Polyazaphosphorus Macrocycles.[1] Synthetic Approaches to Symmetric or Dissymmetric 18-, 20-, 22-, and 30-Membered Rings

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Abstract: High-yield synthetic routes to symmetric, functionalized or unfunctionalized, 18-, 20-, 22-, or 30-membered rings containing P-N-N linkages, i.e., **5c,c'**, **5d,d'**, **6b**, **7a,c**, **8b**, and **9a,b**, via [1 + 1], [2 + 2], or [3 + 3] condensation reactions involving phosphodihydrazides **1a-c** and 1,2, 1,3, or 1,4 dialdehydes are reported. The mechanism of formation of these compounds has been elucidated by ^{31}P NMR studies. The structure of one of these compounds, **5a**, has been resolved by X-ray crystallography. Crystal data at room temperature are a = 16.94 (3) Å, b = 6.16 (4) Å, c = 28.41 (2) Å, β = 93.6 (1)°, Z = 2 for monoclinic system, space group $C2/c$, R = 0.046 for 190 parameters refined with 2400 reflections with $I > 3\sigma(I)$. New phosphorus multifunctionalized 1,11 dialdehydes **13a,b** are prepared and used as starting materials for the synthesis of the dissymmetric 18-membered ring **14**.

Systematic studies on macrocycles started in the sixties and gave rise to a considerable number of reports. The versatile behavior of phosphorus compounds in addition to the complexity and low yield of multistage macrocyclic syntheses presumably explain the slow development of the corresponding phosphorus macrocyclic chemistry. Most of the studies were concerned with the incorporation of phosphorus(III) or-(V) in crown ether links or with the substitution of some oxygen atoms of crown ethers by phosphorus leading to species possessing one or more P-C, P-O, P-S, or, much more scarcely, P-N bonds.[2]

Although tetraimino Schiff base macrocycles derived from heterocyclic dicarbonyls constitute another important class of macrocycles,[3] a few investigations were concerned with the preparation of phosphorus analogues. Only three reports described the preparation of macrocyclic Schiff base mono- or diphosphine diamine complexes. All of the models contain only intracyclic P-C bonds, and in all cases it has been found necessary to use template procedures.[4] To date no free macrocyclic ligand of this type is known.

The dramatic lack of results in this field as well as the known ability of phosphorus to stabilize low oxidation states and the special properties of tetraimino Schiff base large-membered rings[3] prompt us to investigate synthetic routes to free macrocycles.

Our aim was to find a one-step high-yield general and easy preparation of various macrocycles. Moreover the resulting macrocyclic species must be stable enough to be submitted to different chemical procedures in order to modify the cavity size since the ring must be of the optimum size for binding a particular metal. Of course they would also contain specific heteroatom donors (nitrogen, oxygen, etc.) or unsaturated bonds suitable for complexation.

We have already reported[1] that the treatment of oxo- or thiophosphodihydrazides $[RP(Y)(NCH_3NH_2)_2]$ (**1**): R = C_6H_5, C_6H_5O, $N(CH_3)_2$, Y = O, S) with 1,3-dialdehydes such as 2,5-furandicarboxaldehyde (**3a**), 2,6-pyridinecarboxaldehyde (**3b**), or 1,3-benzenedicarboxaldehyde (**3c**) led to 20-membered rings **5** (Scheme I).

We show here the wide scope of this type of reaction leading to new free symmetric or dissymmetric, functionalized 18-, 20-, 22-, or 30-membered rings containing P-N-N linkages and involving either [1 + 1], [2 + 2], or [3 + 3] condensations between phosphodihydrazides and 1,2-, 1,3-, 1,4-, or 1,11-dialdehydes. We

Table I. Selected Interatomic Distances, Bond Lengths, and Angles for **5a**

Interatomic Bond Distances (Å)					
P1-P1*	10.0329	N2-N2*	6.9102	N2-N4*	2.8603
N2-O2*	4.9051	N2-N3*	2.7467	O2-O2*	3.7634
N2-N1*	8.0532	N2-N4	6.0884	N4-N4*	6.3403
Bond Lengths (Å)					
P1-O1	1.474 (2)	P1-C1	1.783 (4)	N3-N4	1.388 (3)
P1-N1	1.686 (3)	N1-N2	1.367 (3)	N3-C14	1.464 (4)
P1-N3*	1.668 (2)	N1-C7	1.460 (4)	N4-C13	1.270 (4)
		N2-C8	1.280 (4)		
Bond Angles (deg)					
O1-P1-N1	114.0 (1)	N1-P1-C1	105.7 (1)	N1-N2-C8	120.4 (2)
O1-P1-N3*	111.7 (1)	N3*-P1-C1	108.0 (1)	P1*-N3-N4	114.0 (2)
O1-P1-C1	112.1 (1)	P1-N1-N2	115.2 (2)	P1*-N3-C14	118.1 (2)
N1-P1-N3*	104.8 (1)	P1-N1-C7	120.3 (3)	N3-N4-C13	117.8 (2)

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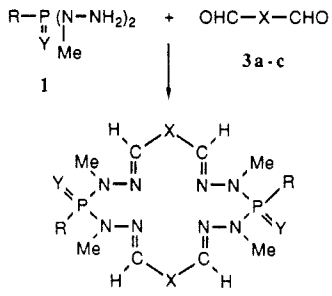
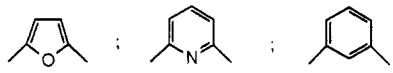
Scheme I

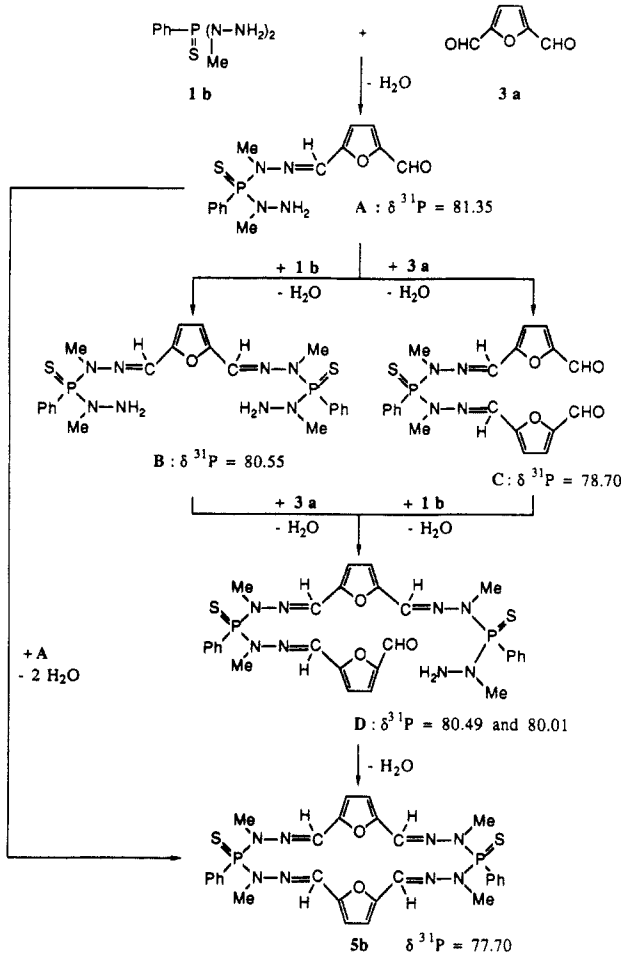


X = 

R = C_6H_5 , C_6H_5O , $(CH_3)_2N$

Y = O, S

Scheme II



also report the X-ray structural determination of one of these macrocycles as well as the preparation of multifunctionalized acyclic phosphorus ligands.

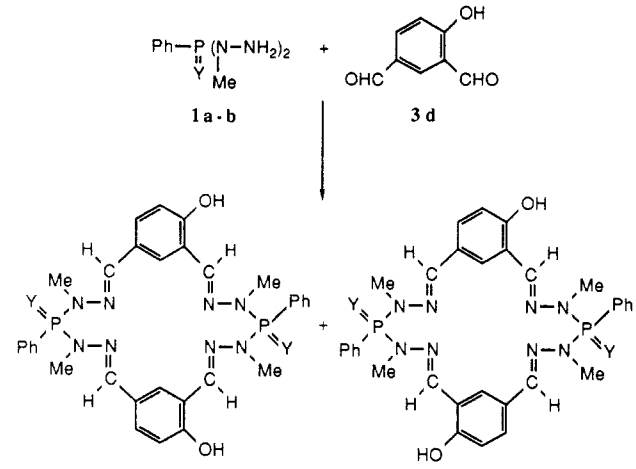
Results and Discussion

The 18-, 20-, and 22-membered rings are prepared by simultaneous slow addition of a methanolic solution of a phosphodihydrazide (**1**) and a solution of a 1,2-, 1,3-, 1,4-dialdehyde (**2**,**3**, or **4**) to methanol (Schemes II to VI).

A number of advantages of this method can be pointed out: (i) the reaction proceeds in very mild conditions (room temperature, stirring for 2 h) and does not necessitate high-dilution techniques, (ii) the desired macrocycles are obtained in nearly quantitative yield and are easily separated from the resulting mixture since they precipitate as soon as they are formed.

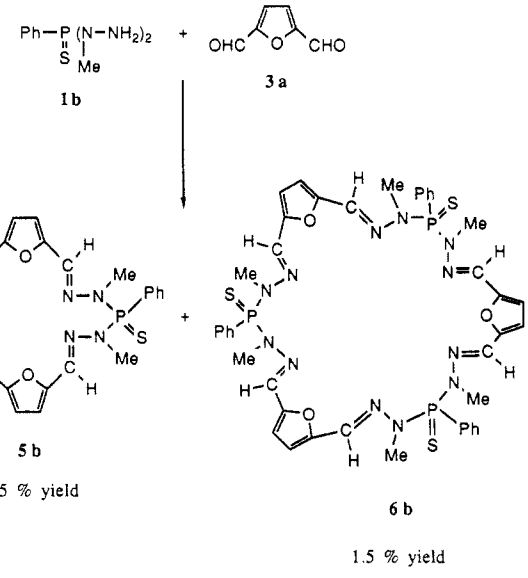
Various phosphorus macrocycles are thus formed in a one-pot procedure from phosphodihydrazides easily synthesized by reacting oxo- or thiodichlorophosphines with methylhydrazine.[5]

Scheme III

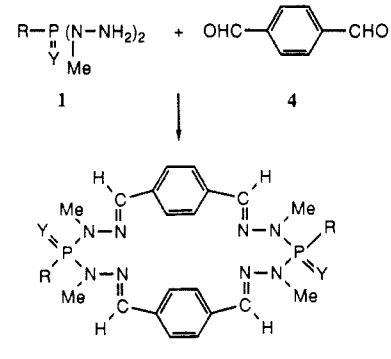


5c-c' : Y = S
5d-d' : Y = O

Scheme IV

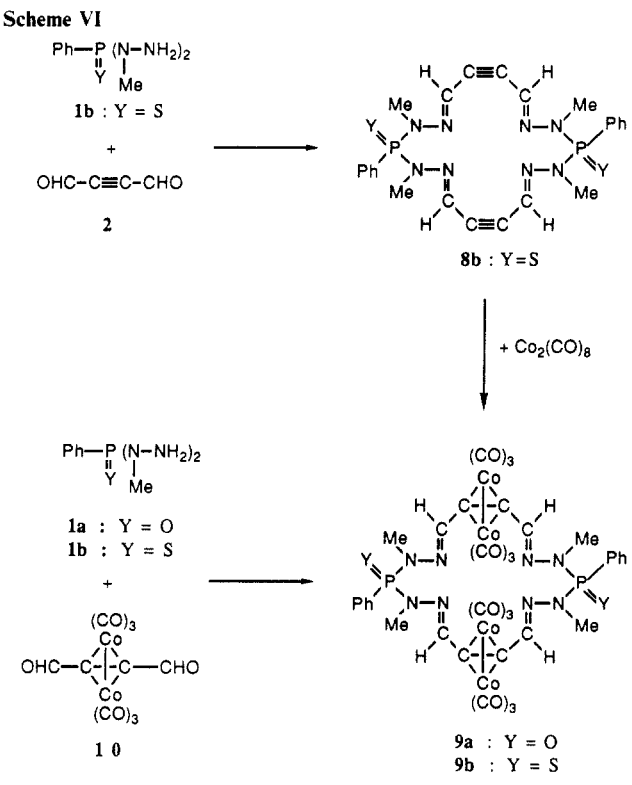


Scheme V



7a R = C_6H_5 Y = O
7b R = C_6H_5 Y = S
7c R = Me_2N Y = O

Scheme VI



All these large-membered rings are stable white or yellow powders nonsensitive to hydrolysis, easily soluble in halogenated solvents, dioxane, THF, etc. Surprisingly, no cleavage of the intracyclic phosphorus–nitrogen bond is detected when they are treated with hydrogen chloride, hydrogen fluoride, or concentrated nitric acid even under drastic conditions.

20- and 30-Membered Rings. Structures of macrocycles **5** were deduced from ^{31}P, ^{1}H, and ^{13}C NMR, IR, mass spectrometry, as well as microanalysis.[1] Nevertheless the significance of reactions affording compounds **5** made it highly desirable to have an unambiguous characterization of the structure of one of these derivatives. Suitable crystals for X-ray analysis were obtained for **5a** (X = furan, R = C_6H_5, Y = O) by recrystallization from a mixture of MeOH and dichloromethane (1:1). The general feature of the macrocycle showing the cavity is given in Figure 1. A view of the molecule along the P–P axis illustrates the unusual butterfly-like structure. Selected bond lengths and interatomic distances are listed in Table I. P–O, P–N, N–N, N=C distances are within the normal range: in particular, C=N bond lengths are similar to those observed in nonphosphorus tetraimine Schiff base macrocycles or in the known corresponding diphosphine diamine complex.[4] The cis position of phosphoryl groups and the short distances between nitrogen atoms in the β position relative to the same phosphorus atom (2.86 Å) are to be noted.

Possible routes to the formation of the [2 + 2] macrocycles **5** are indicated in Scheme II. For the sake of clarity, only attempts to characterize intermediates formed during the synthesis of **5b** (X = furan, R = C_6H_5, Y = S) will be presented here, but both intermediates of types **A**–**D**, whatever the nature of X, Y, and R, were characterized in solution by ^{31}P NMR.

Six signals (81.35, 80.55, 80.49, 80.01, 78.70, 77.70 ppm) are detected in the ^{31}P NMR spectrum in solution when 2,5-furandicarboxaldehyde, (**3a**) in MeOH is added to the phosphodihydrazide **1b** (δ ^{31}P = 86 ppm) in MeOH at 0 °C.

A major signal at 80.55 ppm is observed when the same reaction is performed at −20 °C with 2 equiv of **1b** and 1 equiv of dialdehyde, **3a**. This signal disappears when a second equivalent of **3a** is added while signals at 80.49 and 80.01 ppm slightly increase. Moreover the macrocycle **5b** precipitates (**5b** δ ^{31}P = 77.7 ppm).

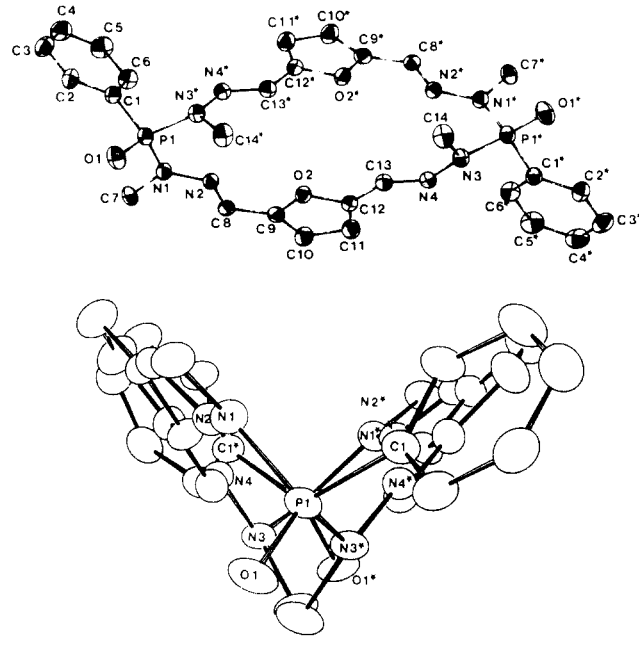


Figure 1. (Top) ORTEP drawing of **5a** showing the atomic numbering scheme. (Bottom) View of the structure of **5a** along the $P_1P_1^*$ axis.

The ^{31}P NMR spectrum of the resulting mixture after addition of 1 equiv of **1b** to 2 equiv of **3a** at 20 °C consists of a main signal at 78.7 ppm. The subsequent ring closure is carried out by slow addition of a second equivalent of **1b**: the signal at 78.7 ppm disappears to the benefit first of the two signals at 80.49 and 80.01 ppm (1/1 ratio) and then of the phosphorus macrocyclic signal.

Last, simultaneous addition of **1b** and **3a** (1/1 ratio) at −40 °C leads to a solution showing predominantly a ^{31}P NMR signal at 81.35 ppm (besides those at 80.49 and 80.01 ppm). Increasing the temperature to −10 °C induces the slow disappearance of this signal while all the other signals (80.55, 80.49, 80.01, 78.7, and 77.7 ppm) increase.

Therefore, the transient formation of intermediates **A** (δ ^{31}P = 81.35 ppm), **B** (δ ^{31}P = 80.55 ppm), **C** (δ ^{31}P = 78.7 ppm), and **D** (δ ^{31}P 80.49 and 80.01 ppm) seems likely although attempts to isolate them failed. Nevertheless a [1 + 1] condensation involving **A**, at least in part, cannot be ruled out.

A functionalized macrocycle with a ring size of 20 atoms is also easily prepared by adding the 4-hydroxy-1,3-benzenedicarboxaldehyde (**3d**)[6] to phenylthiophosphodihydrazide (**1b**) (Scheme III). Two isomers, **5c** and **5c'**, were formed in equal amount as depicted in ^{31}P NMR, which shows three signals in 1:1:2 ratio at 78.47, 78.11 and 77.42 ppm, respectively. The two phosphorus atoms of isomer **5c'** are equivalent (one signal at 77.42 ppm) while the two phosphorus atoms of **5c** are not. The ^{1}H NMR spectrum of the **5c**–**5c'** mixture is in agreement with the proposed structure but did not allow a distinction of one from the other since all the CH=N protons are observed as a singlet at δ 6.60 ppm. Two resonances at δ 157.78 and 157.40 ppm are depicted in the ^{13}C NMR spectrum, pointing out the presence of two imino carbons with different environments. Mass spectrometry shows a molecular ion peak at *m/e* 688.

Treatment of phosphodihydrazide **1a** with **3d** under the same experimental conditions allowed the isolation of the corresponding macrocycles, **5d** and **5d'**. ^{31}P NMR experiments did not distinguish if one or two isomers are formed in this case (only one broad signal at 24.3 ppm). Nevertheless, ^{13}C NMR spectra indicate the presence of two isomers since two singlets are observed at 157.64 and 157.96 ppm for the imino carbons.

The formation of all these 20-membered rings involves [2 + 2] condensation reactions. Actually, a [3 + 3] condensation is also observed when phosphodihydrazide **1b** is treated with 2,5-

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furandicarboxaldehyde **3a** in methanol. In addition to the macrocycle **5b** (95% yield, vide supra), we could isolate in poor yield (1.5%) the corresponding 30-membered ring **6b** possessing three phosphorus atoms in the ring (Scheme IV). The NMR data of this derivative are quite similar to those given by the 20-membered derivative. Mass spectrometry provided a direct confirmation of the structure (*m/e* 954).

22-Membered Rings. [2 + 2] condensation reactions also occurred when a solution of **1** in methanol and a solution of 1,4-benzenedicarboxaldehyde (**4**) in methanol were simultaneously added dropwise at room temperature over a period of 1 h. Macrocycles **7a**, **7b**[1], and **7c** precipitated as soon as they were generated and were obtained as white or yellow powders (40–80% yield) (Scheme V). Structures of **7a–c** have been established by NMR, IR, mass spectrometry, and microanalysis (see Experimental Section). No effect due to the larger ring size is observed.

18-Membered Rings. Symmetric. Acetylenedicarbaldehyde (ADCA)[7] obtained by acidolysis of the corresponding diacetal is a useful starting material for organic synthesis, although it explodes in pure form. We used it in solution in an aprotic solvent such as dichloromethane for the preparation of 18-membered rings. As an example, 1,2-dialdehyde **2**, reacts readily with a solution of phosphodihydrazide **1b** in methanol to give the corresponding macrocycle **8b** as a yellow powder (85% yield) (Scheme VI). **8b** is insoluble in methanol but fairly soluble in chloroform or dichloromethane.

No band in the C≡C absorption range is detected in infrared spectroscopy. This is not really surprising since the same situation occurred with the starting ADCA.[8] However, the N=C stretching frequency is observed at 1685 cm^{-1} while no absorption corresponding to NH_2 or CHO group vibration frequencies is present. Indeed the ^{13}C NMR spectrum indicates the presence of carbon–carbon triple bonds since it exhibits a characteristic singlet at 87.6 ppm, in addition to other signals at 31.89 (broad singlet P–N–CH_3), 121.24 (*C*=N), and 128–133.2 (multiplet C_6H_5) ppm.

^1H NMR is also in agreement with the proposed structure (δ N=CH proton at 6.76 ppm). Satisfactory elemental analyses were obtained and the structure was confirmed by mass spectrometry (*m/e* 552).

In order to demonstrate fully the presence of the carbon–carbon triple bonds, we decided to test the complexation ability of these first C≡C triple bond containing phosphorus macrocycles toward octacarbonyldicobalt.

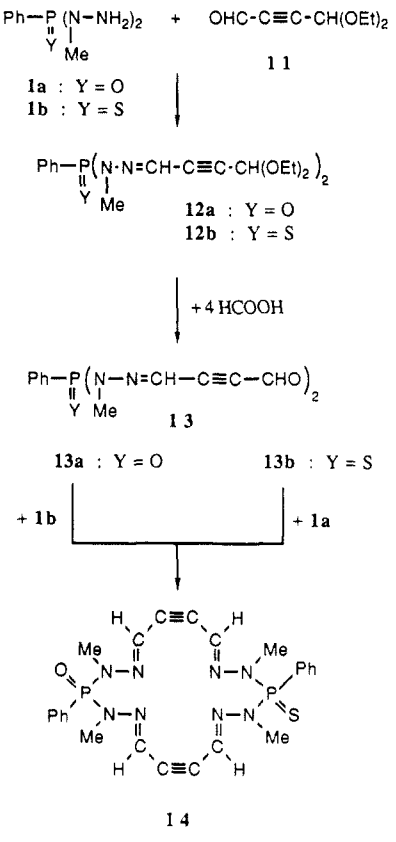
Two approaches were selected. In the first approach, the free macrocycle **8b** was treated with $Co_2(CO)_8$ in large excess. The corresponding complex **9b** was isolated in 90% yield. While no change appears in ^{31}P NMR, except the broadness of the signal (δ = 78.08 ppm), the complexation has a considerable influence on infrared and ^{13}C NMR spectra. ν(C=O) vibrations are located between 2114 and 2040 cm^{-1}, as expected. A similar assignment is indicated[9] for the ADCA hexacarbonyldicobalt complex, **10**. The ^{13}C NMR spectrum shows, among others, broad resonances at 86.43 (C≡C) and 198.64 (CO) ppm.

In the second approach, a solution of complex **10** in dichloromethane and a solution of phosphodihydrazide **1b** in the same solvent were simultaneously added to dichloromethane (Scheme VI). The resulting complex (70% yield) exhibits the same spectroscopic data as **9b**. This cobalt complex proved to be unstable in solution (CH_2Cl_2) and could not be detected by mass spectrometry. Nevertheless, satisfactory elemental analyses were obtained.

Complex **9a** was similarly prepared from **10** and phosphodihydrazide **1a**.

Dissymmetric Rings. All the reactions reported above described the preparation of symmetric phosphorus macrocycles, i.e. compounds in which the two phosphorus atoms of the molecule are linked to the same substituents. To the best of our knowledge, no example of phosphorus large-membered rings in which the two (or more) phosphorus atoms are bonded to different substituents are described. Therefore, we also investigated the potentiality of our method to yield such dissymmetric species. Our strategy, outlined in Scheme VII, involves the preliminary formation of the new polyfunctionalized phosphodihydrazones **12a,b** and **13a,b**.

Scheme VII



Addition of a methanolic solution of the monoacetal of ADCA, **11**, to the phosphodihydrazide **1a** also in methanol leads to the formation of phosphodihydrazone **12a** isolated in 94% yield. The formolysis of **12a** was carried out with anhydrous formic acid in the presence of anhydrous $CuSO_4$. After 1 h of reaction at room temperature, the polyfunctionalized phosphodihydrazone **13a** was easily isolated in 20% yield after workup. **13a** is a pale yellow oil that has been identified by mass spectrometry (*m/e* = 358). The proton NMR spectrum gives evidence of the presence of aldehydic protons: the CHO groups of **13a** exhibit a well-resolved singlet at 9.3 ppm.

It is noteworthy that the chemical behavior of this first phosphorus 1,11-dialdehyde toward phosphodihydrazides **1a** or **1b** is different from that of classical 1,3- or 1,4-dialdehydes.

Indeed, slow addition of 1 equiv of **13a** in methanol to phosphodihydrazide **1b** in the same solvent results in the selective precipitation of the dissymmetric 18-membered ring **14** (80% yield) resulting from a [1 + 1] condensation reaction. Under these experimental conditions, no traces of a 36-membered ring arising from [2 + 2] condensation involving 2 equiv of **13a** and 2 equiv of **1b** were detected. **14** was obtained as a stable yellow powder. Mass spectrometry gives evidence of a parent ion at *m/e* 536. ^{31}P, ^1H, and ^{13}C NMR spectra reveal the dissymmetry due to the presence of phosphoryl and thiophosphoryl groups. ^{31}P NMR shows two singlets at 78.5 (P=S) and 23.1 (P=O) ppm, as expected. The presence of two doublets (δ 3.01 ppm, $^3J_{HP}$ = 5.9 Hz; 3.03 ppm, $^3J_{HP}$ = 7.2 Hz) for the four N–CH_3 groups also points out this phenomena in proton NMR. ^{13}C NMR spectra also allow two different resonances to be distinguished for carbon atoms of the methyl groups (δ 31.82 ppm (d), $^2J_{CP}$ = 8 Hz; 32.75 ppm (d), $^2J_{CP}$ = 7.8 Hz) as well as two signals (87.46 (s), 87.85 ppm (s)) for the C≡C moieties, meanwhile a broad singlet is

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observed for the four imino carbons.

Interestingly, macrocycle **14** can be obtained through the sequence

$$\mathbf{1b} \rightarrow \mathbf{12b} \rightarrow \mathbf{13b} \xrightarrow{\mathbf{1a}} \mathbf{14}$$

(see Scheme VII). Compounds **12b** and **13b** were also isolated and fully characterized.

It seems therefore that, beside their obvious potential in organic synthesis, the multifunctional derivatives **13a,b** are suitable reagents for preparing new classes of phosphorus macrocycles.

Conclusion

An efficient route to original phosphorus macrocycles is described via multiple [phosphodihydrazides–dialdehydes] condensations. Indeed [2 + 2] condensations lead to symmetric 18-, 20-, or 22-membered rings, [3 + 3] to a 30-membered ring, and [1 + 1] a dissymmetric 18-membered ring. The possibility to build a macrocycle bearing both a phosphoryl group P=O and a thiophosphoryl group P=S is of great interest for further complexations.

The simplicity of this general method—one-step from phosphodihydrazides, very mild conditions, easy isolation of macrocycles obtained in high yield—makes it especially attractive.

Detailed information provided by numerous ^{31}P NMR studies can be used to understand the mechanism of formation of these compounds: four different types of intermediates were characterized.

The X-ray determination study of one of these first free polyazaphosphorus macrocycles displays some unique features: butterfly structure, phosphoryl groups in the cis position, and short distances between nitrogen atoms in the β position relative to the same phosphorus atom.

The synthesis of unusual phosphorus multifunctionalized 1,11-dialdehydes **13a,b** gives a new entry for facile preparation of dissymmetric phosphorus macrocycles. Furthermore, compounds **13a,b** should be useful starting materials for organic and inorganic chemistry.

Investigations concerning chemical and complexation properties of these phosphorus macrocycles will be described separately.

Experimental Section

All manipulations were carried out with standard high vacuum or dry argon atmosphere techniques. ^1H and ^{13}C NMR spectra were recorded on a Bruker WM 250 or a Bruker AC80 spectrometer. Chemical shifts are reported in ppm relative to Me_4Si as internal standard. ^{31}P NMR spectra were obtained on a Bruker AC80 instrument and are reported in ppm. Standards for the shifts are 85% H_3PO_4. Infrared spectra were recorded on a Perkin-Elmer 225 instrument. Elemental analyses were performed by the Service Central d'Analyses CNRS. Mass spectra were obtained on a Varian MAT 311A instrument.

Synthesis of Macrocycles 5c, 5c', 5d, 5d', 7a, 7c, and 8b. A solution of phosphodihydrazides **1** (0.02 mol) in 50 mL of methanol and a solution of dialdehydes **2**, **3d**, and **4** (0.02 mol) in 50 mL of methanol were added simultaneously and dropwise at room temperature over a period of 1 h. The mixture was stirred for 2 h, during which a yellow precipitate was formed. The solution was filtered and the precipitate washed with 2 × 20 mL of methanol and recrystallized from acetonitrile/chloroform 4:1. An additional amount of macrocycles **5c**, **5c'**, **5d**, **5d'**, **7a**, **7c**, and **8b** was obtained by evaporation of methanol and recrystallization of the residue from acetonitrile/chloroform 4:1.

5c, 5c': yellow powder; yield 50%; ^{31}P NMR ($CDCl_3$) 77.42, 78.11, 78.47; ^1H NMR ($CDCl_3$) 3.20 (br d, $^3J_{PH}$ = 9.8 Hz, N-CH_3), 6.60 (s, HC=N), 7.8 (m, C_6H_3 and C_6H_5), 10.30 (s, OH); ^{13}C NMR ($CDCl_3$) 31.03 (br s, N-CH_3), 117.81, 130.36, 130.16, 139.15 (m, C_5H_3 and C_6H_5), 157.40 and 157.78 (s, C=N), 162.31 (s, C-OH); IR (KBr) 1665 (C=N) cm^{-1}; MS, *m/e* 688. Anal. Calcd for $C_{32}H_{34}N_8O_2P_2S_2$: C, 55.80; H, 4.98; N, 16.28. Found: C, 55.88; H, 5.02; N, 16.01.

5d, 5d': clear brown powder; yield 50%; ^{31}P NMR ($CDCl_3$) 24.3 (br s); ^1H NMR ($CDCl_3$) 3.20 (v br s, N-CH_3), 6.71 (s, HC=N), 7.70 (m, C_6H_3 and C_6H_5), 10.3 (s, OH); ^{13}C NMR ($CDCl_3$) 31.02 (br s, N-CH_3), 118.10–132.18 (m, C_6H_3 and C_6H_5), 157.64 and 157.96 (s, C=N), 162.00 (s, C-OH); IR (KBr) 1670 (C=N) cm^{-1}; MS, *m/e* 656. Anal. Calcd for $C_{32}H_{34}N_8O_4P_2$: C, 58.52; H, 5.22; N, 17.07. Found: C, 58.64, H, 5.41; N, 16.95.

7a: white powder; yield 68%; ^{31}P NMR ($CDCl_3$) 25.8; ^1H NMR ($CDCl_3$) 3.15 (d, $^3J_{PH}$ = 9.0 Hz, N-CH_3), 7.37 (s, HC=N), 7.5 and 7.9 (m, C_6H_4 and C_6H_5); ^{13}C NMR ($CDCl_3$) 31.46 (d, $^2J_{PC}$ = 9.8 Hz, N-CH_3), 125–135 (m, C_6H_4 and C_6H_5), 136.40 (s, C=N); IR (KBr) 1596 (C=N) cm^{-1}; MS, *m/e* 624. Anal. Calcd for $C_{32}H_{34}N_8O_2P_2$: C, 61.52; H, 5.49; N, 17.95. Found: C, 61.29; H, 5.41; N, 17.78.

7c: yellow powder; yield 80%; mp dec >205 °C; ^{31}P NMR ($CDCl_3$) 17; ^1H NMR ($CDCl_3$) 2.80 (d, $^3J_{PH}$ = 10 Hz, N(CH_3)$_2$), 3.12 (d, $^3J_{PH}$ = 8.2 Hz, N-CH_3), 7.41 (s, HC=N), 7.5 and 7.9 (m, C_6H_4 and C_6H_5); ^{13}C NMR ($CDCl_3$) 32.23 (d, $^2J_{PC}$ = 7.9 Hz, N-CH_3), 37.65 (d, $^2J_{PC}$ = 2.8 Hz, N(CH_3)$_2$), 125–135 (m, C_6H_4 and C_6H_5), 136.48 (s, C=N); IR (KBr) 1601 (C=N) cm^{-1}; MS, *m/e* 558. Anal. Calcd for $C_{24}H_{36}N_{10}O_2P_2$: C, 51.59; H, 6.50; N, 25.08. Found: C, 51.40; H, 6.35; N, 25.21.

8b: pale brown powder; yield 85%; ^{31}P NMR ($CDCl_3$) 77.7; ^1H NMR ($CDCl_3$) 3.00 (d, $^3J_{PH}$ = 9.4 Hz, N-CH_3), 6.78 (br s, HC=N), 7.40 and 7.81 (m, C_6H_5); ^{13}C NMR ($CDCl_3$) 31.89 (br s, N-CH_3), 87.60 (s, C≡C), 121.24 (s, C=N), 128–133 (m, C_6H_5); IR (KBr) 1685 (C=N) cm^{-1}; MS, *m/e* 552. Anal. Calcd for $C_{24}H_{26}N_8P_2S_2$: C, 52.16; H, 4.75; N, 20.29. Found: C, 52.41; H, 4.67; N, 20.01.

Isolation of the 30-Membered Ring, 6b. This compound was prepared according to the procedure of synthesis of **5b**.[1] After filtration of the precipitate (**5b**), the solution was evaporated to dryness. Purification was accomplished by redissolving the crude powder in the minimum amount of dichloromethane and putting it on a silicagel column. Repetitive elutions with a 4:1 [petroleum ether]/[acetone] solution allowed the separation on **6b** (1.5% yield) from the remaining **5b**.

6b: white powder; ^{31}P NMR ($CDCl_3$) 79.6; ^1H NMR ($CDCl_3$) 3.08 (d, $^3J_{PH}$ = 8.4 Hz, N-CH_3), 6.31 (s, C_4OH_2), 7.90 (s, HC=N); ^{13}C NMR ($CDCl_3$) 31.62 (d, $^2J_{PC}$ = 8.6 Hz, N-CH_3), 111.09 (s, *C*-C-O furfural), 132.17 (s, C-*C*-O furfural), 151.68 (s, C=N); IR (KBr) 1660 (C=N) cm^{-1}; MS, *m/e* 954. Anal. Calcd for $C_{42}H_{45}N_{12}O_3P_3S_3$: C, 52.82; H, 4.51; N, 17.61. Found: C, 52.51; H, 4.80; N, 17.36.

Synthesis of Complex 9b. Method A. To a solution of the free macrocycle **8b** (0.50 g, 0.09 mmol) in 20 mL of dry dichloromethane was added $Co_2(CO)_8$ (0.93 g, 2.7 mmol). After the solution was stirred for 2 h in the dark, an excess of $Co_2(CO)_8$ was filtered off on Celite and the solvent evaporated. Crude **9b** was obtained as a bright red powder recrystallized from toluene/dichloromethane 2:1 (90% yield).

Method B. A solution containing 1.84 g (8 mmol) of phosphodihydrazide **1b** dissolved in 50 mL of dry dichloromethane was added dropwise with stirring at room temperature to acetylenedicarbaldehyde cobalt carbonyl [OHCC≡CCHO, $Co_2(CO)_6$] (3 g, 8 mmol) in 50 mL of dichloromethane. The reaction was monitored by ^{31}P NMR. After the complete disappearance of the starting hydrazide **1b**, the resulting mixture was filtered on Celite (elimination of some degradation products). Evaporation of the solvent afforded a bright red powder treated as above (yield 62%).

Method B was also used for the preparation of **9a** (yield 54%).

9b: ^{31}P NMR ($CDCl_3$) 78.08; ^1H NMR ($CDCl_3$) 2.99 (v br s, N-CH_3), 7.31 (v br s, HC=N and C_6H_5); ^{13}C NMR ($CDCl_3$) 31.45 (br s, N-CH_3), 86.43 (br s, C≡C), 127.50 (s, C=N), 131.7–135.17 (m, C_6H_5), 198.64 (s, CO); IR (KBr) 2115 (s), 2079 (vs), 2062 (vs), 2055 (vs), 2040 (vs) (CO), 1675 (C=N) cm^{-1}. Anal. Calcd for $C_{36}H_{26}Co_4N_8O_{12}P_2S_2$; C, 38.44; H, 2.33; N, 9.96. Found: C, 38.02, H, 2.28; N, 9.79.

9a: ^{31}P NMR ($CDCl_3$) 23.5; ^1H NMR ($CDCl_3$) 3.00 (br s, N-CH_3), 7.31 (v br s, HC=N and C_6H_5); ^{13}C NMR ($CDCl_3$) 31.45 (br s, N-CH_3), 86.42 (br s, C≡C), 127.70 (s, C=N), 131.65–135.40 (m, C_6H_5), 198.63 (s, CO); IR (KBr) 2114 (s), 2079 (vs), 2060 (vs), 2057 (vs), 2034 (vs) (CO), 1673 (C=N) cm^{-1}. Anal. Calcd for $C_{36}H_{26}Co_4N_8O_{14}P_2$: C, 39.57; H, 2.40; N, 10.26. Found: C, 39.71; H, 2.29; N, 10.07.

Synthesis of the Phosphodihydrazones 12a,b. A solution of phosphodihydrazides **1a** or **1b** (4.3 mmol) in 30 mL of methanol was added dropwise to a solution of the monoacetal **11** (1.35 g, 8.6 mmol) in 20 mL of methanol at 0 °C. The mixture was stirred at room temperature for 4 h. The solvent was removed under reduced pressure, and the resulting oil was treated with 3 × 20 mL of a 1:1 chloroform/ether solution. **12a** was obtained as white crystals while **12b** was a yellow oil.

12a: yield 94%; ^{31}P NMR ($CDCl_3$) 21.3; ^1H NMR ($CDCl_3$) 1.12 (t, $^3J_{HH}$ = 7 Hz, CH_2CH_3), 2.92 (d, $^3J_{PH}$ = 7 Hz, N-CH_3), 3.52 (q, $^3J_{HH}$ = 7 Hz, CH_2), 5.27 (s, $CH(OCH_2CH_3)_2$), 6.66 (s, HC=N), 7.4–7.8 (m, C_6H_5); ^{13}C NMR ($CDCl_3$) 15.1 (s, CH_2CH_3), 31.41 (d, $^2J_{PC}$ = 8 Hz, N-CH_3), 61.20 (s, CH_2), 81.32 (s, C≡$CCH(OCH_2CH_3)_2$), 86.20 (s, N=CHC≡C), 91.78 (s, $CH(OCH_2CH_3)_2$), 120.06 (d, $^3J_{PC}$ = 15.9 Hz, C=N–), 127.9–133.7 (m, C_6H_5); IR (KBr) 1660 (C=N) cm^{-1}; MS, *m/e* 490. Anal. Calcd for $C_{24}H_{35}N_4O_5P$: C, 58.75; H, 7.20; N, 11.43. Found: C, 58.61; H, 7.09; N, 11.21.

12b: yield 80%; ^{31}P NMR ($CDCl_3$) 78.7; ^1H NMR ($CDCl_3$) 1.21 (t, $^3J_{HH}$ = 7 Hz, CH_2CH_3), 3.02 (d, $^3J_{PH}$ = 9.3 Hz, N-CH_3), 3.59 (q, $^3J_{HH}$ = 7 Hz, CH_2), 5.34 (s, $CH(OCH_2CH_3)_2$), 6.72 (s, HC=N), 7.4–7.8 (m, C_6H_5); ^{13}C NMR ($CDCl_3$) 15.18 (s, CH_2CH_3), 31.70 (d, $^2J_{PC}$ = 10 Hz,

Table II. Crystallographic Parameters for **5a**

formula	$(C_{14}H_{15}N_4O_2P)_2$
T, K	293
cryst syst	monoclinic
space group	C_2/C
a, Å	16.94 (3)
b, Å	6.16 (4)
c, Å	28.41 (2)
β, deg	93.6 (1)
vol, Å^3	2956
d(calcd), g·cm^{-3}	1.358
formula wt	640.5
Z	2
cryst size, mm	0.4 × 0.3 × 0.2
F(000), electrons	632
radiation	Mo Kα
scan-mode	$\theta/2\theta$
scan-rate in ω	(0.85 + 0.347 tan θ)
abs coeff μ, cm^{-1}	0,9
total reflcns	3981
$I > 3\sigma$	2400
no. of variables	190
R	0.046
R_w	0.050
goodness of fit, S	1.37
max shift/esd	0.32
max peak in diff map, eÅ^{-3}	0.38

N-CH_3), 61.09 (s, CH_2), 81.36 (s, C≡*C*CH(OCH_2CH_3)$_2$), 85.96 (s, N=HCC≡C), 91.65 (s, *C*H(OCH_2CH_3)$_2$), 120.26 (d, $^3J_{PC}$ = 16 Hz, C=N-), 127.8-133.9 (m, C_6H_5); MS, *m/e* 506. Anal. Calcd for $C_{24}H_{35}N_4O_4PS$: C, 56.89; H, 6.97; N, 11.06. Found: C, 56.71; H, 7.02; N, 10.82.

Formolysis of Phosphohydrazones 12a,b. To 2.4 mmol of phosphohydrazone **12a** or **12b** in 3 mL of dichloromethane and 2 g of anhydrous $CuSO_4$ was added 1 mL of formic acid. The solution turned deep red. After the mixture was stirred for 45 min at room temperature, 25 mL of dichloromethane were added. The resulting mixture was filtered on glass wool and P_2O_5 (4 g) in 20 mL of dichloromethane was added to the filtrate in order to eliminate formic acid in excess. The solution was stirred for 2 h and filtrated on glass wool and sand. Evaporation of the solvent afforded **13a** or **13b** as yellow oils.

13a: yield 20%; ^{31}P NMR ($CDCl_3$) 21.3; ^{1}H NMR ($CDCl_3$) 2.96 (d, $^3J_{PH}$ = 5.7 Hz, N-CH_3), 6.62 (s, HC=N), 7.4-7.8 (m, C_6H_5), 9.30 (s, HC=O); ^{13}C NMR ($CDCl_3$) 31.39 (d, $^2J_{PC}$ = 8 Hz, N-CH_3), 83.20 and 86.00 (s, -C≡C-), 121.3 (d, $^3J_{PC}$ = 15 Hz, C=N), 128-133.7 (m, C_6H_5), 178.2 (s, HC=O); MS, *m/e* 342. Anal. Calcd for $C_{16}H_{15}N_4O_3P$: C, 56.13; H, 4.42; N, 16.37. Found: C, 55.94; H, 4.31; N, 16.22.

13b: yield 22%; ^{31}P NMR ($CDCl_3$) 78.7; ^{1}H NMR ($CDCl_3$) 3.06 (d, $^3J_{PH}$ = 9.2 Hz, N-CH_3), 6.75 (s, HC=N), 7.4-7.8 (m, C_6H_5), 9.28 (s, HC=O); ^{13}C NMR ($CDCl_3$) 31.70 (d, $^2J_{PC}$ = 9.8 Hz, N-CH_3), 81.45 and 85.70 (s, -C≡C-), 120.30 (d, $^3J_{PC}$ = 16 Hz, C=N), 127.8-133.9 (m, C_6H_5), 178.4 (s, HC=O); MS, *m/e* 358. Anal. Calcd for $C_{16}H_{15}N_4O_2PS$: C, 53.62; H, 4.22; N, 15.64. Found: C, 53.21; H, 4.11; N, 15.34.

Synthesis of the Dissymmetric Macrocycle 14. Compound **14** can be prepared either from the addition of phosphodihydrazide **1a** to phosphodihydrazone **13b** or from the treatment of phosphodihydrazide **1b** with phosphodihydrazone **13a**. In a typical experiment a solution of **1a** (or **1b**) (2 mmol) in 30 mL of methanol and a solution of **13b** (or **13a**) (2 mmol) in 30 mL of methanol were added simultaneously and dropwise at room temperature over a period of 1 h. The mixture was stirred for 3 h during which a yellow precipitate was formed. After usual workup (see preparation of **5, 7, 8**) **14** was obtained as a yellow powder.

14: yield 90%; ^{31}P NMR ($CDCl_3$) 78.5 (s, P=S), 23.1 (s, P=O); ^{1}H NMR ($CDCl_3$) 3.01 (d, $^3J_{PH}$ = 5.9 Hz, N-CH_3), 3.03 (d, $^3J_{PH}$ = 7.2 Hz, N-CH_3), 7.13 (s, HC=N), 7.24 (s, HC=N), 7.54-7.8 (m, C_6H_5); ^{13}C NMR ($CDCl_3$) 31.82 (d, $^2J_{PC}$ = 8 Hz, N-CH_3), 32.75 (d, $^2J_{PC}$ = 7.8 Hz, N-CH_3), 87.46 (s, -C≡C-) 87.85 (s, -C≡C-), 121.20 (v br s, C=N), 128.5-133.58 (m, C_6H_5); MS, *m/e* 536. Anal. Calcd for $C_{24}H_{26}N_8OP_2S$: C, 53.72; H, 4.89; N, 20.89. Found: C, 53.41; H, 4.51; N, 20.49.

Crystallographic Structure Determination of 5a. X-ray data were collected at room temperature with a Enraf-Nonius CAD4 four-circle automated diffractometer equipped with a graphite monochromator. The unit-cell parameters were obtained by least-squares refinement of the setting angles of 25 reflections in the range $8° < \theta < 15°$. No significant change was detected in the intensity of the three standard reflections; Lorentz and polarization corrections were applied to the data; the linear absorption coefficient is 0.9 cm^{-1} for the Mo Kα radiation; an empirical absorption correction was applied to the data between 0.88 and 1.09. Table II provides some important details on crystal parameters, data collection, and refinement.

The crystal structure was solved by using direct methods and refined by full-matrix least-squares calculations (SDP)[10] to a final R index of 0.046. Hydrogen atoms were localized by difference Fourier Map and replaced at idealized positions (at 0.97 Å to the bonded atoms) with an isotropic temperature factor = 1.1, the value of the equivalent isotropic temperature of the bonded atom.

Scattering factors were taken from Cromer and Waber.[11] Anomalous dispersion effects were included in F_c,[12] the values of f' and f'' were those of Cromer.[13] Only the 2400 reflections having intensities greater than 3.0 times their standard deviations were used in the refinements.

Only half of the molecule is refined, and the other half is obtained by the following symmetry operation: $-x, y, {}^1/_2 - z$. The star atoms in the ORTEP representation are those resulting from this symmetry operation.

Table III giving positional parameters and their estimated standard deviations is in the supplementary material.

Supplementary Material Available: Listing of anisotropic and isotropic general temperature factors, refined temperature factors, root mean square amplitude of thermal vibration, and positional parameters (15 pages); tables of observed and calculated structure factors (28 pages). Ordering information is given on any current masthead page.

(10) *CAD4 Operations Manual*; Enraf-Nonius, Delft, 1977.
(11) Cromer, D. T.; Waber, J. T. *International Tables for X-Ray Crystallography*; The Kynoch Press: Birmingham, England, 1974; Vol. IV, Table 2.28.
(12) Ibers, J. A.; Hamilton, W. C. *Acta Crystallogr.* **1964**, *17*, 781.
(13) Cromer, D. T. *International Tables for X-Ray Crystallography*; The Kynoch Press: Birmingham; England, 1974; Vol. IV, Table 2.3.1.