Synthesis and Structural Peculiarities of Homeomorphic Phosphorus Bridgehead Macrobicyclic Compounds and Novel Dioxaphospha[3.1.1.]*p*,*m*,*p*-cyclophanes

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Abstract: The double-capping reaction of *p*,*m*,*p*-trinuclear diphenol **4** with PCl_3 affords the three homeomorphic isomers **5**–**7** of a phosphite macrobicyclic compound in low yields. X-ray structures of *out*,*out*-isomer **5** and *in*,*in*-isomer **6** show very flat macrobicyclic structures with P–P distances of 4.9 Å and 4.5/5.3 Å (two conformers), respectively. The main product of the reaction, however, appears to be diphosphite **8**, which contains two dioxaphospha[3.1.1.]*p*,*m*,*p*-cyclophane subunits. The structural peculiarities of **8** were studied after subsequent oxidation to the corresponding phosphate **12**. At room temperature the free rotation either of the *para*-phenylene rings and the *meta*-phenylene ring in the macrocyclic moieties are hindered as could be demonstrated by means of NOESY measurements. The latter occupies an angled position in respect to the macrocyclic plane. This leads to the existence of conformational isomers due to different relative positions of the *meta*-phenylene ring to the P-OR substituent (*cis*,*trans*). We could isolate the *cis*,*cis*-isomer of **12** and establish its structure by X-ray diffraction.

Keywords: cage compounds · cyclophanes · isomers · phosphates · structure elucidation

Introduction

Phosphorus-containing macrocycles have potential applications in supramolecular and synthetic organic chemistry.[1] The trivalent phosphorus atom can for instance function as donor site for soft transition metals especially in their low valent states. This makes them interesting as ligands for transition-metal-catalyzed reactions such as Heck reaction, hydroformylation, homogenous catalytic hydration, Suzuki coupling, Sonogashira coupling, and others which occupy a more and more important place in standard organic synthesis. The design of the involved ligand systems to optimize catalytic reactions in terms of yield, turnover number and selectivity is therefore an extensively investigated area in organic chemistry.[2]

Trivalent phosphorus atoms easily undergo oxidation reaction to give pentavalent species such as phosphoryl moieties. In those compounds the phosphoryl oxygen can function as a hard donor atom, which upon its integration into macrocyclic systems may be used for metal complexation and for molecular recognition of hydrogen-donating substrates, among them also biologically interesting compounds such as amino acids.[3]

Moreover the trivalent P atom offers a point of attachment for the introduction of additional components with special functions to the macrocylic cores.

Only a few macrobicyclic systems with P-bridgehead atoms have been reported up to now.[4–13] In addition, some medium-sized P-bridgehead bicyclic compounds have been synthesized and investigated.[14–17] All of these compounds show the interesting structural feature of *in*/*out* isomerism.[18] In the case of larger trivalent P-bridgehead macrobicyclic compounds this opens up the chance for reactions on the "inner wall" of the cage by use of the well-defined geometry of *in*-P lone pairs.

Various methods can be applied for the synthesis of macrobicyclic compounds.[18b] The double-capping and tripod-capping reaction should not be very favored. Five components have to be assembled in the right manner under

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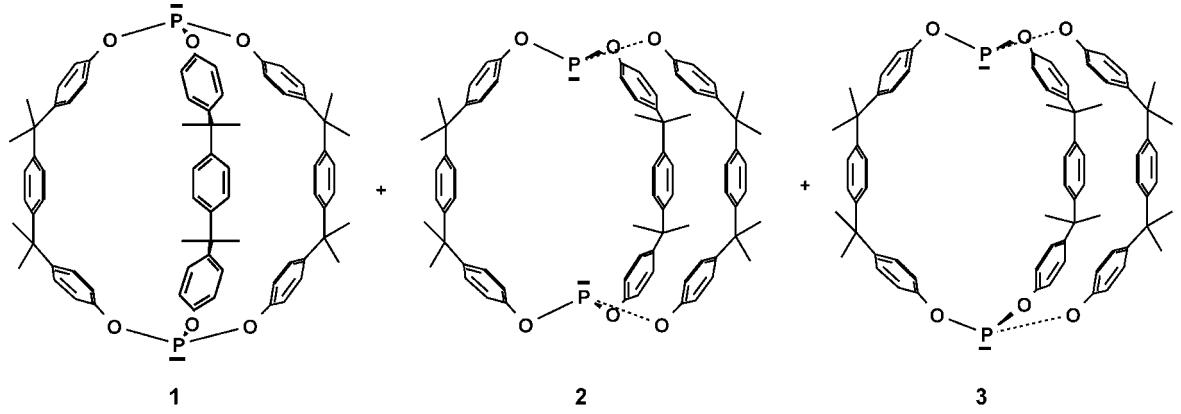
formation of six bonds to form the complex target molecule without control of any intermediate. This seems very unlikely, because even one invalid reaction in an initial step multiplies the yield of side products tremendously. For this reason this method is rarely employed for the synthesis of macrobicyclic compounds. In fact only a few examples of successful double- and tripod-capping reactions have been reported.[19]

We were, however, able to successfully employ the double-capping method for the synthesis of the *out*,*out*- and *in*,*out*-isomer of a sterically hindered, flexible phosphorus-containing cryptand.[13a] Using a nonhindered diphenol we could even isolate all three homeomorphic isomers (**1**–**3**) of a P cage compound in reasonable yields (Scheme 1). The *in*,*out* P atoms showed remarkably different reactivity toward cumene hydroperoxide as an oxidizing agent. The cavity of these cryptands encloses solvent molecules like toluene and chloroform. Depending on the isomer, the P–P distance varies between 8.3/8.5 Å (*in*,*in*-isomer, two conformers) and 10.5 Å (*out*,*out*-isomer).[13c]

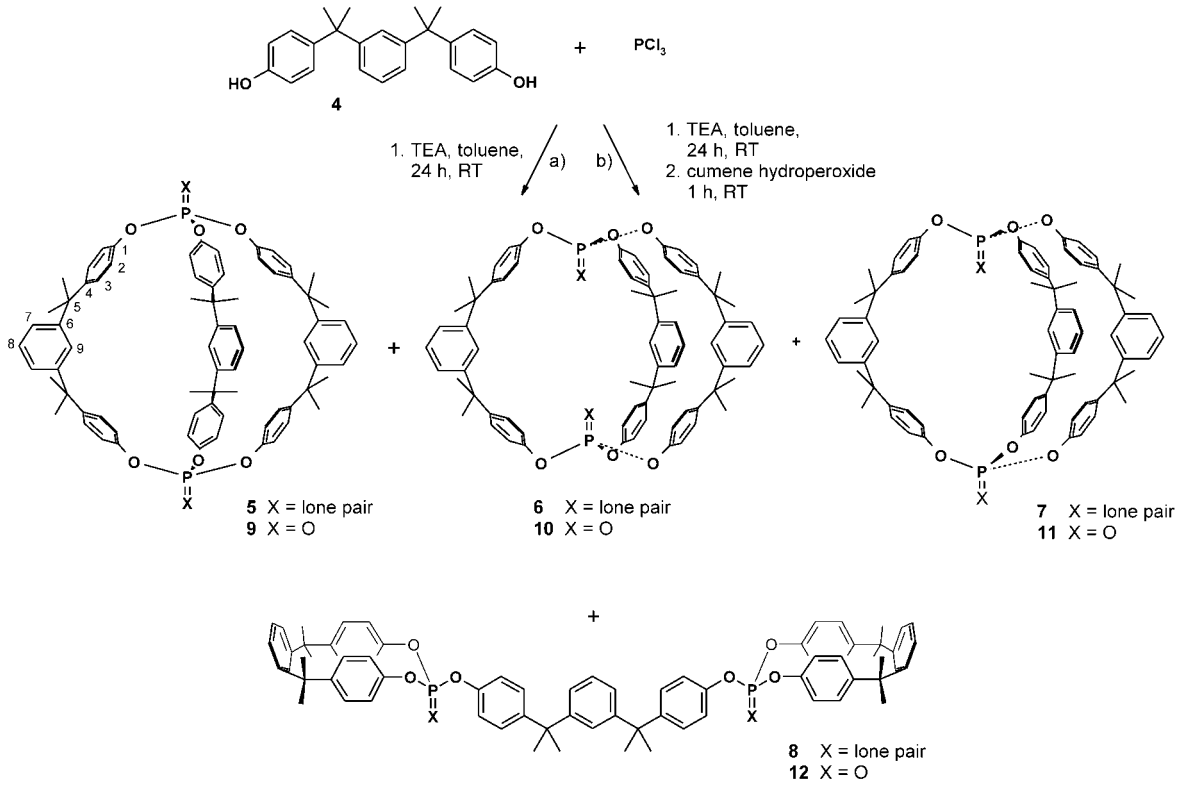
An interconversion of the isomers either by inversion of the P lone pair or by homeomorphic isomerization was not observed for the *in*,*in*-isomer **2** up to 140 °C.

Results and Discussion

Synthesis: In this paper we report on a double-capping synthesis of P macrobicyclic compounds starting from the trinuclear *para-meta*-bridged diphenol **4** and PCl_3 (Scheme 2, path a). The reaction is carried out in toluene at room



Scheme 1. Homeomorphic P-containing macrobicyclic compounds **1**–**3** with all-*para*-phenylene rings.[13c]



Scheme 2. Reaction of diphenol **4** with PCl_3 to the homeomorphic macrobicyclic compounds **5**–**7** and compound **8**, and their subsequent oxidation to the corresponding phosphates **9**–**12**.

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temperature for 1 d in the presence of triethylamine (TEA) as a base.

The product mixture contains the three homeomorphic P cryptands **5**–**7** with a crude yield of about 6% (**5**), 3% (**6**), and 10% (**7**), and compound **8** as the main product with a crude yield of about 35% according to ^{31}P NMR spectroscopy. The yield of the macrobicyclic compounds **5**–**7** turned out to be in the same range as those for macrobicyclic compounds **1**–**3** from the reaction of the corresponding all-*para*-phenylene diphenol with PCl_3.[13c] It could have been expected that in the case of the *para*,*meta*-brigded diphenol **4**, the intrinsic structural information of this building-block is more suitable for the formation of macrocyclic compounds, because of the stronger curvature of the molecule caused by its *meta*-substitution. Hence, the yield of macrobicylic compounds was supposed to be higher in this case. However, this stronger curvature of the diphenolic component permits a competitive reaction namely the intramolecular ring closure of an intermediate phosphorous chloride leading to compound **8**. This reaction is very much favored so that **8** turns out to be the main product, even though the resulting P heterocycles in **8** are slightly strained. An analogous reaction with the corresponding all-*para*-phenylene diphenol was not observed at all. The shortest possible distance between the two OH groups in this compound is still too long to be bridged by a single phosphorus atom.

In the reaction of **4** with PCl_3 open-chain products and other simple macrocycles are formed as byproducts, as can be extracted from the ^{31}P NMR spectrum of the crude product. Such compounds give ^{31}P NMR peaks at around 128 ppm, which is the normal region for this type of aryl phosphite,[20] whereas the peaks for the *in* and *out* positions of the macrobicyclic compounds are shifted to lower or higher field, respectively. The same is true for the P cycle in **8** with an upfield shifted ^{31}P NMR peak at 121 ppm.

The homeomorphic macrobicyclic compounds **5** and **6** and compound **8** could be isolated by column chromatography on silica gel and were characterized by NMR spectroscopy and MALDI-TOF MS; **5** and **6** were also characterized by X-ray analysis (Figure 1).

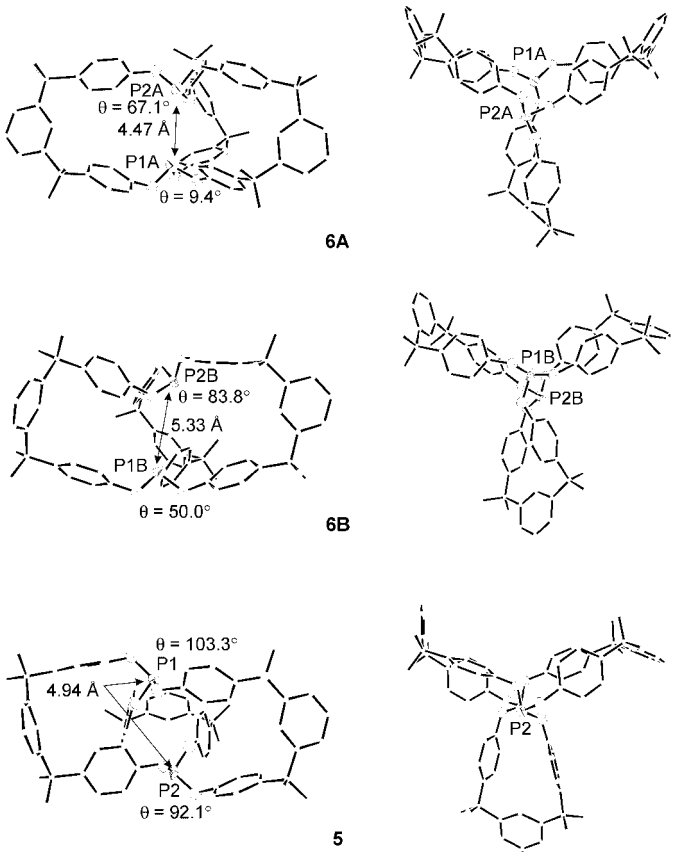
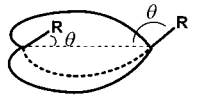


Figure 1. Structures of *out*,*out*-isomer **5** and two conformers (**A**,**B**) of *in*,*in*-isomer **6** in the solid state. Hydrogen atoms and solvent molecules are omitted for clarity. Left: view into the cavity. Right: view along the P–P axis.

Structural investigations: *In*,*in*-isomer **6** crystallizes in two different conformers **A** and **B**, as also observed for the corresponding 1,4-phenylene-*in*,*in*-cryptand **2**.[13c] Regarding the view along the P–P axis, conformer **B** is reminiscent of a C_3 symmetric structure. The central *meta*-phenylene rings all tend to point in the same direction away from each other thus forming a propeller-like geometry. In contrast, in conformer **A** two of the *meta*-phenylene rings point towards each other breaking the pseudo-C_3 symmetry in favor of a Y-shaped structure.

Both homeomorphic isomers **5** and **6** are very crumpled molecules and contain almost no cavity due to the close distance of the opposite parts of the molecules. For this reason no solvent molecules are complexed inside the cavity, but only outside the macrobicyclic compounds.

The P–P distance varies from 4.47 Å to 5.33 Å for the two different *in*,*in*-conformers **6A** and **6B**, whereas *out*,*out*-isomer **5** has a P–P distance of 4.94 Å, which is surprisingly no longer than those of the *in*,*in*-conformers. This is realized by a distinct distortion from an ideal *out* geometry as expressed by the "*out*-ness" of the substituents,[18c] which can be described by the angle θ between the substituent (lone pair), the bridgehead atom to which it is attached and the other bridgehead atom (Scheme 3). An ideal *in* substituent would have $\theta = 0°$, for an ideal *out* position it would be $\theta = 180°$. In case of *in*,*in*-conformer **6A** the angle lone-pair–P1–P2 ($\theta = 9.4°$) is almost ideal for an *in* substituent, but at the P2 center it is 67.1°; this means that this *in* position is extremely distorted towards 90°, an angle that would not permit a reasonable differentiation between *in* and *out* position. For *in*,*in*-conformer **6B** this distortion is even more pronounced with $\theta = 50.0°$ for one side and $\theta = 83.8°$ for the other. In fact this conformer can hardly be regarded as an *in*,*in*-conformer with at least one of the angles being so close to 90°. If it exceeded 90° one should speak of an intertwined *in*,*out*-isomer. However, the strongest distortion from the ideal *in* or *out* position, respectively shows *out*,*out*-isomer **5** with $\theta = 92.1°$ and 103.3°. That means that the lone pairs are almost perpendicularly positioned to the P–P axis, and from



in-R: $0° \le \theta \le 90°$
out-R: $90° \le \theta \le 180°$

Scheme 3. Angle θ to characterize *in* and *out* positions in bicyclic compounds.[18c]

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this geometry a homeomorphic isomerization to an *in*,*in*-isomer should be possible. Averaging θ over all *in* atoms in **6A** and **6B** gives $\bar{\theta} = 52.6^\circ$; for the two *out* positions in **5** it gives 97.7°. In fact it seems even surprising that the two different isomers, which have such small geometric differences with respect to the position of their phosphorus lone pairs, could be isolated at room temperature.

In,*out*-isomer **7** was not obtained in a pure state, due to its retention time being too close to **8**. Its ^{31}P NMR shift, however, could be unambiguously determined from an enriched mixture together with **8**. In comparison to the 1,4-phenylene macrobicyclic compounds **1**–**3** described in reference [13c], cage compounds **5**–**7** are hydrolytically less stable. They were found to be completely hydrolyzed in standard $CDCl_3$ NMR solvent after several days. Also unlike cage compounds **1**–**3** they do not include solvent guest molecules as was proved by NMR spectroscopy and X-ray diffractometry. This is due to the fact that the crumpled shape of these molecules allows almost no cavity formation.

Compound **8** appears to be the hydrolytically least stable compound of the product mixture; this can be attributed to a ring tension effect. A considerable part of the compound is even hydrolyzed during chromatography on silica gel.

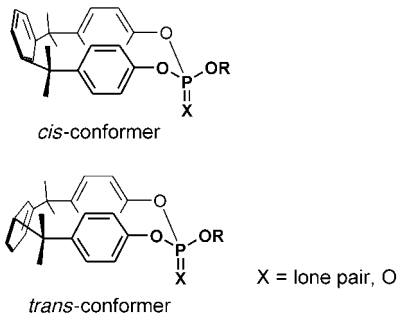
To improve the hydrolytic stability of **8** for structural investigations we carried out the double-capping reaction of **4** and PCl_3 with immediate subsequent oxidation of the mixture by an excess of cumene hydroperoxide. After one hour the oxidation was complete. The corresponding homeomorphic macrobicylic phosphates **9** and **10** could be separated as well as compound **12** as main product (Scheme 2, path b). *In*,*out*-isomer **11** was detected in the crude product by ^{31}P NMR with peaks at -16.7 ppm (*in*) and -18.4 ppm (*out*), but could not be isolated by chromatography.

The oxidation of all phosphorus moieties with cumene hydroperoxide including the *in*-phosphorus atoms of the reaction mixture proceeded relatively fast. This result is rather surprising as no such fast oxidation for *in* positions was obtained earlier with macrobicyclic compounds **2** and **3**.[13c] The reason for this rapid oxidation of normally less available *in* positions is a pronounced distortion from an ideal *in* geometry (Scheme 3), with an averaged $\bar{\theta} = 52.6^\circ$ over the four *in* positions in **6A** and **6B**. This means that the lone pairs point more or less out of the cavity, increasing their reactivity towards oxidizing agents.

Compounds **8** and **12** include a narrow macrocyclic ring. According to ^{1}H NMR measurements the rotation of the *para*-phenylene rings is hindered at room temperature giving four different peaks for their protons. Moreover, the central *meta*-phenylene ring also occupies a fixed location out of the macrocyclic plane. Its different relative position to the P–OR group results in the occurrence of conformational *cis*,*trans*-isomers (Scheme 4).

Three conformers would be possible in **8** and **12**, respectively: *cis*,*cis*, *cis*,*trans* and *trans*,*trans* giving theoretically four ^{31}P NMR signals in total in a mixture.

We could only isolate the *cis*,*cis*-isomer of **12** and most likely also the *cis*,*cis*-isomer of **8**. The structure of **12** was proved by X-ray diffraction (Figure 2). In the crude product of the synthesis of **8**, however, we observed up to four signals in a very narrow range around 121 ppm, which are tentatively assigned to the three conformers of this compound.



Scheme 4. The *cis*- and *trans*-conformers of **8** and **12** with respect to the position of the central *meta*-phenylene ring to the P–OR group.

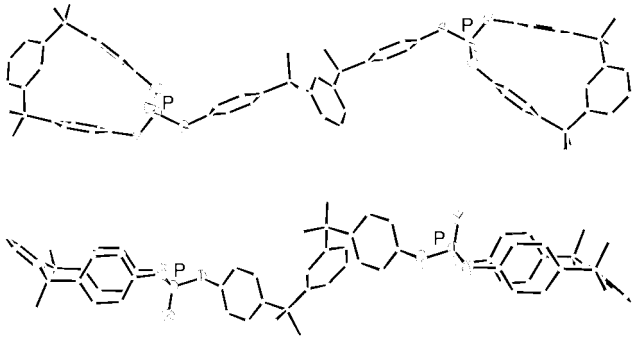


Figure 2. Structure of diphosphate **12**. Hydrogen atoms and solvent molecules are omitted for clarity. Top: view into the cavity of the macrocyclic units. Bottom: side view of the macrocylic subunits showing the *cis*-arrangment of the 1,3-phenylene ring and the P–OR substituent.

NOESY experiments proved that the rotation of the *para*-phenylene rings is not completely suppressed at room temperature, causing a slow interconversion of the conformers. This means that an equilibrium between these conformers will be slowly established in solution.

The macrocyclic components in **12** are rather small so that no large guests can be included. However, the linkage of these two macrocycles through a flexible spacer could permit the enclosure of cations or neutral hydrogen-donating guests in the way of a molecular tweezers. Therein the two phosporyl oxygen atoms might act as binding sites with hard electron-donating and hydrogen-accepting properties, whereas the attached macrocycles should support a complexation either by π donation or by the formation of a nonpolar pocket around the guest molecule.

^{31}P NMR, ^{1}H NMR and ^{13}C NMR studies: In their ^{31}P NMR spectra, the homeomorphic phosphite macrobicylic compounds **5**–**7** show the characteristic pattern as was similarly observed for the compounds **1**–**3**.[13c] All *in*-phosphorus atoms are downfield shifted compared to the normal values at around 128 ppm.[20] *In*,*in*-phoshite **6** gives a ^{31}P NMR peak at 133.0 ppm, and the *in*-P atom in the *in*,*out*-phosphite **7** at 131.2 ppm. *Out*-P atoms are shifted upfield to 123.3 ppm in *out*,*out*-phosphite **5** and 124.6 ppm in *in*,*out*-phosphite **7**.

The same pattern can be observed after oxidation for the corresponding phosphates. However, the differences between *in* and *out* positions are less pronounced. The ^{31}P NMR shift of

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the *in*,*in*-phosphate **10** is observed at −16.0 ppm and that of the *in*-position in *in*,*out*-isomer **11** at −16.7 ppm; these values are in the same range as comparable values of open chain phosphates of this type at around −17 ppm.[20] The *out*-P atoms give slightly upfield shifted peaks, namely −18.6 ppm for the *out*,*out*-isomer **9** and −18.4 ppm for the *in*,*out*-compound **11**.

In compounds **8** and **12**, the phosphorus atom is part of a slightly strained heterocyclic ring; this causes a distortion of the geometry around the phosphorus atom. This is reflected by an upfield shift of the ^{31}P NMR signal at 121.1 ppm for phosphite **8** and −18.5 ppm for phosphate **12**. These peaks correspond to single isolated conformers that equilibrate after a certain time to give rise to the formation of varying amounts (up to 20%) of a second conformer.

In the crude product, however, up to four ^{31}P NMR signals of varying relative intensities can be observed for a mixture of conformers of **8** (121.32, 121.27, 121.12, 121.07 ppm); these signals are due to a different relative position of the central *meta*-phenylene ring to the P−OR group. This effect is less pronounced for the crude product of **12** giving only a broad peak at −18.5 ppm.

^{1}H and ^{13}C NMR measurements for both *out*,*out*-phosphite **5** and *out*,*out*-phosphate **9** give the expected symmetrical spectra with the two sides of the molecules being equivalent. Even though the molecules are very flattened in the solid state (see X-ray structure of **5**) and probably also in solution; the free rotation of the *para*-phenylene rings is not hindered. This is reflected by the occurrence of only one signal each for *ortho*- and *meta*-protons (2-H, 3-H) and *ortho*- and *meta*-carbon atoms (C-2, C-3), respectively. The same is true for *in*,*in*-phosphate **10**. In the ^{13}C NMR spectrum of *in*,*in*-phosphite **6**, however, two signals for the *ortho*-carbon atoms (C-2, C-2′) of the *para*-phenylene ring appear at the same chemical shift of −119.5 ppm. One of them has a $^{3}J_{PC}$ coupling of 8.1 Hz, whereas no such P−C coupling can be observed for the second one. This is an indication of a hindered rotation of the *para*-phenylene rings in this compound.

The NMR spectroscopic properties of compound **12**, which contains two slightly strained heterocyclic rings, have been extensively investigated. The exact assignment of all proton and carbon signals have been achieved by COSY, HMBC, and HSQC measurements. Of special interest thereby is the magnetic nonequivalence of the protons 2-H/11-H and 3-H/10-H. Their assignment to the same phenylene ring is proved by ^{1}H/^{13}C HMBC measurement in which correlations for *ipso*-carbon C-4 with both C-2 and C-11 and for *ipso*-carbon C-1 with C-3 and C-10 are observed (Figure 3). The nonequivalence of the two sides of the 1,4-phenylene rings can only be attributed to a hindered rotation of these groups. Moreover, 10-H gives a NOESY cross peak only with *cis*-5-Me and not with *trans*-5-Me, whereas 3-H shows the corresponding interaction with *trans*-5-Me; this demonstrates a fixed relative position of the two parts of the phenylene rings with respect to the *cis*- and *trans*-Me groups (Figures 3 and 4).

So far this hindered rotation has no chemical consequences. However, NOESY experiments reveal that the position of the central *meta*-phenylene ring is also fixed. The 7-H protons exclusively interact with *cis*-5-Me and not with *trans*-5-Me (Figures 3 and 4). Accordingly 9-H shows a NOESY cross peak only with *trans*-5-Me (Figure 4).

Even though 9-H also interacts with both 3-H and 10-H, indicating that 9-H points very deep into the inside of the cycle, the differentiation between the *cis*- and *trans*-side is again reflected in its cross peak with 2-H, whereas no such is observed with 11-H. The high-field shift of 9-H to 5.16 ppm is due to a strong anisotropic effect caused by its position inside the cyclic system.

The *cis* and *trans* positions with respect to the P−OR group are identified by the interaction of 11-H with 13-H; this leads to the assignment of 11-H, 10-H, *cis*-5-Me, 7-H, and 8-H to the *cis* side of the heterocycle and 2-H, 3-H, *trans*-5-Me, and 9-H to the *trans* side (Figure 3). Both phosphaheterocycles in the molecule are identical; this means that the *cis*,*cis*-isomer of **12** was isolated.

NOESY spectra of **12**, however also reveal that rotation of the *para*-phenylene rings is not completely hindered at room temperature. The spectrum shows weak exchange signals for 10-H/3-H suggesting a slow rotation of the phenylene rings. This gives rise to a slow interconversion of the conformational isomers at room temperature.

Experimental Section

General: The melting points were determined on a Boëtius melting point apparatus. ^{1}H NMR (TMS internal reference), ^{13}C NMR (TMS internal reference), and ^{31}P NMR spectra (85% H_3PO_4 external reference) were recorded on Bruker AC 300 and DRX 500 spectrometers. Exact assignment of ^{1}H and ^{13}C NMR spectra was carried out by two-dimensional NMR techniques (COSY, ^{1}H/^{13}C correlated HSQC, ^{1}H/^{13}C correlated HMBC, NOESY) for **5**, **6** and **12**. The assignment of ^{1}H and ^{13}C NMR spectra for **8**, **9**, and **10** was done in accordance with those of **12**, **5**, and **6**, respectively.

MALDI-TOF mass spectra were measured on a Kratos Kompact MALDI II (Shimadzu Europa GmbH, Duisburg, Germany) by using a N_2-laser source ($\lambda = 337$ nm), a positive polarity, and 20 kV acceleration voltage. The microanalyses were recorded on a CHN-S analyzer (Carlo Erba). Solvents were purified by conventional methods.

Reaction of 4 with PCl_3: Diphenol **4** (4.00 g, 11.5 mmol) and TEA (3.00 g, 29.6 mmol) were dissolved in toluene (1.0 L) in a flame-dried 2 L flask under argon atmosphere (**4** is only partly soluble). Under vigorous stirring PCl_3 (1.06 g, 7.7 mmol) was added dropwise by syringe within 10 min. The solution was stirred for 24 h at 25 °C. The hydrochloride formed was removed by filtration, and the solvent was evaporated in vacuo to yield a viscous oil containing a mixture of **5**, **6**, **7**, and **8** in an approximate ratio of 2:1:3:12, and some noncyclic and simple macrocyclic byproducts according to ^{31}P NMR spectroscopy. Chromatography on silica gel with *n*-pentane/toluene (1:1) afforded *out*,*out*-macrobicycle **5** (190 mg, 4.5%), *in*,*in*-phosphite **6** (71 mg, 1.7%), and phosphite **8** (755 mg, 18.0%, compound partly hydrolyzes on the column), as white solids. *In*,*out*-phosphite **7** has a retention time very close to **8** and could therefore only be enriched in minor amounts together with **8**.

***Out*,*out*-phosphite 5**: M.p. 128–130 °C; ^{31}P NMR (121.5 MHz, $CDCl_3$): $\delta =$ 123.2; ^{1}H NMR (500.1 MHz, $CDCl_3$): $\delta = 7.26-7.25$ (m, 9H; 7,8-H), 6.91 (d, ^{3}J(H,H) = 8.5 Hz, 12H; 2-H), 6.91 (d, ^{3}J(H,H) = 8.5 Hz, 12H; 3-H), 6.63 (s, 3H; 9-H), 1.58 (s, 36H; Me); ^{13}C NMR (75.5 MHz, $CDCl_3$): $\delta = 149.9$ (C-6), 149.3 (d, ^{2}J(P,C) = 2.3 Hz, C-1), 146.0 (C-4), 128.8 (C-9), 127.55 (C-3), 127.5 (C-8), 122.4 (C-7), 119.8 (d, ^{3}J(P,C) = 6.9 Hz, C-2), 42.3 (C-5), 29.7 (5-Me); MALDI-TOF-MS (matrix: 1,8,9-trihydroxyanthracene): *m*/*z*: 1094 [M^{+}+H]; elemental analysis calcd (%) for $C_{72}H_{72}O_6P_2$ (1095.24): C 78.95, H 6.63; found: C 78.35, H 6.96.

***In*,*in*-phosphite 6**: M.p. 222–225 °C; ^{31}P NMR (121.5 MHz, $CDCl_3$): $\delta =$ 133.0; ^{1}H NMR (300.1 MHz, $CDCl_3$): δ 7.26–7.24 (m, 9H; 7,8-H), 6.85 (d, ^{3}J(H,H) = 9.1 Hz, 12H; 3-H), 6.81 (d, ^{3}J(H,H) = 9.0 Hz, 12H; 2-H), 6.4 (s,

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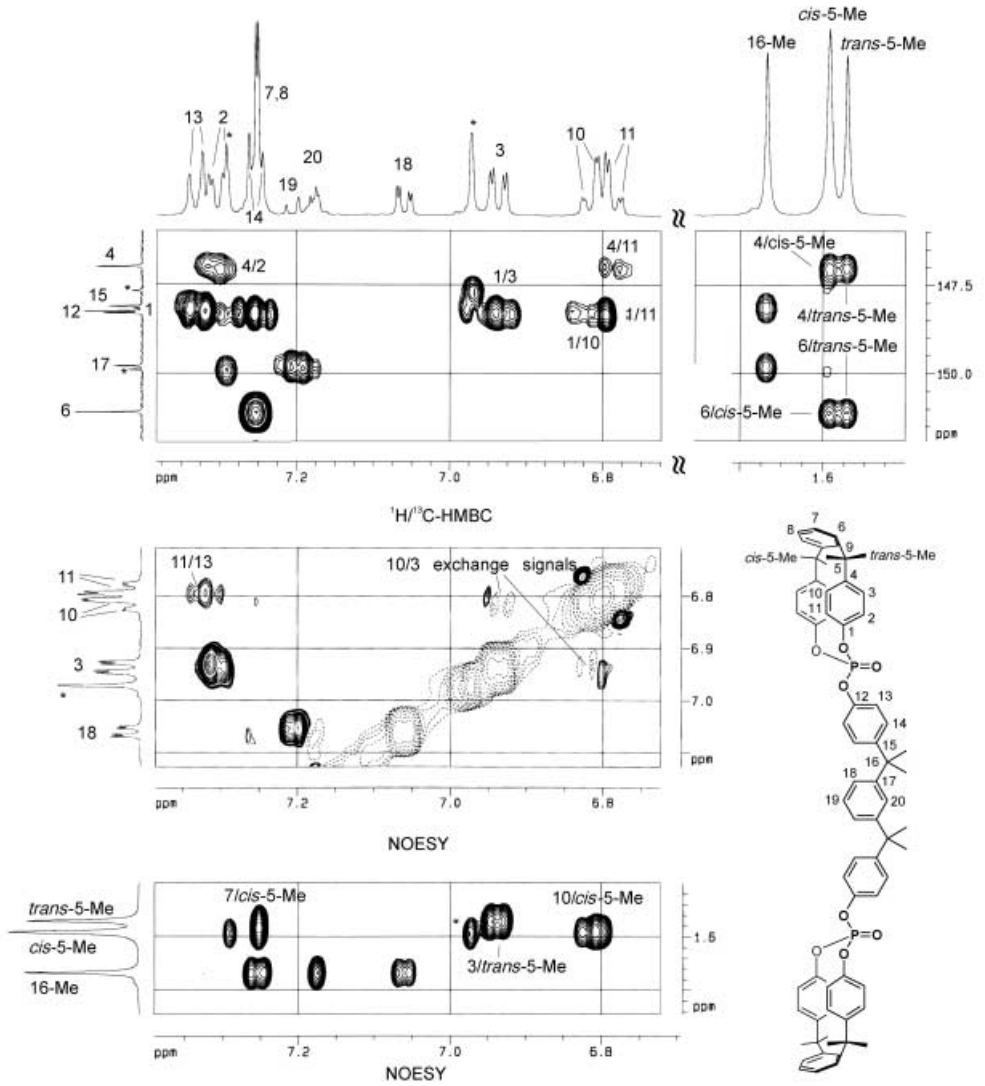

Figure 3. Sections of the $^{1}H/^{13}C$ HMBC and the NOESY spectra of **12**.

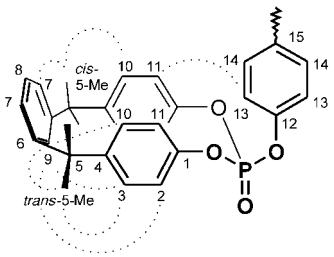

Figure 4. NOESY interactions in compound **12**. Hydrogen atoms are omitted for clarity. The NOE interaction of the protons is illustrated by dotted lines between their corresponding positions on the carbon skeleton.

3H; 9-H), 1.52 (s, 36H; Me); ^{13}C NMR (75.5 MHz, $CDCl_3$): $\delta = 149.9$ (C-6), 149.3 (C-1), 146.0 (C-4), 129.6 (C-9), 127.8 (C-3), 127.5 (C-8), 122.2 (C-7), 119.5 (d, $^{3}J(P,C) = 8.1$ Hz, C-2), 119.5 (s, C-2′), 42.4 (C-5), 30.5 (Me); MALDI-TOF-MS (matrix: 1,8,9-trihydroxyanthracene): *m*/*z*: 1095 [M^{+}+H]; elemental analysis calcd (%) for $C_{72}H_{72}O_6P_2$ (1095.24): C 78.95, H 6.63; found: C 78.23, H 7.02.

***In,out*-phosphite 11**: ^{31}P NMR (121.5 MHz, $CDCl_3$): $\delta = 131.2$ (*in*), 124.6 (*out*).

Diphosphite 8: M.p. 134–137 °C; ^{31}P NMR (121.5 MHz, $CDCl_3$): $\delta = 121.1$; ^{1}H NMR (300.1 MHz, $CDCl_3$): $\delta = 7.25$–7.05 (m, 20H; 13-H, 2-H, 14-H, 7,8-H, 19-H, 20-H), 6.98 (dd, $J(H,H) = 1.7$, 8.8 Hz, 2H; 18-H), 6.86 (dd, $J(H,H) = 2.4$, 9.4 Hz, 4H; 3-H), 6.76–6.71 (m, 8H; 10-H, 11-H), 5.16 (br s, 2H; 9-H), 1.58 (s, 12H; 16-Me), 1.48 (s, 24H; *cis*-5-Me, *trans*-5-Me); MALDI-TOF-MS (matrix: 1,8,9-trihydroxyanthracene): *m*/*z*: 1096 [M^{+}+H]; elemental analysis calcd (%) for $C_{72}H_{72}O_6P_2$ (1095.24): C 78.95, H 6.63; found: C 78.76. H 6.82.

Reaction of 4 with PCl_3 and subsequent oxidation: The reaction between diphenol **4** and PCl_3 was carried out the same way and with the same amounts as described above. The yellow viscous oil obtained mainly containing a mixture of phosphites **5**–**8** was dissolved in toluene (50 mL) and cumene hydroperoxide (2.4 g, 15.5 mmol, two-fold excess) was added. The mixture was stirred for 1 h at room temperature. The solvent was evaporated in vacuo to yield a viscous oil containing a mixture of **9**, **10**, **11**, and **12**, and noncyclic and simple macrocyclic byproducts according to ^{31}P NMR spectroscopy. Isolation of the products by chromatography on silica gel with toluene/Et_2O (20:1) afforded *out,out*-macrobicycle **9** (148 mg, 3.4%), *in,in*-phosphate **10** (56 mg, 1.3%), and phosphate **12** (1.37 g, 31.5%), as white solids. *In,out*-phosphate **7** was obtained only in a mixture with **12**.

***Out,out*-phosphate 9**: M.p. 305–306 °C; ^{31}P NMR (121.5 MHz, $CDCl_3$): $\delta = -18.6$; ^{1}H NMR (300.1 MHz, $CDCl_3$): $\delta = 7.28$–7.27 (m, 9H; 7,8-H), 6.96 (d, $^{3}J(H,H) = 9.3$ Hz, 12H; 2- or 3H), 6.955 (d, $^{3}J(H,H) = 8.7$ Hz, 12H; 3- or 2-H), 6.42 (s, 3H; 9-H), 1.59 (s, 36H; Me); ^{13}C NMR (75.5 MHz, $CDCl_3$): $\delta = 149.9$ (C-6), 148.2 (d, $^{2}J(P,C) = 7.3$ Hz, C-1), 147.7 (C-4), 129.1 (C-9), 127.9 (C-3), 127.6 (C-8), 122.4 (C-7), 119.8 (d, $^{3}J(P,C) = 5.3$ Hz, C-2),

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42.6 (C-5), 30.4 (5-Me); MALDI-TOF-MS (matrix: 1,8,9-trihydroxyanthracene): m/z: 1128 [M^++H], 1150 [M^++Na]; elemental analysis calcd (%) for $C_{72}H_{72}O_8P_2$ (1127.24): C 76.71, H 6.44; found: C 76.12, H 6.78.

***In*,*in*-phosphate 10**: M.p. 268–270 °C; ^{31}P NMR (121.5 MHz, $CDCl_3$): $\delta = -16.0$; ^{1}H NMR (300.1 MHz, $CDCl_3$): $\delta = 7.27-7.29$ (9H; 7,8-H), 7.08 (d, $^3J(H,H) = 8.7$ Hz, 12H; 2-or 3-H), 6.93 (d, $^3J(H,H) = 8.7$ Hz, 12H; 2-or 3-H), 6.94 (br s, 3H; 9-H), 1.59 (s, 36H; Me); ^{13}C NMR (75.5 MHz, $CDCl_3$): $\delta = 149.6$ (C-6), 148.2 (d, $^2J(P,C) = 6.7$ Hz, C-1), 147.3 (C-4), 128.6 (C-9), 127.6 (C-3, C-8), 122.5 (C-7), 119.7 (d, $^3J(P,C) = 4.6$ Hz, C-2), 42.4 (C-5), 30.3 (5-Me); MALDI-TOF-MS (matrix: 1,8,9-trihydroxyanthracene): m/z: 1128 [M^++H], 1150 [M^++Na], 1167 [M^++K]; elemental analysis calcd (%) for $C_{72}H_{72}O_8P_2$ (1127.24): C 76.71, H 6.44; found: C 76.18, H 6.76.

***In*,*out*-phosphate 11**: ^{31}P NMR (121.5 MHz, $CDCl_3$) $\delta = -16.7$ (*in*), -18.4 (*out*).

Diphosphate 12: M.p. 240–243 °C; ^{31}P NMR (121.5 MHz, $CDCl_3$): $\delta = -18.5$; ^{1}H NMR (500.1 MHz, $CDCl_3$): $\delta = 7.33$ (d, $^3J(H,H) = 8.2$ Hz, 4H; 13-H), 7.30 (dd, $J(H,H) = 2.5$, 9.0 Hz, 4H; 2-H), 7.25 (d, $J(H,H) = 8.7$ Hz, 4H; 14-H), 7.25 (m, 6H; 7,8-H), 7.20 (t, $J(H,H) = 7.8$ Hz, 1H; 19-H), 7.18 (t, $J(H,H) = 1.7$ Hz, 1H; 20-H), 7.06 (dd, $J(H,H) = 1.9$, 7.7 Hz, 2H; 18-H), 6.94 (dd, $J(H,H) = 2.2$, 8.7 Hz, 4H; 3-H), 6.82 (dd, $J(H,H) = 2.0$, 8.8 Hz, 4H; 10-H), 6.78 (dd, $J(H,H) = 2.4$, 8.7 Hz, 4H; 11-H), 5.16 (br s, 2H; 9-H), 1.67 (s, 12H; 16-Me), 1.59 (s, 12H; *cis*-5-Me), 1.57 (s, 12H; *trans*-5-Me); ^{13}C NMR (75.5 MHz, $CDCl_3$): $\delta = 151.1$ (C-6), 149.8 (C-17), 148.3 (C-12), 148.2 (C-1), 148.1 (C-15), 147.0 (C-4), 131.3 (C-9), 128.21, 128.18 (C-10,C-14), 127.7 (C-19), 127.4 (C-3), 127.0 (C-8), 125.0 (C-20), 124.3 (C-18), 120.9 (C-7), 120.0 (d, $^3J(P,C) = 6.2$ Hz, C-11), 119.50 (C-2 or C-13), 119.49 (d, $^3J(P,C) = 8.3$ Hz, C-2 or C-13), 42.8 (C-16), 42.3 (C-5), 30.8 (16-Me), 29.7 (*trans*-5-Me), 29.4 (*cis*-5-Me); MALDI-TOF-MS (matrix: 1,8,9-trihydroxyanthracene): m/z: 1127 [M^++H], 1150 [M^++Na]; elemental analysis calcd (%) for $C_{72}H_{72}O_8P_2$ (1127.24): C 76.71, H 6.44; found: C 76.42, H 6.58.

X-ray crystal structure analysis of 5: Formula $C_{72}H_{72}O_6P_2 \cdot CHCl_3 \cdot NCCH_3$, $M_r = 1255.66$, colorless crystal $0.70 \times 0.12 \times 0.12$ mm, $a = 14.601(1)$, $b = 14.720(1)$, $c = 17.743(1)$ Å, $\alpha = 106.44(1)$, $\beta = 104.09(1)$, $\gamma = 104.60(1)°$, $V = 3329.7(4)$ Å^3, $\rho_{calcd} = 1.252$ g cm^{-3}, $\mu = 2.39$ cm^{-1}, empirical absorption correction from SORTAV ($0.851 \le T \le 0.972$), $Z = 2$, triclinic, space group $P\bar{1}$ (No. 2), $\lambda = 0.71073$ Å, $T = 198$ K, ω and ϕ scans, 18925 reflections collected ($\pm h$, $\pm k$, $\pm l$), $[(\sin\theta)/\lambda] = 0.59$ Å^{-1}, 11713 independent ($R_{int} = 0.040$) and 7184 observed reflections [$I > 2\sigma(I)$], 782 refined parameters, $R = 0.087$, $wR^2 = 0.243$, max/min residual electron density 0.71/ -1.36 e Å^{-3}. The solvent molecules were disordered, and the acetonitrile was therefore refined with isotropic thermal parameters; refinement of the chloroform with split positions did not improve the model. Hydrogen atoms were calculated and refined as riding atoms.

X-ray crystal structure analysis of 6: Formula $(C_{72}H_{72}O_6P_2)_2 \cdot CHCl_3$, $M_r = 2309.84$, colorless crystal $0.35 \times 0.25 \times 0.07$ mm, $a = 23.472(1)$, $b = 13.597(1)$, $c = 39.422(1)$ Å, $\beta = 90.22(1)°$, $V = 12581.4(11)$ Å^3, $\rho_{calcd} = 1.219$ g cm^{-3}, $\mu = 1.85$ cm^{-1}, no absorption correction ($0.938 \le T \le 0.987$), $Z = 4$, monoclinic, space group $P2_1/c$ (No. 14), $\lambda = 0.71073$ Å, $T = 198$ K, ω and ϕ scans, 27496 reflections collected ($\pm h$, $\pm k$, $\pm l$), $[(\sin\theta)/\lambda] = 0.65$ Å^{-1}, 18429 independent ($R_{int} = 0.045$) and 9125 observed reflections [$I > 2\sigma(I)$], 1568 refined parameters, $R = 0.065$, $wR^2 = 0.146$, max/min residual electron density 0.55/ -0.32 e Å^{-3}. One linking group in molecule A (C27, C28, C29) was refined with split positions (0.54(1):0.46); the solvent molecule is heavily disordered, also refined with split positions (0.56(1):0.44), in addition geometrical restraints were used. Hydrogen atoms were calculated and refined as riding atoms.

X-ray crystal structure analysis of 12: Formula $C_{72}H_{72}O_8P_2$, $M_r = 1127.24$, colorless crystal $0.40 \times 0.30 \times 0.03$ mm, $a = 6.778(1)$, $b = 13.620(1)$, $c = 16.646(1)$ Å, $\alpha = 75.19(1)$, $\beta = 89.62(1)$, $\gamma = 83.10(1)°$, $V = 1474.4(3)$ Å^3, $\rho_{calcd} = 1.270$ g cm^{-3}, $\mu = 1.32$ cm^{-1}, no absorption correction ($0.949 \le T \le 0.996$), $Z = 1$, triclinic, space group $P\bar{1}$ (No. 2), $\lambda = 0.71073$ Å, $T = 198$ K, ω and ϕ scans, 7976 reflections collected ($\pm h$, $\pm k$, $\pm l$), $[(\sin\theta)/\lambda] = 0.59$ Å^{-1}, 5162 independent ($R_{int} = 0.046$) and 3966 observed reflections [$I > 2\sigma(I)$], 399 refined parameters, $R = 0.093$, $wR^2 = 0.193$, max/min residual electron density 0.87/ -0.43 e Å^{-3}. Owing to symmetry (inversion centre) the central phenyl group was disordered and refined with split positions. Hydrogen atoms were calculated and refined as riding atoms.

Data sets were collected on a Nonius KappaCCD diffractometer, equipped with a rotating anode generator Nonius FR591. Programs used: data collection COLLECT (Nonius B.V., 1998), data reduction Denzo-SMN,[21] absorption correction SORTAV,[22] structure solution SHELXS-97,[23] structure refinement SHELXL-97,[24], and graphics ORTEP-3.[25] CCDC 182712–182714 contain the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/conts/retrieving.html (or from the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; fax: (+44) 1223-336-033; or e-mail: deposit@ccdc.cam.ac.uk).

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