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Polyazaphosphorus Macrocycles: Synthesis, Reactivity, Complexation

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ABSTRACT

A general synthesis of various polyazaphosphorus macrocycles involving [1 + 1], [2 + 2], or [3 + 3] cyclocondensations is reviewed, as well as the attempted synthesis of cryptands. Selective reduction (imino functions) methylation (P=S groups), silylation (P=O groups) are reported. Preparations of some macrocycle complexes are described.

INTRODUCTION

Studies of complex forming properties of macrocycles were mainly initiated by the pioneering work of Pedersen in 1967 [1]. His observations stimulated an extraordinary volume of research over the next decades, and it appeared that macrocycles had a broad scope of applications. Although some phosphorus macrocycles have also been known since the middle of the seventies, it is only in the last ten years that the synthesis of new phosphorus macrocyclic complex forming agents has been intensively investigated [2].

Three main types of reactions can be pointed out, among the various reported preparations of phosphorus macrocycles.

- Ring opening of cyclic phosphonites leading to macrocyclic and oligomeric species [2].
- Condensation reactions between halogenated phosphines or phosphine oxides or sulfides and difunctional reagents such as diols, dithiols, diamines, and dilithiated derivatives. These experiments allow the synthesis of various P—O, P—S, P—C, or more scarcely P—N containing macrocycles [2].
- Template reactions leading to macrocyclic complexes [2].

In most cases these syntheses necessitate either starting reagents difficult to prepare or high dilution techniques. Furthermore, phosphorus macrocycle yields are generally low. These observations have prompted us to investigate synthetic routes to free macrocycles.

Our aim is to find a one-step high yield method of preparing various macrocycles that is also general and easy. 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 (e.g., nitrogen, oxygen, etc.) or unsaturated bonds suitable for complexation.

SYNTHESIS

We have chosen to study the reactivity of phosphodi- or trihydrazides towards 1–2, 1–3, 1–4, 1–6, etc. dialdehydes.

Slow addition of a methanolic solution of a phosphodihydrazide and a solution of a dialdehyde in methanol to methanol leads to the formation of the expected macrocycles (Scheme 1).

A number of advantages of this method can be pointed out: (i) the reaction proceeds under very

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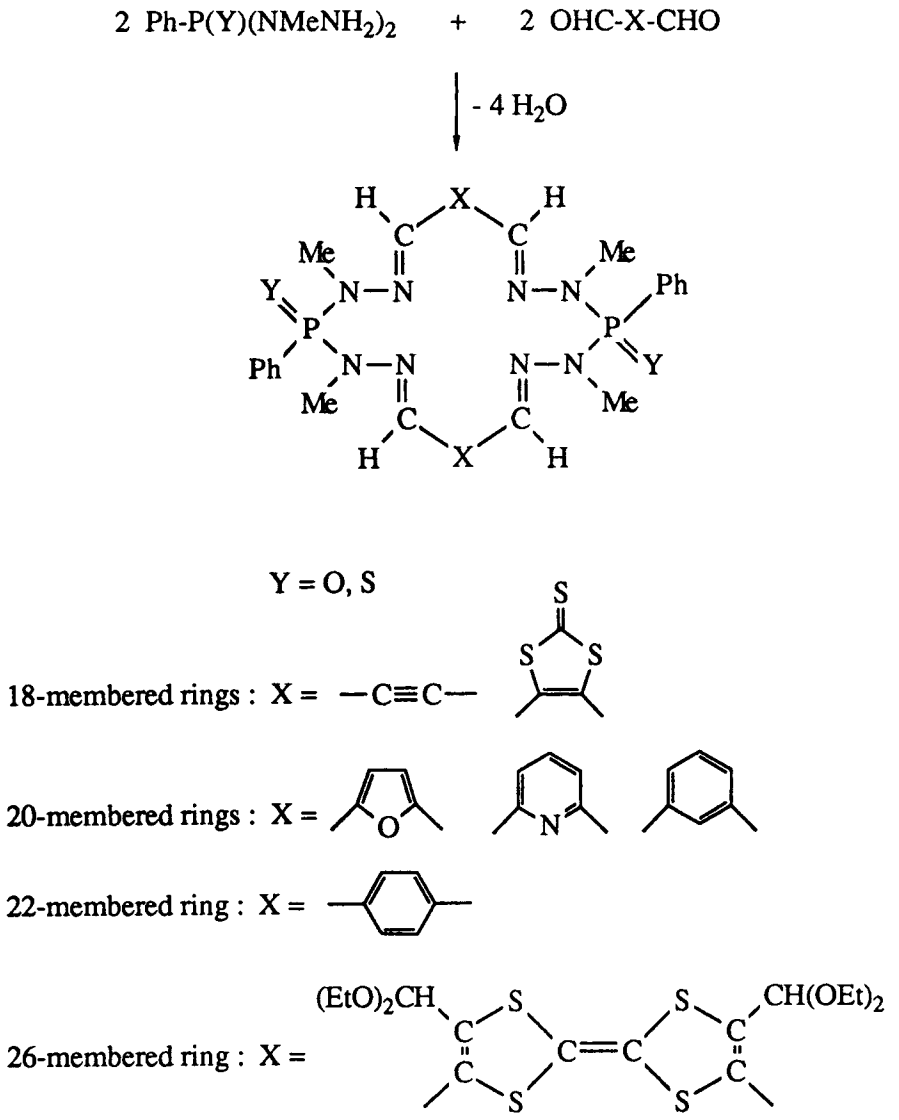


SCHEME 1

mild conditions (room temperature, stirring for two hours) 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.

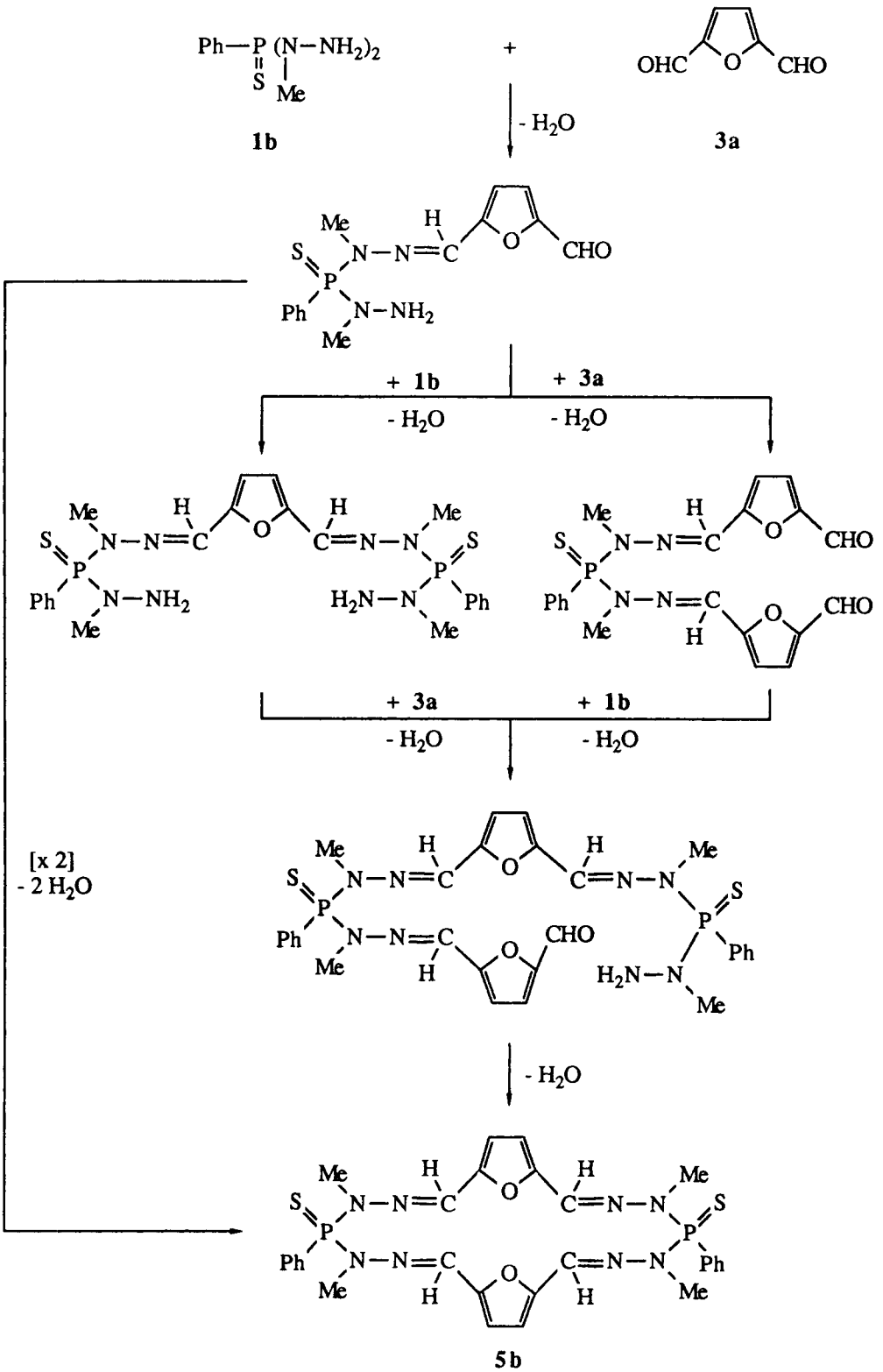
Various phosphorus macrocycles are thus formed in a one-pot procedure from phosphodihydrazides easily synthetized by reacting oxo- or thiodichlorophosphines with methylhydrazine [3].

All of these large-membered rings are stable white or yellow powders nonsensitive to hydrolysis and 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.

[2 + 2] *Cyclocondensations*

[2 + 2] Cyclocondensations take place when 1–2 dialdehydes **2** (acetylene dicarbaldehyde, 4–5 diformyl dithiol thione), 1–3 dialdehydes **3** (2–5 furan dicarboxaldehyde, 2–6 pyridine dicarboxaldehyde, 1–3 benzene dicarboxaldehyde), 1–4 dialdehyde **4** (1–4 benzene dicarboxaldehyde) or 1–6 dialdehyde **6** (diformyl diacetal tetrathiafulvalene, cis isomer) are reacted with oxo- or thiophenyl phosphodihydrazides $PhP(Y)(NCH_3NH_2)_2$ (**1a**: Y = O, **1b**: Y = S). Structures of the resulting 18, 20, 22, or 26 membered rings were deduced from ^{31}P, ^{1}H, ^{13}C NMR, IR, and mass spectrometry as well as microanalysis. Unambiguous characterization of the structure of one of these derivatives was given by X-ray crystallographic studies [4].

Possible routes to the formation of the [2 + 2]



Mechanism of Formation of [2 + 2] Macrocycles: Case of Macrocyle **5b**.

SCHEME 2

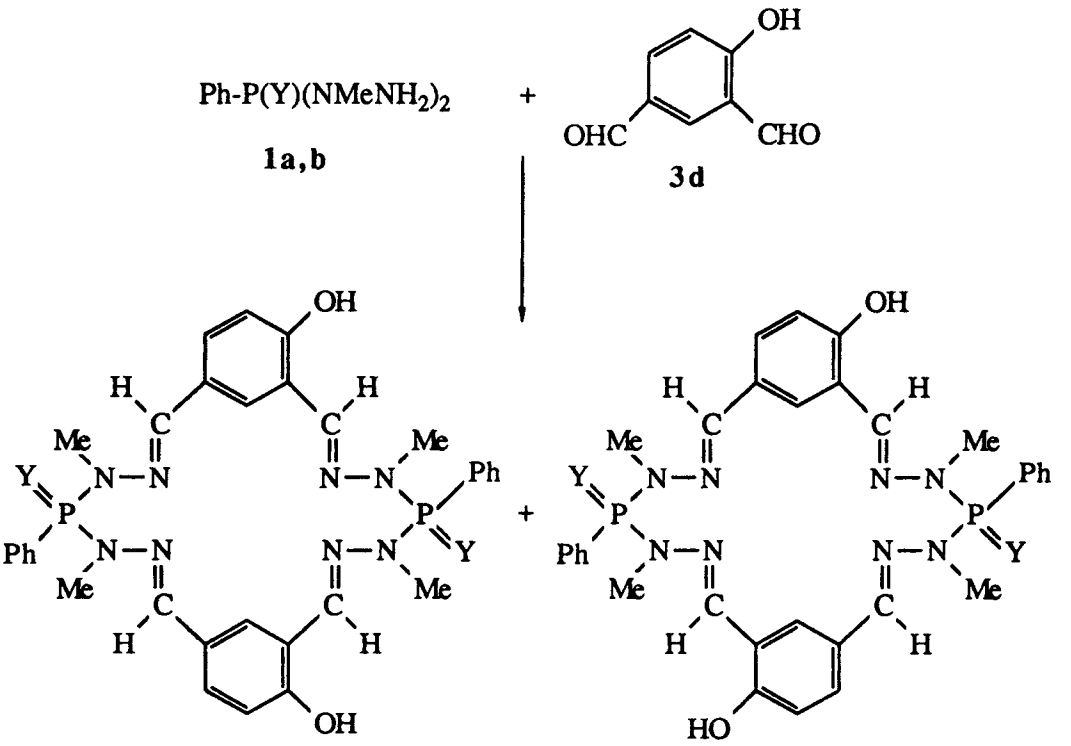
macrocycles are indicated in Scheme 2. Mechanisms of formation of these compounds have been elucidated by variable temperature ^{31}P NMR experiments.

A functionalized macrocycle with a ring size of 20 atoms is also easily prepared by adding the 4-hydroxy-1,3-benzenedicarboxaldehyde, **3d**, to the phenylthiophosphodihydrazide, **1b** (Scheme 3). Two isomers, **5c** and **5c'**, were formed in equal amount as depicted by ^{31}P NMR spectroscopy, which shows three signals in 1:1:2 ratio at δ 78.47, 78.11, and 77.42, respectively. The two phosphorus atoms of isomer **5c'** are equivalent (one signal at δ 77.42) 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 us to distinguish one from the other since all of the CH=N protons are observed as a singlet at δ 6.60. Two resonances at δ 157.78 and 157.40 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**, **5d'**. ^{31}P NMR experiments did not permit us to know whether one or two isomers are formed in this case (there was only one broad signal at δ 24.3). Nevertheless, ^{13}C NMR spectra give a positive answer for the presence of two isomers since two singlets are observed at δ 157.64 and 157.96 for the imino carbons.

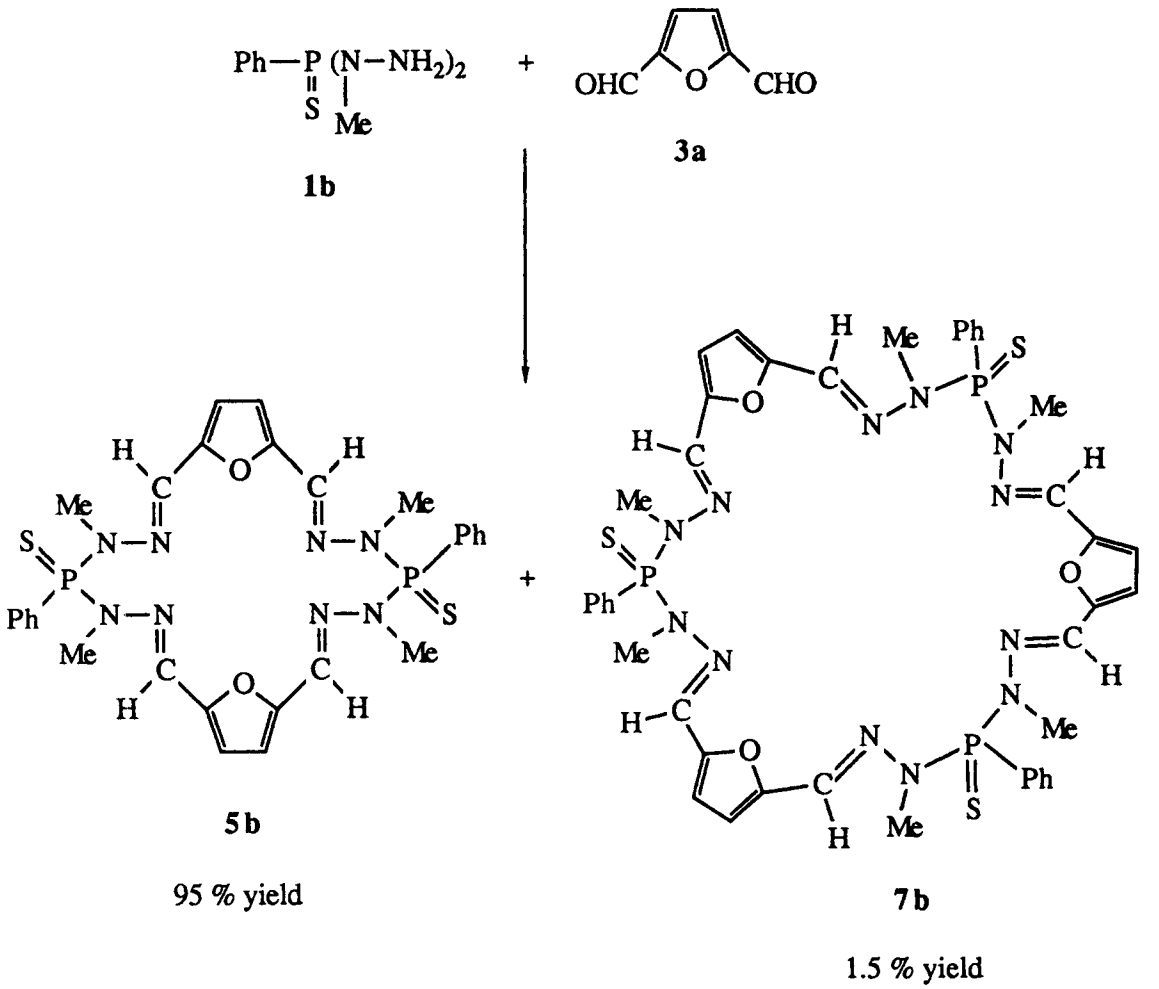
[3 + 3] *Cyclocondensations*

The formation of all of these 20-membered rings involves [2 + 2] condensation reactions. Actually, a [3 + 3] condensation is also observed when the phosphodihydrazide **1b** is treated with the 2,5-furandicarboxaldehyde **3a** in methanol. In addition to the macrocycle **5b** (95% yield) we isolated in poor yield (1.5%) the corresponding 30-membered ring **7b** possessing three phosphorus atoms in the ring (Scheme 4). The NMR data of this derivative are quite similar to those given by the 20-membered one. Mass spectrometry provided a direct confirmation of the structure (*m/e*: 954).



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

SCHEME 3



SCHEME 4

[1 + 1] Cyclocondensations

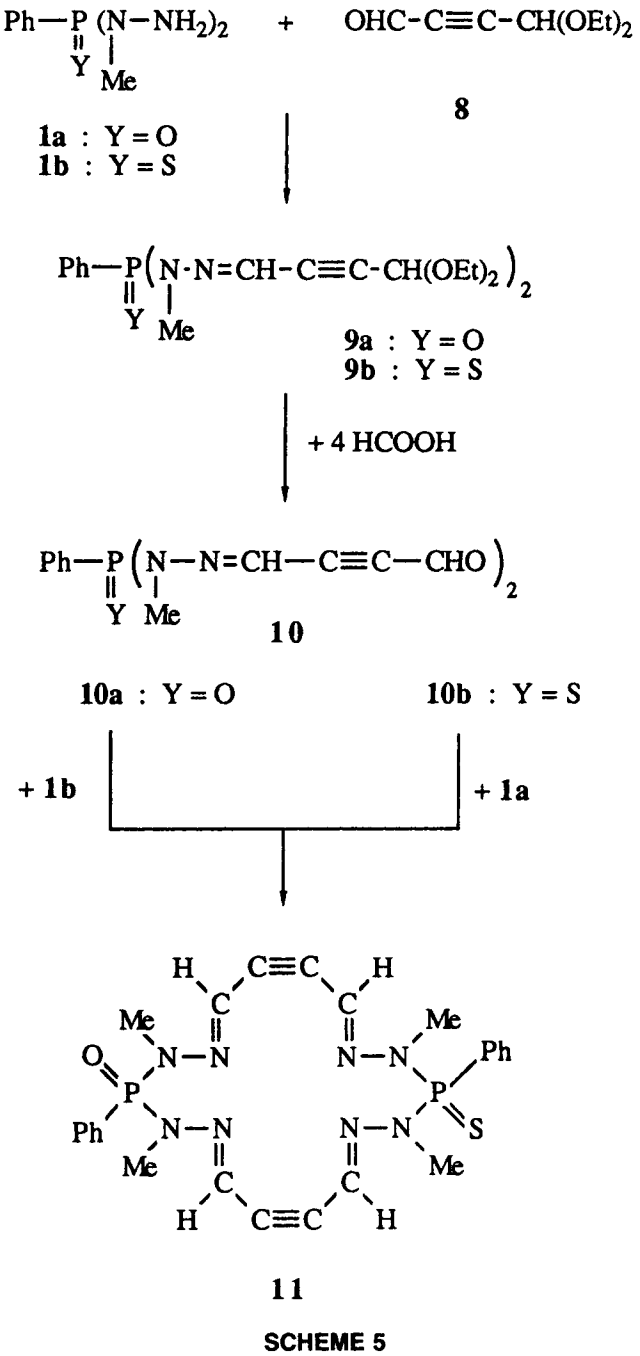
All the reactions reported above described the preparation of symmetric phosphorus macrocycles, i.e. compounds in which the two phosphorus atoms of the molecule are linked to the same substituents. To the best of our knowledge, no example of phosphorus large-membered rings in which the two (or more) 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 5, involves the preliminary formation of the new polyfunctionalized phosphodihydrazides **9a,b**, **10a,b**.

Addition of a methanolic solution of the monoacetal of ADCA, **8**, to the phosphodihydrazide **1a**, also in methanol, led to the formation of the phosphodihydrazide, **9a**, isolated in 94% yield. The formolysis of **9a** was carried out with anhydrous formic acid in the presence of anhydrous $CuSO_4$. After 1 h reaction at room temperature, the polyfunctionalized phosphodihydrazide, **10a**, was easily isolated in 20% yield after work up. Compound **10a** is a pale yellow oil that has been identified by mass spectrometry (m/z = 358). The proton NMR spectrum gives evidence of the presence of aldehydic protons: the CHO groups of **10a** exhibit a well resolved singlet at δ 9.3.

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 one equiv of **10a** in methanol to the phosphodihydrazide **1b** in the same solvent results in the selective precipitation of the dissymmetric eighteen-membered ring **11** (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 **10a** and 2 equiv of **1b** were detected. Compound **11** was obtained as a stable yellow powder. Mass spectrometry gives evidence of a parent ion at m/z 536.

^{31}P, ^{1}H, and ^{13}C NMR spectra reveal the dissymmetry due to the presence of phosphoryl and thio-



SCHEME 5

phosphoryl groups. ^{31}P NMR shows two singlets at δ 78.5 (P=S) and δ 23.1 (P=O), as expected. The presence of two doublets (δ 3.01, $^{3}J_{PH}$ = 5.9 Hz; δ 3.03, $^{3}J_{HP}$ = 7.2 Hz) for the four N—CH_3 groups also points out this phenomena in proton NMR. ^{13}C NMR spectra also allow us to distinguish two different resonances for carbon atoms of the methyl groups (δ 31.82, d, $^{2}J_{CP}$ = 8 Hz; δ 32.75, d, $^{2}J_{CP}$ = 7.8 Hz) as well as two signals (δ 87.46 s, δ 87.85 s) for the C≡C moieties, while a broad singlet is observed for the four imino carbons.

Interestingly, macrocycle **11** can be obtained through the sequence

$$\mathbf{1b} \longrightarrow \mathbf{9b} \longrightarrow \mathbf{10b} \xrightarrow{+\mathbf{1a}} \mathbf{11}$$

Compounds **9b** and **10b** were also isolated and fully characterized.

Attempted Synthesis of Phosphorus Cryptands

Three methods for the preparation of phosphorus cryptands were investigated.

Method 1: The [1 + 1] cyclocondensation of a phosphotrihydrazide such as **12b** with a phosphorus trialdehyde **14** (Scheme 6).

Method 2: The [2 + 3] cyclocondensation of 2 equiv of **12a** or **12b** with 3 equiv of nonphosphorylated dialdehydes (Scheme 6).

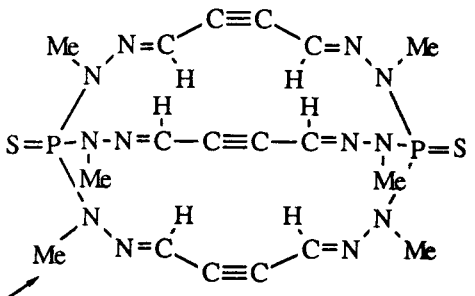
Method 3: The desulfuration of macrocycle **5e** (Scheme 7).

Method 1 necessitates the preliminary synthesis of a phosphorus trialdehyde. Up to now no phosphorus trialdehyde has been reported. The preparation of the first compound of this type is outlined in Scheme 8. Addition of 3 equiv of monoacetal aldehyde **8** to 1 equiv of thiophosphotrihydrazide **12b** leads to the phosphotrihydrazone **13** isolated as white crystals in 85% yield. Treatment of **13** with 6 equiv of formic acid leads to the new aldehyde **14** in 15% yield. The structure of **14** is deduced from ^{31}P, ^{1}H, ^{13}C NMR, IR, and mass spectrometry as well as microanalysis. ^{1}H NMR spectra show a characteristic resonance at δ 9.4 for the aldehyde protons while ^{13}C NMR exhibits a signal at δ 176 for the carbonyl groups. Furthermore IR spectroscopy (intense $\nu_{C=O}$ at 1685 cm^{-1}) and mass spectrometry (*m/e*: 390) are in agreement with the proposed structure.

Use of this multifunctionalized phosphorus trialdehyde **14** should be of the greatest interest in organic and organometallic chemistry since three imino functions and three acetylenic functions are also present in the molecule.

Simultaneous addition of a methanolic solution of **14** to a methanolic solution of the phosphotrihydrazide **12b** (method 1) or the addition of 3 equiv of 2–5 furandicarboxaldehyde or 2.6-benzenedicarboxaldehyde in methanol to a methanolic solution of phósphotrihydrazide **12a** or **12b** (2 equiv) (method 2) does not lead to the desired macrobicyclic derivatives **15a–c**. In each case, polymeric species (**16a,b, 17a,b, 18a,b**) are obtained as poorly soluble yellow orange or brown powders in 60–80% yield.

The most intense ions observed when the species were submitted to mass spectrometry correpond to macrocyclic fragments **19** possessing free hydrazino groups. In addition IR spectroscopy shows the presence of characteristic absorption bands of

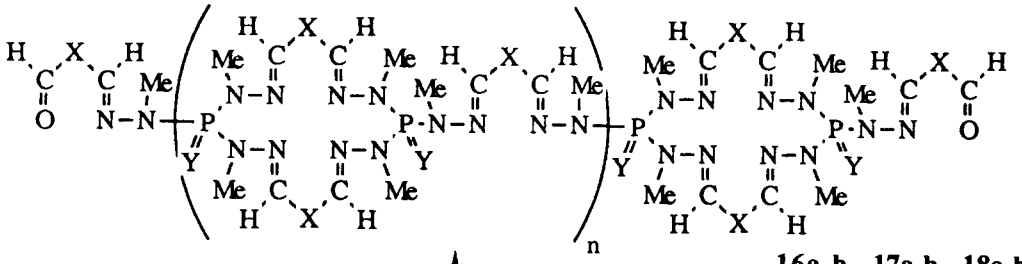


15c

Method 1

(S)P{NMe–N=CH–C≡C-CHO)$_3$ + (S)P{NMe–NH$_2$)$_3$

14 **12b**

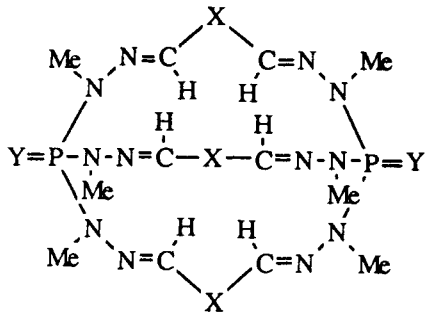


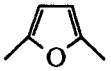
16a,b, 17a,b, 18a,b

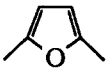
Method 2

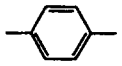
2 (Y)P(NMeNH$_2$)$_3$ + 3 OHC-X-CHO

12a Y = O
12b Y = S



15a, 16a : X =  ; Y = O

15b,16b : X =  ; Y = S

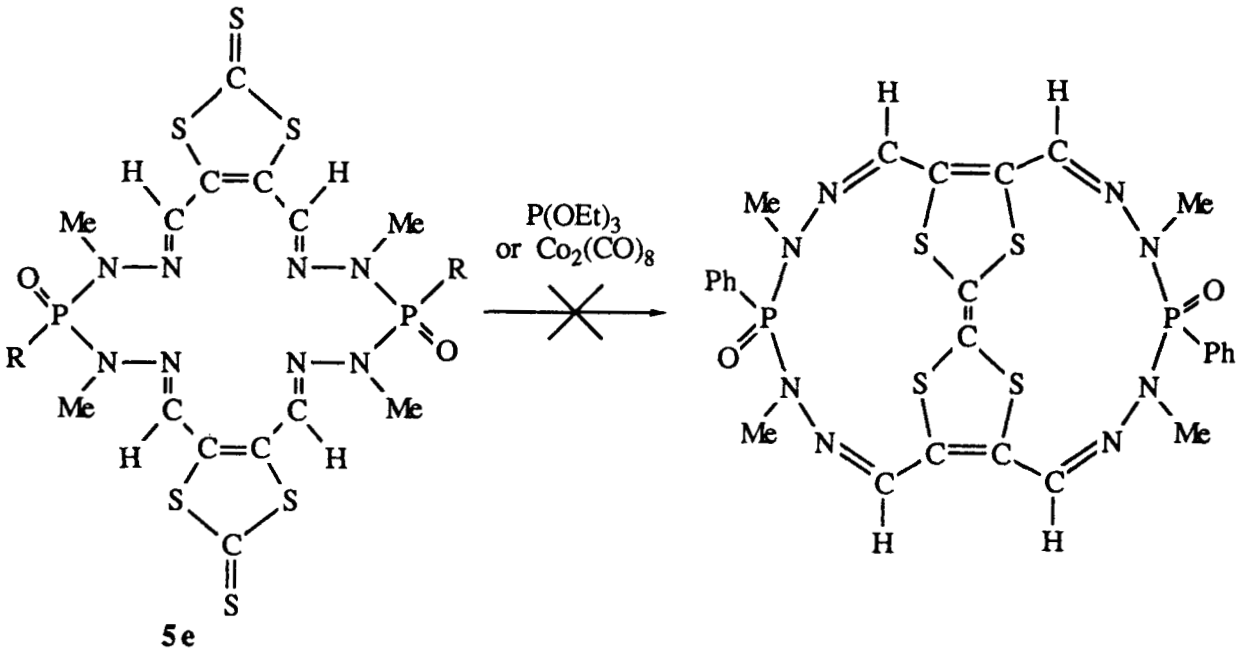
17a : X =  ; Y = O

17b : X =  ; Y = S

18a : X = ; Y = O

18b : X =  ; Y = S

SCHEME 6

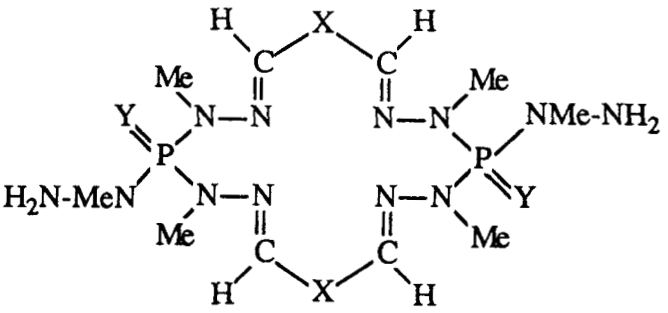


5e

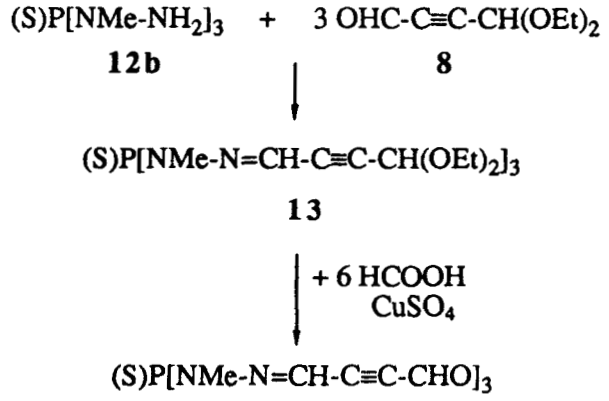
SCHEME 7

carbonyl functions (($\nu_{C=O}$): 1680 cm^{-1} (w)) and imino functions (($\nu_{C=N}$): 1630 cm^{-1} (w)). NMR data are consistent with the proposed polymeric structures; indeed, the presence of terminal aldehyde functions are detected in ^1H NMR as well as ^{13}C NMR.

Method 3 consists of the reaction of the 18-membered ring **5e** with dicobaltoctacarbonyl or with triethyl phosphite. No reaction is detected with $P(OEt)_3$ even under drastic conditions while the addition of $Co_2(CO)_8$ gives only weakly soluble polymeric species (Scheme 7).



19



SCHEME 8

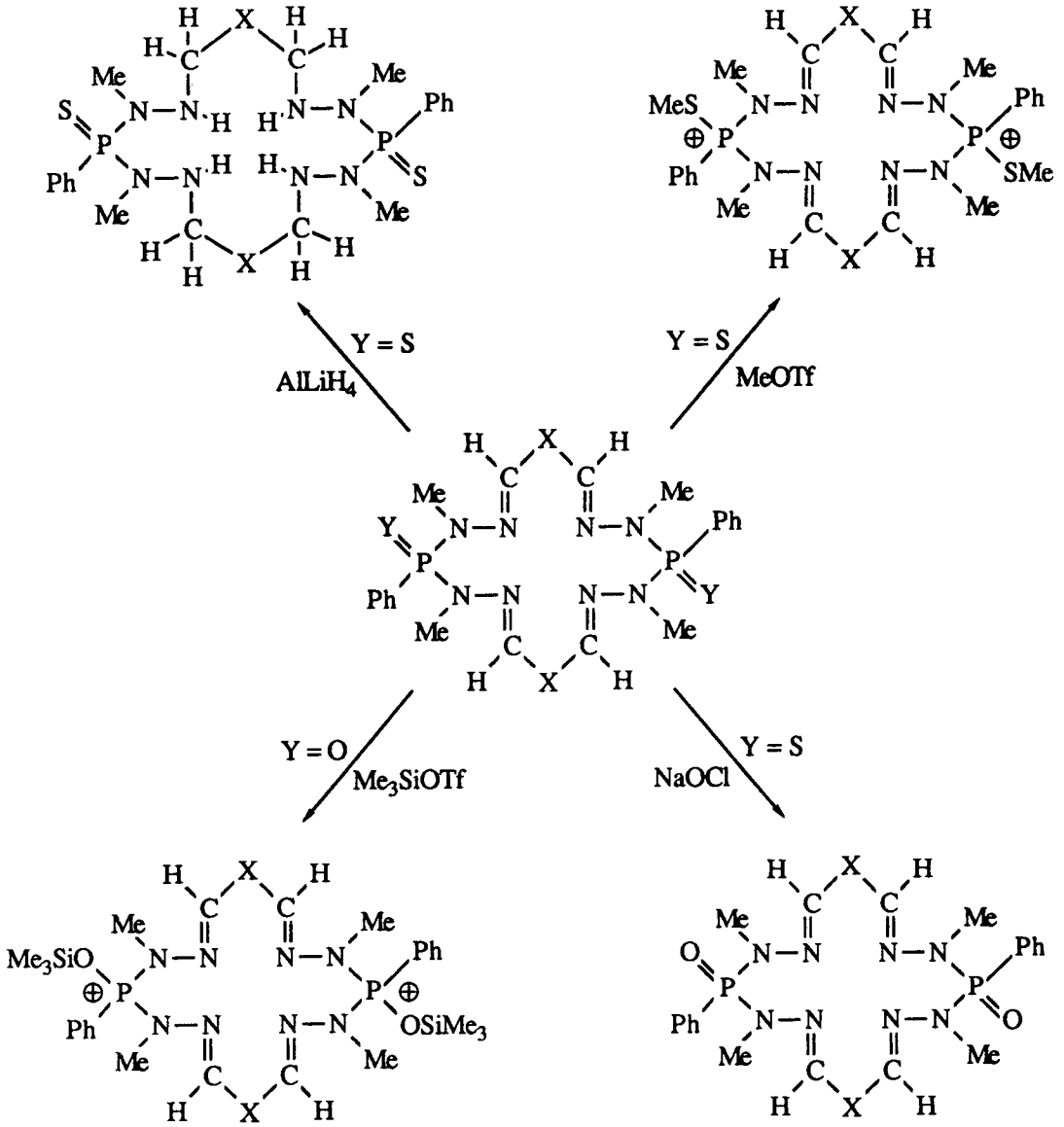
REACTIVITY OF PHOSPHORUS MACROCYCLES

We have found that free polyazadiphosphorus macrocycles are selectively reduced (imino functions) by means of lithium aluminum hydride to give the corresponding NH macrocycles (Scheme 9). Selective methylation of thiophosphoryl groups or selective silylation of phosphoryl groups occur when macrocycles are treated with MeOTf or Me_3SiOTf (OTf = CF_3SO_3).

Thiophosphoryl macrocycles are cleanly transformed into the corresponding phosphoryl derivatives by treatment with aqueous NaOCl.

Complexations

A stable complex **20** is nearly quantitatively obtained when the macrocycle **5a** (2 equiv) in THF

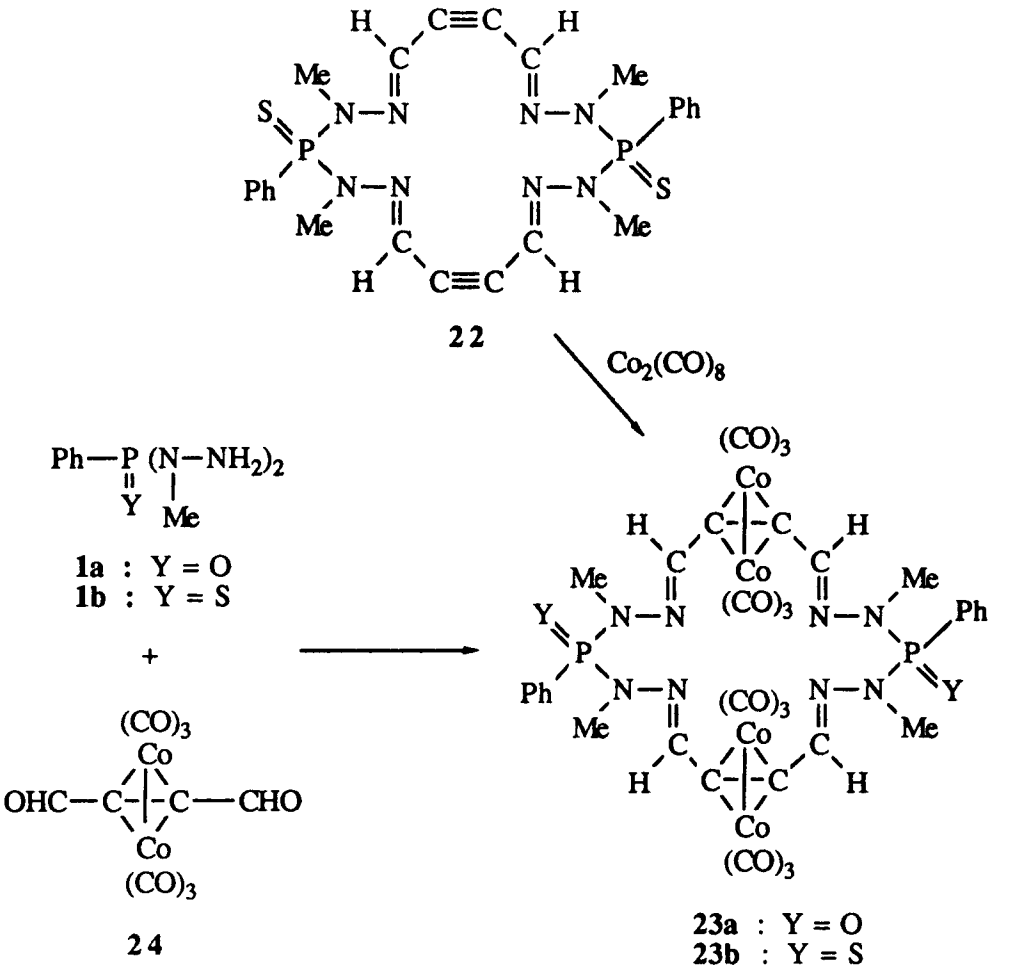


SCHEME 9

and the salt $Ba(ClO_4)_2$ (1 equiv) in the same solvent were simultaneously mixed at room temperature. Compound **20** is isolated as a yellow powder (85% yield) and characterized by its spectroscopic data and elemental analysis indicating a 2:1 macrocycle:metal stoichiometry.

Although no suitable crystals for an X-ray study could be formed, compound **20** may be described as a 12-coordinate Ba^{2+} "sandwich" complex $[BaL_2][ClO_4^-]_2$ (L = **5a**) by analogy with a related 18-membered conjugated tetraimino macrocyclic complex described by Nelson et al. [5]. The occurrence of one $\nu_{(C=N)}$ vibration in the IR spectrum of this bis(macrocycle)barium complex and the equivalence of the hydrogen atoms in the ^1H NMR spectrum suggest that the two molecules of the macrocycles are coordinated in the same way. Indeed the infrared spectrum shows a relatively strong band at 1620 cm^{-1}, which is characteristic of the eight coordinated C=N groups. Moreover the $\nu_{(P=O)}$ absorption is significantly shifted from 1250 to 1210 cm^{-1} suggesting that Ba^{2+} is also coordinated to the four phosphoryl groups and not to the oxygen of the four furfural moieties.

Another synthetic route to complex **20** has been applied by using metal template procedures. The reaction of the phosphodihydrazide **1a** with the 2,5-furan dicarboxaldehyde in the presence of $Ba(ClO_4)_2$ in 2:2:1 molar ratio in methanol at 60°C gave **20** (80% yield). An additional complex of Ba(II) having a 2:1 ligand:metal ratio, **21**, could also be obtained by a methathetical method involving addition of



SCHEME 10

$NaBPh_4$ to the solution of $BaL_2(ClO_4)_2$ in a 1:1 DMF/MeOH solvent mixture.

Complexation ability of the C≡C triple bond containing phosphorus macrocycles toward dicobaltoctacarbonyl was investigated.

Two approaches were selected. In a first approach, the free macrocycle **22** was treated with $Co_2(CO)_8$ in large excess. The corresponding complex **23b** was isolated in 90% yield. While no change appears in ^{31}P NMR, except the broadness of the signal (δ = 78.08), the complexation has a considerable influence on infrared and ^{13}C NMR spectra. As expected, $\nu_{(C=O)}$ vibrations are located between 2114 and 2040 cm^{-1}. A similar assignment is indicated for the ADCA hexacarbonyldicobalt complex, **24**. The ^{13}C NMR spectrum shows broad resonances at δ 86.43 (C≡C) and δ 198.64 (CO), among others.

In a second approach, a solution of complex **24**—easily obtained by treatment of ADCA with dicobalt octacarbonyl—in dichloromethane and a solution of the phosphodihydrazide **1b** in the same solvent were simultaneously added to dichloromethane (Scheme 10). The resulting complex (70% yield) exhibits the same spectroscopic data as **23b**.

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