60. Ditopic Ligands. The Synthesis of a Series of Phosphine-Functionalised Macrocycles

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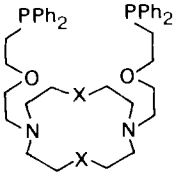
The synthesis of a series of phosphine-functionalised macrocycles, **1–6**, is described. The combination of N- and O-sites with P- and S-sites provides ligands which may bind transition or non-transition metal ions; as a consequence, they give access to dinuclear complexes containing both a *Lewis* acid and a redox metallic site. Compounds **1**,**2** and **6** are heterodinucleating ligands capable of binding two dissimilar metals in proximity. Macrocycles **3–5** are homotopic ligands which may form homodinuclear complexes of transition metals.

Introduction. – Dinucleating macrocycles may be formed by linking together two chelating acyclic sub-units [1–3] or by functionalising a macrocyclic framework by attachment of two or more side chains [4]. Whereas the former may be symmetric or dissymetric, the latter are dissymetric by construction. In both types of ligand, metals may be held in proximity so that they may behave independently or cooperatively. The functionalised macrocyclic systems not only may exhibit the characteristics of mononuclear complexes (*e.g.* catalysis, recognition), but also afford an entry into the study of higher forms of molecular behaviour such as cooperativity and regulation.

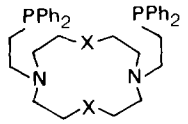
There is a rich coordination chemistry of macrocyclic ligands, and the nature of the metals which may be complexed is determined by the nature, by the number, and by the arrangement of binding heteroatoms. Similarly, there is a very well-defined chemistry of metal-phosphine complexes, and many important catalytic processes depend upon their unique reactivity. Functionalisation of macrocycles with phosphine binding sites combines the features of both classes of substances and defines a versatile series of homo- and heterodinucleating ligands. Such heterotopic ligands may exhibit site selectivity in metal binding [5]: a 'hard' metal ion will preferentially bind to a 'hard' donor site such as a polyoxapolyazamacrocycle, while 'soft' metal ions will prefer phosphine binding sites.

We have studied a series of phosphine-functionalised macrocycles based either on 12-membered $[N_2O_2]$, $[N_2S_2]$, or $[NO_3]$ monocycles or on an 18-membered $[N_2O_4]$ cycle. Their synthesis is reported here. Some of the complexation properties of ligands **1–4** have been described earlier [4].

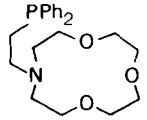
Design of the Macrocyclic Phosphines. – In ligands **1** and **2**, the attachment of the two side chains to the 12-membered macrocycle yields dinucleating ligands capable of binding metals both within the macrocyclic cavity and between the functionalised side arms. A 12-membered ring is chosen so that the metal 'sits' on top of the ring rather than within the macrocycle, and the lateral ether O-atoms provide secondary binding sites so that the bound metal is held close to the P_2 binding site, rather than away from it, as in represen-



1 X=O
2 X=S



3 X=O
4 X=S



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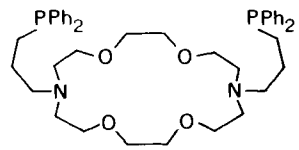

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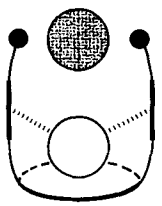
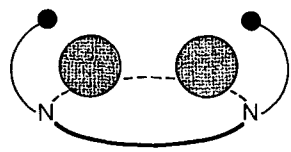


A



B

tation **A**. The 12-[N_2S_2] and 12-[N_2O_2] macrocycles bind quite strongly to Cu^{2+}, Zn^{2+}, Ag^+, and Ni^{2+}[6] [7], and the 12-[N_2O_2] macrocycle with two hydroxyethyl side chains is known to bind strongly to Ca^{2+} [8].

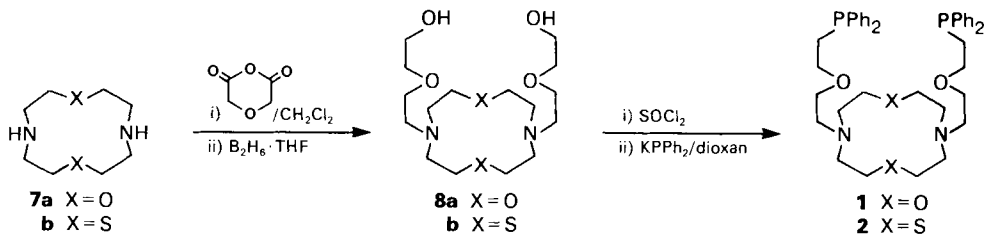
The two P-atoms in **1** and **2** may bind to a metal to give *cis*- or *trans*-constitutional isomers. *trans*-Diphosphine complexes are well established with ligands in which the two P-atoms are well separated [9] and in systems in which the P-atoms are geometrically constrained to span *trans*-positions [10]. Ligands **1** and **2** should, therefore, permit the formation of heterodinuclear metal complexes *via* a two-step sequence. The macrocycle **1** is better suited for this purpose as the [N_2O_2] and P_2 binding sites are clearly dissimilar.

With ligands **3**, **4**, and **5**, a metal may simultaneously bind to the tertiary N-atom and to a P-atom to give a 5- or 6-membered [NP] chelate ring system. Complexes containing small [4] [11] and large ring [12] [NP] chelates are well established with square-planar d^8 systems. The two NP binding units in **5** are sufficiently well separated to permit formation of homodinuclear complexes in which the two metals may either be held on opposite sides or on the same side of the macrocycle as in representation **B**. Ligand **6** may also form a 5-ring chelate with square-planar d^8-metal ions, and the macrocycle O-atoms are still available for weak binding to a hard cation such as Li^+. Alternatively, it may form 1:2 complexes with 2 phosphines binding *trans* or *cis* to a metal, leaving the 12-[NO_3] ring available for coordinating a 'hard' cation either separately or cooperatively.

Synthesis of the Macrocycles 1–6. – All the phosphines were prepared *via* routes formally involving the functionalisation of the secondary N-sites in the parent [N_2O_2], [N_2S_2], [N_2O_4], or [NO_3] monocycles. In each case the diphenylphosphine groups were introduced by reacting potassium diphenylphosphide with the appropriate alkyl chloride in dioxan [13].

Macrocycles **1** *and* **2** were prepared *via* identical routes as shown in *Scheme 1*. Reaction of 1,7-dioxa-4,10-diazacyclododecane (**7a**) with 3-oxaglutaric anhydride followed by reduction with diborane in tetrahydrofuran (THF) gave the diol **8a** in 91%

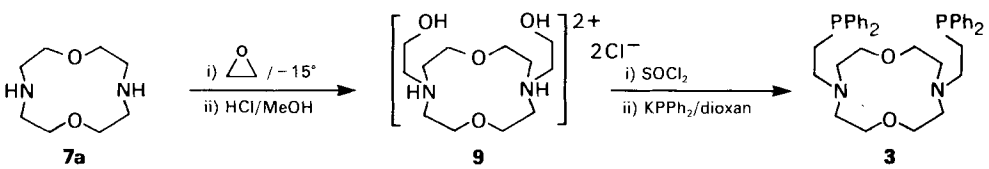
Scheme 1



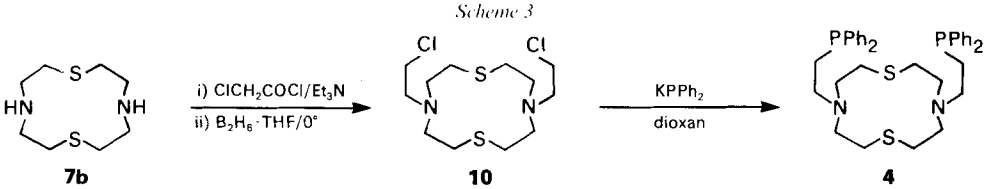
yield. Treatment of **8a** with $SOCl_2$ gave the corresponding dichloride (see **16**, *Exper. Part*) as the dihydrochloride salt. The free amine is unstable in solution at room temperature and was liberated just prior to reaction with diphenylphosphide. The pure phosphine **1** was obtained in 45% yield after recrystallisation from MeOH. The corresponding $[N_2S_2]$-based phosphine **2** was similarly obtained in 65% overall yield from the parent macrocycle **7b**.

Macrocycles **3** *and* **4**. Condensation of **7a** with ethylene oxide afforded the diol **9** which was converted to the corresponding dichloride by reaction with $SOCl_2$ at 0°. The dichloride was isolated as the stable dihydrochloride salt, and the freshly liberated amine reacted with $KPPh_2$ in dioxan at room temperature to give the diphosphine **3** in 44% yield *(Scheme 2)*. The analogous cycle **4** was obtained *via* a different route *(Scheme 3)*.

Scheme 2



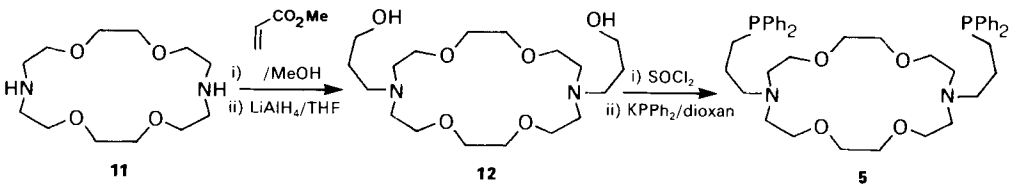
Scheme 3



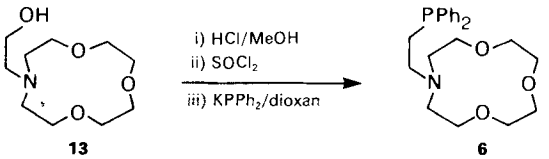
Reaction of **7b** with chloroacetyl chloride in the presence of Et_3N afforded a bis(amide) (see **19**, *Exper. Part*) in 90% yield. The amide groups were selectively reduced using diborane in THF at 0° to yield the dichloride **10** in 62% yield. Treatment of **10** with $KPPh_2$ in dioxan gave the diphosphine **4** in 63% yield.

Macrocyles **5** *and* **6**. The addition of an excess methyl acrylate to the 18-$[N_2O_4]$ macrocycle **11** gave an oily diester (see **20**, *Exper. Part*) in 67% yield. Reduction of the ester groups with $LiAlH_4$ in THF afforded the diol **12** which was converted as above into the diphosphine **5** *(Scheme 4)*. Similarly the ethanol derivative **13** was converted to the monophosphine **6** *(Scheme 5)*.

Scheme 4



Scheme 5



Ligands **1–6** define a series of ditopic macrocycles which may bind two metals in close proximity. It has been shown that **1** and **2** form well defined heterodinuclear complexes [4] in which prior coordination of a cation within the macrocyclic cavity *regulates* the ligand structure aiding coordination of the second metal. The metals may be introduced in a stepwise manner, reacting the P_2 binding site with a d^8-metal ion either prior or subsequent to coordination of a 'hard' cation within the macrocyclic cavity.

Ligands **3–6** have been shown to form [NP] chelate complexes with square planar d^8-metal centres, and with **3** and **5** homodinuclear complexes of Pd(II), Pt(II) and Rh(I) may be isolated. These features and other binding properties of **1–6** will be reported later.

We thank *SERC*, the *Royal Society*, the *British Council*, and the *CNRS* for support.

Experimental Part

1. *General.* Reactions were carried out under Ar, and solvents were distilled prior to use from an appropriate drying agent. M.p.: *Reichert-Kofler* block; uncorrected. ^{1}H-NMR and ^{31}P-NMR: *Bruker WP 200* or *Bruker WH 360*. ^{13}C-NMR: *Varian XL 100* or *Bruker WP 200*. Chemical shifts are given in ppm relative to tetramethylsilane (TMS) or 85% phosphoric acid. MS: *LK-B9000S*, *Thomson-THW-200*, and *VG-7070E* spectrometers. Microanalyses were performed either by the 'Service Central de Microanalyse du *CNRS*' or by Mrs. *M. Cocks*, University of Durham.

2. *1,7-Dioxa-4,10-diazacyclododecane-4,10-bis(γ-oxapentanol)* (**8a**). To a soln. of 1,7-dioxa-4,10-diazacyclododecane (**7a**; 840 mg, 482 mmol) in CH_2Cl_2 (25 ml) was added a soln. of 3-oxaglutaric anhydride (= 1,4-dioxane-2,6-dione; 1.12 g, 9.65 mmol) in CH_2Cl_2 (10 ml), and the mixture was refluxed for 3 h. After evaporation, a 1.0M soln. of B_2H_6 in THF (30 ml) was carefully added at 0° and the mixture refluxed for 6 h. After cooling to 0°, MeOH (10 ml) was cautiously added, and solvents were evaporated. To the residue was added 6M HCl (30 ml). The soln. was refluxed for 3 h and then evaporated. The crude **7a**·2 HCl was dissolved in H_2O (20 ml) and passed over a column of *Dowex 1 × 8* in the basic form. Removal of H_2O gave **8a** as colourless oil (1.46 g, 91%). ^{1}H-NMR ($CDCl_3$): 2.70 (2*t*, 6 CH_2N); 3.56 (*m*, 8 CH_2O); 3.71 (*t*, 2 CH_2OH); 5.25 (br.*s*, 2 OH). ^{13}C-NMR ($CDCl_3$): 72.7, 69.3, 68.9 (CH_2O); 61.4 (CH_2OH); 57.5, 55.7 (CH_2N). CI-MS(NH_3): 351 ($M^+ + 1$), 307, 263, 162, 144, 100. Anal. calc. for $C_{16}H_{34}N_2O_6$ (350.4): C 54.8, H 9.70, N 7.99; found: C 55.0, H 9,83, N 7.61.

3. *4,10-Bis(5-chloro-3-oxapentyl)-1,7-dioxa-4,10-diazacyclododecane* (**16**). To a soln. of **8a** (488 mg, 1.39 mmol) in MeOH (25 ml) was added 26M HCl (2 ml), and the soln. was evaporated to dryness. To the residue was

added freshly distilled $SOCl_2$ (15 ml) and the mixture stirred for 16 h. After removal of $SOCl_2$ under reduced pressure, the residue was twice entrained with abs. EtOH (2 × 10 ml), then redissolved in H_2O (20 ml), washed with CH_2Cl_2 (2 × 20 ml), basified with excess Me_4NOH, and the aq. phase extracted with CH_2Cl_2 (4 × 20 ml). After drying over $MgSO_4$, the solvent was evaporated to yield **16** as a viscous pale yellow oil (557 mg, 90%) which was not stable and was stored as **16**·2 HCl. ^{1}H-NMR ($CDCl_3$): 2.76 (*m*, 6 CH_2N); 3.45 (*m*, 20 H, CH_2O, CH_2Cl). ^{13}C-NMR (**16**·2 HCl, CD_3OD): 73.3, 66.8, 66.6 (CH_2O); 59.7, 57.2 (CH_2N); 44.9 (CH_2Cl). MS (**16**·2 HCl): 388 (M^+ + 1), 307, 293, 180, 150, 100. Anal. calc. for $C_{16}H_{32}Cl_2N_2O_4$ (387.3): C 49.6, H 8.26, N 7.23; found: C 50.0, H 8.48, N 7.51.

4. *[5,5'-(1,7-Dioxa-4,10-diazacyclododecane-4,10-diyl)bis(3-oxapentyl)]bis(diphenylphosphine)* (= 4,10-bis[5-(diphenylphosphino)-3-oxapentyl]-1,7-dioxa-4,10-diazacyclododecane; **1**). K (196 mg, 5.01 mmol) and Na (40 mg) were melted together in a *Schlenk* tube under dry Ar. A soln. of PPh_3 (650 mg, 2.48 mmol) in dioxan (12 ml) was added by steel cannula and the mixture stirred vigorously for 2 h. To the resultant bright orange suspension was added freshly liberated free amine **16** (480 mg, 1.24 mmol) in toluene (10 ml) at −78°, and the mixture was allowed to return to r.t. and stirred for a further 15 min. After filtering through a short pad of *Celite*, the solvents were removed *in vacuo* to yield a pale orange oil which was triturated with MeOH at −78° to give **1** as a white precipitate which was filtered and dried under vacuum (384 mg, 45%), m.p. 78–79°. ^{1}H-NMR ($CDCl_3$): 7.50–7.32 (*m*, 20 arom. H); 3.55 (*t*, 4 CH_2O, ring); 3.46 (*t*, 2 CH_2O); 3.52 (*m*, 2 CH_2O); 2.67 (*t*, 4 CH_2N); 2.64 (*t*, 2 CH_2N); 2.39 (*t*, 2 CH_2P). ^{31}P-NMR ($(CD_3)_2CO$): – 19.8. MS: 686 (M^+), 447, 333, 329, 315, 291. Anal. calc. for $C_{40}H_{52}N_2O_4P_2$ (686.8): C 69.9, H 7.63, N 4.08, P 9.02; found: C 69.9, H 7.70, N 4.20, P 9.10.

5. *1,7-Dithia-4,10-diazacyclododecane-4,10-bis(γ-oxapentanol)* (**8b**). To a soln. of 1,7-dithia-4,10-diazacyclododecane (**7b**; 524 mg, 4.0 mmol) in CH_2Cl_2 (20 ml) was added a soln. of 3-oxaglutaric anhydride (928 mg, 0.8 mmol) in CH_2Cl_2 (10 ml), and the mixture was refluxed for 3 h. After reducing the volume (10 ml), a 1.1M soln. of B_2H_6 in THF (30 ml) was added at 0° and the mixture stirred for 48 h at 40°. Excess borane was destroyed by careful addition of MeOH at 5° (10 ml), and solvents were evaporated. The residue was treated with 6M HCl (30 ml), refluxed for 3 h, and evaporated to dryness. After entraining with MeOH (4 × 15 ml), the soln. was allowed to stand at 4° when the salt **8b**·2 HCl crystallised slowly, m.p. 207–208°. The free amine was liberated by addition of excess Me_4NOH, followed by extraction with CH_2Cl_2 (4 × 20 ml), concentration of the soln. to 10 ml and passage over a short alumina column to yield **8b** as a colourless oil (7.61 g, 90%). ^{1}H-NMR ($CDCl_3$): 2.58 (*t*, 2 CH_2N); 2.71 (*m*, 16 H, CH_2N,CH_2S); 3.45 (2*t*, 4 CH_2O); 3.55 (*t*, 2 CH_2OH). ^{13}C-NMR ($CDCl_3$): 72.9 (NCH_2CH_2O); 69.05 (OCH_2CH_2OH); 62.1 (CH_2OH); 55.4 (NCH_2CH_2O); 54.9 (NCH_2CH_2S); 27.7 (CH_2S). MS: 382 (M^+), 349, 225, 178, 144, 116. Anal. calc. for $C_{36}H_{34}N_2O_4S_2$ (382.6): C 50.2, H 8.96, N 7.32; found: C 50.5, H 9.11, N 7.45.

6. *4,10-Bis(5-chloro-3-oxapentyl)-1,7-dioxa-4,10-diazacyclododecane* (**17**). As in *Exper. 3*, with **8b** (764 mg, 2.0 mmol), MeOH (15 ml), 6M HCl (10 ml), and $SOCl_2$ (15 ml). Following removal of $SOCl_2$ under reduced pressure, the residue was entrained with EtOH (3 × 10 ml) and finally recrystallised from EtOH at 5° to give **17**·2 HCl as a crystalline solid (950 mg, 96%), m.p. 193–195°. ^{13}C-NMR (D_2O): 68.1 (NCH_2CH_2O); 60.2 (OCH_2CH_2); 51.2 (NCH_2CH_2O); 48.6 (NCH_2CH_2S); 40.2 (CH_2Cl); 26.6 (CH_2). MS (**17**·2 HCl): 420 (M^+ + 1), 419 (M^+), 389, 349, 313, 207. Anal. calc. for $C_{16}H_{34}Cl_4N_2O_2S_2$ (492.3): C 39.2, H 6.96, N 5.69, Cl 14.4; found: C 39.2, H 7.07, N 5.80, Cl 14.1.

7. *[5,5'-(1,7-Dithia-4,10-diazacyclododecane-4,10-diyl)bis(3-oxapentyl)]bis(diphenylphosphine)* (= 4,10-bis[5-(diphenylphosphino)-3-oxapentyl]-1,7-dithia-4,10-diazacyclododecane; **2**). As in *Exper. 4* with K (64 mg, 1.64 mmol), Na (15 mg, 0.65 mmol), PPh_3 (210 mg, 0.81 mmol), dioxan (10 ml), and **17** (170 mg, 0.4 mmol) in toluene (5 ml; addition at 0°, 15 min at 0°). After filtration through a short *Celite* pad, solvents were evaporated to yield a pale yellow oil which, on trituration with MeOH (10 ml), gave a white precipitate of **2** which was filtered and dried *in vacuo*: 215 mg (75%), m.p. 93–94°. ^{1}H-NMR (CD_2Cl_2): 2.36 (*t*, 2 CH_2P); 2.58 (*t*, 2 CH_2N); 2.71 (*m*, 16 H, CH_2S,CH_2N); 3.45 (*t*, 2 CH_2O); 3.56 (*t*, 2 CH_2O); 7.30–7.47 (*m*, 20 arom. H). ^{31}P-NMR ($(CD_3)_2CO$): −20.3. MS: 718 (M^+), 685, 684, 360, 346, 326. Anal. calc. for $C_{40}H_{52}N_2O_2P_2S_2$ (718.9): C 66.8, H 7.29, N 3.90, S 8.92; found: C 66.9, H 7.32, N 3.98, S 9.02.

8. *1,7-Dioxa-4,10-diazacyclododecane-4,10-diethanol* (**9**) was prepared as the dihydrochloric salt according to [8], m.p. 198–200° ([8]: m.p. 219–222°). ^{1}H-NMR (D_2O): 3.54 (br. *t*, 2 CH_2N); 3.68 (*m*, 4 CH_2N); 3.94 (*m*, 4 CH_2O); 4.08 (br. *t*, 2 $CH2OH$). ^{13}C-NMR (D_2O): 64.4 (CH_2O); 58.5 (CH_2OH); 55.6 (CH_2N); 54.7 (CH_2N). MS: 263 (M^+ + 1), 262 (M^+), 217, 216, 175, 174. Anal. calc. for $C_{12}H_{28}Cl_2N_2O_4$ (335.2): C 43.0, H 8.36, N 8.36; found: C 43.2, H 8.51, N 8.20.

9. *4,10-Bis(2-chloroethyl)-1,7-dioxa-4,10-diazacyclododecane* (**18**). To **9**·2 HCl (384 mg, 10 mmol) was added $SOCl_2$ (10 ml) and the mixture stirred for 16 h at r.t. After removal of $SOCl_2$ under reduced pressure, the residue

was entrained with EtOH (2 × 10 ml) and recrystallised from abs. EtOH to give **18**·2 HCl as a crystalline solid (378 mg, 90%), m.p. 178–180°. ^{1}H-NMR (D_2O): 3.66 (*m*, 4 CH_2N); 3.78 (*t*, 2 CH_2Cl); 3.92 (*m*, 4 CH_2O); 4.05 (*t*, 2 CH_2N^+). ^{13}C-NMR (D_2O): 64.3 (CH_2O); 57.6 (CH_2N); 54.6 (CH_2N); 36.4 (CH_2Cl). MS: 300 ($M^+ + 1$), 299, 256, 236, 181, 151. Anal. calc. for $C_{12}H_{26}Cl_4N_2O_2$ (371.1): C 38.7, H 6.99, N 7.52; found: C 38.4, H 7.21, N 7.30.

10. *[2,2'-(1,7-Dioxa-4,10-diazacyclododecane-4,10-diyl)bis(ethyl)]bis(diphenylphosphine)* (= 4,10-bis[2-(diphenylphosphino)ethyl]-1,7-dioxa-4,10-diazacyclododecane; **3**). As in *Exper. 4*, with K (156 mg, 4.0 mmol), Na (25 mg), PPh_3 (524 mg, 2.0 mmol), dioxan (10 ml), and **18** (300 mg, 1.0 mmol) in toluene (5 ml; addition at −20°, 15 min at r.t.). After filtering through a short *Celite* pad, solvents were evaporated. The resultant yellow oil was redissolved in toluene, passed over a short alumina column, and, after removal of toluene, triturated with MeOH (10 ml) at −78° yielding a white solid which was filtered and dried under vacuum: 263 mg (44%) of **3**, m.p. 107–109°. ^{1}H-NMR (CD_2Cl_2): 2.25 (*m*, 2 CH_2P); 2.64 (*m*, 6 CH_2N); 3.49 (br. *t*, 4 CH_2O); 7.30–7.47 (*m*, 20 arom. H). ^{31}P-NMR (CD_2Cl_2): −18.9. MS: 598 (M^+), 565, 228, 201, 175, 174. Anal. calc. for $C_{36}H_{44}N_2O_2P_2$ (598.7): C 72.2, H 7.41, N 4.69; found: C 72.0, H 7.09, N 4.81.

11. *2,2'-Dichloro-*N,N':N,N'*-bis(3-thiapentane-1,5-diyl)bis(acetamid)* (= 4,10-bis(chloroacetyl)-1,7-dithia-4,10-diazacyclododecane; **19**). To a soln. of **7b** (415 mg, 1.8 mmol) in CH_2Cl_2 (50 ml) was added dry Et_3N (412 mg, 4.08 mmol) and chloroacetyl chloride (406 mg, 3.6 mmol) at 0°. After stirring for 15 h, the soln. was washed successively with aq. 10M NaOH (2 × 50 ml), 10M HCl (2 × 20 ml), sat. brine (2 × 15 ml), and H_2O (2 × 20 ml), dried over $MgSO_4$, filtered, and reduced to ⅓ of its original volume. The precipitate formed was filtered, washed with acetone (2 × 5 ml), and dried *in vacuo* to give **19** as a colourless solid (570 mg, 90%), m.p. 174–176°. IR (Nujol): 1650, 1644. MS: 360 ($M^+ + 1$), 359 (M^+), 288, 260, 235, 234. Anal. calc. for $C_{12}H_{20}Cl_2N_2O_2S_2$ (359.3): C 40.1, H 5.61, N 7.79; found: C 39.9, H 5.61, N 8.06.

12. *4,10-Bis(2-chloroethyl)-1,7-dithia-4,10-diazacyclododecane* (**10**). To a suspension of **19** (710 mg, 198 mmol) in CH_2Cl_2 (10 ml) was added B_2H_6 in THF (1.0M, 6 ml) at 0°. The suspension was stirred for 24 h, and excess borane destroyed by careful addition of MeOH (15 ml). Removal of solvents gave a residue which was extracted with $CHCl_3$ (3 × 15 ml). The extracted aminoborane was hydrolysed with 6M HCl (20 ml) by refluxing for 3 h. After evaporating to dryness and basifying with Me_4NOH, the product was extracted with CH_2Cl_2 (4 × 15 ml) and passed through a short alumina column and the solvent removed to yield **10** as a colourless solid (406 mg, 62%), m.p. 87–89°. ^{1}H-NMR ($CDCl_3$): 2.76 (*m*, 20 H, CH_2N,CH_2S); 3.54 (*t*, 2 CH_2Cl). ^{13}C-NMR ($CDCl_3$): 57.2 (CH_2N); 54.3 (CH_2N); 41.8 (CH_2Cl); 28.1 (CH_2S). MS: 328 ($M^+ + 1$), 327 (M^+), 299, 297, 261, 199. Anal. calc. for $C_{12}H_{24}Cl_2N_2S$ (327.3): C 44.0, H 6.16, N 8.56; found: C 43.9, H 6.23, N 8.9.

13. *[2,2'-(1,7-Dithia-4,10-diazacyclododecane-4,10-diyl)bis(ethyl)]bis(diphenylphosphine)* (= 4,10-bis[2-(diphenylphosphino)ethyl]-1,7-dithia-4,10-diazacyclododecane; **4**). As in *Exper. 4*, with K (104 mg, 2.66 mmol), Na (25 mg), PPh_3 (348 mg, 133 mmol), dioxan (10 ml), and **10** (218 mg, 0.67 mmol) in dry toluene (5 ml) (addition at 0°, 20 min at 0°). After filtration through a short *Celite* pad, the solvents were evaporated to yield a viscous oil which gave a white solid on trituration with MeOH (10 ml): 410 mg (63%) of **4**, m.p. 131–133°. ^{1}H-NMR ($CDCl_3$): 2.21 (*m*, 2 CH_2P); 2.49 (*m*, 4 CH_2S); 2.63 (*m*, 6 CH_2N); 7.20–7.35 (*m*, 20 arom. H). ^{31}P-NMR ($(CD_3)_2CO$): −18.3. MS: 630 (M^+), 597, 553, 445, 316, 185. Anal. calc. for $C_{24}H_{44}N_2P_2S_2$ (630.8): C 68.5, H 7.03, N 4.44; found: C 68.6, H 7.10, N 4.51.

14. *Dimethyl 1,4,10,13-Tetroxa-7,16-diazacyclooctadeca-7,16-dipropionate* (**20**). To a soln. of **11** (1.5 g, 5.72 mmol) in dry MeOH (15 ml) was added freshly distilled methyl 2-propenoate (2.5 g, 28.5 mmol) and the mixture stirred for 16 h. After evaporation, the residue was chromatographed on neutral alumina with CH_2Cl_2/MeOH 99:1 to yield **20** as a pale yellow oil (1.67 g, 67%). ^{1}H-NMR ($CDCl_3$): 2.77 (*m*, 16 H, CH_2N, CH_2CO); 3.43 (*m*, 22 H, CH_2O, CH_3O). ^{13}C-NMR ($CDCl_3$); 170.7 (CO_2Me); 70.8, 70.1 (CH_2O); 54.4 (CH_3O); 52.1, 51.6 (CH_2N); 33.6 (CH_2CO). Anal. calc. for $C_{20}H_{38}N_2O_8$ (434.5): C 56.2, H 8.81, N 6.45; found: C 55.9, H 9.03, N 6.71.

15. *1,4,10,13-Tetroxa-7,16-diazacyclooctadecane-7,16-dipropanol* (**12**). To a soln. of **20** (1.5 g, 3.45 mmol) in THF (100 ml) was added $LiAlH_4$ (1 g) and the mixture refluxed for 24 h. After cooling, H_2O (2 ml) and a 10% LiOH soln. were added, followed by $MgSO_4$ (1 g). The suspension was filtered, evaporated to dryness, and the residue treated with 1M HCl (50 ml). The aq. phase was washed with CH_2Cl_2 (3 × 50 ml), the pH adjusted to 14 by adding Me_4NOH, and the product extracted with CH_2Cl_2 (4 × 25 ml). After drying over $MgSO_4$, the solvent was evaporated to leave **12** as a colourless oil (1.08 g, 81%). ^{1}H-NMR ($CDCl_3$): 1.70 (*quint.*, 2 CH_2); 2.73 (*m*, 6 CH_2N); 3.63 (*m*, 8 CH_2O). ^{13}C-NMR ($CDCl_3$): 72.3, 71.0 (CH_2O); 65.4 (CH_2OH); 57.2, 55.5 (CH_2N); 30.0 (CH_2). Anal. calc. for $C_{18}H_{38}N_2O_6$ (378.5): C 57.1, H 10.1, N 7.40; found: C 56.8, H 9.91, N 7.13.

16. *7,16-Bis(3-chloropropyl)-1,4,10,13-tetroxa-7,16-diazacyclooctadecane* (**21**). As in *Exper. 3*, with **12** (1.04 g, 2.64 mmol), MeOH (20 ml), 6M HCl (1 ml), and $SOCl_2$ (20 ml) for 16 h at r.t., then for 2 h at reflux. Excess $SOCl_2$ was evaporated and the residue entrained with abs. EtOH (2 × 10 ml). The salt was recrystallised from EtOH/Et_2O 4:1 to give **21**·2 HCl as a colourless solid (1.13 g, 88%), m.p. 176–178°. ^{1}H-NMR ($CDCl_3$): 1.93 (*quint.*, CH_2CH_2); 2.77 (*m*, 6 CH_2N); 3.63 (*m*, 20 H, CH_2O, CH_2Cl_2). ^{13}C-NMR ($CDCl_3$): 72.1, 66.3 (CH_2O); 55.5, 53.6 (CH_2N); 43.4 (CH_2Cl); 28.1 (CH_2). Anal. calc. for $C_{18}H_{38}Cl_4N_2O_4$ (488.2): C 44.3, H 7.84, N 5.73; found: C 44.2, H 7.86, N 5.70.

17. *[3,3'-(1,4,10,13-Tetroxa-7,16-diazacyclooctadecan-7,16-diyl)bis(propyl)]bis(diphenylphosphine)* (= 7,16-bis[3-(diphenylphosphino)propyl]-1,4,10,13-tetroxa-7,16-diazacyclooctadecane; **5**). As in *Exper. 4*, with K (47 mg, 1.12 mmol), Na (15 mg), PPh_3 (157 mg, 0.6 mmol), dioxan (5 ml), and **21** (124 mg, 0.3 mmol) in toluene (5 ml; addition at −10°, 15 min at r.t.). After filtering through a short *Celite* pad, solvents were evaporated, and the residue was taken up in 0.2M degassed HCl (20 ml), washed with CH_2Cl_2 (2 × 10 ml), basified with Me_4NOH, and the product extracted into CH_2Cl_2 (3 × 10 ml). Solvent was evaporated to yield a colourless oil which was triturated with dry EtOH (5 ml) to give **5** as a white solid (100 mg, 45%), m.p. 114–115°. ^{1}H-NMR (CD_2Cl_2): 1.54 (*m*, 2 CH_2CH_2P); 2.05 (*m*, 2 CH_2P); 2.55 (*t*, 2 CH_2N); 2.64 (*t*, 4 CH_2N); 3.49 (*t*, 4 CH_2O); 3.51 (*s*, 4 CH_2O); 7.29–7.45 (*m*, 20 arom. H). ^{31}P-NMR (CD_2Cl_2): −2.47. MS: 714 (M^+), 653, 639, 529, 399. Anal. calc. for $C_{42}H_{56}N_2O_4P_2$ (714.8): C 70.6, H 7.90, N 3.92 ; found: C 70.3, H 8.08, N 3.81.

18. *10-(2-Chloroethyl)-1,4,7-trioxa-10-azacyclododecane* (**22**). As in *Exper. 3*, with **13** (prepared according to [14]; 1.15 g, 5.0 mmol), MeOH (20 ml), a few drops of conc. HCl, and $SOCl_2$ (10 ml) for 16 h at r.t., then for 1 h at reflux. After removal of excess $SOCl_2$ under reduced pressure, the residue was entrained with EtOH (2 × 10 ml) and the product **22**·2 HCl recrystallised from i-PrOH at 5°: 1.14 g (83%), m.p. 182–184°. ^{1}H-NMR (D_2O): 3.60 (*m*, 2 CH_2N); 3.81 (*t*, CH_2Cl); 3.94 (*m*, 6 CH_2O); 4.08 (*t*, CH_2N^+H). MS: 239 ($M^+ + 1$), 238 (M^+), 186, 171, 157, 121, 103. Anal. calc. for $C_{10}H_{21}Cl_2NO_3$ (274.1): C 43.8, H 7.72, N 10.2; found: C 44.0, H 8.01, N 10.1.

19. *Diphenyl [2-(1,4,7-trioxa-10-azacyclododec-10-yl)ethyl]phosphine* (= 10-[2-(diphenylphosphino)ethyl]-1,4,7-trioxa-10-azacyclododecane; **6**). As in *Exper. 4*, with K (296 mg, 7.6 mmol), Na (50 mg, 2.17 mmol), PPh_3 (996 mg, 38 mmol), dioxan (10 ml), and **22** (770 mg, 3.79 mmol) in toluene (10 ml; addition at 10°, 20 min at 10°). After filtration through a short *Celite* pad, solvents were evaporated to give a yellow oil which was redissolved in toluene (5 ml) and passed over a short column of alumina to yield **6** as a colourless oil (600 mg, 41%). ^{1}H-NMR ($C_6D_5CD_3$): 1.8–2.5 (*m*, 8 H, CH_2N,CH_2P); 2.8–3.4 (*m*, 6 CH_2O); 6.9–7.4 (*m*, 10 arom. H). ^{31}P-NMR ($CDCl_3$): −20.9. Cl-MS (Isobutane): 388 ($M^+ + 1$) 387 (M^+), 354, 213, 189, 176. Anal. calc. for $C_{22}H_{30}NO_3P$ (387.5): C 68.2, H 7.76, N 3.62; found: C 67.8, H 7.91, N 3.81.

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