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Synthesis, Derivatisation and Structural Characterisation of a New Macrobicyclic Phosphane Oxide Cryptand

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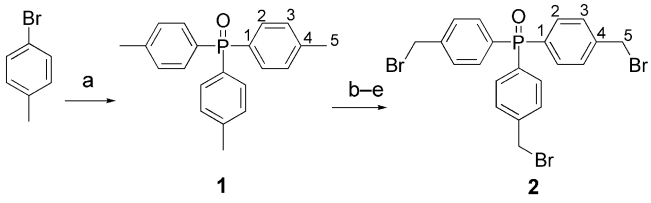
Following a tripod-coupling strategy a new phosphane oxide cage compound was synthesised in comparatively high yield. The X-ray crystal structure obtained shows a large cavity and an *out*-positioned P=O moiety in the solid state. A stable *in*-isomer was not detected, either during synthesis or by isomerisation. We attribute this fact to homeomorphic isomerisation in solution at room temperature.

Introduction

The motive of our work was the interest in *in*-functionalised macrobicycles with large cavities. Bearing a phosphane moiety, such structures could potentially act as ligands for metal-catalysed reactions[1] or as organocatalysts.[2] The exceptional location of the donor centre inside the cavity might give rise to increased regio- and stereospecificity. The corresponding phosphane oxides could also play a role as ionophores.[3] Tsuji et al. pointed out that large bowl-shaped phosphane ligands were highly effective in C–C bond forming reactions, and the depth of the bowl affected the catalytic activity considerably; in general, the deeper bowl ligands were more effective than the shallower ones.[1] The application of chiral phosphane ligands with a pronounced cavity has also been reported for asymmetric metal-catalysed allylic alkylations.[4] In our previous work we investigated the *in*/*out*-isomerism of phosphorus bridgehead cage compounds in the form of phosphites and phosphates.[5–9] The studies presented here deal with related phosphane and phosphane oxide macrobicycles bearing one phosphorus bridgehead atom. Corresponding phosphane and phosphane oxides with two P-bridgeheads are described elsewhere.[10]

Results and Discussion

We intended to assemble a macrobicyclic phosphane oxide cryptand applying a tripod-coupling method.[11] Benzyl bromide **2** as a basic building block was synthesised in 13% overall yield over five steps starting from *p*-bromotoluene and $POCl_3$ by a Grignard coupling,[12] followed by oxidation with $KMnO_4$, esterification, reduction to the corresponding benzylic alcohol and subsequent bromination with $SOBr_2$ (Scheme 1). All steps could be realised on a large scale. Direct Wohl–Ziegler bromination of **1** led only to an inseparable mixture containing compounds of different bromination degree.



Scheme 1. Synthesis of **2**: a) 3.3 equiv. *p*-bromotoluene, Mg, 1 equiv. $POCl_3$, THF, reflux, 2 h, 43%; b) 12 equiv. $KMnO_4$, pyridine/water = 1:2, reflux, 20 h, 99%; c) 6 equiv. $SOCl_2$, EtOH, reflux, 9 h, 87%; d) 9.6 equiv. $LiAlH_4$, THF, reflux, 18 h, 54%; e) $SOBr_2$, 2 drops DMF, room temp., 19 h, 67%.

We were able to determine the crystal structure of **2** by X-ray diffraction (Figure 1).

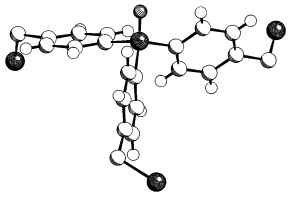


Figure 1. X-ray crystal structure of **2**.

Mono-*O*-acetylated product **3** was obtained from the corresponding, commercially available bisphenol. Williamson ether synthesis using **3** and benzyl bromide **2** followed by in situ deprotection of the ester moieties provided the tripodal compound **4** in 45% yield (Scheme 2).

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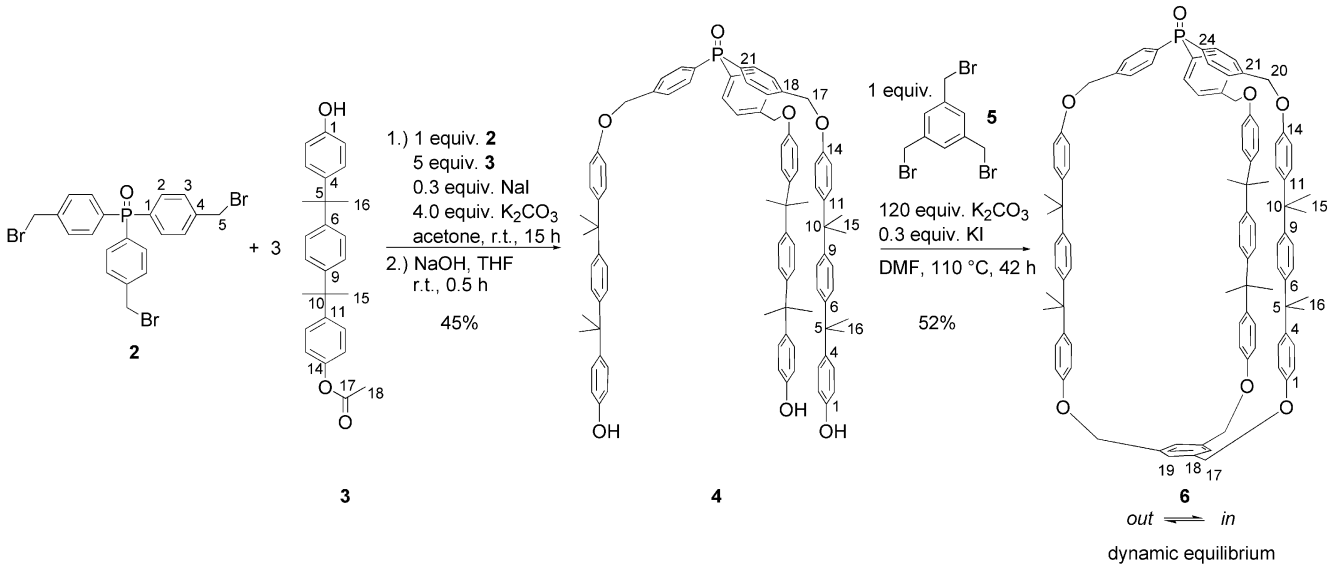


Scheme 2. Synthesis of capping reagent **4** via Williamson ether synthesis and subsequent tripod-coupling of **4** and **5**.

The synthesis of the macrobicyclic product **6** was accomplished by a tripod-coupling reaction of **4** and **5** under dilute conditions (Scheme 2). The phosphane oxide **6** was formed in a comparatively high yield of 52% as a single isomer. To our delight, we obtained single crystals and determined the crystal structure (Figures 2 and 3) showing a huge hole and a distance between the bridgehead fragments of about 11 Å. The P=O moiety is clearly *out*-positioned in the crystalline state. Our primary aim, however, was to gain access to a macrobicyclic phosphane with the phosphorus lone pair directing into the cavity, thus being prepared for ligation inside the macrobicycle. Therefore we applied a reduction protocol to phosphane oxide **6** using trichlorosilane and triethylamine, which is known to lead to inversion of the configuration at the phosphorus.[13–15] Complete conversion was verified by ^{31}P NMR spectroscopy. The ^{31}P NMR peak of starting phosphane oxide **6** at δ = 28.5 ppm had disappeared completely in favour of a peak at –7.3 ppm, corresponding to the phosphane. Due to a high tendency for oxidation during workup and purification, we reoxidised the crude phosphane with H_2O_2 with retention (Scheme 3).[15–18] Thus, we could investigate the stereochemical outcome of the reductive step by making use of the phosphane oxide product distribution. To our surprise, after this reduction/oxidation procedure we exclusively obtained a single product which turned out to be identical with the starting phosphane oxide **6** (Scheme 3).

In contrast to our previously described less flexible macrobicyclic systems[5–9] it was not possible to isolate stable homeomorphic isomers, either during synthesis or by isomerisation. We tentatively attribute this fact to a rapid homeomorphic isomerisation in solution,[19] which is made possible by the long and flexible arms of the macrobicyclic cage. The derivative phosphane-borane complex **7** was synthesised from phosphane oxide **6** via reduction with trichlorosilane proceeding with retention of the configuration at the phosphorus,[12–14] and subsequent quenching with borane-tetrahydrofuran complex (Scheme 3).[13]

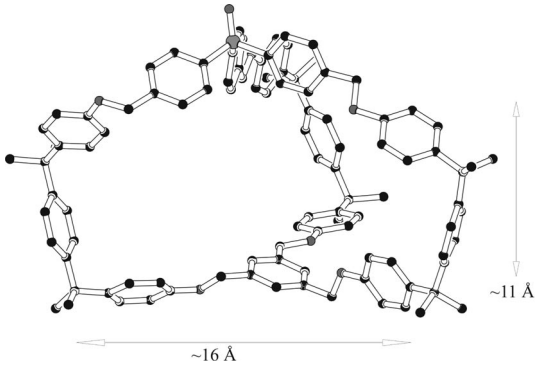


Figure 2. X-ray crystal structure of **6**. Front view into the cavity. Hydrogen atoms are omitted for clarity.

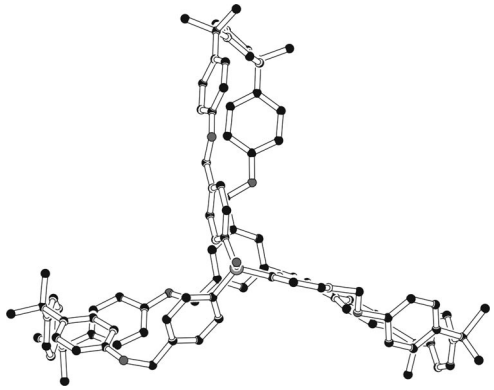
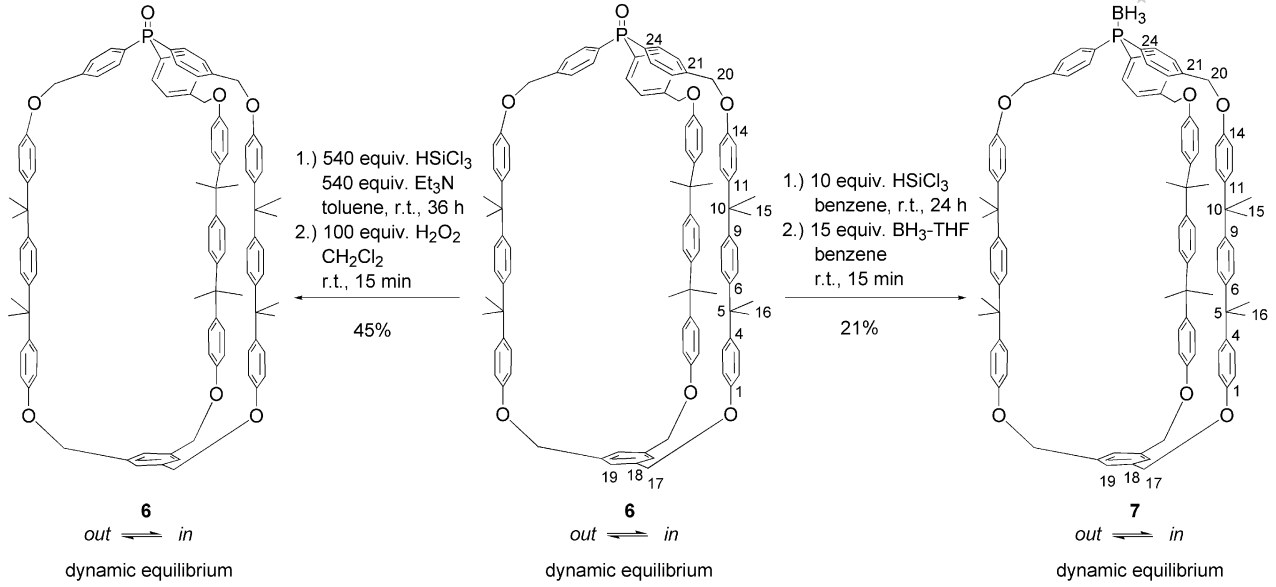


Figure 3. X-ray crystal structure of **6**. Top view along the bridgehead segments. Hydrogen atoms are omitted for clarity.



Scheme 3. Isomerisation experiment of **6** (left) and synthesis of phosphane-borane complex **7** (right).

Conclusions

We synthesised a new phosphane oxide macrobicycle in high yield by a tripod-coupling strategy. The X-ray structure of this new cryptand reveals an *out*-position of the P=O moiety in the solid state; however, in solution we assume a fast homeomorphic isomerisation at room temperature which prevents the isolation of a stable *in*-isomer.

Experimental Section

General: 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 with Bruker DRX-500 and AC300-P spectrometers. For detailed assignment of the NMR peaks based on 2D NMR measurements of **4**, **6** and **7** see numbering in Scheme 2 and Scheme 3. ESI-MS spectra were determined with a Bruker Esquire mass spectrometer with an ion trap detector. Elemental analysis was carried out with a Hekatech EA 3000 Euro Vector instrument. IR spectra were recorded with a Thermo Nicolet Avatar 260 FT-IR instrument. Thin-layer chromatography (TLC) was carried out on aluminum sheets coated with silica gel obtained from Merck. Plates were visualised by UV irradiation. Column chromatography was performed using silica gel (Merck, 0.040–0.063 mm). All reactions were carried out in dry solvents under argon. The solvents were dried using a solvent purification system (MBraun-SPS). Chemicals were used as received from commercial sources. Reagent **5** was synthesised according to a literature procedure.[20]

Tri(*p*-tolyl)phosphane Oxide (1): The synthesis was accomplished according to ref.[12] In a dry flask (1 L), magnesium splints (43.64 g, 1.788 mol) and dry THF (100 mL) were combined under argon. *p*-Bromotoluene (278.00 g, 200 mL, 1.625 mol) was added slowly until the reaction started. The reaction mixture was cooled to 0 °C, and the residual *p*-bromotoluene dissolved in dry THF (300 mL) was added. After 1 h at reflux, the mixture was cooled to 0 °C again and $POCl_3$ (75.52 g, 45.9 mL, 0.493 mol) was added slowly. After refluxing for 1 h, the mixture was cooled to room temperature and then quenched with water and concentrated HCl. After extraction with dichloromethane and washing with $NaHCO_3$, NaCl and 2 M NaOH, the combined organic layers were dried with $MgSO_4$. The solvent was removed under reduced pressure. Recrystallisation of the residue from ethyl acetate/pentane gave product **1** (74.97 g, 0.234 mol, 43%) as a colourless solid; m.p. 140 °C. ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 2.37 (s, 9 H, 5-H), 7.23 (dd, $^4J_{PH}$ = 2.4, $^3J_{HH}$ = 7.9 Hz, 6 H, 3-H), 7.52 (dd, $^3J_{PH}$ = 11.8, $^3J_{HH}$ = 8.1 Hz, 6 H, 2-H) ppm. ^{13}C NMR (76 MHz, $CDCl_3$, 25 °C): δ = 21.53 (C-5), 129.10 (d, $^3J_{PC}$ = 12.5 Hz, C-3), 129.57 (d, $^1J_{PC}$ = 106.5 Hz, C-1), 132.03 (d, $^2J_{PC}$ = 10.2 Hz, C-2), 142.16 (d, $^4J_{PC}$ = 3.0 Hz, C-4) ppm. ^{31}P NMR (122 MHz, $CDCl_3$, 25 °C): δ = 29.40 (s) ppm. ESI-MS (10 V): *m*/*z* (%) = 321.4 (100) $[M + H]^+$.

Tri(*p*-carboxyphenyl)phosphane Oxide: $KMnO_4$ (118.40 g, 749.150 mmol) was added in small portions to a refluxing solution of **1** (20.00 g, 64.429 mmol) in pyridine/water (150 mL, 1:2). After each portion, the reaction mixture was kept stirring under reflux for 1 h until the colour changed from violet to brown. After 20 h, the hot suspension was filtered. The residual MnO_2 was washed with hot water. After acidification of the aqueous phase with semiconcentrated H_2SO_4, the crude product precipitated. The solid was separated and dissolved in NaOH (10%), and the solution was extracted with THF and EtOAc to remove residual starting material **1**. The aqueous phase was again treated with semiconcentrated H_2SO_4 to precipitate the product. This procedure was repeated. The product was powdered and dried at 70 °C under vacuum to obtain the title phosphane oxide compound (25.28 g, 61.611 mmol, 99%) as a colourless solid; m.p. 365 °C. ^{1}H NMR (300 MHz, [D$_6$]-DMSO, 25 °C): δ = 7.80 (dd, $^3J_{PH}$ = 11.6, $^3J_{HH}$ = 8.3 Hz, 6 H, 2-H), 8.11 (dd, $^4J_{PH}$ = 2.5, $^3J_{HH}$ = 8.3 Hz, 6 H, 3-H) ppm. ^{13}C NMR (76 MHz, [D$_6$]DMSO, 25 °C): δ = 129.60 (d, $^3J_{PC}$ = 12.2 Hz, C-3), 131.96 (d, $^2J_{PC}$ = 10.3 Hz, C-2), 134.29 (d, $^4J_{PC}$ = 2.7 Hz, C-4), 136.16 (d, $^1J_{PC}$ = 101.1 Hz, C-1), 166.58 (*C*OOH) ppm. ^{31}P NMR (122 MHz, [D$_6$]DMSO, 25 °C): δ = 24.69 (s) ppm. ESI-MS (25 V): *m*/*z* (%) = 843.1 (34) $[2M + Na]^+$, 821.2 (100) $[2M + H]^+$, 433 (5) $[M + Na]^+$, 411.1 (38) $[M + H]^+$. IR (ATR): $\tilde{\nu}$ = 2880 (w, br, O–

$H_{H\text{-linked}}$), 2619 (w, br), 2500 (w, br), 1690 (st, C=O), 1396, 1235 (P=O), 1162 (st), 1100 (st), 1016, 856, 762, 695 (st) cm^{-1}.

Tri(*p*-ethoxycarbonyl)phosphane Oxide: $SOCl_2$ (70.72 mL, 115.30 g, 0.949 mol) was slowly added to a suspension of tri(*p*-carboxyphenyl)phosphane oxide (64.94 g, 0.158 mol) in EtOH (1 L). The solution was kept stirring under reflux until HCl formation finished (≈ 9 h). The progress of the reaction was monitored by thin-layer chromatography with EtOAc (product: R_f = 0.5). The solution was cooled to room temperature, and the solid precipitate was separated and dissolved in dichloromethane. The solution was washed with water and a saturated NaCl solution and dried with $MgSO_4$. After removal of the solvent under vacuum, the crude product was separated from by-products by column chromatography on silica gel, eluting with CH_2Cl_2, followed by EtOAc to release the product. After removal of the solvent under vacuum, the title ester was obtained as a colourless solid (67.88 g, 0.137 mol, 87%); m.p. 79 °C. ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 1.39 (t, $^3J_{HH}$ = 7.2 Hz, 9 H, –COOCH$_2$C*H*$_3$), 4.40 (q, $^3J_{HH}$ = 7.1 Hz, 6 H, –COOC*H*$_2$CH$_3$), 7.73 (dd, $^3J_{PH}$ = 11.8, $^3J_{HH}$ = 8.5 Hz, 6 H, 2-H), 8.13 (dd, $^4J_{PC}$ = 2.6, $^3J_{HH}$ = 8.4 Hz, 6 H, 3-H) ppm. ^{13}C NMR (76 MHz, $CDCl_3$, 25 °C): δ = 14.25 (–COOCH$_2$*C*H$_3$), 61.57 (–COO*C*H$_2$CH$_3$), 129.62 (d, $^3J_{PC}$ = 12.4 Hz, C-3), 132.02 (d, $^2J_{PC}$ = 10.2 Hz, C-2), 134.09 (d, $^4J_{PC}$ = 2.4 Hz, C-4), 136.10 (d, $^1J_{PC}$ = 101.8 Hz, C-1), 165.52 (–*C*OOEt) ppm. ^{31}P NMR (122 MHz, $CDCl_3$, 25 °C): δ = 26.98 (s) ppm. ESI-MS (25 V): *m*/*z* (%) = 533.0 (16) [M + K]$^+$, 517.1 (6) [M + Na]$^+$, 495.2 (100) [M + H]$^+$. IR (ATR): $\tilde{\nu}$ = 2983 (w), 1712 (st, C=O), 1397, 1366, 1270 (st, CO–O), 1197, 1095 (st, CO–O), 1016 (st), 856, 764, 733 (st), 696 (st) cm^{-1}. $C_{27}H_{27}O_7P$ (494.47): calcd. C 65.58, H 5.50; found C 65.55, H 5.53.

Tri(*p*-hydroxymethylphenyl)phosphane Oxide: A solution of tri(*p*-ethoxycarbonyl)phosphane oxide (67.88 g, 0.137 mol) in dry THF (500 mL) was added dropwise under argon to a refluxing suspension of $LiAlH_4$ (50.02 g, 1.317 mol) in dry THF (800 mL). The progress of the reaction was monitored by thin-layer chromatography with EtOH. After quenching with water and acidification with H_2SO_4 (25%) the solvents (EtOH, water) were removed under reduced pressure. The residue was dissolved in EtOH, and the solution was dried with $MgSO_4$. The product mixture contained about 13% of the corresponding phosphane according to ^{31}P NMR spectroscopy. In order to oxidize the phosphane to the desired product, the solution was treated at room temp. with H_2O_2 (30%, 2 mL) for 30 min. After evaporation of the solvent under reduced pressure, the product was purified by chromatography on silica gel. Elution with CH_2Cl_2 removed nonpolar by-products. Subsequently, the product was eluted with EtOH. The solvent was removed under reduced pressure, and the residue was dried at 75 °C for 10 h under vacuum. Tri(*p*-hydroxymethylphenyl)phosphane oxide was obtained as a yellow, hygroscopic powder (27.32 g, 0.074 mol, 54%); m.p. 230 °C. ^{1}H NMR (300 MHz, [D$_6$]DMSO, 25 °C): δ = 4.57 (d, $^3J_{HH}$ = 5.5 Hz, 6 H, 5-H), 5.36 (t, $^3J_{HH}$ = 5.7 Hz, 3 H, –O*H*), 7.48 (dd, $^4J_{PH}$ = 2.4, $^3J_{HH}$ = 7.8 Hz, 6 H, 3-H), 7.56 (dd, $^3J_{PH}$ = 11.2, $^3J_{HH}$ = 8.0 Hz, 6 H, 2-H) ppm. ^{13}C NMR (126 MHz, [D$_6$]DMSO, 25 °C): δ = 62.47 (C-5), 126.46 (d, $^3J_{PC}$ = 12.0 Hz, C-3), 131.23 (d, $^1J_{PC}$ = 104.1 Hz, C-1), 131.42 (d, $^2J_{PC}$ = 9.9 Hz, C-2), 146.85 (d, $^4J_{PC}$ = 2.4 Hz, C-4) ppm. ^{31}P NMR (122 MHz, [D$_6$]DMSO, 25 °C): δ = 25.70 (s) ppm. ESI-MS (10 V): *m*/*z* (%) = 759.2 (100) [2M + Na]$^+$, 757.1 (24), 743.2 (42), 737.2 (12) [2M + H]$^+$, 735.2 (10), 655.2 (27), 639.2 (18), 633.2 (20), 623.2 (6), 617.2 (11), 607.1 (4), 497.1 (2), 475.1 (4), 391.1 (12) [M + Na]$^+$, 383.1 (4), 369.1 (43) [M + H]$^+$, 260.9 (5). IR (ATR): $\tilde{\nu}$ = 3267 (st, br, ν_{O-H}), 2914 (w), 2856 (w), 1602, 1400 (P–phenyl), 1162, 1114 (st), 1014 (st), 804 670 (st) cm^{-1}.

Tri(*p*-bromomethylphenyl)phosphane Oxide (2): Under argon, $SOBr_2$ (6 mL, 16.10 g, 77.330 mmol) was added at room temperature to tri(*p*-hydroxymethylphenyl)phosphane oxide (100.0 mg, 0.272 mmol) and dry DMF (2 drops). After stirring for 19 h at room temperature, the solution was slowly diluted with CH_2Cl_2 (50 mL) and water (50 mL). NaOH (40%) was added until the solution reached pH 11. After separation of the phases, the aqueous layer was extracted with CH_2Cl_2. The combined organic layers were dried with $MgSO_4$, and the solvent was evaporated under reduced pressure. After column chromatography on silica gel eluting with EtOAc/CH_2Cl_2 = 1:2, product **2** was obtained as a colourless, crystalline solid (101.8 mg, 0.183 mmol, 67%); m.p. 176 °C. ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 4.42 (s, 6 H, 5-H), 7.42 (dd, $^4J_{PH}$ = 2.6, $^3J_{HH}$ = 8.3 Hz, 6 H, 3-H), 7.57 (dd, $^3J_{PH}$ = 11.7, $^3J_{HH}$ = 8.2 Hz, 6 H, 2-H) ppm. ^{13}C NMR (76 MHz, $CDCl_3$, 25 °C): δ = 32.03 (d, $^5J_{PC}$ = 1.2 Hz, C-5), 129.17 (d, $^3J_{PC}$ = 12.6 Hz, C-3), 132.09 (d, $^1J_{PC}$ = 104.7 Hz, C-1), 132.49 (d, $^2J_{PC}$ = 10.4 Hz, C-2), 141.93 (d, $^4J_{PC}$ = 2.9 Hz, C-4) ppm. ^{31}P NMR (122 MHz, $CDCl_3$, 25 °C): δ = 27.45 (s) ppm. ESI-MS (10 V): *m*/*z* (%) = 561.8 (7) [M(3·^{81}Br/1·^{13}C)+H]$^+$, 560.8 (33) [M(3·^{81}Br/^{12}C)+H]$^+$, 559.8 (22) [M(1·^{79}Br/2·^{81}Br/1·^{13}C)+H]$^+$, 558.8 (100) [M(1·^{79}Br/2·^{81}Br/^{12}C)+H]$^+$, 557.8 (23) [M(2·^{79}Br/1·^{81}Br/1·^{13}C)+H]$^+$, 556.8 (99) [M(2·^{79}Br/1·^{81}Br/^{12}C)+H]$^+$, 555.8 (7) [M(3·^{79}Br/1·^{13}C)+H]$^+$, 554.8 (31) [M(3·^{79}Br/^{12}C)+H]$^+$. IR (ATR): $\tilde{\nu}$ = 1600 ($\nu_{C=C}$), 1402 (P-phenyl), 1232 (P=O), 1201, 1178 (st), 1112 (st), 1090, 833, 817, 660 (st, C–Br), 607 (st, C–Br) cm^{-1}. $C_{21}H_{18}Br_3OP$ (557.05): calcd. C 45.28, H 3.26; found C 45.45, H 3.16.

Mono-*O*-acetylated Bisphenol 3: Under argon, Ac_2O (0.78 mL, 0.85 g, 8.326 mmol) was added dropwise (over 1 h) at room temperature with vigorous stirring to a solution of 4,4′-(1,4-phenylenedipropane-2,2-diyl)diphenol (5.71 g, 16.490 mmol) and dry pyridine (3.32 mL, 3.27 g, 41.210 mmol) in dry THF (300 mL). The solution was stirred for 45 min, and the reaction mixture was quenched with water and extracted with CH_2Cl_2. The combined organic layers were washed with saturated solutions of NH_4Cl and NaCl. After drying with $MgSO_4$ and solvent evaporation under vacuum, the crude product was purified by column chromatography on silica gel with pentane/diethyl ether = 2:1. Compound **3** was obtained in 72% yield (Ac_2O was the limiting reagent) as a colourless solid (2.30 g, 5.928 mmol, 72%); m.p. 112 °C. ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 1.56 (s, 6 H, 15-H or 16-H), 1.57 (s, 6 H, 15-H or 16-H), 2.21 (s, 3 H, 18-H), 6.65 (d, $^3J_{HH}$ = 8.8 Hz, 2 H, 2-H), 6.89 (d, $^3J_{HH}$ = 8.7 Hz, 2 H, 3-H), 7.03 (s, 4 H, 7/8-H), 7.03 (d, $^3J_{HH}$ = 8.8 Hz, 2 H, 13-H), 7.15 (d, $^3J_{HH}$ = 8.8 Hz, 2 H, 12-H) ppm. ^{13}C NMR (76 MHz, [D$_6$]DMSO, 25 °C): δ = 20.87 (C-18), 30.43 (C-15 or C-16), 30.62 (C-15 or C-16), 41.27 (C-5 or C-10), 41.77 (C-5 or C-10), 114.67 (C-2 or C-13), 121.20 (C-2 or C-13), 125.95 (C-7 or C-8), 126.07 (C-7 or C-8), 127.37 (C-3 or C-12), 127.48 (C-3 or C-12), 140.42 (C-4 or C-6 or C-9 or C-11 or C-14), 146.84 (C-4 or C-6 or C-9 or C-11 or C-14), 147.73 (C-4 or C-6 or C-9 or C-11 or C-14), 147.99 (C-4 or C-6 or C-9 or C-11 or C-14), 148.24 (C-4 or C-6 or C-9 or C-11 or C-14), 155.04 (C-1), 169.28 (C-17) ppm. ESI-MS (25 V): *m*/*z* (%) = 406.2 (100) [M + NH$_4$]$^+$. IR (ATR): $\tilde{\nu}$ = 3472, 3422 (br., ν_{O-H}), 2965 (st), 1732 (st, C=O), 1612, 1506 (st), 1433, 1368, 1269 (st), 1231 (st, CO–O), 1203 (st, CO–O), 1089, 1016 (st), 916, 844, 830 (st, *p*-disubst. aromatics), 810, 603 cm^{-1}. $C_{26}H_{28}O_3$ (388.50): calcd. C 80.38, H 7.26; found C 80.48, H 7.39.

Phosphane Oxide 4: In a flask (100 mL) under argon, compound **3** (251.1 mg, 0.646 mmol) was dissolved in dry acetone (50 mL). Dry NaI (5.8 mg, 0.039 mmol), dry K_2CO_3 (71.5 mg, 0.517 mmol) and benzyl bromide **2** (72.0 mg, 0.129 mmol) were added. After stirring 15 h at room temperature, the solvent was evaporated under re-

duced pressure. The residue was dissolved in THF, and after addition of NaOH (4%, 10 mL), the solution was stirred for an additional 30 min at room temperature. The solvent was evaporated, and the crude product was dissolved in CH_2Cl_2 and washed with water. After separation of the phases, extraction of the aqueous phase with CH_2Cl_2, treatment of the combined organic layers with saturated solutions of $NaHCO_3$, NH_4Cl and NaCl, and drying with $MgSO_4$, the solvent was evaporated. After column chromatography on silica gel with EtOAc/CH_2Cl_2 = 1:4, compound **4** was obtained as a yellow solid (78.3 mg, 0.058 mmol, 45%); m.p. 126 °C. ^{1}H NMR (500 MHz, [D$_6$]DMSO, 25 °C): δ = 1.54 (s, 18 H, 16-H), 1.56 (s, 18 H, 15-H), 5.12 (s, 6 H, 17-H), 6.64 (d, $^3J_{HH}$ = 8.6 Hz, 6 H, 2-H), 6.89 (d, $^3J_{HH}$ = 8.7 Hz, 6 H, 13-H), 6.99 (d, $^3J_{HH}$ = 8.6 Hz, 6 H, 3-H), 7.07 (s, 12 H, 7/8-H), 7.11 (d, $^3J_{HH}$ = 8.7 Hz, 6 H, 12-H), 7.59 (dd, $^4J_{PH}$ = 1.9, $^3J_{HH}$ = 8.2 Hz, 6 H, 19-H), 7.65 (dd, $^3J_{PH}$ = 11.4, $^3J_{HH}$ = 8.2 Hz, 6 H, 20-H), 9.18 (s, 3 H, O*H*), 11.68 (s, hydrogen bonding, ≈ 0.12 H, weakens after dehydration in the vacuum oven) ppm. ^{13}C NMR (126 MHz, [D$_6$]DMSO, 25 °C): δ = 30.55 (C-15), 30.64 (C-16), 41.25 (C-5), 41.40 (C-10), 68.58 (C-17), 114.17 (C-13), 114.68 (C-2), 125.93 (C-7 or C-8), 125.97 (C-7 or C-8), 127.38 (C-3), 127.57 (C-12), 127.60 (d, $^3J_{PC}$ = 12.1 Hz, C-19, signal partially overlapped by C-12), 131.75 (d, $^2J_{PC}$ = 10.0 Hz, C-20), 132.05 (d, $^1J_{PC}$ = 103.4 Hz, C-21), 140.46 (C-4), 141.62 (C-18), 142.78 (C-11), 147.33 (C-6), 147.80 (C-9), 155.06 (C-1), 156.03 (C-14) ppm. ^{31}P NMR (203 MHz, [D$_6$]DMSO, 25 °C): δ = 25.00 (s) ppm. ESI-MS (–75 V): *m*/*z* (%) = 1351.2 (100) [M – H]$^-$ found, 1351.7 [M – H]$^-$ calcd. IR (ATR): $\tilde{\nu}$ = 3037 (w, br), 2961, 2924, 2852, 1607, 1508 (st, P-phenyl), 1460, 1402, 1361, 1297, 1225 (st, P=O), 1178 (st), 1117, 1089, 1015, 828 (st, *p*-disubst. aromatics), 679 cm^{-1}. $C_{93}H_{93}O_7P$ (1353.70): calcd. C 82.51, H 6.92; found C 82.48, H 6.94.

Macrobicyclic Phosphane Oxide (6): In a flask (1 L) under argon, a suspension of dry K_2CO_3 (7.96 g, 57.620 mmol) and KI (0.024 g, 0.144 mmol) in dry DMF (650 mL) was provided. After heating to 110 °C, a solution of alcohol **4** (0.65 g, 0.480 mmol) in dry DMF (50 mL) and simultaneously a solution of 1,3,5-tri(bromomethyl)-benzene **5**[20] (0.171 g, 0.480 mmol) in dry DMF (50 mL) were added dropwise with two perfusors over about 2 h with equal drop speeds. The reaction mixture was stirred at 110 °C for 42 h, during which the solution colour changed from pink to grey. The reaction was quenched with a saturated $NaHCO_3$ solution, stirred for additional 10 min at 110 °C, and then cooled to room temperature. The solvent was evaporated under reduced pressure, and the residue was dissolved in THF. The organic phase was washed with saturated solutions of NH_4Cl and NaCl, and dried with $MgSO_4$. After evaporation of the solvent and column chromatography on silica gel with CH_2Cl_2/EtOH = 100:5, the product **6** was obtained as a yellow solid (0.364 g, 0.248 mmol, 52%). Compound **6** could be recrystallised from CH_2Cl_2/acetone to form thin plates; m.p. 170 °C. ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 1.58 (s, 36 H, 15/16-H), 4.94 (s, 6 H, 17-H), 4.97 (s, 6 H, 20-H), 6.74* (dd, $^3J_{HH}$ = 8.7, $^4J_{HH}$ = 1.9 Hz, 6 H, 13-H), 6.76* (dd, $^3J_{HH}$ = 8.9, $^4J_{HH}$ = 1.9 Hz, 6 H, 2-H), 7.03* (s, 12 H, 7/8-H), 7.04* (dd, $^3J_{HH}$ = 8.5, $^4J_{HH}$ = 1.9 Hz, 12 H, 3/12-H), 7.35 (s, 3 H, 19-H), 7.41 (dd, $^4J_{PH}$ = 2.4, $^3J_{HH}$ = 8.2 Hz, 6 H, 22-H), 7.58 (dd, $^3J_{PH}$ = 11.7, $^3J_{HH}$ = 8.2 Hz, 6 H, 23-H) ppm. * signal partially superposed. ^{13}C NMR (126 MHz, $CDCl_3$, 25 °C): δ = 30.65 (C-15 or C-16), 30.76 (C-15 or C-16), 41.82 (C-5/10), 69.27 (C-20), 69.67 (C-17), 114.02 (C-2 or C-13), 114.05 (C-2 or C-13), 125.80 (C-19), 126.19 (C-7 or C-8), 126.22 (C-7 or C-8), 127.19 (d, $^3J_{PC}$ = 12.2 Hz, C-22), 127.76 (C-3/12), 131.75 (d, $^1J_{PC}$ = 104.2 Hz, C-24), 132.34 (d, $^2J_{PC}$ = 10.1 Hz, C-23), 137.97 (C-18), 141.53 (d, $^4J_{PC}$ = 2.4 Hz, C-21), 143.38 (C-4 or C-11), 143.64 (C-4 or C-11), 147.73 (C-6 or C-9), 147.76 (C-6 or C-9), 156.28 (C-14), 156.50 (C-1) ppm. ^{31}P NMR (122 MHz, $CDCl_3$, 25 °C): δ = 28.48 (s) ppm. ESI-MS (100 V): *m*/*z* (%) = 1467.8 (100) [M + H]$^+$. IR (ATR): $\tilde{\nu}$ = 2962, 2927, 2866, 1605, 1507, 1459, 1401, 1360, 1297, 1221, 1180, 1113, 1014, 827, 677 cm^{-1}.

Phosphane–Borane Complex 7: The following reaction procedure is based on a method described by Odinets et al. for the reduction of phosphane oxides with trichlorosilane and subsequent trapping of the products as phosphane–borane complexes.[12] In a flask (25 mL) under argon, macrobicycle **6** (95.4 mg, 0.065 mmol) was dissolved in dry benzene. $HSiCl_3$ (0.07 mL, 88.9 mg, 0.650 mmol) was added. The reaction mixture was stirred for 24 h at room temperature, and the progress of the reaction was followed by thin-layer chromatography with CH_2Cl_2 (phosphane: $R_f \approx 1$, phosphane oxide: $R_f \approx 0.4$). Subsequently, the reaction was quenched with a 1 M solution of BH_3–THF (0.97 mL, 83.8 mg, 0.975 mmol) in THF and stirred for 15 min at room temperature. After addition of water and extraction with EtOAc, the combined organic layers were washed with a saturated NaCl solution and dried with $MgSO_4$. After solvent removal and column chromatography on silica gel with pentane/diethyl ether = 3:1, the phospane–borane complex **7** was obtained as a yellow solid (19.8 mg, 0.014 mmol, 21%); m.p. 184 °C. ^{1}H NMR (500 MHz, $CDCl_3$, 25 °C): δ = 1.64 (s, 36 H, 15/16-H), 5.01 (s, 6 H, 17-H), 5.02 (s, 6 H, 20-H), 6.81 (d, $^3J_{HH}$ = 8.8 Hz, 6 H, 13-H), 6.83 (d, $^3J_{HH}$ = 8.9 Hz, 6 H, 2-H), 7.10–7.11 (m, 24 H, 3/7/8/12-H), 7.42 (s, 3 H, 19-H), 7.45 (dd, $^4J_{PH}$ = 1.8, $^3J_{HH}$ = 8.1 Hz, 6 H, 22-H), 7.55 (dd, $^3J_{PH}$ = 10.6, $^3J_{HH}$ = 8.3 Hz, 6 H, 23-H) ppm. ^{13}C NMR (76 MHz, $CDCl_3$, 25 °C): δ = 30.68 (C-15 or C-16), 30.77 (C-15 or C-16), 41.85 (C-5/10), 69.27 (C-20), 69.72 (C-17), 114.04 (C-2 or C-13), 114.09 (C-2 or C-13), 125.83 (C-19), 126.22 (C-7 or C-8), 126.24 (C-7 or C-8), 127.53 (d, $^3J_{PC}$ = 10.4 Hz, C-22), 127.77 (C-3/12), 128.52 (d, $^1J_{PC}$ = 58.4 Hz, C-24), 133.40 (d, $^2J_{PC}$ = 10.0 Hz, C-23), 138.00 (C-18), 140.83 (C-21), 143.43 (C-4 or C-11), 143.67 (C-4 or C-11), 147.75 (C-6 or C-9), 147.77 (C-6 or C-9), 156.34 (C-14), 156.53 (C-11) ppm. ^{31}P NMR (203 MHz, $CDCl_3$, 25 °C): δ = 19.67 (s) ppm. ESI-MS (25 V): *m*/*z* (%) = 1483.6 (88) [M(1·^{11}B/1·^{13}C) + NH_4]$^+$, 1482.6 (100) [M(1·^{11}B/^{12}C) + NH_4]$^+$, 1481.6 (29) [M(1·^{10}B/^{12}C)+NH_4]$^+$. ESI-MS (100 V): *m*/*z* (%) = 1503.7 (34) [M + K]$^+$, 1489.7 (75) [M – BH_3+ K]$^+$, 1487.7 (42) [M + Na]$^+$, 1482.7 (18) [M + NH_4]$^+$, 1473.7 (79) [M – BH_3+Na]$^+$, 1465.8 (19) [M + H]$^+$, 1451.8 (100) [M – BH_3+H]$^+$. IR (ATR): $\tilde{\nu}$ = 2959, 2922, 2852, 1509, 1462, 1378, 1243, 1182, 1018, 829, 739 cm^{-1}.

Crystal Data of 2: $C_{21}H_{18}Br_3OP$, M_r = 557.05 g mol^{-1}, colourless crystal 0.20 × 0.10 × 0.07 mm^3, monoclinic, space group $P2_1/c$ (No. 14), a = 17.0513(5) Å, b = 11.4785(3) Å, c = 10.5829(2) Å, α = 90°, β = 96.511(1)°, γ = 90°, V = 2057.96(9) Å^3, Z = 4, $\rho_{calcd.}$ = 1.798 g cm^{-3}, μ = 5.966 mm^{-1}, empirical absorption correction from SORTAV (0.382 ≤ T ≤ 0.680), λ = 0.71073 Å, T = 223(2) K, ω and ϕ scans, 11364 reflections collected (± h, ± k, ± l), [sinθ/λ] = 0.60 Å^{-1}, 3635 independent (R_{int} = 0.075) and 2239 observed reflections [$I \geq 2\sigma(I)$], 255 refined parameters, R = 0.071, wR^2 = 0.172, max./min. residual electron density 1.53/–0.90 e·Å^{-3}. The structure was solved by direct methods and refined by full-matrix least-squares on F^2. Hydrogen atoms were calculated and refined as riding atoms. Br was disordered and refined with split positions.

Crystal Data of 6: $C_{102}H_{99}O_7P$, M_r = 1467.78 g mol^{-1}, colourless crystal 0.60 × 0.25 × 0.10 mm^3, triclinic, space group $P\bar{1}$ (No. 2), a = 15.214(3) Å, b = 19.131(1) Å, c = 19.787(4) Å, α = 117.15(1)°, β = 108.52(2)°, γ = 94.98(1)°, V = 4672.3(13) Å^3, Z = 2, $\rho_{calcd.}$ = 1.043 g cm^{-3}, μ = 0.080 mm^{-1}, absorption correction from SADABS (0.795 ≤ T ≤ 0.992), λ = 0.71073 Å, T = 198(2) K, ϕ

scans, 110134 reflections collected ($\pm h$, $\pm k$, $\pm l$), [$\sin\theta/\lambda$] = 0.61 Å^{-1}, 17041 independent (R_{int} = 0.104) and 9763 observed reflections [$I \geq 2\sigma(I)$], 973 refined parameters, R = 0.086, wR^2 = 0.212, max./min. residual electron density 0.47/–0.31 e·Å^{-3}. The structure was solved by direct methods and refined by full-matrix least-squares on F^2. Hydrogen atoms were calculated and refined as riding atoms. Solvent free reflection dataset was produced by PLATON/SQUEEZE.

CCDC-685055 (for **2**) and -685056 (for **6**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

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