Template Synthesis

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Phosphorus-Containing [2]Catenanes as an Example of Interlocking Chiral Structures

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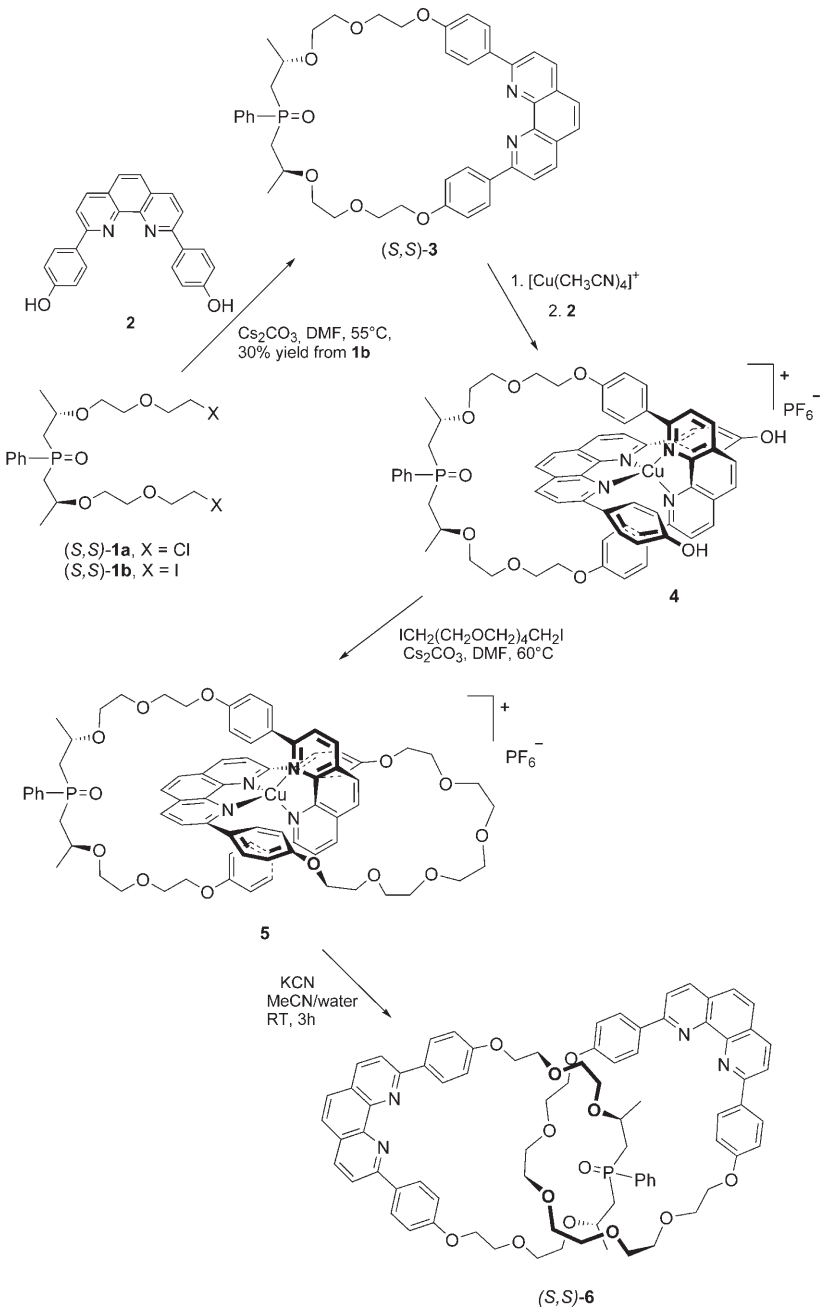
In recent years, several synthetic strategies to [2]catenanes have been designed[1] which allow introduction of various functionalities in their backbone or at their periphery so as to generate targeted physical and chemical properties. For example, suitable functionalities such as coordinating sites and porphyrinic, disulfide, hydroxyl, and halide moieties have allowed the generation of photoinduced electron-transfer processes,[2] the adsorption of catenanes onto gold surfaces,[3] the building of light-driven machine prototypes,[4] and the development of polymerization processes.[5] In the increasingly active search for new structural motifs it is surprising that phosphorus functionalities have been neglected so far. To the best of our knowledge, no catenanes functionalized with phosphorus groups have been described to date. The only reported phosphorus-containing catenanes have phosphine–gold complexes as constitutive elements of the catenane framework itself,[6] and they have been mostly prepared and characterized as solid-state species.

In the present work we envisioned that the synthesis of [2]catenanes bearing phosphine oxide functions would afford potential binding sites for transition metals and, like the corresponding trivalent phosphines, they would open up new ways toward the application of catenanes in coordination chemistry and organometallic catalysis. Described herein is a potentially general, flexible, and modular synthetic approach for the preparation of the first [2]catenanes functionalized with phosphorus groups.

The synthetic approach is based on the strategy established many years ago, which takes advantage of the temporary, three-dimensional template effect of copper(I)/phenanthroline complexes to create the core of the interlocking rings.[7] The key step is a macrocyclization reaction between the phenanthroline diphenol **2**[8] and a suitable biselectrophile. As a new application of the method, the macrocyclization reaction has been performed here by using the phosphorus-containing biselectrophile (*S*,*S*)-**1**. The individual steps leading to catenane **6** are shown in Scheme 1.



Scheme 1. Synthesis of the [2]catenane **6** bearing a phosphine oxide function.

The dichloride **1a** had been designed in previous work as a readily available starting material for building chiral macro-

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Supporting information for this article (full synthetic details and characterization of new compounds) is available on the WWW under http://www.angewandte.org or from the author.

cyclic phosphines in an optically pure form.[9] It was prepared from commercially available phenylphosphine and (*S*)-propylene oxide in a two-step synthesis. Unfortunately, **1a** proved to be insufficiently reactive for the purposes of the present work (incomplete conversion in its reaction with **2**) and so it was converted into the corresponding diiodide (*S*,*S*)-**1b**, whose reaction with the phenanthroline diphenol **2**[8] in DMF in the presence of cesium carbonate under high-dilution conditions led to the expected macrocycle (*S*,*S*)-**3** in 30% yield.

As mentioned above, the tetrahedral cores of catenanes can be formed by combining Cu^{I} salts with two suitable phenanthroline units. One of them can be part of a preformed macrocyclic structure such as **3**. Thus, addition of $[Cu(MeCN)_4]PF_6$ to a solution of **3** in dichloromethane, followed by addition of one equivalent of the phenanthroline diphenol **2** afforded the precatenane **4**, which was treated in situ with 1,14-diiodo-3,6,9,12-tetraoxatetradecane, a usual building block for catenanes, to form the copper catenate **5** containing two different, interlocking macrocycles. After preliminary purification by column chromatography, the copper was removed by means of a ligand-exchange reaction involving treatment of **5** with aqueous KCN under literature conditions.[8]

Not only does (*S*,*S*)-**6** represent the first known catenane bearing a phosphine oxide function, it is a chiral, enantiomerically pure species. The chirality of **6** relies, in a most classical way, on the incorporation of stereogenic carbon centers in the macrocyclic structure. Another interesting case would be that of topologically chiral catenane frameworks. In the case of mechanically interlocking macrocycles, chirality may result from one of two different structural arrangements: on one hand, topological chirality is foreseen for catenanes having oriented segments in their macrocyclic chains. Several examples of topologically chiral [2]catenanes of this family have been reported during the last few years which have generally been resolved by chromatography on chiral stationary phases.[10] On the other hand, enantiomers are expected when both macrocyclic moieties contain prochiral centers, for example, prochiral carbon atoms or phosphorus functions.[11] In this case (Figure 1) both rings are oriented as a consequence of the fact that the prochiral group makes the two faces of the macrocycle different from one another. In other words, each ring has a top face and a bottom face (the P=O and the P–Ph faces, respectively). This arrangement is sufficient to orient the other ring. (Note: strictly speaking, the two objects of Figure 1 are nevertheless not topological enantiomers since they can be interconverted by continuous deformation of bonds at the prochiral phosphorus centers in three-dimensional space.)

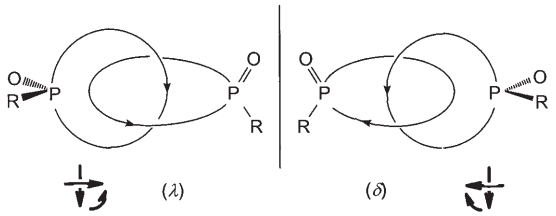
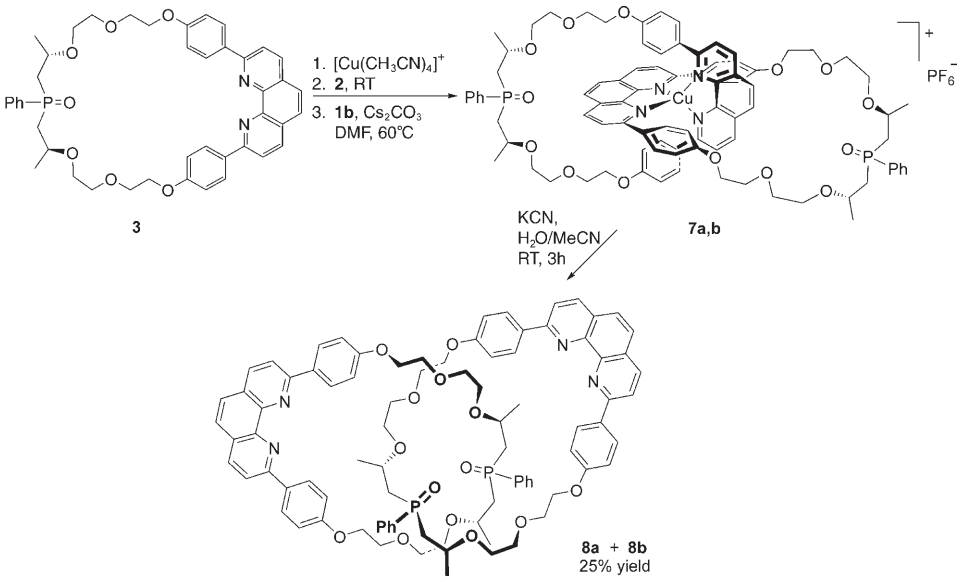


Figure 1. Schematic representation of enantiomeric [2]catenanes with stereogenic phosphorus centers. Assignment of the absolute configuration is made according to the oriented skew-lines convention.[12]

As far as we know, enantiomerically pure [2]catenane derivatives of this type have not been reported to date. In the current study, chiral [2]catenanes bearing prochiral phosphorus centers have been prepared in enantiomerically pure form.

The interlocking rings are obtained by addition of the phosphorus-containing diodide (*S*,*S*)-**1b** to the precatenane generated in situ from (*S*,*S*)-**3**, copper(I) hexafluorophosphate, and the phenanthroline diphenol **2** in the presence of cesium carbonate (Scheme 2). After purification of the reaction mixture by column chromatography, the cationic catenate **7** was characterized by mass spectrometry as well as by ^{1}H and ^{31}P NMR spectroscopy. The most representative ^{1}H NMR signals come from the phenyl groups attached to the phenantroline moiety: in analogous tetrahedral copper/bis(phenanthroline) complexes, the *meta*-phenyl protons are known to lie in the shielding field of the second phenanthroline moiety, which accounts for their high-field shifts at about $\delta = 6$ ppm.[13] The corresponding signals for **7** appear at $\delta =$ 6.03 (d, $J = 9.0$ Hz, 2H, H^{m}), 6.04 (d, $J = 9.0$ Hz, 2H, $H^{m'}$), 6.13 (d, $J = 8.5$ Hz, 2H, H^{m}), and 6.15 ppm (d, $J = 9.0$ Hz, 2H, $H^{m'}$).



Scheme 2. Synthesis of the [2]catenane **8** bearing phosphine oxide functions.

Complete characterization of **7** was prevented by the presence of the two expected diastereoisomers.

After removal of the copper, the two diastereoisomers of the free catenane **8** could be separated by preparative HPLC and fully characterized. Figure 2 shows the HPLC chromatogram as well as the 500 MHz ^{1}H NMR spectra in the aromatic region for the two isomers of **8**. It can be noticed that, in both isomers, the chiral environment markedly differentiates the two halves of the phenanthroline moiety, thus giving well-separated doublets for H^3 and H^8, as well as for H^4 and H^7. The corresponding signals of the parent macrocycle **3** merge into one another in the NMR spectrum despite the presence of stereogenic carbon atoms in the molecule ($\delta = 8.07$ (d, $J =$ 9.0 Hz, 2H, $H^{3,8}$), 8.26 ppm (d, $J = 8.0$ Hz, 2H, $H^{4,7}$)). Thus, it seems that the presence of the interlocking rings results in a more pronounced magnetic differentiation of the two sides of the whole molecule, including the phenanthroline nucleus.

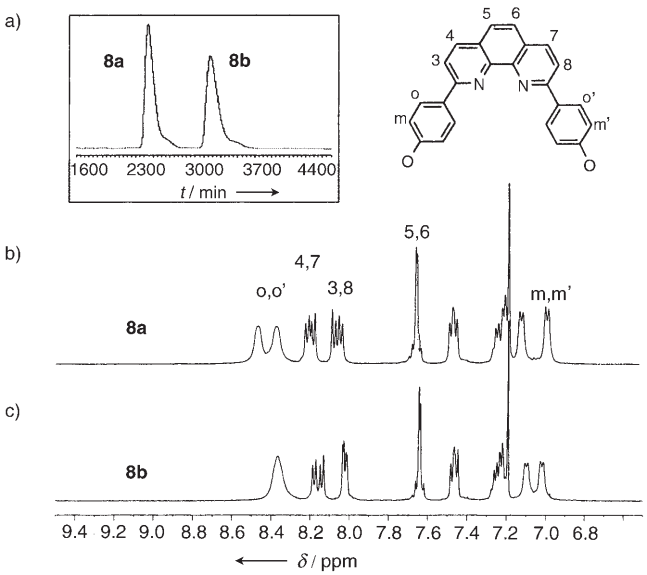


Figure 2. a) HPLC chromatogram of a mixture of **8a** and **8b**. b) Partial ^{1}H NMR spectra of solutions of **8a** and c) **8b** in $CDCl_3$. Assignments have been made by analogy to previously reported data (see ref. [13]).

Phosphine oxides **8** represent an unprecedented class of chiral phosphorus derivatives, that is, phosphorus-containing chiral [2]catenanes, whose properties in coordination chemistry and catalysis will be investigated in the near future.

This exploratory study has established that catenanes containing phosphine oxide functions can be generated by using the template effect of copper/phenanthroline complexes and suitable phosphorus-containing synthons. Stereogenic carbon atoms may be introduced into the above structures so as to produce chiral derivatives. In addition, chiral catenanes are generated as enantiomerically pure diastereomers when both of the interlocking rings bear phosphorus functions.

Experimental Section

8a,b: A degassed solution of $[Cu(MeCN)_4]PF_6$ (130 mg, 0.35 mmol) in MeCN (9 mL) was transferred to a solution of (*S*,*S*)-**3** (240 mg, 0.33 mmol) in CH_2Cl_2 (16 mL) by the double-ended-needle transfer technique. After stirring the mixture at room temperature for 0.5 h, a solution of **2** (120 mg, 0.33 mmol) in DMF (17 mL) was added, which resulted in the generation of a red-brown color corresponding to the formation of **4**. After stirring the mixture at room temperature for 1 h, the solvent was partially removed in vacuo, and then a solution of (*S*,*S*)-**1b** (0.35 mmol) in DMF (20 mL) was added. The mixture was added dropwise, within 8 h, to a suspension of Cs_2CO_3 (0.32 g, 1 mmol) in DMF (50 mL) kept at 55–60 °C. After the end of the addition, the heating was maintained for about 50 h. The DMF was then removed under vacuum and the residue dissolved in H_2O/CH_2Cl_2. The organic layer was washed with brine and water, concentrated to a volume of 20 mL, then stirred overnight with a saturated aqueous solution of KPF_6 to effect anion exchange. The organic layer was washed with brine and water, dried with $MgSO_4$, and the solvent was evaporated to dryness. The crude product was filtered through a column of silica gel using a CH_2Cl_2/MeOH gradient (from 95:5 to 75:15) as the eluent. Complex **7** (150 mg, 0.07 mmol, 29% yield) was obtained as a red-brown oil as a mixture of two diastereoisomers.

Demetalation of **7** (120 mg) was performed by vigorous stirring of a solution of the copper complex in MeCN (4 mL) with an excess of KCN (20 mg, 5 equiv) in water (1 mL) at room temperature for 3 h. The initial reddish-brown color disappeared. The organic layer was separated, dried over $MgSO_4$, and the solvents evaporated to dryness. The crude product was purified by column chromatography on silica gel with an AcOEt/MeOH gradient (from 100:0 to 70:30) as the eluent. Compound **8** was obtained as a mixture of two diastereoisomers in 85% yield (98 mg). ^{31}P NMR ($CDCl_3$): $\delta = 34.0$ ppm; HRMS (ESI): calcd for $C_{88}H_{95}N_4O_{14}P_2$: 1493.6320; found: 1493.6294.

The components of a sample of **8a**+**8b** (60 mg) were separated by preparative HPLC on a Waters SunFire C18 column with a mixture of H_2O/TFA/MeCN (66:0.1:34) as the eluent. The retention times of **8a** and **8b** were 23 and 30 min, respectively. After evaporation of the solvents, the residues were filtered through a short column of silica gel by eluting successively with chloroform and a mixture of AcOEt/MeOH (70:30) to remove the residual inorganic salts.

8a: ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 1.08$ (d, $J = 5.5$ Hz, 6H, Me), 1.28 (d, $J = 5.5$ Hz, 6H, Me), 1.91 (m, 2H, CH_2P), 2.10–2.20 (m, 4H, CH_2P), 2.40 (m, 2H, CH_2P), 3.27 (m, 4H), 3.38 (m, 2H), 3.51 (m, 2H), 3.60–3.70 (m, 10H), 3.82 (m, 4H), 3.90 (m, 6H), 4.20–4.30 (m, 8H), 7.10 (d, $J = 8.0$ Hz, 4H, H^m), 7.22 (d, $J = 6.5$ Hz, 4H, $H^{m'}$), 7.30 (m, 6H, PhH), 7.55 (m, 4H, PhH), 7.74 (m, 4H, $H^{5,6}$), 8.10 (d, $J = 8.5$ Hz, 2H, H^3/H^8), 8.14 (d, $J = 8.0$ Hz, 2H, H^3/H^8), 8.24 (d, $J = 9.0$ Hz, 2H, H^4/H^7), 8.27 (d, $J = 7.5$ Hz, 2H, H^4/H^7), 8.42 (brs, 4H, H^o), 8.51 ppm (brs, 4H, $H^{o'}$).

8b: ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 0.98$ (d, $J = 6.0$ Hz, 6H, Me), 1.27 (d, $J = 5.5$ Hz, 6H, Me), 1.90 (m, 2H, CH_2P), 2.10–2.20 (m, 4H, CH_2P), 2.35 (m, 2H, CH_2P), 3.18 (m, 2H), 3.24 (m, 2H), 3.31 (m, 2H), 3.40, (m, 2H), 3.5–3.7 (m, 12H), 3.70–3.90 (m, 8H), 4.15 (m, 4H), 4.23 (m, 4H), 7.01 (d, $J = 7.5$ Hz, 4H, H^m), 7.10 (d, $J = 7.5$ Hz, 4H, $H^{m'}$), 7.20 (m, 6H, PhH), 7.45 (m, 4H, PhH), 7.64 (m, 2H, $H^{5,6}$), 8.01 (d, $J = 8.5$ Hz, 2H, H^3/H^8), 8.02 (d, $J = 8.5$ Hz, 2H, H^3/H^8), 8.14 (d, $J = 8.5$ Hz, 2H, H^4/H^7), 8.18 (d, $J = 8.5$ Hz, 2H, H^4/H^7), 8.37 ppm (brs, 8H, $H^{o,o'}$).

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[1] For reviews see: a) *Molecular Catenanes, Rotaxanes and Knots* (Eds.: J.-P. Sauvage, C. O. Dietrich-Buchecker), Wiley-VCH, Weinheim, **1999**; b) F. M. Raymo, F. Stoddart, *Chem. Rev.* **1999**,

99, 1643 – 1663; c) J.-C. Chambron, J.-P. Collin, V. Heitz, D. Jouvenot, J.-M. Kern, P. Mobian, D. Pomeranc, J.-P. Sauvage, *Eur. J. Org. Chem.* **2004**, 1627 – 1638, and references therein.
[2] L. Flamigni, A. M. Talarico, J.-C. Chambron, V. Heitz, M. Linke, N. Fujita, J.-P. Sauvage, *Chem. Eur. J.* **2004**, *10*, 2689 – 2699.
[3] L. Raehm, J.-M. Kern, J.-P. Sauvage, C. Hamann, S. Palacin, J.-P. Bourgoin, *Chem. Eur. J.* **2002**, *8*, 2153 – 2162.
[4] P. Mobian, J.-M. Kern, J.-P. Sauvage, *Angew. Chem.* **2004**, *116*, 2446 – 2449; *Angew. Chem. Int. Ed.* **2004**, *43*, 2392 – 2395; J.-P. Sauvage, *Chem. Commun.* **2005**, 1507 – 1510.
[5] a) S. Menzer, A. J. P. White, D. J. Williams, M. Belohradsky, C. Hamers, F. M. Raymo, A. N. Shipway, J. F. Stoddart, *Macromolecules* **1998**, *31*, 295 – 307; b) D. Muscat, W. Köhler, H. J. Räder, K. Martin, S. Mullins, B. Müller, K. Müllen, Y. Geerts, *Macromolecules* **1999**, *32*, 1737 – 1745.
[6] C. P. McArdle, M. J. Irwin, M. C. Jennings, R. J. Puddephatt, *Angew. Chem.* **1999**, *111*, 3571 – 3573; *Angew. Chem. Int. Ed.* **1999**, *38*, 3376 – 3378.
[7] a) C. O. Dietrich-Buchecker, J.-P. Sauvage, J.-P. Kintzinger, *Tetrahedron Lett.* **1983**, *24*, 5095 – 5098; b) C. O. Dietrich-Buchecker, J.-P. Sauvage, J.-M. Kern, *J. Am. Chem. Soc.* **1984**, *106*, 3043 – 3045.
[8] C. Dietrich-Buchecker, J.-P. Sauvage, *Tetrahedron* **1990**, *46*, 503 – 512.
[9] A. Theil, J. Hitce, P. Retailleau, A. Marinetti, *Eur. J. Org. Chem.* **2006**, 154 – 161.
[10] a) D. K. Mitchell, J.-P. Sauvage, *Angew. Chem.* **1988**, *100*, 985 – 986; *Angew. Chem. Int. Ed. Engl.* **1988**, *27*, 930 – 931; b) J.-C. Chambron, D. K. Mitchell, J.-P. Sauvage, *J. Am. Chem. Soc.* **1992**, *114*, 4625 – 4631; c) C. Yamamoto, Y. Okamoto, T. Schmidt, R. Jäger, F. Vögtle, *J. Am. Chem. Soc.* **1997**, *119*, 10547 – 10548; d) C. Reuter, A. Mohry, A. Sobanski, F. Vögtle, *Chem. Eur. J.* **2000**, *6*, 1674 – 1682.
[11] a) C. P. NcArdle, S. Van, M. C. Jennings, R. J. Puddephatt, *J. Am. Chem. Soc.* **2002**, *124*, 3959 – 3965; b) A. Hori, T. Sawada, K. Yamashita, M. Fujita, *Angew. Chem.* **2005**, *117*, 4974 – 4977; *Angew. Chem. Int. Ed.* **2005**, *44*, 4896 – 4899.
[12] D. M. Walba, *Tetrahedron* **1985**, *41*, 3161 – 3212.
[13] C. O. Dietrich-Buchecker, P. A. Marnot, J.-P. Sauvage, J.-P. Kintzinger, P. Maltese, *Nouv. J. Chim.* **1984**, *8*, 573 – 582.

