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Covalently linked phosphoric acids – Applications in self-assembly and organocatalysis

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Declaration of authorship

I declare that I completed this work on my own and did not use any other source than stated.

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Maike Thiele, 29. April 2022

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F. Octa-Smolin, M. Thiele, R. Yadav, A. Platzek, G. H. Clever, J. Niemeyer, *Org. Lett.* **2018**, *20*, 6153-6156

F. Octa-Smolin, R. Mitra, M. Thiele, C. Daniliuc, L. Stegemann, C. Strassert, J. Niemeyer, *Chem. Eur. J.* **2017**, *23*, 10058-10067

R. Mitra, M. Thiele, F. Octa-Smolin, J. Niemeyer, *Chem. Commun.* **2016**, 5977-5980

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1. Introduction

Stereoisomers are molecules that are identical to one another in terms of atomic constitution and sequence of covalent bonds, but which differ in the three-dimensional arrangement of atoms. Among different stereoisomers, molecules that behave like mirror images of each other, which cannot be converted into one another by twisting and turning; are called enantiomers. Such enantiomers are chiral molecules.[1]

Chirality plays an important role in chemical, biological and pharmaceutical sciences as most organic compounds found in nature, e.g. the biomolecular building blocks of life such as amino acids, sugars, proteins, nucleic acids and polysaccharides are chiral.[2] In terms of physiochemical properties, enantiomers differ only in their ability to rotate linearlypolarized light in opposite directions and therefore are also referred to as optical isomers. While enantiomers have identical chemical reactivities under achiral conditions, they often show different physiological behaviours or pharmacological activities in a chiral environment, like the human body.[3,4] In humans, D-amino acids are considered physiologically active compounds and markers of diseases, resulting from racemization of L-isomers.[5] Both D-aspartate and D-serine are involved in processes underlying neurotransmission and neural signaling.[6] Decreased expression and genetic depletion of serine racemase are linked to cognitive disorders such as schizophrenia and addiction.[7] Also, the chiral environment of the human body is highly relevant when chiral molecules are used as drugs. For example, racemic cetirizine is applied against allergic skin diseases, while only the (*R*)-enantiomer shows antiallergic activity.[8]

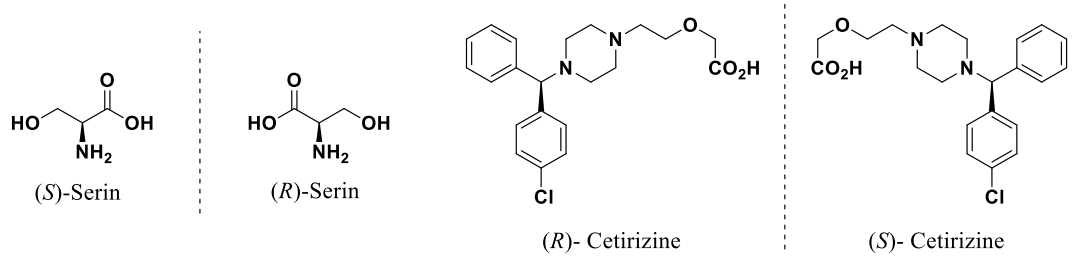


Figure 1: Enantiomers of the amino acid serine (left), enantiomers of the drug cetirizine (right).

[1] C. Pedro, *Angew. Chem. Int. Ed*. **2007**, *46*, 4016-4024.
[2] L. J. Prins, F. De Jong, P. Timmerman, D. N. Reinhoudt, *Nature* **2000**, *408*, 181– 184; M. D. Ward, *Nature* **2003**, *426*, 615–616.
[3] B. Waldeck, *Chirality* **1993**, *5*, 350-355.
[4] N. M. Maier, P. Franco, W. Lindner, *J. Chromatogr. A* **2001**, *906*, 3–33.
[5] G. Genchi, *Amino Acids* **2017**, *49*, 1521–1533.
[6] a) L. Pollegioni, S. Sacchi, *Cell. Mol. Life Sci*. **2010**, *67*, 2387–2404, b) N. Ota, T. Shi, J.V. Sweedler, *Amino Acids* **2012**, *43*, 1873–1886, c) S. H. Snyder, P. M. Kim, *Neurochemical Research* **2000**, *25*, 553–560.
[7] J.T. Coyle, D.T. Balu, *Adv. Pharm*. **2018**, *82*, 35–56.
[8] J. L. Devalia, C. De Vos, F. Hanotte, E. Baltes, *Allergy* **2001**, *56*, 50–57.

The most common source of chirality is the presence of a stereogenic centre, such as a carbon atom with four different substituents. However, there are also other types of molecular chirality, such as planar chirality or axial chirality.[9] For example, dinitrobiphenic acid[10] is an example of an axially chiral molecule, while the chromocene[11] is an example for a molecule with planar chirality (see Figure 2).

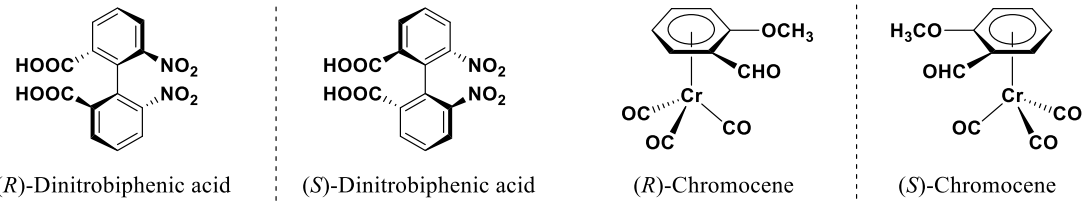


Figure 2: Example of a molecule with axial chirality (left) and a molecule with a planar chirality (right).

1.1. The BINOL-backbone

Axially chiral compounds are present in a plethora of natural products such as, vancomycin,[12] marinopyrrole[13] and TMC-95A,[14] which are highly used in medicine. That makes them interesting building blocks not only in the pharmaceutical industry, but also in chemical industry. Moreover, axially chiral compounds have emerged to be one of the most attractive backbones for the construction of ligands for transition-metal catalysis or for the generation of organocatalysts.[15] One of the most important axially chiral molecular frameworks in general is the 1,1´-binaphthyl-2,2´-diol (BINOL) unit (see Figure 3).

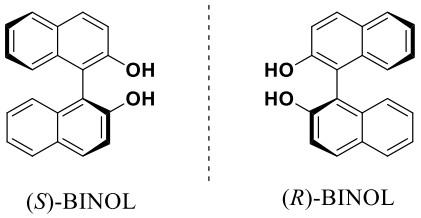
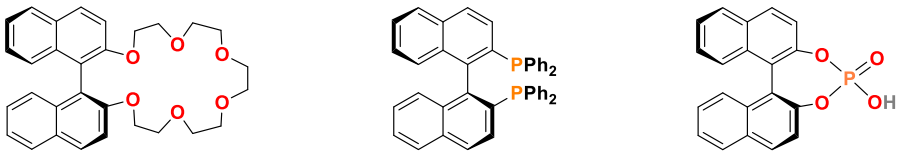


Figure 3: Schematic representation of (*S*)- and (*R*)-BINOL.

[9] R. S. Cahn, C. Ingold, V. Prelog, *Angew. Chem. Int. Ed*. **1966**, *5*, 385-415.
[10] M. Siegel, K. Mislow, *J. Am. Chem. Soc*. **1958**, *80*, 465-473.
[11] A. Solladie-Cavallo, G. Solladie, E. Tsamo, *J. Org. Chem*. **1979**, *44*, 4189-4191.
[12] a) A. Okano, N. A. Isley, D. L. Boger, *Chem. Rev*. **2017**, *117*, 11952−11993.
[13] a) C. C. Hughes, A. Prieto-Davo, P. R. Jensen, W. Fenical, *Org. Lett*. **2008**, *10*, 629-631, b) C. C. Hughes, C. A. Kauffman, P. R. Jensen, W. Fenical, *J. Org. Chem*., **2010**, *75*, 3240–3250,
[14] a) Y. Koguchi, J. Kohno, M. Nishio, K. Takahashi, T. Okuda, T. Ohnuki, S. Komatsubara, *J. Antibiot*. **2000**, *53*, 105-109, b) M. Kaiser, M. Groll, C. Renner, R. Huber, L. Moroder, *Angew. Chem. Int. Ed*. **2002**, *41*, 780-783, c) M. Inoue, H. Sakazaki, H. Furuyama, M. Hirama, *Angew. Chem*. **2003**, *115*, 2758–2761.
[15] M. C. Kozlowski, B. J. Morgan, E. C. Linton, *Chem. Soc. Rev*. **2009**, *38*, 3193–3207; b) G. Bringmann, T. Gulder, T. A. M. Gulder, M. Breuning, *Chem. Rev*. **2011**, *111*, 563–639.

One of the earliest applications of BINOL was the construction of chiral crown ethers such as (*S*)-**1**.[16] These were initially applied for the stereoselective complexation of chiral ammonium salts,[17] but more recently were also applied as ligands in metal-catalysis, e.g. for the lead-catalyzed asymmetric aldol reactions of silyl enol ethers.[18] In the early 1980's *Noyori* reported the synthesis of a novel BINOL-based diphosphane (*S*)-**2**, better known as BINAP (2,2'-bis(diphenylphosphanyl)-1,1'-binaphthyl).[19] It is applied as a chiral ligand in many transition-metal catalyzed reactions e.g. in the asymmetric hydrogenation reaction of ketones.[20] Furthermore, BINOL can be transformed into the chiral phosphoric acid (*S*)-**3** (see Figure 4). One of the first applications of (*S*)-**3** was the use as a chiral resolving agent,[21] but it was also used as a chiral ligand in transition-metal-mediated catalysis e.g. the synthesis of ibuprofen and naproxen.[22]



(*S*)- **1** (*S*)-**2** (*S*)-**3**

Figure 4: BINOL-based structures with application in catalysts: (*S*)-**1** (left), (*S*)-**2** (middle**)** and (*S*)-**3** (right).

[16] E. P. Kyba, R. C. Helheson, k. Madan, G. W. Gokel, T. L. Tarnowski, S.S. Moore, D. J. Cram, *J. Am. Chem. Soc*. **1977**, *99*, 2564-2571.
[17] E. P. Kyba, J. M. Timko, L. J. Kaplan, F. de Jong, G. W. Gokel, D. J. Cram, *J. Am. Chem. Soc.* **1978**, *100*, 4555-4568.
[18] S. Nagayama, S. Kobayashi, *J. Am. Chem. Soc*. **2000**, *122*, 11531–11532.
[19] a) R. Noyori, H. Takaya, *Acc. Chem. Res.* **1990**, *23*, 345-350; b) A. Miyashita, A. Yasuda, H. Takaya, K. Toriumi, T. Ito, T. Souchi, R. Noyori, *J. Am. Chem. Soc.* **1980**, *102*, 7932-7934; c) K. Tani, T. Yamagata, S. Otsuka, S. Akutagawa, H. Kumobayashi, T. Taketomi, H. Takaya, A. Miyashita, R. Noyori, *J. Chem. Soc., Chem. Commun.* **1982**, 600-601; d) K. Tani, T. Yamagata, S. Akutagawa, H. Kumobayashi, T. Taketomi, H. Takaya, A. Miyashita, R. Noyori, S. Otsuka, *J. Am. Chem. Soc.* **1984**, *106*, 5208-5217.
[20] R. Noyori, I. Tomino, Y. Tanimoto, M. Nishizawa, *J. Am. Chem. Soc*. **1984**, *106*, 6709; b) R. Noyori, I. Tomino, M. Yamada, M. Nishizawa, *J. Am. Chem. Soc*. **1984**, *106*, 6717-6725.
[21] W. Arnold, J. J. Daly, R. Imhof, E. Kyburz, *Tetrahedron Lett.* **1983**, *24*, 343-346.
[22] Alper and N. Hamel, *J. Am. Chem. Soc*. **1990**, *112*, 2803-2804.

2. Aim and Objectives

In recent years, BINOL-based phosphoric acid have found widespread use, especially in organocatalysis.[23] Therefore, BINOL-based phosphoric acids are incorporated into different frameworks, consisting of one or more 1,1'-binaphthyl phosphate moieties. However, their use as building blocks for the self-assembly of supramolecular structures remains limited. The first part of this work aims for the synthesis of supramolecular double helices composed of two BINOL-based subunits. The subunits contain either a phosphoric acid moiety or a guanidine functionality, that are bridged by hydrogen bonds upon self-assembly (see Figure 5, see chapter 3.3).

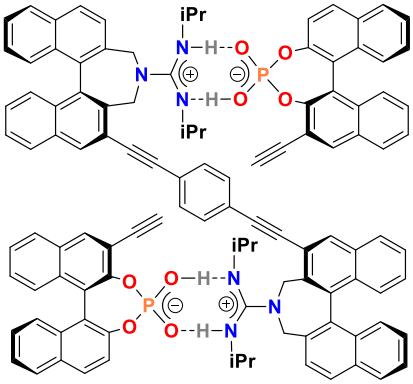


Figure 5: Example for a supramolecular double helix, consisting of a bis-phosphate and a bis-guanidinium fragment.

The work of *Niemeyer* and co-workers illustrates that the BINOL backbone as a chiral element is suitable for the synthesise of chiral sensors and allows good discrimination of enantiomeric analytes using NMR spectroscopy.[24] The identification of structurally related analytes such as the proteinogenic amino acids is already possible with a sensor array using UV/vis- and fluorescence spectroscopy.[25,26] In the second part of this work, the aim is to establish a sensor array for the binding of partially methylated lysine derivatives (**Kme**, **Kme$_2$** and **Kme$_3$**) based on binding to BINOL-phosphates (see Figure 6).

[23] a) D. Parmar, E. Sugiono, S. Raja, M. Rueping, *Chem. Rev.* **2014**, *114*, 9047–9153, b) D. Parmar, E. Sugiono, S. Raja, M. Rueping, *Chem. Rev.* **2017**, *117*, 10608–10620.
[24] F. Octa-Smolin, M. Thiele, Rohan Yadav, André Platzek, Guido Clever, J. Niemeyer, *Org. Lett.* **2018**, *20*, 6153-6156.
[25] A. Buryak, K. Severin, *J. Am. Chem. Soc.* **2005**, *127*, 3700-3701.
[26] F. Octa-Smolin, J. Niemeyer, *Chem. Eur. J.* **2018**, *24*, 6506–16510.

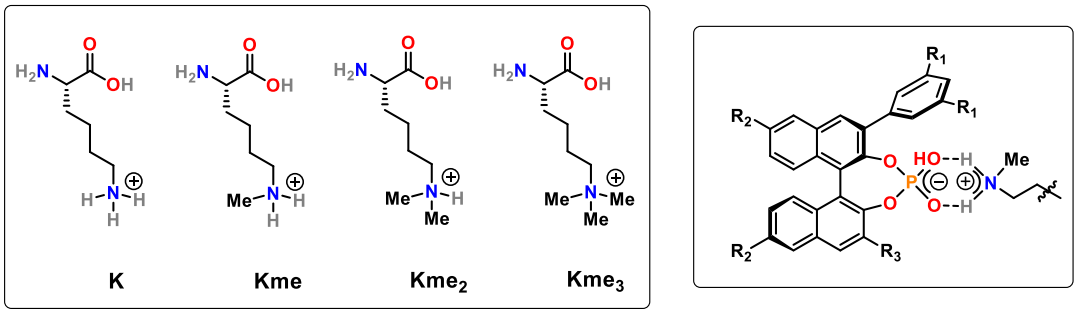


Figure 6: BINOL-phosphates for binding methylated amino acid derivatives using the example of **Kme**.

In the last section of this work it is to investigate the catalytic activity of the BINOL-based phosphoric acids. Based on the results of *Niemeyer* and co-workers,[27,28] the covalent combination of two BINOL-based phosphoric acids has shown to be a promising method to generate cooperative organo catalysts. Since 3,3′-disubstituted BINOL-based phosphoric acids have shown increased stereoselectivity due to the extended steric demand[29,30] this can also be assumed for bis-phosphoric acids with this substitution pattern. In order to investigate the influences of the substituents as well as the linkage in more detail, bis-phosphoric acids were developed which were linked to each other *via* different linkers. Besides, the influence of the number of linkages on the catalytic system is also investigated using singly linked or doubly linked bis-phosphoric acids. Likewise, the corresponding monophosphoric acids were used as comparative systems. On the one hand these systems will be applied in transfer hydrogenation of 2-substituted quinolines and on the other hand in the dearomative fluorination of 2-naphthols.

[27] R. Mitra, M. Thiele, F. Octa-Smolin, M. C. Letzel, J. Niemeyer, *Chem. Commun*. **2016**, *52*, 5977-5980.
[28] S. Thölke, H. Zhu, D. Jansen, F. Octa-Smolin, M. Thiele, K. Kaupmees, I. Leito, S. Grimme, J. Niemeyer, *Eur. J. Org. Chem*. **2019**, *55*, 5190–5195.
[29] D. Uraguchi, M. Terada, *J. Am. Chem. Soc*. **2004**, *126*, 5356–5357.
[30] a) T. Akiyama, J. Itoh, K. Yokota, K. Fuchibe, *Angew. Chem. Int. Ed.* **2004**, *43*, 1566-1568, b) T. Akiyama, *Chem. Rev*. **2007**, *107*, 5744 – 5758.

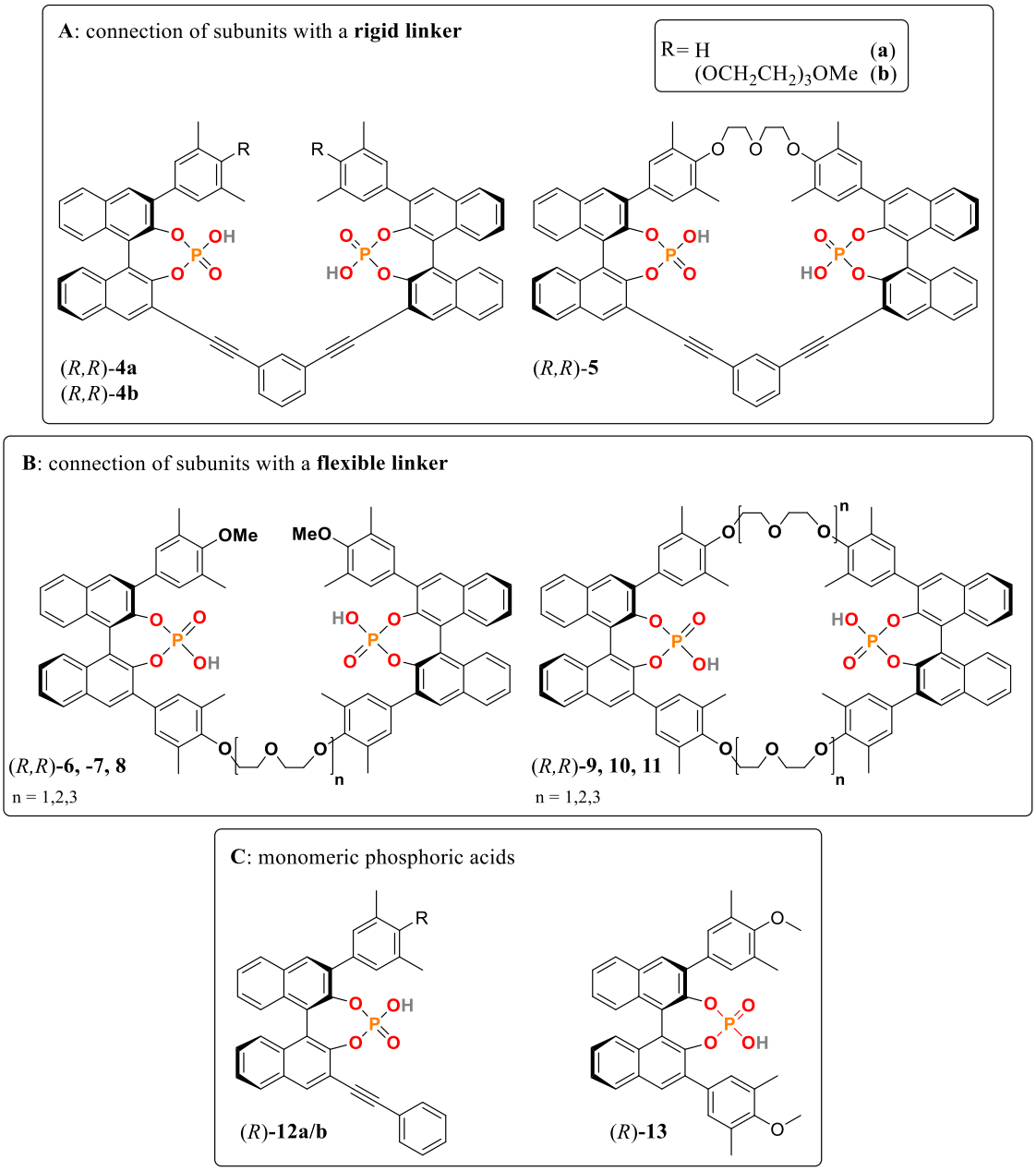


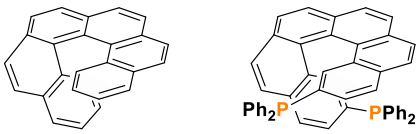
Figure 7: Overview of the twelve monomeric- and bis-phosphoric acids.

3. Complementary Supramolecular Double Helices

3.1. Introduction

Biomacromolecules, such as DNA and proteins, are the most common helical structures in nature. These biomolecules can have architectural elements like a chiral double helix[31] or the single-stranded α-helix.[32] The helical chirality of these structures mostly stems from the homochirality of the constituting building blocks. For instance, amino acids and sugar molecules are involved in cooperative non-covalent interactions, such as hydrogen bonds, π-π- or Coulomb interactions. It is known that the resulting helical superstructures enable the demanding functions of these biomolecules, *e.g.* DNA self-repair, in DNA replication or in signal transduction.[33] Thus, the preparation of synthetic helical structures is of great interest and intimately connected to the helical chirality of these systems.[34]

Inspired by the naturally occurring helical architectures, chemists have tried to mimic their structure and function by constructing artificial helical molecules, both in covalently bonded molecules[35] and in supramolecular aggregates.[36] The first approach was developed by *Martin et al.*, who used steric effects in rigid molecules, to induce a helical structure. The increasing *ortho* annulation of aromatic ring systems leads to a steric interaction between the hydrogen atoms on terminal rings. This results in a non-planar conformation of the arenes. As the number of arenes increases, the terminal rings begin to come into close contact, which causes a helical conformation, which leads to the *helicene* **14**[37] (see Figure 8). More recently *Helicene* **15** has been synthesized and was applied as a catalyst in asymmetric catalysis.[38]



14 **15**

Figure 8: Representation of two helicene, **4** (left) and **5** (right).

[31] J. D Watson, F. H. C. Crick, *Nature*, **1953**, *171*, 737−738.
[32] L. Pauling, R. B. Corey, H. R. Branson, *Proc. Natl. Acad. Sci. U. S. A.*, **1951**, *37*, 205−211.
[33] J. M. Berg, L. Stryer, J. L. Tymoczko and G. Gatto, Biochemistry, WH Freeman, New York, **2019**.
[34] E. Yashima, N. Ousaka, D. Taura, K. Shimomura, T. Ikai, K. Maeda, *Chem. Rev.* **2016**, *116*, 13752-13990.
[35] a.) R. J. M Nolte, A. J. M. Van Beijnen, W. Drenth, *J. Am. Chem. Soc*., **1974**, *96*, 5932−5933, b.) M. M Green, C. Andreola, B. Muñoz, M. P. Reidy, K. Zero, *J. Am. Chem. Soc*. **1988**, *110*, 4063−4065.
[36] Y. Yang, A. Zhang, Z. Wei, *Adv.Mater*., **2013**, *25*, 6039–6049.
[37] R. H. Martin, *Angew. Chem. Int. Ed*. **1974**, *13*, 649-660.
[38] A. Terfort, H. Görls, H. Brunner, *Synthesis*, **1997**, *79*-86.

With respect to supramolecular double-helices, *Lehn* was the first to report on a self-assembled supramolecular double-helical structure (see Figure 9). The double-helix **16** consists of two 2,2′-bipyridine oligomer strands , which wrap around three central copper (I) ions.[39]

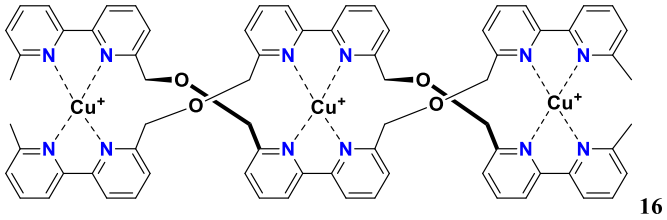


Figure 9: A template-mediated structure of a helix reported by *Lehn*.[39]

Hamilton firstly applied a mixed-template strategy in 1994 (see Figure 10). The strategy was to design a self-assembling receptor for dicarboxylic acids. Here, a copper bis(phenanthroline) complex is initially obtained by reacting **17** with $[Cu(CH_3CN)_4]BF_4$. In the presence of dicarboxylic acids, the ternary helical complex **18** is then formed.[40]

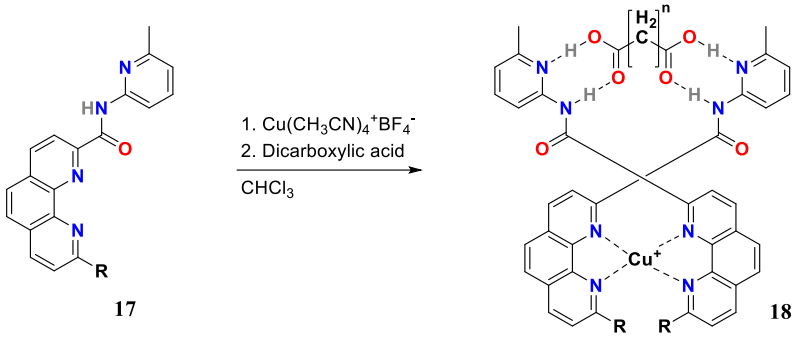


Figure 10: A template-mediated helix formation reported by *Hamilton*.[40]

When using achiral building blocks, a racemic mixture of double-helical species with opposite handedness is formed and the helicates are optically inactive. The handedness of the helix can, however, be influenced by introducing a stereogenic unit into the component.[41] For example, *Lehns* helicates were equipped with axially chiral linkers, such as biphenyls or -BINOL, which allowed for the generation of the helicates with a defined handedness (see Figure 11).[42]

[39] J.-M. Lehn, A. Rigault, J. Siegel, J. Harrowfield, B. Chevrier, D. Moras, *Proc. Natl. Acad. Sci. USA* **1987**, *84*, 2565.
[40] M. S. Goodmann, J. Weiss, A. D. Hamilton, *Tetrahedron Lett*. **1994**, *35*, 8943-8946.
[41] W. Zarges, J. Hall, J.-M. Lehn, C. Bolm, *Helv. Chim. Acta*, **1991**, *74*, 1843−1852.
[42] a.) C. R Woods, M. Benaglia, F. Cozzi, J. S. Siegel, *Angew. Chem., Int. Ed*., **1996**, *35*, 1830−1833.
b.) R. Annunziata, M. Benaglia, M. Cinquini, F.Cozzi, C. R. Woods, J. S. Siegel, *Eur. J. Org. Chem*. **2001**, 173−180.

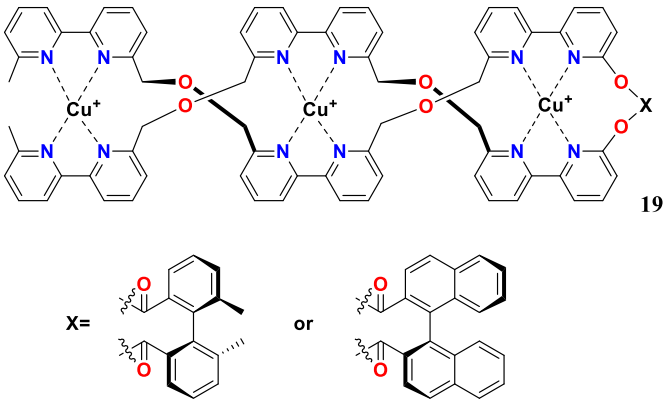


Figure 11:Chiral Helicate synthesised by *Siegel*.[42]

In 1996, *de Mendoza* reported on double-stranded helices in a hydrogen-bonded system (see Figure 12). As shown in Figure 12, the chiral sulfur-bridged bis-guanidinium moieties wrap around the dianionic sulfate ion to form a helical structure. Here, the linker in the bisguanidinium unit **20** is too short to allow the formation of a 1:1 chelate complex with a single sulfate-ion. Therefore, two strands of **20** are forced to bind to two sulfate counterions to form a double helical structure **21**.[43]

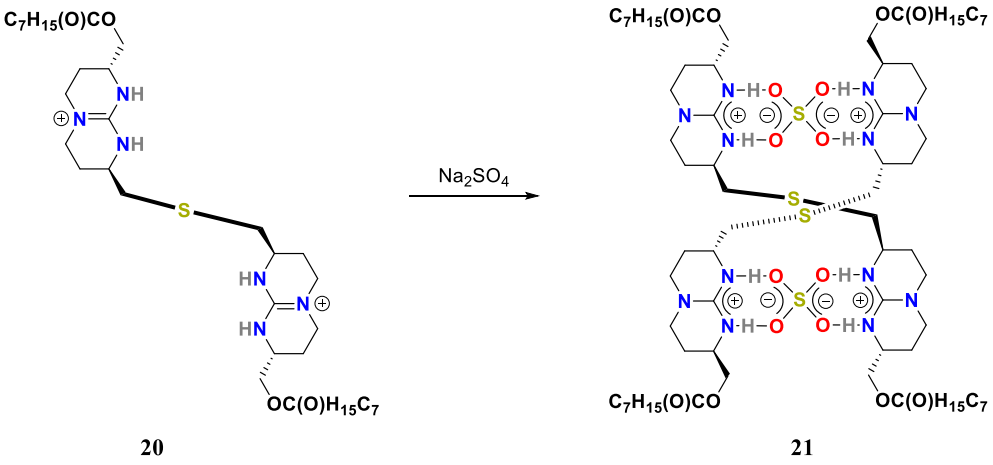


Figure 12: Representation of a bis-guanidinium-based helix of two with two sulfate ions used as templates.[43]

In 2005, *Yashima* showed the first example of a hetero-stranded supramolecular double helix **24** (see Figure 13).[44] There, a bisamidine strand **23** and a complementary biscarboxylic acid strand **22** were synthesized by a modular approach. Upon mixing, the two complementary strands interact *via* ionic hydrogen bonds. Thus, a hetero-stranded double helix is spontaneously formed. In addition, the handedness of the double-helix can be controlled by chiral substituents on the amidine functions. That was the first approach where complementarity between two

[43] J. Sanchez-Quesada, C. Seel, P. Prados, J. de Mendoza, *J. Am. Chem. Soc*. **1996**, *118*, 277.
[44] Y. Tanaka, H. Katagiri, Y. Furusho, E. Yashima, *Angew. Chem. Int. Ed.* **2005**, *44*, 6448-6451.

strands could be exploited, bringing synthetic double-helices closer to DNA, where also two complementary single strands join together to form a double-stranded helical system.

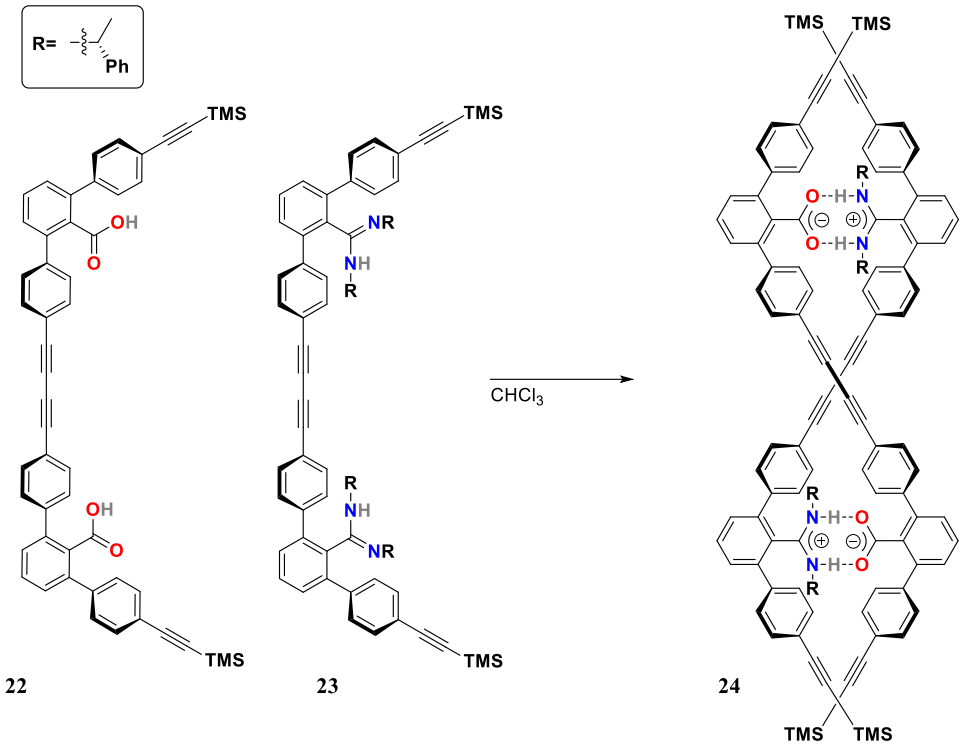


Figure 13: Synthetic double helix formation of a bisamidine and a biscarboxylic acid reported by *Yashima*.[44]

3.2. Aim

Compared to *Yashima's* supramolecular double helical structure,[44] this part of the work aims for the synthesis of a novel generation of hydrogen-bonded supramolecular double-helices based on guanidinum and phosphate pairing. The targeted complementary guanidinium phosphate pair is worth investigating, since it has an important biological relevance,[45] which can also be found in supramolecular applications.[46] In addition, we aim for the use of the axially-chiral BINOL backbone on both binding units, as opposed to *Yashima´s* case where only one subunit is chiral. Thus, we hope that the molecular chirality of the backbone can be directly transferred into the supramolecular helical chirality in the self-assembly process.[44,47] Also, this offers the possibility to investigate cases of matched/mismatched chirality.

The supramolecular interaction of the designated binding motifs has already been found in crystal structures,[48] Thus, 1,1′-binaphthyl-phosphate (*rac*)-**25** was co-crystallized with a 1,1′-binaphthyl-guanidine (*rac*)-**26** yielding the corresponding heterodimeric complex (*rac*)-**25** + (*rac*)-**26** (see Figure 14).

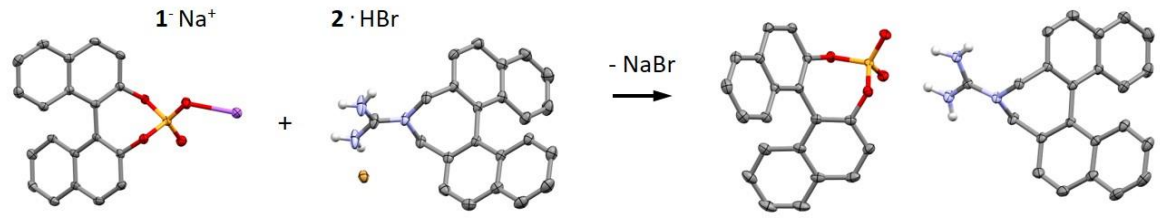


Figure 14: Crystallographic structures on the binding behaviour of binaphthyl-phosphates and -guanidines.

Based on this precedence, the first goal of this work was the synthesis of the bisguanidine (*S*,*S*)-**28**. According to known protocols, the key intermediate (*S*)-**27** (see Figure 15) is available after 7 steps.[49,50,51] The synthesis of the bis-guanidine starting from (*S*,*S*)-**27** are new and synthetic protocols have to be established.

[45] (a) A. Pantos, I. Tsogas, C. A. Paleos, *Biochim. Biophys. Acta*, **2008**, *1778*, 811–823; (b) K. A. Schug, W. Lindner, *Chem. Rev*., **2005**, *105*, 67–113.
[46] (a) T. Schrader, G. Bitan, F.-G. Klärner, *Chem. Commun*. **2016**, *52*, 11318–11334; (b) R. J. T. Houk, S. L. Tobey, E. V. Anslyn, *Top. Curr. Chem*., **2005**, *255*, 199–229.
[47] T. Aida, E. W. Meijer, S. I. Stupp, *Science*, **2012**, *335*, 813– 817.
[48] Frescilia Octa-Smolin, *1,1'-Binaphthyl Based Bis- and Tris-Phosphoric Acids: Syntheses and Application as Fluorescent Chemosensors*, Dissertation, Universität Duisburg-Essen, **2018**.
[49] M. Gingras and F. Dubois, *Tetrahedron Lett.* **1999**, *40*, 1309-1312.
[50] H. Konishi, *Chem. Pharm. Bull.* **2018**, *66*, 1-19.
[51] M. Widhalm, M. Abraham, V. B. Arion, S. Saarsalu and U. Maeorg, *Tetrahedron: Asymmetry* **2010**, *21*, 1971-1982.

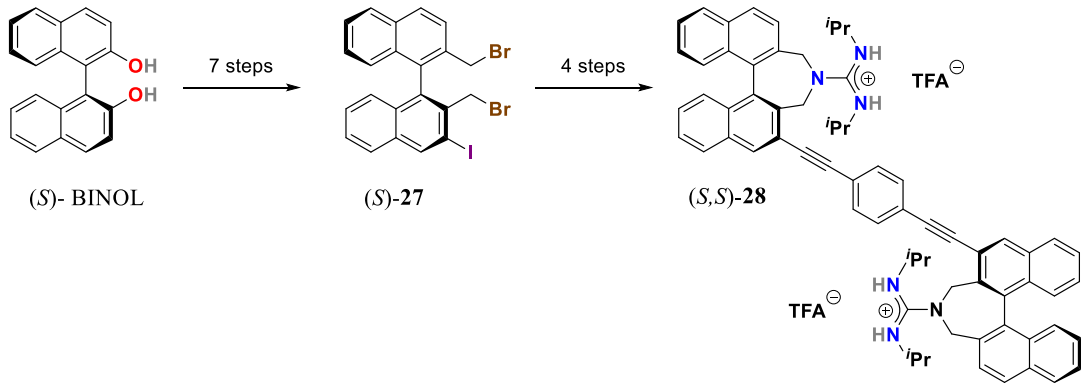


Figure 15: Molecule (*S*)-**27** marks the crucial building block in the synthesis of the guanidine (*S*,*S*)-**28**.

Upon addition of both strands in a homo- or heterochiral fashion, the aim is to investigate the superstructure of (*S*,*S*)-**29**+(*S*,*S*)-**28** on the influence of the strand-chirality on the helix-sense (see Figure 16).

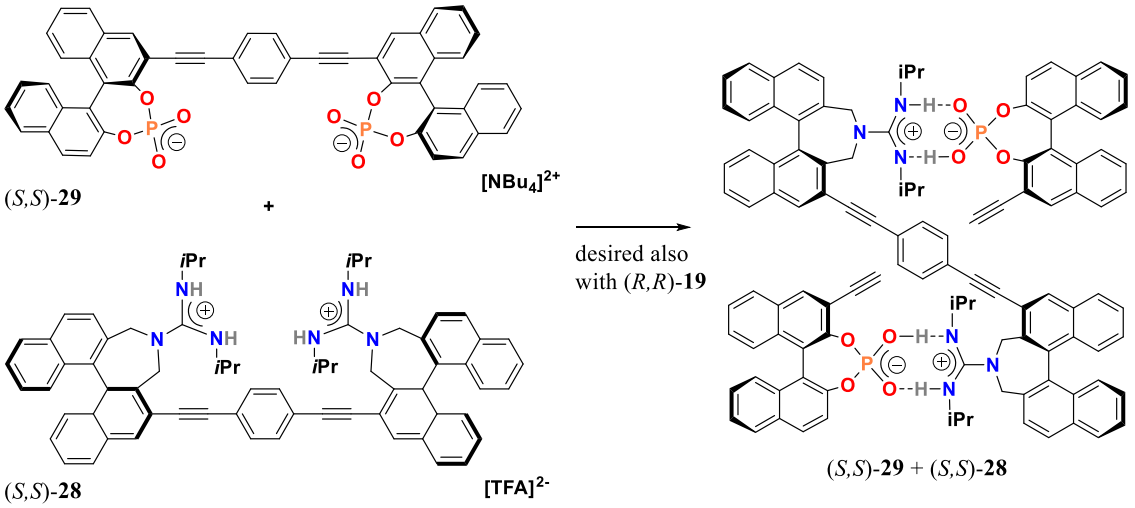


Figure 16: Desired supramolecular double helices of bis-guanidine and bis-phosphate through hydrogen bond formation.

3.3.Synthesis

3.3.1. First Synthetic Route

For the synthesis of the desired bis-guanidine (*S*,*S*)-**28**, we initially pursued a synthetic route previously established in our working group. The central building block (*S*)-**27** was synthesized starting from (*S*)-BINOL. The dibromide (*S*)-**26** is obtained after seven steps, followed by the conversion to the Boc-amine (*S*)-**27** (see Figure 17).

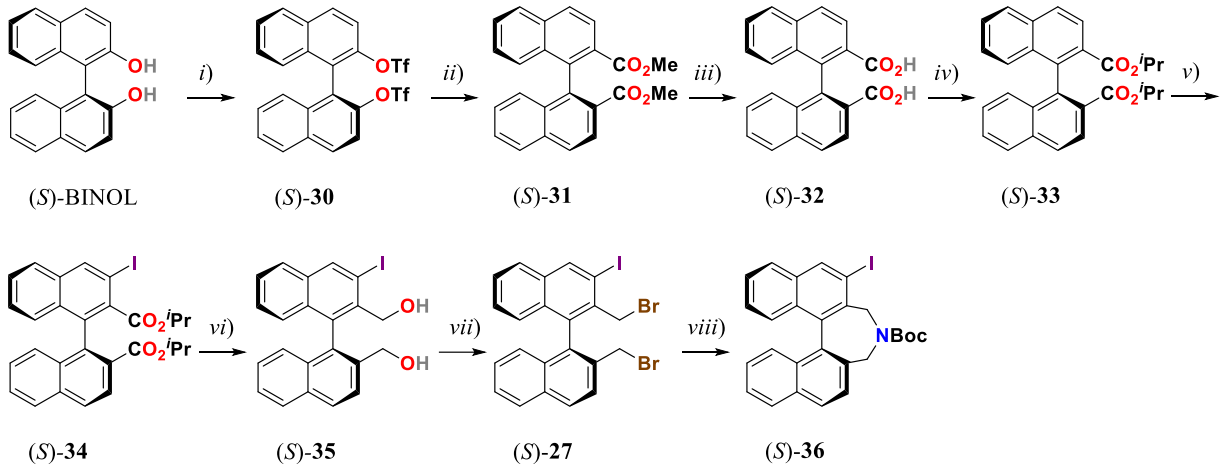


Figure 17: Overview of the original synthetic route to (*S*)-**36**. Reagents and conditions: *i*) trifluoromethanesulfonic anhydride, pyridine, dichloromethane, 25 °C, 97%, *ii*) $Pd(OAc)_2$, dppp, phenylformate, methanol, DMSO, DIPEA, CO-atmosphere, 80 °C, 54%, *iii*) 1. NaOH (5 M), methanol, 2. Hydrochloric acid (5 M), 75 °C, 99%, *iv*) 1. $SOCl_2$, 0 °C to r. t., 2. ^{i}PrOH, 4 °C to r.t., 65%, *v*) $Mg(TMP)_2$, I_2, THF, 0°C to -78 °°C, 26%, *vi*), DIBAL-H, DCM, -78 °C to r.t., 27%, *vii*) PBr_3, DCM, -40 °C to r.t., 93%, *viii*) NaH, *tert*-butyl carbamate, 0°C, THF/DMF, 77%.

First, starting from enantiomerically pure BINOL, the triflate (*S*)-**30** can be obtained by reaction with trifluoromethanesulfonic anhydride. Subsequently, by reacting (*S*)-**30** with CO and methanol in the presence of a palladium catalyst and diisopropylethylamine (DIPEA), the methyl ester (*S*)-**31** was obtained, which was converted into the carboxylic acid (*S*)-**32** in a saponification. Then the acid (*S*)-**32** was converted to the corresponding acid chloride and was reacted *in situ* with isopropanol and pyridine to give the diisopropyl ester (*S*)-**33**. The diisopropyl ester (*S*)-**33** was now reacted with $Mg(TMP)_2$ in a directed *ortho*-metalation (DOM reaction). The lithium intermediate formed in *situ* reacted with iodine to give the monoiodo derivative (*S*)-**34**. In competition, the diiodo derivative is also formed. The sterically demanding reagent $Mg(TMP)_2$ was used here to avoid nucleophilic attack on the isopropyl ester of the isopropyl group. A complete conversion in favour of the product could not be determined, so that 35-70% starting material remained in the product mixture. The desired product (*S*)-**34** was obtained with yields of 26 - 50%. In addition, 4 – 15% of the diiodinated by-product was found. The mixture was then reduced to the alcohol (*S*)-**35** with diisobutylaluminum hydride in order to substitute the hydroxide group for bromine with boron tribromide in the next step to give

(*S*)-**27**. This was followed by reaction with sodium hydride and *tert*-butyl carbamate to give the Boc-protected aminobinaphthyl derivative (*S*)-**36**.

The handling of the carbonylative cross-coupling reaction turned out to be very challenging, due to the use of external CO gas. Further problems during this synthesis occurred during the iodination step. During the iodination, the diiodinated product and the mono iodinated species (*S*)-**34** were formed. Unfortunately, some starting material (*S*)-**33** remained. A separation of the three species was not possible by column chromatography on SiO_2. Also in the following steps, no separation of the three species could be achieved. Furthermore, the percentages of the individual substances could only be estimated by ^{1}H-NMR, since most of the signals were superimposed. Only after introduction of the amine function, it was then possible to separate the three substances. The problems encountered during this synthetic protocol led to the decision to pursue and establish a new protocol to provide the desired 1,1′-binaphthyl-guanidines.

3.3.2. Improved Synthetic Route

In comparison to the described route, the carbonylative cross-coupling reaction was now performed with in *situ* CO gas production. The iodination of the isopropyl ester (*S*)-**23** will be no longer performed instead an adjusted protocol for the introduction of substituents in the 3,3'-positions is pursued (see Figure 18).

Figure 19 shows an overview of the 12-step synthesis of (*S*,*S*)-**28**. The synthesis of the intermediates (*S*)-**30**,[52] (*S*)-**37**,[53] and (*S*)-**41**[54] was previously described. All products (*S*)-**36**, (*S*,*S*)-**43**, (*S*,*S*)-**44** and (*S*,*S*)-**28** were generated for the first time.

[52] H. Hocke, Y. Uozumi, *Synlett*. **2002**, *12*, 2049-2053.
[53] H. Konishi, *Chem. Pharm. Bull.* **2018**, *66*, 1-19.
[54] M. Widhalm, M. Abraham, V. B. Arion, S. Saarsalu and U. Maeorg, *Tetrahedron: Asymmetry* **2010**, *21*, 1971-1982.

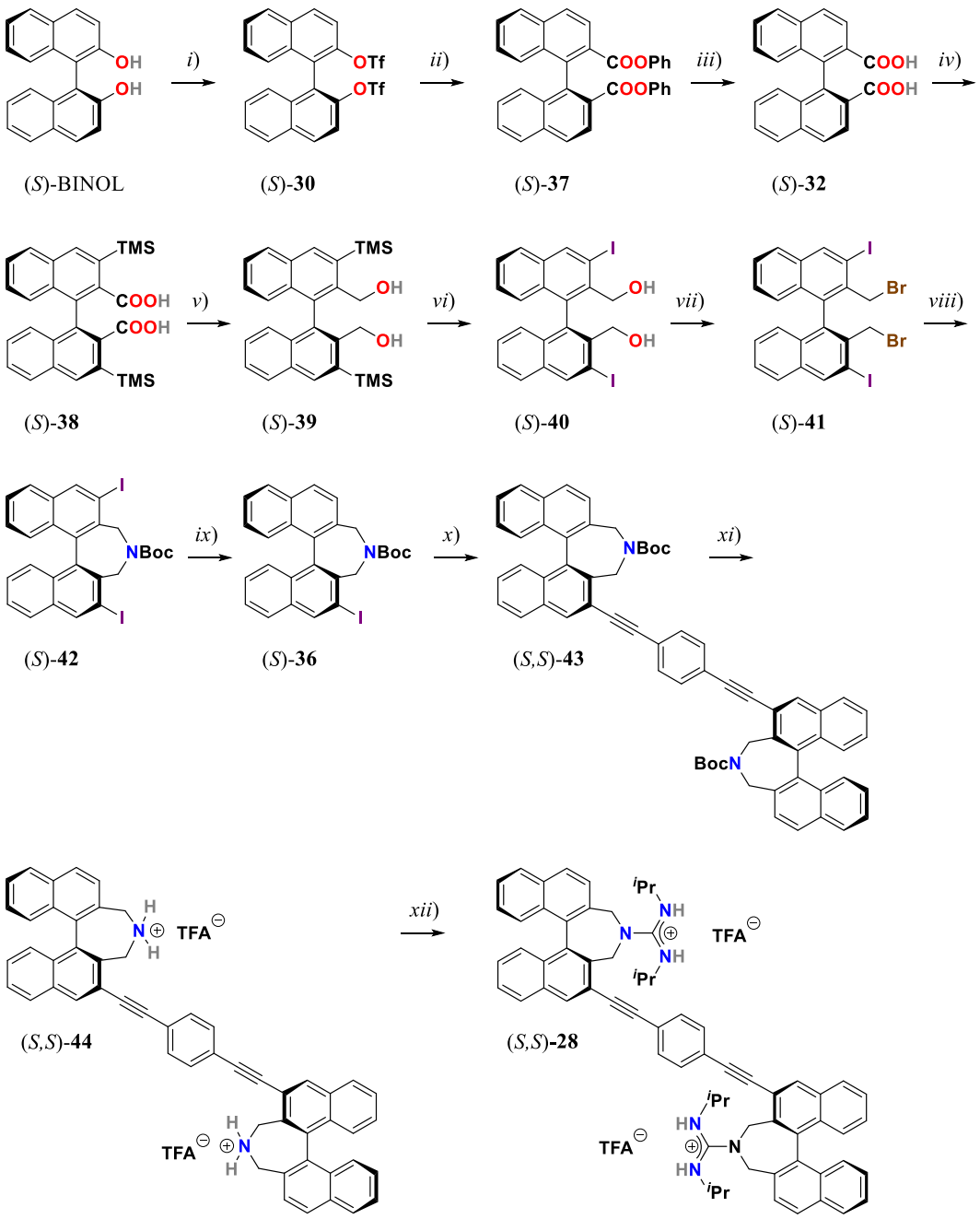


Figure 18: Synthesis of bis-guanidine (*S,S*)-**28**. Reagents and conditions: *i*) trifluoromethanesulfonic anhydride, pyridine, DCM, 25 °C, 97%, *ii*) $Pd(OAc)_2$, dppp, phenylformate, DIPEA, 130 °C, 82%, *iii*) 1. NaOH (5 M), methanol, 2. Hydrochloric acid (5 M), 75 °C, 74%, *iv*) ^{n}BuLi, TMP, TMS-Cl THF/toluene, -78 °C to r.t., 85%, *v*) borane, THF, 80 °C, 97%, *vi*), ICl, DCM, -40 °C to r.t., 87%, *vii*) PBr_3, DCM, -40 °C to r.t., 93%, viii) NaH, *tert*-butyl carbamate, 0°C, THF/DMF, 77%; *ix*) ^{n}BuLi, 0 °C, toluene, then MeOH, 63%; *x*) 1,4-diethynylbenzene, CuI, $Pd(PPh_3)_4$, 80°C, ACN:NEt_3, 86%. *xi*) TFA, r.t., DCM, 76%; *xii*) NaOH, then ^{n}BuLi, diisopropylcarbodiimide, r.t., toluene, 33%.

First, enantiomerically pure (*S*)-BINOL was converted into the triflate (*S*)-**30** by treatment with pyridine and triflic anhydride. The desired product was obtained in quantitative yield. In a carbonylative cross-coupling, the triflate (*S*)-**30** was converted into the cross-coupling product (*S*)-**37**. The reaction was carried out using phenylformate in diisopropylethylamine, using palladium acetate and 1,3-bis(diphenylphosphino)propan as catalysts. The crude product was worked up by column chromatography and obtained in a good yield of 82%. The phenyl ester

(*S*)-**37** is then converted into the dicarboxylic acid (*S*)-**32** by hydrolysis with 2 M sodium hydroxide solution in methanol. The 3,3'-functionalization of (*S*)-**32** occurs by first forming Li-TMP *in situ* by the reaction of *n*-butyl lithium and 2,2,6,6-tetramethylpiperidine. That is reacted with the dicarboxylic acid (*S*)-**32** in a directed *ortho*-metallation, forming a lithium intermediate. The intermediate subsequently reacts with the electrophile, trimethylsilyl chloride, to form the desired compound (*S*)-**38**. Formation of the product was shown in the ^{1}H-NMR spectrum by occurrence of a singlet for the hydrogen atom adjacent to the TMS-group at 8.11 ppm and a singlet for the introduced TMS-group at 0.41 ppm. The carboxylic acid groups were then reduced with the borane–tetrahydrofuran complex to the diol (*S*)-**39**. The protons of the newly formed methylene units are diastereotopic and form an AB spin system due to the axial chirality of the BINOL framework. Their magnetic non-equivalence is reflected in the observation of two different doublets at δ = 4.58 ppm and δ = 4.20 ppm (^{2}J = 11.5 Hz). To introduce iodine in the 3,3′-position, the alcohol (*S*)-**39** was reacted with iodine chloride in dichloromethane to give the product (*S*)-**40** in 81% yield. The structure can be confirmed with the ^{1}H-NMR spectrum, by a significant change in the chemical shift, of the signal adjacent to the iodine, from 8.11 ppm to 8.61 ppm and the loss of the residual proton signal for the TMS-group. In an S_N2-type reaction the hydroxyl groups are substituted for bromine, by reaction of (*S*)-**40** with phosphorus tribromide in dichloromethane to give the product (*S*)-**41** in 93% yield.

This was followed by reaction with sodium hydride and *tert*-butyl carbamate to give the azepine derivative (*S*)-**42**. The ^{1}H-NMR spectrum showed of a new proton signal for the Boc-group at 1.51 ppm. The next step was the removal of one iodine, to get to the main building block (*S*)-**27**. For this, a halogen-lithium exchange was attempted and the then formed lithium intermediate was protonated with methanol. The challenge in this step was to find an appropriate reaction condition. The azepine derivative (*S*)-**42** was dissolved in dry toluene and to the mixture 1.1 equivalent of *n*-butyllithium was added at 0°C. After five minutes, methanol was added and the mixture was stirred for five minutes. The desired product was obtained in a moderate yield of 63%. The reaction mixture consisted also of 12% of non-iodinated species (*S*)-**45** and 25% starting material (*S*)-**42** (see Figure 19). The structures could be isolated by column chromatography and were identified by NMR-spectroscopy (see Figure 21).

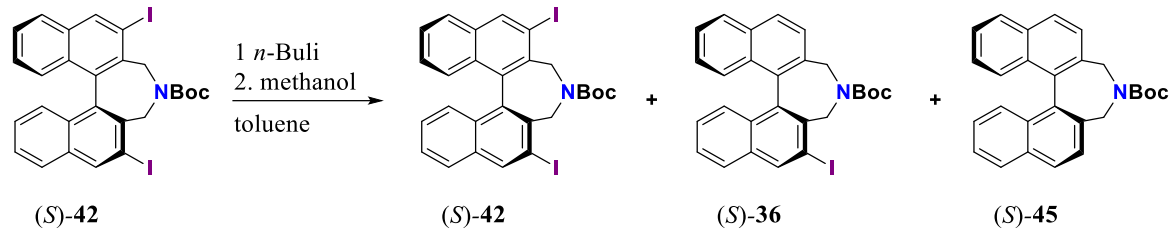


Figure 19: Deiodination reaction of (*R*)-**33** and its products.

The difference in the chemical shift for the methylene protons is most pronounced, as it is directly influenced by the iodine-substituents. In addition, the spectra of (*S*)-**42** and (*S*)-**45** confirm their C_2-symmetric structure, while compound (*S*)-**36** is C_1-symmetric, giving rise to 11 different proton signals in the ^{1}H NMR.

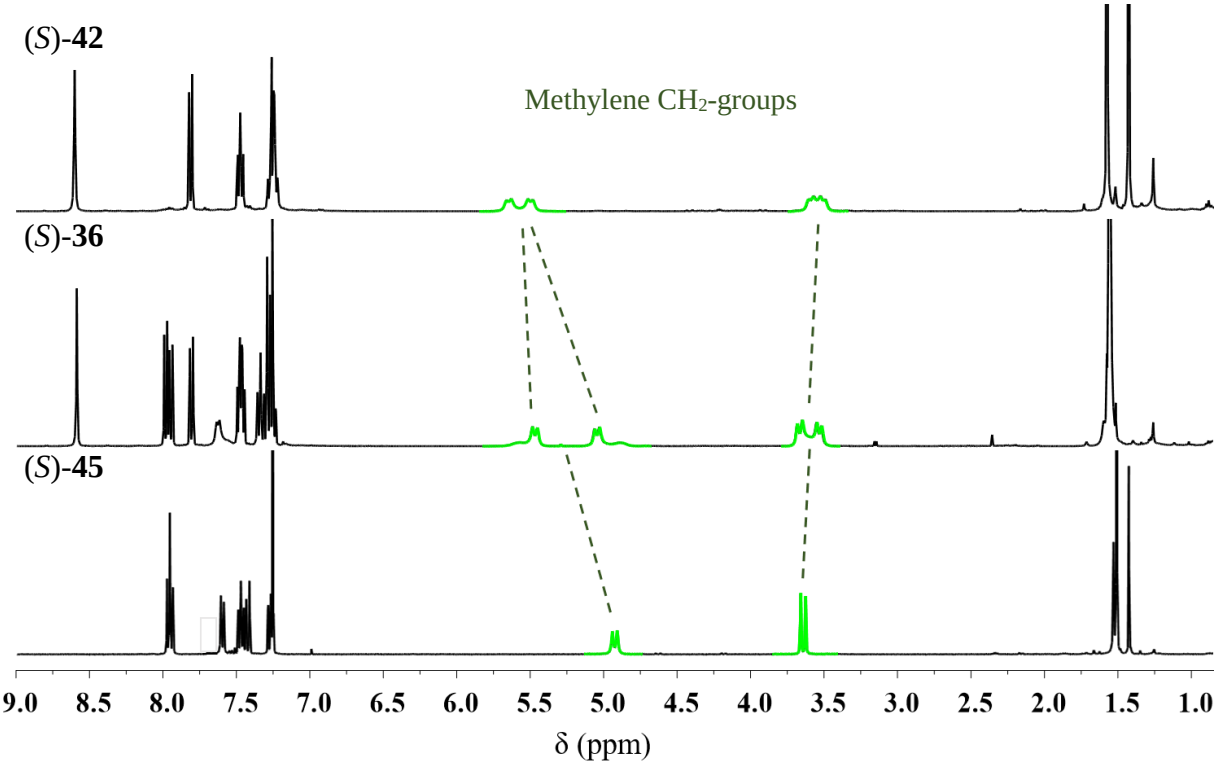


Figure 20: ^{1}H-NMR-spectra of all three azepine derivatives (*S*)-**42**, (*S*)-**36** and (*S*)-**45** [400 MHz, all 298 K, $CDCl_3$].

Furthermore, single crystals suitable for X-ray diffraction could be obtained for compounds **41**, **42**, **36** and **45** by slow evaporation of solutions in ethyl acetate or methanol. „For **41** and **42**, the crystal structures were determined for the (*S*)-enantiomers, for **36** and **45** the crystal structures were determined for the (*R*)-enantiomers (see Figure 21).

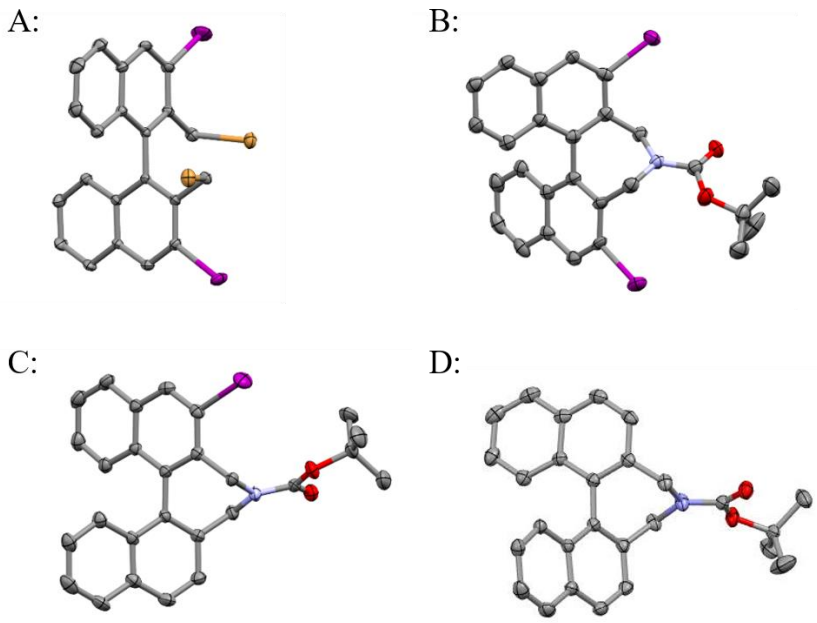


Figure 21: X-Ray crystal structures of A: (*S*)-**41**, B: (*S*)-**42,** C: (*R*)-**36** and D: (*R*)-**45**, Hydrogen atoms omitted for clarity and thermal ellipsoids set at the 50% probability level.

In the next step, the Sonogashira coupling of (*S*)-**36** with 1,4-diethynylbenzene catalyzed by $PdCl_2(PPh_3)_2$ and copper(I) iodide resulted in the bis-binaphthyl amine (*S,S*)-**43** with 86% yield (see Figure 22).

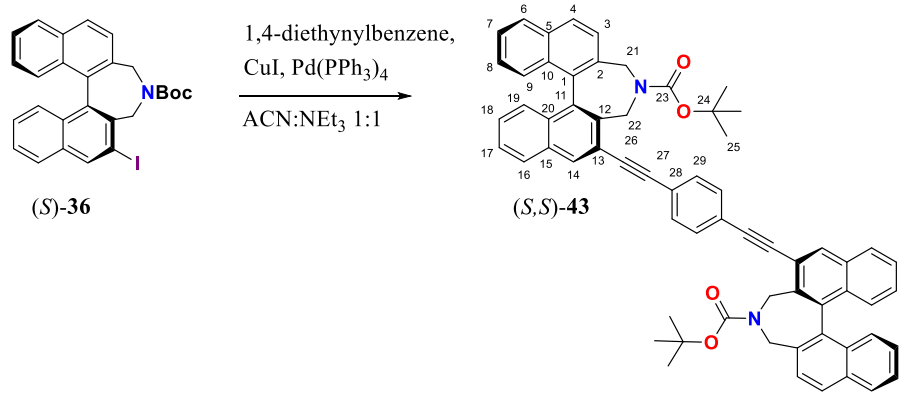


Figure 22: Sonogashira coupling of mono-iodinated boc-protected amine (*S,S*)-**34** with an 1,4-diethynylbenzene linker.

The product was analysed and identified using NMR spectroscopy. In the ^{13}C-NMR new signals for the characteristic ethinyl units are observed (δ= 93.3/90.2 ppm). In the ^{1}H-NMR, the signal for the proton H-14 is shifted (δ: 8.25 ppm for (*S,S*)-**43**, c.f. 8.59 ppm for (*S*)-**36**), as are the signals for the methylene protons (δ: 5.89/5.10/4.88/5.66 ppm/3.58 ppm for (*S,S*)-**43**, c.f. 5.49/5.03/3.65/3.55 ppm for (*S*)-**36**). For both (*S*)-**36** and (*S*)-**43**, the presence of more than four signals for the methylene-groups, together with significant line-broadening, indicates the presence of rotamers due to the Boc-groups (see Figure 23).

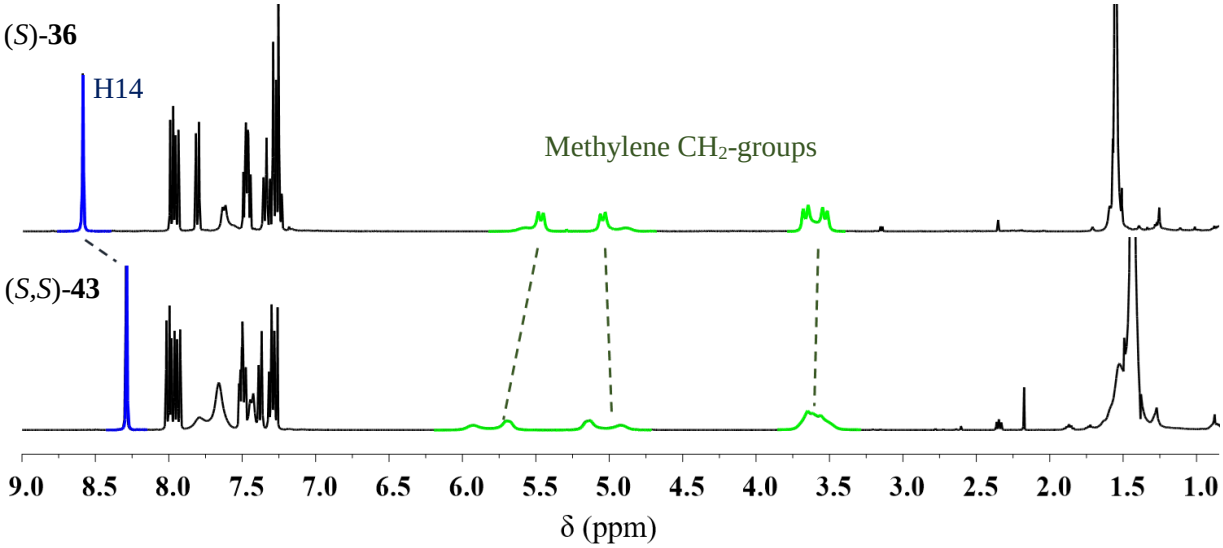


Figure 23: ^{1}H-NMR spectrum of sonogashira coupling product (*S*,*S*)-**43** compared to the mono-iodinated compound (*S*)-**36**. [$CDCl_3$, 400 MHz, 298 K].

Slow evaporation of a solution of (*S*,*S*)-**43** in cyclohexane formed single crystals suitable for X-ray diffraction analysis (see Figure 24).

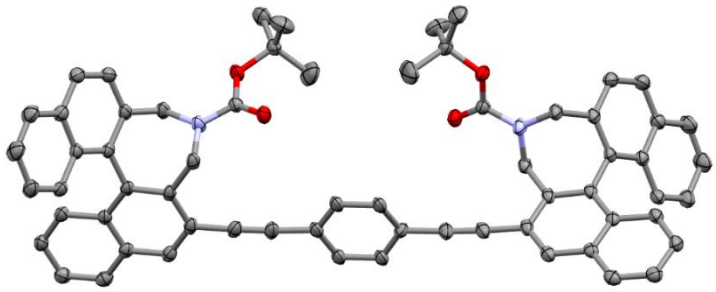


Figure 24: Molecular structure of (*S*,*S*)-**43** in the solid state. Hydrogen atoms omitted for clarity and thermal ellipsoids set at the 50% probability level. Only one orientation of the disordered phenylene-linker is displayed for clarity.

The removal of the Boc-groups was carried out by dissolving compound (*S*,*S*)-**43** in dichlorormethane and addition of trifluoro acetic acid to give the product (*S*,*S*)-**44** as the TFA-salt in 76% yield (see Figure 25).

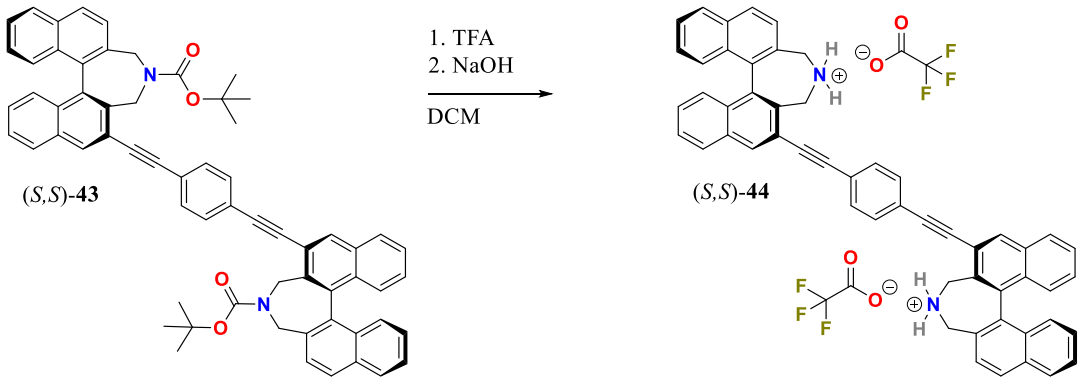


Figure 25: Deprotection oft the Boc-protecting groups.

In the ^{1}H-NMR, the resonance for the Boc-group can no longer be observed, but the resonance of NH_2 protons is observed at 2.51 ppm. The methylene protons appear now as sharp dubletts at 4.61, 3.91, 3.52 and 3.39 ppm (see Figure 26). A final confirmation of the structure of the ammonium salt was achieved by mass spectrometry (signal of the protonated species at m/z = 713.2954 a.u. for $[M+H]^+$, calculated: m/z = 713.2951 a.u. for $[C_{54}H_{37}N_2]^+$).

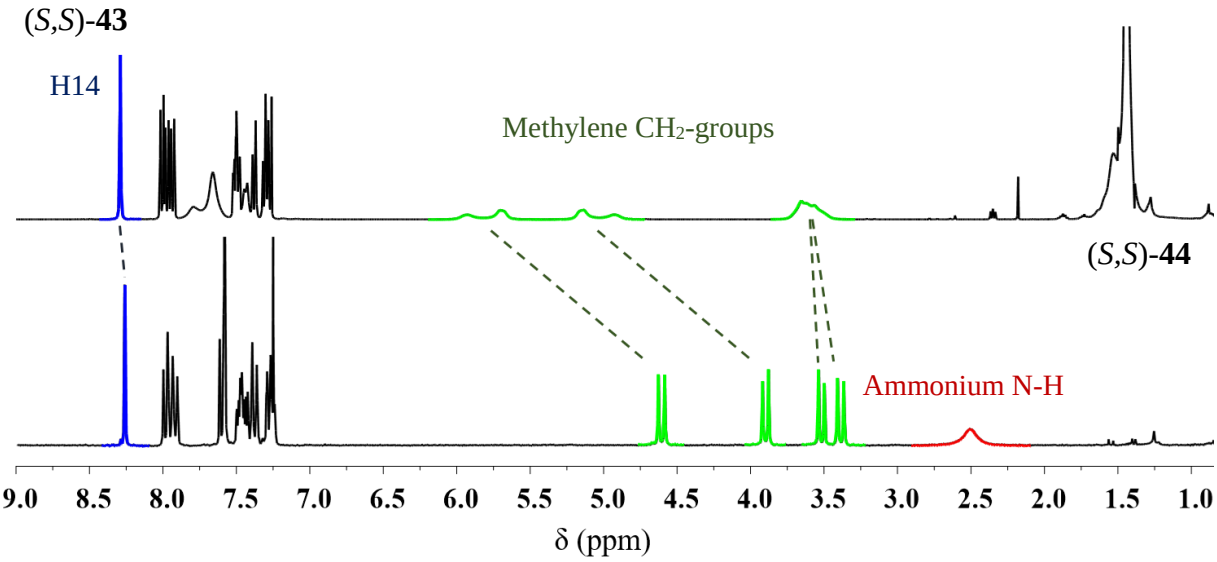


Figure 26: Comparison of the ^{1}H-NMR spectra of compounds (*S*,*S*)-**43** and (*S*,*S*)-**44**. [$CDCl_3$, top 400 MHz, bottom 300 MHz, 298 K].

The finalization of the synthesis route was achieved by the installment of a guanidinium functionality. First, deprotonation was carried out by washing with an aqueous solution of 2 M sodium hydroxide. The solid was then dissolved in dry toluene and *n*-butyllithium was added. The solution directly turned red as a lithium intermediate formed. Subsequently, *N*,*N*′-diisopropylcarbodiimide was added and the mixture was stirred at room temperature for one hour, leading to a brown mixture. To end the reaction methanol was added. The crude product could only be purified by HPLC (RP18-column, methanol/water, 0.1% TFA, 15ml/min). The compound was obtained as the TFA salt (*S*,*S*)-**28** (see Figure 27).

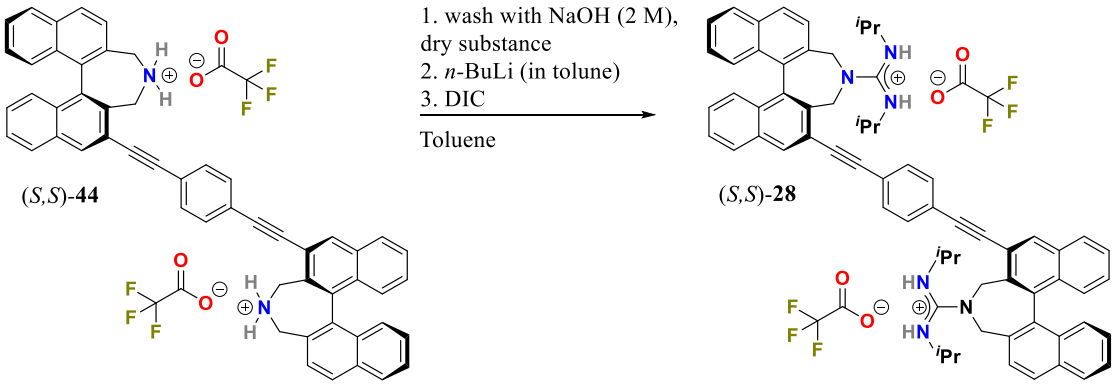


Figure 27: Installment of the guanidine functionality.

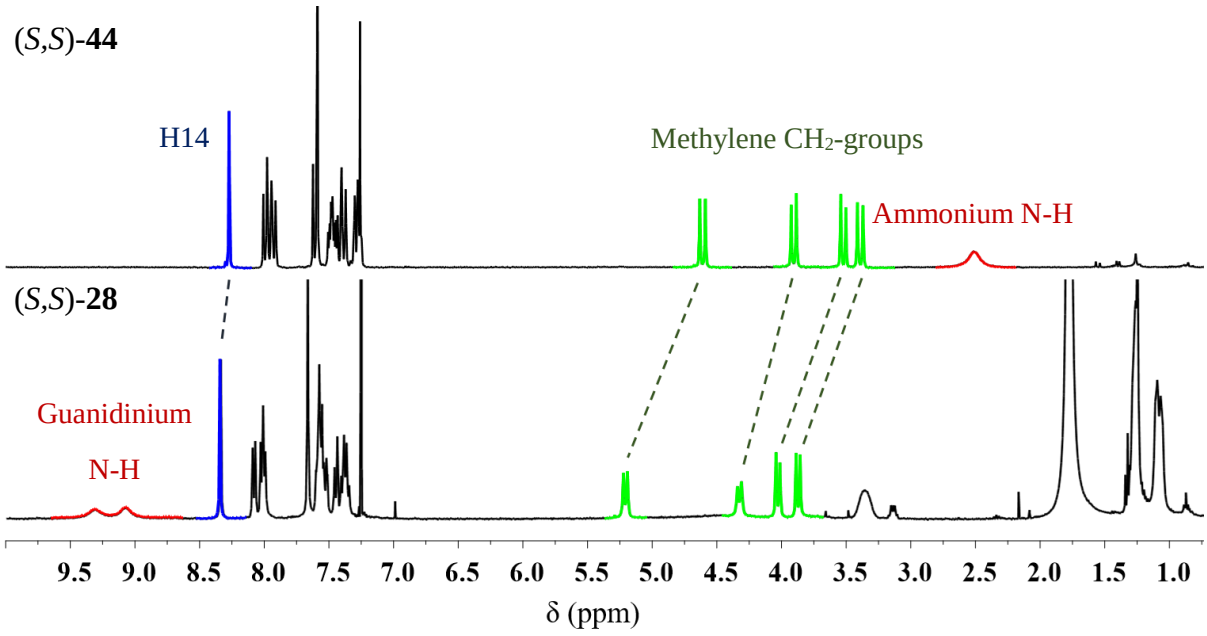


Figure 28: Comparison of the ^{1}H-NMR spectra of the ammonium (*S*,*S*)-**44** and the guanidinium (*S*,*S*)-**28.** [both 600 MHz, $CDCl_3$, 298 K]

The guanidinium compound (*S*,*S*)-**28** was completely analysed. In the ^{1}H-NMR spectrum, new signals for the isopropyl groups were observed at 3.37, 1.25 and 1.10 ppm. Surprisingly, there are two signals for the guanidinium NH protons (δ(NH): 9.32 and 9.08 ppm), indicating that they are in slow exchange (see Figure 28). Furthermore, a mass spectrum confirmed the successful synthesis of the bis-guanidine (*S*,*S*)-**28** (observed m/z = 965.5266 a.u. for $[M+H]^+$, calculated m/z = 965.5265 a.u. for $[C_{68}H_{65}N_6]^+$).

3.3.3. Investigations on supramolecular double helix formation

For the synthesis of the hydrogen-bonded supramolecular double-helices, bis-guanidine (*S*,*S*)-**28** (used as the $(TFA^-)_2$-salt) was mixed in a 1 : 1 stoichiometry with either bisphosphate (*S*,*S*)-**29** or its enantiomer (*R*,*R*)-**29** (used as the $(N^+Bu_4)_2$-salts). The first idea was, that the chirality of the binaphtyl-framework would have a strong influence on the self-assembly, so that possibly only the homochiral (*S*,*S*)-**28**+(*S*,*S*)-**29** pair would be able to form a supramolecular double helix, but not the heterochiral (*S*,*S*)-**28**+(*R*,*R*)-**29** pair. Therefore, ^{1}H-NMR experiments were performed by preparing solutions of the complexes and the single compounds directly in deuterated chloroform (see Figure 29).

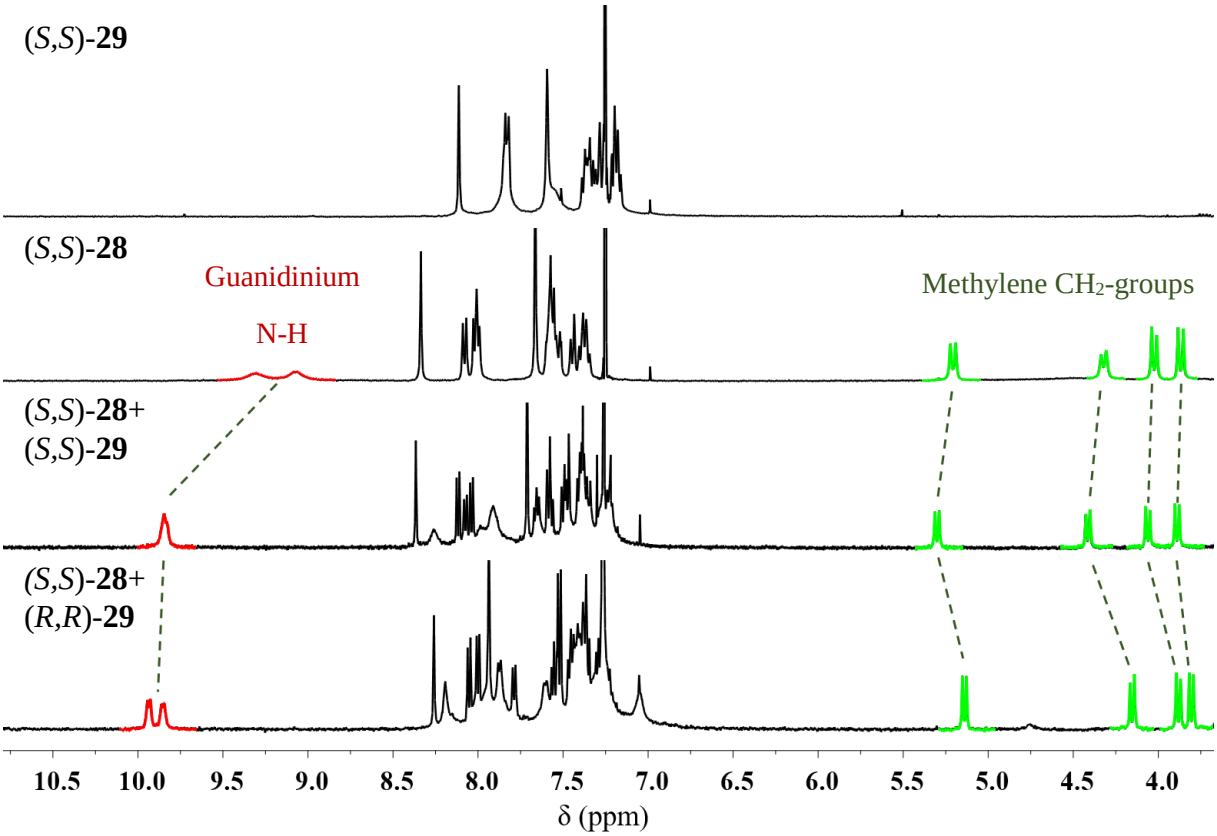


Figure 29: ^{1}H NMR spectra of (*S*,*S*)-**29**, (*S*,*S*)-**28** and the 1:1 complexes (*S*,*S*)-**28** + (*S*,*S*)-**29** and (*S*,*S*)-**28** + (*R*,*R*)-**29** (all: 400 MHz, $CDCl_3$, 298 K, 3 mM for each compound).

Unexpectedly, ^{1}H-NMR analysis proved the formation of the supramolecular complexes for both the homochiral (*S*,*S*)-**28**+(*S*,*S*)-**29** and the heterochiral (*S*,*S*)-**28**+(*R*,*R*)-**29** pair. Most pronounced are the resonances of the guanidinum NH protons that are shifted downfield (δ(NH) = 9.79/ 9.76 ppm for (*S*,*S*)-**28**+(*S*,*S*)-**29**/(*S*,*S*)-**28**+(*R*,*R*)-**29**, c.f. 9.32+9.08 ppm for (*S*,*S*)-**28**. In contrast to that a different behaviour has been observed for the methylene protons, wherethe signals are shifted downfield for the homochiral (*S*,*S*)-**28**+(*S*,*S*)-**29** pair, while an upfield shift

is observed for the heterochiral (*S,S*)-**28**+(*R,R*)-**29** pair. This leads to the indication that there is a difference in complex geometry.

In order to elucidate the geometry of the supramolecular complexes for both pairs, NMR-titrations and DOSY-NMR measurements were carried out. Therefore, stock solutions were prepared (6 mM). Upon titration of (*S,S*)-**28** with (*S,S*)-/(*R,R*)-**29**, sigmoidal binding isotherms were observed in both cases. This hints at a competitive displacement of the triflate counter anions upon addition of the phosphate guest. In addition, the relative binding strenghts[13] were determined according to *Leito*[55]. It was found that the homochiral (*S,S*)-**28**+(*R,R*)-**29** complex and the heterochiral (*S,S*)-**28**+(*R,R*)-**29** complex have an identical association constant within the margin of error (K_{rel} = 0.90±0.18). The DOSY-NMR measurements show a similar result. After complexation, a decrease in diffusion coefficients was observed for both the homochiral and heterochiral pairs (D = 6.00/6.05·10^{-10} m^2s^{-1} for (*S,S*)-**28**+(*S,S*)-**29**/(*S,S*)-**28**+(*R,R*)-**29**; c.f. 6.79 10^{-10} m^2s^{-1} and 6.27·10^{-10} m^2s^{-1} for the components (*S,S*)-**28** and (*S,S*)-**29**). The changes in the diffusion coefficients are rather small, because of the presence of relatively large counter ions and only slightly larger complex structures (*S,S*)-**28**+(*S,S*)-**29**/(*S,S*)-**28**+(*R,R*)-**29** compared to the single strands (*S,S*)-**28** and (*S,S*)-**29**. However, a large change in the diffusion coefficients was found for the N^+Bu_4-cation, which hints at the displacement of the counter ions upon formation of the supramolecular complexes (see Table 1).

Table 1: Association constants and diffusion coefficients as determined by NMR titrations and DOSY NMR. [all 500 MHz, [D_1]-chloroform at 298 K].

Compound		(*S,S*)-**28**	(*S,S*)-**29**	(*S,S*)-**28**+(*S,S*)-**29**	(*S,S*)-**28**+(*R,R*)-**29**
Association constants K_{rel}				1	0.90 ± 0.18
Diffusion coefficients D [10^{-10} m^2 s^{-1}]	CH_{Ar}	6.79 ± 0.32	6.27 ± 0.05	6.00 ± 0.14	6.05 ± 0.23
	N^+Bu_4		6.89 ± 0.09	8.77 ± 0.60	8.69 ± 0.35

To further investigate the geometry of the supramolecular complexes, the structures of the monomers (*S,S*)-**28**/(*S,S*)-**29** and the complexes (*S,S*)-**28**+(*S,S*)-**29** and (*S,S*)-**28**+(*R,R*)-**29** were calculated by means of quantum chemical methods.[56] The geometrical parameters of the monomers and complexes were optimized using B3LYP with the dispersion correction with Becke–Johnson damping (D3BJ). As basis set, 6-31G(d) was applied. Chloroform was

[55] S. A. Kadam, K. Haav, L. Toom, T. Haljasorg and I. Leito, *J. Org. Chem.*, **2014**, *79*, 2501–2513.
[56] These calculations were kindly performed by Prof. Gebhard Haberhauer.

considered as solvent by using the SMD model[57]. The obtained molecular structures are shown in Figure 30. It was found that both supramolecular complexes (*S*,*S*)-**28**+(*S*,*S*)-**29** and (*S*,*S*)-**28** + (*R*,*R*)-**29** are held together by hydrogen bonds between the both guanidinium–phosphate moieties. In case of the homochiral complex, a compact left-handed double helical structure is formed (see Figure 30). Both subunits adopt an *S*-type conformation with an *anti*-orientation of the 1,1′-binaphthyl units and the central 1,4-diethynylbenzene units are nearly parallel to each other. Conversely, in the heterochiral complex, the bisguanidine adopts a *U*-type conformation with a *cis*-orientation of the 1,1′-binaphthyl units, and the aromatic rings of the two central 1,4-diethynylbenzene units are perpendicular to each other. Thus, this supramolecular assembly can be described as a non-helical heterodimer.

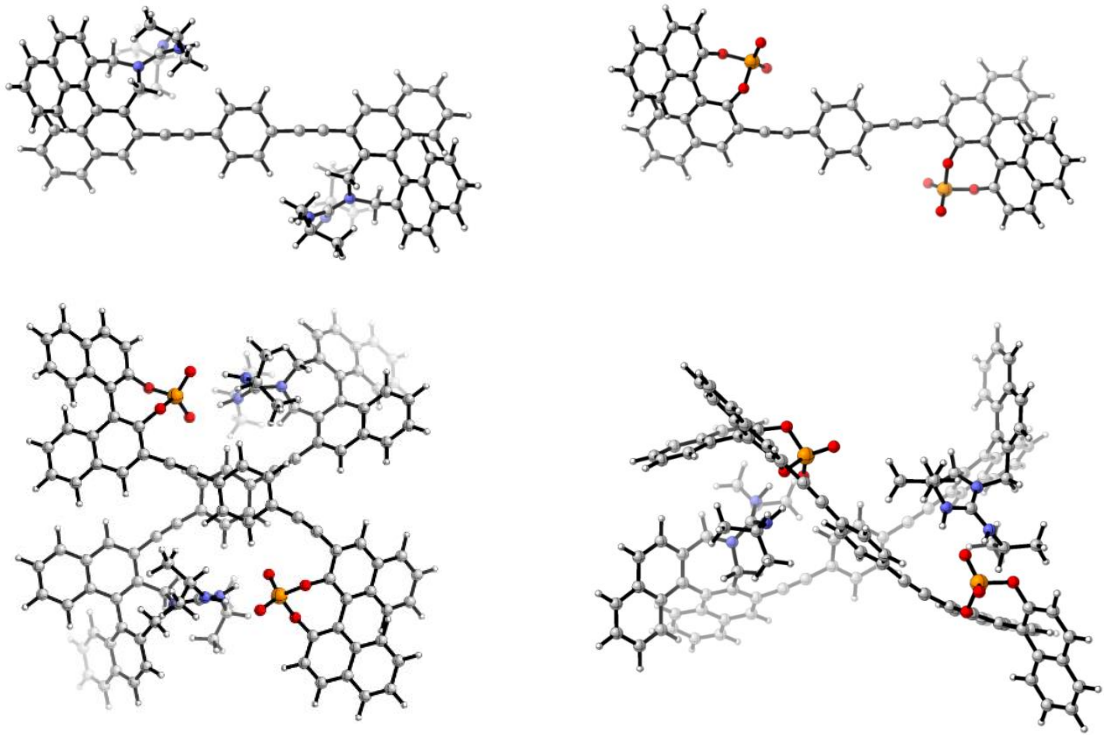


Figure 30: Molecular structures (CYLview20) of (*S*,*S*)-**28**+(*S*,*S*)-**29** and (*S*,*S*)-**28**+(*R*,*R*)-**29** calculated by means of B3LYP-D3BJ(SMD)/6-31G*. Color codes: grey, carbon; white, hydrogen; blue, nitrogen; brown, phosphorus; red, oxygen.

From the computed structures we learned, that the central 1,4-diethynylbenzene unit feature a bent overall structure in both supramolecular structures. In CD-spectra this difference such a bend should be detectable, thus confirming the supramolecular structure. For this reason, ECD spectroscopy of the single strands (*S*,*S*)-**28**, (*S*,*S*)-**29** and (*R*,*R*)-**29** and of the complexes (*S*,*S*)-**28**+(*S*,*S*)-**29** and (*S*,*S*)-**28**+(*R*,*R*)-**29** were carried out. In this purpose, stock solutions of

[57] (a) A. D. Becke, *Phys. Rev. A: At., Mol., Opt. Phys.* **1988**, *38*, 3098–3100; (b) C. Lee, W. Yang, R. G. Parr, *Phys. Rev. B: Condens. Matter Mater. Phys.* **1988**, *37*, 785–789; (c) B. Miehlich, A. Savin, H. Stoll, H. Preuss, *Chem. Phys. Lett.* **1989**, *157*, 200–206; (d) S. Grimme, S. Ehrlich, L. Goerigk, *J. Comput. Chem.*, **2011**, *32*, 1456–1465; (e) A. V. Marenich, C. J. Cramer, D. G. Truhlar, *J. Phys. Chem. B* **2009**, *113*, 6378–6396; (f) T. Yanai, D. P. Tew, N. C. Handy, *Chem. Phys. Lett.* **2004**, *393*, 51–57.

the individual substances were prepared in chloroform (10 µM) for all four substances. Furthermore, all spectra were also simulated by time-dependent density functional theory (TD-DFT) using cam-B3LYP, 6-31G * and the SMD model (chloroform as solvent).[57] The energy, oscillator strength, and rotatory strength were calculated for each of the 150 lowest singlet excitations. For comparison, the experimentally determined and the calculated spectra are shown in Figure 31.

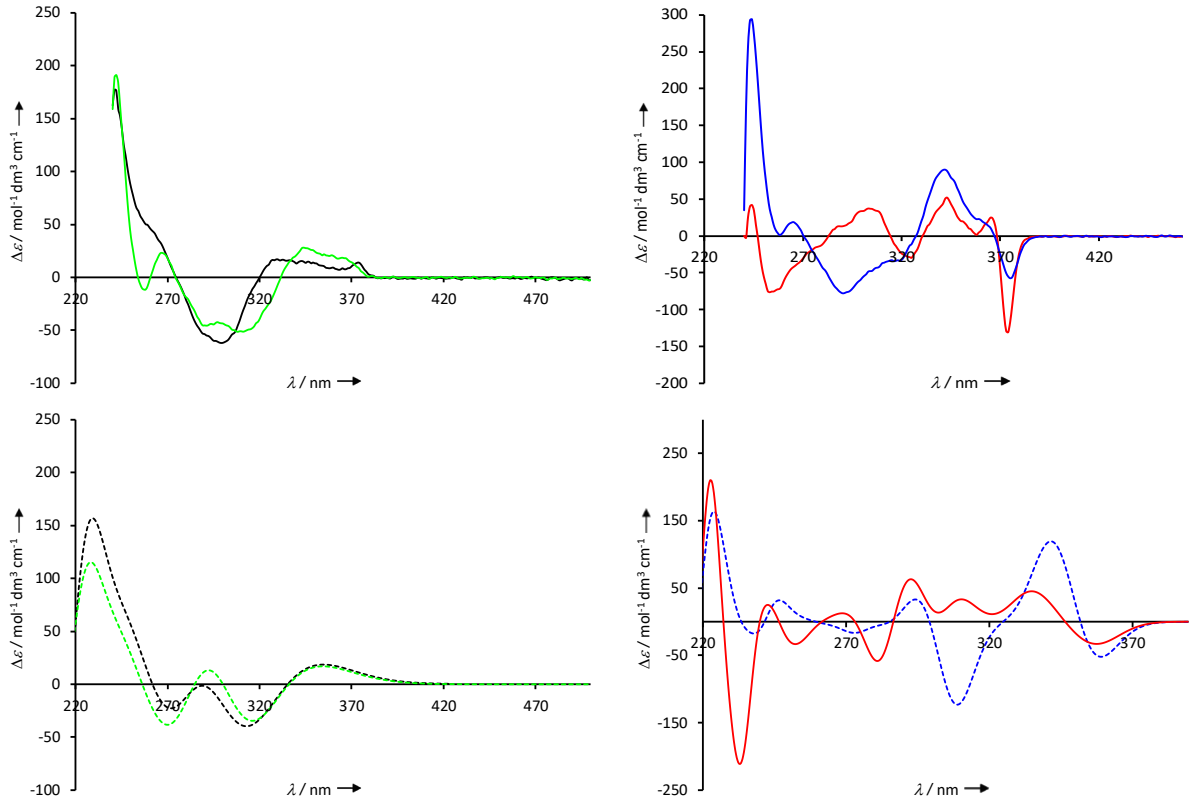


Figure 31: CD spectra of the monomers (S,S)-**28** (green) and (S,S)-**29** (black) and the homochiral complex (S,S)-**28**+(S,S)-**29** (blue) and the heterochiral complex (S,S)-**28**+(R,R)-**29** (red) in $CHCl_3$ (c = 10^{-5} M).(top left and right), TD-cam-B3LYP(SMD)/6-31G*-calculated CD spectra of the monomers (S,S)-**18** (green dashed line) and (S,S)-**29** (black dashed line) and of the homochiral complex (S,S)-**28**+(S,S)-**29** (blue, dashed line) and the heterochiral complex (S,S)-**28**+(R,R)-**29** (red, solid line).(bottom left and right).

In the following, the lowest energy π-π* transition in the monomer units is considered. The diethynylbenzene unit causes an electronic excitation at around 350 nm. For the monomers (*S*,*S*)-**28** and (*S*,*S*)-**29**, this π-π* transition exhibits in both cases a positive Cotton effect. The experimentally determined and the simulated CD spectra of the monomers (*S*,*S*)-**28** and (*S*,*S*)-**29** agree well in this region. In the case of the supramolecular complexe, there are accordingly two bands in this area: the lower (ca. 360 nm) and the higher energy band (ca. 320 and 340 nm) can be assigned to the bisphosphate and bisguanidinium species, respectively. In the computed and measured spectra, the lower energy band shows a negative and the higher energy band a positive Cotton effect. In the calculated spectrum of the complex (*S*,*S*)-**28**+(*R*,*R*)-**29**, however, the negative band is much less pronounced than in the experiment. Qualitatively, the calculated CD

spectra of both complexes agree with the measured ones in this area and thus confirm the structures found by the calculations.

3.4. Conclusion

In summary, we have reported on the successful synthesis of a novel bis-binaphthyl-guanidine based on a 1,4-diethinyl benzene linker. Therefore, a new synthetic route was established, synthesizing the bis-guanidine (*S*,*S*)-**28** in 12 steps starting from BINOL.

Furthermore, we found that the envisioned guanidinium–phosphate pairing was successfully employed for the formation of a complementary double-helical structure. On one hand the homochiral paired complex (*S*,*S*)-**28**+(*S*,*S*)-**29** gives an intertwined double-helical structure with left-handed helicity. On the other hand the heterochiral paired complex (*S*,*S*)-**28**+(*R*,*R*)-**29** forms a non-helical dimeric structure.

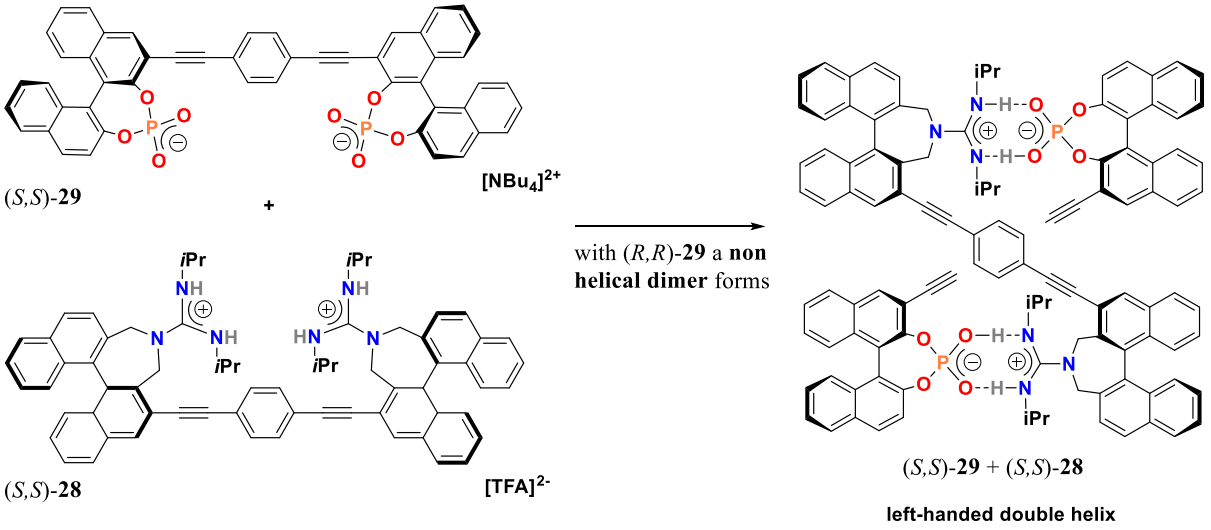


Figure 32: Supramolecular double helices of bis-guanidine and bis-phosphate through hydrogen bond formation.

4. Recognition and Differentiation of Methylated Lysines

4.1. Introduction

Amino acids are ubiquitous components of proteins of all living organisms. Post-translational modifications (PTMs) of amino acids in proteins regulate the function of hundreds of proteins in diverse ways.[58]

The post-translational modification of histone proteins deserves special attention. Histone proteins control and regulate the packing of DNA into its compact form of chromosomes and chromatins.[59] Many PTMs alter the functioning of proteins by introducing a charge at a neutral site through phosphorylation or sulfation, or by neutralizing a charged residue through acetylation or citrullination.[60] Methylation of a lysine side chain, on the other hand, does not significantly change its charge or its pK_a value. The steric demand of the lysine side chains increases only slightly with increasing methylation. Ultimately, the sum of these PTMs on a histone protein results in the so-called histone code, which is scanned by reader proteins and thus, triggers a cascade of subsequent reactions, including the execution or prevention of DNA transcription.[61] Particularly the methylation of lysine side chains is of great interest in research, as it is involved in the regulation of gene transcription. Unlike all other PTMs, methyl groups are installed by enzymes that control the number of resulting methyl groups with high specificity. Lysine can be mono- (**Kme$_1$**), di- (**Kme$_2$**) or tri-methylated (**Kme$_3$**). Because of the biological relevance of the histone-PTMs, analytical methods for the detection of the methylation of lysine are of great interest. In general, antibody-based methods are used, which can be problematic due to poor reproducibility. In addition, a distinction between different histone modifications is often difficult or error-prone.

[58] L. Stryer, *Biochemie*, Spektrum Akademischer Verlag, Heidelberg, **1996**.
[59] a) E. J. Richards, S. C. R. Elgin, *Cell* **2002**, *108*, 489−500; b) K. S. Weiler, B. T. Wakimoto, *Annu. Rev. Genet.* **1995**, *29*, 577−605.
[60] a) H. Wang, W. An, R. Cao, L. Xia, H. Erdjument-bromage, B. Chatton, P. Tempst, R. G. Roeder, Y. Zhang, *Biochem. Soc. Trans.* **2013**, *41*, 751−759; b) S. D. Taverna, H. Li, A. J. Ruthenburg, C. D. Allis, D. Patel, *Nat. Struct. Mol. Biol.* **2007**, *14*, 1025−1040.
[61] S. B. Rothbart, K. Krajewski, B. D. Strahl, S. M. Fuchs, *Methods Enzymol.* **2012**, *512*, 107−135.

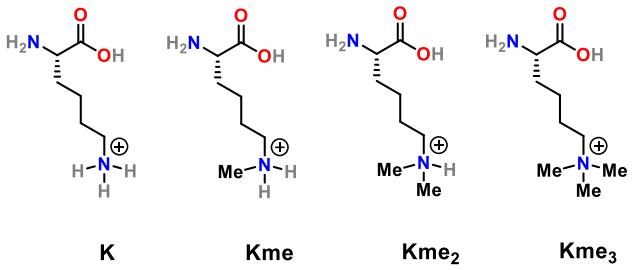
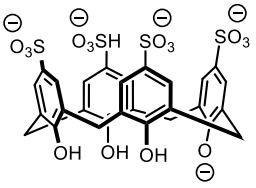


Figure 33: Methylated derivatives of (D)-lysine **K**.

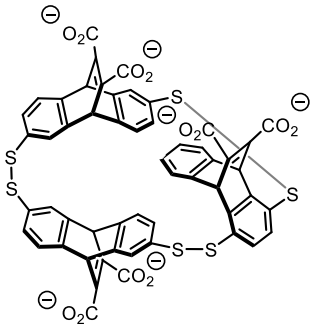
Reader proteins offer binding sites for methylated amino acids, while their electron-rich aromatic cages allow for cation–π interactions to make binding more effective. Therefore, one strategy is to detect methylated amino acids by artificial receptors composed of an electron-rich, macrocyclic π system to mimic reader proteins. *Hof* and co-workers developed a series of receptors with high affinity and selectivity for Kme_3, based on sulfonated calixarenes (see Figure 34).[62] In contrast to the binding of lysine (K_a = 520 M^{-1}), the affinity of receptor **46** to bind the fully methylated amino acid is considerably more pronounced (K_a = 37 000 M^{-1}). Furthermore, it was shown by chemical calculations that the trimethyl-ammonium group of lysine binds in the aromatic cavity. The even higher binding constants for peptides containing a Kme_3 unit (e.g. H3K9me_3, K_a = 139 000 M^{-1}) can be attributed to secondary interactions with the peptide chain. *Waters* and co-workers developed trimeric receptors that self-assemble by dynamic covalent chemistry through the formation of disulfide bridges and thereby incorporate methylated amino acids.[63] In this way, receptors with high affinity, for lysines with different methylation grades were developed. For example, receptor **47** was stabilized in the presence of the fully methylated lysine, resulting in high selectivity for the trimethylated histone derivative H3R8K9me3 (K_a = 3.3x10^{-6} M^{-1}) compared to the other histone derivatives. Once again, secondary interactions result in higher binding constants as shown by comparison with the glycine-containing derivative H3R8GK9me3 (K_a = 770 000 M^{-1}). The groups of *Hof* and *Waters* successfully showed the selective binding of Kme_3 and of Kme_3 in peptides. However, it was not possible to develop synthetic receptors that selectively recognize the double- or mono-methylated lysine species (**Kme2** or **Kme**).

[62] a) C. S. Beshara, C. E. Jones, K. D. Daze, B. J. Lilgert, F. Hof, *ChemBioChem* **2010**, *11*, 63-66, b) C. S. Beshara, F. Hof, *Can. J. Chem.* **2010**, *88*, 1009-1016, c) A. L. Whiting, F. Hof, *Org. Biomol. Chem.* **2012**, *10*, 6885-6892, d) A. L. Whiting, N. M. Neufeld, F. Hof, *Tetrahedron Lett.* **2009**, *50*, 7035-7037.
[63] a) N. K. Pinkin, M. L. Waters, *Org. Biomol. Chem.* **2014**, *12*, 7059-7067, b) N. K. Pinkin, I. Liu, J. D. Abron, M. L. Waters, *Chem. Eur. J.* **2015**, *21*, 17981-17986.



46

Bindungs constants (M^{-1})[a]	
K	520
Kme	4000
Kme_2	16 200
Kme_3	37 000
$H3K9me_3$	139 000



47

Bindungs constants (M^{-1})[b]	
H3R8K9	95 000
H3R8K9me	25 000
$H3R8K9me_2$	240 000
$H3R8K9me_3$	3 300 000
$H3R8GK9Me_3$	770 000

Figure 34: Receptors of *Hof* and *Waters* to detect fully methylated lysine.

An analyte can be successfully detected if the sensor binds the analyte with high selectivity and ideally with high affinity. If the sensor exhibits cross-selectivity, different analytes are bound non-specifically and a clear identification of the analyte is no longer possible. However, *Ansyln* and other scientists have shown that cross-selectivity can still be used to identify structurally related analytes using sensor arrays.[64] In an array-based approach, a signal pattern is generated for each analyte in that each sensor experiences an individual change in the spectroscopic properties with a specific analyte, for example due to different association constants. Here, several output signals are generated for each sensor, which together result in a multidimensional matrix of measured values. A representation in a two- or three-dimensional matrix can be realized by chemometric data reduction and analysis, including principal component analysis (PCA) or linear discriminant analysis (LDA).[65] The time required to identify chemically related analytes can be significantly reduced when using a sensor array. The development of an array can be achieved by different methods: On one hand, multiple sensors that are chemically similar can be synthesized. On the other hand, the measurement parameters, such as the pH value or the solvent, can be varied in order to obtain different responses for different analytes.

Based on the chiral phosphoric acids (*R,R*)-**48a-f** and the use of the metals Eu^{3+} and Ni^{2+}, *Niemeyer* and co-workers developed a sensor array for the chemo- and stereoselective identification of 18 D- and L-amino acids (see Figure 35). This sensor array enables a correct classification of L-amino acids with an accuracy of 100% and a distinction between L- and D-amino acids with an accuracy of 94%.

[64] a) M. A. Palacios, R. Nishiyabu, M. Marquez, P. Anzenbacher, *J. Am. Chem. Soc.* **2007**, *129*, 7538-7544, b) L. You, D. Zha, E. V. Anslyn, *Chem. Rev.* **2015**, *115*, 7840-7892.
[65] a) J. P. Anzenbacher, P. Lubal, P. Bucek, M. A. Palacios, M. E. Kozelkova, *Chem. Soc. Rev.* **2010**, *39*, 3954-3979; b) A. T. Wright, E. V. Anslyn, *Chem. Soc. Rev.* **2006**, *35*, 14-28.

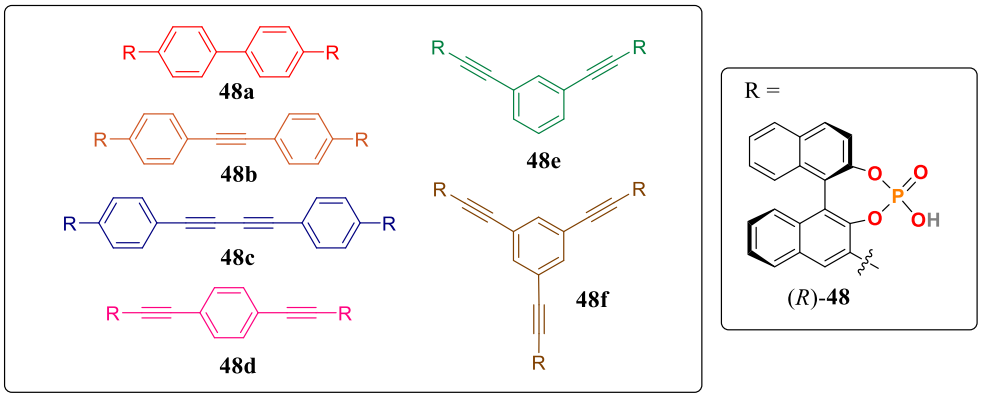


Figure 35: Chiral fluorescent phosphoric acids (*R*,*R*)-**48a-e** and (*R*,*R*,*R*)-**48f** of the sensor array by *Niemeyer*.

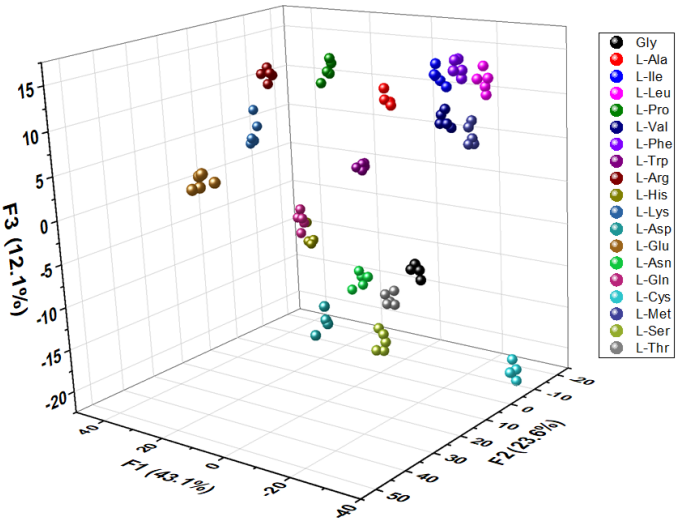
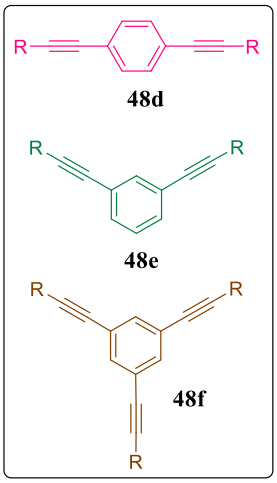
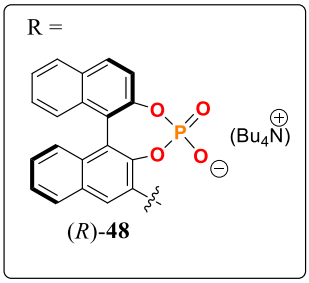


Figure 36: LDA score plot for 18 l-amino acids and glycine based on the reduced parameter set (7 sensors, 3 wavelengths, 21 parameters).

In 2018, *Niemeyer* and co-workers reported the application of (*R*,*R*)-**48d-f** as chiral receptors (see Figure 37). The binding of the enantiomers of lysine to the three chiral receptors was examined by means of NMR titrations. *Niemeyer* and co-workers used the phosphoric acid in the form of the tetrabutylammonium salts and the amino acid in the form of the bishydrochlorides in order to avoid changes in the chemical shift due to proton transfer from the phosphoric acid to the basic amino acid. Here it could be shown that the (*R*,*R*)-**48d** and (*R*,*R*)-**48e** receptors not only have high association constants in the range of 6100 – 40 000 M^{-1} in dimethyl sulfoxide, but also a strong preference for the binding of D-lysine over L-lysine (see Figure 37). The best stereo discrimination was found for (*R*,*R*)-**48d** (K_D/K_L = 6.1).





Association constants K_a [M^{-1}]			
Rezeptor	D-Lysin	L-Lysin	*K*fav/*K*disfav
48d	40000 ± 13000	10000 ± 500	4.0 (D)
48e	37000 ± 3700	6100 ± 170	6.1 (D)
48f	39000 ± 6500	69000 ± 22000	1.8 (L)

Figure 37: Binding constants (M^{-1}) of the three receptors (*R*,*R*)-**48d-e** and (*R*,*R*,*R*)-**48f** with L/D-lysine (used as the bishydrochlorides).

4.2. Aim

The work of *Niemeyer* and co-workers illustrates that the BINOL backbone as a chiral element is a suitable tool for the development of chiral sensors. It allows good discrimination of enantiomeric analytes using NMR spectroscopy. Furthermore, the identification of structurally related analytes such as the proteinogenic amino acids is already possible with a sensor array using fluorescence spectroscopy.

To establish a sensor array for the binding of partially methylated lysine derivatives based on BINOL phosphoric acids, a pool of chiral sensors must be synthesized. In its anionic form the phosphate group can interact with the amino acid side chains *via* Coulomb interactions and/or hydrogen bonds. We envisaged that this might allow for a preferential binding of partially methylated lysine derivatives, since these can interact via one or two hydrogen bonds (for Kme_2 and Kme, respectively), while only Coloumb interactions are formed in case of Kme_3.

However, polar Coloumb and/or hydrogen-bonding interactions might not be sufficiently strong for an application in polar solvent. Thus, we decided to introduce additional aromatic substituents in the 3-position of the BINOL-backbone, allowing for additional hydrophobic and/or cation-π interactions with the analyte. Further substituents can be introduced in the 3'-position, leading to a concave binding pocket. Furthermore, it is synthetically possible to use further substituents in the 6,6'-position to increase the water solubility without affecting the binding properties.

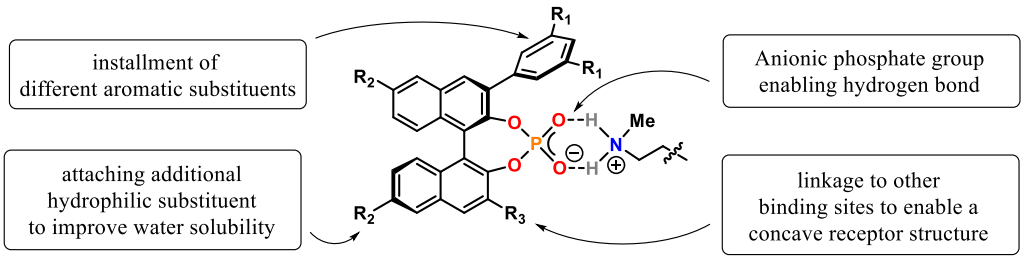


Figure 38: Strategy for the development of a new pool of BINOL-derived phosphoric acids.

The phosphoric acids, synthesized according to these protocols, are meant to serve as sensors for the array to bind partially methylated derivatives of lysine (Kme and Kme_2) with high affinity and selectivity. Therefore, histone modifications, either on individual amino acids or ideally on whole proteins, could be detected by fluorescence spectroscopy

4.3. First attempts

In order to establish a sensor array for the detection and differentiation of methylated lysines, binding behavior potential sensor has to be investigated. For this purpose, binding studies were performed, firstly NMR-titrations, UV/vis titrations and fluorescence titrations. In the first study receptors (*R*,*R*)-**4a** and (*R*)-**12a** will be used (see Figure 39), (for synthesis see chapter 46). In 2018 *Niemeyer* and co-workers have successfully used bis-phosphoric acids (*R*,*R*)-**48d-f** as chiral receptors for the recognition and differentiation of L- and D-lysine. Receptors (*R*,*R*)-**4a** and (*R*)-**12a** are now equipped with an additional aryl substituent in the remaining 3-postion, forming now a sterically demanding binding pocket to improve the recognition of analytes, in this work differently methylated lysines.

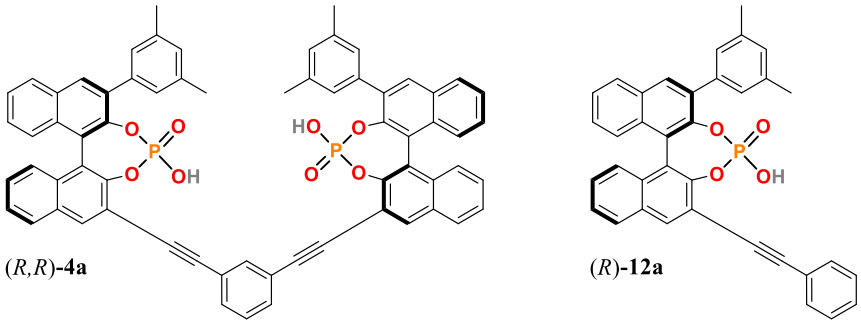


Figure 39: BINOL-based phosphoric acid receptors (*R*,*R*)-**4a** and (*R*)-**12a**.

Then binding behaviour of reference receptor (*R*)-**12a** was first to be investigated, firstly, *via* UV/vis- and secondly *via* fluorescence titration. It turned out that UV/vis spectroscopy was not usable to investigate the binding behaviour of receptor to analyte, because upon addition of analyte to receptor no change in the UV/vis spectrum was observed. In contrast, a change in the intensity of the emission could be observed in the fluorescence spectrum due to the addition of the analyte to receptor. For this reason, only fluorescence titrations were performed. Therefore, stock solutions of both of the receptors (*R*,*R*)-**4a** and (*R*)-**12a** and of the analyte **Kme** were prepared. The solvent used was a mixture of DMSO and water in the ration 70:30. The added equivalents and the resulting emission intensities at 385 nm are given in Table 2. The obtained binding isotherm for the fluorescence titration of (*R*)-**12a** with **Kme** is given in Figure 40. Also, the obtained emission spectra can be found in Figure 40.

Table 2:Results of the fluorescence titration of (*R*)-**12a** with **Kme**. Equivalents and emission intensities at 385 nm are listed.

equivalents of Kme to (*R*)-**12a**	Emission at 385 nm
0	62545
0.5	75406
0.1	61453
10	60998
50	55295
100	51939
250	48737
500	48358

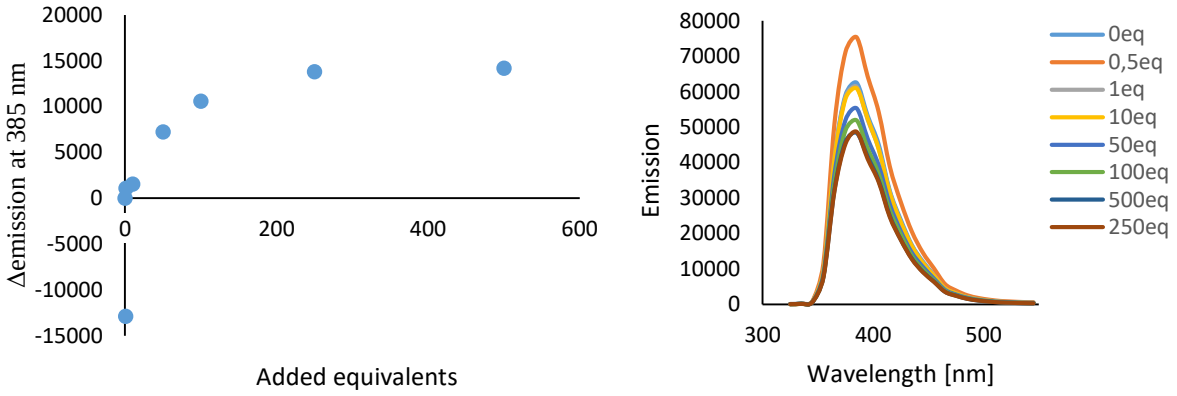


Figure 40: Observed binding isotherm and emission spectra of the titration of (*R*)-**12a** with **Kme**.

Surprisingly, the addition of 0.5 equivalents of analyte resulted in an increase of emission. The addition of further equivalents led to a decrease in emission. From the emission spectra a binding isotherm was generated. However, the association constant could not be determined due to the irregular behaviour at 0.5 equivalents. The same experiment was performed for receptor (*R,R*)-**4a**, but no clear increase or decrease in emission with increasing amounts of added guest could be found.

In addition, it was found that these results were difficult to reproduce. Thus, we attempted to investigate the binding behaviour with an indirect method by an indicator displacement assey (IDA).[66] The use of an IDA might facilitate the detection and differentiation of methylated lysine derivatives. Because of the non-covalent attachment between the fluorescent indicator and the sensor/receptor, it is possible that the analyte displaces the indicator. Due to the interaction between the indicator and the receptor, either no fluorescence is detected or the fluorescence differs after the displacement of the indicator.

[66] a) B. T.Nguyen, E. V.Anslyn, *Coord. Chem. Rev*. **2006**, *250*, 3118-3127, b) A. C. Sedgwick, J. T. Brewster II, T. Wu, X. Feng, S. D. Bull, X. Qian, J. L. Sessler, T. D. James, E. V. Anslyn, X. Sun, *Chem. Soc. Rev*. **2021**, *50*, 9-38.

In this purpose, we used rhodamine B as an indicator and measured the fluorescence of rhodamine B and the fluorescence of the rhodamine B-receptor complex. The last experiment was measuring the fluorescence of the mixture rhodamine B, receptor (*R*)-**12a** and (*R,R*)-**4a** and **Kme**. In the following all three emission spectra are shown.

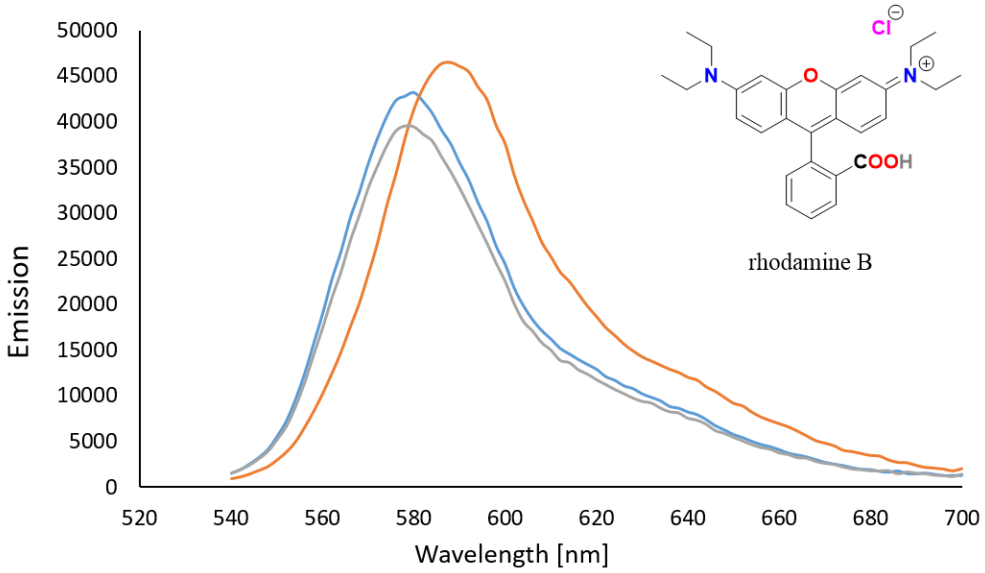


Figure 41: Emission spectra of attempts on an indicator displacement assay.(emission spectra blue: rhodamin B, orange: rhodamin B and (*R,R*)-**4a** and grey**:** rhodamin B, (*R,R*)-**4a** and **Kme**.

The emission maxima of the indicator-receptor-complex was found at 582 nm, while the emission maxima of the mixture of indicator-receptor-complexes was found at 578 nm. Due to this small shift of the emission wavelength, the IDA could not be applied.

4.4.Conclusion

From the fluorescence titrations no clear results were obtained. UV/vis and fluorescence measurements were performed on a well plate reader. Due to some difficulties with the instrument and the well plates, the measurements should be repeated in cuvette.

In the future it is to work on the implementation of the measurements, on the one hand, to obtain reproducible results and, on the other hand, to enable the development of a sensor array.

Due to the SARS-CoV-2 situation, this project was abandoned to the time restraints.

5. BINOL-based Organocatalysts

5.1. Introduction

In recent years, organocatalysis as a form of metal-free catalysis has become increasingly attractive. In particular, the simple chemical structures and low price of organocatalysts represent a major advantage in comparison to metal and/or transition metal-based complexes. Furthermore, the organocatalysts impress with their high stability and wide range of applicability, for example under oxygen-rich or even aqueous conditions.[67] More specifically, the use of chiral organocatalyst has revolutionized the synthesis of chiral organic compounds, as can be seen from the Nobel Prize in Chemistry in 2021, which was awarded to *List* and *MacMillan* for their work on "for the development of asymmetric organocatalysis".

In addition to various classes of organocatalysts, Lewis bases, phase transfer catalysts, or Brønsted acids represent the most important ones. In the following some prominent catalysts structures are presented.

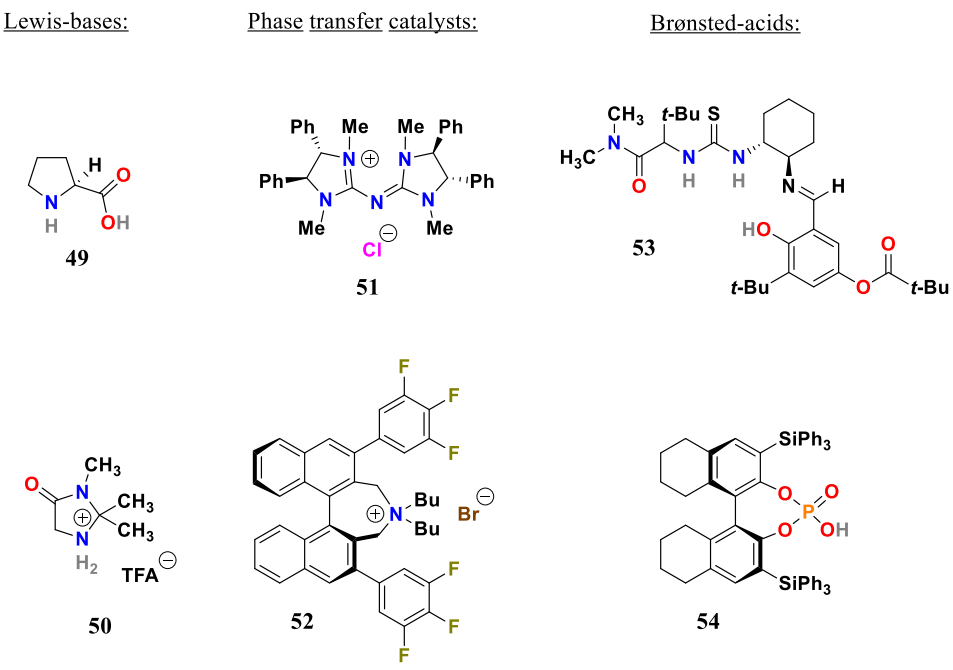


Figure 42: Prominent catalyst: L-Proline **49**, *MacMillan* Imidazolidinone **50**, Guanidinium salt **51**, *Maruoka* azepine **52**, *Jacobsen* thiourea **53**, H_8-BINOL Phosphoric Acid **54**.

Lewis-basic organocatalysts can nucleophilically attack unsaturated substrates such as carbonyl compounds, leading to enamine or iminium-intermediates. This covalent activation allows for various types of organic transformations. L-proline **49** was found to be an effective catalyst e.g.

[67] a) A. Berkessel, H. Gröger, *Asymmetric Organocatalysis*, WILEY-VCH, Weinheim, **2005**, 1-3. b) P. I. Dalko (Ed.), *Comprehensive Enantioselective Organocatalysis*, Wiley-VCH, Weinheim, **2007**.

in Aldol-reactions,[68] Mannich type reactions,[69] α-aminations,[70] α-aminoxylations,[71] intramolecular Michael reactions[72] and many more. *MacMillans* imidazolidinones **50** enables highly enantioselective Diels-Alder reactions, 1,3-dipolar cycloadditions,[73] Friedel–Crafts alkylations,[74] and α-chlorinations[75] and others. In the realm of phase-transfer catalysis, guanidines (e.g. compound **51**) and *Maruoka's* azepin-derived systems (e.g. compound **52**) can be used for asymmetric catalysis. These phase transfer catalysts facilitate the reaction of otherwise insoluble anionic nucleophilic reagents with organic substrates in organic solvents. For example, the guanidinium salts **51** were used as catalysts for the conjugate addition of activated methylene-derivatives to vinyl ketones.[76] *Maruoka's* quaternary ammonium salts **52** were applied for the enantioselective syntheses of α-alkyl α-amino acids through monoalkylation,[77] for Strecker reactions,[78] Aldol reactions[79] and other cycladditionss.[80]

Last but not least, increasing attention has been paid to asymmetric reactions catalysed by Brønsted acids. Depending on the acidity of the Brønsted acid, the mode of substrate activitation ranges from hydrogen-bonding to substrate protonation. Chiral Jacobsen thioureas[81] as weak Brønsted acids, represent hydrogen-bonding catalysts, whereas the BINOL derived phosphoric acids orginally developed by *Terada*[82] and *Akiyama*[83] are examples of stronger Brønsted acids. Thioureas have been successfully applied to reactions such as the Strecker reaction,[81] the hydrophosphorylation of imines[81] or the Mannich reaction.[84] Particularly, the use of chiral phosphoric acids for the synthesis of optically active compounds has become a new and exciting area of contemporary synthetic organic chemistry. This will be discussed in detail in the next chapter.

[68] B. List, R. A. Lerner, C. F. Barbas, *J. Am. Chem. Soc*. **2000**, *122*, 2395-2396.
[69] B. List, P. Pojarliev, W. T. Biller, H. J. Martin, *J. Am. Chem. Soc*. **2002**, *124*, 827.
[70] B. List, *J. Am. Chem. Soc*. **2002**, *124*, 5656-5657.
[71] a) G. Zhong, *Angew. Chem. Int. Ed*. **2003**, *42*, 4247-4250. b) S. P Brown, M. P. Brochu, C. J. Sinz, D. W. C. MacMillan, *J. Am. Chem. Soc*. **2003**, *125*, 10808-10809.
[72] B. List, P. Pojarliev, H. Martin, *J. Org. Lett*. **2001**, *3*, 2423-2425.
[73] W. S. Jen, J. J. M. Wiener, D. W. C. MacMillan, *J. Am. Chem. Soc*. **2000**, *122*, 9874-9875.
[74] N. A. Paras, D. W. C. MacMillan, *J. Am. Chem. Soc*. **2001**, *123*, 4379-4109.
[75] M. P. Brochu, S. P. Brown, D. W. C. MacMillan, *J. Am. Chem. Soc*. **2004**, *126*, 4108-4109.
[76] T. Ma, X. Fu, C. W. Kee, L. Zong, Y. Pan, K.-W. Huang, C.-H. Tan, *J. Am. Chem. Soc.* **2011**, *133*, 2828-2831.
[77] (a) M. Kitamura et al. *Angew. Chem. Int. Ed.* **2005**, *44*, 1549-1550. b) X. Wang, M. Kitamura, K. Maruoka, *J. Am. Chem. Soc.* **2007**, *129*, 1038–1039.
[78] P. Maity, S. D. Lepore, *Angew. Chem*. **2011**,*123*, 8488.
[79] M. Kitamura, S. Shirakawa,Y. Arimura, X. Wang, K. Maruoka, *Chem. Asian J*. **2008**, *3*, 1702.
[80] V. Gembus, S. Postikova, V. Levacher, J.-F. Brière, *J. Org.Chem*. **2011**, *76*, 4194.
[81] a) P. Vachal, E. N. Jacobsen, *J. Am. Chem. Soc*. **2002**, *124*, 10012-10013. b) G. D. Joly, E. N. Jacobsen, *J. Am. Chem. Soc*. **2004**, *126*, 41024103. c) M. S. Taylor, E. N. Jacobsen, *Angew. Chem. Int. Ed* **2006**, *45*, 1520-1543.
[82] D. Uraguchi, M. Terada, *J. Am. Chem. Soc.* **2004**, *126*, 5356-5357.
[83] T. Akiyama, J. Itoh, K. Yokota, K. Fuchibe, *Angew. Chem. Int. Ed., 43*, **2004**, 1566-1568.
[84] A. G. Wenzel, E. N. Jacobsen, *J. Am. Chem. Soc*. **2002**, *124*, 12964-12965.

5.2. BINOL-based Phosphoric Acids

Derivatives of phosphoric acid (*S*)-**48** have been used in various catalytic reactions, due to the advantages of the BINOL-backbone and the phosphoric acid moiety.[85] In most cases the key aspect in chiral Brønsted acid catalysis is the bifunctional character of these phosphoric acids. They can form hydrogen bonds with electrophiles (Brønsted acidic OH-group) whereas the Brønsted basic P=O site forms hydrogen bonds with nucleophiles. For an application in stereoselective catalysis, suitable substitution in the 3,3'-positions of the BINOL-framework is essential, since these substituents point towards the active site, thus generated a chiral pocket around the Brønsted acidic POOH-group.

The group of *List* pioneered on this field by synthesising **55**[86] and **56**,[87] a selection of potent catalysts of BINOL-derived phosphoric acids, that has been used by numerous scientists in many different enantioselective transformations e.g. the Mannich-type reactions,[88] the aza-Friedel-Crafts alkylations[89] or the hydrocyaniation of imines.[90] Another modulation has been made by implementing two phosphoric acid groups into the BINOL- framework[91] or by connecting two BINOL-based phosphoric acid units via an ether linkage.[92] **56** and **58** have been applied to Diels-Alder reactions[91] or 1,3-dipolar cycloadditions.[92]

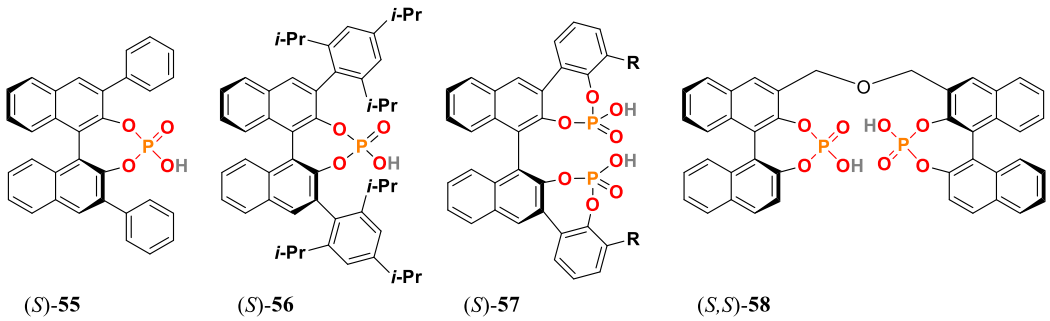


Figure 43: BINOL-based catalysts (*S*)-**55**, (*S*)-**56** (**TRIP**), (*S*)-**57** and (*S,S*)-**58**.

[85] A. Zamfir, S. Schenker, M. Freund, S. B. Tsogoeva, *Org. Biomol. Chem*. **2010**, *8*, 5262-5276.
[86] N. J. A. Martin, B. List, *J. Am. Chem. Soc*. **2006**, *128*, 13368-13369; b) M. Sonja, B. List, *Angew. Chem. Int. Ed*. **2006**, *45*, 4193-4195.
[87] a) S. Hoffmann, A. M. Seayad, B. List, *Angew.Chem*. **2005**, *117*, 7590–7593, b) G. Adair, S. Mukherjee, B. List, *Aldrichimica Acta* **2008**, *41*, 31.
[88] T. Akiyama, J. Itoh, K. Yokota K. Fuchibe, *Angew. Chem. Int. Ed.* **2004**, *43*, 1566–1568, D. Uraguchi, M. Terada, *J. Am. Chem. Soc.* **2004**, *126*, 5356–535.
[89] D. Uraguchi, K. Sorimachi M. Terada, *J. Am. Chem. Soc*. **2004**, *126*, 11804–11805
[90] M. Rueping, E. Sugiono, C. Azap, *Angew. Chem., Int. Ed*. **2006**, *45*, 2617–2619.
[91] a) Q.-X. Guo, H. Liu, C. Guo, S.-W. Luo, Y. Gu, L.-Z. Gong, *J. Am. Chem. Soc.* **2007**, *129*, 3790-3791; b) N. Li, X.-H. Chen, J. Song, S.-W. Luo, W. Fan, L.-Z. Gong, *J. Am. Chem. Soc*. **2009**, *131*, 15301-15310; c) J. M. Goss, S. E. Schaus, *J. Org. Chem.* **2008**, *73*, 7651-7656.
[92] X.-H. Chen, W.-Q. Zhang, L.-Z. Gong, *J. Am. Chem. Soc.* **2008**, *130*, 5652-5653; b) J. Yu, L. He, X.-H. Chen, J. Song, W.-J. Chen, L.-Z. Gong, *Org. Lett.* **2009**, *11*, 4946-4949; c) N. Li, J. Song, X.-F. Tu, B. Liu, X.-H. Chen, L.-Z. Gong, *Org. Biomol. Chem.* **2010**, *8*, 2016-2019; d) L. He, X.-H. Chen, D.-N. Wang, S.-W. Luo, W.-Q. Zhang, J. Yu, L. Ren, L.-Z. Gong, *J. Am. Chem. Soc*. **2011**, *133*, 13504-13518.

Lately, the group of *Niemeyer* developed the synthesis of a mechanically interlocked molecule, a [2]catenane (*S*,*S*)-**61b**, bearing two BINOL- based phosphoric acid groups.[93] Since (*S*,*S*)-**61b** is a bis-Brønsted acid, *Niemeyer* and coworkers. reported on its use as a catalyst in a transfer hydrogenation reaction of quinolines according to previous works of *Rueping*.[94] It was found, by using a catalyst loading of 2.5 mol% [2]catenane (*S*,*S*)-**61b** and a substrate concentration of 5 mM, 2-phenylquinoline was transferred into (*R*)-1,2,3,4-tetrahydrophenylquinoline in 90% yield with an enantiomeric excess of 84%.[95] The macrocyclic counterpart (*S*)-**62b** and the acyclic phosphoric acid (*S*)-**63** showed significantly lower stereoselectivities (-12% *ee* for (*S*)-**62b** and 9% *ee* for (*S*)-**63**).

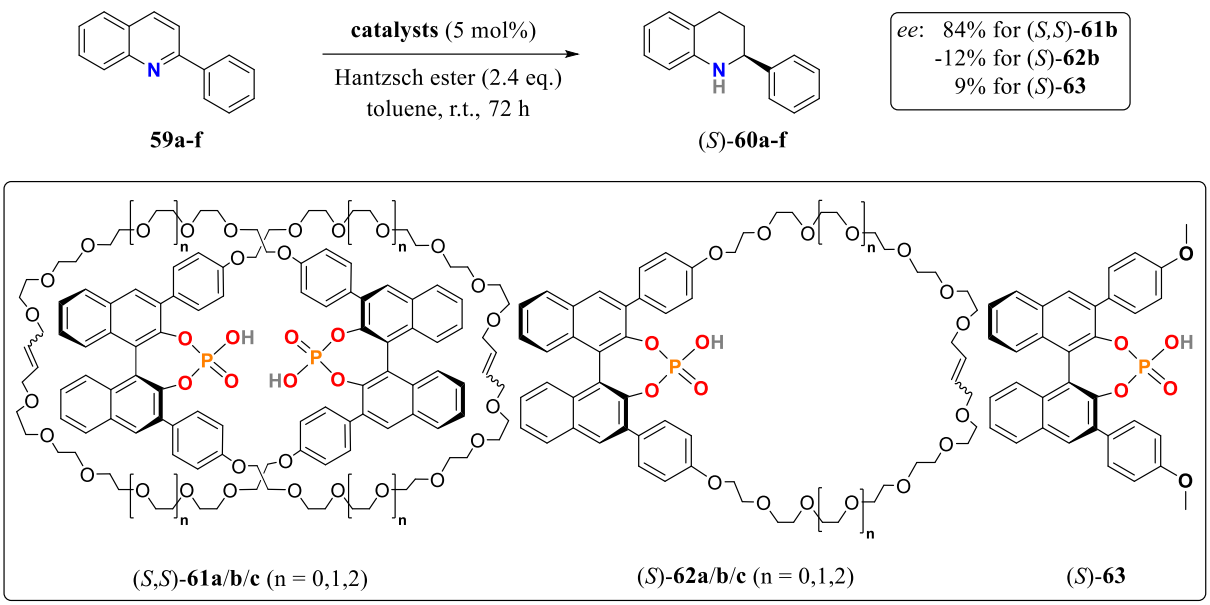


Figure 44: Catenane (*S*,*S*)-**61a/b/c**, macrocycle (*S*,*S*)-**62a/b/c** and mono-phosphoric acid (*S*)-**63** according to *Niemeyer*.

Following this work, *Niemeyer* and co-workers varied the ring size of catenane (*S*,*S*)-**61b** and macrocycle (*S*,*S*)-**62b**. For this purpose catenanes (*S*,*S*)-**61a/c** with ten and fourteen ethylene glycol units per macrocycle were also applied to transferhydrogenation of 2-phenyl quinoline. Surprisingly, there was no influence of the ring-sizes on stereoinduction as catenanes (*S*,*S*)-**61a/c** provided enantiomeric excesses of 81 and 82%. In contrast, the reaction rates of (*S*,*S*)-**61a/b/c** show a distinct dependency on the ring-size. The reaction rate decreases with

[93] R. Mitra, M. Thiele, F. Octa-Smolin, M. C. Letzel, J. Niemeyer, *Chem. Comm.* **2016**, *52*, 5977-5980.
[94] M. Rueping, A. P. Antonchick, T. Theissmann, *Angew. Chem. Int. Ed*. **2006**, *45*, 3683-3686.
[95] R. Mitra, H. Zhu, S. Grimme, J. Niemeyer, *Angew. Chem. Int. Ed.* **2017**, *56*, 11456-11459.

increasing numbers of ethylene glycol units, (v_0= 3.7x10^{-7}, 3.1x10^{-7} and 2.7x10^{-7} for (*S*,*S*)-**61a/b/c**).[96]

The observed high enantioselectivities for the [2]catenane (*S*,*S*)-**61b** and the low enantioselectivities for (*S*)-**62b**/**63** in the transfer hydrogenation were explained using computational modelling. It was found that the phosphoric acid moieties can operate in a dimeric fashion. In the following the calculated catalytic cycle based on a dimer is shown in Figure 46, in contrast, the catalytic cycle based on a monomeric phosphoric acid (comparable to *Rueping´*s case) is shown in Figure 45. It was found that the dimeric catalyst exists primarily as a stable dimer [**ssh2**], which is linked by two P=O···(HO)P hydrogen bonds and is 4.8 kcal mol^{-1} more stable than two individual monomers [**sh**].

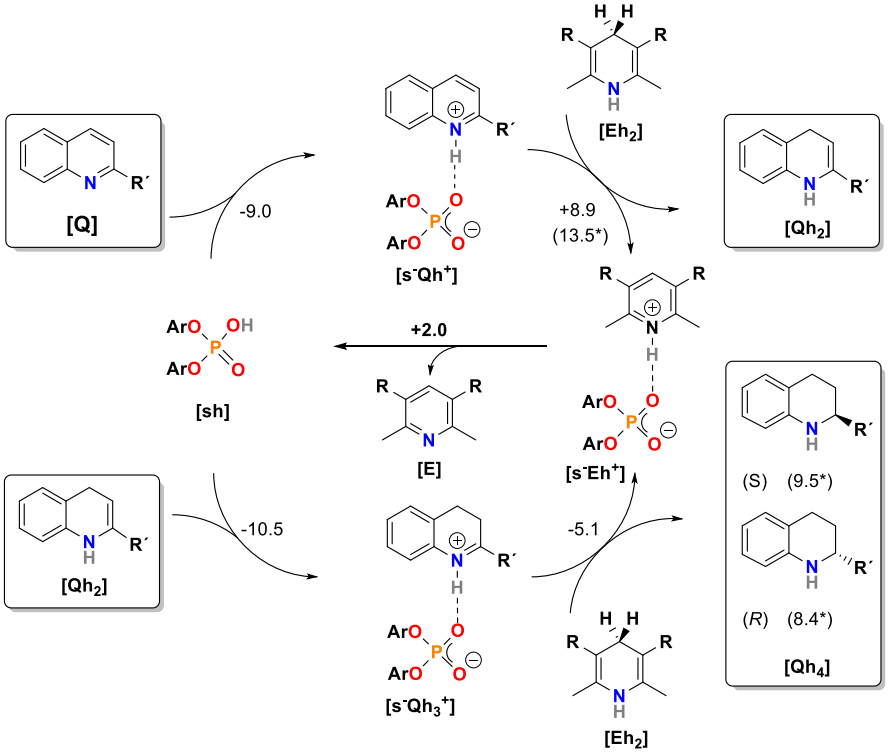


Figure 45: catalytic cycle, calculated for the monomeric species.

[96] D. Jansen, J. Gramüller, F. Niemeyer, T. Schaller, M. C. Letzel, S. Grimme, H. Zhu, R. M. Gschwind, J. Niemeyer, *Chem. Sci*. **2020**, *11*, 4381–4390.

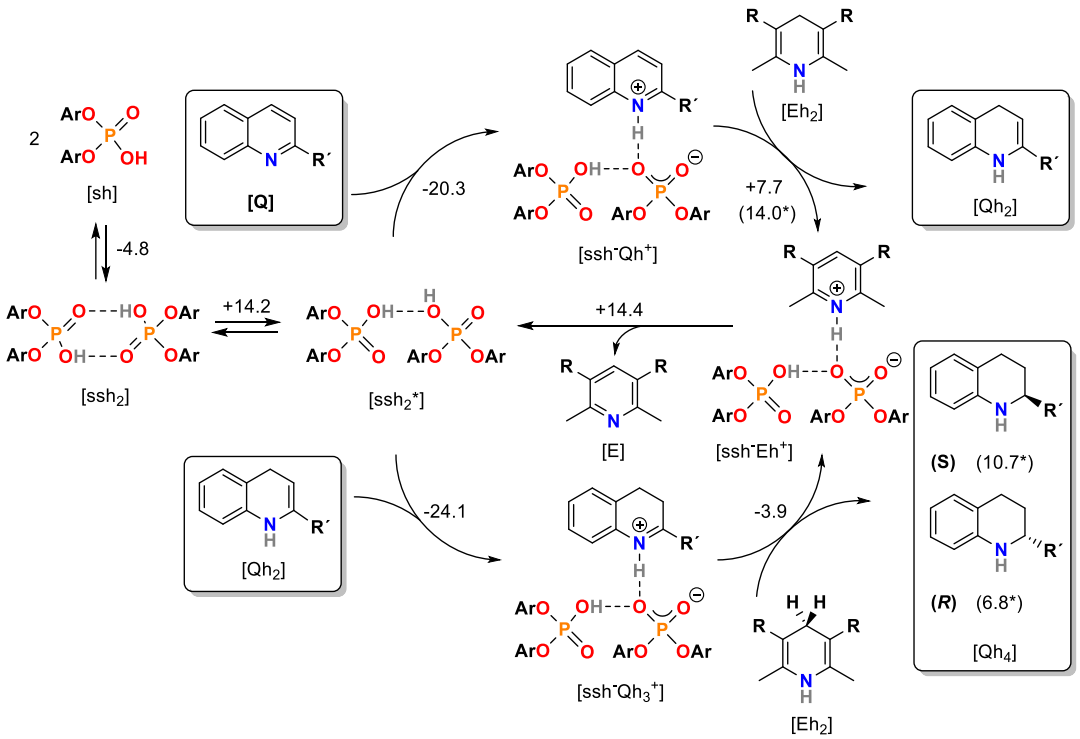


Figure 46: Catalytic cycle, calculated for a 3,3´-bis(4-methoxy-phenyl)-1,1´-binaphthyl-2,2´-phosphoric acid dimer **[ssh$_2$]** as a comparable catalyst to (*S*,*S*)-**53**, with energy barrier values in kcal/mol.

Instead of the quinoline **[Q] (20)** being coordinated and catalysed by one phosphoric acid moiety, it is coordinated by the activated form **[ssh2*]** to form hydrogen bonded complex **[ssh-Qh+]**. By reacting with the Hantsch ester **[Eh2]**, the complex **[ssh-Qh+Eh2]** is formed. The next step is the hydride transfer from the Hantzsch ester and formation of the molecule **[Qh2]**. **[Qh2]** and the **[ssh2*]** form the ion pair **[ssh-Qh3+]**. This can form two diastereomeric transition states with the Hantzsch ester, with one resulting in the (*S*) product and the other in the (*R*) product **[Qh4]** after a second hydride transfer.

In the case of the acyclic phosphoric acid (*S*)-**55**, a competition between these two alternative mechanisms (monomeric vs. dimeric) occurs and mechanism changes depending on the catalyst loading, resulting in concentration-dependent stereoselectivities. For low catalyst loadings the formation of a catalyst-dihydroquinoline-Hantzsch ester complex **[s-Qh3+Eh2]** and for high catalyst loadings the formation of the catalyst-catalyst-dihydroquinoline-Hantzsch ester complex **[ssh-Qh3+Eh2]** is favoured. Furthermore, the relative influence of the dimeric mechanism on the stereoselectivity is stronger than that of the monomeric one, since the reaction rate in the dimeric mechanism is faster in the second reduction step, and thus it dominates even at very low catalyst loadings. The [2]catenane (*S*,*S*)-**61** as a bis-phosphoric acid can always proceed via the dimeric mechanism regardless of the catalyst loading due to the flexible, non-covalent connection. The mechanical interlocking of the two phosphoric acids

prevents them from dissociating. Thus, the high stereoselectivity of the catenane catalyst is due to the cooperative involvement of both phosphoric acids in the dimeric mechanism.[96]

In this context, *Niemeyer* also developed rigid, covalently linked bis- and tris-phosphoric acids (*R*,*R*)-**48d**, (*R*,*R*)-**48e** und (*R*,*R*,*R*)-**48f** and also applied these in transfer hydrogenation of 2-quinolines.[28] Since the mechanical connection of the catenane enabled the dimerization of the phosphoric acid groups to allow a cooperative action in catalysis, this was expected also for (*R*,*R*)-**48d**, (*R*,*R*)-**48e** und (*R*,*R*,*R*)-**48f**. However, almost racemic products were obtained for catalyst (*R*,*R*)-**56** for the transfer hydrogenation of 2-phenylquinoline and 2-biphenylquinoline (-13% ee, 0% *ee*). For (*R*,*R*,*R*)-**48f** moderate enantioselectivities were observed (10% *ee*, 29% *ee*). In contrast, better enantioselectivities (20% *ee*, 61% *ee*) could be achieved with (*R*,*R*)-**48e**. Similar to the [2]catenane (*S*,*S*)-**61**, catalyst (*R*,*R*)-**48e** also acts in a dimeric mechanism, which was confirmed by DFT calculations.

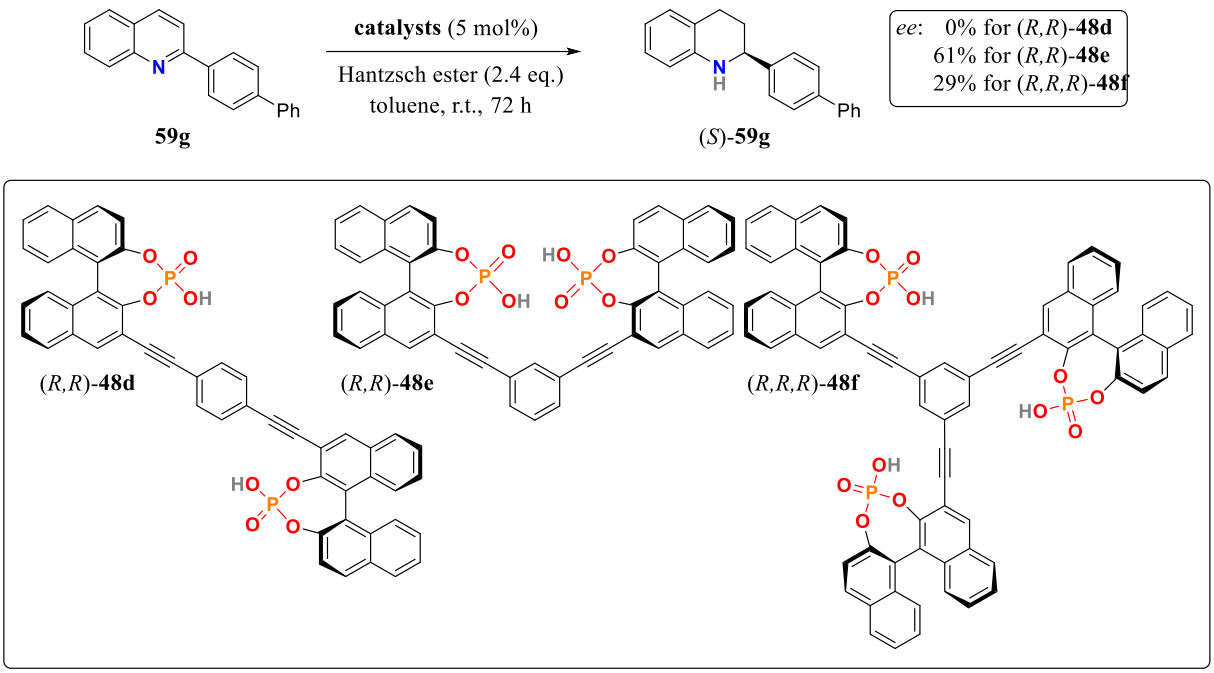


Figure 47: Structures of the covalently linked bis- and trisphosphoric acids (*R*,*R*)-**48e**, (*R*,*R*)-**48e** und (*R*,*R*,*R*)-**48f** for transfer hydrogenation by *Niemeyer*.

BINOL-based phosphoric acids have not only been applied in Brønsted acid mediated catalysis but also in phase transfer catalysis. In 2011 *Toste* started investigating the catalytic activity of chiral anionic salts as phase-transfer catalysts, thus inventing the field of chiral anion phase-transfer catalysis.[97] The approach was to catalyse an electrophilic fluorination reaction, with an

[97] a) V. Rauniyar, A. D. Lackner, G. L. Hamilton, F. D. Toste, Sc*ience* **2011**, 334, 1681-1684; b) R. J. Phipps, K. Hiramatsu, F. D. Toste, *J. Am. Chem. Soc.* **2012,** *134*, 8376-8379; c) R. J. Phipps, F. D. Toste, *J. Am. Chem. Soc.*

insoluble fluorination reagent in conjunction with a chiral phosphate catalyst. Therefore, BINOL-based phosphoric acids like **TRIP** or alkyl-substituted **TRIP**-derivatives (to enhance solubility) were applied together with Selectfluor I as the source of electrophilic F^+. The asymmetric fluorination of **64** with **TRIP** and **C_8-TRIP** yielded gave the products in enantiomeric excesses of 87% and 92%, respectively.

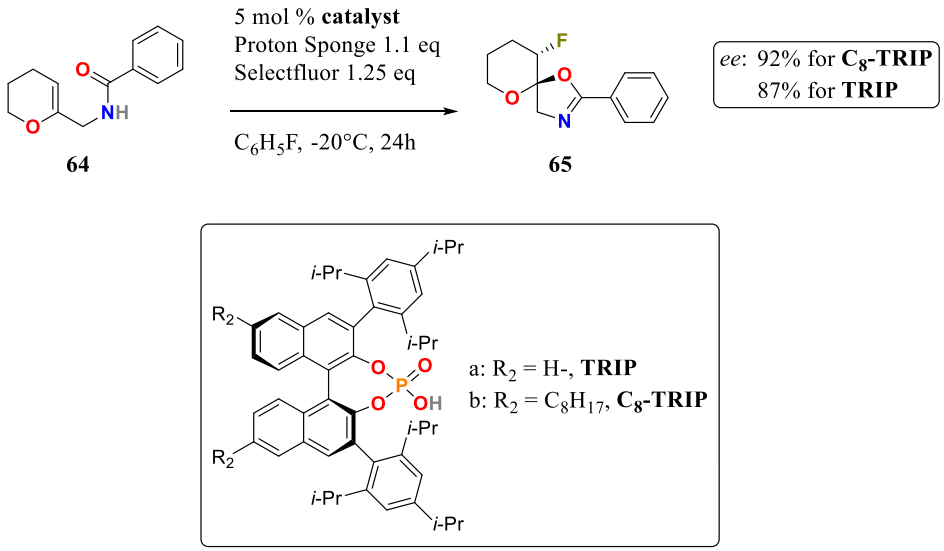


Figure 48: Asymmetric Fluorination of a dihydropyran-derived substrate by the use of **TRIP** and **C_8-TRIP**.

Based on the findings of *Maruoka* and co-workers on the development of carboxylic acids based on the chiral 1,1'-binaphthyl framework and its applications in asymmetric organocatalysis, axially chiral dicarboxylic acids have been used in a wide range of enantioselective transformations ever since.[98] The group of *Hamashima* extended the use of chiral 1,1'-binaphthyl carboxylic acids towards chiral anionic phase-transfer catalysis, developing also new derivatives of the original carboxylic acids of *Maruoka*.

2013, *135*, 1268-1271; d) H. P. Shunatona, N. Früh, Y.-M. Wang, V. Rauniyar, F. D. Toste, An*gew. Chem. Int. Ed.* **2013,** *52*, 7724-7727; e) J. Wu, Y.-M. Wang, A. Drljevic, V. Rauniyar, R. J. Phipps, F. D. Toste, *Proceedings of the National Academy of Science* **2013,** *110*, 13729-13733; f) H. M. Nelson, S. H. Reisberg, H. P. Shunatona, J. S. Patel, F. D. Toste, *Angew. Chem. Int. Ed.* **2014,** *53*, 5600-5603; g) X. Yang, R. J. Phipps, F. D. Toste, *J. Am. Chem. Soc.* **2014,** *136*, 5225-5228; h) W. Zi, Y.-M. Wang, F. D. Toste, *J. Am. Chem. Soc.* **2014,** *136*, 12864-12867.

[98] a) T. Hashimoto, N. Uchiyama, K. Maruoka, *J. Am. Chem. Soc.* **2008**, *130*, 14380-14381; b) T. Hashimoto, K. Maruoka, *J. Am. Chem. Soc.* **2007**, *129*, 10054-10055, b) T. Hashimoto, H. Kimura, Y. Kawamata, K. Maruoka, *Angew. Chem. Int. Ed.* **2012**, *51*, 7279–7281, c) T. Hashimoto, H. Kimura, Y. Kawamata, K. Maruoka, *Nat. Chem.* **2011**, *3*, 642–646, d) T. Hashimoto, H. Kimura, H. Nakatsu, K. Maruoka, *J. Org. Chem.* **2011**, *76*, 6030–6037.

The idea was to use BINOL-based dicarboxylic acids as dianonic phase-transfer catalysts (as opposed to the monoanionic nature of Toste´s BINOL-phosphates). Among other fluorination reactions,[99] dicarboxylic acid (*S*,*S*)-**69** was applied in asymmetric dearomative fluorination of 2-naphthols.[100] First, the dicarboxylic acid is deprotonated by sodium carbonate to form the chiral anionic salt, that transfers Selectfluor I from the solid phase to the liquid phase.

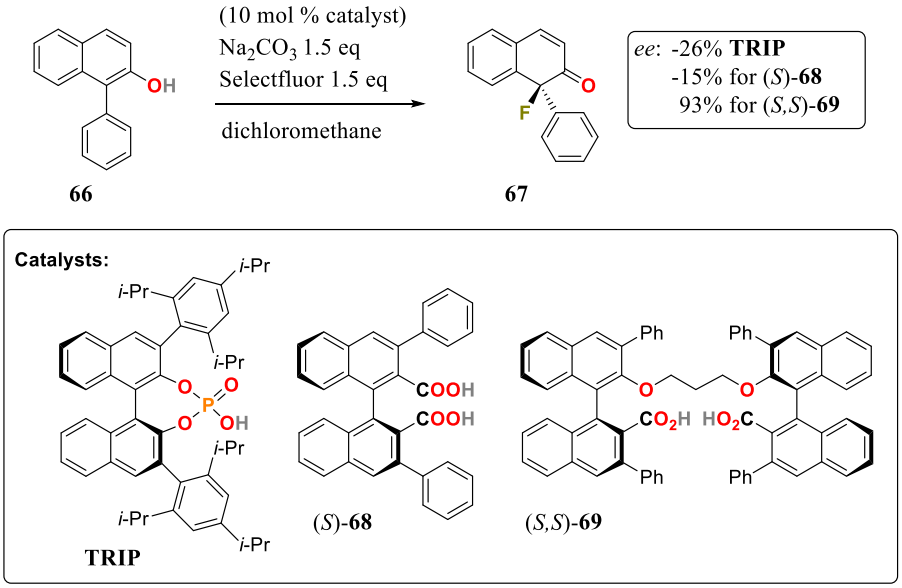


Figure 49: Dearomative fluorination reaction of 1-phenyl-2-naphthol by catalysts **TRIP**, (*S*)-**68** and (*S*,*S*)-**69**.

The asymmetric dearomative fluorination of **66** with (*S*,*S*)-**69** gave the product **67** with an enantiomeric excess of 83%. In comparison, **TRIP** and related dicarboxylic acid (*S*)-**68** only gave enantiomeric excesses of -26% and -16%, respectively.

[99] a) H. Egami, T. Niwa, H. Sato, R. Hotta, D. Rouno, Y. Kawato, Y. Hamashima, *J. Am. Chem. Soc.* **2018**, *140*, 2785-2788; b) T. Niwa, K. Ujiie, H. Sato, H. Egami, Y. Hamashima, C*hem. Pharm. Bull.* **2018**, *66*, 920-922; c) T. Rouno, T. Niwa, K. Nishibashi, N. Yamamoto, H. Egami, Y. Hamashima, *Molecules* **2019**, *24*, 3464; d) H. Egami, R. Hotta, M. Otsubo, T. Rouno, T. Niwa, K. Yamashita, Y. Hamashima, *Org. Lett.* **2020**, *22*, 5656-5660; e) T. Niwa, K. Nishibashi, H. Sato, K. Ujiie, K. Yamashita, H. Egami, Y. Hamashima, *J. Am. Chem. Soc.* **2021**, *143*, 16599-16609; f) M. Otsubo, K. Sakimoto, H. Egami, Y. Hamashima, *Tetrahedron* **2021**, *96*, 132355.

[100] H. Egami, T. Rouno, T. Niwa, K. Masuda, K. Yamashita, Y. Hamashima, *Angew. Chem. Int. Ed.* **2020**, *59*, 14101–14105.

5.3. Aim

Since the first reports by *Terada* and *Akiyama* of chiral phosphoric acids,[88] especially BINOL-based phosphoric acids as organocatalysts, these have been applied to a wide range of enantioselective transformations. Among others, the group of *Niemeyer* has developed a series of potent bis-phosphoric acids as catalysts (see chapter 5.1), foremost the [2]catenane (*S*,*S*)-**61** which achieved high enantioselectivities in transfer hydrogenation of quinolines. In contrast the rigidly, covalently linked bis-phosphoric acid only achieved moderate enantioselectivities, presumably due to the absence of a substituent in the other 3-position. Due to the cooperativity of the two phosphoric acid subunits, the enantioselectivities are still significantly higher than those of mono functionalized phosphoric acids.

This work, now, attempts to generate covalently linked bisphosphoric acids that incorporate different substituents in the 3,3'-position. For this purpose, 3,5-dimethylphenyl substituents should be installed in the 3-postion, while in the 3'-position a flexible polyethylene based linker of different length or a rigid diethynylphenyl-based linker was chosen to connect the two phosphoric acid subunits. Furthermore, the catalytic performance of singly linked catalysts compared to doubly linked (i.e. macrocyclic) phosphoric acids should be investigated. Finally, the applicability of the systems in phase-transfer catalysis should also be investigated.

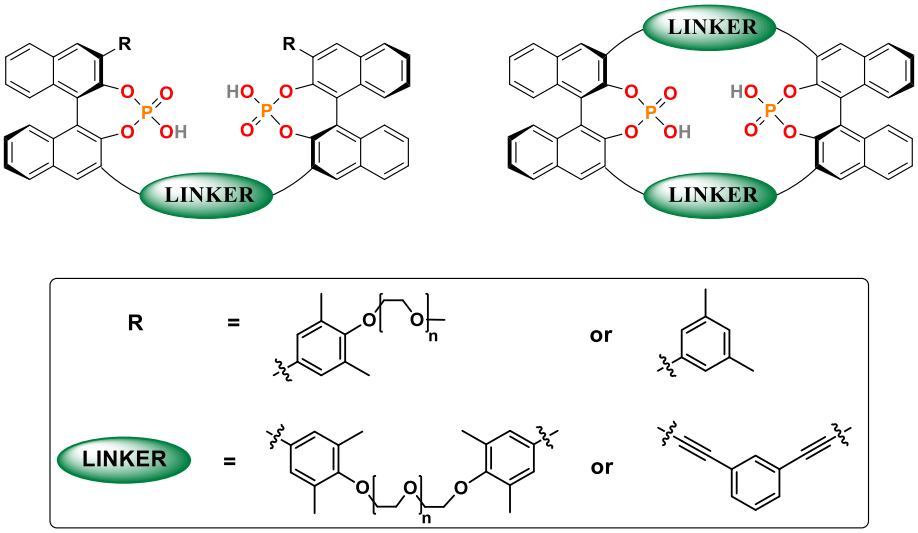


Figure 50: Overview of the different catalyst structures that will be examined in this work.

5.4. Synthesis of 3,3'-Unsymmetrically Substituted BINOL-based Phosphoric Acids

In the following (Figure 51), an overview of all twelve successfully synthesized monomeric- and bis-phosphoric acids is given. The bis-phosphoric acids are divided into rigidly (A) and flexibly (B) linked catalysts. In the next chapter (5.4.1) the first steps of the possible synthetic routes towards unsymmetrically substituted 3,3'-BINOL-derived phosphoric acids are shown, as all phosphoric acids have similar key building blocks.

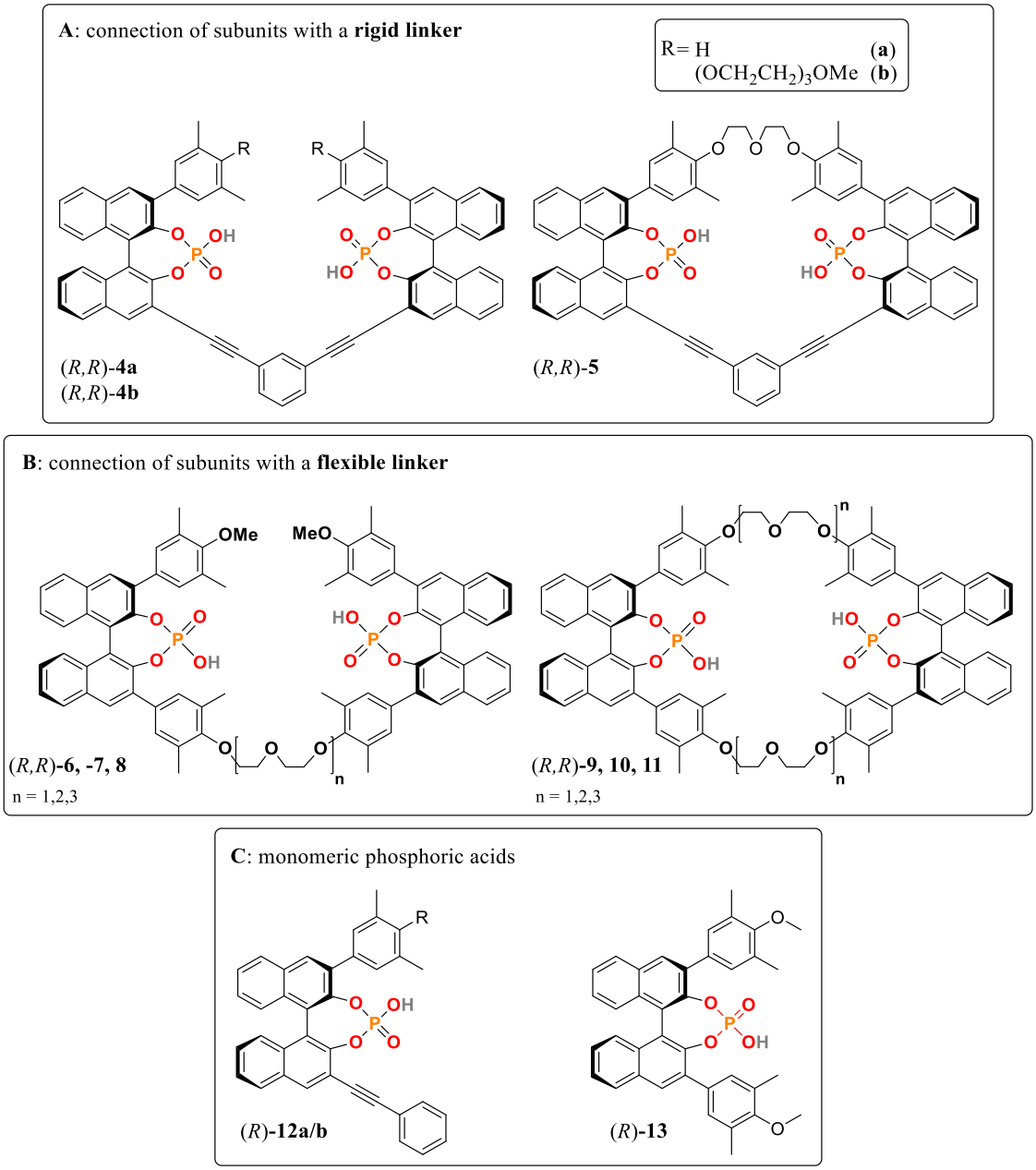


Figure 51: Overview of the twelve monomeric- and bis-phosphoric acids.

5.4.1. Synthesis of the Main Building Block

In this part of the chapter, the basis for further syntheses for the preparation of the bisphosphoric acids is presented by illustrating the synthesis of the building block (*R*)-**70a/c/e**. The group of *Niemeyer* reported on the synthesis of the monoiodide (*R*)-**72** and on the diiodide (*R*)-**73** as essential building blocks in the synthesis of the [2]catenane **61**[93] and of the rigid bis-phosphoric acid **48e.**[101] However, these protocols were not applicable for the unsymmetric functionalization of the 3,3'-positions, so that a new route towards unsymmetrically 3,3´-disubstited BINOL-derivatives had to be developed. The final synthesis has been applied to all different key building blocks (*R*)-**70a/c/e** (see Figure 52). In the following, three possible strategies to obtain the key building block (*R*)-**70a/c/e** are shown (see Figure 53). The search for the most suitable synthesis route towards asymmetric 3,3´-disubstited BINOL-derivatives was only pursued for compound (*R*)-**70a**.

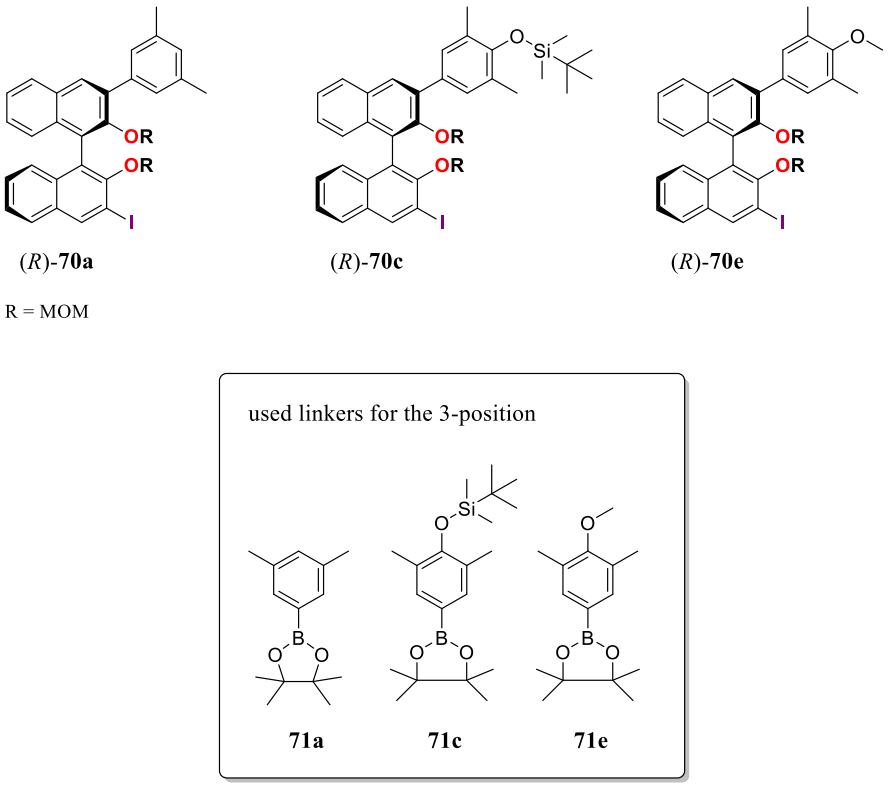


Figure 52: Used key building blocks (*R*)-**70a-c** with its corresponding linkers **71a-e**.[102,103]

[101] F. Octa-Smolin, M. Thiele, Rohan Yadav, A. Platzek, G. Clever, J. Niemeyer, *Org. Lett*. **2018**, *20*, 6153-6156.
[102] R. Rausch, D. Schmidt, D. Bialas, I. Krummenacher, H. Braunschweig, F. Würthner, *Chem. Eur. J.* **2018**, *24*, 3420 – 3424.
[103] N. Pairault, H. Zhu, D. Jansen, A. Huber, C. G. Daniliuc, S. Grimme, J. Niemeyer, *Angew. Chem. Int. Ed*., **2020**, *59*,5102 –5107.

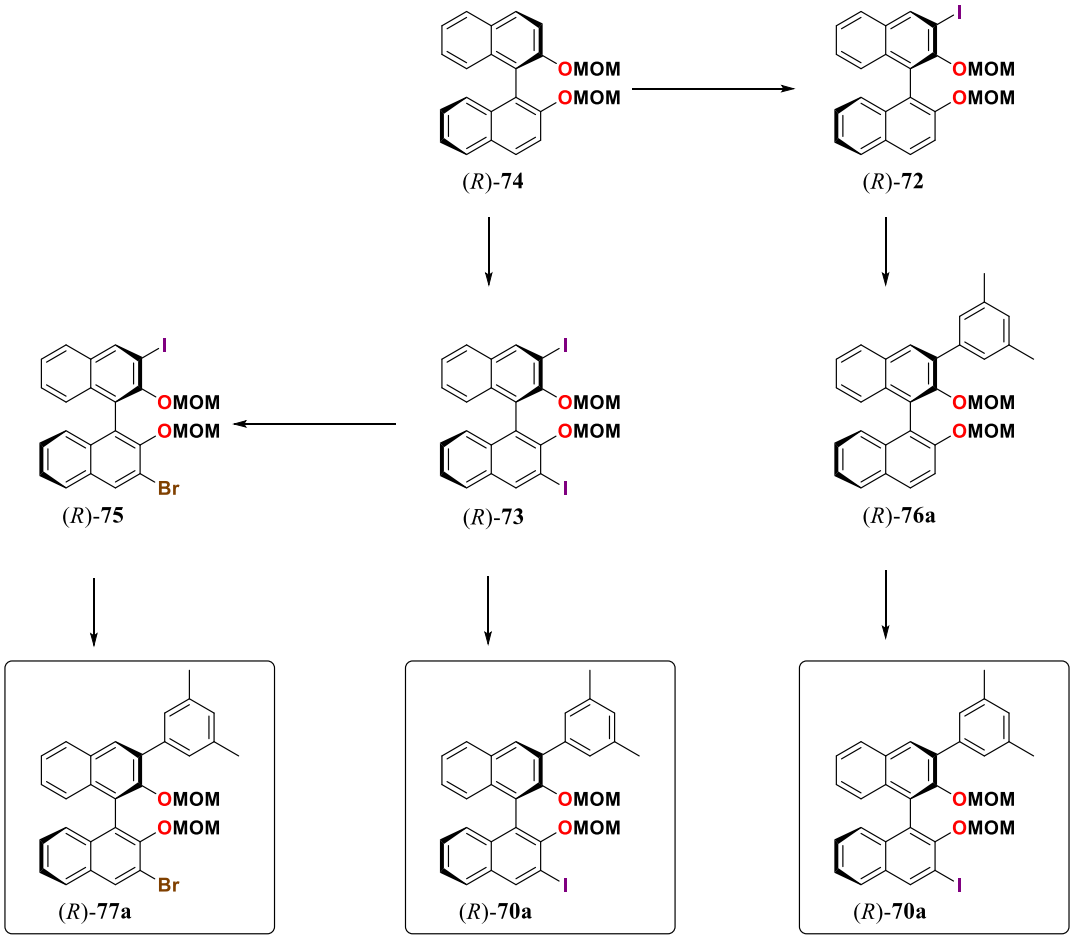


Figure 53: Three possible synthetic routes to key compound (*R*)-**77a/70a**.

Firstly, the BINOL-derivative (*R*)-**74** was transformed into either the monoiodide (*R*)-**72** or the diiodide (*R*)-**73** by established protocols.[104] First, the diiodide (*R*)-**73** was reacted according to *Suzuki* in a metal mediated cross-coupling reaction[105] with 3,5-dimethylphenyl boronic acid ester **71a** (1.15 eq), but this reaction not only gave the desired product (*R*)-**70a**, but the reaction mixture contained also the disubstituted compound and starting material. All these compounds are very similar in terms of polarity, which made a separation via column chromatography challenging. Recrystallization was tried, but failed. Therefore, another attempt towards asymmetric 3,3´-disubstited BINOL-derivatives was pursued, also using diiodide (*R*)-**73** as a starting point. In this attempt one iodine was to be substituted against bromine, still having the possibility to react it in metal-mediated cross-coupling reactions. But the advantage is the different reactivity of the carbon-halogen bonds towards the oxidative addition step, allowing only one product to form. At first the diiodide (*R*)-**73** was reacted with *n*-butyl lithium to form a lithiated intermediate by halogen-lithium-exchange. This was followed by the addition of

[104] a) Y. Li, Q. Li, *Org. Lett.* **2012**, *14*, 4362-4365, b) N. Lv, M. Xie, W. Gu, H. Ruan, S. Qiu, C. Zhou, Z. Cui, *Org. Lett.*, **2013**, *15*, 2382-2385; c) D. Cai, D. L. Hughes, T. R. Verhoeven and P. J. Reider, *Org. Synth.* **1999**, *76*, 1; d) T. R. Wu, L. Shen, J. M. Chong, *Org. Lett.* **2004**, *6*, 2701-2704.
[105] N. Miyaura, T. Yanagi, A. Suzuki, *Synth. Commun*. **1981**, *11*, 513-519.

bromine, which should give the asymmetrically halogenated BINOL-derivative (*R*)-**75**. Unfortunately, also this attempt failed as there are too many side-products that are formed. In addition to the product (*R*)-**75**, the monoiodide (*R*)-**73** and MOM-BINOL (*R*)-**74** were also observed. At last, the monoiodide (*R*)-**72** was chosen as a starting point reacting it in a *Suzuki* coupling reaction to give the *Suzuki*-product (*R*)-**76a** in a good yield of 88%. The product was identified by ^{1}H-NMR spectroscopy through the additional singlet for the methyl group of the newly introduced substituent at 2.34 ppm. This was followed by a second iodination. This time, the starting material was dissolved in diethyl ether and *n*-butyl lithium was added at 0°C, after stirring for 30 minutes, iodine was added in tetrahydrofuran. The reaction was stopped after 10 additional minutes of stirring by the addition of a solution of sodium sulfite. The key building block (*R*)-**70a** was successfully isolated by column chromatography in 81% yield. Formation of the product was shown in the ^{1}H NMR spectrum by occurrence of a new singlet, which is distinctive for the hydrogen atom adjacent to the iodine at 8.53 ppm.

With the sequential protocol for functionalization of the 3,3´-positions in hand, compounds (*R*)-**75c/e** were also synthesized. Therefore, the monoidodide (*R*)-**72** was dissolved in a degassed solution of toluene and water (1:5) alongside with the boronic acid ester **70c** and **70e,** respectively, tetrabutylammonium hydroxide 30-hydrate, tris(dibenzylideneacetone)dipalladium(0) and tri(*o*-tolyl)phosphine to give the crude products. After column chromatography the corresponding products (*R*)-**78c/e** were obtained in good yields of 76% and 86%. This was followed by a second iodination step analogously to the procedure of (*R*)-**70a**. The products (*R*)-**70c/e** were obtained in 82% and 66% yield. Formation of the products was proven by ^{1}H NMR spectroscopy, based on the new singlet from the hydrogen atom adjacent to the iodine at 8.71 ppm and 8.72 ppm.
For compounds (*R*)-**76a** and (*R*)-**70a** , single crystals suitable for X-ray diffraction were by slow evaporation of a solution in cyclohexane and methanol (see Figure 54).

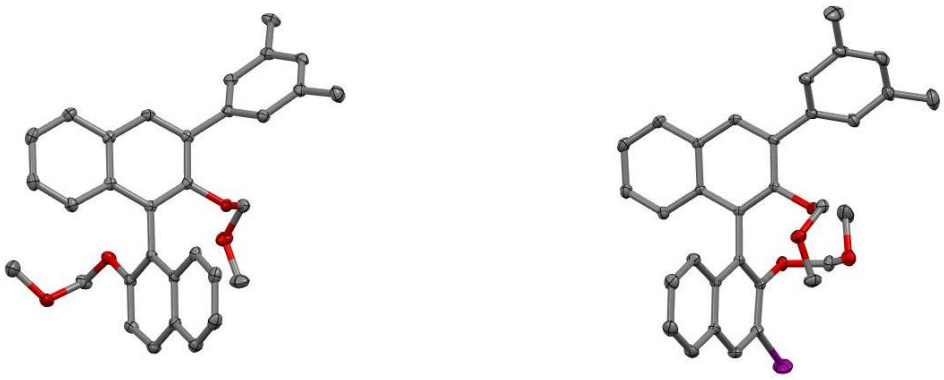


Figure 54: X-Ray crystal structures of (*R*)-**76a** and (*R*)-**70a**, Hydrogen atoms omitted for clarity and thermal ellipsoids set at the 50% probability level.

5.4.2. Synthesis of Rigidly Linked Bis-Phosphoric Acids

In this chapter the synthesis of the bis-phosphoric acids (*R*,*R*)-**4a/b** and (*R*,*R*)-**5** is described. In order to show the whole synthetic sequence, Figure 55 also shows the synthesis of the key intermediates (*R*)-**70a/c** (*vide supra*).

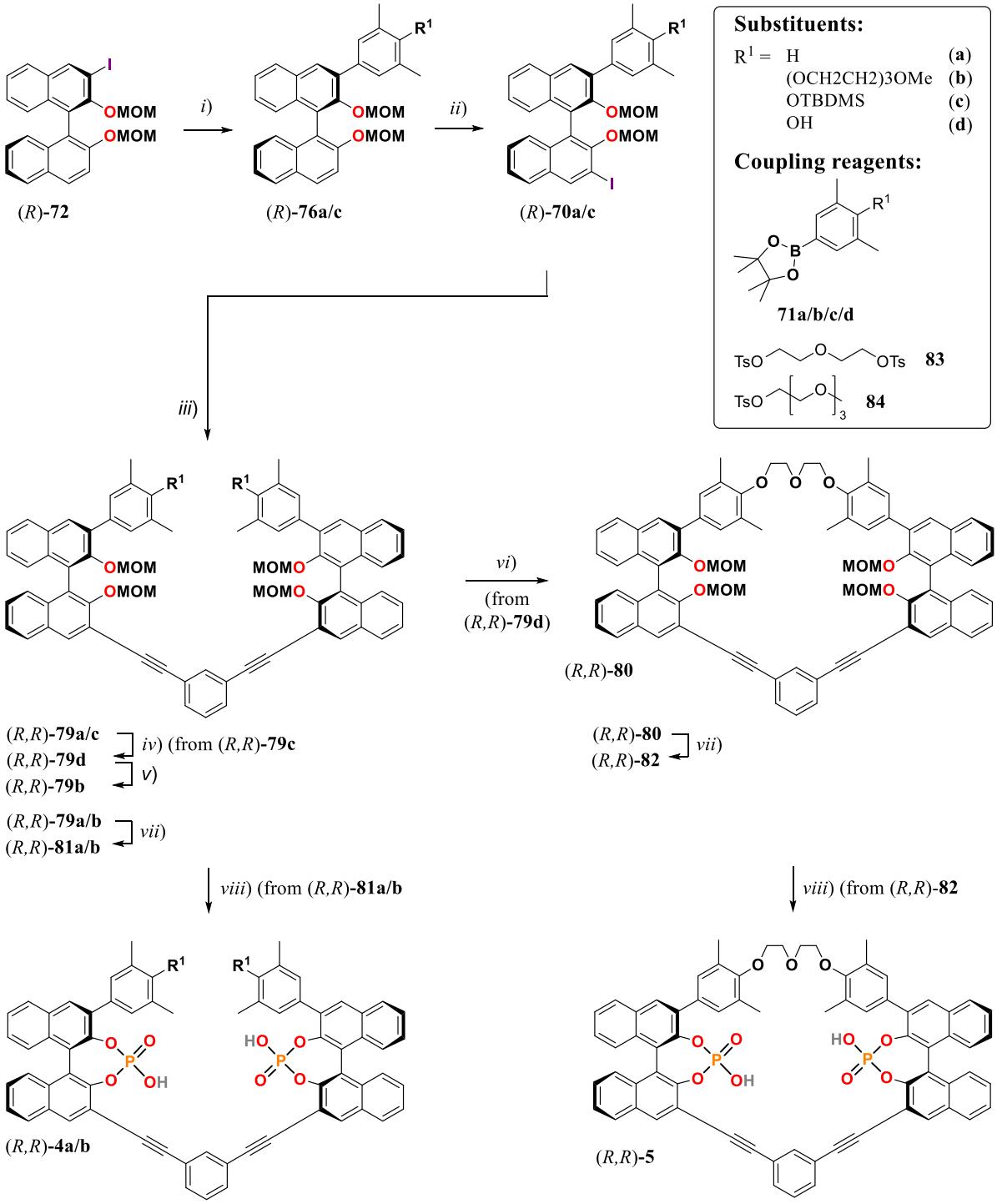


Figure 55: Synthesis of the bis-phosphoric acid catalysts (*R*,*R*)-**4a/b** and (*R*,*R*)-**5**. Reagents and conditions: *i*) arylboronic acid ester **71a/c**, $Pd(PPh_3)_4$, DME/Na_2CO_3 (aq), 90 °C, 88%/76% (for (*R*)-**76a/c**) *ii*) ^{n}BuLi, I_2, Et_2O/THF, 0 °C to r.t., 70%/82% (for (*R*)-**70a/c**), *iii*) 1,3-diethynylbenzene or ethynylbenzene, $Pd(PPh_3)_4$,CuI, CH_3CN/Et_3N, 80 °C, 91%/92% (for (*R*,*R*)-**79a/c**, *iv*) TBAF, THF, r.t., 97% (for (*R*,*R*)-**79d**, *v*) $Ts(OCH_2CH_2)_3OMe$, Cs_2CO_3, CH_3CN, 90 °C, 87%(for (*R*,*R*)-**79b**, *vi*) $Ts(OCH_2CH_2OCH_2CH_2)OTs$) 70% (for (*R*,*R*)-**80**), *vii*) TMSBr, CH_2Cl_2, r.t. 93/94/95%(for (*R*,*R*)-**81a/b**, (*R*,*R*)-**82**), *viii*) $POCl_3$, pyridine, 65 °C, 32/71/55% (for (*R*,*R*)-**4a/b**, (*R*,*R*)-**5**.

The monoiodides (*R*)-**70a/c** were reacted in a *Sonogashira* coupling reaction with 1,3-diethynylbenzene and palladium-tetrakis(triphenylphosphine) and copper iodide in a degassed solution of acetonitrile and triethyl amine (1:1). Full conversion was confirmed by TLC and the crude product was purified by column chromatography. The structures were confirmed by NMR spectroscopy. For example, proton signals at 7.79, 7.57 and 7.39 ppm for (*R,R*)-**79a** and 7.84, 7.69 and 7.57 ppm for (*R,R*)-**79c** could be observed for the new aromatic systems. Furthermore, the characteristic carbon signals for ethinyl-units were observed in the ^{13}C NMR (for (*R,R*)-**79a** at 92.81 and 87.62 ppm, for (*R,R*)-**79c** at 92.20 and 87.45 ppm). The silyl protected species (*R,R*)-**79c** was dissolved in tetrahydrofuran and deprotected by addition of a solution of 1 M tetra-*n*-butylammonium fluoride in tetrahydrofuran to give the product (*R,R*)-**79d**. Thereafter, the bis-BINOL-derivative (*R,R*)-**79d** was reacted with the tosylate **84**[106] in the presence of caesium carbonate to yield the triethyleneglycol-substituted compound (*R,R*)-**81b**. On the other hand (*R,R*)-**79d** was also used as a starting material for the synthesis of the macrocyclic molecule (*R,R*)-**80**. To successfully synthesize both molecules (*R,R*)-**79b** and (*R,R*)-**80** the concentration of the reaction has to be precisely adjusted to avoid product mixtures as the products are very difficult to separate by column chromatography or recrystallization. To obtain the acyclic molecule (*R,R*)-**79b,** it was prepared a concentrated solution of (*R,R*)-**79d** in acetonitrile (45.8 mM). After the addition of caesium carbonate and stirring of 15 minutes, the tosylate **84** was added in acetonitrile (100 mM) to give the product in 87% yield. In comparison, to obtain (*R,R*)-**80**, a rather diluted solution of (*R,R*)-**79d** in acetonitrile (0.381 mM) had to be prepared. As before, caesium carbonate was added, the mixture was stirred for 15 minutes and then the bistosylate **83** in acetonitrile (6.31 mM) was added. Both products were identified by ^{1}H-NMR spectra showing new proton signals for the ethyleneglycol chain in the range of 3.95 -3.43 ppm. The removal of the MOM-protecting groups turned out to be very challenging, at least for compounds (*R,R*)-**79b** and (*R,R*)-**80**. While alcohol (*R,R*)-**81a** was accessible using standard conditions by reacting (*R,R*)-**79a** with the Lewis acid bromotrimethylsilane in dichloromethane, the alcohols (*R,R*)-**81b** and (*R,R*)-**82** could not be obtained using this protocol due to the formation of many by-products. For this purpose, a new deprotection protocol was developed. Thus, the starting materials (*R,R*)-**79b** and (*R,R*)-**80** were suspended in a mixture of ethanol and diethyl ether (5:3, each) and then acetyl chloride was added to give the products (*R,R*)-**81b** and (*R,R*)-**82**. The main advantage of this route is that no side products are formed in the reaction and thus, purification by column chromatography was not necessary. For further deprotections, the new protocol was applied as the reaction is easy to perform and pure products

[106] D. B. Mohler, G. Shen, *Org. Biomol. Chem*., **2006**, *4*, 2082–2087.

are obtained. The successful deprotection was shown in the ^{1}H-NMR, where resonances for the hydroxyl groups are now observed at 8.97 ppm and at 8.21 ppm (for (*R*,*R*)-**81a**) or at 8.97 ppm and 8.20 ppm (for (*R*,*R*)-**81b**), respectively (for (*R*,*R*)-**82** the signal for the hydroxyl group is too broad). Finally, the synthesis is completed with the phosphorylation of the alcohols. Therefore, the starting materials were, each, dissolved in pyridine, and phosphoryl chloride was added. After stirring for 18 hours at 65°C, the crude products were purified by washing with a solution of 2 M of hydrochloric acid. The products were identified by NMR-spectroscopy. Firstly, the introduction of the phosphoric acid moieties was examined by ^{31}P-NMR. The signals at 1.18/1.09/1.98 ppm (for (*R*,*R*)-**4a**/(*R*,*R*)-**4b**/(*R*,*R*)-**5**) confirm a successful introduction of the phosphoric acid functionality. Additionally, successful introduction of the phosphoric acid moiety was shown by ^{13}C-NMR from the carbon-phosphorus coupling seen in the resonances for C-2 and C-12, with coupling constants in the range of 9.5 - 9.7 Hz, Finally, the structures were confirmed by mass spectra. In the following the ^{1}H-NMR spectra of compounds (*R*,*R*)-**4a/b**, and (*R*,*R*)-**5** are shown.

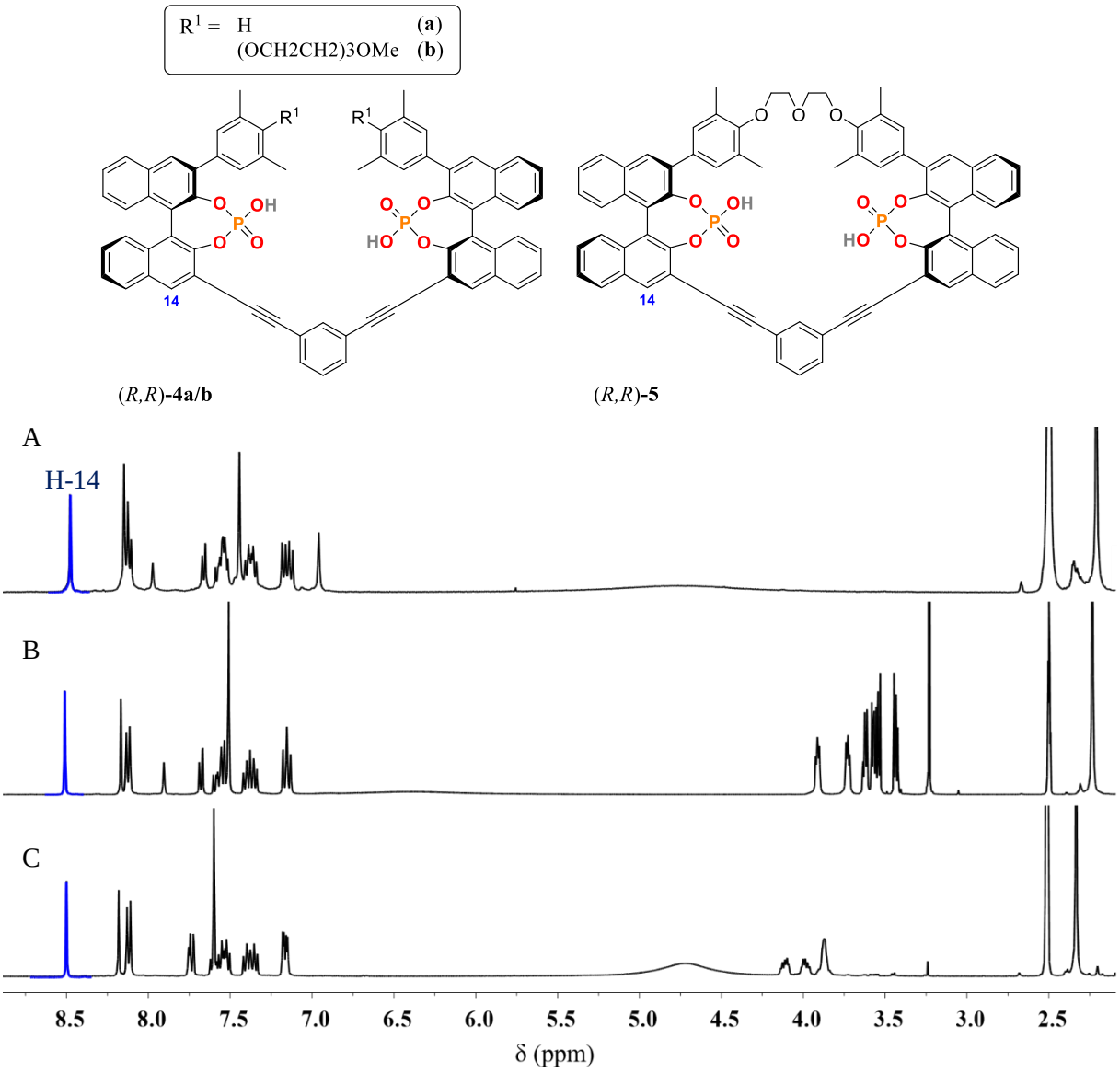


Figure 56: ^{1}H-NMR spectra of A: (*R*,*R*)-**4a**, B: (*R*,*R*)-**4b** and C: (*R*,*R*)-**5** [d_6-DMSO, 400 MHz, 298 K].

For all three phosphoric acids, proton 14 shows the most pronounced downfield shift (marked in blue). While the other signals of the aromatic protons of all three compounds show similar chemical shifts, the difference in the ^{31}P NMR is clearly pronounced.

5.4.3. Synthesis of flexibly linked bis-phosphoric acids

In this chapter the synthesis of molecules (*R,R*)-**6, -7**, **-8** and (*R,R*)-**9, -10**, **-11** is described.

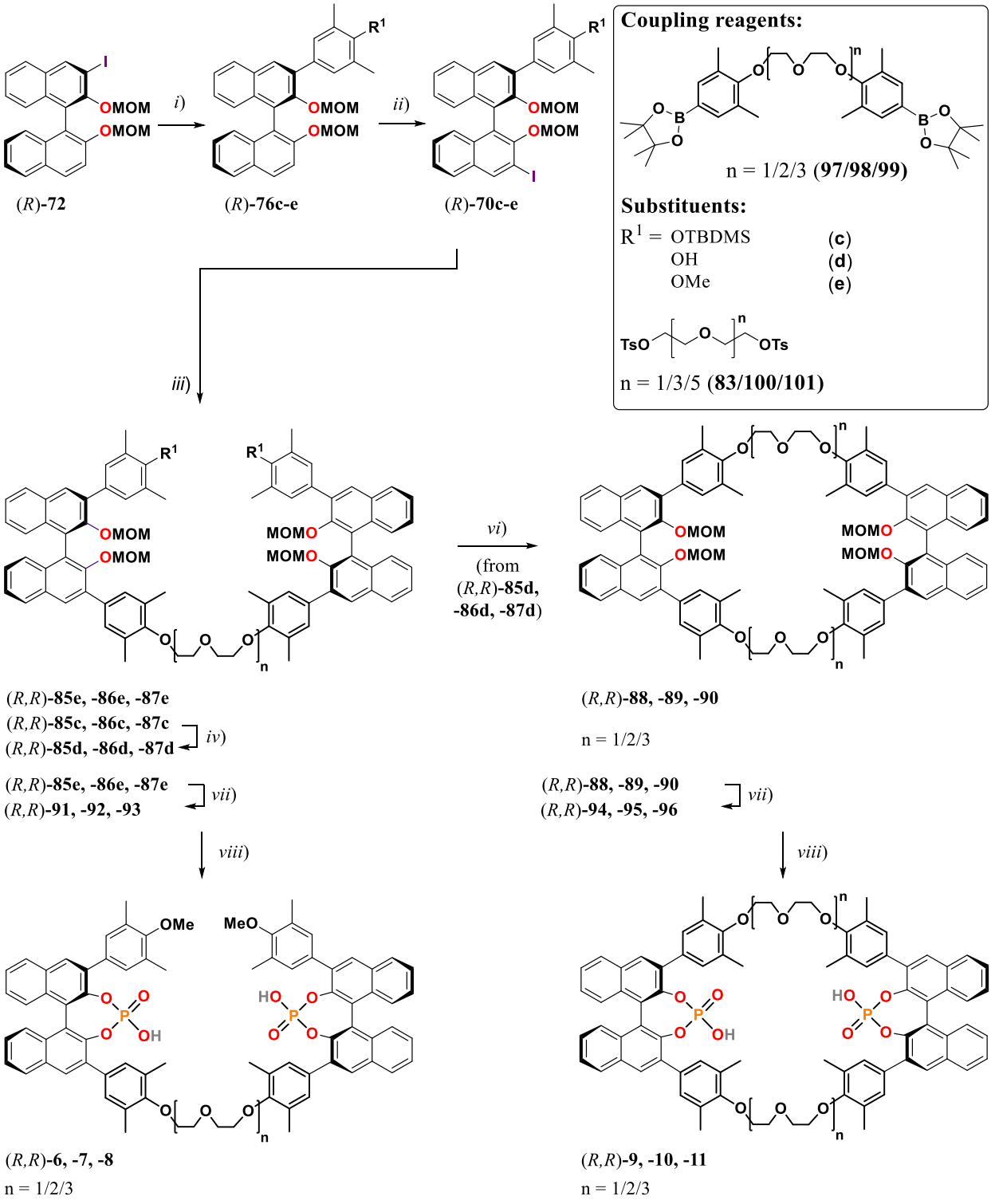


Figure 57: Synthesis of the bisphosphoric acid catalysts (*R,R*)-**6, -7, -8 and** (*R,R*)-**9, -10, -11**. Reagents and conditions: *i*) arylboronic ester **71c**/**e**, $PdPd_2(dba)_3$, $^nBuN_4^+OH^-$, P(*o*-tol)$_3$, toluene/H_2O, 90 °C, 88/76/86%, *ii*) ^{n}BuLi, I_2, Et_2O/THF, 0 °C to r.t., 82/66/82%, *iii*) linked diarylboronic ester **97-99**, $Pd_2(dba)_3$, $^nBuN_4^+OH^-$, P(*o*-tol)$_3$, toluene/H_2O, 90 °C, 51/53/51% (for (*R,R*)- **85e, -86e, -87e**) and 59/40/59% ((*R,R*)- **85c, -86c, -87c**); *iv*) TBAF, THF, r.t., 91/91/98% (for (*R,R*)- **85d, 86d, 87d**), *vi*) $TsO(CH_2OCH_2)_nOTs$ **83**, **100-101**, Cs_2CO_3, CH_3CN, 90 °C, 44/84/49% (for (*R,R*)- **88, -89, -90**); *vii*) AcCl, EtOH/Et_2O, r.t., 95/84/91% (for (*R,R*)- **91, 92, 93**) and 83/87/63% (for (*R,R*)- **94, 95, 96**), *viii*) $POCl_3$, pyridine, 65 °C, 79/69/69/73/74/78% (for (*R,R*)-**6, -7, -8** and (*R,R*)- **9, -10, -11**).

The synthesis begins by reacting the monoiodide (*R*)-**70e** to (*R,R*)-**85e**, -**86e** and -**87e** according *Suzuki*. Therefore, the monoidodide (*R*)-**70c/e** was dissolved in a degassed solution of toluene and water (1:5), followed by the addition of the corresponding bisboronic ester **97**-**99**, tetrabutylammonium hydroxide 30-hydrate, tris(dibenzylideneacetone)dipalladium(0) and tri(*o*-tolyl)phosphine. During this reaction many side products are formed. There are impurities of decomposed starting material and also small amounts of remaining starting materials. Thus, it is important to adjust the equivalents and the concentration precisely as too much solvent leads to singly linked compounds and less solvent to decomposition of starting materials. The most suitable reaction conditions are as follows: 2.1 equivalents of the monoiodide (*R*)-**70e**, 1.0 equivalents of the boronic acid ester **97**-**99** and 1.15 equivalents of tetrabutylammoniumhydroxide 30-hydrate, 0.05 equivalents of tris(dibenzylideneacetone)dipalladium(0) (eq) and 0.12 equivalents of tri(o-tolyl)phosphine in a mixture of toluene and water (1:5) at a concentration of 3 mM (for the BINOL-derivative). The progress of the reaction is followed by TLC and terminated when the starting material is fully consumed. After column chromatography the *Suzuki* products are obtained in yield of 51%, 53% and 51%, respectively. The products were identified by ^{1}H-NMR spectroscopy, by resonances for the ethylene glycol chain in the range of 4.0 ppm to 3.4 ppm. In the next step, the MOM-protecting groups are removed by reacting (*R,R*)-**85e**, -**86e** and -**87e** in diethyl ether (5:3) with acetyl chloride. Formation of the products was shown in the ^{1}H NMR spectrum by occurrence of a singlet for the protons of the hydroxyl groups at 8.16 ppm, 8.15 ppm and 8.15 ppm. Since the molecule is substituted unsymmetrically in the in the 3,3'-position, two signals were expected for the hydroxyl groups, but only one signal with an integral of 4 was observed. This is attributed to the similarity of the substituents in the 3,3'-position. The alcohols (*R,R*)-**91**, -**92** and -**93** are then dissolved in pyridine and reacted with phosphoryl chloride to give the corresponding bis-phosphoric acids (*R,R*)-**6**, -**7** and -**8** (see Figure 58). The formation of the bis-phosphoric acids was confirmed by a singlet in the ^{31}P-NMR at 1.30 ppm, at 1.06 ppm and at 1.16 ppm, respectively. The formation of the desired products was also confirmed by high resolution mass spectrometry.

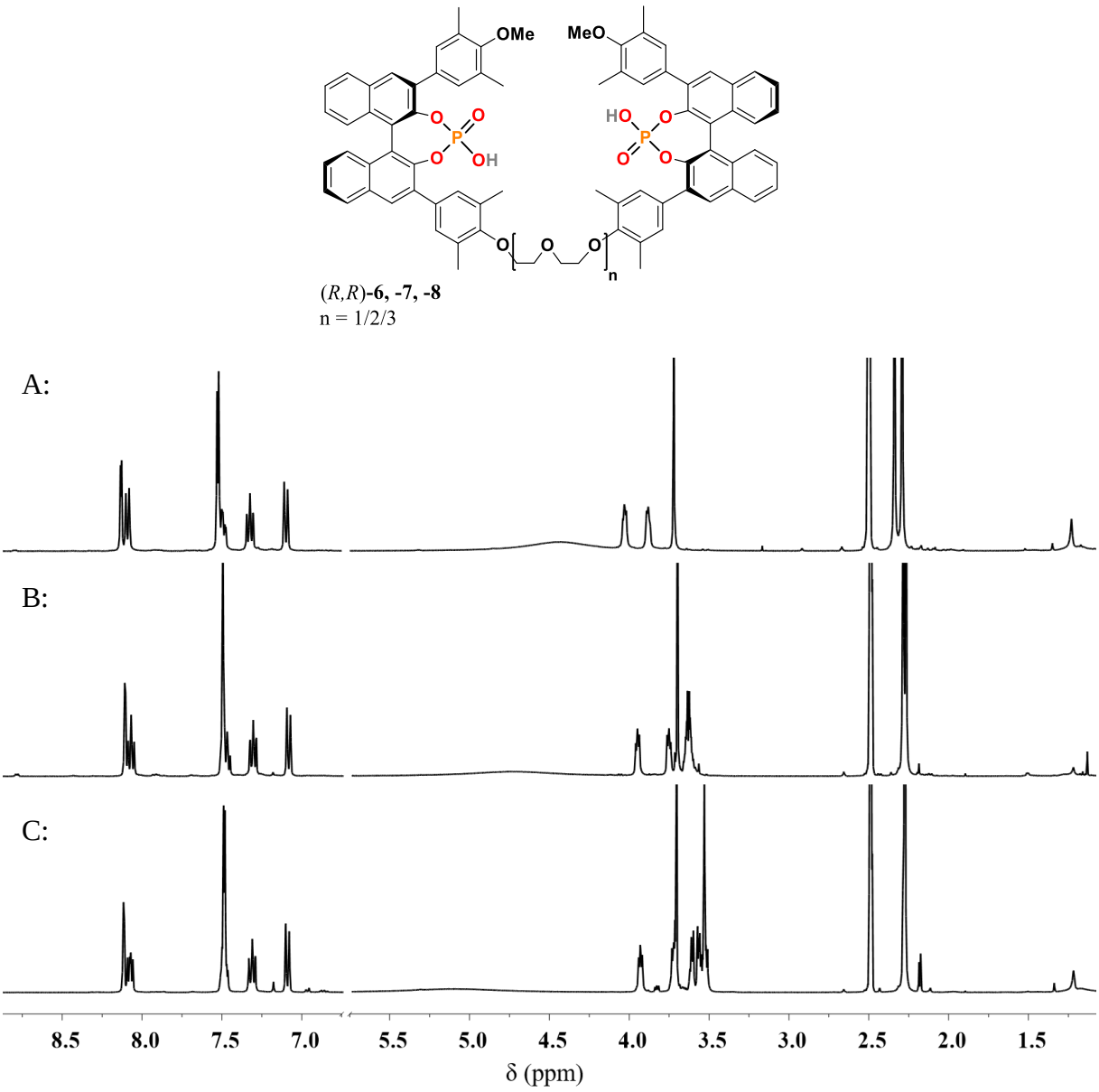


Figure 58: A: ^{1}H-NMR spectra of A: (*R*,*R*)-**6**, B: (*R*,*R*)-**7** and C: (*R*,*R*)-**8** [d_6-DMSO, 400 MHz, 298 K].

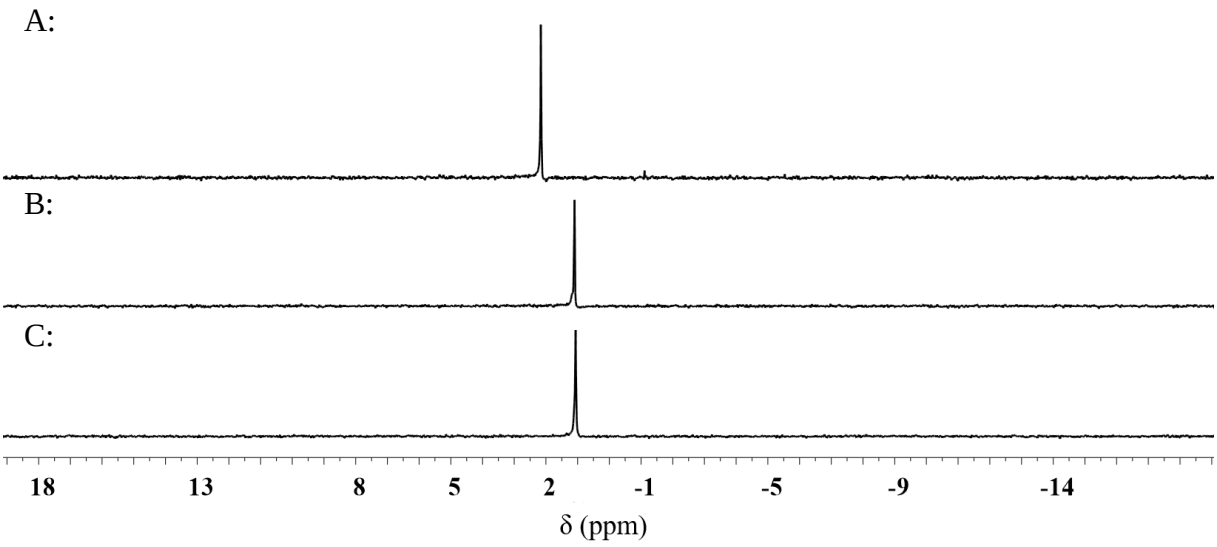


Figure 59: A: ^{31}P-NMR spectra of A: (*R*,*R*)-**6**, B: (*R*,*R*)-**7** and C: (*R*,*R*)-**8** [d_6-DMSO, 162 MHz, 298 K].

The ^{1}H-NMR spectra of the three compounds look very similar, especially the aromatic proton signals. As the ethylene glycol unit in the molecule becomes longer, its proton signals in ^{1}H-NMR are increasingly shifted to higher field. Also similar resonances for the phosphoric acid moiety were found in the ^{31}P NMR spectra of (*R*,*R*)-**6**, -**7** and -**8**.

The synthesis of the macrocyclic systems begins with the TBDMS-protected monoiodide (*R*)-**70c**, reacting it in a *Suzuki* type of reaction to give (*R*,*R*)-**85c**, -**86c** and -**87c**. According to the findings on synthesising the acyclic compounds, the optimized conditions were used. After column chromatography the products were obtained in yields of 59%, 40% and 59%, respectively. The products were identified by ^{1}H-NMR spectroscopy, by resonances for the ethylene glycol chain in the range of 4.0 ppm to 3.4 ppm. The removal of the silyl protecting groups was achieved by the use of tetra-*n*-butylammonium fluoride as a fluoride source. In the ^{1}H-NMR a singlet for the proton of the hydroxyl group was found (8.38 ppm, 8.38 ppm and 8.38 ppm for (*R*,*R*)-**85d**, **-86d** and **-87d**). Thereafter, the macrocycles (*R*,*R*)-**88**, -**89** and -**90** are synthesised in a twofold S_N2 reaction using the bistosylates **83**, **100** and **101** as reagents. To generate the macrocyclic structures, it is necessary to work in very dilute solution, otherwise two linker molecules are bound to the starting material. For this purpose, a solution of (*R*,*R*)-**85d**, **-86d** and **-87d** in acetonitrile (0.38 mM) was prepared, after the addition of caesium carbonate and stirring for 15 minutes the reaction mixture turned yellow due to deprotonation. The tosylates **83**, **100**-**101** (100 mM), were then dissolved in ACN and added portionwise. After complete conversion the crude product was purified by column chromatography. After obtaining the macrocycles (*R*,*R*)-**88**, **-89** and **-90**, a simplified data set corresponding to a symmetrical BINOL-backbone is observed. The removal of the MOM-protecting groups is achieved by reacting (*R*,*R*)-**88**, **-89** and **-90** in diethyl ether (5:3) with acetyl chloride. Formation of the products was shown in the ^{1}H NMR spectrum by occurrence of a singlet for the protons of the hydroxyl groups at 8.15/8.09/8.10 ppm (for (*R*,*R*)-**94**/**95**/**96**). Finally, the phosphoric acid functionality was installed. Therefore, the alcohols (*R*,*R*)-**94**, **-95** and **-96** are reacted with phosphoryl chloride in pyridine giving the corresponding bis-phosphoric acids (*R*,*R*)-**9**, -**10** and -**11**. The formation of the bis-phosphoric acids was confirmed by a singlet in the ^{31}P-NMR at 2.16 ppm, at 0.94 ppm and at 1.29 ppm, respectively (see . Furthermore, with the mass spectra proved the successful synthesis of (*R*,*R*)-**9**, -**10** and -**11**. The corresponding 1H-NMR spectra of bis-phosphoric acids (*R*,*R*)-**9**, -**10** and -**11** is shown in Figure 60.

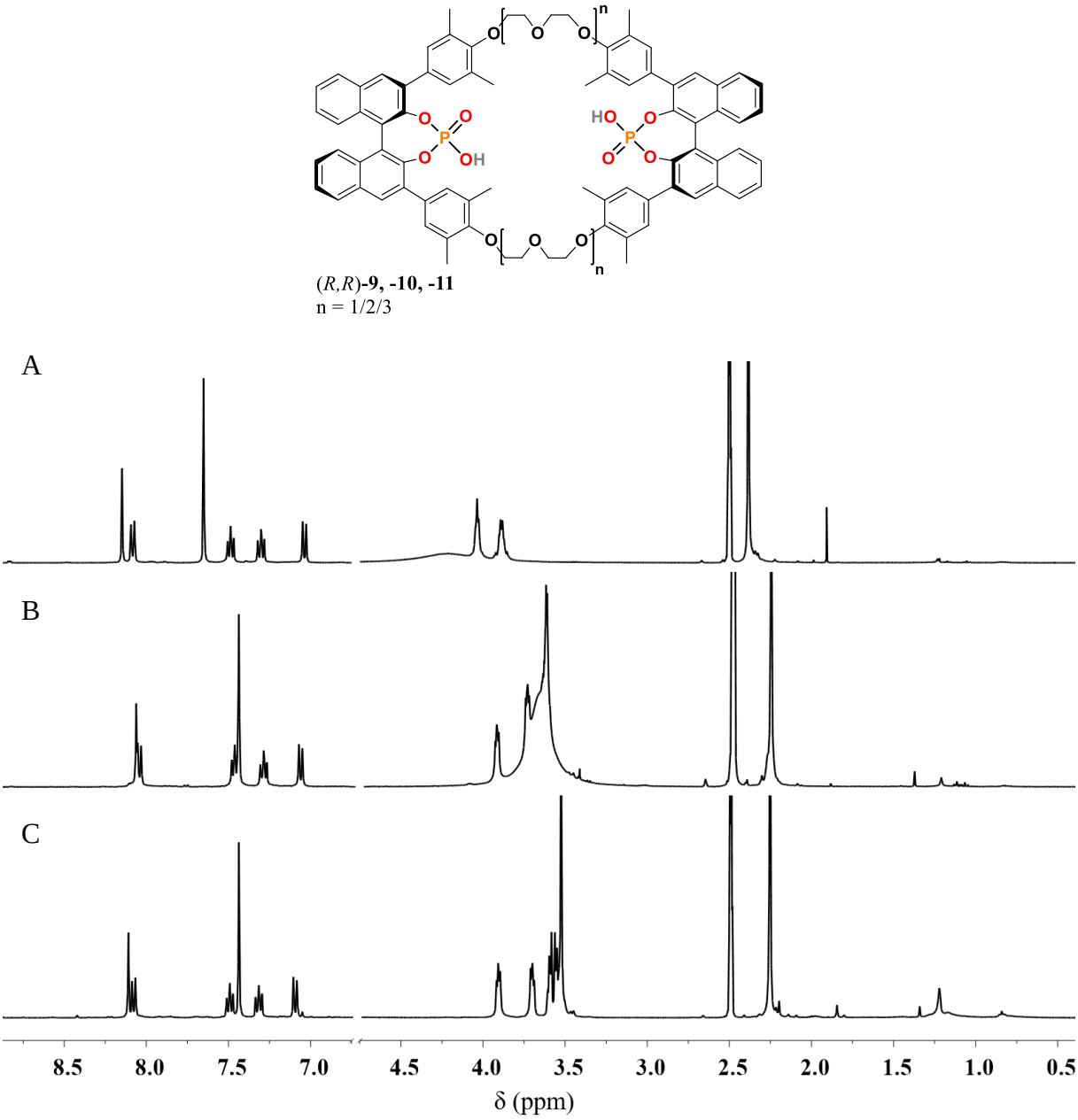


Figure 60: A: ^{1}H-NMR spectra of A: (*R*,*R*)-**9**, B: (*R*,*R*)-**10** and C: (*R*,*R*)-**11** [d_6-DMSO, 400 MHz, 298 K].

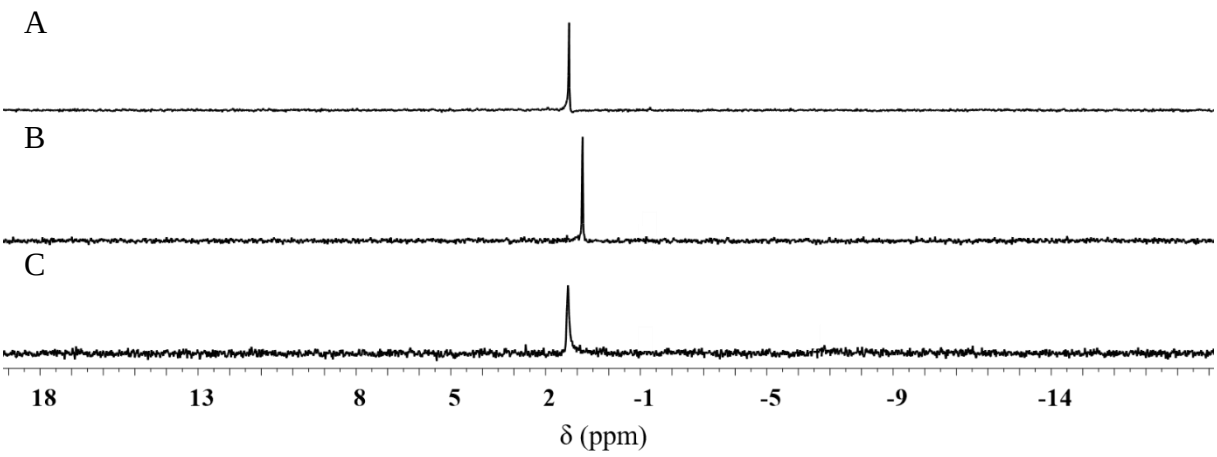


Figure 61: A: ^{31}P-NMR spectra of A: (*R*,*R*)-**9**, B: (*R*,*R*)-**10** and C: (*R*,*R*)-**11** [d_6-DMSO, 162 MHz, 298 K].

The ^{1}H-NMR spectra of the three macrocycles are very similar. Especially in the aromatic region, the proton signals show almost identical chemical shifts. A small difference becomes apparent when looking at the chemical shift of the proton signals of the ethylene glycol units. Similar chemical shifts were also observed in the ^{31}P-NMR for bis-phosphoric acids (*R*,*R*)-**9**, -**10** and -**11**.

5.4.4. Synthesis of reference catalysts

As reference catalysts, we also synthesized the monophosphoric acids (*R*)-**12a/b** and (*R*)-**13** (see Figure 62) via analogous synthetic routes

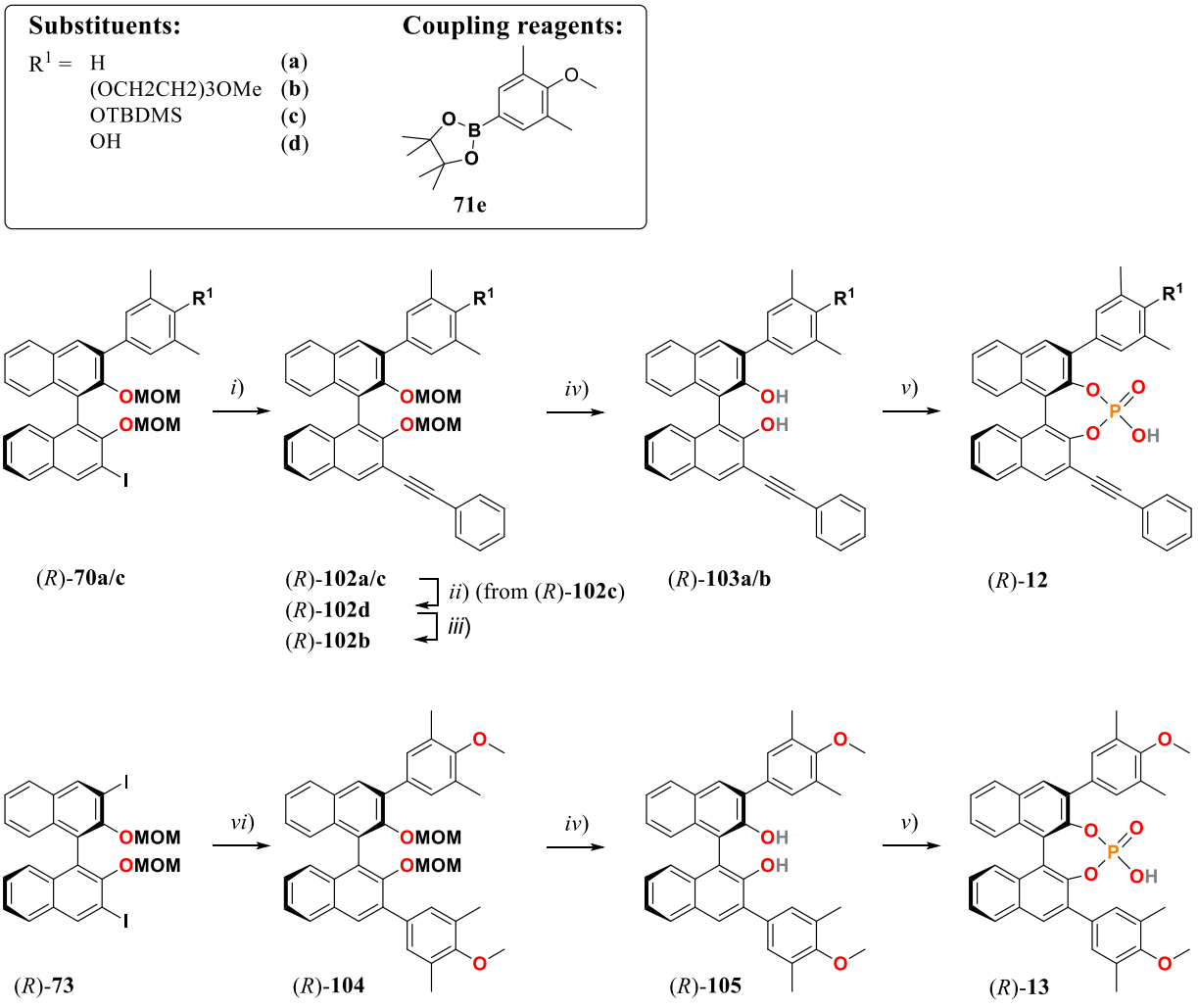


Figure 62: Synthesis of the reference catalysts (*R*)-**12a/b** and (*R*)-**13**. Reagents and conditions: *i*) phenylacetylene, $Pd(PPh_3)_4$, CuI, CH_3CN/Et_3N, 80 °C, 94%/74% (for (*R*)-**102a/c**), *ii*) TBAF, THF, r.t., 95% for (*R*)-**102d**, *iii*) $Ts(OCH_2CH_2)_3OMe$, Cs_2CO_3, CH_3CN, 90 °C, 98% for (*R*)-**102b**, *iv*) TMSBr, CH_2Cl_2, r.t., 80% (for (*R*)-**103a**) or AcCl, $EtOH/Et_2O$, r.t., 84%/94%% (for (*R*)-**103b**/-**105**); *v*) $POCl_3$, pyridine, 65 °C, 89%/69%/77% (for (*R*)-**12a**/**12b**/**13**); *vi*) $Pd_2(dba)_3$, $^{n}BuN_4^{+}OH^{-}$, P(*o*-tol)$_3$, toluene/H_2O, 90 °C, 85%.

In the following the ^{1}H-NMR-spectra of the monomeric reference catalysts are shown.

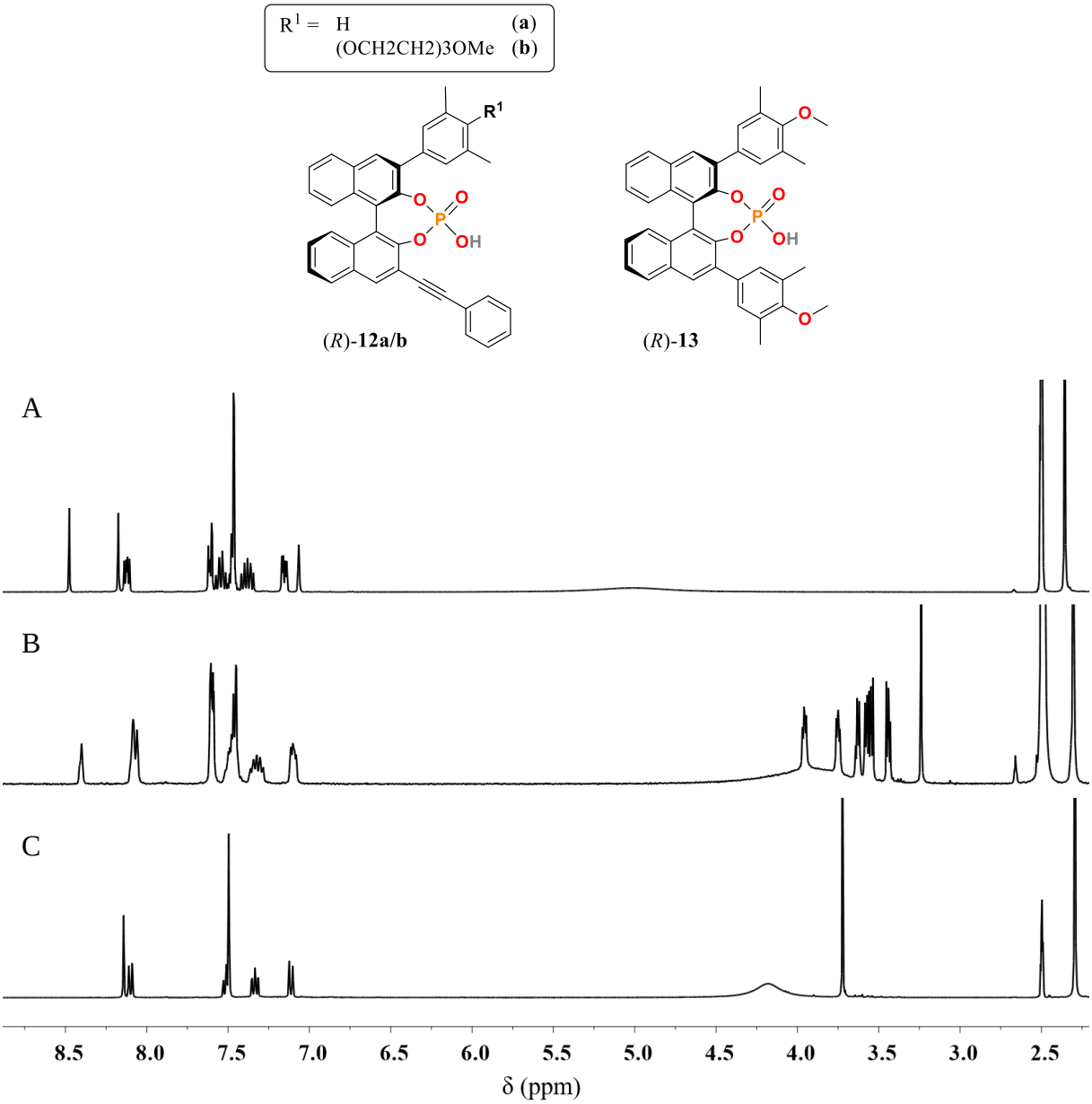


Figure 63: A: ^{1}H-NMR spectra of A: (*R*)-**12a**, B: (*R*)-**12b** and C: (*R*,*R*)-**13** [d_6-DMSO, 400 MHz, 298 K].

5.4.5. Synthesis of naphtalenes for dearomative fluorination

The naphtalenes **109a-d** have been synthesized according to literature procedures.[100] These substrates were chosen to evaluate the substrate scope in catalysis and thus investigating steric and electronic influences of the substituent on catalysis.

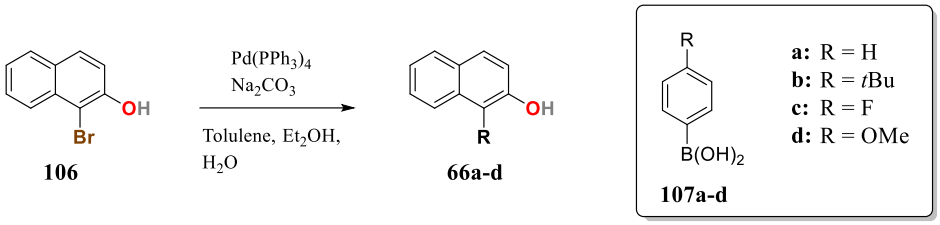


Figure 64: Synthesis of naphtalene derivatives **66a-d**.

Starting with commercially available 1-bromo-2-naphthol **106** substrates **66a-d** have been synthesized. Therefore, 1-bromo-2-naphthol, was reacted with the corresponding boronic acid **107a-d** and with tetrakis(triphenylphosphine)palladium(0) and sodium carbonate in a degassed solution of toluene (7 ml), ethanol (2 ml) and water (2 ml). The crude products were purified by column chromatography. The products **66a-d** were identified by ^{1}H-NMR spectroscopy. New signals for the phenyl substituent were observed for **66a**. In the ^{1}H-NMR spectrum of **66b** a new signal for the *tert*-butyl substituent was found at 1.32 ppm. Product **66c** was identified by ^{19}F-NMR by a fluorine signal at -113.06 ppm. The proton signal of the methyl group from the methoxy moiety of **66d** was found at 3.82 ppm in the ^{1}H-NMR spectrum.

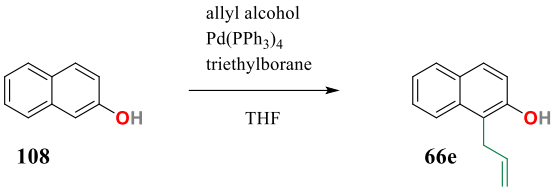


Figure 65: Synthesis of substrate **66e**.

Recently, it was found that the allylation of benzene polyols and naphtols can be pursued by the combinational use of catalytic amounts of palladium(0) species and triethylborane. The substrate **109e** was synthesized by reacting 2-naphtol with allyl alcohol, triethylborane and tetrakis(triphenylphosphine)palladium(0) in tetrahydrofuran for 24 hours.[107] The product **66e** was obtained after column chromatography in relatively poor yield of 25.1%.

The product was identified by the characteristic signals of the allyl-group at 6.03 ppm, 5.13 – 5.05 ppm and at 3.85 – 3.82 ppm in the ^{1}H-NMR spectrum.

[107] M. Kimura, M.Fukasaka, Y. Tamaru, *Synthesis* **2006**, *21*, 3611–3616.

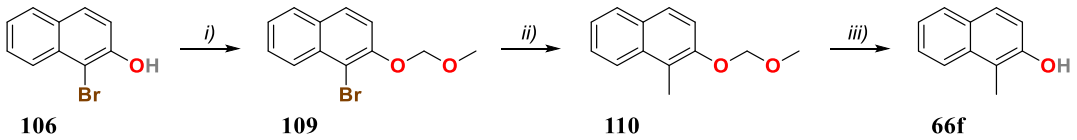


Figure 66: Synthesis of substrate **66f**. Reagents and conditions: *i*) DIPEA, MOM-Cl, DCM, r.t., *ii*) ^{n}BuLi, MeI, THF, 0 °C to r.t., *iii*) conc. HCl, MeOH, r.t.

To synthesize **66f**[108], the OH-group in **106** was protected with a MOM-group under standard conditions. In the ^{1}H-NMR new signals at 5.37 ppm and 3.58 ppm were observed and assigned to the MOM-protecting group. This was followed by methylation of **109** by reacting it with *n* butyllithium and subsequent reaction of the lithiated species with methyliodide. The crude product was purified by column chromatography, but unluckily the pure product could not be obtained. The remaining impurities were assigned to the already deproctected compound **66f.** Therefore, **110** was reacted with concentrated hydrochloric acid in methanol to fully remove the MOM-group to yield **66f** as a pure substance without further purification.

5.5. Transfer Hydrogenation[109]

5.5.1. Transfer Hydrogenation of 2-Phenyl Quinoline

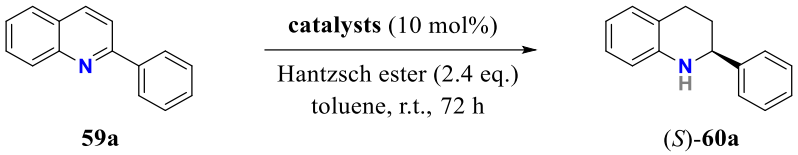
In the past, both the [2]catenane (*S*,*S*)-**61** and the covalently linked bis-phosphoric acid (*R*,*R*)-**48e** have been used successfully in transfer hydrogenation of 2-substituted quinolines (see chapter 5.2). The new library of catalysts (**4**-**12**) was used to answer the following questions:

- Are the stereoselectivities improved by covalently linked bis-phosphoric acids featuring substituents in both the 3- and 3´-positions (as opposed to (*R*,*R*)-**48e** with only one substituent)?
- Can the mechanical bond in (*S*,*S*)-**61** be replaced by a covalent bond for an easier entry towards cooperative bisphosphoric acid catalysts?
- If so, is there a difference between singly linked catalysts compared to doubly linked (macrocyclic) catalysts in catalysis?

An overview of the catalysts employed for the transfer hydrogenation of 2-phenyl quinoline is shown in Figure 51 in chapter 5.4. This encompasses the bisethinylphenyl-linked catalysts

[108] T. Oguma, T. Katsuki, *J. Am. Chem. Soc.* **2012**, *134*, 20017–20020.
[109] This part of the work was developed together with Sophia Stadtfeld, see: Sophia Stadtfeld, *BINOL-basierte Phosphorsäuren in der Organokatalyse - Makrozyklische vs. azyklische Katalysatoren*, Bachelor thesis, University of Duisburg-Essen, 2021.

(*R*,*R*)-**4a/b** and the macrocyclic counterpart (*R*,*R*)-**5**, together with the corresponding reference catalysts (*R*)-**12a/b**. Also, the ethylene glycol linked catalysts were used, both in the singly linked and macroccylic form, first focusing on the shortest diethyleneglycol linker (catalysts (*R*,*R*)-**6** and (*R*,*R*)-**9**). Here, the monophosphoric acid (*R*)-**13** was used as a reference.The previously established optimized conditions for this reaction described by *Niemeyer* for different quinolines[95] were used. Thus, the newly prepared phosphoric acids were applied in the organocatalytic reduction of **59a**.



59a (*S*)-**60a**

Figure 67: Transfer hydrogenation of 2-phenyl quinoline **59a** by different catalysts.

Surprisingly, the rigidly connected alkyne-linked bisphosphoric acids and their counterparts, the monomeric phosphoric acids gave only moderate stereoselectivities (37/36/24/28/52% *ee* for catalysts (*R*,*R*)-**5**, (*R*,*R*)-**4a/b** and (*R*)-**12a/b**). In contrast, the flexibly linked ethyleneglycol based phosphoric acids and their monomeric counterpart gave moderate to good stereoselectivities (87/64/80% *ee* for catalysts (*R*,*R*)-**6**, **-9** and (*R*)-**13**) (see Table 3).

Table 3: Transfer hydrogenation of 2-phenyl quinoline; reaction conditions, yield and ee for different catalysts.

Entry	catalyst	cat.-loading [mol%]	solvent	temperature [°C]	time [h]	yield [%]	*ee*[a][b] [%]
1	(*R*)-**13**	10	toluene	25	72	89	80
2	(*R*)-**12a**	10	toluene	25	72	99	28
3	(*R*)-**12b**	10	toluene	25	72	71	52
4	(*R*,*R*)-**4a**	10	toluene	25	140	90	36
5	(*R*,*R*)-**4a**	10	toluene	25	72	52	36
6	(*R*,*R*)-**4b**	10	toluene	25	140	68	23
7	(*R*,*R*)-**4b**	10	toluene	25	72	95	24
8	(*R*,*R*)-**5**	10	toluene	25	140	73	38
9	(*R*,*R*)-**5**	10	toluene	25	72	51	37
10	(*R*,*R*)-**6**	10	toluene	25	72	91	87
11	(*R*,*R*)-**9**	10	toluene	25	140	72	64
12	(*R*,*R*)-**9**	10	toluene	25	72	63	64

[a] Isolated yields. [b] Determined by chiral HPLC. Values are given for the (*S*)-enantiomer.

Our previous findings had shown that the [2]catenane (*S*,*S*)-**61** (Figure 44) is capable of highly stereoselective cooperative catalysis in the transfer hydrogenation of quinolines. We assumed

that also the catalysts (*R*,*R*)-**6** and (*R*,*R*)-**9** might allow for a stereoselective cooperative catalytic mechanism. Accordingly, these catalysts should give higher stereoselectivities than the reference catalyst (*R*)-**13**. However, compound (*R*)-**13** gave an *ee* of 80%, which is only slightly worse than the result for (*R*,*R*)-**6** (87% *ee*) and even better than the result for (*R*,*R*)-**9** (64% *ee*). A reason for this might lie in the competition between a cooperative and a non-cooperative mechanism depending on catalyst loading and thus on the concentration of the catalyst. At higher concentration (*R*)-**13** can also act as a dimer (even in the absence of a covalent linker), thus allowing for the cooperative mechanism. In the next chapter (5.5.2) this will be investigated. In addition, it is surprising that the macrocycle (*R*,*R*)-**9** provides comparatively poorer stereoselectivities in contrast to the acyclic system (*R*,*R*)-**6**. For these systems we hypothesized that the presence of the second linker might prevent the correct relative positioning of the 1,1´-binaphthyl phosphoric acids and/or the correct positioning of the substrates within the active site. Accordingly, longer linkers were investigated (see chapter 5.5.4).

5.5.2. Concentration series

Due to the high stereoselectivity of catalyst (*R*)-**13** at a catalyst loading of 10 mol% in the transfer hydrogenation of 2-phenyl quinoline, this is examined now more closely with regard to its mode of action. In addition, catalysts (*R,R*)-**6** and (*R,R*)-**9** are also investigated in this respect to test the monomer/dimer hypothesis. For this purpose, a concentration series with catalyst loadings of 0.25%, 1%, 2.9%, 5.9%, 10% and 20% was carried out (see Table 4). The catalysis was also carried out as described in Section 5.5.1 (Table 3).

Table 4: Concentration series in transfer hydrogenation of 2-phenyl quinoline; reaction conditions, yield and ee for the used catalysts (*R,R*)-**6**, (*R,R*)-**9** and (*R*)-**13**.

Entry	catalyst	cat.-loading [mol%]	solvent	temperature [°C]	time [h]	yield [%]	*ee*[a][b] [%]
1	(*R*)-**13**	0.25	toluene	25	72	61	18
2	(*R*)-**13**	1.00	toluene	25	72	56	56
3	(*R*)-**13**	2.90	toluene	25	72	88	70
4	(*R*)-**13**	5.90	toluene	25	72	87	76
5	(*R*)-**13**	10	toluene	25	72	89	80
6	(*R*)-**13**	20	toluene	25	72	93	86
7	(*R,R*)-**6**	0.25	toluene	25	72	83	84
8	(*R,R*)-**6**	1	toluene	25	72	94	87
9	(*R,R*)-**6**	5.9	toluene	25	72	75	84
10	(*R,R*)-**6**	10	toluene	25	72	91	87
11	(*R,R*)-**6**	20	toluene	25	72	86	84
12	(*R,R*)-**9**	0.25	toluene	25	72	63	65
13	(*R,R*)-**9**	1	toluene	25	72	67	57
14	(*R,R*)-**9**	5.9	toluene	25	72	81	-
15	(*R,R*)-**9**	10	toluene	25	72	63	64
16	(*R,R*)-**9**	20	toluene	25	72	61	62

[a] Isolated yields. [b] Determined by chiral HPLC. Values are given for the (*S*)-enantiomer.

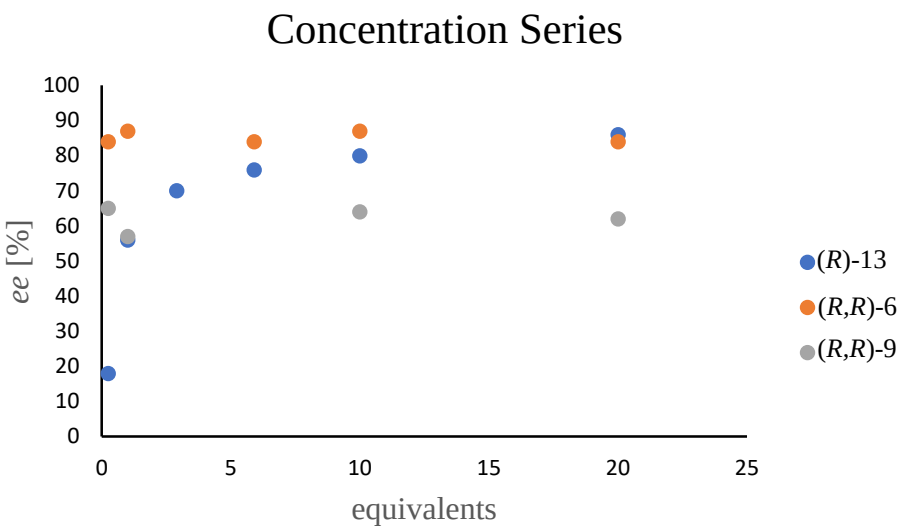


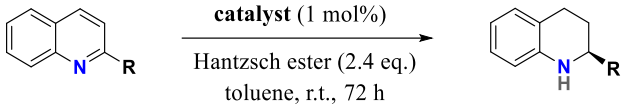
Figure 68: Plot of stereoselectivity (*ee* [%]) versus catalyst loading ([mol%]) of (*R*,*R*)-**6**, (*R*,*R*)-**9** and (*R*)-**13**.

As the catalyst loading of (*R*)-**13** decreases, the stereoselectivity also decreases, meaning a concentration-dependent stereoselectivity is observed for catalyst (*R*)-**13**. In contrast for (*R*,*R*)-**6** and (*R*,*R*)-**9** no concentration-dependent stereoselectivity was found. Thus, it can be confirmed that for catalyst (*R*)-**13**, catalysis proceeds via the non-cooperative mechanism at low catalyst loadings (less stereoselective) and via the cooperative mechanism at high catalyst loadings (more stereoselective). For the covalently linked catalysts (*R*,*R*)-**6** and (*R*,*R*)-**9**, the cooperative mechanism is dominant even at low catalyst loadings.

5.5.3. Transfer Hydrogenation Reaction of Quinoline Derivatives

Catalysts (*R*)-**13**, (*R*,*R*)-**6** and (*R*,*R*)-**9** gave high stereoselectivities in the transfer hydrogenation of 2-phenylquinolines, which makes them promising candidates to investigate the influence of the substrate structure on the effectiveness of the catalysis. Therefore, the chosen catalysts were applied to transfer hydrogenation with substrates **59b-f**. These 2-quinoline derivatives were already in stock in the group of *Niemeyer*, synthesized by *Xiang*[110] in her master thesis and were directly used. Since low catalyst loadings are desirable, the experiments were conducted at a catalyst loading of 1 mol% were used (as opposed to 10 mol% used for the catalyst screening). The results are shown in Table 5.

[110] Hongxiao Xiang, *Unsymmetrically Substituted Organophosphoric Acids - Synthesis and Application in Organocatalysis*, Master thesis, University of Duisburg-Essen, 2020.



59b-f **60b-f**

b: R = C_6H_5-F
c: R = C_6H_5-OMe
d: R = C_6H_5-CO_2Me
e: R = C_6H_6-^{t}Bu
f: R = C_4H_4O

b: R = C_6H_5-F
c: R = C_6H_5-OMe
d: R = C_6H_5-CO_2Me
e: R = C_6H_6-^{t}Bu
f: R = C_4H_4O

Figure 69: Substrate scope for the transfer hydrogenation of 2-substiuted quinolines with catalysts (*R*)-**13**, (*R*,*R*)-**6** and (*R*)-**9**.

Table 5: Transfer hydrogenation of 2-quinoline derivatives; reaction conditions, yield and *ee* for the used catalysts (*R*)-**13**, (*R*,*R*)-**6** and (*R*)-**9**.

Entry	catalyst	substrate	cat.-loading [mol%]	solvent	temperature [°C]	time [h]	yield [%]	*ee*[a][b] [%]
1	(*R*)-**13**	**59a**	1	toluene	25	72	56	56
2	(*R*,*R*)-**6**	**59a**	1	toluene	25	72	94	87
3	(*R*,*R*)-**9**	**59a**	1	toluene	25	72	67	57
4	(*R*)-**13**	**59b**	1	toluene	25	72	98	57
5	(*R*,*R*)-**6**	**59b**	1	toluene	25	72	90	87
6	(*R*,*R*)-**9**	**59b**	1	toluene	25	72	59	58
7	(*R*)-**13**	**59c**	1	toluene	25	72	98	70
8	(*R*,*R*)-**6**	**59c**	1	toluene	25	72	61	76
9	(*R*,*R*)-**9**	**59c**	1	toluene	25	72	30	82
10	(*R*)-**13**	**59d**	1	toluene	25	72	90	86
11	(*R*,*R*)-**6**	**59d**	1	toluene	25	72	78	78
12	(*R*,*R*)-**9**	**59d**	1	toluene	25	72	34	78
13	(*R*)-**13**	**59e**	1	toluene	25	72	99	81
14	(*R*,*R*)-**6**	**59e**	1	toluene	25	72	70	84
15	(*R*,*R*)-**9**	**59e**	1	toluene	25	72	62	48
16	(*R*)-**13**	**59f**	1	toluene	25	72	25	27
17	(*R*,*R*)-**6**	**59f**	1	toluene	25	72	73	86
18	(*R*,*R*)-**9**	**59f**	1	toluene	25	72	52	26

[a] Isolated yields. [b] Determined by chiral HPLC. Values are given for the (*S*)-enantiomer.

The enantiomeric excesses for the monomeric phosphoric acids are in the range of 27% to 86% *ee*. Similarly, the enantiomeric excesses for the macrocycle (*R*,*R*)-**9** range from 26% to 82% *ee*. However, catalyst (*R*,*R*)-**6** gave consistently good stereoselectivity in the range of 76% to 87% *ee*. Even for challenging substrates with rather small 2-aryl-substituents, catalyst (*R*,*R*)-**6** gave high stereoselectivities (88/87/86% *ee* for **59ab/f**).

5.5.4. Systems with longer ethylene glycol units

Based on the assumption (see chapter 5.5.1) that in case of macrocycle (*R,R*)-**72** the second linker is preventing the correct relative positioning of the 1,1´-binaphthyl phosphoric acids and/or the correct positioning of the substrates within the active site, we also synthesised the acyclic and macrocyclic systems with four and six ethylene glycol units (*R,R*)-**7**, **-8** and (*R,R*)-**10**, **-11** (see chapter 5.4.3). In that way, enough flexibility for optimal spatial arrangement, to enhance stereoselectivity, should be given. The use of the new catalyst systems in the transfer hydrogenation of 2-phenyl quinoline showed that even better stereoselectivities (92.5/93/92/93% *ee* for (*R,R*)-**7**, **-8** and (*R,R*)-**10**, **-11**) could be achieved than with the original systems (87/57% *ee* for (*R,R*)-**6** and (*R,R*)-**9**), confirming our hypothesis. Furthermore, there is no difference in selectivity between the different linkers and between acyclic and macrocyclic catalysts. This is shown in Table 6.

Table 6: Transfer hydrogenation of 2-phenyl quinoline; reaction conditions, yield and ee for the used catalysts (*R,R*)-**7**, **-8** and (*R,R*)-**10**, **-11**.

Entry	catalyst	substrate	cat.-loading [mol%]	solvent	temperature [°C]	time [h]	yield [%]	*ee*[a][b] [%]
1	(*R,R*)-**7**	**59a**	1	toluene	25	72	80	92.5
2	(*R,R*)-**8**	**59a**	1	toluene	25	72	83	93
3	(*R,R*)-**10**	**59a**	1	toluene	25	72	67	92
4	(*R,R*)-**11**	**59a**	1	toluene	25	72	96	93

[a] Isolated yields. [b] Determined by chiral HPLC. Values are given for the (*S*)-enantiomer.

As expected, the new catalyst systems also showed no dependency of catalyst loading on stereoselectivity, indicating that these systems can also act as cooperative catalysts even at low catalyst loading (see Table 7).

Table 7: Concentration series in transfer hydrogenation of 2-phenyl quinoline; reaction conditions, yield and ee for the used catalysts (*R,R*)-**8**, (*R,R*)-**11**.

Entry	catalyst	substrate	cat.-loading [mol%]	solvent	temperature [°C]	time [h]	yield [%]	*ee*[a][b] [%]
1	(*R,R*)-**8**	**59a**	0.25	toluene	25	72	83	87
2	(*R,R*)-**8**	**59a**	1	toluene	25	72	83	93
3	(*R,R*)-**8**	**59a**	2.9	toluene	25	72	75	94
4	(*R,R*)-**8**	**59a**	20	toluene	25	72	85	92.5
5	(*R,R*)-**11**	**59a**	0.25	toluene	25	72	73	78
6	(*R,R*)-**11**	**59a**	1	toluene	25	72	96	92.5
7	(*R,R*)-**11**	**59a**	2.9	toluene	25	72	78	95
8	(*R,R*)-**11**	**59a**	20	toluene	25	72	91	94.5

[a] Isolated yields. [b] Determined by chiral HPLC. Values are given for the (*S*)-enantiomer.

5.5.5. Transfer hydrogenation of 2-quinoline derivatives

As catalysts (*R*,*R*)-**8** and (*R*,*R*)-**11** show excellent stereoselectivities in the transfer hydrogenation of 2-phenyl quinoline, the influence of the substrate structure and electronic properties on the effectiveness of the catalysis is also investigated.

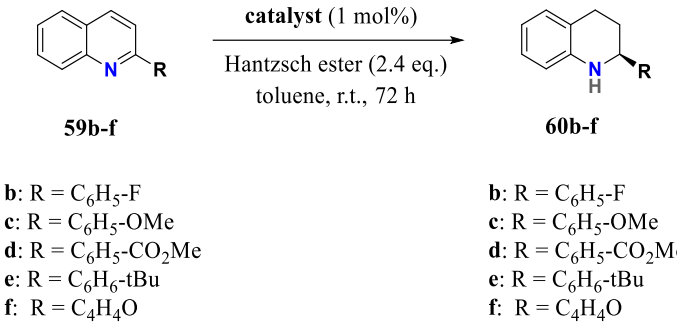


Figure 70: Substrate scope for the transfer hydrogenation of 2-substiuted quinolines with catalysts (*R*,*R*)-**8**, (*R*,*R*)-**11**.

For this purpose, transfer hydrogenations with the substrates **59b-f** were carried out with (*R*,*R*)-**8** and (*R*,*R*)-**11**. Once again, a catalyst loading of 1 mol% was chosen. The corresponding yields and enantiomeric excesses are shown in Table 8.

Table 8: Transfer hydrogenation of 2-quinoline derivatives; reaction conditions, yield and ee for the used catalysts (*R*,*R*)-**8** and (*R*,*R*)-**11**.

Entry	catalyst	substrate	cat.-loading [mol%]	solvent	temperature [°C]	time [h]	yield [%]	*ee*[a][b] [%]
1	(*R*,*R*)-**8**	**59a**	1	toluene	25	72	83	93
2	(*R*,*R*)-**11**	**59a**	1	toluene	25	72	96	92.5
3	(*R*,*R*)-**8**	**59b**	1	toluene	25	72	77	93
4	(*R*,*R*)-**11**	**59b**	1	toluene	25	72	83	94
5	(*R*,*R*)-**8**	**59c**	1	toluene	25	72	85	95.5
6	(*R*,*R*)-**11**	**59c**	1	toluene	25	72	79	95
7	(*R*,*R*)-**8**	**59d**	1	toluene	25	72	76	93
8	(*R*,*R*)-**11**	**59d**	1	toluene	25	72	75	90
9	(*R*,*R*)-**8**	**59e**	1	toluene	25	72	82	92
10	(*R*,*R*)-**11**	**59e**	1	toluene	25	72	92	94.5
11	(*R*,*R*)-**8**	**59f**	1	toluene	25	72	74	91
12	(*R*,*R*)-**74**	**59f**	1	toluene	25	72	87	91

[a] values for the (*S*)-enantiomer; [b] determined by chiral HPLC.

Both, the acyclic and the macrocyclic catalysts (*R*,*R*)-**8** and (*R*,*R*)-**11**, consistently gave excellent stereoselectivities (90-95% *ee*) for all used substrates. The impact of modifying the chain length of the macrocyclic system is more pronounced compared to the acyclic system. For the macrocycle (*R*,*R*)-**9** (diethyleneglycol linker) stereoselectivities in the range of 26-82% *ee* were found compared to (*R*,*R*)-**11** (hexaethyleneglycol linker) with stereoselectivities in the range of 91-95% *ee*. In comparison, the singly linked system (*R*,*R*)-**6** (diethyleneglycol linker) already gave good stereoseletivities (76-87% *ee*), which was only slightly improved for (*R*,*R*)-**8** (hexaethyleneglycol linker, 91-95.5% *ee*). This might be based on the more pronounced flexibility of the acyclic system. For longer chain lengths, no difference between the macrocyclic and the acyclic system was observed. In summary, we found that catalysts with longer ethylene glycol chains feature an excellent balance between molecular flexibility and a high local concentration of phosphoric acids, making them excellent candidates for cooperative phosphoric acid catalysis.

5.6. Phase transfer catalysis

The works of *Toste*[97] and *Hamashima*[99] have shown that BINOL-based systems have been used successfully as catalysts in anionic chiral phase transfer catalysis. We hypothesized that our newly synthesized phosphoric acids might also be suitable for this purpose.

Therefore, the enantioselective dearomative fluorination of 2-naphtols was investigated. At first we applied the newly synthesized catalysts to the dearomative fluorination of 1-phenyl-2-naphtol.

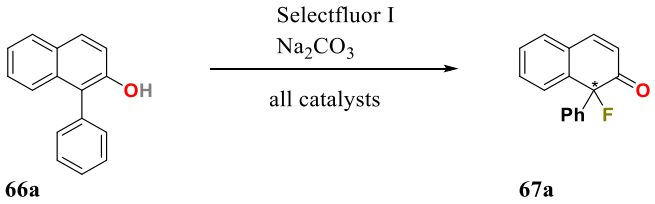


Figure 71: Dearomative fluorination reaction of 1-phenyl-2-naphtol by different catalysts.

Surprisingly, it was found that the flexibly linked bis-phosphoric acids **6**-**11**, which were successfully applied in transfer hydrogenation, revealed only poor stereoselectivities from -5% to 27% *ee*. In contrast the rigidly linked bis-phosphoric acids achieved promising stereoselectivities (81/79% *ee* for (*R*,*R*)-**4a/b**). The monomeric counterparts also gave poor stereoselectivities in all cases (-6% *ee* for (*R*)-**12a**/**12b**/**13**). For (*R*,*R*)-**4a/b**, the (*R*)-product enantiomer was obtained as the major isomer, which is in line with the application of the

(*R*,*R*)-configuration of the catalysts (*Toste* observed the (*S*)-product as the main product when using (*S*)-BINOL based catalysts).[100]

Table 9: reaction conditions, yields and enantiomeric excesses for different catalysts.

entry	cat.	cat.-loading [mol%]	solvent	temperature [°C]	time [h]	yield [%]	*ee*[a][b] [%]
1	(*R*)-**12a**	10	DCM	0	18	49	–6
2	(*R*)-**12b**	10	DCM	0	18	52	–6
3	(*R*)-**13**	10	DCM	0	18	63	–6
4	(*R*,*R*)-**4a**	10	DCM	0	18	92	81
5	(*R*,*R*)-**4b**	10	DCM	0	18	85	79
6	(*R*,*R*)-**5**	10	DCM	0	18	62	30
7	(*R*,*R*)-**6**	10	DCM	0	18	70	27
8	(*R*,*R*)-**7**	10	DCM	0	18	76	27
9	(*R*,*R*)-**8**	10	DCM	0	18	62	<5[c]
11	(*R*,*R*)-**9**	10	DCM	0	18	65	<5[c]
12	(*R*,*R*)-**10**	10	DCM	0	18	69	22
13	(*R*,*R*)-**11**	10	DCM	0	18	59	<5[c]

[a] values for the (*R*)-enantiomer; [b] determined by chiral HPLC.

Based on these results, the reaction conditions were examined in terms of solvent, temperature and catalyst loading. Based on the near-identical enantioselectivities found for (*R*,*R*)-**4a**/**b**, only (*R*,*R*)-**4a** was used for further experiments. At first four other solvents, in which sodium carbonate and selectfluor I, both were insoluble, were investigated. It was found, that catalyst (*R*,*R*)-**4a** gave slightly better stereoselectivities in chloroform than in dichloromethane (86/81% *ee*). The stereoselectivities in brombenzene and toluene dropped to 72% and 47% *ee*, respectively. Thus, further investigations on the influence of temperature were performed in chloroform. For this purpose, the dearomative fluorination was performed in chloroform at -25 °C, 0 °C and 25 °C. At all three temperatures the same stereoselectivities were found (86% *ee*). Thus, 25 °C was chosen as this allows the simplest experimental setup. Decreasing the catalyst loading to 5 mol% resulted in a decrease in stereoselectivity (86% *ee* to 48% *ee*).

Table 10: Results on different reaction conditions of dearomative fluorination with (*R*,*R*)-**4a** as catalyst and **66a** as substrate.

entry	cat.	cat.-loading [mol%]	solvent	temperature [°C]	time [h]	yield [%]	*ee*[a][b] [%]
1	(*R*,*R*)-**4a**	10	toluene	0	18	69	47
2	(*R*,*R*)-**4a**	10	dichloromethane	0	18	92	81
3	(*R*,*R*)-**4a**	10	brombenzene	0	18	72	72
4	(*R*,*R*)-**4a**	10	chloroform	-25	18	75	86
5	(*R*,*R*)-**4a**	10	chloroform	25	18	95	86
6	(*R*,*R*)-**4a**	5	chloroform	25	18	82	48

[a] values for the (*R*)-enantiomer; [b] determined by chiral HPLC.

Thus, the optimized conditions (chloroform, 25 °C, 10% catalyst loading) were applied for further investigations on different substrates in this reaction. In this respect, rigidly linked catalyst (*R*,*R*)-**4a**, its monomeric counterpart and macrocycle (*R*,*R*)-**5** were used.

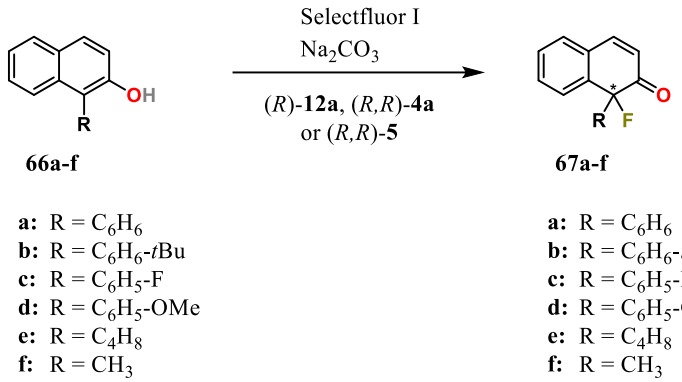


Figure 72: Dearomative fluorination reaction of different 2-naphtol by (*R*,*R*)-**4a**, (*R*,*R*)-**5** and (*R*)-**12a**.

Both, the macrocycle (*R*,*R*)-**5** and the reference catalyst (*R*)-**12a** showed poor stereoselectivities (-6% to 12% *ee*) for all of the substrates used. In contrast, catalyst (*R*,*R*)-**4a** gave moderate to good stereoselectivities for the phenyl-based substituents (86/50/53/78% *ee* for **67a**-**d**), while small substituents in the 1-position (*R*,*R*)-**4a** gave no stereoselectivities (0/1.4% *ee* for **67d**/**e**). It is therefore clear, that (*R*,*R*)-**4a** is a suitable catalyst for the dearomatizing fluorination. Interestingly, larger substituents do not necessary lead to higher stereoselectivities, as can be seen for the 4-*tert*-butylphenyl derivative **66b** (50% *ee*) in comparison to the phenyl/methoxyphenyl derivatives **66a**/**d** (86/78% *ee*). However, the results are an excellent starting point for further investigations (see Table 11).

Table 11: reaction conditions, yields and enantiomeric excesses for different substrates.

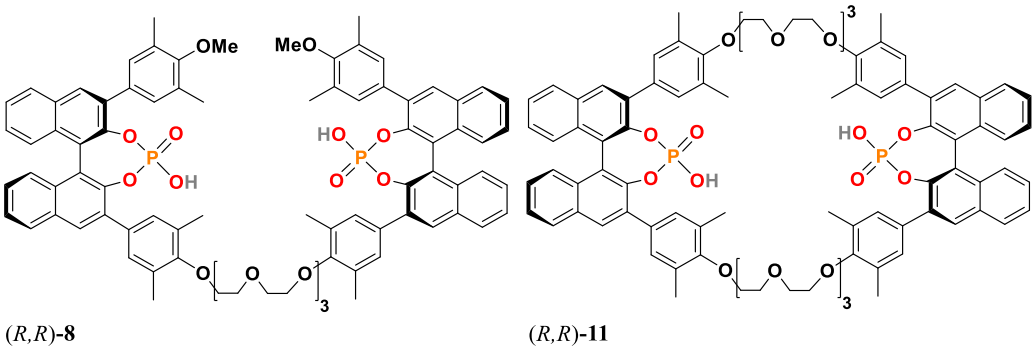
entry	substrate	cat.	cat. loading [mol%]	solvent	temperature [°C]	time [h]	yield [%]	*ee*[a][b] [%]
1	**66a**	(*R*)-**12a**	10	Chloroform	25	18	75	7
2	**66a**	(*R*,*R*)-**5**	10	Chloroform	25	18	79	-6
3	**66a**	(*R*,*R*)-**4a**	10	Chloroform	25	18	90	86
4	**66b**	(*R*)-**12a**	10	Chloroform	25	18	69	0
5	**66b**	(*R*,*R*)-**5**	10	Chloroform	25	18	82	2
6	**66b**	(*R*,*R*)-**4a**	10	Chloroform	25	18	96	50
7	**66c**	(*R*)-**12a**	10	Chloroform	25	18	66	12
8	**66c**	(*R*,*R*)-**5**	10	Chloroform	25	18	86	3
9	**66c**	(*R*,*R*)-**4a**	10	Chloroform	25	18	97	53
10	**66d**	(*R*)-**12a**	10	Chloroform	25	18	53	-2
11	**66d**	(*R*,*R*)-**5**	10	Chloroform	25	18	79	-2
12	**66d**	(*R*,*R*)-**4a**	10	Chloroform	25	18	92	78
13	**66e**	(*R*)-**12a**	10	Chloroform	25	18	49	-11
14	**66e**	(*R*,*R*)-**5**	10	Chloroform	25	18	82	12
15	**66e**	(*R*,*R*)-**4a**	10	Chloroform	25	18	94	1.4
16	**66f**	(*R*)-**12a**	10	Chloroform	25	18	59	7
17	**66f**	(*R*,*R*)-**5**	10	Chloroform	25	18	77	7
18	**66f**	(*R*,*R*)-**4a**	10	Chloroform	25	18	93	0

[a] values for the (*R*)-enantiomer; [b] determined by chiral HPLC.

5.7. Conclusion

In this work, a library of catalysts was prepared (see Figure 51). The flexibly linked bisphosphoric acids (*R*,*R*)-**8** and (*R*,*R*)-**11** have shown to be excellent catalysts in the transfer hydrogenation of different 2-substituted quinoline derivatives. These catalysts provide high stereoselectivities (90-96% *ee*) for all substrates investigated. Even for 2-furanyl quinoline, which is very difficult to reduce in a stereoselective fashion, the catalysts (*R*,*R*)-**8** and (*R*,*R*)-**11** gave excellent stereoselectivity. (see Figure 73).

A:



(*R*,*R*)-**8** (*R*,*R*)-**11**

B:

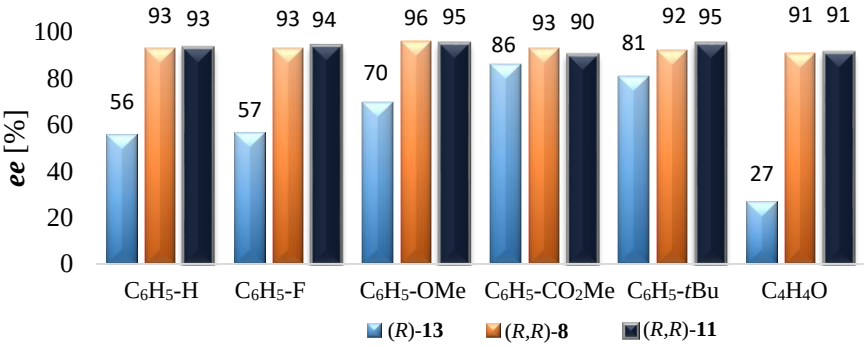
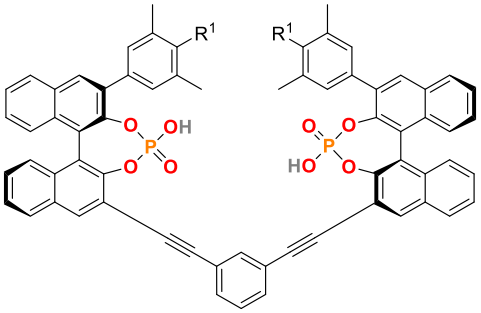


Figure 73: A: Catalysts (*R*,*R*)-**71** and (*R*,*R*)-**74**, B: Representation of the stereoselectivity (*ee* [%]) against various 2-substituted quinoline derivatives. The nature of the 2-substituent is noted.

Besides, our BINOL-based phosphoric acids have also been applied in chiral anionic phase transfer catalysis, for the first time in our group. It was found, that rigidly linked catalyst (*R*,*R*)-**4a** provides moderate to good enantioselectivities (50-78% *ee*) in case of phenyl-based 1-substituted 2-naphtols, where the flexibly linked bis-phosphoric acids provide only poor to moderate stereoselectivities (see Table 9). For smaller substituents in the 1-position even (*R*,*R*)-**4a** gave poor stereoselectivities (0/0% *ee*).

A:



(*R*,*R*)-**4a/b**

B:

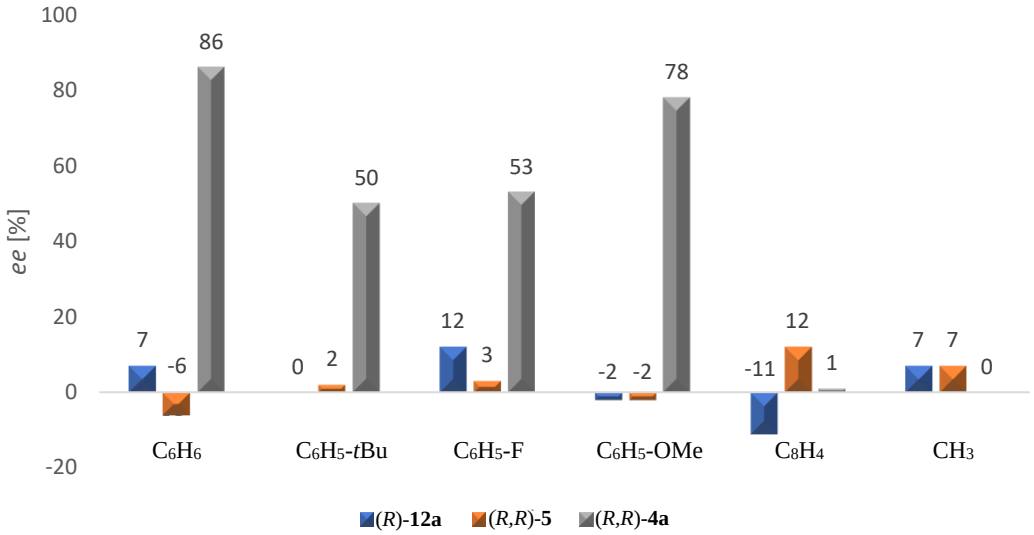


Figure 74: A: catalyst (*R*,*R*)-**65a**, B: Representation of the stereoselectivity (*ee* [%]) against various 1-substituted 2-naphtols. The nature of the 1-substituent is noted

6. Summary

6.1. Complementary supramolecular double helices

In this chapter, we have first reported the successful synthesis of a novel bis-binaphthyl-guanidine. To this end, a new synthetic route was established, synthesizing the bis-guanidine (*S*,*S*)-**28** in 12 steps starting from BINOL. Furthermore, guanidinium–phosphate pairing was successfully employed for the formation of a complementary double-helical structure. Here, the homochiral complex ((*S*,*S*)-**28**+ (*S*,*S*)-**29** gives an intertwined double-helical structure with left-handed helicity. In contrast, the heterochiral paired complex (*S*,*S*)-**28**+(*R*,*R*)-**29** forms a non-helical dimeric structure.

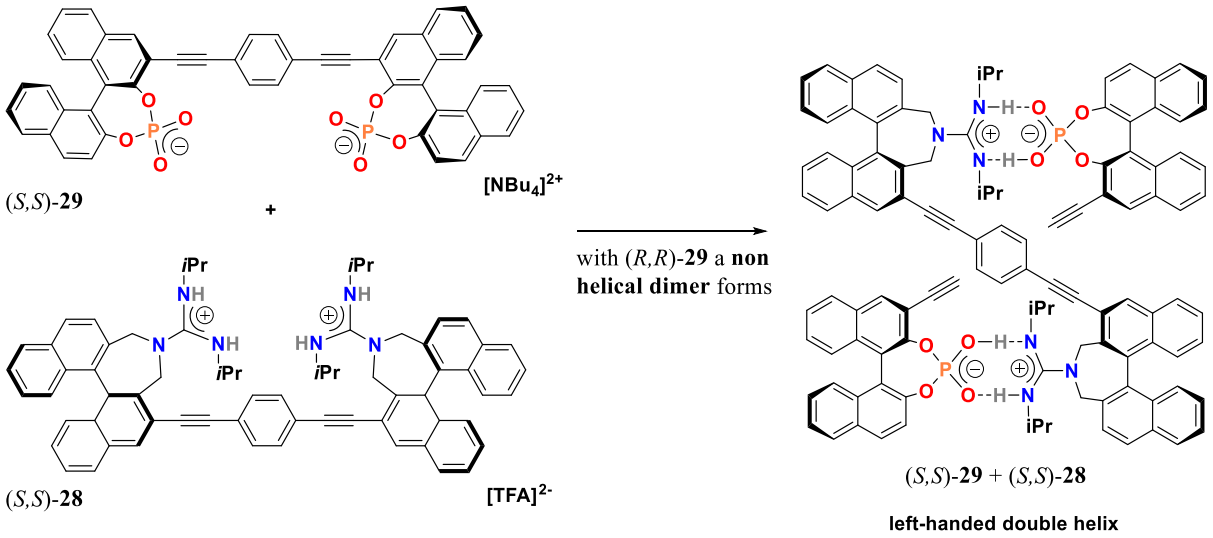
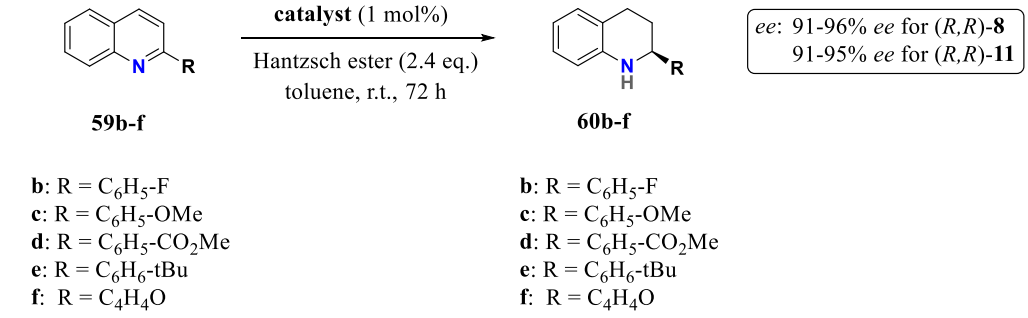


Figure 75: Supramolecular double helices of bis-guanidine and bis-phosphate through hydrogen bond formation.

6.2. BINOL based phosphoric acids as organocatalysts

In this chapter, a library of novel catalysts was synthesized. We were able to successfully apply this new generation of phosphoric acids for the transfer hydrogenation of 2-substituted quinoline derivatives. In this context, the flexibly linked bisphosphoric acids (*R*,*R*)-**8** and (*R*,*R*)-**11** provided excellent stereoselectivities (90-96% *ee*) for all substrates investigated (see Figure 76). In Addition, chiral anionic phase transfer catalysis was also investigated. The dearomative fluorination reaction of 1-aryl-2-naphtols with the rigidly linked catalyst (*R*,*R*)-**4a** gave moderate to good stereoselectivities (50-78% *ee*)(see Figure 77).



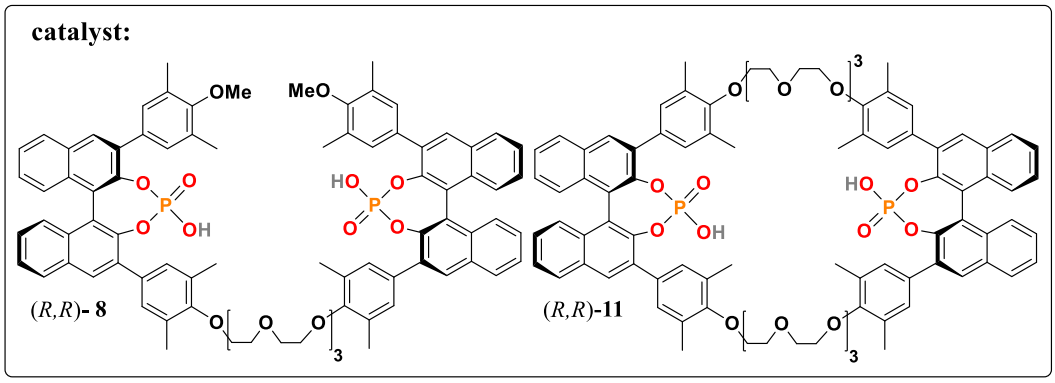
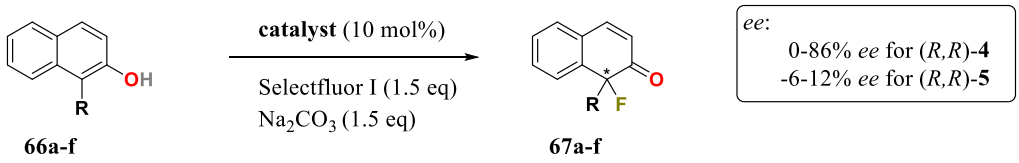


Figure 76: Transferhydrogenation of 2-quinolines with (*R*,*R*)-**8**,-**11**.



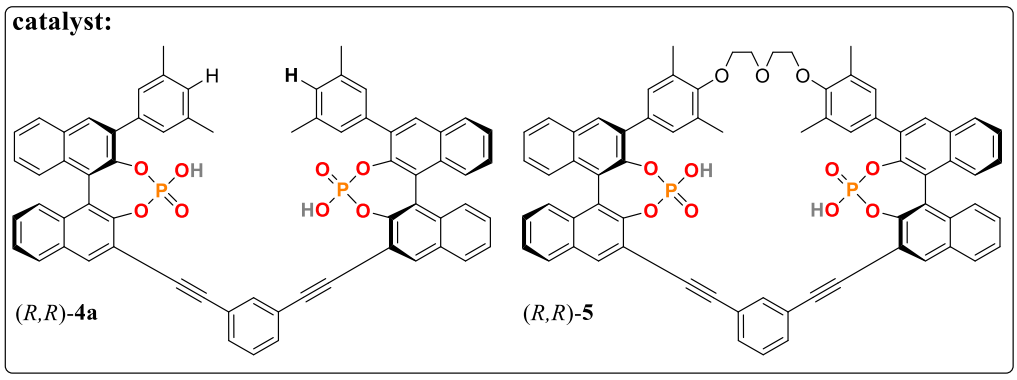


Figure 77: Dearomative fluorination of 2-naphtols with (*R*,*R*)-**4**,-**5**.

7. Zusammenfassung

7.1. Komplementäre Supramolekulare Doppelhelix

In diesem Kapitel haben wir erstmals über die erfolgreiche Synthese eines neuartigen Bis-binaphthylguanidins berichtet. Zu diesem Zweck wurde ein neuer Syntheseweg etabliert, der ausgehend von BINOL das Bisguanidin (*S*,*S*)-**28** in 12 Schritten erfolgt. Darüber hinaus wurde die Guanidinium-Phosphat-Paarung erfolgreich zur Bildung einer komplementären Doppelhelix-Struktur eingesetzt. Hier ergibt der homochirale Komplex ((*S*,*S*)-**28**+ (*S*,*S*)-**29** eine Doppelhelixs-Struktur mit linksgängiger Helizität. Im Gegensatz dazu ergibt der heterochiral gepaarte Komplex (*S*,*S*)-**28**+(*R*,*R*) **29** eine nicht helikale dimere Struktur.

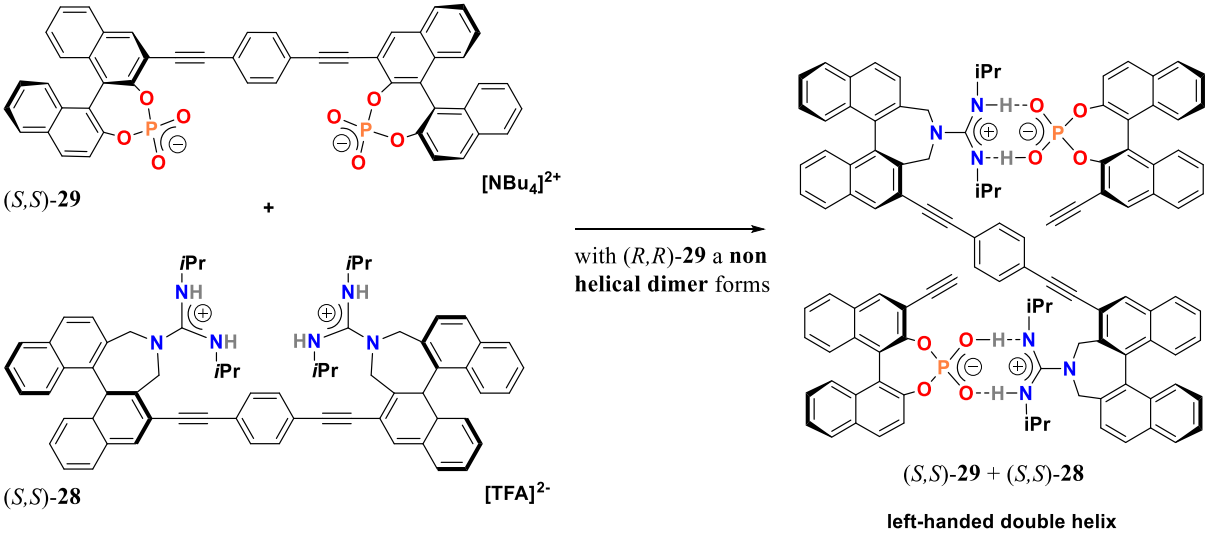
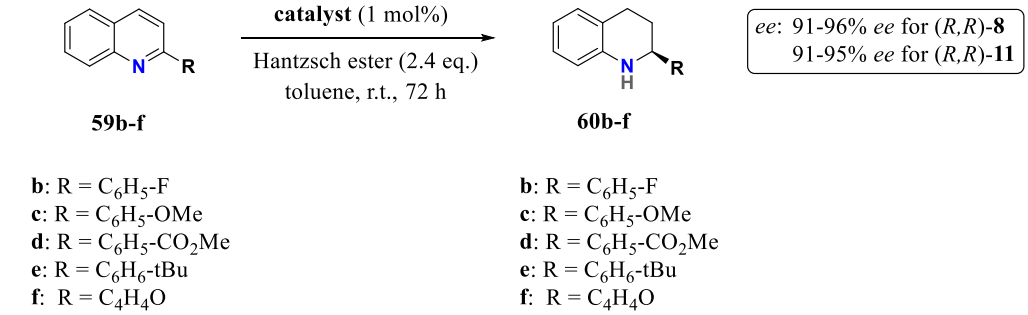


Figure 78: Supramolekulare Doppelhelix bestehend aus Bisguanidin und Bisphosphat durch Wasserstoffbrückenbildung.

7.2. BINOL-basierte Phosphorsäuren als Organokatalysatoren

In diesem Kapitel wurde eine Bibliothek neuartiger Katalysatoren synthetisiert. Wir konnten diese neue Generation von Phosphorsäuren erfolgreich für die Transferhydrierung von 2-substituierten Chinolin-derivaten einsetzen. Dabei lieferten die flexibel verknüpften Bisphosphorsäuren (*R*,*R*)-**8** und (*R*,*R*)-**11** hervorragende Stereoselektivitäten (90–96 % *ee*) für alle untersuchten Substrate (siehe Abbildung 1). Darüber hinaus wurde auch die chirale anionische Phasentransferkatalyse untersucht. Die dearomatisierende Fluorierung von 1-Aryl-2-naphtholen mit dem starr verknüpften Katalysator (*R*,*R*)-**4a** ergab mäßige bis gute Stereoselektivitäten (50–78 % *ee*) (siehe Abbildung 2).



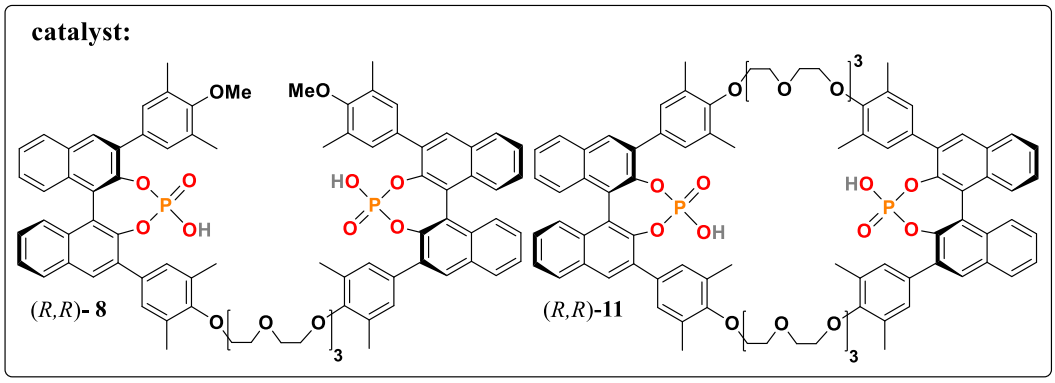
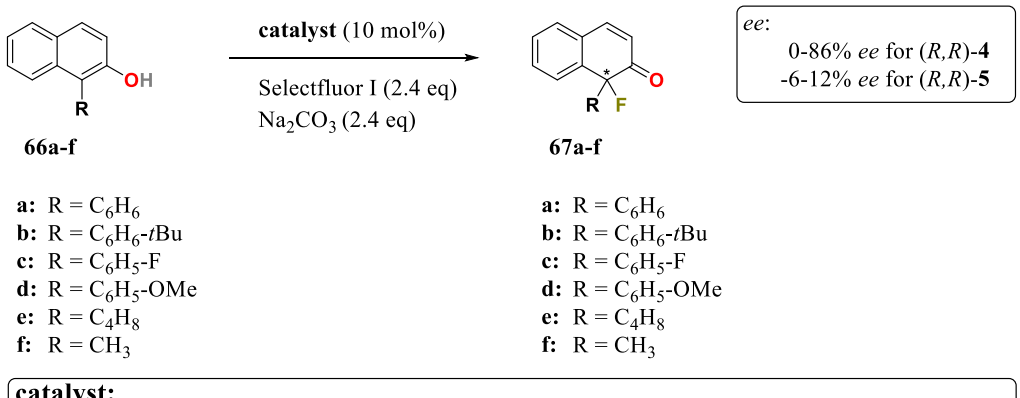


Abbildung 1: Transferhydrierung von 2-Chinolinen mit (*R*,*R*)-**8**,-**11**.



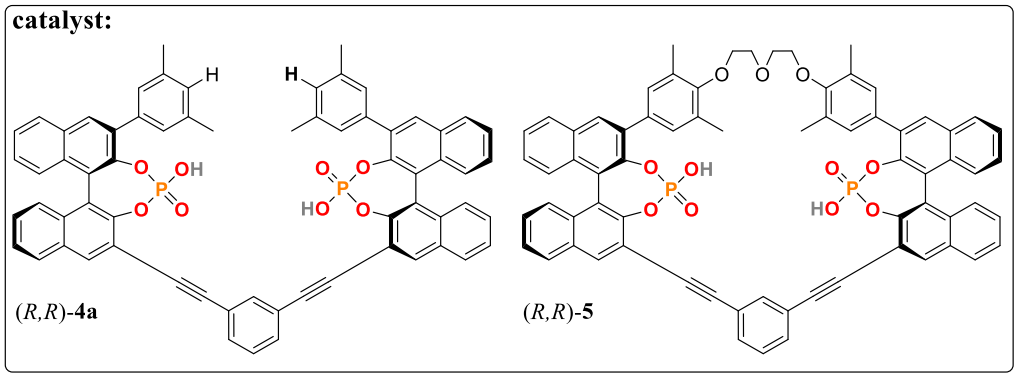


Abbildung 2: Dearomtisierende Fluorierung von 2-Naphtolen mit (*R*,*R*)-**4**,-**5**.

8. Experimental part

8.1.Materials and methods

8.1.1. Chemicals and general techniques

All reactions that needed exclusion of residual air or humidity were performed under an argon inert gas atmosphere using common Schlenk-techniques. Unless otherwise stated, all commercially purchased chemicals were not purified before use. Solvents for synthetic procedures were used analytically pure, solvents for aqueous extraction processes or flash column chromatographies were of technical grade. Technical grade ethyl acetate and cyclohexane were always distilled before being used for work-ups or columns. Anhydrous dichloromethane was dried over calcium hydride, whilst anhydrous tetrahydrofuran was dried over sodium, both solvents being freshly distilled prior to use. *N,N*-diisopropylethylamine (DIPEA) and 2,2,6,6-Tetramethylpiperidine (TMP) were dried over calcium hydride, distilled and stored over molecular sieves under argon. Pyridine was dried over potassium hydroxide, distilled and stored over molecular sieves under argon. Phosphoryl chloride ($POCl_3$) was distilled under vacuum and stored in a Schlenk flask under argon. Dimethoxyethane (DME) and aqueous sodium carbonate solution (2 M) were degassed by bubbling with argon for 15 minutes. Sodium hydride (60% dispersion in mineral oil), *1,3*- diethynylbenzene, *1,4*-diethynylbenzene, *1,3,5*-triethynylbenzene, Pd(dppf)$Cl_2 \cdot CH_2Cl_2$, trimethylsilyl bromide, trimethylsilyl chloride, *tert*-butyl carbamate, iodine, *1,3*-Bis(diphenylphosphino)propane, bromotrimethylsilane and tris(dibenzylideneacetone)dipalladium(0) were purchased from TCI and used without further purification. (*R*)-1,1′-Binaphthyl-2,2′-diol (>99.9% *ee*) and (*S*)-1,1′-Binaphthyl-2,2′-diol (>99.9% *ee*) were purchased from RCA Separations and used without further purification. Phosphourus tribromide (1.0 M in dichlormethane), *n*-butyllithium (2.7 M in toluene), borane-tetrahydrofuran complex (1.0 M in tetrahydrofuran), tetrabutylammonium fluoride (1.0 M in tetrahydrofuran), *tert*-butyldimethylsilyl chloride, 2-naphtol, ethynylbenzene, triethyl borane, allyl alcohol and methyl iodide were purchased from ACROS Organics and were used without further purification. Sodium chloride, sodium bicarbonate and sodium sulfate were purchased from VWR. Hydrochloric acid (12 M) was purchased from Bernd Kraft GmbH and used without further purification. Trifluoromethanesulfonic anhydride (>98%), palladium(II) acetate, *N,N*'-diisopropylcarbodiimide, trifluoroacetic acid, 3,5-Dimethylphenylboronic acid were purchased from Fluorochem. Palladiumtetrakistriphenylphosphine(0), acetyl chloride, tetrabutylammonium hydroxide 30-hydrate were purchased from Sigma-Aldrich. Imidazole, 2,6-Dimetyl-4-bromophenol, Iodine monochloride were purchased from Alfa Aesar. Bis(pinacolato)diboron and 1-Brom-2-naphthol were purchased from abcr.

8.1.2. Chromatography

POLYGRAM® SIL G / UV254 TLC plates (silica gel 0.2 mm, 40 × 80 mm) were used for thin-layer chromatography, and a UV Hand Lamp (Herolab GmbH) with the wavelengths 254 nm and 366 nm was used for the evaluation. Purifications were carried out by column chromatography with silica gel of the type MN 60 M (Machery-Nagel) with a particle size of 0.04-0.063 mm.

8.1.3. Analytical methods

8.1.3.1. NMR spectroscopy

The NMR spectra were recorded on a Bruker DMX 300 spectrometer (^{1}H: 300 MHz), a Bruker Avance NEO 400 spectrometer (^{1}H: 400 MHz, ^{13}C: 101 MHz, ^{19}F: 376 MHz, ^{31}P: 162 MHz), DMX 500 spectrometer (^{1}H: 500 MHz) and DRX 600 spectrometer (^{1}H: 600 MHz, ^{13}C: 151 MHz, ^{31}P: 243 MHz) All NMR-experiments were performed at room temperature except otherwise stated. The residual proton signals of the deuterated solvents were used to reference the spectra. The chemical shifts of the residual proton signals of the solvents in the ^{1}H-NMR are: $CDCl_3$: δ = 7.26 ppm, d_6-DMSO: δ = 2.50 ppm, d_4-MeOD: 3.31 ppm. The apparent coupling constants are given in Hertz. The description of the fine structure means: s = singlet, br s = broad singlet, d = doublet, ps d = pseudo doublet, br d = broad doublet, t = triplet, m = multiplet.

8.1.3.2. Mass Spectrometry

Low resolution ESI mass spectra were recorded on a Bruker Amazon SL spectrometer.

High resolution ESI mass spectra were recorded on a Bruker Maxis 4G spectrometer or a Thermo Scientific Orbitrap

8.1.3.3. Meltingpoints

Melting points were measured with a Büchi Melting-Point B-540 apparatus with open end glass capillary tubes.

8.1.3.4. IR Spectroscopy

All IR spectra were measured on a Jasco FT/IR-430 spectrometer. The data was analyzed using the supplementary software.

8.1.3.5. UV-Vis-Spectroscopy

UV/Vis spectra were recorded on a JASCO V-660 spectrophotometer. The quartz cuvettes were from Hellma®Analytics type 100-QS (10 mm light path). All solvents were spectrometric grade.

8.1.3.6. CD-Spectroscopy

CD absorption spectra were recorded on a JASCO J-815 spectrophotometer. The quartz cuvettes were from Hellma®Analytics type 100-QS (10 mm light path). All solvents were spectrometric grade.

8.1.3.7. MPLC and HPLC

Reversed phase medium performance liquid chromatography (MPLC) was performed with the following setup: Armen Instrument Spot Liquid Chromatography Flash system (detection wavelength: 263 nm), YMC GEL ODS-AQ 12 nm, S-50 μm in Kronlab glass columns with 10 mm diameter and 500 mm length. Methanol for MPLC was used analytically pure (VWR). Water for MPLC was purified with a TKA MicroPure ultrapure water system.

Reversed phase analytical high performance liquid chromatography (HPLC) was performed with the following setup: Dionex HPLC system: P680 pump, ASI-100 automated sample injector, UVD-340U UV detector (detection wavelength: 263 nm), UltiMate 3000 Column Compartment; YMC-Pack ODS-A column (3.0 x 150 mm, 5 μm, 12 nm; type: AA12S05-1503QT).

8.1.3.8. Chiral HPLC

Normal phase analytical high performance liquid chromatography (HPLC) was performed with the following setup: Erma Degasser ERC-3512, Merck Hitachi Intelligent Pump L-6200A, Chiralcel OD-H column (0.46 x 25 cm) and Chiralcel IC-3 column (0.46 x 25 cm), Knauer Smartline UV-Detector 2600 (detection wavelength 225 nm).

8.1.3.9. Elemental analysis

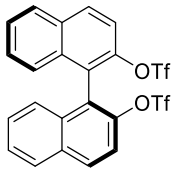
Elemental analyses were performed on Euro EA – CHNSO Elemental Analyser from HEKAtech GmbH.

8.2.Syntheses Procedures and Analytical Data

8.2.1. Syntheses of a Bis- 1,1'-Binaphtylguanidine

8.2.1.1. Synthesis of compound (*S*)-**30**[52]

Described experiment: MT186 Repeated:



(*S*)-BINOL (15.0 g, 52.4 mmol, 1 eq.) was dissolved in dichloromethane, then pyridine (33.1 g, 33.8 ml, 419 mmol, 8 eq.) was added. At 0 °C trifluoromethanesulfonic anhydride (32.5 g, 20.1 ml, 115.0 mmol, 2.2 eq.) was added in a dropwise manner with rapid stirring. The mixture was warmed up to room temperature and the reaction mixture was stirred for 16 hours. The solvent was evaporated and the residue was dissolved in ethyl acetate. The organic phase was washed with hydrochloric acid (1 M, 100 ml), then with a statured solution of sodium hydrogen carbonate (100 ml) and with a statured solution of sodium chloride (100 ml). The combined organic layers were dried over anhydrous sodium sulfate and concentrated *in vacuo.* The desired product was a colorless crystal (28.2 g, 51.3 mmol, 97.9%).

$C_{22}H_{12}F_6O_6S_2$, MW = 550.4 g/mol.

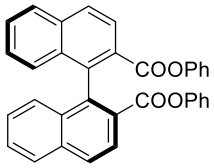
^{1}H-NMR (300 MHz, [D$_1$]-Chloroform, 298 K) δ [in ppm] 8.13 (d, ^3J = 9.2 Hz, 2H, H_{Aryl}), 8.00 (d, ^3J = 8.16 Hz, 2H, H_{Aryl}), 7.61 (d, ^3J = 8.87 Hz, 2H, H_{Aryl}), 7.58 (ddd, ^3J = 8.1, 6.7, ^4J = 1.3 Hz, 2H, H_{Aryl}), 7.40 (ddd, ^3J = 8.2, 6.8, ^4J = 1.2 Hz, 2H, H_{Aryl}), 7.24 (m, 2H, H_{Aryl}, merged with $CHCl_3$ signal).

^{19}F-NMR (282.23 MHz, [D$_1$]-Chloroform, 298 K) δ [in ppm] -74.6.

[MT186-2]

8.2.1.2. Synthesis of compound (*S*)-**37**[53]

Described experiment: MT248 Repeated: MT246, MT253, MT264, MT270, MT274, MT287, AxK001 (*rac*)



Compound (*S*)-**30** (5.01 g, 9.12 mmol, 1 eq.) was weighted into an *ACE pressure tube*, then phenylformate (0.444 g, 4.06 ml, 35.5 mmol, 4 eq.), 1,3-Bis(diphenylphosphino)propan (0.572 g, 1.39 mmol, 0.15 eq.), palladium(II)acetate (0.204 g, 0.913 mmol, 0.1 eq.) and *N*,*N*-diisopropylethylamin (14.2 g, 18.6 ml, 0.109 mol, 12 eq.) were added. The closed tube was stirred at 135 °C for 48 h. After cooling to room temperature the reaction mixture was diluted with ethyl acetate (70 ml) and the organic phase was washed with sodium hydroxide (2 M, 50 ml) hydrochloric acid (2 M, 50 ml), then with a statured solution of sodium chloride (50 ml). The organic layer was dried over anhydrous sodium sulfate and concentrated *in vacuo.* The crude product was purified by column chromatography (10x2 cm, *n*Hex:DCM 1:1) gaining a white crystalline solid (3.61 g, 7.28 mmol, 80.0%).

Same procedure was applied to synthesize (*rac*)-**37:** (*rac*)-**37** (8.00 g, 14.6 mmol, 1 eq.) gave the desired product (*rac*)-**37** (5.91 g, 12.0 mmol, 82.1 %).

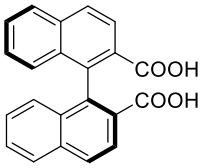
$C_{34}H_{22}O_4$, MW = 494.5 g/mol.

^{1}H-NMR (300 MHz, [D$_1$]-Chloroform, 298 K) δ [in ppm] 8.31 (d, ^3J = 8.7 Hz, 2H, H_{Aryl}), 8.05 (d, ^3J = 8.56 Hz, 2H, H_{Aryl}), 7.97 (d, ^3J = 8.2 Hz, 2H, H_{Aryl}), 7.56 (ddd, ^3J = 8.1, 6.7, ^4J = 1.3 Hz, 2H, H_{Aryl}), 7.32 (ddd, ^3J = 8.5, 6.6, ^4J = 1.2 Hz, 2H, H_{Aryl}), 7.24 (m, 2H, H_{Aryl}, merged with $CHCl_3$ signal), 7.17 (m, 4H, H_{Aryl}), 7.09 (tdd, ^3J = 8.5, 6.6, ^4J = 1.1 Hz, 2H, H_{Aryl}), 6.65 (m, 4H, H_{Aryl}).

[MT248-2]

8.2.1.3. Synthesis of compound (*S*)-**32**[52]

Described experiment: MT290 Repeated: MT277, AxK002 (*rac*)



Compound (*S*)-**37** (7.61 g, 1.41 mmol, 1 eq.) was dissolved in 250 ml methanol and aqueous sodium hydroxide solution (14.2 ml, 5 M, 70.8 mmol, 5 eq.) was added. The solution was stirred at 75°C for 18 hours. The reaction mixture was concentrated in *vacuo*. Addition of hydrochloric acid (2 M, 200 ml) gave a suspension with a white precipitate. The suspension was extracted with ethyl acetate (3 x 150 ml). The combined organic layers were washed with water (100 ml) and dried over anhydrous sodium sulfate and concentrated in *vacuo*. The desired product was a brown solid (5.01 g, 14.6 mmol, 95.4%)

Same procedure was applied to synthesize (*rac*)-**32:** (*rac*)-**32** (5.91 g, 14.6 mmol, 1 eq.) gave the desired product (*rac*)-**32** (3.16 mg, 8.87 mmol, 74.2 %).

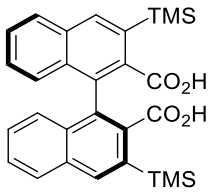
$C_{22}H_{14}O_4$, MW = 356.3 g/mol.

^{1}H-NMR (300 MHz, [D$_1$]-chloroform, 298 K) δ [in ppm] 8.11 (d, ^3J = 8.7 Hz, 2H, H_{Aryl}), 7.94 (d, ^3J = 9.0 Hz, 2H, H_{Aryl}), 7.90 (d, ^3J = 8.3 Hz, 2H, H_{Aryl}), 7.52-7.40 (m, 2H, H_{Aryl}), 7.19-7.05 (m, 2H, H_{Aryl},), 6.88 (d, ^3J = 8.5 Hz, 2H, H_{Aryl}).

[MT290-1]

8.2.1.4. Synthesis of compound (*S*)-**38**[54]

Described experiment: MT282 Repeated: MT262, MT291, AxK003 (*rac*)



2,2,6,6-Tetramethylpiperidine (12.4 g, 14.9 ml, 88.2 mmol, 6.84 eq.) was dissolved in dry tetrahydrofuran (40 mL). *n*-butyl lithium (32.7 mL, 2.7 M, 88.2 mmol, 6.84 eq.) in toluene was added to the Schlenk flask at 0 °C. The reaction mixture was stirred for 20 minutes at that temperature. Then, Chlor(trimethyl)silane (15.4 g, 9.22 ml, 141.9 mmol, 11 eq.) was added dropwise at -78 °C and was stirred for additional 20 minutes. Afterwards, the carboxylic acid (*S*)-**32** (4.41 g, 12.9 mmol, 1 eq.) in dry tetrahydrofuran (40 ml) was added and the reaction mixture was stirred for 16 hours at room temperature. Then hydrochloric acid (60 ml, 4 N) and diethyl ether (60 ml) were added with stirring and the organic layer was separated. The aqueous layer was extracted with diethyl ether (40 ml). The combined organic layer was basified with sodium hydroxide (200 ml) and stirred for 15 minutes. The alkaline layer was separated and this was repeated 3 times. The combined aqueous extracts were acidified with hydrochloric acid (80 ml, 6 N) and extracted with diethyl ether (2x100 ml). The organic layer was washed with saturated sodium chloride solution, dried over anhydrous sodium sulfate and concentrated in *vacuo* to give the product as a light yellow solid (5.31 g, 10.9 mmol, 85.1%).

Same procedure was applied to synthesize (*rac*)-**32:** (*rac*)-**32** (3.06 g, 8.41 mmol, 1 eq.) gave the desired product (*rac*)-**32** (3.36 mg, 6.90 mmol, 82.1 %).

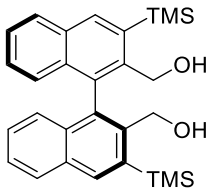
$C_{28}H_{30}O_4Si_2$, MW = 486.2 g/mol.

^{1}H-NMR (300 MHz, [D$_1$]-chloroform, 298 K) δ [in ppm] 8.11 (s, 2H, H_{Aryl}), 7.91 (d, ^3J = 7.8 Hz, 2H, H_{Aryl}), 7.50 (t, ^3J = 7.5 Hz, 2H, H_{Aryl}), 7.30 (t, ^3J = 7.5 Hz, 2H, H_{Aryl}), 7.01 (d, ^3J = 8.5 Hz, 2H, H_{Aryl}), 0.41 (s, 18H, H_{Methyl}).

[MT282-1]

8.2.1.5. Synthesis of compound (*S*)-**39**[54]

Described experiment: MT283 Repeated: MT295, MT269, ME13 (*rac*)



Compound (*S*)-**38** (3.91 g, 8.04 mmol, 1 eq.) was dissolved in dry tetrahydrofuran (50 ml), then borane (48.25 ml, 1 M in THF, 48.3 mmol, 6 eq.) was added slowly to the solution. The reaction mixture was stirred at 80 °C for 16 hours, when the TLC showed complete conversion hydrochloric acid (20 ml, 2 M) was added carefully at 0 °C and tetrahydrofurane was evaporated. The aqueous phase was extracted with dichlormethane (2x100 ml) and the combined organic layer was washed with a statured solution of sodium chloride (50 ml). The organic layer was dried over anhydrous sodium sulfate and concentrated in *vacuo* to afford the product as a yellow solid (3.60 g, 7.81 mmol, 97.6%).

Same procedure was applied to synthesize (*rac*)-**39:** (*rac*)-**39** (3.01 g, 6.17 mmol, 1 eq.) gave the desired product (*rac*)-**39** (2.81 g, 6.12 mmol, 99.3 %).

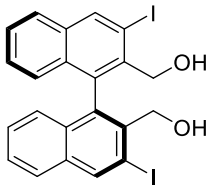
$C_{28}H_{34}O_2Si_2$, MW = 458.7 g/mol.

^{1}H-NMR (300 MHz, [D$_1$]-chloroform, 298 K) δ [in ppm] 8.22 (s, 2H, H_{Aryl}), 7.92 (d, ^3J = 8.1 Hz, 2H, H_{Aryl}), 7.50 (ddd, ^3J = 8.1, 6.8, ^4J = 1.2 Hz, 2H, H_{Aryl}), 7.23 (ddd, ^3J = 8.0, 6.9, ^4J = 1.3 Hz, 2H, H_{Aryl}), 6.94 (d, ^3J = 8.5 Hz, 2H, H_{Aryl}), 4.58 (d, ^2J = 11.5 Hz, 2H, $H_{Methylene}$), 4.20 (d, ^2J = 11.6 Hz, 2H, $H_{Methylene}$), 0.50 (s, 18H, H_{Methyl}).

[MT283-1]

8.2.1.6. Synthesis of compound (*S*)-**40**[54]

Described experiment: MT323 Repeated: MT315, MT285, MT379 (*rac*)



Compound (*S*)-**39** (3.6 g, 7.81 mmol, 1 eq.) was dissolved in dry dichlormethane (40 ml) and was cooled to -40 °C, then iodine monochloride (3.80 g, 1.22 ml, 23.5 mmol, 3.5 eq.) in dichlormethane (40 ml) was added slowly to the solution. The reaction mixture was stirred at -40 °C for two hours. When the TLC showed complete conversion the reaction mixture was warmed to room temperature. A saturated $NaHSO_3$ solution (30 mL) was added. The organic layer was separated and the aqueous phase was extracted with dichlormethane (2x40 ml) and the combined organic layer was washed with a statured solution of sodium chloride (50 ml). The organic layer was dried over anhydrous sodium sulfate and concentrated in *vacuo* to afford the product as a yellow solid (3.85 g, 6.80 mmol, 87.3%).

Same procedure was applied to synthesize (*rac*)-**40:** (*rac*)-**40** (2.89 g, 6.29 mmol, 1 eq.) gave the desired product (*rac*)-**40** (2.89 g, 6.11 mmol, 81.4 %).

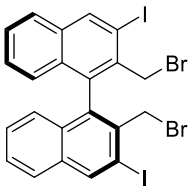
$C_{22}H_{16}O_2I_2$, MW = 565.92 g/mol.

^{1}H-NMR (300 MHz, [D$_1$]-chloroform, 298 K) δ [in ppm] 8.61 (s, 2H, H_{Aryl}), 7.82 (d, ^3J = 8.2 Hz, 2H, H_{Aryl}), 7.49 (ddd, ^3J = 8.1, 6.9, ^4J = 1.2 Hz, 2H, H_{Aryl}), 7.32-7.23 (m, 2H, H_{Aryl} merged with $CHCl_3$ signal), 6.90 (d, ^3J = 8.6 Hz, 2H, H_{Aryl}), 4.61 (d, ^2J = 12.2 Hz, 2H, $H_{Methylene}$), 4.16 (d, ^2J = 12.3 Hz, 2H, $H_{Methylene}$).

[MT315-1]

8.2.1.7. Synthesis of compound (*S*)-**41**[54]

Described experiment: MT324 Repeated: MT316, MT286, MT436, MT388 (*rac*)



Compound (*S*)-**40** (3.85 g, 6.81 mmol, 1 eq.) was dissolved in dry dichlormethane (40 ml).
At -40 °C phosphorus tribromide (10.2 ml, 1 M, 20.1 mmol, 1.5 eq.) was added slowly and the reaction mixture was stirred for 16 hours. The reaction mixture was poured onto water (15 ml), and the organic layer was separated and the aqueous layer was extracted with ethyl acetate (2x50 ml). The combined organic layer was washed with water (50 ml). The organic layer was dried over anhydrous sodium sulfate and was concentrated in *vacuo* to afford the product as an orange solid (4.32 g, 2.43 mmol, 93.1%).

Same procedure was applied to synthesize (*rac*)-**40:** (*rac*)-**40** (2.28 g, 4.03 mmol, 1 eq.) gave the desired product (*rac*)-**40** (680 mg, 0.986 mmol, 25.1 %).

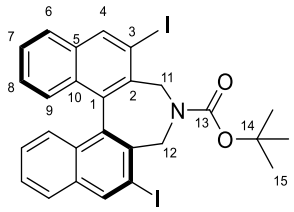
$C_{22}H_{14}Br_2I_2$, MW = 689.75 g/mol.

^{1}H-NMR (300 MHz, [D$_1$]-chloroform, 298 K) δ [in ppm] 8.65 (s, 2H, H_{Aryl}), 7.82 (d, ^3J = 8.2 Hz, 2H, H_{Aryl}), 7.51 (ddd, ^3J = 8.2, 6.8, ^4J = 1.2 Hz, 2H, H_{Aryl}), 7.33-7.23 (m, 2H, H_{Aryl} merged with $CHCl_3$ signal), 6.98 (d, ^3J = 8.6 Hz, 2H, H_{Aryl}), 4.41 (d, ^2J = 10.4 Hz, 2H, $H_{Methylene}$), 4.32 (d, ^2J = 10.4 Hz, 2H, $H_{Methylene}$).

[MT286-2]

8.2.1.8. Synthesis of compound (*S*)-**42**[111,112]

Described experiment: MT288 Repeated: MT317, MT326, MT389 (*rac*)



Compound (*S*)-**41** (1.81 g, 2.61 mmol, 1 eq) and *tert*-butyl carbamate (0.458 g, 3.91 mmol, 1.5 eq) were dissolved in dry tetrahydrofuran (40 ml). Sodium hydride (60% in petroleum ether, 0.510 g, 13.1 mmol, 5 eq) was suspended in dry dimethylformamide (40 mL). At 0 °C, the solution of compound (*S*)-**3** and *tert*-butyl carbamate was slowly added to the sodium hydride suspension. The reaction mixture was stirred for 24 hours. After complete conversion a saturated solution of sodium chloride (50 ml) was added and the organic layer was separated. The aqueous phase was extracted with ethyl acetate (5x50 ml). The combined organic layer was dried over anhydrous sodium sulfate and was concentrated in *vacuo*. The crude product was purified by column chromatography (20x4 cm, cyclohexane:ethyl acetate 20:1) and afforded the product (*S*)-**4** as a white crystalline solid (1.30 g, 2.01 mmol, 77.4%).

Same procedure was applied to synthesize (*rac*)-**41:** (*rac*)-**41** (340 mg, 0.985 mmol, 1 eq.) gave the desired product (*rac*)-**41** (415 mg, 0.640 mmol, 65.1 %).

$C_{27}H_{23}NO_2I_2$, MW = 646.98 g/mol.

NMR: For compound (*S*)-**41**, we observe separate signals for the methylene-groups 11 and 12, probably due to slow rotation around the N-C amide bond. However, for the binaphthyl-backbone only one set of signals was observed.

^{1}H-NMR (600 MHz, [D$_1$]-chloroform, 298 K) δ [in ppm] = 8.60 (s, 2 H, H-4), 7.81 (d, ^3J = 8.5 Hz, 2 H, H-6), 7.48 (t, ^3J = 7.4 Hz, 2 H, H-7), 7.27-7.24 (m, 4 H, H-8/9), 5.64 (d, ^2J = 12.4 Hz, 1 H, H-11/12), 5.49 (d, ^2J = 12.4 Hz, 1 H, H-11/12), 3.59 (d, ^2J = 12.9 Hz, 1 H, H-11/12), 3.50 (d, ^2J = 12.9 Hz, 1 H, H-11/12), 1.51 (s, 9 H, H-25).

^{13}C-NMR (151 MHz, [D$_1$]-chloroform, 298 K) δ [in ppm] = 153.3 (C-13), 140.2 (C-4), 136.2 (C-1), 134.5 (C-10), 130.9 (C-5), 127.5 (C-9), 127.3 (C-6), 126.9 (C-7/8), 98.0 (C-3), 97.8 (C-2), 80.4 (C-14), 51.8 (C-11/12), 51.1 (C-11/12), 28.6 (C-15).

^{1}H,^{1}H-COSY (600 MHz / 600 MHz, [D$_1$]-chloroform, 298 K) δ [in ppm] = 7.81 / 7.48 (H-6 / H-7), 7.48 / 7.81, 7.27-7.24 (H-7 / H-6, H-8/9), 7.27-7.24 / 7.48 (H-8/9 / H-7), 5.64 / 3.50 (H-11 / H-12), 5.49 / 3.60 (H-11 / H-12), 3.60 / 5.49 (H-12 / H-11), 3.50 / 5.64 (H-12 / H-11).

^{1}H,^{13}C-GHSQC (600 MHz / 151 MHz, [D$_1$]-chloroform, 298 K) δ (^{1}H) / δ (^{13}C) [in ppm] = 8.60 / 140.2 (H-4 / C-4), 7.81 / 127.3 (H-6 / C-6), 7.48 / 126.9 (H-7 / C-7/8), 7.27-7.24 / 126.9 (H-8/9 / C-7/8),

[111] The synthesis of compound (*S*)-**42** was developed at the same time by *Widhalm* (see: A. Manaprasertsak, S. Tharamak, C. Schedl, A. Roller, M. Widhalm, *Molecules*, **2019**, *24*, 3844)

[112] Compound (*S*)-**42** was synthesized following a procedure of *Maruoka* (see: S. B. J. Kan, H. Maruyama, M. Akaura, T. Kano, K. Maruoka, *Angew. Chem. Int. Ed.*, **2017**, *56*, 9487-9491).

7.27-7.24 / 127.5 (H-8/9 / C-9), 5.64 / 51.1 (H-11/12 / C-11/12), 5.49 / 51.8 (H-11/12 / C-11/12), 3.59 / 51.8 (H-11/12 / C-11/12), 3.50 / 51.1 (H-11/12 / C-11/12), 1.57 / 28.6 (H-15 / C-15).

^{1}H,^{13}C-GHMBC (600 MHz / 151 MHz, [D$_1$]-chloroform, 298 K) δ (^{1}H) / δ (^{13}C) [in ppm] = 8.60 / 134.5, 130.9, 127.3, 98,0/97.8 (H-4 / C-10, C-5, C-6, C-3/2), 7.81 / 140.2, 130.5, 126,9 (H-6 / C-4, C-5,C-7/8), 7.48 / 134.5, 127.5, (H-7 / C-10, C-9), 7.27-7.24 / 136.2, 130.9, 127.3, 126.9, 134.5 (H-8/9 / C-1, C-5, C-6, C-7/8, C-10), 5.64 / 136.2, 98.0, 97.8 (H-11/12 / C-1, C-3, C-2), 5.63 / 136.2, 98.0, 97.8 (H-11/12 / C-1, C-3, C-2), 3.59 / 136.2, 98.0, 97.8 (H-11/12 / C-1, C-3, C-2), 3.50 / 136.2, 98.0, 97.8 (H-11/12 / C-1, C-3, C-2). [MT318-5]

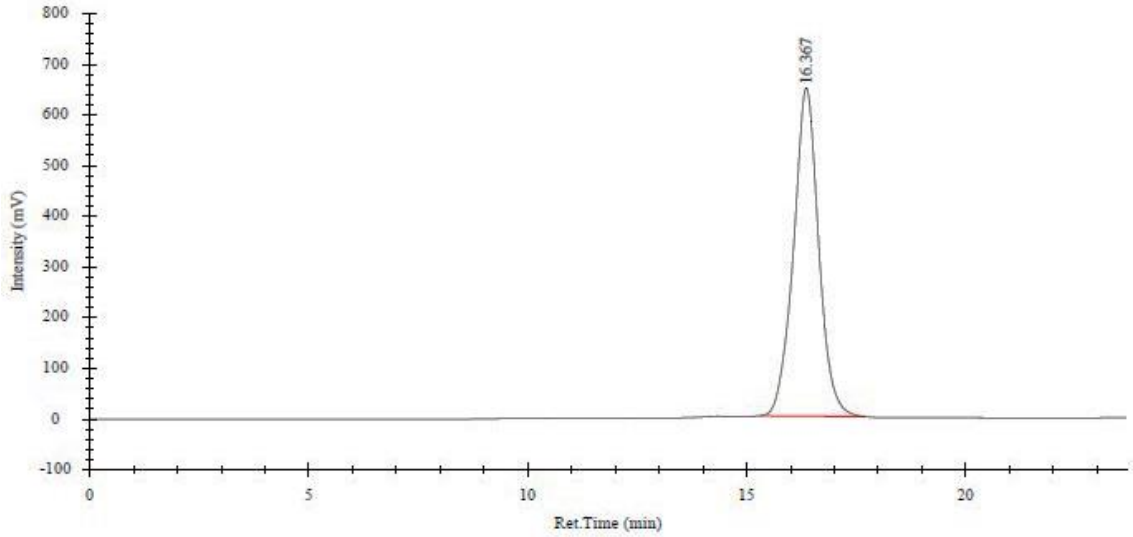
Elemental analysis = calcd (%) for $C_{27}H_{23}NO_2I_2$: C: 50.10, H: 3.58, I: 39.21. N: 2.16, O: 4.94; found: C: 50.05, H: 3.48, I: 37.10 N: 2.17, O: 4.77.

MS (ESI-pos, MeOH**)**: *m/z* = 647.9892 ([M+H]$^+$, calcd. 647.9891 [$C_{27}H_{24}NO_2I_2$]$^+$)

IR (ATR-FT): $\tilde{\nu}$ (cm^{-1}) = 3054, 2969, 2923, 2877, 2360, 2113, 1689, 1550, 1457, 1396, 1241, 1157, 1110, 1025, 964, 925, 871, 817, 740.

Chiral HPLC of (*S*)-**41** and (*rac*)-**41:**

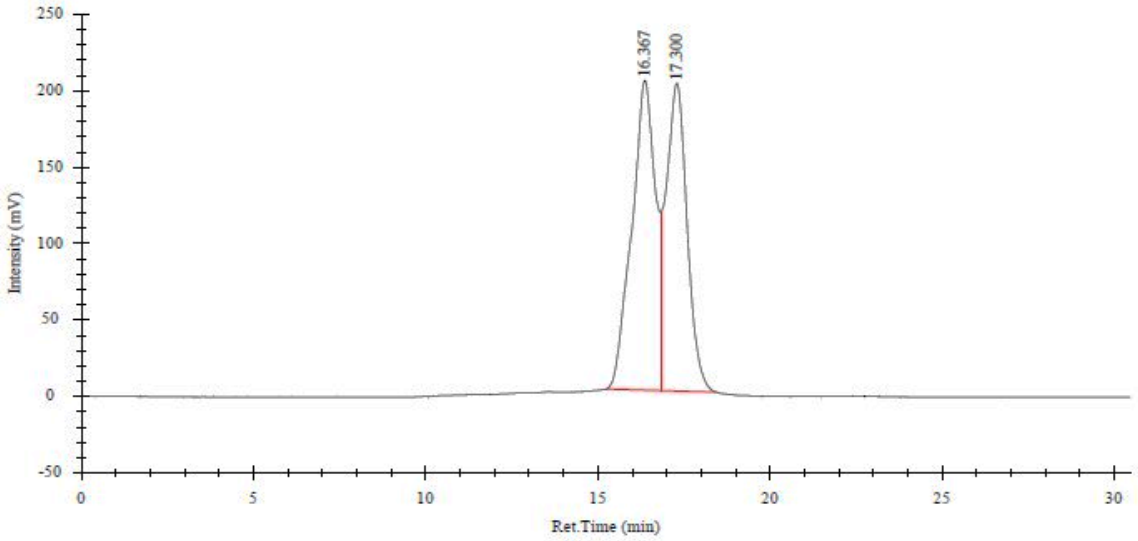
Because the X-ray analysis of (*S*)-**41** showed a small amount of co-crystallized (*R*)-**4**, we checked the enantiopurity by chiral HPLC. Although no baseline-separation for the racemate could be achieved, HPLC proves high stereopurity for (*S*)-**41**.



Calculation Method: Percent

Peak-No.	Window-No.	Ret. Time (min)	Area	Response-Factor	Percent	Name
1	0	16.367	25942520.00		100.000	

Figure 79: Chiral HPLC chromatogram and integration table of (*S*)-**41** (hexane : isopropanol 25 : 75, 0.3 ml/min); t_R (area): 16.36 min (100%).



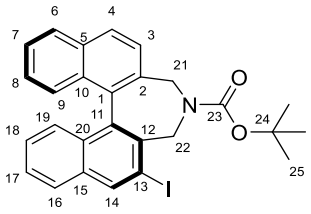
Calculation Method: Percent

Peak-No.	Window-No.	Ret. Time (min)	Area	Response-Factor	Percent	Name
1	0	16.367	9579010.00		52.504	
2	0	17.300	8665431.00		47.496	

Figure 80: Chiral HPLC chromatogram and integration table of (*rac*)-**41** (hexane : isopropanol 25 : 75, 0.3 ml/min); t_R (area): 16.36 min (52.5%), 17.3 min (47.5%).

8.2.1.9. Synthesis of compound (*S*)-**36**[113]

Described experiment: MT318 Repeated:



Compound (*S*)-**42** utyl lithium (0.377 mL, 2.7 M solution in toluene, 1.02 mmol, 1.1 eq.) in toluene was added at 0 °C. The reaction mixture was stirred for 5 minutes. Then methanol (5 ml) was added and the mixture was stirred for additional 10 minutes. Removal of the solvent was followed by purification of the crude product by column chromatography (20x4 cm, cyclohexane:acetone 30:1) and afforded the product (*S*)-**5**[3] as a white crystalline solid (0.304 g, 5.83 mmol, 63.1%).

$C_{27}H_{24}INO_2$, MW = 521.08 g/mol.

^{1}H-NMR (400 MHz, [D$_1$]-chloroform, 298 K) δ [in ppm] = 8.59 (s, 1 H, H-14), 7.98 (d, ^3J = 8.4 Hz, 1 H, H-4), 7.95 (d, ^3J = 8.2 Hz, 1 H, H-6), 7.81 (d, ^3J = 8.5 Hz, 1 H, H-16), 7.63 (br d, ^3J = 7.9 Hz, 1 H, H-3), 7.48 (dt, ^3J = 6.9 Hz, ^4J = 1.2 Hz 1 H, H-7), 7.45 (dt, ^3J = 7.0 Hz, ^4J = 1.2 Hz 1 H, H-17), 7.35 (d, ^3J = 8.5 Hz, 1 H, H-9), 7.30 (d, ^3J = 8.5 Hz, 1 H, H-19), 7.29-7.26 (m, 2 H, merged with chloroform, H-8+H-18), 5.64-5.45 (m, 1 H, H-21/22), 5.06-4.86 (m, 1 H, H-21/22), 3.67 (d, ^2J = 13.3 Hz 1 H, H-21/22), 3.53 (d, ^2J = 13.3 Hz 1 H, H-21/22), 1.55 (s, 9 H, merged with water signal, H-25).

^{13}C-NMR (100.61 MHz, [D$_1$]-chloroform, 298 K) δ [in ppm] = 153.9 (C-23), 139.8 (C-14), 136.6 (C-2), 135.1 (C-12), 134.6 (C-15), 133.29 (C-5), 133.22 (C-13), 131.30 (C-10/20), 131.23 (C-10/20), 129.8 (C-4), 128.5 (C-6), 127.83 (C-8), 127.74 (C-3), 127.31 (C-9), 127.24 (C-16), 126.89 (C-17), 126.77 (C-18), 126.4 (C-8), 126.0 (C-7), 116.7 (C-11), 98.1 (C-1), 80.32 (C-24) 52.00 (C-21/22), 47.2 (C-21/22), 28.7 (C-25).

^{1}H,^{1}H-COSY (400 MHz / 600 MHz, [D$_1$]-chloroform, 298 K) δ [in ppm] = 7.98 / 7.63 (H-4 / H-3), 7.95 / 7.48 (H-6 / H-7), 7.81 / 7.45 (H-16 / H-17), 7.63 / 7.98 (H-3 / H-4), 7.48 / 7.27 (H-7 / H-8+H-18), 7.45 / 7.81, 7.27 (H-17 / H-16, H-8+H-18), 7.35 / 7.27 (H-9 / H-8+H-18), 7.27 / 7.48, 7.45, 7.35 (H-8+H-18 / H-7, H-17, H-9), 5.48 / 3.67 (H-21/22/ H-21/22), 5.03 / 3.53 (H-21/22/ H-21/22), 3.67 / 5.48 (H-21/22 / H-21/22), 3.53 /5.03 (H-21/22 / H-21/22).

^{1}H,^{13}C-GHSQC (400 MHz / 100.61 MHz, [D$_1$]-chloroform, 298 K) δ (^{1}H) / δ (^{13}C) [in ppm] = 8.59 / 139.78 (H-14 / C-14), 7.98 / 129.8 (H-4 / C-4), 7.95 / 128.5 (H-6 / C-6), 7.81 / 127.24 (H-16 / C-16), 7.63 / 127.74 (H-3 / C-3), 7.48 / 126.0 (H-7 / C-7), 7.45 / 126.89 (H-17 / C-17), 7.35 / 127.31/127.24 (H-9 / C-9/16), 7.30 / 127.83 (H-19 / C-19), 7.29-7.25 / 126.4/126.77 (H-8/18 / C-8+C-18), 5.46 / 52.0 (H-21/22 / C-21/22), 5.02 / 47.2 (H-21/22 / C-21/22), 3.67 / 52.0 (H-21/22 / C-21/22), 3.53 / 47.2 (H-21/22 / C-21/22), 1.55 / 28.7 (H-25 / C25).

[113] Compound (*S*)-**36** was synthesized following a procedure of *Sayed* (see: W. E. Parham, L. D. Jones, Y. A. Sayed, *J. Org. Chem*., **1976**, *41*, 7, 1184-1186).

^{1}H,^{13}C-GHMBC (400 MHz / 100.61 MHz, [D$_1$]-chloroform, 298 K) δ (^{1}H) / δ (^{13}C) [in ppm] = 8.59 / 135.1, 131.30/131.23, 127.31/127.24 (H-14 / C-12, C-10/20, C-9/16), 7.98 / 136.6, 133.29, 131.30, 128.5 (H-4 / C-2, C-5, C-10, C-6), 7.95 / 131.30/131.23, 129.8, 126.4 (H-6 / C-10/20, C-4, C8), 7.81 / 139.8, 131.3/131.21, 126.77 (H-16 / C-14, C-10/20, C-18), 7.48 / 133.31, 127.31/127.24 (H-7 / C-5, C-9/16), 7.45 / 134.6, 127.83 (H-17 / C-15, C-19), 7.35 / 133.29, 126.0 (H-9 / C-5, C-7), 7.30 / 134.6, 126.89 (H-19 / C-15, C-17), 7.29-7.26 / 131.30/131.23, 128.5, 126.89 (H-8+H18 / C-10/20, C-6, C-17), 1.55 / 80.1 (H-25 / C-24). [MT496-5]

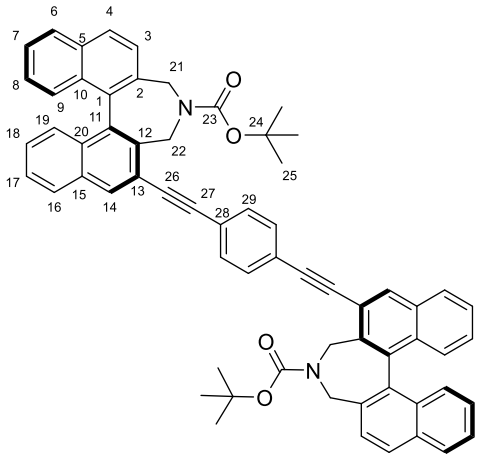
MS (ESI-pos, MeOH**)**: *m/z* = 522.0927 ([M+H]$^{+}$, calcd. 522.0925 [$C_{27}H_{25}INO_2$]$^{+}$)

IR (ATR-FT): $\tilde{\nu}$ (cm^{-1}) = 2975, 1687, 1552, 1402, 1365, 1272, 1245, 1155, 1105, 960, 910, 869, 823, 750, 732, 626.

[MT240-24]

8.2.1.10. Synthesis of compound (*S*,*S*)-**43**

Described experiment: MT319 Repeated: MT383, MT499



Compound (*S*)-**36** (570 mg, 1.10 mmol, 2.1 eq), 1,4-diethynylbenzene (65.1 mg, 0.516 mmol, 1 eq), copper iodide (8.58 mg, 45.1 µmol, 0.1 eq) and palladiumtetrakistriphenylphosphine(0) (52.1 mg, 45.1 µmol, 0.1 eq) were dissolved in a dry and degassed mixture of acetonitrile:triethylamine (1:1 ratio, 30 ml total). The reaction mixture was stirred at 80 C for 18 hours. After cooling to room temperature all volatiles were evaporated and the crude product was purified by column chromatography (20x4 cm, cyclohexane:ethyl acetate 10:1) and afforded the product (*S*,*S*)-**6**[4] as a yellow solid (0.401 g, 0.505 mmol, 86%).

$C_{64}H_{52}N_2O_4$, MW = 912.13 g/mol.

^{1}H-NMR (600 MHz, [D$_1$]-chloroform, 323 K) δ [in ppm] = 8.28 (s, 2 H, H-14), 7.99 (d, ^3J = 8.4 Hz, 2 H, H-4), 7.96 (d, ^3J = 8.1 Hz, 2 H, H-6), 7.92 (d, ^3J = 8.2 Hz, 2 H, H-16), 7.69 (br s, 4 H, H-29), 7.63 (d, ^3J = 7.5 Hz, 2 H, H-3), 7.49 (t, ^3J = 7.4 Hz, 2 H, H-17), 7.48 (t, ^3J = 7.4 Hz, 2 H, H-7), 7.42 (d, ^3J = 8.4 Hz, 2 H, H-9), 7.36 (d, ^3J = 8.7 Hz, 2 H, H-19), 7.29 (t, ^3J = 7.6 Hz, 2 H, H-8), 7.27 (t, ^3J = 7.4 Hz, 2 H, H-18), 5.76 (br s, 2 H, H-21/22), 5.06 (br s, 2 H, H-21/22), 3.64 (d, ^2J = 13.5 Hz, 2 H, H-21/22), 3.53 (d, ^2J = 12.4 Hz, 2 H, H-21/22), 1.46 (br s, 18 H, H-25).

^{13}C-NMR (151 MHz, [D$_1$]-chloroform, 323 K) δ [in ppm] = 154.4 (C-23), 136.6 (C-11), 134.72 (C-1), 133.69 (C-2), 133.5 (C-5+C-12), 133.3 (C-14), 133.0 (C-15), 132.0 (C-29), 131.6 (C-10), 131.5 (C-20), 129.7 (C-4), 128.5 (C-6), 128.3 (C-16), 127.8 (C-19), 127.59 (C-3/9), 127.53 (C-3/9), 127.1 (C-18), 126.7 (C-17), 126.3 (C-8), 126.0 (C-7), 123.6 (C-13/18), 121.2 (C-13/18), 93.3 (C-27), 90.2 (C-26), 80.1 (C-24), 47.7 (C-21/22), 45.2 (C-21/22), 28.70 (C-25).

^{1}H,^{1}H-COSY (600 MHz / 600 MHz, [D$_1$]-chloroform, 323 K) δ [in ppm] = 7.99 / 7.63 (H-4 / H-3), 7.63 / 7.99 (H-3 / H-4) 7.96 / 7.48 (H-6 / H-7), 7.92 / 7.49 (H-16 / H-17), 7.48 / 7.96 (H-7 / H-6), 7.49 / 7.92 (H-17 / H-16), 7.42 / 7.29 (H-9 / H-8), 7.29 / 7.42 (H-8 / H-9), 7.36 / 7.27 (H-19 / H-18), 7.27 / 7.36 (H-18 / H-19).

^{1}H,^{13}C-GHSQC (600 MHz / 151 MHz, [D$_1$]-chloroform, 323 K) δ (^{1}H) / δ (^{13}C) [in ppm] = 8.28 / 133.3 (H-14 / C-14), 7.99 / 129.7 (H-4 / C-4), 7.96 / 128.5 (H-6 / C-6), 7.92 / 128.3 (H-16 / C-16), 7.69 / 132.0 (H-29 / C-29), 7.63 / 127.59/127.53 (H-3 / C-3/9), 7.49 / 126.7 (H-17 / C-17), 7.48 / 126.0 (H-7

/ C-7), 7.42 / 127.59/127.53 (H-9 / C-3/9), 7.36 / 127.8 (H-19 / C-19), 7.29 / 126.3 (H-8 / C-8), 7.27 / 127.1 (H-18 / C-18), 3.53 / 45.2 (H-21/22 / C-21/22), 1.46 / 28.7 (H-25 / C25).

^{1}H,^{13}C-GHMBC (600 MHz / 151 MHz, [D$_1$]-chloroform, 323 K) δ (^{1}H) / δ (^{13}C) [in ppm] = 8.28 / 133.5, 131.5, 128.3, 90.17 (H-14 / C-5+C12, C-20, C-16, C-26), 7.99 / 133.69, 131.6, 128.5 (H-4 / C-2, C-10, C-6), 7.96 / 131.6, 129.7, 126.3 (H-6 / C-10, C-4, C8), 7.92 / 133.3, 131.5, 127.1 (H-16 / C-14, C-20, C-18), 7.63 / 134.7, 133.5 (H-3 / C-1, C-5), 7.49 / 133.0, 131.5, 127.8 (H-17 / C-15, C-20, C-19), 7.48 / 131.63 (H-7 / C-10), 7.42 / 134.7, 133.5, 126.0 (H-9 / C-1, C-5, C-7), 7.36 / 136.6, 133.0, 131.5, 126.7 (H-19 / C-11, C-15, C-20, C-17), 7.29 / 131.6, 128.5 (H-8 / C-10, C-6), 7.27 / 131.5, 128.3 (H-18 / C-20, C-16). [MT319VT]

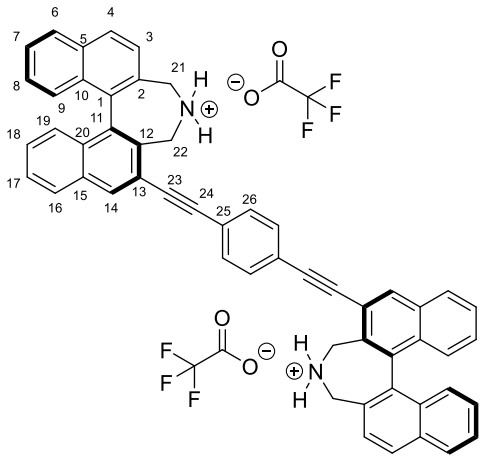
Elemental analysis = calcd (%) for $C_{64}H_{52}N_2O_4$: C: 84.18, H: 5.75 N: 3.07, O: 7.01; found: C: 83.9, H: 5.62, N: 3.25, O: 6.98.

MS (ESI-pos, MeOH**)**: *m/z* = 935.3817 ([M+Na]$^+$, calcd. 935.3819 [$C_{64}H_{52}N_2O_4Na$]$^+$)

IR (ATR-FT): $\tilde{\nu}$ (cm^{-1}) = 3054, 2977, 2923, 2869, 2360, 1920, 1689, 1504., 1457.92, 1396, 1249, 1157, 1103, 871, 825, 748.

8.2.1.11. Synthesis of compound (*S,S*)-**44**

Described experiment: MT327 Repeated: MT518



Compound (*S,S*)-**43**(18.5 mg, 0.0203 mmol, 1 eq), was dissolved in a dry and degassed dichloromethane (3 ml), then trifluoric acetic acid (63.6 mg, 0.557 mmol, 27.5 eq) was added and the mixture was stirred at room temperature for 18 hours. The organic layer was washed with water (5 ml), dried over sodium sulfate and concentrated in *vacuo* to give the product (*S,S*)-**7**[2,5] as a yellow solid (11.0 mg, 0.0154 mmol, 76.1%).

$C_{58}H_{38}F_6N_2O_4$, MW = 940.94 g/mol.

^{1}H-NMR (600 MHz, [D$_1$]-chloroform, 298 K) δ [in ppm] = 8.27 (s, 2 H, H-14), 7.99 (d, ^3J = 7.5 Hz, 2 H, H-4), 7.96 (d, ^3J = 7.5 Hz, 2 H, H-6), 7.92 (d, ^3J = 7.9 Hz, 2 H, H-16), 7.62 (d, ^3J = 8.4 Hz, 2 H, H-3), 7.58 (s, 4 H, H-26), 7.48 (t, ^3J = 7.3 Hz, 2 H, H-17), 7.47 (t, ^3J = 7.8 Hz, 2 H, H-7), 7.41 (d, ^3J = 8.5 Hz, 2 H, H-9), 7.38 (d, ^3J = 8.6 Hz, 2 H, H-19), 7.30-7.27 (m, 2 H, H-8), 7.27-7.25 (m, 2 H, H-18), 4.62 (d, ^2J = 13.3 Hz, 2 H, H-21), 3.92 (d, ^2J = 13.3 Hz, 2 H, H-22), 3.53 (d, ^2J = 11.8 Hz, 2 H, H-22), 3.40 (d, ^2J = 11.8 Hz, 2 H, H-21). [MT327]

^{1}H-NMR (400 MHz, [D$_6$]-dimethylsulfoxid, 298 K) δ [in ppm] = 8.44 (s, 2 H, H-14), 8.09 (d, ^3J = 8.69 Hz, 4 H, H-4+H-16), 8.06 (d, ^3J = 8.19 Hz, 2 H, H-6), 7.72 (s, 4 H, H-26), 7.66 (d, ^3J = 8.46 Hz, 2 H, H-3), 7.54 (dt, ^3J = 7.48 Hz, ^4J = 1.05 Hz, 2 H, H-17), 7.50 (d, ^3J = 7.48 Hz, ^4J = 1.21 Hz, 2 H, H-7), 7.35 (dt, ^3J = 8.82 Hz, ^4J = 1.21 Hz, 2 H, H-18), 7.33 (dt, ^3J = 8.54 Hz, ^4J = 1.29 Hz, 2 H, H-8), 7.24 (d, ^3J = 8.33 Hz, 2 H, H-9), 7.20 (d, ^3J = 8.54 Hz, 2 H, H-19), 4.41 (d, ^2J = 12.09 Hz, 2 H, H-22$_{1/2}$), 3.79 (d, ^2J = 12.09 Hz, 2 H, H-21$_{1/2}$), 3.20 (d, ^2J = 12.09 Hz, 2 H, H-22$_{1/2}$), 3.12 (d, ^2J = 12.09 Hz, 2 H, H-21$_{1/2}$).

^{13}C-NMR (100.61 MHz, [D$_6$]-dimethylsulfoxid, 298 K) δ [in ppm] = 135.6 (C-2), 135.20 (C-11/12), 135.11 (C-11/12), 133.4 (C-1), 132.9 (C-14), 132.5 (C-5), 131.97 (C-15), 131.82 (C-26), 130.6 (C-10+C-20), 129.0 (C-4), 128.47 (C-6), 128.42 (C-16), 127.4 (C-3), 127.2 (C-18), 126.6 (C-19), 126.33 (C-9/17), 126.28 (C-9/17), 126.1 (C-8), 125.4 (C-7), 122.7 (C-25), 119.6 (C-13) 92.1 (C-24), 90.5 (C-23), 47.9 (C-21), 45.0 (C-22).

^{1}H,^{1}H-COSY (400 MHz / 400 MHz, [D$_6$]-dimethylsulfoxid, 298 K) δ [in ppm] = 8.09 / 7.66, 7.54 (H-4+H-16 / H-3, H-17), 8.06 / 7.50 (H-6 / H-7), 7.66/7.54 / 8.09 (H-3, H-17 / H-4+H-16), 7.50 / 8.06

(H-7 / H-6), 7.54/7.50 / 7.35/7.33 (H-17/7 / H-18/8), 7.35/7.33 / 7.54/7.50, 7.24/7.20 (H-18/8 / H-17/7, H-9/19), 7.24/7.20 / 7.35/7.33 (H-9/19 / H-18/8), 4.41 / 3.12 ($H\text{-}22_{1/2}$ / $H\text{-}22_{1/2}$), 3.79 / 3.20 ($H\text{-}21_{1/2}$ / $H\text{-}21_{1/2}$), 3.12 / 4.41 ($H\text{-}22_{1/2}$ / $H\text{-}22_{1/2}$), 3.20 / 3.79 ($H\text{-}21_{1/2}$ / $H\text{-}21_{1/2}$).

^{1}H,^{13}C-GHSQC (400 MHz / 100.61 MHz, [D$_6$]-dimethylsulfoxid, 298 K) δ (^{1}H) / δ (^{13}C) [in ppm] = 8.44 / 132.9 (H-14 / C-14), 8.09 / 129.0, 128.42 (H-4/16 / C-4/16), 8.06 / 128.47 (H-6 / C-6), 7.72 / 131.82 (H-26 / C-26), 7.66 / 127.4 (H-3 / C-3), 7.54 / 126.33, 126.28 (H-17 / C-9/17), 7.50 / 125.4 (H-7 / C-7), 7.35 / 127.2 (H-18 / C-18), 7.33 / 126.1 (H-8 / C-8), 7.24 / 126.33, 126.28 (H-9 / C-9/17), 7.20 / 126.6 (H-19 / C-19), 4.41 / 45.0 ($H\text{-}22_{1/2}$ / C-22), 3.79 / 47.9 ($H\text{-}21_{1/2}$ / C-21), 3.20 / 47.9 ($H21_{1/2}$ / C-21), 3.12 / 45.0 ($H\text{-}22_{1/2}$ / C22).

^{1}H,^{13}C-GHMBC (400 MHz / 100.61 MHz, [D$_6$]-dimethylsulfoxid, 298 K) δ (^{1}H) / δ (^{13}C) [in ppm] = 8.44 / 135.20/135.11, 130.6, 128.42, 90.5 (H-14 / C-11/12, C-10/20, C-16, C-23), 8.09 / 135.6, 130.6, 128.47, 127.2 (H-4+H-16 / C-2, C-10+C-20, C-6, C-18), 8.06 / 130.6, 129.0, 126.1 (H-6 / C-10+C-20, C-4, C-8), 7.72 / 122.7, 92.1 (H-26 / C-25, C-24), 7.66 / 133.4, 132.5, 47.9 (H-3 / C-1, C-5, C-21), 7.54 / 131.82, 126.6 (H-17 / C-15, C-19), 7.50 / 132.5, 126.33/126.28 (H-7 / C-5, C-9/17), 7.35 / 130.6, 128.42 (H-18 / C-10+C-20, C-16), 7.33 / 130.6, 128.47/128.42 (H-8 / C-10+C-20, C-6/16), 7.24 / 132.5, 125.4 (H-9 / C-5, C-7), 7.20 / 135.20/135.11, 131.97, 126.33/126.28 (H-19 / C-11/12, C-15, C-9/17), 4.41 / 135.20/135.11, 119.6 ($H\text{-}22_{1/2}$ / C-11/12, C-13), 3.79 / 135.6, 133.4, 127.4 ($H21_{1/2}$ / C-2, C-1, C-3), 3.20 / 135.6 ($H21_{1/2}$ / C-2), 3.12 / 135.20/135.11, 119.6 ($H22_{1/2}$ / C-11/12, C-13). [MT518-3]

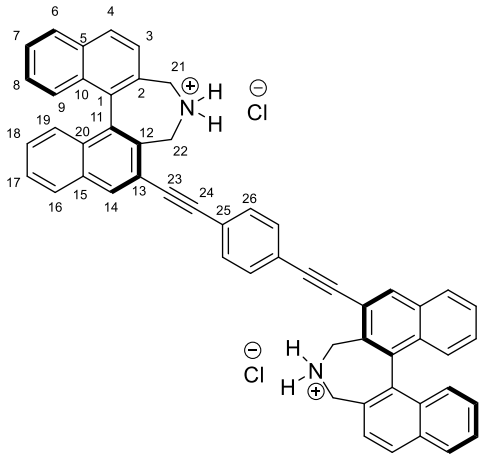
^{19}F-NMR (376.5 MHz, [D$_6$]-Dimethylsulfoxid, 298 K) δ [in ppm] -73.41

MS (ESI-pos, MeOH**)**: *m/z* = 713.2954 ($[M+H]^+$, calcd. 713.2951 $[C_{54}H_{37}N_2]^+$)

IR (ATR-FT): $\tilde{\nu}$ (cm^{-1}) = 3744, 3045, 2952, 2923, 2848, 2673, 2489, 2360, 2331, 2206, 1733, 1699, 1683, 1652, 1575, 1558, 1538, 1506, 1423, 1209, 1184, 1105, 1029, 880, 827, 806, 748, 649, 609.

8.2.1.12. Synthesis of compound (*S*,*S*)-**44b**

Described experiment: MT339 Repeated:



Compound (*S*,*S*)-**44** (33.10 mg, 46.3 µmol, 1 eq), was dissolved in distilled tetrahydrofurane (4 ml), then concentrated hydrochloric acid (9.6 µl, 4.22 mg, 0.116 mmol, 2.5 eq) was added and the mixture was stirred at room temperature for 30 minutes. Then ethyl acetate (15 ml) was added and the organic layer was separated. The organic layer was washed with water (5 ml), dried over sodium sulfate and concentrated in *vacuo* to give the product as a yellow solid (32.1 mg, 40.9 µmol, 88.2%).

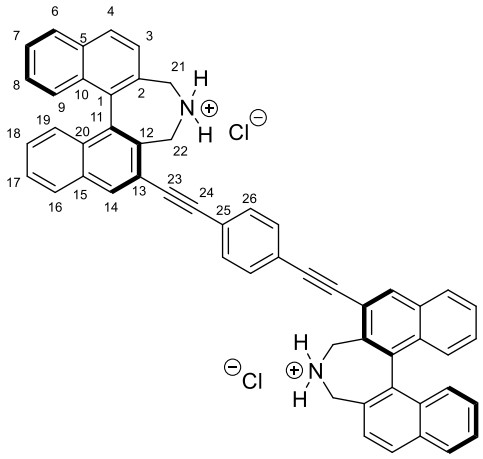
$C_{54}H_{38}N_2Cl_2$, MW = 785.79 g/mol.

^{1}H-NMR (400 MHz, [D_6]- dimethylsulfoxid, 298 K) δ [in ppm] = 8.57 (s, 2 H, H-14), 8.23 (d, ^3J = 8.53 Hz, 2 H, H-4), 8.19 (d, ^3J = 8.34 Hz, 2 H, H-6), 8.14 (d, ^3J = 8.34 Hz, 2 H, H-16), 7.84 (s, 4 H, H-26), 7.82 (d, ^3J = 8.42 Hz, 2 H, H-3), 7.66 (t, ^3J = 7.93 Hz, 2 H, H-7), 7.61 (d, ^3J = 7.36 Hz, 2 H, H-17), 7.44 (ddd, ^3J = 6.79 Hz, 2 H, H-8), 7.40 (ddd, ^3J = 7.43 Hz, 2 H, H-18), 7.23 (d, ^3J = 9.13 Hz, 2 H, H-19), 7.20 (d, ^3J = 8.85 Hz, 2 H, H-9), 4.85 (d, ^2J = 9.17 Hz, 2 H, H-$22_{1/2}$), 4.41 (d, ^2J = 9.17 Hz, 2 H, H-$21_{1/2}$), 3.63 – 3.52 (m, 4 H, H-21/22, signal merged with H_2O signal).

[MT339-1]

8.2.1.13. Synthesis of compound (*S*,*S*)-**44b**

Described experiment: MT385 Repeated: MT462



Compound (*S*,*S*)-**43** (39.5 mg, 43.3 µmol, 1 eq), was dissolved in degassed methanol (3 ml), then concentrated hydrochloric acid (10.39 ml, 0.866 mmol, 10 eq) was added and the mixture was stirred at room temperature for 18 hours. Then dichloromethane 10 ml was added and the organic layer was washed with water (15 ml), dried over sodium sulfate and concentrated in *vacuo* to give the product (*S*,*S*)-**10**[5] as a yellow solid (31.7 mg, 40.3 µmol, 93.2%).

$C_{54}H_{38}N_2Cl_2$, MW = 785.81 g/mol

^{1}H-NMR (400 MHz, [D$_4$]-methanol, 298 K) δ [in ppm] = 8.47 (s, 2 H, H_{Aryl}), 8.19 (d, ^3J = 8.35 Hz, 2 H, H_{Aryl}), 8.08 (d, ^3J = 8.14 Hz, 4 H, H_{Aryl}), 7.80 (d, ^3J = 8.48 Hz, 2 H, H_{Aryl}), 7.78 (s, 4 H, H_{Aryl}), 7.61 (t, ^3J = 7.04 Hz, 2 H, H_{Aryl}), 7.57 (t, ^3J = 7.38 Hz, 2 H, H_{Aryl}), 7.38 - 7.27 (m, 8 H, H_{Aryl}), 5.06 (d, ^2J = 13.29 Hz, 2 H, $H_{Methylene}$), 4.43 (d, ^2J = 12.84 Hz, 2 H, $H_{Methylene}$), 3.72 (d, ^2J = 12.38 Hz, 2 H, $H_{Methylene}$), 3.66 (d, ^2J = 13.00 Hz, 2 H, $H_{Methylene}$).

[MT385-1]

^{1}H-NMR (600 MHz, [D$_6$]-dimethylsulfoxid, 298 K) δ [in ppm] = 9.94 (br s, 4H, H-27), 8.58 (s, 2 H, H-14), 8.25-8.23 (m, 2 H, H-4), 8.18 (d, ^3J = 8.1 Hz, 2 H, H-16), 8.15 (d, ^3J = 8.8 Hz, 2 H, H-6), 7.85 (s, 4 H, H-26), 7.82 (d, ^3J = 8.2 Hz, 2 H, H-3), 7.66 (t, ^3J = 7.5 Hz, 2 H, H-17), 7.62 (t, ^3J = 7.5 Hz, 2 H, H-7), 7.44 (t, ^3J = 7.4 Hz, 2 H, H-18), 7.41 (t, ^3J = 7.9 Hz, 2 H, H-8), 7.24 (d, ^3J = 8.6 Hz, 2 H, H-9), 7.21 (d, ^3J = 8.6 Hz, 2 H, H-19), 4.84 (d, ^2J = 14.4 Hz, 2 H, H-22$_{1/2}$), 4.40 (d, ^2J = 12.3 Hz, 2 H, H-21$_{1/2}$), 3.61 (d, ^2J = 12.6 Hz, 2 H, H-22$_{1/2}$), 3.56 (d, ^2J = 13.7 Hz, 2 H, H-21$_{1/2}$).

^{13}C-NMR (151 MHz, [D$_6$]-dimethylsulfoxid, 298 K) δ [in ppm] = 136.13 (C-11), 134.07 (C-1), 133.54 (C-5/14), 132.97 (C-15), 131.99 (C-2/26), 130.54 (C-10/12), 130.49 (C-20), 129.66 (C-4), 128.64 (C-6), 128.57 (C-16), 127.99 (C-3/18), 127.69 (C-17), 126.93 (C-19), 126.83 (C-7/8), 126.79 (C-7/8), 126.60 (C-9), 122.62 (C-25), 119.96 (C-13), 93.39 (C-24), 89.51 (C-23), 45.32 (C-21) 42.72 (C-22).

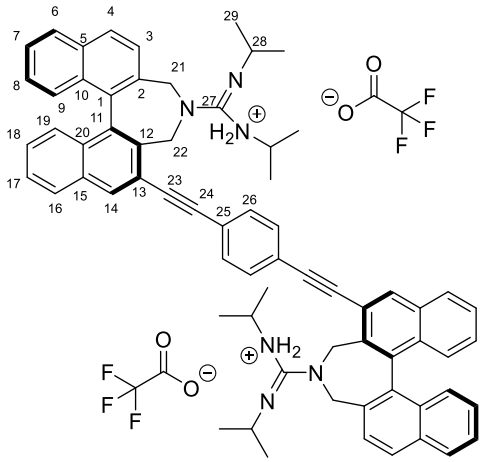
^{1}H,^{1}H-COSY (600 MHz / 600 MHz, [D$_6$]-dimethylsulfoxid, 298 K) δ [in ppm] = 8.24 / 7.82 (H-4 / H-3), 8.18 / 7.66 (H-16 / H-17), 8.15 / 7.62 (H-6 / H-7), 7.66 / 7.44 (H-17 / H-18), 7.62 / 7.41 (H-7 / H-8), 7.44 / 7.21 (H-18 / H-19), 7.41 / 7.24 (H-8 / H-9), 4.84 / 3.56 (H-22$_{1/2}$ / H-22$_{1/2}$), 4.40 / 3.61 (H-21$_{1/2}$ / H-21$_{1/2}$).

^{1}H,^{13}C-GHSQC (600 MHz / 151 MHz, [D$_6$]-dimethylsulfoxid, 298 K) δ (^{1}H) / δ (^{13}C) [in ppm] = 8.58 / 133.54 (H-14 / C-5/14), 8.24 / 129.66 (H-4 / C-4), 8.18 / 128.57 (H-16 / C-16), 8.15 / 128.64 (H-6 / C-6), 7.85 / 131.99 (H-26 / C-2/26), 7.82 / 127.99 (H-3 / C-3/18), 7.66 / 127.69 (H-17 / C-17), 7.62 / 126.83, 126.79 (H-7 / C-7/8), 7.44 / 127.99 (H-18 / C-3/18), 7.41 / 126.83, 126.79 (H-8 / C-7/8), 7.24 / 126.60 (H-9 / C-9), 7.21 /126.60 (H-9 / C-9), 4.84 / 42.72 (H-22$_{1/2}$ / C-22), 4.40 / 45.32 (H-21$_{1/2}$ / C-21), 3.61 / 45.32 (H21$_{1/2}$ / C-21), 3.56 / 42.72 (H-22$_{1/2}$ / C22).

^{1}H,^{13}C-GHMBC (600 MHz / 151 MHz, [D$_6$]-dimethylsulfoxid, 298 K) δ (^{1}H) / δ (^{13}C) [in ppm] = 8.58 / 130.54/130.49, 128.64/128.57, 89.51 (H-14 / C-10/12, C-6/16, C-23), 8.24 / 130.54/130.49, 128.64/128.57 (H-4 / C-10/12/20, C-6/16), 8.18 / 133.54, 130.54/130.49, 127.99 (H-16 / C-5/14, C-10/12/20, C-3/18), 8.15 / 130.54/13049, 129.66, 126.83/126.79 (H-6 / C-10/12/20, C-4, C-7/8), 7.85 / 122.62, 93.39 (H-26 / C-25, C-24), 7.82 / 134.07, 133.52, 45.32 (H-3 / C-1, C-5/14, C-21), 7.66 / 132.98, 126.93 (H-17 / C-15, C-19), 7.62 / 133.54, 126.60 (H-7 / C-5/14, C-9), 7.44 / 130.49, 128.57 (H-18 / C-20, C-16), 7.41 / 130.54, 128.64 (H-8 / C-10/12, C-6), 7.24 / 134.07, 133.54, 126.83/126.79 (H-9 / C-1, C-5/14, C-7/8), 7.21 / 136.13, 132.97, 127.69 (H-19 / C-11, C-15, C-17). [MT462_1]

8.2.1.14. Synthesis of compound (*S*)-**28**

Described experiment: MT503 Repeated:



First, compound (*S,S*)-**44** (33.1 mg, 46.5 µmol, 1 eq), was dissolved in dichloromethane (10 ml), then sodium hydroxide solution (1 M, 2.00 ml, 2.00 mmol, 16 eq), was added and the organic layer was separated, dried over sodium sulfate and concentrated in *vacuo*. It was then dissolved in dry toluene (2 ml), *n*-butyl lithium (51.1 µL, 2.7 M in toluene, 0.138 mmol, 3 eq.) was added and the solution immediately turned dark red. Then *N,N'*-diisopropylcarbodiimide (14.9 µl, 12.2 mg, 96.1 µmol, 2.1 eq) was added and the mixture was stirred at room temperature for one hour, leading to formation of a brown mixture. Methanol (5 ml) was added and all volatiles were removed to give the crude product as a yellow solid. The crude product was purified by HPLC (methanol/water, 15ml/min) and was obtained as the TFA salt (*S,S*)-**8**. (10.5 mg, 8.79 µmol, 32.5%).

$C_{72}H_{66}F_6N_6O_4$, MW = 1193.35 g/mol.

^{1}H-NMR (400 MHz, [D$_4$]-methanol, 298 K) δ [in ppm] = 8.44 (s, 2 H, H_{Aryl}), 8.16 (d, ^3J = 8.4 Hz, 2 H, H_{Aryl}), 8.08 (d, ^3J = 8.1 Hz, 4 H, H_{Aryl}), 7.71 (d, ^3J = 8.4 Hz, 2 H, H_{Aryl}), 7.67 (s, 4 H, H_{Aryl}), 7.65-7.56 (m, 4 H, H_{Aryl}), 7.47-7.36 (m, 8 H, H_{Aryl}), 5.22 (d, ^2J = 12.8 Hz, 2 H, $H_{Methylen}$), 4.51 (d, ^2J = 11.9 Hz, 2 H, $H_{Methylen}$), 4.08 (d, ^2J = 12.4 Hz, 2 H, $H_{Methylen}$), 3.99 (d, ^2J = 12.1 Hz, 2 H, $H_{Methylen}$), 3.80 (s br, 4 H, $H_{Isopropyl}$), 1.31 (d, ^2J = 6.5 Hz, 12 H, $H_{Isopropyl}$), 1.22 (d, ^2J = 6.4 Hz, 12 H, $H_{Isopropyl}$).

^{1}H-NMR (400 MHz, [D$_1$]-chloroform, 298 K) δ [in ppm] = 9.32 (s, 2 H, N-H), 9.08 (s, 2 H, NH), 8.34 (s, 2 H, H_{Aryl}), 8.09 (d, ^3J = 7.9 Hz, 2 H, H_{Aryl}), 8.04 – 7.99 (m, 4 H, H_{Aryl}), 7.67 (s, 4 H, H_{Aryl}), 7.61 – 7.52 (m, 8 H, H_{Aryl}), 7.45 (d, ^3J = 8.4 Hz, 2 H, H_{Aryl}), 7.42-7.34 (m, 4 H, H_{Aryl}), 5.12 (d, ^2J = 12.2 Hz, 2 H, $H_{Methylen}$), 4.33 (d, ^2J = 12.2 Hz, 2 H, $H_{Methylen}$), 4.03 (d, ^2J = 12.5 Hz, 2 H, $H_{Methylen}$), 3.87 (d, ^2J = 12.2 Hz, 2 H, $H_{Methylen}$), 3.36 (s br, 4 H, $H_{Isopropyl}$), 1.31 – 1.22 (m, 12 H, $H_{Isopropyl}$), 1.08 (d, ^2J = 10.3 Hz, 12 H, $H_{Isopropyl}$).

^{1}H-NMR (600 MHz, [D$_6$]-dimethylsulfoxid, 298 K) δ [in ppm] = 8.56 (s, 2 H, H-14), 8.21 (d, ^3J = 8.3 Hz, 2 H, H-4), 8.17 (d, ^3J = 8.3 Hz, 2 H, H-6), 8.14 (d, ^3J = 8.3 Hz, 2 H, H-16), 7.83 (d, ^3J = 8.4 Hz, 2 H, H-3), 7.70 (br s, 2 H, H-28),7.68 (s, 4 H, H-26 merged with NH_2 signal), 7.66 (t, ^3J = 7.5 Hz, 2 H, H-17), 7.61 (t, ^3J = 7.5 Hz, 2 H, H-7), 7.47 (t, ^3J = 7.7 Hz, 2 H, H-8), 7.44 (t, ^3J = 7.6 Hz, 2 H, H-18), 7.36 (d, ^3J = 8.5 Hz, 2 H, H-9), 7.31 (d, ^3J = 8.5 Hz, 2 H, H-19), 4.97 (d,

^{2}J = 13.2 Hz, 2 H, H-22$_{1/2}$), 4.46 (d, ^{2}J = 12.3 Hz, 2 H, H-21$_{1/2}$), 4.00 (d, ^{2}J = 12.8 Hz, 2 H, H-21$_{1/2}$), 3.94 (d, ^{2}J = 12.7 Hz, 2 H, H-22$_{1/2}$), 3.75 (br s, 4 H, H-29 merged with water signal), 1.20 (d, ^{2}J = 5.70 Hz, 12 H, H-30$_{1/2}$), 1.10 (br s, 12 H, H-30$_{1/2}$).

^{13}C-NMR (151 MHz, [D$_6$]-dimethylsulfoxid, 298 K) δ [in ppm] = 157.7 (q, ^{2}J = 30.6 Hz, TFA-Carbon), 155.7 (C-27), 135.6 (C-11), 133.85 (C-1/14), 133.82 (C-1/14), 133.2 (C-5), 132.7 (C-15), 131.8 (C-26), 131.4 (C-2), 130.7 (C-12), 130.4 (C-10/20), 130.0 (C-4), 128.6 (C-6/16), 128.1 (C-8), 127.54 (C-3), 127.47 (C-17), 126.9 (C-18), 126.7 (C-19), 126.6 (C-7), 126.5 (C-9), 122.4 (C-25), 119.2 (C-13), 92.5 (C-24) 89.3 (C-23), 51.3 (C-21), 48.8 (C-22), 46.4 (C-29), 23.2 (C-30$_{1/2}$), 21.9 (C-30$_{1/2}$).

^{1}H,^{1}H-COSY (600 MHz / 600 MHz, [D$_6$]-dimethylsulfoxid, 298 K) δ [in ppm] = 8.21 / 7.83 (H-4 / H-3), 8.17 / 7.61 (H-6 / H-7), 8.14 / 7.66 (H-16 / H-17), 7.83 / 8.21 (H-3 / H-4), 7.66 / 8.14, 7.44 (H-17 / H-16, H-18), 7.61 / 8.17, 7.47 (H-7 / H-6, H-8), 7.47 / 7.61 (H-8 / H-7), 7.44 / 7.66 (H-18 / H-17), 4.97 / 3.94 (H-22$_{1/2}$ / H-22$_{1/2}$), 4.46 / 4.00 (H-21$_{1/2}$ / H-21$_{1/2}$), 4.00 / 4.46 (H-21$_{1/2}$ / H-21$_{1/2}$),3.94 / 4.97 (H-22$_{1/2}$ / H-22$_{1/2}$).

^{1}H,^{13}C-GHSQC (600 MHz / 151 MHz, [D$_6$]-dimethylsulfoxid, 298 K) δ (^{1}H) / δ (^{13}C) [in ppm] = 8.56 / 133.85/133.82 (H-14 / C-1/14), 8.21 / 130.0 (H-4 / C-4), 8.17 / 128.6 (H-6 / C-6/16), 8.14 / 128.6 (H-16 / C-6/16), 7.83 / 127.54 (H-3 / C-3), 7.68 / 131.8 (H-26 / C26), 7.66 / 127.47 (H-17 / C-17), 7.61 / 126.6 (H-7 / C-7), 7.47 / 128.1 (H-8 / C-8), 7.44 / 126.9 (H-18 / C-18), 7.36 / 126.5 (H-9 / C-9), 7.31 / 126.7 (H-19 / C-19), 4.97 / 48.8 (H-22$_{1/2}$ / C-22), 4.46 / 51.3 (H-21$_{1/2}$ / C-21), 4.00 / 51.3 (H21$_{1/2}$ / C-21) 3.94 / 48.8 (H-22$_{1/2}$ / C22), 1.20 / 21.9 (H-30$_{1/2}$ / C-30$_{1/2}$), 1.10 / 23.2 (H-30$_{1/2}$ / C-30$_{1/2}$).

^{1}H,^{13}C-GHMBC (600 MHz / 151 MHz, [D$_6$]-dimethylsulfoxid, 298 K) δ (^{1}H) / δ (^{13}C) [in ppm] = 8.56 / 130.7, 130.4, 128.6, 89.3 (H-14 / C-12, C-10/20, C-6/16, C-23), 8.21 / 131.4, 130.4, 128.6 (H-4 / C-2, C-10/20, C-6/16), 8.17 / 133.85/133.82, 130.4, 128.1 (H-6 / C-1/14, C-10/20, C-8), 8.14 / 130.4, 126.9 (H-16 / C-10/20, C-18), 7.83 / 133.85/133.82, 133.2, 51.3 (H-3 / C-1/14, C-5, C-21), 7.68 / 122.4, 92.5 (H-26 / C-25, C-24), 7.66 / 132.7, 126.7 (H-17 / C-15, C-19), 7.61 / 133.2, 126.5 (H-7 / C-5, C-9), 7.47 / 130.4, 128.6 (H-8 / C-10/20, C-6/16), 7.44 / 130.4, 128.56 (H-18 / C-10/20, C-6/16), 7.36 / 133.85/133.82, 133.2, 126.6 (H-9 / C-1/14, C-5, C-7), 7.31 / 135.7, 132.7, 127.47 (H-19 / C-11, C-15, C-17), 4.97 / 135.6, 130.7, 119.2 (H-22$_{1/2}$ / C-11, C-12, C-13), 4.46 / 133.85/133.82, 131.4, 127.54 (H21$_{1/2}$ / C-1/14, C-2, C-3), 4.00 / 133.85/133.82, 131.4, 127.54 (H21$_{1/2}$ / C-1/14, C-2, C-3), 3.94 / 135.6, 130,7, 119.2 (H22$_{1/2}$ / C-11, C-12, C-13), 1.20 / 46.4, 23.2 (H-30$_{1/2}$ / C-29, C-30$_{1/2}$), 1.10 / 21.9 (H-30$_{1/2}$ / C-30$_{1/2}$). [MT503 DMSO]

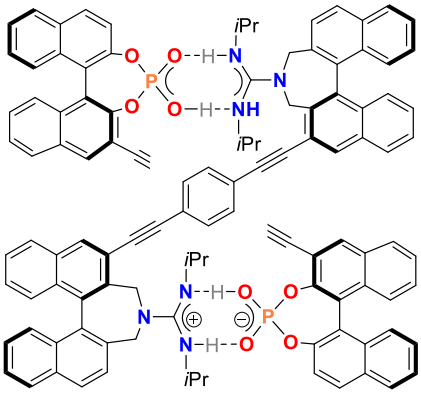
^{19}F-NMR (376.5 MHz, [D$_6$]-dimethylsulfoxid, 298 K) δ [in ppm] -73.61

MS (ESI-pos, MeOH**)**: *m/z* = 965.5266 ([M+H]$^{+}$, calcd. 965.5265 [$C_{68}H_{65}N_6$]$^{+}$)

IR (ATR-FT): $\tilde{\nu}$ (cm^{-1}) = 3240, 3061, 2973, 2927, 2878, 2853, 1683, 1606, 1455, 1267, 1250, 1200, 1128, 834, 799, 751, 718.

8.2.1.15. Synthesis of compound (*S*,*S*)-**28**+(*S*,*S*)-**29**

Described experiment: MT403 Repeated:



First, compound (*S*,*S*)-**28** (2.61 mg, 2.19 µmol, 1 eq), was dissolved in dimethylsulfoxid (0.729 ml), and directly added into a NMR-tube. Then compound (*S*,*S*)-**29** in dimethylsulfoxid (75 mM, 7.8 µl, 2.19 µmol, 1 eq), was added and the resulting solution was analyzed by NMR-spectroscopy.

Compound (*S*,*S*)-**28** (5.31 mg, 5.11 µmol, 1 eq), was dissolved in chloroform (0.852 ml), and 0.250 ml were transferred into a NMR-tube, Compound (*S*,*S*)-**29** (5.62 mg, 4.32 µmol, 1 eq), was dissolved in chloroform (0.721 ml), and 0.250 ml were transferred into the same NMR tube to give an overall concentration of 3 mM of the helix. The solution was analyzed by NMR-spectroscopy.

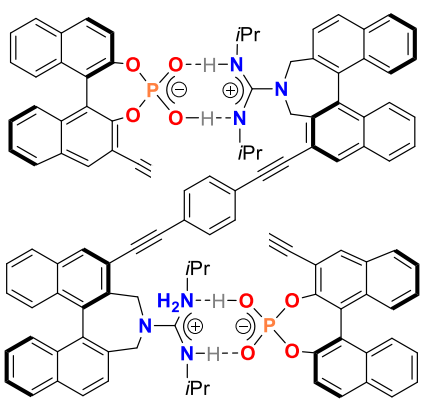
^{1}H-NMR (500 MHz, [D$_6$]-dimethylsulfoxid, 298 K) δ [in ppm] = 8.51 (s, 3 H, H_{Aryl}), 8.32 (s, 6 H, H_{Aryl}), 8.16-8.09 (m, 12 H, H_{Aryl}), 8.04-7.99 (m, 21 H, H_{Aryl}), 7.80-7.75 (m, 10 H, H_{Aryl}), 7.59 (s, 18 H, H_{Aryl}), 7.46-7.39 (m, 27 H, H_{Aryl}), 7.34-7.26 (m, 21 H, H_{Aryl}), 7.16-7.13 (m, 14 H, H_{Aryl}), 5.02 (d, ^2J = 13.2 Hz, 2 H, $H_{methylene}$), 4.37 (d, ^2J = 12.4 Hz, 2 H, $H_{methylene}$), 3.96 (d, ^2J = 12.8 Hz, 2 H, $H_{methylene}$), 3.88 (d, ^2J = 12.7 Hz, 2 H, $H_{methylene}$), 3.74 (br s, 4 H, $H_{isoprppyl}$), 1.22-1.01 (m, 24 H, $H_{isoprppyl}$, merged with tetrabutylammonium signals).

^{1}H-NMR (400 MHz, [D$_1$]-chloroform, 298 K) δ [in ppm] = 9.78 (s, 2 H, H_{Aryl}), 8.35 (s, 2 H, H_{Aryl}), 8.25 (s, 2 H, H_{Aryl}), 8.11 (d, ^3J = 8.9 Hz, 2 H, H_{Aryl}), 8.07-8-02 (m, 4 H, H_{Aryl}), 7.99-7.97 (m, 2 H, H_{Aryl}), 7.93-7.89 (m, 14 H, H_{Aryl}), 7.71 (s, 4 H, H_{Aryl}), 7.66-7.63 (m, 4 H, H_{Aryl}), 7.59-7.55 (m, 4 H, H_{Aryl}), 7.51-7.46 (m, 6 H, H_{Aryl}), 7.41-7.34 (m, 10 H, H_{Aryl}), 7.29-7.26 (m, 2 H, merged with chlorform signal, H_{Aryl}), 7.26-7.21 (m, 4 H, merged with chlorform signal H_{Aryl}), 5.29 (d, ^2J = 10.6 Hz, 2 H, $H_{methylene}$), 4.41 (d, ^2J = 12.4 Hz, 2 H, $H_{methylene}$), 4.05 (d, ^2J = 12.8 Hz, 2 H, $H_{methylene}$), 3.88 (d, ^2J = 12.7 Hz, 2 H, $H_{methylene}$), 3.36 (br s, 4 H, $H_{isoprppyl}$), 1.28-1.26 (m, 16 H, $H_{isoprppyl}$,), 1.16-1.12 (m, 8 H, $H_{isoprppyl}$).

[MT403-8]

8.2.1.16. Synthesis of compound (*S*,*S*)-**28**+(*R*,*R*)-**29**

Described experiment: MT402 Repeated:



First, compound (*S*,*S*)-**28** (2.61 mg, 2.19 µmol, 1 eq), was dissolved in dimethylsulfoxid (0.729 ml), and directly added into a NMR tube. Then compound (*R*,*R*)-**29** in dimethylsulfoxid (75 mM, 7.8 µl, 2.19 µmol, 1 eq), was added and the resulting solution was analyzed by NMR spectroscopy.

Compound (*S*,*S*)-**28** (5.31 mg, 5.11 µmol, 1 eq), was dissolved in chloroform (0.852 ml), and 0.250 ml were transferred into a NMR tube. Compound (*R*,*R*)-**29** (5.71 mg, 4.39 µmol, 1 eq), was dissolved in chloroform (0.732 ml), and 0.250 ml were transferred into the same NMR tube to give an overall concentration of 3 mM of the helix. The solution was analyzed by NMR spectroscopy.

^{1}H-NMR (500 MHz, [D$_6$]-dimethylsulfoxid, 298 K) δ [in ppm] = 8.51 (s, 3 H, H_{Aryl}), 8.34 (s, 4 H, H_{Aryl}), 8.31 (s, 3 H, H_{Aryl}), 8.16-8.08 (m, 11 H, H_{Aryl}), 8.05-7.98 (m, 23 H, H_{Aryl}), 7.81-7.76 (m, 10 H, H_{Aryl}), 7.58 (s, 21 H, H_{Aryl}), 7.46-7.38 (m, 29 H, H_{Aryl}), 7.32-7.26 (m, 24 H, H_{Aryl}), 7.17-7.13 (m, 17 H, H_{Aryl}), 4.99 (d, ^2J = 13.2 Hz, 2 H, $H_{methylene}$), 4.37 (d, ^2J = 12.4 Hz, 2 H, $H_{methylene}$), 3.96 (d, ^2J = 12.8 Hz, 2 H, $H_{methylene}$), 3.88 (d, ^2J = 12.7 Hz, 2 H, $H_{methylene}$), 3.74 (br s, 4 H, $H_{isoprppyl}$), 1.22-1.13 (m, 40 H, $H_{isoprppyl}$, merged with tetrabutylammonium signals), 1.02-1.01 (m, 18 H, $H_{isoprppyl}$).

^{1}H-NMR (400 MHz, [D$_1$]-chloroform, 298 K) δ [in ppm] = 9.76 (s, 2 H, H_{Aryl}), 8.26 (s, 2 H, H_{Aryl}), 8.18 (s, 2 H, H_{Aryl}), 8.06-8-7.74 (m, 22 H, H_{Aryl}), 7.61-7.48 (m,14 H, H_{Aryl}), 7.46-7.33 (m, 17 H, H_{Aryl}), 7.32-7.23 (m, 21 H, merged with chlorform signal, H_{Aryl}), 5.15 (d, ^2J = 10.6 Hz, 2 H, $H_{methylene}$), 4.33-4.10 (m, 4 H, $H_{methylene}$), 3.96-3.78 (m, 6 H, $H_{methylene}$), 3.36 (br s, 4 H, $H_{isoprppyl}$), 1.25-1.00 (m, 24 H, $H_{isoprppyl}$).

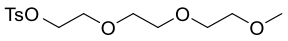
[MT402-8]

8.2.2. Synthesis of 1,1'- Binaphtyl based Phosphoric acids

8.2.2.1. Precursors

8.2.2.1.1. Synthesis of compound **84**[106]

Described experiment: MT355 Repeated:



Triethyleneglycol methyl ether (0.974 ml, 1.01 g, 6.09 mmol, 1 eq), 4-toluenesulfonyl chloride (1.45 g, 7.61 mmol, 1.25 eq), triethylamine (1.36 ml, 0.985 g, 9.7 mmol, 1.6 eq) and 4-dimethylaminopyridine (0.148 g, 1.22 mmol, 0.2 eq) were dissolved in dry dichloromethane (100 ml). The solution was stirred at 25 °C for 18 hours under argon atmosphere. Then the reaction mixture was diluted with diethylether and water (100 ml each). The organic layer was separated and then washed with 2 M hydrochloric acid (60 ml), a saturated solution of sodium bicarbonate (60 ml) and a saturated solution of sodium chloride (60 ml). The organic layer was dried over sodium sulfate, the solvent was removed to afford the product as a colourless oil (1.71 g, 5.38 mmol, 90.1%).

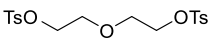
$C_{14}H_{22}O_6S$, MW = 318.1 g/mol.

^{1}H-NMR (400 MHz, [D$_1$]-chloroform, 298 K) δ [in ppm] = 7.70 (d, ^3J = 8.4 Hz, 2 H, CH_{Aryl}), 7.25 (d, ^3J = 8.4 Hz, 2 H, CH_{Aryl}), 4.08 -. 4.05 (m, 2 H, CH_2), 3.60 – 3.57 (m, 2 H, CH_2), 3.53 – 3.49 (m, 6 H, CH_2), 3.45 – 3.42 (m, 2 H, CH_2), 3.27 (s, 3H, CH_3), 2.35 (s, 3H, CH_3).

[MT355-1]

8.2.2.1.2. Synthesis of compound **83**[106]

Described experiment: THA17 Repeated:



Diethylene glycol (5.01 g, 47.1 mmol, 1 eq), 4-toluenesulfonyl chloride (17.96 g, 94.2 mmol, 2.2 eq), triethylamine (10.1 ml, 9.51 g, 94.2 mmol, 2 eq) and 4-dimethylaminopyridine (0.172 g, 1.43 mmol, 0.3 eq) were dissolved in dry dichloromethane (100 ml). The solution was stirred at 25 °C for 18 hours under argon atmosphere. Then the reaction mixture was diluted with diethylether and water (100 ml each). The organic layer was separated and then washed with 2 M hydrochloric acid (60 ml), a saturated solution of sodium bicarbonate (60 ml) and a saturated solution of sodium chloride (60 ml). The organic layer was dried over sodium sulfate, the solvent was removed to afford the product as a colourless oil (13.1 g, 31.6 mmol, 67.1%).

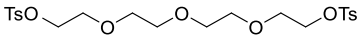
$C_{18}H_{22}O_7S_2$, MW = 414.5 g/mol.

^{1}H-NMR (400 MHz, [D$_1$]-chloroform, 298 K) δ [in ppm] = 7.79 (d, ^3J = 8.4 Hz, 4 H, CH_{Aryl}), 7.34 (d, ^3J = 8.4 Hz, 4 H, CH_{Aryl}), 4.16 -. 4.14 (m, 4 H, CH_2), 3.69 – 3.66 (m, 4 H, CH_2), 2.44 (s, 6H, CH_3).

[THA17-1]

8.2.2.1.3. Synthesis of compound **100**[106]

Described experiment: MT642 Repeated:



Tetraethylene glycol (5.01 g, 25.7 mmol, 1 eq), 4-toluenesulfonyl chloride (10.8 g, 56.5 mmol, 2.2 eq), triethylamine (7.17 ml, 5.20 g, 51.4 mmol, 2 eq) and 4-dimethylaminopyridine (0.942 g, 7.71 mmol, 0.3 eq) were dissolved in dry dichloromethane (100 ml). The solution was stirred at 25 °C for 18 hours under argon atmosphere. Then the reaction mixture was diluted with diethylether and water (100 ml each). The organic layer was separated and then washed with 2 M hydrochloric acid (60 ml), a saturated solution of sodium bicarbonate (60 ml) and a saturated solution of sodium chloride (60 ml). The organic layer was dried over sodium sulfate, the solvent was removed to afford the product as a colourless oil (10.9 g, 21.8 mmol, 84.9%).

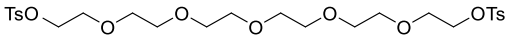
$C_{22}H_{30}O_9S_2$, MW = 502.6 g/mol.

^{1}H-NMR (400 MHz, [D$_1$]-chloroform, 298 K) δ [in ppm] = 7.79 (d, ^3J = 8.4 Hz, 4 H, CH_{Aryl}), 7.34 (d, ^3J = 8.4 Hz, 4 H, CH_{Aryl}), 4.16 - 4.14 (m, 4 H, CH_2), 3.69 – 3.66 (m, 4 H, CH_2), 3.57 – 3.55 (m, 8 H, CH_2), 2.44 (s, 6H, CH_3).

[MT642-1]

8.2.2.1.4. Synthesis of compound **101**[106]

Described experiment: SF064 Repeated:



Hexaethylene glycol (5.01 g, 17.7 mmol, 1 eq), 4-toluenesulfonyl chloride (7.42 g, 38.9 mmol, 2.2 eq), triethylamine (4.92 ml, 3.58 g, 35.4 mmol, 2 eq) and 4-dimethylaminopyridine (0.649 g, 5.31 mmol, 0.3 eq) were dissolved in dry dichloromethane (100 ml). The solution was stirred at 25 °C for 18 hours under argon atmosphere. Then the reaction mixture was diluted with diethylether and water (100 ml each). The organic layer was separated and then washed with 2 M hydrochloric acid (60 ml), a saturated solution of sodium bicarbonate (60 ml) and a saturated solution of sodium chloride (60 ml). The organic layer was dried over sodium sulfate, the solvent was removed to afford the product as a colourless oil (8.91 g, 15.1 mmol, 85.2%).

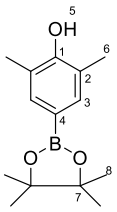
$C_{26}H_{38}O_{11}S_2$, MW = 590.7 g/mol.

^{1}H-NMR (400 MHz, [D$_1$]-chloroform, 298 K) δ [in ppm] = 7.79 (d, ^3J = 8.4 Hz, 4 H, CH_{Aryl}), 7.33 (d, ^3J = 8.4 Hz, 4 H, CH_{Aryl}), 4.16 -. 4.14 (m, 4 H, CH_2), 3.69 – 3.66 (m, 4 H, CH_2), 3.61 (s, 4H, CH_2), 3.57 (s, 4H, CH_2), 3.57 – 3.55 (m, 8 H, CH_2), 2.44 (s, 6H, CH_3).

[SF064-1]

8.2.2.1.5. Synthesis of compound **71d**[102,103]

Described experiment: MT348 Repeated: MT390



4-Bromo-2,5-dimethylphenol (1.00 g, 4.97 mmol, 1 eq.), bis(pinacolato)diboron (1.70 g, 6.71 mmol, 1.35 eq), [1,1′-bis(diphenylphosphino)ferrocene]dichloropalladium(II) (164 mg, 0.223 mmol, 0.045 eq) and potassium acetate (1.27 g, 12.9 mmol, 2.6 eq), were dissolved degassed 1,4-dioxane (20 mL). The solution was stirred at 90 °C for 2 hours under argon atmosphere. After cooling down to room temperature the solid was removed by filtration. The solvent was removed and the crude product was purified by silica gel flash column chromatography (cyclohexane:ethyl acetate:toluene = 5:1:5) to afford the product as a white solid (0.757 g, 3.054 mmol, 61.5%).

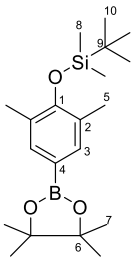
$C_{14}H_{21}O_3B$, MW = 248.1g/mol.

^{1}H-NMR (400 MHz, [D_1]-chloroform, 298 K) δ [in ppm] = 7.45 (s, 2 H, H-3), 4.83 (s, 1 H, H-5), 2.26 (s, 6 H, H-6), 1.33 (s, 12 H, H-8).

[MT390-3]

8.2.2.1.6. Synthesis of compound **71c**

Described experiment: MT455 Repeated: THA15



Compound **71d** (1.86 g, 7.52 mmol, 1 eq), *tert*-butyldimethylsilyl chloride (5.60 g, 37.6 mmol, 5 eq) and imidazole (2.55 g, 37.6 mmol, 5 eq), were dissolved in dry dimethylformamide (10 ml). The solution was stirred at 60 °C for five hours under argon atmosphere. After cooling down to room temperature the reaction mixture was diluted with diethylether (20 ml), was washed with water (10 ml) and an aqueous solution of lithium chloride (5%, 20 ml). The organic layer was dried over sodium sulfate, the solvent was removed and the crude product was purified by silica gel flash column chromatography (hexane:dichloromethane = 7:3) to afford the product as a white solid (1.97 g, 5.44 mmol, 72.4%).

$C_{20}H_{35}BO_3Si$, MW = 362.4 g/mol.

^{1}H-NMR (400 MHz, [D$_1$]-chloroform, 298 K) δ [in ppm] = 7.45 (s, 2 H, H-3), 2.22 (s, 6 H, H-5), 1.34 (s, 12 H, H-7), 1.02 (s, 9 H, H-10), 0.19 (s, 6 H, H-8),

^{13}C-NMR (101 MHz, [D$_1$]-chloroform, 298 K) δ [in ppm] = 155.36 (C-1), 135.73 (C-2+3), 128.24 (C-4), 83.62 (C-6), 26.23 (C-10), 25.00 (C-7), 18.93 (C-9), 17.73 (C-5), -2.79 (C-8).

^{1}H,^{1}H-COSY (400 MHz / 400 MHz, [D$_1$]-chloroform, 298 K) δ [in ppm] = 7.45 / 2.22 (H-3 / H-5), 2.22 / 7.45 (H-5 / H-3).

^{1}H,^{13}C-GHSQC (400 MHz / 101 MHz, [D$_1$]-chloroform, 298 K) δ (^{1}H) / δ (^{13}C) [in ppm] = 7.45 / 135.73 (H-3 / C-2+3), 2.22 / 17.73 (H-5 / C-5), 1.34 / 25.00 (H-7 / C-7), 1.02 / 26.23 (H-10 / C-10), 0.19 / -2.79 (H-8 / C-8).

^{1}H,^{13}C-GHMBC (400 MHz / 101 MHz, [D$_1$]-chloroform, 298 K) δ (^{1}H) / δ (^{13}C) [in ppm] = 7.45 / 155.36, 135.73, 17.73 (H-3 / C-1, C-2+3, C-5), 2.22 / 155.36, 135.73, 128.24 (H-5 / C-1, C-2+3, C-4), 1.34 / 83.62, 25.00 (H-7 / C-6, C-7), 1.02 / 26.23, 18.93 (H-10 / C-10, C-9), 0.19 / -2.79 (H-8 / C-8). [MT455-2]

Elemental analysis = calcd (%) for $C_{64}H_{52}N_2O_4$: C: 66.29, H: 9.74, O: 13.24; found:

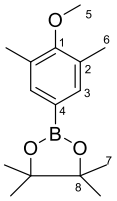
C: 65.9, H: 9.21, O: 13.2.

MS (ESI-pos, MeOH**)**: *m/z* = 363.2522 ([M+H]$^+$, calcd 363.2525 for [$C_{32}H_{31}O_4^+$]).

IR (ATR-FT): $\tilde{\nu}$ (cm^{-1}) = 2977, 2923, 2877, 1603, 1478, 1321, 1197, 1133, 1055, 966, 882, 855, 683. [MT455-3]

8.2.2.1.7. Synthesis of compound **71e**

Described experiment: MT563 Repeated:



Compound **71d** (3.69 g, 14.9 mmol, 1 eq) and potassium carbonate (2.55 g, 37.6 mmol, 5 eq), were suspended in acetone (40 ml). Then freshly destilled methyl iodide (2.77 ml, 6.31 g, 44.7 mmol, 3 eq) was added. The solution was stirred at 65 °C for 12 hours under argon atmosphere. After cooling down to room temperature the reaction mixture was diluted with water (20 ml), and the organic solvent was removed under reduced pressure. The residual aqueous phase was extracted with dichloromethane (50 ml) and the organic phase was washed with water (10 ml) and a saturated solution of sodium chloride (30 ml). The organic layer was dried over sodium sulfate, the solvent was removed and the product was obtained as a white solid (3.81 g, 14.5 mmol, 97.4%).

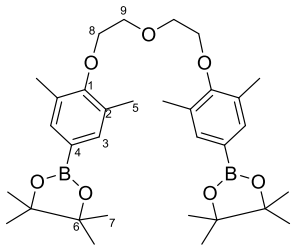
$C_{15}H_{23}BO_3$, MW = 262.2 g/mol.

^{1}H-NMR (400 MHz, [D_1]-chloroform, 298 K) δ [in ppm] = 7.49 (s, 2 H, H-3), 3.73 (s, 3 H, H-5), 2.29 (s, 6 H, H-6), 1.33 (s, 12 H, H-7).

[MT563-2]

8.2.2.1.8. Synthesis of compound **97**

Described experiment: MT575 Repeated:



Compound **71d** (3.00 g, 12.1 mmol, 2 eq) and caesium carbonate (5.91 g, 18.2 mmol, 3 eq) were dissolved in degassed acetonitrile (10 ml) and stirred for 15 minutes under argon. After the addition of diethyleneglycol bistosylate (2.88 g, 6.95 mmol, 1 eq) the reaction mixture was stirred at 90 °C for one hour. After cooling to room temperature ethyl acetate (10 ml) was added. Caesium carbonate was removed by filtration and all volatiles were removed in *vacuo*. The crude product was purified by column chromatography (21x3 cm, cyclohexane:ethyl acetatecyclohexane:ethyl acetate 10:1) and afforded the product as a colourless oil (3.10 g, 3.21 mmol, 78.6%).

$C_{32}H_{48}O_7B_2$, MW = 566.4 g/mol.

^{1}H-NMR (400 MHz, [D$_1$]-chloroform, 298 K) δ [in ppm] = 7.49 (s, 4 H, H-3), 4.00 – 3.98 (m, 4 H, H-8), 3.92 – 3.90 (m, 4 H, H-9), 2.30 (s, 12 H, H-5), 1.33 (s, 24 H, H-7).

^{13}C-NMR (101 MHz, [D$_1$]-chloroform, 298 K) δ [in ppm] = 158.71 (C-1), 135.76 (C-2+3), 130.58 (C-4), 83.80 (C-6), 71.44 (C-8), 70.89 (C-9), 24.99 (C-7), 16.17 (C-5).

^{1}H,^{1}H-COSY (400 MHz / 400 MHz, [D$_1$]-chloroform, 298 K) δ [in ppm] = 7.49 / 2.30 (H-3 / H-5), 4.00 – 3.98 / 3.92 – 3.90 (H-8 / H-9), 3.92 – 3.90 / 4.00 – 3.98 (H-9 / H-8), 2.30 / 7.49 (H-5 / H-3).

^{1}H,^{13}C-GHSQC (400 MHz / 101 MHz, [D$_1$]-chloroform, 298 K) δ (^{1}H) / δ (^{13}C) [in ppm] = 7.49 / 135.76 (H-3 / C-2+3), 4.00 – 3.98 / 71.44 (H-8 / C-8), 3.92 – 3.90 / 70.89 (H-9 / C-9), 2.30 / 16.17 (H-5 / C-5), 1.33 / 24.99 (H-7 / C-7).

^{1}H,^{13}C-GHMBC (400 MHz / 101 MHz, [D$_1$]-chloroform, 298 K) δ (^{1}H) / δ (^{13}C) [in ppm] = 7.49 / 158.71, 135.76, 16.17 (H-3 / C-1, C-2+3, C-5), 2.30 / 158.71, 135.76, 130.58 (H-5 / C-1, C-2+3, C-4), 1.33 / 83.80, 24.99 (H-7 / C-6, C-7). [MT575-5]

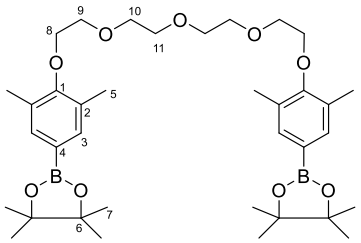
MS (ESI-pos, MeOH**)**: *m/z* = 589.3487 ([M+Na]$^+$, calcd. 589.3489 for [$C_{32}H_{48}O_7B_2Na^+$].

IR (ATR-FT): $\tilde{\nu}$ (cm^{-1}) = 2975, 2924, 2870, 1603, 1468, 1362, 1311, 1197, 1130, 1053, 966, 892, 853, 683.

[MT575]

8.2.2.1.9. Synthesis of compound **98**

Described experiment: MT646 Repeated:



Compound **71d** (2.00 g, 8.06 mmol, 2 eq) and caesium carbonate (3.93 g, 12.09 mmol, 3 eq), were dissolved in degassed acetonitrile (15 ml) and stirred for 15 minutes under argon. After the addition of tetraethyleneglycol bistosylate (1.99 g, 4.03 mmol, 1 eq) the reaction mixture was stirred at 90 °C for one hour. After cooling to room temperature ethyl acetate (10 ml) was added. Caesium carbonate was removed by filtration and all volatiles were removed in *vacuo*. The crude product was purified by column chromatography (21x3 cm, cyclohexane:ethyl acetate 6:1) and afforded the product as a colourless oil (2.11 g, 3.21 mmol, 80.1%).

$C_{36}H_{56}O_9B_2$, MW = 654.4 g/mol.

^{1}H-NMR (400 MHz, [D$_1$]-chloroform, 298 K) δ [in ppm] = 7.48 (s, 4 H, H-3), 3.96 – 3.93 (m, 4 H, H-8), 3.83 – 3.81 (m, 4 H, H-9), 3.76 – 3.70 (m, 8 H, H-10+11), 2.28 (s, 12 H, H-5), 1.33 (s, 24 H, H-7).

^{13}C-NMR (101 MHz, [D$_1$]-chloroform, 298 K) δ [in ppm] = 158.80 (C-1), 135.75 (C-2+3), 130.53 (C-4), 83.79 (C-6), 71.47 (C-8), 71.04 (C-10/11), 70.92 (C-10/11), 70.68 (C-9), 24.99 (C-7), 16.21 (C-5).

^{1}H,^{1}H-COSY (400 MHz / 400 MHz, [D$_1$]-chloroform, 298 K) δ [in ppm] = 7.48 / 2.28 (H-3 / H-5), 3.96 – 3.93 / 3.83 – 3.81 (H-8 / H-9), 3.83 – 3.81 / 3.96 – 3.93 (H-9 / H-8), 2.28 / 7.48 (H-5 / H-3).

^{1}H,^{13}C-GHSQC (600 MHz / 151 MHz, [D$_1$]-chloroform, 298 K) δ (^{1}H) / δ (^{13}C) [in ppm] = 7.48 / 135.75 (H-3 / C-2+3), 3.96 – 3.93 / 71.47 (H-8 / C-8), 3.83 – 3.81 / 70.68 (H-9 / C-9), 3.76 – 3.70 / 71.04/70.92 (H-10+11 / C-10/11), 2.28 / 16.21 (H-5 / C-5), 1.33 / 24.99 (H-7 / C-7).

^{1}H,^{13}C-GHMBC (400 MHz / 101 MHz, [D$_1$]-chloroform, 298 K) δ (^{1}H) / δ (^{13}C) [in ppm] = 7.48 / 158.80, 135.75, 16.21 (H-3 / C-1, C-2+3, C-5), 2.28 / 158.80, 135.75, 130.53 (H-5 / C-1, C-2+3, C-4), 1.33 / 83.79, 24.99 (H-7 / C-6, C-7). [MT646-5]

Elemental analysis = calcd (%) for $C_{36}H_{56}O_9B_2$: C: 66.07, H: 8.63, O: 22.00; found: C: 64.9, H: 9.3, O: -.

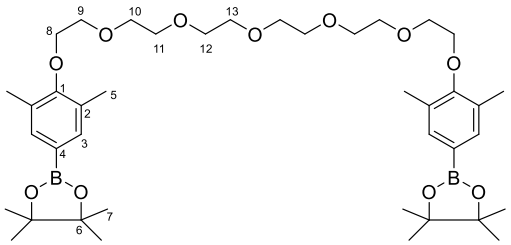
MS (ESI-pos, MeOH**)**: *m/z* = 677.4016 ([M+Na]$^+$, calcd. 677.4016 for [$C_{36}H_{56}O_9B_2Na^+$].

IR (ATR-FT): $\tilde{\nu}$ (cm^{-1}) = 2974, 2938, 2909, 2866, 1602, 1466, 1400, 1389, 1365, 1350, 1315, 1100, 1101, 1050, 964, 931, 892, 852, 684.

[MT646]

8.2.2.1.10. Synthesis of compound **99**

Described experiment: MT650 Repeated:



Compound **71d** (2.00 g, 8.06 mmol, 2.1 eq) and caesium carbonate (3.93 g, 12.09 mmol, 3 eq), were dissolved in degassed acetonitrile (15 ml) and stirred for 15 minutes under argon. After the addition of hexaethyleneglycol bistosylate (2.26 g, 3.83 mmol, 1 eq) the reaction mixture was stirred at 90 °C for one hour. After cooling to room temperature ethyl acetate (10 ml) was added. Caesium carbonate was removed by filtration and all volatiles were removed in *vacuo*. The crude product was purified by column chromatography (21x3 cm, cyclohexane:ethyl acetate 2:1) and afforded the product as a colourless oil (2.45 g, 3.29 mmol, 86.3%).

$C_{40}H_{64}O_{11}B_2$, MW = 742.6 g/mol.

^{1}H-NMR (400 MHz, [D$_1$]-chloroform, 298 K) δ [in ppm] = 7.48 (s, 4 H, H-3), 3.95 – 3.93 (m, 4 H, H-8), 3.83 – 3.80 (m, 4 H, H-9), 3.74 – 3.72 (m, 4 H, H-10), 3.70 – 3.68 (m, 4 H, H-11), 3.67 – 3.65 (m, 8 H, H-12+13), 2.28 (s, 12 H, H-5), 1.33 (s, 24 H, H-7).

^{13}C-NMR (101 MHz, [D$_1$]-chloroform, 298 K) δ [in ppm] = 158.80 (C-1), 135.74 (C-2+3), 130.53 (C-4), 83.79 (C-6), 71.47 (C-8), 71.01 (C-10), 70.83 (C-11/12/13), 70.77 (C-11/12/13), 70.66 (C-9), 24.99 (C-7), 16.21 (C-5).

^{1}H,^{1}H-COSY (400 MHz / 400 MHz, [D$_1$]-chloroform, 298 K) δ [in ppm] = 7.48 / 2.28 (H-3 / H-5), 3.95 – 3.93 / 3.83 – 3.80 (H-8 / H-9), 3.83 – 3.80 / 3.95 – 3.93 (H-9 / H-8), 2.28 / 7.48 (H-5 / H-3).

^{1}H,^{13}C-GHSQC (400 MHz / 101 MHz, [D$_1$]-chloroform, 298 K) δ (^{1}H) / δ (^{13}C) [in ppm] = 7.48 / 135.74 (H-3 / C-2+3), 3.95 – 3.93 / 71.47 (H-8 / C-8), 3.83 – 3.80 / 70.66 (H-9 / C-9), 3.74 – 3.72 / 71.01 (H-10 / C-10), 3.70 – 3.68 / 70.83/70.77 (H-11 / C-11/12/13), 3.67 – 3.65 / 70.83/70.77 (H-12+13 / C-11/12/13), 2.28 / 16.21 (H-5 / C-5), 1.33 / 24.99 (H-7 / C-7).

^{1}H,^{13}C-GHMBC (400 MHz / 101 MHz, [D$_1$]-chloroform, 298 K) δ (^{1}H) / δ (^{13}C) [in ppm] = 7.48 / 158.80, 135.74, 16.21 (H-3 / C-1, C-2+3, C-5), 2.28 / 158.80, 135.74, 130.53 (H-5 / C-1, C-2+3, C-4), 1.33 / 83.79, 24.99 (H-7 / C-6, C-7). [MT650-5]

Elemental analysis = calcd (%) for $C_{64}H_{52}N_2O_4$: C: 64.70, H: 8.69, O: 23.70; found: C: 64.3, H: 8.4.

MS (ESI-pos, MeOH**)**: *m/z* = 765.4540 ([M+Na]$^+$, calcd. 765.4540 for [$C_{40}H_{64}O_{11}B_2Na^+$].

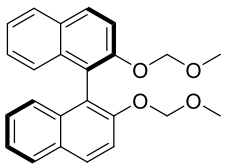
IR (ATR-FT): $\tilde{\nu}$ (cm^{-1}) = 2975, 2868, 1603, 1468, 1400, 1383, 1363, 1311, 1275, 1199, 1140, 1110, 1054, 853.

[MT650]

8.2.2.2. Synthesis of 3,3- Disubstituted compounds

8.2.2.2.1. Synthesis of compound (*R*)-**74**[104]

Described experiment: MT077 Repeated: MT528, 635



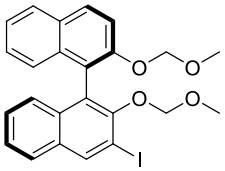
Sodium hydride (60 % in mineral oil, 3.07 g, 76.7 mmol 2.2 eq) was dissolved in dry tetrahydrofurane (200 ml) and the mixture was cooled to 0 °C. Then a solution of BINOL (10.1 g, 34.9 mmol, 1 eq) in tetrahydrofurane (100 ml) was added in a dropwise manner with rapid stirring. The solution was stirred at 0 °C for 1 hour, then at room temperature for further 30 minutes. After cooling down to 0 °C (chloromethyl)methylether (5.83 mL, 6.17 g, 76.7 mmol, 2.2 eq) was added carefully, and the suspension was stirred for another 24 hours. The reaction mixture was diluted with saturated ammonium chloride (75 ml), the organic layer was separated and then washed with saturated sodium chloride solution (25 ml), dried over sodium sulfate and concentrated in *vacuo*. The desired product was a light brown solid (12.9 g 34.7 mmol, 98.7 %).

$C_{24}H_{22}O_4$, MW = 374.4 g/mol.

^{1}H-NMR (300 MHz, [D$_1$]-Chloroform, 298 K) δ [in ppm] 8.00 (d, ^3J = 8.4 Hz, 2 H, CH_{Aryl}), 7.92 (d, ^3J = 8.4 Hz, 2 H, CH_{Aryl}), 7.64 (d, ^3J = 8.4 Hz, 2 H, CH_{Aryl}), 7.39 (m, 2 H, CH_{Aryl}), 7.30-7.19 (m, 4 H, CH_{Aryl}), 5.10 (d, ^2J = 14.1 Hz, 2 H, MOM-CH_2), 5.08 (d, ^2J = 14.1 Hz, 2 H, MOM-CH_2), 1.34 (s, 6 H, MOM-CH_3).
[MT077]

8.2.2.2.2. Synthesis of compound (*R*)-**72**[104]

Described experiment: MT078 Repeated: MT346, 399, 529, 571, 636



Compound (*R*)-**74** (8.00 g, 21.4 mmol, 1 eq) was dissolved in dry tetrahydrofurane (450 mL). After cooling down to -78 °C, ^{n}butyllithium (2.7 M in toluene, 9.88 mL, 26.7 mmol, 1.25 eq) was added. The solution was then stirred for 2 hours under argon atmosphere. At -78 °C a solution of iodine (7.57 g, 29.96 mmol, 1.4 eq) in tetrahydrofurane (100 ml) was added in a dropwise manner with rapid stirring. Then the reaction mixture was warmed to room temperature and stirred for further 12 hours. At 0 °C, a solution of sodium sulfite (37%, 200 mL) was added, the mixture was then stirred for another hour. After diluting with water (200 mL), the organic layer was separated. The aqueous layer was extracted with ethyl acetate (3 x 100 mL), and the combined organic layer was washed with saturated sodium chloride solution (50 mL), dried over sodium sulfate and concentrated in *vacuo*. The crude product was purified by silica gel flash column chromatography (cyclohexane:ethyl acetate = 20:1) to afford the product as a bright yellow solid (7.91 g, 15.8 mmol, 73.9 %).

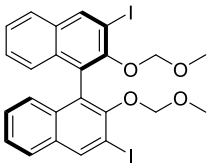
$C_{24}H_{21}IO_4$, MW = 500.3 g/mol.

^{1}H-NMR (300 MHz, [D$_1$]-Chloroform, 298 K) δ [in ppm] 8.52 (s, 1 H, CH_{Aryl}), 7.96 (d, ^3J = 8.98 Hz, 1 H, CH_{Aryl}), 7.86 (d, ^3J = 8.1 Hz, 1 H, CH_{Aryl}), 7.78 (d, ^3J = 8.1 Hz, 1 H, CH_{Aryl}), 7.58 (d, ^3J = 9.1 Hz 1 H, CH_{Aryl}), 7.58 (d, ^3J = 9.06 Hz 1 H, CH_{Aryl}), 7.42 – 7.34 (m, 2 H, CH_{Aryl}), 7.31 – 7.22 (m, merged with $CDCl_3$ – signal, 1 H, CH_{Aryl}), 7.19 – 7.13 (m, 2 H, CH_{Aryl}), 5.14 (d, ^2J = 6.9 Hz, 1 H, MOM-CH_2), 5.04 (d, ^2J = 6.9 Hz, 1 H, MOM-CH_2), 4.73 (d, ^2J = 5.2 Hz, 1 H, MOM-CH_2), 4.69 (d, ^2J = 5.2 Hz, 1 H, MOM-CH_2), 3.20 (s, 3 H, MOM-CH_3), 2.72 (s, 3 H, MOM-CH_3).

[MT078-2]

8.2.2.2.3. Synthesis of compound (*R*)-**73**[104]

Described experiment: MT571 Repeated:



Compound (*R*)-**74** (4.00 g, 10.7 mmol, 1 eq) was dissolved in dry tetrahydrofurane (120 ml). After cooling down to -78 °C, *n*butyllithium (2.7 M in toluene, 8.91 ml, 24.1 mmol, 2.25 eq) was added. The solution was then stirred for 2 hours under argon atmosphere. At -78 °C a solution of iodine (8.13 g, 52.1 mmol, 3 eq) in tetrahydrofurane (100 ml) was added in a dropwise manner with rapid stirring. Then the reaction mixture was warmed to room temperature and stirred for further 12 hours. At 0 °C, a solution of sodium sulfite (37%, 200 mL) was added, the mixture was then stirred for another hour. After diluting with water (200 ml), the organic layer was separated. The aqueous layer was extracted with ethyl acetate (3 x 100 ml), and the combined organic layer was washed with saturated sodium chloride solution (50 ml), dried over sodium sulfate and concentrated in *vacuo*. The crude product was purified by silica gel flash column chromatography (cyclohexane:ethyl acetate = 20:1) to afford the product as a bright yellow solid (3.34 g, 5.33 mmol, 50 %).

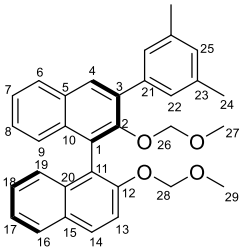
$C_{24}H_{20}I_2O_4$, MW = 626.2 g/mol.

^{1}H-NMR (400 MHz, [D$_1$]-Chloroform, 298 K) δ [in ppm] 8.54 (s, 2 H, CH_{Aryl}), 7.78 (d, ^3J = 8.4 Hz, 2 H, CH_{Aryl}), 7.43 (dt, ^3J = 7.5 Hz, ^4J = 1.2 Hz, 2 H, CH_{Aryl}), 7.30 (dt, ^3J = 7.7 Hz, ^4J = 1.3 Hz, 2 H, CH_{Aryl}), 7.17 (d, ^3J = 8.7 Hz, 2 H, CH_{Aryl}), 4.81 (d, ^2J = 5.6 Hz, 2 H, MOM-CH_2), 4.69 (d, ^2J = 5.6 Hz, 2 H, MOM-CH_2), 2.60 (s, 6 H, MOM-CH_3).

[MT571-1]

8.2.2.2.4. Synthesis of compound (*R*)-**76a**[114]

Described experiment: TCH9 Repeated: JT69, TCH26



(*R*)-3-Iodo-2,2´-bis(methoxymethoxy)-1,1´-binaphthyl (3.52 g, 7.03 mmol, 1 eq), 3,5-dimethylphenylboronic ester **71a** (1.32 g, 8.79 mmol, 1.25 eq), tetrakis(triphenylphosphine)palladium(0) (0.725 g, 0.703 mmol, 0.1 eq) were dissolved in a mixture of degassed sodium carbonate (2 M, 18.3 ml, 36.6 mmol, 5.2 eq) and degassed dimethoxy ethane (40 ml). The reaction mixture was stirred at 90 °C for five hours. After cooling to room temperature a saturated solution of ammonium chloride (50 ml) and ethyl acetate (50 ml) were added. After separating the two layers, the aqueous layer was extracted with ethyl acetate (2x 30 ml), and the combined organic layers were dried over sodium sulfate and were concentrated in *vacuo*. The crude product was purified by silica gel flash column chromatography (21x3 cm, cyclohexane:ethyl acetate = 20:1) to afford the product as a bright yellow solid (2.97 g, 6.21 mmol, 88.1%).

$C_{32}H_{30}O_4$, MW = 478.6 g/mol.

^{1}H-NMR (600 MHz, [D$_1$]-chloroform, 298 K) δ [in ppm] = 8.08 (d, ^3J = 9.05 Hz, 1 H, H-14), 8.03 (d, ^3J = 7.7 Hz, 1 H, H-6), 8.02 (s, 1 H, H-4), 7.96 (d, ^3J = 7.9 Hz, 1 H, H-16), 7.65 (d, ^3J = 9.1 Hz, 1 H, H-13), 7.44 (t, ^3J = 7.7 Hz, 1 H, H-7), 7.38 (t, ^3J = 7.3 Hz, 1 H, H-17), 7.31 (t, ^3J = 9.1 Hz, 1 H, H-18), 7.29 (s, 2 H, H-22), 7.27 (m, 1 H, H-8), 7.07 (d, ^3J = 8.2 Hz, 1 H, H-19), 7.04 – 7.03 (m, 2 H, H-9+25), 5.21 (d, ^2J = 6.8 Hz, 1 H, H-26$_{1/2}$/ H-28$_{1/2}$), 5.16 (d, ^2J = 6.6 Hz, 1 H, H-26$_{1/2}$/ H-27$_{1/2}$), 4.29 (d, ^2J = 5.5 Hz, 1 H, H-26$_{1/2}$/ H-27$_{1/2}$), 4.23 (d, ^2J = 5.5 Hz, 1 H, H-26$_{1/2}$/ H-27$_{1/2}$), 3.16 (s, 3 H, H-27/29), 2.34 (s, 6 H, H-24), 2.30 (s, 3 H, H-27/29).

^{13}C-NMR (151 MHz, [D$_1$]-chloroform, 298 K) δ [in ppm] = 152.40 (C-2), 150.38 (C-12), 138.36 (C-21), 137.20 (C-23), 135.27 (C-3), 133.43 (C-20), 132.56 (C-10), 130.61 (C-5), 129.90 (C-4), 129.62 (C-14), 129.02 (C-15), 128.71 (C-25), 128.17 (C-6), 127.95 (C-16), 127.07 (C-22), 126.61 (C-18), 126.32 (C-8), 125.78 (C-1), 125.16 (C-7), 124.99 (C-9), 124.84 (C-19), 123.84 (C-17), 119.50 (C-11), 115.96 (C-13), 97.77 (C-26/28), 93.85 (C-26/28), 55.41 (C-27/29), 55.38 (C-27/29), 21.02 (C-24).

^{1}H,^{1}H-COSY (600 MHz / 600 MHz, [D$_1$]-chloroform, 298 K) δ [in ppm] = 8.08 / 7.65 (H-14 / H-13), 8.03 / 7.44 (H-6 / H-7), 7.96 / 7.38 (H-16 / H-17), 7.65 / 8.08 (H-13 / H-14), 7.44 / 8.03 (H-7 / H-6), 7.38 / 7.96 (H-17 / H-16), 7.29 / 7.04 – 7.03, 2.34 (H-22 / H-9+25, H-24), 7.04 – 7.03 / 7.29, 2.34 (H-9/25 / H-22, H-24), 2.34 / 7.29, 7.04 – 7.03 (H-24 / H-22, H-9/25).

^{1}H,^{13}C-GHSQC (600 MHz / 151 MHz, [D$_1$]-chloroform, 298 K) δ (^{1}H) / δ (^{13}C) [in ppm] = 8.08 / 129.62 (H-14 / C-14), 8.03 / 128.17 (H-6 / C-6), 8.02 / 129.90 (H-4 / C-4), 7.96 / 127.95 (H-16 / C-16), 7.65 / 115.96 (H-13 / C-13), 7.44 / 125.16 (H-7 / C-7), 7.38 / 123.84 (H-17 / C-17), 7.31 / 126.61 (H-18 / C-18), 7.29 / 127.07 (H-22 / C-22), 7.27 / 126.32 (H-8 / C-8), 7.07 / 124.84 (H-19 / C-19), 7.04 – 7.03

[114] First done by John Toddenhöfer (former trainee in the Niemeyer Group, Supervision Maike Thiele)

/ 128.71, 124.99 (H-9+25 / C-25+9), 5.21 / 93.85 (H-$26_{1/2}$/ H-$28_{1/2}$/ C-26/28), 5.16 / 93.85 (H-$26_{1/2}$/ H-$28_{1/2}$/ C-26/28), 4.29 / 97.77 (H-$26_{1/2}$/ H-$28_{1/2}$/ C-26/27), 4.23 / 97.77 (H-$26_{1/2}$/ H-$28_{1/2}$/ C-26/28), 3.16 / 55.41 (H-27/29 / C-27/29), 2.34 / 21.02 (H-24 / C-24), 2.30 / 55.38 (H-27/29 / C-27/29).

^{1}H,^{13}C-GHMBC (600 MHz / 151 MHz, [D_1]-chloroform, 298 K) δ (^{1}H) / δ (^{13}C) [in ppm] = 8.08 / 133.43, 127.95 (H-14 / C-20, C-16), 8.03 / 132.56, 129.90, 126.32 (H-6 / C-10, C-4, C-8), 8.02 / 138.36, 132.56, 128.17 (H-4 / C-21, C-10, C-6), 7.96 / 133.41, 129.62, 126.61 (H-16 / C-20, C-14, C-18), 7.65 / 129.02, 119.50 (H-13 / C-15, C-11), 7.44 / 130.61, 124.99 (H-7 / C-5, C-9), 7.38 / 129.02, 124.84 (H-17 / C-15, C-19), 7.31 / 133.43, 127.95 (H-18 / C-20, C-16), 7.29 / 135.27, 128.71, 127.07 (H-22 / C-3, C-25, C-22), 7.27 / 132.56 (H-8 / C-10), 7.07 / 129.02, 123.84 (H-19 / C-15, C-17), 7.04 – 7.03 / 130.61, 127.07, 125.16 (H-9+25 / C-5, C-22, C-7), 3.16 / 93.85 (H-27/29 / C-26/28), 2.34 / 137.20, 128.71, 127.07 (H-24 / C-23, C-25, C-22), 2.30 / 97.77 (H-27/29 / C-26/28).

[TCH9-3]

Elemental analysis = calcd (%) for $C_{64}H_{52}N_2O_4$: C: 63.58, H: 4.84, O: 10.59, I: 20.99; found:

C: 64.9, H: 5.21, O: 10.2.

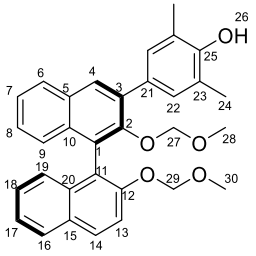
MS (ESI-pos, MeOH**)**: *m/z* = 501.2100 ([M+Na]$^+$, calcd. 501.2036 for [$C_{32}H_{30}O_4Na^+$].

IR (ATR-FT): $\tilde{\nu}$ (cm^{-1}) = 3064, 2982, 2973, 2938, 2916, 2851, 2818, 1621, 1594, 1509, 1495, 1471, 1433, 1414, 1389, 1235, 1157, 1146.

[TCH9-3]

8.2.2.2.5. Synthesis of compound (*R*)-**76d**

Described experiment: MT366 Repeated:



Compound (*R*)-**72** (100.0 mg, 0.199 mmol, 1 eq), the boronic ester **71d** (61.99 mg, 0.249 mmol, 1.25 eq), tetrabutylammoniumhydroxide 30 hydrate (183 mg, 0.229 mmol, 1.15 eq), tris(dibenzylideneacetone)dipalladium(0) (9.11 mg, 9.95 µmol, 0.05 eq) and tri(*o*-tolyl)phosphine (7.26 mg, 23.8 µmol, 0.12 eq) were dissolved in a degassed solution of toluene and water (1:5, 5 ml total). The reaction mixture was stirred at 90 °C for three hours. After cooling to room temperature, water (10 ml) and ethyl acetate (10 ml) were added. The aqueous phase was extracted with ethyl acetate (10 ml) and the combined organic layer was washed with a saturated solution of sodium chloride (10 ml). The organic layer was dried over sodium sulfate and concentrated in *vacuo*. The crude product was purified by column chromatography (21x2 cm, Cy:EA 8:1) and afforded the product as a white solid (70.0 mg, 0.142 mmol, 71.1%).

$C_{32}H_{30}O_5$, MW = 494.2 g/mol.

^{1}H-NMR (400 MHz, [D$_6$]-dimethylsulfoxid, 298 K) δ [in ppm] = 8.56 (s, 1 H, H-26), 8.27 (d, ^3J = 8.9 Hz, 1 H, H-14), 8.19 (d, ^3J = 8.5 Hz, 1 H, H-6), 8.16 (s, 1 H, H-4), 8.15 (d, ^3J = 7.7 Hz, 1 H, H-16), 7.84 (d, ^3J = 9.2 Hz, 1 H, H-13), 7.61 (t, ^3J = 7.6 Hz, 1 H, H-7), 7.57 (t, ^3J = 7.6 Hz, 1 H, H-17), 7.50 (t, ^3J = 7.4 Hz, 1 H, H-18), 7.45 – 7.43 (m, 3 H, H-8+22), 7.26 (d, ^3J = 8.6 Hz, 1 H, H-19), 7.21 (d, ^3J = 8.6 Hz, 1 H, H-9), 5.40 (d, ^2J = 6.9 Hz, 1 H, H-29$_{1/2}$), 5.35 (d, ^2J = 6.9 Hz, 1 H, H-29$_{1/2}$), 4.49 (d, ^2J = 5.4 Hz, 1 H, H-27$_{1/2}$), 4.45 (d, ^2J = 5.4 Hz, 1 H, H-27$_{1/2}$), 3.36 (s, 3 H, H-30), 2.50 (s, 3 H, H-28), 2.43 (s, 6 H, H-24).

^{13}C-NMR (101 MHz, [D$_6$]-dimethylsulfoxid, 298 K) δ [in ppm] = 152.73 (C-25), 152.39 (C-12), 150.45 (C-2), 135.18 (C-3), 133.48 (C-20), 132.22 (C-10), 130.71 (C-5), 129.51 (C-4/14), 129.49 (C-4/14), 129.17 (C-21), 129.12 (C-22), 129.00 (C-15), 128.00 (C-6), 127.91 (C-16), 126.53 (C-18), 125.97 (C-8), 125.68 (C-1), 125.02 (C-7), 124.97 (C-19), 124.92 (C-9), 124.05 (C-23), 123.80 (C-17), 119.70 (C-11), 115.99 (C-13), 97.52 (C-27), 93.84 (C-29), 55.38 (C-28/30), 16.74 (C-24).

^{1}H,^{1}H-COSY (400 MHz / 400 MHz, [D$_6$]-dimethylsulfoxid, 298 K) δ [in ppm] = 8.27 / 7.84 (H-14 / H-13), 8.19 / 7.61 (H-6 / H-7), 8.15 / 7.57 (H-16 / H-17), 7.84 / 8.27 (H-13 / H-14), 7.61 / 8.19 (H-7 / H-6), 7.57 / 8.15 (H-17 / H-16), 7.50 / 7.26 (H-18 / H-19), 7.44 / 7.21, 2.43 (H-8+22 / H-9, H-24), 7.21 /, 7.45-7.43 (H-9 / H-8+22), 2.43 / 7.45-7.43 (H-24 / H-8/22).

^{1}H,^{13}C-GHSQC (400 MHz / 101 MHz, [D$_6$]-dimethylsulfoxid, 298 K) δ (^{1}H) / δ (^{13}C) [in ppm] = 8.27 / 129.51/129.49 (H-14 / C-4/14), 8.19 / 128.00 (H-6 / C-6), 8.16 / 129.51/129.49 (H-4 / C-4/14), 8.15 / 127.91 (H-16 / C-16), 7.84 / 115.99 (H-13 / C-13), 7.61 / 125.02 (H-7 / C-7), 7.57 / 123.80 (H-17 / C-17), 7.50 / 126.53 (H-18 / C-18), 7.45 – 7.43 / 129.12, 125.97 (H-8+22 / C-22, C-8), 7.26 / 124.97

(H-19 / C-19), 7.21 / 124.92 (H-9 / C-9), 5.40 / 93.84 (H-$29_{1/2}$ / C-29), 5.35 / 93.84 (H-$29_{1/2}$ / C-29), 4.49 / 97.52 (H-$27_{1/2}$ / C-27), 4.45 / 97.52 (H-$27_{1/2}$ / C-27), 3.36 / 55.38 (H-30 / C-28/30), 2.50 / 55.38 (H-28 / C-28/30), 2.43 / 16.74 (H-24 / C-24).

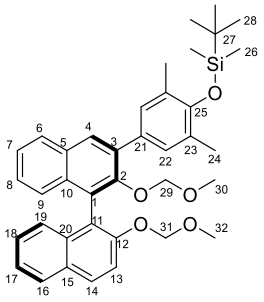
^{1}H,^{13}C-GHMBC (400 MHz / 101 MHz, [D$_6$]-dimethylsulfoxid, 298 K) δ (^{1}H) / δ (^{13}C) [in ppm] = 8.56 / 124.05 (H-26 / C-23), 8.27 / 152.39, 133.48, 127.91 (H-14 / C-12, C-20, C-16), 8.19 / 132.22, 129.51/129.49, 125.97 (H-6 / C-10, C-4/14, C-8), 8.16 / 150.45, 132.22, 129.17 (H-4 / C-2, C-10, C-21), 8.15 / 133.48, 126.53 (H-16 / C-20, C-18), 7.84 / 129.00, 119.67 (H-13 / C-15, C-11), 7.61 / 130.71, 124.92 (H-7 / C-5, C-9), 7.57 / 129.00, 124.97 (H-17 / C-15, C-19), 7.50 / 133.48, 127.91 (H-18 / C-20, C-16), 7.45 – 7.43 / 152.73, 135.18, 132.22, 129.17, 128.00, 16.74 (H-8+22 / C-25, C-3, C-10, C-21, C-6, C24), 7.26 / 129.00, 123.80, 119.70 (H-19 / C-15, C-17, C-11), 7.21 / 130.71, 125.68, 125.02 (H-9 / C-5, C-1, C-7), 5.40 / 152.39, 55.38 (H-$29_{1/2}$ / C-12, C-28/30), 5.35 / 152.39, 55.38 (H-$29_{1/2}$ / C-12, C-28/30), 4.49 / 150.45, 55.38 (H-$27_{1/2}$ / C-2, C-28/30), 4.45 / 150.45, 55.38 (H-$27_{1/2}$ / C-2, C-28/30), 3.36 / 93.84 (H-30 / C-29), 2.50 / 97.52 (H-28 / C-27), 2.43 / 152.73, 129.12, 124.05 (H-24 / C-25, C-22, C23).

[MT366-2]

Elemental analysis = calcd (%) for $C_{32}H_{30}O_5$: C: 77.71, H: 6.11, O: 16.17; found: C: 71.95, H: 5.70, O: 15.95
MS (ESI-pos, MeOH**)**: *m/z* = 517.1991 ([M+Na]$^+$, calcd for $C_{32}H_{30}O_5Na^+$ = 517.1985)
IR (ATR-FT): $\tilde{\nu}$ (cm^{-1}) = 3519, 3451, 3056, 2925, 2852, 2827, 2364, 2248, 1617, 1592, 1492, 1430, 1390, 1330, 1259, 1240, 1197, 1151, 1076,1039, 1014, 979, 910, 813, 732.
[MT366-2]

8.2.2.2.6. Synthesis of compound (*R*)-**76c**

Described experiment: MT473 Repeated: MT460, MT577, MT639



(*R*)-3-Iodo-2,2´-bis(methoxymethoxy)-1,1´-binaphthyl (3.51 g, 6.99 mmol, 1 eq), the boronic ester **71d** (3.16 g, 8.74 mmol, 1.25 eq), tetrabutylammonium hydroxide 30-hydrate (6.43 g, 8.04 mmol, 1.15 eq), tris(dibenzylideneacetone)dipalladium(0) (321 mg, 0.349 mmol, 0.05 eq) and tri(*o*-tolyl)phosphine (255 mg, 0.838 mmol, 0.12 eq) were dissolved in a degassed mixture of toluene and water (1:5, 20 ml total). The reaction mixture was stirred at 90 °C for three hours. After cooling to room temperature water (100 ml) and ethyl acetate (100 ml) were added. The aqueous phase was extracted with ethyl acetate (100 ml) and the combined organic layer was washed with a saturated solution of sodium chloride (100 ml). The organic layer was dried over sodium sulfate and concentrated in *vacuo*. The crude product was purified by column chromatography (21x2 cm, cyclohexane:ethyl acetate 15:1) and afforded the product as a white solid (3.21 g, 5.26 mmol, 76.1%).

$C_{38}H_{44}O_5Si$, MW = 608.8 g/mol.

^{1}H-NMR (400 MHz, [D$_6$]-dimethylsulfoxid, 298 K) δ [in ppm] = 8.08 (d, ^3J = 9.1 Hz, 1 H, H-14), 8.02 (s, 1 H, H-4), 8.00 (d, ^3J = 8.1 Hz, 1 H, H-6), 7.96 (d, ^3J = 8.1 Hz, 1 H, H-16), 7.65 (d, ^3J = 9.1 Hz, 1 H, H-13), 7.43 (dt, ^3J = 7.5 Hz, 1.29 Hz, 1 H, H-7), 7.38 (dt, ^3J = 7.5 Hz, 1.3 Hz, 1 H, H-17), 7.33 – 7.29 (m, 3 H, H-18+22), 7.27 (dt, ^3J = 7.6 Hz, 1.31 Hz, 1 H, H-8), 7.07 (d, ^3J = 8.6 Hz, 1 H, H-19), 7.02 (d, ^3J = 8.5 Hz, 1 H, H-9), 5.21 (d, ^2J = 7.0 Hz, 1 H, H-31), 5.16 (d, ^2J = 7.0 Hz, 1 H, H-31), 4.31 (d, ^2J = 5.5 Hz, 1 H, H-29), 4.24 (d, ^2J = 5.5 Hz, 1 H, H-29), 3.16 (s, 3 H, H-32), 2.35 (s, 3 H, H-30), 2.24 (s, 6 H, H-24), 1.01 (s, 9 H, H-28), 0.20 (s, 6 H, H-26).

^{13}C-NMR (101 MHz, [D$_6$]-dimethylsulfoxid, 298 K) δ [in ppm] = 152.39 (C-12), 151.09 (C-25), 150.50 (C-2), 134.93 (C-3), 133.41 (C-20), 132.40 (C-10), 131.42 (C-21), 130.67 (C-5), 129.70 (C-22), 129.62 (C-4/14), 129.58 (C-4/14), 129.03 (C-15), 128.08 (C-6), 127.96 (C-16), 127.78 (C-23), 126.61 (C-18), 126.14 (C-8), 125.67 (C-1), 125.10 (C-7), 124.94 (C-9), 124.82 (C-19), 123.84 (C-17), 119.56 (C-11), 115.97 (C-13), 97.72 (C-29), 93.86 (C-31), 55.44 (C-30/32), 55.41 (C-30/32), 25.97 (C-28), 18.53 (C-27), 17.61 (C-24), -3.10 (C-26).

^{1}H,^{1}H-COSY (400 MHz / 400 MHz, [D$_6$]-dimethylsulfoxid, 298 K) δ [in ppm] = 8.08 / 7.65 (H-14 / H-13), 8.00 / 7.43 (H-6 / H-7), 7.96 / 7.38 (H-16 / H-17), 7.65 / 8.08 (H-13 / H-14), 7.43 / 8.00 (H-7 / H-6), 7.38 / 7.96 (H-17 / H-16), 7.33 – 7.29 / 7.07, 2.24 (H-18+22 / H-19, H-24), 7.27 / 7.02 (H-8 / H-9), 7.07 / 7.33 – 7.29 (H-19 / H-18+22), 7.02 / 7.27 (H-9 / H-8), 2.24 / 7.33 – 7.29 (H-24 / H-18+22).

^{1}H,^{13}C-GHSQC (400 MHz / 101 MHz, [D$_6$]-dimethylsulfoxid, 298 K) δ (^{1}H) / δ (^{13}C) [in ppm] = 8.08 / 129.62/129.58 (H-14 / C-4/14), 8.02 / 129.62/129.58 (H-4 / C-4/14), 8.00 / 128.08 (H-6 / C-6), 7.96 / 127.96 (H-16 / C-16), 7.65 / 115.97 (H-13 / C-13), 7.43 / 125.10 (H-7 / C-7), 7.38 / 123.84 (H-17 / C-17), 7.33 – 7.29 / 129.70, 126.61 (H-18 / C-22, C-18), 7.27 / 126.14 (H-8 / C-8), 7.07 / 124.82 (H-19

/ C-19), 7.02 / 124.94 (H-9 / C-9), 5.21 / 93.86 (H-$31_{1/2}$ / C-31), 5.16 / 93.86 (H-$31_{1/2}$ / C-31), 4.31 / 97.72 (H-$29_{1/2}$ / C-29), 4.24 / 97.72 (H-$29_{1/2}$ / C-29), 3.16 / 55.44/55.41 (H-32 / C-30/32), 2.35 / 55.44/55.41 (H-30 / C-30/32), 2.24 / 17.61 (H-24 / C-24), 1.01 / 25.97 (H-28 / C-28), 0.20 / -3.10 (H-26 / C-31).

^{1}H,^{13}C-GHMBC (400 MHz / 101 MHz, [D$_6$]-dimethylsulfoxid, 298 K) δ (^{1}H) / δ (^{13}C) [in ppm] = 8.08 / 152.39, 133.41, 128.08 (H-14 / C-12, C-20, C-16), 8.02 / 150.50, 132.40, 131.42, 128.08 (H-4 / C-2, C-10, C-21, C-6), 8.00 / 132.40, 129.62/129.58, 126.14 (H-6 / C-10, C-4/14, C-8), 7.96 / 133.41, 129.62/129.58, 126.61 (H-16 / C-20, C-4/14, C-18), 7.65 / 129.03, 119.56 (H-13 / C-15, C-11), 7.43 / 130.67, 124.94 (H-7 / C-5, C-9), 7.38 / 129.03, 124.82 (H-17 / C-15, C-19), 7.33 – 7.29 / 151.09, 134.93, 133.41, 129.70, 127.96, 17.61 (H-18+22 / C-25, C-3, C-20, C-22, C-16, C-24), 7.27 / 132.40, 128.08 (H-8 / C-10, C-6), 7.07 / 129.03, 123.84, 119.56 (H-19 / C-15, C-17, C-11), 7.02 / 130.67, 125.10 (H-9 / C-5, C-7), 5.21 / 152.39 (H-$31_{1/2}$ / C-12), 5.16 / 152.39 (H-$31_{1/2}$ / C-12), 4.31 / 150.50 (H-$29_{1/2}$ / C-2), 4.24 / 150.50 (H-$29_{1/2}$ / C-2), 3.16 / 93.86 (H-32 / C-31), 2.35 / 97.72 (H-30 / C-29), 2.24 / 151.09, 129.70, 127.78 (H-24 / C-25, C-22, C-23), 1.01 / 25.97, 18.53 (H-28 / C-28, C-27), 0.20 / -3.10 (H-26 / C-26).

[MT473-4]

Elemental analysis = calcd (%) for $C_{38}H_{44}O_5Si$: C: 74.96, H: 7.28, O: 13.14, Si: 4.61; found:

C: 76.3, H: 7.28.

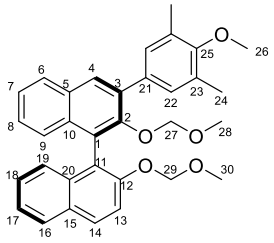
MS (ESI-pos, MeOH**)**: *m/z* = 631.2850 ([M+Na]$^+$, calcd. 631.2836 for [$C_{38}H_{44}O_5SiNa^+$].

IR (ATR-FT): $\tilde{\nu}$ (cm^{-1}) = 3061, 2952, 2928, 2894, 2857, 2823, 1917, 1592, 1472, 1428, 1388, 1240, 1153, 1072, 1031, 1012, 970, 920, 877, 837, 806, 778, 745, 681, 618.

[MT473]

8.2.2.2.7. Synthesis of compound (*R*)-**71e**

Described experiment: MT671 Repeated: MT620



(*R*)-3-Iodo-2,2´-bis(methoxymethoxy)-1,1´-binaphthyl (2.01 g, 3.99 mmol, 1 eq), the boronic ester **71e** (1.26 g, 4.71 mmol, 1.2 eq), tetrabutylammonium hydroxide 30-hydrate (7.02 g, 8.77 mmol, 2.2 eq), tris(dibenzylideneacetone)dipalladium(0) (365 mg, 0.399 mmol, 0.1 eq) and tri(*o*-tolyl)phosphine (242 mg, 0.798 mmol, 0.2 eq) were dissolved in a degassed mixture of toluene and water (1:5, 20 ml total). The reaction mixture was stirred at 90 °C for three hours. After cooling to room temperature water (100 ml) and ethyl acetate (100 ml) were added. The aqueous phase was extracted with ethyl acetate (100 ml) and the combined organic layer was washed with a saturated solution of sodium chloride (100 ml). The organic layer was dried over sodium sulfate and concentrated in *vacuo*. The crude product was purified by column chromatography (21x2 cm, cyclohexane:ethyl acetate 15:1) and afforded the product as a white solid (1.74 g, 3.42 mmol, 86.1%).

$C_{33}H_{32}O_5$, MW = 508.6 g/mol.

^{1}H-NMR (400 MHz, [D$_6$]-dimethylsulfoxid, 298 K) δ [in ppm] = 8.08 (d, ^3J = 9.1 Hz, 1 H, H-14), 8.03 (s, 1 H, H-4), 8.01 (d, ^3J = 8.1 Hz, 1 H, H-6), 7.97 (d, ^3J = 8.1 Hz, 1 H, H-16), 7.66 (d, ^3J = 9.2 Hz, 1 H, H-13), 7.43 (t, ^3J = 7.5 Hz, 1 H, H-7), 7.38 (t, ^3J = 7.2 Hz, 1 H, H-17), 7.35 (s, 2 H, H-22), 7.33 – 7.32 (m, 1 H, H-18), 7.30 – 7.26 (m, 1 H, H-8), 7.07 (d, ^3J = 8.4, 1 H, H-19), 7.02 (d, ^3J = 8.3, 1 H, H-9), 5.21 (d, ^2J = 6.5 Hz, 1 H, H-29$_{1/2}$), 5.16 (d, ^2J = 6.5 Hz, 1 H, H-29$_{1/2}$), 4.31 (d, ^2J = 5.5 Hz, 1 H, H-27$_{1/2}$), 4.24 (d, ^2J = 5.5 Hz, 1 H, H-27$_{1/2}$), 3.70 (s, 3 H, H-26), 3.17 (s, 3 H, H-30), 2.32 (s, 3 H, H-28), 2.29 (s, 6 H, H-24).

^{13}C-NMR (101 MHz, [D$_6$]-dimethylsulfoxid, 298 K) δ [in ppm] = 156.04 (C-25), 152.40 (C-12), 150.39 (C-2), 134.85 (C-3), 133.79 (C-21), 133.42 (C-20), 132.49 (C-10), 130.62 (C-5), 130.06 (C-23), 129.78 (C-4), 129.68 (C-22), 129.62 (C-14), 129.01 (C-15), 128.12 (C-6), 127.96 (C-16), 126.61 (C-18), 126.26 (C-8), 125.77 (C-1), 125.15 (C-7), 124.98 (C-9), 124.83 (C-19), 123.84 (C-17), 119.50 (C-11), 115.95 (C-13), 97.75 (C-27), 93.84 (C-29), 59.39 (C-26), 55.40 (C-28/C-30), 55.38 (C-28/30), 15.93 (C-24).

^{1}H,^{1}H-COSY (400 MHz / 400 MHz, [D$_6$]-dimethylsulfoxid, 298 K) δ [in ppm] = 8.08 / 7.66 (H-14 / H-13), 8.01 / 7.43 (H-6 / H-7), 7.97 / 7.38 (H-16 / H-17), 7.66 / 8.08 (H-13 / H-14), 7.43 / 8.01 (H-7 / H-6), 7.38 / 7.97 (H-17 / H-16), 7.35 / 2.29 (H-22 / H-24), 7.33 – 7.32 / 7.07 (H-18 / H-19), 7.30 – 7.26 / 7.02 (H-8 / H-9), 7.07 / 7.33 – 7.32 (H-19 / H-18), 7.02 / 7.30 – 7.26 (H-9 / H-8), 2.29 / 7.35 (H-24 / H-22).

^{1}H,^{13}C-GHSQC (400 MHz / 101 MHz, [D$_6$]-dimethylsulfoxid, 298 K) δ (^{1}H) / δ (^{13}C) [in ppm] = 8.08 / 129.62 (H-14 / C-14), 8.03 / 129.78 (H-4 / C-4), 8.01 / 128.12 (H-6 / C-6), 7.97 / 127.96 (H-16 / C-16), 7.66 / 115.95 (H-13 / C-13), 7.43 / 125.15 (H-7 / C-7), 7.38 / 123.84 (H-17 / C-17), 7.35 / 129.68 (H-22 / C-22), 7.33 – 7.32 / 126.61 (H-18 / C-18), 7.30 – 7.26 / 126.26 (H-8 / C-8), 7.07 / 124.83 (H-19 / C-19), 7.02 / 124.98 (H-9 / C-9), 5.21 / 93.84 (H-29$_{1/2}$ / C-29), 5.16 / 93.84 (H-29$_{1/2}$ / C-29), 4.31 / 97.75 (H-27$_{1/2}$ / C-27), 4.24 / 97.75 (H-27$_{1/2}$ / C-27), 3.70 / 59.39 (H-26 / C-26), 3.17 / 55.40/55.38 (H-30 / C-28/30), 2.32 / 55.40/55.38 (H-28 / C-28/30), 2.29 / 15.93 (H-24 / C-24).

^{1}H,^{13}C-GHMBC (400 MHz / 101 MHz, [D$_6$]-dimethylsulfoxid, 298 K) δ (^{1}H) / δ (^{13}C) [in ppm] = 8.08 / 152.40, 133.42, 127.96 (H-14 / C-12, C-20, C-16), 8.03 / 150.39, 133.79, 132.49, 128.12 (H-4 / C-2, C-21, C-10, C-6), 8.01 / 132.49, 129.78, 126.26 (H-6 / C-10, C-4, C-8), 7.97 / 133.42, 129.62, 126.61 (H-16 / C-20, C-14, C-18), 7.66 / 129.01, 119.50 (H-13 / C-15, C-11), 7.43 / 130.62, 124.98 (H-7 / C-5, C-9), 7.38 / 129.01, 124.83 (H-17 / C-15, C-19), 7.35 / 156.04, 134.85, 129.68, 15.93 (H-22 / C-25, C-3, C-22, C-24), 7.33 – 7.32 / 133.42, 127.96 (H-18 / C-20, C-16), 7.30 – 7.26 / 132.49, 128.12 (H-8 / C-10, C-6), 7.07 / 129.01, 123.84, 119.50 (H-19 / C-15, C-17, C-11), 7.02 / 130.62, 125.15 (H-9 / C-5, C-7), 5.21 / 152.40, 55.40/55.38 (H-29$_{1/2}$ / C-12, C-28/30), 5.16 / 152.40, 55.40/55.38 (H-29$_{1/2}$ / C-12, C-28/30), 4.31 / 150.39, 55.40/55.39 (H-27$_{1/2}$ / C-2, C-28/30), 4.24 / 150.39, 55.40/55.39 (H-27$_{1/2}$ / C-2, C-28/30), 3.70 / 156.04 (H-26 / C-25), 3.17 / 93.84 (H-30 / C-29), 2.32 / 97.75 (H-28 / C-27), 2.29 / 156.04, 130.06, 129.68 (H-24 / C-25, C-23, C-22). [MT620-3]

Elemental analysis = calcd (%) for $C_{33}H_{32}O_5$: C: 77.93, H: 6.34, O: 15.73; found:

C: 77.1, H: 5.70, O: 15.95

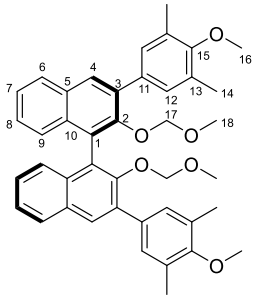
MS (ESI-pos, MeOH**)**: *m/z* = 531.2140 ([M+Na]$^+$, calcd. 531.2142 for [$C_{33}H_{32}O_5Na^+$].

IR (ATR-FT): $\tilde{\nu}$ (cm^{-1}) = 3050, 2988, 2977, 2951, 2917, 2908, 2888, 2875, 2827, 1597, 1485, 1447, 1421, 1401, 1388, 1353, 1335, 1298, 1271, 1254, 1224, 1201, 1153, 1127, 1088, 1051, 1015.

[MT620]

8.2.2.2.8. Synthesis of compound (*R*)-**76d**

Described experiment: MT566 Repeated: SF001



(*R*)-3,3´-Diiodo-2,2´-bis(methoxymethoxy)-1,1´-binaphthyl (102 mg, 0.163 mmol, 1 eq), the boronic ester **71e** (93.9 mg, 0.358 mmol, 2.2 eq), tetrabutylammonium hydroxide 30-hydrate (286 mg, 0.358 mmol, 2.2 eq), tris(dibenzylideneacetone)dipalladium(0) (14.9 mg, 16.3 µmol, 0.1 eq) and tri(*o*-tolyl)phosphine (99.2 mg, 32.6 µmol, 0.2 eq) were dissolved in a degassed solution of toluene and water (1:5, 5 ml total). The reaction mixture was stirred at 90 °C for three hours. After cooling to room temperature water (100 ml) and ethyl acetate (100 ml) were added. The aqueous phase was extracted with ethyl acetate (100 ml) and the combined organic layer was washed with a saturated solution of sodium chloride (100 ml). The organic layer was dried over sodium sulfate and concentrated in *vacuo*. The crude product was purified by column chromatography (21x2 cm, cyclohexane:ethyl acetate 15:1) and afforded the product as a white solid (88.1 mg, 0.137 mmol, 85.1%).

$C_{42}H_{42}O_6$, MW = 642.8 g/mol.

^{1}H-NMR (400 MHz, [D$_6$]-dimethylsulfoxid, 298 K) δ [in ppm] = 8.04 (s, 2 H, H-4), 8.02 (d, ^3J = 8.1 Hz, 2 H, H-6), 7.45 (t, ^3J = 7.4 Hz, 2 H, H-7), 7.36 (s, 4 H, H-12), 7.31 (t, ^3J = 7.9 Hz, 2 H, H-8), 7.07 (d, ^3J = 8.5 Hz, 2 H, H-9), 4.39 (d, ^2J = 5.5 Hz, 2 H, H-17$_{1/2}$), 4.29 (d, ^2J = 5.5 Hz, 2 H, H-17$_{1/2}$), 3.70 (s, 6 H, H-16), 2.32 (s, 6 H, H-18), 2.30 (s, 12 H, H-14).

^{13}C-NMR (101 MHz, [D$_6$]-dimethylsulfoxid, 298 K) δ [in ppm] = 156.13 (C-15), 150.49 (C-2), 134.68 (C-3), 133.79 (C-11), 132.83 (C-10), 130.45 (C-5), 130.20 (C-4+13), 129.58 (C-12), 128.04 (C-6), 126.37 (C-8), 125.82 (C-1), 125.58 (C-9), 125.15 (C-7), 97.56 (C-17), 59.41 (C-16), 55.26 (C-18), 15.92 (C-14).

^{1}H,^{1}H-COSY (400 MHz / 400 MHz, [D$_6$]-dimethylsulfoxid, 298 K) δ [in ppm] = 8.02 / 7.45 (H-6 / H-7), 7.36 / 2.30 (H-12 / H-14), 7.45 / 8.02, 7.31 (H-7 / H-6, H-8), 7.31 / 7.45, 7.07 (H-8 / H-7, H-9), 7.07 / 7.31 (H-9 / H-8), 2.30/ 7.36 (H-14 / H-12).

^{1}H,^{13}C-GHSQC (400 MHz / 101 MHz, [D$_6$]-dimethylsulfoxid, 298 K) δ (^{1}H) / δ (^{13}C) [in ppm] = 8.04 / 130.20 (H-4 / C-4+13), 8.02 / 128.04 (H-6 / C-6), 7.45 / 125.15 (H-7 / C-7), 7.36 / 129.58 (H-12 / C-12), 7.31 / 126.37 (H-8 / C-8), 7.07 / 125.58 (H-9 / C-9), 4.39 / 97.56 (H-17$_{1/2}$ / C-17), 4.29 / 97.56 (H-17$_{1/2}$ / C-17), 3.70 / 59.41 (H-16 / C-16), 2.32 / 55.26 (H-18 / C-18), 2.30 / 16.01 (H-14 / C-14).

^{1}H,^{13}C-GHMBC (600 MHz / 151 MHz, [D$_6$]-dimethylsulfoxid, 298 K) δ (^{1}H) / δ (^{13}C) [in ppm] = 8.04 / 150.49, 133.79, 132.83, 128.04 (H-4 / C-2, C-11, C-10, C-6), 8.02 / 132.83, 130.20, 126.37 (H-6 / C-10, C-4+13, C-8), 7.45 / 130.45, 125.58 (H-7 / C-5, C-9), 7.36 / 156.13, 134.68, 129.58, 15.92 (H-12 / C-15, C-3, C-12, C-14), 7.31 / 132.83, 128.04 (H-8 / C-10, C-6), 7.07 / 130.45, 125.82, 125.15 (H-9 / C-5, C-1, C-7), 4.39 / 150.49, 55.26 (H-17$_{1/2}$ / C-2, C-18), 4.29 / 150.49, 55.26 (H-17$_{1/2}$ / C-2, C-18),

3.70 / 156.13 (H-16 / C-15), 2.32 / 97.56 (H-18 / C-16), 2.30 / 156.13, 130.20, 129.58 (H-14 / C-15, C-4+13, C-12). [SF001-5]

Elemental analysis = calcd (%) for $C_{42}H_{42}O_6$: C: 78.48, H: 6.59, O: 14.93; found:

C: 78.4, H: 7.31, O: -

MS (ESI-pos, MeOH**)**: *m/z* = 665.2888 ($[M+Na]^+$, calcd. 665.2874 for $[C_{42}H_{42}O_6Na^+]$.

IR (ATR-FT): $\tilde{\nu}$ (cm^{-1}) = 3048, 2980, 2970, 2946, 2917, 2903, 2883, 2871, 2824, 1591, 1485, 1447, 1428, 1408, 1387, 1353, 1337, 1298, 1270, 1254, 1222, 1203, 1152, 1127, 1083, 1050, 1015.

[MT566]

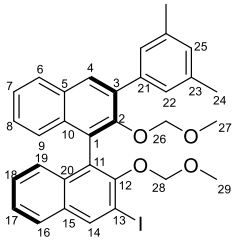
8.2.2.3. Synthesis of 3'-iodo-BINOL- derivatives with an existing substituent in the 3-positon

A: General procedure for the 3´-iodination of 3-substituted BINOL-derivatives:

The corresponding BINOL-derivative was dissolved in dry diethyl ether (40 ml/mmol). After cooling to 0 °C, *n*-butyllithium (2.7 M in toluene, 1.5 eq.) was added carefully and the solution was stirred for 30 minutes. At 0°C iodine (1.4 eq.) in dry tetrahydrofurane (15 ml/mmol BINOL-derivative) was added, then the reaction mixture was warmed up to room temperature and stirred for 1 additional hour. Afterwards a solution of sodium sulfite (37%, 20 ml/mmol BINOL-derivative) was added and the mixture was stirred for 60 minutes. Then ethyl acetate (50 ml/mmol BINOL-derivative) was added. After separating the two layers, the aqueous layer was extracted with ethyl acetate (2x 50 ml/mmol BINOL-derivative), and the combined organic layers were dried over sodium sulfate and concentrated in *vacuo* to afford the crude product as a yellow solid. The crude product was purified by silica gel flash column chromatography (cyclohexane:ethyl acetate = 20:1) to afford the product as a bright yellow solid.

8.2.2.3.1. Synthesis of compound (*R*)-**70a**[115]

Described experiment: TCH9 Repeated: MT669



According to general procedure **A**, compound (*R*)-**76a** (0.595 g, 1.24 mmol, 1 eq) gave the product as a bright yellow solid (0.524 g, 0.867 mmol, 69.9%).

$C_{32}H_{29}IO_4$, MW = 604.48 g/mol.

^{1}H-NMR (600 MHz, [D$_1$]-chloroform, 298 K) δ [in ppm] = 8.53 (s, 1 H, H-14), 7.94 (s, 1 H, H-4), 7.88 (d, ^3J = 8.29 Hz, 1 H, H-6), 7.77 (d, ^3J = 8.02 Hz, 1 H, H-16), 7.43 (t, ^3J = 6.69 Hz, 1 H, H-7), 7.41 (t, ^3J = 6.43 Hz, 1 H, H-17), 7.33 (s, 2 H, H-22), 7.29 (t, ^3J = 6.17 Hz, 1 H, H-8), 7.27 (t, 1 H, H-18), 7.24 (d, ^3J = 8.26 Hz, 1 H, H-19), 7.16 (d, ^3J = 8.41 Hz, 1 H, H-9), 7.01 (s, 1 H, H-25), 4.88 (d, ^2J = 5.22, 1 H, H-26$_{1/2}$ / H-28$_{1/2}$), 4.71 (d, ^2J = 5.22, 1 H, H-26$_{1/2}$ / H-28$_{1/2}$), 4.34 (d, ^2J = 6.39, 1 H, H-26$_{1/2}$/ H-28$_{1/2}$), 4.33 (d, ^2J = 5.89, 1 H, H-26$_{1/2}$ / H-28$_{1/2}$), 2.75 (s, 3 H, H-27/29), 2.39 (s, 6 H, H-24), 2.21 (s, 3 H, H-27/29).

^{13}C-NMR (151 MHz, [D$_1$]-chloroform, 298 K) δ [in ppm] = 151.96 (C-12), 151.65 (C-2), 139.70 (C-14), 138.87 (C-21), 138.05 (C-23), 135.56 (C-3), 134.31 (C-20), 133.44 (C-10), 132.45 (C-15), 131.24 (C-4), 130.85 (C-5), 129.22 (C-25), 128.04 (C-6), 127.33 (C-22), 127.16 (C-11/1), 127.01 (C-19), 126.91 (C-17), 126.74 (C-8), 126.62 (C-16), 126.25 (C-9), 125.83 (C-18), 125.76 (C-1/11), 125.35 (C-7), 99.36 (C-26/28), 98.65 (C-26/28), 92.80 (C-13), 56.83 (C-27/29), 55.85 (C-27/29), 21.51 (C-24).

^{1}H,^{1}H-COSY (600 MHz / 600 MHz, [D$_1$]-chloroform, 298 K) δ [in ppm] = 7.88 / 7.43 (H-6 / H-7), 7.77 / 7.41 (H-16 / H-17), 7.43 / 7.88, 7.29 (H-7 / H-6, H-8), 7.41 / 7.77, 7.27 (H-17 / H-16, H-18), 7.33 / 7.01, 2.39 (H-22 / H-25, H-24), 7.29 / 7.43, 7.16 (H-8 / H-7, H-9), 7.27 / 7.41, 7.24 (H-18 / H-17, H-19), 7.24 / 7.27 (H-19 / H-18), 7.16 / 7.29 (H-9 / H-8), 7.01 / 7.33, 2.39 (H-25 / H-22, H-24), 4.88 / 4.71 (H-26$_{1/2}$ / H-28$_{1/2}$ / H-26$_{1/2}$ / H-28$_{1/2}$), 4.71 / 4.88 (H-26$_{1/2}$ / H-28$_{1/2}$ / H-26$_{1/2}$ / H-28$_{1/2}$), 2.39 / 7.33, 7.01 (H-24 / H-22, H-25).

^{1}H,^{13}C-GHSQC (600 MHz / 151 MHz, [D$_1$]-chloroform, 298 K) δ (^{1}H) / δ (^{13}C) [in ppm] = 8.53 / 139.70 (H-14 / C-14), 7.94 / 131.24 (H-4 / C-4), 7.88 / 128.04 (H-6 / C-6), 7.77 / 126.62 (H-16 / C-16), 7.43 / 125.35 (H-7 / C-7), 7.41 / 126.91 (H-17 / C-17), 7.33 / 127.33 (H-22 / C-22), 7.29 / 126.74 (H-8 / C-8), 7.27 / 125.83 (H-18 / C-18), 7.24 / 127.01 (H-19 / C-19), 7.16 / 126.25 (H-9 / C-9), 7.01 / 129.22 (H-25 / C-25), 4.88 / 99.36 (H-26$_{1/2}$/ H-28$_{1/2}$ / C-26/28), 4.71 / 99.36 (H-26$_{1/2}$/ H-28$_{1/2}$ / C-26/28), 4.34 / 98.65 (H-26$_{1/2}$/ H-28$_{1/2}$ / C-26/28), 4.33 / 98.65 (H-26$_{1/2}$/ H-28$_{1/2}$ / C-26/28), 2.75 / 56.83 (H-27/28 / C-27/29), 2.39 / 21.51 (H-24/ C-24), 2.21 / 55.85 (H-27/29 / C-27/29).

^{1}H,^{13}C-GHMBC (600 MHz / 151 MHz, [D$_1$]-chloroform, 298 K) δ (^{1}H) / δ (^{13}C) [in ppm] = 8.53 / 151.96, 134.31, 126.62, 92.80 (H-14 / C-12, C-20, C-16, C-13), 7.94 / 151.65, 138.87, 133.44, 128.04

[115] First done by Tasja Hermann (former trainee in the Niemeyer Group, Supervision Maike Thiele)

(H-4 / C-2, C-21, C-10, C-6), 7.88 / 133.44, 131.24, 126.74 (H-6 / C-10, C-4, C-8), 7.77 / 139.70, 134.31 (H-16 / C-14, C-20), 7.43 / 130.85, 126.25 (H-7 / C-5, C-9), 7.41 / 132.45, 127.01, (H-17 / C-15, C-19), 7.33 / 129.22, 127.33 (H-22 / C-25, C-22), 7.29 / 133.44, 126.25 (H-8 / C-10, C-9), 7.16 / 130.85, 125.35 (H-9 / C-5, C-7), 7.27 / 134.31, (H-18 / C-20), 7.24 / 132.45, 125.83 (H-19 / C-15, C-17), 2.75 / 99.36 (H-27/29 / C-26/28), 2.21 / 98.65 (H-27/29 / C-26/28), 2.39 / 138.87, 129.22, 127.33 (H-24 / C-21, C-25, C-22).

[TCH9-2]

Elemental analysis = calcd (%) for $C_{32}H_{29}IO_4$: C: 63.58, H: 4.84, O: 10.59; found:

C: 64.9, H: 5.21, O: 10.2.

MS (ESI-pos, MeOH**)**: *m/z* = 627.1023 ([M+Na]$^+$, calcd. 627.1003 for [$C_{32}H_{29}IO_4Na^+$].

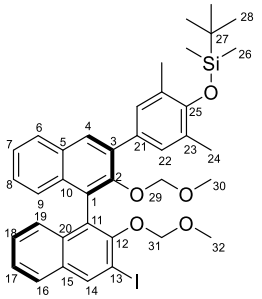
IR (ATR-FT): $\tilde{\nu}$ (cm^{-1}) = 3051, 2989, 2920, 2849, 2824, 1617, 1561, 1491, 1446, 1348, 1231, 1202, 1148, 964.

[TCH9-2]

X-ray crystal structure analysis: X-ray quality crystals were grown by slow evaporation of a solution of **2a** in methanol [Data: MT364Edukt for experiment MT364].

8.2.2.3.2. Synthesis of compound (*R*)-**70c**

Described experiment: MT475 Repeated: MT460, MT491, MT578, MT643



According to general procedure **A**, compound (*R*)-**76c** (2.51 g, 4.11 mmol, 1 eq) gave the product as a bright yellow solid (2.49 g, 3.39 mmol, 82.1%).

$C_{38}H_{43}IO_5Si$, MW = 734.7 g/mol.

^{1}H-NMR (400 MHz, [D$_6$]-dimethylsulfoxid, 298 K) δ [in ppm] = 8.71 (s, 1 H, H-14), 8.06 (s, 1 H, H-4), 8.03 (d, ^3J = 8.09 Hz, 1 H, H-6), 8.01 (d, ^3J = 8.4 Hz, 1 H, H-16), 7.47 – 7.45 (m, 1 H, H-17), 7.44 – 7.42 (m, 1 H, H-7), 7.34 – 7.27 (m, 4 H, H-8+18+22), 7.06 (d, ^3J = 9.1 Hz, 1 H, H-19), 7.00 (d, ^3J = 9.1 Hz, 1 H, H-9), 4.79 (d, ^2J = 5.2 Hz, 1 H, H-31$_{1/2}$), 4.58 (d, ^2J = 5.1, 1 H, H-31$_{1/2}$), 4.26 (d, ^2J = 5.5, 1 H, H-29$_{1/2}$), 4.19 (d, ^2J = 5.7, 1 H, H-29$_{1/2}$), 2.64 (s, 3 H, H-32), 2.24 (s, 6 H, H-24), 2.19 (s, 3 H, H-30), 1.00 (s, 9 H, H-28), 0.19 (s, 3 H, H-26).

^{13}C-NMR (101 MHz, [D$_6$]-dimethylsulfoxid, 298 K) δ [in ppm] = 151.23 (C-25), 151.17 (C-12), 150.06 (C-2), 139.31 (C-14), 134.47 (C-3), 133.38 (C-20), 132.46 (C-10), 131.99 (C-15), 131.20 (C-21), 130.44 (C-4/5), 130.42 (C-4/5), 129.42 (C-22), 128.06 (C-6), 128.02 (C-23), 126.94 (C-16), 126.50 (C-8), 126.09 (C-11), 125.88 (C-19), 125.64 (C-17), 125.32 (C-9), 125.18 (C-7), 125.03 (C-1), 98.26 (C-31), 97.42 (C-29), 93.40 (C-13), 55.94 (C-32), 55.12 (C-30), 25.93 (C-28), 18.49 (C-27), 17.56 (C-24), -3.12 (C-26).

^{1}H,^{1}H-COSY (400 MHz / 400 MHz, [D$_6$]-dimethylsulfoxid, 298 K) δ [in ppm] = 8.03 / 7.44 – 7.42 (H-6 / H-7), 8.01 / 7.47 – 7.45 (H-16 / H-17), 7.47 – 7.45 / 8.01 (H-17 / H-16), 7.44 – 7.42 / 8.03 (H-7 / H-6), 7.34 – 7.27 / 7.06, 7.00, 2.24 (H-8+18+22 / H-19, H-9, H-24), 7.06 / 7.34 – 7.27 (H-19 / H-8+18+22), 7.00 / 7.34 – 7.27 (H-9 / H-8+18+22), 4.79 / 4.58 (H-31$_{1/2}$ / H-31$_{1/2}$), 4.58 / 4.79 (H-31$_{1/2}$ / H-31$_{1/2}$), 4.26 / 4.19 (H-29$_{1/2}$ / H-29$_{1/2}$), 4.19 / 4.26 (H-29$_{1/2}$ / H-29$_{1/2}$), 2.24 / 7.34 – 7.27 (H-24 / H-8/18/22).

^{1}H,^{13}C-GHSQC (400 MHz / 101 MHz, [D$_6$]-dimethylsulfoxid, 298 K) δ (^{1}H) / δ (^{13}C) [in ppm] = 8.71 / 139.31 (H-14 / C-14), 8.06 / 130.44/130.42 (H-4 / C-4/5), 8.03 / 128.06 (H-6 / C-6), 8.01 / 126.94 (H-16 / C-16/18), 7.47 – 7.45 / 125.64 (H-17 / C-17), 7.44 – 7.42 / 125.18 (H-7 / C-7), 7.34 – 7.27 / 129.42, 126.94, 126.50 (H-8+18+22 / C-22, C-16/18, C-8), 7.06 / 125.88 (H-19 / C-19), 7.00 / 125.32 (H-9 / C-9), 4.79 / 98.26 (H-31$_{1/2}$ / C-31), 4.58 / 98.26 (H-31$_{1/2}$ / C-31), 4.26 / 97.42 (H-29$_{1/2}$ / C-29), 4.19 / 97.42 (H-29$_{1/2}$ / C-29), 2.64 / 55.94 (H-32 / C-32), 2.24 / 17.56 (H-24 / C-24), 2.19 / 55.12 (H-30 / C-30), 1.00 / 25.93 (H-28 / C-28), 0.19 / -3.12 (H-26 / C-26).

^{1}H,^{13}C-GHMBC (400 MHz / 101 MHz, [D$_6$]- dimethylsulfoxid, 298 K) δ (^{1}H) / δ (^{13}C) [in ppm] = 8.71 / 151.17, 133.38, 126.94, 93.40 (H-14 / C-12, C-20, C-16/18, C-13), 8.06 / 150.06, 132.46, 131.20, 128.02, 125.03 (H-4 / C-2, C-10, C-21, C-23, C-1), 8.03 / 132.46, 130.44/130.42, 126.50 (H-6 / C-10, C-4/5, C-8), 8.01 / 139.31, 133.38, 126.94 (H-16 / C-14, C-20, C-16/18), 7.47 – 7.45 / 131.99, 125.88

(H-17 / C-15, C-19), 7.44 – 7.42 / 130.44/130.42, 125.32 (H-7 / C-4/5, C-9), 7.34 – 7.27 / 151.23, 134.47, 133.38, 132.46, 129.42, 128.06/128.02, 126.94, 17.56 (H-8+18+22 / C-25, C-3, C-20, C-10, C-22, C-6/23, C-16/18, C-24), 7.06 / 131.99, 125.64 (H-19 / C-15, C-17), 7.00 / 130.44/130.42, 125.18, 125.03 (H-9 / C-4/5, C-7, C-1), 4.79 / 151.17, 55.94 ($H\text{-}31_{1/2}$ / C-12, C-32), 4.58 / 151.17, 55.94 ($H\text{-}31_{1/2}$ / C-12, C-32), 4.26 / 150.06, 55.12 ($H\text{-}29_{1/2}$ / C-2, C-30), 4.19 / 150.06, 55.12 ($H\text{-}29_{1/2}$ / C-2, C-30), 2.64 / 98.26 (H-32 / C-31), 2.24 / 151.23, 129.42, 128.06/128.02 (H-24 / C-25, C-22, C-6/23), 2.19 / 97.42, (H-30 / C-29), 1.00 / 25.93, 18.49 (H-28 / C-28, C-27).

[MT475-4]

Elemental analysis = calcd (%) for $C_{38}H_{43}IO_5Si$: C: 62.12, H: 5.90, O: 10.89, Si: 3.82, I: 17.27; found: C: 62.8, H: 5.78

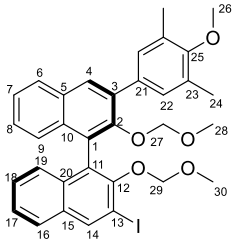
MS (ESI-pos, MeOH**)**: *m/z* = 757.1815 ($[M+Na]^+$, calcd. 757.1817for $[C_{38}H_{43}IO_5SiNa^+]$.

IR (ATR-FT): $\tilde{\nu}$ (cm^{-1}) = 3053, 2980, 2969, 2955, 2927, 2891, 2856, 2823, 2359, 1559, 1484, 1471, 1462, 1386, 1348, 1338, 1271, 1252, 1227, 1201, 1155, 1149, 1083, 1038, 967.

[MT475]

8.2.2.3.3. Synthesis of compound (*R*)-**70e**

Described experiment: MT673 Repeated: MT621



According to general procedure **A**, compound (*R*)-**76e** (1.74 g, 3.41 mmol, 1 eq) gave the product as a bright yellow solid (1.39 g, 2.18 mmol, 64.6%).

$C_{33}H_{31}IO_5$, MW = 634.5 g/mol.

^{1}H-NMR (400 MHz, [D$_6$]-dimethylsulfoxid, 298 K) δ [in ppm] = 8.72 (s, 1 H, H-14), 8.07 (s, 1 H, H-4), 8.03 (d, ^3J = 8.3 Hz, 1 H, H-6), 7.96 (d, ^3J = 8.3 Hz, 1 H, H-16), 7.47 (t, 2 H, ^3J = 7.2 Hz, H-7+17), 7.36 – 7.34 (m, 3 H, H-18+22), 7.32 (t, ^3J = 7.2 Hz, 1 H, H-8), 7.05 (d, ^3J = 8.3 Hz, 1 H, H-19), 7.00 (d, ^3J = 8.3 Hz, 1 H, H-9), 4.80 (d, ^2J = 5.1 Hz, 1 H, H-29$_{1/2}$), 4.58 (d, ^2J = 5.1, 1 H, H-29$_{1/2}$), 4.29 (d, ^2J = 5.1, 1 H, H-27$_{1/2}$), 4.20 (d, ^2J = 5.1, 1 H, H-27$_{1/2}$), 2.70 (s, 3 H, H-26), 2.64 (s, 3 H, H-30), 2.30 (s, 6 H, H-24), 2.17 (s, 3 H, H-28).

^{13}C-NMR (101 MHz, [D$_6$]-dimethylsulfoxid, 298 K) δ [in ppm] = 156.18 (C-25), 151.17 (C-12), 150.59 (C-2), 139.32 (C-14), 134.38 (C-3), 133.59 (C-21), 133.38 (C-20), 132.55 (C-10), 132.01 (C-15), 130.66 (C-4), 130.39 (C-5), 130.32 (C-23), 129.41 (C-22), 128.13 (C-6), 126.97 (C-16+18), 126.66 (C-8), 126.08 (C-11), 125.92 (C-19), 125.68 (C-17), 125.35 (C-9), 125.25 (C-7), 125.12 (C-1), 98.27 (C-29), 97.51 (C-27), 93.43 (C-13), 59.40 (C-26), 55.94 (C-30), 55.09 (C-28), 15.91 (C-24).

^{1}H,^{1}H-COSY (400 MHz / 400 MHz, [D$_6$]-dimethylsulfoxid, 298 K) δ [in ppm] = 8.03 / 7.47 (H-6 / H-7+17), 7.96 / 7.47 (H-16 / H-7+17), 7.47 / 8.03, 7.96, 7.32 (H-7+17 / H-6, H-16, H-8), 7.36 – 7.34 / 7.05, 2.30 (H-18+22 / H-19, H-24), 7.32 / 7.00 (H-8 / H-9), 7.05 / 7.36 – 7.34 (H-19 / H-18+22), 7.00 / 7.32 (H-9 / H-8), 4.80 / 4.58 (H-29$_{1/2}$ / H-29$_{1/2}$), 4.58 / 4.80 (H-29$_{1/2}$ / H-29$_{1/2}$), 4.29 / 4.20 (H-27$_{1/2}$ / H-27$_{1/2}$), 4.20 / 4.29 (H-27$_{1/2}$ / H-27$_{1/2}$), 2.30 / 7.36 – 7.34 (H-24 / H-18+22).

^{1}H,^{13}C-GHSQC (400 MHz / 101 MHz, [D$_6$]-dimethylsulfoxid, 298 K) δ (^{1}H) / δ (^{13}C) [in ppm] = 8.72 / 139.32 (H-14 / C-14), 8.07 / 130.66 (H-4 / C-4), 8.03 / 128.13 (H-6 / C-6), 7.96 / 126.97 (H-16 / C-16+18), 7.47 / 125.68, 125.25 (H-7+17 / C-17, C-7), 7.36 – 7.34 / 129.41, 126.97 (H-18+22 / C-22, C-16+18), 7.32 / 126.66 (H-8 / C-8), 7.05 / 125.92 (H-19 / C-19), 7.00 / 125.35 (H-9 / C-9), 4.80 / 98.27 (H-29$_{1/2}$ / C-29), 4.58 / 98.27 (H-29$_{1/2}$ / C-29), 4.29 / 97.51 (H-27$_{1/2}$ / C-27), 4.20 / 97.51 (H-27$_{1/2}$ / C-27), 2.70 / 59.40 (H-26 / C-26), 2.64 / 55.94 (H-30 / C-30), 2.30 / 15.91 (H-24 / C-24), 2.17 / 55.09 (H-28 / C-28).

^{1}H,^{13}C-GHMBC (400 MHz / 101 MHz, [D$_6$]-dimethylsulfoxid, 298 K) δ (^{1}H) / δ (^{13}C) [in ppm] = 8.72 / 151.17, 133.38, 126.97, 93.43 (H-14 / C-12, C-20, C-16+18, C-13), 8.07 / 150.59, 133.59, 132.55, 128.13 (H-4 / C-2, C-21, C-10, C-6), 8.03 / 132.55, 130.66, 126.66 (H-6 / C-10, C-4, C-8), 7.96 / 139.32, 133.38, 126.97 (H-16 / C-14, C-20, C-16+18), 7.47 / 132.01, 130.39, 126.97 (H-7+17 / C-15, C-5, C-16+18), 7.36 – 7.34 / 156.18, 134.38, 133.38, 129.41, 126.97, 15.91 (H-18+22 / C-25, C-3, C-20, C-22, C-16+18, C-24), 7.32 / 132.55, 128.13 (H-8 / C-10, C-6), 7.05 / 132.01, 126.08, 125.68 (H-19 / C-15, C-11, C-17), 7.00 / 130.39, 125.25, 125.12 (H-9 / C-5, C-7, C-1), 4.80 / 151.17, 55.94 (H-29$_{1/2}$ / C-12,

C-30), 4.58 / 151.17, 55.94 (H-$29_{1/2}$ / C-12, C-30), 4.29 / 150.59, 55.09 (H-$27_{1/2}$ / C-2, C-28), 4.20 / 150.59, 55.09 (H-$27_{1/2}$ / C-2, C-28), 2.64 / 98.27 (H-30 / C-29), 2.30 / 156.18, 130.32, 129.41 (H-24 / C-25, C-23, C-22), 2.17 / 97.51 (H-28 / C-27). [MT621-7]

Elemental analysis = calcd (%) for $C_{33}H_{31}IO_5$: C: 62.47, H: 4.92, O: 12.61 found: C: 63.3, H: 4.86, O: 12.6

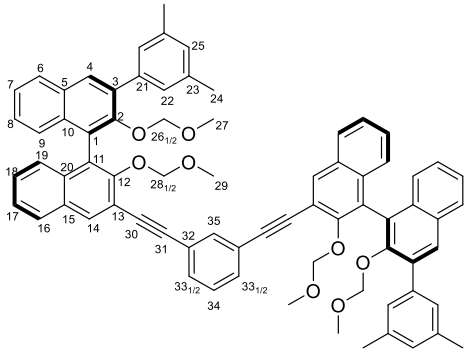
MS (ESI-pos, MeOH**)**: *m/z* = 657.1112 ($[M+Na]^+$, calcd. 657.1142 for $[C_{33}H_{31}IO_5Na^+]$.

IR (ATR-FT): $\tilde{\nu}$ (cm^{-1}) = 3420, 3411, 3052, 2980, 2971, 2930, 2902, 2890, 2823, 1559, 1487, 1462, 1446, 1431, 1417, 1386, 1349, 1269, 1252, 1225,1202, 1152, 1083, 1037, 1007, 984, 966.

[MT621]

8.2.2.3.4. Synthesis of compound (*R*,*R*)-**79a**

Described experiment: MT332 Repeated: MT364



Compound (*R*)-**70a** (1.00 g, 1.65 mmol, 3 eq.), 1,3-diethynylbenzene, (69.6 mg, 71.0 µl, 0.551 mmol, 1 eq), copper(I)-iodide (10.5 mg, 55.1 µmol, 0.1 eq) and tetrakis(triphenylphosphine)palladium(0) (63.7 mg, 55.1 µmol, 0.1 eq), were dispersed in a degassed mixture of acetonitrile:triethylamine (1:1, 50 ml total). The reaction mixture was strirred at 80 °C for 12 hours. The solvent was removed and the crude product was purified by silica gel flash column chromatography (21x4 cm, cyclohexane:ethyl acetate = 10:1) to afford the product as a white solid (0.543 g, 0.504 mmol, 91.4%).

$C_{74}H_{62}O_8$, MW = 1079.28 g/mol.

^{1}H-NMR (600 MHz, [D$_1$]-chloroform, 298 K) δ [in ppm] = 8.26 (s, 2 H, H-14), 7.95 (s, 2 H, H-4), 7.89 (d, ^3J = 9.1 Hz, 2 H, H-6), 7.87 (d, ^3J = 9.1 Hz, 2 H, H-16), 7.79 (t, ^3J = 1.4 Hz, 1 H, H-35), 7.57 (dd, ^3J = 7.7 Hz, ^4J = 1.6 Hz, 2 H, H-33), 7.45-7.43 (m, 2 H, H-17), 7.42-7.41 (m, 2 H, H-7), 7.39 (t, ^3J = 7.9 Hz, 1 H, H-34), 7.36 (s, 4 H, H-22), 7.32-7.30 (m, 2 H, H-18), 7.29-7.27 (m, 4 H, H-8+19), 7.22 (d, ^3J = 8.5 Hz, 2 H, H-9), 7.02 (s, 2 H, H-25), 5.18 (d, ^2J = 5.9, 2 H, H-28$_{1/2}$), 5.06 (d, ^2J = 5.9, 2 H, H-28$_{1/2}$), 4.43 (d, ^2J = 5.9, 2 H, H-26$_{1/2}$), 4.38 (d, ^2J = 5.9, 2 H, H-26$_{1/2}$), 2.64 (s, 6 H, H-29), 2.39 (s, 12 H, H-24), 2.23 (s, 3 H, H-27).

^{13}C-NMR (151 MHz, [D$_1$]-chloroform, 298 K) δ [in ppm] = 153.02 (C-12), 151.66 (C-2), 139.00 (C-21), 138.01 (C-23), 135.60 (C-3), 134.48 (C-35), 134.42 (C-14), 134.28 (C-20), 133.51 (C-10), 131.60 (C-33), 131.02 (C-4), 130.95 (C-5), 130.49 (C-15), 129.16 (C-25), 128.79 (C-34), 127.92 (C-6), 127.72 (C-16), 127.43 (C-22), 127.34 (C-18), 126.96 (C-19), 126.47 (C-9), 126.41 (C-8), 125.79 (C-11), 125.66 (C-17), 125.30 (C-7), 123.89 (C-32), 117.28 (C-13), 99.05 (C-28), 98.82 (C-26), 92.82 (C-31), 87.62 (C-30), 56.23 (C-29), 55.89 (C-27), 21.49 (C-24).

^{1}H,^{1}H-COSY (600 MHz / 600 MHz, [D$_1$]-chloroform, 298 K) δ [in ppm] = 7.79 / 7.57 (H-35 / H-33), 7.57 / 7.79, 7.39 (H-33 / H-35, H-34), 7.45 – 7.43 / 7.32 – 7.30 (H-17 / H-18), 7.42 – 7.41 / 7.29 – 7.27 (H-7 / H-8+19), 7.39 / 7.57 (H-34 / H-33), 7.36 / 2.39 (H-22 / H-24), 7.32 – 7.30 / 7.45 – 7.43 (H-18 / H-17), 7.29 – 7.27 / 7.42 – 7.41 (H-8+19 / H-7), 5.18 / 5.06 (H-28$_{1/2}$ / H-28$_{1/2}$), 5.06 / 5.18 (H-28$_{1/2}$ / H-28$_{1/2}$), 4.43 / 4.38 (H-26$_{1/2}$ / H-26$_{1/2}$). 4.38 / 4.43 (H-26$_{1/2}$ / H-26$_{1/2}$), 2.39 / 7.36 (H-24 / H-22).

^{1}H,^{13}C-GHSQC (600 MHz / 151 MHz, [D$_1$]-chloroform, 298 K) δ (^{1}H) / δ (^{13}C) [in ppm] = 8.26 / 134.39 (H-14 / C-14), 7.95 / 131.02 (H-4 / C-4), 7.89 / 127.92 (H-6 / C-6), 7.87 / 127.72 (H-16 / C-16), 7.79 / 134.48 (H-35 / C-35), 7.57 / 131.60 (H-33 / C-33), 7.45 – 7.43 / 125.66 (H-17 / C-17), 7.42 - 7.41 / 125.30 (H-7 / C-7), 7.39 / 128.79 (H-34 / C-34), 7.36 / 127.43 (H-22 / C-22), 7.32 – 7.30 / 127.34 (H-18 / C-18), 7.29 - 7.27 / 126.96, 126.41 (H-8+19 / C-19, C-8), 7.22 / 126.47 (H-9 / C-9), 7.02 / 129.16 (H-25 / C-25), 5.18 / 99.05 (H-28$_{1/2}$ / C-28), 5.06 / 99.05 (H-28$_{1/2}$/ C-28), 4.43 / 98.81 (H-26$_{1/2}$ / C-26),

4.38 / 98.81 (H-$26_{1/2}$ / C-26), 2.64 / 56.23 (H-29 / C-29), 2.39 / 21.49 (H-24 / C-24), 2.23 / 55.89 (H-27/ C-27).

^{1}H,^{13}C-GHMBC (600 MHz / 151 MHz, [D_1]-chloroform, 298 K) δ (^{1}H) / δ (^{13}C) [in ppm] = 8.26 / 153.02, 134.28, 127.72, 87.62 (H-14 / C-12, C-20, C-16, C-30), 7.95 / 151.66, 139.05, 133.51, 127.92 (H-4 / C-2, C-21, C-10, C-6), 7.89 / 133.51, 131.02, 126.41 (H-6 / C-10, C-4, C-8), 7.87 / 134.28, 127.34 (H-16 / C-20, C-18), 7.79 / 131.60, 92.82 (H-35 / C-33, C-31), 7.57 / 134.48, 131.60, 92.82 (H-33 / C-35, C-33, C-31), 7.45 – 7.43 / 130.49, 126.96 (H-17 / C-15, C-19), 7.42 - 7.41 / 130.95, 126.47 (H-7 / C-5, C-9), 7.39 / 123.89 (H-34 / C-32), 7.36 / 135.60, 129.16, 127.43 (H-22 / C-3, C-25, C-22), 7.32 – 7.30 / 134.28, 127.72, 125.66 (H-18 / C-20, C-16, C-17), 7.29 - 7.27 / 133.51, 130.49, 127.92, 126.96, 125.30 (H-8+19 / C-10, C-15, C-6, C-19, C-7), 7.22 / 130.95, 125.79, 125.30 (H-9 / C-5, C-11, C-7), 7.02 / 127.43 (H-25 / C-22), 5.18 / 153.02, 56.23 (H-$28_{1/2}$ / C-12, C-29), 5.06 / 153.02, 56.23 (H-$28_{1/2}$ / C-12, C-29), 4.43 / 151.66, 55.89 (H-$26_{1/2}$ / C-2, C-2), 4.38 / 151.66, 55.89 (H-$26_{1/2}$ / C-2, C-27), 2.64 / 99.05 (H-29 / C-28), 2.39 / 138.01, 129.16, 127.43 (H-24 / C-23, C-25, C-22), 2.23 / 98.81 (H-27 / C-26).

Elemental analysis = calcd (%) for $C_{74}H_{62}O_8$: C: 82.35, H: 5.79, O: 11.86; found: C: 82.8, H: 5.60, O: 10.7.

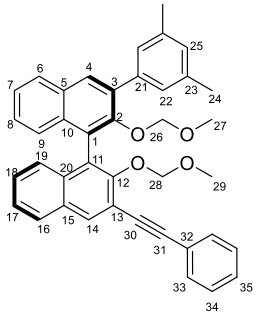
MS (ESI-pos, MeOH**)**: *m/z* = 1101.4329 ([M+Na]$^+$, calcd. 1101.4337for [$C_{74}H_{62}O_8Na^+$].

IR (ATR-FT): $\tilde{\nu}$ (cm^{-1}) = 3048, 2994, 2921, 2823, 2360, 2339, 1598, 1428, 1390, 1355, 1232, 1203, 1157, 1060, 973, 916, 848, 790, 750, 703, 640, 613.

[MT332-2]

8.2.2.3.5. Synthesis of compound (*R*)-**102a**

Described experiment: MT333 Repeated:



Compound (*R*)-**70a** (0.501 g, 0.827 mmol, 1 eq), ethynylbenzene, (80.8 mg, 82.0 µl, 1.03 mmol, 1.25 eq), copper(I)-iodide (15.8 mg, 82.7 µmol, 0.1 eq) and tetrakis(triphenylphosphine)palladium(0) (95.6 mg, 82.7 µmol, 0.1 eq), were dispersed in a degassed mixture of acetonitrile:triethylamine (1:1, 25 ml total). The reaction mixture was strirred at 80 °C for 12 hours. The solvent was removed and the crude product was purified by silica gel flash column chromatography (cyclohexane:ethyl acetate = 10:1) to afford the product as a white solid (0.450 g, 0.779 mmol, 94.1%).

$C_{40}H_{34}O_4$, MW = 578.2 g/mol.

^{1}H-NMR (600 MHz, [D$_6$]-dimethylsulfoxid, 298 K) δ [in ppm] = 8.42 (s, 1 H, H-14), 8.08 (s, 1 H, H-4), 8.05 (d, ^3J = 4.20 Hz, 1 H, H-6), 8.03 (d, ^3J = 4.34 Hz, 1 H, H-16), 7.63 (d, 1 H, ^3J = 4.64 Hz, H-33$_{1/2}$), 7.61 (d, ^3J = 2.27 Hz, 1 H, H-33$_{1/2}$), 7.51 – 7.50 (m, 1 H, H-17), 7.49 – 7.48 (m, 4 H, H-7/34/35), 7.40 (t, ^3J = 8.27 Hz, 1 H, H-18), 7.33 (t, ^3J = 8.26 Hz, 1 H, H-8), 7.31 (s, 2 H, H-22), 7.10 (d, ^3J = 8.42 Hz, 1 H, H-19), 7.06 (d, ^3J = 6.37 Hz, 1 H, H-9), 7.05 (s, 1 H, H-25), 4.99 (s, 2 H, H-28), 4.28 (d, ^2J = 5.63, 1 H, H-26a), 4.23 (d, ^2J = 5.63, 1 H, H-26b), 2.62 (s, 3 H, H-29), 2.35 (s, 6 H, H-24), 2.19 (s, 3 H, H-27).

^{13}C-NMR (151 MHz, [D$_6$]-dimethylsulfoxid, 298 K) δ [in ppm] = 152.18 (C-12), 150.60 (C-2), 138.25 (C-21), 137.41 (C-13/23), 134.86 (C-3), 133.97 (C-14), 133.39 (C-20), 132.65 (C-10), 131.33 (C-33), 130.54 (C-4), 130.44 (C-5), 130.00 (C-15), 129.05 (C-25), 128.90 (C-34), 128.12 (C-6), 127.92 (C-16), 127.57 (C-18), 126.88 (C-22), 126.53 (C-8), 126.01 (C-32), 125.86 (C-19), 125.63 (C-17), 125.48 (C-9), 125.24 (C-7), 125.01 (C-35), 122.25 (C-11), 116.55 (C-1), 98.08 (C-28) 97.60 (C-26), 93.28 (C-31) 86.54 (C-30), 55.52 (C-29) 55.16 (C-27), 21.01 (C-24).

^{1}H,^{1}H-COSY (600 MHz / 600 MHz, [D$_6$]-dimethylsulfoxid, 298 K) δ [in ppm] = 8.05 / 7.49 – 7.48 (H-6 / H-7/34/35), 7.63/7.61 / 7.49 – 7.48 (H-33$_{1/2}$ / H-7/34/35), 7.49 – 7.48 / 8.05, 7.63/7.61 (H-7/34/35 / H-6, H-33$_{1/2}$), 7.40 / 7.10 (H-18 / H-19), 7.33 / 7.06 (H-8 / H-9), 7.31 / 7.05, 2.35 (H-22 / H-25, H-24), 7.10 / 7.40 (H-19 / H-18), 7.06 / 7.33 (H-9 / H-8), 7.05 / 7.31, 2.35 (H-25 / H-22, H-24). 2.35 / 7.31, 7.05 (H-24 / H-22, H-25).

^{1}H,^{13}C-GHSQC (600 MHz / 151 MHz, [D$_1$]-dimethylsulfoxid, 298 K) δ (^{1}H) / δ (^{13}C) [in ppm] = 8.42 / 133.97 (H-14 / C-14), 8.08 / 130.54 (H-4 / C-4), 8.05 / 128.12 (H-6 / C-6), 8.03 / 127.92 (H-16 / C-16), 7.63/761 / 131.33 (H-33a/b / C-33), 7.51 – 7.50 / 125.63 (H-17 / C-17), 7.49 – 7.48 / 125.24/125.01/128.90 (H-7/34/35 / C-7/35/34), 7.40 / 127.57 (H-18 / C-18), 7.33 / 126.53 (H-8 / C-8), 7.31 / 126.88 (H-22 / C-22), 7.10 / 125.86 (H-19 / C-19), 7.06 / 125.48 (H-9 / C-9), 7.05 / 129.05 (H-25 / C-25), 4.99 / 98.08 (H-28 / C-28), 4.28 / 97.60 (H-26a / C-26), 4.23 / 97.60 (H-26b / C-26), 2.62 / 55.52 (H-29 / C-29), 2.35 / 21.01 (H-24 / C-24), 2.19 / 55.16 (H-27 / C-27).

^{1}H,^{13}C-GHMBC (600 MHz / 151 MHz, [D$_1$]-dimethylsulfoxid, 298 K) δ (^{1}H) / δ (^{13}C) [in ppm] = 8.42 / 152.18, 133.39, 127.92, 86.54 (H-14 / C-12, C-20, C-16, C-30), 8.08 / 150.60, 133.25, 132.65, 128.12 (H-4 / C-2, C-21, C-10, C-6), 8.05 / 130.53, 132.65, 126.51 (H-6 / C-10, C-4, C-8), 8.03 / 133.39, 127.59 (H-16 / C-20, C-18), 7.61/7.63 / 93.28 (H-33a/b / C-31), 7.51 – 7.50 / 130.00 (H-17 / C-15), 7.49 – 7.48 / 131.33, 130.42, 128.90, 125.48, 122.24 (H-7/34/35 / C-33, C-5, C-34, C-9, C-32), 7.40 / 133.39, 127.92 (H-18 / C-20, C-16), 7.33 / 132.65, 128.12 (H-8 / C-10, C-6), 7.31 / 134.86, 129.05, 126.88, 21.01 (H-22 / C-3, C-25, C-22, C-24), 7.10 / 130.00, 125.63 (H-19 / C-15, C-17), 7.05 / 126.88, 21.01 (H-25 / C-22, C-24), 2.62 / 98.08 (H-29 / C-28), 2.35 / 137.41, 129.05, 126.88 (H-24 / C-13/23, C-25, C-22), 2.19 / 97.60 (H-27 / C-26).

Elemental analysis = calcd (%) for $C_{40}H_{34}O_4$: C: 83.02, H: 5.92, O: 11.06; found:

C: 82.7, H: 5.89, O: 11.7

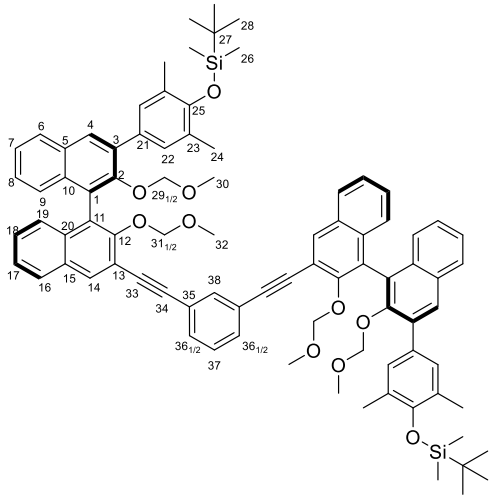
MS (ESI-pos, MeOH**)**: *m/z* = 601.2363 ([M+Na]$^+$, calcd. 601.2349for [$C_{40}H_{34}O_4Na^+$].

IR (ATR-FT): $\tilde{\nu}$ (cm^{-1}) = 3052, 2994, 2948, 2911, 2823, 2360, 2341, 1598, 1492, 1444, 1427, 1392, 1355, 1334, 1232, 1203, 1157, 1058, 1016, 973, 916, 848, 792, 752, 690, 669, 628, 619.

[MT333-2]

8.2.2.3.6. Synthesis of compound (*R*,*R*)-**79c**

Described experiment: MT492 Repeated: MT476



Compound (*R*)-**70c** (1.31 g, 1.77 mmol, 2.1 eq), 1,3-diethynylbenzene, (123mg, 126 µl, 0.972 mmol, 1 eq), copper(I)-iodide (18.5 mg, 97.2 µmol, 0.1 eq) and tetrakis(triphenylphosphine)palladium(0) (112 mg, 97.2 µmol, 0.1 eq), were dispersed in a degassed mixture of acetonitrile:triethylamine (1:1, 30 ml total). The reaction mixture was stirred at 80 °C for two hours. The solvent was removed and the crude product was purified by silica gel flash column chromatography (21x3 cm, cyclohexane:ethyl acetate = 30:1) to afford the product as a white solid (1.13 g, 0.775 mmol, 91.9%).

$C_{86}H_{90}O_{10}Si_2$, MW = 1339.8 g/mol.

^{1}H-NMR (400 MHz, [D$_6$]-dimethylsulfoxid, 298 K) δ [in ppm] = 8.44 (s, 2 H, H-14), 8.07 (s, 2 H, H-4), 8.05 (d, ^3J = 4.06 Hz, 2 H, H-6), 8.03 (d, ^3J = 4.06 Hz, 2 H, H-16), 7.84 (s, 1 H, H-38), 7.69 (d, ^3J = 7.98 Hz, 2 H, H-36), 7.57 (t, ^3J = 7.38 Hz, 1 H, H-37), 7.50 (t, ^3J = 6.99 Hz, 2 H, H-17), 7.45 (t, ^3J = 7.87 Hz, 2 H, H-7), 7.38 (t, ^3J = 7.48 Hz, 2 H, H-18), 7.33 (s, 4 H, H-22), 7.31 (t, ^3J = 6.99 Hz, 2 H, H-8), 7.10 (d, ^3J = 8.27 Hz, 2 H, H-19), 7.04 (d, ^3J = 8.36 Hz, 2 H, H-9), 5.00 (s, 4 H, H-31), 4.28 (d, ^2J = 5.67, 2 H, H-29$_{1/2}$), 4.24 (d, ^2J = 5.64, 2 H, H-29$_{1/2}$), 2.60 (s, 6 H, H-32), 2.24 (s, 12 H, H-24), 2.23 (s, 6 H, H-30), 1.01 (s, 18 H, H-28), 0.20 (s, 12 H, H-26).

^{13}C-NMR (101 MHz, [D$_6$]-dimethylsulfoxid, 298 K) δ [in ppm] = 152.20 (C-12), 151.20 (C-25), 150.69 (C-2), 134.51 (C-3), 134.20 (C-14), 133.73 (C-38), 133.51 (C-20), 132.47 (C-10), 131.70 (C-36), 131.27 (C-21), 130.48 (C-5), 130.24 (C-4), 129.95 (C-15), 129.66 (C-37), 129.49 (C-22), 127.98 (C-6+16+23), 127.71 (C-18), 126.35 (C-8), 126.09 (C-1), 125.85 (C-19), 125.68 (C-17), 125.44 (C-9), 125.17 (C-7), 124.86 (C-11), 123.03 (C-35), 116.26 (C-13), 98.15 (C-31), 97.51 (C-29), 92.20 (C-34) 87.45 (C-33), 55.49 (C-32) 55.22 (C-30), 25.96 (C-28) 18.52 (C-27), 17.57 (C-24), -3.09 (C-26$_{1/2}$), -3.12 (C-26$_{1/2}$).

^{1}H,^{1}H-COSY (400 MHz / 400 MHz, [D$_6$]-dimethylsulfoxid, 298 K) δ [in ppm] = 8.05 / 7.45 (H-6 / H-7), 8.03 / 7.50 (H-16 / H-17), 7.69 / 7.57 (H-36 / H-37), 7.57 / 7.69 (H-37 / H-36), 7.50 / 8.03 (H-17 / H-16), 7.45 / 8.05 (H-7 / H-6), 7.38 / 7.10 (H-18 / H-19), 7.33 / 2.24 (H-22 / H-24), 7.31 / 7.04 (H-8 / H-9), 7.10 / 7.38 (H-19 / H-18), 7.04 / 7.31 (H-9 / H-8), 2.24 / 7.33 (H-22 / H-24).

^{1}H,^{13}C-GHSQC (400 MHz / 101 MHz, [D$_6$]-dimethylsulfoxid, 298 K) δ (^{1}H) / δ (^{13}C) [in ppm] = 8.44 / 134.20 (H-14 / C-14), 8.07 / 130.24 (H-4 / C-4), 8.05 / 127.98 (H-6 / C-6+16+23), 8.03 / 127.98

(H-16 / C-6+16+23), 7.84 / 133.73 (H-38 / C-38), 7.69 / 131.70 (H-36 / C-36), 7.57 / 129.66 (H-37 / C-37), 7.50 / 125.68 (H-17 / C-17), 7.45 / 125.17 (H-7 / C-7), 7.38 / 127.71 (H-18 / C-18), 7.33 / 129.49 (H-22 / C-22), 7.31 / 126.35 (H-8 / C-8), 7.10 / 125.85 (H-19 / C-19), 7.04 / 125.44 (H-9 / C-9), 5.00 / 98.15 (H-31 / C-31), 4.28 / 97.51 (H-$29_{1/2}$ / C-29), 4.24 / 97.51 (H-$29_{1/2}$ / C-29), 2.60 / 55.49 (H-32 / C-32), 2.24 / 17.57 (H-24 / C-24), 2.23 / 55.22 (H-30 / C-30), 1.01 / 25.96 (H-28 / C-28), 0.20 / -3.09/-3.12 (H-26 / C-$26_{1/2}$).

^{1}H,^{13}C-GHMBC (400 MHz / 101 MHz, [D_6]-dimethylsulfoxid, 298 K) δ (^{1}H) / δ (^{13}C) [in ppm] = 8.44 / 152.20, 133.51, 127.98, 87.45 (H-14 / C-12, C-20, C-6+16+23, C-33), 8.07 / 150.69, 132.47, 131.27, 127.98 (H-4 / C-2, C-10, C-21, C-6+16+23), 8.05 / 132.47, 130.24, 126.35 (H-6 / C-10, C-4, C-8), 8.03 / 134.20, 127.71, 124.86 (H-16 / C-14, C-18, C-), 7.84 / 131.70, 92.20 (H-38 / C-36, C-34), 7.69 / 133.73, 131.70, 92.20 (H-36 / C-38, C-36, C-34), 7.57 / 123.03 (H-37 / C-35), 7.50 / 129.95, 125.85 (H-17 / C-15, C-19), 7.45 / 130.48, 125.44 (H-7 / C-5, C-9), 7.38 / 133.51, 127.98 (H-18 / C-20, C-6+16+23), 7.33 / 151.20, 134.51, 129.49, 17.57 (H-22 / C-25, C-3, C-22, C-24), 7.31 / 132.47, 127.98 (H-8 / C-10, C-6+16+23), 7.10 / 129.95, 125.68 (H-19 / C-15, C-17), 7.04 / 130.48, 125.17 (H-9 / C-5, C-7), 5.00 / 152.20, 55.49 (H-31 / C-12, C-32), 4.28 / 150.69, 55.22 (H-$29_{1/2}$ / C-2, C-30), 4.24 / 152.20, 55.49 (H-$29_{1/2}$ / C-2, C-30), 2.60 / 98.15 (H-32 / C-31), 2.24 / 151.20, 129.49, 127.98 (H-24 / C-25, C-22, C-6+16+23), 2.23 / 97.51 (H-30 / C-29), 1.01 / 25.96, 18.52 (H-28 / C-28, C-27). [MT476-4]

Elemental analysis = calcd (%) for $C_{86}H_{90}O_{10}Si_2$: C: 77.10, H: 6.77, O: 11.94, Si: 4.19; found:

C: 77.7, H: 6.74

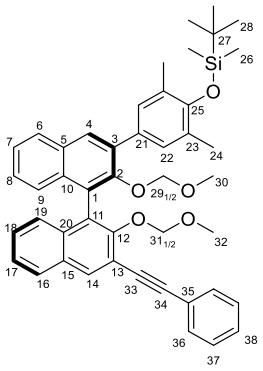
MS (ESI-pos, MeOH**)**: *m/z* = 1362.5993 ($[M+Na]^+$, calcd. 1362.5995 for $[C_{74}H_{62}O_8Na^+]$.

IR (ATR-FT): $\tilde{\nu}$ (cm^{-1}) = 3057, 2952, 2928, 2894, 2857, 2819, 1592, 1483, 1428, 1389, 1227, 1156, 1058, 968, 923, 880, 836, 803, 778, 745, 684, 620.

[MT492]

8.2.2.3.7. Synthesis of compound (*R*)-**102c**

Described experiment: MT536 Repeated:



Compound (*R*)-**70c** (0.672 g, 0.915 mmol, 1 eq), ethynylbenzene (80.1 mg, 82.1 µl, 1.14 mmol, 1.25 eq), copper(I)-iodide (17.4 mg, 91.5 µmol, 0.1 eq) and tetrakis(triphenylphosphine)palladium(0) (105 mg, 91.5 µmol, 0.1 eq), were dispersed in a degassed mixture of acetonitrile:triethylamine (1:1, 30 ml total). The reaction mixture was stirred at 80 °C for two hours. The solvent was removed and the crude product was purified by silica gel flash column chromatography (cyclohexane:ethyl acetate = 30:1) to afford the product as a white solid (0.478 g, 0.674 mmol, 74.1%).

$C_{46}H_{48}O_5Si$, MW = 708.9 g/mol.

^{1}H-NMR (400 MHz, [D$_6$]-dimethylsulfoxid, 298 K) δ [in ppm] = 8.41 (s, 1 H, H-14), 8.07 (s, 1 H, H-4), 8.04 (d, ^3J = 8.2 Hz, 2 H, H-6+16), 7.63-7.61 (m, 2 H, H-36), 7.51 (t, 1 H, ^3J = 6.5 Hz, H-17), 7.49-7.44 (m, 4 H, H-7+37+38), 7.37 (t, ^3J = 7.2 Hz, 1 H, H-18), 7.34 (s, 2 H, H-22), 7.31 (t, ^3J = 7.6 Hz, 1 H, H-8), 7.09 (d, ^3J = 8.6 Hz, 1 H, H-19), 7.04 (d, ^3J = 8.5 Hz, 1 H, H-9), 4.98 (s, 2 H, H-31), 4.28 (d, ^2J = 5.6, 1 H, H-29$_{1/2}$), 4.24 (d, ^2J = 5.6, 1 H, H-29$_{1/2}$), 2.61 (s, 3 H, H-32), 2.25 (s, 6 H, H-24), 2.23 (s, 3 H, H-30), 1.01 (s, 9 H, H-28), 0.21 (s, 6 H, H-26).

^{13}C-NMR (101 MHz, [D$_6$]-dimethylsulfoxid, 298 K) δ [in ppm] = 152.15 (C-12), 151.20 (C-25), 150.67 (C-2), 134.51 (C-3), 133.95 (C-14), 133.37 (C-20), 132.47 (C-10), 131.31 (C-36), 131.27 (C-21), 130.48 (C-5), 130.22 (C-4), 129.98 (C-15), 129.49 (C-22), 129.03 (C-38), 128.89 (C-37), 128.02 (C-6), 127.98 (C-23), 127.91 (C-16), 127.56 (C-18), 126.34 (C-8), 126.02 (C-11), 125.82 (C-19), 125.62 (C-17), 125.43 (C-9), 125.16 (C-7), 124.90 (C-1), 122.24 (C-35), 116.55 (C-13), 98.05 (C-31), 97.49 (C-29), 93.26 (C-34) 86.53 (C-33), 55.51 (C-32) 55.22 (C-30), 25.97 (C-28) 18.52 (C-27), 17.58 (C-24), -3.09 (C-26$_{1/2}$), -3.11 (C-26$_{1/2}$).

^{1}H,^{1}H-COSY (600 MHz / 600 MHz, [D$_6$]-dimethylsulfoxid, 298 K) δ [in ppm] = 8.04 / 7.51, 7.49 - 7.44 (H-6+16 / H-17, H-7+37+38), 7.63-7.61 / 7.49 - 7.44 (H-36 / H-7+37+38), 7.51 / 8.04, 7.37 (H-17 / H-6+16, H-18), 7.49 - 7.44 / 8.04, 7.63-7.61, 7.31 (H-7+37+38 / H-6+16, H-36, H-8), 7.37 / 7.51, 7.09 (H-18 / H-17, H-19), 7.34 / 2.25 (H-22 / H-24), 7.31 / 7.49 - 7.44, 7.04 (H-8 / H-7, H-9), 7.09 / 7.37 (H-19 / H-18), 7.04 / 7.31 (H-9 / H-8), 2.25 / 7.34 (H-24 / H-22).

^{1}H,^{13}C-GHSQC (400 MHz / 101 MHz, [D$_6$]-dimethylsulfoxid, 298 K) δ (^{1}H) / δ (^{13}C) [in ppm] = 8.41 / 133.95 (H-14 / C-14), 8.07 / 130.22 (H-4 / C-4), 8.04 / 128.02, 127.91 (H-6+H16 / C-6+C-16), 7.63-7.61 / 131.31 (H-36 / C-36), 7.51 / 125.62 (H-17 / C-17), 7.49-7.44 / 129.03, 128.89, 125.16 (H-7+H-37+H-38 / C-38, C-37, C-7), 7.37 / 127.56 (H-18 / C-18), 7.34 / 129.49 (H-22 / C-22), 7.31 / 126.34 (H-8 / C-8), 7.09 / 125.82 (H-19 / C-19), 7.04 / 125.43 (H-9 / C-9), 4.98 / 98.05 (H-31 / C-31),

4.28 / 97.49 (H-29$_{1/2}$ / C-29), 4.24 / 97.49 (H-29$_{1/2}$ / C-29), 2.61 / 55.51 (H-32 / C-32), 2.25 / 17.58 (H-24 / C-24), 2.23 / 55.22 (H-30 / C-30), 1.01 / 25.97 (H-28 / C-28), 0.21 / -3.09, -3.12 (H-26 / C-26$_{1/2}$).

^{1}H,^{13}C-GHMBC (400 MHz / 101 MHz, [D$_6$]-dimethylsulfoxid, 298 K) δ (^{1}H) / δ (^{13}C) [in ppm] = 8.41 / 152.15, 133.37, 127.91, 126.02, 86.53 (H-14 / C-12, C-20, C-16, C-11, C-33), 8.07 / 150.67, 132.47, 131.27, 128.02 (H-4 / C-2, C-10, C-21, C-6), 8.04 / 133.95, 133.37, 132.47, 130.22, 127.56, 126.34 (H-6+H16 / C-14, C-20, C-10, C-4, C-18, C-8), 7.63-7.61 / 131.31, 129.03, 93.26 (H-36 / C-36, C-38, C-34), 7.51 / 129.98, 125.82 (H-17 / C-15, C-19), 7.49-7.44 / 130.48, 128.89, 125.43, 122.24 (H-7+H-37+H-38 / C-5, C-37, C-9, C-35), 7.37 / 133.37, 127.91 (H-18 / C-20, C-16), 7.34 / 151.20, 134.51, 129.49, 17.58 (H-22 / C-25, C-3, C-22, C-24), 7.31 / 132.47, 128.02 (H-8 / C-10, C-6), 7.09 / 129.98, 125.82 (H-19 / C-15, C-17), 7.04 / 130.48, 125.16 (H-9 / C-5, C-7), 4.98 / 152.15, 55.51 (H-31 / C-12, C-32), 4.28 / 150.67, 55.22 (H-29$_{1/2}$ / C-2, C-30), 4.23 / 150.67, 55.22 (H-29$_{1/2}$ / C-2, C-30), 2.61 / 98.05 (H-32 / C-31), 2.25 / 151.20, 129.49 (H-24 / C-25, C-22), 2.23 / 97.49 (H-30 / C-29), 1.01 / 25.97, 18.52 (H-28 / C-28, C-27).

[MT536-4]

Elemental analysis = calcd (%) for $C_{46}H_{48}O_5Si$: C: 77.93, H: 6.82, O: 11.28; found:

C: 78.3, H: 6.79, O: 9.67 [MT536]

MS (ESI-pos, MeOH**)**: *m/z* = 731.3168 ([M+Na]$^+$, calcd. 731.3163 for [$C_{46}H_{48}O_5SiNa^+$].

[MT536-1]

IR (ATR-FT): $\tilde{\nu}$ (cm^{-1}) = 3057, 2955, 2925, 2853, 1728, 1623, 1593, 1509, 1485, 1471, 1427, 1389, 1357, 1338, 1272, 1259, 1240, 1226, 1153, 1013, 970, 921, 877.

[MT536]

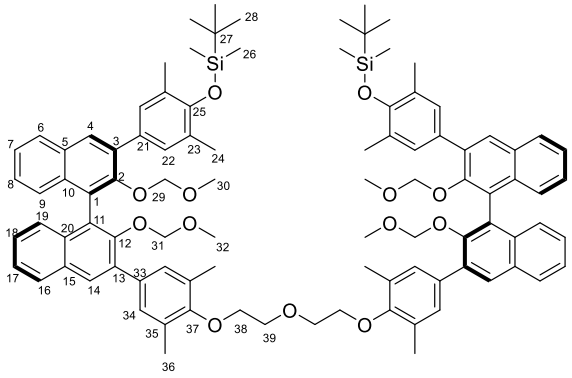
8.2.2.4. Suzuki couplings

B: General procedure for the coupling of BINOL-monoiodides with bis-boronic esters:

The corresponding BINOL-monoiodide (2.1 eq), the bis-boronic ester (1.25 eq), tetrabutylammoniumhydroxide 30-hydrate (1.15 eq) and tris(dibenzylideneacetone)dipalladium(0) (0.05 eq) and tri(*o*-tolyl)phosphine (0.12 eq) were dissolved in a degassed solution of toluene and water (1:5, 25 ml/mmol BINOL-monoiodide). The reaction mixture was stirred at 90 °C for three hours. After cooling to room temperature water (50 ml/mmol BINOL-monoiodide) and ethyl acetate (50 ml/mmol BINOL-monoiodide) were added. The aqueous phase was extracted with ethyl acetate (1 x 50 ml/mmol BINOL-monoiodide) and the combined organic layer was washed with a saturated solution of sodium chloride (1 x 50 ml/mmol BINOL-monoiodide). The organic layer was dried over sodium sulfate and concentrated in *vacuo*. The crude product was purified by column chromatography (cyclohexane:ethyl acetate 10:1) and afforded the product as a white to yellow solid.

8.2.2.4.1. Synthesis of compound (*R*,*R*)-**85c**

Described experiment: MT585 Repeated: MT579, MT594



According to general procedure **B**, compound (*R*)-**70c** (0.999 g, 1.36 mmol, 2.2 eq) and bis-boronicester **97** (0.353 g, 0.618 mmol, 1 eq) gave the product as a yellow solid (0.557 g, 0.365 mmol, 59.1%).

$C_{96}H_{110}O_{13}Si_2$, MW = 1528.1 g/mol.

^{1}H-NMR (600 MHz, [D$_6$]-dimethylsulfoxid, 298 K) δ [in ppm] = 8.03 (s, 4 H, H-4+14), 8.02 (d, ^3J = 6.3 Hz, 2 H, H-6/16), 8.01 (d, ^3J = 6.3 Hz, 2 H, H-6/16), 7.43 (t, ^3J = 7.4 Hz, 4 H, H-7+17), 7.35 (s, 4 H, H-22/34), 7.32 (s, 4 H, H-22/34), 7.31 – 7.28 (m, 4 H, H-8+18), 7.06 (d, ^3J = 8.8 Hz, 2 H, H-9/19), 7.05 (d, ^3J = 8.8 Hz, 2 H, H-9/19), 4.37 (d, ^2J = 5.4 Hz, 2 H, H-29$_{1/2}$/31$_{1/2}$), 4.36 (d, ^2J = 5.4, 2 H, H-29$_{1/2}$/31$_{1/2}$), 4.29 (d, ^2J = 5.4, 2 H, H-29$_{1/2}$/31$_{1/2}$), 4.28 (d, ^2J = 5.4, 2 H, H-29$_{1/2}$/31$_{1/2}$), 4.00 – 3.98 (m, 4 H, H-38/39), 3.86 – 3.84 (m, 4 H, H-38/39), 2.34 (s, 12 H, H-24/36), 2.33 (s, 6 H, H-30/32), 2.32 (s, 6 H, H-30/32), 2.24 (s, 12 H, H-24/36), 1.01 (s, 18 H, H-28), 0.20 (s, 6 H, H-26), 0.19 (s, 6 H, H-26).

^{13}C-NMR (151 MHz, [D$_6$]- dimethylsulfoxid, 298 K) δ [in ppm] = 154.96 (C-25/37), 151.16 (C-25/37), 150.56 (C-2/12), 150.48 (C-2/12), 134.73 (C-3/13), 134.72 (C-3/13), 133.75 (C-21/33), 132.80 (C-10/20), 132.71 (C-10/20), 131.39 (C-21/33), 130.47 (C-5/15), 130.43 (C-5/15), 130.39 (C-23/35), 130.15 (C-4/14), 130.01 (C-4/14), 129.57 (C-22/34), 129.53 (C-22/34), 128.01 (C-6/16), 128.98 (C-6/16), 127.89 (C-23/35), 126.33 (C-8/18), 126.23 (C-8/18), 125.82 (C-1/11), 125.71 (C-1/11), 125.53

(C-9+19), 125.11 (C-7/17), 125.07 (C-7/17), 97.54 (C-29/31), 97.46 (C-29/31), 71.48 (C-38/39), 70.00 (C-38/39), 55.28 (C-30/32), 55.25 (C-30/32), 25.97 (C-28), 18.53 (C-27), 17.58 (C-24/36), 16.05 (C-24/36), -3.09 (C-$26_{1/2}$), -3.10 (C-$26_{1/2}$).

^{1}H,^{1}H-COSY (600 MHz / 600 MHz, [D$_6$]- dimethylsulfoxid, 298 K) δ [in ppm] = 8.02 / 7.43 (H-6/16 / H-7+17), 8.01 / 7.43 (H-6/16 / H-7+17), 7.43 / 8.02, 8.01, 7.31 – 7.28 (H-7+17 / H-6/16, H6/16, H-8+18), 7.35 / 2.34 (H-22/34 / H-24/36), 7.32 / 2.24 (H-22/34 / H-24/36), 7.31 – 7.28 / 7.43, 7.06, 7.05 (H-8+18 / H7+17, H-9/19, H-9/19), 7.06 / 7.31 – 7.28 (H-9/19 / H-8+18), 7.05 / 7.31 – 7.28 (H-9/19 / H-8+18), 4.37 / 4.29, 4.28 (H-$29_{1/2}$/$31_{1/2}$ / H-$29_{1/2}$/$31_{1/2}$), 4.36 / 4.29, 4.28 (H-$29_{1/2}$/$31_{1/2}$ / H-$29_{1/2}$/$31_{1/2}$), 4.29 / 4.37, 4.36 (H-$29_{1/2}$/$31_{1/2}$ / H-$29_{1/2}$/$31_{1/2}$), 4.28 / 4.37, 4.36 (H-$29_{1/2}$/$31_{1/2}$ / H-$29_{1/2}$/$31_{1/2}$), 4.00 – 3.98 / 3.86 – 3.84 (H-38 / H-39), 3.86 – 3.84 / 4.00 – 3.98 (H-39 / H-38).

^{1}H,^{13}C-GHSQC (400 MHz / 151 MHz, [D$_6$]- dimethylsulfoxid, 298 K) δ (^{1}H) / δ (^{13}C) [in ppm] = 8.03 / 130.15 + 130.01 (H-4+14 / C-4/14, C-4/14), 8.02 / 128.01/127.98 (H-6/16 / C-6/16), 8.01 / 128.01/127.98 (H-6/16 / C-6/16), 7.43 / 125.11/125.07 (H-7+17 / C-7/17), 7.35 / 129.57/129.53 (H-22/34 / C-22/34), 7.32 / 129.57/129.53 (H-22/34 / C-22/34), 7.31 – 7.28 / 126.33/126.23 (H-8+18 / C-8/18), 7.06 / 125.53 (H-9/19 / C-9+19), 7.05 / 125.53 (H-9/19 / C-9+19), 4.37 / 97.54/97.46 (H-$29_{1/2}$/$31_{1/2}$ / C-29/31), 4.36 / 97.54/97.46 (H-$29_{1/2}$/$31_{1/2}$ / C-29/31), 4.29 / 97.54/97.46 (H-$29_{1/2}$/$31_{1/2}$ / C-29/31), 4.28 / 97.54/97.46 (H-$29_{1/2}$/$31_{1/2}$ / C-29/31), 4.00 – 3.98 / 71.48 (H-38/39 / C-38/39), 3.86 – 3.84 / 71.48 (H-38/39 / C-38/39), 2.34 / 16.05 (H-24/36 / C-24/36), 2.33 / 55.28/55.25 (H-30/32 / C-30/32), 2.32 / 55.28/55.25 (H-30/32 / C-30/32), 2.24 / 17.58 (H-24/36 / C-24/36), 1.01 / 25.97 (H-28 / C-28), 0.20 / -3.09/-3.10 (H-26 / C-$26_{1/2}$), 0.19 / -3.09/-3.10 (H-26 / C-$26_{1/2}$).

^{1}H,^{13}C-GHMBC (600 MHz / 151 MHz, [D$_6$]- dimethylsulfoxid, 298 K) δ (^{1}H) / δ (^{13}C) [in ppm] = 8.03 / 150.56/150.48, 133.75, 132.80/132.71, 131.39, 128.01/127.98 (H-4+14 / C-2/12, C-21/33, C-10/20, C-21/33, C-6/16), 8.02 / 132.80/132.71, 130.15/130.01, 126.33/126.23 (H-6/16 / C-10/20, C-4/14, C-8/18), 8.01 / 132.80/132.71, 130.15/130.01, 126.33/126.23 (H-6/16 / C-10/20, C-4/14, C-8/18), 7.43 / 130.47/130.43, 125.53 (H-7+17 / C-5/15, C-9+19), 7.35 / 154.96, 134.73/134.72, 129.57/129.53, 16.05 (H-22/34 / C-25/37, C-3/13, C-22/34, C-24/36), 7.32 / 151.16, 134.73/134.72, 129.57/129.53, 17.58 (H-22/34 / C-25/37, C-3/13, C-22/34, C-24/36), 7.31 – 7.28 / 132.80/132.71, 128.01/127.98 (H-8+18 / C-10/20, C-6/16), 7.06 / 130.47/130.43, 125.82/125.71, 125.11/125.07 (H-9/19 / C-5/15, C-1/11, C-7/17), 7.05 / 130.47/130.43, 125.82/125.71, 125.11/125.07 (H-9/19 / C-5/15, C-1/11, C-7/17), 4.37 / 150.56/150.48, 55.28/55.25 (H-$29_{1/2}$/$31_{1/2}$ / C-2/12, C-30/32), 4.36 / 150.56/150.48, 55.28/55.25 (H-$29_{1/2}$/$31_{1/2}$ / C-2/12, C-30/32), 4.29 / 150.56/150.48, 55.28/55.25 (H-$29_{1/2}$/$31_{1/2}$ / C-2/12, C-30/32), 4.28 / 150.56/150.48, 55.28/55.25 (H-$29_{1/2}$/$31_{1/2}$ / C-2/12, C-30/32), 3.86 – 3.84 / 71.48 (H-38/39 / C-38/39), 2.34 / 154.96 (H-24/36 / C-25/37), 2.33 / 97.54/97.46 (H-30/32 / C-29/31), 2.32 / 97.54/97.46 (H-30/32 / C-29/31), 2.24 / 151.16, 129.57/129.53 (H-24/36 / C-25/37, C-22/34), 1.01 / 25.97, 18.53 (H-28 / C-28, C-27), 0.20 / -3.09/-3.10 (H-26 / C-$26_{1/2}$), 0.19 / -3.09/-3.10 (H-26 / C-$26_{1/2}$).

[MT585]

Elemental analysis = calcd (%) for $C_{96}H_{110}O_{13}Si_2$: C: 75.46, H: 7.26, O: 13.61; found: C: 77.4, H: 7.80, O: 11.3

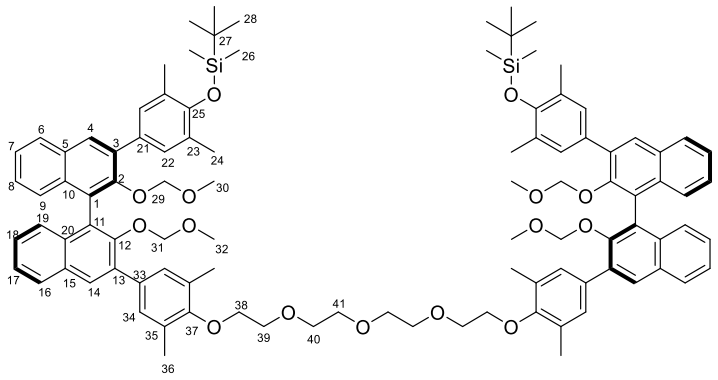
MS (ESI-pos, MeOH**)**: *m/z* = 1550.7413 ([M+Na]$^+$, calcd. 1550.7408 for $C_{96}H_{110}O_{13}Si_2Na^+$][MT583_2][116]

IR (ATR-FT): $\tilde{\nu}$ (cm^{-1}) = 3050, 2952, 2925, 2856, 1592, 1484, 1426, 1387, 1353, 1337, 1271, 1254, 1224, 1202, 1156, 1080, 1051, 971, 923, 876, 837

[116] Sample name was interchanged in the department of mass spectrometry

8.2.2.4.2. Synthesis of compound (*R*,*R*)-**86c**

Described experiment: MT647 Repeated:



According to general procedure **B**, compound (*R*)-**70c** (1.22 g, 1.63 mmol, 2.2 eq) and bis-boronicester **98** (99.7 mg, 0.175 mmol, 1 eq) gave the product as a yellow solid (0.750 g, 0.464 mmol, 62.6%).

$C_{100}H_{118}O_{15}Si_2$, MW = 1614.2 g/mol.

^{1}H-NMR (400 MHz, [D$_6$]-dimethylsulfoxid, 298 K) δ [in ppm] = 8.03 (s, 2 H, H-4/14), 8.02 (d, ^3J = 8.1 Hz, 2 H, H-6/16), 8.01 (s, 2 H, H-4/14), 7.98 (d, ^3J = 8.3 Hz, 2 H, H-6/16), 7.42 (t, ^3J = 7.4 Hz, 4 H, H-7+17), 7.33 (s, 4 H, H-22/34), 7.31 (s, 4 H, H-22/34), 7.29 – 7.25 (m, 4 H, H-8+18), 7.05 (d, ^3J = 8.3 Hz, 2 H, H-9/19), 7.04 (d, ^3J = 8.3 Hz, 2 H, H-9/19), 4.35 (d, ^2J = 5.4 Hz, 2 H, H-29$_{1/2}$/31$_{1/2}$), 4.34 (d, ^2J = 5.4, 2 H, H-29$_{1/2}$/31$_{1/2}$), 4.26 (d, ^2J = 5.4, 4 H, H-29$_{1/2}$/31$_{1/2}$), 3.94 – 3.92 (m, 4 H, H-38), 3.75 – 3.73 (m, 4 H, H-39), 3.64 – 3.60 (m, 8 H, H-40+41), 2.30 (s, 6 H, H-30/32), 2.29 (s, 12 H, H-24/36), 2.28 (s, 6 H, H-30/32), 2.22 (s, 12 H, H-24/36), 1.00 (s, 18 H, H-28), 0.19 (s, 6 H, H-26$_{1/2}$), 0.18 (s, 6 H, H-26$_{1/2}$).

^{13}C-NMR (101 MHz, [D$_6$]-dimethylsulfoxid, 298 K) δ [in ppm] = 154.99 (C-25/37), 151.16 (C-25/37), 150.56 (C-2/12), 150.49 (C-2/12), 134.72 (C-3+13), 133.69 (C-21/33), 132.79 (C-10/20), 132.71 (C-10/20), 131.39 (C-21/33), 130.47 (C-5/15), 130.42 (C-5/15), 130.34 (C-23/35), 130.13 (C-4/14), 130.02 (C-4/14), 129.56 (C-22/34), 129.51 (C-22/34), 127.99 (C-6+16), 127.89 (C-23/35), 126.31 (C-8/18), 126.23 (C-8/18), 125.82 (C-1/11), 125.71 (C-1/11), 125.54 (C-9+19), 125.09 (C-7/17), 125.06 (C-7/17), 97.53 (C-29/31), 97.46 (C-29/31), 71.46 (C-38), 70.02 (C-40/41), 69.96 (C-40/41), 69.84 (C-39), 55.26 (C-30/32), 55.22 (C-30/32), 25.96 (C-28), 18.51 (C-27), 17.55 (C-24/36), 16.05 (C-24/36), -3.12 (C-26).

^{1}H,^{1}H-COSY (400 MHz / 400 MHz, [D$_6$]-dimethylsulfoxid, 298 K) δ [in ppm] = 8.02 / 7.42 (H-6/16 / H-7+17), 7.98 / 7.42 (H-6/16 / H-7+17), 7.42 / 8.02, 7.98, 7.29 – 7.25 (H-7+17 / H-6/16, H6/16, H-8+18), 7.33 / 2.29, 2.22 (H-22/34 / H-24/36, H-24/36), 7.31 / 2.29, 2.22 (H-22/34 / H-24/36, H-24/36), 7.29 – 7.25 / 7.42, 7.05, 7.04 (H-8+18 / H7+17, H-9/19, H-9/19), 7.05 / 7.29 – 7.25 (H-9/19 / H-8+18), 7.04 / 7.29 – 7.25 (H-9/19 / H-8+18), 4.35 / 4.26 (H-29$_{1/2}$/31$_{1/2}$ / H-29$_{1/2}$/31$_{1/2}$), 4.34 / 4.26 (H-29$_{1/2}$/31$_{1/2}$ / H-29$_{1/2}$/31$_{1/2}$), 4.26 / 4.35, 4.34 (H-29$_{1/2}$/31$_{1/2}$ / H-29$_{1/2}$/31$_{1/2}$), 3.94 – 3.92 / 3.75 – 3.73 (H-38 / H-39), 3.75 – 3.73 / 3.94 – 3.92 (H-39 / H-38).

^{1}H,^{13}C-GHSQC (400 MHz / 101 MHz, [D$_6$]-dimethylsulfoxid, 298 K) δ (^{1}H) / δ (^{13}C) [in ppm] = 8.03 / 130.13/130.02 (H-4/14 / C-4/14), 8.02 / 127.99 (H-6/16 / C-6+16), 8.01 / 130.13/130.02 (H-4/14 / C-4/14), 7.98 / 127.99 (H-6/16 / C-6+16), 7.42 / 125.09, 125.06 (H-7+17 / C-7/17), 7.33 / 129.56/129.51 (H-22/34 / C-22/34), 7.31 / 129.56/129.51 (H-22/34 / C-22/34), 7.29 – 7.25 /

126.31/126.23 (H-8+18 / C-8/18), 7.05 / 125.54 (H-9/19 / C-9+19), 7.04 / 125.54 (H-9/19 / C-9+19), 4.35 / 97.53/97.46 (H-$29_{1/2}$/$31_{1/2}$ / C-29/31), 4.34 / 97.53/97.46 (H-$29_{1/2}$/$31_{1/2}$ / C-29/31), 4.26 / 97.53/97.46 (H-$29_{1/2}$/$31_{1/2}$ / C-29/31), 3.94 – 3.92 / 71.46 (H-38 / C-38), 3.75 – 3.73 / 69.84 (H-39 / C-39), 3.64 – 3.60 / 70.02, 69.96 (H-40+41 / C-40+41), 2.30 / 55.26/55.22 (H-30/32 / C-30/32), 2.29 / 16.05 (H-24/36 / C-24/36), 2.28 / 55.26/55.22 (H-30/32 / C-30/32), 2.22 / 17.55 (H-24/36 / C-24/36), 1.00 / 25.96 (H-28 / C-28), 0.19 / -3.12 H-$26_{1/2}$ / C-26), 0.18 / -3.12 (H-$26_{1/2}$ / C-26).

^{1}H,^{13}C-GHMBC (400 MHz / 101 MHz, [D_6]- dimethylsulfoxid, 298 K) δ (^{1}H) / δ (^{13}C) [in ppm] = 8.03 / 150.56/150.49, 133.69, 132.79/132.71, 131.39, 127.99 (H-4/14 / C-2/12, C-21/33, C-10/20, C-21/33, C-6+16), 8.02 / 132.79/132.71, 130.13/130.02, 126.31/126.23 (H-6/16 / C-10/20, C-4/14, C-8/18), 8.01 / 150.56/150.49, 133.69, 132.79/132.71, 131.39, 127.99 (H-4/14 / C-2/12, C-21/33, C-10/20, C-21/33, C-6+16), 7.98 / 132.79/132.71, 130.13/130.02, 126.31/126.23 (H-6/16 / C-10/20, C-4/14, C-8/18), 7.42 / 130.47/130.42, 125.54 (H-7+17 / C-5/15, C-9+19), 7.33 / 154.99, 134.72, 129.51, 16.05 (H-22/34 / C-25/37, C-3+13, C-22/34, C-24/36), 7.31 / 151.16, 134.72, 129.56, 17.55 (H-22/34 / C-25/37, C-3+13, C-22/34, C-24/36), 7.29 – 7.25 / 132.79/132.71, 127.99 (H-8+18 / C-10/20, C-6+16), 7.05 / 130.47/130.42, 125.09/125.06, (H-9/19 / C-5/15, C-7/17), 7.04 / 130.47/130.42, 125.09/125.06 (H-9/19 / C-5/15, C-7/17), 4.35 / 150.56/150.49, 55.26/55.22 (H-$29_{1/2}$/$31_{1/2}$ / C-2/12, C-30/32), 4.34 / 150.56/150.49, 55.26/55.22 (H-$29_{1/2}$/$31_{1/2}$ / C-2/12, C-30/32), 4.26 / 150.56/150.49, 55.26/55.22 (H-$29_{1/2}$/$31_{1/2}$ / C-2/12, C-30/32), 3.94 – 3.92 / 69.84 (H-38 / C-39), 3.75 – 3.73 / 71.46 (H-39 / C-38), 2.30 / 97.53/97.46 (H-30/32 / C-29/31), 2.29 / 154.99, 130.34, 129.56/129.51, 127.89 (H-24/36 / C-25/37, C-23/35, C-22/34, C-23/35), 2.28 / 97.53/97.46 (H-30/32 / C-29/31), 2.22 / 151.16, 130.34, 129.56/129.51, 127.89 (H-24/36 / C-25/37, C-23/35, C-22/34, C-23/35), 1.00 / 25.96, 18.51 (H-28 / C-28, C-27).

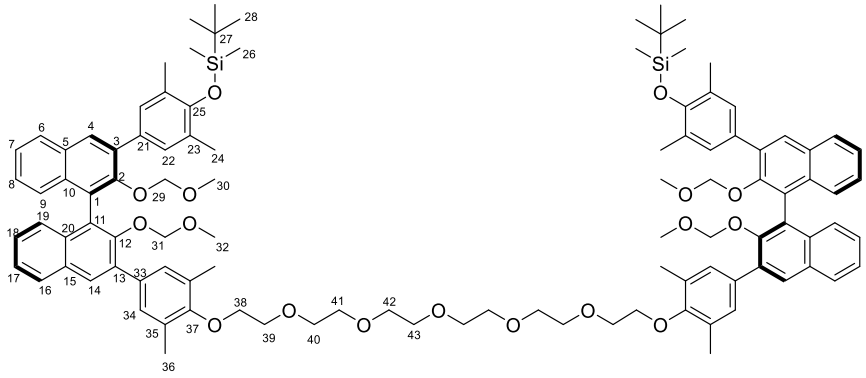
Elemental analysis = calcd (%) for $C_{100}H_{118}O_{15}Si_2$: C: 74.32, H: 7.36, O: 14.85; found: C: 74.1, H: 8.18, O: 10.5

MS (ESI-pos, MeOH**)**: *m/z* = 1638.7972 ([M+Na]$^+$, calcd. 16387932for [$C_{100}H_{118}O_{15}Si_2Na^+$].

IR (ATR-FT): $\tilde{\nu}$ (cm^{-1}) = 3051, 2955, 2925, 2856, 1736, 1592, 1484, 1471, 1463, 1426, 1409, 1387, 1355, 1337, 1298, 1257, 1225, 1204, 1155, 1128, 1083, 1051, 1017, 972.

8.2.2.4.3. Synthesis of compound (*R*,*R*)-**87c**

Described experiment: MT654 Repeated:



According to general procedure **B**, compound (*R*)-**70c** (1.21 g, 1.63 mmol, 2.2 eq) and the bis-boronic ester **99** (0.551 mg, 0.742 mmol, 1 eq) gave the product as a yellow solid (0.747 g, 0.438 mmol, 59.2%).

$C_{104}H_{126}O_{17}Si_2$, MW = 1704.3 g/mol.

^{1}H-NMR (600 MHz, [D$_6$]-dimethylsulfoxid, 298 K) δ [in ppm] = 8.03 (s, 2 H, H-4/14), 8.02 (s, 2 H, H-4/14), 8.01 (d, ^3J = 8.1 Hz, 2 H, H-6/16), 7.99 (d, ^3J = 8.3 Hz, 2 H, H-6/16), 7.43 (t, ^3J = 7.4 Hz, 4 H, H-7+17), 7.33 (s, 4 H, H-22/34), 7.32 (s, 4 H, H-22/34), 7.29 (dt, ^3J = 9.1 Hz, ^4J = 1.1 Hz, 2 H, H-8/18), 7.28 (dt, ^3J = 9.1 Hz, ^4J = 1.1 Hz, 2 H, H-8/18), 7.05 (d, ^3J = 8.3 Hz, 2 H, H-9/19), 7.04 (d, ^3J = 8.3 Hz, 2 H, H-9/19), 4.36 (d, ^2J = 5.5 Hz, 2 H, H-29$_{1/2}$/31$_{1/2}$), 4.35 (d, ^2J = 5.5, 2 H, H-29$_{1/2}$/31$_{1/2}$), 4.27 (d, ^2J = 5.5, 2 H, H-29$_{1/2}$/31$_{1/2}$), 4.26 (d, ^2J = 5.5, 2 H, H-29$_{1/2}$/31$_{1/2}$), 3.92 – 3.91 (m, 4 H, H-38), 3.73 – 3.71 (m, 4 H, H-39), 3.61 – 3.59 (m, 4 H, H-40), 3.57 – 3.55 (m, 4 H, H-41), 3.54 – 3.52 (m, 8 H, H-42+43), 2.32 (s, 6 H, H-30/32), 2.30 (s, 6 H, H-30/32), 2.28 (s, 12 H, H-24/36), 2.23 (s, 12 H, H-24/36), 1.00 (s, 18 H, H-28), 0.20 (s, 6 H, H-26$_{1/2}$), 0.19 (s, 6 H, H-26$_{1/2}$).

^{13}C-NMR (151 MHz, [D$_6$]-dimethylsulfoxid, 298 K) δ [in ppm] = 154.97 (C-25/37), 151.16 (C-25/37), 150.56 (C-2/12), 150.49 (C-2/12), 134.72 (C-3+13), 133.69 (C-21/33), 132.80 (C-10/20), 132.71 (C-10/20), 131.39 (C-21/33), 130.48 (C-5/15), 130.43 (C-5/15), 130.34 (C-23/35), 130.13 (C-4/14), 130.01 (C-4/14), 129.57 (C-22/34), 129.51 (C-22/34), 127.99 (C-6+16), 127.89 (C-23/35), 126.32 (C-8/18), 126.22 (C-8/18), 125.82 (C-1/11), 125.71 (C-1/11), 125.52 (C-9+19), 125.10 (C-7/17), 125.07 (C-7/17), 97.53 (C-29/31), 97.46 (C-29/31), 71.42 (C-38), 69.98 (C-40), 69.88 (C-41/42/43), 69.85 (C-41/42/43), 69.83 (C-41/42/43), 69.80 (C-39), 55.27 (C-30/32), 55.23 (C-30/32), 25.96 (C-28), 18.51 (C-27), 17.55 (C-24/36), 16.04 (C-24/36), -3.12 (C-26).

^{1}H,^{1}H-COSY (600 MHz / 600 MHz, [D$_6$]- dimethylsulfoxid, 298 K) δ [in ppm] = 8.01 / 7.43 (H-6/16 / H-7+17), 7.99 / 7.43 (H-6/16 / H-7+17), 7.43 / 8.01, 7.99, 7.29, 7.28 (H-7+17 / H-6/16, H6/16, H-8/18, H-8/18), 7.33 / 2.28/2.23 (H-22/34 / H-24/36, H-24/36), 7.32 / 2.28/2.23 (H-22/34 / H-24/36, H-24/36), 7.29 / 7.43, 7.05, 7.04 (H-8+18 / H7+17, H-9/19, H-9/19), 7.28 / 7.43, 7.05, 7.04 (H-8+18 / H7+17, H-9/19, H-9/19), 7.05 / 7.29/7.28 (H-9/19 / H-8/18), 7.04 / 7.29/7.28 (H-9/19 / H-8/18), 4.36 / /4.27/4.26 (H-29$_{1/2}$/31$_{1/2}$ / H-29$_{1/2}$/31$_{1/2}$/ H-29$_{1/2}$/31$_{1/2}$), 4.35 / /4.27/4.26 (H-29$_{1/2}$/31$_{1/2}$ / H-29$_{1/2}$/31$_{1/2}$/ H-29$_{1/2}$/31$_{1/2}$), 4.27 / 4.36/4.35 (H-29$_{1/2}$/31$_{1/2}$ / H-29$_{1/2}$/31$_{1/2}$/ H-29$_{1/2}$/31$_{1/2}$), 4.26 / 4.36/4.35 (H-29$_{1/2}$/31$_{1/2}$ / H-29$_{1/2}$/31$_{1/2}$/ H-29$_{1/2}$/31$_{1/2}$), 3.92 – 3.91 / 3.73 – 3.71 (H-38 / H-39), 3.73 – 3.71 / 3.92 – 3.91 (H-39 / H-38).

^{1}H,^{13}C-GHSQC (600 MHz / 151 MHz, [D$_6$]- dimethylsulfoxid, 298 K) δ (^{1}H) / δ (^{13}C) [in ppm] = 8.03 / 130.01 (H-4/14 / C-4/14), 8.02 / 130.13 (H-4/14 / C-4/14), 8.01 / 127.99 (H-6/16 / C-6+16), 7.99

/ 127.99 (H-6/16 / C-6+16), 7.43 / 125.10, 125.07 (H-7+17 / C-7/17), 7.33 / 129.51 (H-22/34 / C-22/34), 7.32 / 129.57 (H-22/34 / C-22/34), 7.29 / 126.32 (H-8/18 / C-8/18), 7.28 / 126.22 (H-8/18 / C-8/18), 7.05 / 125.52 (H-9/19 / C-9+19), 7.04 / 125.52 (H-9/19 / C-9+19), 4.36 / 97.53/97.46 ($H\text{-}29_{1/2}/31_{1/2}$ / C-29/31), 4.35 / 97.53/97.46 ($H\text{-}29_{1/2}/31_{1/2}$ / C-29/31), 4.27 / 97.53/97.46 ($H\text{-}29_{1/2}/31_{1/2}$ / C-29/31), 4.26 / 97.53/97.46 ($H\text{-}29_{1/2}/31_{1/2}$ / C-29/31), 3.92 – 3.91 / 71.42 (H-38 / C-38), 3.73 – 3.71 / 69.80 (H-39 / C-39), 3.61 – 3.59 / 69.98 (H-40 / C-40), 3.57 – 3.55 / 69.88/69.85/69.83 (H-41 / C-41/42//43), 3.54 – 3.52 / 69.88/69.85/69.83 (H-42+43 / C-41/42/43), 2.32 / 55.27/55.23 (H-30/32 / C-30/32), 2.30 / 55.27/55.23 (H-30/32 / C-30/32), 2.28 / 16.04 (H-24/36 / C-24/36), 2.23 / 17.55 (H-24/36 / C-24/36), 1.00 / 25.96 (H-28 / C-28), 0.20 / -3.12 (H-26 / C-26), 0.19 / -3.12 (H-26 / C-26).

^{1}H,^{13}C-GHMBC (400 MHz / 101 MHz, [D$_6$]-dimethylsulfoxid, 298 K) δ (^{1}H) / δ (^{13}C) [in ppm] = 8.03 / 150.56, 132.80/132.71, 131.39, 127.99 (H-4/14 / C-2/12, C-10/20, C-21/33, C-6+16), 8.02 / 150.49, 133.69, 132.80/132.71, 127.99 (H-4/14 / C-2/12, C-21/33, C-10/20, C-6+16), 8.01 / 132.80/132.71, 130.01, 126.22 (H-6/16 / C-10/20, C-4/14, C-8/18), 7.99 / 132.80/132.71, 130.13, 126.32 (H-6/16 / C-10/20, C-4/14, C-8/18), 7.43 / 130.48/130.43, 125.52 (H-7+17 / C-5/15, C-9+19), 7.33 / 154.97, 134.72, 129.51, 17.55/16.05 (H-22/34 / C-25/37, C-3+13, C-22/34, C-24/36), 7.32 / 151.16, 134.72, 129.57, 17.55/16.05 (H-22/34 / C-25/37, C-3+13, C-22/34, C-24/36), 7.29 / 132.80, 127.99 (H-8/18 / C-10/20, C-6+16), 7.28 / 132.71, 127.99 (H-8/18 / C-10/20, C-6+16), 7.05 / 130.48/130.43, 125.82/125.71, 125.10/125.07 (H-9/19 / C-5/15, C-1/11, C-7/17), 7.05 / 130.48/130.43, 125.82/125.71, 125.10/125.07 (H-9/19 / C-5/15, C-1/11, C-7/17), 4.36 / 150.56/150.49, 55.27/55.23 ($H\text{-}29_{1/2}/31_{1/2}$ / C-2/12, C-30/32), 4.35 / 150.56/150.49, 55.27/55.23 ($H\text{-}29_{1/2}/31_{1/2}$ / C-2/12, C-30/32), 4.27 / 150.56/150.49, 55.27/55.23 ($H\text{-}29_{1/2}/31_{1/2}$ / C-2/12, C-30/32), 4.26 / 150.56/150.49, 55.27/55.23 ($H\text{-}29_{1/2}/31_{1/2}$ / C-2/12, C-30/32), 3.92 – 3.91 / 69.80 (H-38 / C-39), 3.73 – 3.71 / 69.98 (H-39 / C-40), 3.61 – 3.59 / 69.88/69.85/69.83/69.80 (H-40 / C-39/40/41/42), 3.57 – 3.55 / 69.88/69.85/69.83/69.80 (H-41 / C-39/40/41/42), 3.54 – 3.52 / 69.88/69.85/69.83/69.80 (H-42+43 / C-39/40/41/42), 2.32 / 97.46 (H-30/32 / C-29/31), 2.30 / 97.53 (H-30/32 / C-29/31), 2.28 / 154.97, 130.34, 129.51 (H-24/36 / C-25/37, C-23/35, C-22/34), 2.23 / 151.16, 129.57, 127.89 (H-24/36 / C-25/37, C-22/34, C-23/35), 1.00 / 25.96, 18.51 (H-28 / C-28, C-27).

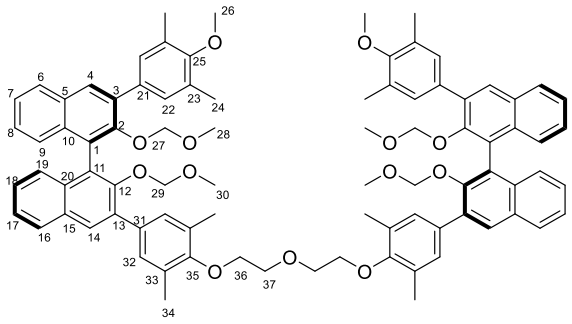
Elemental analysis = calcd (%) for $C_{96}H_{110}O_{13}Si_2$: C: 73.29, H: 7.45, O: 15.96; found: C: 71.3, H: 7.98, O: 13.3

MS (ESI-pos, MeOH**)**: *m/z* = 1726.8485 ($[M+Na]^+$, calcd. 1726.8457 for $[C_{104}H_{126}O_{17}Si_2Na^+]$.

IR (ATR-FT): $\tilde{\nu}$ (cm^{-1}) = 3049, 3022, 2979, 2952, 2926, 2884, 2858, 1592, 1484, 1471, 1426, 1409, 1388, 1353, 1338, 1298, 1271, 1254, 1225, 1203, 1154, 1128, 1101, 1089, 1051, 1029, 1018.

8.2.2.4.4. Synthesis of compound (*R*,*R*)-**85e**

Described experiment: MT622 Repeated:



According to general procedure **B**, compound (*R*)-**70e** (0.244 g, 0.385 mmol, 2.2 eq) and the bis-boronic ester **97** (99.7 mg, 0.175 mmol, 1 eq) gave the product as a yellow solid (0.120 g, 90.1 µmol, 51.1%).

$C_{86}H_{86}O_{13}$, MW = 1327.6 g/mol.

^{1}H-NMR (600 MHz, [D$_6$]-dimethylsulfoxid, 298 K) δ [in ppm] = 8.03 (s, 4 H, H-4+14), 8.02 (d, ^3J = 8.2 Hz, 2 H, H-6/16), 8.01 (d, ^3J = 8.2 Hz, 2 H, H-6/16), 7.44 (t, ^3J = 7.5 Hz, 4 H, H-7+17), 7.34 (s, 8 H, H-22+32), 7.32 – 7.29 (m, 4 H, H-8+18), 7.05 (d, ^3J = 8.5 Hz, 4 H, H-9+19), 4.38 (d, ^2J = 5.5 Hz, 2 H, H-27$_{1/2}$/29$_{1/2}$), 4.37 (d, ^2J = 5.5, 2 H, H-27$_{1/2}$/29$_{1/2}$), 4.28 (d, ^2J = 5.4, 2 H, H-27$_{1/2}$/29$_{1/2}$), 4.27 (d, ^2J = 5.4, 2 H, H-27$_{1/2}$/29$_{1/2}$), 4.00 – 3.98 (m, 4 H, H-36), 3.86 – 3.84 (m, 4 H, H-37), 3.69 (s, 6 H, H-26), 2.33 (s, 12 H, H-34), 2.32 (s, 6 H, H-28/30), 2.31 (s, 6 H, H-28/30), 2.29 (s, 12 H, H-24).

^{13}C-NMR (151 MHz, [D$_6$]-dimethylsulfoxid, 298 K) δ [in ppm] = 156.11 (C-25), 154.97 (C-35), 150.49 (C-2/12), 150.47 (C-2/12), 134.71 (C-3/13), 134.66 (C-3/13), 133.77 (C-21/31), 133.75 (C-21/31), 132.80 (C-10+20), 130.43 (C-5/15), 130.40 (C-5/15), 130.18 (C-4+14+23+33), 129.56 (C-22/32), 129.54 (C-22/32), 128.02 (C-6+16), 126.35 (C-8+18), 125.80 (C-1/11), 125.79 (C-1/11), 125.56 (C-9+19), 125.12 (C-7+17), 97.54 (C-27+29), 71.49 (C-36), 70.00 (C-37), 59.40 (C-26), 55.25 (C-28/30), 55.23 (C-28/30), 16.05 (C-34), 15.91 (C-24).

^{1}H,^{1}H-COSY (600 MHz / 600 MHz, [D$_6$]- dimethylsulfoxid, 298 K) δ [in ppm] = 8.02 / 7.44 (H-6/16 / H-7+17), 8.01 / 7.44 (H-6/16 / H-7+17), 7.44 / 8.02, 8.01, 7.32 – 7.29 (H-7+17 / H-6/16, H-6/16, H-8+18), 7.34 / 2.33, 2.29 (H-22+32 / H-34, H-24), 7.32 – 7.29 / 7.44, 7.05 (H-8+18 / H-7+17, H-9+19), 7.05 / 7.32 – 7.29 (H-9+19 / H-8+18), 4.38/4.37 / 4.28/4.27 (H-27$_{1/2}$/29$_{1/2}$ / H-27$_{1/2}$/29$_{1/2}$), 4.00 – 3.98 / 3.86 – 3.84 (H-36 / H-37), 3.86 – 3.84 / 4.00 – 3.98 (H-37 / H-36).

^{1}H,^{13}C-GHSQC (600 MHz / 151 MHz, [D$_6$]-dimethylsulfoxid, 298 K) δ (^{1}H) / δ (^{13}C) [in ppm] = 8.03 / 130.18 (H-4+14 / C-4+14+23+33), 8.02 / 128.02 (H-6/16 / C-6+16), 8.01 / 128.02 (H-6/16 / C-6+16), 7.44 / 125.12 (H-7+17 / C-7+17), 7.34 / 129.56, 129.54 (H-22+23 / C-22+32), 7.32 – 7.29 / 126.35 (H-8+18 / C-8+18), 7.05 / 125.56 (H-9+19 / C-9+19), 4.38 / 97.54 (H-27$_{1/2}$/29$_{1/2}$ / C-27+29), 4.37 / 97.54 (H-27$_{1/2}$/29$_{1/2}$ / C-27+29), 4.28 / 97.54 (H-27$_{1/2}$/29$_{1/2}$ / C-27/29), 4.27 / 97.54 (H-27$_{1/2}$/29$_{1/2}$ / C-27+29), 4.00 – 3.98 / 71.49 (H-36 / C-36), 3.86 – 3.84 / 70.00 (H-37 / C-37), 3.69 / 59.40 (H-26 / C-26), 2.33 / 16.05 (H-34 / C-34), 2.32 / 55.25/55.23 (H-28/30 / C-28/30), 2.31 / 55.25/55.23 (H-28/30 / C-28/30), 2.29 / 15.91 (H-24 / C-24).

^{1}H,^{13}C-GHMBC (600 MHz / 151 MHz, [D$_6$]-dimethylsulfoxid, 298 K) δ (^{1}H) / δ (^{13}C) [in ppm] = 8.03 / 150.49/150.47, 133.77/133.75, 132.80, 128.02, 125.80/125.79 (H-4+14 / C-2/12, C-21/31, C-10+20, C-6+16, C-1/11), 8.02 / 132.80, 130.18, 126.35 (H-6/16 / C-10+20, C-4+14+23+33, C-8+18),

8.01 / 132.80, 130.18, 126.35 (H-6/16 / C-10+20, C-4+14+23+33, C-8+18), 7.44 / 130.43/130.40, 126.35, 125.56 (H-7+17 / C-5/15, C-8+18, C-9+19), 7.34 / 156.11/154.97, 134.71/134.66, 129.56/129.54, 16.05/15.91 (H-22+32 / C-25/35 C-3/13, C-22/32, C-24/34), 7.32 – 7.29 / 132.80, 128.02, 125.12 (H-8+18 / C-10+20, C-6+16, C-7+17), 7.05 / 130.43/130.40, 125.80/125.79, 125.12 (H-9+19 / C-5+15, C-1/11, C-7+17), 4.38 / 150.49/150.47, 55.25/55.23 (H-$27_{1/2}$/$29_{1/2}$ / C-2/12, C-28/30), 4.37 / 150.49/150.47, 55.25/55.23 (H-$27_{1/2}$/$29_{1/2}$ / C-2/12, C-28/30), 4.28 / 150.49/150.47, 55.25/55.23 (H-$27_{1/2}$/$29_{1/2}$ / C-2/12, C-28/30), 4.27 / 150.49/150.47, 55.25/55.23 (H-$27_{1/2}$/$29_{1/2}$ / C-2/12, C-28/30), 3.69 / 156.11 (H-26 / C-25), 2.33 / 154.97, 130.18, 129.56/129.54 (H-34 / C-35, C-4+14+23+33, C-22/32), 2.32 / 97.54 (H-28/30 / C-27/29), 2.31 / 97.54 (H-28/30 / C-27/29), 2.29 / 156.11, 130.18, 129.56/129.54 (H-24 / C-25, C-4+14+23+33, C-22/32).

[MT622-3_b]

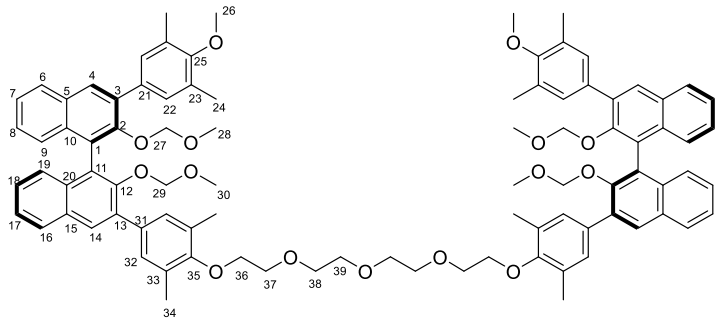
Elemental analysis = calcd (%) for $C_{96}H_{110}O_{13}Si_2$: C: 77.8, H: 6.53, O: 15.67; found: C: 77.9, H: 6.48, O: 15.6

MS (ESI-pos, MeOH**)**: *m/z* = 1349.5951 ($[M+Na]^+$, calcd. 1349.5961 for $[C_{90}H_{94}O_{15}Na^+]$.

IR (ATR-FT): $\tilde{\nu}$ (cm^{-1}) = 3055, 2922, 2872, 2857, 2823, 1734, 1592, 1485, 1428, 1387, 1353, 1222, 1203, 1155, 1127, 1080, 1050, 1015.

8.2.2.4.5. Synthesis of compound (*R*,*R*)-**86e**

Described experiment: MT684 Repeated: MT672



According to general procedure **B**, compound (*R*)-**70e** (0.599 g, 0.816 mmol, 2.2 eq) and the bis-boronic ester **98** (0.253 g, 0.388 mmol, 1 eq) gave the product as a yellow solid (0.298 g, 0.211 mmol, 54.3%).

$C_{90}H_{94}O_{15}$, MW = 1414.7 g/mol.

^{1}H-NMR (400 MHz, [D$_6$]-dimethylsulfoxid, 298 K) δ [in ppm] = 8.03 (s, 2 H, H-4/14), 8.01 (s, 2 H, H-4/14), 7.99 (d, ^3J = 8.6 Hz, 4 H, H-6+16), 7.45 – 7.41 (m, 4 H, H-7+17), 7.34 (s, 4 H, H-22), 7.33 (s, 4 H, H-32), 7.30 – 7.26 (m, 4 H, H-8+18), 7.05 (d, ^3J = 8.8 Hz, 4 H, H-9+19), 4.37 (d, ^2J = 5.5 Hz, 2 H, H-27$_{1/2}$/29$_{1/2}$), 4.36 (d, ^2J = 5.5, 2 H, H-27$_{1/2}$/29$_{1/2}$), 4.27 (d, ^2J = 5.4, 4 H, H-27$_{1/2}$/29$_{1/2}$), 3.94 – 3.92 (m, 4 H, H-36), 3.76 – 3.74 (m, 4 H, H-37), 3.69 (s, 6 H, H-26), 3.64-3.61 (m, 8 H, H-38+39), 2.30 (s, 24 H, H-24+34), 2.29 (s, 12 H, H-28+30).

^{13}C-NMR (101 MHz, [D$_6$]-dimethylsulfoxid, 298 K) δ [in ppm] = 156.10 (C-25), 154.99 (C-35), 150.49 (C-2/12), 150.47 (C-2/12), 134.69 (C-3/13), 134.65 (C-3/13), 133.77 (C-21/31), 133.69 (C-21/31), 132.79 (C-10+20), 130.42 (C-5/15), 130.36 (C-5/15), 130.17 (C-4+14), 129.55 (C-22/32), 129.50 (C-22/32), 127.99 (C-6+16), 126.33 (C-8+18), 125.80 (C-1/11), 125.78 (C-1/11), 125.55 (C-9+19), 125.11 (C-7+17), 97.53 (C-27+29), 71.45 (C-36), 70.01 (C-38/39), 69.95 (C-38/39), 69.83 (C-37), 59.38 (C-26), 55.23 (C-28+30), 16.06 (C-24/34), 15.89 (C-24/34).

^{1}H,^{1}H-COSY (400 MHz / 400 MHz, [D$_6$]-dimethylsulfoxid, 298 K) δ [in ppm] = 7.99 / 7.45-7.41 (H-6+16 / H-7+17), 7.45 – 7.41 / 7.99, 7.30 – 7.26 (H-7+17 / H-6/16, H-8+18), 7.34 / 2.30 (H-22 / H-24/34), 7.33 / 2.30 (H-32 / H-24/34), 7.30 – 7.26 / 7.45 – 7.41, 7.05 (H-8+18 / H7+17, H-9+19), 7.05 / 7.30 (H-9+19 / H-8+18), 4.37 / 4.27 (H-27$_{1/2}$/29$_{1/2}$ / H-27$_{1/2}$/29$_{1/2}$), 4.36 / 4.27 (H-27$_{1/2}$/29$_{1/2}$ / H-27$_{1/2}$/29$_{1/2}$), 4.27 / 4.37, 4.36 (H-27$_{1/2}$/29$_{1/2}$ / H-27$_{1/2}$/29$_{1/2}$), 3.94 – 3.92 / 3.76 – 3.74 (H-36 / H-37), 3.76 – 3.74/ 3.94 – 3.92 (H-37 / H-36).

^{1}H,^{13}C-GHSQC 400 MHz / 101 MHz, [D$_6$]-dimethylsulfoxid, 298 K) δ (^{1}H) / δ (^{13}C) [in ppm] = 8.03 / 130.17 (H-4/14 / C-4+14), 8.01 / 130.17 (H-4/14 / C-4+14), 7.99 / 127.99 (H-6+16 / C-6+16), 7.45 – 7.41 / 125.11 (H-7+17 / C-7+17), 7.34 / 129.55/129.50 (H-22 / C-22/32), 7.33 / 129.55/129.50 (H-32 / C-22/32), 7.30 – 7.26 / 126.33 (H-8+18 / C-8+18), 7.05 / 125.55 (H-9+19 / C-9+19), 4.37 / 97.53 (H-27$_{1/2}$/29$_{1/2}$ / C-27+29), 4.36 / 97.53 (H-27$_{1/2}$/29$_{1/2}$ / C-27/29), 4.27 / 97.53 (H-27$_{1/2}$/29$_{1/2}$ / C-27/29), 3.94 – 3.92 / 71.45 (H-36 / C-36), 3.76 – 3.74 / 69.83 (H-37 / C-37), 3.69 / 59.38 (H-26 / C-26), 3.64-3.61 / 70.01/69.95 (H-38+39 / C-38/39), 2.30 / 16.06, 15.89 (H-24+34 / C-24/34, C-24/34), 2.29 / 55.23 (H-28+30 / C-28+30).

^{1}H,^{13}C-GHMBC (400 MHz / 101 MHz, [D$_6$]-dimethylsulfoxid, 298 K) δ (^{1}H) / δ (^{13}C) [in ppm] = 8.03 / 150.49/150.47, 133.77/133.69, 132.79, 127.99 (H-4+14 / C-2/12, C-21/31, C-10+20, C-6+16),

8.01 / 150.49/150.47, 133.75/133.69, 132.79, 131.39, 127.99 (H-4+14 / C-2/12, C-21/31, C-10+20, C-6+16), 7.99 / 132.79, 130.17, 126.33 (H-6+16 / C-10+20, C-4+14, C-8+18), 7.45 – 7.41 / 130.42/130.36, 125.55 (H-7+17 / C-5/15, C-9+19), 7.34 / 156.10, 134.69/134.65, 129.55/129.50, 16.06/15.89 (H-22 / C-25, C-3/13, C-22/32, C-24/34), 7.33 / 156.10, 134.69/134.65, 129.55/129.50, 16.06/15.89 (H-32 / C-25, C-3/13, C-22/32, C-24/34), 7.30 – 7.26 / 132.79, 127.99 (H-8+18 / C-10+20, C-6+16), 7.05 / 130.42/130.36, 125.11 (H-9+19 / C-5+15, C-7+17), 4.37 / 150.49/150.47, 55.23 (H-$27_{1/2}$/$29_{1/2}$ / C-2/12, C-28/30), 4.36 / 150.49/150.47, 55.23 (H-$27_{1/2}$/$29_{1/2}$ / C-2/12, C-28/30), 4.27 / 150.49/150.47, 55.23 (H-$27_{1/2}$/$29_{1/2}$ / C-2/12, C-28/30), 3.94 – 3.92 / 69.83 (H-36 / C-37), 3.76 – 3.74 / 71.45 (H-37 / C-36), 3.69 / 156.10 (H-26 / C-25), 3.64-3.61 / 69.83 (H-38/39 / C-37), 2.30 / 156.10/154.99, 129.55/129.50 (H-24+34 / C-25/35, C-22/32), 2.29 / 97.53 (H-28+30 / C-27/29).

[MT684-4]

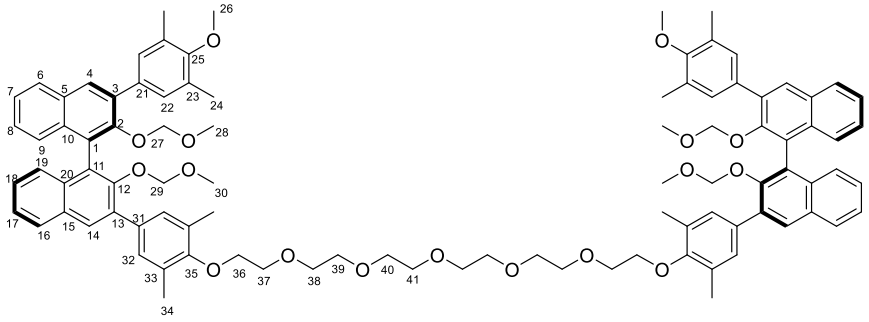
Elemental analysis = calcd (%) for $C_{96}H_{110}O_{13}Si_2$: C: 76.36, H: 6.69, O: 16.95; found: C: 74.0, H: 7.13, O: -

MS (ESI-pos, MeOH**)**: *m/z* = 1437.6492 ($[M+Na]^+$, calcd. 1437.6485 for $[C_{90}H_{94}O_{15}Na^+]$.

IR (ATR-FT): $\tilde{\nu}$ (cm^{-1}) = 3051, 2979, 2922, 2873, 2824, 1591, 1485, 1447, 1428, 1387, 1270, 1222, 1203.

8.2.2.4.6. Synthesis of compound (*R*,*R*)-**87e**

Described experiment: MT677 Repeated:



According to general procedure **B**, compound (*R*)-**70e** (0.601 g, 0.816 mmol, 2.1 eq) and the bis-boronic ester **99** (0.288 g, 0.388 mmol, 1 eq) gave the product as a yellow solid (0.283 g, 0.188 mmol, 48.5%).

$C_{94}H_{102}O_{17}$, MW = 1503.8 g/mol.

^{1}H-NMR (400 MHz, [D$_6$]-dimethylsulfoxid, 298 K) δ [in ppm] = 8.03 (s, 2 H, H-4/14), 8.02 (s, 2 H, H-4/14), 8.01 (d, ^3J = 7.1 Hz, 2 H, H-6/16), 7.98 (d, ^3J = 7.5 Hz, 2 H, H-6/16), 7.43 (t, ^3J = 7.1 Hz, 4 H, H-7+17), 7.35 (s, 4 H, H-22), 7.33 (s, 4 H, H-32), 7.32 – 7.27 (m, 4 H, H-8+18), 7.06 (d, ^3J = 8.1 Hz, 4 H, H-9+19), 4.37 (d, ^2J = 5.5 Hz, 2 H, H-27$_{1/2}$/29$_{1/2}$), 4.36 (d, ^2J = 5.5, 2 H, H-27$_{1/2}$/29$_{1/2}$), 4.27 (d, ^2J = 5.4, 4 H, H-27$_{1/2}$/29$_{1/2}$), 3.93 – 3.90 (m, 4 H, H-36), 3.73 – 3.71 (m, 4 H, H-37), 3.69 (s, 6 H, H-26), 3.62 -3.60 (m, 4 H, H-38), 3.57 -3.53 (m, 12 H, H-39+40+41), 2.30 (s, 12 H, H-28+30), 2.29 (s, 24 H, H-24+34).

^{13}C-NMR (101 MHz, [D$_6$]-dimethylsulfoxid, 298 K) δ [in ppm] = 156.11 (C-25), 154.98 (C-35), 150.51 (C-2/12), 150.49 (C-2/12), 134.70 (C-3/13), 134.66 (C-3/13), 133.78 (C-21/31), 133.70 (C-21/31), 132.80 (C-10+20), 130.44 (C-23+33), 130.36 (C-5+15), 130.17 (C-4+14), 129.56 (C-22/32), 129.51 (C-22/32), 128.02 (C-6+16), 126.33 (C-8+18), 125.82 (C-1/11), 125.80 (C-1/11), 125.56 (C-9+19), 125.16 (C-7+17), 97.55 (C-27+29), 71.43 (C-36), 69.99 (C-37/38/39/40/41), 69.89 (C-37/38/39/40/41), 69.86 (C-37/38/39/40/41), 69.84 (C-37/38/39/40/41), 69.82 (C-37/38/39/40/41), 59.39 (C-26), 55.23 (C-28/30), 55.22 (C-28/30) 16.04 (C-24/34), 15.89 (C-24/34).

^{1}H,^{1}H-COSY (400 MHz / 400 MHz, [D$_6$]-dimethylsulfoxid, 298 K) δ [in ppm] = 8.01 / 7.43 (H-6/16 / H-7+17), 7.98 / 7.43 (H-6/16 / H-7+17), 7.43 / 8.01, 7.99, 7.32 – 7.27 (H-7+17 / H-6/16, H-6/16, H-8+18), 7.35 / 2.29 (H-22 / H-24+34), 7.33 / 2.29 (H-32 / H-24+34), 7.32 – 7.27 / 7.43, 7.06 (H-8+18 / H-7+17, H-9+19), 7.06 / 7.32 – 7.27 (H-9+19 / H-8+18), 4.37 / 4.27 (H-27$_{1/2}$/29$_{1/2}$ / H-27$_{1/2}$/29$_{1/2}$), 4.36 / 4.27 (H-27$_{1/2}$/29$_{1/2}$ / H-27$_{1/2}$/29$_{1/2}$), 4.27 / 4.37, 4.36 (H-27$_{1/2}$/29$_{1/2}$ / H-27$_{1/2}$/29$_{1/2}$), 3.93 – 3.90 / 3.73 – 3.71 (H-36 / H-37), 3.73 – 3.71 / 3.93 – 3.90 (H-37 / H-36).

^{1}H,^{13}C-GHSQC (400 MHz / 101 MHz, [D$_6$]- dimethylsulfoxid, 298 K) δ (^{1}H) / δ (^{13}C) [in ppm] = 8.03 / 130.17 (H-4/14 / C-4+14), 8.02 / 130.17 (H-4/14 / C-4+14), 8.01 / 128.02 (H-6/16 / C-6+16), 7.98 / 128.02 (H-6/16 / C-6+16), 7.43 / 125.16 (H-7+17 / C-7+17), 7.35 / 129.56/129.51 (H-22 / C-22/32), 7.33 / 129.56/129.51 (H-32 / C-22/32), 7.32 – 7.27 / 126.33 (H-8+18 / C-8+18), 7.06 / 125.56 (H-9+19 / C-9+19), 4.37 / 97.55 (H-27$_{1/2}$/29$_{1/2}$ / C-27+29), 4.36 / 97.55 (H-27$_{1/2}$/29$_{1/2}$ / C-27/29), 4.27 / 97.55 (H-27$_{1/2}$/29$_{1/2}$ / C-27+29), 3.93 – 3.90 / 71.43 (H-36 / C-36), 3.73 – 3.71 / 69.99/69.89/69.86/69.84/69.82 (H-37 / C-37/38/39/40/41), 3.69 / 59.39 (H-26 / C-26), 3.62 -3.60 / 69.99/69.89/69.86/69.84/69.82 (H-38

/ C-37/38/39/40/41), 3.57 -3.53 / 69.99/69.89/69.86/69.84/69.82 (H-39+40+41 / C-37/38/39/40/41), 2.29 / 16.04, 15.89 (H-24 / C-24/34, C-24/34), 2.30 / 55.23/55.22 (H-28+30 / C-28/30).

^{1}H,^{13}C-GHMBC (400 MHz / 101 MHz, [D$_6$]- dimethylsulfoxid, 298 K) δ (^{1}H) / δ (^{13}C) [in ppm] = 8.03 / 150.51/150.49, 133.78/133.70, 132.80, 128.02 (H-4+14 / C-2/12, C-21/31, C-10+20, C-6+16), 8.02 / 150.51/150.49, 133.78/133.70, 132.80, 128.02 (H-4+14 / C-2/12, C-21/31, C-10+20, C-6+16), 8.01 / 132.80, 130.17, 126.33 (H-6+16 / C-10+20, C-4+14, C-8+18), 7.98 / 132.80, 130.17, 126.30 (H-6+16 / C-10+20, C-4+14, C-8+18), 7.43 / 130.36, 125.56 (H-7+17 / C-5+15, C-9+19), 7.35 / 156.11, 134.70/134.66, 129.56/129.51, 16.04/15.89 (H-22 / C-25, C-3/13, C-22/32, C-24/34), 7.33 / 154.98, 134.70/134.66, 129.56/129.51, 16.04/15.89 (H-23 / C-35, C-3/13, C-22/32, C-24/34), 7.32 – 7.27 / 132.80, 128.02 (H-8+18 / C-10+20, C-6+16), 7.06 / 130.36, 125.16 (H-9+19 / C-5+15, C-7+17), 4.37 / 150.51/150.49, 55.23/55.22 (H-27$_{1/2}$/29$_{1/2}$ / C-2/12, C-28/30), 4.36 / 150.51/150.49, 55.23/55.22 (H-27$_{1/2}$/29$_{1/2}$ / C-2/12, C-28/30), 4.27 / 150.51/150.49, 55.23/55.22 (H-27$_{1/2}$/29$_{1/2}$ / C-2/12, C-28/30), 3.93 – 3.90 / 69.99/69.89/69.86/69.84/69.82 (H-36 / C-37/38/39/40/41), 3.73 – 3.71 / 71.43 (H-37 / C-36), 3.69 / 156.11 (H-26 / C-25), 3.62-3.60 / 69.99/69.89/69.86/69.84/69.82 (H-38 / C-37/38/39/40/41), 3.57 -3.53 / 69.99/69.89/69.86/69.84/69.82 (H-39+40+41 / C-37/38/39/40/41), 2.30 / 97.55 (H-28+30 / C-27+29), 2.29 / 156.11/154.98, 129.56/129.51 (H-24+34 / C-25/35, C-22/32).

[MT677-7]

Elemental analysis = calcd (%) for $C_{94}H_{102}O_{17}$: C: 75.08, H: 6.84; found: C: 74.4, H: 6.67

MS (ESI-pos, MeOH**)**: *m/z* = 1525.7009 ([M+Na]$^+$, calcd. for 1525.7024 [$C_{96}H_{110}O_{13}Si_2Na^+$].

IR (ATR-FT): $\tilde{\nu}$ (cm^{-1}) = 3048, 2980, 2970, 2946, 2917, 2903, 2883, 2871, 2824, 1591, 1485, 1447, 1428, 1408, 1387, 1353, 1337, 1298, 1270, 1254, 1222, 1203, 1152, 1127, 1083, 1050, 1015.

[MT677]

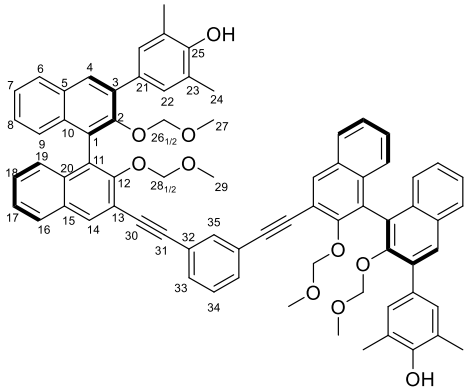
8.2.2.5. Deprotection of *tert*-butyldimethylsilyl protectinggroups

C: General procedure for the TBDMS-deprotection:

The corresponding TBDMS-protected compound was dissolved in dry tetrahydrofuran (10 ml / mmol TBDMS-protected compound). Then a solution of freshly pepared tetrabutylammoniumfluorid 30 hydrate in tetrahydrofuran (1 mM, 1.1 eq if one TBDMS-group is present or 2.2 eq if two TBDMS-groups are present) was added in a dropwise manner with rapid stirring. The solution was stirred at 25 °C for 3 minutes. Then, water (25 mL/mmol TBDMS-protected compound) and ethyl acetate (40 mL/mmol TBDMS-protected compound) were added. The organic layer was separated and then washed with a saturated solution of sodium chloride (1 x 25 mL/mmol TBDMS-protected compound). The organic layer was dried over sodium sulfate and concentrated in *vacuo.* The crude product was purified by column chromatography (cyclohexane:ethyl acetate 5:1) to afford the product as a yellow solid.

8.2.2.5.1. Synthesis of compound (*R*,*R*)-**79d**

Described experiment: MT537 Repeated: MT493



According to general procedure **C**, compound (*R*,*R*)-**79c** (1.24 g, 0.925 mmol, 1 eq.) gave the product as a yellow solid (0.998 g, 0.898 mmol, 97.1%).

$C_{74}H_{62}O_{10}$, MW = 1111.3 g/mol.

^{1}H-NMR (400 MHz, [D$_6$]-dimethylsulfoxid, 298 K) δ [in ppm] = 8.44 (s, 2H, H-14), 8.39 (s, 2 H, OH), 8.04 (d, ^3J = 8.3 Hz, 2 H, H-16), 8.02 (d, ^3J = 8.0 Hz, 2 H, H-6), 8.01 (s, 2 H, H-4), 7.84 (br s, 1 H, H-35), 7.70 (dd, ^3J = 7.8 Hz, J = 1.5 Hz, 2 H, H-33), 7.57 (t, ^3J = 7.8 Hz, 1 H, H-34), 7.50 (t, ^3J = 7.5 Hz, 2 H, H-17), 7.45 (t, ^3J = 7.2 Hz, 2 H, H-7), 7.37 (t, ^3J = 7.81 Hz, 2 H, H-18), 7.30 (t, ^3J = 7.8 Hz, 2 H, H-8), 7.27 (s, 4 H, H-22), 7.10 (d, ^3J = 9.0 Hz, 2 H, H-19), 7.03 (d, ^3J = 8.7 Hz, 2 H, H-9), 4.99 (s, 4 H, H-28), 4.30 (d, ^2J = 5.6, 2 H, H-26$_{1/2}$), 4.25 (d, ^2J = 5.6, 2 H, H-26$_{1/2}$), 2.62 (s, 6 H, H-29), 2.24 (s, 12 H, H-24), 2.18 (s, 6 H, H-27).

^{13}C-NMR (101 MHz, [D$_6$]-dimethylsulfoxid, 298 K) δ [in ppm] = 152.84 (C-25), 152.15 (C-12), 150.70 (C-2), 134.77 (C-3), 134.13 (C-14), 133.66 (C-20), 133.56 (C-35), 132.28 (C-10), 131.71 (C-33), 130.52 (C-5), 130.13 (C-4), 129.95 (C-15), 129.66 (C-34), 129.02 (C-21), 128.91 (C-22), 127.96 (C-6/16), 127.91 (C-6/16), 127.61 (C-18), 126.23 (C-11), 126.19 (C-8), 125.93 (C-19), 125.64 (C-17), 125.42 (C-9), 125.09 (C-7), 124.82 (C-1), 124.23 (C-23), 123.04 (C-32), 116.24 (C-13), 98.12 (C-28), 97.18 (C-26), 92.14 (C-31), 87.49 (C-30), 55.52 (C-29), 55.13 (C-27), 16.71 (C-24).

^{1}H,^{1}H-COSY (400 MHz / 400 MHz, [D$_6$]-dimethylsulfoxid, 298 K) δ [in ppm] = 8.04 / 7.50 (H-16 / H-17), 8.02 / 7.45 (H-6 / H-7), 7.70 / 7.57 (H-33 / H-34), 7.57 / 7.70 (H-34 / H-33), 7.50 / 8.04, 7.37 (H-17 / H-16, H-18), 7.45 / 8.01, 7.30 (H-7 / H-6, H-8), 7.37 / 7.50, 7.10 (H-18 / H-17, H-19), 7.30 / 7.45, 7.03 (H-8 / H-7, H-9), 7.27 / 2.24 (H-22 / H-24), 7.10 / 7.37 (H-19 / H-18), 7.03 / 7.30 (H-9 / H-8), 4.30 / 4.25 (H-26$_{1/2}$ / H-26$_{1/2}$), 4.25 / 4.30 (H-26$_{1/2}$ / H-26$_{1/2}$), 2.24 / 7.27 (H-24 / H-22).

^{1}H,^{13}C-GHSQC (400 MHz / 101 MHz, [D$_6$]-dimethylsulfoxid, 298 K) δ (^{1}H) / δ (^{13}C) [in ppm] = 8.44 / 134.13 (H-14 / C-14), 8.04 / 127.96/127.91 (H-16 / C-6/16), 8.02 / 127.96/127.91 (H-6 / C-6/16), 8.01 / 130.13 (H-4 / C-4), 7.84 / 133.56 (H-35 / C-35), 7.70 / 131.71 (H-33 / C-33), 7.57 / 129.66 (H-34 / C-34), 7.50 / 125.64 (H-17 / C-17), 7.45 / 125.09 (H-7 / C-7), 7.37 / 127.61 (H-18 / C-18), 7.30 / 126.19 (H-8 / C-8), 7.27 / 128.91 (H-22 / C-22), 7.10 / 125.93 (H-19 / C-19), 7.03 / 125.42 (H-9 / C-9), 4.99 / 98.12 (H-28 / C-28), 4.30 / 97.18 (H-26$_{1/2}$ / C-26), 4.25 / 97.18 (H-26$_{1/2}$ / C-26), 2.62 / 55.52 (H-29 / C-29), 2.24 / 16.71 (H-24/ C-24), 2.18 / 55.13 (H-27 / C-27).

^{1}H,^{13}C-GHMBC (400 MHz / 101 MHz, [D$_6$]- dimethylsulfoxid, 298 K) δ (^{1}H) / δ (^{13}C) [in ppm] = 8.44 / 152.15, 133.66, 127.96/127.91, 126.23, 87.49 (H-14 / C-12, C-20, C-6/16, C-11, C-30), 8.39 / 152.84, 124.23 (OH / C-25, C-23), 8.04 / 134.13, 133.66, 126.61 (H-16 / C-14, C-20, C-18), 8.02 / 132.28, 130.13, 126.19, 125.42 (H-6 / C-10, C-4, C-8, C-9), 8.01 / 150.70, 132.28, 129.02, 127.96/127.91, 124.82 (H-4 / C-2, C-10, C-21, C6/16, C-1), 7.84 / 131.71, 92.14 (H-35 / C-33, C-31), 7.70 / 133.56, 131.71, 92.14 (H-33 / C-35, C-33, C-31), 7.57 / 123.04 (H-34 / C-32), 7.50 / 129.95, 127.61, 125.93 (H-17 / C-15, C-18, C-19), 7.45 / 130.52, 125.42, 124.82 (H-7 / C-5, C-9, C-1), 7.37 / 133.66, 127.96/127.91, 125.64 (H-18 / C-20, C-6/16, C-17), 7.30 / 132.28, 127.96/127.91, 125.09 (H-8 / C-10, C-6/16, C-7), 7.27 / 152.84, 134.77, 128.91, 16.71 (H-22 / C-25, C-3, C-22, C-24), 7.10 / 129.95, 126.23, 125.64 (H-19 / C-15, C-11, C-17), 7.03 / 130.52, 125.09 (H-9 / C-5, C-7), 4.99 / 152.15, 55.52 (H-28 / C-12, C-29), 4.30 / 150.70, 55.13 (H-26$_{1/2}$ / C-2, C-27), 4.29 / 150.70, 55.13 (H-26$_{1/2}$ / C-2, C-27), 2.62 / 98.12, (H-29 / C-28), 2.24 / 152.84, 128.91, 124.23 (H-24 / C-25, C-22, C-23), 2.18 / 97.18 (H-27 / C-26). [MT537-3]

Elemental analysis = calcd (%) for $C_{74}H_{62}O_{10}$: C: 79.98, H: 5.62, O: 14.40; found:

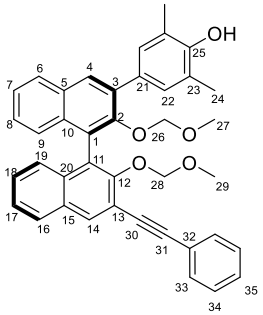
C: 78.9, H: 5.59, O: 14.4. [MT537]

MS (ESI-pos, MeOH**)**: *m/z* = 1133.4233 ([M+Na]$^{+}$, calcd. 1133.4235 for [$C_{74}H_{62}O_{10}Na^{+}$].

IR (ATR-FT): $\tilde{\nu}$ (cm^{-1}) = 3569, 3459, 3053, 2904, 2824, 1588, 1566, 1489, 1474, 1446, 1427, 1389, 1355, 1337, 1316, 1251, 1227, 1196, 1149, 1080, 1057, 1016, 966, 909, 887, 789. [MT537]

8.2.2.5.2. Synthesis of compound (*R*)-**102d**

Described experiment: MT540 Repeated:



According to general procedure **C**, compound (*R*)-**102c** (0.464 g, 0.654 mmol, 1 eq), gave the product as a yellow solid (0.366 g, 0.616 mmol, 94.8%).

$C_{40}H_{34}O_5$, MW = 594.7 g/mol.

^{1}H-NMR (400 MHz, [D$_6$]-dimethylsulfoxid, 298 K) δ [in ppm] = 8.41 (s, 1 H, H-14), 8.40 (s, 1 H, H-OH), 8.04 (d, ^3J = 7.6 Hz, 1 H, H-16), 8.03 – 8.01 (m, 2 H, H-4+6), 7.63 – 7.61 (m, 2 H, H-33), 7.50 (t, ^3J = 8.0 Hz, 1 H, H-17), 7.47 – 7.45 (m, 3 H, H-34+35), 7.45 (t, ^3J = 8.0 Hz, 1 H, H-7), 7.36 (t, ^3J = 8.1 Hz, 1 H, H-18), 7.30 (t, ^3J = 8.1 Hz, 1 H, H-8), 7.28 (s, 2 H, H-22), 7.09 (d, ^3J = 8.6 Hz, 1 H, H-19), 7.03 (d, ^3J = 8.6 Hz, 1 H, H-9), 4.98 (s, 2 H, H-28), 4.30 (d, ^2J = 5.8, 1 H, H-26$_{1/2}$), 4.25 (d, ^2J = 5.6, 1 H, H-26$_{1/2}$), 2.63 (s, 3 H, H-29), 2.24 (s, 6 H, H-24), 2.18 (s, 3 H, H-27).

^{13}C-NMR (101 MHz, [D$_6$]-dimethylsulfoxid, 298 K) δ [in ppm] = 152.85 (C-25), 152.10 (C-12), 150.69 (C-2), 134.78 (C-3), 133.86 (C-14), 133.43 (C-20), 132.29 (C-10), 131.31 (C-33), 130.52 (C-5), 130.11 (C-4), 129.98 (C-15), 129.03 (C-21), 128.92 (C-34+35), 128.89 (C-22), 127.95 (C-6), 127.86 (C-16), 127.47 (C-18), 126.16 (C-8), 125.91 (C-19), 125.59 (C-17), 125.42 (C-9), 125.09 (C-7), 124.87 (C-1), 124.23 (C-11+23), 122.26 (C-32), 116.53 (C-13), 98.03 (C-28), 97.35 (C-26), 93.21 (C-31), 86.58 (C-30), 55.53 (C-29), 55.12 (C-27), 16.71 (C-24).

^{1}H,^{1}H-COSY (400 MHz / 400 MHz, [D$_6$]-dimethylsulfoxid, 298 K) δ [in ppm] = 8.04 / 7.48 (H-16 / H-17), 8.03 – 8.01 / 7.45 (H-4+6 / H-7), 7.50 / 8.04, 7.36 (H-17 / H-16, H-18), 7.45 / 8.03 – 8.01, 7.30 (H-7 / H-4+6, H-8), 7.36 / 7.50, 7.09 (H-18 / H-17, H-19), 7.30 / 7.45, 7.03 (H-8 / H-7, H-9), 7.28 / 2.24 (H-22 / H-24), 7.09 / 7.36 (H-19 / H-18), 7.03 / 7.30 (H-9 / H-8), 4.30 / 4.25 (H-26$_{1/2}$ / H-26$_{1/2}$), 4.25 / 4.30 (H-26$_{1/2}$ / H-26$_{1/2}$), 2.24 / 7.28 (H-24 / H-22).

^{1}H,^{13}C-GHSQC (400 MHz / 101 MHz, [D$_6$]- dimethylsulfoxid, 298 K) δ (^{1}H) / δ (^{13}C) [in ppm] = 8.41 / 133.86 (H-14 / C-14), 8.04 / 127.86 (H-16 / C-16), 8.03 – 8.01 / 130.11, 127.95 (H-4+6 / C-4+6), 7.63 – 7.61 / 131.31 (H-33 / C-33), 7.50 / 125.59 (H-17 / C-17), 7.47 – 7.45 / 128.92 (H-34+35 / C-34+35), 7.45 / 125.09 (H-7 / C-7), 7.36 / 127.47 (H-18 / C-18), 7.30 / 126.16 (H-8 / C-8), 7.28 / 128.89 (H-22 / C-22), 7.09 / 125.91 (H-19 / C-19), 7.03 / 125.42 (H-9 / C-9), 4.98 / 98.03 (H-28 / C-28), 4.30 / 97.35 (H-26$_{1/2}$ / C-26), 4.25 / 97.35 (H-26$_{1/2}$ / C-26), 2.63 / 55.53 (H-29 / C-29), 2.24 / 16.71 (H-24/ C-24), 2.18 / 55.12 (H-27 / C-27).

^{1}H,^{13}C-GHMBC (400 MHz / 101 MHz, [D$_6$]- dimethylsulfoxid, 298 K) δ (^{1}H) / δ (^{13}C) [in ppm] = 8.41 / 152.10, 133.43, 127.86, 86.58 (H-14 / C-12, C-20, C-16, C-30), 8.40 / 124.23 (OH / C-11+23), 8.04 / 133.43, 127.47 (H-16 / C-20, C-18), 8.03 – 8.01 / 150.69, 132.29, 130.11, 129.03, 126.16 (H-4+6 / C-2, C-10, C-4, C-21, C-8), 7.63 – 7.61 / 131.31, 128.92, 93.21 (H-33 / C-33, C-34+35, C-31), 7.47 –

7.45 / 131.31, 128.92, 122.26 (H-34+35 / C-33, C-34+35, C-32), 7.45 / 130.52, 125.42 (H-7 / C-5, C-9), 7.36 / 133.43, 127.86 (H-18 / C-20, C-16), 7.30 / 132.29, 127.95 (H-8 / C-10, C-6), 7.28 / 152.85, 134.78, 128.89, 16.71 (H-22 / C-25, C-3, C-22, C-24), 7.09 / 129.98, 125.59, 124.23 (H-19 / C-15, C-17, C-11+23), 7.03 / 130.52, 125.09, 124.87 (H-9 / C-5, C-7, C-1), 4.98 / 152.10, 55.53 (H-28 / C-12, C-29), 4.30 / 150.69, 55.12 (H-$26_{1/2}$ / C-2, C-27), 4.25 / 150.69, 55.12 (H-$26_{1/2}$ / C-2, C-27), 2.63 / 98.03, (H-29 / C-28), 2.24 / 152.85, 128.89, 124.23 (H-24 / C-25, C-22, C-11+23), 2.18 / 97.35 (H-27 / C-26).

[MT540-2]

Elemental analysis = calcd (%) for $C_{40}H_{34}O_5$: C: 80.79, H: 5.76, O: 13.45; found:

C: 80.6, H: 5.76, O: 14.2

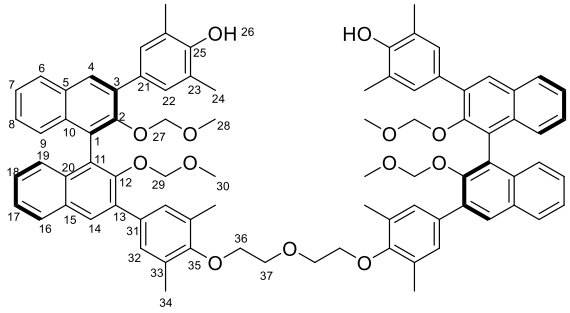
MS (ESI-pos, MeOH**)**: *m/z* = 617.2307 ($[M+Na]^+$, calcd. 617.2298 for $[C_{40}H_{34}O_5Na^+]$ [MT540-2]

IR (ATR-FT): $\tilde{\nu}$ (cm^{-1}) = 3448, 3051, 2922, 2824, 1735, 1719, 1708, 1596, 1489, 1442, 1426, 1389, 1355, 1335, 1254, 1226, 1197, 1150.

[MT540]

8.2.2.5.3. Synthesis of compound (*R*,*R*)-**85d**

Described experiment: MT586 Repeated: MT582, MT564, MT572, MT580



According to general procedure **C**, compound (*R*,*R*)-**85c** (0.479 g, 0.314 mmol, 1 eq), gave the product as a yellow solid (0.372 g, 0.286 mmol, 91.4%).

$C_{84}H_{82}O_{13}$, MW = 1299.54 g/mol.

^{1}H-NMR (400 MHz, [D$_6$]-dimethylsulfoxid, 298 K) δ [ppm]= 8.38 (s, 2H, H-26), 8.02 (d, ^{3}J = 6.0 Hz, 4H, H-14), 7.99 (m, 6H, H-4+6+16), 7.45 – 7.40 (m, 4H, H-7+17), 7.35 (s, 4H, H-22/32), 7.32 – 7.27 (m, 4H, H-8+18), 7.26 (s, 4H, H-22/32), 7.06 (d, ^{3}J = 8.6 Hz, 2H, H-9/19), 7.05 (d, ^{3}J = 8.6 Hz, 2H, H-9/19), 4.38 (d, ^{2}J = 3.3 Hz, 2H, H-27$_{1/2}$/H-29$_{1/2}$), 4.37 (d, ^{2}J = 3.3 Hz, 2H, H-27$_{1/2}$/H-29$_{1/2}$), 4.30 (d, ^{2}J = 5.2 Hz, 2H, H-27$_{1/2}$/H-29$_{1/2}$), 4.28 (d, ^{2}J = 5.2 Hz, 2H, H-27$_{1/2}$/H-29$_{1/2}$), 4.01 – 3.98 (m, 4H, H-36/37), 3.87 – 3.84 (m, 4H, H-36/37), 2.34 (s, 12H, H-24/34), 2.33 (s, 6H, H-28/30), 2.29 (s, 6H, H-28/30), 2.24 (s, 12H, H-24/34).

^{13}C-NMR (101 MHz, [D$_6$]-dimethylsulfoxid, 298 K) δ [ppm] = 154.95 (C-25/35), 152.80 (C-25/35), 150.57 (C-2/12), 150.45 (C-2/12), 135.01 (C-3/13), 134.72 (C-3/13), 133.80 (C-21/31), 132.86 (C-10/20), 132.54 (C-10/20), 130.53 (C-5/15), 130.43 (C-5/15), 130.38 (C-23/33), 130.06 (C-4/14), 129.91 (C-4/14), 129.56 (C-22/32), 129.14 (C-21/31), 129.01 (C-22/32), 127.97 (C-6/16), 127.92 (C-6/16), 126.26 (C-8/18), 126.09 (C-8/18), 125.95 (C-1/11), 125.72 (C-1/11), 125.63 (C-9/19), 125.53 (C-9/19), 125.09 (C-7/17), 125.01 (C-7/17), 124.16 (C-23/33), 97.53 (C-27/29), 97.32 (C-27/29), 71.48 (C-36/C-37), 70.00 (C-36/C-37), 55.27 (C-28/30), 55.19 (C-28/C-30), 16.71 (C-24/34), 16.05 (C-24/34).

COSY (400 MHz / 400 MHz, [D$_6$]-dimethylsulfoxid, 298 K) δ [ppm] = 8.01 / 7.45 – 7.40 (H-4+6+16 / H-7+17), 7.45 – 7.40 / 8.01, 7.32 – 7.27 (H-7+17 / H-4+6+16, H-8/18), 7.35 / 2.34 (H-22/32 / H-24/34), 7.32 – 7.27 / 7.45 – 7.40, 7.06, 7.05 (H-8+18 / H-7+17, H-9/19, H-9/19), 7.26 / 2.24 (H-22/32 / H-24/34), 7.06 / 7.32 – 7.27 (H-9/19 / H-8+18), 7.05 / 7.32 – 7.27 (H-9/19 / H-8+18), 4.38 / 4.30/4.28 (H-27$_{1/2}$/H-29$_{1/2}$ / H-27$_{1/2}$/H-29$_{1/2}$/ H-27$_{1/2}$/H-29$_{1/2}$), 4.37 / 4.30/4.28 (H-27$_{1/2}$/H-29$_{1/2}$ / H-27$_{1/2}$/H-29$_{1/2}$/ H-27$_{1/2}$/H-29$_{1/2}$), 4.30 / 4.38/4.37 (H-27$_{1/2}$/H-29$_{1/2}$ / H-27$_{1/2}$/H-29$_{1/2}$/ H-27$_{1/2}$/H-29$_{1/2}$), 4.28 / 4.38/4.37 (H-27$_{1/2}$/H-29$_{1/2}$ / H-27$_{1/2}$/H-29$_{1/2}$ / H-27$_{1/2}$/H-29$_{1/2}$), 4.01 – 3.98 / 3.87 – 3.84 (H-36/37 / H-36/37), 3.87 – 3.84 / 4.01 – 3.98 (H-36/37 / H-36/37), 2.34 / 7.35 (H-24/34 / H-22/32), 2.24 / 7.26 (H-24/34 / H-22/32).

HSQC (400 MHz / 101 MHz, [D$_6$]-dimethylsulfoxid, 298 K): δ (^{1}H) / δ (^{13}C) [in ppm] = 8.02 / 130.06/129.91 (H-14 / C-4/14), 7.99 / 130.06/129.91, 127.97/127.92 (H-4+6+16 / C-4/6/16), 7.45 – 7.40 / 125.09/125.01 (H-7+17 / C-7/17), 7.35 / 129.56 (H-22/32 / C-22/32), 7.32 – 7.27 / 126.26/126.09 (H-8+18 / C-8/18), 7.26 / 129.01 (H-22/32 / C-22/32), 7.06 / 125.63/125.53 (H-9/19 / C-9/19), 7.05 / 125.63/125.53 (H-9/19 / C-9/19), 4.38 / 97.53/97.32 (H-27$_{1/2}$/H-29$_{1/2}$ / C-27/29), 4.37 / 97.53/97.32

(H-$27_{1/2}$/H-$29_{1/2}$ / C-27/29), 4.30 / 97.53/97.32 (H-$27_{1/2}$/H-$29_{1/2}$ / C-27/29), 4.28 / 97.53/97.32 (H-$27_{1/2}$/H-$29_{1/2}$ / C-27/29), 4.01 – 3.98 / 71.48 (H-36/37 / C-36/37), 3.87 – 3.84 / 70.00 (H-36/37 / C-36/37), 2.34 / 16.05 (H-24/34 / C-24/34), 2.33 / 55.27/55.19 (H-28/30 / C-28/30), 2.29 / 55.27/55.19 (H-28/30 / C-28/30), 2.24 / 16.71 (H-24/34 / C-24/34).

HMBC (400 MHz / 101 MHz, [D_6]-dimethylsulfoxid, 298 K): δ (^{1}H) / δ (^{13}C) [in ppm] = 8.38 / 124.16 (H-26 / C-23/33), 8.02 / 150.45, 133.80, 132.86, 127.97/127.92 (H-14 / C-2/12, C-21/31, C-10/20, C-6/16), 7.99 / 150.57, 130.06/129.91, 132.54, 129.14, 127.97/127.92, 125.95/126.09 (H-4+6+16 / C-2/12, C-4/14, C-10/20, C-21/31, C-6/16, C-8/18), 7.45 – 7.40 / 130.53/130.43, 125.63/125.53 (H-7+17 / C-5/15, C-9/19), 7.35 / 154.95, 134.72, 129.56, 16.05 (H-22/32 / C-25/35, C-3/13, C-22/32, C-24/34), 7.32 – 7.27 / 132.86, 132.54, 127.97/127.92 (H-8+18 / C-10/20, C-10/20, C-6/16), 7.26 / 152.80, 135.01, 129.14, 16.71 (H-22/32 / C-25/35, C-3/13, C-21/31, C-24/34), 7.05 / 130.53/130.43, 125.09/125.01 (H-9/19 / C-5/15, C-7/17), 7.04 / 130.53/130.43, 125.09/125.01 (H-9/19 / C-5/15, C-7/17), 4.38 / 150.57/150.45, 55.27/55.19 (H-$27_{1/2}$/H-$29_{1/2}$ / C-2/12, C-28/C-30), 4.37 / 150.57/150.45, 55.27/55.19 (H-$27_{1/2}$/H-$29_{1/2}$ / C-2/12, C-28/C-30), 4.30 / 150.57/150.45, 55.27/55.19 (H-$27_{1/2}$/H-$29_{1/2}$ / C-2/12, C-28/C-30), 4.28 / 150.57/150.45, 55.27/55.19 (H-$27_{1/2}$/H-$29_{1/2}$ / C-2/12, C-28/C-30), 2.34 / 154.95, 130.38, 129.56 (H-24/34 / C-25/35, C-23/33, C-22/32), 2.33 / 97.53 (H-28/30 / C-27/29), 2.29 / 97.32 (H-28/30 / C-27/29), 2.24 / 152.80, 124.16 (H-24/34 / C-25/35, C-23/33).

[MT586]

Elemental analysis = calcd (%) for $C_{84}H_{82}O_{13}$: C: 77.63, H: 6.36, O: 16.01; found:

C: 80.90, H: 6.73, O: 16.3.

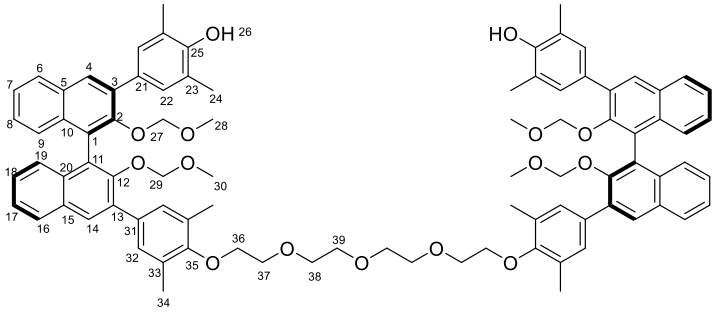
MS (ESI-pos, MeOH**)**: *m/z* = 1321.5620 ($[M+Na]^+$, calcd. 1321.5617for $[C_{84}H_{82}O_{13}Na^+]$.

IR (ATR-FT): $\tilde{\nu}$ (cm^{-1}) = 3438, 3050, 2920, 2849, 2825, 1593, 1487, 1426, 1387, 1353, 1336, 1197, 1147, 1079, 1049, 971, 920, 876, 747.

[MT586]

8.2.2.5.4. Synthesis of compound (*R*,*R*)-**86d**

Described experiment: MT653 Repeated:



According to general procedure **C**, compound (*R*,*R*)-**86c** (0.417 g, 0.258 mmol, 1 eq), gave the product as a yellow solid (0.248 g, 0.178 mmol, 69.3%).

$C_{88}H_{90}O_1$, MW = 1387.7 g/mol.

^{1}H-NMR (400 MHz, [D$_6$]-dimethylsulfoxid, 298 K): δ [ppm]= 8.38 (s, 2H, H-26), 8.00 – 7.97 (m, 8H, H-4+14+6+16), 7.42 (t, ^3J = 7.5 Hz, 4H, H-7+17), 7.33 (s, 4H, H-22), 7.32 – 7.24 (m, 4H, H-8+18), 7.26 (s, 4H, H-32), 7.05 (d, ^3J = 8.4 Hz, 2H, H-9/19), 7.04 (d, ^3J = 8.4 Hz, 2H, H-9/19), 4.37 (d, ^2J = 5.5 Hz, 4H, H-27$_{1/2}$/H-29$_{1/2}$), 4.28 (d, ^2J = 5.5 Hz, 2H, H-27$_{1/2}$/H-29$_{1/2}$), 4.26 (d, ^2J = 5.5 Hz, 2H, H-27$_{1/2}$/H-29$_{1/2}$), 3.94 – 3.92 (m, 4H, H-36), 3.76 – 3.73 (m, 4H, H-37), 3.65 – 3.61 (m, 8H, H-38+39), 2.31 (s, 6H, H-28/30), 2.30 (s, 12H, H-24), 2.27 (s, 6H, H-28/30), 2.23 (s, 12H, H-34).

^{13}C-NMR (101 MHz, [D$_6$]-dimethylsulfoxid, 298 K) δ [ppm] = 154.98 (C-25), 152.80 (C-35), 150.57 (C-2/12), 150.46 (C-2/12), 135.00 (C-3/13), 134.72 (C-3/13), 132.85 (C-10/20), 132.53 (C-10/20), 130.53 (C-5/15), 130.43 (C-5/15), 130.35 (C-21/31), 130.04 (C-4/14), 129.92 (C-4/14), 129.53 (C-22), 129.14 (C-21/31), 129.01 (C-32), 127.95 (C-6/16), 127.93 (C-6/16), 126.25 (C-8/18), 126.07 (C-8/18), 125.95 (C-1/11), 125.72 (C-1/11), 125.63 (C-9/19), 125.52 (C-9/19), 125.08 (C-7/17), 125.01 (C-7/17), 124.16 (C-23+33), 97.52 (C-27/29), 97.31 (C-27/29), 71.46 (C-36), 70.02 (C-38/39), 69.96 (C-38/39), 69.85 (C-37), 55.26 (C-28/30), 55.18 (C-28/30), 16.70 (C-34), 16.06 (C-24).

COSY (400 MHz / 400 MHz, [D$_6$]-dimethylsulfoxid, 298 K): δ [ppm] = 8.00 – 7.97/ 7.42 (H-4+14+6+16 / H-7+17), 7.42 / 8.00 – 7.97, 7.32 – 7.24 (H-7+17 / H-4+14+6+16, H-8+18), 7.33 / 2.30 (H-22 / H-24), 7.32 – 7.24 / 7.42, 7.05, 7.04 (H-8+18 / H-7+17, H-9/19, H-9/19), 7.26 / 2.23 (H-32 / H-34), 7.05 / 7.32 – 7.24 (H-9/19 / H-8+18), 7.04 / 7.32 – 7.24 (H-9/19 / H-8+18), 4.37 / 4.28/4.26 (H-27$_{1/2}$/H-29$_{1/2}$ / H-27$_{1/2}$/H-29$_{1/2}$/ H-27$_{1/2}$/H-29$_{1/2}$), 4.28 / 4.37 (H-27$_{1/2}$/H-29$_{1/2}$ / H-27$_{1/2}$/H-29$_{1/2}$), 4.26 / 4.37 (H-27$_{1/2}$/H-29$_{1/2}$ / H-27$_{1/2}$/H-29$_{1/2}$), 3.94 – 3.92 / 3.76 – 3.73 (H-36 / H-37), 3.76 – 3.73/ 3.94 – 3.92 (H-37 / H-36), 2.30 / 7.33 (H-24 / H-22), 2.23 / 7.26 (H-34 / H-32).

HSQC (400 MHz / 101 MHz, [D$_6$]-dimethylsulfoxid, 298 K): δ (^{1}H) / δ (^{13}C) [in ppm] = 8.00 – 7.97/ 130.04, 129.92, 127.95, 129.93 (H-4+14+6+16 / C-4, C-14, C-6, C-16), 7.42 / 125.08/125.01 (H-7+17 / C-7/17), 7.33 / 129.53 (H-22 / C-22), 7.32 – 7.24 / 126.25/126.07 (H-8+18 / C-8/18), 7.26 / 129.01 (H-32 / C-32), 7.05 / 125.63/125.52 (H-9/19 / C-9/19), 7.04 / 125.63/125.52 (H-9/19 / C-9/19), 4.37 / 97.52/97.31 (H-27$_{1/2}$/H-29$_{1/2}$ / C-27/29), 4.28 / 97.52/97.31 (H-27$_{1/2}$+H-29$_{1/2}$ / C-27/29), 4.26 / 97.52/97.31 (H-27$_{1/2}$/H-29$_{1/2}$ / C-27/29), 3.94 – 3.92 / 71.46 (H-36 / C-36), 3.76 – 3.73/ 69.85 (H-37 / C-37), 3.65 – 3.61 / 70.02, 69.96 (H-38+39 / C-38, C-39), 2.31 / 55.26/55.18 (H-28/30 / C-28/30), 2.30 / 16.06 (H-24 / C-24/34), 2.27 / 55.26/55.18 (H-28/30 / C-28/30), 2.23 / 16.70 (H-34 / C-24/34).

HMBC (400 MHz / 101 MHz, [D_6]-dimethylsulfoxid, 298 K): δ (^{1}H) / δ (^{13}C) [in ppm] = 8.38 / 124.16 (H-26 / C-23+33), 8.00 – 7.97/ 150.57/150.46, 132.85/132.53, 130.35, 130.04/129.92, 129.14, 127.95/127.93, 126.25/126.07 (H-4+14+6+16 / C-2/12, C-10/20, C-21/31, C-4/14, C-21/31, C-6/16, C-8/18), 7.42 / 130.53/130.43, 125.63/125.52 (H-7+17 / C-5/15, C-9/19), 7.33 / 154.98, 134.72, 129.53, 16.06 (H-22 / C-25, C-3/13, C-22, C-24), 7.32 – 7.24 / 132.85/132.53, 127.95/127.93 (H-8+18 / C-10/20, C-6/16), 7.26 / 152.80, 135.00, 129.01, 16.70 (H-32 / C-35, C-3/13, C-32, C-34), 7.05 / 130.53/130.43, 125.95/125.72, 125.08/125.01 (H-9/19 / C-5/15, C-1/11, C-7/17), 7.04 / 130.53/130.43, 125.95/125.72, 125.08/125.01 (H-9/19 / C-5/15, C-1/11, C-7/17), 4.37 / 150.57/150.46, 55.26/55.18 (H-$27_{1/2}$/H-$29_{1/2}$ / C-2/12, C-28/30), 4.28 / 150.57/150.46, 55.26/55.18 (H-$27_{1/2}$/H-$29_{1/2}$ / C-2/12, C-28/30), 4.26 / 150.57/150.46, 55.26/55.18 (H-$27_{1/2}$/H-$29_{1/2}$ / C-2/12, C-28/30), 3.94 – 3.92 / 69.85 (H-36 / C-37), 3.76 – 3.73/ 71.46 (H-37 / C-36), 2.31 / 97.52 (H-28/30 / C-27/29), 2.30 / 154.98, 130.35, 129.53 (H-24 / C-25, C-21/31, C-22), 2.27 / 97.31 (H-28/30 / C-27/29), 2.23 / 152.80, 129.01, 124.16 (H-34 / C-35, C-32, C23+33). [MT653-4]

Elemental analysis = calcd (%) for $C_{88}H_{90}O_1$: C: 76.17, H: 6.54, O: 17.29; found:

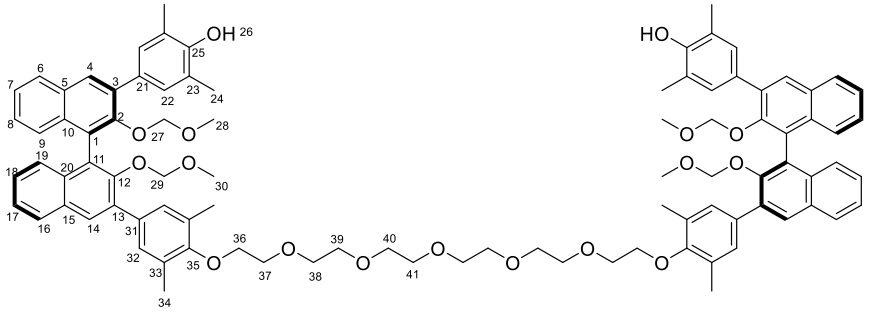
C: 75.5, H: 6.5, O: -.

MS (ESI-pos, MeOH**)**: *m/z* = 1409.6159 ([M+Na]$^+$, calcd. 1409.6172 for [$C_{88}H_{90}O_1Na^+$].

IR (ATR-FT): $\tilde{\nu}$ (cm^{-1}) = 3434, 3412, 3048, 2979, 2969, 2917, 2888, 1700, 1594, 1487, 1427, 1387, 1353, 1337, 1199, 1147, 1127, 1082, 1050, 1017, 970. [MT653]

8.2.2.5.5. Synthesis of compound (*R*,*R*)-**87d**

Described experiment: MT657 Repeated:



According to general procedure **C**, compound (*R*,*R*)-**87c** (0.661 g, 0.388 mmol, 1 eq), gave the product as a yellow solid (0.566 g, 0.384 mmol, 98.8%).

$C_{92}H_{98}O_{17}$, MW = 1475.8 g/mol.

^{1}H-NMR (400 MHz, [D$_6$]-dimethylsulfoxid, 298 K): δ [ppm]= 8.38 (s, 2H, H-26), 8.01 (s, 2H, H-4/14), 8.00 (d, ^{3}J = 8.1 Hz, 4H, H-6+16), 7.99 (s, 2H, H-4/14), 7.45 – 7.40 (m, 4H, H-7+17), 7.33 (s, 4H, H-22), 7.31 – 7.27 (m, 4H, H-8+18), 7.26 (s, 4H, H-32), 7.05 (d, ^{3}J = 8.9 Hz, 2H, H-9/19), 7.04 (d, ^{3}J = 8.4 Hz, 2H, H-9/19), 4.37 (d, ^{2}J = 5.7 Hz, 4H, H-27$_{1/2}$/H-29$_{1/2}$), 4.28 (d, ^{2}J = 5.6 Hz, 2H, H-27$_{1/2}$/H-29$_{1/2}$), 4.27 (d, ^{2}J = 5.9 Hz, 2H, H-27$_{1/2}$/H-29$_{1/2}$), 3.93 – 3.90 (m, 4H, H-36), 3.73 – 3.71 (m, 4H, H-37), 3.62 – 3.60 (m, 4H, H-38), 3.57 – 3.52 (m, 12H, H-39+40+41), 2.32 (s, 6H, H-28/30), 2.29 (s, 12H, H-24), 2.28 (s, 6H, H-28/30), 2.23 (s, 12H, H-34).

^{13}C-NMR (101 MHz, [D$_6$]-dimethylsulfoxid, 298 K) δ [ppm] = 154.97 (C-25), 152.80 (C-35), 150.57 (C-2/12), 150.46 (C-2/12), 135.00 (C-3/13), 134.72 (C-3/13), 133.74 (C-21/31), 132.85 (C-10/20), 132.53 (C-10/20), 130.53 (C-5/15), 130.43 (C-5/15), 130.34 (C-33), 130.06 (C-4/14), 129.91 (C-4/14), 129.53 (C-22), 129.14 (C-21/31), 129.01 (C-32), 127.96 (C-6+16), 126.25 (C-8/18), 126.07 (C-8/18), 125.95 (C-1/11), 125.72 (C-1/11), 125.63 (C-9/19), 125.52 (C-9/19), 125.08 (C-7/17), 125.01 (C-7/17), 124.16 (C-23), 97.52 (C-27/29), 97.32 (C-27/29), 71.43 (C-36), 69.99 (C-38), 69.89 (C-37/39/40/41), 69.86 (C-37/39/40/41), 69.83 (C-37/39/40/41), 69.81 (C-37/39/40/41), 55.26 (C-28/30), 55.18 (C-28/C-30), 16.70 (C-24/34), 16.05 (C-24/34).

COSY (400 MHz / 400 MHz, [D$_6$]-dimethylsulfoxid, 298 K): δ [ppm] = 8.00 / 7.45 – 7.40 (H-6+16 / H-7+17), 7.45 – 7.40 / 8.00, 7.31 – 7.27 (H-7+17 / H-6+16, H-8+18), 7.33 / 2.29 (H-22 / H-24), 7.31 – 7.27 / 7.45 – 7.40, 7.05, 7.04 (H-8+18 / H-7+17, H-9/19, H-9/19), 7.26 / 2.23 (H-32 / H-34), 7.05 / 7.31 – 7.27 (H-9/19 / H-8+18), 7.04 / 7.31 – 7.27 (H-9/19 / H-8+18), 4.37 / 4.28/4.27 (H-27$_{1/2}$/H-29$_{1/2}$ / H-27$_{1/2}$/H-29$_{1/2}$/ H-27$_{1/2}$/H-29$_{1/2}$), 4.28 / 4.37 (H-27$_{1/2}$/H-29$_{1/2}$ / H-27$_{1/2}$/H-29$_{1/2}$), 4.27 / 4.37 (H-27$_{1/2}$/H-29$_{1/2}$ / H-27$_{1/2}$/H-29$_{1/2}$), 3.93 – 3.90/ 3.73 – 3.71 (H-36 / H-37), 3.73 – 3.71 / 3.93 – 3.90 (H-37 / H-36), 2.29 / 7.33 (H-24 / H-22), 2.23 / 7.26 (H-34 / H-32).

HSQC (400 MHz / 101 MHz, [D$_6$]-dimethylsulfoxid, 298 K): δ (^{1}H) / δ (^{13}C) [in ppm] = 8.01 / 130.06/129.91 (H-4/14 / C-4/14), 8.00 / 127.96 (H-6+16 / C-6+16), 7.99 / 130.06/129.91 (H-4/14 / C-4/14), 7.45 – 7.40 / 125.08/125.01 (H-7+17 / C-7/17), 7.33 / 129.53 (H-22 / C-22), 7.31 – 7.27 / 126.25/126.07 (H-8+18 / C-8/18), 7.26 / 129.01 (H-32 / C-32), 7.05 / 125.63/125.52 (H-9/19 / C-9/19), 7.04 / 125.63/125.52 (H-9/19 / C-9/19), 4.37 / 97.52/97.32 (H-27$_{1/2}$/H-29$_{1/2}$ / C-27/29), 4.28 / 97.52/97.32 (H-27$_{1/2}$/H-29$_{1/2}$ / C-27/29), 4.27 / 97.52/97.32 (H-27$_{1/2}$/H-29$_{1/2}$ / C-27/29), 3.93 – 3.90/ 71.43 (H-36 / C-36), 3.73 – 3.71 / 69.89/69.86/69.83/69.81 (H-37 / C-37/39/40/41), 3.62 – 3.60 / 69.99

(H-38 / C-38), 3.57 – 3.52 / 69.89/69.86/69.83/69.81 (H-39+40+41 / C-37/39/40/41), 2.32 / 55.26 (H-28/30 / C-28/30), 2.29 / 16.05 (H-24 / C-24/34), 2.28 / 55.18 (H-28/30 / C-28/30), 2.23 / 16.70 (H-34 / C-24/34).

HMBC (400 MHz / 101 MHz, [D_6]-dimethylsulfoxid, 298 K): δ (^{1}H) / δ (^{13}C) [in ppm] = 8.38 / 124.16 (H-26 / C-23), 8.01 / 150.57/150.46, 133.74, 127.96 (H-4/14 / C-2/12, C-21/31, C6+16), 8.00 / 132.85, 132.53 (H-6+16 / C-10/20), 7.99 / 150.57/150.46, 133.74, 127.96 (H-4/14 / C-2/12, C-21/31, C6+16) 7.45 – 7.40 / 130.53/130.43, 125.63/125.52 (H-7+17 / C-5/15, C-9/19), 7.33 / 154.97, 134.72, 129.53, 16.70/16.05 (H-22 / C-25, C-3/13, C-22, C-24/34), 7.31 – 7.27 / 132.85, 132.53, 127.96 (H-8+18 / C-10/20, C-6+16), 7.26 / 152.80, 135.00, 129.01, 16.71/16.05 (H-32 / C-35, C-3/13, C-32, C-24/34), 7.05 / 130.53/130.43, 125.08/125.01 (H-9/19 / C-5/15, C-7/17), 7.04 / 130.53/130.43, 125.08/125.01 (H-9/19 / C-5/15, C-7/17), 4.37 / 150.57/150.46, 55.26/55.18 (H-$27_{1/2}$+H-$29_{1/2}$ / C-2/12, C-28/30), 4.28 / 150.57/150.46, 55.26/55.18 (H-$27_{1/2}$+H-$29_{1/2}$ / C-2/12, C-28/30), 4.27 / 150.57/150.46, 55.26/55.18 (H-$27_{1/2}$+H-$29_{1/2}$ / C-2/12, C-28/30), 3.93 – 3.90/ 69.89/69.86/69.83/69.81, (H-36 / C-37/39/40/41), 3.73 – 3.71 / 71.43 (H-37 / C-36), 3.57 – 3.52 / 69.89/69.86/69.83/69.81 (H-39/40/41 / C-37/39/40/41), 2.32 / 97.52 (H-28/30 / C-27/29), 2.29 / 154.97, 130.34, 129.53 (H-24 / C-25, C-23/33, C-22), 2.28 / 97.32 (H-28/30 / C-27/29), 2.23 / 152.80, 129.01, 124.16 (H-34 / C-35, C-32, C23/33). [MT657-4]

Elemental analysis = calcd (%) for $C_{92}H_{98}O_{17}$: C: 74.88, H: 6.69, O: 18.43; found:

C: 73.6, H: 7.26, O: -.

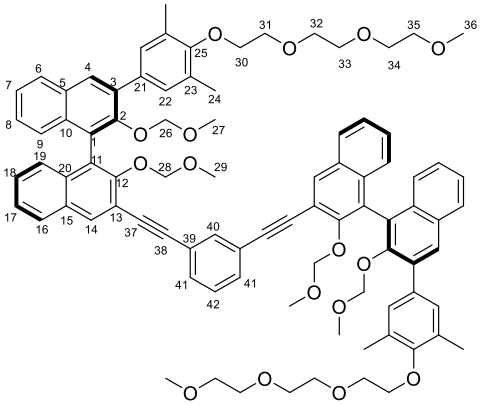
MS (ESI-pos, MeOH**)**: *m/z* = 1498.6732 ([M+Na]$^+$, calcd. 1498.6730 for [$C_{92}H_{98}O_{17}Na^+$].

IR (ATR-FT): $\tilde{\nu}$ (cm^{-1}) = 3426, 3049, 2979, 2970, 2913, 2884, 1701, 1594, 1488, 1427, 1387, 1352, 1337, 1255, 1199, 1147, 1127, 1086, 1050, 1017, 970.

[MT657]

8.2.2.5.6. Synthesis of compound (*R*,*R*)-**79b**

Described experiment: MT538 Repeated: MT498



Compound (*R*,*R*)**79d** (0.509 g, 0.458 mmol, 1 eq) and caesium carbonate (0.446 g, 1.37 mmol, 3 eq) were dissolved in degassed acetonitrile (10 ml) and stirred for 15 minutes under argon. After the addition of triethyleneglycol methyl ether tosylate (0.313 g, 0.985 mmol, 2.15 eq) dissolved in 10 ml acetonitrile, the reaction mixture was stirred at 90 °C for one hour. After cooling to room temperature caesium carbonate was removed by filtration. Then water (10 ml) and ethyl acetate (10 ml) were added. The aqueous phase was extracted with ethyl acetate (20 ml) and the combined organic layer was washed with a saturated solution of sodium chloride (20 ml). The organic layer was dried over sodium sulfate and concentrated in *vacuo*. The crude product was purified by column chromatography (21x3 cm, cyclohexane:ethyl acetate 1:2) and afforded the product as a white solid (0.559 g, 0.398 mmol, 87.2%).

$C_{88}H_{90}O_{16}$, MW = 1403.7 g/mol.

^{1}H-NMR (600 MHz, [D$_6$]-dimethylsulfoxid, 298 K) δ [in ppm] = 8.45 (s, 2 H, H-14), 8.07 (s, 2 H, H-4), 8.05 (d, ^3J = 8.2 Hz, 2 H, H-16), 8.03 (d, ^3J = 8.4 Hz, 2 H, H-6), 7.84 (br s, 1 H, H-40), 7.69 (d, ^3J = 7.3 Hz, 2 H, H-41), 7.57 (t, ^3J = 7.3 Hz, 1 H, H-42), 7.50 (t, ^3J = 7.5 Hz 2 H, H-17), 7.47 (t, ^3J = 7.5 Hz, 2 H, H-7), 7.38 (t, ^3J = 7.5 Hz, 2 H, H-18), 7.35 (s, 4 H, H-22), 7.32 (t, ^3J = 7.9 Hz, 2 H, H-8), 7.10 (d, ^3J = 8.4 Hz, 2 H, H-19), 7.05 (d, ^3J = 8.6 Hz, 2 H, H-9), 5.01 (d, ^2J = 5.7 Hz, 2 H, H-28$_{1/2}$), 4.99 (d, ^2J = 5.7 Hz, 2 H, H-28$_{1/2}$), 4.30 (d, ^2J = 5.8 Hz, 2 H, H-26$_{1/2}$), 4.25 (d, ^2J = 5.8 Hz, 2H, H-26$_{1/2}$), 3.94 – 3.92 (m, 4 H, H-30), 3.74 – 3.73 (m, 4 H, H-31), 3.63 – 3.61 (m, 4 H, H-32), 3.57 – 3.55 (m, 4 H, H-33), 3.54 – 3.53 (m, 4 H, H-34/35), 3.44 – 3.43 (m, 4 H, H-34/35), 3.23 (s, 6 H, H-36), 2.61 (s, 6 H, H-29), 2.30 (s, 12 H, H-24), 2.21 (s, 6 H, H-27).

^{13}C-NMR (151 MHz, [D$_6$]- dimethylsulfoxid, 298 K) δ [in ppm] = 155.03 (C-25), 152.20 (C-12), 150.62 (C-2), 134.46 (C-3), 134.22 (C-14), 133.69 (C-40), 133.57 (C-21), 133.50 (C-20), 132.55 (C-10), 131.73 (C-41), 130.46 (C-4/5/23), 130.42 (C-4/5/23), 129.95 (C-15), 129.67 (C-12), 129.42 (C-22), 128.07 (C-6), 127.97 (C-16), 127.71 (C-18), 126.46 (C-8), 126.07 (C-11), 125.87 (C-19), 125.68 (C-17), 125.45 (C-9), 125.21 (C-7), 124.93 (C-1), 123.02 (C-39), 116.25 (C-13), 98.15 (C-28), 97.59 (C-26), 92.20 (C-38), 87.44 (C-37), 71.44 (C-30), 71.29 (C-35), 69.99 (C-32), 69.85 (C-33), 69.81 (C-31), 69.66 (C-34), 58.05 (C-36), 55.48 (C-29), 55.18 (C-27), 16.06 (C-24).

^{1}H,^{1}H-COSY (600 MHz / 600 MHz, [D$_6$]- dimethylsulfoxid, 298 K) δ [in ppm] = 8.05 / 7.50 (H-16 / H-17), 8.03 / 7.47 (H-6 / H-7), 7.69 / 7.57 (H-41 / H-42), 7.57 / 7.69 (H-42 / H-41), 7.50 / 8.05, 7.38 (H-17 / H-16, H-18), 7.47 / 8.03, 7.32 (H-7 / H-6, H-8), 7.38 / 7.50, 7.10 (H-18 / H-17, H-19), 7.35 / 2.30 (H-22 / H-24), 7.32 / 7.47, 7.05 (H-8 / H-7, H-9), 7.10 / 7.38 (H-19 / H-18), 7.05 / 7.32 (H-9 / H-

8), 5.01 / 4.99 (H-$28_{1/2}$ / H-$28_{1/2}$), 4.99 / 5.01 (H-$28_{1/2}$ / H-$28_{1/2}$), 4.30 / 4.25 (H-$26_{1/2}$ / H-$26_{1/2}$), 4.25 / 4.30 (H-$26_{1/2}$ / H-$26_{1/2}$), 3.94 – 3.92 / 3.74 – 3.73 (H-30 / H-31), 3.74 – 3.73 / 3.94 – 3.92 (H-31 / H-30), 3.63 – 3.61 / 3.57 – 3.55 (H-32 / H-33), 3.57 – 3.55 / 3.63 – 3.61 (H-33 / H-32), 3.54 – 3.53 / 3.44 – 3.43 (H-34/35 / H-34/35), 3.44 – 3.43 / 3.54 – 3.53 (H-34/35 / H-34/35), 2.30 / 7.35 (H-24 / H-22).

^{1}H,^{13}C-GHSQC (600 MHz / 151 MHz, [D$_6$]- dimethylsulfoxid, 298 K) δ (^{1}H) / δ (^{13}C) [in ppm] = 8.45 / 134.22 (H-14 / C-14), 8.07 / 130.46/130.42 (H-4 / C-4/5/23), 8.05 / 127.97 (H-16 / C-16), 8.03 / 128.07 (H-6 / C-6), 7.84 / 133.69 (H-40 / C-40), 7.69 / 131.73 (H-41 / C-41), 7.57 / 129.67 (H-42 / C-42), 7.50 / 125.68 (H-17 / C-17), 7.47 / 125.21 (H-7 / C-7), 7.38 / 127.71 (H-18 / C-18), 7.35 / 129.42 (H-22 / C-22), 7.32 / 126.46 (H-8 / C-8), 7.10 / 125.87 (H-19 / C-19), 7.05 / 125.45 (H-9 / C-9), 5.01 / 98.15 (H-$28_{1/2}$ / C-28), 4.99 / 98.15 (H-$28_{1/2}$ / C-28), 4.30 / 97.59 (H-$26_{1/2}$ / C-26), 4.25 / 97.59 (H-$26_{1/2}$ / C-26), 3.94 – 3.92 / 71.44 (H-30 / C-30), 3.74 – 3.73 / 69.81 (H-31 / C-31), 3.63 – 3.61 / 69.99 (H-32 / C-32), 3.57 – 3.55 / 69.85 (H-33 / C-33), 3.54 – 3.53 / 69.66 (H-34/35 / C-34/35), 3.44 – 3.43 / 71.29 (H-34/35 / C-34/35), 3.23 / 58.05 (H-36 / C-36), 2.61 / 55.48 (H-29 / C-29), 2.30 / 16.06 (H-24 / C-24), 2.21 / 55.18 (H-27 / C-27).

^{1}H,^{13}C-GHMBC (600 MHz / 151 MHz, [D$_6$]- dimethylsulfoxid, 298 K) δ (^{1}H) / δ (^{13}C) [in ppm] = 8.45 / 152.20, 133.57/133.50, 127.97, 87.44 (H-14 / C-12, C-20/21, C-16, C-37), 8.07 / 150.62, 133.57/133.50, 132.55, 128.07 (H-4 / C-2, C-20/21, C-10, C-6), 8.05 / 134.22, 133.50, 127.71 (H-16 / C-14, C-20, C-18), 8.03 / 132.55, 130.46/130.42, 126.46 (H-6 / C-10, C-4/5/23, C-8), 7.84 / 131.73, 92.20 (H-40 / C-41, C-38), 7.69 / 133.69, 131.73, 92.20 (H-41 / C-40, C-41, C-38), 7.57 / 123.02 (H-42 / C-39), 7.50 / 129.95, 125.87 (H-17 / C-15, C-19), 7.47 / 130.46/130.42, 125.45 (H-7 / C-4/5/23, C-9), 7.38 / 133.50, 127.97 (H-18 / C-20, C-16), 7.35 / 155.03, 134.46, 129.42, 16.06 (H-22 / C-25, C-3, C-22, C-24), 7.32 / 132.55, 128.07 (H-8 / C-10, C-6), 7.10 / 129.95, 126.07, 125.68 (H-19 / C-15, C-11, C-17), 7.05 / 130.46/130.42, 125.21, 124.93 (H-9 / C-4/5/23, C-7, C-1), 5.01 / 152.20, 55.48 (H-$28_{1/2}$ / C-12, C-29), 4.99 / 152.20, 55.48 (H-$28_{1/2}$ / C-12, C-29), 4.30 / 150.62, 55.18 (H-$26_{1/2}$ / C-2, C-27), 4.25 / 150.62, 55.18 (H-$26_{1/2}$ / C-2, C-27), 3.63 – 3.61 / 69.81 (H-32 / C-31), 3.57 – 3.55 / 69.65 (H-33 / C-34), 3.54 – 3.53 / 71.29, 69.85 (H-34/35 / C-35, C-33), 3.44 – 3.43 / 58.05 (H-34/35 / C-36), 3.23 / 71.29 (H-36 / C-35), 2.61 / 98.15 (H-29 / C-28), 2.30 / 155.03, 130.46/130.42, 129.42 (H-24 / C-25, C-4/5/23, C-22), 2.21 / 97.59 (H-27 / C-26).

[MT538-3]

Elemental analysis = calcd (%) for $C_{39}H_{44}O_8$: C: 73.10, H: 6.92, O: 19.98; found:

C: 70.5, H: 7.0, O: -

MS (ESI-pos, MeOH**)**: *m/z* = 724.3009 ([M+Na]$^{2+}$, calcd. 724.3007for [$C_{39}H_{44}O_8$ Na_2^{2+}].

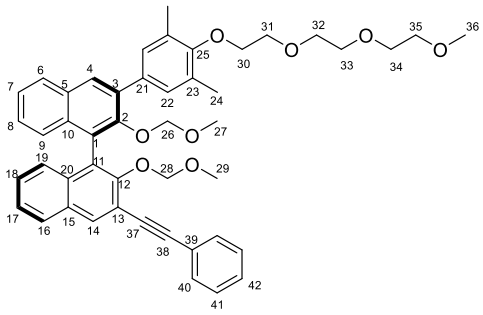
[MT498-2]

IR (ATR-FT): $\tilde{\nu}$ (cm^{-1}) = 3050, 2921, 2872, 2823, 1620, 1597, 1571, 1485, 1443, 1425, 1389, 1351, 1331, 1287, 1263, 1221, 1198, 1151, 1095, 1087, 1059, 1027, 969, 916, 884, 851, 751.

[MT498]

8.2.2.5.7. Synthesis of compound (*R*)-**102b**

Described experiment: MT541 Repeated:



Compound (*R*)-**102d** (0.268 g, 0.451 mmol, 1 eq) and caesium carbonate (0.219 g, 0.675 mmol, 1.5 eq) were dissolved in degassed acetonitrile (10 ml) and stirred for 15 minutes under argon. After the addition of triethyleneglycol methyl ether tosylate (0.165 g, 0.521 mmol, 1.15 eq), dissolved in 5 ml acetonitrile, the reaction mixture was stirred at 90 °C for one hour. After cooling to room temperature caesium carbonate was removed by filtration. Then water (10 ml) and ethyl acetate (10 ml) were added. The aqueous phase was extracted with ethyl acetate (20 ml) and the combined organic layer was washed with a saturated solution of sodium chloride (20 ml). The organic layer was dried over sodium sulfate and concentrated in *vacuo*. The crude product was purified by column chromatography (21x2 cm, cyclohexane:ethyl acetate 1:2) and afforded the product as a white solid (0.326 g, 0.440 mmol, 97.8%).

$C_{47}H_{48}O_8$, MW = 740.9 g/mol.

^{1}H-NMR (400 MHz, [D$_6$]-dimethylsulfoxid, 298 K) δ [in ppm] = 8.42 (s, 1 H, H-14), 8.07 (s, 1 H, H-4), 8.04 (d, ^3J = 8.1 Hz, 2 H, H-6+16), 7.63 – 7.61 (m, 2 H, H-40), 7.51 – 7.45 (m, 5 H, H-7+17+41+42), 7.37 (t, ^3J = 9.0 Hz, 1 H, H-18), 7.36 (s, 2 H, H-22), 7.32 (t, ^3J = 6.8 Hz, 1 H, H-8), 7.09 (d, ^3J = 8.7 Hz, 1 H, H-19), 7.04 (d, ^3J = 8.6, 1 H, H-9), 4.99 (s, 2 H, H-28), 4.30 (d, ^2J = 5.5 Hz, 1 H, H-26$_{1/2}$), 4.26 (d, ^2J = 5.5 Hz, 1H, H-26$_{1/2}$), 3.95 – 3.93 (m, 2 H, H-30), 3.75 – 3.73 (m, 2 H, H-31), 3.63 – 3.61 (m, 2 H, H-32), 3.58 – 3.54 (m, 4 H, H-33+34), 3.45 – 3.43 (m, 2 H, H-35), 3.24 (s, 3 H, H-36), 2.61 (s, 3 H, H-29) 2.31 (s, 6 H, H-24), 2.22 (s, 3 H, H-27).

^{13}C-NMR (101 MHz, [D$_6$]-dimethylsulfoxid, 298 K) δ [in ppm] = 155.03 (C-25), 152.16 (C-12), 150.61 (C-2), 134.47 (C-3), 133.95 (C-14), 133.58 (C-21), 133.38 (C-20), 132.56 (C-10), 131.31 (C-40), 130.46 (C-5+23), 130.40 (C-4), 129.99 (C-15), 129.43 (C-22), 129.04 (C-42), 128.89 (C-41), 128.06 (C-6), 127.91 (C-16), 127.56 (C-18), 126.44 (C-8), 126.01 (C-11), 125.84 (C-19), 125.62 (C-17), 125.45 (C-9), 125.21 (C-7), 124.98 (C-1), 122.24 (C-39), 116.54 (C-13), 98.06 (C-28), 97.58 (C-26), 93.27 (C-38), 86.53 (C-37), 71.44 (C-30), 71.29 (C-35), 69.99 (C-32), 69.85 (C-31), 69.81 (C-33/34), 69.66 (C-33/34), 58.06 (C-36), 55.50 (C-29), 55.18 (C-27), 16.07 (C-24).

^{1}H,^{1}H-COSY (400 MHz / 400 MHz, [D$_6$]-dimethylsulfoxid, 298 K) δ [in ppm] = 8.04 / 7.51 – 7.45 (H-6+16 / H-7+17+41+42), 7.63 – 7.61 / 7.51 – 7.45 (H-40 / H-7+17+41+42), 7.51 – 7.45 / 8.04, 7.63 – 7.61 (H-7+17+41+42 / H-6+16, H-40), 7.37 / 7.09 (H-18 / H-19), 7.36 / 2.31 (H-22 / H-24), 7.32 / 7.04 (H-8 / H-9), 7.09 / 7.37 (H-19 / H-18), 7.04 / 7.32 (H-9 / H-8), 4.30 / 4.26 (H-26$_{1/2}$ / H-26$_{1/2}$), 4.26 / 4.30 (H-26$_{1/2}$ / H-26$_{1/2}$), 3.95 – 3.93 / 3.75 – 3.73 (H-30 / H-31), 3.75 – 3.73/ 3.95 – 3.93 (H-31 / H-30), 3.58 – 3.54 / 3.45 – 3.43 (H-33+34 / H-35), 3.45 – 3.43 / 3.58 – 3.54 (H-35 / H-33+34), 2.31 / 7.36 (H-24 / H-22).

^{1}H,^{13}C-GHSQC (400 MHz / 101 MHz, [D$_6$]-dimethylsulfoxid, 298 K) δ (^{1}H) / δ (^{13}C) [in ppm] = 8.42 / 133.95 (H-14 / C-14), 8.07 / 130.40 (H-4 / C-4), 8.04 / 128.06, 127.91 (H-6+16 / C-6, C-16), 7.63 – 7.61 / 131.31 (H-40 / C-40), 7.51 – 7.45 / 129.04, 128.89, 125.62, 125.21 (H-7+17+41+42 / C-42, C-41, C-17, C-7), 7.37 / 127.56 (H-18 / C-18), 7.36 / 129.43 (H-22 / C-22), 7.32 / 126.44 (H-8 / C-8), 7.09 / 125.84 (H-19 / C-19), 7.04 / 125.45 (H-9 / C-9), 4.99 / 98.06 (H-28 / C-28), 4.30 / 97.58 (H-26$_{1/2}$ / C-26), 4.26 / 97.58 (H-26$_{1/2}$ / C-26), 3.95 – 3.93 / 71.44 (H-30 / C-30), 3.75 – 3.73/ 69.85 (H-31 / C-31), 3.63 – 3.61 / 69.99 (H-32 / C-32), 3.58 – 3.54 / 69.81, 69.66 (H-33+34 / C-33+34), 3.45 – 3.43 / 71.29 (H-35 / C-35), 3.24 / 58.06 (H-36 / C-36), 2.61 / 55.50 (H-29 / C-29), 2.31 / 16.07 (H-24 / C-24), 2.22 / 55.18 (H-27 / C-27).

^{1}H,^{13}C-GHMBC (400 MHz / 101 MHz, [D$_6$]- dimethylsulfoxid, 298 K) δ (^{1}H) / δ (^{13}C) [in ppm] = 8.42 / 152.16, 133.38, 127.91, 86.53 (H-14 / C-12, C-20, C-16, C-37), 8.07 / 150.61, 133.58, 132.56, 128.06 (H-4 / C-2, C-21, C-10, C-6), 8.04 / 133.95, 133.38, 132.56, 130.40, 127.56, 126.44 (H-6+16 / C-14, C-20, C-10, C-4, C-18, C-8), 7.63 – 7.61 / 131.31, 129.04, 93.27 (H-40 / C-40, C-42, C-38), 7.51 – 7.45 / 131.31, 130.46/130.40, 129.99, 128.89, 125.84, 125.45, 122.24 (H-7+17+41+42 / C-40, C-5+23/C-4, C-15, C-41, C-19, C-9, C-39), 7.37 / 133.38, 127.91 (H-18 / C-20, C-16), 7.36 / 155.03, 134.47, 129.43, 16.07 (H-22 / C-25, C-3, C-22, C-24), 7.32 / 132.56, 128.06 (H-8 / C-10, C-6), 7.09 / 129.99, 126.01, 125.62 (H-19 / C-15, C-11, C-17), 7.04 / 130.46, 125.21, 124.98 (H-9 / C-5+23, C-7, C-1), 4.99 / 152.16, 55.50 (H-28 / C-12, C-29), 4.30 / 150.61, 55.18 (H-26$_{1/2}$ / C-2, C-27), 4.26 / 150.61, 55.18 (H-26$_{1/2}$ / C-2, C-27), 3.95 – 3.93 / 69.85/69.81 (H-30 / C-31/33+34), 3.75 – 3.73/ 71.44 (H-31 / C-30), 3.24 / 71.29 (H-36 / C-35), 2.61 / 98.06 (H-29 / C-28), 2.31 / 155.03, 130.46/130.40, 129.43 (H-24 / C-25, C-5+23/4, C-22), 2.22 / 97.58 (H-27 / C-26). [MT541-6]

Elemental analysis = calcd (%) for $C_{47}H_{48}O_8$: C: 76.19, H: 6.53, O: 17.28; found:

C: 76.4, H: 6.98, O: 17.8

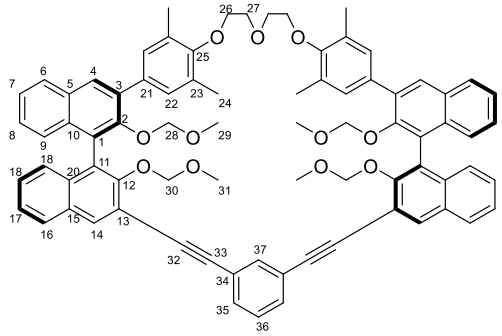
MS (ESI-pos, MeOH**)**: *m/z* = 763.3247 ([M+Na]$^{2+}$, calcd. 763.3241 for [$C_{47}H_{48}O_8$ Na_2^{2+}] [MT541_2]

IR (ATR-FT): $\tilde{\nu}$ (cm^{-1}) = 3052, 2920, 2872, 2823, 1618, 1596, 1571, 1489, 1443, 1426, 1389, 1353, 1335, 1288, 1263, 1221, 1199, 1151, 1099, 1084, 1056, 1027, 969, 916, 884, 851, 750

[MT541]

8.2.2.5.8. Synthesis of compound (*R*,*R*)-**80**

Described experiment: MT525 Repeated:MT539



Compound (*R*,*R*)-**79d** (64.1 mg, 0.0576 mmol, 1 eq) and caesium carbonate (46.4 mg, 0.143 mmol, 2.5 eq), were dissolved in degassed acetonitrile (150 ml) and stirred for 15 minutes under argon. After the addition of diethyleneglycol bistosylate (26.3 mg, 0.063 mmol, 1.1 eq), dissolved in 10 ml acetonitrile, the reaction mixture was stirred at 90 °C for one hour. After cooling to room temperature caesium carbonate was removed by filtration. Then water (10 ml) and ethyl acetate (10 ml) were added. The aqueous phase was extracted with ethyl acetate (20 ml) and the combined organic layer was washed with a saturated solution of sodium chloride (20 ml). The organic layer was dried over sodium sulfate and concentrated in *vacuo*. The crude product was purified by column chromatography (21x2 cm, cyclohexane:ethyl acetate 1:2) and afforded the product as a white solid (67.3 mg, 0.0401 mmol, 70.4%).

$C_{78}H_{68}O_{11}$, MW = 1181.4 g/mol.

^{1}H-NMR (400 MHz, [D$_6$]-dimethylsulfoxid, 298 K) δ [in ppm] = 8.43 (s, 2 H, H-14), 8.07 (s, 2 H, H-4), 8.04 (d, ^{3}J = 7.4 Hz, 2 H, H-16), 8.02 (d, ^{3}J = 7.6 Hz, 2 H, H-6), 7.92 (s, 1 H, H-37), 7.70 (d, ^{3}J = 7.8 Hz, 2 H, H-35), 7.58 (t, ^{3}J = 8.2 Hz, 1 H, H-36), 7.48 (t, ^{3}J = 7.2 Hz 2 H, H-17), 7.45 (t, ^{3}J = 7.5 Hz, 2 H, H-7), 7.40 (s, 4 H, H-22), 7.36 (t, ^{3}J = 7.8, 2 H, H-18), 7.30 (t, ^{3}J = 8.1, 2 H, H-8), 7.09 (d, ^{3}J = 8.7 Hz, 2 H, H-19), 7.03 (d, ^{3}J = 8.7 Hz, 2 H, H-9), 4.93 (s, 4 H, H-30), 4.23 (d, ^{2}J = 5.81 Hz, 2 H, H-28$_{1/2}$), 4.19 (d, ^{2}J = 5.8 Hz, 2 H, H-28$_{1/2}$), 4.07 – 4.04 (m, 2 H, H-26/27), 3.95 – 3.92 (m, 2 H, H-26/27), 3.86 – 3.76 (m, 4 H, H-26/27), 2.48 (s, 6 H, H-31), 2.36 (s, 12 H, H-24) 2.15 (s, 6 H, H-29).

^{13}C-NMR (101 MHz, [D$_6$]-dimethylsulfoxid, 298 K) δ [in ppm] = 154.88 (C-25), 152.73 (C-12), 150.99 (C-2), 134.32 (C-3), 134.06 (C-37), 133.92 (C-14), 133.58 (C-23), 133.43 (C-20), 132.51 (C-10), 131.66 (C-35), 130.59 (C-21), 130.45 (C-5), 130.16 (C-4), 129.90 (C-15), 129.58 (C-36), 129.23 (C-22), 128.12 (C-6), 128.05 (C-16), 127.60 (C-18), 126.40 (C-8), 126.00 (C-11), 125.90 (C-19), 125.53 (C-17), 125.45 (C-9), 125.11 (C-7), 125.06 (C-1), 123.06 (C-34), 116.30 (C-13), 98.15 (C-30), 97.75 (C-28), 92.07 (C-33), 87.21 (C-32), 71.96 (C-26/27), 70.21 (C-26/27), 55.29 (C-31), 55.10 (C-29), 16.33 (C-24).

^{1}H,^{1}H-COSY (400 MHz / 400 MHz, [D$_6$]- dimethylsulfoxid, 298 K) δ [in ppm] = 8.04 / 7.48 (H-16 / H-17), 8.02 / 7.45 (H-6 / H-7), 7.70 / 7.58 (H-35 / H-36), 7.58 / 7.70 (H-36 / H-35), 7.48 / 8.04 (H-17 / H-16), 7.45 / 8.03 (H-7 / H-6), 7.40 / 2.36 (H-22 / H-24), 7.36 / 7.09 (H-18 / H-19), 7.30 / 7.03 (H-8 / H-9), 7.09 / 7.36 (H-19 / H-18), 7.03 / 7.30 (H-9 / H-18). 4.23 / 4.19 (H-28$_{1/2}$ / H-28$_{1/2}$), 4.19 / 4.23 (H-28$_{1/2}$ / H-28$_{1/2}$).

^{1}H,^{13}C-GHSQC (400 MHz / 101 MHz, [D$_6$]-dimethylsulfoxid, 298 K) δ (^{1}H) / δ (^{13}C) [in ppm] = 8.43 / 133.92 (H-14 / C-14), 8.07 / 130.16 (H-4 / C-4), 8.04 / 128.05 (H-16 / C-16), 8.02 / 128.12 (H-6 / C-6), 7.92 / 134.06 (H-37 / C-37), 7.70 / 131.66 (H-35 / C-35), 7.58 / 129.58 (H-36 / C-36), 7.48 / 125.53 (H-17 / C-17), 7.45 / 125.11 (H-7 / C-7), 7.40 / 129.23 (H-22 / C-22), 7.36 / 127.60 (H-18 / C-18), 7.30 / 126.40 (H-8 / C-8), 7.09 / 125.90 (H-19 / C-19), 7.03 / 125.45 (H-9 / C-9), 4.93 / 98.15 (H-30 / C-30), 4.23 / 97.75 (H-28$_{1/2}$ / C-28), 4.19 / 97.75 (H-28$_{1/2}$ / C-28), 4.07 – 4.04 / 71.96 (H-26/27 / C-26/27), 3.95 – 3.92 / 71.91 (H-26/27 / C-26/27), 3.86 – 3.76 / 70.21 (H-26/27 / C-26/27), 2.48 / 55.29 (H-31 / C-31), 2.36 / 16.33 (H-24 / C-24), 2.15 / 55.10 (H-29 / C-29).

^{1}H,^{13}C-GHMBC (400 MHz / 101 MHz, [D$_6$]-dimethylsulfoxid, 298 K) δ (^{1}H) / δ (^{13}C) [in ppm] = 8.43 / 152.72, 133.43, 128.05, 87.21 (H-14 / C-12, C-20, C-16, C-32), 8.07 / 150.99, 132.51, 128.12, 125.06 (H-4 / C-2, C-10, C-6, C-1), 8.04 / 133.58, 133.43, 127.60 (H-16 / C-23, C-20, C-18), 8.02 / 132.51, 130.16, 126.40 (H-6 / C-10, C-4, C-8), 7.92 / 131.66, 92.07 (H-37 / C-35, C-33), 7.70 / 134.06, 131.66, 92.07 (H-35 / C-37, C-35, C-33), 7.58 / 123.06 (H-36 / C-34), 7.48 / 129.90, 125.90 (H-17 / C-15, C-19), 7.45 / 130.45, 125.45 (H-7 / C-5, C-9), 7.40 / 154.88, 134.32, 129.23, 16.33 (H-22 / C-25, C-3, C-22, C-24), 7.36 / 133.43, 128.05 (H-18 / C-20, C-16), 7.30 / 132.51, 128.12 (H-8 / C-10, C-6), 7.09 / 129.90, 125.53 (H-19 / C-15, C-17), 7.03 / 130.45, 125.06 (H-9 / C-5, C-1), 4.93 / 152.73, 55.29 (H-30 / C-12, C-31), 4.23 / 150.99, 55.10 (H-28$_{1/2}$ / C-2, C-29), 4.19 / 150.99, 55.10 (H-28$_{1/2}$ / C-2, C-29), 2.48 / 98.15 (H-31 / C-30), 2.36 / 154.88, 130.59, 129.23 (H-24 / C-25, C-21, C-22), 2.15 / 97.75 (H-29 / C-28).[MT525-2]

Elemental analysis = calcd (%) for $C_{78}H_{68}O_{11}$: C: 79.30, H: 5.80, O: 14.9; found:

C: 75.8, H: 5.50, O: 15.2

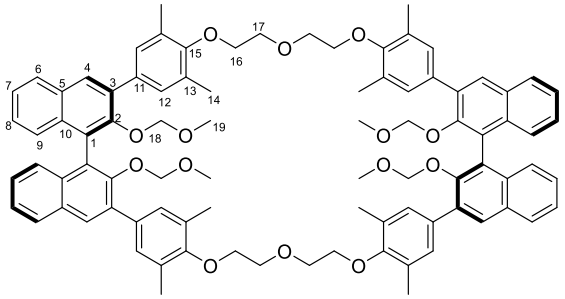
MS (ESI-pos, MeOH**)**: *m/z* = 724.3009 ([M+Na]$^{2+}$, calcd. 724.3007 for [$C_{39}H_{44}O_8Na_2^{2+}$] [MT525-2]

IR (ATR-FT): $\tilde{\nu}$ (cm^{-1}) = 3054, 2921, 2872, 2823, 1619, 1585, 1482, 1446, 1426, 1388, 1354, 1336, 1201, 1154, 1058.

[MT525]

8.2.2.5.9. Synthesis of compound (*R*,*R*)-**88**

Described experiment: MT581 Repeated: MT568, MT589



Compound (*R*,*R*)-**85d** (0.269 g, 0.207 mmol, 1 eq) and caesium carbonate (0.219 g, 0.621 mmol, 3 eq), were dissolved in degassed acetonitrile (550 ml) and stirred for 15 minutes under argon. After the addition of diethyleneglycol bistosylate (94.4 mg, 0.227 mmol, 1.1 eq), dissolved in 20 ml acetonitrile, the reaction mixture was stirred at 90 °C for one hour. After cooling to room temperature caesium carbonate was removed by filtration. Then water (10 ml) and ethyl acetate (10 ml) were added. The aqueous phase was extracted with ethyl acetate (20 ml) and the combined organic layer was washed with a saturated solution of sodium chloride (20 ml). The organic layer was dried over sodium sulfate and concentrated in *vacuo*. The crude product was purified by column chromatography (21x2 cm, cyclohexane:ethyl acetate 1:2) and afforded the product as a white solid (0.126 g, 0.0921 mmol, 44.1%).

$C_{88}H_{88}O_{14}$, MW = 1369.63 g/mol.

^{1}H-NMR (400 MHz, [D$_6$]-dimethylsulfoxid, 298 K) δ [in ppm] = 8.06 (s, 4 H, H-4), 8.01 (d, ^3J = 8.2Hz, 4 H, H-6), 7.44 (t, ^3J = 6.9 Hz, 4 H, H-7), 7.41 (s, 8 H, H-12), 7.28 (t, ^3J = 8.0 Hz, 4 H, H-8), 7.01 (d, ^3J = 8.4 Hz, 4 H, H-9), 4.33 (d, ^2J = 5.53 Hz, 4 H, H-18$_{1/2}$), 4.19 (d, ^2J = 5.53 Hz, 4 H, H-18$_{1/2}$), 3.99 (br s, 8 H, H-16/17), 3.91 – 3.81 (m, 8 H, H-16/17), 2.38 (s, 24 H, H-14), 2.21 (s, 12 H, H-19).

^{13}C-NMR (101 MHz, [D$_6$]-dimethylsulfoxid, 298 K) δ [in ppm] = 154.70 (C-15), 150.74 (C-2), 134.58 (C-3), 133.80 (C-11), 132.84 (C-10), 130.62 (C-13), 130.47 (C-5), 130.10 (C-4), 129.50 (C-12), 128.05 (C-6), 126.27 (C-8), 125.87 (C-1), 125.64 (C-9), 125.06 (C-7), 97.61 (C-18), 71.53 (C-16/17), 70.06 (C-16/17), 55.04 (C-19), 15.96 (C-14).

^{1}H,^{1}H-COSY (400 MHz / 400 MHz, [D$_6$]-dimethylsulfoxid, 298 K) δ [in ppm] = 8.01 / 7.44 (H-6 / H-7), 7.44 / 8.01, 7.28 (H-7 / H-6, H-8), 7.41 / 2.38 (H-12 / H-14), 7.28 / 7.44, 7.01 (H-8 / H-7, H-9), 7.01 / 7.28 (H-9 / H-8), 4.33 / 4.19 (H-18$_{1/2}$ / H-18$_{1/2}$), 4.19 / 4.33 (H-18$_{1/2}$ / H-18$_{1/2}$), 3.99 / 3.91 – 3.81 (H-16/17 / H-16/17), 3.91 – 3.81 / 3.99 (H-16/17 / H-16/17).

^{1}H,^{13}C-GHSQC (400 MHz / 101 MHz, [D$_6$]- dimethylsulfoxid, 298 K) δ (^{1}H) / δ (^{13}C) [in ppm] = 8.06 / 130.10 (H-4 / C-4), 8.01 / 128.05 (H-6 / C-6), 7.44 / 125.07 (H-7 / C-7), 7.41 / 129.50 (H-12 / C-12), 7.28 / 126.27 (H-8 / C-8), 7.01 / 125.64 (H-9 / C-9), 4.33 / 97.61 (H-18$_{1/2}$ / C-18), 4.19 / 97.61 (H-18$_{1/2}$ / C-18), 3.99 / 71.53 (H-16/17 / C-16/17), 3.91 – 3.81 / 70.06 (H-16/17 / C-16/17), 2.38 / 15.96 (H-14 / C-14), 2.20 / 55.04 (H-19 / C-19).

^{1}H,^{13}C-GHMBC (400 MHz / 101 MHz, [D$_6$]- dimethylsulfoxid, 298 K) δ (^{1}H) / δ (^{13}C) [in ppm] = 8.06 / 150.74, 133.80, 132.84, 128.05, 125.87 (H-4 / C-2, C-11, C-10, C-6, C-1), 8.01 / 132.84, 130.10, 126.27 (H-6 / C-10, C-4, C-8), 7.44 / 130.47, 125.64 (H-7 / C-5, C-9), 7.41 / 154.70, 134.59, 129.50, 15.96 (H-12 / C-15, C-3 C-12, C-14), 7.28 / 132.84, 128.05 (H-8 / C-10, C-6), 7.01 / 130.47, 125.87,

125.06 (H-9 / C-5, C-1, C-7), 4.33 / 150.74, 55.04 (H-$18_{1/2}$ / C-2, C-19), 4.19 / 150.74, 55.04 (H-$18_{1/2}$ / C-2, C-19), 2.38 / 154.70, 130.62, 129.50 (H-14 / C-15, C-13, C-12), 2.21 / 97.61 (H-19 / C-18).

[MT589-3]

Elemental analysis = calcd (%) for $C_{88}H_{88}O_{14}$: C: 77.17, H: 6.48, O: 16.35; found:

C: 79.05, H: 6.40, O: 16.35

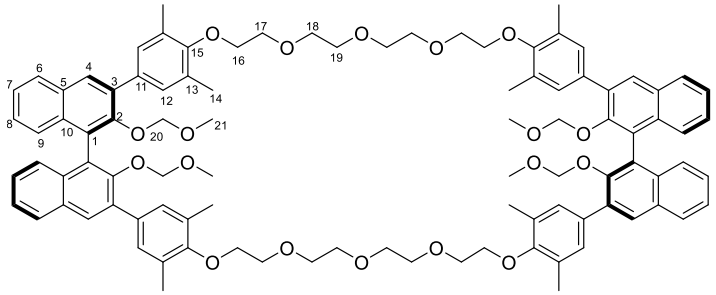
MS (ESI-pos, MeOH**)**: *m/z* = 1391.6053 ($[M+Na]^+$, calcd. 1391.6066 for $[C_{88}H_{88}O_{14}Na^+]$.

IR (ATR-FT): $\tilde{\nu}$ (cm^{-1}) = 3050, 2919, 2871, 2824, 1620, 1591, 1484, 1427, 1387, 1352, 1299, 1270,1233, 1201, 1155, 1080, 1051, 1018, 970, 921, 851, 786, 747, 665, 623

[MT589-3]

8.2.2.5.10. Synthesis of compound (*R*,*R*)-**89**

Described experiment: MT656 Repeated:



Compound (*R*,*R*)-**86d** (0.172 g, 0.124 mmol, 1 eq) and caesium carbonate (0.131 g, 0.372 mmol, 3 eq), were dissolved in degassed acetonitrile (400 ml) and stirred for 15 minutes under argon. After the addition of the tetraethyleneglycol bistosylate (73.8 mg, 0.149 mmol, 1.2 eq), dissolved in 15 ml acetonitrile, the reaction mixture was stirred at 90 °C for one hour. After cooling to room temperature caesium carbonate was removed by filtration. Then water (10 ml) and ethyl acetate (10 ml) were added. The aqueous phase was extracted with ethyl acetate (20 ml) and the combined organic layer was washed with a saturated solution of sodium chloride (20 ml). The organic layer was dried over sodium sulfate and concentrated in *vacuo*. The crude product was purified by column chromatography (21x2 cm, cyclohexane:ethyl acetate 1:2) and afforded the product as a white solid (0.161 g, 0.104 mmol, 84.2%).

$C_{96}H_{104}O_{18}$, MW = 1545.8 g/mol.

^{1}H-NMR (400 MHz, [D$_6$]-dimethylsulfoxid, 298 K) δ [in ppm] = 7.98 (s, 4 H, H-4), 7.96 (d, ^3J = 8.6Hz, 4 H, H-6), 7.41 (t, ^3J = 7.3 Hz, 4 H, H-7), 7.29 (t, ^3J = 7.5 Hz, 4 H, H-8) 7.28 (s, 8 H, H-12), 7.04 (d, ^3J = 8.6 Hz, 4 H, H-9), 4.30 (d, ^2J = 5.5 Hz, 4 H, H-20$_{1/2}$), 4.21 (d, ^2J = 5.5 Hz, 4 H, H-20$_{1/2}$), 3.92 – 3.90 (m, 8 H, H-16), 3.75 – 3.73 (m, 8 H, H-17), 3.64 – 3.59 (m, 16 H, H-18+19), 2.26 (s, 24 H, H-14), 2.23 (s, 12 H, H-21).

^{13}C-NMR (101 MHz, [D$_6$]-dimethylsulfoxid, 298 K) δ [in ppm] = 154.98 (C-15), 150.45 (C-2), 134.63 (C-3), 133.63 (C-11), 132.75 (C-10), 130.39 (C-5), 130.32 (C-13), 130.10 (C-4), 129.44 (C-12), 127.96 (C-6), 126.30 (C-8), 125.76 (C-1), 125.53 (C-9), 125.09 (C-7), 97.47 (C-20), 71.48 (C-16), 70.08 (C-18/19), 70.07 (C-18/19), 69.86 (C-17), 55.12 (C-21), 16.01 (C-14).

^{1}H,^{1}H-COSY (400 MHz / 400 MHz, [D$_6$]-dimethylsulfoxid, 298 K) δ [in ppm] = 7.96 / 7.41 (H-6 / H-7), 7.41 / 7.96, 7.29 (H-7 / H-6, H-8), 7.29 / 7.41, 7.04 (H-8 / H-7, H-9), 7.28 / 2.26 (H-12 / H-14), 7.04 / 7.29 (H-9 / H-8), 4.30 / 4.21 (H-20$_{1/2}$ / H-20$_{1/2}$), 4.21 / 4.30 (H-20$_{1/2}$ / H-20$_{1/2}$), 3.92 – 3.90 / 3.75 – 3.73 (H-16 / H-17), 3.75 – 3.73 / 3.92 – 3.90 (H-17 / H-16).

^{1}H,^{13}C-GHSQC (400 MHz / 101 MHz, [D$_6$]- dimethylsulfoxid, 298 K) δ (^{1}H) / δ (^{13}C) [in ppm] = 7.98 / 130.10 (H-4 / C-4), 7.96 / 127.96 (H-6 / C-6), 7.41 / 125.09 (H-7 / C-7), 7.29 / 126.30 (H-8 / C-8), 7.28 / 129.44 (H-12 / C-12), 7.04 / 125.53 (H-9 / C-9), 4.30 / 97.47 (H-20$_{1/2}$ / C-20), 4.21 / 97.47 (H-20$_{1/2}$ / C-20), 3.92 – 3.90 / 71.48 (H-16 / C-16), 3.75 – 3.73 / 69.86 (H-17 / C-17), 3.64 – 3.59 / 70.08/70.07 (H-18+19 / C-18/19), 2.26 / 16.01 (H-14 / C-14), 2.23 / 55.12 (H-21 / C-21).

^{1}H,^{13}C-GHMBC (400 MHz / 101 MHz, [D$_6$]- dimethylsulfoxid, 298 K) δ (^{1}H) / δ (^{13}C) [in ppm] = 7.98 / 150.45, 133.63, 132.75, 127.96 (H-4 / C-2, C-11, C-10, C-6), 7.96 / 132.75, 130.10, 126.30 (H-6 / C-10, C-4, C-8), 7.41 / 130.39, 125.53 (H-7 / C-5, C-9), 7.29 / 132.75, 127.96 (H-8 / C-10, C-6), 7.28 / 154.98, 134.63, 129.44, 16.01 (H-12 / C-15, C-3, C-12, C-14), 7.04 / 130.39, 125.09 (H-9 / C-5, C-7),

4.30 / 150.45, 55.12 (H-$20_{1/2}$ / C-2, C-21), 4.21 / 150.45, 55.12 (H-$20_{1/2}$ / C-2, C-21), 3.92 – 3.90 / 69.86 (H-16 / C-17), 3.75 – 3.73 / 71.48 (H-17 / C-16), 3.64 – 3.59 / 70.08/70.07/69.86 (H-18+19 / C-17/18/19), 2.26 / 154.98, 130.32, 129.44 (H-14 / C-15, C-13, C-12), 2.23 / 97.47 (H-21 / C-20).

[MT656-7]

Elemental analysis = calcd (%) for $C_{96}H_{104}O_{18}$: C: 74.59, H: 6.78, O: 18.63; found:

C: 74.9, H: 7.49, O: -

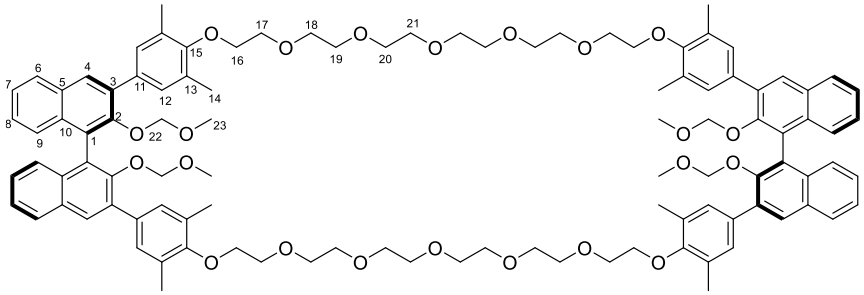
MS (ESI-pos, MeOH**)**: *m/z* = 1568.7168 ($[M+Na]^+$, calcd. 1568.7149 for $[C_{96}H_{104}O_{18}Na^+]$.

IR (ATR-FT): $\tilde{\nu}$ (cm^{-1}) = 3050, 2919, 2866, 1727, 1591, 1484, 1426, 1388, 1353, 1202, 1147, 1088, 1050, 970, 921, 748.

[MT656]

8.2.2.5.11. Synthesis of compound (*R*,*R*)-**90**

Described experiment: MT658 Repeated:



Compound (*R*,*R*)-**87d** (0.255 g, 0.173 mmol, 1 eq) and caesium carbonate (0.183 g, 0.519 mmol, 3 eq), were dissolved in degassed acetonitrile (450 ml) and stirred for 15 minutes under argon. After the addition of the hexaethyleneglycol bistosylate (0.122 g, 0.207 mmol, 1.2 eq), dissolved in 20 ml acetonitrile, the reaction mixture was stirred at 90 °C for one hour. After cooling to room temperature caesium carbonate was removed by filtration. Then water (10 ml) and ethyl acetate (10 ml) were added. The aqueous phase was extracted with ethyl acetate (20 ml) and the combined organic layer was washed with a saturated solution of sodium chloride (20 ml). The organic layer was dried over sodium sulfate and concentrated in *vacuo*. The crude product was purified by column chromatography (21x2 cm, cyclohexane:ethyl acetate 1:2) and afforded the product as a white solid (0.146 g, 0.0851 mmol, 49.3%).

$C_{104}H_{120}O_{22}$, MW = 1722.1 g/mol.

^{1}H-NMR (400 MHz, [D$_6$]-dimethylsulfoxid, 298 K) δ [in ppm] = 8.00 (s, 4 H, H-4), 7.98 (d, ^3J = 8.5Hz, 4 H, H-6), 7.42 (t, ^3J = 7.2 Hz, 4 H, H-7), 7.30 (s, 8 H, H-12), 7.28 (t, ^3J = 7.6 Hz, 4 H, H-8), 7.04 (d, ^3J = 8.6 Hz, 4 H, H-9), 4.32 (d, ^2J = 5.5 Hz, 4 H, H-22$_{1/2}$), 4.23 (d, ^2J = 5.5 Hz, 4 H, H-22$_{1/2}$), 3.90 – 3.88 (m, 8 H, H-16), 3.71 – 3.69 (m, 8 H, H-17), 3.60 – 3.58 (m, 8 H, H-18), 3.56 – 3.54 (m, 8 H, H-19), 3.52 (br s, 16 H, H-20+21), 2.25 (s, 36 H, H-14+23).

^{13}C-NMR (101 MHz, [D$_6$]-dimethylsulfoxid, 298 K) δ [in ppm] = 154.97 (C-15), 150.50 (C-2), 134.66 (C-3), 133.64 (C-11), 132.77 (C-10), 130.41 (C-5), 130.33 (C-13), 130.11 (C-4), 129.46 (C-12), 127.99 (C-6), 126.30 (C-8), 125.71 (C-1), 125.54 (C-9), 125.09 (C-7), 97.51 (C-22), 71.42 (C-16), 70.01 (C-17/18/19/20/21), 69.92 (C-17/18/19/20/21), 69.88 (C-17/18/19/20/21), 69.85 (C-17/18/19/20/21), 69.79 (C-17/18/19/20/21), 55.15 (C-23), 16.00 (C-14).

^{1}H,^{1}H-COSY (400 MHz / 400 MHz, [D$_6$]-dimethylsulfoxid, 298 K) δ [in ppm] = 7.98 / 7.42 (H-6 / H-7), 7.42 / 7.98, 7.28 (H-7 / H-6, H-8), 7.30 / 2.25 (H-12 / H-14+23), 7.28 / 7.42, 7.04 (H-8 / H-7, H-9), 7.04 / 7.28 (H-9 / H-8), 4.32 / 4.23 (H-22$_{1/2}$ / H-22$_{1/2}$), 4.23 / 4.32 (H-22$_{1/2}$ / H-22$_{1/2}$), 3.90 – 3.88 / 3.71 – 3.69 (H-16 / H-17), 3.71 – 3.69 / 3.90 – 3.88 (H-17 / H-16).

^{1}H,^{13}C-GHSQC (400 MHz / 101 MHz, [D$_6$]-dimethylsulfoxid, 298 K) δ (^{1}H) / δ (^{13}C) [in ppm] = 8.00 / 130.11 (H-4 / C-4), 7.98 / 127.99 (H-6 / C-6), 7.42 / 125.09 (H-7 / C-7), 7.30 / 129.46 (H-12 / C-12), 7.28 / 126.30 (H-8 / C-8), 7.04 / 125.54 (H-9 / C-9), 4.32 / 97.51 (H-22$_{1/2}$ / C-22), 4.23 / 97.51 (H-22$_{1/2}$ / C-22), 3.90 – 3.88 / 71.42 (H-16 / C-16), 3.71 – 3.69 / 70.01/69.92/69.88/69.85/69.79 (H-17 / C-17/18/19/20/21), 3.60 – 3.58 / 70.01/69.92/69.88/69.85/69.79 (H-18 / C-17/18/19/20/21), 3.56 – 3.54 / 70.01/69.92/69.88/69.85/69.79 (H-19 / C-17/18/19/20/21), 3.52 / 70.01/69.92/69.88/69.85/69.79 (H-20+21 / C-17/18/19/20/21), 2.25 / 55.15, 16.00 (H-14+23 / C-14, C-23).

^{1}H,^{13}C-GHMBC (400 MHz / 101 MHz, [D$_6$]-dimethylsulfoxid, 298 K) δ (^{1}H) / δ (^{13}C) [in ppm] = 8.00 / 150.50, 133.64, 132.77, 127.99 (H-4 / C-2, C-11, C-10, C-6), 7.98 / 132.77, 130.11, 126.30 (H-6 / C-10, C-4, C-8), 7.42 / 130.41, 125.54 (H-7 / C-5, C-9), 7.30 / 154.97, 134.66, 129.46, 16.00 (H-12 / C-15, C-3 C-12, C-14), 7.28 / 132.77, 127.99 (H-8 / C-10, C-6), 7.04 / 130.41, 125.09 (H-9 / C-5, C-7), 4.32 / 150.50, 55.15 (H-22$_{1/2}$ / C-2, C-23), 4.23 / 150.50, 55.15 (H-22$_{1/2}$ / C-2, C-23), 3.90 – 3.88 / 70.01/69.92/69.88/69.85/69.79 (H-16 / C-17/18/19/20/21), 3.71 – 3.69 / 71.42 (H-17 / C-16), 3.60 – 3.58 / 70.01/69.92/69.88/69.85/69.79 (H-18 / C-17/18/19/20/21), 3.56 – 3.54 / 70.01/69.92/69.88/69.85/69.79 (H-19 / C-17/18/19/20/21), 3.52 / 70.01/69.92/69.88/69.85/69.79 (H-20+21 / C-17/18/19/20/21), 2.25 / 154.97, 130.33, 129.46, 97.51 (H-14+23 / C-15, C-13, C-12, C-22).

[MT658-5]

Elemental analysis = calcd (%) for $C_{104}H_{120}O_{22}$: C: 72.54, H: 7.02, O: 20.44; found:

C: 66.9, H: 6.99, O: -

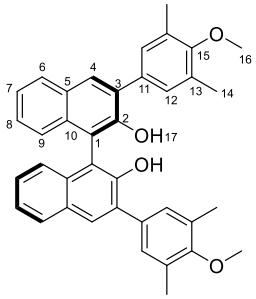
MS (ESI-pos, MeOH**)**: *m/z* = 1744.8248 ([M+Na]$^+$, calcd. 1744.8197 for [$C_{104}H_{120}O_{22}Na^+$].

IR (ATR-FT): $\tilde{\nu}$ (cm^{-1}) = 3051, 2980, 2970, 2916, 2904, 2882, 2869, 2736, 1591, 1485, 1448, 1427, 1408, 1387, 1351, 1338, 1297, 1270, 1252, 1234, 1202, 1147, 1125, 1101, 1088, 1051, 971.

[MT658]

8.2.2.5.12. Synthesis of compound (*R*,*R*)-**105**

Described experiment: MT576 Repeated: SF005



Compound (*R*)-**104** (43.1 mg, 67.1 µmol, 1 eq), was dissolved in a mixture of dry ethanol:diethyl ether (5:3, 1 ml total). Then acetyl chloride (95.1 µl, 104 mg, 1.33 µmol, 20 eq) was added in a dropwise manner over 15 minutes and the mixture was stirred for 18 hours. Then 15 ml water were added to end the reaction and ethanol and ethyl ether were removed in *vacuo*. Then ethyl acetate (20 ml) was added to the aqueous residue. The organic layer was separated and then washed with a saturated solution of sodium chloride (15 ml). The organic layer was dried over sodium sulfate and was concentrated in *vacuo* to afford the product as a yellow solid (37.1 mg, 66.9 µmol, 99.7%).

$C_{38}H_{34}O_4$, MW = 554.7 g/mol.

^{1}H-NMR (400 MHz, [D$_6$]-dimethylsulfoxid, 298 K) δ [in ppm] = 8.16 (s, 2 H, H-17), 7.91 (d, ^3J = 8.1 Hz, 2 H, H-6), 7.89 (s, 2 H, H-4), 7.36 (s, 4 H, H-12), 7.27 (t, ^3J = 7.6 Hz, 2 H, H-7), 7.19 (t, ^3J = 7.4 Hz, 2 H, H-8), 6.88 (d, ^3J = 8.5 Hz, 2 H, H-9), 3.72 (s, 6 H, H-16), 2.31 (s, 12 H, H-14).

^{13}C-NMR (101 MHz, [D$_6$]-dimethylsulfoxid, 298 K) δ [in ppm] = 155.82 (C-15), 151.30 (C-2), 134.19 (C-11), 133.38 (C-10), 131.48 (C-3), 130.01 (C-12), 129.64 (C-4+13), 128.61 (C-5), 128.04 (C-6), 125.95 (C-8), 124.01 (C-9), 122.88 (C-7), 114.99 (C-1), 59.32 (C-16), 15.98 (C-14).

^{1}H,^{1}H-COSY (400 MHz / 400 MHz, [D$_6$]-dimethylsulfoxid, 298 K) δ [in ppm] = 7.91 / 7.27 (H-6 / H-7), 7.36 / 2.31 (H-12 / H-14), 7.27 / 7.91, 7.19 (H-7 / H-6, H-8), 7.19 / 7.27, 6.88 (H-8 / H-7, H-9), 6.88 / 7.19 (H-9 / H-8), 2.31 / 7.36 (H-14 / H-12).

^{1}H,^{13}C-GHSQC (400 MHz / 101 MHz, [D$_6$]-dimethylsulfoxid, 298 K) δ (^{1}H) / δ (^{13}C) [in ppm] = 7.91 / 128.04 (H-6 / C-6), 7.89 / 129.64 (H-4 / C-4+13), 7.36 / 130.01 (H-12 / C-12), 7.27 / 122.88 (H-7 / C-7), 7.19 / 125.95 (H-8 / C-8), 6.88 / 124.01 (H-9 / C-9), 3.72 / 59.32 (H-16 / C-16), 2.31 / 15.98 (H-14 / C-14).

^{1}H,^{13}C-GHMBC (400 MHz / 101 MHz, [D$_6$]-dimethylsulfoxid, 298 K) δ (^{1}H) / δ (^{13}C) [in ppm] = 8.16 / 151.30, 131.47, 114.99 (H-17 / C-2, C-3, C-1), 7.91 / 133.38, 129.64, 125.95 (H-6 / C-10, C-4+13, C-8), 7.89 / 151.30, 134.19, 133.38, 128.04 (H-4 / C-2, C-11, C-10, C-6), 7.36 / 155.82, 131.48, 130.01, 15.98 (H-12 / C-15, C-3, C-12, C-14), 7.27 / 128.61, 124.01 (H-7 / C-5, C-9), 7.19 / 133.38, 128.04 (H-8 / C-10, C-6), 6.88 / 128.61, 122.88, 114.99 (H-9 / C-5, C-7, C-1), 3.72 / 155.82 (H-16 / C-15), 2.31 / 155.82, 130.01, 129.64 (H-14 / C-15, C-12, C-4+13). [MT576-5]

Elemental analysis = calcd (%) for $C_{38}H_{34}O_4$: C: 82.28, H: 6.18, O: 11.54; found:

C: 81.8, H: 6.77, O: 11.4

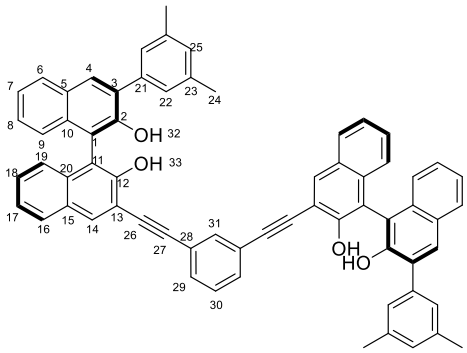
MS (ESI-pos, MeOH**)**: *m/z* = 555.2524 ([M+H]$^+$, calcd. 555.2530 for [$C_{38}H_{35}O_4^+$].

IR (ATR-FT): $\tilde{\nu}$ (cm^{-1}) = 3052, 2981, 2970, 2920, 2910, 2888, 2875, 2736, 1591, 1481, 1446, 1408, 1388, 1353, 1338, 1297, 1235, 1202, 1147, 1127, 1102, 1089, 1051, 970.

[MT576]

8.2.2.5.13. Synthesis of compound (*R*,*R*)-**81a**

Described experiment: MT350 Repeated:-



Compound (*R*,*R*)-**79a** (0.420 g, 0.389 mmol, 1 eq), was dissolved in dry dichlormethane (40 ml). After cooling down to 0 °C, bromotrimethylsilane (0.821 ml, 0.953 g, 6.23 mmol, 16 eq) was added carefully and the mixture was stirred for 18 hours at 25°C. The organic layer was dried over sodium sulfate and was concentrated in *vacuo* to afford the product as a yellow solid (0.327 g, 0.363 mmol, 93.1%).

$C_{66}H_{46}O_4$ MW = 902.3 g/mol.

^{1}H-NMR (600 MHz, [D$_6$]-dimethylsulfoxid, 298 K) δ [in ppm] = 8.97 (s, 2 H, H-33), 8.28 (s, 2 H, H-14), 8.21 (s, 2 H, H-32) 7.93 (m, 5 H, H-6+16+31), 7.95 – 7.91 (s, 2 H, H-4), 7.68 (d, ^3J = 7.77 Hz, 2 H, H-29), 7.54 (t, ^3J = 7.9 Hz, 1 H, H-30), 7.32 (t, ^3J = 7.3 Hz 2 H, H-17), 7.29 (s, 4 H, H-22), 7.29 - 7.25 (m, 4 H, H-7/18), 7.21 (t, ^3J = 7.7 Hz, 2 H, H-8), 7.01 (s, 2 H, H-25), 6.94 (d, ^3J = 8.4 Hz, 2 H, H-19), 6.87 (d, ^3J = 8.7 Hz, 2 H, H-9), 2.35 (s, 12 H, H-24).

^{13}C-NMR (151 MHz, [D$_6$]-dimethylsulfoxid, 298 K) δ [in ppm] = 152.94 (C-12), 150.91 (C-2), 138.54 (C-21), 136.80 (C), 134.35 (C-20), 134.10 (C-31), 133.62 (C-14), 133.13 (C-10), 131.83 (C-3), 131.39 (C-29), 129.66 (C-4), 129.30 (C-30), 128.89 (C), 128.46 (C), 128.43 (C-25), 128.12 (C), 128.09 (C), 128.03 (C), 127.36 (C-22), 126.06 (C-8), 124.22 (C-19), 123.89 (C-9), 123.40 (C-28), 123.27 (C-17), 122.93 (C-18), 115.57 (C-11), 114.93 (C-1), 113.05 (C-13) 92.63 (C-27), 87.65 (C-26), 21.07 (C-24).

^{1}H,^{1}H-COSY (600 MHz / 600 MHz, [D$_6$]-dimethylsulfoxid, 298 K) δ [in ppm] = 7.95 – 7.91 / 7.68, 7.31, 7.29 - 7.25 (H-6+16+30 / H-29, H-17, H7/18), 7.32 / 7.95 – 7.91 (H-17/ H-6+16+30), 7.29 - 7.25 / 7.95 – 7.91 (H7/18 / H-6+16+30), 7.68 / 7.95 – 7.91, 7.54 (H-29 / H-6+16+30, H-31), 7.54 / 7.68 (H-31 / H-29), 7.29 / 7.01 (H-22 / H-25), 7.01 / 7.29 (H-25 / H-22).

^{1}H,^{13}C-GHSQC (600 MHz / 151 MHz, [D$_6$]- dimethylsulfoxid, 298 K) δ (^{1}H) / δ (^{13}C) [in ppm] = 8.28 / 133.62 (H-14 / C-14), 7.95 – 7.91 / 134.10, 128.09/128.03/128.12 (H-31/6/16 / C-31/6/16), 7.91 / 129.66 (H-4 / C-4), 7.68 / 131.39 (H-29 / C-29), 7.54 / 129.30 (H-30 / C-30), 7.32 / 123.27 (H-17 / C-17), 7.29 / 127.36 (H-22 / C-22), 7.29 - 7.25 / 122.93 (H-7/18 / C-18), 7.21 / 126.06 (H-8 / C-8), 7.01 / 128.43 (H-25 / C-25), 6.94 / 124.22 (H-19 / C-19), 6.87 / 123.89 (H-9 / C-9), 2.35 / 21.07 (H-24 / C-24).

^{1}H,^{13}C-GHMBC (600 MHz / 151 MHz, [D$_6$]- dimethylsulfoxid, 298 K) δ (^{1}H) / δ (^{13}C) [in ppm] = 8.97 / 152.94, 115.57, 113.05 (H-33 / C-12, C-11, C-13), 8.28 / 152.94, 134.35, 128.12/128.09/128.03, 115.57, 87.65 (H-14 / C-12, C-20, C, C-11, C-26), 8.21 / 150.91, 131.83, 114.93 (H-32 / C-2, C-3, C-1), 7.95 – 7.91 / 134.35, 133.13, 131.39, 129.66, 127.36, 126.06, 92.63 (H-6/16/30 / C-20, C-10, C-29, C-4, C-22, C-8, C-27), 7.91 / 150.91, 138.54, 133.13, 128.12/128.09/128.03 (H-4 / C-2, C-21, C-10, C),

7.68 / 134.10, 131.39, 92.63 (H-29 / C-31, C-29, C-27), 7.54 / 123.40 (H-30 / C-28), 7.32 / 128.12/128.09/128.03, 124.22 (H-17 / C, C-19), 7.29 / 131.83, 128.43, 127.36, 21.07 (H-22 / C-3, C-25, C-20, C24), 7.29 - 7.25 / 134.35, 128.12/128.09/128.03, 123.89 (H-7/18 / C-20, C, C-9), 7.21 / 128.12/128.09/128.03 (H-8 / C), 7.01 / 127.36, 21.07 (H-25 / C-22, C-24), 6.94 / 128.03, 128.09, 128.12, 123.27, 115.57 (H-19 / C, C-17, C-11), 6.87 / 128.46, 114.93, (H-9 / C-, C-1).

[MT350-4]

Elemental analysis = calcd (%) for $C_{66}H_{46}O_4$: C: 87.87, H: 5.13, O: 7.09; found:

C: 84.6, H: 5.82, O: 7.08

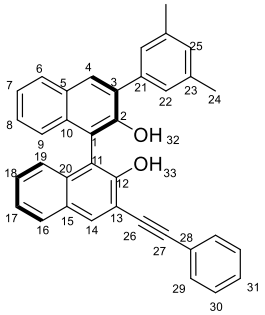
MS (ESI-pos, MeOH**)**: *m/z* = 903.3471 ($[M+H]^+$, calcd. 903.3469 for $[C_{66}H_{47}O_4^+]$.

IR (ATR-FT): $\tilde{\nu}$ (cm^{-1}) = 3502, 3052, 3025, 3000, 2960, 2914, 2853, 1619, 1595, 1495, 1477, 1432, 1411, 1382, 1360, 1259, 1209, 1146, 1020, 934, 887, 847, 745.

[MT350-4]

8.2.2.5.14. Synthesis of compound (*R*)-**103a**

Described experiment: MT351 Repeated:-



Compound (*R*)-**102a** (0.160 g, 0.271 mmol, 1 eq) was dissolved in dry dichlormethane (40 ml). After cooling down to 0 °C bromotrimethylsilane (0.292 ml, 0.338 g, 2.21 mmol, 8 eq) was added carefully and the mixture was stirred for 18 hours at 25°C. Then water (10 ml) and dichloromethane (10 ml) were added. The aqueous phase was extracted with ethyl acetate (20 ml) and the combined organic layer was washed with a saturated solution of sodium chloride (20 ml). The organic layer was dried over sodium sulfate and was concentrated in *vacuo* to afford the product as a yellow solid (0.106 g, 0.216 mmol, 80.3%).

$C_{36}H_{26}O_2$ MW = 490.2 g/mol.

^{1}H-NMR (600 MHz, [D$_6$]-dimethylsulfoxid, 298 K) δ [in ppm] = 8.89 (s, 1 H, H-33), 8.25 (s, 1 H, H-14), 8.19 (s, 1 H, H-32), 7.92 (d, ^3J = 7.9 Hz, 2 H, H-6+16), 7.90 (s, 1 H, H-4), 7.63 (dd, ^3J = 8.2 Hz ^4J = 1.3 Hz, 2 H, H-29), 7.48 – 7.41 (m, 3 H, H-30+31), 7.34 – 7.25 (s, 5 H, H-7+17+18+22), 7.20 (d, ^3J = 6.2 Hz, 1 H, H-8), 7.01 (s, 1 H, H-25), 6.93 (d, ^3J = 8.3 Hz, 1 H, H-19), 6.86 (d, ^3J = 8.3 Hz, 1 H, H-9), 2.35 (s, 6 H, H-24).

^{13}C-NMR (151 MHz, [D$_6$]-dimethylsulfoxid, 298 K) δ [in ppm] = 152.92 (C-12), 150.95 (C-2), 138.66 (C-21), 136.81 (C-23), 134.24 (C-20), 133.43 (C-14), 133.17 (C-10), 131.43 (C-29), 129.67 (C-4), 128.73 (C-30/31), 128.68 (C-30/31), 128.48 (C-25), 128.44 (C-5), 128.15 (C-15), 128.10 (C-6), 127.98 (C-16), 127.37 (C-22), 127.23 (C-18), 126.07 (C-8), 124.20 (C-19), 123.90 (C-9), 123.36 (C-17), 122.94 (C-7), 122.82 (C-28), 115.62 (C-11), 114.92 (C-1), 113.35 (C-13), 93.51 (C-27), 86.84 (C-26) 21.07 (C-24).[117]

^{1}H,^{1}H-COSY (600 MHz / 600 MHz, [D$_6$]-dimethylsulfoxid, 298 K) δ [in ppm] = 7.92 / 7.34 – 7.25 (H-6+16 / H-7+17+18+22), 7.63 / 7.48 – 7.41 (H-29 / H-30+31), 7.48 – 7.41 / 7.64/7.62 (H-30+31 / H-29), 7.34 – 7.25 / 7.92, 6.93, 2.35 (H-7+17+18+22 / H-6+16 H-19, H-24), 6.93 / 7.34 – 7.25 (H-19 / H-7+17+18+22), 7.20 / 6.86 (H-8 / H-9), 6.86 / 7.20 (H-9 / H-8), 7.01 / 2.35 (H-25 / H-24), 2.35 / 7.01, 7.34 – 7.25 (H-24 / H-7+17+18+22, H-25).

^{1}H,^{13}C-GHSQC (600 MHz / 151 MHz, [D$_6$]-dimethylsulfoxid, 298 K) δ (^{1}H) / δ (^{13}C) [in ppm] = 8.25 / 133.43 (H-14 / C-14), 7.92 / 128.10/127.98 (H-6+16 / C-6+16), 7.90 / 129.67 (H-4 / C-4), 7.63 / 131.43 (H-29 / C-29), 7.48 – 7.41 / 128.73/128.68 (H-30+31 / C-30/31), 7.34 – 7.25 / 127.37, 127.23, 123.36, 122.94 (H-7+17+18+22 / C-7, C-17, C-18, C-22), 7.20 / 126.07 (H-8 / C-8), 7.01 / 128.48 (H-25 / C-25), 6.93 / 124.20 (H-19 / C-19), 6.86 / 123.90 (H-9 / C-9), 2.35 / 21.07 (H-24 / C-24).

[117] One Carbon signal was not found

^{1}H,^{13}C-GHMBC (600 MHz / 151 MHz, [D$_6$]-dimethylsulfoxid, 298 K) δ (^{1}H) / δ (^{13}C) [in ppm] = 8.89 / 115.62, 113.35 (H-33 / C-11, C-13), 8.25 / 152.92, 134.24, 127.98, 86.84 (H-14 / C-12, C-20, C-16, C-26), 8.19 / 114.92 (H-32 / C-1), 7.92 / 134.24, 133.17 129.67, 127.23, 126.07 (H-6+16 / C-20, C-10, C-4, C-18, C-8), 7.90 / 150.95, 138.66, 133.17, 128.15 (H-4 / C-2, C-21, C-10, C-15), 7.63 / 131.43, 128.68, 93.51 (H-29 / C-29, C-30/31, C-27), 7.48 – 7.41 / 131.43, 122.82 (H-30+31 / C-29, C-28), 7.34 – 7.25 / 134.24, 128.48, 128.44, 128.15, 127.37 (H-7+17+18+22 / C-20, C-25, C-5, C-15, C-22), 7.20 / 133.17, 128.16 (H-8 / C-10, C-6), 7.01 / 127.37 (H-25 / C-22), 6.93 / 128.15, 123.36, 115.62 (H-19 / C-15, C-17, C-11), 6.86 / 128.44, 122.94, 114.92 (H-9 / C-5, C-7, C-1), 2.35 / 136.81, 128.48, 127.37 (H-24 / C-23, C-25, C-22).

[MT351-4]

Elemental analysis = calcd (%) for $C_{36}H_{26}O_2$: C: 87.7, H: 5.34, O: 6.52; found:

C: 87.6, H: 5.58, O: 6.62

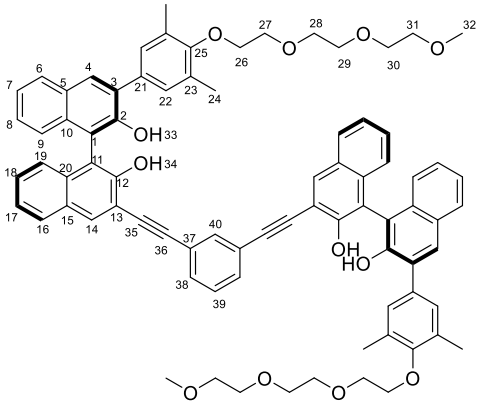
MS (ESI-pos, MeOH**)**: *m/z* = 491.2012 ([M+H]$^+$, calcd. 491.2006 for [$C_{36}H_{27}O_2^+$]

IR (ATR-FT): $\tilde{\nu}$ (cm^{-1}) = 3503, 3051, 2949, 2910, 2865, 2840, 2807, 1618, 1494, 1432, 1379, 1360, 1245, 1228, 1206, 1174, 1147, 1128, 1072, 923, 888, 848, 823, 802, 779.

[MT351-2]

8.2.2.5.15. Synthesis of compound (*R,R*)-**81b**

Described experiment: MT544 Repeated: MT543



Compound (*R,R*)-**79b** (0.410 g, 0.292 mmol, 1 eq), was dissolved in a mixture of dry ethanol:diethyl ether (5:3, 30 ml total). Then acetyl chloride (0.833 ml, 0.917 g, 11.7 mmol, 40 eq) was added in a dropwise manner over 15 minutes and the mixture was stirred for 18 hours. Then water (15 ml) was added to end the reaction and ethanol and ethyl ether were removed in *vacuo*. Then ethyl acetate (50 ml) was added to the aqueous residue. The organic layer was separated and then washed with a saturated solution of sodium chloride (25 ml). The organic layer was dried over sodium sulfate and was concentrated in *vacuo* to afford the product as a yellow solid (0.347 g, 0.283 mmol, 97.1%).

$C_{80}H_{74}O_{12}$ MW = 1227.4 g/mol.

^{1}H-NMR (400 MHz, [D$_6$]-dimethylsulfoxid, 298 K) δ [in ppm] = 8.97 (s, 2 H, H-34), 8.27 (s, 2 H, H-14), 8.20 (s, 2 H, H-33), 7.94 – 7.90 (m, 5 H, H-6+16+40), 7.89 (s, 2 H, H-4) 7.67 (dd, ^3J = 7.8Hz, ^4J = 1.5 Hz, 2 H, H-38), 7.53 (t, ^3J = 7.9 Hz, 1 H, H-39), 7.33 (s, 4 H, H-22), 7.32 – 7.30 (m, 2 H, H-17), 7.29 – 7.27 (m, 2 H, H-7), 7.26 (dt, ^3J = 6.8 Hz, ^4J = 1.4 Hz, 2 H, H-18), 7.20 (dt, ^3J = 7.5 Hz, ^4J = 1.2 Hz, 2 H, H-8), 6.92 (d, ^3J = 8.3 Hz, 2 H, H-19), 6.85 (d, ^3J = 8.7 Hz, 2 H, H-9), 3.95 – 3.93 (m, 4 H, H-26), 3.76 – 3.73 (m, 4 H, H-27), 3.64 – 3.62 (m, 4 H, H-28/29), 3.58 – 3.56 (m, 4 H, H-28/29), 3.55 – 3.53 (m, 4 H, H-30), 3.45 – 3.38 (m, 4 H, H-31), 3.24 (s, 6 H, H-32), 2.30 (s, 12 H, H-24).

^{13}C-NMR (101 MHz, [D$_6$]-dimethylsulfoxid, 298 K) δ [in ppm] = 154.83 (C-25), 152.98 (C-12), 150.97 (C-2), 134.41 (C-20), 134.18 (C-21), 134.08 (C-40), 133.70 (C-14), 133.11 (C-10), 131.48 (C-3/38), 131.45 (C-3/38), 129.97 (C-22), 129.64 (C-4), 129.40 (C-39), 128.88 (C-15), 128.56 (C-5+23), 128.19 (C-6/16), 128.13 (C-6/16), 127.43 (C-18), 126.09 (C-8), 124.28 (C-19), 123.94 (C-9), 123.51 (C-17), 123.42 (C-37), 123.02 (C-7), 115.69 (C-11), 115.01 (C-1), 113.10 (C-13), 92.72 (C-36), 87.70 (C-35), 71.45 (C-26), 71.36 (C-31), 70.06 (C-28/29), 69.92 (C-28/29), 69.73 (C-27+30), 58.13 (C-32), 16.17 (C-24).

^{1}H,^{1}H-COSY (400 MHz / 400 MHz, [D$_6$]-dimethylsulfoxid, 298 K) δ [in ppm] = 7.94 – 7.90 / 7.32 – 7.30, 7.29 – 7.27 (H-6+16+40 / H-7/17), 7.67 / 7.53 (H-38 / H-39), 7.53 / 7.67 (H-39 / H-38), 7.33 / 2.30 (H-22 / H-24), 7.32 – 7.30/7.29 – 7.27 / 7.94 – 7.90 (H-7/17 / H-6+16+40), 7.26 / 6.92 (H-18 / H-19), 7.20 / 6.85 (H-8 / H-9), 6.92 / 7.26 (H-19 / H-18), 6.85 / 7.20 (H-9 / H-8), 3.95 – 3.93 / 3.76 – 3.73 (H-26 / H-27), 3.76 – 3.73 / 3.95 – 3.93 (H-27 / H-26), 3.64 – 3.62 / 3.58 – 3.56 (H-28/29 / H-28/29), 3.58 – 3.56 / 3.64 – 3.62, 3.45 – 3.38 (H-28/29 / H-28/29, H-31), 3.55 – 3.53 / 3.45 – 3.38 (H-30 / H-31), 3.45 – 3.38 / 3.58 – 3.56, 3.55 – 3.53 (H-31 / H-28/29, H-30), 2.30 / 7.33 (H-24 / H-22).

^{1}H,^{13}C-GHSQC (400 MHz / 101 MHz, [D$_6$]-dimethylsulfoxid, 298 K) δ (^{1}H) / δ (^{13}C) [in ppm] = 8.27 / 133.70 (H-14 / C-14), 7.94 – 7.90 / 134.08, 128.19, 128.13 (H-6+16+40 / C-40, C-6/16, C-6/16), 7.89 / 129.64 (H-4 / C-4), 7.67 / 131.45, (H-38 / C-3/38), 7.53 / 129.40 (H-39 / C-39), 7.33 / 129.97 (H-22 / C-22), 7.32 – 7.30 / 123.51 (H-17 / C-17), 7.29 – 7.27 / 123.02 (H-7 / C-7), 7.26 / 127.43 (H-18 / C-18), 7.20 / 126.09 (H-8 / C-8), 6.92 / 124.28 (H-19 / C-19), 6.85 / 123.94 (H-9 / C-9), 3.95 – 3.93 / 71.45 (H-26 / C-26), 3.76 – 3.73 / 69.73 (H-27 / C-27+C30), 3.64 – 3.62 / 70.06 (H-28/29 / C-28/29), 3.58 – 3.56 / 69.92 (H-28/29 / C-28/29), 3.55 – 3.53 / 69.73 (H-30 / C-27+30), 3.45 – 3.38 / 71.36 (H-31 / C-31), 3.24 / 58.13 (H-32 / C-32), 2.30 / 16.17 (H-24 / C-24),.

^{1}H,^{13}C-GHMBC (400 MHz / 101 MHz, [D$_6$]-dimethylsulfoxid, 298 K) δ (^{1}H) / δ (^{13}C) [in ppm] = 8.97 / 115.69, 113.10 (H-34 / C-11, C-13), 8.27 / 152.98, 134.41, 128.19/128.13, 87.70 (H-14 / C-12, C-20, C-6/16, C-35), 8.20 / 131.45/131.48, 115.01 (H-33 / C-3/38, C-1), 7.94 – 7.90 / 134.41, 133.70, 129.64, 127.43, 126.09 (H-6+16+40 / C-20, C-14, C-4, C-18, C-8), 7.89 / 150.97, 134.18, 133.11 (H-4 / C-2, C-21, C-10), 7.67 / 134.08, 131.48/131.45, 123.42, 92.72 (H-38 / C-40, C-3/38, C-37, C-36), 7.53 / 123.42 (H-39 / C-37), 7.33 / 154.83, 131.48/131.45, 129.97, 16.17 (H-22 / C-25, C-3/28, C-22, C-24), 7.32 – 7.30 / 128.19/128.13, 124.28 (H-17 / C-6/16, C-19), 7.29 – 7.27 / 128.56, 123.94 (H-7 / C-5+23, C-9), 7.26 / 134.41 (H-18 / C-20), 7.20 / 133.11 (H-8 / C-10), 6.92 / 128.88, 128.19/128.13, 123.51, 115.69 (H-19 / C-15, C-6/16, C-17, C-11), 6.85 / 128.56, 123.02, 115.01 (H-9 / C-5/23, C-7, C-1), 3.95 – 3.93 / 69.92 (H-26 / C-28/29), 3.76 – 3.73 / 71.36 (H-27 / C-31), 3.64 – 3.62 / 69.92 (H-28/29 / C-28/29), 3.58 – 3.56 / 69.92 (H-28/29 / C-28/29), 3.55 – 3.53 / 69.92 (H-30 / C-28/29) 3.24 / 71.36 (H-32 / C-31) 2.30 / 154.83, 129.97, 128.56 (H-24 / C-25, C-22, C-5+23). [MT544-4]

Elemental analysis = calcd (%) for $C_{80}H_{74}O_{12}$: C: 78.28, H: 6.08, O: 15.64; found:

C: 75.0, H: 5.69, O: -

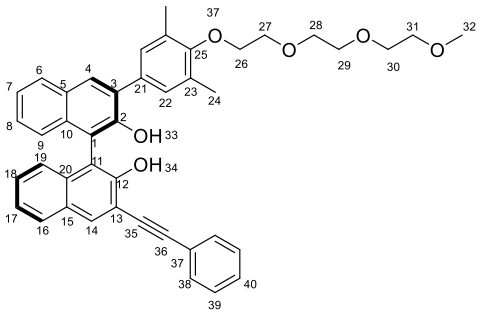
MS (ESI-pos, MeOH**)**: *m/z* = 636.2475 ([M+Na]$^{2+}$, calcd. 636.2482 for [$C_{80}H_{74}O_{12}Na_2^{2+}$].

IR (ATR-FT): $\tilde{\nu}$ (cm^{-1}) = 3503, 3054, 3033, 2980, 2972, 2884, 2360, 2331, 1618, 1589, 1568, 1541, 1521, 1479, 1434, 1399, 1381, 1361, 1340, 1323, 1299, 1246, 1200, 1171, 1140, 1124, 1092.

[MT544]

8.2.2.5.16. Synthesis of compound (*R*)-**103b**

Described experiment: MT545 Repeated:-



Compound (*R*)-**102b** (0.213 g, 0.287 mmol, 1 eq), was dissolved in a mixture of dry ethanol:diethyl ether (5:3, 10 ml total). Then acetyl chloride (0.410 ml, 0.451 g, 5.75 mmol, 20 eq) was added in a dropwise manner over 15 minutes and the mixture was stirred for 18 hours. Then water (15 ml) was added to end the reaction and ethanol and ethyl ether were removed in *vacuo*. Then ethyl acetate (40 ml) was added to the aqueous residue. The organic layer was separated and then washed with a saturated solution of sodium chloride (25 ml). The organic layer was dried over sodium sulfate and was concentrated in *vacuo* to afford the product as a yellow solid (0.156 g, 0.241 mmol, 84.2%).

$C_{43}H_{40}O_6$ MW = 652.8 g/mol.

^{1}H-NMR (400 MHz, [D$_6$]-dimethylsulfoxid, 298 K) δ [in ppm] = 8.90 (s, 1 H, H-34), 8.25 (s, 1 H, H-14), 8.19 (s, 1 H, H-33), 7.93 (d, ^3J = 8.0 Hz, 1 H, H-16), 7.91 (d, ^3J = 8.0Hz, 1 H, H-6), 7.89 (s, 1 H, H-4) 7.66 – 7.62 (m, 2 H, H-38), 7.48 – 7.42 (m, 3 H, H-39+40), 7.33 (s, 2 H, H-22), 7.31 – 7.29 (m, 1 H, H-17), 7.28 – 7.27 (m, 1 H, H-7), 7.25 (dt, ^3J = 7.5 Hz, ^4J = 1.4 Hz, 1 H, H-18), 7.20 (dt, ^3J = 7.5 Hz, ^4J = 1.2 Hz, 1 H, H-8), 6.92 (d, ^3J = 8.6 Hz, 1 H, H-19), 6.85 (d, ^3J = 8.6 Hz, 1 H, H-9), 3.95 – 3.93 (m, 2 H, H-26), 3.76 – 3.73 (m, 2 H, H-27), 3.64 – 3.62 (m, 2 H, H-28), 3.58 – 3.53 (m, 4 H, H-29+30), 3.45 – 3.43 (m, 2 H, H-31), 3.24 (s, 3 H, H-32), 2.30 (s, 6 H, H-24).

^{13}C-NMR (101 MHz, [D$_6$]-dimethylsulfoxid, 298 K) δ [in ppm] = 154.81 (C-25), 152.93 (C-12), 150.99 (C-2), 134.27 (C-20), 134.08 (C-21), 133.47 (C-14), 133.12 (C-10), 131.48 (C-3/38), 131.45 (C-3/38), 129.95 (C-22), 129.62 (C-4), 128.78 (C-39+40/23), 128.75 (C-39+40/23), 128.55 (C-5), 128.20 (C-15), 128.11 (C-6/16), 128.05 (C-6/16), 127.28 (C-18), 126.06 (C-8), 124.24 (C-19), 123.93 (C-9), 123.44 (C-17), 123.00 (C-7), 122.84 (C-37), 115.56 (C-11), 114.98 (C-1), 113.38 (C-13), 93.58 (C-36), 86.07 (C-35), 71.43 (C-26/31), 71.35 (C-26/31), 70.04 (C-28), 69.90 (C-27 + C-29/30), 69.72 (C-29/30), 58.12 (C-32), 16.16 (C-24).

^{1}H,^{1}H-COSY (400 MHz / 400 MHz, [D$_6$]- dimethylsulfoxid, 298 K) δ [in ppm] = 7.93 / 7.31 – 7.29 (H-16 / H-17), 7.91 / 7.28 – 7.27 (H-6 / H-7), 7.66 – 7.62/ 7.48 – 7.42 (H-38 / H-39+40), 7.48 – 7.42 / 7.66 – 7.62 (H-39+40 / H-38), 7.33 / 2.30 (H-22 / H-24), 7.31 – 7.29 / 7.93 (H-17 / H-16), 7.28 – 7.27 / 7.91 (H-7 / H-6), 7.25 / 6.92 (H-18 / H-19), 7.20 / 6.85 (H-8 / H-9), 6.92 / 7.25 (H-19 / H-18), 6.85 / 7.20 (H-9 / H-8), 3.95 – 3.93 / 3.76 – 3.73 (H-26 / H-27), 3.76 – 3.73 / 3.95 – 3.93 (H-27 / H-26), 3.64 – 3.62 / 3.58 – 3.53 (H-28 / H-29+30), 3.58 – 3.53 / 3.64 – 3.62, 3.45 – 3.43 (H-29+30 / H-28, H-31), 3.45 – 3.43 / 3.58 – 3.53 (H-31 / H-29+30), 2.30 / 7.33 (H-24 / H-22).

^{1}H,^{13}C-GHSQC (400 MHz / 101 MHz, [D$_6$]- dimethylsulfoxid, 298 K) δ (^{1}H) / δ (^{13}C) [in ppm] = 8.25 / 133.47 (H-14 / C-14), 7.93 / 128.11/128.05 (H-16 / C-6/16), 7.91 / 128.11/128.05 (H-6 / C-6/16), 7.89 / 129.62 (H-4 / C-4), 7.66 – 7.62 / 131.48/131.45 (H-38 / C-3/38), 7.48 – 7.42 / 128.78/128.75

(H-39+40 / C-39+40/C-23), 7.33 / 129.95 (H-22 / C-22), 7.31 – 7.29 / 123.44 (H-17 / C-17), 7.28 – 7.27 / 123.00 (H-7 / C-7), 7.25 / 127.28 (H-18 / C-18), 7.20 / 126.06 (H-8 / C-8), 6.92 / 124.24 (H-19 / C-19), 6.85 / 123.93 (H-9 / C-9), 3.95 – 3.93 / 71.43/71.35 (H-26 / C-26/31), 3.76 – 3.73 / 69.90 (H-27 / C-27 + C-29/30), 3.64 – 3.62 / 70.04 (H-28 / C-28), 3.58 – 3.53 / 69.90, 69.72 (H-29+30 / C-27 + C-29/30, C-29/30), 3.45 – 3.43 / 71.43/71.35 (H-31 / C-26/31), 3.24 / 58.12 (H-32 / C-32), 2.30 / 16.16 (H-24 / C-24).

^{1}H,^{13}C-GHMBC (400 MHz / 101 MHz, [D$_6$]- dimethylsulfoxid, 298 K) δ (^{1}H) / δ (^{13}C) [in ppm] = 8.25 / 152.93, 134.27, 128.11/128.05, 86.07 (H-14 / C-12, C-20, C-6/16, C-35), 7.93/7.91 / 133.97, 127.28, 126.04 (H-6/16 / C-14, C-18, C-8), 7.89 / 150.99, 134.08, 133.12, 128.11/128.05 (H-4 / C-2, C-21, C-10, C-6/16), 7.66 – 7.62/ 131.48/131.45, 128.78/128.75, 93.58 (H-38 / C-3/38, C-39+40/23, C-36), 7.48 – 7.42 / 131.48/131.45, 128.78/128.75, 122.84 (H-39+40 / C-3/38, C39+40/23, C37), 7.33 / 154.81, 131.48/131.45, 129.95, 16.16 (H-22 / C-25, C-3/38, C-22, C-24), 7.31 – 7.29 / 128.20, 124.24 (H-17 / C-15, C-19), 7.28 – 7.27 / 128.55, 123.93 (H-7 / C-5, C-9), 7.25 / 134.27, 128.11/128.05 (H-18 / C-20, C-6/16), 7.20 / 133.12, 128.11/128.05 (H-8 / C-10, C-6/16), 6.92 / 128.20, 123.44, 115.56 (H-19 / C-15, C-17, C-11), 6.85 / 128.55, 123.00, 114.98 (H-9 / C-5, C-7, C-1), 3.95 – 3.93 / 69.90 (H-26 / C-27 + C-29/30), 3.76 – 3.73 / 71.43 (H-27 / C-26/31), 3.24 / 71.35 (H-32 / C-26/31) 2.30 / 154.81, 129.95, 128.78/128.75 (H-24 / C-25, C-22, C-39+40/23).

[MT545-4]

Elemental analysis = calcd (%) for $C_{43}H_{40}O_6$: C: 79.12, H: 6.18, O: 14.71; found:

C: 77.1, H: 5.99, O: 14.4

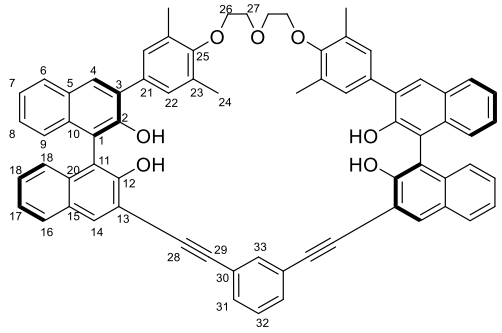
MS (ESI-pos, MeOH**)**: *m/z* = 675.2727 ([M+Na]$^+$, calcd. 675.2717 for [$C_{43}H_{40}O_6Na^+$].

IR (ATR-FT): $\tilde{\nu}$ (cm^{-1}) = 3499, 3305, 3052, 2915, 2870, 1618, 1591, 1489, 1432, 1402, 1379, 1360, 1338.

[MT545]

8.2.2.5.17. Synthesis of compound (*R*,*R*)-**82**

Described experiment: MT548 Repeated:-



Compound (*R*,*R*)-**80** (0.200 g, 0.169 mmol, 1 eq), was dissolved in a mixture of dry ethanol:diethyl ether (5:3, 5 ml total). Then acetyl chloride (0.483 ml, 0.531 g, 6.77 mmol, 40 eq) was added in a dropwise manner over 15 minutes and the mixture was stirred for 18 hours. Then water (15 ml) was added to end the reaction and ethanol and ethyl ether were removed in *vacuo*. Then ethyl acetate (40 ml) was added to the aqueous residue. The organic layer was separated and then washed with a saturated solution of sodium chloride (25 ml). The organic layer was dried over sodium sulfate and was concentrated in *vacuo* to afford the product as a yellow solid (0.161 g, 0.160 mmol, 95.3%).

$C_{70}H_{52}O_7$ MW = 1005.2 g/mol.

^{1}H-NMR (400 MHz, [D$_6$]-dimethylsulfoxid, 298 K) δ [in ppm] = 8.25 (s, 2 H, H-14), 8.10 (s, 1 H, H-33), 7.93 (d, ^3J = 8.5 Hz, 2 H, H-16) 7.90 (d, ^3J = 8.5 Hz, 2 H, H-6), 7.86 (s, 2 H, H-4), 7.64 – 7.62 (m, 2 H, H-31), 7.56 – 7.52 (m, 1 H, H-32), 7.34 (s, 4 H, H-22), 7.31 (t, ^3J = 7.7 Hz, 2 H, H-17), 7.26 (t, ^3J = 7.5 Hz, 2 H, H-7), 7.24 (t, ^3J = 7.5 Hz, 2 H, H-18), 7.16 (t, ^3J = 7.5 Hz, 2 H, H-8), 6.90 (d, ^3J = 8.4 Hz, 2 H, H-19), 6.79 (d, ^3J = 8.4 Hz, 2 H, H-9), 4.10 – 4.05 (m, 1 H, H-26/27), 4.03 – 3.99 (m, 1 H, H-26/27), 3.84 (br s, 2 H, H-26/27), 2.33 (s, 2 H, H-24).

^{13}C-NMR (101 MHz, [D$_6$]-dimethylsulfoxid, 298 K) δ [in ppm] = 154.93 (C-25), 153.08 (C-12), 151.08 (C-2), 136.24 (C-33), 134.48 (C-20), 133.95 (C-21), 133.12 (C-10), 132.87 (C-14), 131.56 (C-23), 130.48 (C-31), 129.85 (C-3), 129.73 (C-22), 129.47 (C-4), 129.33 (C-32), 128.40 (C-5), 128.10 (C-6/16), 128.07 (C-6/16), 128.00 (C-15), 127.22 (C-18), 125.92 (C-8), 124.54 (C-19), 124.02 (C-9), 123.36 (C-17/30), 123.32 (C-17/30), 122.85 (C-7), 115.62 (C-11), 114.76 (C-1), 113.12 (C-13), 92.78 (C-29), 87.48 (C-28), 71.93 (C-26/27), 70.22 (C-26/27), 16.46 (C-24).

^{1}H,^{1}H-COSY (400 MHz / 400 MHz, [D$_6$]-dimethylsulfoxid, 298 K) δ [in ppm] = 7.93 / 7.31 (H-16 / H-17), 7.90 / 7.26 (H-6 / H-7), 7.64 – 7.62 / 7.56 – 7.52 (H-31 / H-32), 7.56 – 7.52 / 7.64 – 7.62 (H-32 / H-31), 7.31 / 7.93 (H-17 / H-16), 7.26 / 7.90 (H-7 / H-6), 7.24 / 6.90 (H-18 / H-19), 7.16 / 6.79 (H-8 / H-9), 6.90 / 7.24 (H-19 / H-18), 6.79 / 7.16 (H-9 / H-8). 4.10 – 4.05 / 4.03 – 3.99 (H-26/27 / H-26/27), 4.03 – 3.99 / 4.10 – 4.05 (H-26/27 / H-26/27).

^{1}H,^{13}C-GHSQC (400 MHz / 101 MHz, [D$_6$]-dimethylsulfoxid, 298 K) δ (^{1}H) / δ (^{13}C) [in ppm] = 8.25 / 132.87 (H-14 / C-14), 8.10 / 136.24 (H-33 / C-33), 7.93 / 128.10/128.07 (H-16 / C-6/16), 7.90 / 128.10/128.07 (H-6 / C-6/16), 7.86 / 129.47 (H-4 / C-4), 7.64 – 7.62 / 130.48 (H-31 / C-31), 7.56 – 7.52 / 129.33 (H-32 / C-32), 7.34 / 129.73 (H-22 / C-22), 7.31 / 123.36/123.32 (H-17 / C-17/30), 7.26 / 122.85 (H-7 / C-7), 7.24 / 127.22 (H-18 / C-18), 7.16 / 125.92 (H-8 / C-8), 6.90 / 124.54 (H-19 / C-19), 6.79 /

124.02 (H-9 / C-9), 4.10 – 4.05 / 71.93 (H-26/27 / C-26/27), 4.03 – 3.99 / 70.22 (H-26/27 / C-26/27), 2.33 / 16.46 (H-24 / C-24).

^{1}H,^{13}C-GHMBC (400 MHz / 101 MHz, [D$_6$]-dimethylsulfoxid, 298 K) δ (^{1}H) / δ (^{13}C) [in ppm] = 8.25 / 153.08, 134.48, 128.10/128.07, 87.48 (H-14 / C-12, C-20, C-6/16, C-28), 8.10 / 130.48, 92.78 (H-33 / C-31, C-29), 7.93 / 134.48, 132.87, 127.22 (H-16 / C-20, C-14, C-18), 7.90 / 133.12, 129.47, 125.92 (H-6 / C-10, C-4, C-8), 7.86 / 151.08, 133.95, 133.12, 128.10/128.07 (H-4 / C-2, C-21, C-10, C-6/16), 7.64 – 7.62 / 136.24, 130.48, 92.78 (H-31 / C-33, C-31, C-29), 7.56 – 7.52 / 123.36/123.32 (H-32 / C-17/30), 7.34 / 154.93, 131.56, 129.73, 16.46 (H-22 / C-25, C-23, C-22, C-24), 7.31 / 128.00, 128.10/128.07, 124.55 (H-17 / C-15, C-6/16, C-19), 7.26 / 128.10/128.07 (H-7 / C-6/16), 7.24 / 134.48 (H-18 / C-20), 7.16 / 133.12 (H-8 / C-10), 6.90 / 128.00, 123.36/123.32, 115.62 (H-19 / C-15, C-17/30, C-11), 6.79 / 128.40, 122.85, 114.76 (H-9 / C-5, C-7, C-1), 2.33 / 154.93, 129.73 (H-24 / C-25, C-22).

[MT548-4]

Elemental analysis = calcd (%) for $C_{70}H_{52}O_7$: C: 81.3, H: 5.53, O: 13.17; found:

C: 81.0, H: 5.15, O: 11.4

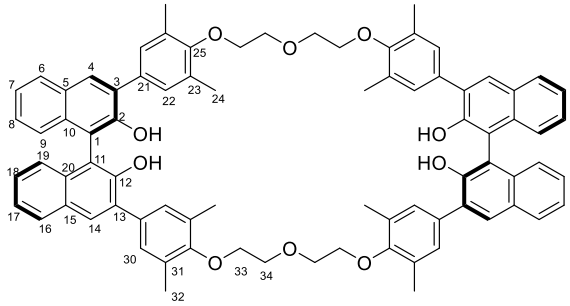
MS (ESI-pos, MeOH**)**: *m/z* = 1027.3588 ([M+Na]$^+$, calcd. 1027.3605 for [$C_{70}H_{52}O_7Na^+$].

IR (ATR-FT): $\tilde{\nu}$ (cm^{-1}) = 3509, 3052, 2941, 2917, 2865, 1619, 1587, 1570, 1480, 1427, 1400, 1383, 1362, 1301, 1259, 1247, 1202, 1171, 1146, 1125, 1067, 1015, 934, 883, 791, 775, 745.

[MT548-4]

8.2.2.5.18. Synthesis of compound (*R*,*R*)-**94**

Described experiment: MT583 Repeated: MT591



Compound (*R*,*R*)-**88** (0.126 g, 0.0919 mmol, 1 eq), was dissolved in a mixture of dry ethanol:diethyl ether (5:3, 5 ml total). Then acetyl chloride (0.262 ml, 0.288 mg, 3.61 mmol, 40 eq) was added in a dropwise manner over 15 minutes and the mixture was stirred for 18 hours. Then water (15 ml) was added to end the reaction and ethanol and ethyl ether were removed in *vacuo*. Then ethyl acetate (40 ml) was added to the aqueous residue. The organic layer was separated and then washed with a saturated solution of sodium chloride (25 ml). The organic layer was dried over sodium sulfate and was concentrated in *vacuo* to afford the product as a yellow solid (91.3 mg, 0.0765 mmol, 83.3%).

$C_{80}H_{72}O_{10}$, MW = 1193.4 g/mol.

^{1}H-NMR (400 MHz, [D$_1$]-chloroform, 298 K) δ [in ppm] = 7.96 (s, 4 H, H-4), 7.88 (d, ^{3}J = 7.8 Hz, 4 H, H-6), 7.39 (s, 8 H, H-12), 7.34 (dt, ^{3}J = 7.5 Hz, ^{4}J = 1.3 Hz, 4 H, H-7), 7.26 (dt, ^{3}J = 7.2 Hz, ^{4}J = 1.3 Hz, 4 H, H-8), 7.15 (d, ^{3}J = 8.5 Hz, 4 H, H-9), 5.43 (br s, 4 H, H-18), 4.11 – 4.03 (m, 8 H, H-16/17), 3.99 – 3.91 (m, 8 H, H-16/17), 2.39 (s, 24 H, H-14).

^{13}C-NMR (101 MHz, [D$_1$]-chloroform, 298 K) δ [in ppm] = 155.56 (C-15), 150.06 (C-2), 133.20 (C-10), 132.94 (C-11), 131.49 (C-13), 130.94 (C-4), 130.49 (C-3), 130.09 (C-12), 129.52 (C-5), 128.41 (C-6), 127.10 (C-8), 124.65 (C-9), 124.29 (C-7), 112.73 (C-1), 71.75 (C-16/17), 70.89 (C-16/17), 16.53 (C-14).

^{1}H,^{1}H-COSY (400 MHz / 400 MHz, [D$_1$]-chloroform, 298 K) δ [in ppm] = 7.88 / 7.34 (H-6 / H-7), 7.39 / 2.39 (H-12 / H-14), 7.34 / 7.88, 7.26 (H-7 / H-6, H-8), 7.26 / 7.34, 7.15 (H-8 / H-7, H-9), 7.15 / 7.26 (H-9 / H-8), 4.11 – 4.03 / 3.99 – 3.91 (H-16/17 / H-16/17), 3.99 – 3.91 / 4.11 – 4.03 (H-16/17 / H-16/17), 2.39 / 7.39 (H-14 / H-12).

^{1}H,^{13}C-GHSQC (400 MHz / 101 MHz, [D$_1$]-chloroform, 298 K) δ (^{1}H) / δ (^{13}C) [in ppm] = 7.96 / 130.94 (H-4 / C-4), 7.88 / 128.41 (H-6 / C-6), 7.39 / 130.09 (H-12 / C-12), 7.34 / 124.29 (H-7 / C-7), 7.26 / 127.10 (H-8 / C-8), 7.15 / 124.65 (H-9 / C-9), 4.11 – 4.03 / 71.75 (H-16/17 / C-16/17), 3.99 – 3.91 / 70.89 (H-16/17 / C-16/17), 2.39 / 16.53 (H-14 / C-14).

^{1}H,^{13}C-GHMBC (400 MHz / 101 MHz, [D$_1$]-chloroform, 298 K) δ (^{1}H) / δ (^{13}C) [in ppm] = 7.96 / 150.06, 133.20, 132.94, 128.41 (H-4 / C-2, C-10, C-11, C-6), 7.88 / 133.20, 130.93, 127.10 (H-6 / C-10, C-4, C-8), 7.39 / 155.56, 130.49, 130.09, 16.53 (H-12 / C-15, C-3, C-12, C-14), 7.34 / 129.52, 124.65 (H-7 / C-5, C-9), 7.26 / 133.20, 128.41 (H-8 / C-10, C-6), 7.15 / 129.52, 124.29, 112.73 (H-9 / C-5, C-7, C-1), 2.39 / 155.56, 131.49, 130.09 (H-14 / C-15, C-13, C-12).

[MT591-6]

Elemental analysis = calcd (%) for $C_{80}H_{72}O_{10}$: C: 80.51, H: 6.08, O: 13.41; found:

C: 80.75, H: 5.86, O: 13.5

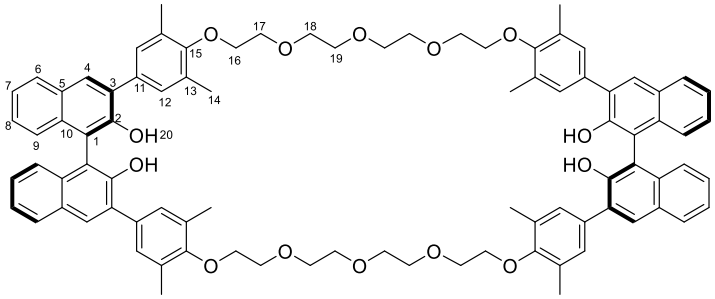
MS (ESI-pos, MeOH**)**: *m/z* = 491.2012 ([M+H]$^+$, calcd. 491.2006 for [$C_{36}H_{27}O_2^+$].

IR (ATR-FT): $\tilde{\nu}$ (cm^{-1}) = 3512, 3058, 2915, 2871, 1719, 1625, 1588, 1487, 1435, 1401, 1367, 1309, 1248, 1203, 1177, 1127, 1059, 1021, 877, 747.

[MT591]

8.2.2.5.19. Synthesis of compound (*R*,*R*)-**95**

Described experiment: MT659 Repeated:



Compound (*R*,*R*)-**89** (79.9 mg, 0.052 mmol, 1 eq), was dissolved in a mixture of dry ethanol:diethyl ether (5:3, 5 ml total). Then acetyl chloride (0.148 ml, 0.102 mg, 2.07 mmol, 40 eq) was added in a dropwise manner over 15 minutes and the mixture was stirred for 18 hours. Then water (15 ml) was added to end the reaction and ethanol and ethyl ether were removed in *vacuo*. Then ethyl acetate (40 ml) was added to the aqueous residue. The organic layer was separated and then washed with a saturated solution of sodium chloride (25 ml). The organic layer was dried over sodium sulfate and was concentrated in *vacuo* to afford the product as a yellow solid (62.1 mg, 0.0453 mmol, 87.5%).

$C_{88}H_{88}O_{14}$, MW = 1369.6 g/mol.

^{1}H-NMR (600 MHz, [D$_6$]-dimethylsulfoxid, 298 K) δ [in ppm] = 8.09 (s, 4 H, H-20), 7.87 (d, ^{3}J = 8.0 Hz, 4 H, H-6), 7.84 (s, 4 H, H-4), 7.30 (s, 8 H, H-12), 7.24 (t, ^{3}J = 7.1 Hz, 4 H, H-7), 7.16 (t, ^{3}J = 7.6 Hz, 4 H, H-8), 6.83 (d, ^{3}J = 8.7 Hz, 4 H, H-9), 3.93 – 3.91 (m, 8 H, H-16), 3.76 – 3.75 (m, 8 H, H-17), 3.65 – 3.61 (m, 16 H, H-18+19), 2.28 (s, 24 H, H-14).

^{13}C-NMR (151 MHz, [D$_6$]-dimethylsulfoxid, 298 K) δ [in ppm] = 154.71 (C-15), 151.24 (C-2), 134.06 (C-11), 133.34 (C-10), 131.44 (C-3), 129.91 (C-12), 129.79 (C-13), 129.55 (C-4), 128.55 (C-5), 128.01 (C-6), 125.91 (C-8), 123.98 (C-9), 122.84 (C-7), 114.93 (C-1), 71.44 (C-16), 70.12 (C-18/19), 70.09 (C-18/19), 69.90 (C-17), 16.08 (C-14).

^{1}H,^{1}H-COSY (600 MHz / 600 MHz, [D$_6$]-dimethylsulfoxid, 298 K) δ [in ppm] = 7.87 / 7.24 (H-6 / H-7), 7.30 / 2.28 (H-12 / H-14), 7.24 / 7.87, 7.16 (H-7 / H-6, H-8), 7.16 / 7.24, 6.83 (H-8 / H-7, H-9), 6.83 / 7.16 (H-9 / H-8), 3.93 – 3.91 / 3.76 – 3.75 (H-16 / H-17), 3.76 – 3.75 / 3.93 – 3.91 (H-16 / H-17), 2.28 / 7.30 (H-14 / H-12).

^{1}H,^{13}C-GHSQC (600 MHz / 151 MHz, [D$_6$]-dimethylsulfoxid, 298 K) δ (^{1}H) / δ (^{13}C) [in ppm] = 7.87 / 128.01 (H-6 / C-6), 7.84 / 129.55 (H-4 / C-4), 7.30 / 129.91 (H-12 / C-12), 7.24 / 122.84 (H-7 / C-7), 7.16 / 125.91 (H-8 / C-8), 6.83 / 123.98 (H-9 / C-9), 3.93 – 3.91 / 71.44 (H-16 / C-16), 3.76 – 3.75 / 69.90 (H-17 / C-17), 3.65 – 3.61 / 70.12, 70.09 (H-18+19 / C-18+19), 2.28 / 16.08 (H-14 / C-14).

^{1}H,^{13}C-GHMBC (600 MHz / 151 MHz, [D$_6$]-dimethylsulfoxid, 298 K) δ (^{1}H) / δ (^{13}C) [in ppm] = 8.09 / 131.44, 114.93 (H-20 / C-3, C-1), 7.87 / 133.34, 129.55, 125.91 (H-6 / C-10, C-4, C-8), 7.84 / 151.24, 134.06, 133.34, 128.01 (H-4 / C-2, C-11, C-10, C-6), 7.30 / 154.71, 131.44, 129.91, 129.79, 16.08 (H-12 / C-15, C-3, C-12, C-13, C-14), 7.24 / 128.55, 123.98 (H-7 / C-5, C-9), 7.16 / 133.34, 128.01 (H-8 / C-10, C-6), 6.83 / 128.55, 122.84, 114.93 (H-9 / C-5, C-7, C-1), 3.93 – 3.91 / 69.90 (H-16 / C-17), 3.76 – 3.75 / 70.12/70.09 (H-17 / C-18/19), 2.28 / 154.71, 129.91, 129.79 (H-14 / C-15, C-12, C-13).

[MT659-4-2]

Elemental analysis = calcd (%) for $C_{88}H_{88}O_{14}$: C: 77.17, H: 6.48, O: 16.35; found:

C: 76.0, H: 6.56, O: -

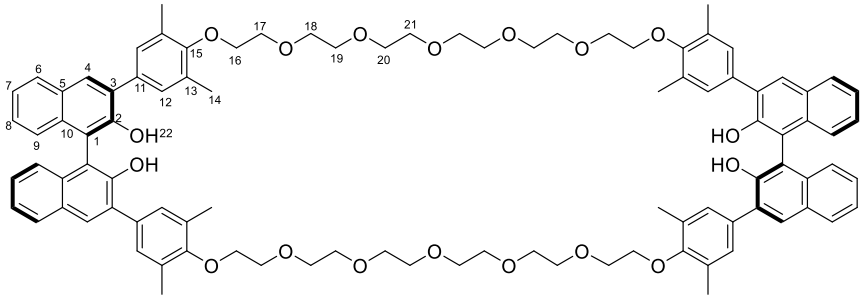
MS (ESI-pos, MeOH**)**: *m/z* = 707.2983 ($[M+2Na]^{2+}$, calcd. 707.2979 for $[C_{88}H_{88}O_{14}Na_2^{2+}]$.

IR (ATR-FT): $\tilde{\nu}$ (cm^{-1}) = 3511, 3054, 2917, 2861, 1716, 1620, 1594, 1484, 1435, 1400, 1360, 1303, 1251, 1203, 1177, 1124, 1059, 1029, 877, 747.

[MT659]

8.2.2.5.20. Synthesis of compound (*R*,*R*)-**96**

Described experiment: MT660 Repeated:



Compound (*R*,*R*)-**90** (79.9 mg, 0.0465 mmol, 1 eq), was dissolved in a mixture of dry ethanol:diethyl ether (5:3, 5 ml total). Then acetyl chloride (0.132 ml, 0.146 mg, 1.86 mmol, 40 eq) was added in a dropwise manner over 15 minutes and the mixture was stirred for 18 hours. Then water (15 ml) was added to end the reaction and ethanol and ethyl ether were removed in *vacuo*. Then ethyl acetate (40 ml) was added to the aqueous residue. The organic layer was separated and then washed with a saturated solution of sodium chloride (25 ml). The organic layer was dried over sodium sulfate and was concentrated in *vacuo* to afford the product as a yellow solid (45.1 mg, 0.0291 mmol, 63.2%).

$C_{96}H_{104}O_{18}$, MW = 1545.8 g/mol.

^{1}H-NMR (600 MHz, [D$_6$]-dimethylsulfoxid, 298 K) δ [in ppm] = 8.10 (s, 4 H, H-22), 7.88 (d, ^{3}J = 8.2 Hz, 4 H, H-6), 7.85 (s, 4 H, H-4), 7.31 (s, 8 H, H-12), 7.24 (t, ^{3}J = 7.1 Hz, 4 H, H-7), 7.16 (t, ^{3}J = 7.7 Hz, 4 H, H-8), 6.84 (d, ^{3}J = 8.8 Hz, 4 H, H-9), 3.92 – 3.90 (m, 8 H, H-16), 3.73 – 3.71 (m, 8 H, H-17), 3.62 – 3.60 (m, 8 H, H-18), 3.58 – 3.56 (m, 8 H, H-19), 3.54 – 3.53 (m, 16 H, H-20+21), 2.27 (s, 24 H, H-14).

^{13}C-NMR (151 MHz, [D$_6$]-dimethylsulfoxid, 298 K) δ [in ppm] = 154.72 (C-15), 151.26 (C-2), 134.06 (C-11), 133.35 (C-10), 131.46 (C-3), 129.93 (C-12), 129.80 (C-13), 129.56 (C-4), 128.58 (C-5), 128.02 (C-6), 125.92 (C-8), 124.00 (C-9), 122.85 (C-7), 114.96 (C-1), 71.39 (C-16), 70.03 (C-18), 69.92 (C-17/19/20/21), 69.90 (C-17/19/20/21), 69.87 (C-17/19/20/21), 16.10 (C-14).

^{1}H,^{1}H-COSY (600 MHz / 600 MHz, [D$_6$]-dimethylsulfoxid, 298 K) δ [in ppm] = 7.88 / 7.24 (H-6 / H-7), 7.31 / 2.27 (H-12 / H-14), 7.24 / 7.88 (H-7 / H-6), 7.16 / 6.84 (H-8 / H-9), 6.84 / 7.16 (H-9 / H-8), 3.92 – 3.90 / 3.73 – 3.71 (H-16 / H-17), 3.73 – 3.71 / 3.92 – 3.90 (H-16 / H-17), 2.27 / 7.31 (H-14 / H-12).

^{1}H,^{13}C-GHSQC (600 MHz / 151 MHz, [D$_6$]-dimethylsulfoxid, 298 K) δ (^{1}H) / δ (^{13}C) [in ppm] = 7.88 / 128.02 (H-6 / C-6), 7.85 / 129.56 (H-4 / C-4), 7.31 / 129.93 (H-12 / C-12), 7.24 / 122.85 (H-7 / C-7), 7.16 / 125.92 (H-8 / C-8), 6.84 / 124.00 (H-9 / C-9), 3.92 – 3.90 / 71.39 (H-16 / C-16), 3.73 – 3.71 / 69.92/69.90/69.87 (H-17 / C-17/19/20/21), 3.62 – 3.60 / 70.03 (H-18 / C-18), 3.58 – 3.56 / 69.92/69.90/69.87 (H-19 / C-17/19/20/21), 3.54 – 3.53 / 69.92/69.90/69.87 (H-20+21 / C-17/19/20/21), 2.27 / 16.10 (H-14 / C-14).

^{1}H,^{13}C-GHMBC (600 MHz / 151 MHz, [D$_6$]- chloroform, 298 K) δ (^{1}H) / δ (^{13}C) [in ppm] = 8.10 / 131.46 (H-22 / C-3), 7.88 / 133.35, 129.56, 125.92 (H-6 / C-10, C-4, C-8), 7.85 / 151.26, 134.06, 133.35, 128.02 (H-4 / C-2, C-11, C-10, C-6), 7.31 / 154.72, 131.46, 129.93, 129.80, 16.10 (H-12 / C-15, C-3, C-12, C-13, C-14), 7.24 / 128.58, 124.00 (H-7 / C-5, C-9), 7.16 / 133.35, 128.02 (H-8 / C-10, C-6), 6.84

/ 128.58, 122.85, 114.96 (H-9 / C-5, C-7, C-1), 3.54 – 3.53 / 69.92/69.90/69.87 (H-20+21 / C-17/19/20/21), 2.27 / 154.72, 129.93, 129.80 (H-14 / C-15, C-12, C-13).

[MT660-4-2]

Elemental analysis = calcd (%) for $C_{96}H_{104}O_{18}$: C: 74.59, H: 6.78, O: 18.63; found:

C: 73.1, H: 6.06, O: -

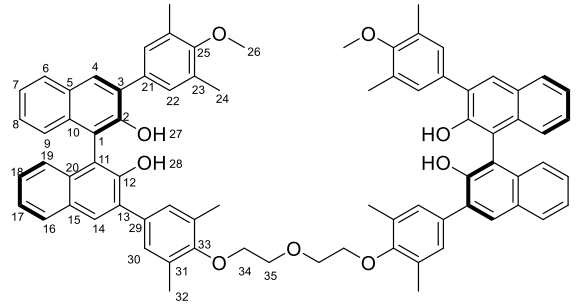
MS (ESI-pos, MeOH**)**: *m/z* = 795.3506 ($[M+2Na]^{2+}$, calcd 795.3504 for $[C_{96}H_{104}O_{18}Na_2^{2+}]$.

IR (ATR-FT): $\tilde{\nu}$ (cm^{-1}) = 3511, 3054, 2917, 2861, 1716, 1620, 1594, 1484, 1435, 1400, 1360, 1303, 1251, 1203, 1177, 1124, 1059, 1029, 877, 747.

[MT660]

8.2.2.5.21. Synthesis of compound (*R*,*R*)-**91**

Described experiment: MT624 Repeated:



Compound (*R*,*R*)-**85e** (0.110 g, 0.0828 mmol, 1 eq), was dissolved in a mixture of dry ethanol:diethyl ether (5:3, 5 ml total). Then acetyl chloride (0.236 ml, 0.260 mg, 3.31 mmol, 40 eq) was added in a dropwise manner over 15 minutes and the mixture was stirred for 18 hours. Then water (15 ml) was added to end the reaction and ethanol and ethyl ether were removed in *vacuo*. Then ethyl acetate (40 ml) was added to the aqueous residue. The organic layer was separated and then washed with a saturated solution of sodium chloride (25 ml). The organic layer was dried over sodium sulfate and was concentrated in *vacuo* to afford the product as a yellow solid (90.1 mg, 0.0781 mmol, 95.2%).

$C_{78}H_{70}O_9$, MW = 1151.4 g/mol.

^{1}H-NMR (600 MHz, [D$_6$]-dimethylsulfoxid, 298 K) δ [in ppm] = 8.16 (s, 4 H, H-27+28), 7.91 (d, ^3J = 7.9 Hz, 4 H, H-6+16), 7.89 (s, 2 H, H-4/14), 7.88 (s, 2 H, H-4/14), 7.36 (s, 4 H, H-22/30), 7.35 (s, 4 H, H-22/30), 7.26 (t, ^3J = 7.5 Hz, 4 H, H-7+17), 7.18 (t, ^3J = 7.2 Hz, 4 H, H-8+18), 6.87 (d, ^3J = 8.1 Hz, 4 H, H-9+19), 4.02 – 4.00 (m, 4 H, H-34), 3.88 – 3.87 (m, 4 H, H-35), 3.71 (s, 6 H, H-26), 2.34 (s, 12 H, H-24/32), 2.30 (s, 12 H, H-24/32).

^{13}C-NMR (151 MHz, [D$_6$]-dimethylsulfoxid, 298 K) δ [in ppm] = 155.80 (C-25), 154.68 (C-33), 151.28 (C-2+12), 134.17 (C-21+29), 133.35 (C-10+20), 131.46 (C-3+13), 129.99 (C-23/31), 129.97 (C-23/31), 129.86 (C-22+30), 129.61 (C-4+14), 128.59 (C-5+15), 128.02 (C-6+16), 125.93 (C-8+18), 123.99 (C-9+19), 122.85 (C-7+17), 114.97 (C-1+11), 71.42 (C-34), 70.02 (C-35), 59.75 (C-26), 16.08 (C-24/32), 15.96 (C-24/32).

^{1}H,^{1}H-COSY (600 MHz / 600 MHz, [D$_6$]-dimethylsulfoxid, 298 K) δ [in ppm] = 7.91 / 7.26 (H-6+16 / H-7+17), 7.36 / 2.34 (H-22/30 / H-24/32), 7.35 / 2.30 (H-22/30 / H-24/32), 7.26 / 7.91, 7.18 (H-7+17 / H-6+16, H-8+18), 7.18 / 7.26, 6.87 (H-8+18 / H-7+17, H-9+19), 6.87 / 7.18 (H-9+19 / H-8+18), 4.02 – 4.00 / 3.88 – 3.87 (H-34 / H-35), 3.88 – 3.87 / 4.02 – 4.00 (H-35 / H-34), 2.34 / 7.36 (H-24/32 / H-22/30), 2.30 / 7.35 (H-24/32 / H-22/30).

^{1}H,^{13}C-GHSQC (600 MHz / 151 MHz, [D$_6$]-dimethylsulfoxid, 298 K) δ (^{1}H) / δ (^{13}C) [in ppm] = 7.91 / 128.02 (H-6+16 / C-6+16), 7.89 / 129.61 (H-4/14 / C-4+14), 7.88 / 129.61 (H-4/14 / C-4+14), 7.36 / 129.86 (H-22/30 / C-22+30), 7.35 / 129.86 (H-22/30 / C-22+30), 7.26 / 122.85 (H-7+17 / C-7+17), 7.18 / 125.93 (H-8+18 / C-8+18), 6.87 / 123.99 (H-9+19 / C-9+19), 4.02 – 4.00 / 71.42 (H-34 / C-34), 3.88 – 3.87 / 70.02 (H-35 / C-35), 3.71 / 59.75 (H-26 / C-26), 2.34 / 16.08 (H-24/32 / C-24/32), 2.30 / 15.96 (H-24/32 / C-24/32).

^{1}H,^{13}C-GHMBC (600 MHz / 151 MHz, [D$_6$]- dimethylsulfoxid, 298 K) δ (^{1}H) / δ (^{13}C) [in ppm] = 8.16 / 131.46, 114.97 (H-27+28 / C-3+13, C-1+11), 7.91 / 133.35, 129.61, 125.93 (H-6+16 / C-10+20, C-4+14, C-8+18), 7.89 / 151.28, 134.17, 133.35, 128.02, 114.97 (H-4/14 / C-2+12, C-21+29, C-10+20,

C-6+16, C-1+11), 7.88 / 151.28, 134.17, 133.35, 128.02, 114.97 (H-4/14 / C-2+12, C-21+29, C-10+20, C-6+16, C-1+11), 7.36 / 155.80, 131.46, 129.99/129.97, 16.08 (H-22/30 / C-25, C-3+13, C-23+31, C24/32), 7.35 / 154.68, 131.46, 129.99/129.97, 15.97 (H-22/30 / C-33, C-3+13, C-23+31, C24/32), 7.26 / 128.59, 123.99 (H-7+17 / C-5+15, C-9+19), 7.18 / 133.95, 128.02 (H-8+18 / C-10+20, C-6+16), 6.87 / 128.59, 122.85, 114.97 (H-9+19 / C-5+15, C-7+17, C-1+11), 4.02 – 4.00 / 70.02 (H-34 / C-35), 3.88 – 3.87 / 71.42 (H-35 / C-34), 3.71 / 155.80 (H-26 / C-25), 2.34 / 154.68, 129.86 (H-24/32 / C-33, C-22+30), 2.30 / 155.80, 129.87 (H-24/32 / C-25, C-22+30).

[MT624-1]

Elemental analysis = calcd (%) for $C_{78}H_{70}O_9$: C: 81.37, H: 6.13, O: 12.51; found:

C: 79.9, H: 6.20, O: 12.6

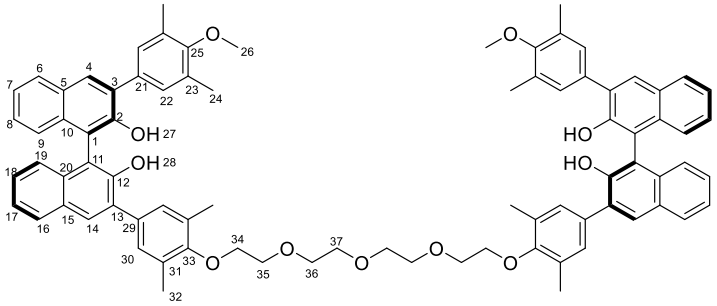
MS (ESI-pos, MeOH**)**: *m/z* = 1349.4951 ($[M+Na]^+$, calcd. 1349.4961 for $[C_{78}H_{70}O_9Na^+]$.

IR (ATR-FT): $\tilde{\nu}$ (cm^{-1}) = 3511, 2924, 2515, 2363, 2363, 2029, 1977, 1719, 1620, 1597, 1485, 1437, 1400, 1362, 1304, 1256, 1206, 1146, 1125, 1084, 1061, 1013, 932, 876, 806, 779, 746, 702, 664, 627.

[MT624]

8.2.2.5.22. Synthesis of compound (*R*,*R*)-**92**

Described experiment: MT686 Repeated:



Compound (*R*,*R*)-**86e** (0.295 g, 0.208 mmol, 1 eq), was dissolved in a mixture of dry ethanol:diethyl ether (5:3, 5 ml total). Then acetyl chloride (0.594 ml, 0.654 mg, 8.33 mmol, 40 eq) was added in a dropwise manner over 15 minutes and the mixture was stirred for 18 hours. Then water (15 ml) was added to end the reaction and ethanol and ethyl ether were removed in *vacuo*. Then ethyl acetate (40 ml) was added to the aqueous residue. The organic layer was separated and then washed with a saturated solution of sodium chloride (25 ml). The organic layer was dried over sodium sulfate and was concentrated in *vacuo* to afford the product as a yellow solid (216 mg, 0.174 mmol, 84.1%).

$C_{82}H_{78}O_{11}$, MW = 1239.5 g/mol.

^{1}H-NMR (400 MHz, [D$_6$]-dimethylsulfoxid, 298 K) δ [in ppm] = 8.15 (s, 4 H, H-27+28), 7.91 (d, ^3J = 7.9 Hz, 2 H, H-6/16), 7.90 (d, ^3J = 7.9 Hz, 2 H, H-6/16), 7.88 (s, 4 H, H-4+14), 7.35 (br s, 8 H, H-22+30), 7.26 (t, ^3J = 7.6 Hz, 4 H, H-7+17), 7.18 (dt, ^3J = 6.6 Hz, ^4J = 1.3 Hz, 2 H, H-8/18), 7.17 (d, ^3J = 6.6 Hz, 2 H, H-8/18), 6.86 (d, ^3J = 8.5 Hz, 4 H, H-9+19), 3.96 – 3.93 (m, 4 H, H-34), 3.78 – 3.75 (m, 4 H, H-35), 3.70 (s, 6 H, H-26), 3.67 – 3.61 (m, 8 H, H-36/37), 2.31 (s, 12 H, H-32), 2.29 (s, 12 H, H-24).

^{13}C-NMR (101 MHz, [D$_6$]-dimethylsulfoxid, 298 K) δ [in ppm] = 155.80 (C-25), 154.73 (C-33), 151.28 (C-2+12), 134.17 (C-21/29), 134.11 (C-21/29), 133.35 (C-10+20), 131.46 (C-3+13), 129.99 (C-22/30), 129.95 (C-22/30), 129.82 (C-23+31), 129.61 (C-4+14), 128.59 (C-5+15), 128.02 (C-6+16), 125.93 (C-8+18), 124.00 (C-9+19), 122.85 (C-7+17), 114.98 (C-1+11), 71.40 (C-34), 70.03 (C-36/37), 69.96 (C-36/37), 69.89 (C-35), 59.30 (C-26), 16.11 (C-24/32), 15.97 (C-24/32).

^{1}H,^{1}H-COSY (400 MHz / 400 MHz, [D$_6$]-dimethylsulfoxid, 298 K) δ [in ppm] = 7.91 / 7.26 (H-6/16 / H-7+17), 7.90 / 7.26 (H-6/16 / H-7+17), 7.35 / 2.31 (H-22+30 / H-32), 7.35 / 2.29 (H-22+30 / H-24), 7.26 / 7.91, 7.90 (H-7+17 / H-6/16, H-6/16), 7.18 / 6.86 (H-8/18 / H-9+19), 7.17 / 6.86 (H-8/18 / H-9+19), 6.86 / 7.18, 7.17 (H-9+19 / H-8/18, H8/18), 3.96 – 3.93 / 3.78 – 3.75 (H-34 / H-35), 3.78 – 3.75 / 3.96 – 3.93 (H-35 / H-34), 2.31 / 7.35 (H-24/32 / H-22+30), 2.29 / 7.35 (H-24/32 / H-22+30).

^{1}H,^{13}C-GHSQC (400 MHz / 101 MHz, [D$_6$]-dimethylsulfoxid, 298 K) δ (^{1}H) / δ (^{13}C) [in ppm] = 7.91 / 128.02 (H-6/16 / C-6+16), 7.90 / 128.02 (H-6/16 / C-6+16), 7.88 / 129.61 (H-4+14 / C-4+14), 7.35 / 129.99+129.95 (H-22+30 / C-22 + C-30), 7.26 / 122.85 (H-7+17 / C-7+17), 7.18 / 125.93 (H-8/18 / C-8+18), 7.17 / 125.93 (H-8/18 / C-8+18), 6.86 / 124.00 (H-9+19 / C-9+19), 3.96 – 3.93 / 71.40 (H-34 / C-34), 3.78 – 3.75 / 69.89 (H-35 / C-35), 3.70 / 59.30 (H-26 / C-26), 3.67 – 3.61 / 70.03, 69.96 (H-36+37 / C-36/37, C-36/37), 2.31 / 16.11/15.97 (H-32 / C-24/32), 2.29 / 16.11/15.97 (H-24 / C-24/32).

^{1}H,^{13}C-GHMBC (400 MHz / 101 MHz, [D$_6$]-dimethylsulfoxid, 298 K) δ (^{1}H) / δ (^{13}C) [in ppm] = 8.15 / 131.46 (H-27+28 / C-3+13), 7.91 / 133.35, 125.93 (H-6/16 / C-10+20, C-8+18), 7.90 / 133.35,

125.93 (H-6/16 / C-10+20, C-8+18), 7.88 / 151.28, 134.17/134.11, 133.35, 128.02 (H-4+14 / C-2+12, C-21/29, C-10+20, C-6+16), 7.35 / 155.80, 154.73, 131.46, 129.99/129.95, 129.82 (H-22+30 / C-25, C-33, C-3+13, C-22/30, C-23+31), 7.26 / 128.59, 124.00 (H-7+17 / C-5+15, C-9+19), 7.18 / 133.35, 128.03 (H-8/18 / C-10+20, C-6+16), 7.17 / 133.35, 128.02 (H-8/18 / C-10+20, C-6+16), 6.86 / 128.59, 122.85, 114.98 (H-9+19 / C-5+15, C-7+17, C-1+11), 3.96 – 3.93 / 69.89 (H-34 / C-35), 3.78 – 3.75 / 71.40 (H-35 / C-34), 3.70 / 155.80 (H-26 / C-25), 3.67 – 3.61 / 70.03, 69.96 (H-36+37 / C-36/37, C-36/37), 2.31 / 154.73, 129.99/129.95, 129.82 (H-32 / C-33, C-22/30, C-23+31), 2.29 / 155.80, 129.99/129.95, 129.82 (H-24 / C-25, C-22/30, C-23+31).

[MT686-4]

Elemental analysis = calcd (%) for $C_{82}H_{78}O_{11}$: C: 79.46, H: 6.34, O: 14.20; found:

C: 77.2, H: 6.39, O: -

MS (ESI-pos, MeOH**)**: *m/z* = 1261.5442 ($[M+Na]^+$, calcd. 1261.5436 for $[C_{82}H_{77}O_{11}Na^+]$.

MS (ESI-pos, MeOH): m/z = 634.12621 ($[M+H]^+$, calcd. 634.12879 for $[C_{33}H_{29}F_5FeNOSi]^+$);

IR (ATR-FT): $\tilde{\nu}$ (cm^{-1}) = 3505, 3051, 3031, 2979, 2970, 2919, 2869, 1730, 1718, 1704, 1646, 1620, 1594, 1485, 1435, 1400, 1379.

[MT686]

8.2.2.5.23. Synthesis of compound (*R,R*)-**93**

Described experiment: MT682 Repeated:

Compound (*R,R*)-**87e** (0.384 g, 0.255 mmol, 1 eq), was dissolved in a mixture of dry ethanol:diethyl ether (5:3, 10 ml total). Then acetyl chloride (0.729 ml, 0.802 mg, 10.2 mmol, 40 eq) was added in a dropwise manner over 15 minutes and the mixture was stirred for 18 hours. Then water (30 ml) was added to end the reaction and ethanol and ethyl ether were removed in *vacuo*. Then ethyl acetate (40 ml) was added to the aqueous residue. The organic layer was separated and then washed with a saturated solution of sodium chloride (25 ml). The organic layer was dried over sodium sulfate and was concentrated in *vacuo*to afford the product as a yellow solid (306 mg, 0.231 mmol, 91.5%).

$C_{86}H_{86}O_{13}$, MW = 1327.6 g/mol.

^{1}H-NMR (400 MHz, [D$_6$]-dimethylsulfoxid, 298 K) δ [in ppm] = 8.15 (s, 4 H, H-27+28), 7.91 (d, ^{3}J = 7.9 Hz, 2 H, H-6/16), 7.90 (d, ^{3}J = 7.9 Hz, 2 H, H-6/16), 7.89 (s, 4 H, H-4+14), 7.35 (s, 4 H, H-22), 7.34 (s, 4 H, H-30), 7.26 (t, ^{3}J = 7.6 Hz, 4 H, H-7+17), 7.20 – 7.16 (m, 4 H, H-8+18), 6.86 (d, ^{3}J = 8.5 Hz, 4 H, H-9+19), 3.94 – 3.92 (m, 4 H, H-34), 3.75 – 3.73 (m, 4 H, H-35), 3.71 (s, 6 H, H-26), 3.64 – 3.62 (m, 4 H, H-36), 3.59 – 3.53 (s, 12 H, H-37+38+39), 2.30 (s, 24 H, H-24+32).

^{13}C-NMR (101 MHz, [D$_6$]-dimethylsulfoxid, 298 K) δ [in ppm] = 155.80 (C-25), 154.72 (C-33), 151.29 (C-2+12), 134.17 (C-21/29), 134.11 (C-21/29), 133.35 (C-10+20), 131.46 (C-3+13), 129.99 (C-22/30), 129.94 (C-22/30), 129.81 (C-23+31), 129.61 (C-4+14), 128.58 (C-5+15), 128.02 (C-6+16), 125.92 (C-8+18), 124.00 (C-9+19), 122.84 (C-7+17), 114.98 (C-1+11), 71.37 (C-34), 69.98 (C-36), 69.88 (C-35/37/38/39), 69.86 (C-35/37/38/39), 59.30 (C-26), 16.10 (C-24/32), 15.97 (C-24/32).

^{1}H,^{1}H-COSY (400 MHz / 400 MHz, [D$_6$]-dimethylsulfoxid, 298 K) δ [in ppm] = 7.91 / 7.26 (H-6/16 / H-7+17), 7.90 / 7.26 (H-6/16 / H-7+17), 7.35 / 2.30 (H-22 / H-24+32), 7.34 / 2.30 (H-30 / H-24+32), 7.26 / 7.91, 7.90 (H-7+17 / H-6/16, H-6/16), 7.20 – 7.16 / 6.86 (H-8+18 / H-9+19), 6.86 / 7.20 – 7.16 (H-9+19 / H-8+18), 3.94 – 3.92 / 3.75 – 3.73 (H-34 / H-35), 3.75 – 3.73 / 3.94 – 3.92 (H-35 / H-34), 2.30 / 7.35, 7.34 (H-24+32 / H-22, H-30).

^{1}H,^{13}C-GHSQC (400 MHz / 101 MHz, [D$_6$]-dimethylsulfoxid, 298 K) δ (^{1}H) / δ (^{13}C) [in ppm] = 7.91 / 128.02 (H-6/16 / C-6+16), 7.90 / 128.02 (H-6/16 / C-6+16), 7.89 / 129.61 (H-4+14 / C-4+14), 7.35 / 129.99/129.94 (H-22 / C-22/30), 7.34 / 129.99/129.94 (H-30 / C-22/30), 7.26 / 122.84 (H-7+17 / C-7+17), 7.20 – 7.16 / 125.92 (H-8+18 / C-8+18), 6.86 / 124.00 (H-9+19 / C-9+19), 3.94 – 3.92 / 71.37 (H-34 / C-34), 3.75 – 3.73 / 69.88/69.86 (H-35 / C-35/37/38/39), 3.71 / 59.30 (H-26 / C-26), 3.64 – 3.62 / 69.98 (H-36 / C-36), 3.59 – 3.53 / 69.88/69.86 (H-37/38/39 / C-35/37/38/39), 2.30 / 16.10, 15.97 (H-24+32 / C-24+32).

^{1}H,^{13}C-GHMBC (400 MHz / 101 MHz, [D$_6$]-dimethylsulfoxid, 298 K) δ (^{1}H) / δ (^{13}C) [in ppm] = 8.15 / 131.46 (H-27+28 / C-3+13), 7.91 / 133.35, 125.92 (H-6/16 / C-10+20, C-8+18), 7.90 / 133.35,

125.92 (H-6/16 / C-10+20, C-8+18), 7.89 / 151.29, 134.17/134.11, 133.35, (H-4+14 / C-2+12, C-21/29, C-10+20), 7.35 / 155.80, 131.46, 129.99/129.95 (H-22 / C-25, C-3+13, C-22/30), 7.34 / 154.72, 131.46, 129.99/129.95 (H-30 / C-33, C-3+13, C-22/30), 7.26 / 128.58, 124.00 (H-7+17 / C-5+15, C-9+19), 7.20 – 7.16 / 133.35, 128.02 (H-8+18 / C-10+20, C-6+16), 6.86 / 128.58, 122.84, 114.98 (H-9+19 / C-5+15, C-7+17, C-1+11), 3.94 – 3.92 / 69.88/69.86 (H-34 / C-35/37/38/39), 3.75 – 3.73 / 71.37 (H-35 / C-34), 3.71 / 155.80 (H-26 / C-25), 3.59 – 3.53 / 69.88/69.86 (H-37+38+39 / C-35/37/38/39), 2.30 / 155.80, 154.72, 129.81 (H-24+32 / C-25, C-33, C-23+31).

[MT682-4]

Elemental analysis = calcd (%) for $C_{86}H_{86}O_{13}$: C: 77.80, H: 6.53, O: 15.67; found:

C: 76.9, H: 6.78, O: -

MS (ESI-pos, MeOH**)**: *m/z* = 1349.5962 ($[M+Na]^+$, calcd. 1349.5961 for $[C_{86}H_{85}O_{13}Na^+]$.

IR (ATR-FT): $\tilde{\nu}$ (cm^{-1}) = 3510, 3053, 3032, 2979,2970, 2919, 2869, 2735, 1701, 1619, 1594, 1485, 1436, 1400, 1379,3 1360.

[MT682]

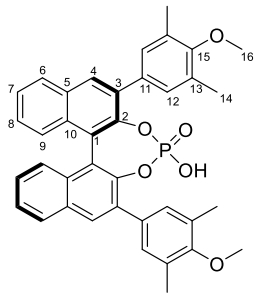
8.2.2.6. Synthesis of phosphoric acid derivatives

D: General procedure for the phosphorylation[118]:

The corresponding BINOL-derivative (1eq) was dissolved in dry pyridine (300 eq. per BINOL-derivative). To that mixture freshly distilled phosphorus oxychloride (30 eq. per BINOL-derivative) was added in a dropwise manner with rapid stirring. The solution was stirred at 65 °C for 12 hours under argon atmosphere. After cooling down to room temperature, water (90 mL/mmol BINOL-derivative) was carefully added and the suspension was stirred at 60 °C for another 2 hours. The reaction mixture was diluted with dichloromethane (225 mL/mmol BINOL-derivative) and then washed with HCl (6 M, 5 x 67 mL/mmol BINOL-derivative) to remove pyridine. The organic layer was dried over sodium sulfate and concentrated in *vacuo* to afford the product as a yellow solid.

8.2.2.6.1. Synthesis of compound (*R*)-**13**

Described experiment: SF003 Repeated: MT588



According to general procedure **D**, compound (*R*)-**105** (0.320 g, 0.577 mmol, 1 eq) gave the product as a yellow solid (0.285 g, 0.462 mmol, 80.1%).

$C_{38}H_{33}O_6P$, MW = 616.7 g/mol.

^{1}H-NMR (400 MHz, [D$_6$]-dimethylsulfoxid, 298 K) δ [in ppm] = 8.12 (s, 2 H, H-4), 8.09 (d, ^3J = 8.8 Hz, 2 H, H-6), 7.54 (s, 4 H, H-12), 7.50 (t, ^3J = 7.4 Hz, 2 H, H-7), 7.32 (t, ^3J = 7.4 Hz, 2 H, H-8), 7.09 (d, ^3J = 8.5 Hz, 2 H, H-9), 3.73 (s, 6 H, H-16), 2.30 (s, 12 H, H-14).

^{13}C-NMR (101 MHz, [D$_6$]-dimethylsulfoxid, 298 K) δ [in ppm] = 156.19 (C-15), 146.00 (d, $^2J_{PC}$ =9.7 Hz, C-2), 133.58 (C-3), 132.60 (C-11), 132.31 (C-10), 130.60 (C-4+5), 130.37 (C-12), 129.75 (C-13), 128.52 (C-6), 126.49 (C-8), 125.98 (C-9), 125.46 (C-7), 122.22 (C-1), 59.29 (C-16), 16.01 (C-14).

^{1}H,^{1}H-COSY (400 MHz / 400 MHz, [D$_6$]-dimethylsulfoxid, 298 K) δ [in ppm] = 8.09 / 7.50 (H-6 / H-7), 7.54 / 2.30 (H-12 / H-14), 7.50 / 8.09, 7.32 (H-7 / H-6, H-8), 7.32 / 7.50, 7.09 (H-8 / H-7, H-9), 7.09 / 7.32 (H-9 / H-8), 2.30/ 7.54 (H-14 / H-12).

^{1}H,^{13}C-GHSQC (400 MHz / 101 MHz, [D$_6$]-dimethylsulfoxid, 298 K) δ (^{1}H) / δ (^{13}C) [in ppm] = 8.12 / 130.60 (H-4 / C-4+5), 8.09 / 128.52 (H-6 / C-6), 7.54 / 130.37 (H-12 / C-12), 7.50 / 125.46 (H-7 / C-7), 7.32 / 126.49 (H-8 / C-8), 7.09 / 125.98 (H-9 / C-9), 3.73 / 59.29 (H-16 / C-16), 2.30 / 16.01 (H-14 / C-14).

[118] F. Octa-Smolin, R. Mitra, M. Thiele, C. G. Daniliuc, L. Stegemann, C. Strassert, J. Niemeyer, *Chem. Eur. J.*, **2017**, *23*, 10058 – 10067.

^{1}H,^{13}C-GHMBC (600 MHz / 151 MHz, [D$_6$]-dimethylsulfoxid, 298 K) δ (^{1}H) / δ (^{13}C) [in ppm] = 8.12 / 146.00, 132.60, 131.31, 128.52 (H-4 / C-2, C-11, C-10, C-6), 8.09 / 131.31, 130.60 (H-6 / C-10, C-4+5), 7.54 / 156.19, 133.58, 130.32, 130.60, 16.01 (H-12 / C-15, C-3, C-12, C-4+5, C-14), 7.50 / 130.60, 125.98 (H-7 / C-4+5, C-9), 7.32 / 131.31, 128.52 (H-8 / C-10, C-6), 7.09 / 130.60, 125.46, 122.22 (H-9 / C-4+5, C-7, C-1), 3.73 / 156.19 (H-16 / C-15), 2.30 / 156.19, 130.37, 129.75 (H-14 / C-15, C-12, C13). [MT588-5]

^{31}P-NMR (162 MHz, [D$_6$]- dimethylsulfoxid, 298 K) δ [in ppm] = 1.26

Elemental analysis = calcd (%) for $C_{38}H_{33}O_6P$: C: 74.02, H: 5.39, O: 15.57; found:

C: 74.3, H: 5.94, O: 15.5

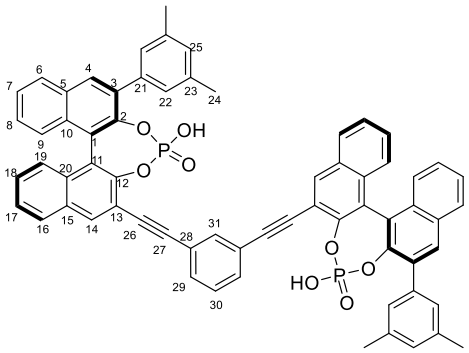
MS (ESI-pos, MeOH**)**: *m/z* = 617.2088 ([M-H]$^+$, calcd. 617.2088 for [$C_{38}H_{34}O_6P^+$]

IR (ATR-FT): $\tilde{\nu}$ (cm^{-1}) = 2924, 2160, 3031, 1977, 1719, 1487, 1397, 1373, 1337, 1260, 1215, 1150, 1126, 1086, 1017, 968, 930, 883, 872, 841, 88, 775, 750, 694, 665, 627.

[MT588]

8.2.2.6.2. Synthesis of compound (*R*,*R*)-**4a**

Described experiment: MT356 Repeated: MT565



According to general procedure **D**, compound (*R*,*R*)**81a** (0.150 g, 0.222 mmol, 1 eq), gave the product as a yellow solid (0.0738 g, 0.0719 mmol, 32.4%).

$C_{66}H_{44}O_8P_2$, MW = 1026.3 g/mol.

^{1}H-NMR (600 MHz, [D$_6$]-dimethylsulfoxid, 298 K) δ [in ppm] = 8.50 (s, 2 H, H-14), 8.17 (s, 2 H, H-4), 8.14 (d, ^3J = 8.7 Hz, 2 H, H-6), 8.12 (d, ^3J = 9.2 Hz, 2 H, H-16), 7.93 (s, 1 H, H-31), 7.67 (d, ^3J = 7.8 Hz, 2 H, H-29), 7.59 – 7.57 (m, 1 H, H-30), 7.57 – 7.55 (m, 2 H, H-17), 7.55 – 7.53 (m, 2 H, H-7), 7.44 (s, 4 H, H-22), 7.41-7.39 (m, 2 H, H-18), 7.38 – 7.35 (m, 2 H, H-8), 7.18 (d, ^3J = 8.4 Hz, 2 H, H-9), 7.14 (d, ^3J = 8.8 Hz, 2 H, H-19), 6.99 (s, 2 H, H-25), 2.25 (s, 12 H, H-24).

^{13}C-NMR (151 MHz, [D$_6$]-dimethylsulfoxid, 298 K) δ [in ppm] = 146.87 (d, $^2J_{pc}$ = 9.7 Hz, C-12), 145.61 ((d, $^2J_{pc}$ = 9.5 Hz, C-2), 136.91 (C-21), 136.85 (C-23), 135.14 (C-31), 134.09 (C-3), 133.76 (C-14), 131.70 (C-20), 131.32 (C-29), 131.08 (C-4+10), 130.65 (C-5), 130.40 (C-15), 129.48 (C-30), 128.91 (C-25), 128.68 (C-16), 128.60 (C-6), 127.79 (C-18), 127.70 (C-22), 126.71 (C-8), 126.14 (C-19), 126.06 (C-17), 125.92 (C-9), 125.68 (C-7), 123.11 (C-28), 122.25 (C-11), 121.24 (C-1), 115.52 (C-13), 92.94 (C-27), 86.43 (C-26), 20.93 (C-24).

^{1}H,^{1}H-COSY (600 MHz / 600 MHz, [D$_6$]-dimethylsulfoxid, 298 K) δ [in ppm] = 8.14 / 7.55 – 7.53 (H-6 / H-7), 8.12 / 7.57 – 7.55 (H-16 / H-17), 7.67 / 7.59 – 7.57 (H-29 / H-30), 7.59 – 7.57 / 7.67 (H-30 / H-29), 7.57 – 7.55 / 8.12 (H-17 / H-16), 7.55 – 7.53 / 8.14 (H-7 / H-6), 7.44 / 6.99 (H-22 / H-25), 7.41-7.39 / 7.14 (H-18 / H-19), 7.38 – 7.35 / 7.18 (H-8 / H-9), 7.18 / 7.38 – 7.35 (H-9 / H-8), 7.14 / 7.41-7.39 (H-19 / H-18), 6.99 / 7.44 (H-25 / H-22).

^{1}H,^{13}C-GHSQC (600 MHz / 151 MHz, [D$_6$]-dimethylsulfoxid, 298 K) δ (^{1}H) / δ (^{13}C) [in ppm] = 8.50 / 133.76 (H-14 / C-14), 8.17 / 131.08 (H-4 / C-4), 8.14 / 128.60 (H-6 / C-6), 8.12 / 128.68 (H-16 / C-16), 7.93 / 135.14 (H-31 / C-31), 7.67 / 131.32 (H-29 / C-29), 7.59 – 7.57 / 129.48 (H-30 / C-30), 7.57 – 7.55 / 126.06 (H-17 / C-17), 7.55 – 7.53 / 125.69 (H-7 / C-7), 7.44 / 127.70 (H-22 / C-22), 7.41-7.39 / 127.79 (H-18 / C-18), 7.38 – 7.35 / 126.71 (H-8 / C-8), 7.18 / 125.92 (H-9 / C-9), 7.14 / 126.14 (H-19 / C-19), 6.99 / 128.91 (H-25 / C-25), 2.25 / 20.93 (H-24 / C-24).

^{1}H,^{13}C-GHMBC (600 MHz / 151 MHz, [D$_6$]-dimethylsulfoxid, 298 K) δ (^{1}H) / δ (^{13}C) [in ppm] = 8.50 / 146.87, 131.70, 128.68, 86.43 (H-14 / C-12, C-20, C-16, C-26), 8.17 / 145.61, 136.91, 131.08, 128.60 (H-4 / C-2, C-21, C-4+10, C-6), 8.14 / 131.08, 126.71 (H-6 / C-4+10, C-8), 8.12 / 131.70, 127.79 (H-16 / C-20, C-18), 7.93 / 131.32, 92.94 (H-31 / C-29, C-27), 7.67 / 135.14, 131.32, 92.94 (H-29 / C-31, C-29, C-27), 7.59 – 7.57 / 123.11 (H-30 / C-28), 7.57 – 7.55 / 130.40, 126.14 (H-17 / C-15, C-19), 7.55 – 7.53 / 130.65, 125.92 (H-7 / C-5, C-9), 7.44 / 134.09, 128.91, 127.70 (H-22 / C, C-25, C-22),

7.14 / 130.40, 126.06, 122.25 (H-19 / C-15, C-17, C-11), 6.99 / 127.70 (H-25 / C-22), 2.25 / 136.91, 136.85, 128.91, 127.70 (H-24 / C-21, C-23, C-25, C-22).

[MT356-1]

^{31}P-NMR (243 MHz, [D_6]- dimethylsulfoxid, 298 K) δ [in ppm] = 1.18

Elemental analysis = calcd (%) for $C_{66}H_{44}O_8P_2$: C: 77.19, H: 4.32, O: 12.46; found:

C: 75.2, H: 4.50, O: 14.2

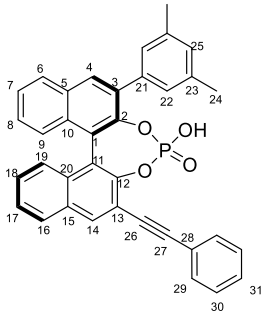
MS (ESI-neg, MeOH**)**: *m/z* = 1025.24386 ([M-H]$^-$, calcd. 1025.24405for [$C_{66}H_{43}O_8P_2^-$].

IR (ATR-FT): $\tilde{\nu}$ (cm^{-1}) = 3426, 3270,2360, 2252, 2127, 1658, 1051, 1024, 1002, 821, 759, 619.

[MT356-1]

8.2.2.6.3. Synthesis of compound (*R*)-**12a**

Described experiment: MT380 Repeated:



According to general procedure **D**, compound (*R*)-**103a** (0.0631 g, 0.128 mmol, 1 eq) gave the product as a yellow solid (0.0634 g, 0.115 mmol, 89.6%).

$C_{36}H_{25}O_4P$, MW = 552.6 g/mol.

^{1}H-NMR (400 MHz, [D$_6$]-dimethylsulfoxid, 298 K) δ [in ppm] = 8.48 (s, 1 H, H-14), 8.13 (s, 1 H, H-4), 8.12 (d, ^3J = 8.1 Hz, 1 H, H-6), 8.11 (d, ^3J = 8.2 Hz, 1 H, H-16), 7.62 – 7.59 (m, 2H, H-29), 7.55 (t, ^3J = 8.7 Hz, 1 H, H-17), 7.53 (t, ^3J = 8.4 Hz, 1 H, H-7), 7.49 – 7.45 (m, 5 H, H-22/30/31), 7.39 (t, ^3J = 8.1 Hz, 1 H, H-18), 7.36 (t, ^3J = 8.1 Hz, 1 H, H-8), 7.16 (d, ^3J = 8.5, 1 H, H-9), 7.14 (d, ^3J = 8.5, 1 H, H-19), 7.06 (s, 1 H, H-25), 2.35 (s, 6 H, H-24).

^{13}C-NMR (101 MHz, [D$_6$]-dimethylsulfoxid, 298 K) δ [in ppm] = 146.72 (d, $^2J_{pc}$ = 9.7 Hz, C-12), 145.42 (d, $^2J_{pc}$ = 9.7 Hz, C-2), 136.96 (C-23), 136.94 (C-21), 134.04 (C-3), 133.97 (C-14), 131.60 (C-20), 131.47 (C-29), 131.16 (C-4), 131.09 (C-10), 130.69 (C-5), 130.41 (C-15), 129.05 (C-31), 128.96 (C-25), 128.83 (C-30), 128.63 (C-6/16), 128.57 (C-6/16), 127.73 (C-18), 127.70 (C-22), 126.77 (C-8), 126.15 (C-17), 126.08 (C-19), 125.88 (C-9), 125.74 (C-7), 122.39 (C-28), 122.20 (C-11), 121.39 (C-1), 115.80 (C-13), 93.66 (C-27), 85.37 (C-26), 21.03 (C-24).

^{1}H,^{1}H-COSY (400 MHz / 400 MHz, [D$_6$]-dimethylsulfoxid, 298 K) δ [in ppm] = 8.12 / 7.53 (H-6 / H-7), 8.11 / 7.55 (H-16 / H-17), 7.62 – 7.59 / 7.49 – 7.45 (H-29 / H-22/30/31), 7.55 / 8.11, 7.39 (H-17 / H-16, H-18), 7.53 / 8.12, 7.36 (H-7 / H-6, H-8), 7.49 – 7.45 / 7.62 – 7.59 (H-22/30/31 / H-29), 7.39 / 7.55, 7.14 (H-18 / H-17, H-19), 7.36 / 7.53, 7.16 (H-8 / H-7, H-9).

^{1}H,^{13}C-GHSQC (400 MHz / 101 MHz, [D$_6$]-dimethylsulfoxid, 298 K) δ (^{1}H) / δ (^{13}C) [in ppm] = 8.48 / 133.97 (H-14 / C-14), 8.13 / 131.16 (H-4 / C-4), 8.12/8.11 / 128.63/128.57 (H-6/16 / C-6/16), 7.62 – 7.59 / 131.47 (H-29 / C-29), 7.55 / 126.15 (H-17 / C-17), 7.53 / 125.74 (H-7 / C-7), 7.49 – 7.45 / 128.83, 127.70 (H-22/30/31 / C-30, C-22), 7.39 / 127.73 (H-18 / C-18), 7.36 / 126.77 (H-8 / C-8), 7.16 / 125.88 (H-9 / C-9), 7.14 / 126.08 (H-19 / C-19), 7.06 / 128.96 (H-25 / C-25), 2.35 / 21.03 (H-24 / C-24).

^{1}H,^{13}C-GHMBC (400 MHz / 101 MHz, [D$_6$]-dimethylsulfoxid, 298 K) δ (^{1}H) / δ (^{13}C) [in ppm] = 8.48 / 146.72, 131.60, 128.63/128.57, 85.37 (H-14 / C-12, C-20, C-6/16, C-26), 8.13 / 145.42, 136.94, 131.09, 128.63/128.57 (H-4 / C-2, C-21, C-10, C-6/16), 8.12 / 131.16, 131.09, 126.77 (H-6 / C-4, C-10, C-8), 8.11 / 131.60, 127.73 (H-16 / C-20, C-18), 7.62 – 7.59 / 129.05, 93.66 (H-29 / C-31, C-27), 7.55 / 130.41, 126.08 (H-17 / C-15, C-19), 7.53 / 130.69, 125.88 (H-7 / C-5, C-9), 7.49 – 7.45 / 131.47, 128.96, 127.70, 122.39, 21.04 (H-22/30/31 / C-29, C-25, C-22, C-28, C-24), 7.39 / 131.60, 128.63/128.57 (H-18 / C-20, C-6/16), 7.36 / 131.09, 128.63/128.57 (H-8 / C-10, C-6/16), 7.16 / 130.69,

125.74, 121.39 (H-9 / C-5, C-7, C-1), 7.14 / 130.41, 126.15, 122.20 (H-19 / C-15, C-17, C-11), 7.06 / 127.70, 21.03 (H-25 / C-22, C-24), 2.35 / 136.94, 127.70, (H-24 / C-21, C-22).

[MT380-1.3]

^{31}P-NMR (162 MHz, [D_6]-dimethylsulfoxid, 298 K) δ [in ppm] = 1.63

Elemental analysis = calcd (%) for $C_{36}H_{25}O_4P$: C: 78.25, H: 4.56, O: 11.58; found:

C: 75.4, H: 4.64, O: 12.5

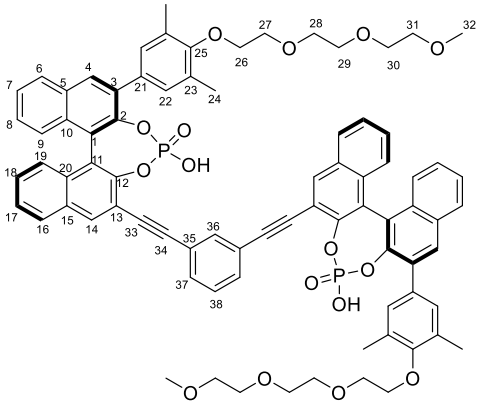
MS (ESI-neg, MeOH**)**: *m/z* = 551.14132 ([M-H]$^-$, calcd. 551.14177 for [$C_{36}H_{24}O_4P^-$].

IR (ATR-FT): $\tilde{\nu}$ (cm^{-1}) = 3051, 3017, 2961, 2915, 2856, 1599, 1491, 1441, 1423, 1408, 1363, 1336, 1258, 1224, 1201, 1180, 1149, 1094, 1064, 1014, 967, 918, 885, 847, 828, 748, 659, 610.

[MT380-1.3]

8.2.2.6.4. Synthesis of compound (*R*,*R*)-**4b**

Described experiment: MT554 Repeated:MT549



According to general procedure **D**, compound (*R*,*R*)-**81b** (0.237 g, 0.193 mmol, 1 eq), gave the product as a yellow solid (0.187 g, 0.138 mmol, 71.7%).

$C_{80}H_{72}O_{16}P_2$, MW = 1351.4 g/mol.

^{1}H-NMR (400 MHz, [D$_6$]-dimethylsulfoxid, 298 K) δ [in ppm] = 8.51 (s, 2 H, H-14), 8.17 (s, 2 H, H-4), 8.12 (d, ^3J = 8.6 Hz, 4 H, H-6+16), 7.91 (br s, 1 H, H-36), 7.68 (d, ^3J = 7.7 Hz, 2 H, H-37), 7.60 – 7.58 (m, 1 H, H-38), 7.58 – 7.53 (m, 4 H, H-7+17), 7.51 (s, 4 H, H-22), 7.40 (t, ^3J = 7.6 Hz, 2 H, H-18), 7.36 (t, ^3J = 7.6 Hz, 2 H, H-8), 7.17 (d, ^3J = 9.0 Hz, 2 H, H-19), 7.14 (d, ^3J = 9.00 Hz, 2 H, H-9), 3.92 – 3.90 (m, 4 H, H-26), 3.74 – 3.72 (m, 4 H, H-27), 3.64 – 3.61 (m, 4 H, H-28), 3.58 – 3.53 (m, 8 H, H-29+30), 3.45 – 3.42 (m, 4 H, H-31), 3.23 (s, 6 H, H-32), 2.24 (s, 12 H, H-24).

^{13}C-NMR (101 MHz, [D$_6$]-dimethylsulfoxid, 298 K) δ [in ppm] = 155.18 (C-25), 146.71 (d, $^2J_{pc}$ = 9.7 Hz, C-12), 145.49 (d, $^2J_{pc}$ = 9.7 Hz, C-2), 134.78 (C-36), 133.96 (C-14), 133.57 (d, $^2J_{pc}$ = 9.7 Hz, C-3), 132.28 (C-21), 131.71 (C-20), 131.54 (C-37), 131.17 (C-4), 131.00 (C-10), 130.71 (C-15), 130.46 (C-5), 130.29 (C-22), 130.00 (C-23), 129.54 (C-38), 128.71 (C-6/16), 128.59 (C-6/16), 127.86 (C-18), 126.71 (C-8), 126.16 (C-9+19), 125.93 (C-7), 123.75 (C-17), 123.10 (C-35), 122.29 (C-1), 121.26 (C-11), 115.49 (C-13), 92.90 (C-34), 86.34 (C-33), 71.31 (C-31), 69.99 (C-27/28/29/30), 69.86 (C-27/28/29/30), 69.69 (C-29/30), 58.06 (C-32), 16.06 (C-24).

^{1}H,^{1}H-COSY (400 MHz / 400 MHz, [D$_6$]-dimethylsulfoxid, 298 K) δ [in ppm] = 8.12 / 7.58 – 7.53 (H-6+16 / H-7+17), 7.68 / 7.60 – 7.58 (H-37 / H-38), 7.60 – 7.58 / 7.68 (H-38 / H-37), 7.58 – 7.53/ 8.12, 7.40, 7.36 (H-7+17 / H-6+16, H-18, H-8), 7.51 / 2.24 (H-22 / H-24), 7.40 / 7.58 – 7.53 (H-18 / H-7+17), 7.36 / 7.56 (H-8 / H-7+17), 3.92 – 3.90 / 3.74 – 3.72 (H-26 / H-27), 3.74 – 3.72 / 3.92 – 3.90 (H-27 / H-26), 3.58 – 3.53 / 3.45 – 3.42 (H-29+30 / H-31), 3.45 – 3.42 / 3.58 – 3.53 (H-31 / H-29+30), 2.24 / 7.51 (H-24 / H-22).

^{1}H,^{13}C-GHSQC (400 MHz / 101 MHz, [D$_6$]-dimethylsulfoxid, 298 K) δ (^{1}H) / δ (^{13}C) [in ppm] = 8.51 / 133.96 (H-14 / C-14), 8.17 / 131.17 (H-4 / C-4), 8.12 / 128.71, 128.59 (H-6+16 / C-6/16, C-6/16), 7.91 / 134.78 (H-36 / C-36), 7.60 – 7.58 / 129.54 (H-38 / C-38), 7.58 – 7.53/ 125.93, 123.75 (H-7+17 / C-7/17, C7/17), 7.51 / 130.29 (H-22 / C-22), 7.40 / 127.86 (H-18 / C-18), 7.36 / 126.71 (H-8 / C-8), 7.17 / 126.16 (H-19 / C-9+19), 7.14 / 126.16 (H-9 / C-9+19), 3.92 – 3.90 / 71.31 (H-26 / C-26+31), 3.74 – 3.72 / 69.86 (H-27 / C-27/28/29/30), 3.64 – 3.61 / 69.86 (H-28 / C-27/28/29/30), 3.58 – 3.53 / 69.86/69.69 (H-29+30 / C-27/28/29/30), 3.45 – 3.42 / 71.31 (H-31 / C-26+31), 3.23 / 58.06 (H-32 / C-32), 2.24 / 16.06 (H-24 / C-24).

^{1}H,^{13}C-GHMBC (400 MHz / 101 MHz, [D$_6$]-dimethylsulfoxid, 298 K) δ (^{1}H) / δ (^{13}C) [in ppm] = 8.51 / 146.71, 131.71, 128.71/128.59, 86.34 (H-14 / C-12, C-20, C-6/16, C-33), 8.17 / 145.49, 132.28, 131.00, 128.71/128.59 (H-4 / C-2, C-21, C-10, C-6/16), 8.12 / 133.96, 131.71, 131.17, 127.86, 126.71 (H-6+16 / C-14, C-20, C-4, C-18, C-8), 7.91 / 131.54, 92.90 (H-36 / C-37, C-34), 7.68 / 134.78, 131.54, 92.90 (H-37 / C-36, C-37, C-34), 7.60 – 7.58 / 123.10 (H-38 / C-35), 7.58 – 7.53/ 126.16 (H-7+17 / C-9+19), 7.51 / 155.18, 133.57, 130.29, 16.06 (H-22 / C-25, C-3, C-22, C-24), 7.40 / 131.71, 128.71/128.59 (H-18 / C-20, C-6/16), 7.36 / 131.00, 128.71/128.59 (H-8 / C-10, C-6/16), 7.17 / 130.71, 123.75, 121.26 (H-19 / C-15, C-17, C-11), 7.14 / 130.46, 125.93, 122.29 (H-9 / C-5, C-7, C-1), 3.92 – 3.90 / 69.86 (H-26 / C-27/28/29/30), 3.74 – 3.72 / 71.31 (H-27 / C-26+31), 3.64 – 3.61 / 69.68 (H-28 / C-29+30), 3.58 – 3.53 / 69.86 (H-29+30 / C-27/28/29/30), 3.45 – 3.42 / 69.86 (H-28 / C-27/28/29/30), 3.23 / 71.31 (H-32 / C-26+31), 2.24 / 155.18, 130.29, 130.00 (H-24 / C-25, C-22, C-23).[MT554-6]

^{31}P-NMR (162 MHz, [D$_6$]-dimethylsulfoxid, 298 K) δ [in ppm] = 1.09

[MT554-5]

Elemental analysis = calcd (%) for $C_{80}H_{72}O_{16}P_2$: C: 71.10, H: 5.37, O: 18.94; found:

C: 69.4, H: 5.54, O: 19.0

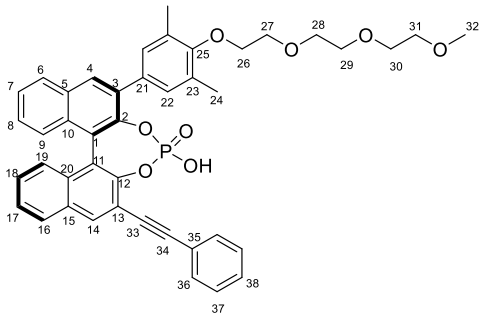
MS (ESI-neg, MeOH**)**: *m/z* = 674.20693 ([M-2H]$^{2-}$, calcd. 674.20750for [$C_{80}H_{70}O_{16}P_2^{2-}$].

IR (ATR-FT): $\tilde{\nu}$ (cm^{-1}) = 3427, 3053, 2919, 2871, 1598, 1486, 1447, 1422, 1391, 1371, 1336, 1258, 1201, 1147, 1127, 1091, 1016, 968, 920, 882, 748.

[MT554]

8.2.2.6.5. Synthesis of compound (*R*)-**12b**

Described experiment: MT555 Repeated:



According to general procedure **D**, compound (*R*)-**103b** (87.7 mg, 0.133 mmol, 1 eq) gave the product as a yellow solid (65.3 mg, 91.4 µmol, 68.7%).

$C_{43}H_{39}O_8P$, MW = 714.4 g/mol.

^{1}H-NMR (600 MHz, [D$_6$]- dimethylsulfoxid, 298 K) δ [in ppm] = 8.42 – 8.39 (m, 1 H, H-14), 8.09 – 8.07 (m, 3 H, H-4+6+16), 7.62 – 7.60 (m, 4 H, H-22+36), 7.52 – 7.44 (m, 5 H, H-7+17+37+38), 7.36 – 7.30 (m, 2 H, H-8+18), 7.12 – 7.08 (m, 2 H, H-9+19), 3.97 – 3.96 (m, 2 H, H-26), 3.77 – 3.75 (m, 2 H, H-27), 3.65 – 3.63 (m, 2 H, H-28), 3.59 – 3.57 (m, 2 H, H-29), 3.56 – 3.55 (m, 2 H, H-30), 3.46 – 3.44 (m, 2 H, H-31), 3.25 (s, 3 H, H-32), 2.31 (s, 6 H, H-24).

^{13}C-NMR (151 MHz, [D$_6$]- dimethylsulfoxid, 298 K) δ [in ppm] = 155.06 (C-25), 147.83 (C-12), 146.58 (C-2), 133.96 (C-3), 133.49 (C-14), 132.80 (C-21), 131.79 (C-20), 131.46 (C-36), 131.16 (C-10), 130.63 (C-4), 130.50 (C-22), 130.34 (C-5/15), 130.09 (C-5/15), 129.78 (C-23), 128.87 (C-38), 128.77 (C-37), 128.45 (C-6+16), 127.36 (C-8/18), 126.32 (C-8/18), 126.08 (C-9/19), 125.82 (C-9/19), 125.58 (C-7/17), 125.20 (C-7/17), 122.66 (C-35), 122.45 (C-1/11), 121.57 (C-1/11), 116.32 (C-13), 93.27 (C-34), 86.13 (C-33), 71.32 (C-26/31), 71.30 (C-26/31), 69.99 (C-28), 69.89 (C-27/29), 69.85 (C-27/29), 69.67 (C-30), 58.07 (C-32), 16.13 (C-24).

^{1}H,^{1}H-COSY (600 MHz / 600 MHz, [D$_6$]- dimethylsulfoxid, 298 K) δ [in ppm] = 8.09 – 8.07 / 7.52 – 7.44 (H-4+6+16 / H-7+17+37+38), 7.62 – 7.60 / 7.52 – 7.44, 2.31 (H-22+36 / H-7+17+37+38, H-24), 7.52 – 7.44 / 8.09 – 8.07, 7.62 – 7.60, 7.36 – 7.30 (H-7+17+37+38 / H-4+6+16, H-22+36, H-8+18), 7.36 – 7.30/ 7.52 – 7.44, 7.12 – 7.08 (H-8+18 / H-7+17+37+38, H-9+19), 7.12 – 7.08 / 7.36 – 7.30 (H-9+19 / H-8+18), 3.97 – 3.96 / 3.77 – 3.75 (H-26 / H-27), 3.77 – 3.75 / 3.97 – 3.96 (H-27 / H-26), 3.63 – 3.59 / 3.59 – 3.57 (H-28 / H-29), 3.59 – 3.57 / 3.63 – 3.59 (H-29 / H-28), 3.56 – 3.55 / 3.46 – 3.44 (H-30 / H-31), 3.46 – 3.44 / 3.56 – 3.55 (H-31 / H-30), 2.31 / 7.51 (H-24 / H-22+36).

^{1}H,^{13}C-GHSQC (600 MHz / 151 MHz, [D$_6$]-dimethylsulfoxid, 298 K) δ (^{1}H) / δ (^{13}C) [in ppm] = 8.42 – 8.39 / 133.49 (H-14 / C-14), 8.09 – 8.07 / 130.63, 128.45 (H-4+6+16 / C-4, C-6+16), 7.62 – 7.60 / 131.46, 130.50 (H-22+36 / C-36, C-22), 7.52 – 7.44 / 128.87, 128.77, 125.58, 125.20 (H-7+17+37+38 / C-38, C-37, C-7/17, C-7/17), 7.36 – 7.30 / 127.36, 126.32 (H-8+18 / C-8/18, C-8/18), 7.12 – 7.08 / 126.08, 125.82 (H-9+19 / C-9/19, C9/19), 3.97 – 3.96 / 71.32/71.30 (H-26 / C-26/31), 3.77 – 3.75 / 69.89/69.85 (H-27 / C-27/29), 3.65 – 3.63 / 69.99 (H-28 / C-28), 3.59 – 3.57 / 69.89/69.85 (H-29 / C-27/29), 3.56 – 3.55 / 69.67 (H-30 / C-30), 3.46 – 3.44 / 71.32/71.30 (H-31 / C-26/31), 3.25 / 58.07 (H-32 / C-32), 2.31 / 16.13 (H-24 / C-24).

^{1}H,^{13}C-GHMBC (600 MHz / 151 MHz, [D$_6$]-dimethylsulfoxid, 298 K) δ (^{1}H) / δ (^{13}C) [in ppm] = 8.42 – 8.39 / 147.83, 131.79, 128.45, 86.13 (H-14 / C-12, C-20, C-6+16, C-33), 8.09 – 8.07 / 146.58, 133.49, 132.80, 131.79, 131.16, 130.63, 128.45, 127.36, 126.32 (H-4+6+16 / C-2, C-14, C-21, C-20, C-10, C-4, C-6+16, C-8/18, C-8/18), 7.62 – 7.60 / 155.06, 133.96, 131.46, 130.50, 128.77, 93.27, 16.13 (H-22+36 / C-25, C-3, C-36, C-22, C-37, C-34, C-24), 7.52 – 7.44 / 131.46, 130.34, 130.09, 128.77, 126.08, 125.82, 122.66 (H-7+17+37+38 / C-36, C-5/15, C-5/15, C-37, C-9/19, C-9/19, C-35), 7.36 – 7.30 / 131. 79, 131.16, 128.46 (H-8+18 / C-20, C-10, C-6+16), 7.12 – 7.08 / 130.34, 130.09, 125.58, 125.20, 121.57 (H-9+19 / C-5/15, C-5/15, C-7/17, C-7/17, C-1/11), 2.31 / 155.06, 130.50, 129.78 (H-24 / C-25, C-22, C-23).[MT555-4]

^{31}P-NMR (243 MHz, [D$_6$]-dimethylsulfoxid, 298 K) δ [in ppm] = 2.66

Elemental analysis = calcd (%) for $C_{43}H_{39}O_8P$: C: 72.26, H: 5.50, O: 17.91; found:

C: 70.0, H: 5.60, O: 17.9

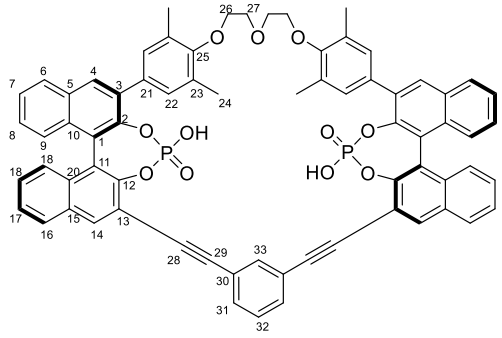
MS (ESI-neg, MeOH**)**: *m/z* = 713.22877 ([M-H]$^-$), calcd. 713.23098 for [$C_{43}H_{37}O_8P^-$]

IR (ATR-FT): $\tilde{\nu}$ (cm^{-1}) = 3048, 2960, 2915, 2866, 2323, 1599, 1489, 1442, 1419, 1395, 1362, 1336, 1260, 1202, 1093, 966, 881, 798, 750.

[MT555]

8.2.2.6.6. Synthesis of compound (*R*,*R*)-**5**

Described experiment: MT556 Repeated:MT689



According to general procedure **D**, compound (*R*,*R*)-**82** (43.6 mg, 0.0436 mmol, 1 eq) gave the product as a yellow solid (27.1 mg, 24.1 µmol, 54.6%).

$C_{70}H_{50}O_{11}P_2$, MW = 1128.1 g/mol.

^{1}H-NMR (400 MHz, [D$_6$]-dimethylsulfoxid, 298 K) δ [in ppm] = 8.49 (s, 2 H, H-14), 8.17 (s, 2 H, H-4), 8.11 (d, ^3J = 8.4 Hz, 4 H, H-6+16), 7.74 – 7.71 (m, 3 H, H-31+33), 7.59 (s, 5 H, H-22+32), 7.58 – 7.49 (m, 4 H, H-7+17), 7.39 (t, ^3J = 7.5 Hz, 2 H, H-18), 7.34 (t, ^3J = 7.5 Hz, 2 H, H-8), 7.16 (d, ^3J = 8.5, 2 H, H-19), 7.15 (d, ^3J = 8.50, 2 H, H-9), 4.13 – 4.08 (m, 2 H, H-26/27), 4.00 – 3.95 (m, 25 H, H-26/27), 3.86 (br s, 4 H, H-26/27), 2.32 (s, 12 H, H-24).

^{13}C-NMR (101 MHz, [D$_6$]-dimethylsulfoxid, 298 K) δ [in ppm] = 155.23 (C-25), 147.08 (d, $^2J_{pc}$ = 9.7 Hz, C-12), 146.10 (d, $^2J_{pc}$ = 9.7 Hz, C-2), 134.20 (C-14), 133.96 (C-33), 133.75 (C-3), 132.21 (C-21), 131.96 (C-31), 131.80 (C-20), 131.08 (C-10+15), 130.60 (C-4), 130.45 (C-22), 130.33 (C-5), 129.82 (C-23), 129.52 (C-33), 128.63 (C-6/16), 128.60 (C-6/16), 127.70 (C-18), 126.53 (C-8), 126.15 (C-7), 125.89 (C-9+19), 125.51 (C-17), 123.17 (C-30), 122.42 (C-13), 121.33 (C-1+11), 115.87 (C-13), 92.25 (C-29), 86.39 (C-28), 71.32 (C-26/27), 70.18 (C-26/27), 16.34 (C-24).

^{1}H,^{1}H-COSY (400 MHz / 400 MHz, [D$_6$]-dimethylsulfoxid, 298 K) δ [in ppm] = 8.11 / 7.58 – 7.49 (H-6+16 / H-7+17), 7.74 – 7.71 / 7.59 (H-31+33 / H-22+32), 7.59 / 7.74 – 7.71 (H-22+32 / H-31+33), 7.58 – 7.49 / 8.11, 7.39, 7.34 (H-7+17 / H-6+16, H-18, H-8), 7.39 / 7.58 – 7.49, 7.16/7.15 (H-18 / H-7+17, H-19/9), 7.34 / 7.54, 7.16/7.15 (H-8 / H-7+17, H-19/9), 7.16/7.15 / 7.39, 7.34 (H-9/19 / H-18, H-8), 4.13 – 4.08 / 4.00 – 3.95 (H-26/27 / H-26/27), 4.00 – 3.95 / 4.13 – 4.08, 3.86 (H-26/27 / H-26/27, H26/27), 3.86 / 4.00 – 3.95 (H-26/27 / H-26/27).

^{1}H,^{13}C-GHSQC (400 MHz / 101 MHz, [D$_6$]-dimethylsulfoxid, 298 K) δ (^{1}H) / δ (^{13}C) [in ppm] = 8.49 / 134.20 (H-14 / C-14), 8.17 / 130.60 (H-4 / C-4), 8.11 / 128.63, 128.60 (H-6+16 / C-6/16, C-6/16), 7.74 – 7.71 / 133.96, 131.96 (H-31+33 / C-33, C-31), 7.59 / 130.45, 129.52 (H-22+32 / C-22, C-32), 7.58 – 7.49 / 126.15, 125.51 (H-7+17 / C-7, C-17), 7.39 / 127.70 (H-18 / C-18), 7.34 / 126.53 (H-8 / C-8), 7.16 / 125.89 (H-19 / C-9+19), 7.15 / 125.89 (H-9 / C-9+19), 4.13 – 4.08 / 71.32 (H-26/27 / C-26/27), 4.00 – 3.95 / 71.32 (H-26/27 / C-26/27), 3.86 / 70.18 (H-26/27 / C-26/27), 2.32 / 16.34 (H-24 / C-24),

^{1}H,^{13}C-GHMBC (400 MHz / 101 MHz, [D$_6$]-dimethylsulfoxid, 298 K) δ (^{1}H) / δ (^{13}C) [in ppm] = 8.49 / 147.08, 131.80, 128.63/128.60, 86.39 (H-14 / C-12, C-20, C-6/16, C-28), 8.17 / 146.10, 132.21, 131.08, 128.63/128.60 (H-4 / C-2, C-21, C-10+15, C-6/16), 8.11 / 134.20, 131.80, 131.08, 127.70, 126.53 (H-6+16 / C-14, C-20, C-10+15, C-18, C-8), 7.74 – 7.71 / 133.96, 131.96, 92.25 (H-31+33 / C-32, C-31, C-29), 7.59 / 133.96, 133.75, 130.45, 123.17 (H-22+32 / C-33, C-3, C-22, C-30), 7.58 – 7.49

/ 126.15 (H-7+17 / C-7), 7.39 / 131.80, 128.63/128.60 (H-18 / C-20, C-6/16), 7.34 / 131.08, 128.63/128.60, 126.15 (H-8 / C-10+15, C-6/16, C-7), 7.16 / 131.08, 125.51, 121.33 (H-19 / C-10+15, C-17, C-1+11), 7.15 / 130.33, 126.15, 121.33 (H-9 / C-5, C-7, C-1+11), 2.32 / 155.23, 129.82 (H-24 / C-25, C-23).

[MT556-5]

^{31}P-NMR (162 MHz, [D$_6$]-dimethylsulfoxid, 298 K) δ [in ppm] = 1.98

[MT556-3]

Elemental analysis = calcd (%) for $C_{70}H_{50}O_{11}P_2$: C: 74.46, H: 4.46, O: 15.59; found:

C: 68.7, H: 4.66, O: 16.2

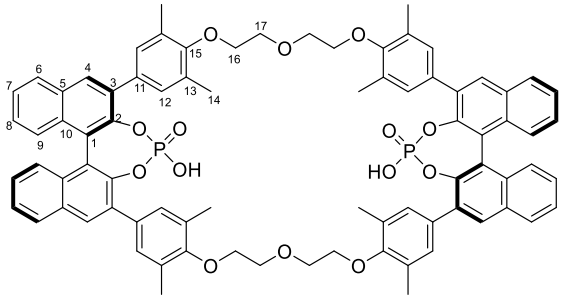
MS (ESI-neg, MeOH**)**: *m/z* = 563.13401 ([M-2H]$^{2-}$, calcd. 563.13414 for [$C_{70}H_{48}O_{11}P_2^{2-}$].

IR (ATR-FT): $\tilde{\nu}$ (cm^{-1}) = 3390, 2953, 2919, 2863, 1701, 1592, 1571, 1482, 1447, 1420, 1371, 1336, 1247, 1205, 1149, 1131, 1094, 1018, 967, 943, 883, 851, 748, 684, 668.

[MT556-6]

8.2.2.6.7. Synthesis of compound (*R*,*R*)-**9**

Described experiment: MT598 Repeated: MT593, MT587



According to general procedure **D**, compound (*R*,*R*)-**94** (64.4 mg, 54.2 µmol, 1 eq) gave the product as a yellow solid (52.1 mg, 39.5 µmol, 73.1%).

$C_{80}H_{70}O_{14}P_2$, MW = 1317.4 g/mol.

^{1}H-NMR (400 MHz, [D$_6$]-dimethylsulfoxid, 298 K) δ [in ppm] = 8.15 (s, 4 H, H-4), 8.08 (d, ^3J = 8.4 Hz, 4 H, H-6), 7.65 (s, 8 H, H-12), 7.49 (t, ^3J = 7.4 Hz, 4 H, H-7), 7.30 (t, ^3J = 7.6 Hz, 4 H, H-8), 7.04 (d, ^3J = 8.6 Hz, 4 H, H-9), 4.05 – 4.03 (m, 8 H, H-16), 3.90 – 3.87 (m, 8 H, H-17), 2.38 (s, 24 H, H-14).

^{13}C-NMR (101 MHz, [D$_6$]-dimethylsulfoxid, 298 K) δ [in ppm] = 154.97 (C-15), 145.55 (d, $^2J_{pc}$ = 9.7 Hz, C-2), 133.34 (d, $^2J_{pc}$ = 9.7 Hz, C-3), 132.23 (C-11), 131.31 (C-10), 130.66 (C-4/5), 130.62 (C-4/5), 130.45 (C-12), 130.15 (C-13), 128.51 (C-6), 126.46 (C-8), 126.02 (C-9), 125.47 (C-7), 121.98 (d, $^2J_{pc}$ = 9.7 Hz, C-1), 71.48 (C-16), 69.99 (C-17) 16.15 (C-14).

^{1}H,^{1}H-COSY (400 MHz / 400 MHz, [D$_6$]-dimethylsulfoxid, 298 K) δ [in ppm] = 8.08 / 7.49 (H-6 / H-7), 7.65 / 2.38 (H-12 / H-14), 7.49 / 8.08, 7.30 (H-7 / H-6, H-8), 7.30 / 7.49, 7.04 (H-8 / H-7, H-9), 7.04 / 7.30 (H-9 / H-8), 4.05 – 4.03 / 3.90 – 3.87 (H-16 / H-17), 3.90 – 3.87 / 4.05 – 4.03 (H-17 / H-16), 2.38/ 7.65 (H-14 / H-12).

^{1}H,^{13}C-GHSQC (400 MHz / 101 MHz, [D$_6$]-dimethylsulfoxid, 298 K) δ (^{1}H) / δ (^{13}C) [in ppm] = 8.15 / 130.66/130.62 (H-4 / C-4/5), 8.08 / 128.51 (H-6 / C-6), 7.65 / 130.45 (H-12 / C-12), 7.49 / 125.47 (H-7 / C-7), 7.30 / 126.46 (H-8 / C-8), 7.04 / 126.02 (H-9 / C-9), 4.05 – 4.03 / 71.48 (H-16 / C-16), 3.90 – 3.87 / 69.99 (H-17 / C-17), 2.38 / 16.15 (H-14 / C-14).

^{1}H,^{13}C-GHMBC (600 MHz / 151 MHz, [D$_6$]-dimethylsulfoxid, 298 K) δ (^{1}H) / δ (^{13}C) [in ppm] = 8.15 / 145.55, 132.23, 131.31, 128.51, 121.98 (H-4 / C-2, C-11, C-10, C-6, C-1), 8.08 / 131.31, 126.46 (H-6 / C-10, C-8), 7.65 / 154.97, 133.34, 130.45, 16.15 (H-12 / C-15, C-3, C-12, C-14), 7.49 / 130.66/130.62, 126.02 (H-7 / C-4/5, C-9), 7.30 / 131.31, 128.51 (H-8 / C-10, C-6), 7.04 / 130.66/130.62, 125.47, 121.98 (H-9 / C-4/5, C-7, C-1), 2.38 / 154.97, 130.45, 130.15 (H-14 / C-15, C-12, C13). [MT598-5]

^{31}P-NMR (162 MHz, [D$_6$]-dimethylsulfoxid, 298 K) δ [in ppm] = 2.16

Elemental analysis = calcd (%) for $C_{80}H_{70}O_{14}P_2$: C: 72.94, H: 5.36, O: 17.00; found:

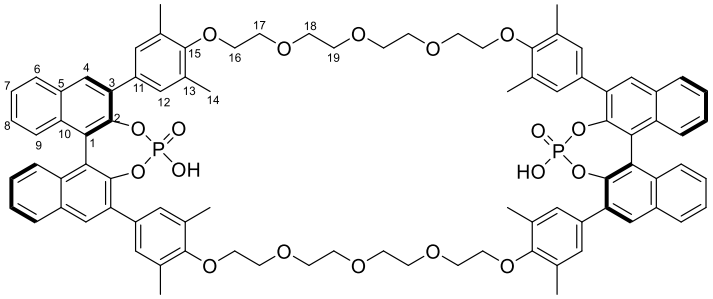
C: 67.4, H: 7.10, O: 17.7

MS (ESI-neg, MeOH**)**: *m/z* = 1315.41742 ([M-H]$^-$), calcd 1315.41680 for [$C_{80}H_{70}O_{14}P_2^-$].

IR (ATR-FT): $\tilde{\nu}$ (cm^{-1}) = 3051, 2960, 2921, 2860, 1593,1485, 1423, 1259, 1208, 1127, 1086, 1013, 965, 931, 871, 797, 748. [MT593-6]

8.2.2.6.8. Synthesis of compound (*R*,*R*)-**10**

Described experiment: MT664 Repeated:



According to general procedure **D**, compound (*R*,*R*)-**95** (55.8 mg, 40.7 µmol, 1 eq) gave the product as a yellow solid (45.1 mg, 30.1 µmol, 74.2%).

$C_{88}H_{86}O_{18}P_2$, MW = 1493.6 g/mol.

^{1}H-NMR (600 MHz, [D$_6$]-dimethylsulfoxid, 298 K) δ [in ppm] = 8.08 (s, 4 H, H-4), 8.06 (d, ^3J = 8.3 Hz, 4 H, H-6), 7.48 (t, ^3J = 7.2 Hz, 4 H, H-7), 7.46 (s, 8 H, H-12), 7.31 (t, ^3J = 7.6 Hz, 4 H, H-8), 7.08 (d, ^3J = 8.3 Hz, 4 H, H-9), 3.94 – 3.93 (m, 8 H, H-16), 3.76 – 3.75 (m, 8 H, H-17), 3.66 – 3.51 (m, 16 H, H-18+19), 2.27 (s, 24 H, H-14).

^{13}C-NMR (151 MHz, [D$_6$]-dimethylsulfoxid, 298 K) δ [in ppm] = 155.60 (C-15), 145.79 (d, $^2J_{pc}$ = 9.7 Hz, C-2), 133.95 (C-3), 133.83 (C-11), 131.68 (C-10), 131.13 (C-4/5), 131.12 (C-4/5), 130.69 (C-12), 130.42 (C-13), 128.99 (C-6), 126.95 (C-8), 126.43 (C-9), 125.97 (C-7), 122.58 (d, $^2J_{pc}$ = 9.7 Hz, C-1), 71.86 (C-16), 70.56 (C-18/19), 70.54 (C-18/19), 70.40 (C-17), 16.58 (C-14).

^{1}H,^{1}H-COSY (600 MHz / 600 MHz, [D$_6$]-dimethylsulfoxid, 298 K) δ [in ppm] = 8.06 / 7.48 (H-6 / H-7), 7.48 / 8.06, 7.31 (H-7 / H-6, H-8), 7.46 / 2.27 (H-12 / H-14), 7.31 / 7.48, 7.08 (H-8 / H-7, H-9), 7.08 / 7.31 (H-9 / H-8), 3.94 – 3.93 / 3.76 – 3.75 (H-16 / H-17), 3.76 – 3.75 / 3.94 – 3.93 (H-17 / H-16), 2.27/ 7.46 (H-14 / H-12).

^{1}H,^{13}C-GHSQC (600 MHz / 151 MHz, [D$_6$]-dimethylsulfoxid, 298 K) δ (^{1}H) / δ (^{13}C) [in ppm] = 8.08 / 130.13/131.12 (H-4 / C-4/5), 8.06 / 128.99 (H-6 / C-6), 7.48 / 125.97 (H-7 / C-7), 7.46 / 130.69 (H-12 / C-12), 7.31 / 126.95 (H-8 / C-8), 7.08 / 126.43 (H-9 / C-9), 3.94 – 3.93 / 71.86 (H-16 / C-16), 3.76 – 3.75 / 70.40 (H-17 / C-17), 3.66 – 3.51 / 70.56, 70.54 (H-18+19 / C-18+19), 2.27 / 16.58 (H-14 / C-14).

^{1}H,^{13}C-GHMBC (600 MHz / 151 MHz, [D$_6$]-dimethylsulfoxid, 298 K) δ (^{1}H) / δ (^{13}C) [in ppm] = 8.08 / 145.79, 133.83, 131.68, 128.99 (H-4 / C-2, C-11, C-10, C-6), 8.06 / 131.68, 131.13/131.12, 126.95 (H-6 / C-10, C-4/5, C-8), 7.48 / 131.13/131.12, 126.43 (H-7 / C-4/5, C-9), 7.46 / 155.60, 133.95, 130.69, 16.58 (H-12 / C-15, C-3, C-12, C-14), 7.31 / 131.68, 128.99 (H-8 / C-10, C-6), 7.08 / 131.13/131.12, 125.97, 122.58 (H-9 / C-4/5, C-7, C-1), 2.27 / 155.60, 130.69, 130.42 (H-14 / C-15, C-12, C13). [MT664-9]

^{31}P-NMR (243 MHz, [D$_6$]-dimethylsulfoxid, 298 K) δ [in ppm] = 0.94

Elemental analysis = calcd (%) for $C_{88}H_{86}O_{18}P_2$: C: 70.77, H: 5.80, O: 19.28; found:

C: 66.8, H: 5.91, O: 18.5

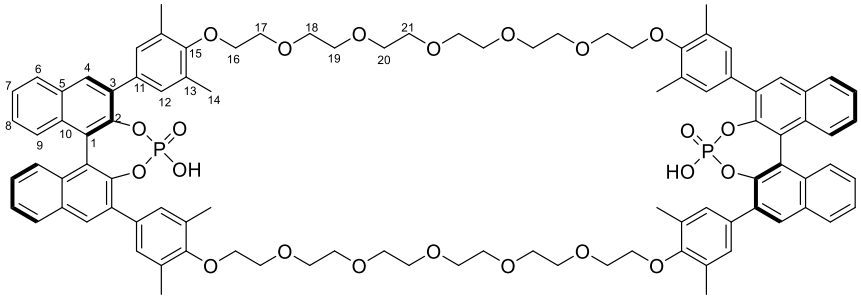
MS (ESI-neg, MeOH**)**: *m/z* = 1491.52267 ([M-H]$^-$, calcd. 1491.52166 for [$C_{88}H_{85}O_{18}P_2^-$].

IR (ATR-FT): $\tilde{\nu}$ (cm^{-1}) = 3048, 3033, 2980, 2971, 2914, 2884, 2871, 2357, 2324, 1594, 1486, 1455, 1448, 1422, 1392, 1374, 1362, 1338, 1303, 1270, 1257, 1232, 1205, 1162, 1147, 1126, 1086.

[MT664-9]

8.2.2.6.9. Synthesis of compound (*R*,*R*)-**11**

Described experiment: MT665 Repeated:



According to general procedure **D**, compound (*R*,*R*)-**96** (32.1 mg, 20.7 µmol, 1 eq) gave the product as a yellow solid (26.9 mg, 16.1 µmol, 78.1%).

$C_{96}H_{102}O_{22}P_2$, MW = 1669.8 g/mol.

^{1}H-NMR (400 MHz, [D$_6$]-dimethylsulfoxid, 298 K) δ [in ppm] = 8.12 (s, 4 H, H-4), 8.10 (d, ^3J = 7.8 Hz, 4 H, H-6), 7.50 (t, ^3J = 7.3 Hz, 4 H, H-7), 7.45 (s, 8 H, H-12), 7.32 (t, ^3J = 8.6 Hz, 4 H, H-8), 7.10 (d, ^3J = 8.8 Hz, 4 H, H-9), 3.93 – 3.90 (m, 8 H, H-16), 3.72 – 3.70 (m, 8 H, H-17), 3.62 – 3.59 (m, 8 H, H-18), 3.57 – 3.55 (m, 8 H, H-19), 3.54 – 3.52 (m, 16 H, H-20+21), 2.26 (s, 24 H, H-14).

^{13}C-NMR (101 MHz, [D$_6$]-dimethylsulfoxid, 298 K) δ [in ppm] = 155.17 (C-15), 145.00 (d, $^2J_{pc}$ = 9.7 Hz, C-2), 133.37 (d, $^2J_{pc}$ = 9.7 Hz, C-3), 132.24 (C-11), 131.18 (C-10), 130.84 (C-4), 130.76 (C-5), 130.16 (C-12), 130.01 (C-13), 128.56 (C-6), 126.61 (C-8), 125.98 (C-9), 125.67 (C-7), 122.06 (d, $^2J_{pc}$ = 9.7 Hz, C-1), 71.34 (C-16), 70.00 (C-18), 69.90 (C-17/19/20/21), 69.87 (C-17/19/20/21), 69.85 (C-17/19/20/21), 16.10 (C-14).

^{1}H,^{1}H-COSY (400 MHz / 400 MHz, [D$_6$]-dimethylsulfoxid, 298 K) δ [in ppm] = 8.10 / 7.50 (H-6 / H-7), 7.50 / 8.10, 7.32 (H-7 / H-6, H-8), 7.45 / 2.26 (H-12 / H-14), 7.32 / 7.50, 7.10 (H-8 / H-7, H-9), 7.10 / 7.32 (H-9 / H-8), 3.93 – 3.90 / 3.72 – 3.70 (H-16 / H-17), 3.72 – 3.70 / 3.93 – 3.90 (H-17 / H-16), 3.62 – 3.59 / 3.57 – 3.55 (H-18 / H-19), 3.57 – 3.55 / 3.62 – 3.59 (H-19 / H-18), 2.26/ 7.45 (H-14 / H-12).

^{1}H,^{13}C-GHSQC (400 MHz / 101 MHz, [D$_6$]-dimethylsulfoxid, 298 K) δ (^{1}H) / δ (^{13}C) [in ppm] = 8.12 / 130.84 (H-4 / C-4), 8.10 / 128.56 (H-6 / C-6), 7.50 / 125.67 (H-7 / C-7), 7.45 / 130.16 (H-12 / C-12), 7.32 / 126.61 (H-8 / C-8), 7.10 / 125.98 (H-9 / C-9), 3.93 – 3.90 / 71.34 (H-16 / C-16), 3.72 – 3.70 / 69.90/69.87/69.85 (H-17 / C-17/20/21/22), 3.62 – 3.59 / 70.00 (H-18 / C-18), 3.57 – 3.55 / 69.90/69.87/69.85 (H-19 / C-17/20/21/22), 3.54 – 3.52 / 69.90/69.87/69.85 (H-20+21 / C-17/20/21/22), 2.26 / 16.10 (H-14 / C-14).

^{1}H,^{13}C-GHMBC (400 MHz / 101 MHz, [D$_6$]-dimethylsulfoxid, 298 K) δ (^{1}H) / δ (^{13}C) [in ppm] = 8.12 / 145.00, 132.24, 131.18, 128.56 (H-4 / C-2, C-11, C-10, C-6), 8.10 / 130.84, 126.61 (H-6 / C-4, C-8), 7.50 / 130.76, 125.98 (H-7 / C-5, C-9), 7.45 / 155.17, 133.37, 130.16, 130.01, 16.10 (H-12 / C-15, C-3, C-12, C-13, C-14), 7.32 / 131.18, 128.56 (H-8 / C-10, C-6), 7.10 / 130.76, 125.67, 122.06 (H-9 / C-5, C-7, C-1), 3.93 – 3.90 / 69.90/69.87/69.85 (H-16 / C-17/20/21/22), 3.72 – 3.70 / 71.34 (H-17 / C-16), 3.62 – 3.59 / 69.90/69.87/69.85 (H-18 / C-17/20/21/22), 3.57 – 3.55 / 69.90/69.87/69.85 (H-19 / C-17/20/21/22), 2.26 / 155.17, 130.16, 130.01 (H-14 / C-15, C-12, C13).

[MT665-6]

^{31}P-NMR (162 MHz, [D_6]- dimethylsulfoxid, 298 K) δ [in ppm] = 1.29

Elemental analysis = calcd (%) for $C_{96}H_{102}O_{22}P_2$: C: 69.05, H: 6.16, O: 21.08; found:

C: 65.6, H: 5.91, O: -

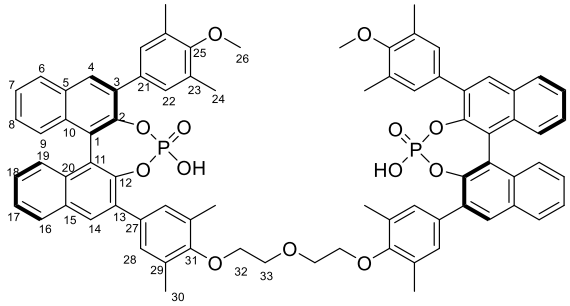
MS (ESI-neg, MeOH**)**: *m/z* = 833.30852 ([M-2H]$^{2-}$, calcd. 833.30962 for [$C_{96}H_{100}O_{22}P_2^{2-}$].

IR (ATR-FT): $\tilde{\nu}$ (cm^{-1}) = 3064, 3048, 3032, 2980, 2970, 2918, 2884, 2871, 2736, 2357, 2313, 1486, 1456, 1423, 1392, 1349, 1338, 1306, 1271, 1254, 1232, 1206, 1161, 1146, 1126, 1086, 1052, 1018, 965.

[MT665]

8.2.2.6.10. Synthesis of compound (*R*,*R*)-**6**[119]

Described experiment: MT629 Repeated: SF025



According to general procedure **D**, compound (*R*,*R*)-**91** (68.1 mg, 59.1 µmol, 1 eq) gave the product as a yellow solid (59.7 mg, 46.8 µmol, 79.2%).

$C_{78}H_{68}O_{13}P_2$, MW = 1275.34 g/mol.

^{1}H-NMR (400 MHz, [D$_6$]-dimethylsulfoxid, 298 K) δ [in ppm] = 8.14 (s, 2 H, H-4/14), 8.13 (s, 2 H, H-4/14), 8.09 (d, ^3J = 8.6 Hz, 4 H, H-6+16), 7.53 (s, 4 H, H-28), 7.52 (s, 4 H, H-22), 7.49 – 7.47 (m, 4 H, H-7+17), 7.32 (t, ^3J = 8.3 Hz, 4 H, H-8+18), 7.10 (d, ^3J = 7.6 Hz, 4 H, H-9+19), 4.04 – 4.02 (m, 4 H, H-32), 3.89 – 3.87 (m, 4 H, H-33), 3.72 (s, 6 H, H-26), 2.34 (s, 12 H, H-30), 2.29 (s, 12 H, H-24).

^{13}C-NMR (101 MHz, [D$_6$]-dimethylsulfoxid, 298 K) δ [in ppm] = 156.20 (C-25), 155.12 (C-31), 145.38 (d, $^2J_{pc}$ = 9.7 Hz, C-2/12), 133.49 (d, $^2J_{pc}$ = 9.7 Hz, C-3/13), 132.49 (C-21+27), 131.26 (C-10+20), 130.76 (C-4/14+C-5/15), 130.67 (C-4/14+C-5/15), 130.32 (C-22/28), 130.29 (C-22/28), 130.03 (C-29), 129.78 (C-23), 128.54 (C-6+16), 126.53 (C-8+18), 125.98 (C-9+19), 125.53 (C-7+17), 122.15 (C-1+11), 71.39 (C-32), 70.04 (C-33), 59.27 (C-26), 16.11 (C-30), 15.98 (C-24).

^{1}H,^{1}H-COSY (400 MHz / 400 MHz, [D$_6$]-dimethylsulfoxid, 298 K) δ [in ppm] = 8.09 / 7.50 (H-6+16 / H-7+17), 7.53 / 2.34 (H-28 / H-30), 7.52 / 2.29 (H-22 / H-24), 7.49 – 7.47 / 8.09, 7.32 (H-7+17 / H-6+16, H-8+18), 7.32 / 7.49 – 7.47, 7.10 (H-8+18 / H-7+17, H-9+19), 7.10 / 7.32 (H-9+19 / H-8+18), 2.34 / 7.53 (H-30 / H-28), 2.29 / 7.52 (H-24 / H-22).

^{1}H,^{13}C-GHSQC (400 MHz / 101 MHz, [D$_6$]-dimethylsulfoxid, 298 K) δ (^{1}H) / δ (^{13}C) [in ppm] = 8.14 / 130.76/130.67 (H-4/14 / C-4/14+C5/15), 8.13 / 130.76/130.67 (H-4/14 / C-4/14+C5/15), 8.09 / 128.54 (H-6+16 / C-6+16), 7.53 / 130.32/130.29 (H-28 / C-22/28), 7.52 / 130.32/130.29 (H-22 / C-22/28), 7.49 – 7.47 / 125.53 (H-7+17 / C-7+17), 7.32 / 126.53 (H-8+18 / C-8+18), 7.10 / 125.98 (H-9+19 / C-9+19), 4.04 – 4.02 / 71.39 (H-32 / C-32), 3.89 – 3.87 / 70.04 (H-33 / C-33), 3.72 / 59.27 (H-26 / C-26), 2.34 / 16.11 (H-30 / C-30), 2.29 / 15.98 (H-24 / C-24).

^{1}H,^{13}C-GHMBC (400 MHz / 101 MHz, [D$_6$]-dimethylsulfoxid, 298 K) δ (^{1}H) / δ (^{13}C) [in ppm] = 8.14 / 145.38, 132.49, 131.26, 128.54 (H-4/14 / C-2+12, C-21+27, C-10+20, C-6+16), 8.13 / 145.38, 132.49, 131.26, 128.54 (H-4/14 / C-2+12, C-21+27, C-10+20, C-6+16), 8.09 / 131.26, 130.76/130.67, 126.53 (H-6+16 / C-10+20, C-4/14+C5/15, C-8+18), 7.53 / 155.12, 133.49, 130.32/130.29, 16.11 (H-28 / C-31, C-3+13, C-22/28, C-30), 7.52 / 156.20, 133.49, 130.32/130.29, 15.98 (H-22 / C-25, C-3+13, C-22/28, C-24), 7.49 / 130.76/130.67, 125.98 (H-7/17 / C-4/14+C5/15, C-9+19), 7.32 / 131.26, 128.54 (H-8+18 / C-10+20, C-6+16), 7.10 / 130.76/130.67, 125.53, 122.15 (H-9+19 / C-4/14+C-5/15, C-7+17,

[119] First done by Sophia Stadtfeld, former Bachelor student. Supervision and evaluation of data by Maike Thiele.

C-1+11), 3.72 / 156.20 (H-26 / C-25), 2.34 / 155.12, 130.03 (H-30 / C-31, C-29), 2.29 / 156.20, 129.78 (H-24 / C-25, C-23).

[MT629-2]

^{31}P-NMR (162 MHz, [D_6]-dimethylsulfoxid, 298 K) δ [in ppm] = 1.30

Elemental analysis = calcd (%) for $C_{78}H_{68}O_{13}P_2$: C: 73.46, H: 5.37, O: 16.31; found:

C: 71.2, H: 5.89, O: 16.3

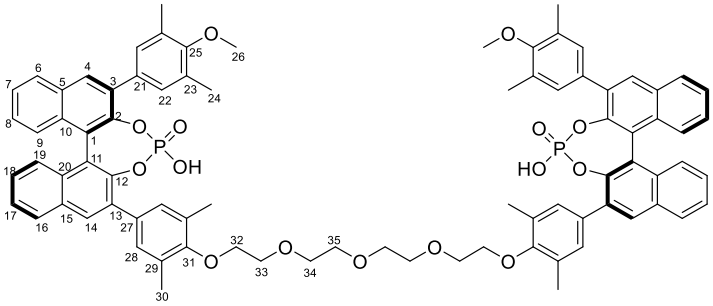
MS (ESI-neg, MeOH**)**: *m/z* = 1273.40754 ([M-H]$^-$, calcd. 1273.40624 for [$C_{78}H_{67}O_{13}P_2^-$].

IR (ATR-FT): $\tilde{\nu}$ (cm^{-1}) = 2924, 2160, 3031, 1977, 1719, 1487, 1397, 1373, 1337, 1260, 1215, 1150, 1126, 1086, 1017, 968, 930, 883, 872, 841, 88, 775, 750, 694, 665, 627.

[MT629]

8.2.2.6.11. Synthesis of compound (*R*,*R*)-**7**

Described experiment: MT688 Repeated:



According to general procedure **D**, compound (*R*,*R*)-**92** (54.1 mg, 43.6 µmol, 1 eq), gave the product as a yellow solid (41.2 mg, 30.2 µmol, 69.2%).

$C_{82}H_{76}O_{15}P_2$, MW = 1363.4 g/mol.

^{1}H-NMR (400 MHz, [D$_6$]-dimethylsulfoxid, 298 K) δ [in ppm] = 8.12 (br s, 4 H, H-4+14), 8.09 (d, ^3J = 7.6 Hz, 2 H, H-6/16), 8.07 (d, ^3J = 7.6 Hz, 2 H, H-6/16), 7.51 (s, 8 H, H-22+28), 7.48 (t, ^3J = 7.1 Hz, 4 H, H-7+17), 7.32 (t, ^3J = 7.8 Hz, 4 H, H-8+18), 7.09 (d, ^3J = 7.6 Hz, 4 H, H-9+19), 3.97 – 3.95 (m, 4 H, H-32), 3.77 – 3.75 (m, 4 H, H-33), 3.71 (s, 6 H, H-26), 3.66 – 3.61 (m, 8 H, H-34+35), 2.30 (s, 12 H, H-30), 2.28 (s, 12 H, H-24).

^{13}C-NMR (101 MHz, [D$_6$]-dimethylsulfoxid, 298 K) δ [in ppm] = 156.19 (C-25), 155.17 (C-31), 145.35 (d, $^2J_{pc}$ = 9.7 Hz, C-2/12), 133.47 (d, $^2J_{pc}$ = 9.7 Hz, C-3/13), 132.48 (C-21/27), 132.41 (C-21/27), 131.25 (C-10+20), 130.72 (C-4/14+C-5/15), 130.67 (C-4/14+C-5/15), 130.30 (C-22/28), 130.25 (C-22/28), 129.98 (C-23/29), 129.77 (C-23/29), 128.52 (C-6+16), 126.52 (C-8+18), 125.96 (C-9+19), 125.53 (C-7+17), 122.14 (C-1+11), 71.36 (C-32), 71.01 (C-33/34/35), 69.95 (C-33/34/35), 69.90 (C-33/34/35), 59.26 (C-26), 16.13 (C-24/30), 15.97 (C-24/30).

^{1}H,^{1}H-COSY (400 MHz / 400 MHz, [D$_6$]-dimethylsulfoxid, 298 K) δ [in ppm] = 8.09 / 7.48 (H-6/16 / H-7+17), 8.07 / 7.48 (H-6/16 / H-7+17), 7.51 / 2.30, 2.28 (H-22+28 / H-24, H-30), 7.48 / 8.09, 8.07, 7.32 (H-7+17 / H-6/16, H-6/16, H-8+18), 7.32 / 7.48, 7.09 (H-8+18 / H-7+17, H-9+19), 7.09 / 7.32 (H-9+19 / H-8+18), 2.30 / 7.51 (H-30 / H-22+28), 2.28 / 7.51 (H-24 / H-22+28).

^{1}H,^{13}C-GHSQC (400 MHz / 101 MHz, [D$_6$]-dimethylsulfoxid, 298 K) δ (^{1}H) / δ (^{13}C) [in ppm] = 8.12 / 130.72/130.67 (H-4/14 / C-4/14+C5/15), 8.09 / 128.52 (H-6+16 / C-6+16), 8.07 / 128.52 (H-6+16 / C-6+16), 7.51 / 130.30/130.25 (H-22+28 / C-22/28), 7.48 / 125.53 (H-7+17 / C-7+17), 7.32 / 126.52 (H-8+18 / C-8+18), 7.09 / 125.96 (H-9+19 / C-9+19), 3.97 – 3.95 / 71.36 (H-32 / C-32), 3.77 – 3.75 / 70.01/69.95/69.90 (H-33 / C-33/34/35), 3.71 / 59.26 (H-26 / C-26), 3.66 – 3.61 / 70.01/69.95/69.90 (H-34+35 / C-33/34/35), 2.30 / 16.13/15.97 (H-30 / C-24/30), 2.28 / 16.13/15.97 (H-24 / C-24/30).

^{1}H,^{13}C-GHMBC (400 MHz / 101 MHz, [D$_6$]-dimethylsulfoxid, 298 K) δ (^{1}H) / δ (^{13}C) [in ppm] = 8.12 / 145.35, 132.48/132.41, 131.25, 128.52 (H-4+14 / C-2+12, C-21+27, C-10+20, C-6+16), 8.09 / 131.25, 126.52 (H-6/16 / C-10+20, C-8+18), 8.07 / 131.25, 126.52 (H-6/16 / C-10+20, C-8+18), 7.51 / 156.19, 155.17, 133.47, 130.30/130.25, 16.13, 15.97 (H-22+28 / C-25, C-31, C-3+13, C-22+28, C-30, C-24), 7.48 / 130.72/130.67, 125.96 (H-7+17 / C-4/14+C5/15, C-9+19), 7.32 / 131.25, 128.52 (H-8+18 / C-10+20, C-6+16), 7.09 / 130.72/130.67, 125.53, 122.14 (H-9+19 / C-4/14+C-5/15, C-7+17, C-1+11), 3.97 – 3.95 / 70.01/69.95/69.90 (H-32 / C-33/34/35), 3.77 – 3.75 / 71.36 (H-33 / C-32), 3.71 / 156.19

(H-26 / C-25), 2.30 / 155.17, 130.30/130.25, 129.98/129.77 (H-30 / C-31, C-22/28, C-23/29), 2.28 / 156.19, 130.30/130.25, 129.98/129.77 (H-24 / C-25, C-22/28, C-23/29).

[MT688-5]

^{31}P-NMR (162 MHz, [D_6]- dimethylsulfoxid, 298 K) δ [in ppm] = 1.16

Elemental analysis = calcd (%) for $C_{82}H_{76}O_{15}P_2$: C: 72.24, H: 5.62, O: 17.60; found:

C: 70.2, H: 6.03, O: -

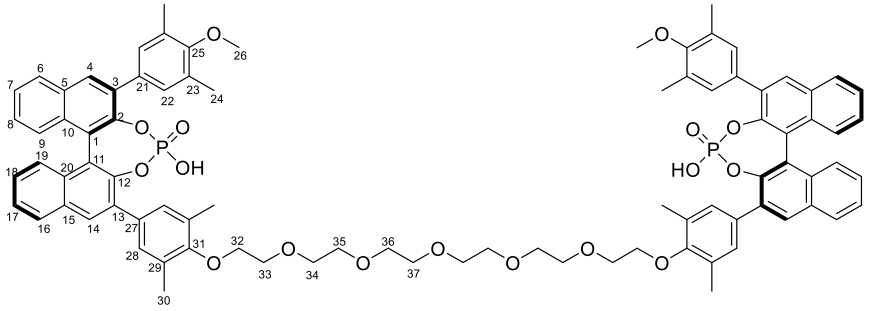
MS (ESI-neg, MeOH**)**: *m/z* = 1361.45968 ([M-H]$^-$, calcd. 1361.45867 for [$C_{82}H_{75}O_{15}P_2^-$].

IR (ATR-FT): $\tilde{\nu}$ (cm^{-1}) = 3063, 3050, 3032, 2980, 2971, 2917, 2886, 2870, 1618, 1593, 1486, 1448, 1392, 1374, 1337, 1297, 1257, 1211, 1160, 1148, 1127, 1086, 1053, 965.

[MT688]

8.2.2.6.12. Synthesis of compound (*R*,*R*)-**8**

Described experiment: MT687 Repeated:



According to general procedure **D**, compound (*R*,*R*)-**93** (91.1 mg, 68.5 µmol, 1 eq), gave the product as a yellow solid (68.7 mg, 47.3 µmol, 69.1%).

$C_{86}H_{84}O_{17}P_2$, MW = 1451.5 g/mol.

^{1}H-NMR (400 MHz, [D$_6$]- dimethylsulfoxid, 298 K) δ [in ppm] = 8.12 (s, 4 H, H-4+14), 8.09 (d, ^3J = 8.3 Hz, 2 H, H-6/16), 8.08 (d, ^3J = 8.1 Hz, 2 H, H-6/16), 7.51 – 7.48 (m, 4 H, H-7+17), 7.50 (s, 4 H, H-22), 7.49 (s, 4 H, H-28), 7.32 (t, ^3J = 7.7 Hz, 4 H, H-8+18), 7.10 (d, ^3J = 7.6 Hz, 4 H, H-9+19), 3.95 – 3.93 (m, 4 H, H-32), 3.74 – 3.72 (m, 4 H, H-33), 3.71 (s, 6 H, H-26), 3.63 – 3.61 (m, 4 H, H-34), 3.58 – 3.52 (m, 12 H, H-35+36+37), 2.29 (s, 24 H, H-24+30).

^{13}C-NMR (101 MHz, [D$_6$]- dimethylsulfoxid, 298 K) δ [in ppm] = 156.21 (C-25), 155.18 (C-31), 145.25 (d, $^2J_{pc}$ = 9.7 Hz, C-2+12), 133.44 (d, $^2J_{pc}$ = 9.7 Hz, C-3+13), 132.45 (C-21/27), 132.37 (C-21/27), 131.23 (C-10+20), 130.78 (C-4/14+C-5/15), 130.70 (C-4/14+C-5/15), 130.29 (C-22/28), 130.23 (C-22/28), 130.00 (C-23/29), 129.80 (C-23/29), 128.54 (C-6+16), 126.56 (C-8+18), 125.97 (C-9+19), 125.58 (C-7+17), 122.12 (C-1+11), 71.34 (C-32), 69.97 (C-34), 69.87 (C-33/35/36/37), 69.85 (C-33/35/36/37), 69.83 (C-33/35/36/37), 59.27 (C-26), 16.13 (C-24/30), 15.98 (C-24/30).

^{1}H,^{1}H-COSY (400 MHz / 400 MHz, [D$_6$]- dimethylsulfoxid, 298 K) δ [in ppm] = 8.09 / 7.51 - 7.48 (H-6/16 / H-7+17), 8.08 / 7.51 - 7.48 (H-6/16 / H-7+17), 7.51 – 7.48 / 8.09, 8.08, 7.32 (H-7+17 / H-6/16, H-6/16, H-8+18), 7.50 / 2.29 (H-22 / H-24+30), 7.49 / 2.29 (H-28 / H-24+30), 7.32 / 7.51 – 7.48, 7.10 (H-8+18 / H-7+17, H-9+19), 7.10 / 7.32 (H-9+19 / H-8+18), 2.29 / 7.50, 7.49 (H-24+30 / H-22, H-28).

^{1}H,^{13}C-GHSQC (400 MHz / 101 MHz, [D$_6$]-dimethylsulfoxid, 298 K) δ (^{1}H) / δ (^{13}C) [in ppm] = 8.12 / 130.78/130.70 (H-4+14 / C-4/14+C5/15), 8.09 / 128.54 (H-6/16 / C-6+16), 8.08 / 128.54 (H-6/16 / C-6+16), 7.51 – 7.48 / 125.58 (H-7+17 / C-7+17), 7.50 / 130.29/130.23 (H-22 / C-22/28), 7.49 / 130.29/130.23 (H-28 / C-22/28), 7.32 / 126.56 (H-8+18 / C-8+18), 7.10 / 125.97 (H-9+19 / C-9+19), 3.95 – 3.93 / 71.34 (H-32 / C-32), 3.74 – 3.72 / 69.87/69.85/69.83 (H-33 / C-33/35/36/37), 3.71 / 59.27 (H-26 / C-26), 3.63 – 3.61/ 69.97 (H-34 / C-34), 3.58 – 3.52 / 69.87/69.85/69.83 (H-35+36+37 / C-33/35/36/37), 2.29 / 16.13, 15.98 (H-24+30 / C-24, C-30).

^{1}H,^{13}C-GHMBC (400 MHz / 101 MHz, [D$_6$]-dimethylsulfoxid, 298 K) δ (^{1}H) / δ (^{13}C) [in ppm] = 8.12 / 145.25, 132.45/132.37, 131.23, 128.54 (H-4+14 / C-2+12, C-21+27, C-10+20, C-6+16), 8.09 / 131.23, 126.56 (H-6/16 / C-10+20, C-8+18), 8.08 / 131.23, 126.56 (H-6/16 / C-10+20, C-8+18), 7.51 – 7.48 / 130.78/130.70, 125.97 (H-7+17 / C-4/14+C5/15, C-9+19), 7.50 / 156.21, 133.44, 130.29/130.23, 130.00/129.80, 15.98 (H-22 / C-25, C-3+13, C-22/28, C-23/29, C-24/30), 7.49 / 155.18, 133.44, 130.29/130.23, 130.00/129.80, 16.13 (H-28 / C-31, C-3+13, C-22/28, C-23/29, C-24/30), 7.32 / 131.23, 128.54, 125.97 (H-8+18 / C-10+20, C-6+16, C-9+19), 7.10 / 130.78/130.70, 125.58, 122.12 (H-9+19 /

C-4/14+C-5/15, C-7+17, C-1+11), 3.74 – 3.72 / 71.34 (H-33 / C-32), 3.71 / 156.21 (H-26 / C-25), 3.58 – 3.52 / 69.87/69.85/69.83 (H-35+36+37 / C-33/35/36/37), 2.29 / 156.21, 155.18 130.00, 129.80 (H-24+30 / C-25, C-31, C-23/29, C-23/29). [MT687-5]

^{31}P-NMR (162 MHz, [D$_6$]- dimethylsulfoxid, 298 K) δ [in ppm] = 1.06

Elemental analysis = calcd (%) for $C_{86}H_{84}O_{17}P_2$: C: 71.16, H: 5.83, O: 18.74; found:

C: 69.8, H: 6.26, O: 18.6

MS (ESI-neg, MeOH**)**: *m/z* = 1449.51283 ([M-H]$^-$, calcd. 1449.51110 for [$C_{86}H_{83}O_{17}P_2^-$].

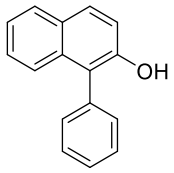
IR (ATR-FT): $\tilde{\nu}$ (cm^{-1}) = 3052, 2980, 2970, 2919, 2889, 2870, 1593, 1486, 1456, 1448, 1421, 1407, 1392, 1337, 1298, 1258, 1213, 1148, 1127, 1086, 1053, 1012, 956.

[MT687]

8.2.3. Substrates

8.2.3.1. Synthesis of compound **66a**[100]

Described experiment: MT632 Repeated:



1-Bromo-2-naphthol (1.00 g, 4.48 mmol, 1 eq), phenylboronic acid **107a** (0.601 g, 4.93 mmol, 1.1 eq), tetrakis(triphenylphosphine)palladium(0) (259 mg, 0.224 mmol, 0.05 eq) and sodium carbonate (0.997 g, 9.41 mmol, 2.1 eq), were dissolved in a degassed solution of toluene (7 ml), ethanol (2 ml) and water (2 ml). The solution was stirred at 95 °C for 20 hours under argon atmosphere. After cooling down to room temperature the solution was diluted with ethyl acetate and water (each 50 ml). The organic layer was separated and washed with a saturated solution of sodium chloride (30 ml). The organic phase was dried over anhydrous sodium sulfate, concentrated in *vacuo* and the crude product was purified by silica gel flash column chromatography (cyclohexane:ethyl acetate = 20:1) to afford the product as a white solid (0.605 g, 2.75 mmol, 61.1 %).

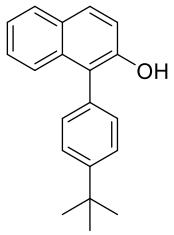
$C_{16}H_{12}O$, MW = 220.3 g/mol.

^{1}H-NMR (400 MHz, [D$_1$]-chloroform, 298 K) δ [in ppm] = 7.83 – 7.80 (m, 2 H, H_{Aryl}), 7.62 – 7.57 (m, 2 H, H_{Aryl}), 7.54 – 7.49 (m, 1 H, H_{Aryl}), 7.44 – 7.38 (m, 3 H, H_{Aryl}), 7.36 – 7.31 (m, 2 H, H_{Aryl}), 7.27 (d, ^3J = 7.7 Hz, 1 H, H_{Aryl}), 5.17 (s, 1 H, H-OH).

[MT632-1]

8.2.3.2. Synthesis of compound **66b**[100]

Described experiment: MT667 Repeated:



1-Brom-2-naphthol (1.00 g, 4.48 mmol, 1 eq), the 4-*tert*-butyl-phenyl boronic acid **107b** (0.872 g, 4.93 mmol, 1.1 eq), tetrakis(triphenylphosphine)palladium(0) (258.84 mg, 0.224 mmol, 0.05 eq) and sodium carbonate (0.997 g, 9.41 mmol, 2.1 eq), were dissolved in a degassed solution of toluene (7 ml), ethanol (2 ml) and water (2 ml). The solution was stirred at 95 °C for 20 hours under argon atmosphere. After cooling down to room temperature the solution was diluted with ethyl acetate and water (each 50 ml). The organic layer was separated and washed with a saturated solution of sodium chloride (30 ml). The organic phase was dried over anhydrous sodium sulfate, concentrated in *vacuo* and the crude product was purified by silica gel flash column chromatography (cyclohexane:ethyl acetate = 20:1) to afford the product as a white solid (0.961 g, 3.48 mmol, 77.6 %).

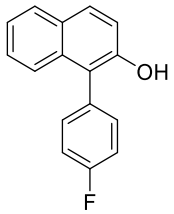
$C_{20}H_{20}O$, MW = 276.4 g/mol.

^{1}H-NMR (400 MHz, [D$_1$]-chloroform, 298 K) δ [in ppm] = 7.71 – 7.67 (m, 2 H, H_{Aryl}), 7.50 – 7.48 (m, 2 H, H_{Aryl}), 7.36 – 7.34 (m, 1 H, H_{Aryl}), 7.26 – 7.20 (m, 4 H, H_{Aryl}), 7.16 (d, ^3J = 7.7 Hz, 1 H, H_{Aryl}), 1.32 (s, 9 H, $H_{tert\text{-butyl}}$).

[MT667-4]

8.2.3.3. Synthesis of compound **66c**[100]

Described experiment: MT662 Repeated:



1-Bromo-2-naphthol (1.00 g, 4.48 mmol, 1 eq), the 4-fluorophenyl boronic acid **107c** (0.689 g, 4.93 mmol, 1.1 eq), tetrakis(triphenylphosphine)palladium(0) (258.84 mg, 0.224 mmol, 0.05 eq) and sodium carbonate (0.997 g, 9.41 mmol, 2.1 eq), were dissolved in a degassed solution of toluene (7 ml), ethanol (2 ml) and water (2 ml). The solution was stirred at 95 °C for 20 hours under argon atmosphere. After cooling down to room temperature the solution was diluted with ethyl acetate and water (each 50 ml). The organic layer was separated and washed with a saturated solution of sodium chloride (30 ml). The organic phase was dried over anhydrous sodium sulfate, concentrated in *vacuo* and the crude product was purified by silica gel flash column chromatography (cyclohexane:ethyl acetate = 20:1) to afford the product as a white solid (0.623 g, 2.62 mmol, 58.4 %).

$C_{16}H_{11}OF$, MW = 238.3 g/mol.

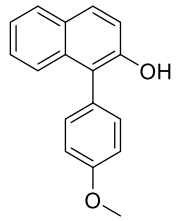
^{1}H-NMR (400 MHz, [D$_1$]-chloroform, 298 K) δ [in ppm] = 7.73 – 7.71 (m, 2 H, H_{Aryl}), 7.33 – 7.29 (m, 2 H, H_{Aryl}), 7.26 – 7.23 (m, 3 H, H_{Aryl}), 7.21 – 7.15 (m, 3 H, H_{Aryl}), 4.94 (s, 1 H, H-OH).

^{19}F-NMR (377 MHz, [D$_1$]-chloroform, 298 K) δ [in ppm] = -113.06

[MT662-4]

8.2.3.4. Synthesis of compound **66d**[100]

Described experiment: MT670 Repeated:



1-Brom-2-naphthol (1.00 g, 4.48 mmol, 1 eq), 4-methoxyphenyl boronic acid **107d** (0.744 g, 4.93 mmol, 1.1 eq), tetrakis(triphenylphosphine)palladium(0) (258.84 mg, 0.224 mmol, 0.05 eq) and sodium carbonate (0.997 g, 9.41 mmol, 2.1 eq), were dissolved in a degassed solution of toluene (7 ml), ethanol (2 ml) and water (2 ml). The solution was stirred at 95 °C for 20 hours under argon atmosphere. After cooling down to room temperature the solution was diluted with ethyl acetate and water (each 50 ml). The organic layer was separated and washed with a saturated solution of sodium chloride (30 ml). The organic phase was dried over anhydrous sodium sulfate, concentrated in *vacuo* and the crude product was purified by silica gel flash column chromatography (cyclohexane:ethyl acetate = 20:1) to afford the product as a white solid (0.901 g, 3.59 mmol, 80.4 %).

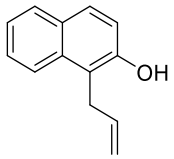
$C_{16}H_{11}OF$, MW = 238.3 g/mol.

^{1}H-NMR (400 MHz, [D$_1$]-chloroform, 298 K) δ [in ppm] = 7.75 – 7.71 (m, 2 H, H_{Aryl}), 7.37 – 7.34 (m, 1 H, H_{Aryl}), 7.29 – 7.23 (m, 4 H, H_{Aryl}), 7.20 – 7.18 (m, 1 H, H_{Aryl}), 7.06 – 7.02 (m, 2 H, H_{Aryl}), 5.13 (s, 1 H, H-OH), 3.82 (s, 3 H, H_{Methyl}).

[MT670-4]

8.2.3.5. Synthesis of compound **66e**[107]

Described experiment: MT676 Repeated:



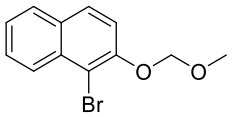
2-Naphthol (1.00 g, 6.94 mmol, 1 eq), allyl alcohol (1.21 g, 1.42 ml, 20.8 mmol, 3 eq), tetrakis(triphenylphosphine)palladium(0) (400 mg, 0.347 mmol, 0.05 eq) were dissolved in dry tetrahydrofurane (15 ml). Then triethylborane (20.8 ml, 1 M in hexane, 20.8 mmol, 3 eq) was carefully added. The solution was stirred at 25 °C for 24 hours under argon atmosphere. The solution was diluted with ethyl acetate and water (each 50 ml). The organic layer was washed with a solution of 2 M hydrochloric acid, a saturated solution of sodium hydrogencarbonate and a saturated solution of sodium chloride (50 ml each). The organic phase was dried over anhydrous sodium sulfate, concentrated in *vacuo* and the crude product was purified by silica gel flash column chromatography (cyclohexane:ethyl acetate = 20:1) to afford the product as a white solid (0.315 mg, 1.71 mmol, 25.1 %).

$C_{13}H_{12}O$, MW = 238.3 g/mol.

^{1}H-NMR (400 MHz, [D$_1$]-chloroform, 298 K) δ [in ppm] = 7.91 (d, ^3J = 8.6 Hz, 1 H, H_{Aryl}), 7.79 (d, ^3J = 7.6 Hz, 1 H, H_{Aryl}), 7.68 (d, ^3J = 8.9 Hz, 1 H, H_{Aryl}), 7.48 (ddd, ^3J = 8.3 Hz, 6.8 Hz, ^4J = 1.2 Hz,1 H, H_{Aryl}), 7.34 (ddd, ^3J = 7.6 Hz, 6.7 Hz, ^2J = 1.4 Hz,1 H, H_{Aryl}), 7.10 (d, ^3J = 8.6 Hz, 1 H, H_{Aryl}), 6.13 – 6.03 (m, 1 H, H_{allyl}), 5.13 – 5.05 (m, 2 H, H_{allyl}), 3.85 – 3.82 (m, 2 H, H_{allyl}) [MT676-1]

8.2.3.6. Synthesis of compound **109**[108]

Described experiment: MT683 Repeated:



1-Brom-2-naphthol (1.00 g, 4.48 mmol, 1 eq.) was dissolved in dried dichloromethane (25 ml). Then at 0 °C *N*-Ethyl-*N*-(propan-2-yl)propan-2-amine (0.637 g, 0.858 ml, 4.93 mmol, 1.1 eq.) and (chlormethyl)methylether (396 mg, 374 µl, 0.224 mmol, 1.1 eq.) were added. The solution was stirred at 25 °C for 20 hours under argon atmosphere. The solution was diluted with methanol (20 ml). The organic layer was washed with a saturated solution of sodium chloride (20 ml). The organic phase was dried over anhydrous sodium sulfate, concentrated in *vacuo* and the crude product was purified by silica gel flash column chromatography (cyclohexane:ethyl acetate = 10:1) to afford the product as a white solid (1.01 g, 3.78 mmol, 84.4 %).

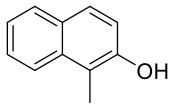
$C_{16}H_{11}OF$, MW = 238.3 g/mol.

^{1}H-NMR (400 MHz, [D$_1$]-chloroform, 298 K) δ [in ppm] = 8.24 (d, ^3J = 8.7 Hz, 2 H, H_{Aryl}), 7.79 (d, ^3J = 8.7 Hz, 2 H, H_{Aryl}), 7.58 (ddd, ^3J = 7.8 Hz, 6.8 Hz, ^4J = 1.3 Hz, 1 H, H_{Aryl}), 7.45 – 7.41 (m, 2 H, H_{Aryl}), 5.37 (s, 2 H, $H_{Methylen}$), 3.58 (s, 3 H, H_{Methyl}).

[MT683-3]

8.2.3.7. Synthesis of compound **66f**[108]

Described experiment: MT685 Repeated:



Compound **109** (1.01 g, 3.78 mmol, 1 eq) was dissolved in dry tetrahydrofuran (25 ml). Then at -78 °*n*-butyllithium (1.81 ml, 2.7 M in toluene, 4.16 mmol, 1.1 eq) was added and stirred for one hour at -78 °C. Then at -78 °C methyl iodide (5.37 g, 2.36 ml, 37.8 mmol, 10 eq) was added. The solution was stirred at -78 °C for 15 minutes and slowly warmed to 25 °C. Then ammonium chloride (50 ml) and ethyl acetate were added. The organic layer was separated and was washed with a saturated solutio of sodium chloride (50 ml). The organic phase was dried over anhydrous sodium sulfate, concentrated in *vacuo* and the crude product was purified by silica gel flash column chromatography (cyclohexane:ethyl acetate = 10:1). The pure product **110** could not be isolated, due to impurities of already MOM-deprotected compound, but was used for the next step. The solid was dissolved in dry methanol (10 ml). Then concentrated hydrochloric acid (0.815 ml) was added and the solution was stirred at 25 °C for 24 hours. The solvent was removed to afford the product as a white solid (1.01 g, 3.78 mmol, 84.4 %).

$C_{11}H_{10}O$, MW = 158.2 g/mol.

^{1}H-NMR (400 MHz, [D_1]-chloroform, 298 K) δ [in ppm] = 7.92 (d, ^3J = 8.7 Hz, 1 H, H_{Aryl}), 7.77 (d, ^3J = 8.7 Hz, 1 H, H_{Aryl}), 7.63 (d, ^3J = 8.7 Hz, 1 H, H_{Aryl}), 7.49 (dt, ^3J = 7.9 Hz, ^4J = 1.4 Hz, 1 H, H_{Aryl}), 7.34 (ddd, ^3J = 7.9 Hz, 6.5 Hz, ^4J = 1.4 Hz, 1 H, H_{Aryl}), 7.07 (d, ^3J = 8.7 Hz, 1 H, H_{Aryl}), 2.54 (s, 3 H, H_{Methyl}) [MT693-2]

8.3.X-Ray crystal structure analyses

8.3.1. Compounds **25-43**

The crystals were mounted on nylon loops in inert oil. Data were collected on a Bruker AXS D8 Kappa diffractometer with APEX2 detector (mono-chromated $Mo_{K\alpha}$ radiation, λ = 0.71073 Å) at 100(2) K. Data of mt_383m_sq were collected on a Bruker AXS D8 Venture diffractometer with Photon II detector (mono-chromated $Cu_{K\alpha}$ radiation, λ = 1.54178 Å, mirco-focus source).The structures were solved by Direct Methods (SHELXS-97)[120] and refined anisotropically by full-matrix least-squares on F^2 (SHELXL-2014)[121,122]. Absorption corrections were performed semi-empirically from equivalent reflections on basis of multi-scans (Bruker AXS APEX2/3). Hydrogen atoms were refined using a riding model or rigid methyl groups. The OH hydrogen atoms of fos016_4[123] and mt_317_2 were refined freely. In fos016_27 the hydrogen atoms of NH groups were refined freely. Those of the methanol molecule were refined using AFIX 147 i.e. rotating refinement with a bond angle fixed to the tetrahedral angle. In case of the disordered molecules they were restraint to point towards the most reasonable H bond acceptor employing a FLAT restraint. This was not possible for H95K. Since its position did not converge properly the refinement was damped to settle its position. In st010_4[124] the NH hydrogen atoms were refined freely with its NH bond length restraint to 0.87 Å and its displacement parameter constrained to 1.2 times the U eq of the connecting N atom.

In fos016_27 the atoms of the disordered solvent molecules could only be refined isotropically. The phenyl ring of the toluene molecule was constraint to a regular hexagon. Despite the use of distance restraints (SADI, DFIX) in some cases the bond length are not very realistic and should be ignored. The residual electron density suggests further disorder components of methanol 95 which could not be modeled properly. Mt_240_23 and mt_317_2 were refined as an inversion twin. Thus, the enantiopurity of Mt_240_23 cannot be confirmed. In mt_383m_sq the central phenyl ring is disordered over the two-fold axis. Two alternate positions were used in the refinement and the local symmetry was ignored in the refinement (negative PART). The bond lengths were restrained to be equal to 1.39 Å (DFIX, σ = 0.001) and the angle were restrained to be equal (SADI, σ = 0.001). The ring was restrained to planarity (FLAT, σ = 0.001). All atoms of both positions were refined with common displacement parameters (EADP) and the connecting atoms (C30, C30' and C36, C36') were constrained to equal positions (EXYZ). In addition, the structure contains highly disordered solvent – possibly methanol. The final refinement was done with a solvent free dataset from a PLATON/SQUEEZE[125] run. Since the nature and amount of the solvent is not clear it was not included in the sum formula. The Flack parameter suggests twinning by inversion, however refining so yields a very high standard uncertainty for the BASF rendering it meaningless. Thus, the twinning model was discarded. The chosen chirality resembles chemical expectation but should not be considered reliable. St_010 contains highly disordered solvent – possibly chloroform. The final refinement was done with a solvent free dataset from a

[120] G. M. Sheldrick, *Acta Crystallogr.* 1990, **A46**, 467
[121] G. M. Sheldrick, SHELXL-2014, Program for the Refinement of Crystal Structures University of Göttingen, Göttingen (Germany) **2014**. (see also: Sheldrick, G. M. Acta Crystallogr. 2008, **A64**, 112).
[122] shelXle, *A Qt GUI for SHELXL*, C. B. Hübschle, G. M. Sheldrick, B. Dittrich, *J. Appl. Cryst.* **2011**, *44*, 1281-1284.
[123] F. Octa-Smolin, *1,1'-Binaphthyl Based Bis- and Tris-Phosphoric Acids: Syntheses and Application as Fluorescent Chemosensors*, Dissertation, Universität Duisburg-Essen, **2018**.
[124] S. Thölke, *Versuche zur Herstellung von 3,3´-disubstituierten Binaphthyl-Guanidinen*, Bachelor thesis, Universität Duisburg-Essen, **2015**.
[125] PLATON/SQUEEZE, P. van der Sluis, A. L. Spek, *Acta Crystallogr.* **1990**, *A46*, 194-201

PLATON/SQUEEZE[125] run. Since the nature and amount of the solvent is not clear it was not included in the sum formula.

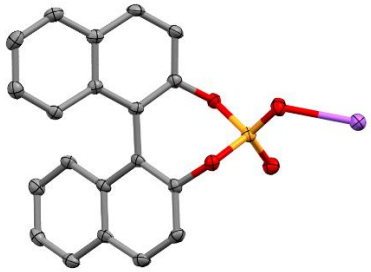


Figure 81: Molecular structure of (*rac*)-**25** in the solid state. Only (*S*)-isomer shown, solvent molecules and hydrogen atoms omitted for clarity and thermal ellipsoids set at the 60% probability level.

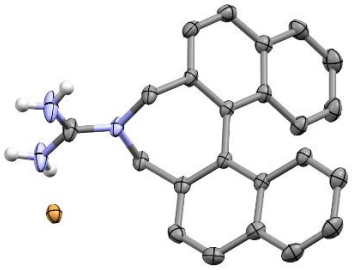


Figure 82: Molecular structure of (*rac*)-**26** in the solid state. Only (*S*)-isomer shown, hydrogen atoms omitted for clarity and thermal ellipsoids set at the 60% probability level.

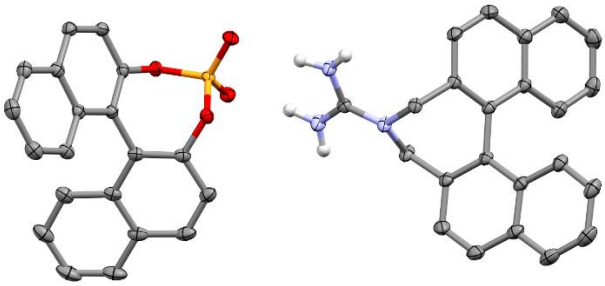


Figure 83: Molecular structure of complex (*rac*)-**25** + (*rac*)-**26** in the solid state. Only (*S*,*S*)-isomer shown, solvent molecules and hydrogen atoms omitted for clarity and thermal ellipsoids set at the 60% probability level.

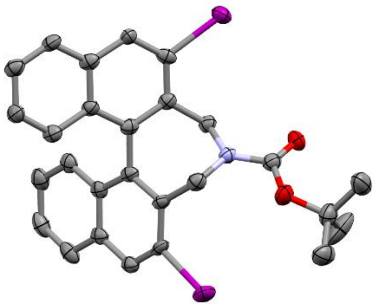


Figure 84: Molecular structure of (*S*)-**42** in the solid state. Solvent molecules and hydrogen atoms omitted for clarity and thermal ellipsoids set at the 50% probability level.

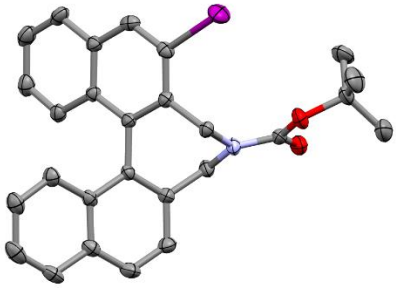


Figure 85: Molecular structure of (*R*)-**36** in the solid state. Hydrogen atoms omitted for clarity and thermal ellipsoids set at the 50% probability level. Monoiodide **36** was analyzed as the (*R*)-isomer because suitable crystals could only be obtained in this case.

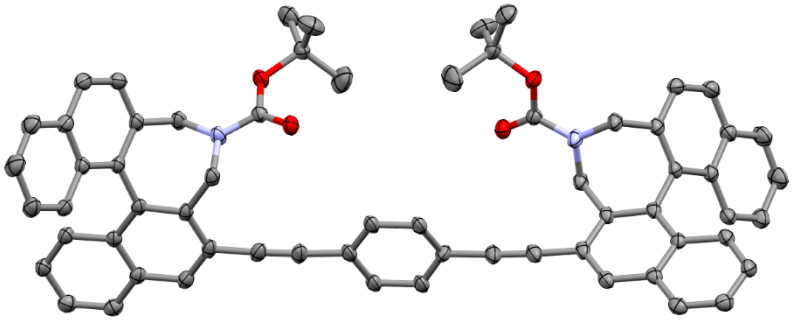


Figure 86: olecular structure of (*S*,*S*)-**43** in the solid state. Hydrogen atoms omitted for clarity and thermal ellipsoids set at the 50% probability level. Only one orientation of the disorder is displayed for clarity.

Table 12: Details of the X-ray crystal structure analyses of (*rac*)-**25**, (*rac*)-**26** and (*S*)-**36**.

Compound	(*rac*)-**1**	(*rac*)-**1** + (*rac*)-**2**	(*S*)-**5**
Identification code	**fos016_4m**	**fos016_27m**	**mt_240_23_mom**
CCDC-Number	2078130	2078131	2078132
Empirical formula	$C_{22}H_{20}NaO_6P$	$C_{44.92}H_{38.29}N_3O_{5.43}P$	$C_{27}H_{24}I\ NO_2$
M	434.34	738	521.37
Crystal size [mm]	0.325 × 0.189 × 0.076	0.259 × 0.258 × 0.201	0.378 × 0.246 × 0.192
T [K]	100(1)	100(1)	100(2)
Crystal system	monoclinic	triclinic	monoclinic
Space group	$P2_1/c$	*P* -1	$P2_1$
a [Å]	19.211(2)	18.1178(12)	10.158(5)
b [Å]	8.5749(9)	19.5762(12)	9.420(4)
c [Å]	12.3647(13)	22.3911(12)	12.633(5)
α [°]	90	80.708(3)	90
β [°]	97.328(7)	72.212(2)	108.94(2)
γ [°]	90	86.459(3)	90
V [Å$_3$]	2020.2(4)	7462.1(8)	1143.4(8)
Z	4	8	2
D_{calc} [g·cm^{-1}]	1.428	1.314	1.514
μ(Mo$K\alpha$ [mm^{-1}])	0.195	0.127	1.424
Transmissions	1/0.77	0.75/0.68	0.75/0.51
F(000)	904	3098	524
Index ranges	-28 ≤ *h* ≤ 27	-27 ≤ *h* ≤ 27	-15 ≤ *h* ≤ 15
	-12 ≤ *k* ≤ 9	-27 ≤ *k* ≤ 27	-14 ≤ *k* ≤ 13
	-17 ≤ *l* ≤ 18	-32 ≤ *l* ≤ 33	-19 ≤ *l* ≤ 19
ϑ_{max} [°]	33.235	33.203	33.14
Reflections collected	20004	153929	40148
Independent reflections	6780	50065	8111
R_{int}	0.0491	0.0315	0.0541
Refined parameters	281	2038	284
R_1 [$I > 2\sigma(I)$]	0.049	0.0545	0.0544
wR_2 [all data]	0.1348	0.1584	0.1386
x(Flack)			0.22(3)
GooF	1.011	1.032	1.052
$\Delta\rho_{final}$ (max/min) [e·Å^{-3}]	0.454/-0.618	1.466/-0.801	2.000/-1.129

Table 13: Details of the X-ray crystal structure analyses of (*S,S*)-**42**, (*S*)-**43** and (*rac*)-**26**.

Compound	(*S,S*)-**6**	(*S*)-**4**	(*rac*)-**2**
Identification code	**mt_317_2m**	**mt_383m_sq**	**st010_4m**
CCDC-Number	2078133	2078134	2078135
Empirical formula	$C_{28}H_{27}I_2NO_3$	$C_{64}H_{52}N_2O_4$	$C_{23}H_{20}BrN_3$
M	679.3	913.07	418.33
Crystal size [mm]	0.261 × 0.173 × 0.011	0.101 × 0.079 × 0.052	0.173 × 0.125 × 0.095
T [K]	100(2)	104(2)	100(1)
Crystal system	monoclinic	tetragonal	triclinic
Space group	$P2_1$	$P4_32_12$	*P* -1
a [Å]	11.8508(16)	10.0422(3)	8.8577(2)
b [Å]	9.1039(12)	10.0422(3)	8.9307(2)
c [Å]	13.2298(17)	53.3248(16)	18.7699(4)
α [°]	90	90	91.7000(10)
β [°]	115.219(6)	90	93.9750(10)
γ [°]	90	90	108.2000(10)
V [Å3]	1291.3(3)	5377.6(4)	1405.06(5)
Z	2	4	2
D_{calc} [g·cm-3]	1.747	1.128	0.989
μ(Cu$K\alpha$ [mm-1])	19.363	0.547	1.471
Transmissions	0.75/0.44	0.75/0.68	0.75/0.61
F(000)	664	1928	428
Index ranges	-15 ≤ *h* ≤ 15	-12 ≤ *h* ≤ 12	-10 ≤ *h* ≤ 13
	-11 ≤ *k* ≤ 10	-11 ≤ *k* ≤ 12	-13 ≤ *k* ≤ 9
	-16 ≤ *l* ≤ 16	-68 ≤ *l* ≤ 66	-28 ≤ *l* ≤ 27
ϑ_{max} [°]	81.331	79.876	32.575
Reflections collected	49382	84164	38397
Independent reflections	5431	5790	9887
R_{int}	0.0778	0.0412	0.033
Refined parameters	316	328	260
R_1 [$I > 2\sigma(I)$]	0.0427	0.0453	0.0464
wR_2 [all data]	0.1088	0.1217	0.1212
x(Flack)	0.163(12)	0.24(5)	
GooF	1.064	1.028	1.052
$\Delta\rho_{final}$ (max/min) [e·Å-3]	2.152/-0.577	0.521/-0.574	0.851/-0.381

8.3.2. Compounds **76a** and **70a**

The crystals were mounted on nylon loops in inert oil. The data of **mt_364edukt** were collected on a Bruker AXS D8 Kappa diffractometer with APEX2 detector (mono-chromated $Mo_{K\alpha}$ radiation, λ = 0.71073 Å) and the data of **mt_610** on a Bruker AXS D8 Venture diffractometer with Photon II detector (mono-chromated $Cu_{K\alpha}$ radiation, λ = 1.54178 Å, mirco-focus source) at 100(2) K. The structures were solved by Direct Methods (SHELXS-97)[120] and refined anisotropically by full-matrix least-squares on F^2 (SHELXL-2017)[121,122]. Absorption corrections were performed semi-empirically from equivalent reflections on basis of multi-scans (Bruker AXS APEX3). Hydrogen atoms were refined using a riding model or rigid methyl groups. The absolute structure of **mt_364edukt** and **mt_610** could be determined reliably. Parsons quotient method was used to determine the absolute structure parameter *x*. For more details see S. Parsons, H. D. Flack, *Acta Cryst. A60* (**2004**), s61 and S. Parsons, H. D. Flack, T. Wagner, *Acta Cryst. B69* (**2013**), 249-259. However, the found enantiomer of **mt_364edukt** is the inverse of the expected one.

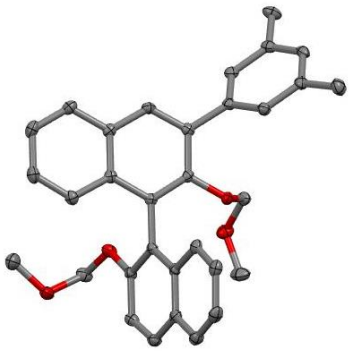


Figure 87: Molecular structure of (*R*)-**76a** in the solid state. Solvent molecules and hydrogen atoms omitted for clarity and thermal ellipsoids set at the 50% probability level.

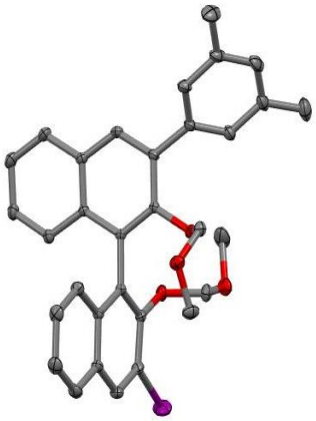


Figure 88: Molecular structure of (*R*)-**70a** in the solid state. Solvent molecules and hydrogen atoms omitted for clarity and thermal ellipsoids set at the 50% probability level.

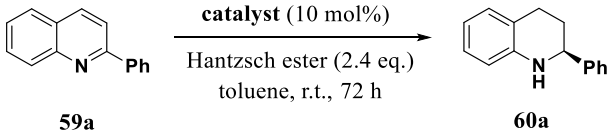
Table 14: Details of the X-ray crystal structure analyses of (*R*)-**76a** and (*R*)-**70a**.

Identification code	**mt_364eduktm**	**mt_610m**
CCDC deposition number		
Empirical formula	$C_{32}H_{29}IO_4$	$C_{32}H_{30}O_4$
M	604.45	478.56
Crystal size [mm]	0.257 × 0.208 × 0.090	0.246 × 0.180 × 0.093
T [K]	100(2)	100(2)
Crystal system	monoclinic	orthorhombic
Space group	$P2_1$	$P2_12_12_1$
a [Å]	10.8890(7)	7.4811(5)
b [Å]	10.8895(7)	9.1846(6)
c [Å]	11.8792(8)	36.885(2)
α [°]	90	90
β [°]	105.4902(19)	90
γ [°]	90	90
V [Å^3]	1357.42(15)	2534.4(3)
Z	2	4
D_{calc} [g·cm^{-3}]	1.479	1.254
μ(Mo/CuK_α [mm^{-1}])	1.215	0.649
Transmissions	0.75/0.67	0.75/0.65
F(000)	612	1016
Index ranges	-18 ≤ *h* ≤ 18	-7 ≤ *h* ≤ 9
	-18 ≤ *k* ≤ 18	-11 ≤ *k* ≤ 11
	-19 ≤ *l* ≤ 19	-47 ≤ *l* ≤ 46
ϑ_{max} [°]	36.602	80.311
Reflections collected	81592	78891
Independent reflections	13378	5538
R_{int}	0.0261	0.0397
Refined parameters	338	329
R_1 [$I > 2\sigma(I)$]	0.0297	0.0261
wR_2 [all data]	0.0778	0.0670
x(Flack)	0.025(3)	-0.01(2)
GooF	1.037	1.030
$\Delta\rho_{final}$ (max/min) [e·Å^{-3}]	2.194/-0.568	0.161/-0.177

8.4.Catalyzed transfer hydrogenation reaction[95,126]

8.4.1. Catalyst and conditions screening

Described experiments: SF006 (entry 1), SF011 (entry 2), SF007 (entry 3), SF012 (entry 4), SF008 (entry5), SF027 (entry 6), SF014 (entry7), SF026 (entry 8), SF009 (entry9), SF016 (entry 10), SF015 (entry 11), SF024 (entry 12), SF030 (entry 13), SF010 (entry 14), SF023 (entry 15), SF076 (entry 16), SF078 (entry 17), SF077 (entry 18), SF079 (entry 19), SF104 (entry 20).



59a **60a**

Under argon atmosphere 2-phenyl-quinoline (**59a**, 7.00 mg, 34.1 µmol, 1 eq) and Hantzsch ethyl ester (20.7 mg, 81.8 µmol, 2.4 eq) were dissolved. in dry toluene (3 mL). The respective catalyst was also dissolved in dry toluene (2 mL) and was added to the reaction mixture. After stirring for 140 or 72 hours the solvent was evaporated *in vacuo*. After purification of the crude product by flash column chromatography on silica gel (1.5 x 30 cm, cyclohexane : ethyl acetate = 31:1), the pure product **60a** was obtained as an off-white solid.

The enantiomeric excess was determined by chiral HPLC (Chiralcel OD-H column (0.46 x 25 cm), *n*-hexane : isopropanol = 95:5, 1.0 mL/min).

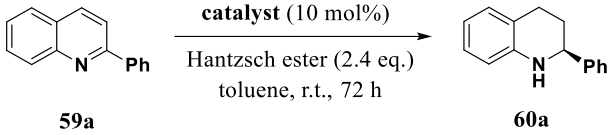
[126] This chapter is developed in the bachelor thesis of Sophia Stadtfeld, Supervisor Maike Thiele

Table 15: reaction conditions, yields and enantiomeric excesses for different catalysts.

entry	cat.	cat. loading [mol%]	solvent	temperature [°C]	time [h]	yield [%]	*ee*[a][b] [%]
1	(rac*)*-**43**	10	toluene[c]	25	72	77	0
2	(*R*)-**13**	10	toluene	25	72	89	80
3	(*R*)-**12a**	10	toluene	25	72	99	28
4	(*R*)-**12a**	10	toluene	25	72	82	28
5	(*R*)-**12b**	10	toluene	25	72	71	52
6	(*R*)-**12b**	10	toluene	25	72	77	48
7	(*R*,*R*)-**4a**	10	toluene	25	140	90	36
8	(*R*,*R*)-**4a**	10	toluene	25	72	52	36
9	(*R*,*R*)-**4b**	10	toluene	25	140	68	23
10	(*R*,*R*)-**4b**	10	toluene	25	72	95	24
11	(*R*,*R*)-**5**	10	toluene	25	140	73	38
12	(*R*,*R*)-**5**	10	toluene	25	72	51	37
16	(*R*,*R*)-**6**	10	toluene	25	72	91	87
14	(*R*,*R*)-**9**	10	toluene	25	140	72	64
15	(*R*,*R*)-**9**	10	toluene	25	72	63	64
16	(*R*,*R*)-**7**	1	toluene	25	72	80	93
17	(*R*,*R*)-**10**	1	toluene	25	72	67	92
18	(*R*,*R*)-**8**	1	toluene	25	72	83	93
19	(*R*,*R*)-**11**	1	toluene	25	72	96	93
20	**TRIP**	1	toluene	25	72	86	96

[a] values for the (*R*)-enantiomer; [b] determined by chiral HPLC. Values are given for the (*S*)-enantiomer.

Described experiments: SF032 (entry 1), SF022 (entry 2), SF019 (entry 3), SF011 (entry 4), SF021 (entry 5), SF033 (entry 6), SF033 (entry 7), SF068 (entry 8), SF030 (entry 9), SF069 (entry 10), SF021 (entry 11), SF034 (entry 12), SF071 (entry 13), SF010 (entry 14), SF023 (entry 15).



59a **60a**

Table 16: Reaction conditions, yields and enantiomeric excesses for different concentrations of catalyst (*R*,*R*)-**6**/**9** and (*R*)-**13**.

entry	cat.	cat. loading [mol%]	solvent	temperature [°C]	time [h]	yield [%]	*ee*[a][b] [%]
1	(*R*)-**13**	0.25	toluene	25	72	61	18
2	(*R*)-**13**	1	toluene	25	72	56	56
3	(*R*)-**13**	6	toluene	25	72	87	76
4	(*R*)-**13**	10	toluene	25	72	89	80
5	(*R*)-**13**	20	toluene	25	72	93	86
6	(*R*,*R*)-**6**	0.25	toluene	25	72	83	84
7	(*R*,*R*)-**6**	1	toluene	25	72	94	87
8	(*R*,*R*)-**6**	6	toluene	25	72	75	84
9	(*R*,*R*)-**6**	10	toluene	25	72	91	87
10	(*R*,*R*)-**6**	20	toluene	25	72	86	84
11	(*R*,*R*)-**9**	0.25	toluene	25	72	63	65
12	(*R*,*R*)-**9**	1	toluene	25	72	67	57
13	(*R*,*R*)-**9**	6	toluene	25	72	81	-
14	(*R*,*R*)-**9**	10	toluene	25	72	63	64
15	(*R*,*R*)-**9**	20	toluene	25	72	61	62

[a] values for the (*R*)-enantiomer; [b] determined by chiral HPLC. Values are given for the (*S*)-enantiomer.

8.4.2. Influence of chain-length in catalysts (*R*,*R*)-**6/7/8** and (*R*,*R*)-**9/10/11**

Described experiments: SF033 (entry 1), SF076 (entry 2), SF077 (entry 3), SF034 (entry 4), SF078 (entry 5), SF079 (entry 6), SF094 (entry 7), SF077 (entry 8), SF090 (entry 9), SF098 (entry 10), SF102 (entry 11), SF079 (entry 12), SF089 (entry 13), SF099 (entry 14).

Under argon atmosphere 2-phenyl-quinoline (**59a**, 7.00 mg, 34.1 µmol, 1 eq) and Hantzsch ethyl ester (20.7 mg, 81.8 µmol, 2.4 eq) were dissolved. in dry toluene (3 mL). The respective catalyst was also dissolved in dry toluene (2 mL) and was added to the reaction mixture. After stirring for 140 or 72 hours the solvent was evaporated *in vacuo*. After purification of the crude product by flash column chromatography on silica gel (1.5 x 30 cm, cyclohexane : ethyl acetate = 31:1), the pure product **60a** was obtained as an off-white solid.

The enantiomeric excess was determined by chiral HPLC (Chiralcel OD-H column (0.46 x 25 cm), *n*-hexane : isopropanol = 95:5, 1.0 mL/min).

Table 17: Influence of chain length in the transfer-hydrogenation of 2 phenylquinoline **59a** for catalysts (*R*,*R*)-**6**/**7**/**8**/**9**/**10**/**11**.

entry	cat.	cat. loading [mol%]	solvent	temperature [°C]	time [h]	yield [%]	*ee*[a][b] [%]
1	(*R*,*R*)-**6**	1	toluene	25	72	94	87
2	(*R*,*R*)-**7**	1	toluene	25	72	80	92.5
3	(*R*,*R*)-**8**	1	toluene	25	72	83	93
4	(*R*,*R*)-**9**	1	toluene	25	72	67	57
5	(*R*,*R*)-**10**	1	toluene	25	72	67	92
6	(*R*,*R*)-**11**	1	toluene	25	72	96	93

[a] values for the (*R*)-enantiomer; [b] determined by chiral HPLC. Values are given for the (*S*)-enantiomer.

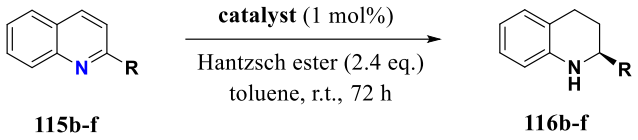
Table 18: Influence of catalyst loadings in the transfer-hydrogenation of 2 phenylquinoline 59a for catalysts (*R*,*R*)-**8**/**11**.

entry	cat.	cat. loading [mol%]	solvent	temperature [°C]	time [h]	yield [%]	*ee*[a][b] [%]
7	(*R*,*R*)-**8**	0.25	toluene	25	72	83	87
8	(*R*,*R*)-**8**	1	toluene	25	72	83	93
9	(*R*,*R*)-**8**	3	toluene	25	72	75	94
10	(*R*,*R*)-**8**	20	toluene	25	72	85	92.5
11	(*R*,*R*)-**11**	0.25	toluene	25	72	73	78
12	(*R*,*R*)-**11**	1	toluene	25	72	96	92.5
13	(*R*,*R*)-**11**	3	toluene	25	72	78	95
14	(*R*,*R*)-**11**	20	toluene	25	72	91	94.5

[a] values for the (*R*)-enantiomer; [b] determined by chiral HPLC. Values are given for the (*S*)-enantiomer.

8.4.3. Catalyzed transfer hydrogenation reaction of quinoline derivates

Described experiments: SF022 (entry 1), SF050 (entry 2), SF039 (entry 3), SF048 (entry 4), SF058 (entry 5), SF056 (entry 6), SF033 (entry 7), SF037 (entry 8), SF041 (entry 9), SF057 (entry 10), SF051 (entry 11), SF054 (entry 12), SF034 (entry 13), SF038 (entry 14), SF042 (entry 15), SF046 (entry 16), SF052 (entry 17), SF055 (entry 18), SF077 (entry 19), SF084 (entry 20), SF087 (entry 21), SF081 (entry 22), SF096 (entry 23), SF092 (entry 24), SF079 (entry 25), SF085 (entry 26), SF086 (entry 27), SF083 (entry 28), SF097 (entry 29), SF093 (entry 30).



115b-f **116b-f**

b: R = C_6H_5-F
c: R = C_6H_5-OMe
d: R = C_6H_5-CO_2Me
e: R = C_6H_6-tBu
f: R = C_4H_4O

b: R = C_6H_5-F
c: R = C_6H_5-OMe
d: R = C_6H_5-CO_2Me
e: R = C_6H_6-tBu
f: R = C_4H_4O

Under argon atmosphere the quinoline derivative **59a-g** (1 eq) and Hantzsch ethyl ester (2.4 eq) were dissolved. in dry toluene (3 mL). The respective catalyst (0.01 eq) was also dissolved in dry toluene (2 mL) and was added to the reaction mixture. After stirring for 72 hours the solvent was evaporated *in vacuo*. After the purification of the crude product by flash column chromatography on silica gel (1.5 x 30 cm, cyclohexane : ethyl acetate = 25:1 (**59a**), 20:1 (**59b**), 5:1 (**59c**), 35:1 (**59d**), 20:1 (**59e**), 15:1 (**59f**), the pure product **60a-f** was obtained.

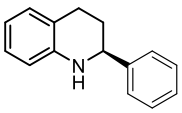
The enantiomeric excess was determined by chiral HPLC (Chiralcel OD-H column (0.46 x 25 cm), *n*-hexane : isopropanol = 95:5, 1.0 mL/min for **60a/b/c/d/f**).

Table 19: reaction conditions, yields and enantiomeric excesses for different catalysts.

entry	cat.	substrate	cat. loading [mol%]	solvent	temperature [°C]	time [h]	yield [%]	*ee*[a][b] [%]
1	(*R*)-**13**	**59a**	1	toluene	25	72	56	56
2	(*R*)-**13**	**59b**	1	toluene	25	72	98	57
3	(*R*)-**13**	**59c**	1	toluene	25	72	98	70
4	(*R*)-**13**	**59d**	1	toluene	25	72	90	86
5	(*R*)-**13**	**59e**	1	toluene	25	72	99	81
6	(*R*)-**13**	**59f**	1	toluene	25	72	93	38
7	(*R*,*R*)-**6**	**59a**	1	toluene	25	72	94	87
8	(*R*,*R*)-**6**	**59b**	1	toluene	25	72	90	87
9	(*R*,*R*)-**6**	**59c**	1	toluene	25	72	61	76
10	(*R*,*R*)-**6**	**59d**	1	toluene	25	72	78	78
11	(*R*,*R*)-**6**	**59e**	1	toluene	25	72	70	84
12	(*R*,*R*)-**6**	**59f**	1	toluene	25	72	73	86
13	(*R*,*R*)-**9**	**59a**	1	toluene	25	72	67	57
14	(*R*,*R*)-**9**	**59b**	1	toluene	25	72	59	58
15	(*R*,*R*)-**9**	**59c**	1	toluene	25	72	30	82
16	(*R*,*R*)-**9**	**59d**	1	toluene	25	72	34	78
17	(*R*,*R*)-**9**	**59e**	1	toluene	25	72	62	48
18	(*R*,*R*)-**9**	**59f**	1	toluene	25	72	52	26
19	(*R*,*R*)-**8**	**59a**	1	toluene	25	72	83	93
20	(*R*,*R*)-**8**	**59b**	1	toluene	25	72	77	93
21	(*R*,*R*)-**8**	**59c**	1	toluene	25	72	85	95.5
22	(*R*,*R*)-**8**	**59d**	1	toluene	25	72	76	93
23	(*R*,*R*)-**8**	**59e**	1	toluene	25	72	82	92
24	(*R*,*R*)-**8**	**59f**	1	toluene	25	72	74	91
25	(*R*,*R*)-**11**	**59a**	1	toluene	25	72	96	92.5
26	(*R*,*R*)-**11**	**59b**	1	toluene	25	72	83	94
27	(*R*,*R*)-**11**	**59c**	1	toluene	25	72	79	95
28	(*R*,*R*)-**11**	**59d**	1	toluene	25	72	75	90
29	(*R*,*R*)-**11**	**59e**	1	toluene	25	72	92	94.5
30	(*R*,*R*)-**11**	**59f**	1	toluene	25	72	87	91

[a] values for the (*R*)-enantiomer; [b] determined by chiral HPLC. Values are given for the (*S*)-enantiomer.

1,2,3,4-Tetrahydro-2-phenyl-quinoline **60a**[94]

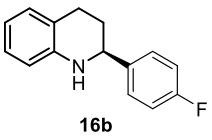


$C_{15}H_{15}N$, MW = 209.29 g/mol.

^{1}H-NMR (400 MHz, [D$_1$]-chloroform, 298 K) δ [in ppm] = 7.43 – 7.38 (m, 2H, H_{Aryl}), 7.38 – 7.32 (m, 2H, H_{Aryl}), 7.32 – 7.27 (m, 1H, H_{Aryl}), 7.04 – 6.99 (m, 2H, H_{Aryl}), 6.68 (t, ^3J = 7.3 Hz, 1H, H_{Aryl}), 6.57 (d, ^3J = 8.1 Hz, 1H, H_{Aryl}), 4.44 (dd, ^3J = 9.4 Hz, ^4J = 3.3 Hz, 1H, NC-H), 2.93 (ddd, ^2J = 16.2 Hz, ^3J = 10.6 Hz, ^3J = 5.6 Hz, 1H, CH_2), 2.75 (dt, ^2J = 16.5 Hz, ^3J = 4.8 Hz, 1H, CH_2), 2.18 – 2.10 (m, 1H, CH_2), 2.09 – 1.97 (m, 1H, CH_2).

[NMR-data: SF019-1]

1,2,3,4-Tetrahydro-2-(4-fluorophenyl)-quinoline **60b**[94]



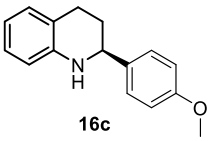
16b

$C_{15}H_{15}N$, MW = 209.29 g/mol

^{1}H-NMR (400 MHz, [D$_1$]-Chloroform, 298 K) δ [in ppm] = 7.39 – 7.35 (m, 2H, H_{Aryl}), 7.06 – 7.00 (m, 4H, H_{Aryl}), 6.69 (t, ^3J = 7.3 Hz, 1H, H_{Aryl}), 6.56 (dd, ^3J = 8.4 Hz, ^4J = 1.0 Hz, 1H, H_{Aryl}), 4.43 (dd, ^3J = 9.4 Hz, ^4J = 3.2 Hz, 1H, NC-H), 2.93 (ddd, ^2J = 16.3 Hz, ^3J = 10.6 Hz, ^3J = 5.5 Hz, 1H, CH_2), 2.74 (dt, ^2J = 16.5 Hz, ^3J = 4.8 Hz, 1H, CH_2), 2.14 – 2.06 (m, 1H, CH), 2.04 – 1.93 (m, 1H, CH).

[NMR-data: SF037-1]

1,2,3,4-Tetrahydro-2-(4-methoxyphenyl)-quinoline **60c**[94]



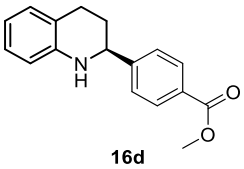
16c

$C_{16}H_{17}NO$, MW = 239.32 g/mol

^{1}H-NMR (400 MHz, [D$_1$]-Chloroform, 298 K) δ [in ppm] = 7.35 – 7.30 (m, 2H, H_{Aryl}), 7.02 – 6.98 (m, 2H, H_{Aryl}), 6.92 – 6.87 (m, 2H, H_{Aryl}), 6.67 (t, ^3J = 7.3 Hz, 1H, H_{Aryl}), 6.53 (dd, ^3J = 8.2 Hz, ^4J = 1.0 Hz, 1H, H_{Aryl}), 4.38 (dd, ^3J = 9.6 Hz, ^4J = 3.2 Hz, 1H, NC-H), 3.82 (s, 3H, OMe), 2.93 (ddd, ^2J = 16.4 Hz, ^3J = 10.9 Hz, ^3J = 5.6 Hz, 1H, CH_2), 2.74 (dt, ^2J = 16.4 Hz, ^3J = 4.6 Hz, 1H, CH_2), 2.13 – 2.06 (m, 1H, CH), 2.05 – 1.93 (m, 1H, CH).

[NMR-data: SF041-1]

Benzoic acid-4-(1,2,3,4-tetrahydro-2-quinolinyl)-methyl ester **60d**[95]



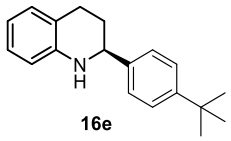
16d

$C_{17}H_{17}NO_2$, MW = 267.33 g/mol

^{1}H-NMR (400 MHz, [D$_1$]-Chloroform, 298 K) δ [in ppm] = 8.04–8.00 (m, 2H, H_{Aryl}), 7.47 (d, ^3J = 8.3 Hz, 2H, H_{Aryl}), 7.02 (dd, ^3J = 11.5, 7.5 Hz, 2H, H_{Aryl}), 6.69 (t, ^3J = 7.4 Hz, 1H, H_{Aryl}), 6.60 (d, ^3J = 7.9 Hz, 1H, H_{Aryl}), 4.52 (dd, ^3J = 8.9, ^4J = 3.4 Hz, 1H, NC-H), 3.92 (s, 3H, CH_3), 2.91 (ddd, ^2J = 15.9 Hz, ^3J = 10.1 Hz, ^3J = 5.4 Hz, 1H, CH_2), 2.72 (dt, ^2J = 16.4 Hz, ^3J = 5.0 Hz, 1H, CH_2), 2.18–2.10 (m 1H, CH), 2.06–1.95 (m, 1H, CH).

[NMR-data: SF043-1]

1,2,3,4-Tetrahydro-2-(4-*tert*-butylphenyl)-quinoline **60e**[127]



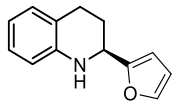
16e

$C_{19}H_{23}N$, MW = 265.40 g/mol

^{1}H-NMR (400 MHz, [D$_1$]-Chloroform, 298 K) δ [in ppm] = 7.40 – 7.36 (m, 2H, H_{Aryl}), 7.36 – 7.31 (m, 2H, H_{Aryl}), 7.04 – 6.98 (m, 2H, H_{Aryl}), 6.67 (t, ^3J = 7.0 Hz, 1H, H_{Aryl}), 6.57 (d, ^3J = 8.1 Hz, 1H, H_{Aryl}), 4.42 (dd, ^3J = 9.5 Hz, ^4J = 3.2 Hz, 1H, H_{Aryl}), 2.94 (ddd, ^2J = 16.3 Hz, ^3J = 10.7 Hz, ^3J = 5.6 Hz, 1H, CH_2), 2.76 (dt, ^2J = 16.4 Hz, ^3J = 4.7 Hz, 1H, CH_2), 2.17 – 2.09 (m, 1H, CH), 2.07 – 1.96 (m, 1H, CH), 1.33 (s, 9H, C(C*H*$_3$)$_3$).

[NMR-data: SF044-1]

2-(2-Furanyl)-1,2,3,4-tetrahydro-quinoline **60f**[94]



16f

$C_{13}H_{13}NO$, MW = 199.25 g/mol

^{1}H-NMR (400 MHz, [D$_1$]-Chloroform, 298 K) δ [in ppm] = 7.37 (d, ^{3}J = 1.0 Hz, 1H, H_{Aryl}), 7.04 – 6.97 (m, 2H, H_{Aryl}), 6.69 (t, ^3J = 7.3 Hz, 1H, H_{Aryl}), 6.62 (d, ^3J = 7.8 Hz, 1H, H_{Aryl}), 6.33 (dd, ^3J = 3.1 Hz, ^4J =1.8 Hz, 1H, H_{Aryl}), 6.23 (d, ^3J = 3.2 Hz, 1H, H_{Aryl}), 4.55 (dd, ^3J = 8.2 Hz, ^4J = 3.6 Hz, 1H, NC-H), 2.92-2.82 (m, 1H, CH_2), 2.76 (dt, ^2J = 16.3 Hz, ^3J = 5.5 Hz, 1H, CH_2), 2.28-2.10 (m, 2H, CH).

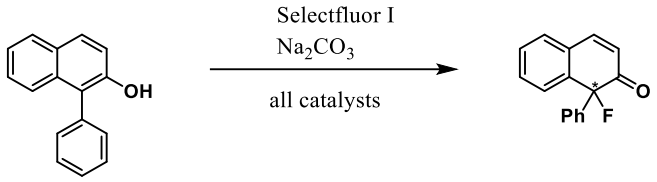
[NMR-data: SF059-1]

[127] N. T. Patil, V. S. Raut, R. B. Tella, *Chem. Commun*. **2013**, *49*, 570-572.

8.5. Dearomative fluorination reaction[100]

8.5.1. Catalyst and condition screening

Described experiments: MT661 (entry 1), MT651 (entry 2), MT648 (entry 3), MT645 (entry 4), MT649 (entry 5), MT644 (entry 6), MT634 (entry 7), MT714 (entry 8), MT715 (entry 9), MT652 (entry 10), MT718 (entry 11), MT719 (entry 12).



66a **67a**

Under argon atmosphere 1-phenyl-2-naphthol **66a** (1 eq), the catalyst (0.1 eq) and sodium carbonate (5.055 mg, 47.7 µmol, 1.5 eq) were suspended in the respective solvent (dry solvent, 159 µL). Then selectfluor I (16.9 mg, 47.7 µmol, 1.5 eq) was also added to the reaction mixture. After stirring for18 hours the solids were filtered off and the solid was washed with ethyl acetate (10 ml). Then the solvent was evaporated *in vacuo*. After the purification of the crude product by flash column chromatography on silica gel (1.5 x 30 cm, cyclohexane : ethyl acetate = 10:1), the pure product67 was obtained.

The enantiomeric excess was determined by chiral HPLC (Chiralcel IC-3 column (0.46 x 25 cm), *n*-hexane : isopropanol = 95:5, 0.5 mL/min).

Table 20: reaction conditions, yields and enantiomeric excesses for different catalysts.

entry	cat.	cat.-loading [mol%]	solvent	temperature [°C]	time [h]	yield [%]	*ee*[a][b] [%]
1	(*R*)-**12a**	10	DCM	0	18	49	–6
2	(*R*)-**12b**	10	DCM	0	18	52	–6
3	(*R*)-**13**	10	DCM	0	18	63	–6
4	(*R*,*R*)-**4a**	10	DCM	0	18	92	81
5	(*R*,*R*)-**4b**	10	DCM	0	18	85	79
6	(*R*,*R*)-**5**	10	DCM	0	18	62	30
7	(*R*,*R*)-**6**	10	DCM	0	18	70	27
8	(*R*,*R*)-**7**	10	DCM	0	18	76	27
9	(*R*,*R*)-**8**	10	DCM	0	18	62	<5[c]
10	(*R*,*R*)-**9**	10	DCM	0	18	65	<5[c]
11	(*R*,*R*)-**10**	10	DCM	0	18	69	22
12	(*R*,*R*)-**11**	10	DCM	0	18	59	<5[c]

[a] values for the (*R*)-enantiomer; [b] determined by chiral HPLC, [c] Enantiomeric excesses between –5% and +5% ee are reported as <5%.

Described experiments: MT697 (entry 1), MT694 (entry 2), MT645 (entry 3), MT698 (entry 4), MT700 (entry5), MT701 (entry 6), MT704 (entry 7).

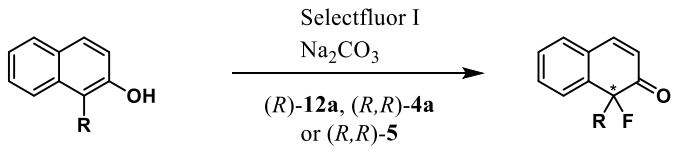
Table 21: Results on different reaction conditions of dearomative fluorination with (R,R)-4a as catalyst and 66a as substrate.

entry	cat.	cat.-loading [mol%]	solvent	temperature [°C]	time [h]	yield [%]	*ee*[a][b] [%]
1	(*R*,*R*)-**4a**	10	toluene	0	18	69	47
2	(*R*,*R*)-**4a**	10	dichloromethane	0	18	92	81
3	(*R*,*R*)-**4a**	10	brombenzene	0	18	72	72
4	(*R*,*R*)-**4a**	10	chloroform	-25	18	75	86
5	(*R*,*R*)-**4a**	10	chloroform	25	18	95	86
6	(*R*,*R*)-**4a**	5	chloroform	25	18	82	70

[a] values for the (*R*)-enantiomer; [b] determined by chiral HPLC.

8.5.2. Substrate screening

Described experiments: MT711 (entry 1), MT710 (entry 2), MT701 (entry 3), MT713 (entry 4), MT703 (entry 5), MT702 (entry 6), MT725 (entry 7), MT724 (entry 8), MT723 (entry 9), MT729 (entry 10), MT728 (entry 11), MT727 (entry 12), MT737 (entry 13), MT736 (entry 14), MT735 (entry 15), MT721 (entry 16), MT720 (entry 17), MT717 (entry 15).



66a-f **67a-f**

a: R = C_6H_6
b: R = C_6H_6-*t*Bu
c: R = C_6H_5-F
d: R = C_6H_5-OMe
e: R = C_4H_8
f: R = CH_3

a: R = C_6H_6
b: R = C_6H_6-*t*Bu
c: R = C_6H_5-F
d: R = C_6H_5-OMe
e: R = C_4H_8
f: R = CH_3

Under argon atmosphere the naphtalene derivates **66b-f** (1 eq), the catalyst (0.1 eq) and sodium carbonate (1.5 eq) were suspended in chloroform (159 µL). Then selectfluor I (1.5 eq) was also added to the reaction mixture. After stirring for18 hours the solids were filtered off and the solid was washed with ethyl acetate (10 ml). Then the solvent was evaporated *in vacuo*. After the purification of the crude product by flash column chromatography on silica gel (1.5 x 30 cm, cyclohexane : ethyl acetate = 10:1), the pure products **67a-f** were obtained.

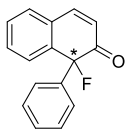
The enantiomeric excesses were determined by chiral HPLC (Chiralcel IC-3 column (0.46 x 25 cm), *n*-hexane : isopropanol = 95:5, 0.5 mL/min for **67a**, *n*-hexane : isopropanol = 90:10, 1.0 mL/min for **67b-f**).

Table 22: reaction conditions, yields and enantiomeric excesses for different substrates.

entry	substrate	cat.	cat. loading [mol%]	solvent	temperature [°C]	time [h]	yield [%]	*ee*[a][b] [%]
1	**66a**	(*R*)-**12a**	10	Chloroform	25	18	75	7
2	**66a**	(*R,R*)-**5**	10	Chloroform	25	18	79	-6
3	**66a**	(*R,R*)-**4a**	10	Chloroform	25	18	94	86
4	**66b**	(*R*)-**12a**	10	Chloroform	25	18	69	0
5	**66b**	(*R,R*)-**5**	10	Chloroform	25	18	82	2
6	**66b**	(*R,R*)-**4a**	10	Chloroform	25	18	96	50
7	**66c**	(*R*)-**12a**	10	Chloroform	25	18	66	12
8	**66c**	(*R,R*)-**5**	10	Chloroform	25	18	86	3
9	**66c**	(*R,R*)-**4a**	10	Chloroform	25	18	97	53
10	**66d**	(*R*)-**12a**	10	Chloroform	25	18	53	-2
11	**66d**	(*R,R*)-**5**	10	Chloroform	25	18	79	-2
12	**66d**	(*R,R*)-**4a**	10	Chloroform	25	18	92	78
13	**66e**	(*R*)-**12a**	10	Chloroform	25	18	49	0
14	**66e**	(*R,R*)-**5**	10	Chloroform	25	18	82	12
15	**66e**	(*R,R*)-**4a**	10	Chloroform	25	18	94	0
16	**66f**	(*R*)-**12a**	10	Chloroform	25	18	59	0
17	**66f**	(*R,R*)-**5**	10	Chloroform	25	18	77	7
18	**66f**	(*R,R*)-**4a**	10	Chloroform	25	18	93	0

[a] values for the (*R*)-enantiomer; [b] determined by chiral HPLC.

1-Fluoro-1-phenylnaphthalen-2(1H)-one **67a**

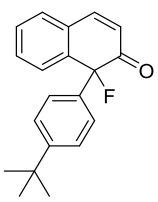


$C_{16}H_{11}FO$, MW = 238.3 g/mol.

^{1}H-NMR (400 MHz, [D$_1$]-Chloroform, 298 K) δ [in ppm] = 7.53 – 7.49(m, 1H, CH_{Aryl}), 7.47 – 7.44 (m, 2H, CH_{Aryl}), 7.43 – 7.39 (m, 2H, CH_{Aryl}), 7.32 – 7.24 (m, merged with $CDCl_3$ – Signal 5H, CH_{Aryl}), 6.06 (dd, ^3J = 10.1 Hz, ^4J = 4.1 Hz, 1H, CH_{Aryl}).

[MT701-1]

1-Fluoro-1-*tert*-butylphenylnaphthalen-2(1H)-one **67b**[100]

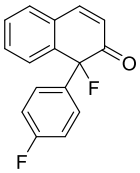


$C_{20}H_{19}FO$, MW = 294.4 g/mol

^{1}H-NMR (400 MHz, [D$_1$]-Chloroform, 298 K) δ [in ppm] = 7.54 – 7.42 (m, 1H, CH), 7.46 – 7.44 (m, 2H, CH), 7.40 – 7.38 (m, 2H, CH), 7.30 (d, ^3J = 8.4 Hz, 2H, CH), 7.16 (d, ^3J = 8.4 Hz, 2H, CH), 6.05 (dd, ^3J = 10.1 Hz, ^4J = 4.1 Hz, 1H, CH), 1.26 (s, 12H, CH_3).

[MT702-1]

1-Fluoro-1-(4-fluorophenyl)naphthalen-2(1H)-one **67c**[100]

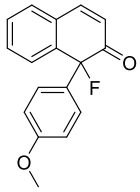


$C_{16}H_{10}F_2O$, MW = 265.3 g/mol

^{1}H-NMR (400 MHz, [D$_1$]-Chloroform, 298 K) δ [in ppm] = 7.52 – 7.45 (m, 3H, CH), 7.43 – 7.38 (m, 2H, CH), 7.23 (dd, ^3J = 8.4 Hz, ^4J = 5.2 Hz, 2H, CH), 6.97 (t, ^3J = 8.4 Hz, 2H, CH), 6.06 (dd, ^3J = 10.1 Hz, ^4J = 4.1 Hz, 1H, CH).

[MT724-1]

1-Fluoro-1-(4-methoxyphenyl)naphthalen-2(1H)-one **67d**[100]

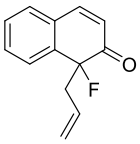


$C_{17}H_{13}FO_2$, MW = 268.3 g/mol

^{1}H-NMR (400 MHz, [D$_1$]-Chloroform, 298 K) δ [in ppm] = 7.55 – 7.52 (m, 1H, CH), 7.49 – 7.43 (m, 2H, CH), 7.39 – 7.35 (m, 2H, CH), 7.15 (d, ^3J = 9.1 Hz, 2H, CH), 6.80 (d, ^3J = 9.1 Hz, 2H, CH), 6.06 (dd, ^3J = 10.1 Hz, ^4J = 4.1 Hz, 1H, CH), 3.76 (s, 3H, OMe).

[MT727-1]

1-Allyl-1-fluoronaphthalen-2(1H)-one **67e**[100]

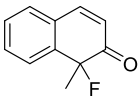


$C_{13}H_{11}FO$, MW = 202.2 g/mol

^{1}H-NMR (400 MHz, [D$_1$]-Chloroform, 298 K) δ [in ppm] = 7.58 (d, ^3J = 7.5 Hz, 1H, CH), 7.45 (dt, ^3J = 8.1Hz, ^4J = 1.5 Hz, 1H, CH), 7.41 – 7.36 (m, 2H, CH), 7.30 (d, ^3J = 7.5 Hz, 1H, CH), 6.12 (dd, ^3J = 10.1 Hz, ^4J = 4.1 Hz, 1H, CH), 5.63 – 5.52 (m, 1H, CH_{Vinyl}), 5.08 (d, ^3J = 9.7 Hz, 1H, CH), 4.98 (d, ^3J = 17.2 Hz, 1H, CH), 2.84 – 2.69 (m, 2H, CH_2),

[MT736-1]

1-Methyl-1-fluoronaphthalen-2(1H)-one **67f**[100]**Fehler! Textmarke nicht definiert.**



$C_{11}H_9FO$, MW = 176.2 g/mol

^{1}H-NMR (400 MHz, [D$_1$]-Chloroform, 298 K) δ [in ppm] = 7.64 (d, ^3J = 7.5 Hz, 1H, CH), 7.46 (t, ^3J = 7.5 Hz, 1H, CH), 7.42 – 7.37 (m, 1H, CH), 7.30 (d, ^3J = 8.4 Hz, 2H, CH), 6.05 (dd, ^3J = 10.1 Hz, ^4J = 4.1 Hz, 1H, CH), 1.74 (d, J = 22 Hz, 12H, CH_3).

[MT717-1]

9. Appendix

9.1.NMR Spectroscopy

9.1.1. NMR-Spectra of selected compounds

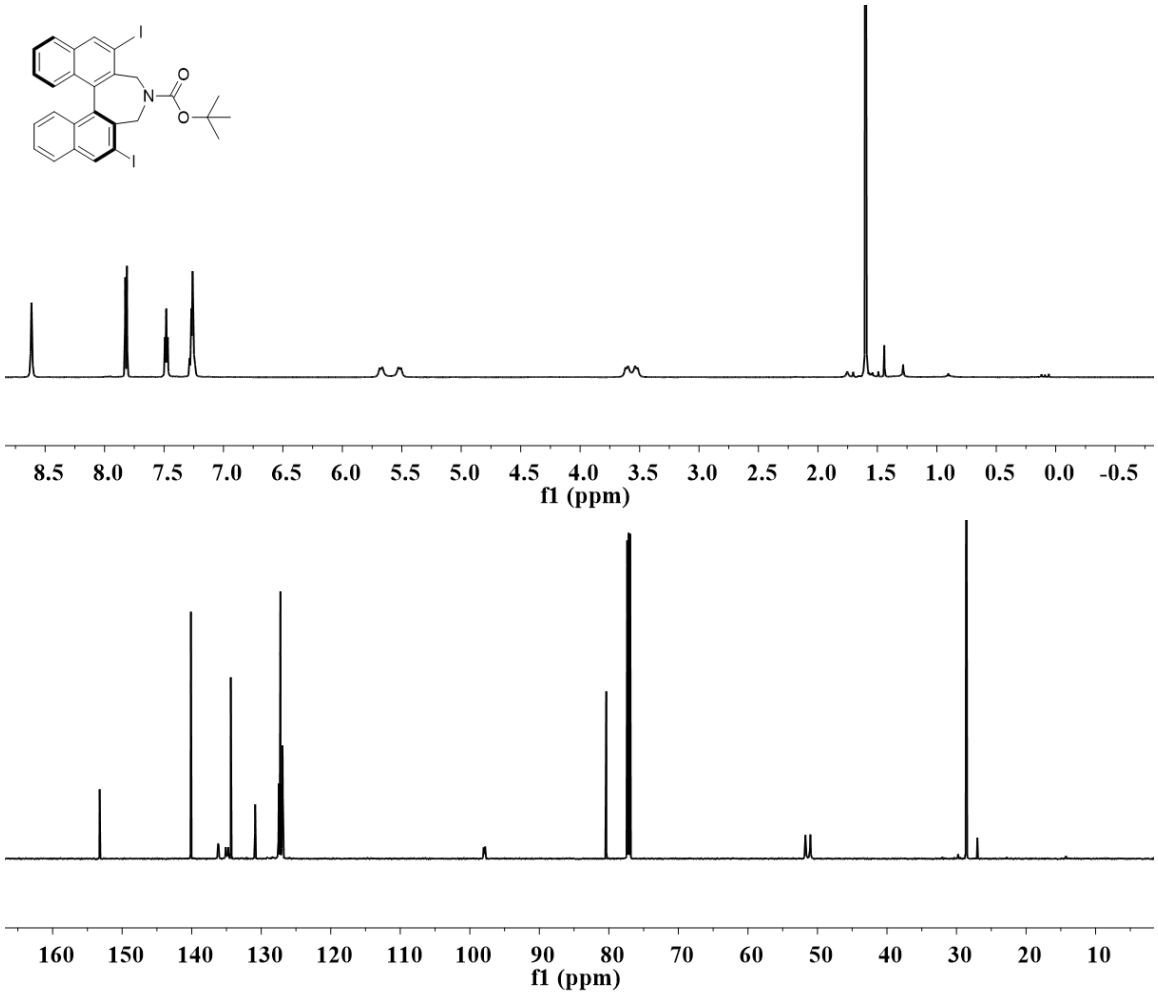


Figure 89: NMR-spectra of (*S*)-**42** in [D_1]- chloroform (298 K): top ^{1}H (600 MHz), bottom ^{13}C (151 MHz) [MT318-5].

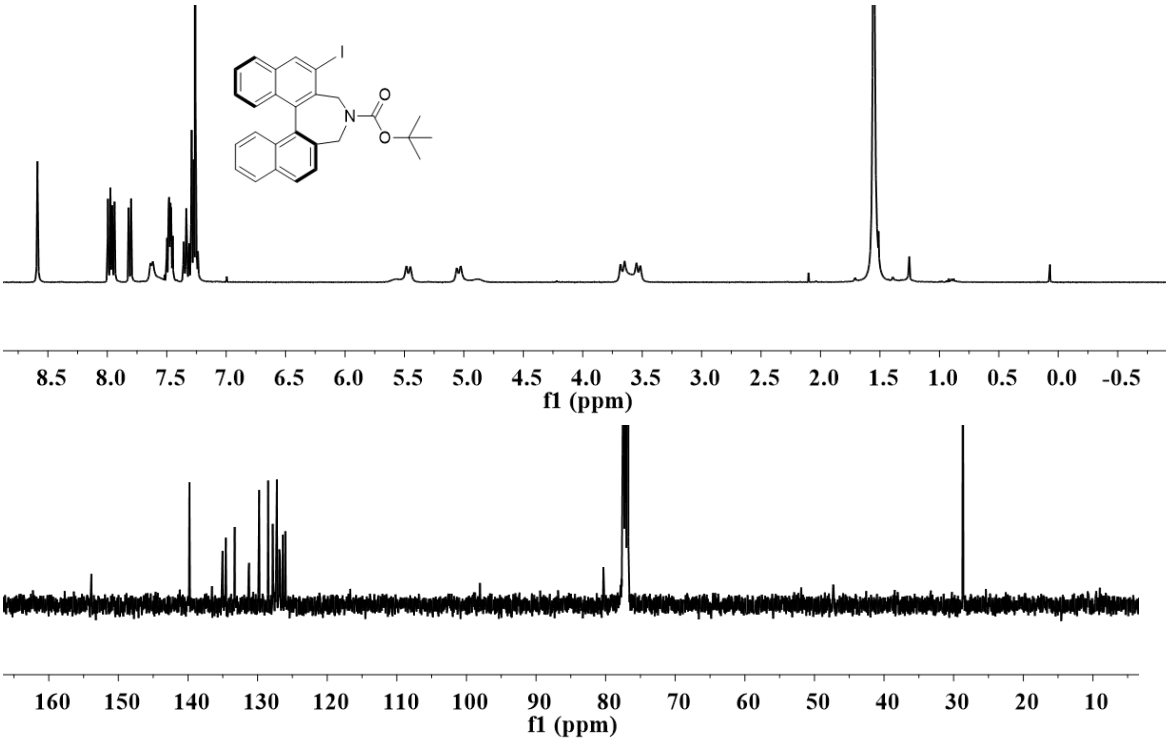


Figure 90: NMR-spectra of (*S*)-**36** in [D_1]- chloroform (298 K): top ^{1}H (400 MHz), bottom ^{13}C (101 MHz) [MT496-5]

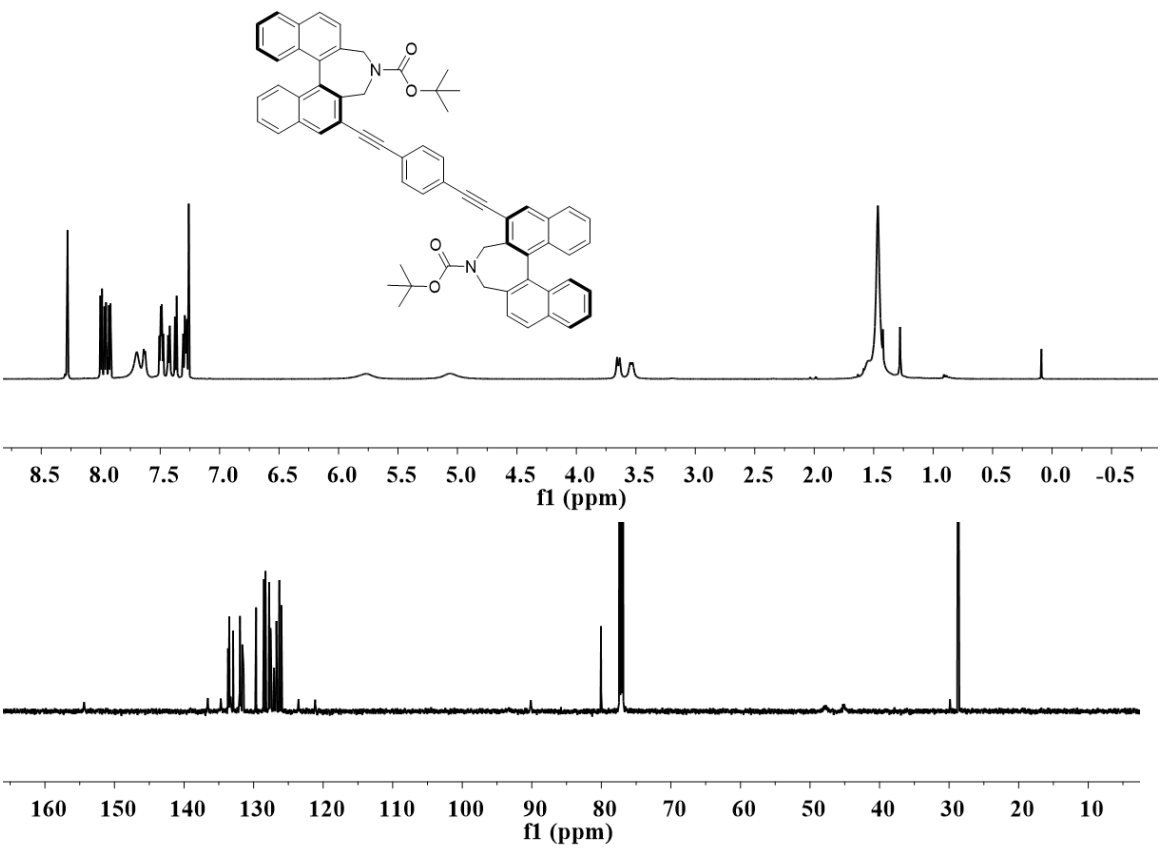


Figure 91: NMR-spectra of (*R*,*R*)-**43** in [D_1]- chloroform (298 K): top ^{1}H (600 MHz), bottom ^{13}C (151 MHz) [MT319VT]

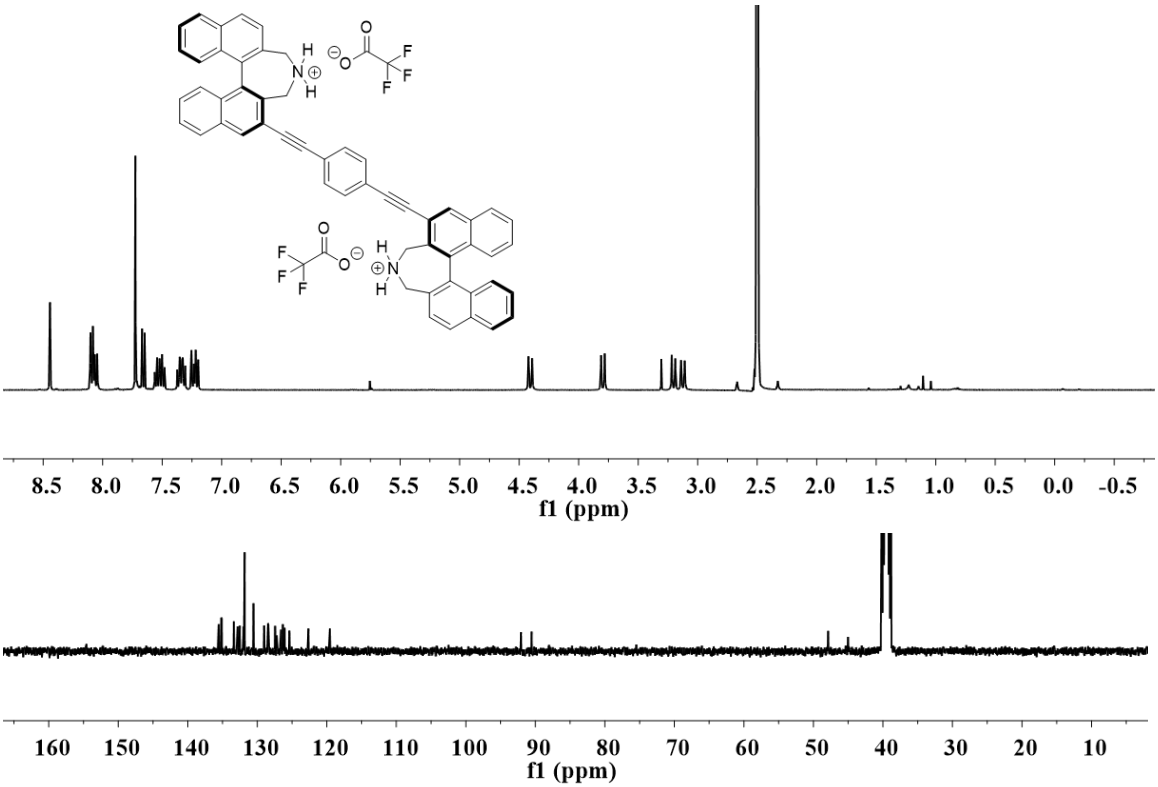


Figure 92: NMR-spectra of (*R*,*R*)-**44** in [D_6]- dimethylsulfoxid (298 K): top ^{1}H (400 MHz), bottom ^{13}C (101 MHz) [MT518-3]

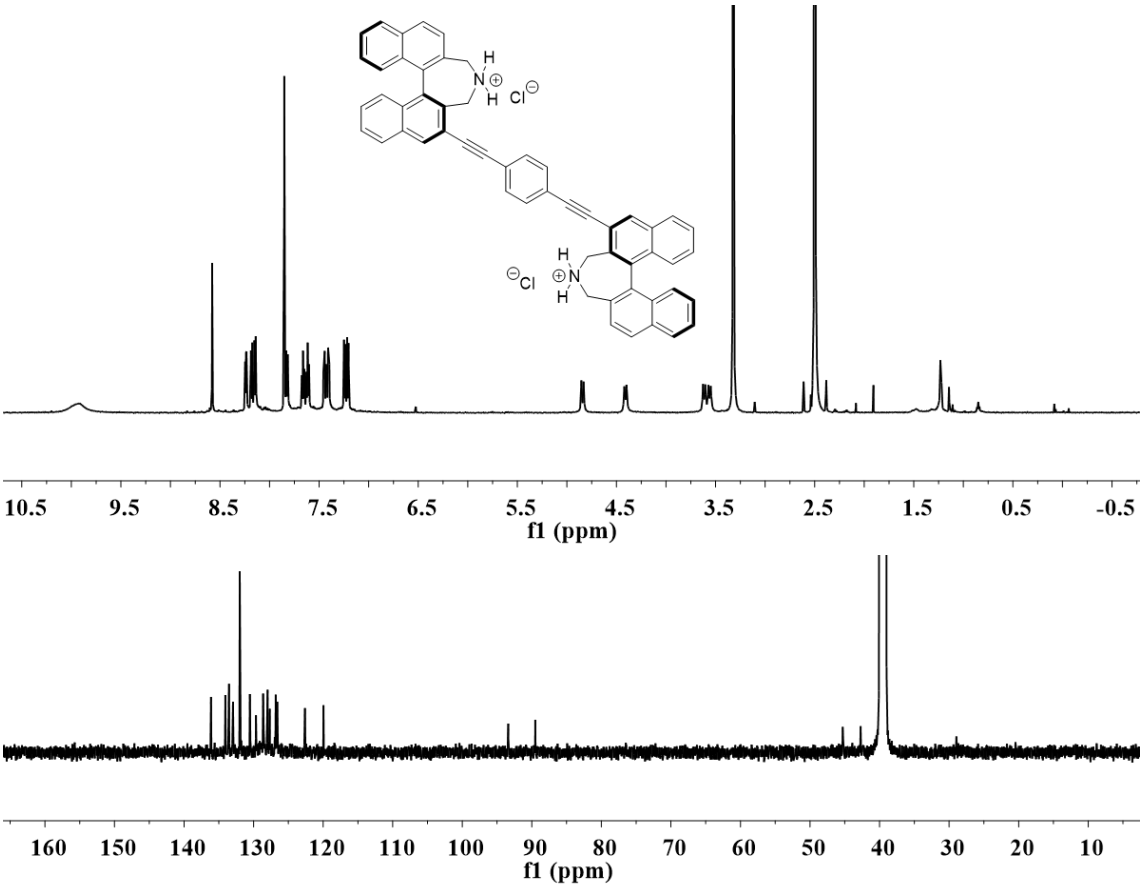


Figure 93: NMR-spectra of (*R*,*R*)-**44b** in [D_6]- dimethylsulfoxid (298 K): top ^{1}H (600 MHz), bottom ^{13}C (151 MHz) [MT462_1]

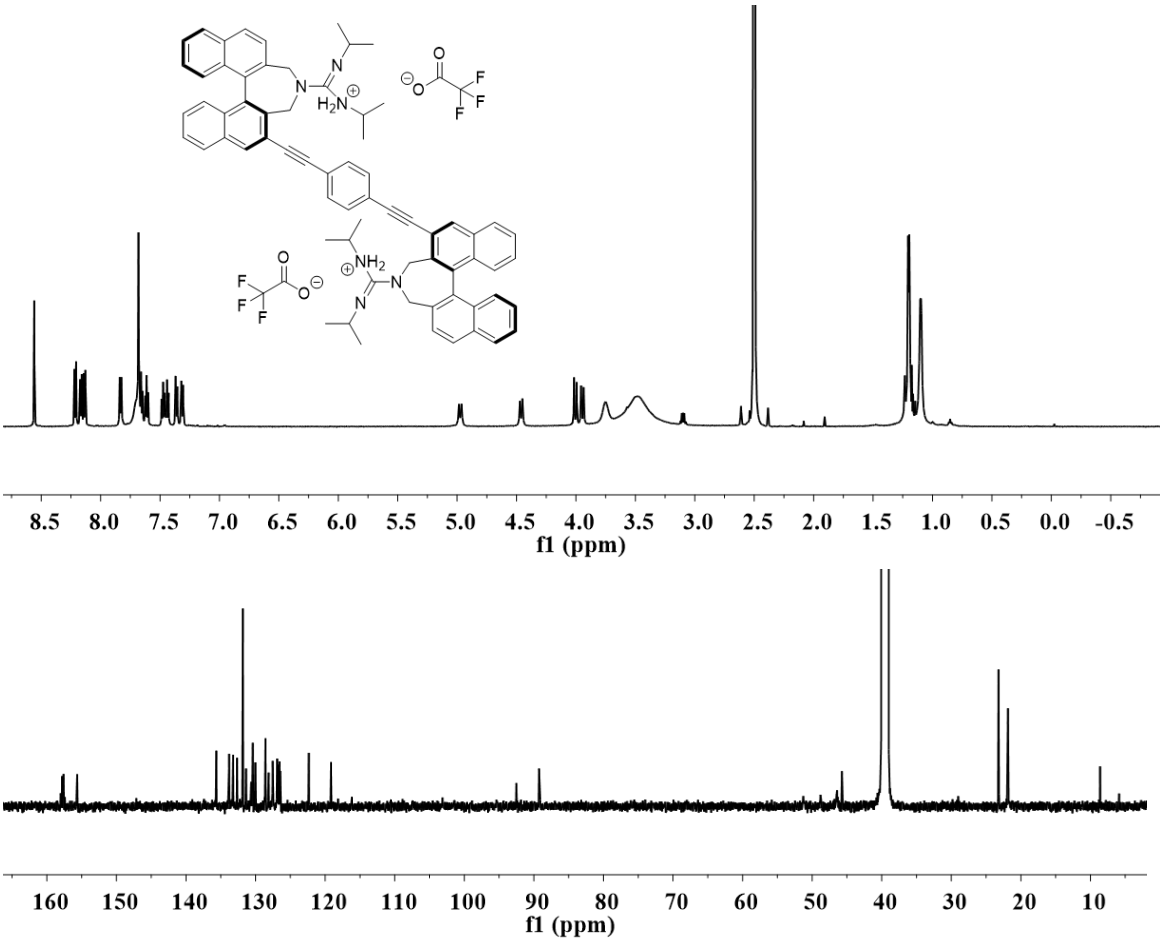


Figure 94: NMR-spectra of (*S*,*S*)-**28** in [D_6]- dimethylsulfoxid (298 K): top ^{1}H (600 MHz), bottom ^{13}C (151 MHz) [MT503 DMSO]

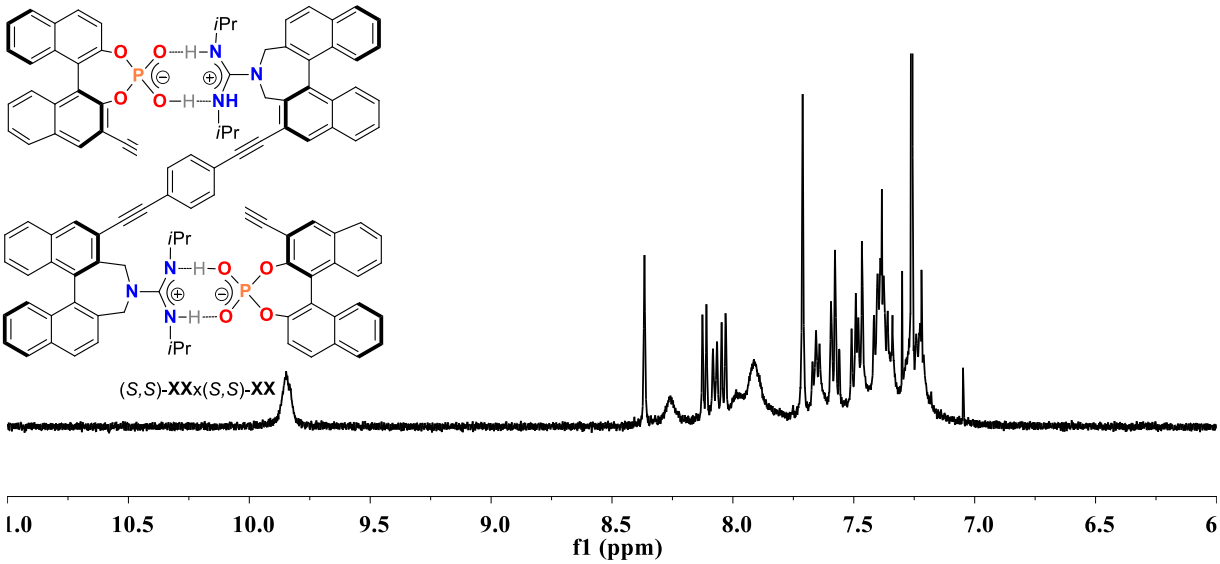


Figure 95: ^{1}H NMR spectrum (aromatic region) of (*S*,*S*)-**28** (3 mM) + (*S*,*S*)-**29** (3 mM) ($CDCl_3$, 600 MHz, 298 K).

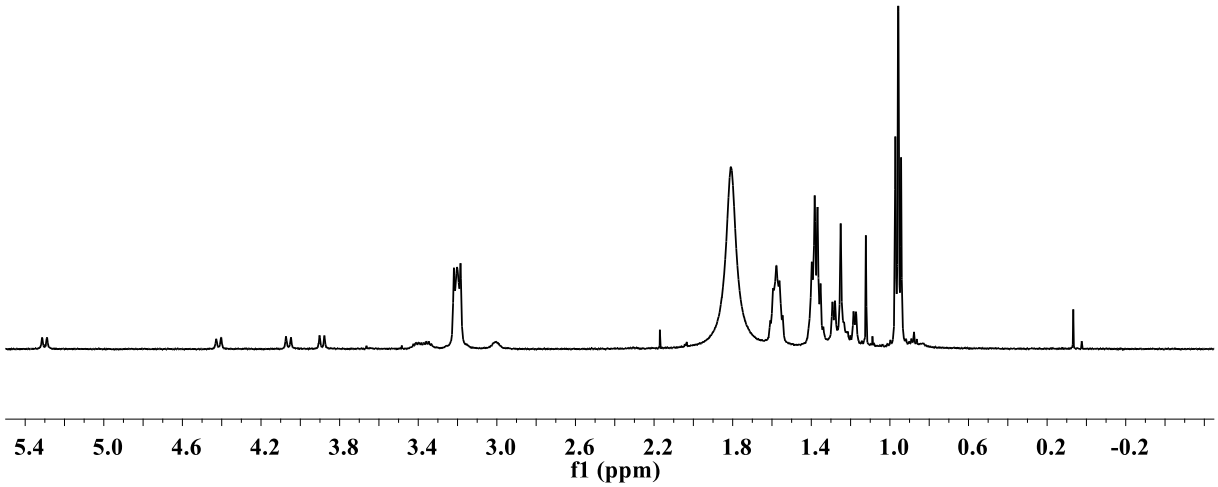


Figure 96: ^{1}H NMR spectrum (aliphatic region) of (*S*,*S*)-**28** (3 mM) + (*S*,*S*)-**29** (3 mM) ($CDCl_3$, 600 MHz, 298 K).

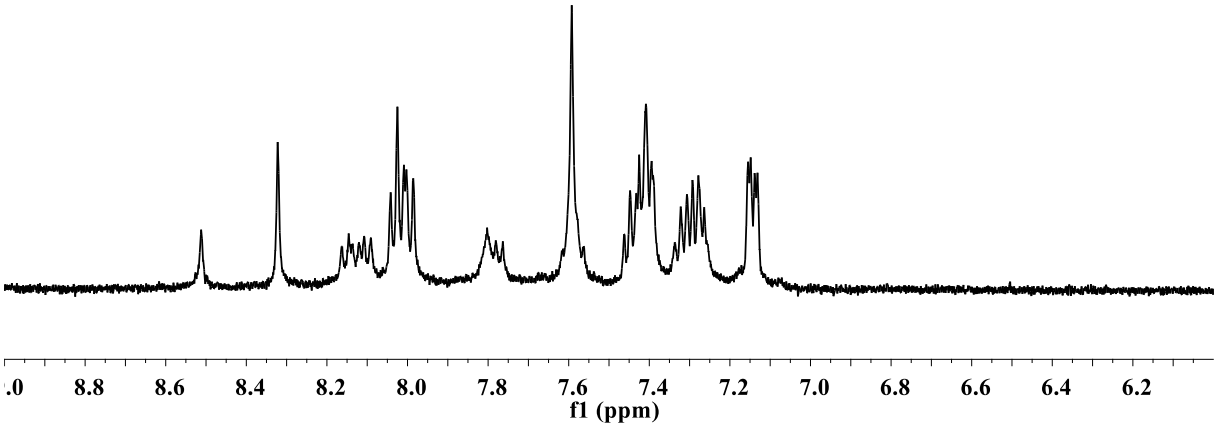


Figure 97: ^{1}H NMR spectrum (aromatic region) of (*S*,*S*)-**28** (1 mM) + (*S*,*S*)-**29** (1 mM) (DMSO-d_6 500 MHz, 298 K).

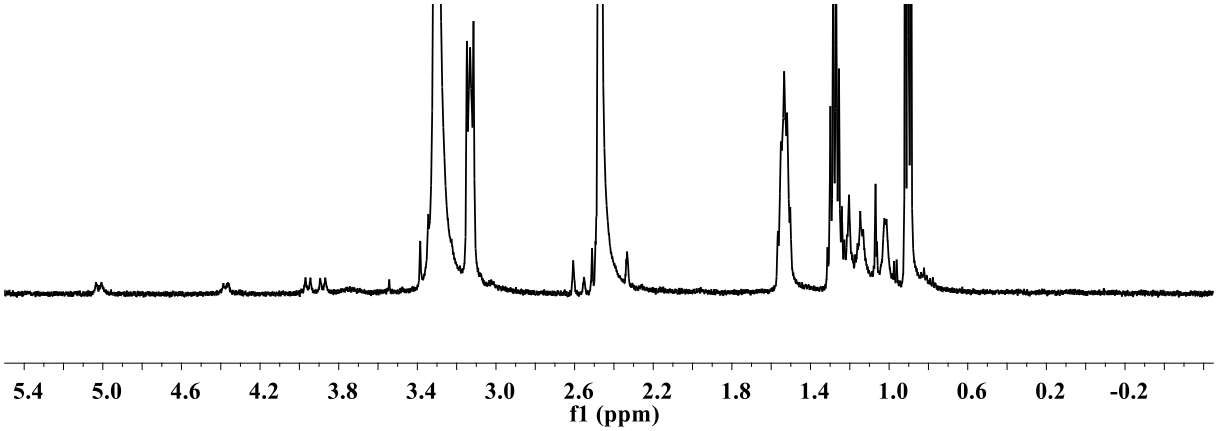


Figure 98: ^{1}H NMR spectrum (aliphatic region) of (*S*,*S*)-**28** (1 mM) + (*S*,*S*)-**29** (1 mM) (DMSO-d_6 500 MHz, 298 K).

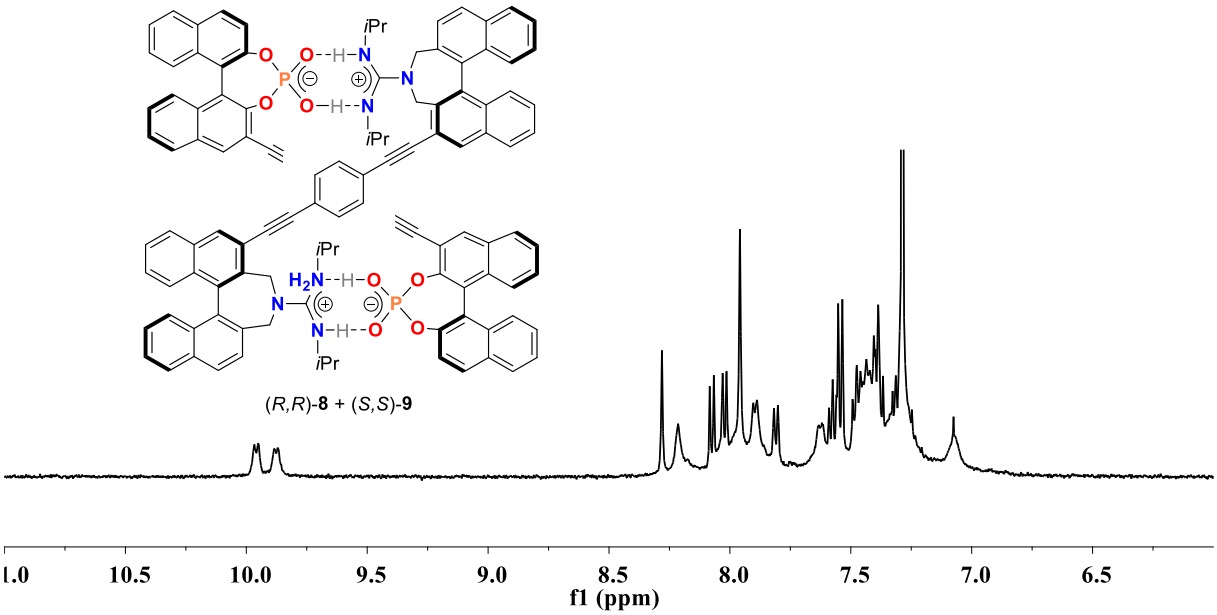


Figure 99: ^{1}H NMR spectrum (aromatic region) of (*S*,*S*)-**28** (3 mM) + (*R*,*R*)-**29** (3 mM) ($CDCl_3$, 500 MHz, 298 K).

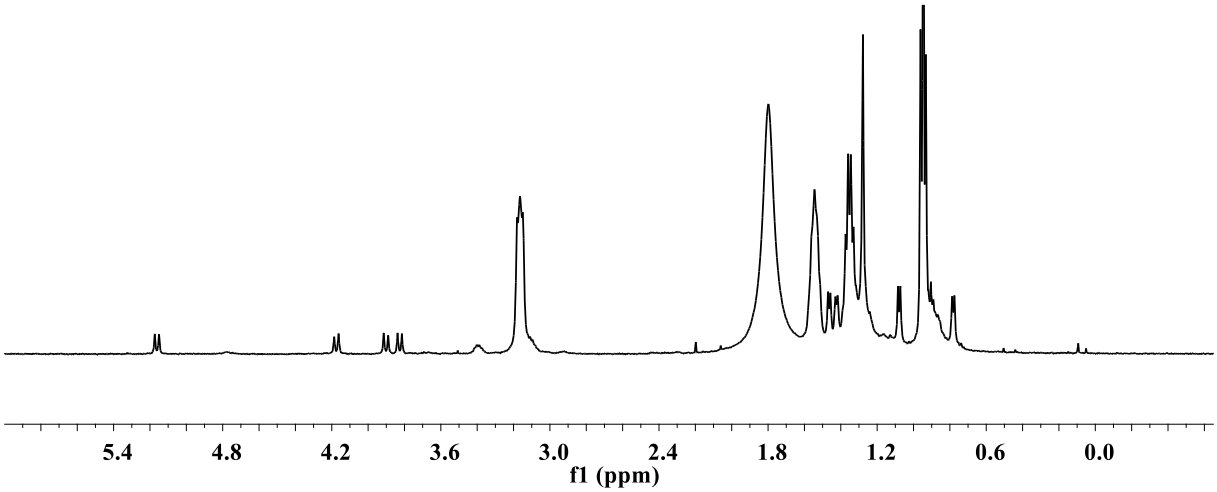


Figure 100: ^{1}H NMR spectrum (aliphatic region) of (*S*,*S*)-**28** (3 mM) + (*R*,*R*)-**29** (3 mM) ($CDCl_3$, 500 MHz, 298 K).

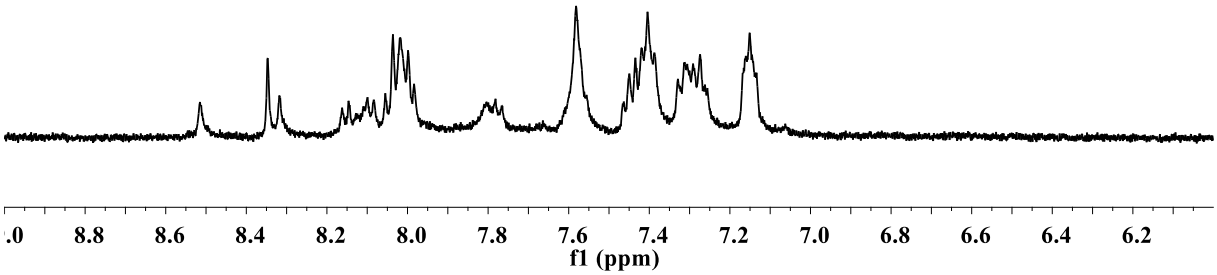


Figure 101: ^{1}H NMR spectrum (aromatic region) of (*S,S)*-**28** (1 mM) + (*R,R*)-**29** (1 mM) (DMSO-d_6 500 MHz, 298 K).

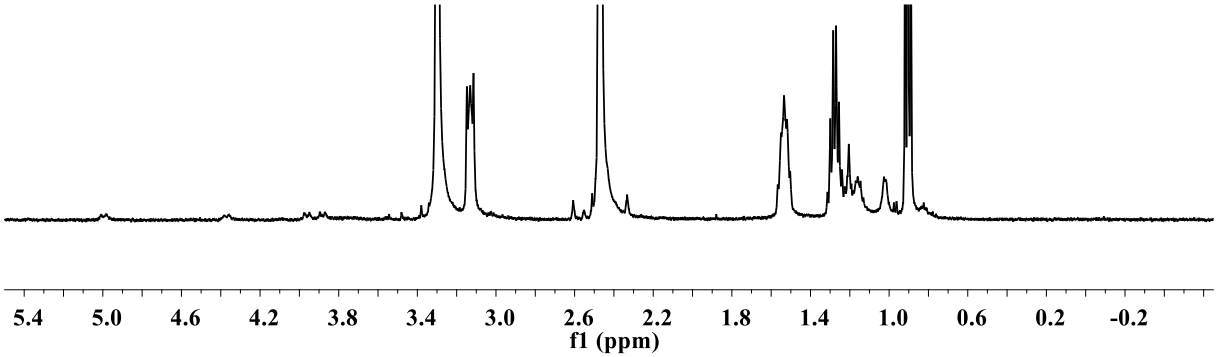


Figure 102: ^{1}H NMR spectrum (aliphatic region) of (*S,S)*-**28** (1 mM) + (*R,R*)-**29** (1 mM) (DMSO-d_6 500 MHz, 298 K).

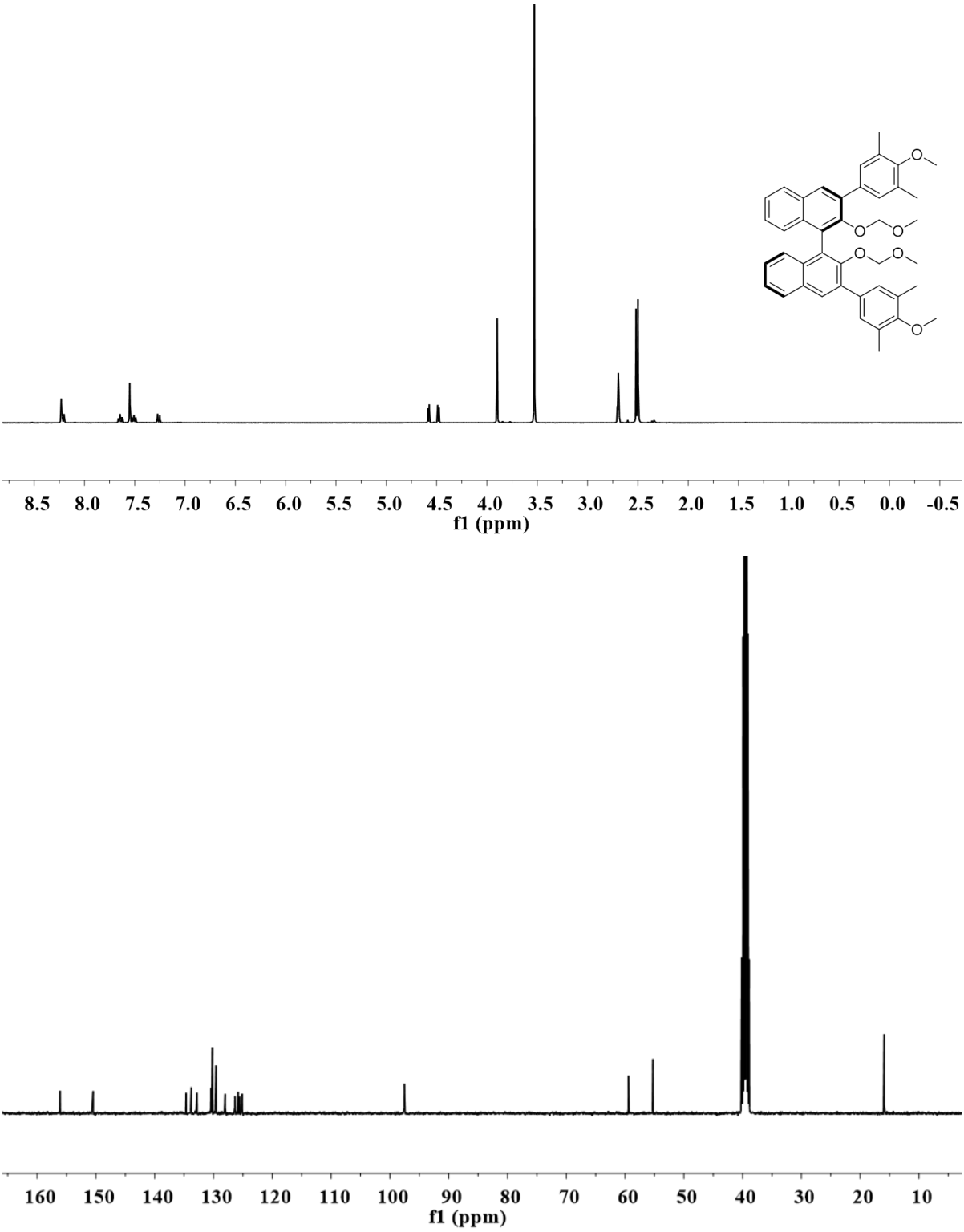


Figure 103: NMR-spectra of (*R*)-**13** in [D_6]- dimethylsulfoxid (298 K): top ^{1}H (400 MHz), bottom ^{13}C (101 MHz).

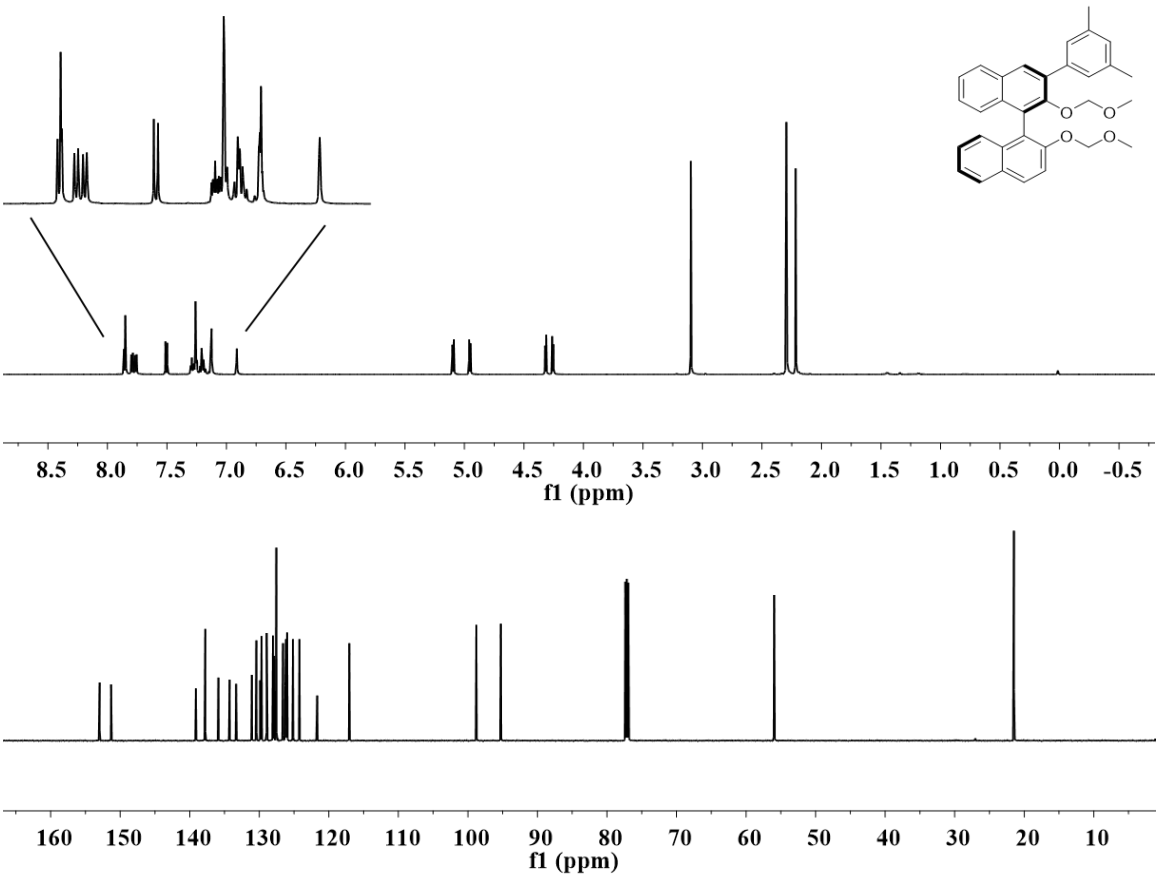


Figure 104: NMR-spectra of (*R*)-**76a** in [D_1]-chloroform (298 K): top ^{1}H (600 MHz), bottom ^{13}C (151 MHz) [TCH9-3].

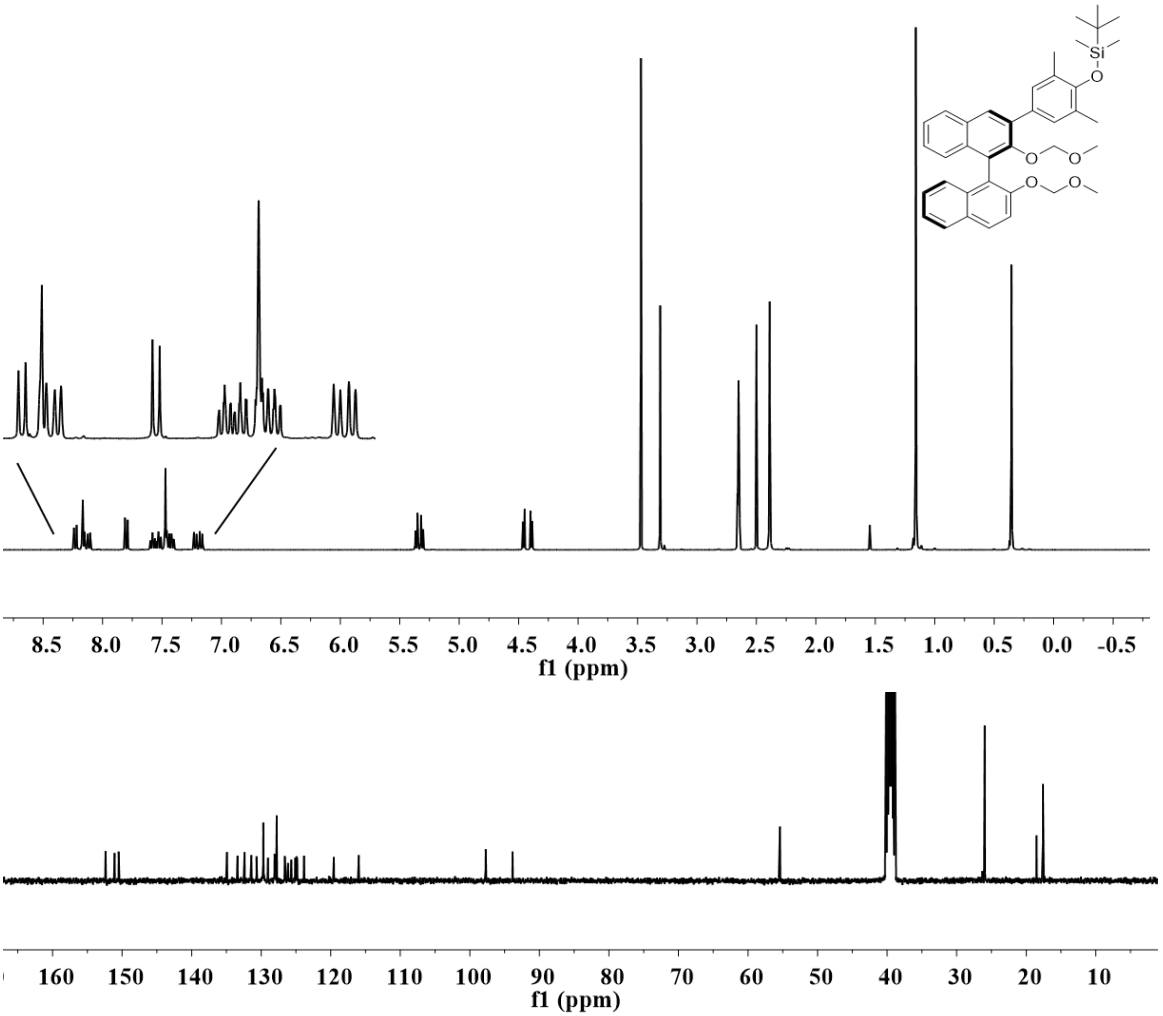


Figure 105: NMR-spectra of (*R*)-**76c** in [D_6]- dimethylsulfoxid (298 K): top ^{1}H (400 MHz), bottom ^{13}C (101 MHz) [MT473-4]

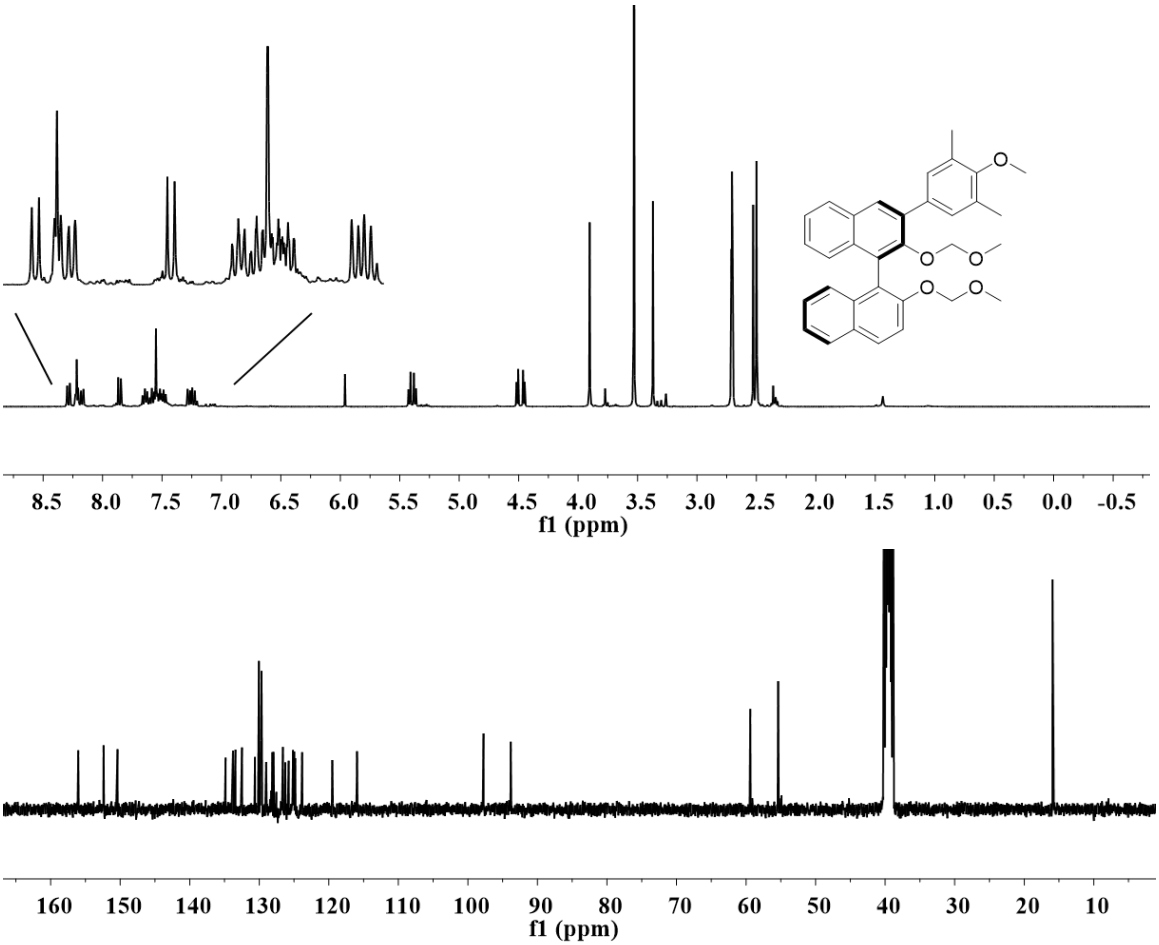


Figure 106: NMR-spectra of (*R*)-**76e** in [D_6]- dimethylsulfoxid (298 K): top ^{1}H (400 MHz), bottom ^{13}C (101 MHz) [MT620-3].

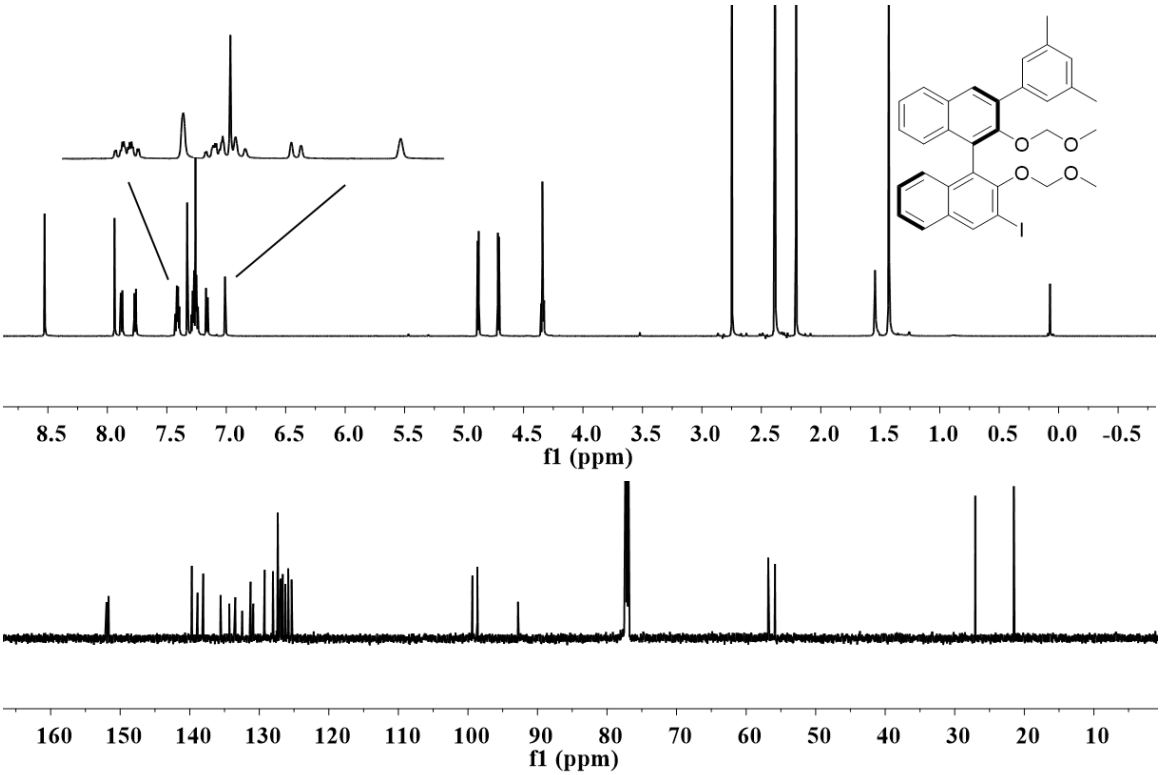


Figure 107: NMR-spectra of (*R*)-**70a** in [D_1]-chloroform (298 K): top ^{1}H (600 MHz), bottom ^{13}C (151 MHz) [TCH9-2].

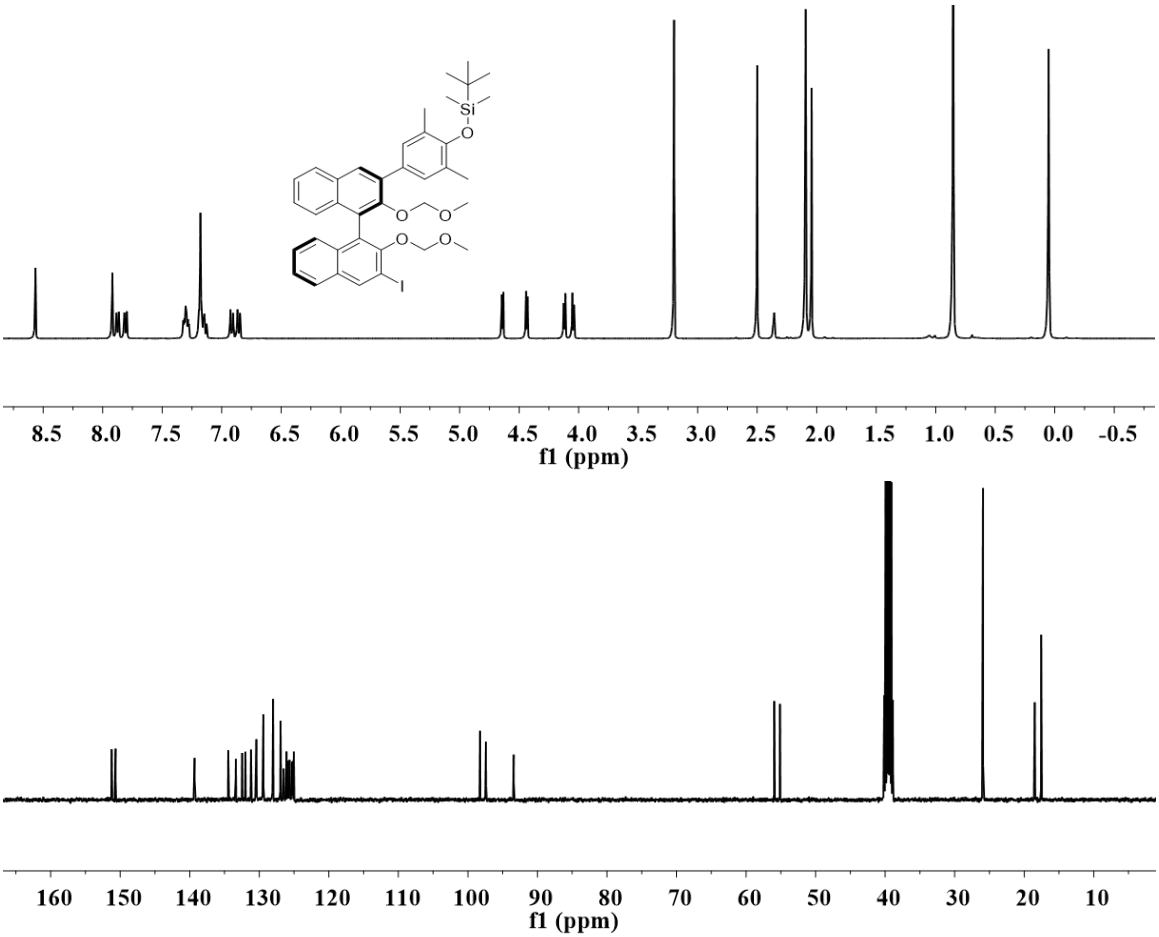


Figure 108: NMR-spectra of (*R*)-**70c** in [D_6]- dimethylsulfoxid (298 K): top ^{1}H (400 MHz), bottom ^{13}C (101 MHz) [MT475-4].

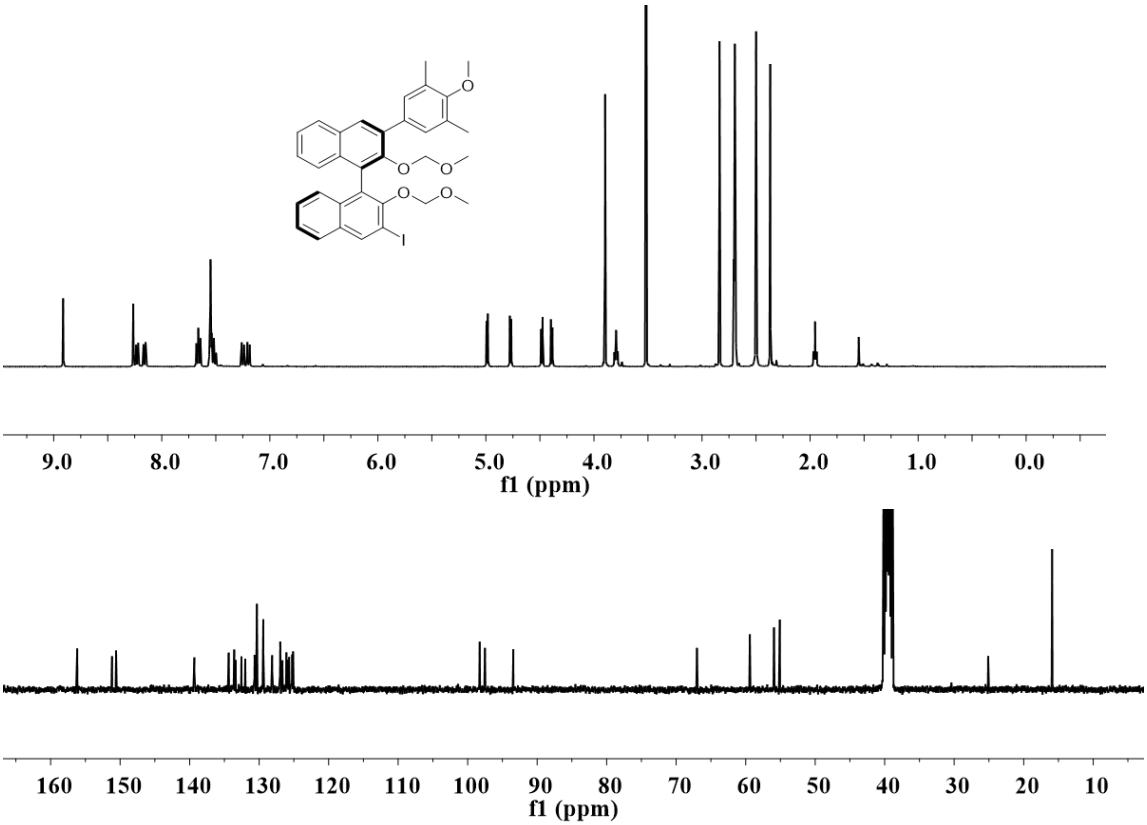


Figure 109: NMR-spectra of (*R*)-**70e** in [D_6]- dimethylsulfoxid (298 K): top ^{1}H (600 MHz), bottom ^{13}C (151 MHz) [MT621-7].

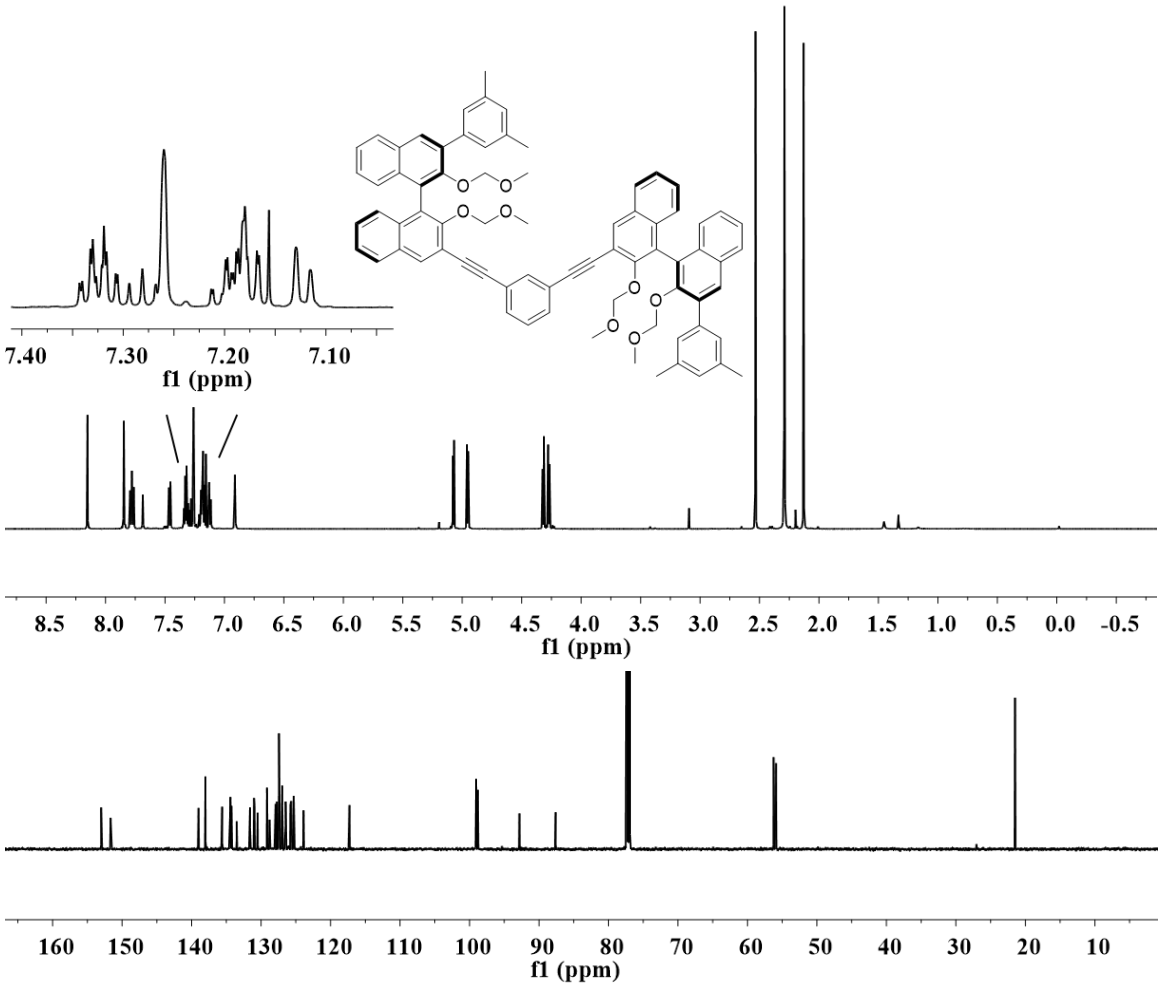


Figure 110: NMR-spectra of (*R*,*R*)-**79a** in [D_1]-chloroform (298 K): top ^{1}H (600 MHz), bottom ^{13}C (151 MHz) [MT332-2].

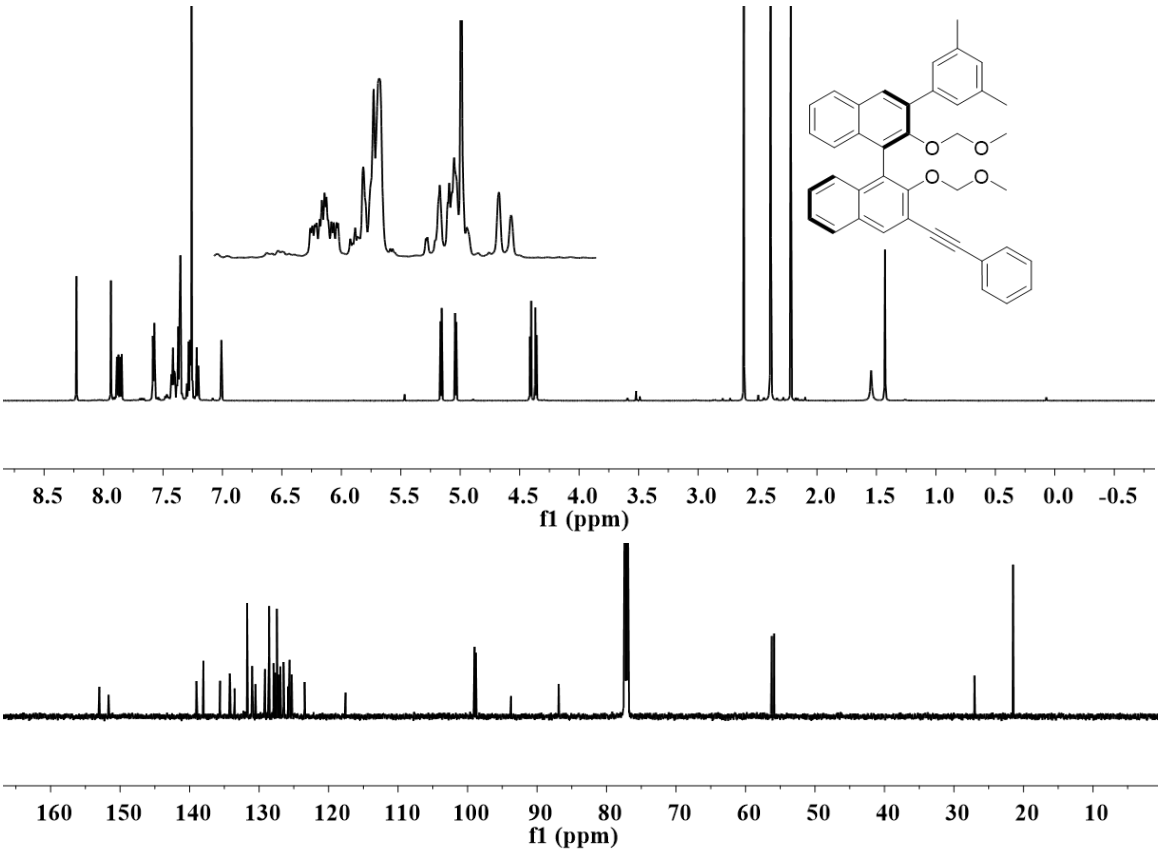


Figure 111: NMR-spectra of (*R*)-**102a** in [D_1]-chloroform (298 K): top ^{1}H (600 MHz), bottom ^{13}C (151 MHz) [MT333-2].

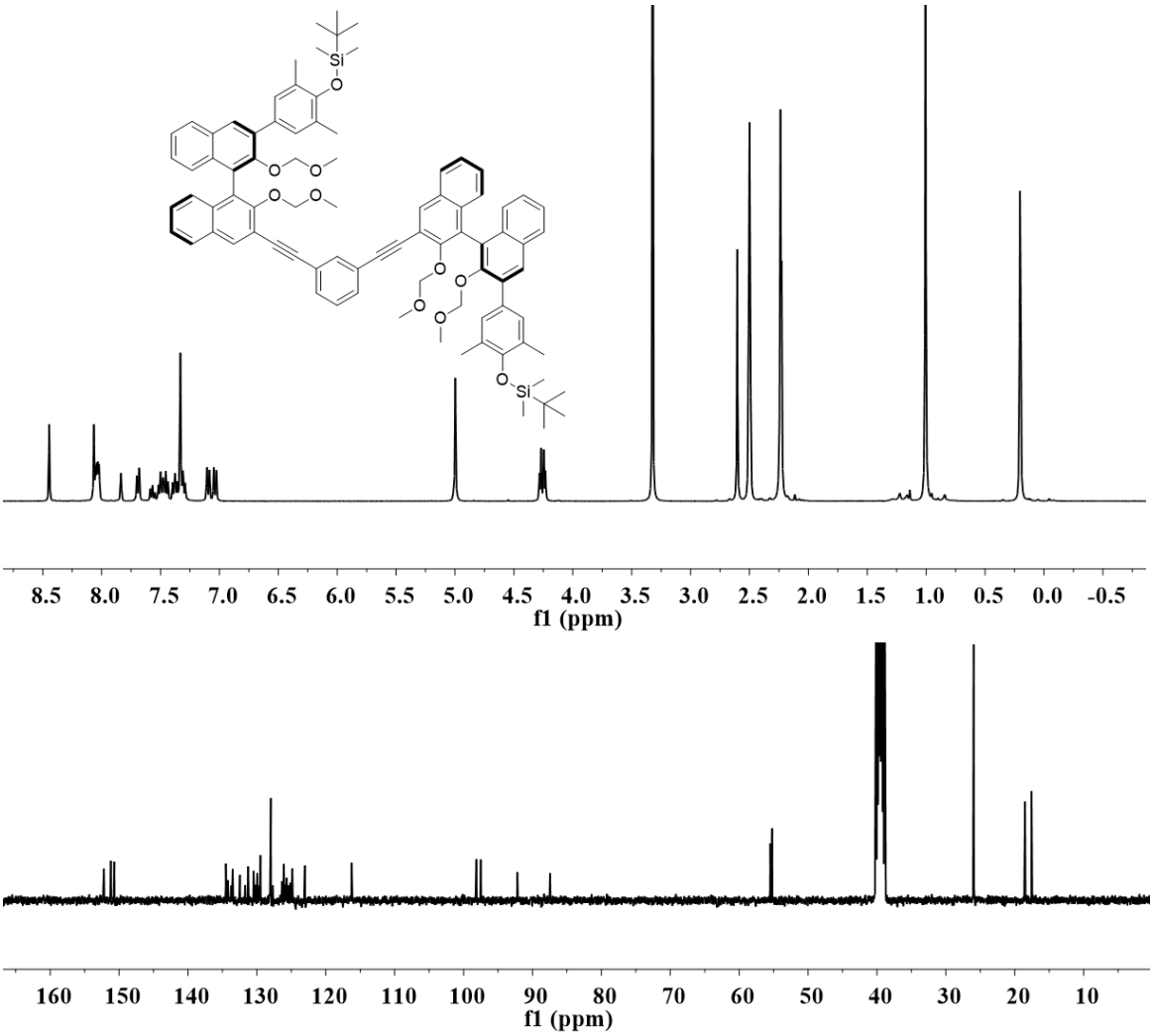


Figure 112: NMR-spectra of (*R*,*R*)-**79c** in [D_6]- dimethylsulfoxid (298 K): top ^{1}H (400 MHz), bottom ^{13}C (101 MHz) [MT476-4].

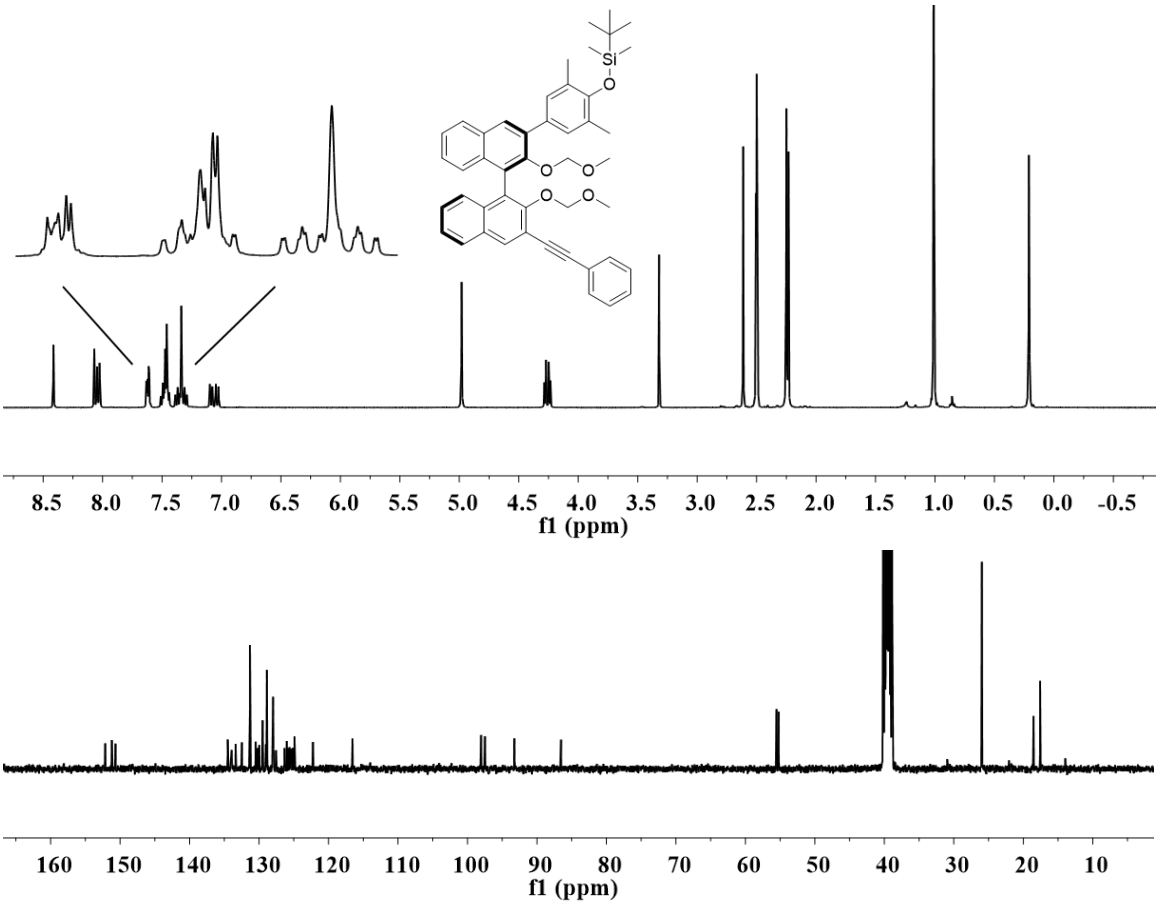


Figure 113: NMR-spectra of (*R*)-**102c** in [D_6]- dimethylsulfoxid (298 K): top ^{1}H (400 MHz), bottom ^{13}C (101 MHz) [MT536-4].

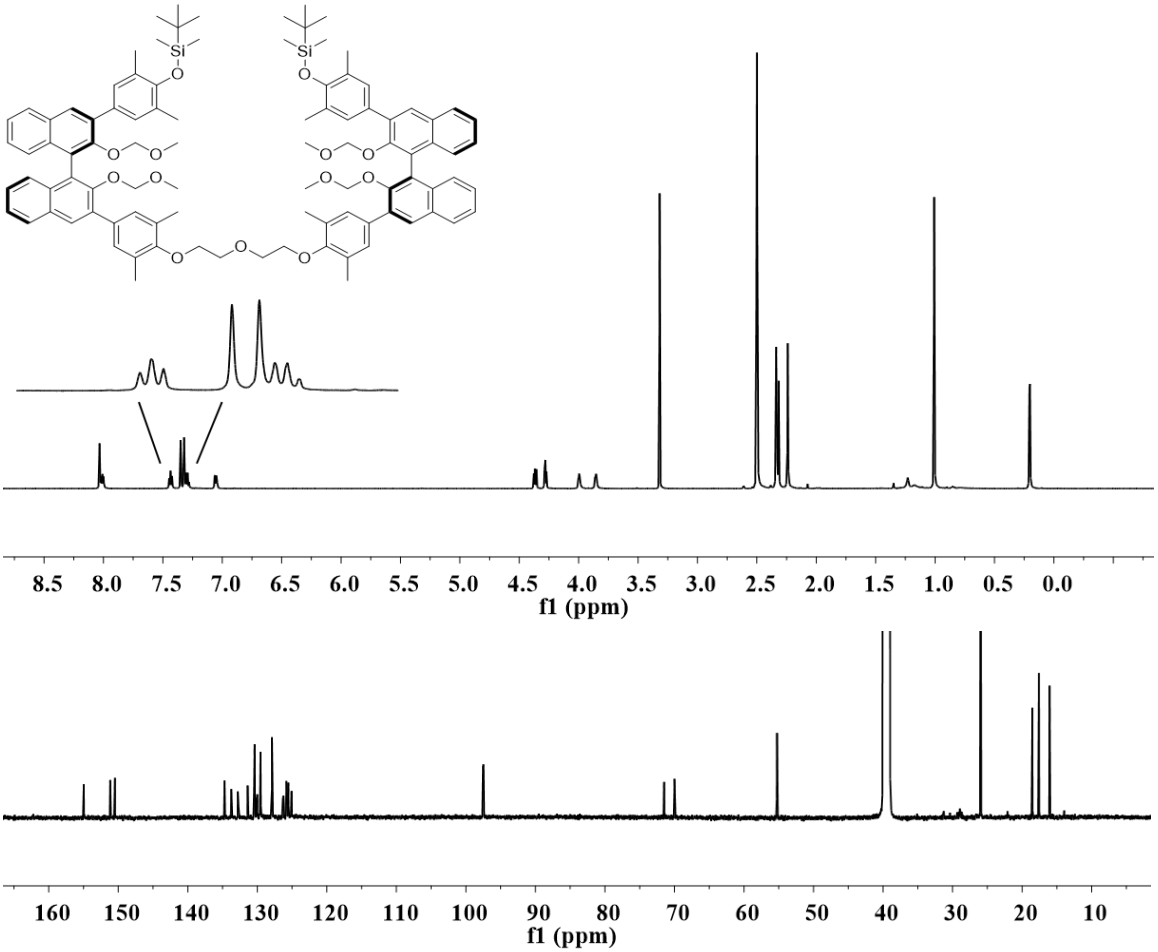


Figure 114: NMR-spectra of (*R*,*R*)-**85c** in [D_6]- dimethylsulfoxid (298 K): top ^{1}H (600 MHz), bottom ^{13}C (151 MHz) [MT585].

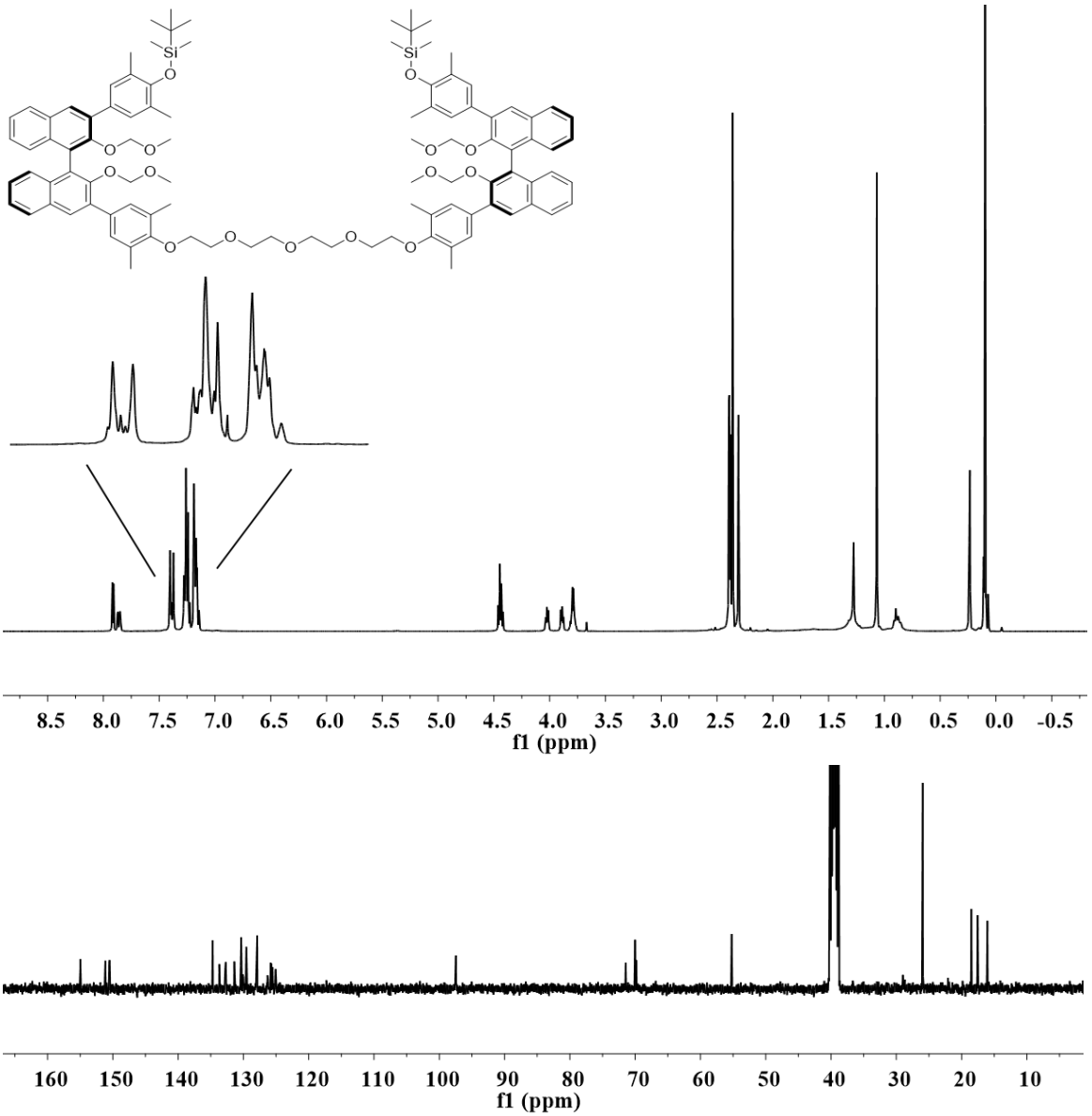


Figure 115: NMR-spectra of (*R*,*R*)-**86c** in [D_6]- dimethylsulfoxid (298 K): top ^{1}H (400 MHz), bottom ^{13}C (101 MHz) [MT647-7].

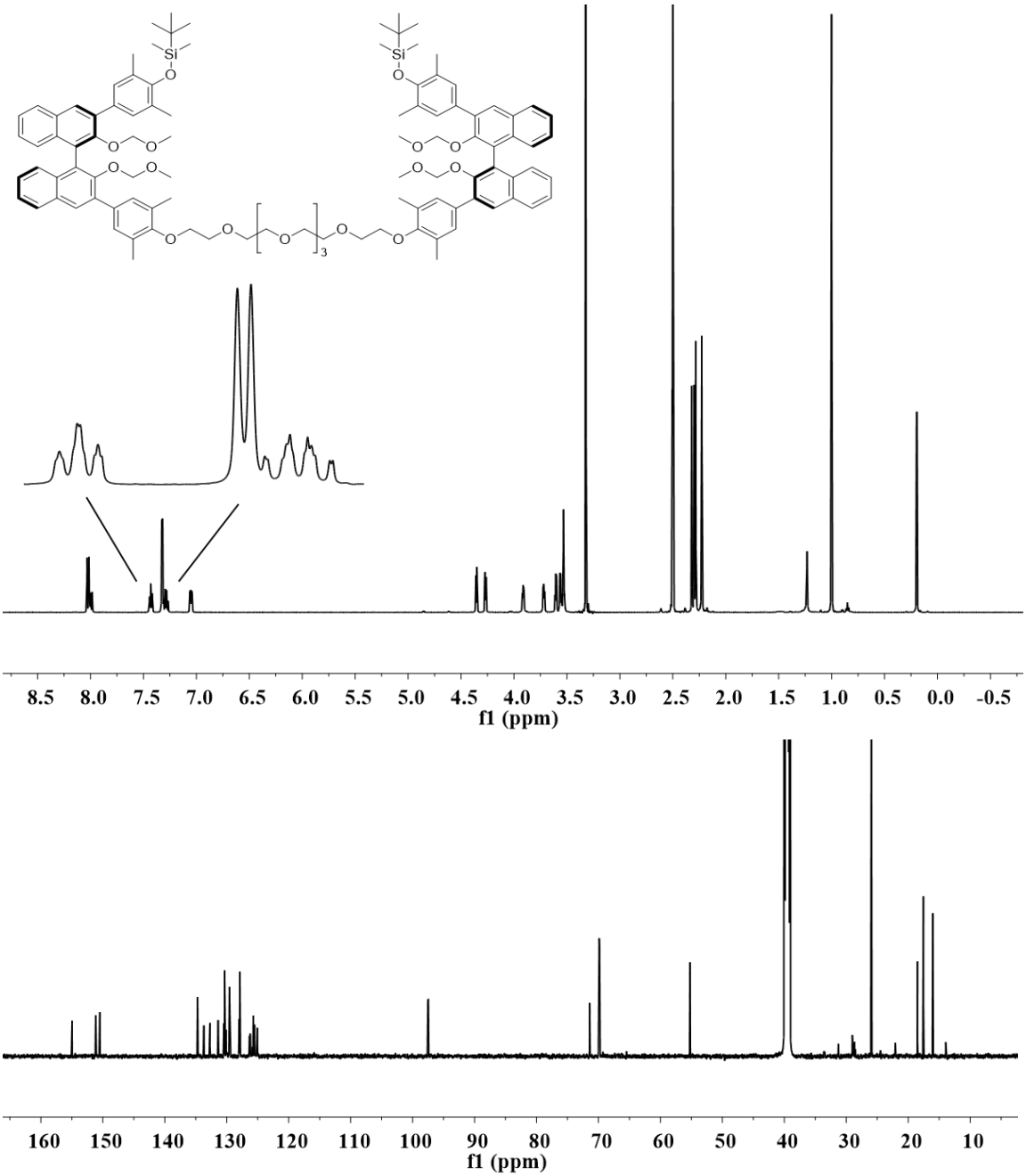


Figure 116: NMR-spectra of (*R*,*R*)-**87c** in [D_6]- dimethylsulfoxid (298 K): top ^{1}H (600 MHz), bottom ^{13}C (151 MHz) [MT654-7].

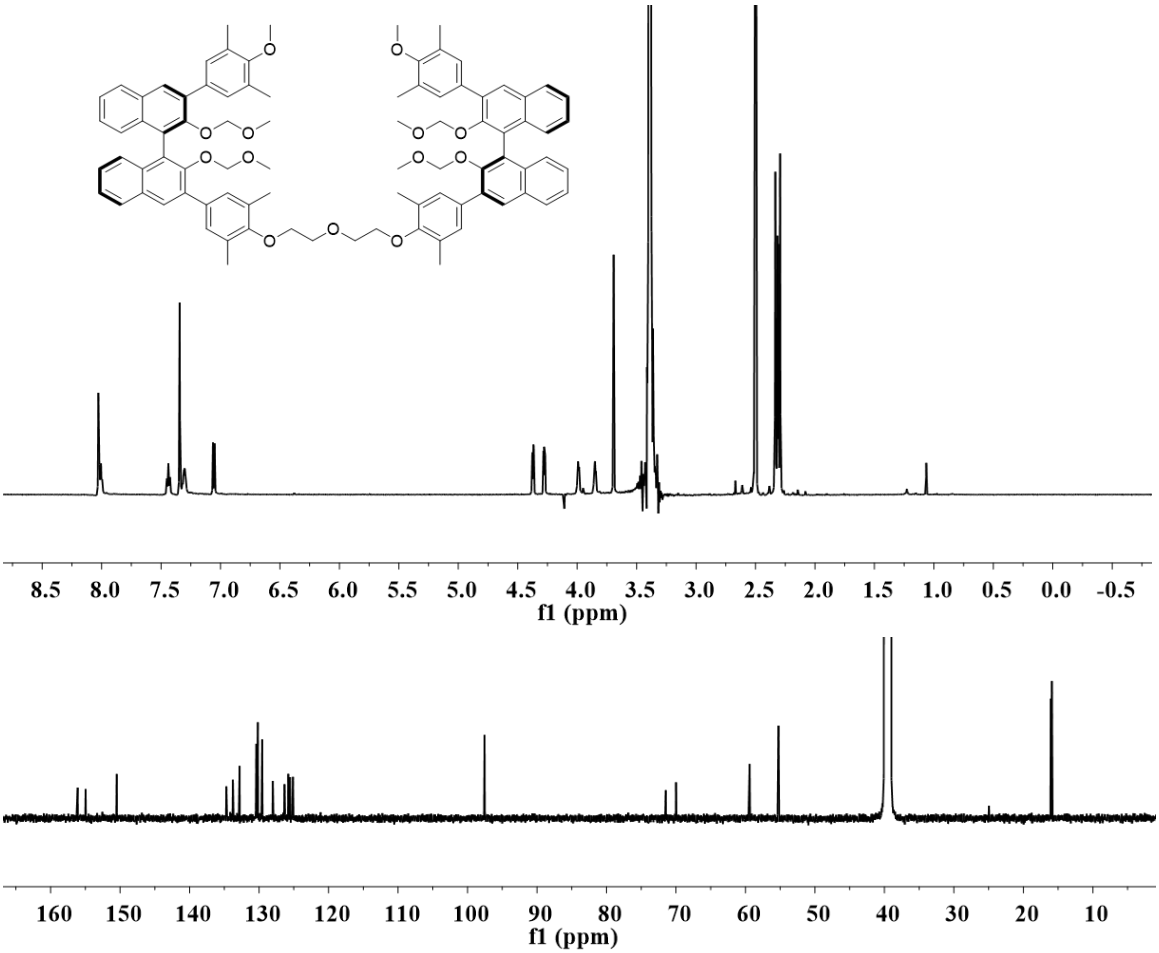


Figure 117: NMR-spectra of (*R*,*R*)-**85e** in [D_6]- dimethylsulfoxid (298 K): top ^{1}H (600 MHz), bottom ^{13}C (151 MHz) [MT622-3].

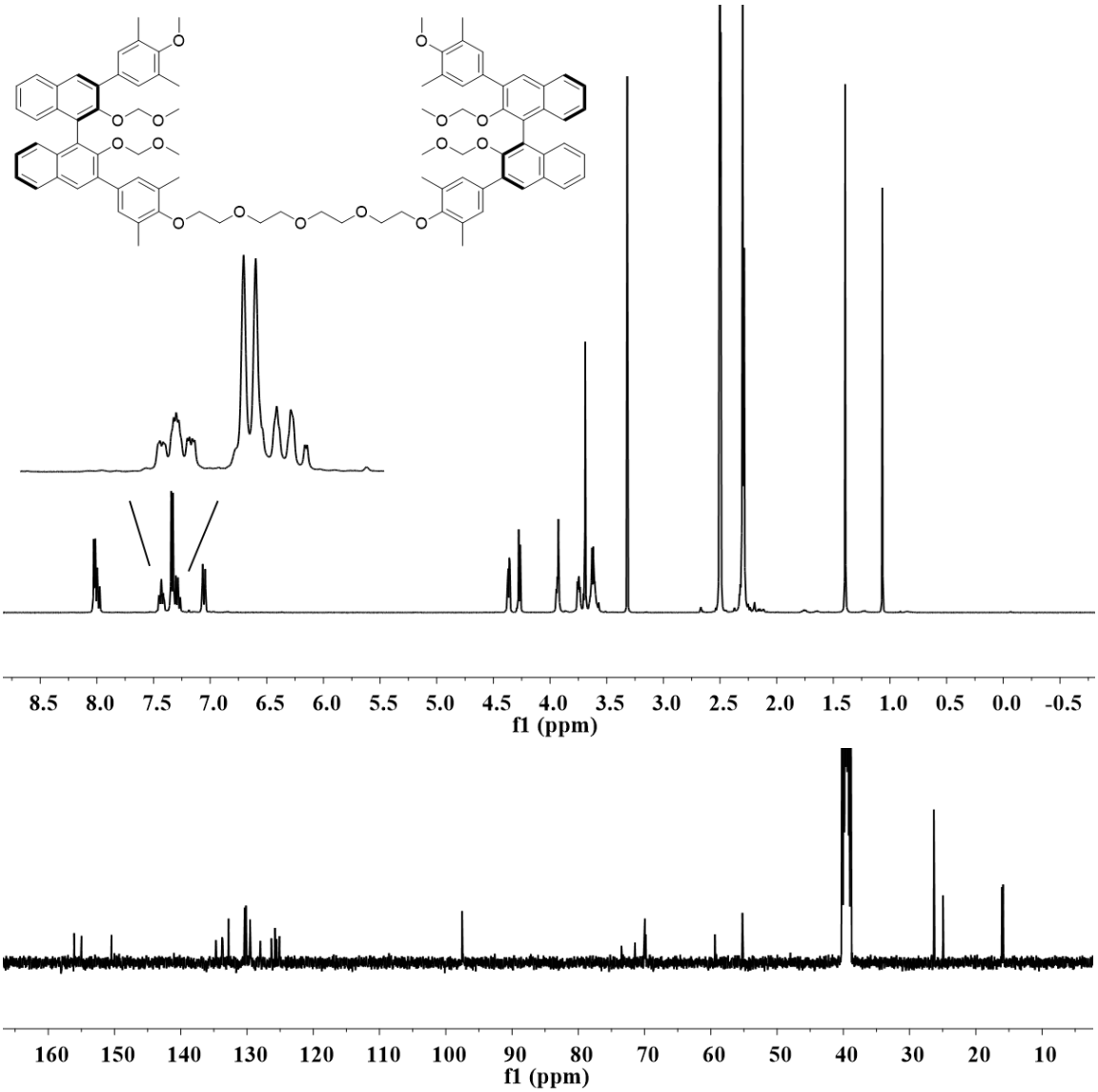


Figure 118: NMR-spectra of (*R*,*R*)-**86e** in [D_6]- dimethylsulfoxid (298 K): top ^{1}H (400 MHz), bottom ^{13}C (101 MHz) [MT684-4].

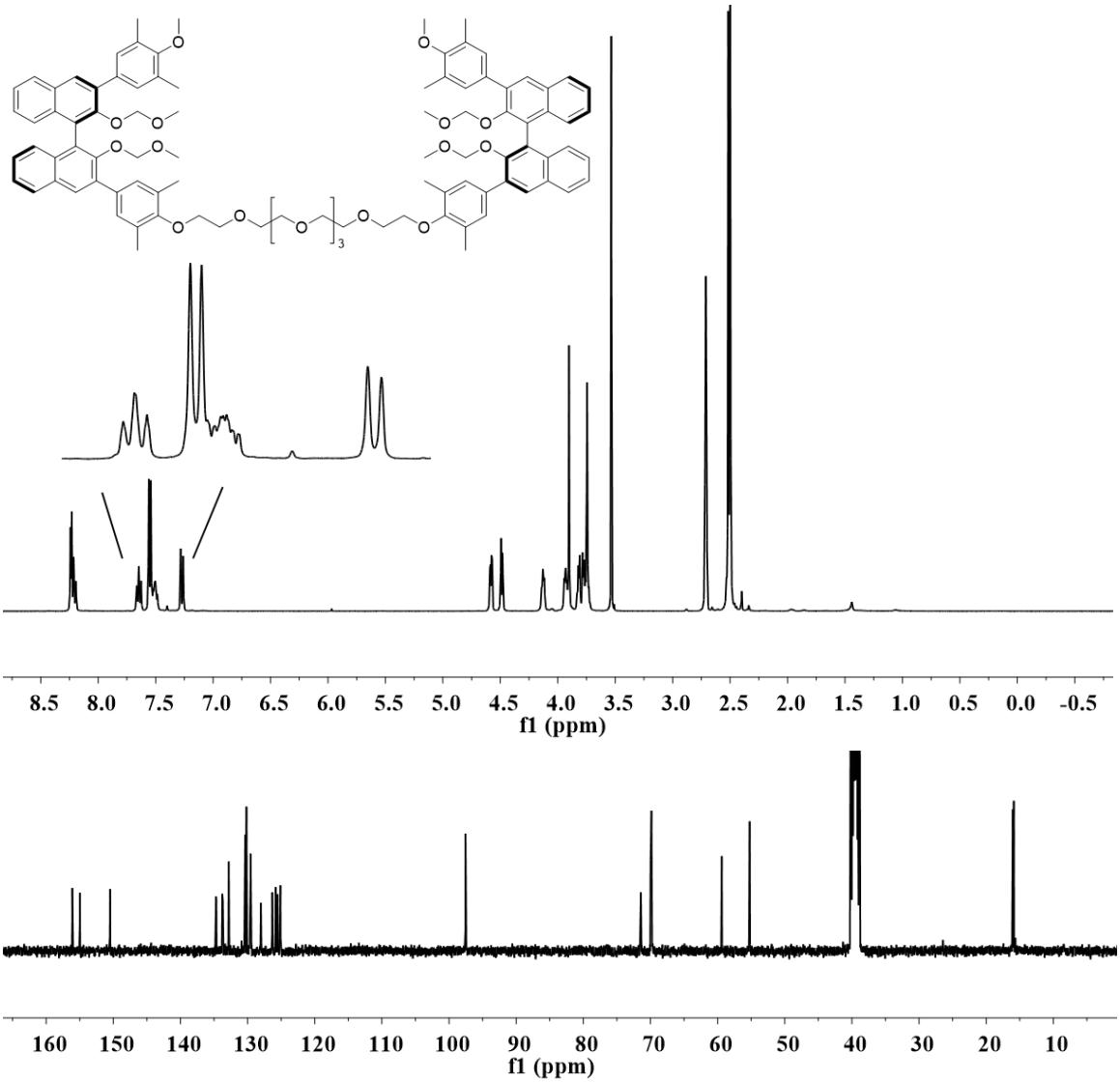


Figure 119: NMR-spectra of (*R*,*R*)-**87e** in [D_6]- dimethylsulfoxid (298 K): top ^{1}H (400 MHz), bottom ^{13}C (101 MHz) [MT677-7].

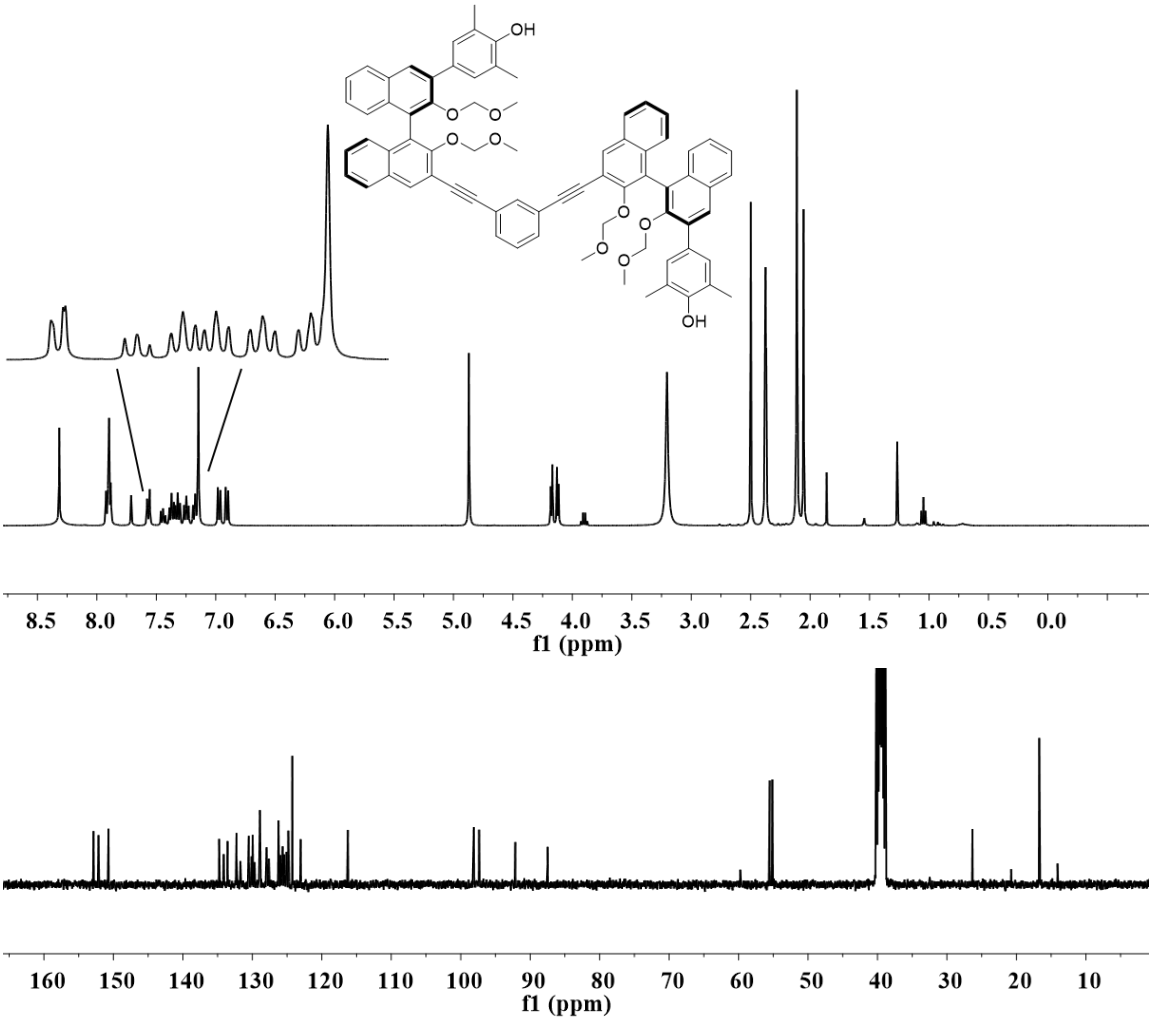


Figure 120: NMR-spectra of (*R*,*R*)-**79d** in [D_6]- dimethylsulfoxid (298 K): top ^{1}H (400 MHz), bottom ^{13}C (101 MHz) [MT537-3].

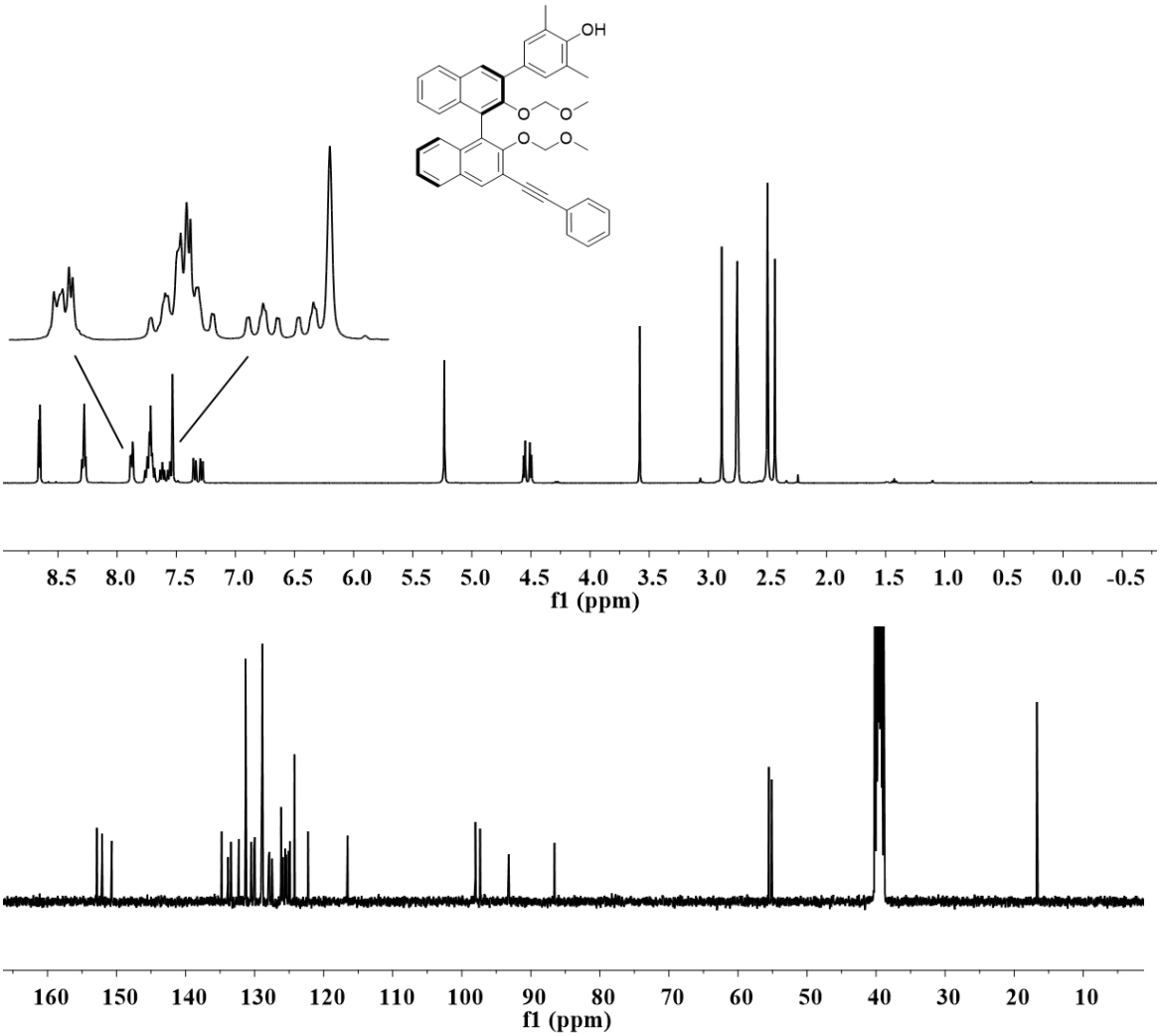


Figure 121: NMR-spectra of (*R*)-**102d** in [D_6]- dimethylsulfoxid (298 K): top ^{1}H (400 MHz), bottom ^{13}C (101 MHz) [MT540-2].

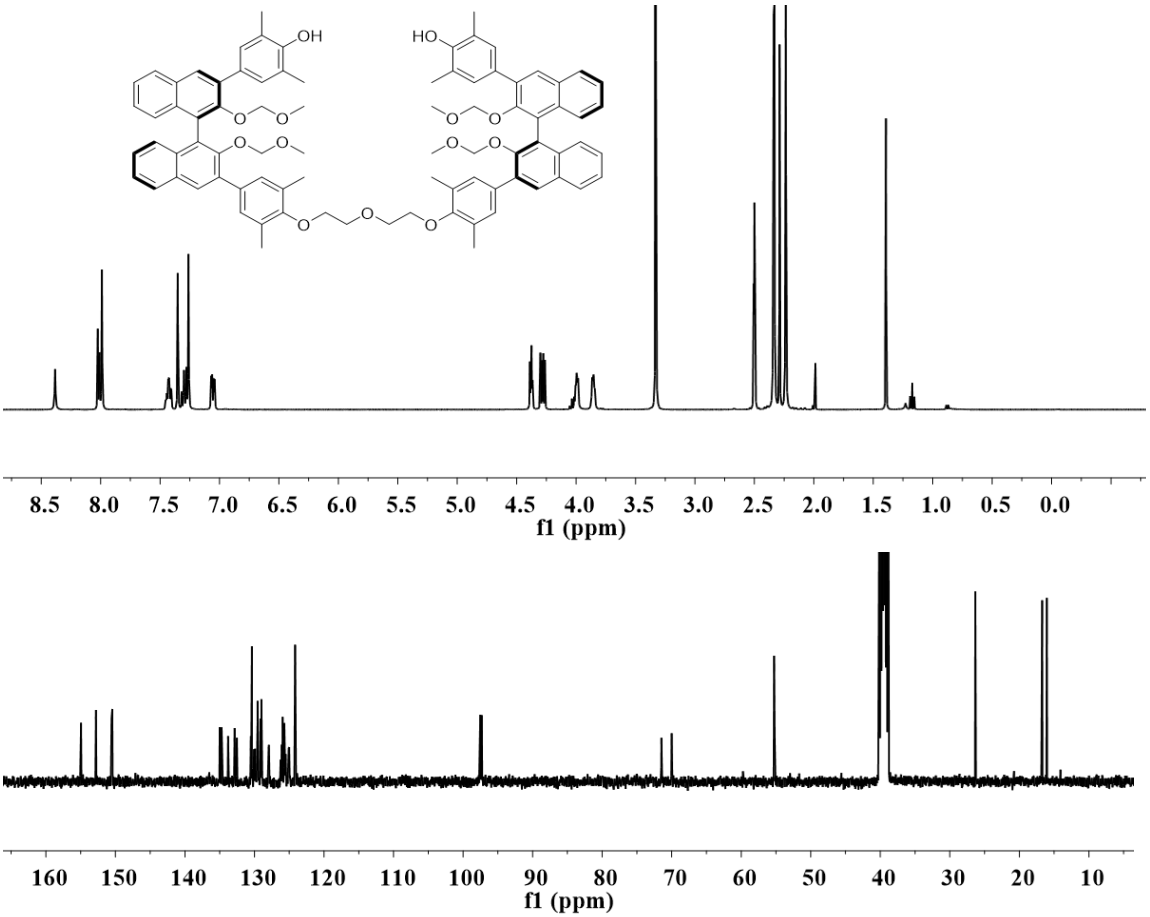


Figure 122: NMR-spectra of (*R*,*R*)-**85d** in [D_6]- dimethylsulfoxid (298 K): top ^{1}H (400 MHz), bottom ^{13}C (101 MHz) [MT586].

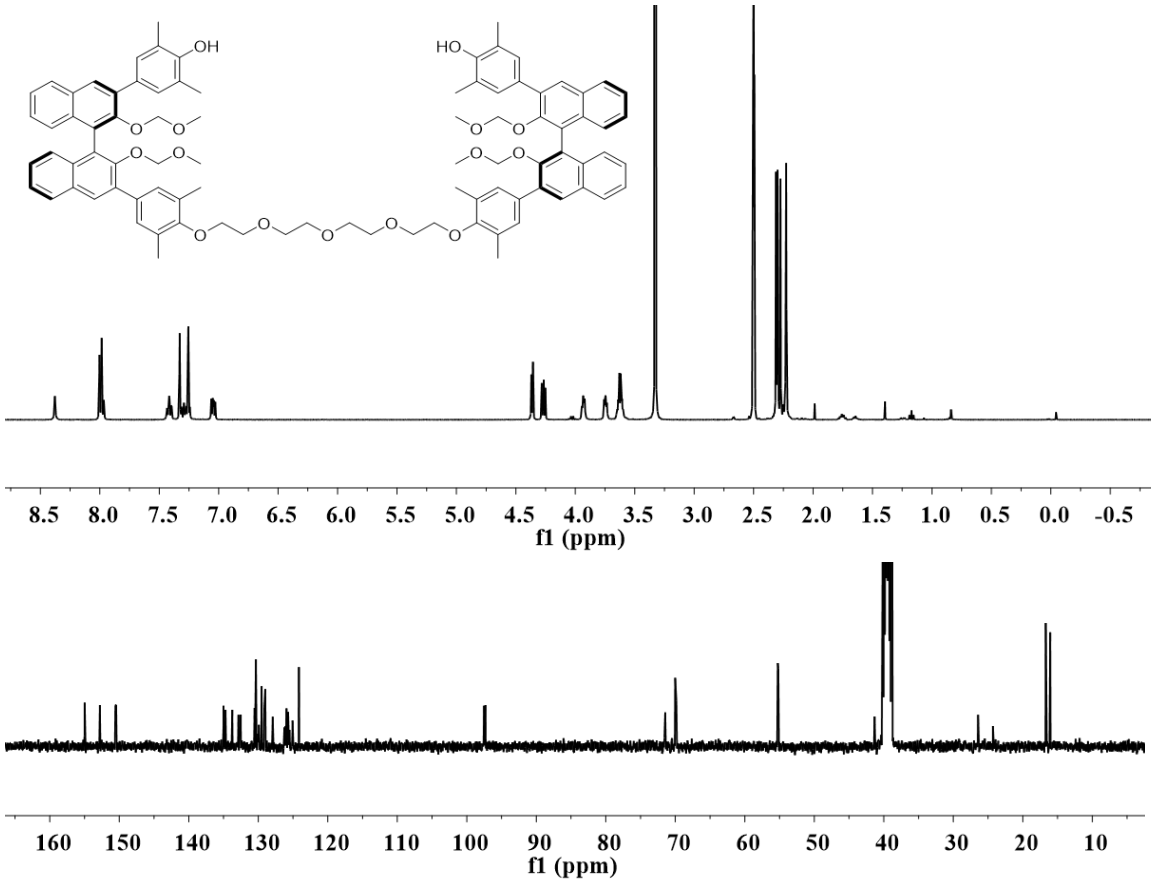


Figure 123: NMR-spectra of (*R*,*R*)-**86d** in [D_6]- dimethylsulfoxid (298 K): top ^{1}H (400 MHz), bottom ^{13}C (101 MHz) [MT653-4].

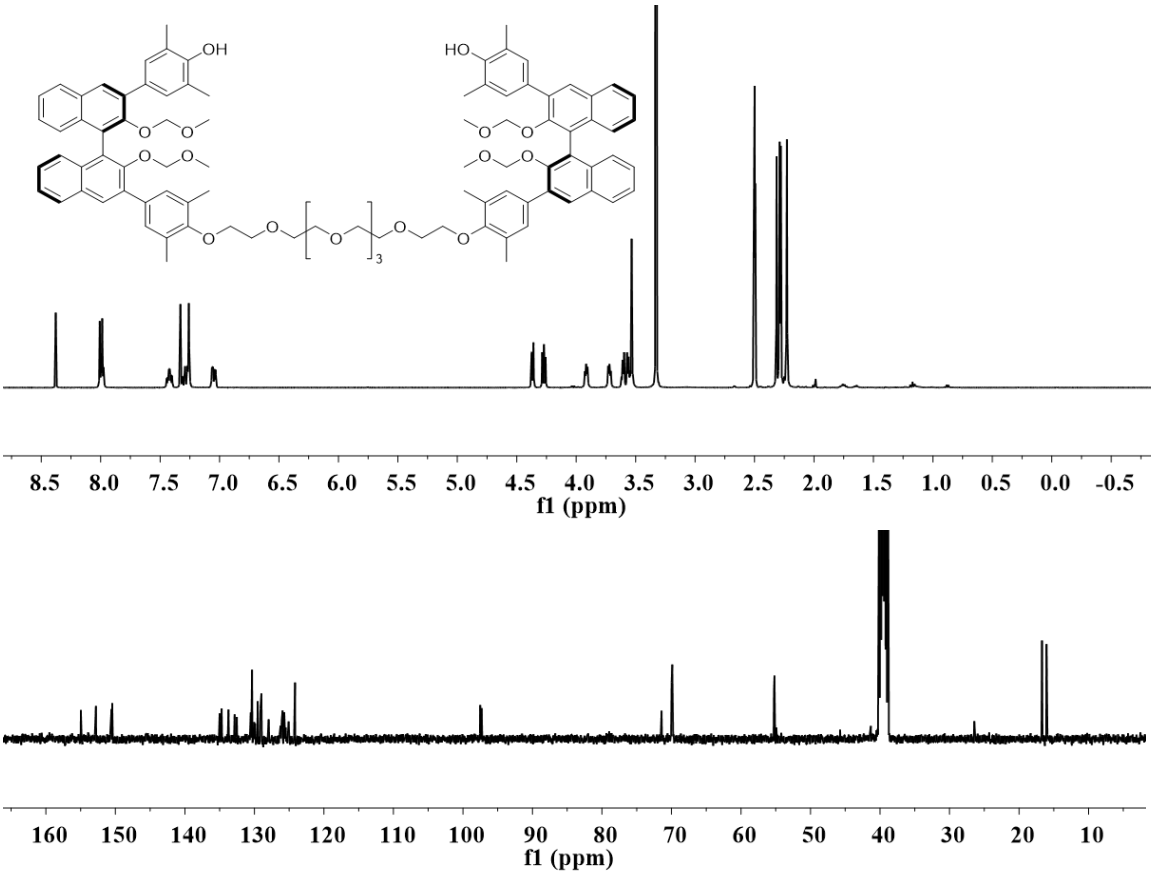


Figure 124: NMR-spectra of (*R*,*R*)-**87d** in [D_6]- dimethylsulfoxid (298 K): top ^{1}H (400 MHz), bottom ^{13}C (101 MHz) [MT657-4].

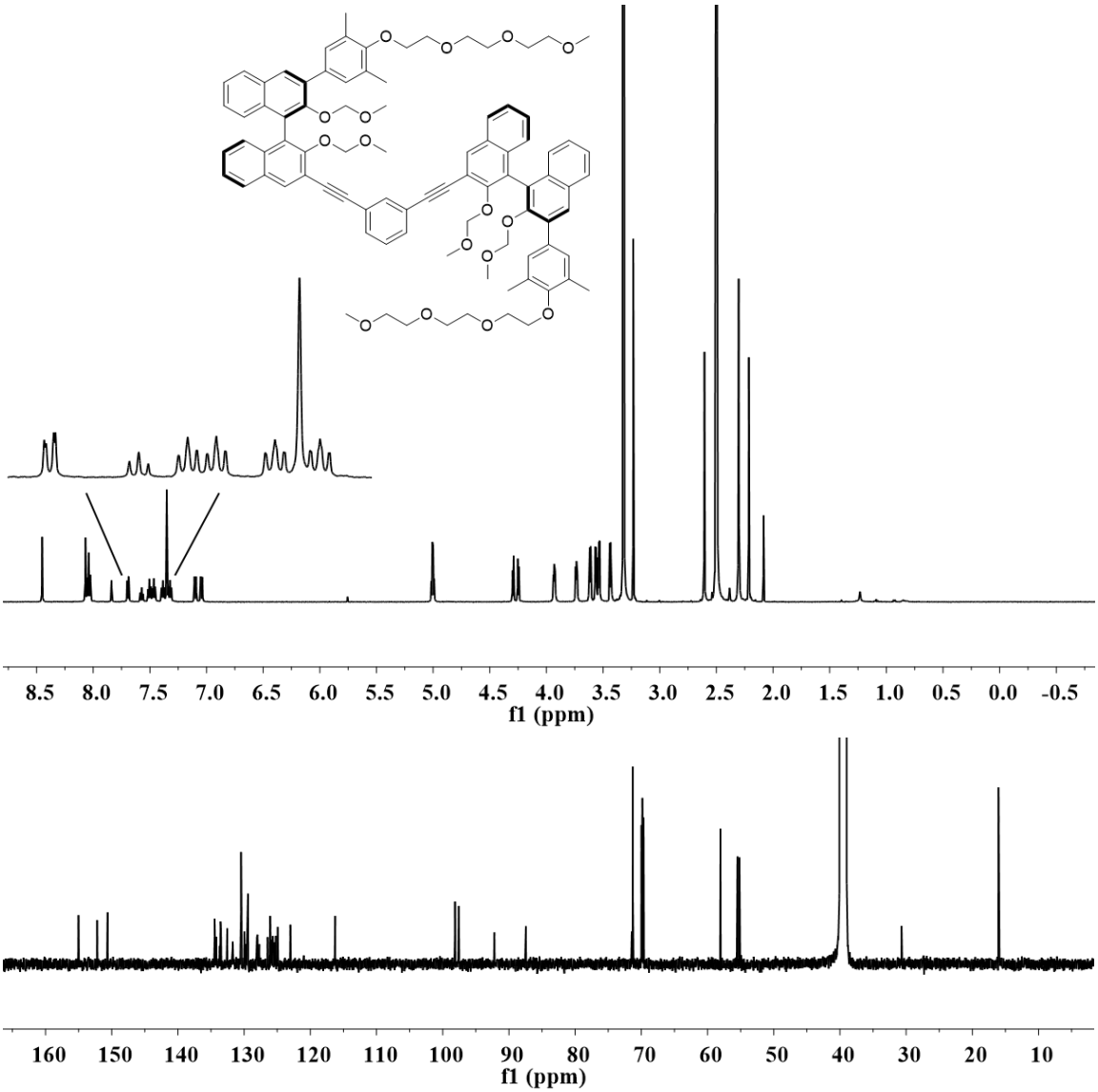


Figure 125: NMR-spectra of (*R*,*R*)-**79b** in [D_6]- dimethylsulfoxid (298 K): top ^{1}H (600 MHz), bottom ^{13}C (151 MHz) [MT538-3].

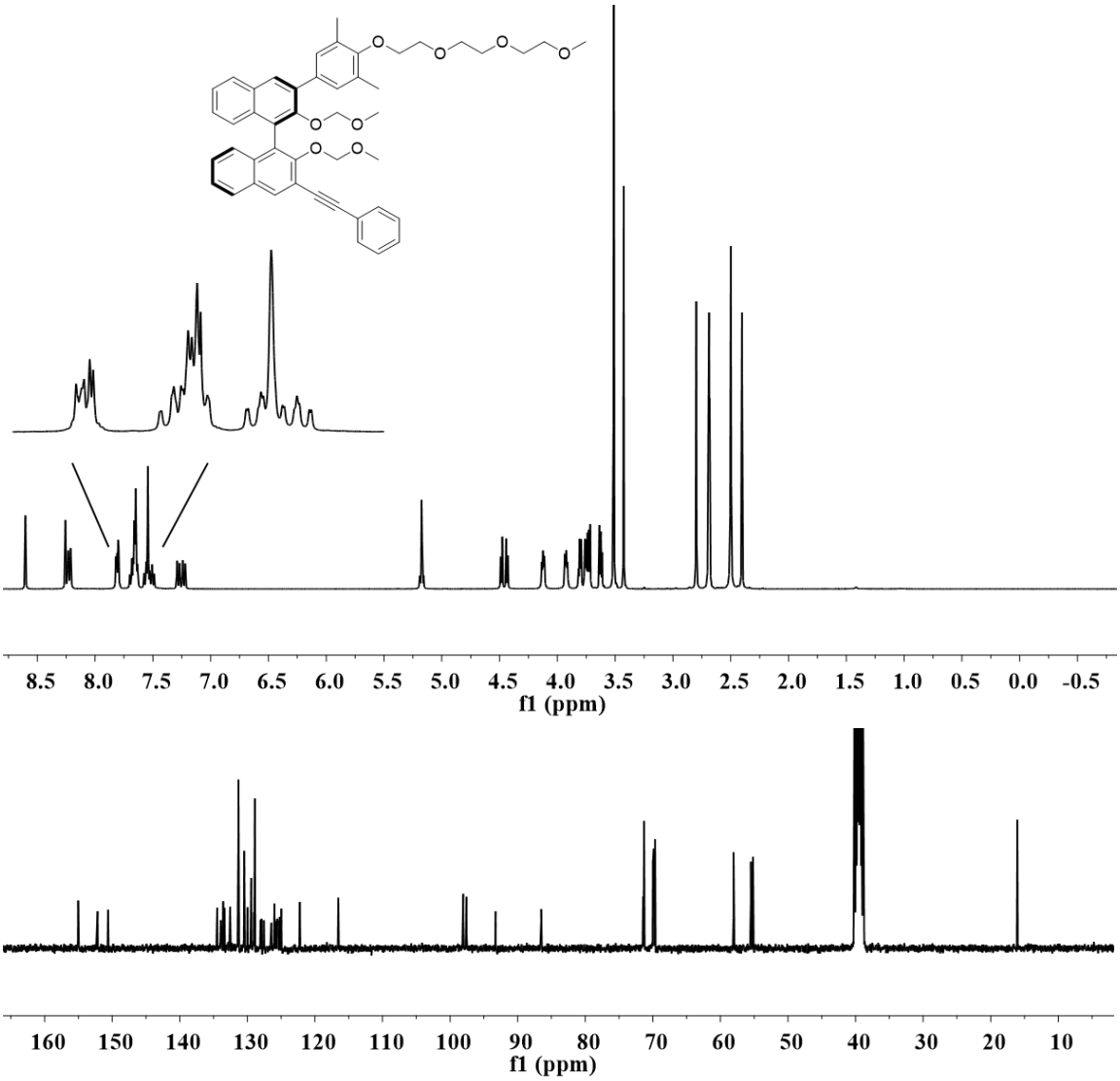


Figure 126: NMR-spectra of (*R*)-**102b** in [D_6]- dimethylsulfoxid (298 K): top ^{1}H (400 MHz), bottom ^{13}C (101 MHz) [MT541-6].

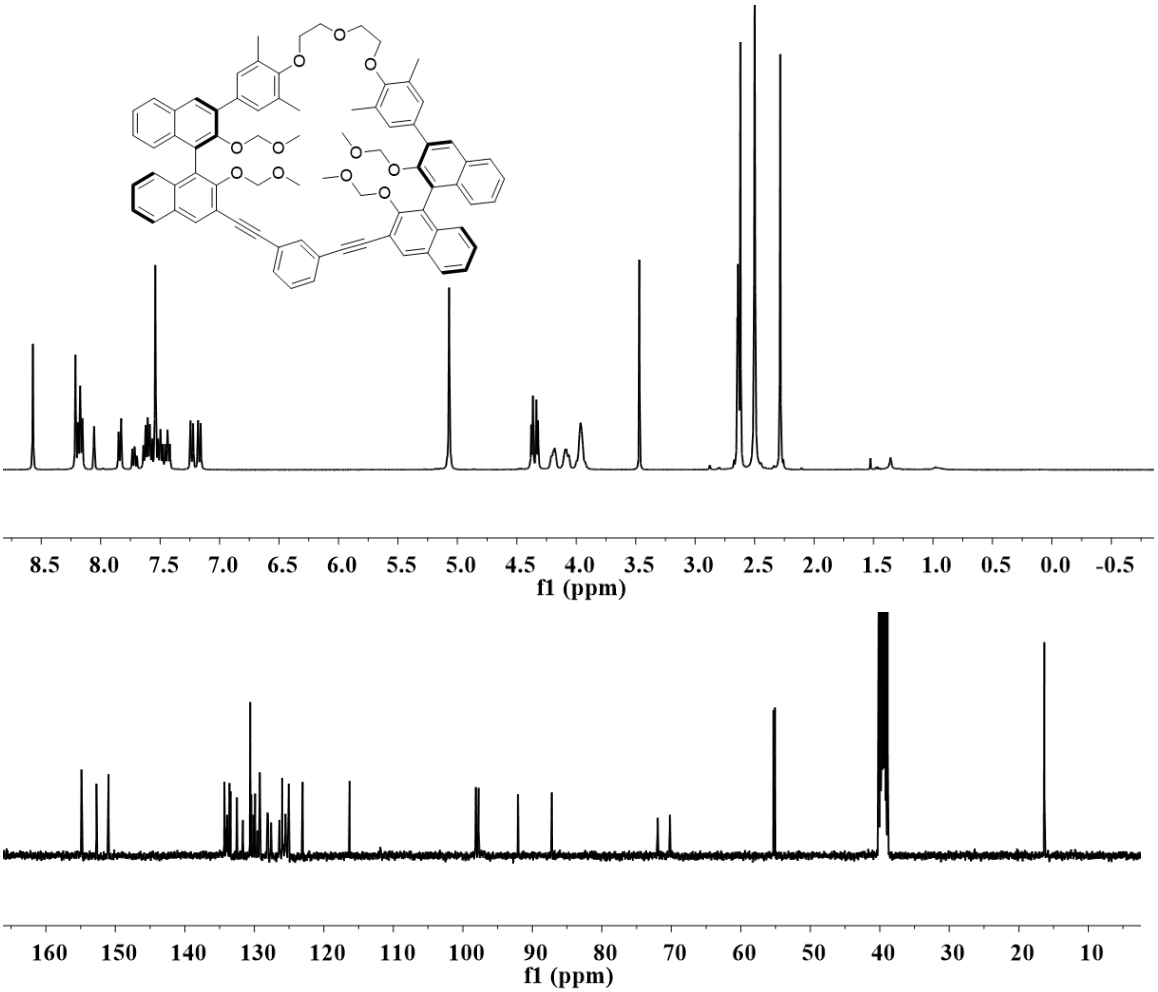


Figure 127 NMR-spectra of (*R*,*R*)-**80** in [D_6]- dimethylsulfoxid (298 K): top ^{1}H (400 MHz), bottom ^{13}C (101 MHz) [MT525-2].

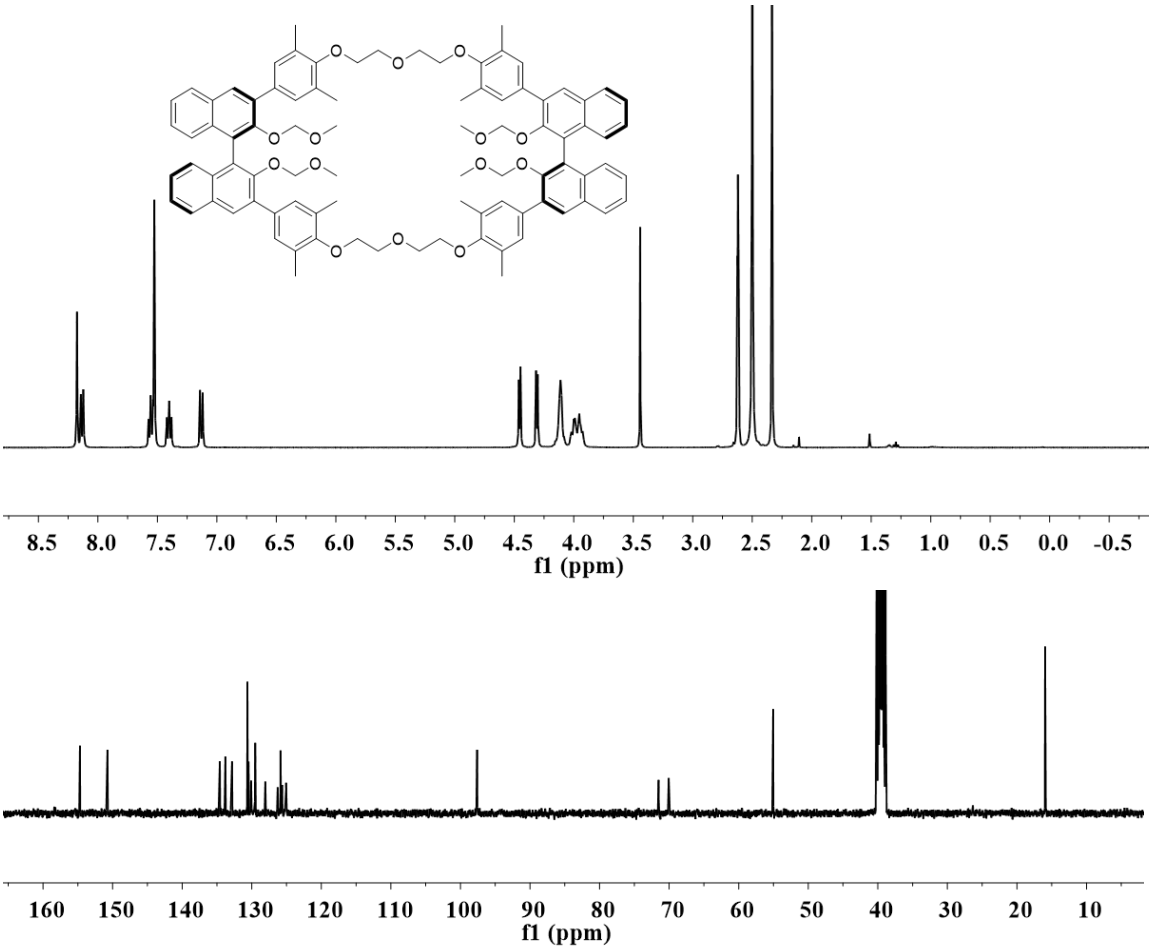


Figure 128: NMR-spectra of (*R*,*R*)-**88** in [D_6]- dimethylsulfoxid (298 K): top ^{1}H (400 MHz), bottom ^{13}C (101 MHz) [MT589-3].

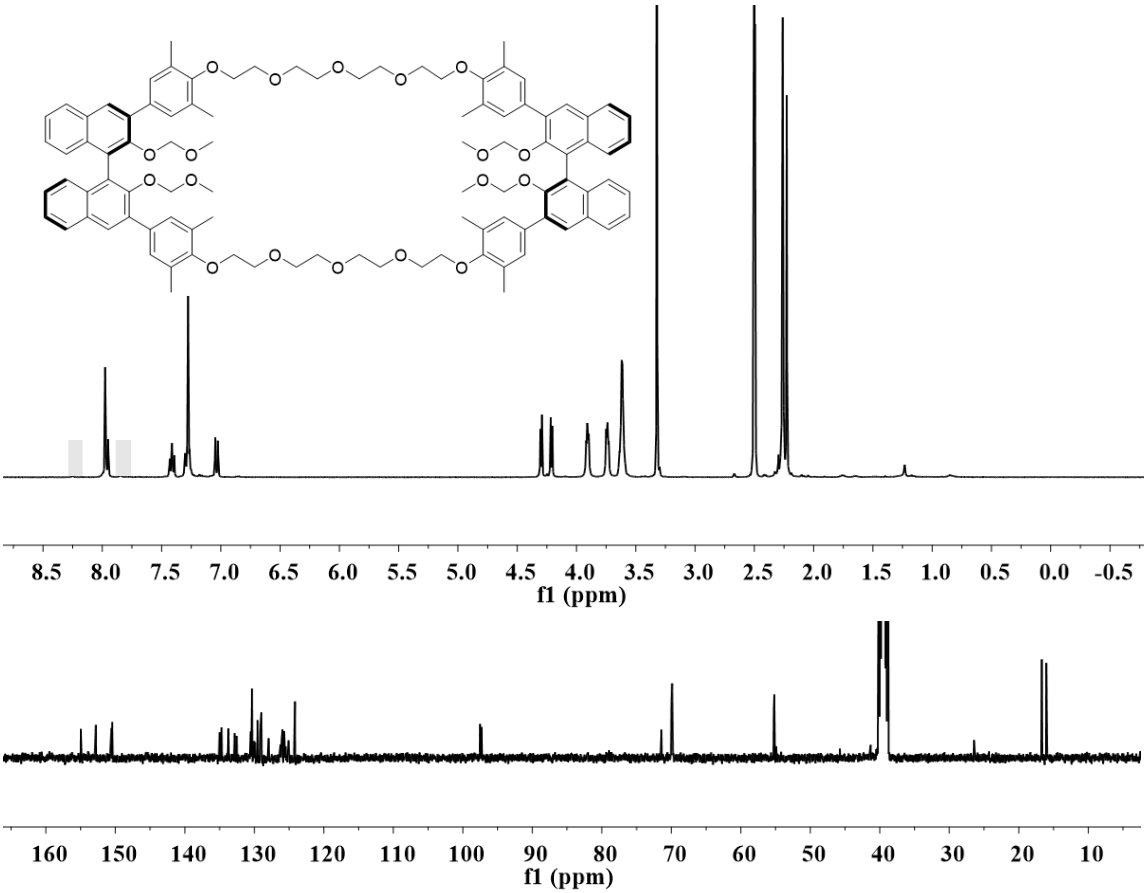


Figure 129: NMR-spectra of (*R*,*R*)-**89** in [D_6]- dimethylsulfoxid (298 K): top ^{1}H (400 MHz), bottom ^{13}C (101 MHz) [MT656-7].

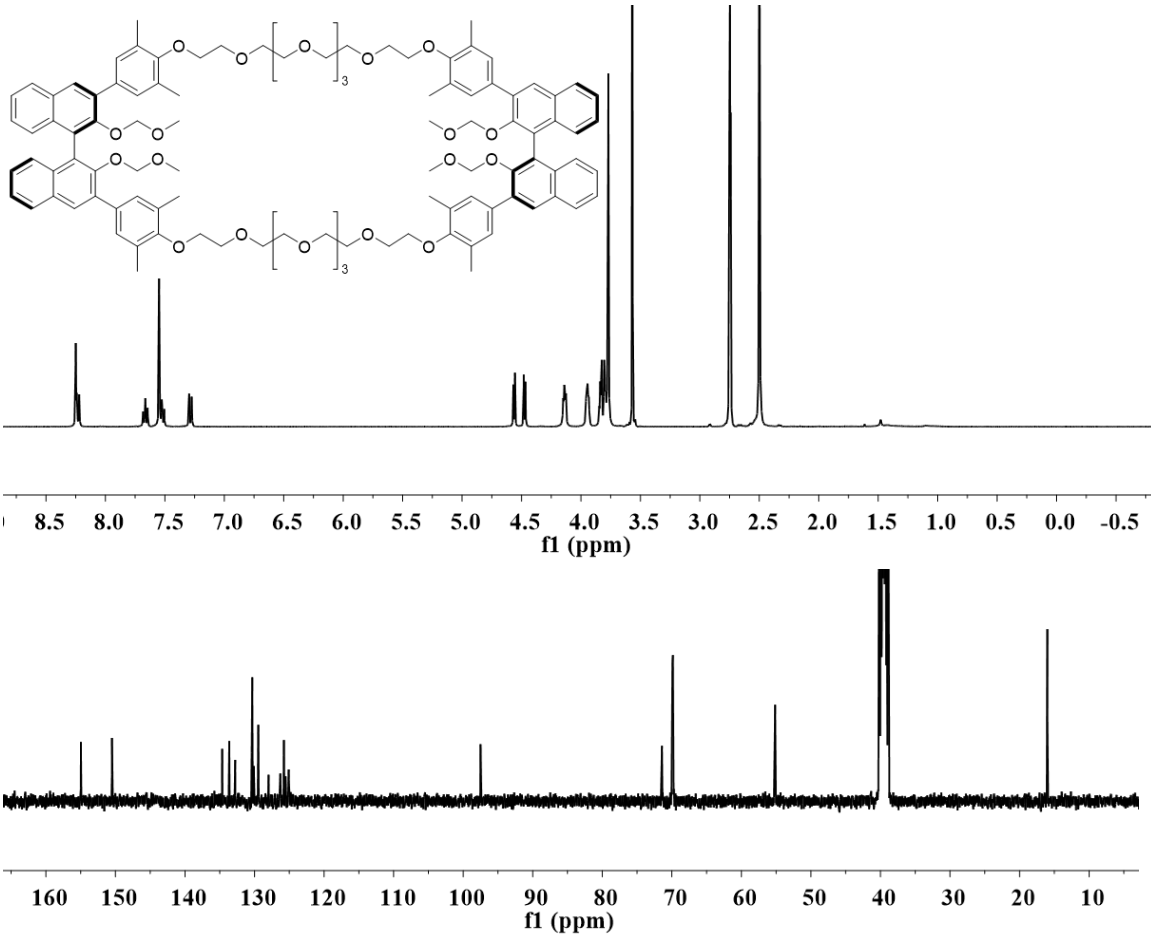


Figure 130: NMR-spectra of (*R*,*R*)-**90** in [D_6]- dimethylsulfoxid (298 K): top ^{1}H (400 MHz), bottom ^{13}C (101 MHz) [MT658-5].

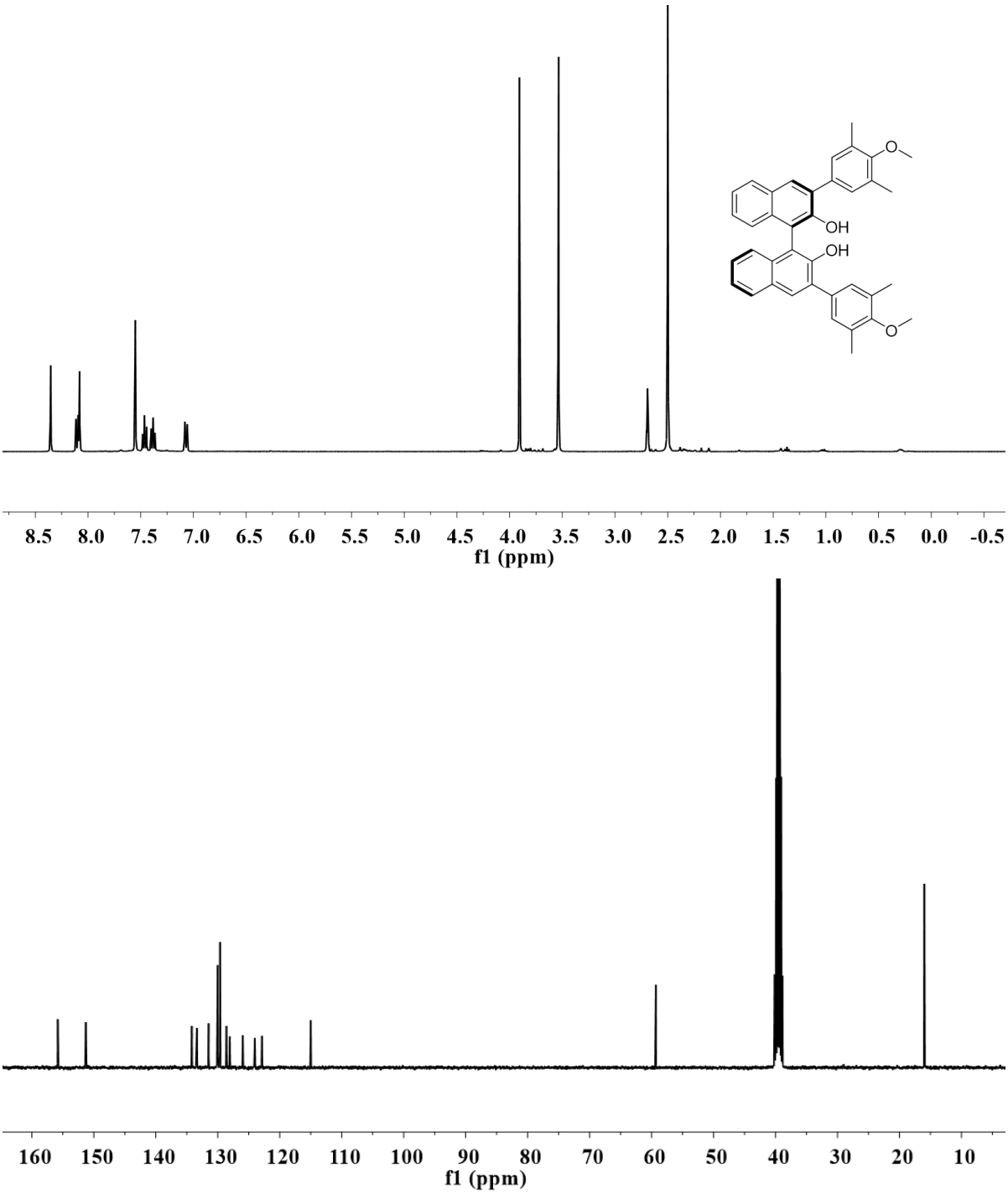


Figure 131: NMR-spectra of (*R*)-**105** in [D_6]- dimethylsulfoxid (298 K): top ^{1}H (400 MHz), bottom ^{13}C (101 MHz).

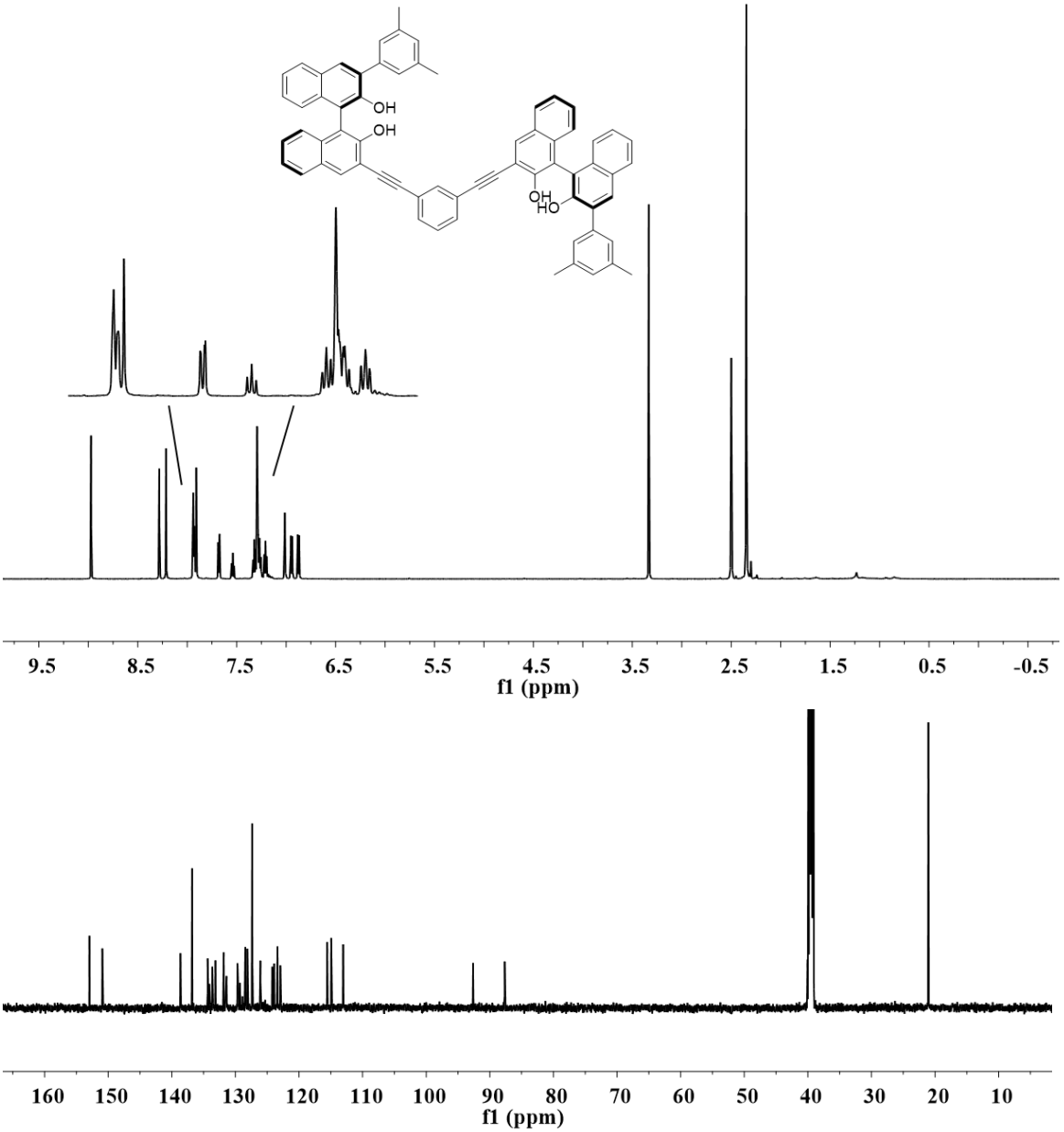


Figure 132: NMR-spectra of (*R*,*R*)-**81a** in [D_6]- dimethylsulfoxid (298 K): top ^{1}H (600 MHz), bottom ^{13}C (151 MHz) [MT350-4].

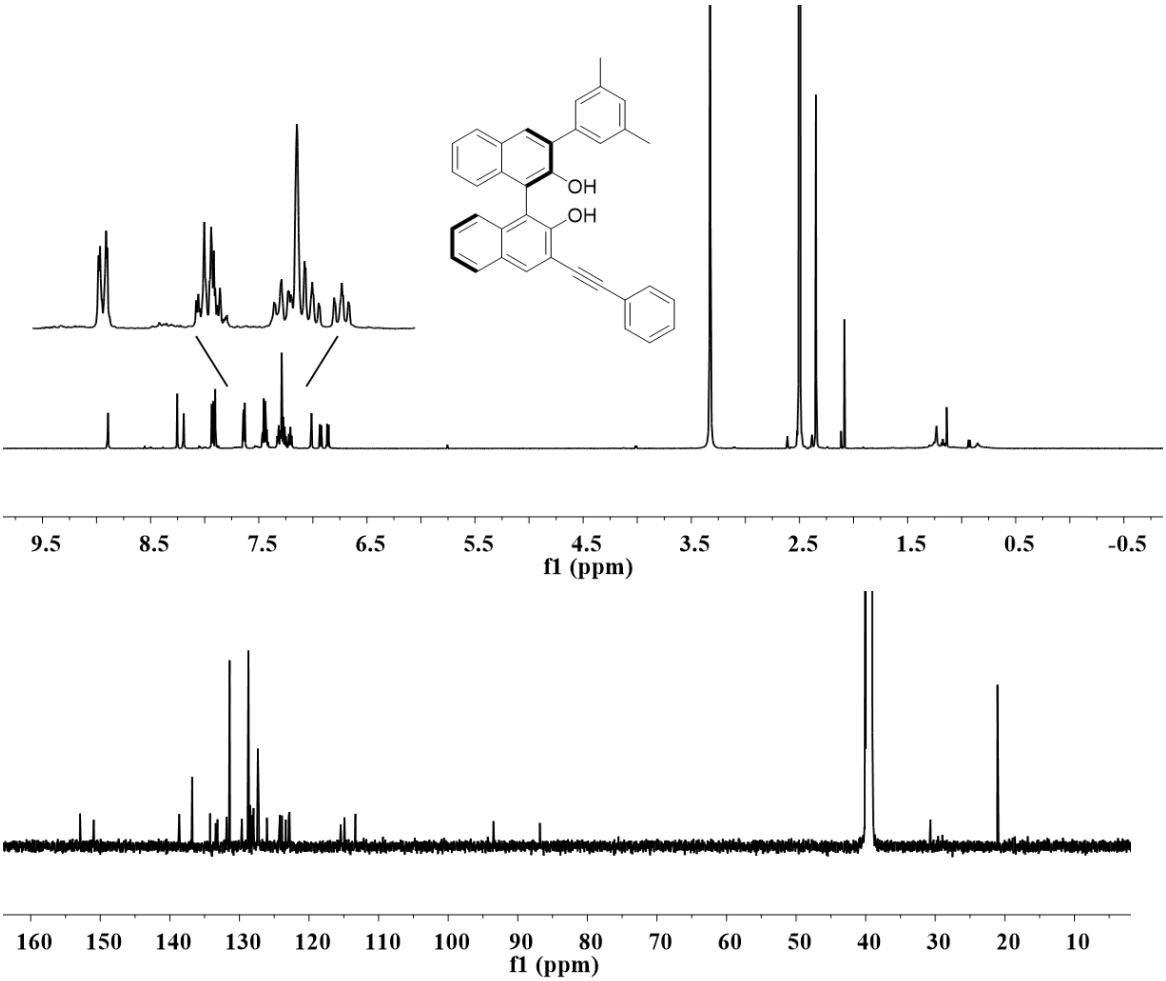


Figure 133: NMR-spectra of (*R*)-**103a** in [D_6]- dimethylsulfoxid (298 K): top ^{1}H (600 MHz), bottom ^{13}C (151 MHz) [MT351-4].

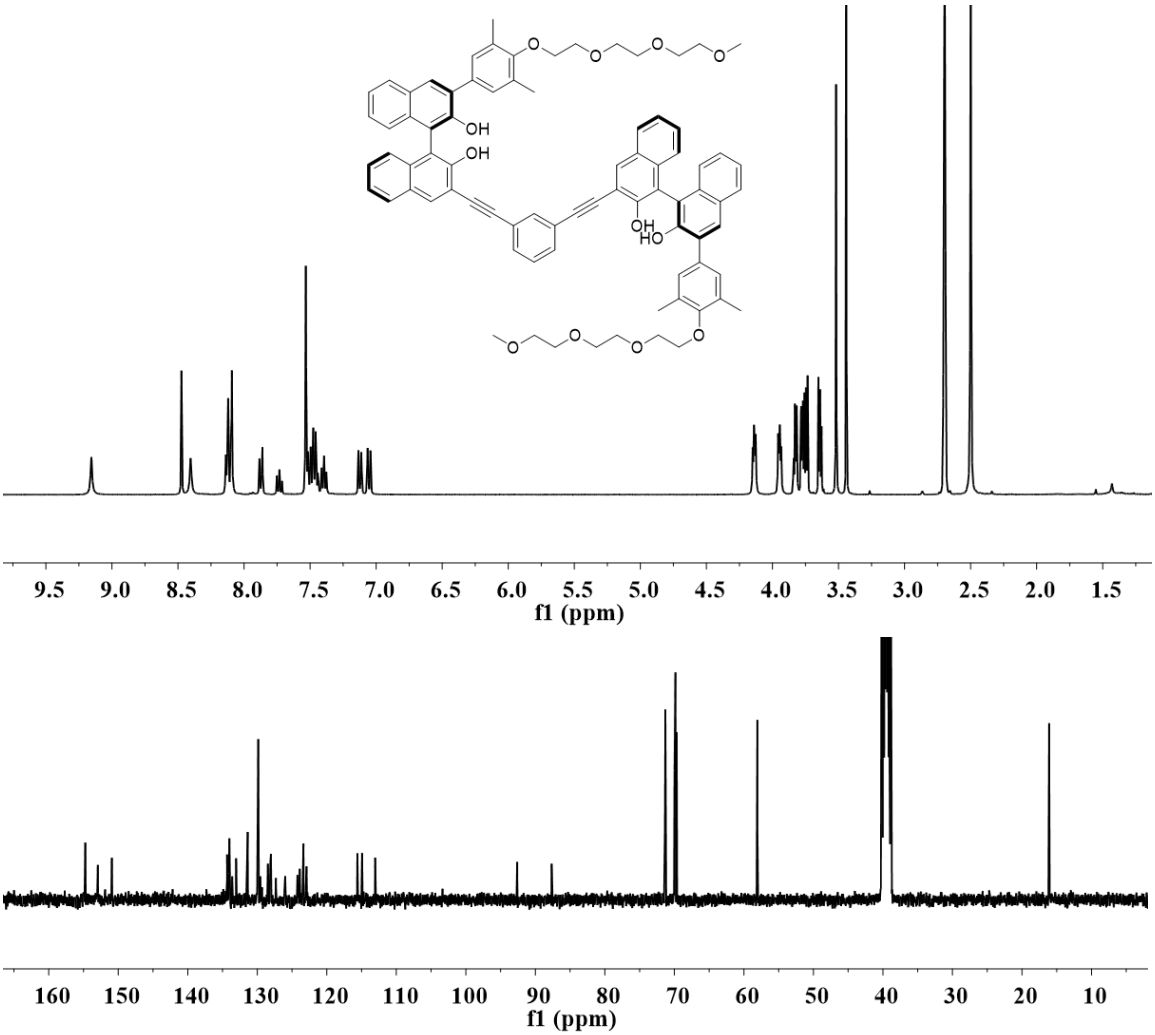


Figure 134: NMR-spectra of (*R*,*R*)-**81b** in [D_6]- dimethylsulfoxid (298 K): top ^{1}H (400 MHz), bottom ^{13}C (101 MHz) [MT544-4].

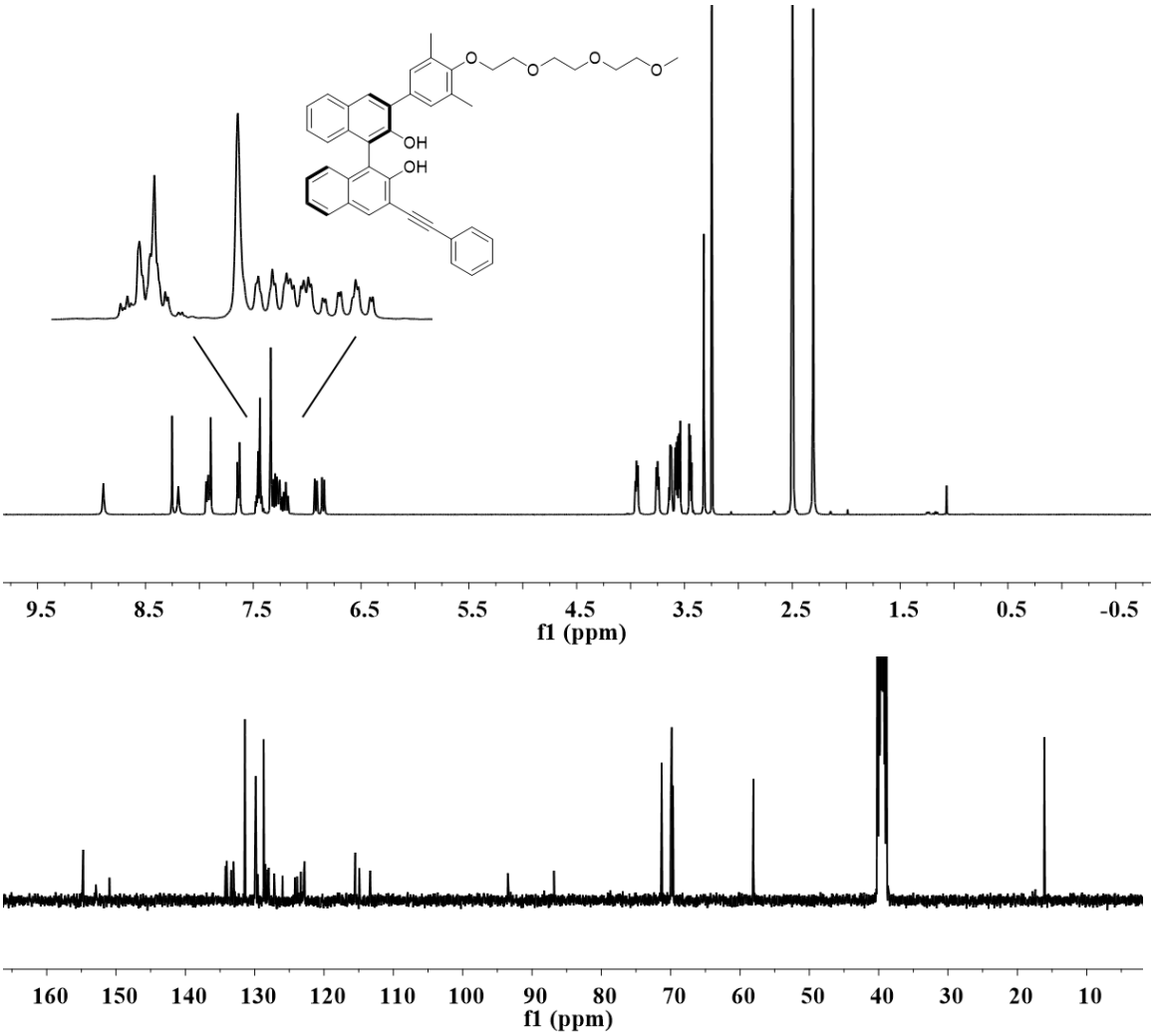


Figure 135: NMR-spectra of (*R*)-**103b** in [D_6]- dimethylsulfoxid (298 K): top ^{1}H (400 MHz), bottom ^{13}C (101 MHz) [MT545-4].

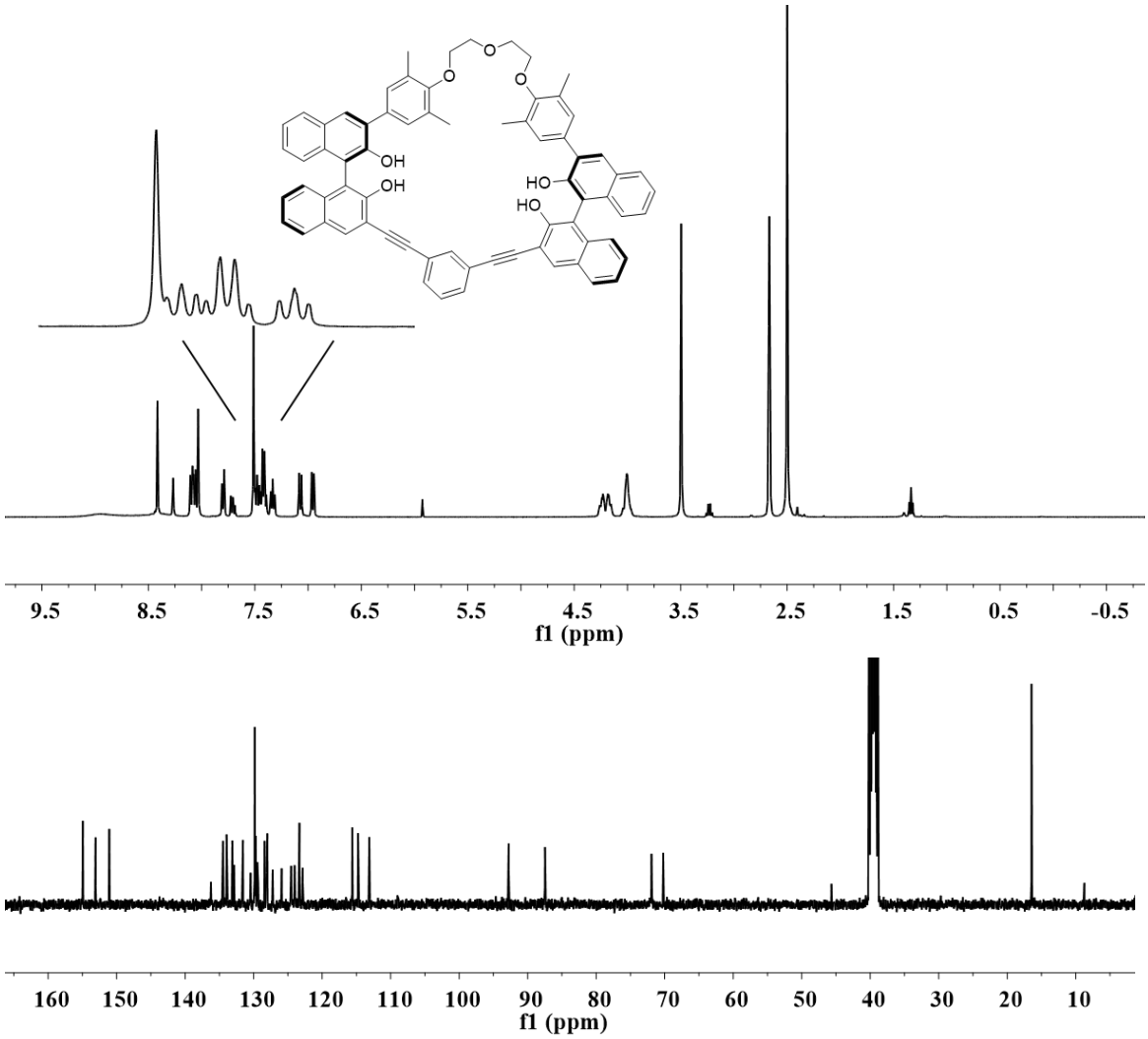


Figure 136: NMR-spectra of (*R*,*R*)-**82** in [D_6]- dimethylsulfoxid (298 K): top ^{1}H (400 MHz), bottom ^{13}C (101 MHz) [MT548-4].

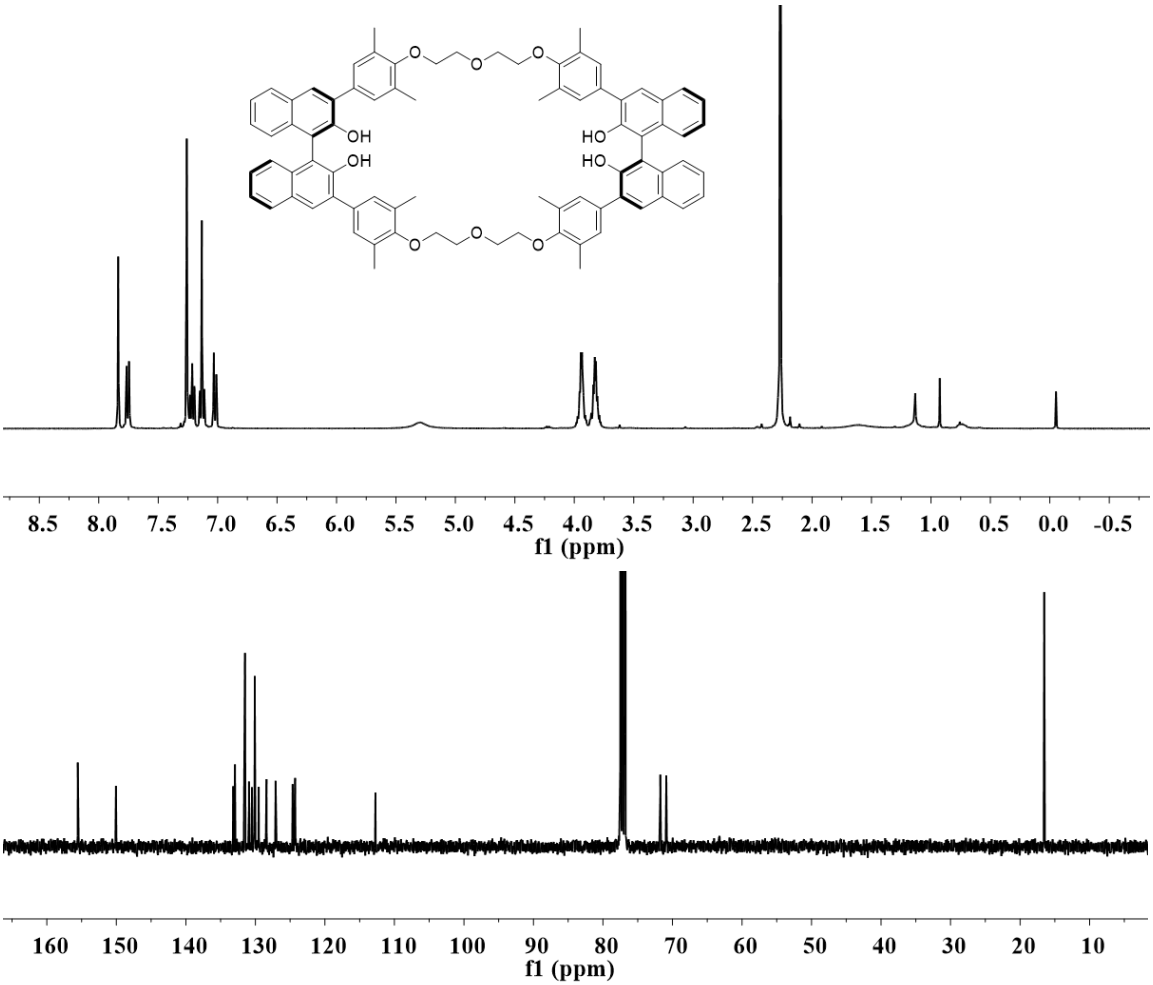


Figure 137: NMR-spectra of (*R*,*R*)-**94** in [D_1]- chloroform (298 K): top ^{1}H (400 MHz), bottom ^{13}C (101 MHz) [MT591-6]

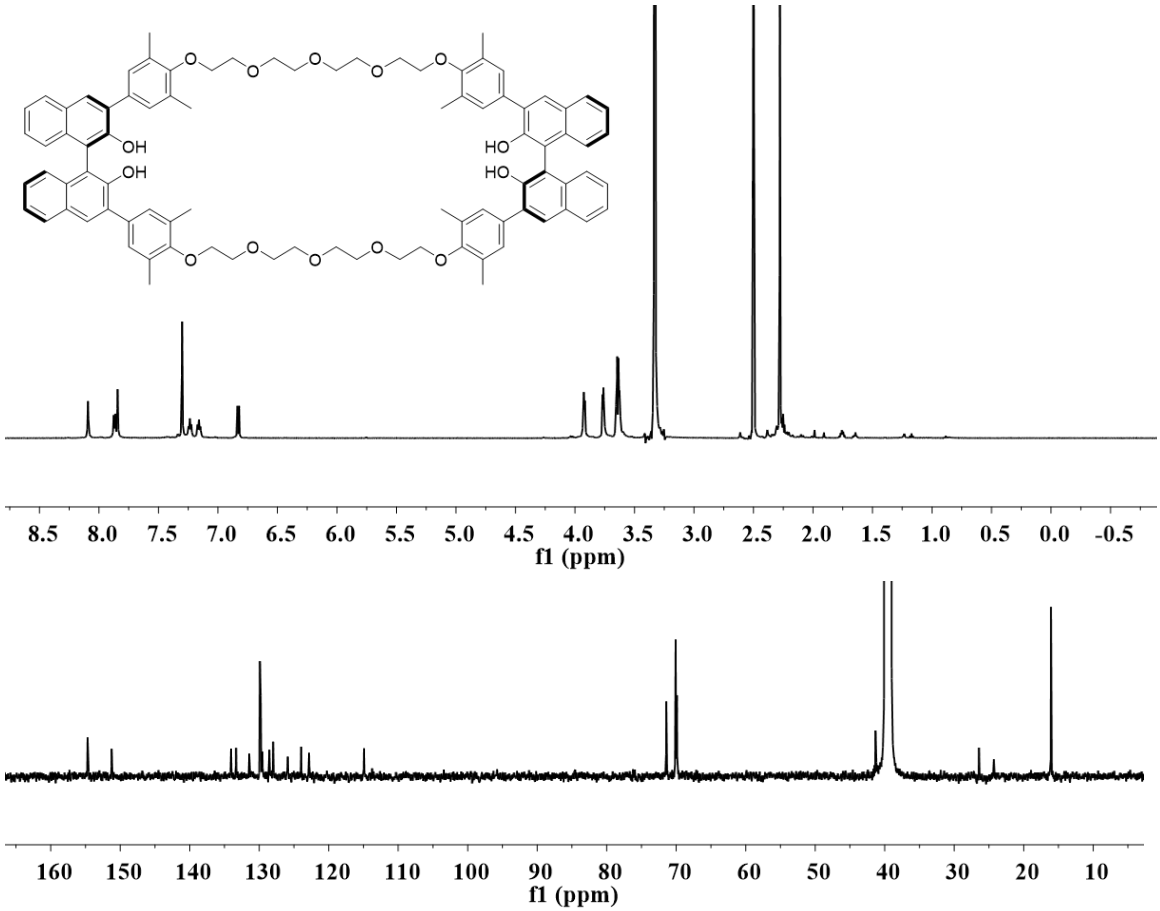


Figure 138: NMR-spectra of (*R*,*R*)-**95** in [D_6]- dimethylsulfoxid (298 K): top ^{1}H (600 MHz), bottom ^{13}C (151 MHz) [MT659-4-2].

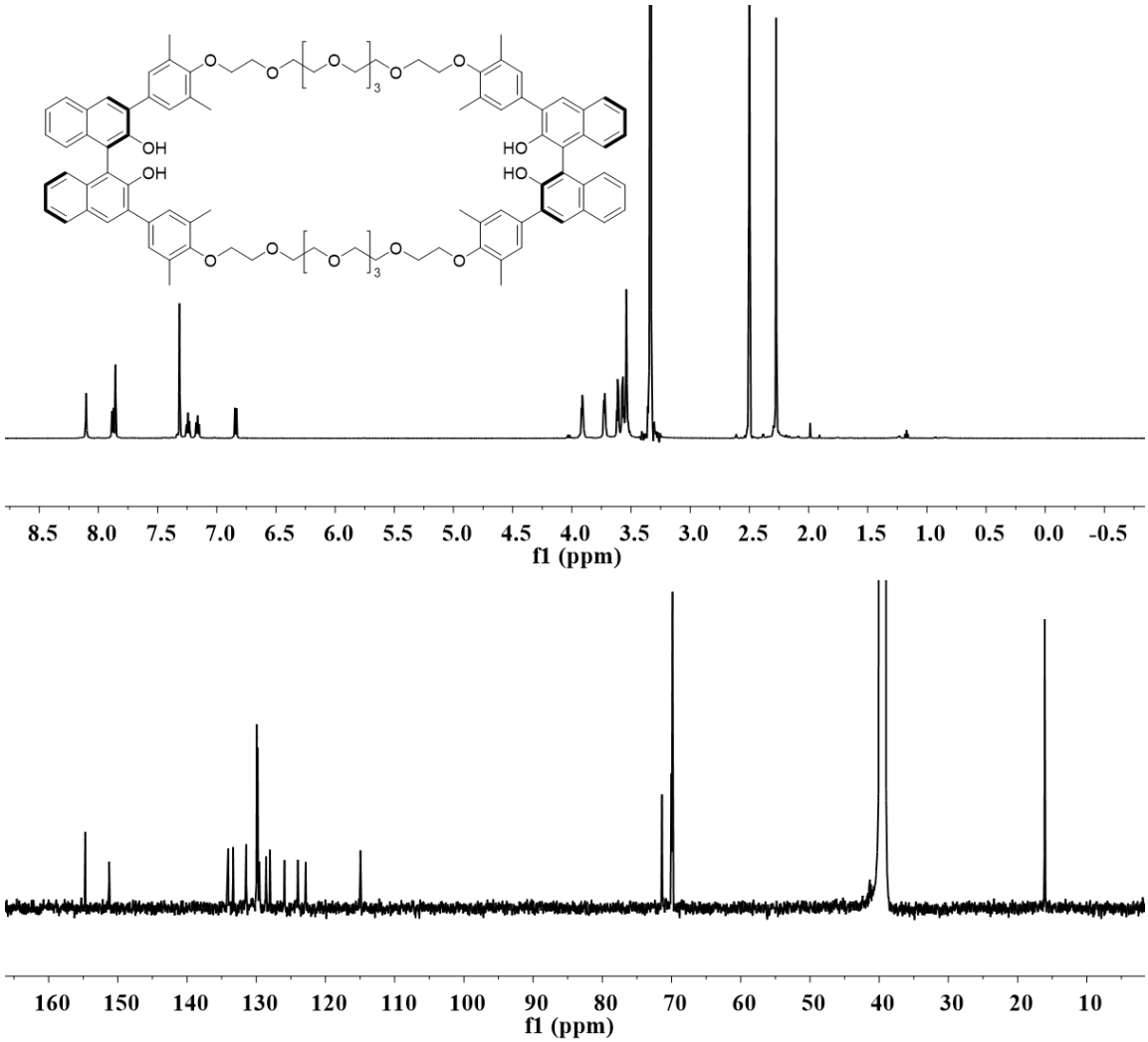


Figure 139: NMR-spectra of (*R*,*R*)-**96** in [D_6]- dimethylsulfoxid (298 K): top ^{1}H (600 MHz), bottom ^{13}C (151 MHz) [MT660-4-2].

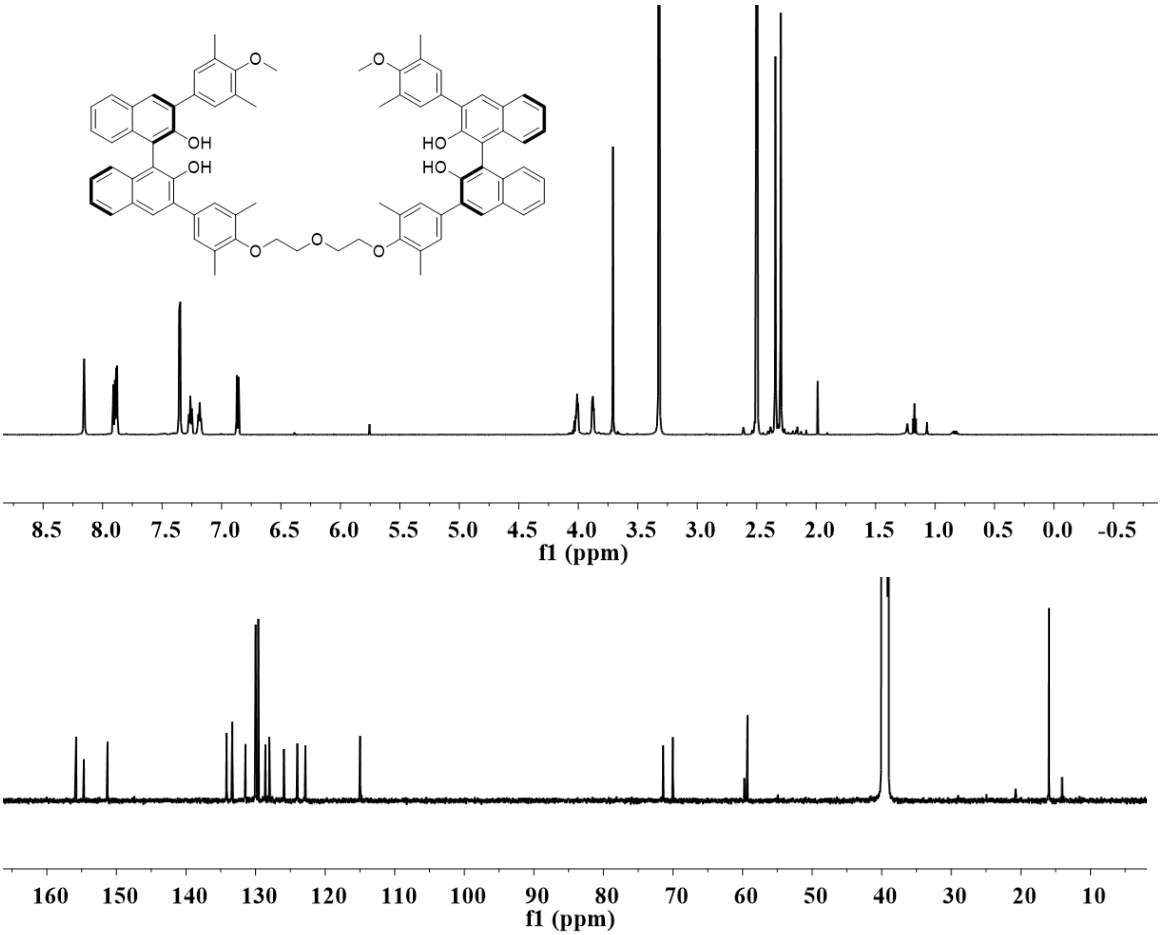


Figure 140: NMR-spectra of (*R*,*R*)-**91** in [D_6]- dimethylsulfoxid (298 K): top ^{1}H (600 MHz), bottom ^{13}C (151 MHz) [MT624-1].

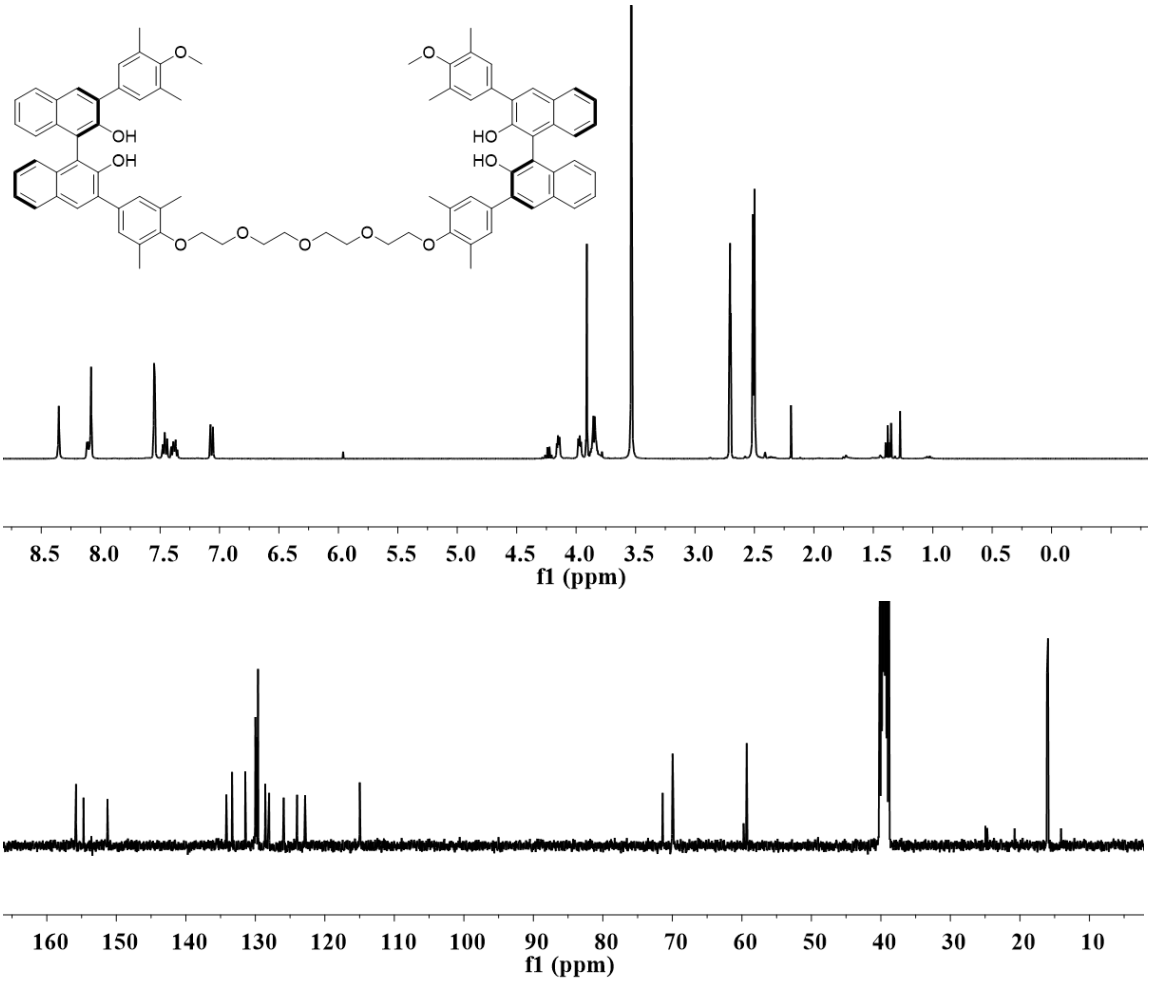


Figure 141: NMR-spectra of (*R*,*R*)-**92** in [D_6]- dimethylsulfoxid (298 K): top ^{1}H (400 MHz), bottom ^{13}C (101 MHz) [MT686-4].

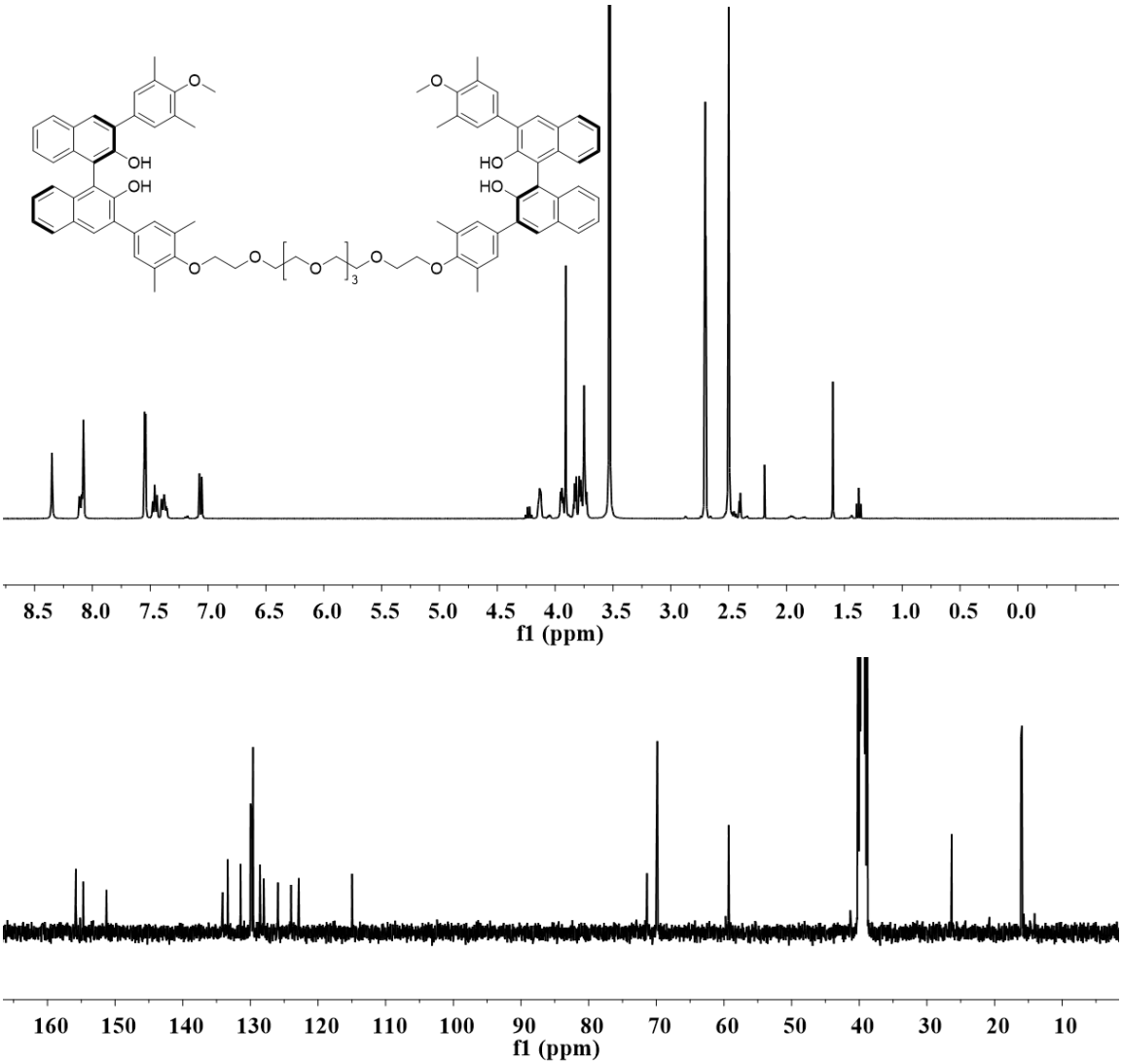


Figure 142: NMR-spectra of (*R*,*R*)-**93** in [D_6]- dimethylsulfoxid (298 K): top ^{1}H (400 MHz), bottom ^{13}C (101 MHz) [MT682-4].

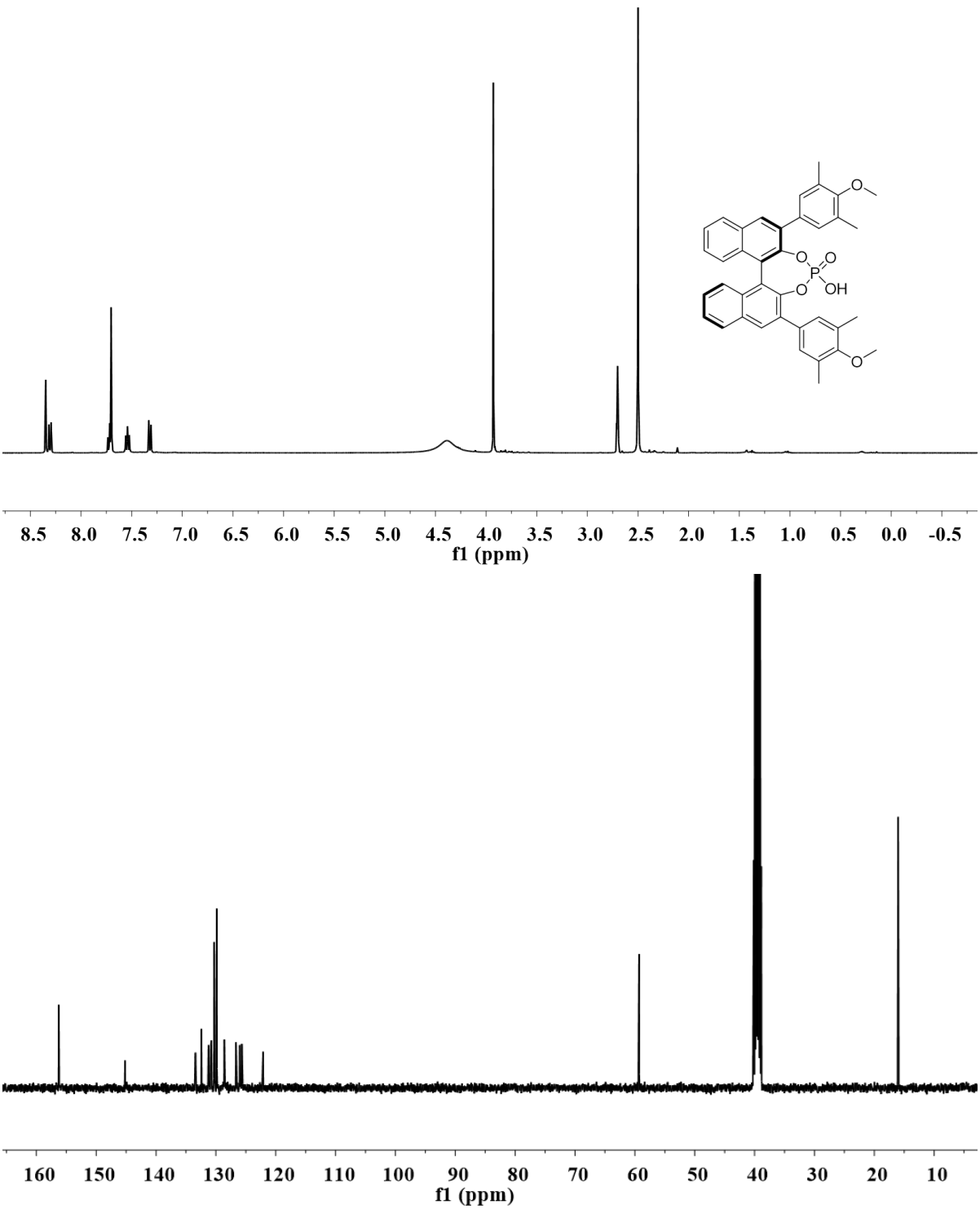


Figure 143: NMR-spectra of (*R*)-**13** in [D_6]- dimethylsulfoxid (298 K): top ^{1}H (400 MHz), bottom ^{13}C (101 MHz).

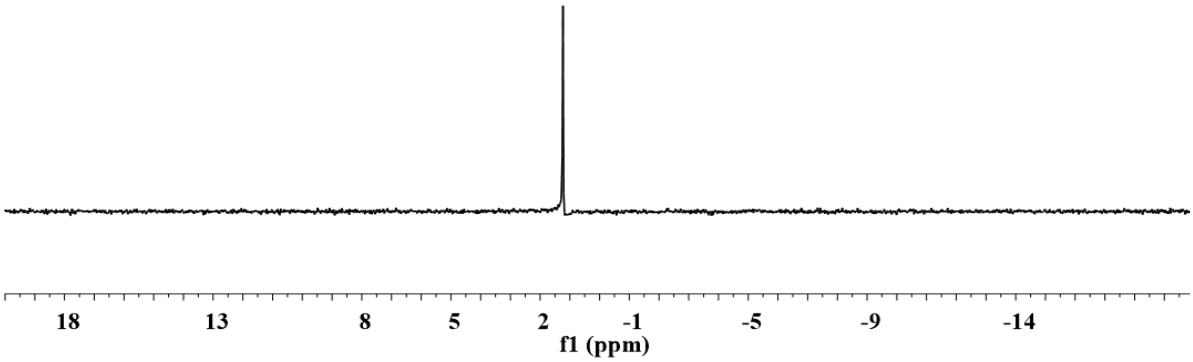


Figure 144: NMR-spectra of (*R*)-**13** in [D_6]- dimethylsulfoxid (298 K), ^{31}P (162 MHz).

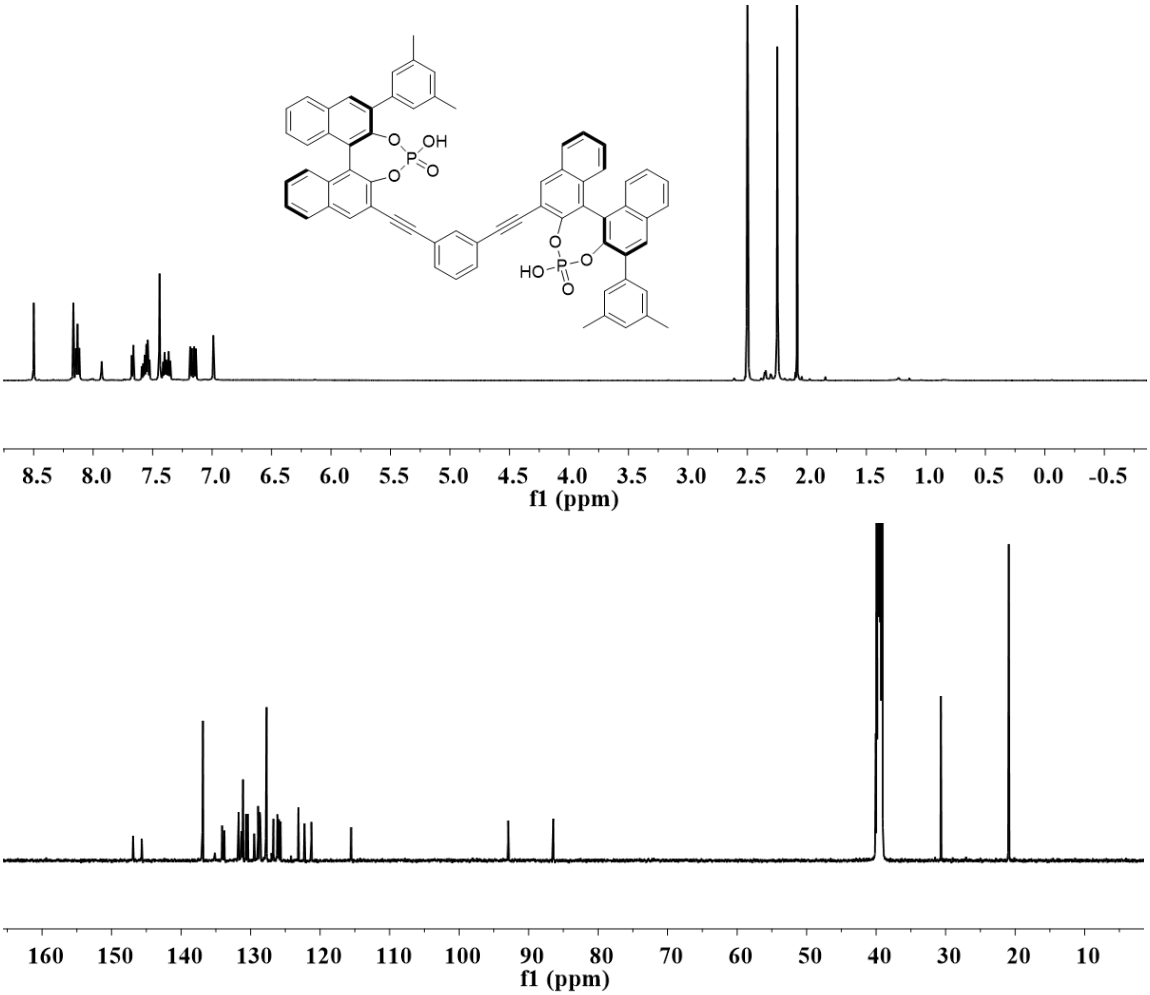


Figure 145: NMR-spectra of (*R*,*R*)-**4a** in [D_6]- dimethylsulfoxid (298 K): top ^{1}H (600 MHz), bottom ^{13}C (151 MHz) [MT356-1].

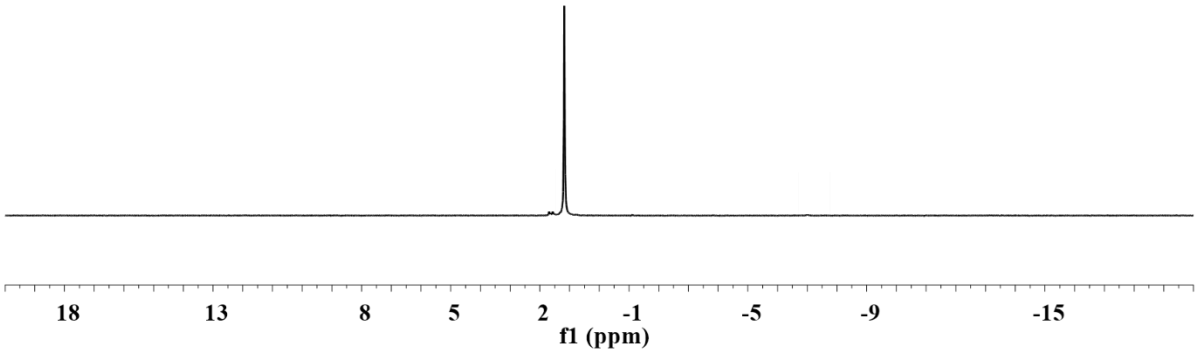


Figure 146: NMR-spectra of (*R*,*R*)-**4a** in [D_6]- dimethylsulfoxid (298 K), ^{31}P (243 MHz).

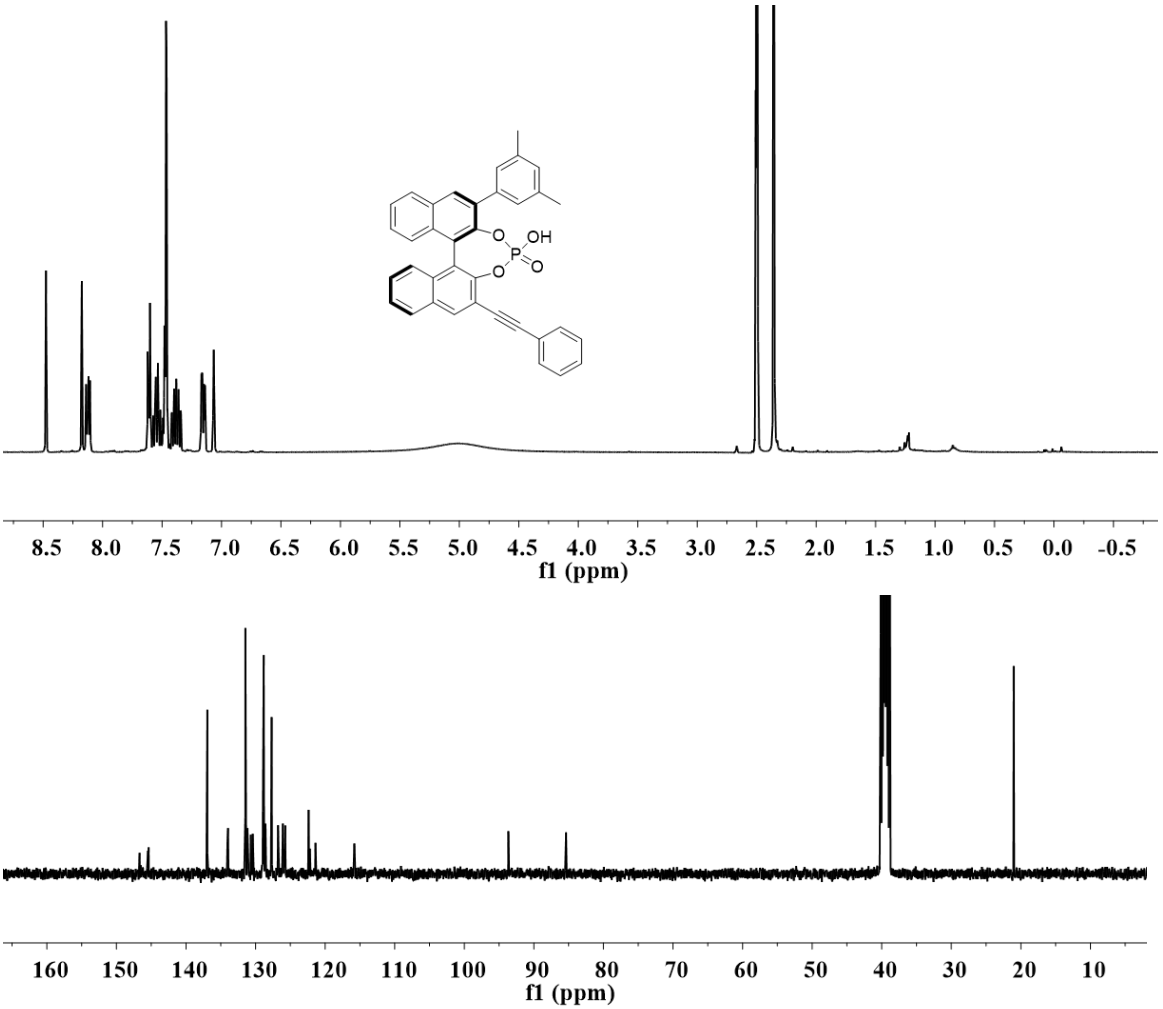


Figure 147: NMR-spectra of (*R*)-**12a** in [D_6]- dimethylsulfoxid (298 K): top ^{1}H (400 MHz), bottom ^{13}C (101 MHz) [MT380-1.3].

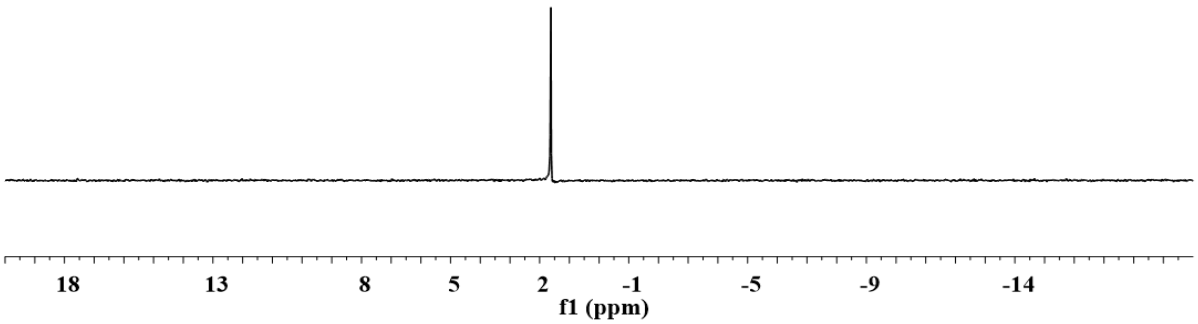


Figure 148: NMR-spectra of (*R*)-**12a** in [D_6]- dimethylsulfoxid (298 K), ^{31}P (162 MHz).

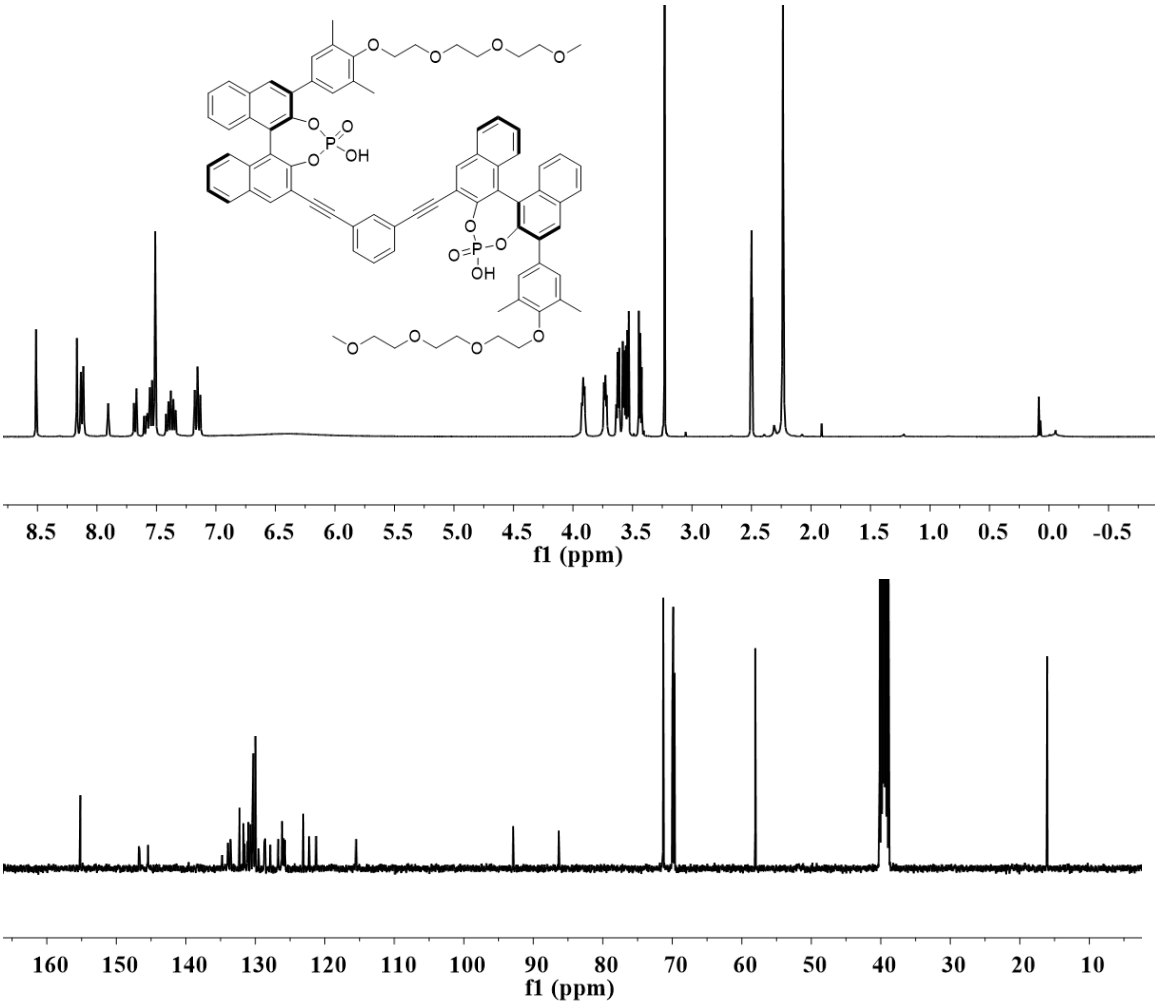


Figure 149: NMR-spectra of (*R*,*R*)-**4b** in [D_6]- dimethylsulfoxid (298 K): top ^{1}H (400 MHz), bottom ^{13}C (101 MHz) [MT554-6].

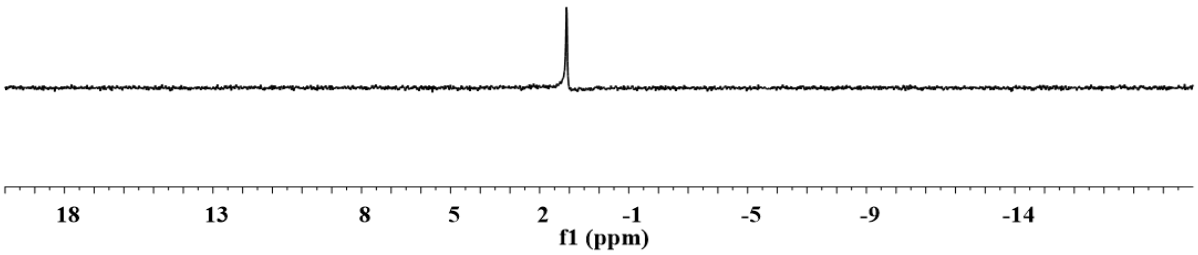


Figure 150: NMR-spectra of (*R*,*R*)-**4b** in [D_6]- dimethylsulfoxid (298 K), ^{31}P (162 MHz).

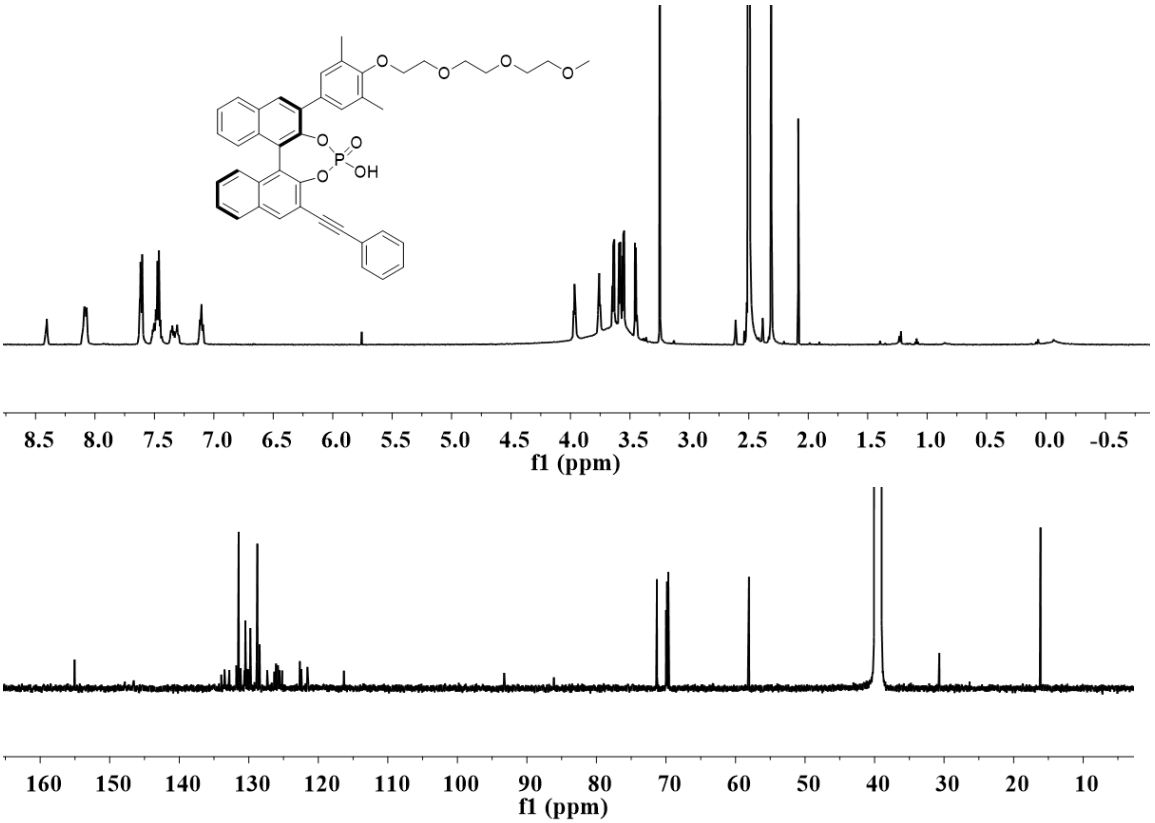


Figure 151: NMR-spectra of (*R*,*R*)-**12b** in [D_6]- dimethylsulfoxid (298 K): top ^{1}H (400 MHz), bottom ^{13}C (101 MHz) [MT555-4].

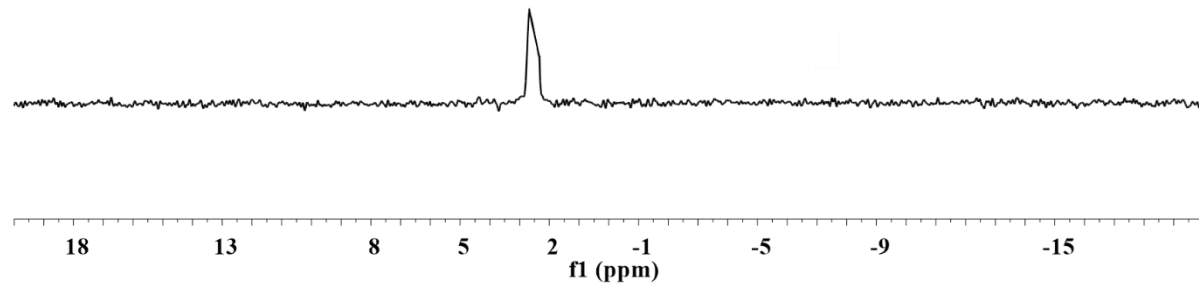


Figure 152: NMR-spectra of (*R*)-**12b** in [D_6]- dimethylsulfoxid (298 K), ^{31}P (162 MHz).

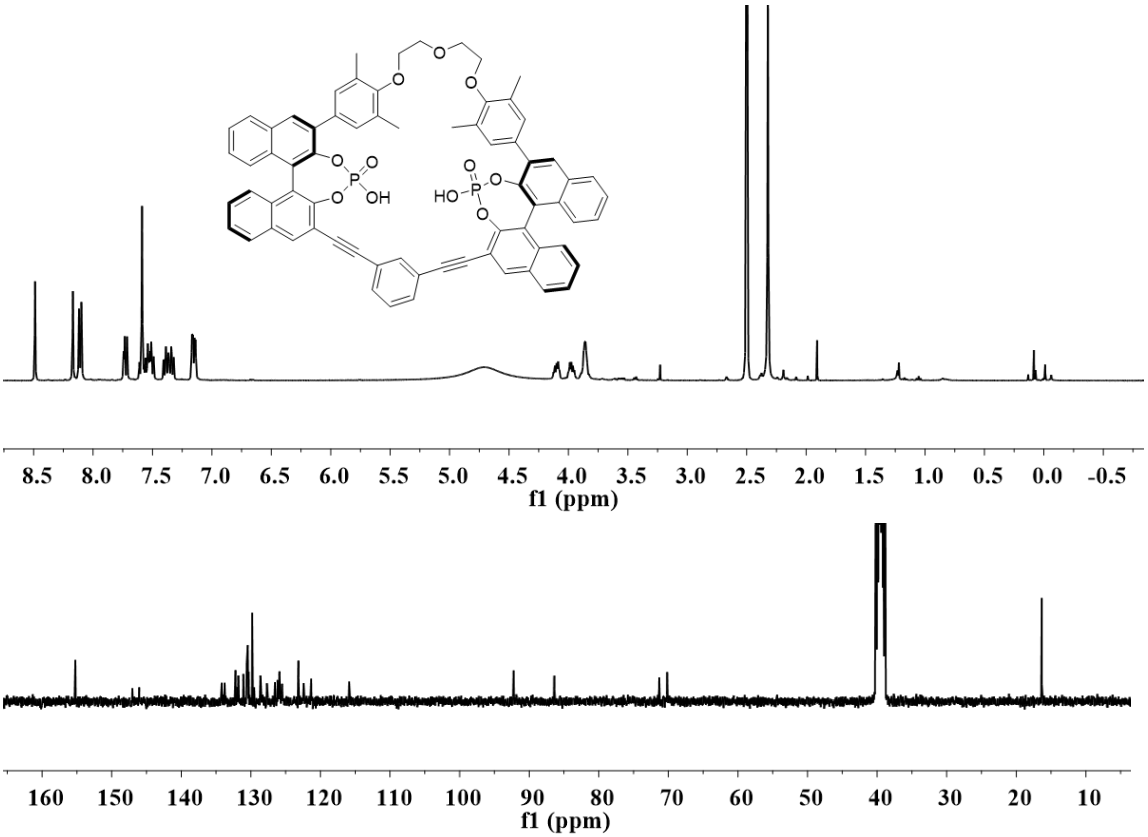


Figure 153: NMR-spectra of (*R*,*R*)-**5** in [D_6]- dimethylsulfoxid (298 K): top ^{1}H (400 MHz), bottom ^{13}C (101 MHz) [MT556-6].

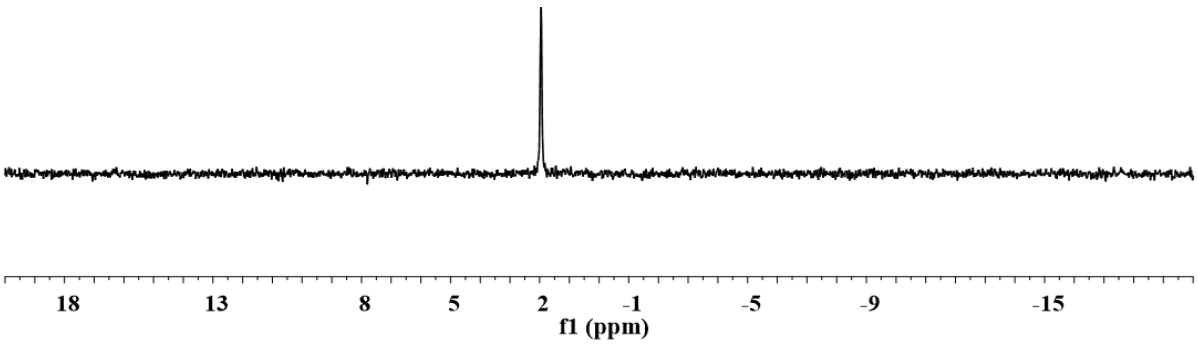


Figure 154: NMR-spectra of (*R*,*R*)-**5** in [D_6]- dimethylsulfoxid (298 K), ^{31}P (162 MHz).

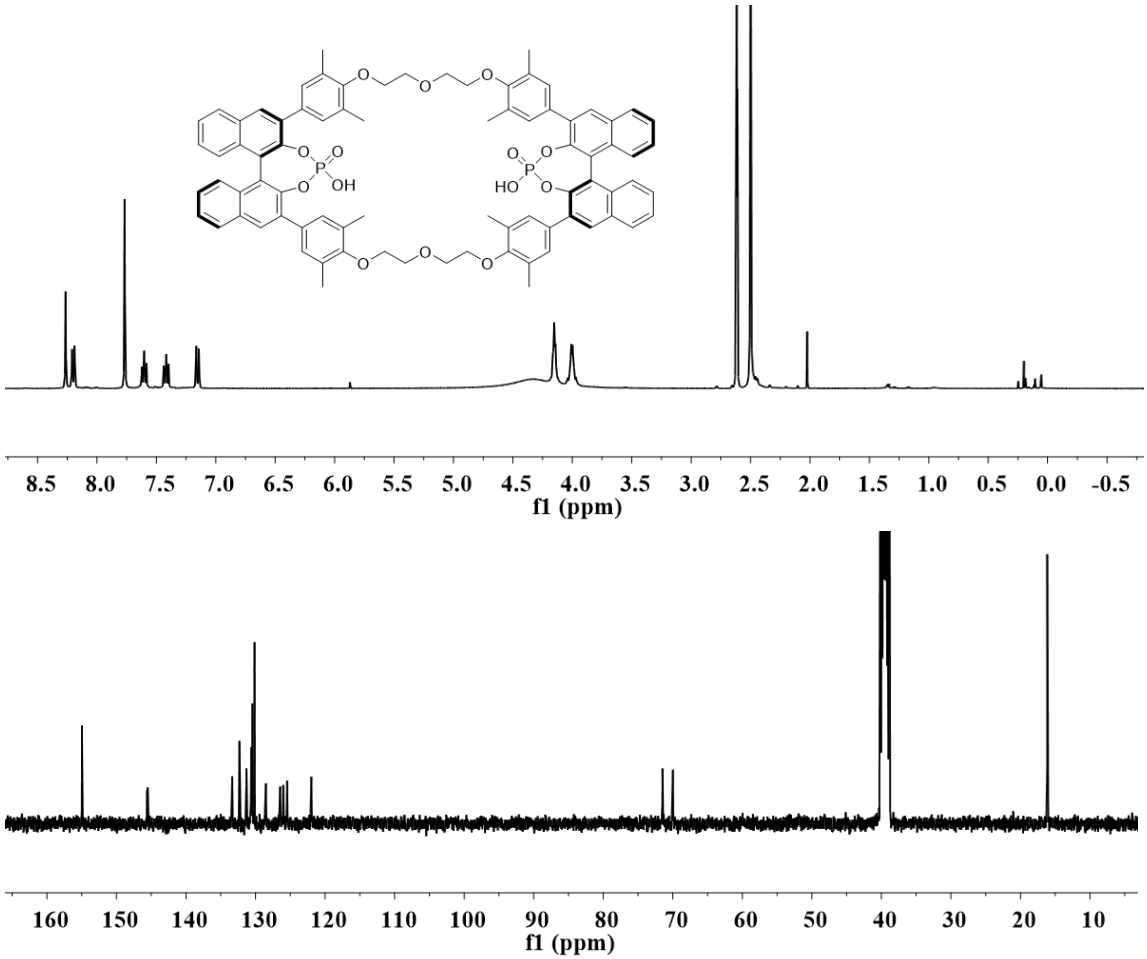


Figure 155: NMR-spectra of (*R*,*R*)-**9** in [D_6]- dimethylsulfoxid (298 K): top ^{1}H (400 MHz), bottom ^{13}C (101 MHz) [MT598-5].

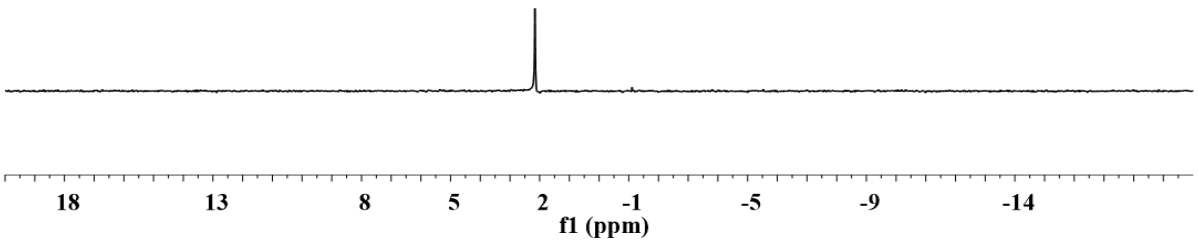


Figure 156: NMR-spectra of (*R*,*R*)-**9** in [D_6]- dimethylsulfoxid (298 K), ^{31}P (162 MHz).

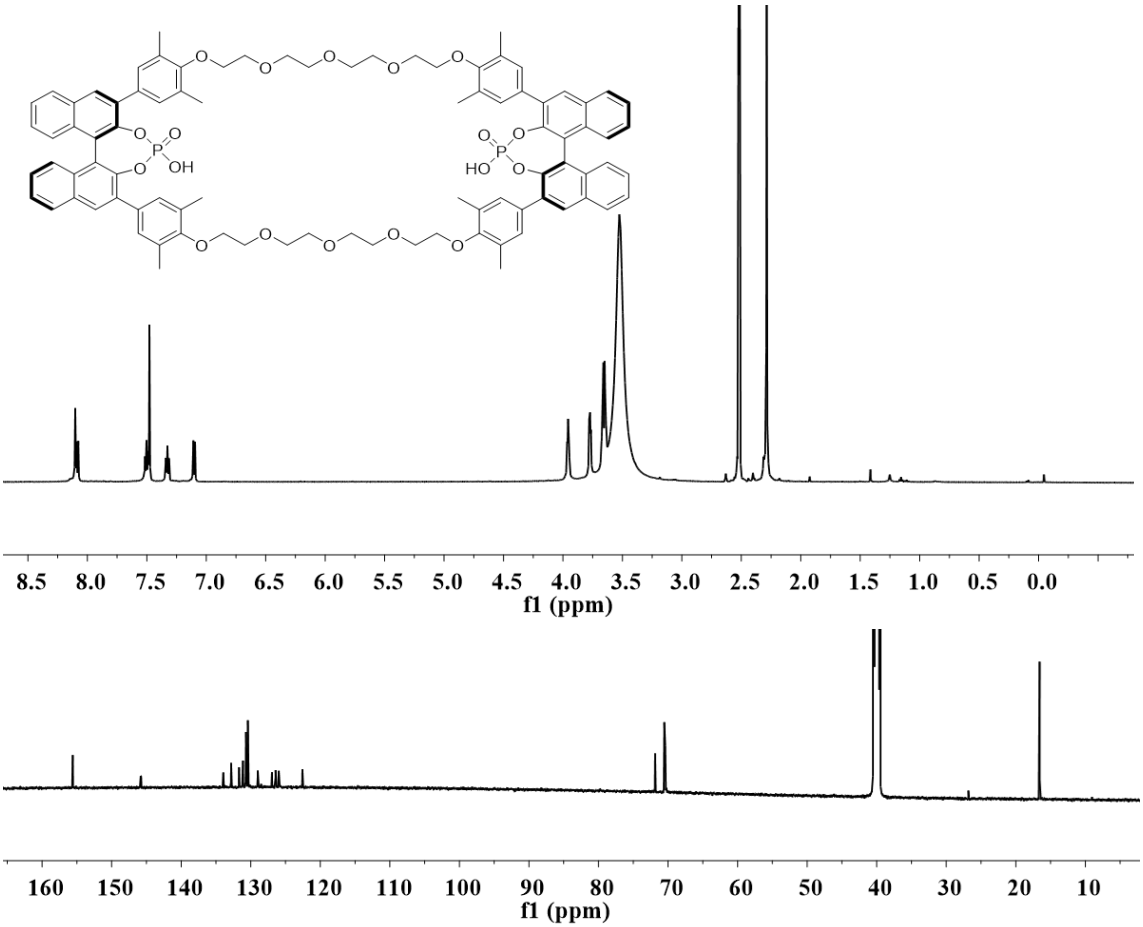


Figure 157: NMR-spectra of (*R*,*R*)-**10** in [D_6]- dimethylsulfoxid (298 K): top ^{1}H (600 MHz), bottom ^{13}C (151 MHz) [MT664-9].

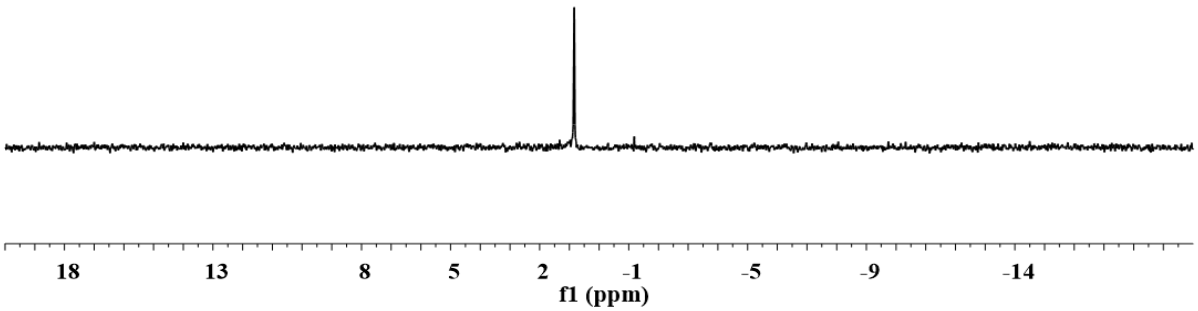


Figure 158: NMR-spectra of (*R*,*R*)-**10** in [D_6]- dimethylsulfoxid (298 K), ^{31}P (162 MHz).

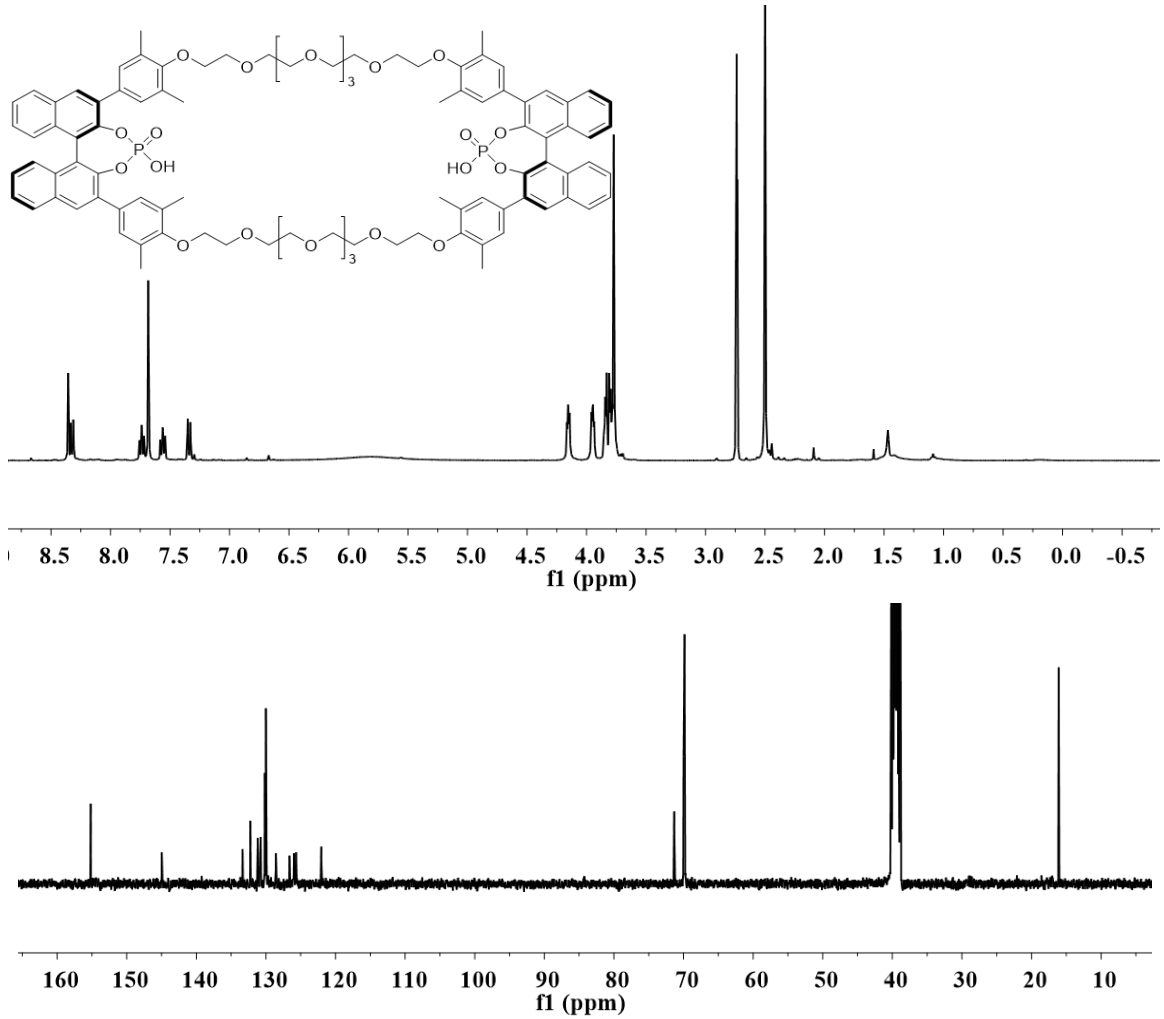


Figure 159: NMR-spectra of (*R*,*R*)-**11** in [D_6]- dimethylsulfoxid (298 K): top ^{1}H (400 MHz), bottom ^{13}C (101 MHz) [MT665-6].

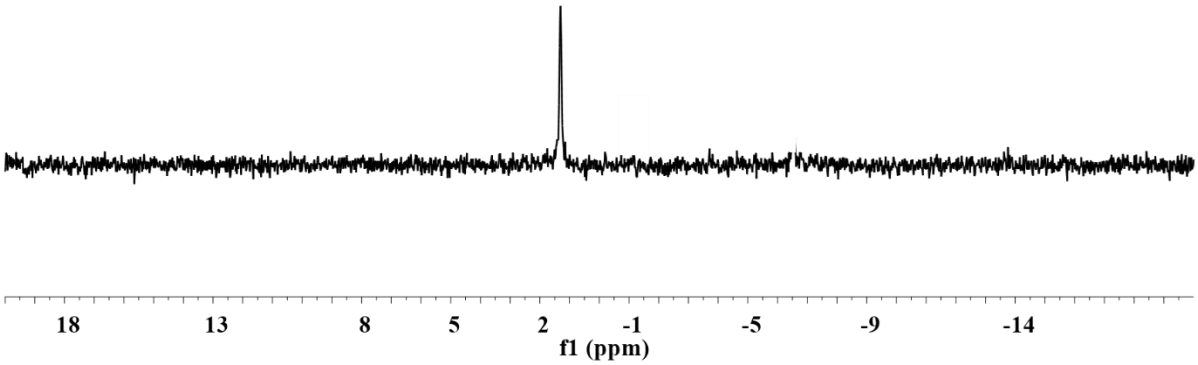


Figure 160: NMR-spectra of (*R*,*R*)-**11** in [D_6]- dimethylsulfoxid (298 K), ^{31}P (162 MHz).

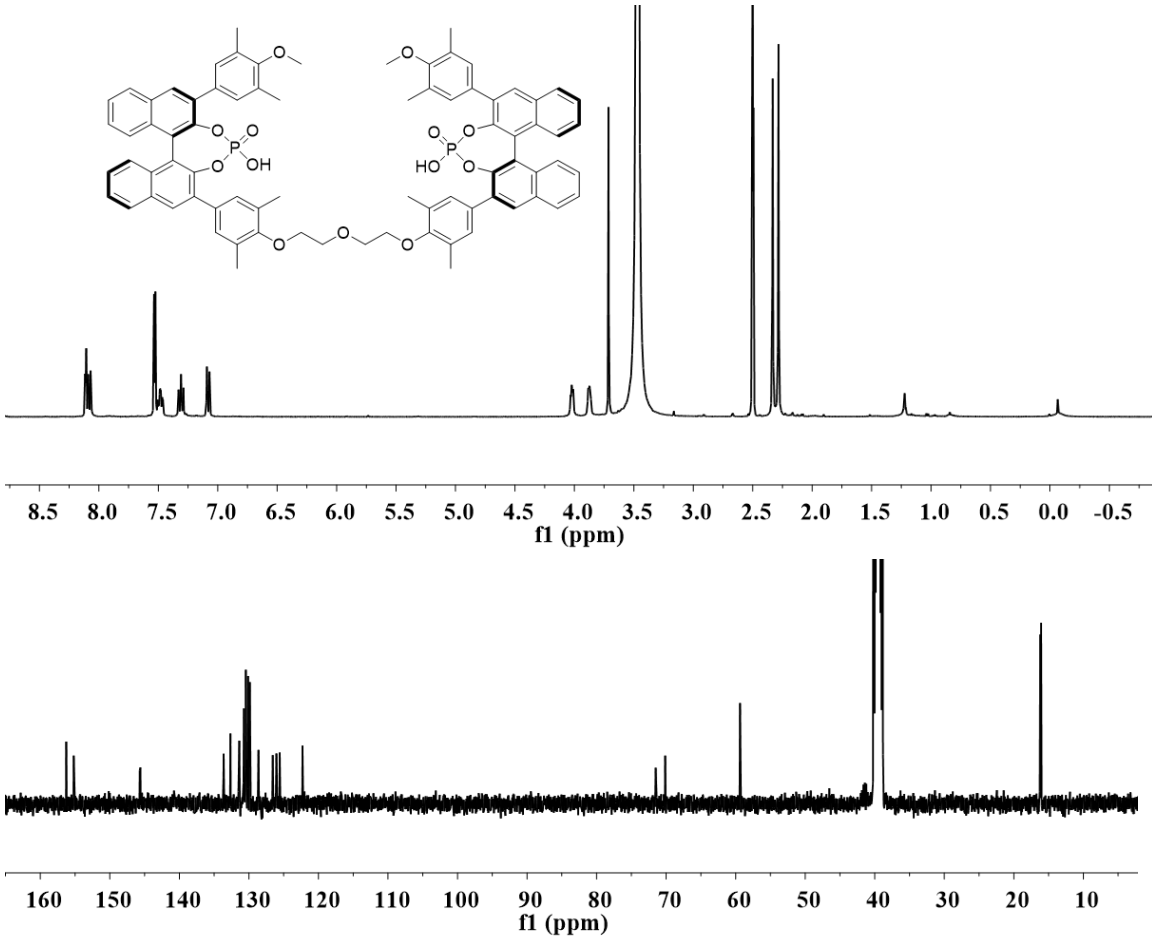


Figure 161: NMR-spectra of (*R,R*)-**6** in [D_6]- dimethylsulfoxid (298 K): top ^{1}H (400 MHz), bottom ^{13}C (101 MHz) [MT629-2].

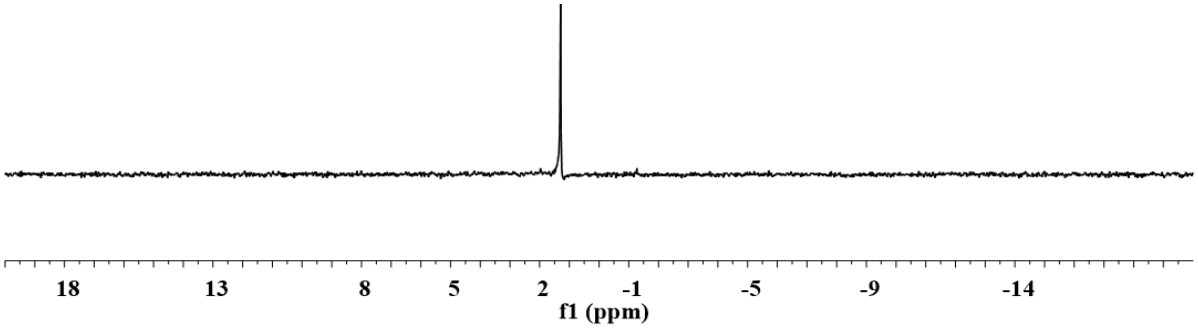


Figure 162: NMR-spectra of (*R,R*)-**6** in [D_6]- dimethylsulfoxid (298 K), ^{31}P (162 MHz).

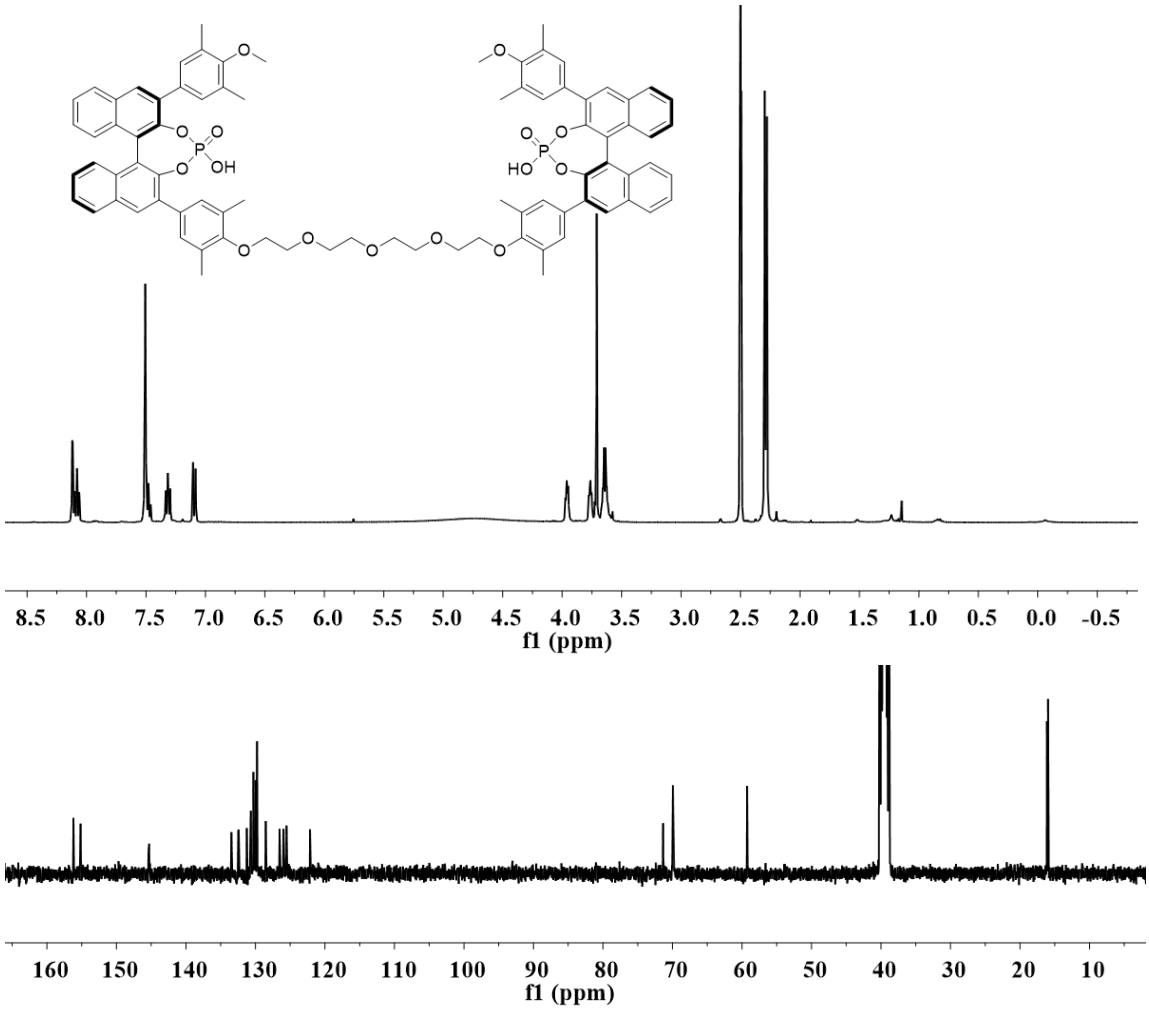


Figure 163: NMR-spectra of (*R*,*R*)-**7** in [D_6]- dimethylsulfoxid (298 K): top ^{1}H (400 MHz), bottom ^{13}C (101 MHz) [MT688-5].

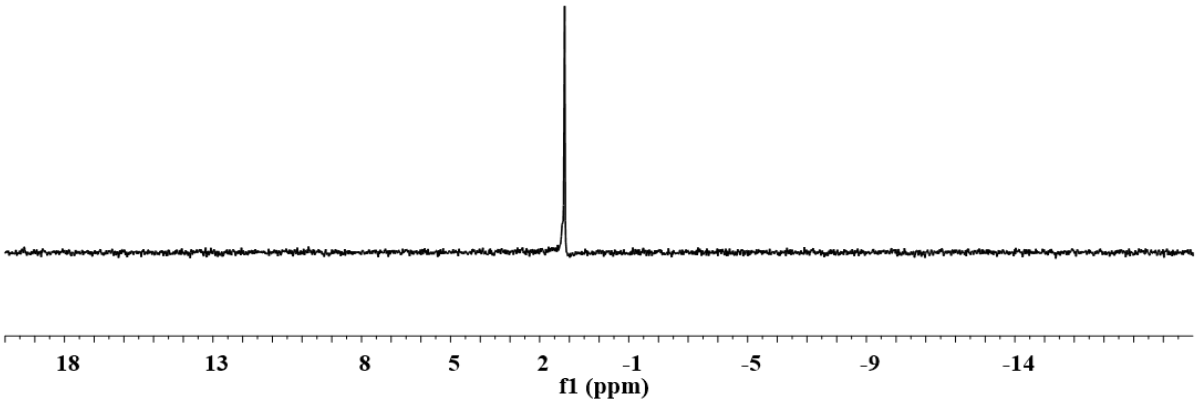


Figure 164: NMR-spectra of (*R*,*R*)-**7** in [D_6]- dimethylsulfoxid (298 K), ^{31}P (162 MHz).

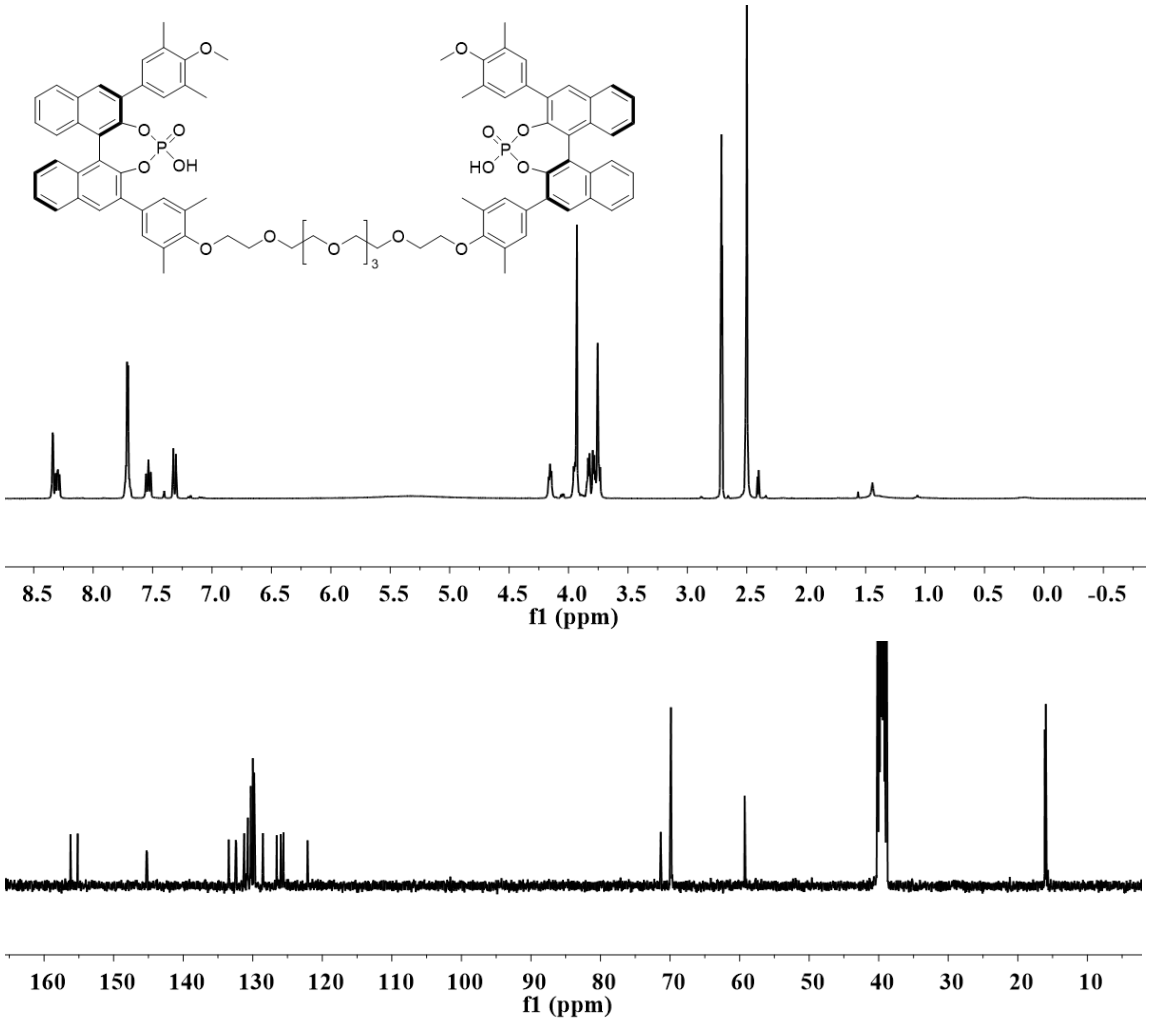


Figure 165: NMR-spectra of (*R*,*R*)-**8** in [D_6]- dimethylsulfoxid (298 K): top ^{1}H (400 MHz), bottom ^{13}C (101 MHz) [MT687-5].

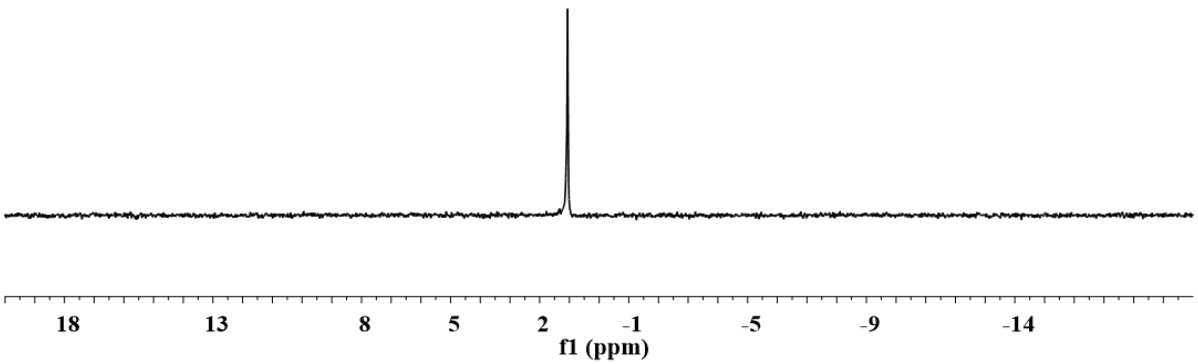


Figure 166: NMR-spectra of (*R*,*R*)-**8** in [D_6]- dimethylsulfoxid (298 K), ^{31}P (162 MHz).

9.1.2. Determination of association constants *K*a via NMR spectroscopy:

9.1.2.1. NMR Titration experiments:

To perform the ^{1}H NMR titration, stock solutions of compounds (*S*,*S*)-**28** - (*S*,*S*)-**29**, the guanidine bis-tetrafluoric acid salt [(*S*,*S*)-**28**$^{2+}$(TFA^{-})$_2$, host] (3 mM) and the ammoniumphosphates [(*R*,*R*)-**29**$^{2-}$(Bu$_4$N^{+})$_2$] and [(*S*,*S*)-**29**$^{2-}$(Bu$_4$N^{+})$_2$, guest] (75 mM) were prepared in [D$_1$]-chloroform. [D$_1$]-chloroform was treated with basic Alox before use. The titration was performed as detailed below. All samples were prepared by subsequent addition of the guest stock solution (samples 1-13).

Table 23: Titration protocol.

Sample No	Eq Guest to Host	V (Guest) added [µl]	V (Host) [ml]	V (Solvent) [ml]	V (total) [ml]
1	0	0.00	0.2	0.4	0.600
2	0.1	0.80			0.601
3	0.2	0.80			0.602
4	0.35	1.20			0.603
5	0.5	1.20			0.604
6	0.65	1.20			0.605
7	0.8	1.20			0.606
8	1	1.60			0.608
9	1.15	1.20			0.609
10	1.3	1.20			0.610
11	1.5	1.60			0.612
12	1.8	2.40			0.614
13	2	1.60			0.616

9.1.2.2. NMR stacked plots

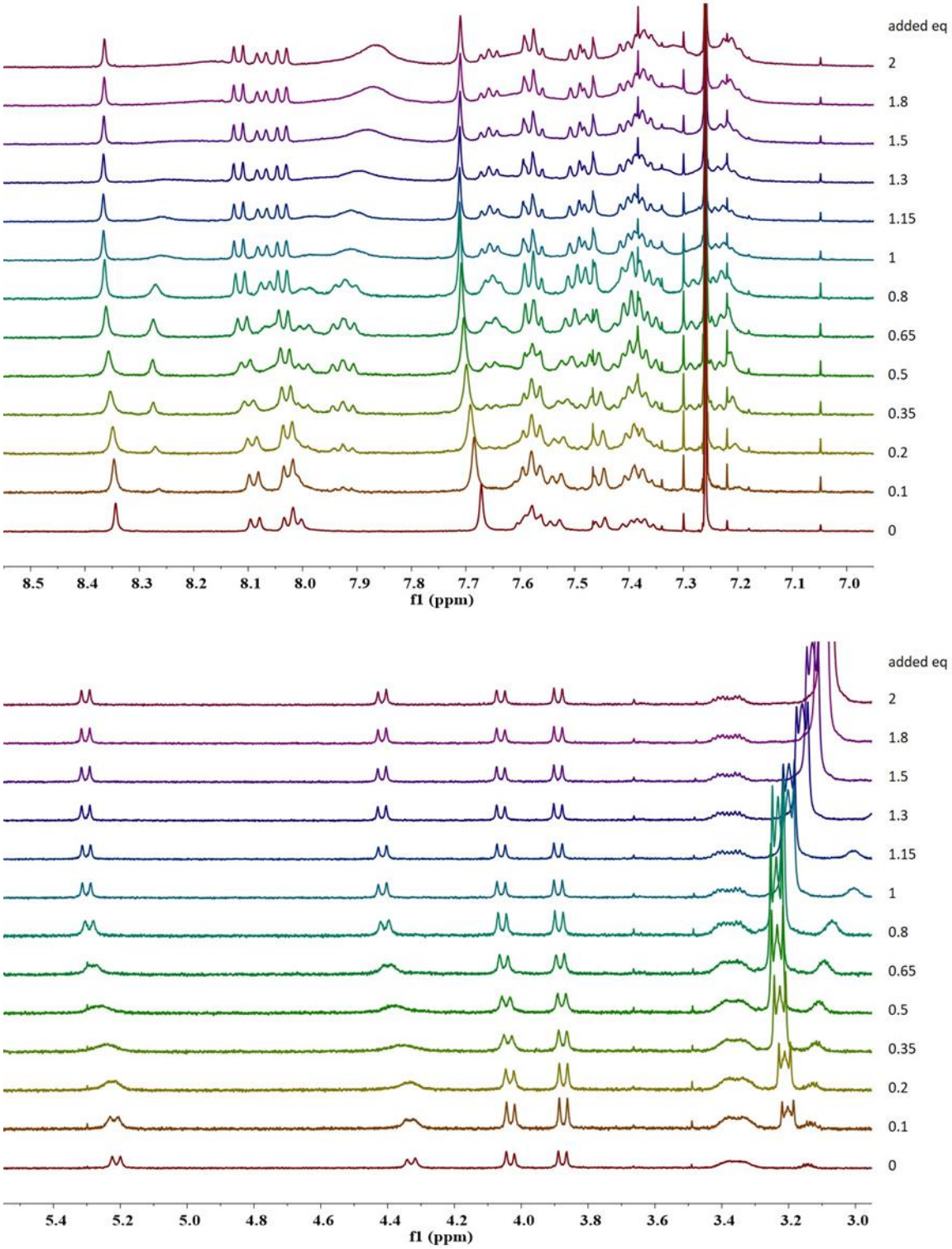


Figure 167: Stacked NMR spectra (top: aromatic region, bottom: aliphatic region) for the binding of [(*S*,*S*)-**9**$^{2-}$(Bu_4N^+)$_2$] (0.10 to 2 equivalents) to [(*S*,*S*)-**28**$^{2+}$(TFA^-)$_2$] [all: 500 MHz, [D_1]-chloroform, 298K, initial concentration of [(*S*,*S*)-**28**$^{2+}$(TFA^-)$_2$]: 1 mM].

The chemical shift of H-$22_{1/2}$ was used for the construction of the binding isotherms.

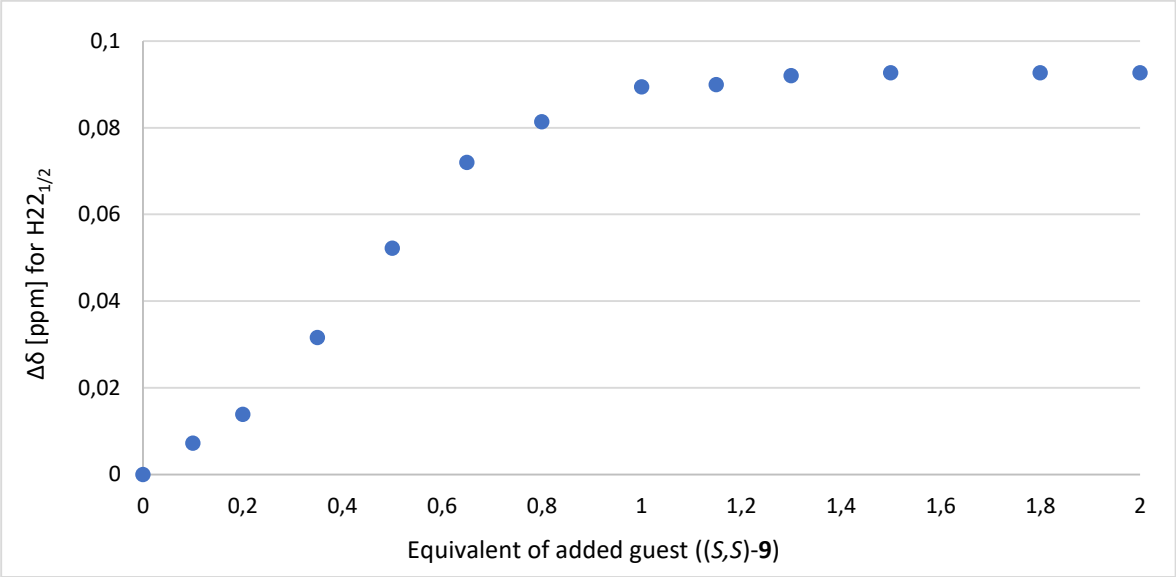


Figure 168: Binding isotherm for the binding of (*S,S*)-**29** (as $(Bu_4N^+)_2$ -salt) to (*S,S*)-**28** (as $(TFA^-)_2$ salt) in [D_1]-chloroform [initial concentration of host: 1 mM, plotted for H-22.

Table 24: The added equivalents of (*S,S*)-**29**$^{2-}$$(Bu4N^+)_2$], the measured chemical shifts are given, and the change in chemical shift (Δδ) of the titration of [(*S,S*)-**29**$^{2-}$$(Bu4N^+)_2$]) to [(*S,S*)-**28**$^{2+}$$(TFA^-)_2$] are given.

equivalents of (*S,S*)-**29** to (*S,S*)-**28**	δ (ppm)	H$22_{1/2}$ Δδ (ppm)
0	5.2115	0
0.1	5.2187	0.0072
0.2	5.2254	0.0139
0.35	5.2431	0.0316
0.5	5.2637	0.0522
0.65	5.2835	0.072
0.8	5.2929	0.0814
1	5.3009	0.0894
1.15	5.3014	0.0899
1.3	5.3035	0.092
1.5	5.3042	0.0927
1.8	5.3042	0.0927
2	5.3042	0.0927

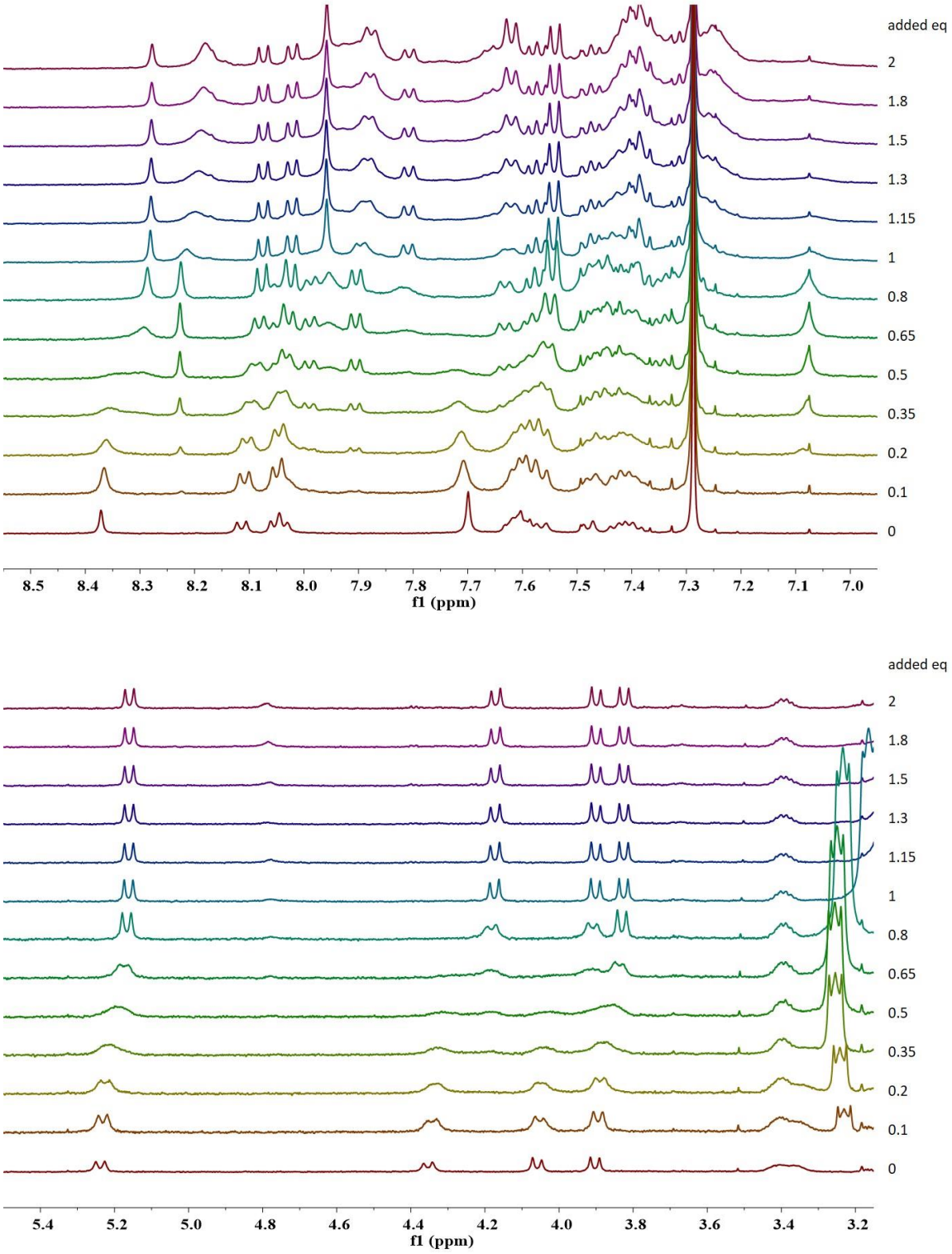


Figure 169: Stacked NMR spectra (top: aromatic region, bottom: aliphatic region) for the binding of [(*R*,*R*)-**9**$^{2-}$(Bu_4N^+)$_2$](0.10 to 2 equivalents) to [(*S*,*S*)-**28**$^{2+}$(TFA^-)$_2$] [all: 500 MHz, [D_1]-chloroform, 298K, initial concentration of [(*S*,*S*)-**28**$^{2+}$(TFA^-)$_2$]: 1 mM].

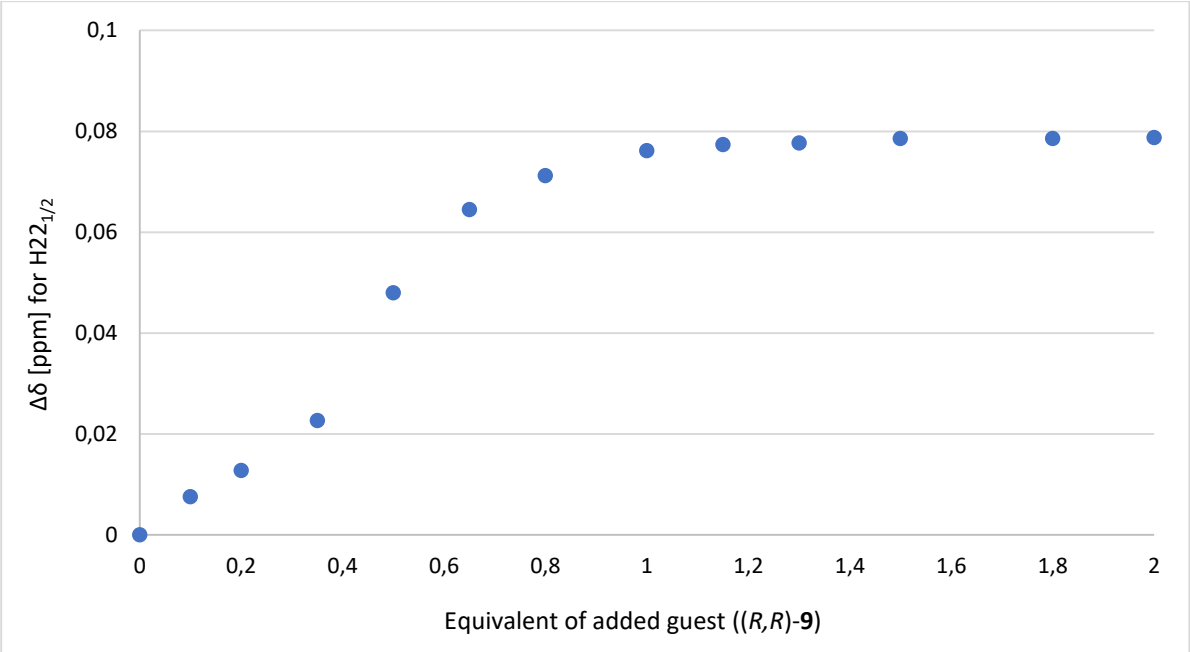


Figure 170: Binding isotherm for the binding of (*R*,*R*)-**29** (as $(Bu_4N^+)_2$ -salt) to (*S*,*S*)-**28** (as $(TFA^-)_2$ salt) in [D_1]-chloroform [initial concentration of host: 1 mM, plotted for H-22.

Table 25: The added equivalents of (*R*,*R*)-**29**$^{2-}$(Bu4N$^+$)$_2$], the measured chemical shifts are given, and the change in chemical shift (Δδ) of the titration of [(*R*,*R*)-**29**$^{2-}$(Bu4N$^+$)$_2$]) to [(*S*,*S*)-**28**$^{2+}$(TFA$^-$)$_2$] are given.

equivalents of (*R*,*R*)-**29** to (*S*,*S*)-**28**	δ (ppm)	H22$_{1/2}$ Δδ (ppm)
0	5.2389	0
0.1	5.2313	0.0076
0.2	5.2261	0.0128
0.35	5.2162	0.0227
0.5	5.1909	0.048
0.65	5.1744	0.0645
0.8	5.1677	0.0712
1	5.1627	0.0762
1.15	5.1615	0.0774
1.3	5.1612	0.0777
1.5	5.1603	0.0786
1.8	5.1603	0.0786
2	5.1601	0.0788

9.2. Data analysis

The sigmoidal binding isotherms indicate competitive displacement of the triflate counterions from the bisguanidinium-salt (*S*,*S*)-**28** upon addition of the bisphosphates (*S*,*S*)-**29** / (*R*,*R*)-**29**. Thus, we did not determine absolute association constants of the bisphosphate-guests to the bisguanidinium-host, but used Leito´s method for relative binding constant determination.[128] This is based on determination of the relative molar fraction of complex (*S*,*S*)-**28** + (*S*,*S*)-**29** and (*S*,*S*)-**28** + (*R*,*R*)-**29** at identical stoichiometries of the components, determined from the chemical shift Δδ in relation to the maximum chemical shift Δδmax observed at the end of the titration.

Table 26: Determination of the relative binding constants of the complexes (*S*,*S*)-**28**+(*S*,*S*)-**29** and (*S*,*S*)-**28**+(*R*,*R*)-**29**

titration No	1	2	3	4	5	6	7	8	9	10	11	12	13	
equivalents of **29**	0	0.1	0.2	0.35	0.5	0.65	0.8	1	1.15	1.3	1.5	1.8	2	
δ (^{1}H) for (*S*,*S*)-**29**	5.212	5.219	5.225	5.243	5.264	5.284	5.293	5.301	5.301	5.304	5.304	5.304	5.304	
Δδ (^{1}H) for (*S*,*S*)-**29**	0	0.007	0.014	0.032	0.052	0.072	0.081	0.089	0.090	0.092	0.093	0.093	0.093	= Δδmax
δ (^{1}H) for (*R*,*R*)-**29**	5.239	5.231	5.226	5.216	5.191	5.174	5.168	5.163	5.162	5.161	5.160	5.160	5.160	
Δδ (^{1}H) for (*R*,*R*)-**29**	0	-0.008	-0.013	-0.023	-0.048	-0.064	-0.071	-0.076	-0.077	-0.078	-0.079	-0.079	-0.079	= Δδmax
α = Δδ / Δδmax for (*S*,*S*)-**29**	0	0.078	0.150	0.341	0.563	0.777	0.878	0.964	0.970	0.992	1	1	1	
α = Δδ / Δδmax for (*R*,*R*)-**29**	0	0.096	0.162	0.288	0.609	0.819	0.904	0.967	0.982	0.986	0.997	0.997	1	
K(A)/K(B)	-	0.7889	0.9095	1.2782	0.827	0.7711	0.7689	0.9244	0.5807	1.8606	-	-	-	
		Mean:	0.90	+-	0.1803									

[128] S. A. Kadam, K. Haav, L. Toom, T. Haljasorg and I. Leito, *J. Org. Chem.*, **2014**, *79*, 2501-2513

9.3.DOSY NMR

The ^{1}H DOSY NMR experiments were run on a Bruker Avance Neo II 500 MHz spectrometer (Bruker BioSpin, Rheinstetten, Germany) at a hydrogen resonance frequency of 500 MHz. Simple single-pulse excitation was used to obtain hydrogen line spectra. An external standard was used for a reliable determination of the chemical shifts. Spin-lattice relaxation times were determined in a conventional inversion recovery experiment. ^{1}H NMR diffusion experiments were run with a Bruker DIFBBI probe head. All measurements were performed at 298 K. For all measurements, the stimulated echo pulse sequence with two gradient pulses was used. 64 scans were accumulated for each setting. The time between two gradient pulses Δ was 25 ms. The gradients were adjusted to strengths G between 1 and 150 G/cm with a duration δ of 1.0 ms. All measurements (the full set of gradient strengths under the variation from 1 to 150 G/cm) were repeated two times.

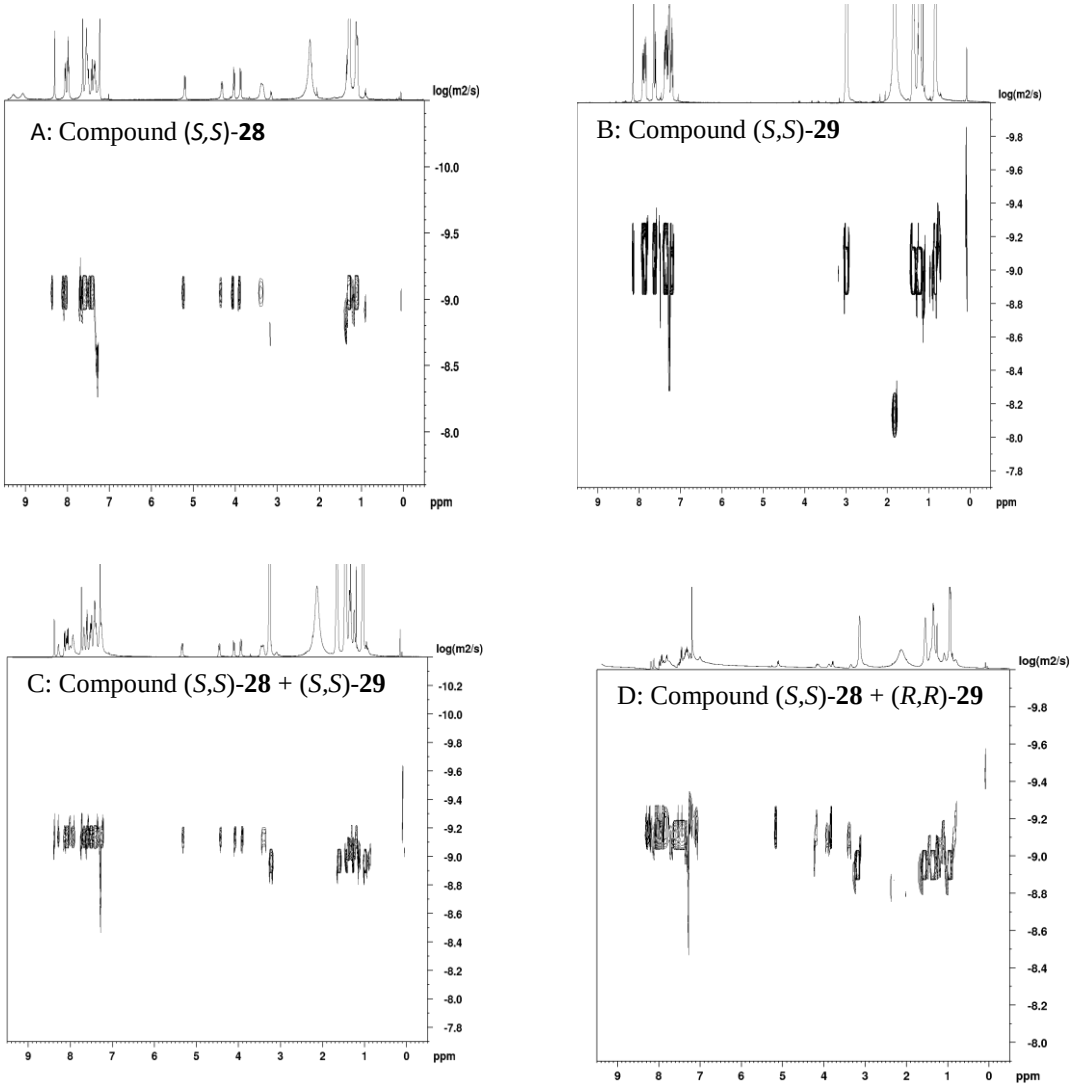


Figure 171: DOSY plots A) Compound (*S,S*)-**28**; B) Compound (*S,S*)-**29**, C) Compound (*S,S*)-**28** + (*S,S*)-**29**, D) Compound (*S,S*)-**28** + (*R,R*)-**29**.

Table 27: Diffusion coefficients as determined per DOSY NMR. All measurements were performed in [D_1]-chloroform at 298 K.

Compound		(*S,S*)-**28**		(*S,S*)-**29**		(*S,S*)-**28**+ (*S,S*)-**29**		(*S,S*)-**28**+ (*R,R*)-**29**	
Assignment	**Integral region**	**Diffusion coefficient**	**Mean diffusion coefficient**	**Diffusion coefficient**	**Mean diffusion coefficient**	**Diffusion coefficient**	**Mean diffusion coefficient**	**Diffusion coefficient**	**Mean diffusion coefficient**
	[ppm]	**[10^{-10} m^2s^{-1}]**	**[10^{-10} m^2s^{-1}]**	**[10^{-10} m^2s^{-1}]**	**[10^{-10} m^2s^{-1}]**	**[10^{-10} m^2s^{-1}]**	**[10^{-10} m^2s^{-1}]**	**[10^{-10} m^2s^{-1}]**	**[10^{-10} m^2s^{-1}]**
Aromatic signals	8.4	6.78	6.79 ± 0.32	-	6.27 ± 0.05	6.01	6.00 ± 0.14	-	6.05 ± 0.23
	8.3	-		-		5.77		6.03	
	8.2	-		-		6.02		5.76	
	8.1	7.00		6.25		5.99		6.09	
	8.0	6.96		6.23		5.78		6.04	
	7.9	-		6.33		-		5.79	
	7.7	6.91		-		6.00		-	
	7.6	-		-		5.95		6.17	
Benzylic signals	5.2-5.3	6.93		-		6.06		6.07	
	4.2-4.4	6.09		-		6.11		-	
	3.8-3.9	-		-		6.06		6.00	
	3.4	6.87		-		6.28		6.54	
Tetrabutyl-ammonium signals	1.4	-	-	-	6.89 ± 0.09	8.33	8.77 ± 0.60	8.71	8.69 ± 0.35
	1.2	-		6.95		8.53		8.33	
	1.0	-		6.82		9.46		9.03	

9.4. Circular dichroism

9.4.1. CD measurements

In order to further characterize the structures of (*S*,*S*)-**28**+(*S*,*S*)-**29** and (*S*,*S*)-**28**+(*R*,*R*)-**29**, we carried out ECD measurements. To perform ECD measurements stock solutions of (*S*,*S*)-**28**, (*S*,*S*)-**29** and (*R*,*R*)-**29** (1 mM each) were prepared. Stock solutions were used to prepare the samples with concentrations of 10 µM in chloroform. The samples were measured at 25 °C.

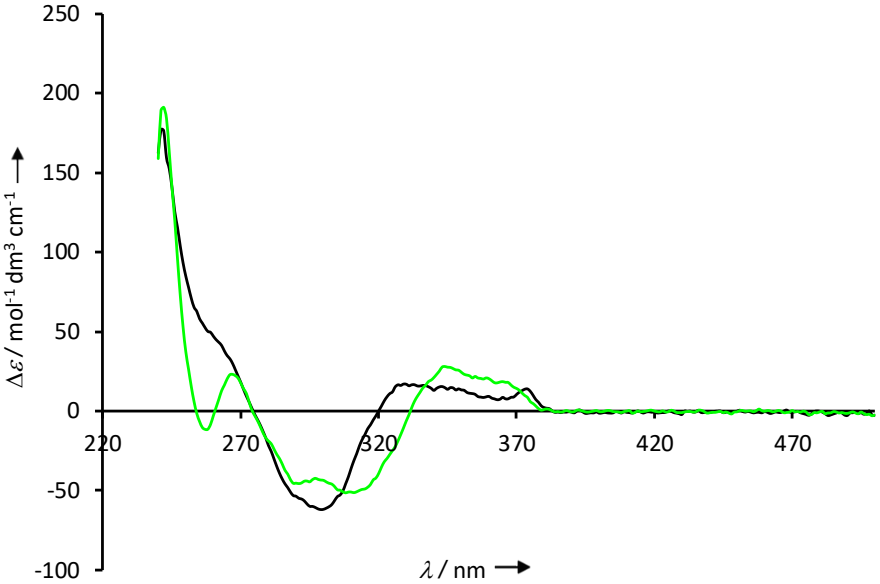


Figure 172: CD spectra of the monomers (*S*,*S*)-**28** (green) and (*S*,*S*)-**29** (black) in $CHCl_3$ (c = 10^{-5} M).

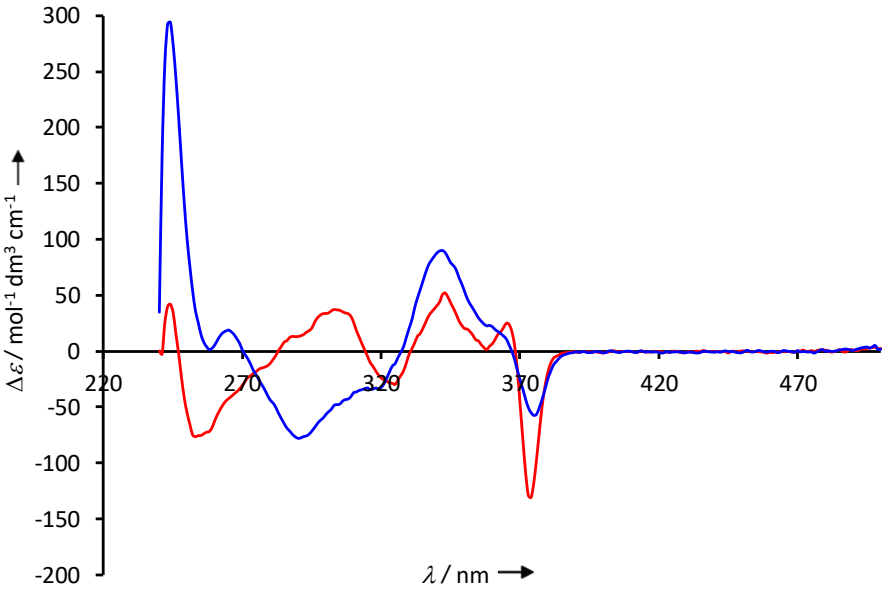


Figure 173: CD spectra of the homochiral complex (*S*,*S*)-**28**+(*S*,*S*)-**29** (blue) and the heterochiral complex (*S*,*S*)-**28**+(*R*,*R*)-**29** (red) in $CHCl_3$ (c = 10^{-5} M).

9.5. Calculated structures and CD spectra

9.5.1. Computational details

All calculations were performed by using the program package Gaussian 16[129]. The geometrical parameters of all stationary points were optimized by means of the density functional B3LYP[130,131,132]together with the dispersion correction with Becke-Johnson damping[133] (D3BJ). As basis set 6-31G(d) was applied. In order to take solvent effects into account, chloroform was considered as solvent by using the SMD[134] model. For all structures C1 symmetry was applied. Frequency calculations were carried out at each of the stationary points to verify the nature of the stationary point. It turned out that all stationary states have no imaginary frequency. The CD spectra were simulated with time-dependent density functional theory (TD-DFT), using the functional cam-B3LYP[135], the basis set 6-31G* and the SMD model (chloroform as solvent). The energy, oscillator strength, and rotatory strength were calculated for each of the 150 lowest singlet excitations

[129] M. J. Frisch, G. W. Trucks, H. B. Schlegel, G. E. Scuseria, M. A. Robb, J. R. Cheeseman, G. Scalmani, V. Barone, G. A. Petersson, H. Nakatsuji, X. Li, M. Caricato, A. V. Marenich, J. Bloino, B. G. Janesko, R. Gomperts, B. Mennucci, H. P. Hratchian, J. V. Ortiz, A. F. Izmaylov, J. L. Sonnenberg, D. Williams-Young, F. Ding, F. Lipparini, F. Egidi, J. Goings, B. Peng, A. Petrone, T. Henderson, D. Ranasinghe, V. G. Zakrzewski, J. Gao, N. Rega, G. Zheng, W. Liang, M. Hada, M. Ehara, K. Toyota, R. Fukuda, J. Hasegawa, M. Ishida, T. Nakajima, Y. Honda, O. Kitao, H. Nakai, T. Vreven, K. Throssell, J. A. Montgomery, Jr.; , J. E. Peralta, F. Ogliaro, M. J. Bearpark, J. J. Heyd, E. N. Brothers, K. N. Kudin, V. N. Staroverov, T. A. Keith, R. Kobayashi, J. Normand, K. Raghavachari, A. P. Rendell, J. C. Burant, S. S. Iyengar, J. Tomasi, M. Cossi, J. M. Millam, M. Klene, C. Adamo, R. Cammi, J. W. Ochterski, R. L. Martin, K. Morokuma, O. Farkas, J. B. Foresman, D. J. Fox, Gaussian, Inc., Wallingford CT, **2016**.

[130] A. D. Becke, *Phys. Rev. A* **1988**, *38*, 3098-3100.

[131] C. Lee, W. Yang, R. G. Parr, *Phys. Rev. B* **1988**, *37*, 785-789.

[132] B. Miehlich, A. Savin, H. Stoll, H. Preuss, *Chem. Phys. Lett.* **1989**, *157*, 200-206.

[133] S. Grimme, S. Ehrlich, L. Goerigk, *J. Comp. Chem.* **2011**, *32*, 1456-1465.

[134] A. V. Marenich, C. J. Cramer, D. G. Truhlar, *J. Phys. Chem. B* **2009**, *113*, 6378-6396.

[135] T. Yanai, D. P. Tew, N. C. Handy, *Chem. Phys. Lett.* **2004**, *393*, 51-57.

9.6. Structures of the monomers and dimers

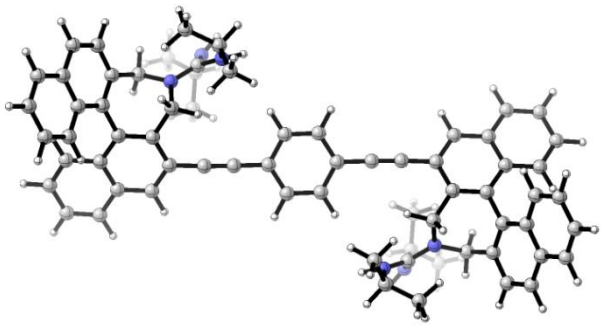


Figure 174: Molecular structures (CYLview20) of the cationic part of (*S*,*S*)-**28** calculated by means of B3LYP-D3BJ(SMD)/6-31G*. Color codes: grey, carbon; white, hydrogen; blue, nitrogen.

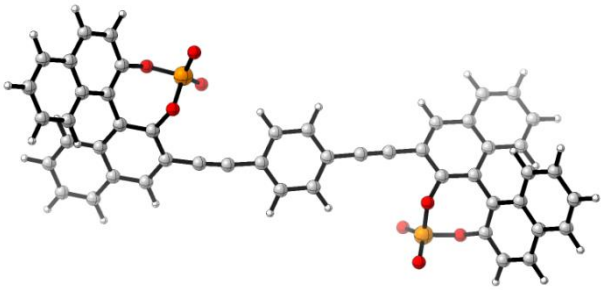


Figure 175: Molecular structures (CYLview20) of the anionic part of (*S*,*S*)-**29** calculated by means of B3LYP-D3BJ(SMD)/6-31G*. Color codes: grey, carbon; white, hydrogen; brown, phosphorus; red, oxygen.

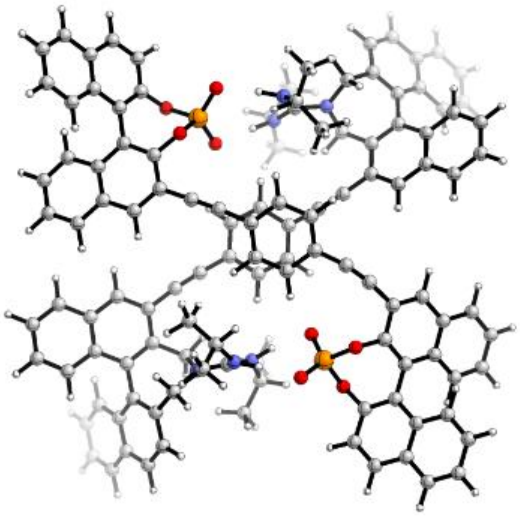


Figure 177: Molecular structures (CYLview20) of the homochiral complex (*S*,*S*)-**28**+(*S*,*S*)-**29** calculated by means of B3LYP-D3BJ(SMD)/6-31G*. Color codes: grey, carbon; white, hydrogen; brown, phosphorus; blue, nitrogen; red, oxygen.

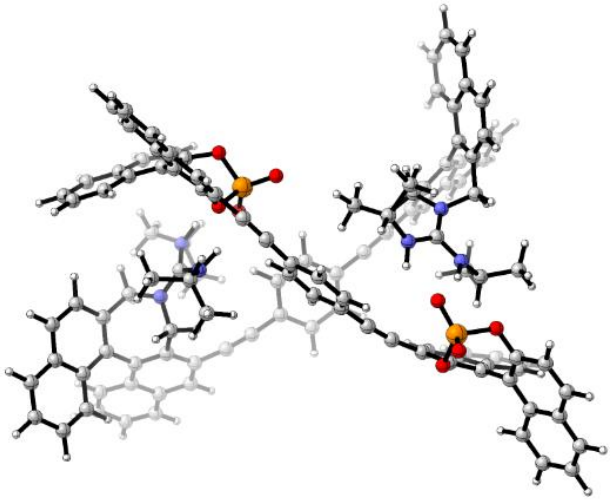


Figure 176: Molecular structures (CYLview20) of the heterochiral complex (*S*,*S*)-**28**+(*R*,*R*)-**29** calculated by means of B3LYP-D3BJ(SMD)/6-31G*. Color codes: grey, carbon; white, hydrogen; brown, phosphorus; blue, nitrogen; red, oxygen.

9.7. Calculated transition orbitals

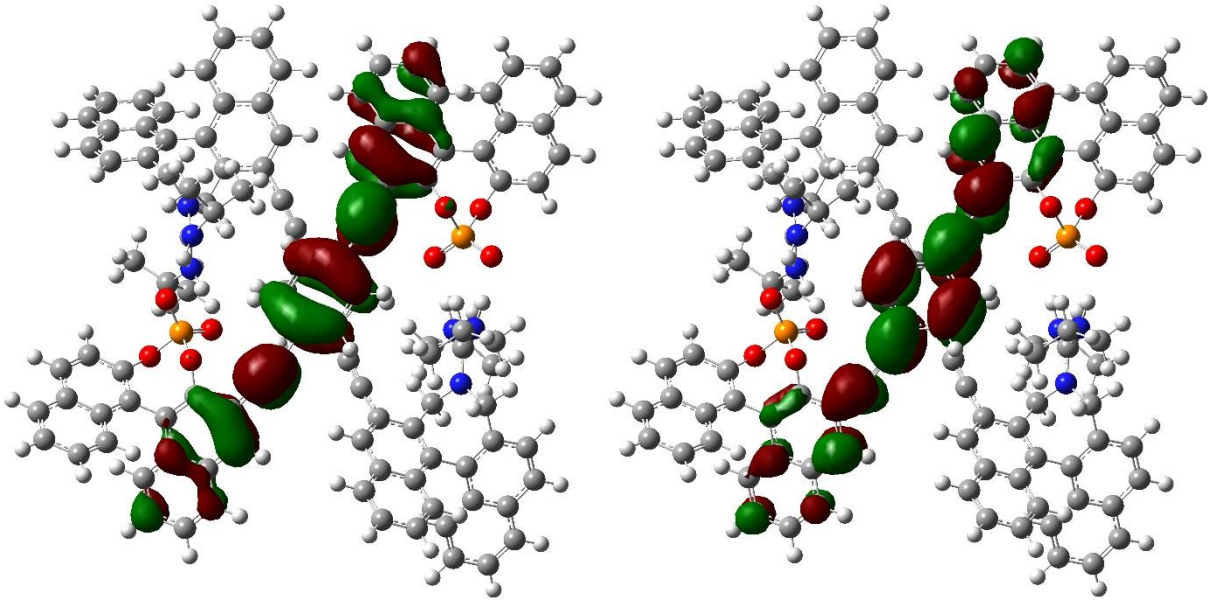


Figure 178: Occupied (left) and virtual (right) natural transition orbitals of the π-π* band at 355 nm of the homochiral complex (*S*,*S*)-**28**+(*S*,*S*)-**29** calculated by means of TD-cam-B3LYP(SMD)/6-31G*.

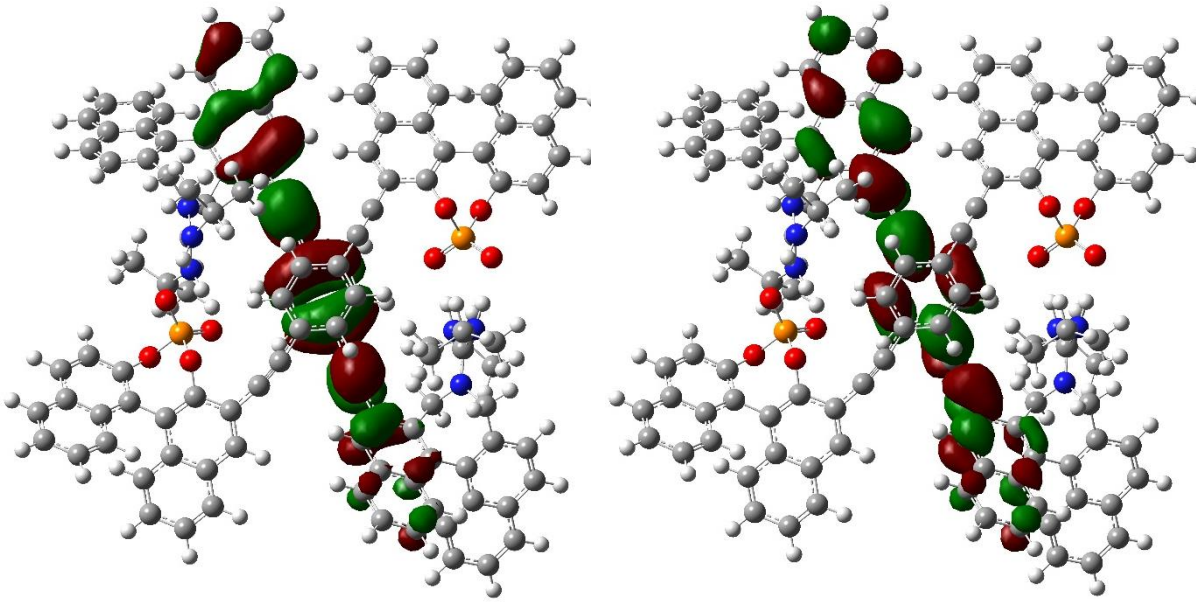


Figure 179: Occupied (left) and virtual (right) natural transition orbitals of the π-π* band at 343 nm of the homochiral complex (*S*,*S*)-**28**+(*S*,*S*)-**29** calculated by means of TD-cam-B3LYP(SMD)/6-31G*.

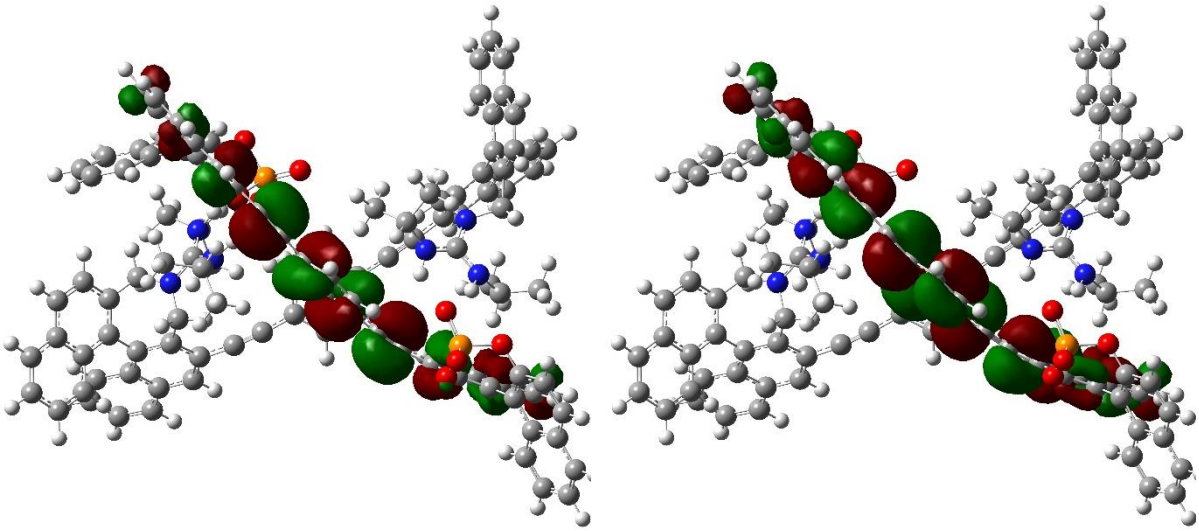


Figure 180: Occupied (left) and virtual (right) natural transition orbitals of the π-π* band at 357 nm of the heterochiral complex (*S*,*S*)-**28**+(*R*,*R*)-**29** calculated by means of TD-cam-B3LYP(SMD)/6-31G*.

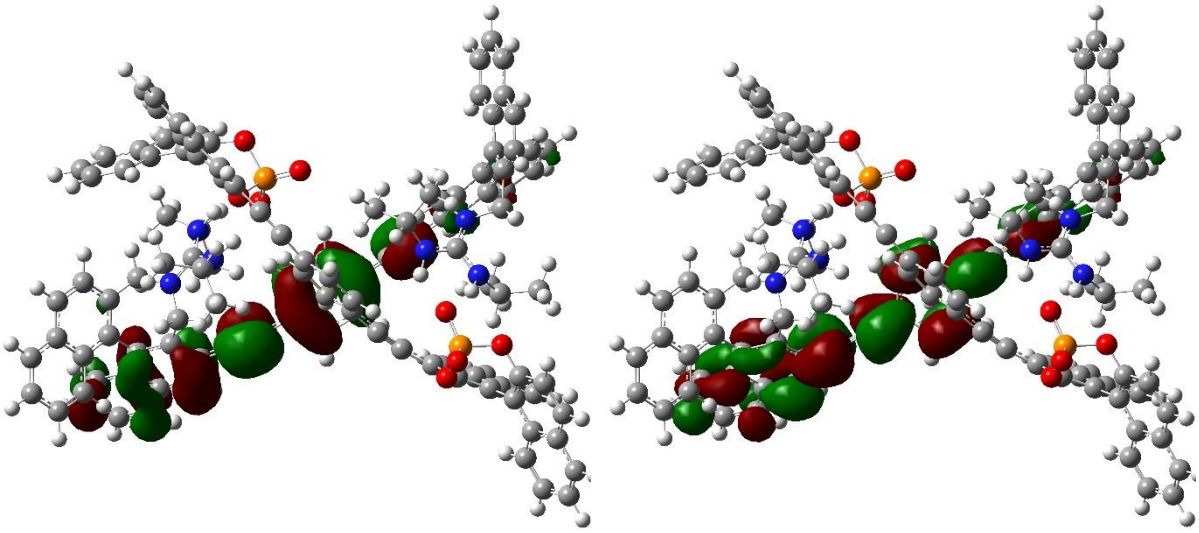


Figure 181: Occupied (left) and virtual (right) natural transition orbitals of the π-π* band at 323 nm of the heterochiral complex (*S*,*S*)-**28**+(*R*,*R*)-**29** calculated by means of TD-cam-B3LYP(SMD)/6-31G*.

9.8. Calculated CD spectra

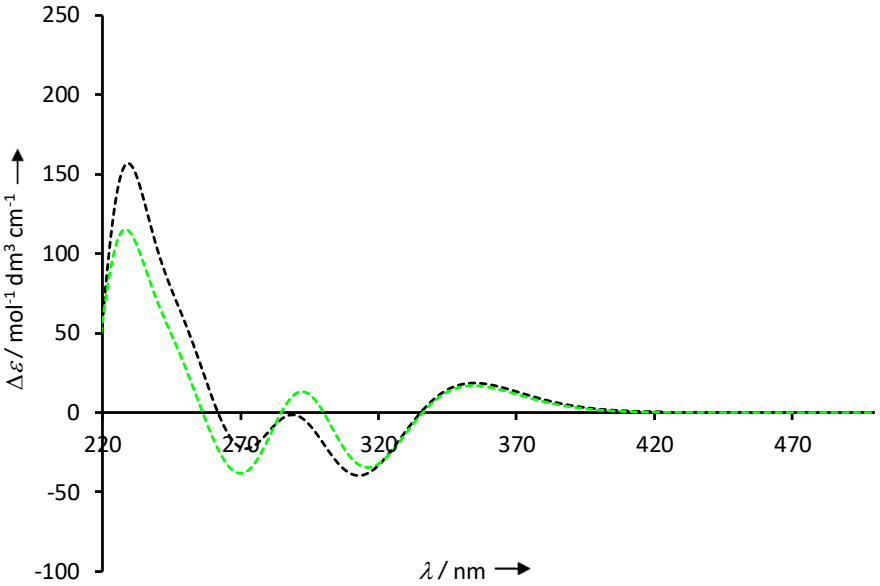


Figure 182: TD-cam-B3LYP(SMD)/6-31G*-calculated CD spectra of the monomers (*S*,*S*)-**28** (green) and (*S*,*S*)-**29** (black).

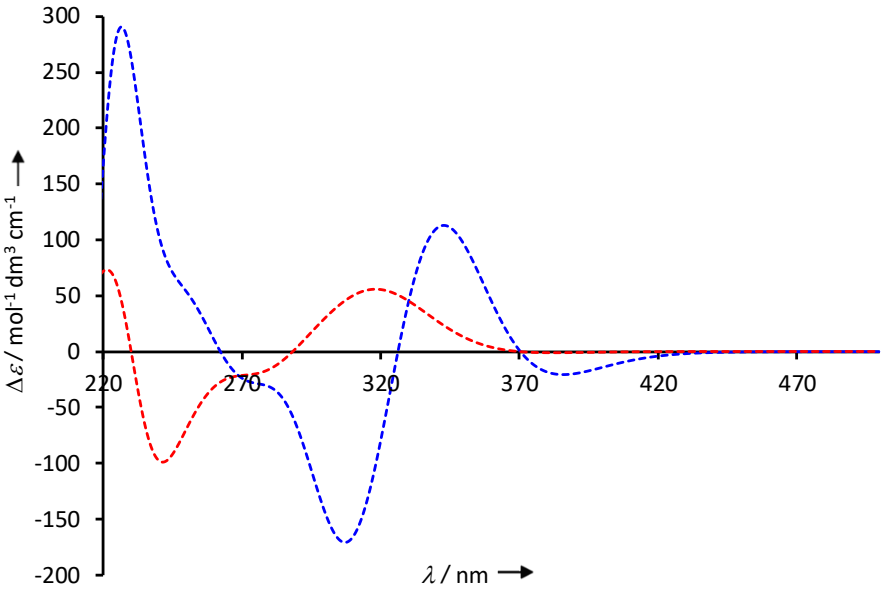
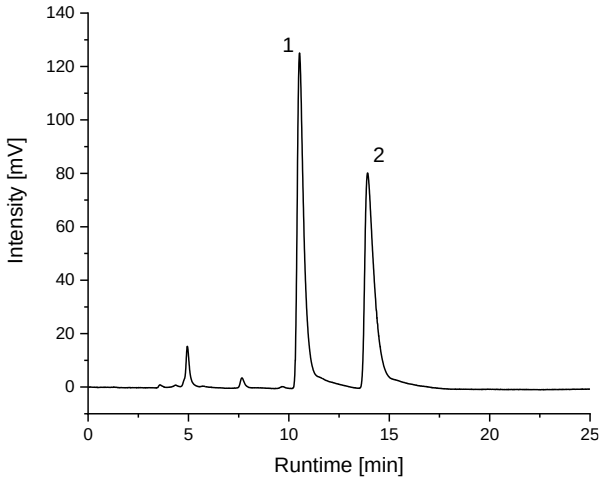


Figure 183: TD-cam-B3LYP(SMD)/6-31G*-calculated CD spectra of the monomers of the homochiral complex (*S*,*S*)-**28**+(*S*,*S*)-**29** (blue) and the heterochiral complex (*S*,*S*)-**28**+(*R*,*R*)-**29** (red) in $CHCl_3$ (c = 10^{-5} M).

9.9.HPLC-Runs

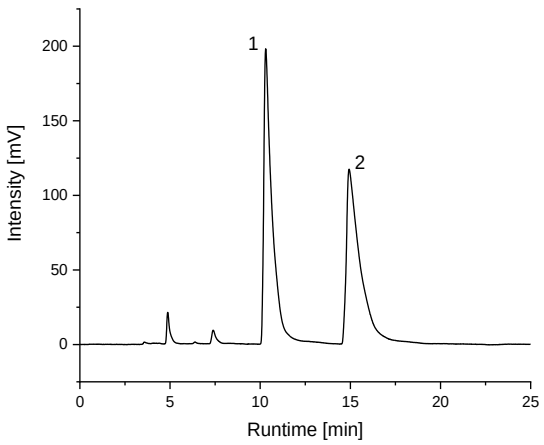
9.9.1. Chromatograms of Transferhydrogenation

9.9.1.1. Chromatograms for all substrates with racemic catalyst



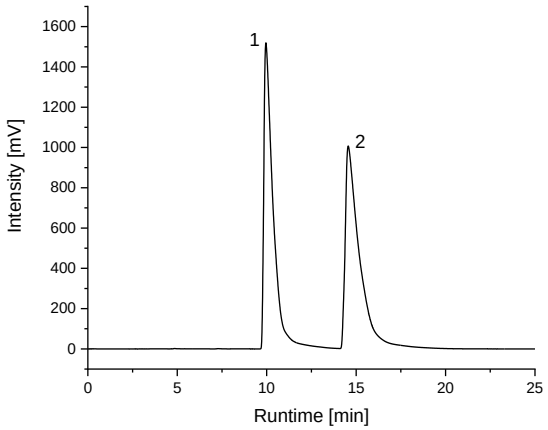
number	retention time	percentage
1	10.525	50.94043
2	13.91667	49.05957

Figure 184: Chiral HPLC chromatogram of **60a** catalyzed by 10% (*rac*)- BNDHP**.**



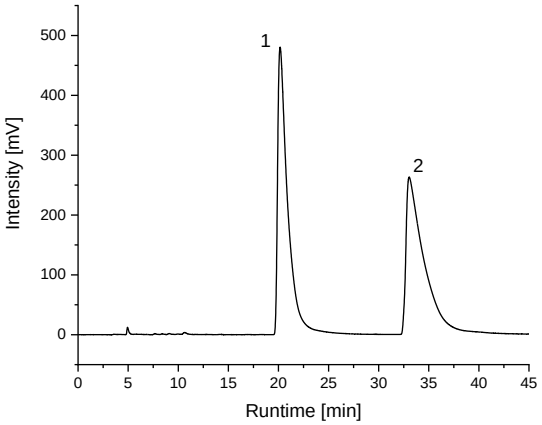
retention time	percentage
10.3	50.91286
14.925	49.08714

Figure 185: Chiral HPLC chromatogram of **60b** catalyzed by 10% (*rac*)-BNDHP.



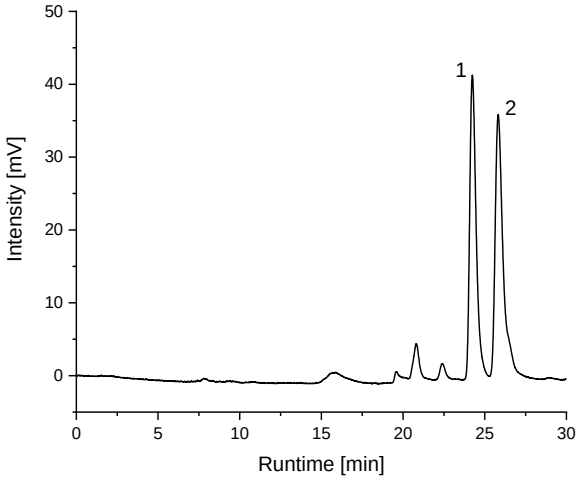
number	retention time	percentage
1	9.95	50.28891
2	14.56667	49.71109

Figure 186: Chiral HPLC chromatogram of **60c** catalyzed by 10% (*rac*)-BNDHP**.**



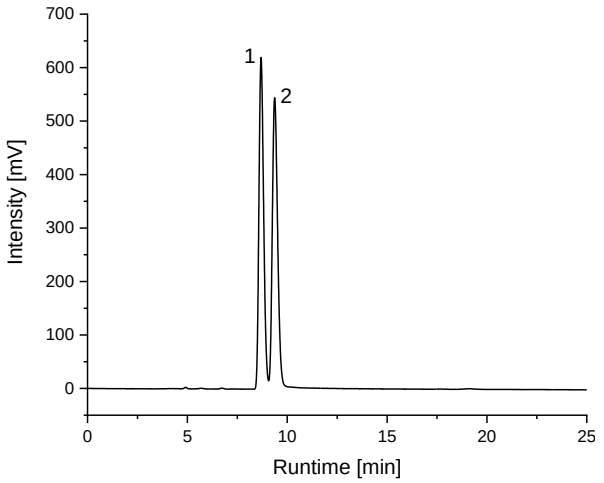
retention time	percentage
20.15833	50.45487
33.05	49.54513

Figure 187: Chiral HPLC chromatogram of **60d** catalyzed by 10% (*rac*)-BNDHP**.**



number	retention time	percentage
1	24.23333	49.96378
2	25.81667	50.03622

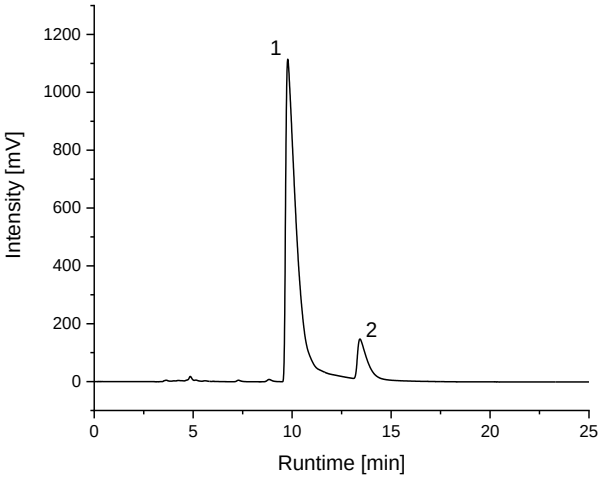
Figure 188: Chiral HPLC chromatogram of **60e** catalyzed by 10% (*rac*)-BNDHP**.**



retention time	percentage
8.683333	50.29367
9.375	49.70633

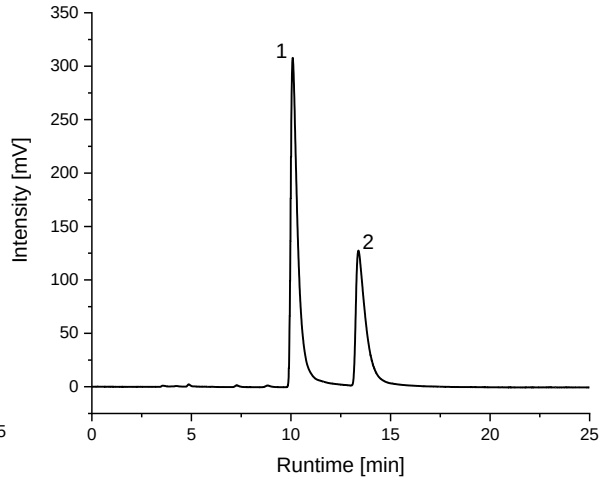
Figure 189: Chiral HPLC chromatogram of **60f** catalyzed by 10% (*rac*)-BNDHP**.**

9.9.1.2. Chromatograms of 2-phenyl-quinoline with a catalyst loading of 10% and a reaction time of 72 hours



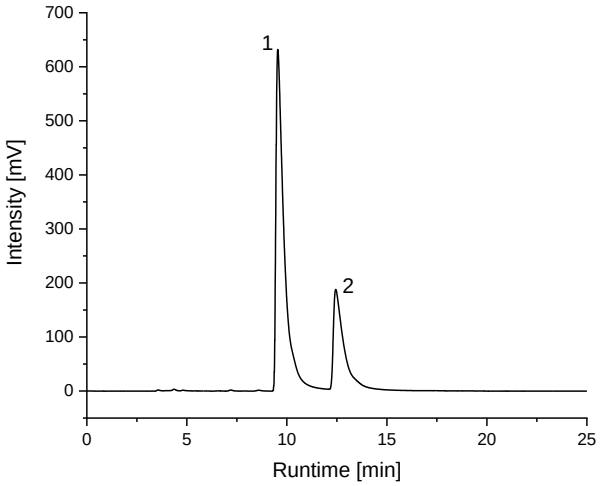
number	retention time	percentage
1	9.775	90.52799
2	13.43333	9.472011

Figure 190: Chiral HPLC chromatogram of **60a** catalyzed by 10% (*R*)-**13.**



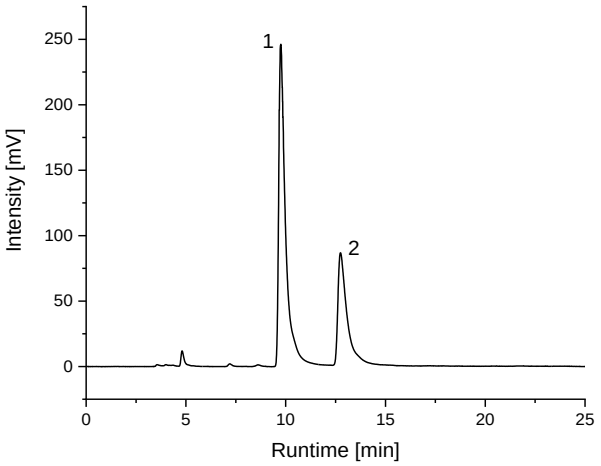
retention time	percentage
10.09167	64.21548
13.39167	35.78452

Figure 191: Chiral HPLC chromatogram of **60a** catalyzed by 10% (*R*)-**12a.**



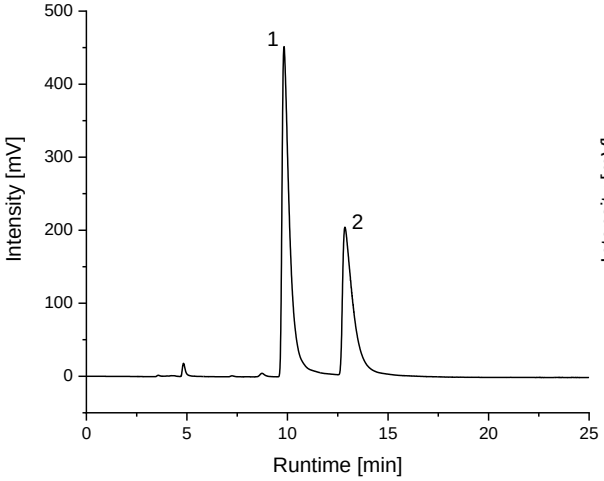
number	retention time	percentage
1	9.541667	73.96033
2	12.45	26.03966

Figure 192: Chiral HPLC chromatogram of **60a** catalyzed by 10% (*R*)-**12b.**



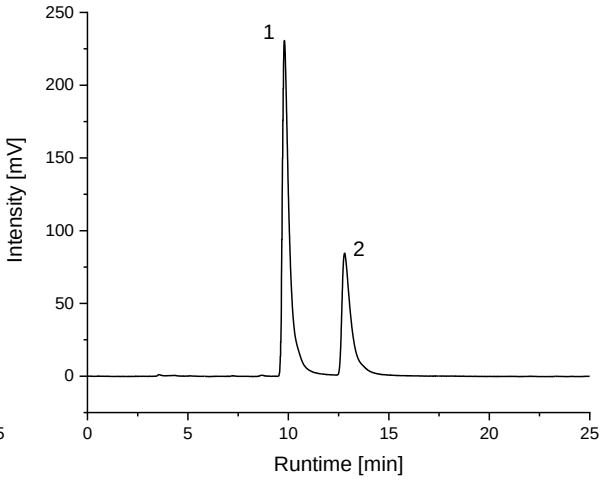
retention time	percentage
9.75	67.99802
12.75	32.00198

Figure 193: Chiral HPLC chromatogram of **60a** catalyzed by 10% (*R*,*R*)-**4a.**



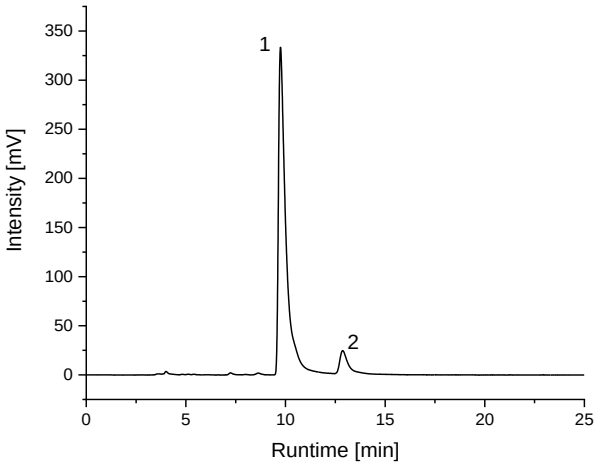
number	retention time	percentage
1	9.833333	62.10015
2	12.86667	37.89985

Figure 194: Chiral HPLC chromatogram of **60a** catalyzed by 10% (*R*,*R*)-**4b**.



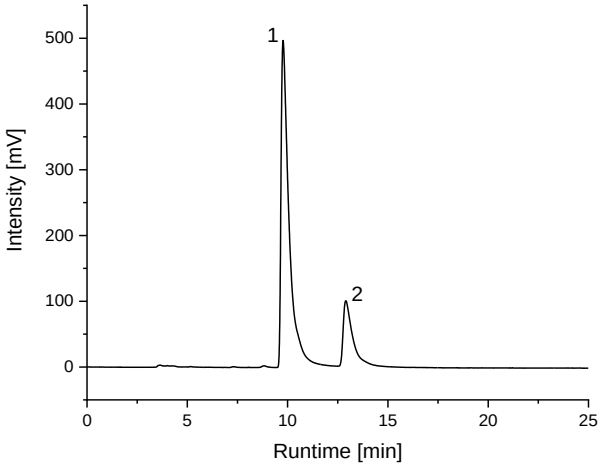
retention time	percentage
9.808333	68.3845
12.79167	31.6155

Figure 195: Chiral HPLC chromatogram of **60a** catalyzed by 10% (*R*,*R*)-**45.**



number	retention time	percentage
1	9.741667	93.50741
2	12.86667	6.492589

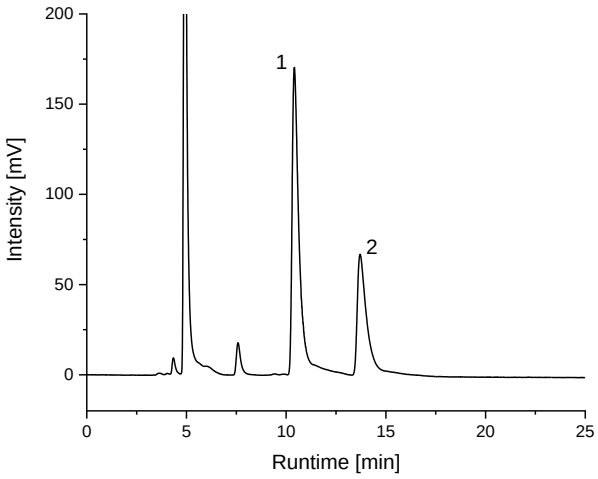
Figure 196: Chiral HPLC chromatogram of **60a** catalyzed by 10% (*R*,*R*)-**6.**



retention time	percentage
9.766666	82.15453
12.90833	17.84548

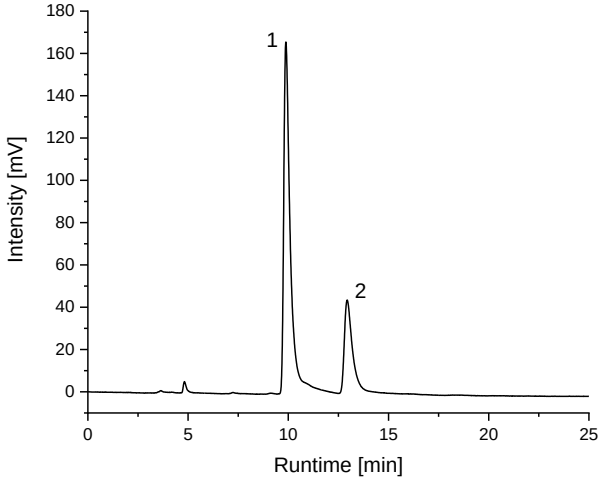
Figure 197: Chiral HPLC chromatogram of **60a** catalyzed by 10% (*R*,*R*)-**9.**

9.9.1.3. Chromatograms of 2-phenyl-quinoline with a catalyst loading of 10% and a reaction time of 140 hours



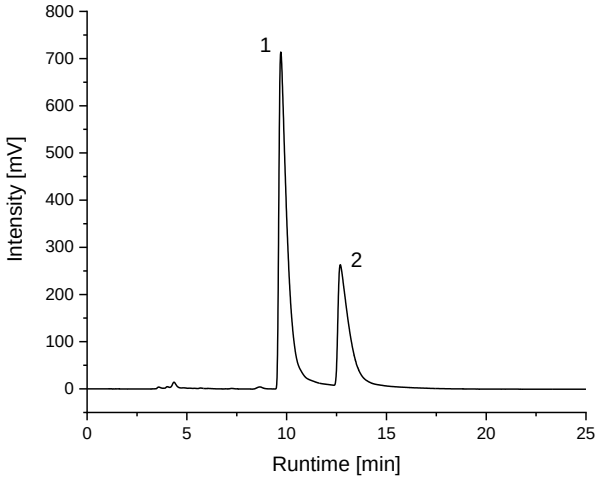
number	retention time	percentage
1	10.41667	66.63564
2	13.7	33.36436

Figure 198: Chiral HPLC chromatogram of **60a** catalyzed by 10% (*R*)-**12a.**



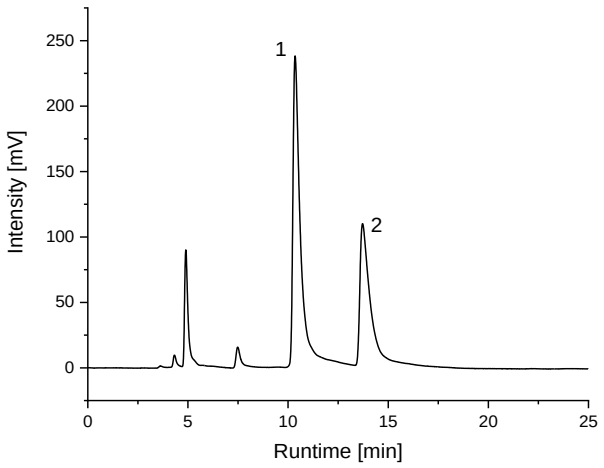
retention time	percentage
9.875	75.80424
12.93333	24.19576

Figure 199: Chiral HPLC chromatogram of **60a** catalyzed by 10% (*R*)-**12b.**



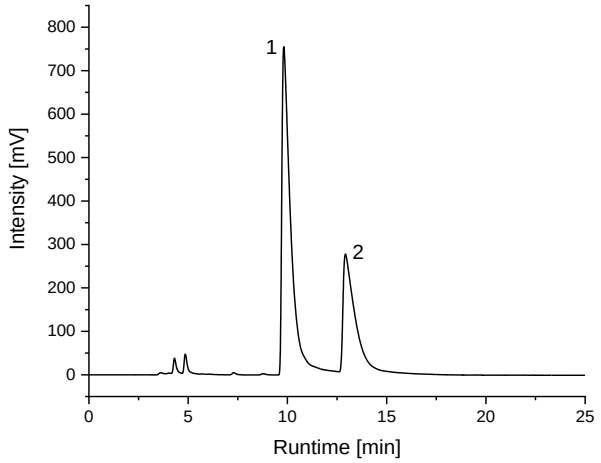
number	retention time	percentage
1	9.7	68.39439
2	12.68333	31.60562

Figure 200: Chiral HPLC chromatogram of **60a** catalyzed by 10% (*R*,*R*)-**4a.**



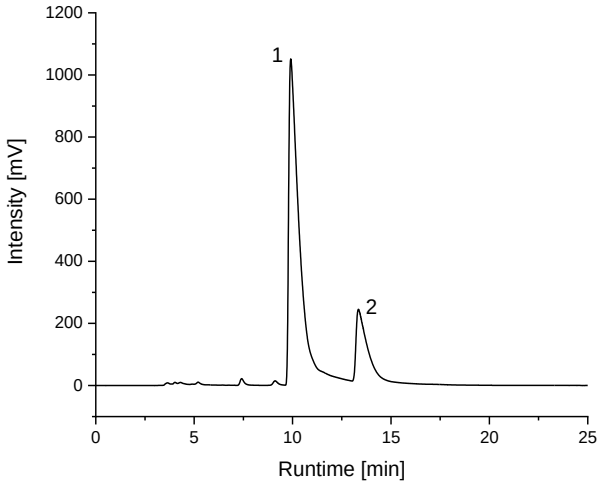
retention time	percentage
10.35833	61.71014
13.725	38.28986

Figure 201: Chiral HPLC chromatogram of **60a** catalyzed by 10% (*R*,*R*)-**4b.**



number	retention time	percentage
1	9.825	68.84393
2	12.91667	31.15607

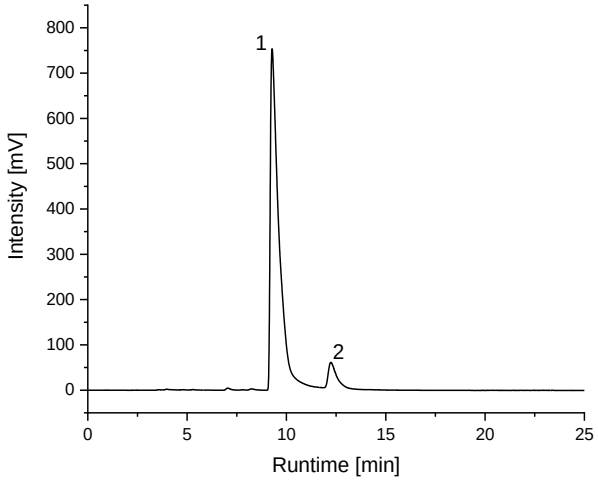
Figure 202: Chiral HPLC chromatogram of **60a** catalyzed by 10% (*R*,*R*)-**5.**



retention time	percentage
9.916667	81.51507
13.34167	18.48494

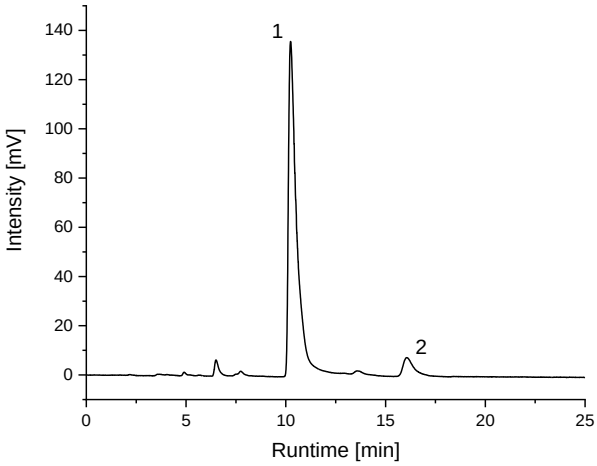
Figure 203: Chiral HPLC chromatogram of **60a** catalyzed by 10% (*R*,*R*)-**9.**

9.9.1.4. Chromatograms of 2-quinoline derivatives with a catalyst loading of 1% and a reaction time of 72 hours



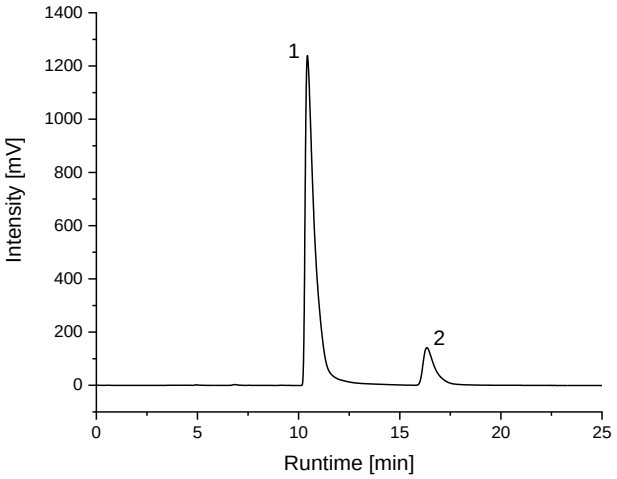
number	retention time	percentage
1	9.283334	93.49123
2	12.24167	6.508773

Figure 204: Chiral HPLC chromatogram of **60a** catalyzed by 1% (*R*,*R*)-**6.**



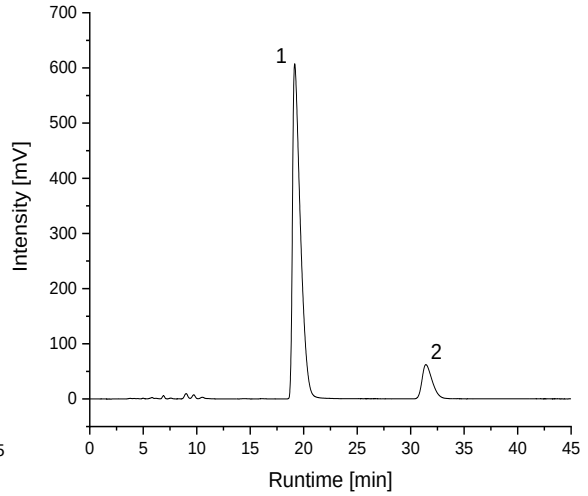
retention time	percentage
10.23333	93.61012
16.075	6.38988

Figure 205: Chiral HPLC chromatogram of **60b** catalyzed by 1% (*R*,*R*)-**6.**



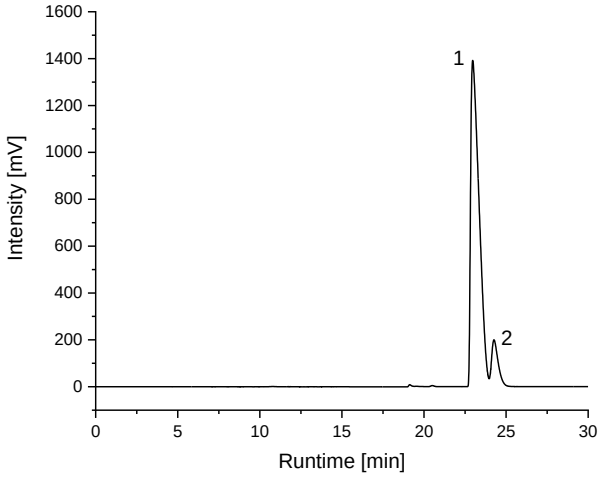
number	retention time	percentage
1	10.44167	87.84078
2	16.33333	12.15922

Figure 206: Chiral HPLC chromatogram of **60c** catalyzed by 1% (*R*,*R*)-**6.**



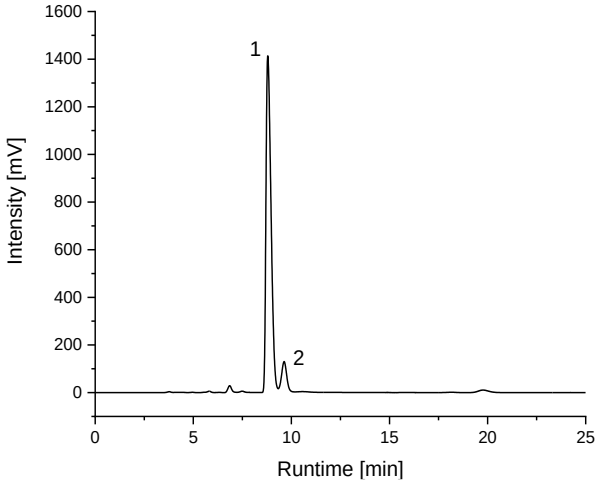
retention time	percentage
19.16667	88.93777
31.425	11.06223

Figure 207: Chiral HPLC chromatogram of **60d** catalyzed by 1% (*R*,*R*)-**6.**



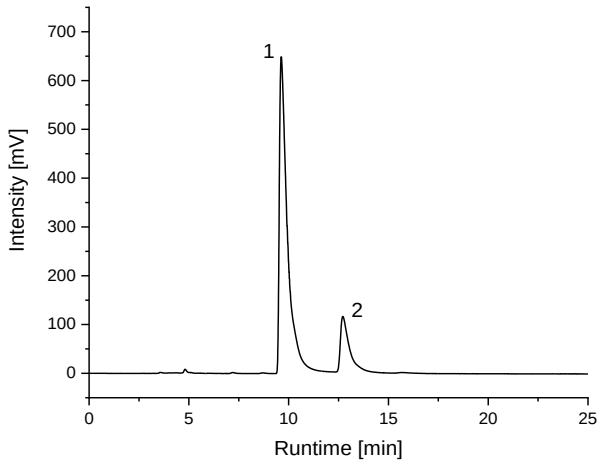
number	retention time	percentage
1	22.975	91.80817
2	24.25833	8.191824

Figure 208: Chiral HPLC chromatogram of **60e** catalyzed by 1% (*R*,*R*)-**6.**



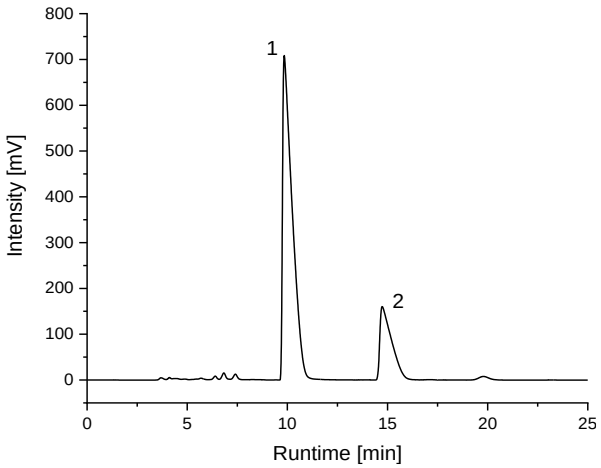
retention time	percentage
8.791667	92.60001
9.625	7.399992

Figure 209: Chiral HPLC chromatogram of **60f** catalyzed by 1% (*R*,*R*)-**6.**



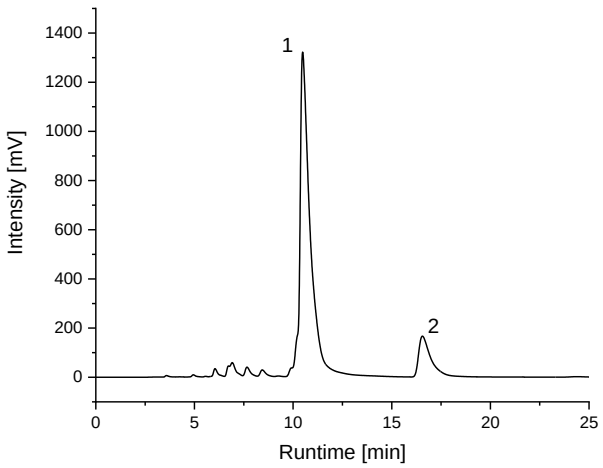
number	retention time	percentage
1	10.10833	77.61721
2	13.36667	22.38279

Figure 210: Chiral HPLC chromatogram of **60a** catalyzed by 1% (*R*)-**13.**



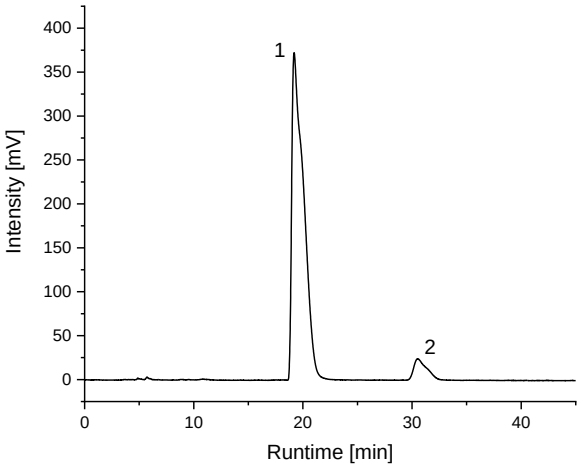
retention time	percentage
9.85	78.35873
14.74167	21.64127

Figure 211: Chiral HPLC chromatogram of **60b** catalyzed by 1% (*R*)-**13.**



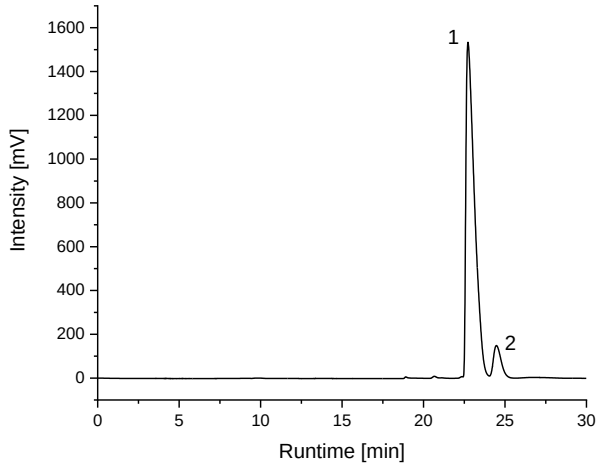
number	retention time	percentage
1	10.49167	85.05753
2	16.55	12.92474

Figure 212: Chiral HPLC chromatogram of **60c** catalyzed by 1% (*R*)-**13.**



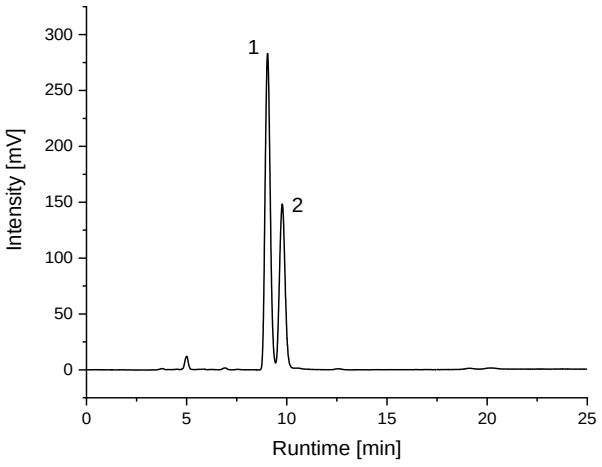
retention time	percentage
19.19167	93.23022
30.51667	6.76978

Figure 213: Chiral HPLC chromatogram of **60d** catalyzed by 1% (*R*)-**13.**



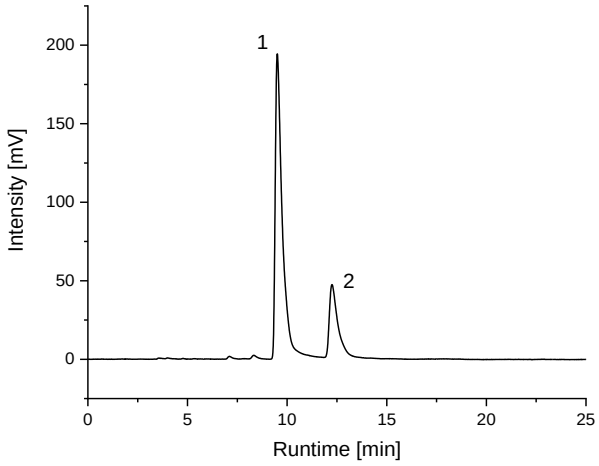
number	retention time	percentage
1	22.73333	
2	24.46667	

Figure 214: Chiral HPLC chromatogram of **60e** catalyzed by 1% (*R*)-**13.**



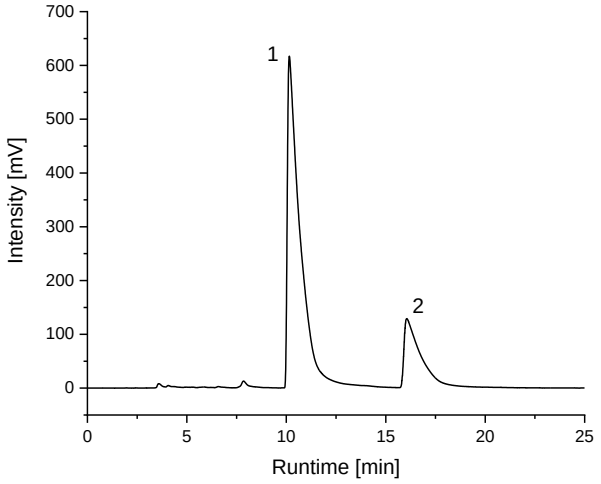
retention time	percentage
9.033334	63.39811
9.766666	36.60189

Figure 215: Chiral HPLC chromatogram of **60f** catalyzed by 1% (*R*)-**13.**



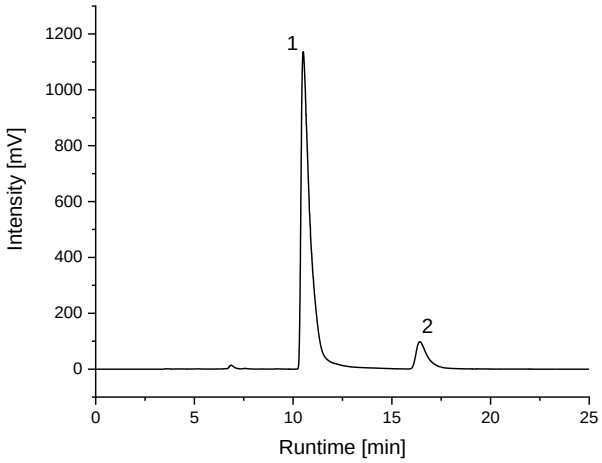
number	retention time	percentage
1	9.5	77.39766
2	12.25833	22.60234

Figure 216: Chiral HPLC chromatogram of **60a** catalyzed by 1% (*R*,*R*)-**9.**



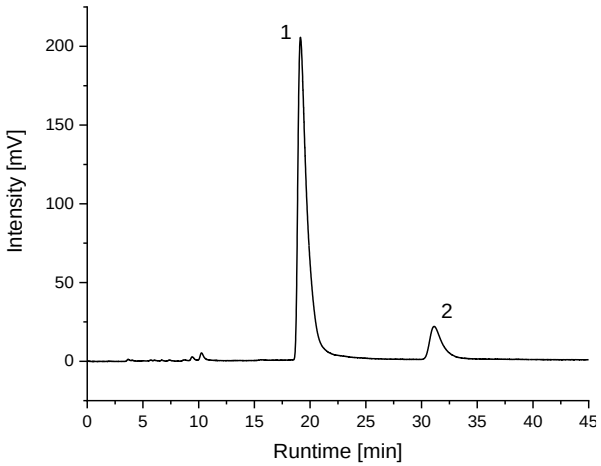
retention time	percentage
10.15833	79.18779
16.06667	20.81221

Figure 217: Chiral HPLC chromatogram of **60b** catalyzed by 1% (*R*,*R*)-**9.**



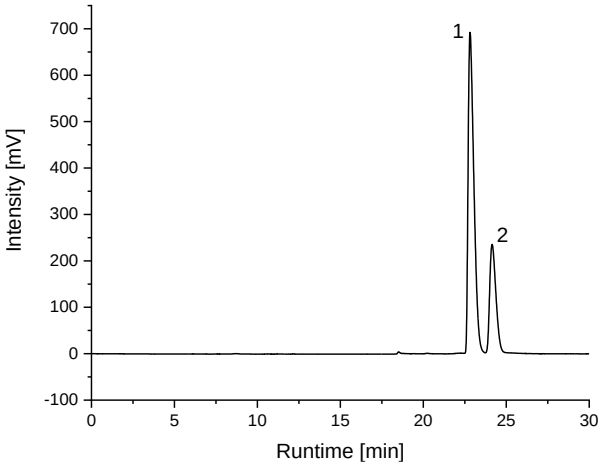
number	retention time	percentage
1	10.51667	90.54131
2	16.40833	9.458694

Figure 218: Chiral HPLC chromatogram of **60c** catalyzed by 1% (*R*,*R*)-**9.**



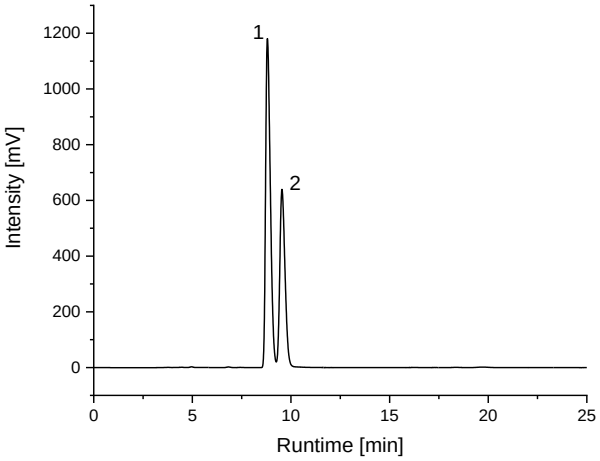
retention time	percentage
19.125	89.37986
31.13333	10.62014

Figure 219: Chiral HPLC chromatogram of **60d** catalyzed by 1% (*R*,*R*)-**9.**



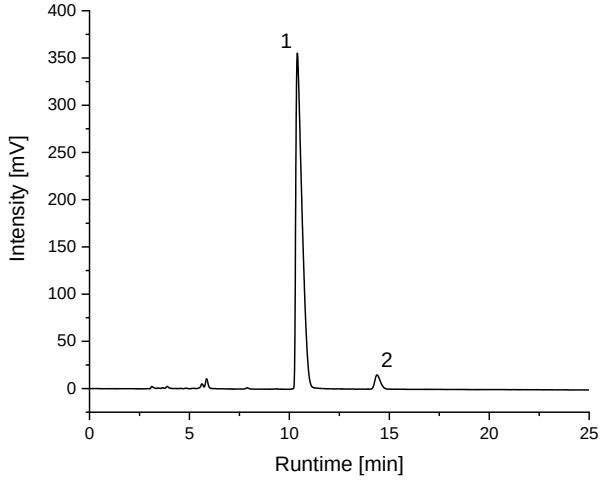
number	retention time	percentage
1	22.825	73.99845
2	24.14167	26.00155

Figure 220: Chiral HPLC chromatogram of **60e** catalyzed by 1% (*R*,*R*)-**9.**



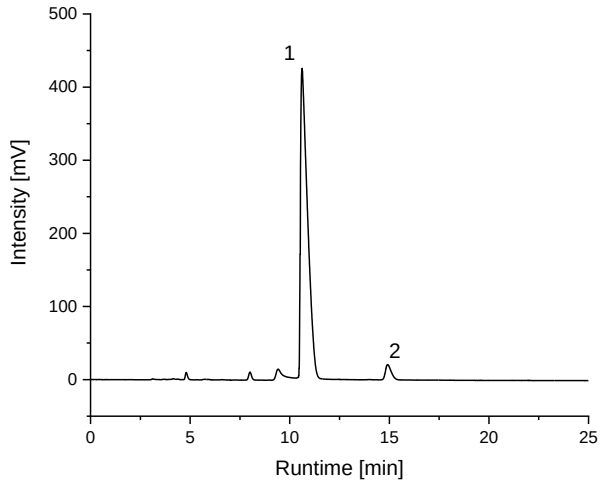
retention time	percentage
8.8	62.63076
9.55	37.36924

Figure 221: Chiral HPLC chromatogram of **60f** catalyzed by 1% (*R*,*R*)-**9.**



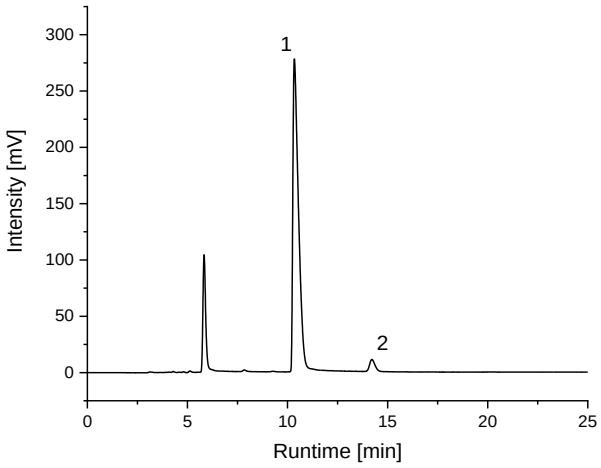
number	retention time	percentage
1	10.39167	96.25383
2	14.39167	3.746173

Figure 222: Chiral HPLC chromatogram of **60a** catalyzed by 1% (*R*,*R*)-**7.**



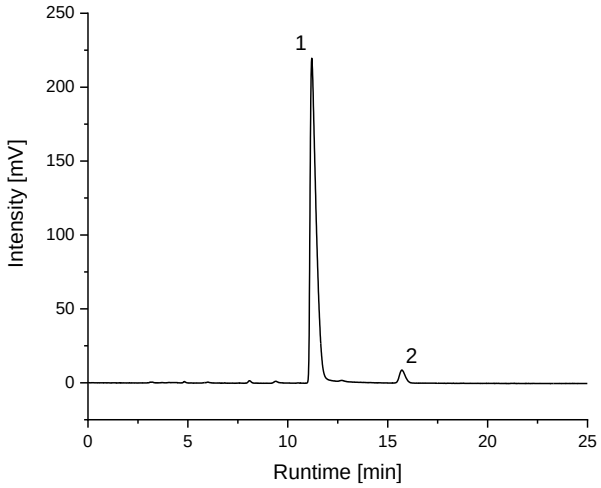
retention time	percentage
423.64	96.08005
20.92258	3.919951

Figure 223: Chiral HPLC chromatogram of **60a** catalyzed by 1% (*R*,*R*)-**10.**



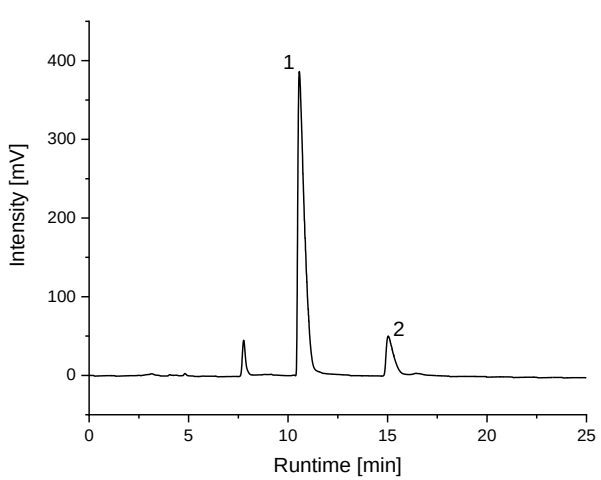
number	retention time	percentage
1	10.35	96.4524
2	14.20833	3.547597

Figure 224: Chiral HPLC chromatogram of **60a** catalyzed by 1% (*R*,*R*)-**8.**



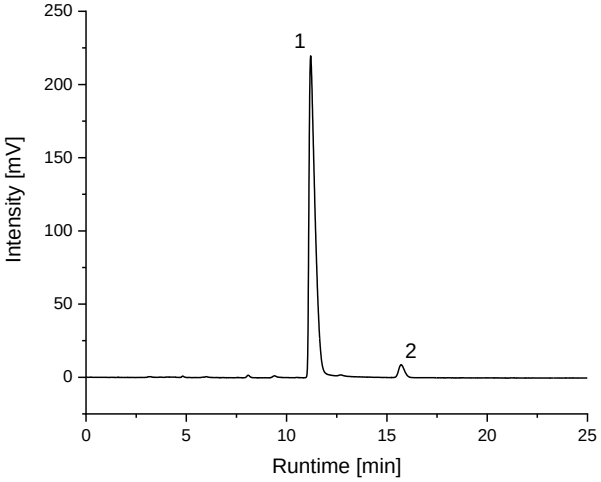
retention time	percentage
11.19167	96.26923
15.71667	3.730768

Figure 225: Chiral HPLC chromatogram of **60a** catalyzed by 1% (*R*,*R*)-**11**



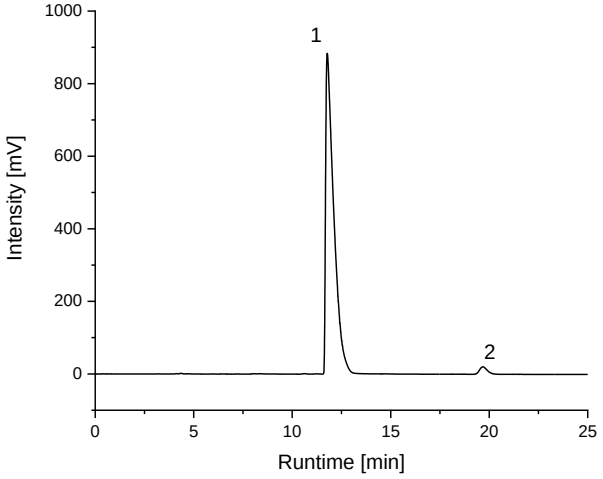
number	retention time	percentage
1	10.55833	87.79343
2	15.025	12.20656

Figure 226: Chiral HPLC chromatogram of **60b** catalyzed by 1% (*R*,*R*)-**8.**



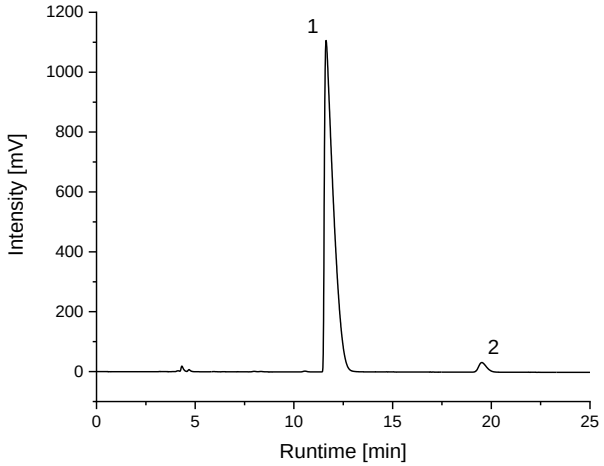
retention time	percentage
11.19167	96.26923
15.71667	3.730768

Figure 227: Chiral HPLC chromatogram of **60b** catalyzed by 1% (*R*,*R*)-**11.**



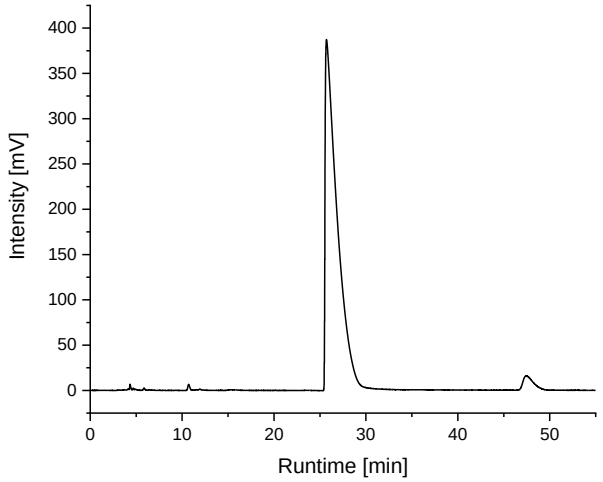
number	retention time	percentage
1	11.775	97.85862
2	19.66667	2.141384

Figure 228: Chiral HPLC chromatogram of **60c** catalyzed by 1% (*R*,*R*)-**8.**



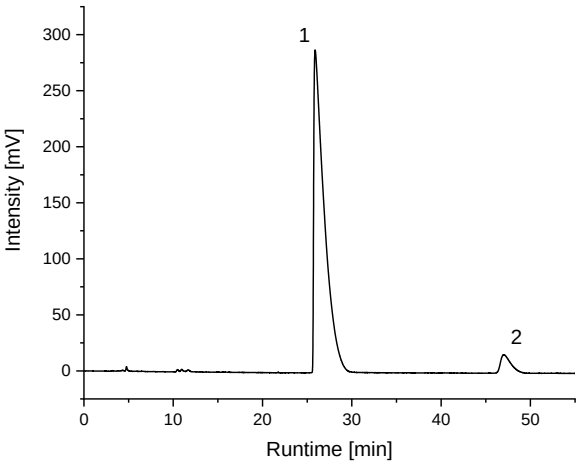
retention time	percentage
11.625	97.45364
19.51667	2.546353

Figure 229: Chiral HPLC chromatogram of **60c** catalyzed by 1% (*R*,*R*)-**11.**



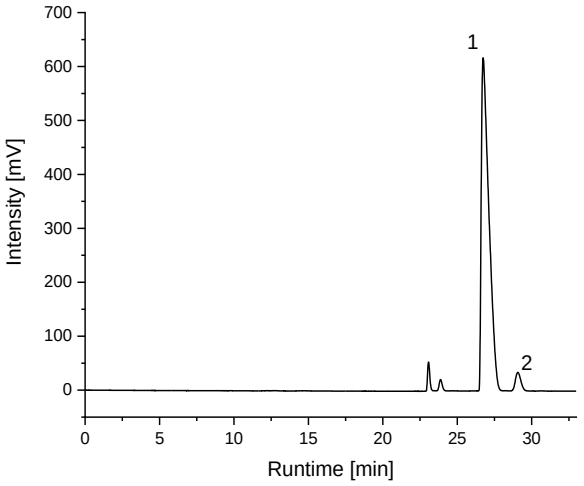
number	retention time	percentage
1	25.71667	96.50325
2	47.45	3.496747

Figure 230: Chiral HPLC chromatogram of **60d** catalyzed by 1% (*R*,*R*)-**8.**



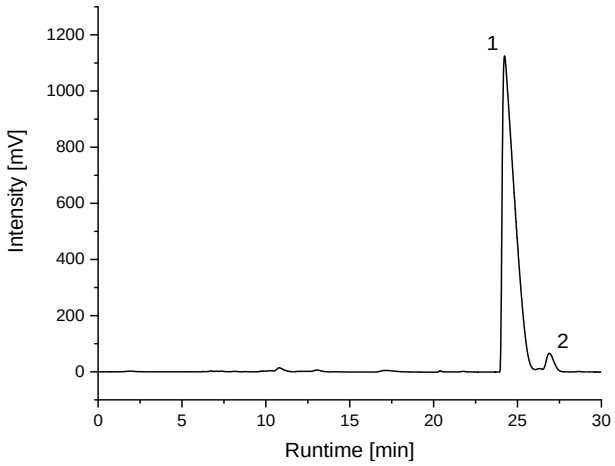
retention time	percentage
25.9	94.67974
47.03333	5.320259

Figure 231: Chiral HPLC chromatogram of **60d** catalyzed by 1% (*R*,*R*)-**11.**



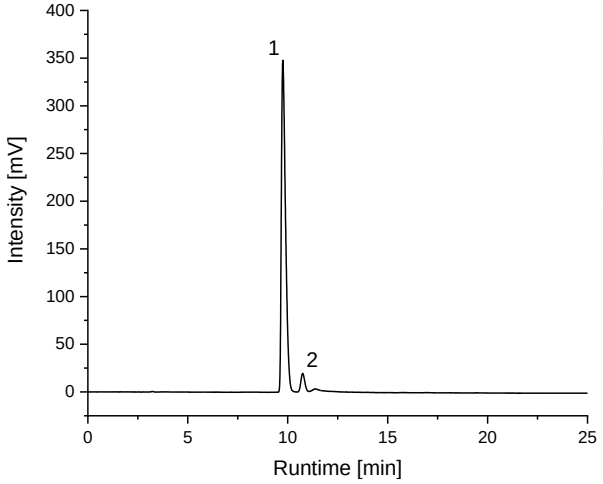
number	retention time	percentage
1	26.73333	96.13071
2	29.075	3.869287

Figure 232: Chiral HPLC chromatogram of **60e** catalyzed by 1% (*R*,*R*)-**8.**



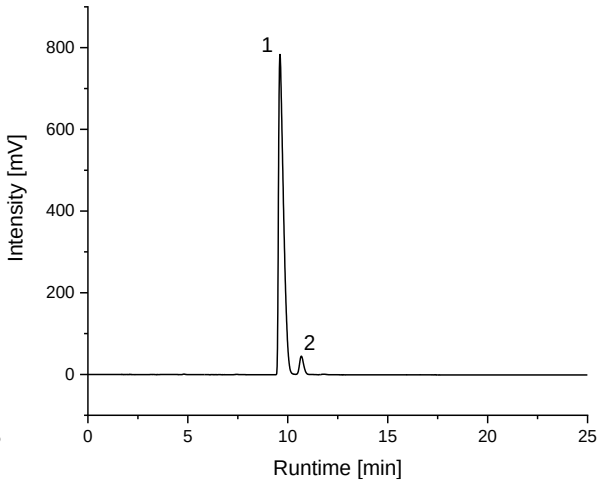
retention time	percentage
24.23333	97.26305
26.89167	2.736955

Figure 233: Chiral HPLC chromatogram of **60e** catalyzed by 1% (*R*,*R*)-**11.**



number	retention time	percentage
1	9.75	95.48155
2	10.74167	4.518451

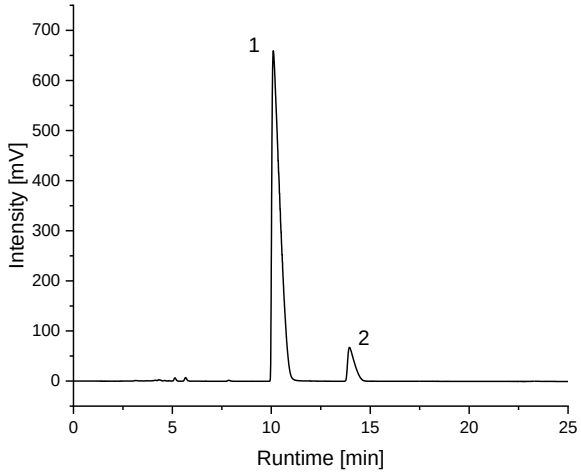
Figure 234: Chiral HPLC chromatogram of **60f** catalyzed by 1% (*R*,*R*)-**8.**



retention time	percentage
9.616667	95.55984
10.68333	4.440152

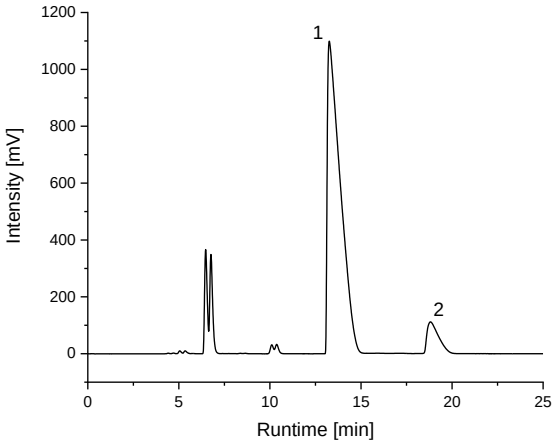
Figure 235: Chiral HPLC chromatogram of **60f** catalyzed by 1% (*R*,*R*)-**11.**

9.9.1.5. Concentration series



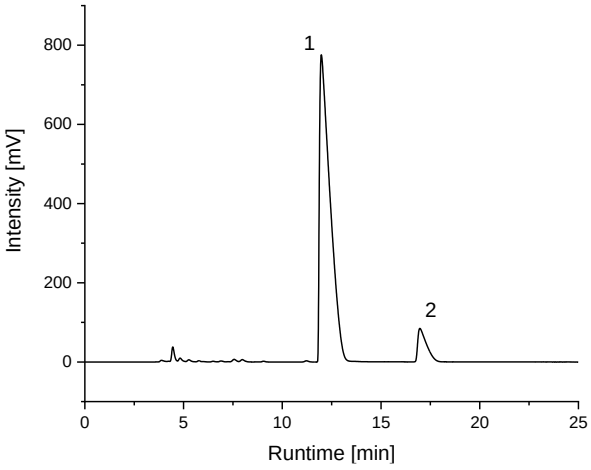
number	retention time	percentage
1	10.10833	91.92901
2	13.95833	8.070995

Figure 236: Chromatogramm der chiralen HPLC von **16f** durch 0.25% (*R*,*R*)-**6** katalysiert.



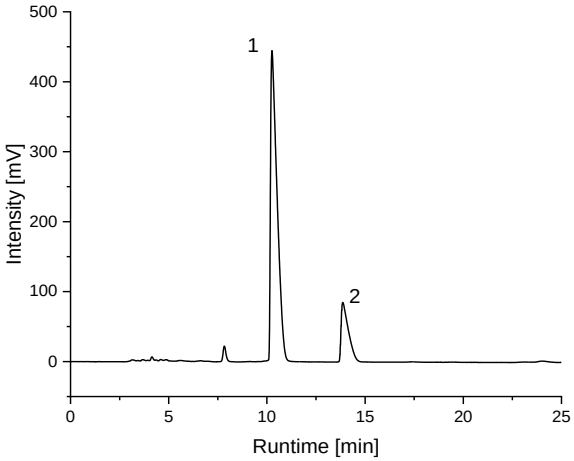
retention time	percentage
11.625	97.45364
19.51667	2.546353

Figure 237: Chiral HPLC chromatogram of **60a** catalyzed by 5.9% (*R*,*R*)-**6.**



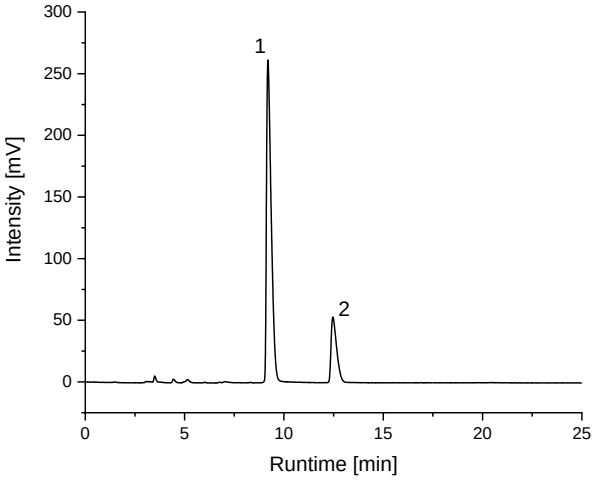
number	retention time	percentage
1	11.98333	91.77915
2	16.975	8.220848

Figure 238: Chiral HPLC chromatogram of **60a** catalyzed by 20% (*R*,*R*)-**6.**



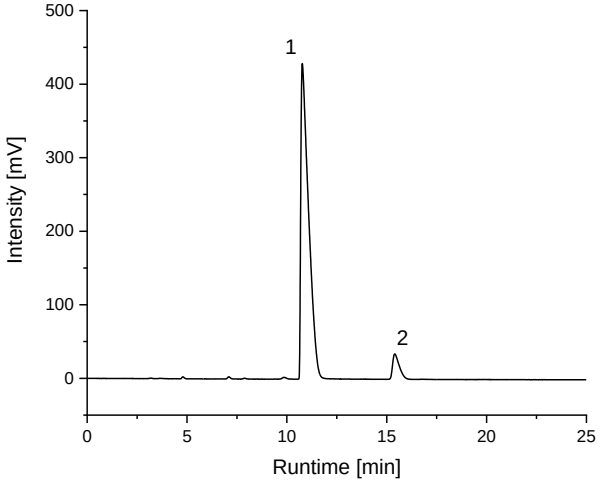
number	retention time	percentage
1	10.25	82.45493
2	13.85833	17.54507

Figure 239: Chromatogramm der chiralen HPLC von **16a** durch 0.25% (*R*,*R*)-**9** katalysiert.



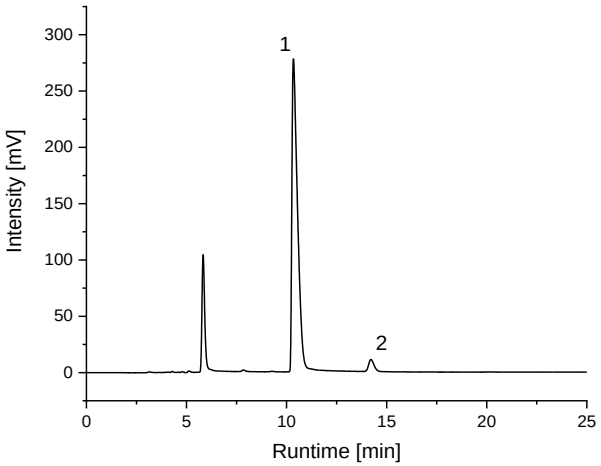
retention time	percentage
9.191667	80.90214
12.45833	19.09786

Figure 240: Chiral HPLC chromatogram of **60a** catalyzed by 20% (*R*,*R*)-**9.**



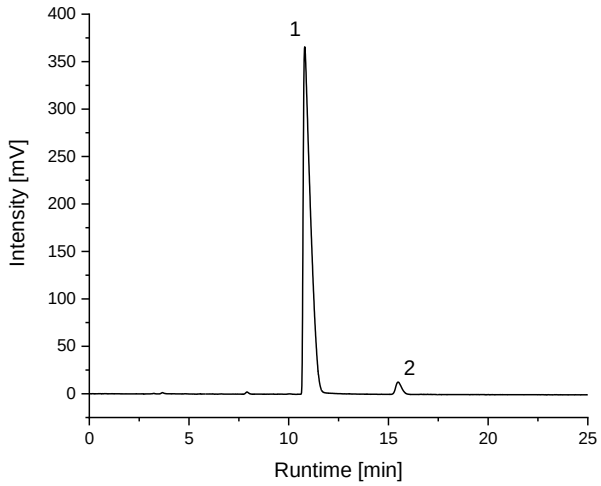
number	retention time	percentage
1	10.76667	93.56168
2	15.40833	6.43832

Figure 241: Chiral HPLC chromatogram of **60a** catalyzed by 0.25% (*R*,*R*)**-8.**



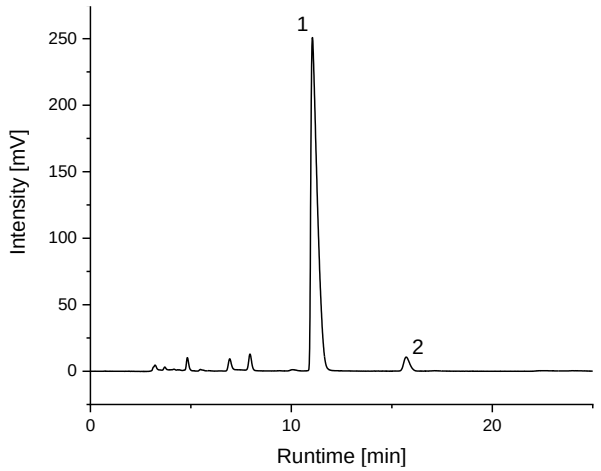
retention time	percentage
10.35	96.4524
14.20833	3.547597

Figure 242: Chiral HPLC chromatogram of **60a** catalyzed by 1% (*R*,*R*)**-8.**



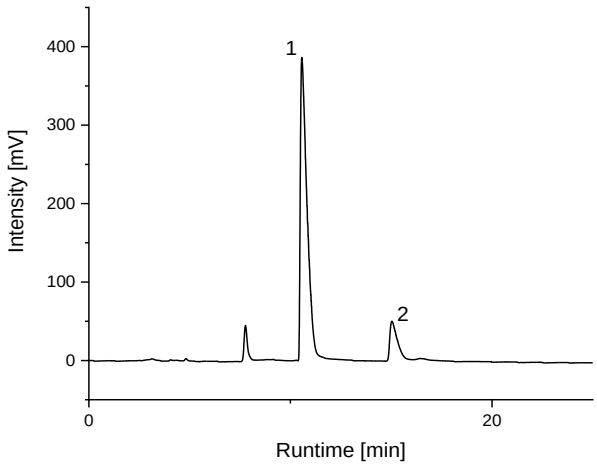
number	retention time	percentage
1	10.80833	97.14745
2	15.49167	2.852548

Figure 243: Chiral HPLC chromatogram of **60a** catalyzed by 2.9% (*R*,*R*)**-8.**



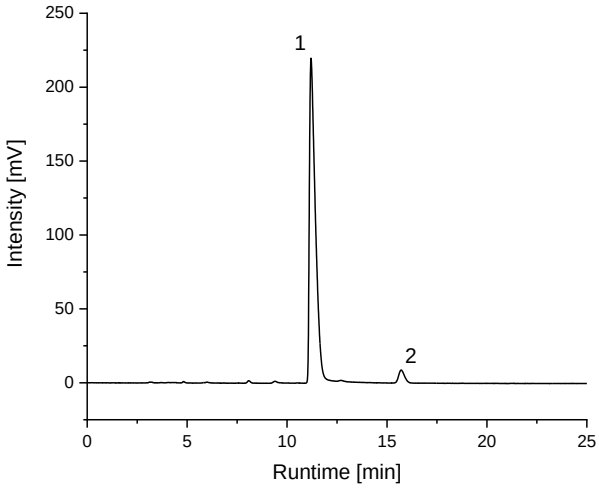
retention time	percentage
11.04167	96.2534
15.70833	3.7466

Figure 244: Chiral HPLC chromatogram of **60a** catalyzed by 20% (*R*,*R*)**-8.**



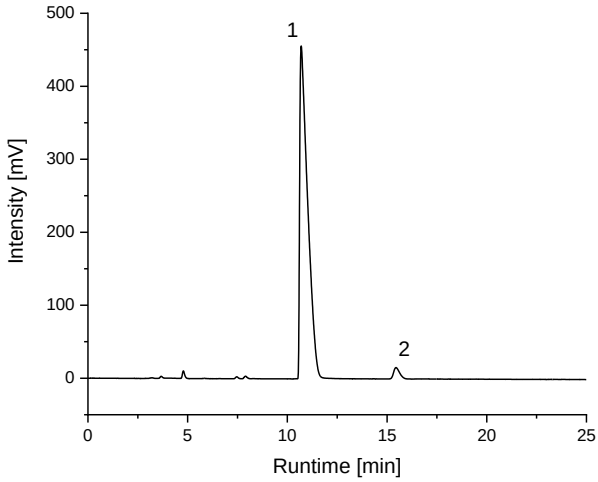
number	retention time	percentage
1	10.55833	87.79343
2	15.025	12.20656

Figure 245: Chiral HPLC chromatogram of **60a** catalyzed by 0.25% (*R*,*R*)-**11.**



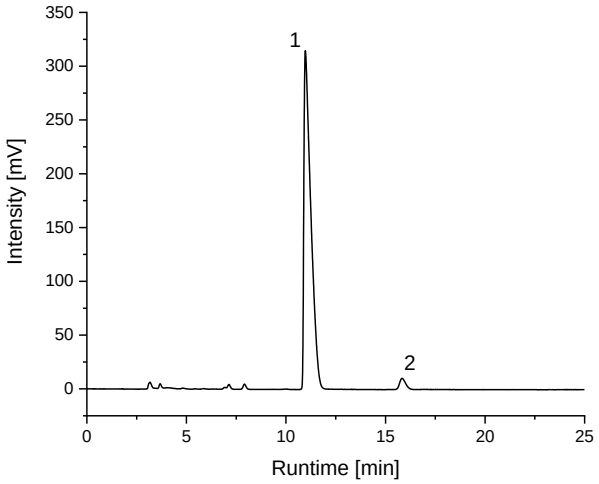
retention time	percentage
11.19167	96.26923
15.71667	3.730768

Figure 246: Chiral HPLC chromatogram of **60a** catalyzed by 1% (*R*,*R*)-**11.**



number	retention time	percentage
1	10.7	97.50211
2	15.44167	2.497892

Figure 247: Chiral HPLC chromatogram of **60a** catalyzed by 2.9% (*R*,*R*)-**11.**

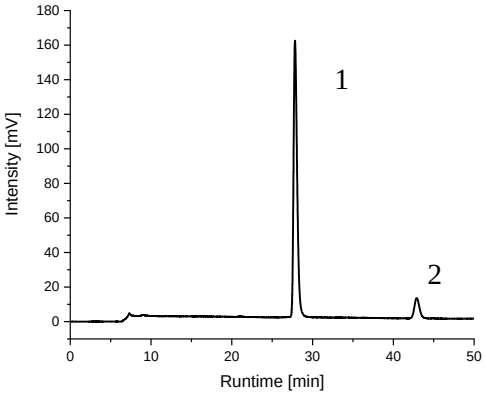


retention time	percentage
10.98333	97.23843
15.84167	2.761576

Figure 248: Chiral HPLC chromatogram of **60a** catalyzed by 20% (*R*,*R*)-**11.**

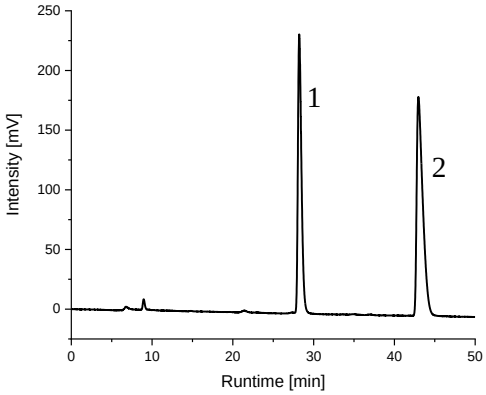
9.9.2. Chromatograms of dearomative fluorination reaction

9.9.2.1. Chromatograms of **67a** with all catalysts at literature conditions



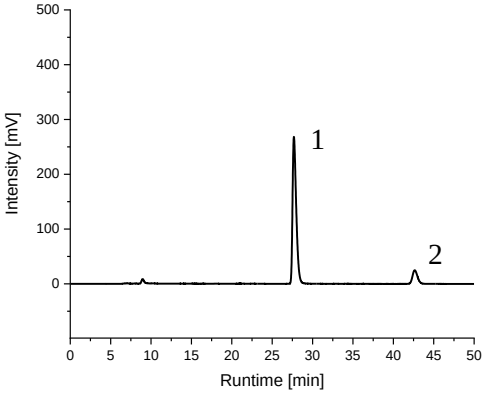
number	retention time	percentage
1	27.816	90.55
2	42.875	9.45

Figure 249: Chiral HPLC chromatogram of **67a** catalyzed by 10% (*R*,*R*)-**4a.**



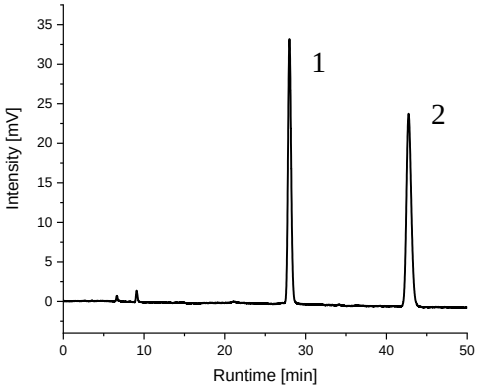
retention time	percentage
28.225	43.07
42.983	56.93

Figure 250: Chiral HPLC chromatogram of **67a** catalyzed by 10% (*R*)-**12a.**



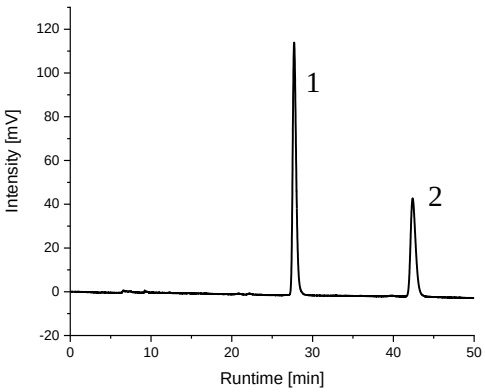
number	retention time	percentage
1	27.683	88.72
2	42.641	11.28

Figure 251: Chiral HPLC chromatogram of **67a** catalyzed by 10% (*R*,*R*)-**4b.**



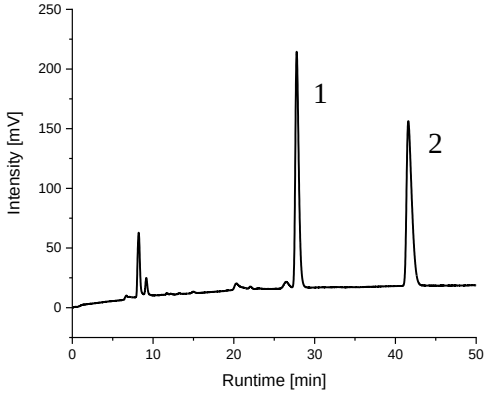
Retentionszeit	percentage
28.008	47.61
42.741	52.39

Figure 252: Chiral HPLC chromatogram of **67a** catalyzed by 10% (*R*)-**12b.**



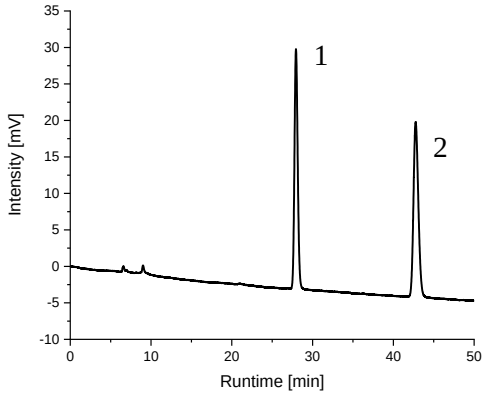
number	retention time	percentage
1	27.716	64.67
2	42.383	35.33

Figure 253: Chiral HPLC chromatogram of **67a** catalyzed by 10% (*R*,*R*)-**5.**



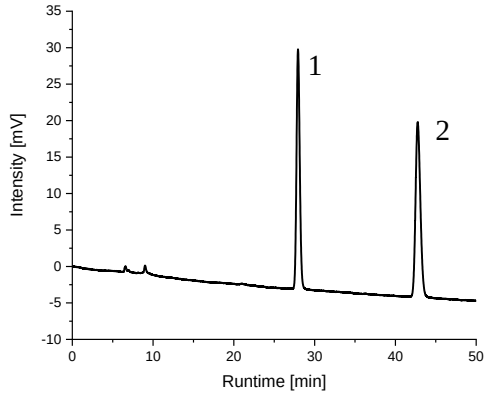
retention time	percentage
27.783	47.75
41.608	52.25

Figure 254: Chiral HPLC chromatogram of **67a** catalyzed by 10% (*S*)-**TRIP.**



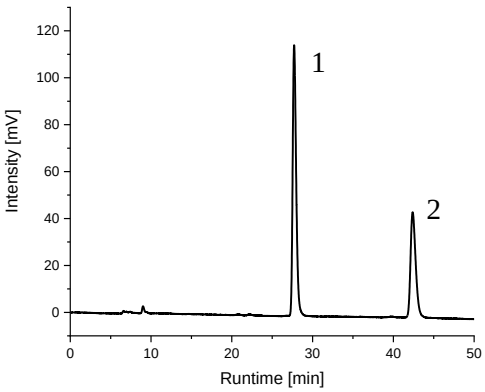
number	retention time	Prozentanteil
1	27.95	47.91
2	42.75	52.09

Figure 255: Chiral HPLC chromatogram of **67a** catalyzed by 10% (*R*,*R*)-**9.**



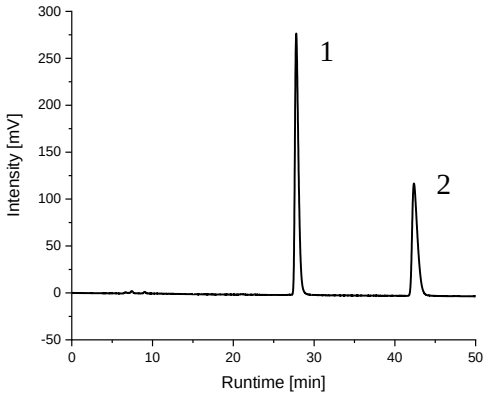
retention time	percentage
27.083	63.42
40.933	36.58

Figure 256: Chiral HPLC chromatogram of **67a** catalyzed by 10% (*R*,*R*)-**6.**.



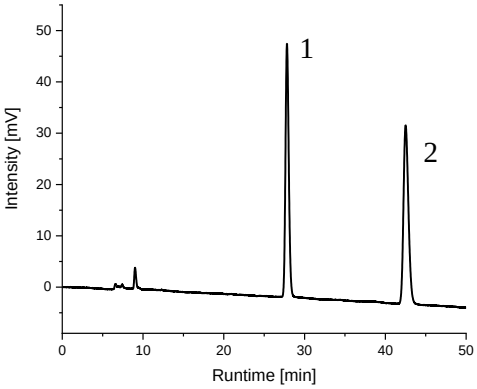
number	retention time	percentage
1	27.725	63.58
2	42.383	36.42

Figure 257: Chiral HPLC chromatogram of **67a** catalyzed by 10% (*R*,*R*)-**7.**



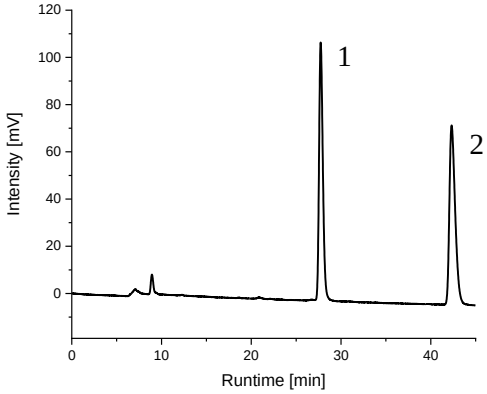
retention time	percentage
27.791	60.80
42.366	39.20

Figure 258: Chiral HPLC chromatogram of **67a** catalyzed by 10% (*R*,*R*)-**10.**



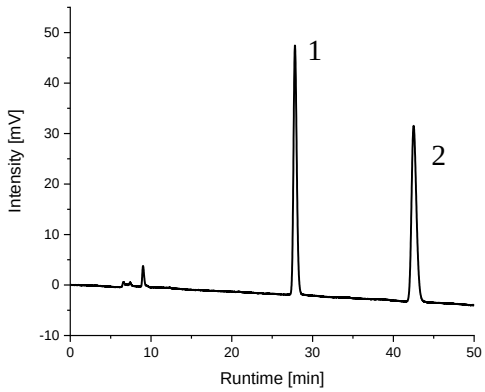
number	retention time	percentage
1	27.825	48.78
2	42.516	51.22

Figure 259: Chiral HPLC chromatogram of **67a** catalyzed by 10% (*R*,*R*)-**8.**



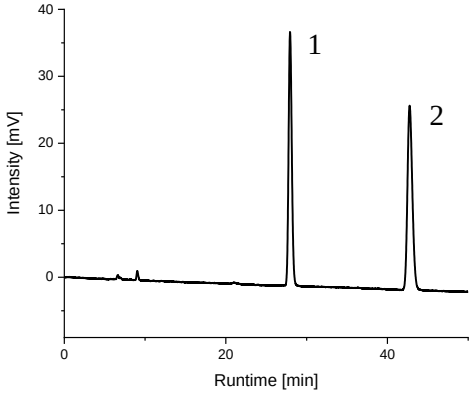
retention time	percentage
27.741	49.16
42.316	50.84

Figure 260: Chiral HPLC chromatogram of **67a** catalyzed by 10% (*R*,*R*)-**11.**



number	retention time	percentage
1	27.825	48.75
2	42.516	51.25

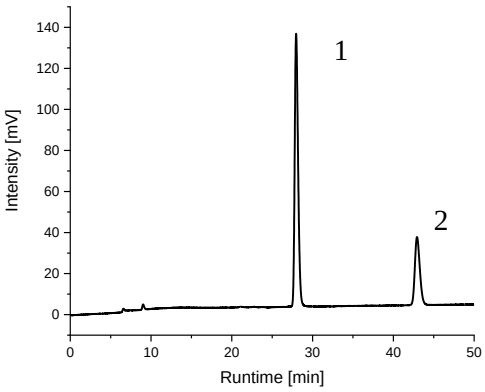
Figure 261: Chiral HPLC chromatogram of **67a** catalyzed by 10% (*rac*)-BNDHP**.**



retention time	percentage
27.95	47.59
42.758	52.41

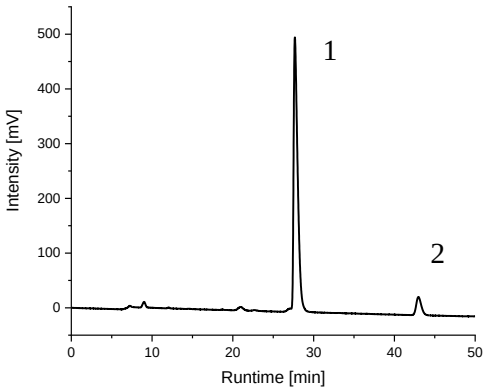
Figure 262: Chiral HPLC chromatogram of **67a** catalyzed by 10% (*R*)-**13.**.

9.9.2.2. Chromatograms of **67a** with different solvent at 0°C for 18 hours



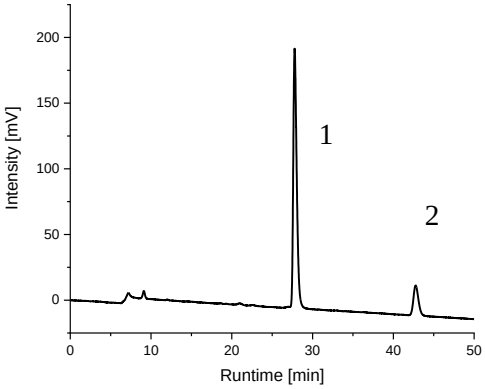
number	retention time	percentage
1	27.966	73.32
2	42.933	26.68

Figure 263: Chiral HPLC chromatogram of **67a** catalyzed by 10% (*R*,*R*)-**4a** in toluene at 0°C.



retention time	percentage
27.683	92.36
42.975	7.64

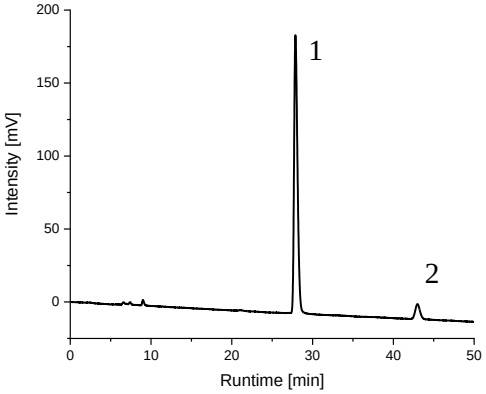
Figure 264: Chiral HPLC chromatogram of **67a** catalyzed by 10% (*R*,*R*)-**4a** in chloroform at 0°C



number	retention time	percentage
1	27.783	86.20
2	42.758	13.80

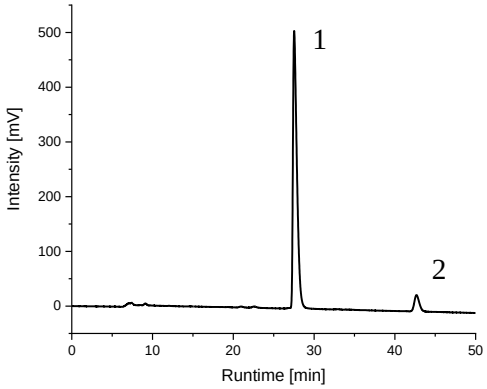
Figure 265: Chiral HPLC chromatogram of **67a** catalyzed by 10% (*R*,*R*)-**4a** in brombenzene at 0°C

9.9.2.3. Chromatograms of **67a** in chloroform at different temperatures for 18 hours



number	retention time	percentage
1	27.875	92.75
2	42.966	7.25

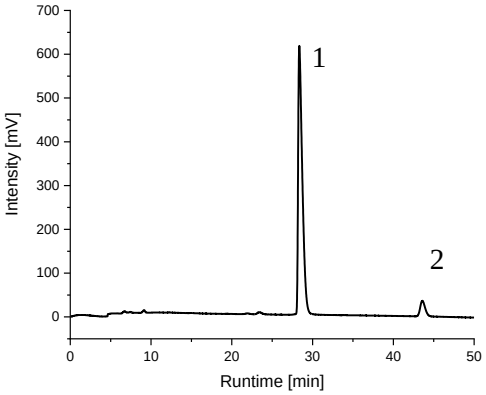
Figure 266: Chiral HPLC chromatogram of **67a** catalyzed by 10% (*R*,*R*)-**4a** in chloroform at -25°C



retention time	percentage
27.541	92.07
42.683	6.93

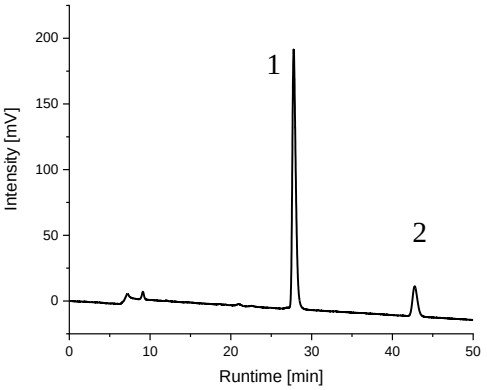
Figure 267: Chiral HPLC chromatogram of **67a** catalyzed by 10% (*R*,*R*)-**4a** in chloroform at 25°C**.**

9.9.2.4. Chromatograms of **67a** in chloroform at 25 °C with different catalyst loadings for 18 hours



number	retention time	percentage
1	28.366	93.48
2	43.575	6.52

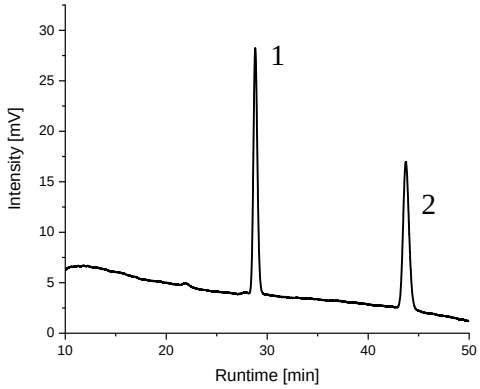
Figure 268: Chiral HPLC chromatogram of **67a** catalyzed by 1% (*R*,*R*)-**4a** in chloroform at 25°C**.**



retention time	percentage
22.833	86.19
40.866	13.81

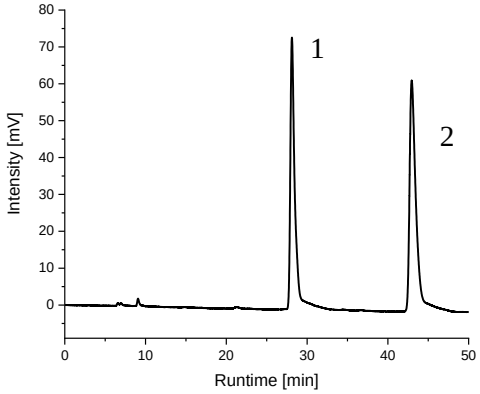
Figure 269: Chiral HPLC chromatogram of **67a** catalyzed by 5% (*R*,*R*)-**4a** in chloroform at 25°C**.**

9.9.2.5. Chromatograms of all subtrates with (*R*,*R*)-**4a**, -**5** and (*R*)-**12a** in chloroform at 25 °C with catalyst loading of 10 % for 18 hours



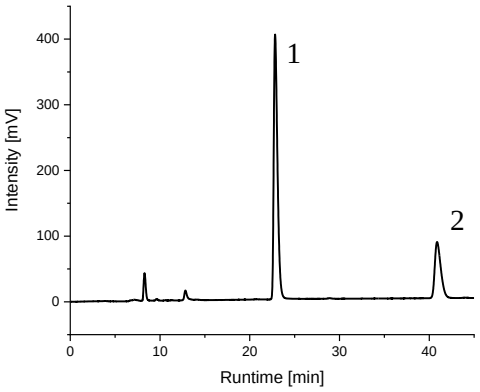
number	retention time	percentage
1	27.758	53.67
2	42.536	46.33

Figure 270: Chiral HPLC chromatogram of **67a** catalyzed by 10% (*R*,*R*)-**12a** in chloroform at 25°C**.**



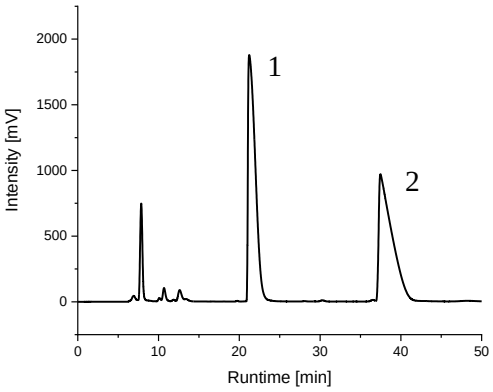
retention time	percentage
27.802	46.86
42.687	53.14

Figure 271: Chiral HPLC chromatogram of **67a** catalyzed by 10% (*R*,*R*)-**5** in chloroform at 25°C



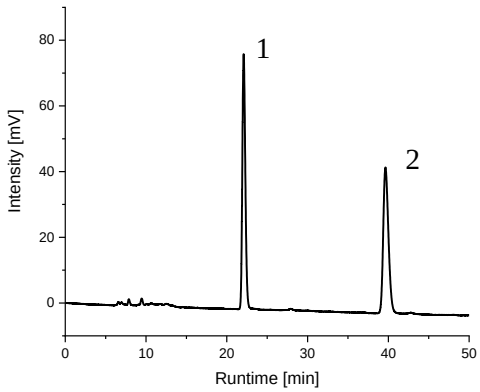
number	retention time	percentage
1	22.833	74.42
2	40.866	25.58

Figure 272: Chiral HPLC chromatogram of **67b** catalyzed by 10% (*R*,*R*)-**4a** in chloroform at 25°C**.**



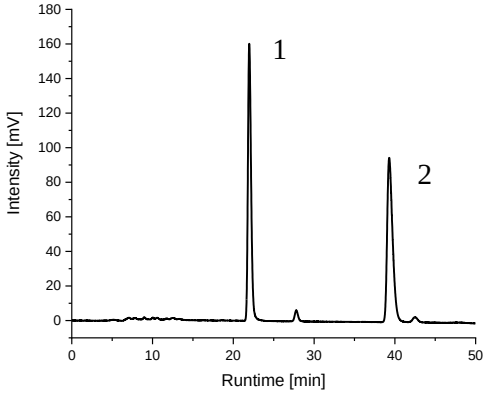
retention time	percentage
21.23	51.85
37.475	48.15

Figure 273: Chiral HPLC chromatogram of **67b** catalyzed by 10% (*R*,*R*)-**5** in chloroform at 25°C**.**



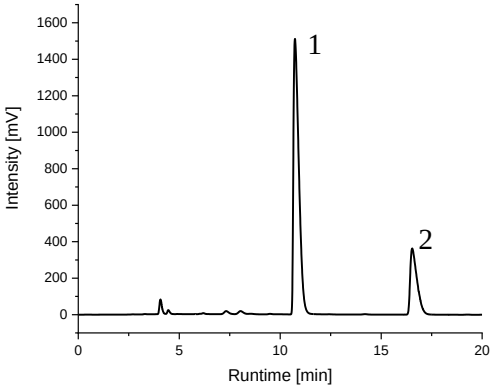
number	retention time	percentage
1	22.092	50.32
2	39.633	49.68

Figure 274: Chiral HPLC chromatogram of **67b** catalyzed by 10% (*R*)-**12a** in chloroform at 25°C**.**



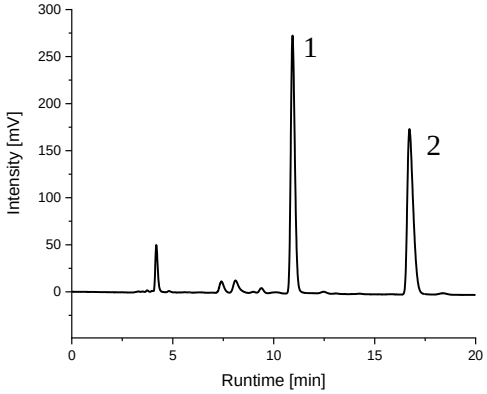
retention time	percentage
21.966	49.96
39.308	50.04

Figure 275: Chiral HPLC chromatogram of **67b** catalyzed by 10% (*rac*)-BNDHP in chloroform at 25°C**.**



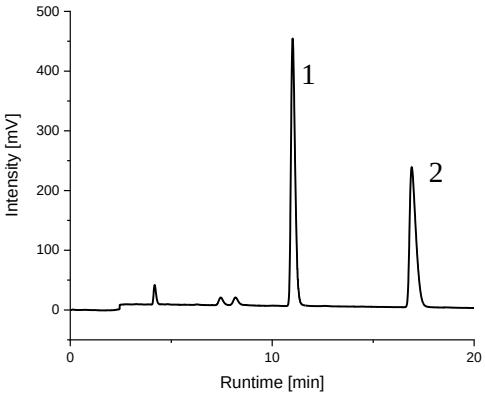
number	retention time	percentage
1	10.725	76.80
2	16.533	23.20

Figure 276: Chiral HPLC chromatogram of **67c** catalyzed by 10% (*R*,*R*)-**4a** in chloroform at 25°C**.**



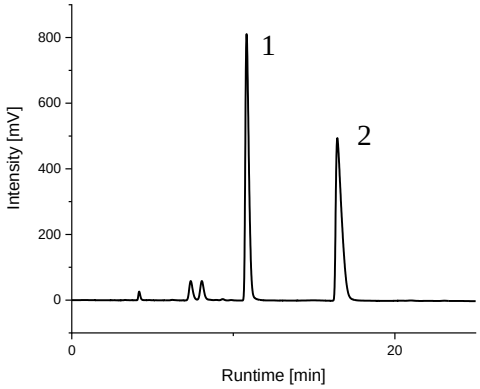
retention time	percentage
10.925	51.62
16.71	48.38

Figure 277: Chiral HPLC chromatogram of **67c** catalyzed by 10% (*R*,*R*)-**5** in chloroform at 25°C**.**



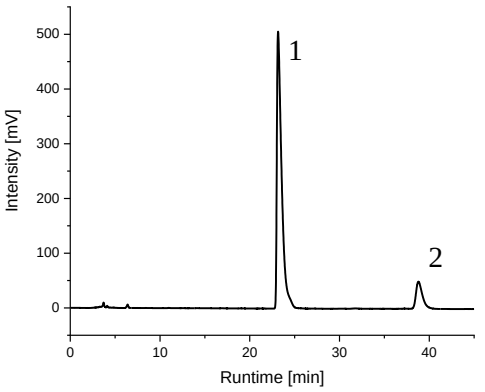
number	retention time	percentage
1	11.016	55.75
2	16.91	44.25

Figure 278: Chiral HPLC chromatogram of **67c** catalyzed by 10% (*R*)-**12a** in chloroform at 25°C**.**



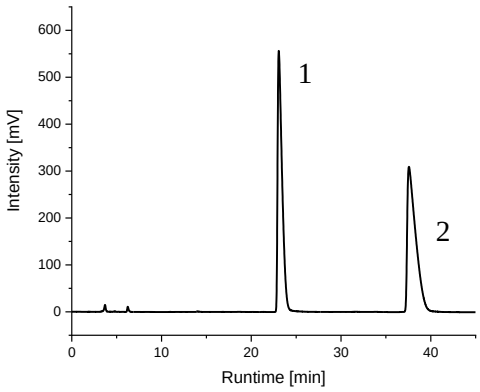
retention time	percentage
10.816	49.33
16.433	50.67

Figure 279: Chiral HPLC chromatogram of **67c** catalyzed by 10% (*rac*)-BNDHP in chloroform at 25°C**.**



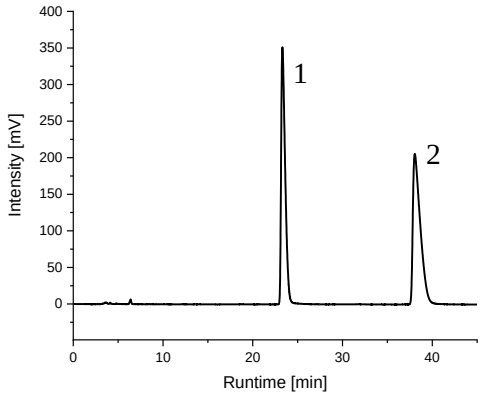
number	retention time	percentage
1	23.15	88.38
2	38.791	11.62

Figure 280: Chiral HPLC chromatogram of **67d** catalyzed by 10% (*R*,*R*)-**4a** in chloroform at 25°C**.**



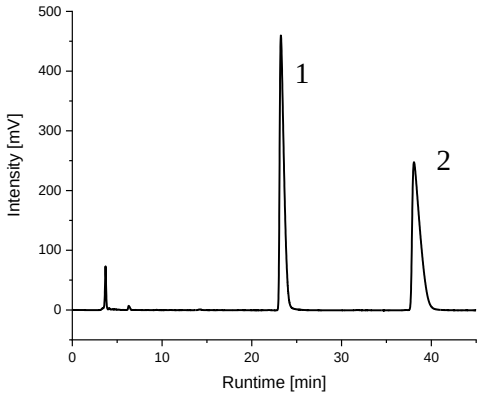
retention time	percentage
23.058	48.92
37.575	51.08

Figure 281: Chiral HPLC chromatogram of **67d** catalyzed by 10% (*R*,*R*)-**5** in chloroform at 25°C**.**



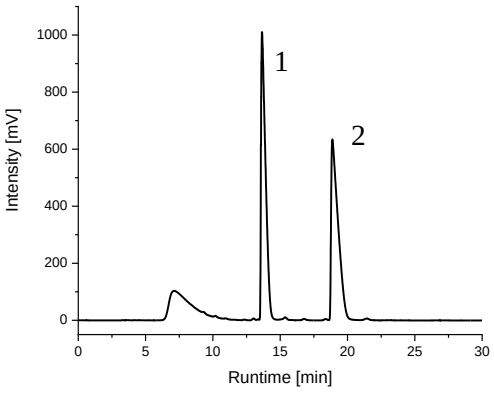
number	retention time	percentage
1	23.3	48.47
2	38.05	51.53

Figure 282: Chiral HPLC chromatogram of **67d** catalyzed by 10% (*R*)-**12a** in chloroform at 25°C**.**



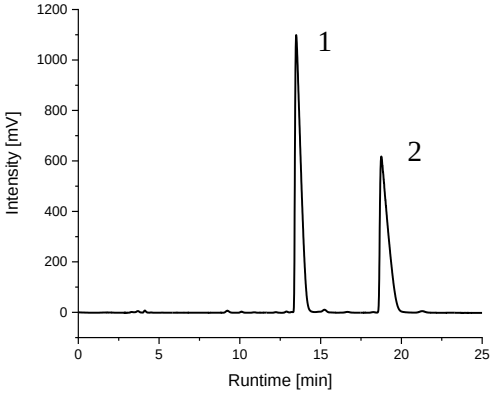
retention time	percentage
23.233	50.26
38.066	49.74

Figure 283: Chiral HPLC chromatogram of **67d** catalyzed by 10% (*rac*)-BNDHP in chloroform at 25°C**.**



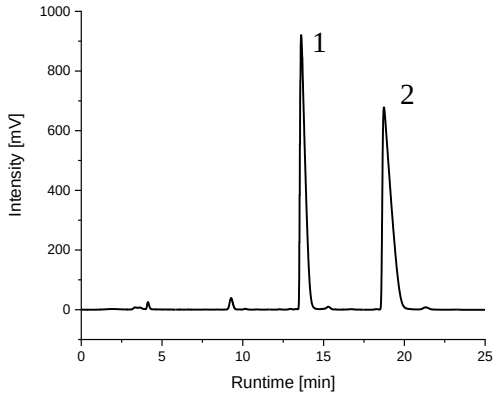
number	retention time	percentage
1	13.65	50.69
2	18.883	49.31

Figure 284: Chiral HPLC chromatogram of **67e** catalyzed by 10% (*R*,*R*)-**4a** in chloroform at 25°C**.**



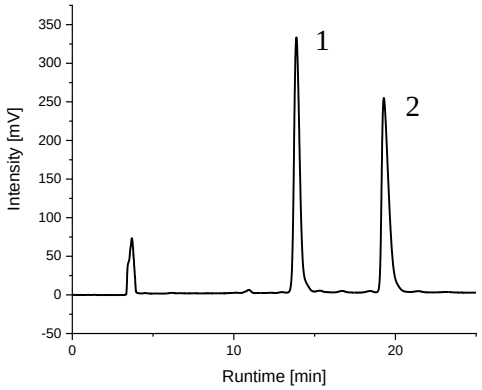
retention time	percentage
13.483	56.10
18.75	43.90

Figure 285: Chiral HPLC chromatogram of **67e** catalyzed by 10% (*R*,*R*)-**5** in chloroform at 25°C**.**



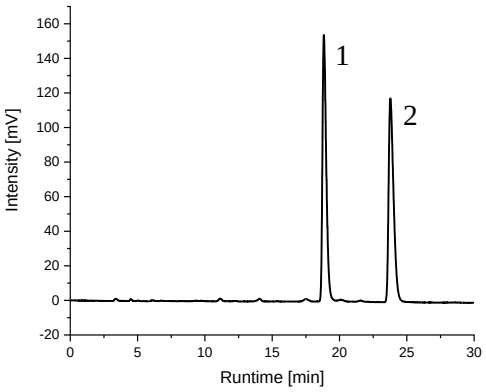
number	retention time	percentage
1	13.608	44.39
2	18.741	55.61

Figure 286: Chiral HPLC chromatogram of **67e** catalyzed by 10% (*R*)-**12a** in chloroform at 25°C**.**



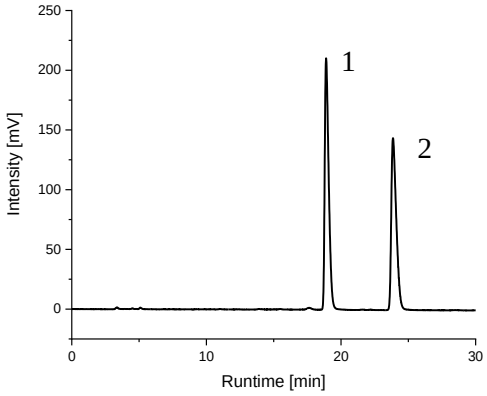
retention time	percentage
13.866	51.23
19.291	48.77

Figure 287: Chiral HPLC chromatogram of **67e** catalyzed by 10% (*rac*)-BNDHP in chloroform at 25°C**.**



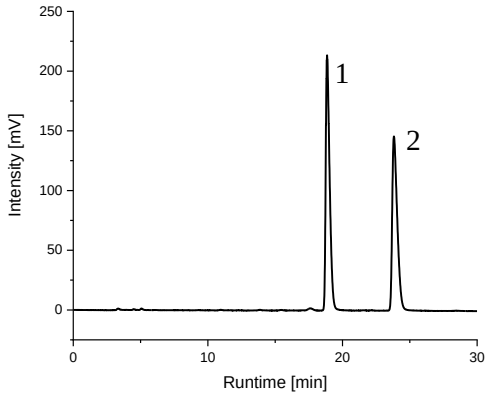
number	retention time	percentage
1	18.841	50.30
2	23.78	49.70

Figure 288: Chiral HPLC chromatogram of **67f** catalyzed by 10% (*R*,*R*)-**4a** in chloroform at 25°C**.**



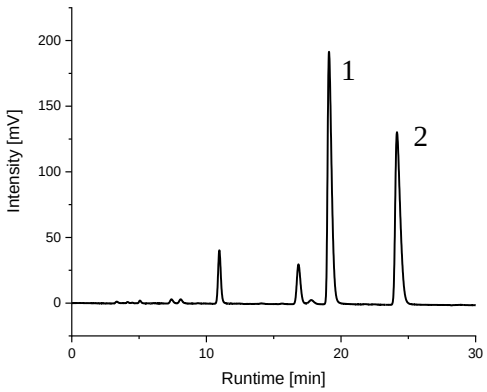
Retentionszeit	percentage
18.9	53.50
23.866	46.50

Figure 289: Chiral HPLC chromatogram of **67f** catalyzed by 10% (*R*,*R*)-**5** in chloroform at 25°C**.**



number	retention time	percentage
1	18.858	53.41
2	23.825	46.59

Figure 290: Chiral HPLC chromatogram of **67f** catalyzed by 10% (*R*)-**12a** in chloroform at 25°C**.**



retention time	percentage
19.116	50.41
24.15	49.58

Figure 291: Chiral HPLC chromatogram of **67f** catalyzed by 10% (*rac*)-BNDHP in chloroform at 25°C**.**

9.10. Acknowledgements

An dieser Stelle bedanke ich mich bei Herrn Prof. Dr. Niemeyer für das spannende Thema und die Gelegenheit, diese Arbeit unter seiner Anleitung anzufertigen. Im Rahmen dieser Arbeit durfte ich viel Neues lernen.

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9.11. Curriculum Vitae

Der Lebenslauf ist in der Online-Version aus Gründen des Datenschutzes nicht enthalten.