Synthesis of achiral and new chiral crown ethers containing a triphenylphosphane unit

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Abstract

Synthesis and characterization of achiral **1** and new chiral macrocycles (*R*,*R*)-**2**, (*S*,*S*)-**3** and (*S*,*S*)-**4** containing a triphenylphosphanone unit have been accomplished. A new method was used for the reduction of phosphanones to phosphanes. Using this method new potential catalyst ligands **15**, (*R*,*R*)-**16**, (*S*,*S*)-**17** and (*S*,*S*)-**18** containing a triphenylphosphane unit were synthesized and characterized. These ligands are promising candidates for coordination chemistry studies and homogeneous catalytic reactions.

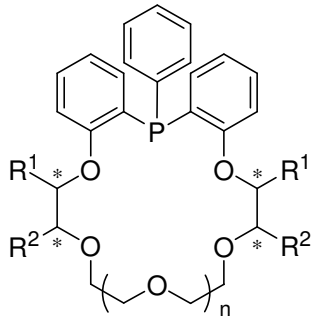
Keywords: Macrocycles, triarylphosphanes, triarylphosphanones, crown ethers

Introduction

Trivalent phosphane compounds have gained great attention in organic chemistry since 1948[1-8] due to their complexing ability and their potential use as catalysts in homogenous reactions, such as hydrogenation[9,10] for example. Although P-heterocyclic ligands are becoming the subjects of a more and more important research area,[11] there are only a few P(III)-containing macrocycles reported in the literature due to the difficulties of their preparation.[12-14] The advantageous features of these macrocycles are as follows. Beside the trivalent phosphorus, the oxygen atoms of the crown ethers can improve the complexation with transition metals. The macrocycle of the crown ethers containing the triphenylphosphane unit induces a rigid conformation, which can increase the selectivity of the catalysis.

A few years ago we reported the synthesis of crown ethers containing an ethyl diarylphosphinate moiety.[15] In the present paper we describe a method for an ethyl diarylphosphinate-triarylphosphanone transformation including crown ether derivatives as well.

Silane compounds are commonly used for the reduction of phosphanones to phosphanes.[16-23] However, with most of these reported methods the phosphane is difficult to purify. There are reported reductions using triethoxysilane, but in all cases Ti compounds and a solvent, for example benzene are used.[24-30] In this paper we report an easy way to deoxygenate phosphanones using trimethoxy- or triethoxysilanes without a solvent and a catalyst, gaining macrocycles **1**, (*R*,*R*)-**2**, (*S*,*S*)-**3**, (*S*,*S*)-**4** containing a triphenylphosphane unit. Crown ethers **1** and **5** are already known compounds[14], here we describe a new route for their preparation, which gives better yields. Enantiopure macrocycles (*R*,*R*)-**2**, (*S*,*S*)-**3**, (*S*,*S*)-**4**, (*R*,*R*)-**6,** (*S*,*S*)-**7**, and (*S*,*S*)-**8** are new compounds.

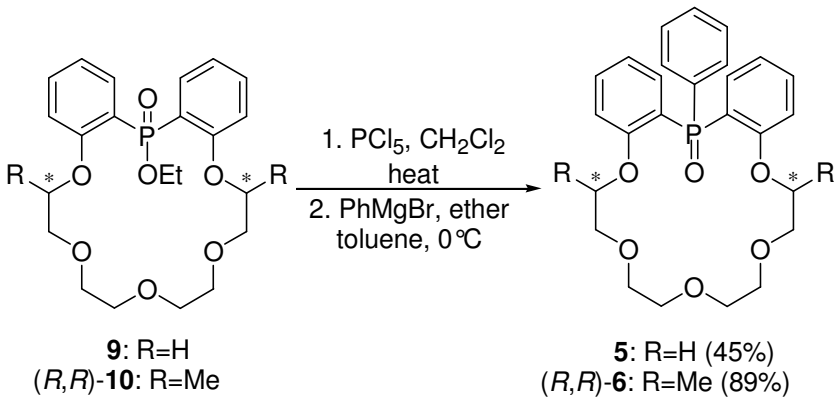


1: R^1=R^2=H, n=1
(*R*,*R*)-**2**: R^1=Me, R^2=H, n=1
(*S*,*S*)-**3**: R^1=H, R^2=Oct, n=2
(*S*,*S*)-**4**: R^1=H, R^2=Me, n=1

Figure 1. Structures of crown ethers **1**-(*S*,*S*)-**4** containing a triphenylphosphane unit.

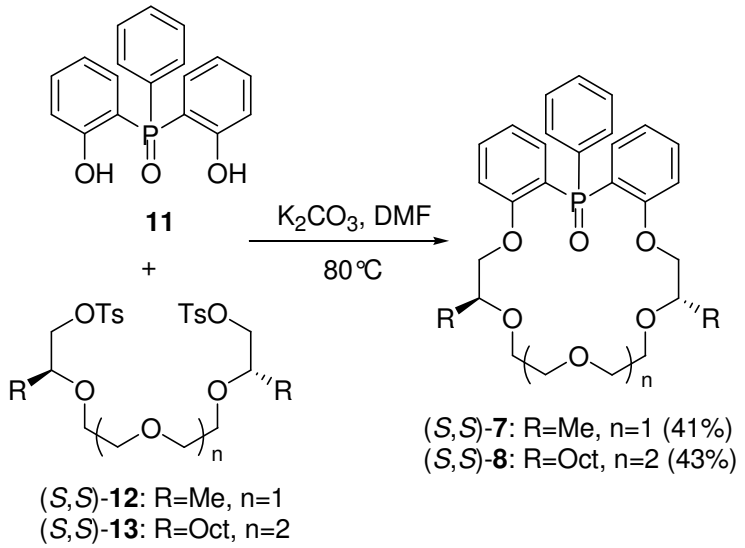
Results and Discussion

The preparation of ligands containing a phenyl diarylphosphanone unit [**5**, (*R*,*R*)-**6,** (*S*,*S*)-**7**, and (*S*,*S*)-**8**] was achieved in two ways. Phosphanones **5** and (*R*,*R*)-**6** were respectively prepared from the already reported macrocycles **9**[15] and (*R*,*R*)-**10**[15] *via* the appropriate phosphine chlorides with phenylmagnesium bromide adopting a known procedure[31] (see Scheme 1).



Scheme 1. Preparation of crown ethers containing a triphenylphosphanone unit.

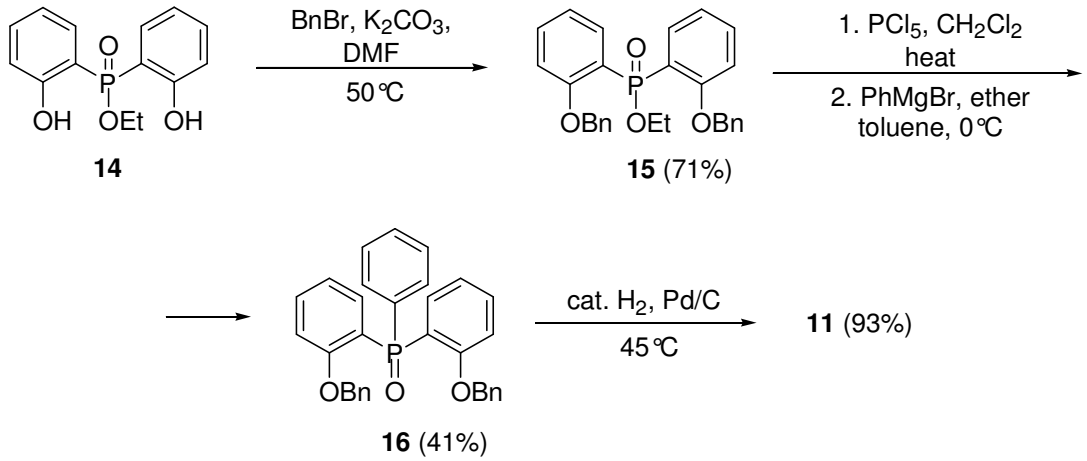
It was planned to prepare new crown ethers (*S*,*S*)-**7** and (*S*,*S*)-**8** by macrocyclization of the reported phenyl bis(2-hydroxyphenyl)phosphanone (**11**)[32] and the reported enantiopure dimethyl- and dioctyl-substituted tetra- and pentaethylene glycol ditosylates[33] [(*S*,*S*)-**12**, (*S*,*S*)-**13**] at 80 °C in DMF using K_2CO_3 as a base (see Scheme 2).



Scheme 2. Preparation of crown ethers containing a triphenylphosphanone unit.

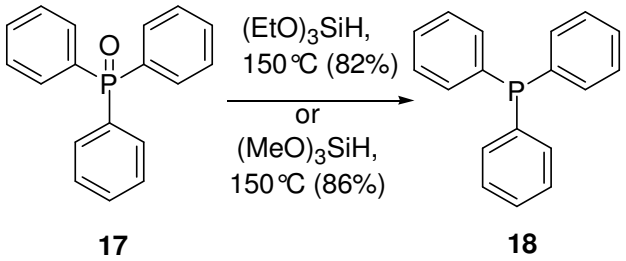
Although there is a reported procedure[32] for the preparation of phosphanone **11**, we could not reproduce it with acceptable yields, so we tried to find another way.

The free hydroxyl groups of the known ethyl bis(2-hydroxyphenyl)phosphinate (**14**)[34] were protected by *O*-benzylation using benzyl bromide and K_2CO_3. *O*-benzyl ethyl phosphinate **15** was obtained in 71% yield and transformed to triphenylphosphanone derivative **16** using the same method as described above for **5** and (*R*,*R*)-**6**. The benzyl protecting groups were removed by hydrogenolys in a very good yield (see Scheme 3).



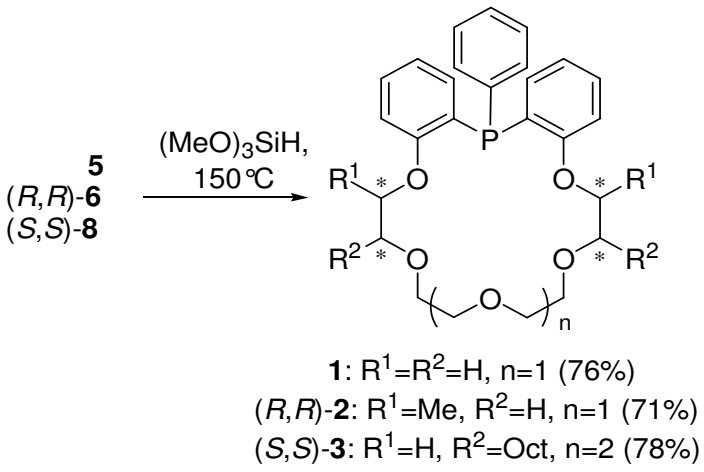
Scheme 3. Preparation of **11** bis(2-hydroxyphenyl)phenyl-λ^5-phosphanone.

There are numerous silane reducing agents for the preparation of phosphanes from phosphanones in the literature, but in most of those cases it is difficult to get the product from the reaction mixture, or to avoid using a solvent, such as benzene.[24,28,29] We tried to find an easy and simple way for the deoxygenation of phosphanones. First triphenylphosphanone (**17**) was used as a model compound to investigate the reduction. Triethoxysilane and trimethoxysilane were applied as the reducing agents in a sealed tube. The experiments showed that both reducing agents were effective, and the purification was easy in both cases. The silanes were both the reagent and the solvent, and after completion of the reaction the unreacted silanes were removed by simple evaporation under reduced pressure. Using trimethoxysilane we obtained a slightly better yield for **18** than applying triethoxysilane (see Scheme 4).



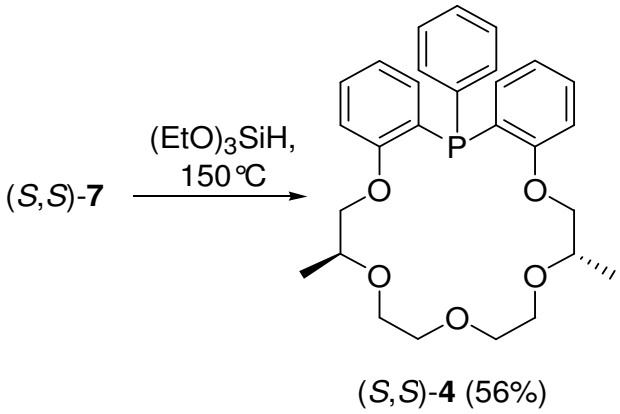
Scheme 4. Reduction of triphenylphosphanone to triphenylphosphane.

The reduction of the crown ethers containing the triarylphosphanone unit was carried out as well. Macrocycles **5**, (*R*,*R*)-**6** and (*S*,*S*)-**8** were deoxygenated using trimethoxysilane in good yields (see Scheme 5).



Scheme 5. Reduction of phosphanone-crown ethers using trimethoxysilane.

We wanted to know if the reduction procedure using triethoxysilane also works in the case of crown ethers. Macrocycle (*S*,*S*)-**7** was also deoxygenated using triethoxysilane (see Scheme 6). Thus we can say that both reducing agents are suitable for the reduction of phosphanone-crown ethers as well.



Scheme 6. Reduction of phosphanone crown ether (*S*,*S*)-**7** using triethoxysilane.

Although macrocycles **1** and **5** were prepared earlier, the reported yields were rather low and the compounds were not well characterized.[14]

In our hands, the compounds are fully characterized. We note here that in the MS spectra of the phosphanes **1**, (*R*,*R*)-**2**, (*S*,*S*)-**3** and (*S*,*S*)-**4** only the molecular peaks for the appropriate phosphanones could be found. The completion of the phosphanone-phosphane transformation was proved by ^{31}P-NMR (the difference of the concerning δ values was larger than 45), IR (the lack of the peaks for phosphanones in the spectra of phosphanes) and TLC analysis (big differences in R_f values).

Conclusions

The synthesis and characterization of achiral **1** and new enantiopure (*R*,*R*)-**2**, (*S*,*S*)-**3** and (*S*,*S*)-**4** crown ethers containing a triarylphosphane unit have been carried out successfully. The appropriate phosphanones were reduced to phosphanes applying trialkoxy silanes. As a reducing agent neat trimethoxysilane or triethoxysilane without any solvents and/or catalysts was used successfully. These macrocycles containing a triphenylphosphane unit are promising precursors of catalysts for transition metal catalytic reactions. We plan to study the metal ion complexing ability and homogeneous catalytic behavior of these crown ethers.

Experimental Section

General. Infrared spectra were recorded on a PerkinElmer Spectrum 400 FT-IR spectrometer, with Universal ATR Sampling Accessory, Composite Diamond/ZnSe Crystal. PerkinElmer Spectrum 6.3.2 software was used for data acquisition and qualitative analyses. Optical rotations were taken on a Perkin–Elmer 241 polarimeter that was calibrated by measuring the optical rotations of both enantiomers of menthol. ^{1}H-NMR spectra were taken either on a Bruker DRX-500 Avance spectrometer (500 MHz, reference: TMS) or on a Brucker 300 Avance spectrometer (300 MHz, reference: TMS) and it is indicated in each individual case. ^{13}C-NMR spectra were taken either on a Bruker DRX-500 Avance spectrometer (125.8 MHz, reference: TMS) or on a Brucker 300 Avance spectrometer (75.5 MHz, reference: TMS) and it is indicated in each individual case. ^{31}P-NMR spectra were recorded on a Brucker 300 Avance spectrometer (121.5 MHz, reference: H_3PO_4). HPLC-DAD-MS/MS experiments were performed on an Agilent 1200 HPLC system(G1379B degasser, G1312B binary gradient pump, G1367C autosampler, G1316B column thermostat and G1315C diode array detector) coupled with an Agilent 6410 triple quadrupole mass spectrometer equipped with an ESI ion source (Agilent Technologies, Waldbronn, Germany). Masshunter B.03.01 software was used for data acquisition and qualitative analyses. Chiral HPLC measurements were carried out on a Phenomenex, Lux Cellulose-2 column (5 µm, 250x6 mm). Elemental analyses were performed in the Microanalytical Laboratory of the Department of Organic Chemistry, Institute of Chemistry, L. Eötvös University, Budapest, Hungary. Starting materials were purchased from Sigma-Aldrich Corporation unless otherwise noted. Melting points were taken on a Boetius micro-melting point apparatus and were uncorrected. Silica gel 60 F_{254} (Merck) plates were used for TLC. Silica gel 60 (70–230 mesh, Merck) were used for column chromatography. Silica gel 60 F_{254} and aluminium oxide 150 F_{254} (Merck) plates were used for PLC (preparative layer chromatography). Ratios of solvents for the eluents are given in volumes (mL/mL). Solvents were dried and purified according to well-established[35] methods. Evaporations were carried out under reduced pressure unless otherwise stated.

Ethyl bis(2-benzyloxyphenyl)phosphinate (15). Ethyl bis(2-hydroxyphenyl)phosphinate (**14**)[34] (10.00 g, 37 mmol), benzyl bromide (10.77 mL, 90 mmol) and finely powdered anhydrous K_2CO_3 (49.67 g, 360 mmol) were mixed with vigorous stirring in dry DMF (330 mL) under Ar. The temperature of the reaction mixture was raised to 50 °C and kept stirring at this temperature until TLC analysis showed the total consumption of the starting materials (2 days). The solvent was removed at 40 °C and CH_2Cl_2 (400 mL) and water (300 mL) were added to the residue. The phases were shaken well and separated. The aqueous phase was extracted with CH_2Cl_2 (3x150 mL). The combined organic phase was dried over $MgSO_4$, filtered and the solvent was removed. The crude product was recrystallized from toluene to give **15** (11.63 g, 71%). mp 111-113 °C (from toluene). R_f: 0.36 (silica gel TLC, acetone-hexane 1:2). ^{1}H-NMR (500 MHz, $CDCl_3$) δ 1.33 (t, *J* 7 Hz, 3H, CH_3), 4.11 (m, 2H, OCH_2), 4.94 (s, 4H, Ar CH_2), 6.85-6.91 (m, 4H, ArH), 7.05-7.07 (m, 4H, ArH), 7.23-7.29 (m, 6H, ArH), 7.39-7.41 (m, 2H, ArH), 7.93-7.95 (m, 2H, ArH). ^{13}C-NMR (75 MHz, $CDCl_3$) δ 16.65 (d, *J* 6.75 Hz, CH_3), 60.55 (d, *J* 6 Hz, OCH_2), 70.09 (Ar CH_2), 112.01 (d, *J* 8.25 Hz, ArC), 120.61 (d, *J* 12 Hz, ArC), 120.81 (d, *J* 140.25 Hz, ArC), 127.41, 127.79, 128.40 (ArC), 133.54 (d, *J* 2.25 Hz, ArC), 135.42 (d, *J* 6 Hz, ArC), 136.48 (ArC), 160.05 (d, *J* 4.5 Hz, ArC). ^{31}P-NMR (121.5 MHz, $CDCl_3$): δ 26.23; MS: 459.2 $(M+H)^+$.

Bis(2-benzyloxyphenyl)phenyl-λ^5-phosphanone (16). To the solution of phosphinate **15** (10.00 g, 21.8 mmol) in dry CH_2Cl_2 (330 mL) PCl_5 (4.86 g, 23.3 mmol) was added under Ar. The mixture was stirred at reflux temperature for 3 hours and then at rt for 15 minutes. The solvent was removed and dry toluene (300 mL) and dry ether (100 mL) were added to the residue under Ar. The stirred mixture was cooled to 0 °C and PhMgBr (43.4 mmol, 29 mL, 1.5 M solution in ether) was added dropwise. After stirring the reaction mixture for 10 minutes at 0 °C the temperature was raised to rt and it was kept stirring for 2 hours. The mixture was poured into ice-water (500 mL) and CH_2Cl_2 (150 mL) was added. The phases were shaken well, separated, and the organic phase was shaken with water (2x150 mL), dried over $MgSO_4$, filtered and the solvent was removed. The crude product was purified by chromatography on silica gel using acetone–hexane mixtures (gradient elution with increasing polarity from 1:3 to 2:1) as eluents to give **16** (4.41 g, 41%) as a white solid. mp 192-194 °C (from acetone); R_f: 0.29 (silica gel TLC, acetone-hexane 1:2). ^{1}H-NMR (500 MHz, $CDCl_3$) δ 4.90 (s, 4H, Ar CH_2), 6.88-6.93 (m, 6H, ArH), 6.99-7.01 (m, 2H, ArH), 7.15-7.26 (m, 8H, ArH), 7.38-7.47 (m, 3H, ArH), 7.66-7.77 (m, 4H, ArH); ^{13}C-NMR (75 MHz, $CDCl_3$) δ 70.34 (Ar CH_2), 112.22 (d, *J* 6 Hz, ArC), 121.12 (d, *J* 12 Hz, ArC), 127.42, 127.83, 127.96, 128.43, 131.14 (ArC), 132.21 (d, *J* 10.5 Hz, ArC), 133.75 (ArC), 134.86 (d, *J* 8.25 Hz, ArC), 136.20, 160.24 (ArC). ^{31}P-NMR (121.5 MHz, $CDCl_3$): δ 25.35; MS: 491.2 $(M+H)^+$.

Bis(2-hydroxyphenyl)phenyl-λ^5-phosphanone (11). To Pd/C catalyst (10% Pd on charcoal, 1.20 g) methanol (10 mL) was added under Ar. The Ar protecting gas was exchanged by H_2 and the mixture was stirred under atmospheric H_2 for 10 minutes. The solution of **16** (4.01 g, 8.20 mmol) in methanol (150 mL) was added to the prehydrogenated catalyst and this mixture was stirred vigorously at 45 °C until the consumption of H_2 stopped. H_2 was exchanged by Ar and the mixture was filtered using a celite pad. The solvent was removed to obtain pure **11** (2.36 g,

93%). mp 236-237 °C (from methanol). MS: 311.1 $(M+H)^+$. Other physical and spectroscopic data were very similar to those of reported in the literature[32].

22-Phenyl-6,7,9,10,12,13,15,16-octahydro-22*H*-22λ^5-dibenzo[*n,q*][1,4,7,10,13,16]pentaoxaphosphacyclooctadecin-22-one (5). To the solution of the reported macrocycle **9**[15] (3.10 g, 7.1 mmol) in dry CH_2Cl_2 (100 mL) PCl_5 (1.63 g, 7.8 mmol) was added under Ar. The mixture was stirred at reflux temperature for 3 hours and then at rt for 15 minutes. The solvent was removed and dry toluene (100 mL) and dry ether (30 mL) were added to the residue under Ar. The stirred mixture was cooled to 0 °C and PhMgBr (15.0 mmol, 10 mL, 1.5 M solution in ether) was added dropwise. After stirring the reaction mixture for 10 minutes at 0 °C the temperature of it was raised to rt and stirring was continued for 24 hours. The mixture was poured into ice-water (150 mL) and CH_2Cl_2 (150 mL) was added to it. The phases were shaken well and separated. The aqueous phase was shaken with CH_2Cl_2 (3x50 mL). The combined organic phase was dried over $MgSO_4$, filtered and the solvent was removed. The crude product was purified by chromatography on silica gel using methanol–CH_2Cl_2 (1:30) as an eluent to give **5** (1.50 g, 45%) as a white solid. mp 173-175 °C (from methanol); R_f: 0.38 (silica gel TLC, methanol-CH_2Cl_2 1:20). IR (neat) ν_{max} 1166 cm^{-1} ν P=O; ^{1}H-NMR (500 MHz, $CDCl_3$) δ 3.22-3.54 (m, 12H, OCH_2), 4.00-4.02 (m, 2H, OCH_2), 4.20-4.24 (m, 2H, OCH_2), 7.00-7.05 (m, 4H, ArH), 7.43-7.48 (m, 5H, ArH), 7.69-7.73 (m, 2H, ArH), 8.04-8.08 (m, 2H, ArH). ^{13}C-NMR (75 MHz, $CDCl_3$) δ 66.52, 69.92, 70.81, 71.34 (OCH_2). 111.86 (d, *J* 6.6 Hz, ArC), 120.39 (d, *J* 12.2 Hz, ArC), 121.30 (d, *J* 107.5 Hz, ArC), 127.67 (d, *J* 12.9 Hz, ArC), 130.68, 130.71 (ArC), 132.21 (d, *J* 10.6 Hz, ArC). 133.09, 133.11, 134.25, 134.35 (ArC), 160.27 (d, *J* 2.9 Hz, ArC). ^{31}P-NMR (121.5 MHz, $CDCl_3$): δ 24.90. MS: 469.2 $(M+H)^+$. Anal Calcd for $C_{26}H_{29}O_6P$: C, 66.66; H, 6.24. Found: C, 66.55; H, 6.14.

(6*R*,16*R*)-6,16-Dimethyl-22-phenyl-6,7,9,10,12,13,15,16-octahydro-22*H*-22λ^5-dibenzo[*n,q*]-[1,4,7,10,13,16]pentaoxaphosphacyclooctadecin-22-one [(*R*,*R*)-6]. Macrocycle (*R*,*R*)-**6** was prepared from the reported crown ether (*R*,*R*)-**10**[15] (0.252 g, 0.54 mmol) in the same way as described above for **5**. The crude product was purified by PLC on silica gel using methanol–CH_2Cl_2 (1:30) as an eluent to give (*R*,*R*)-**6** (0.239 g, 89%) as a white solid. mp168-170 °C (from methanol). R_f: 0.36 (silica gel TLC, methanol-CH_2Cl_2 1:20); $[\alpha]_D^{34}$ -92.28 (c 2.57, CH_2Cl_2); IR (neat) ν_{max} 1163, 1181 cm^{-1} ν P=O. ^{1}H-NMR (300 MHz, $CDCl_3$) δ 1.01 (d, *J* 6.2 Hz, 3H, CH_3), 1.13 (d, *J* 6.3 Hz, 3H, CH_3), 2.57-2.66 (m, 1H, OCH, OCH_2), 3.01-3.03 (m, 2H, OCH, OCH_2), 3.10-3.15 (m, 1H, OCH, OCH_2), 3.23-3.30 (m, 2H, OCH, OCH_2), 3.39-3.62 (m, 6H, OCH, OCH_2), 4.47-4.60 (m, 2H, OCH, OCH_2), 6.83-6.91 (m, 1H, ArH), 6.97-7.05 (m, 3H, ArH), 7.18-7.25 (m, 1H, ArH), 7.35-7.48 (m, 5H, ArH), 7.98-8.04 (m, 3H, ArH). ^{13}C-NMR (75 MHz, $CDCl_3$) δ 16.76, 17.74 (CH_3), 70.68, 70.95, 71.21, 71.39, 71.67, 73.68, 73.77, 74.54 (OCH, OCH_2), 105.07 (ArC), 111.71 (d, *J* 6.8 Hz, ArC), 113.14 (d, *J* 6.3 Hz, ArC), 119.99 (d, *J* 12.8 Hz, ArC), 120.35 (d, *J* 11.9 Hz, ArC), 122.48 (d, *J* 108.3 Hz, ArC), 124.06 (d, *J* 108.9 Hz, ArC), 127.98 (d, *J* 12.4 Hz, ArC), 131.28 (d, *J* 2.7 Hz, ArC), 132.43 (d, *J* 10.0 Hz, ArC), 132.45, 132.82, (d, *J* 1.9 Hz, ArC), 132.93, (d, *J* 1.8 Hz, ArC), 133.80, (d, *J* 9.7 Hz, ArC), 133.89 (ArC), 134.49, (d, *J* 6.4 Hz, ArC), 158.35, (d, *J* 3.7 Hz, ArC), 160.33 (d, *J* 1.8 Hz, ArC). ^{31}P-NMR

(121.5 MHz, $CDCl_3$): δ 23.35; MS: 497.2 $(M+H)^+$. Anal Calcd for $C_{28}H_{33}O_6P$: C, 67.73; H, 6.70. Found: C, 67.48; H, 6.47.

(7*S*,15*S*)-7,15-Dimethyl-22-phenyl-6,7,9,10,12,13,15,16-octahydro-22*H*-22λ^5-dibenzo[*n,q*]-[1,4,7,10,13,16]pentaoxaphosphacyclooctadecin-22-one [(*S*,*S*)-7]. Triphenyl phosphanone **11** (0.58 g, 1.9 mmol), dimethyl-substituted tetraethylene glycol ditosylate (*S*,*S*)-**12**[33] (1.00 g, 1.9 mmol) and finely powdered anhydrous K_2CO_3 (2.88 g, 20.9 mmol) were mixed with vigorous stirring in dry DMF (40 mL) under Ar. The temperature of the reaction mixture was raised to 80 °C and kept stirring at this temperature until TLC analysis showed the total consumption of the starting materials (4 days). The solvent was removed at 40 °C, the residue was suspended in water (200 mL) and it was extracted with CH_2Cl_2 (4x100 mL). The combined organic phase was shaken with H_2O (50 mL), dried over $MgSO_4$, filtered and the solvent was removed. The crude product was purified by chromatography on silica gel using methanol–CH_2Cl_2 (1:30) as an eluent to give (*S*,*S*)-**7**. This product was triturated with diisopropyl ether to give a yellow solid (0.39 g, 41%). mp 136-138 °C (from methanol). R_f: 0.34 (silica gel TLC, ethyl acetate-hexane 1:1); $[\alpha]_D^{25}$ +56.1 (c 0.97, methanol); IR (neat) ν_{max} 1161 cm^{-1} ν P=O; ^{1}H-NMR (300 MHz, $CDCl_3$) δ 0.98-1.04 (m, 6H, CH_3), 2.79-2.81 (m, 1H, OCH, OCH_2), 3.09-3.16 (m, 2H, OCH, OCH_2), 3.21-3.24 (m, 1H, OCH, OCH_2), 3.33-3.35 (m, 1H, OCH, OCH_2), 3.40-3.51 (m, 4H, OCH, OCH_2), 3.57-3.59 (m, 1H, OCH, OCH_2), 3.68-3.71 (m, 1H, OCH, OCH_2), 3.78-3.81 (m, 1H, OCH, OCH_2), 3.93-3.96 (m, 1H, OCH, OCH_2), 4.12-4.15 (m, 1H, OCH, OCH_2), 6.94-7.06 (m, 4H, ArH), 7.42-7.47 (m, 6H, ArH), 7.75-7.79 (m, 1H, ArH), 7.98-8.02 (m, 2H, ArH). ^{13}C-NMR (75 MHz, $CDCl_3$) δ 17.13, 17.43 (CH_3), 69.68, 70.00, 71.32, 71.51, 72.05, 73.06, 75.18, 75.60 (OCH, OCH_2), 112.54 (d, *J* 6.75 Hz, ArC), 112.97 (d, *J* 6.4 Hz, ArC), 120.67 (d, *J* 4.7 Hz, ArC), 120.68 (d, *J* 17.4 Hz, ArC), 122.50 (d, *J* 198.1 Hz, ArC), 122.51 (d, *J* 16.4 Hz, ArC), 128.15 (d, *J* 12.75 Hz, ArC), 131.21 (ArC), 132.21 (d, *J* 10.3 Hz, ArC), 133.11, 133.32, 134.07, 134.17,134.64 (ArC), 160.65 (d, *J* 42.2 Hz, ArC). ^{31}P-NMR (121.5 MHz, $CDCl_3$): δ 24.01; MS: 497.2 $(M+H)^+$. Anal Calcd for $C_{28}H_{33}O_6P$: C, 67.73; H, 6.70. Found: C, 67.61; H, 6.77.

(7*S*,15*S*)-7,15-Dioctyl-22-phenyl-6,7,9,10,12,13,15,16,18,19-decahydro-25*H*-25λ^5-dibenzo-[*q,t*][1,4,7,10,13,16,19]hexaaoxaphosphacyclooctahenicosin-22-one [(*S*,*S*)-8]. Macrocycle (*S*,*S*)-**8** was prepared from the reported ditosylate (*S*,*S*)-**13**[33] (0.55 g, 0.76 mmol) and **11** (0.24 g, 0.76 mmol) in the same way as described above for (*S*,*S*)-**7**. The reaction was completed in 7 days. The crude product was purified by PLC on aluminium oxide using acetone–hexane (1:2) as an eluent to give (*S*,*S*)-**8** (0.241 g, 43%) as a colorless oil. R_f: 0.85 (aluminium oxide TLC, acetone-hexane 1:2); $[\alpha]_D^{34}$ +16.18 (c 1.36, CH_2Cl_2); IR (neat) ν_{max} 1163, 1188 cm^{-1} ν P=O; ^{1}H-NMR (300 MHz, $CDCl_3$) δ 0.90 (t, *J* 6.3 Hz, 6H, CH_3), 1.09-1.27 (m, 28H, CH_2), 2.52-6.13 (m, 1H, OCH, OCH_2), 2.84-2.92 (m, 1H, OCH, OCH_2), 3.13-3.25 (m, 2H, OCH, OCH_2), 3.36-3.67 (m, 8H, OCH, OCH_2), 3.77-3.84 (m, 2H, OCH, OCH_2), 3.89-4.00 (m, 2H, OCH, OCH_2), 6.91-7.03 (m, 3H, ArH), 7.03-7.11 (m, 1H, ArH), 7.21-7.26 (m, 1H, ArH), 7.42-7.54 (m, 5H, ArH), 7.91-8.02 (m, 3H, ArH); ^{13}C-NMR (75 MHz, $CDCl_3$) δ 14.15, 22.71, 25.11, 25.47, 29.33, 29.55, 29.63, 29.73, 29.75, 31.90, 31.91, 32.42, 32.97 (CH_2, CH_3), 70.19, 70.58, 70.61, 70. 83, 70.99, 71.06, 71.23, 72.28, 78.46, 78.68 (OCH, OCH_2), 112.46 (d, *J* 6.7 Hz, ArC), 112.76 (d, *J* 5.8 Hz,

ArC), 120.69 (d, *J* 12.7 Hz, ArC), 121.17 (d, *J* 12.3 Hz, ArC), 122.82 (d, *J* 23.4 Hz, ArC), 123.94 (d, *J* 68.2 Hz, ArC), 128.15 (d, *J* 12.3 Hz, ArC), 131.30, 131.33 (ArC), 131.93 (d, *J* 10.0 Hz, ArC), 133.08, 133.12, 133.14 (ArC), 133.64 (d, *J* 9.4 Hz, ArC), 134.06 (ArC), 134.07 (d, *J* 6.6 Hz, ArC), 159.68 (d, *J* 2.4 Hz, ArC), 160.99 (d, *J* 1.9 Hz, ArC). ^{31}P-NMR (121.5 MHz, $CDCl_3$): δ 22.75; MS: 737.5 $(M+H)^+$. Anal Calcd for $C_{44}H_{65}O_7P$: C, 71.71; H, 8.89. Found: C, 71.96; H, 9.02.

General procedure for the reduction of phosphanones to phosphanes. Triphenylphosphanone (**17**) (0.1 g, 0.36 mmol), and triethoxysilane (2.00 mL, 10.8 mmol) were mixed with vigorous stirring in a sealed tube under Ar. The temperature of the reaction mixture was raised to 150 °C and kept stirring at this temperature for 2 days. The solvent was removed at 40 °C and the crude product was purified by PLC on silica gel using hexane as an eluent to give triphenylphosphane **18** (0.082 g, 82%). $R_{f,\mathbf{13}}$: 0.20, $R_{f,\mathbf{14}}$: 0.92 (silica gel TLC, acetone-hexane 1:3). The product was pure according to TLC analysis, ^{1}H- and ^{31}P-NMR.

Triphenylphosphanone (**17**) (0.1 g, 0.36 mmol), and trimethoxysilane (2.00 mL, 15.7 mmol) were mixed with vigorous stirring in a sealed tube under Ar. The temperature of the reaction mixture was raised to 150 °C and kept stirring at this temperature for 2 days. The solvent was removed at 40 °C and the crude product was purified by PLC on silica gel using hexane as an eluent to give triphenylphosphane **18** (0.086 g, 86%). $R_{f,\mathbf{13}}$: 0.20, $R_{f,\mathbf{14}}$: 0.92 (silica gel TLC, acetone-hexane 1:3). The product was pure according to TLC analysis, ^{1}H- and ^{31}P-NMR.

22-Phenyl-6,7,9,10,12,13,15,16-octahydro-22*H*-dibenzo[*n,q*][1,4,7,10,13,16]pentaoxa-phosphacyclooctadecin (1). Macrocycle **1** was prepared from phosphanone **5** (0.16 g, 0.35 mmol) and trimethoxysilane (2 mL, 15.7 mmol) in the same way as described above for **18**. The reaction was completed in 4 days. The solvent was removed at 30 °C and the crude product was purified by PLC on silica gel using methanol-CH_2Cl_2 (1:40) as an eluent to give **1** (0.119 g, 76%) as a white solid. mp112-114 °C (from methanol). R_f: 0.55 (silica gel TLC, methanol-CH_2Cl_2 1:30). IR (neat) no peak at 1166±30 cm^{-1} for ν P=O. ^{1}H-NMR (300 MHz, $CDCl_3$) δ 3.66-3.85 (m, 12H, OCH_2), 4.04-4.18 (m, 4H, OCH_2), 6.69-6.72 (m, 2H, ArH), 6.83-6.91 (m, 4H, ArH), 7.28-7.34 (m, 7H, ArH). ^{13}C-NMR (75 MHz, $CDCl_3$) δ 68.89, 69.73, 70.73, 70.76, 71.88, 71.92 (OCH_2), 111.01 (d, *J* 1.1 Hz, ArC), 111.15, 121.03, 125.94 (ArC), 126.03 (d, *J*14.2 Hz, ArC), 128.30 (d, *J* 7.2 Hz, ArC), 128.50, 129.89, 133.69 (ArC), 134.34 (d, *J* 21.5 Hz, ArC), 136.75 (d, *J* 12.9 Hz, ArC), 160.59 (d, *J* 16.9 Hz, ArC). ^{31}P-NMR (121.5 MHz, $CDCl_3$): δ -28.33; Anal Calcd for $C_{26}H_{29}O_5P$: C, 69.01; H, 6.46. Found: C, 68.93. H, 6.14.

(6*R*,16*R*)-6,16-Dimethyl-22-phenyl-6,7,9,10,12,13,15,16-octahydro-22*H*-dibenzo[*n,q*]-[1,4,7,10,13,16]pentaoxaphosphacyclooctadecin [(*R,R*)-2]. Macrocycle (*R*,*R*)-**2** was prepared from phosphanone (*R*,*R*)-**6** (0.11 g, 0.23 mmol) and trimethoxysilane (2 mL, 15.7 mmol) in the same way as described above for **18**. The reaction was completed in 4 days. The solvent was removed at 30 °C and the crude product was purified by PLC on silica gel using methanol-CH_2Cl_2 (1:40) as an eluent to give (*R*,*R*)-**2** (0.0973 g, 71%) as a colorless oil. R_f: 0.62 (silica gel TLC, methanol-CH_2Cl_2 1:30). $[\alpha]_D^{29}$ -194.2 (c 0.97, CH_2Cl_2); IR (neat) no peaks between 1130-

1234 cm^{-1} for ν P=O. ^{1}H-NMR (300 MHz, $CDCl_3$) δ 0.91 (d, *J* = 6.2 Hz, 3H, CH_3), 1.13 (d, *J* = 6.2 Hz, 3H, CH_3), 3.44-3.85 (m, 12H, OCH, OCH_2), 4.53-4.66 (m, 2H, OCH, OCH_2), 6.72-6.94 (m, 6H, ArH), 7.26-7.40 (m, 7H, ArH). ^{13}C-NMR (75 MHz, $CDCl_3$) δ 15.54, 16.16 (CH_3), 70.50, 70.52, 70.73, 70.75, 71.07, 71.10, 72.06, 72.10, 73.62, 73.63, 73.79, 73.80, 74.25, 74.93 (OCH, OCH_2), 111.79 (d, *J* 1.7 Hz, ArC), 112.17 (d, *J* 1.2 Hz, ArC), 120.24 (ArC), 120.98 (d, *J* 1.2 Hz, ArC), 125.87 (d, *J* 10.9 Hz, ArC), 126.80 (d, *J* 12.7 Hz, ArC), 128.20 (d, *J* 7.5 Hz, ArC), 128.51 (ArC), 129.68 (d, *J* 6.0 Hz, ArC), 133.42, 134.47, 134.49, 134.53 (ArC), 134.65 (d, *J* 21.4 Hz, ArC), 136.46 (d, *J* 10.5 Hz, ArC), 159.25 (d, *J* 13.1 Hz, ArC), 159.45 (d, *J* 15.5 Hz, ArC). ^{31}P-NMR (121.5 MHz, $CDCl_3$): δ -24.03. Anal Calcd for $C_{28}H_{33}O_5P$: C, 69.98, H, 6.92. Found: C, 69.88, H, 6.96.

(7*S*,15*S*)-7,15-Dioctyl-22-phenyl-6,7,9,10,12,13,15,16,18,19-decahydro-25*H*-dibenzo[*q*,*t*]-[1,4,7,10,13,16,19]hexaaoxaphosphacyclooctahenicosin [(*S*,*S*)-3]. Macrocycle (*S*,*S*)-**3** was prepared from phosphanone (*S*,*S*)-**8** (0.10 g, 0.15 mmol) and trimethoxysilane (2 mL, 15.7 mmol) in the same way as described above for **18**. The reaction was completed in 4 days. The solvent was removed at 30 °C and the crude product was purified by PLC on silica gel using methanol-CH_2Cl_2 (1:60) as an eluent to give (*S*,*S*)-**3** (0.0779 g, 78%) as a colorless oil. R_f: 0.88 (silica gel TLC, methanol-CH_2Cl_2 1:30). $[\alpha]_D^{29}$ +73.2 (c 1.11, CH_2Cl_2); IR (neat) no peaks between 1131-1239 cm^{-1} for ν P=O. ^{1}H-NMR (300 MHz, $CDCl_3$) δ 0.91 (t, *J* 6.6 Hz, 6H, CH_3), 1.20-1.45 (m, 28H, CH_2), 3.22-3.29 (m, 1H, OCH, OCH_2), 3.45-3.52 (m, 2H, OCH, OCH_2), 3.60-3.70 (m, 10H, OCH, OCH_2), 3.78-4.05 (m, 5H, OCH, OCH_2), 6.60-6.63 (m, 1H, ArH), 6.77-6.87 (m, 5H, ArH), 7.31-7.34 (m, 7H, ArH); ^{13}C-NMR (75 MHz, $CDCl_3$) δ 14.17 (CH_3), 22.73, 25.22, 25.65, 29.34, 29.60, 29.63, 29.67, 31.86, 31.93, 32.23 (CH_2), 70.32, 70.37, 70.50, 70.56, 71.30, 71.40, 71.88, 71.92, 78.67, 78.71 (OCH, OCH_2), 110.58 (d, *J* 13.1 Hz, ArC), 110.56, 115.55 (ArC), 120.89 (d, *J* 34.9 Hz, ArC), 125.24 (d, *J* 12.9 Hz, ArC), 125.91 (d, *J* 14.7 Hz, ArC), 128.30 (d, *J* 7.4 Hz, ArC), 128.64 (ArC), 129.85 (d, *J* 5.1 Hz, ArC), 133.22, 133.72, 133.73 (ArC), 134.51 (d, *J* 21.6 Hz, ArC), 136.43 (d, *J* 11.7 Hz, ArC), 160.37 (d, *J* 4.5 Hz, ArC), 160.58 (d, *J* 3.3 Hz, ArC). ^{31}P-NMR (121.5 MHz, $CDCl_3$): δ -24.99; Anal Calcd for $C_{44}H_{65}O_6P$: C, 73.30; H, 9.09. Found: C, 73.12; H, 8.97.

(7*S*,15*S*)-7,15-Dimethyl-22-phenyl-6,7,9,10,12,13,15,16-octahydro-22*H*-dibenzo[*n*,*q*]-[1,4,7,10,13,16]pentaoxaphosphacyclooctadecin [(*S*,*S*)-4]. Macrocycle (*S*,*S*)-**4** was prepared from phosphanone (*S*,*S*)-**7** (0.10 g, 0.20 mmol) and triethoxysilane (2 mL, 10.8 mmol) in the same way as described above for **18**. The reaction was completed in 4 days. The crude product was purified by PLC on silica gel using methanol-CH_2Cl_2 (1:40) as an eluent to give (*S*,*S*)-**4** (0.054 g, 56%) as a yellow oil. R_f: 0.62 (silica gel TLC, ethyl acetate-hexane 1:1); $[\alpha]_D^{25}$ +111.18 (c 0.85, CH_2Cl_2); IR (neat) no significant peaks between 1130-1236 cm^{-1} for ν P=O. ^{1}H-NMR (300 MHz, $CDCl_3$) δ 1.06 (d, *J* 6.4 Hz, 3H, CH_3), 1.11 (d, *J* 6.4 Hz, 3H, CH_3), 3.49-4.04 (m, 3H, OCH, OCH_2), 4.14-4.19 (m, 1H, OCH, OCH_2), 6.61-6.65 (m, 1H, ArH), 6.77-6.88 (m, 5H, ArH), 7.31-7.35 (m, 7H, ArH). ^{13}C-NMR (75 MHz, $CDCl_3$) δ 17.08, 17.72 (CH_3), 70.26, 70.27, 70.30, 70.33, 73.04, 74.02, 74.64, 74.88 (OCH, OCH_2), 110.91 (d, *J* 1.2 Hz, ArC), 111.06 (d, *J* 1.7 Hz, ArC), 121.09 (d, *J* 33.0 Hz, ArC), 125.77 (d, *J* 13.2 Hz, ArC), 126.36 (d, *J* 14.7 Hz, ArC),

128.43 (d, *J* 7.4 Hz, ArC), 128.70 (ArC), 130.00 (d, *J* 4.1 Hz, ArC), 133.25, 134.04, 134.44, 134.72 (ArC), 136.83 (d, *J* 12.5 Hz, ArC), 160.59 (d, *J* 1.4 Hz, ArC), 160.81 (d, *J* 2.8 Hz, ArC). ^{31}P-NMR (121.5 MHz, $CDCl_3$): δ -26.99. Anal Calcd for $C_{28}H_{33}O_5P$: C, 69.98, H, 6.92. Found: C, 69.79, H, 6.81.

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References

1. Reppe, W.; Schweckendiek, W. J. *Justus Liebigs Annalen der Chemie* **1948**, *560*, 104. http://dx.doi.org/10.1002/jlac.19485600104
2. Young, J. F.; Osborn, J. A.; Jardine, F. H.; Wilkinson, G. *Chem. Comm. (London)* **1965**, 131.
3. Dang, T. P.; Kagan, H. B. *J. Chem. Soc. D: Chem. Comm.* **1971**, 481.
4. Ohta, T.; Takaya, H.; Kitamura, M.; Nagai, K.; Noyori, R. *J. Org. Chem.* **1987**, *52*, 3174. http://dx.doi.org/10.1021/jo00390a043
5. Noyori, R.; Ohkuma, T.; Kitamura, M.; Takaya, H.; Sayo, N.; Kumobayashi, H.; Akutagawa, S. *J. Am. Chem. Soc.* **1987**, *109*, 5856. http://dx.doi.org/10.1021/ja00253a051
6. Kitamura, M.; Ohkuma, T.; Inoue, S.; Sayo, N.; Kumobayashi, H.; Akutagawa, S.; Ohta, T.; Takaya, H.; Noyori, R. *J. Am. Chem. Soc.* **1988**, *110*, 629. http://dx.doi.org/10.1021/ja00210a070
7. Boezio, A. A.; Pytkowicz, J.; Cote, A.; Charette, A. B. *J. Am. Chem. Soc.* **2003**, *125*, 14260. http://dx.doi.org/10.1021/ja038291+
8. Brauer, David J.; Kottsieper, Konstantin W.; Roßenbach, S.; Stelzer, O. *Eur. J. Inorg. Chem.* **2003**, 1748. http://dx.doi.org/10.1002/ejic.200200388
9. Brunner, H.; Zettlmeier, W. *Handbook of Enantioselective Catalysis with Transition Metal Compounds*; VCH: Weinheim **1993**.
10. Botteghi, C.; Marchetti, M.; Paganelli, S. in *Transition Metals for Organic Synthesis*; Beller M.; Bolm C. Eds.; Wiley-VCH: Weinheim **1998**, pp 25-48.
11. Kollar, L.; Keglevich, G. *Chem. Rev.* **2010**, *110*, 4257. http://dx.doi.org/10.1021/cr900364c
12. DelDonno, T. A.; Rosen, W. *J. Am. Chem. Soc.* **1977**, *99*, 8051.

http://dx.doi.org/10.1021/ja00466a048
13. Ciampolini, M.; Dapporto, P.; Nardi, N.; Zanobini, F. *J. Chem. Soc.: Chem. Comm.* **1980**, 177.
14. Van Zon, A.; Torny, G. J.; Frijns, J. H. G. *Recl. Trav. Chim. Pays-Bas* **1983**, *102*, 326. http://dx.doi.org/10.1002/recl.19831020609
15. Huszthy, P.; Farkas, V.; Tóth, T.; Székely, G.; Hollósi, M. *Tetrahedron* **2008**, *64*, 10107. http://dx.doi.org/10.1016/j.tet.2008.07.111
16. Maier, L. *Organic Phosphorus Compounds*; Wiley: New York, 1972.
17. Engel, R. in *Handbook of Organophosphorus Chemistry*; Engel, R. Ed. Marcel Dekker, New York. **1992**, p 193.
18. Fritzsche, H.; Hasserodt, U.; Korte, F. *Chemische Berichte* **1964**, *97*, 1988. http://dx.doi.org/10.1002/cber.19640970729
19. Fritzsche, H.; Hasserodt, U.; Korte, F. *Chemische Berichte* **1965**, *98*, 171. http://dx.doi.org/10.1002/cber.19650980122
20. Myers, D. K.; Quin, L. D. *J. Org. Chem.* **1971**, *36*, 1285. http://dx.doi.org/10.1021/jo00808a025
21. Quin, L. D.; Caster, K. C.; Kisalus, J. C.; Mesch, K. A. *J. Am. Chem. Soc.* **1984**, *106*, 7021. http://dx.doi.org/10.1021/jo00808a025
22. Quin, L. D.; Szewczyk, J. *Phosphorous and Sulfur and the Related Elements* **1984**, *21*, 161. http://dx.doi.org/10.1080/03086648408077652
23. Coumbe, T.; Lawrence, N. J.; Muhammad, F. *Tetrahedron Letters* **1994**, *35*, 625. http://dx.doi.org/10.1016/S0040-4039(00)75855-2
24. Montel, S.; Jia, T.; Walsh, P. J. *Org. Lett.* **2014**, *16*, 130. http://dx.doi.org/10.1021/ol403124g
25. Trudeau, S.; Morken, J. P. *Tetrahedron* **2006**, *62*, 11470. http://dx.doi.org/10.1016/j.tet.2006.05.043
26. Snieckus, V.; Demchuk, O.; Yoruk, B.; Blackburn, T. *Synlett* **2006**, 2908.
27. Vandyck, K.; Matthys, B.; Willen, M.; Robeyns, K.; Van Meervelt, L.; Van der Eycken, J. *Org. Lett.* **2006**, *8*, 363. http://dx.doi.org/10.1021/ol0522788
28. Odinets, I. L.; Vinogradova, N. M.; Matveeva, E. V.; Golovanov, D. D.; Lyssenko, K. A.; Keglevich, G.; Kollár, L.; Roëschenthaler, G.-V.; Mastryukova, T. A. *J. Organometall. Chem.* **2005**, *690*, 2559. http://dx.doi.org/10.1016/j.jorganchem.2004.09.030
29. Ngo, H. L.; Lin, W. *J. Org. Chem.* **2005**, *70*, 1177. http://dx.doi.org/10.1021/jo048333s
30. Hatano, M.; Horibe, T.; Ishihara, K. *Angew. Chem. Int. Ed. Engl.* **2013**, *52*, 4549. http://dx.doi.org/10.1002/anie.201300938
31. Keglevich, G.; Kovács, A.; Tőke, L.; Újszászy, K.; Argay, G.; Czugler, M.; Kálmán, A. *Heteroatom Chem.* **1993**, *4*, 329.

http://dx.doi.org/10.1002/hc.520040405
32. Tanke, R. S.; Holt, E. M.; Crabtree, R. H. *Inorg. Chem.* **1991**, *30*, 1714. http://dx.doi.org/10.1021/ic00008a009
33. Székely, G.; Csordás, B.; Farkas, V.; Kupai, J.; Pogány, P.; Sánta, Z.; Szakács, Z.; Tóth, T.; Hollósi, M.; Nyitrai, J.; Huszthy, P. *Eur. J. Org. Chem.* **2012**, 3396. http://dx.doi.org/10.1002/ejoc.201101769
34. Dhawan, B.; Redmore, D. *J. Org. Chem.* **1986**, *51*, 179. http://dx.doi.org/10.1021/jo00352a010
35. Riddick, J. A.; Bunger, W. B.; Sakano, T. K. *Organic Solvents: Physical Properties and Methods of Purification*; Wiley-Interscience: New York, 1986.

