Design of New Tools for Macrocyclic Synthesis. Applications to the Preparation of Polyphosphorus Macrocycles

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New diphosphorus *m,m'* or *p,p'* dialdehydes **2–7** were prepared by treatment of 1,3-di-*tert*-butyldiaza-2,4-dichlorodiphosphetidine, **1**, with 3- or 4-hydroxybenzaldehyde, and in the case of **4–7** in the presence of S_8. These initial compounds when reacted with phosphodihydrazides $RP(X)(NCH_3NH_2)_2$ **9** and **10** allowed the preparation, via [2 + 2] cyclocondensation reactions, of macrocycles **11–13**, **15**, and **16** possessing six phosphorus atoms in the skeleton, different coordination modes (tri- or tetracoordinate) and both N–P–N and O–P–N linkages. Reaction of the tetraphosphorus dihydrazide **20** with 1,2-benzenedicarboxaldehyde gave macrocycle **22** with a total annular size of 29 ring atoms. Macrocycles **23** or **24** were obtained by reacting **20** with 2,6-pyridinedicarboxaldehyde or 1,3-benzenedicarboxaldehyde. Asymmetry can also be introduced via [1 + 1] cyclocondensation of tetraphosphorus dihydrazides **18** or **19** with diphosphorus dialdehydes **3** or **2**; these reactions led to the 38-membered cyclic product **25**. Two macrocycles **27**, **28** incorporating five phosphorus atoms with three different types of phosphorus environments (C–P–C, N–P–N, and O–P–N) were obtained when tetraphosphorus dihydrazides **18** or **20** were reacted with the phosphorus dialdehyde **26**. All the reactions were found stereospecific.

Polyphosphamacrocycles have only recently received considerable attention as potential ligands.[1] However, interest in their synthesis, reactivity, and complexing properties is growing very rapidly. Macrocyclic compounds containing tricoordinated trivalent or tetracoordinated pentavalent phosphorus atoms bonded to carbon, oxygen, sulfur, or less frequently nitrogen have been obtained but only specific syntheses have been reported so far.

Our goal in this area is to develop a general strategy for the synthesis of macrocycles possessing P–N–N linkages. The inclusion of such a group may be advantageous for the following reasons: (i) phosphorus nitrogen bonds in this type of compounds are insensitive to acid or basic hydrolysis even under very forcing conditions, (ii) phosphodihydrazides $-P(X)(NNH_2)_2$ and $-P(X)(NN{=}C<)_2$ and related compounds are powerful ligands. Thus, imino nitrogen atoms participate in the complexation of a large variety of metal ions,[2] and we recently demonstrated that, for example, a dinuclear copper complex $[[C_6H_5P(S)[N(CH_3)N{=}CHC_5H_4FeC_5H_5]_2,Cu]]_2[CF_3SO_3]_2$ can be easily prepared by reacting $C_6H_5P(S)[N(CH_3)N{=}CHC_5H_4FeC_5H_5]_2$ with $Cu(CF_3SO_3)_2$.[3] Lastly, sandwich complexes were formed from phosphorus-containing macrocycles incorporating P–N–N linkages,[4] (iii) the different coordination modes of phosphorus may increase the possibilities of complexation, it is well-known that phosphine oxides or sulfides are good complexing agents for alkali or alkali earth metals while the corresponding phosphines easily complex transition metal,[5] (iv) various functional groups can be linked to phosphorus, thus dramatically increasing the potential reactivity of the resulting macrocyclic species.

We have recently reported the synthesis of various diphosphorus (exclusively P–N–N) macrocycles[6] and the preparation of tetraphosphorus macrocycles with intracyclic P–N and P–C bonds.[7]

All these reactions involve the treatment of phosphodihydrazides $RP(X)(NCH_3NH_2)_2$ with a large variety of dialdehydes including in one case a phosphorus dialdehyde.[7]

The next challenge is to demonstrate the possibility of using the same type of reaction for the preparation of larger macrocycles including more than four phosphorus atoms with different coordination modes and different phosphorus environments (N–P–N, O–P–N, C–P–C, etc.).

It would also be of great interest to extend this method to the formation of asymmetric molecules, the cyclic chain being formed with two or three different skeletons. Until now, the asymmetry in such systems was derived from the presence of differently substituted phosphorus atoms in the ring.[6]

Investigations concerning the formation of odd link macrocycles are also of interest since all the P–N–N macrocycles reported so far present an even number of intracyclic bonds.

We report here the synthesis of new diphosphorus *m,m'*- or *p,p'*-dialdehydes **2–7** (phosphorus atoms are tri- or tetracoordinated). Stereospecific reactions involving these dialdehydes and easily available phosphodihydrazides, $C_6H_5P(X)(NCH_3NH_2)_2$, will be described allowing thus the preparation of macrocyclic compounds **11–13**, **15**, and **16** possessing for the first time six phosphorus atoms in the skeleton, different coordination modes, and both N–P–N and O–P–N linkages.

Lastly, the design of useful reagents, the long-chain acyclic phosphorus hydrazides **18–20**, will be presented as well as their use in the preparation of asymmetric phosphorus macrocycles **22–25**, **27**, and **28** incorporating four, five, or six phosphorus atoms and, in two cases (**27**, **28**), N–P–N, O–P–N, and C–P–C fragments in the same ring.

Results and Discussion

In order to increase and to vary the number of bonds in the macrocycles, we first prepared new dialdehydes

† UP 8241 liée par conventions à l'Université Paul Sabatier et à l'Institut National Polytechnique.

(1) See for example: Wei, L.; Bell, A.; Ahn, K. Y.; Holl, M. M.; Warner, S.; Williams, I. D.; Lippard, S. J. *Inorg. Chem.* **1990**, *29*, 825 and references cited therein.

(2) Ricker-Nappier, J.; Meek, P. W. *Chem. Commun.* **1974**, 442. Cabral, J. de O.; Cabral, M. F.; Drew, M. G. B.; Nelson, S. M.; Rodgers, A. G. *Inorg. Chim. Acta* **1977**, *25*, L 77. Scanlon, L. G.; Tsao, Y. Y.; Cummings, S. C.; Toman, K.; Meck, D. W. *J. Am. Chem. Soc.* **1980**, *102*, 6849. Scanlon, L. G.; Tsao, Y. Y.; Toman, K.; Cummings, S. C.; Meck, D. W. *Inorg. Chem.* **1982**, *21*, 1215.

(3) Delavaud-Nicot, B.; Lugan, N.; Majoral, J.-P.; Mathieu, R. *Inorg. Chem.*, in press.

(4) Majoral, J.-P.; Badri, M.; Caminade, A.-M.; Delmas, M.; Gaset, A. *Inorg. Chem.* **1988**.

(5) *Comprehensive Coordination Chemistry*; Pergamon Press: New York, 1987; Vol. 2, 715–738, 899–958.

(6) Badri, M.; Majoral, J. P.; Caminade, A. M.; Delmas, M.; Gaset, A.; Gorgues, A.; Jaud, J. *J. Am. Chem. Soc.* **1990**, *112*, 5618. Majoral, J. P.; Badri, M.; Caminade, A. M.; Delmas, M.; Gaset, A. *Inorg. Chem.* **1991**, *30*, 344.

(7) Gonce, F.; Caminade, A. M.; Majoral, J. P. *Tetrahedron Lett.* **1991**, *2*, 203.

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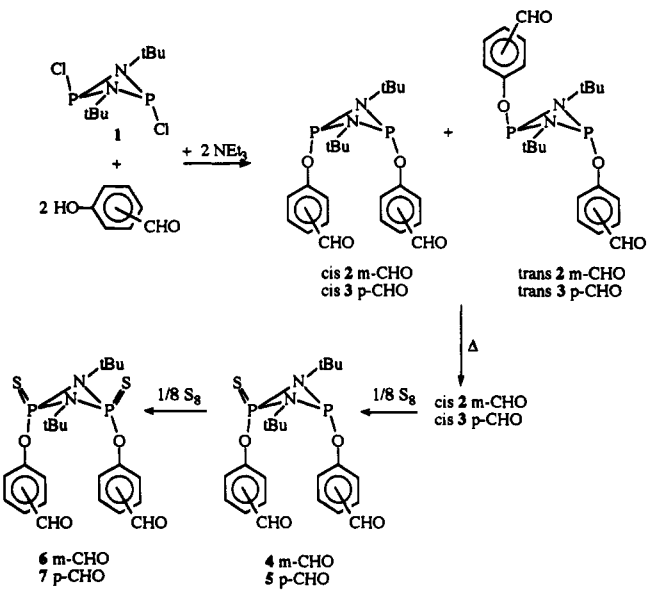
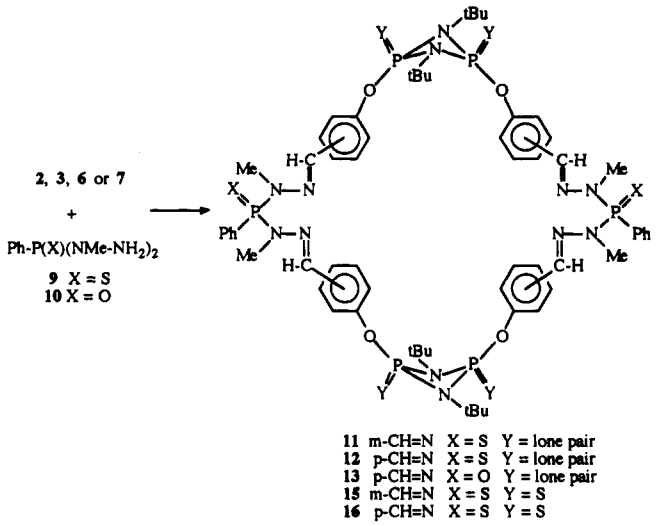
Scheme I



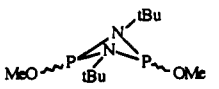
starting from 1,3-di-*tert*-butyldiaza-2,4-dichlorodiphosphetidine, 1.[8] Addition of 3- or 4-hydroxybenzaldehyde (2 equiv) to 1 (1 equiv) in the presence of triethylamine (2 equiv) leads to the formation of the diphospha 1,11- or 1,13-dialdehyde (**2** or **3**, respectively) in 90% yield. Both reactions result in the formation of two isomers (trans and cis) with a $\Delta\delta$ ^{31}P of 91 ppm (**2**, δ ^{31}P = 234.6 and 142.9 ppm; **3**, δ ^{31}P = 235.6 and 144.7 ppm), but the "high-field" isomer is always predominant. On standing or more quickly on heating, the equilibrium is totally shifted to the thermodynamically favored high-field isomer. There is now a considerable body of evidence that the high-field isomers of 1,3-di-*tert*-butyldiaza-2,4-dialkoxydiphosphetidine have *cis* structures.[8] Therefore, signals at 142.9 (**2**) and 144.7 (**3**) ppm can be assigned to the *cis*-1,11- and 1-13-dialdehydes, respectively. All previous studies reportedly show that the *trans*-diazadiphosphetidines are planar while the P_2N_2 ring of the cis isomer is slightly puckered.[9]

Dialdehydes **6** or **7** are directly obtained from the sulfurization of the parent trivalent derivatives **2** or **3** (THF, 67 °C, 10 days) (Scheme I). The formation of the monosulfurized dialdehyde **4** or **5** can be detected by ^{31}P NMR (**4** or **5**: δ = 107.9 (d), 54.9 (d) ppm; $^2J_{PP}$ = 18 Hz) since the monosulfurization is significantly faster than the disulfurization. The dialdehyde **4** was isolated and fully characterized. Two different structures are expected for **4–7** considering the possible different respective orientations of the phenoxy groups. Indeed, one isomer is observed in each case. There is no clear evidence to determine which of the two possible structures for either **6** and **7** is obtained, since in ^{31}P NMR the $\Delta\delta$ between *cis*- and *trans*-diazadiphosphetidine disulfide signals is usually very small (between 2 and 5 ppm) and strongly dependent on the phosphorus environment.[10,11]

Scheme II



Nevertheless, it has been shown that the reactions of the parent compounds **8** (*cis* isomer) and **8'** (*trans* isomer) with



8 cis
8' trans

elemental sulfur were essentially stereospecific so that each isomeric form gave an isomerically pure mono- or dioxidation product.[8] So, we might postulate that, similarly, the diazadiphosphetidine mono- or disulfides **4–7** are obtained as *cis* isomers.

All these new dialdehydes **2**, **3**, **6**, and **7** were also characterized by spectral data (^1H, ^{13}C NMR, IR, and MS) (see Experimental Section).

A facile condensation occurs when *m*- or *p*-dialdehydes **2** and **3** are reacted with phosphodihydrazides, $C_6H_5P(X)(NCH_3NH_2)_2$, **9** or **10** (**9**, X = S, **10**, X = O) in THF. The reactions require 20 to 45 h of stirring at room temperature to go to completion, and the expected macrocycles **11–13** have been obtained in 75 to 85% yield (Scheme II). (Surprisingly, we have never observed formation of significant amounts of linear products at the end of the reaction leading to **11–13**, **15**, and **16**.)

It is worth noting that the reaction can be dramatically accelerated in the presence of a catalytic amount of $Pb(ClO_4)_2$. Under these conditions, only 1 h of stirring is then sufficient to obtain macrocycles **11** and **12** with improved yields! One can reasonably postulate that compounds **11–13** are obtained via template reactions with formation of unstable macrocyclic lead complexes which dissociate into the corresponding free macrocycles and the starting $Pb(ClO_4)_2$. (The fact that Pb(II) a "soft" metal ion is so effective as a template ion is not really curious since the heavier donor atoms S, P (as well as Se, As) coordinate well to the soft metal ions [Ag(I), Au(I), Hg(II), Pb(II)].[13])

Structures of species **11–13** were deduced from ^{31}P, ^1H, and ^{13}C NMR, IR, and mass spectrometry as well as analysis. For example, ^{13}C NMR spectra are fully consistent with the presence of imine carbon atoms: the CH=N signal appears as a doublet ($^3J_{CP}$ = 13.1 to 14.1 Hz) centered at 136.0–136.5 ppm, depending on the macrocycle. Fast atom bombardment mass spectrometries of

(8) Keat, R.; Rycroft, D. G.; Thompson, D. S. *J. Chem. Soc., Dalton Trans.* **1979**, 1224.

(9) See for example: Keat, R. *Top. Curr. Chem.* **1982**, *102*, 89. Jefferson, R.; Nixon, J. F.; Painter, T. M.; Keat, R.; Stobbs, L. *J. Chem. Soc., Dalton Trans.* **1973**, 1414. Scherer, O. J.; Schnabl, G. *Angew. Chem., Int. Ed. Engl.* **1976**, *15*, 772. Niecke, E.; Flick, W.; Pohl, S. *Angew. Chem., Int. Ed. Engl.* **1976**, *15*, 309. Chen, H. J.; Haltiwanger, R. C.; Hill, T. G.; Thompson, M. L.; Coons, D. E.; Norman, A. D. *Inorg. Chem.* **1985**, *24*, 4725.

(10) Scherer, O. J.; Schnabl, G. *Chem. Ber.* **1976**, *109*. 2996. Zeiss, W.; Feldt, C.; Weis, J.; Dunkel, G. *Chem. Ber.* **1978**, *111*, 1180.

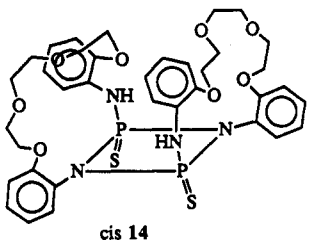
(11) Dutasta, J. P.; Declercq, J. P.; Esteban-Calderon, C.; Tinant, B. *J. Am. Chem. Soc.* **1989**, *111*, 7136.

11–13 show molecular ion peaks m/e corresponding to [2 + 2] cyclocondensations. No peak due to [1 + 1], [3 + 3], or other types of cyclocondensation between dialdehydes and phosphodihydrazides were detected.

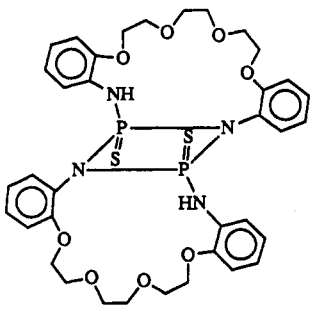
In ^{31}P NMR, in addition to the signal due to P–N–N moieties, compounds 11–13 exhibit singlets at 143.9 (11), 142.3 (12), and 141.8 (13) ppm (O–P–N linkages).

We have already observed[6] that in the case of macrocycle formation cyclization does not have a very great effect on ^{31}P chemical shift. Indeed, there is generally a slight increase in shielding ($\Delta\delta^{31}P$ from 0 to 7 ppm). Considering that only one ^{31}P signal is observed in the P_{III} region of the spectra and that this signal is close to that of the starting linear product, we may postulate that reactions are stereospecific and lead to cis–cis macrocycles. Formation of trans–trans isomers would have resulted in very different ^{31}P chemical shifts. On the other hand, cis–trans isomers would give at least two signals in the O–P–N area.

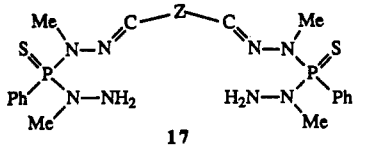
These observations are in marked contrast with results reported recently. The synthesis of bis crown ether annelated diazadiphosphetidines 14 is not stereospecific:[11] two isomers could be detected with a $\Delta\delta$ ^{31}P of 51.6 ppm (cis δ = 112.8, trans δ = 164.4 ppm). In fact, even if this reaction and our reactions lead to macrocyclic species incorporating one[11] or two (this work) diazadiphosphetidine rings, the two syntheses are fundamentally different. In the literature procedure, the diazadiphosphetidine ring is *created* while we start from an already formed P_2N_2 ring.



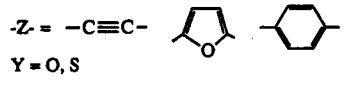
cis 14



trans 14



17



Y = O, S

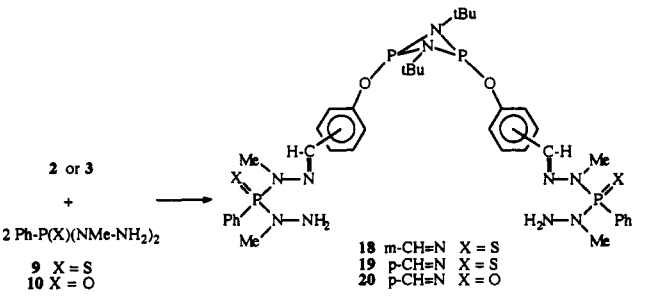
Although it seems reasonable to postulate analogous cis–cis configuration for the macrocycles 15 and 16 obtained from the meta or para diphosphorus dialdehydes 6 and 7, one must keep in mind that ^{31}P chemical shifts are almost independent of the configuration of the diphosphazane disulfide ring as previously demonstrated.[6,9,11,12]

Remarkably, all these original hexaphosphorus macrocyclic species are stable enough to be stored for months at room temperature in inert atmosphere, in contrast with, for example, the annelated diazadiphosphetidine macrocycle 14 which is extremely sensitive to moisture.[11] To the best of our knowledge, no multiphosphorus 36- and 40-membered rings have been reported so far. Compounds

(12) Keat, R.; Muir, K. W.; Thompson, D. G. *Tetrahedron Lett.* **1977**, 3087.

(13) Mancock, R. D.; Martell, A. E. *Chem. Rev.* **1989**, *89*, 1875.

Scheme III



11–13, 15, and 16 are the first examples of macrocycles possessing six phosphorus atoms. Also worthy of note is the presence of two types of linkage, N–P–N and O–P–N, in the ring and the possibility of varying the number of tricoordinated phosphorus atoms incorporated in the macrocycle: four or zero.

Condensation reactions between phosphodihydrazides and dialdehydes proved to be a convenient method for the synthesis of macrocycles possessing an even number of links. Since no example of odd number link macrocycles has been reported in this series, we decided to investigate the possible use of our method for the preparation of such compounds.

We have already demonstrated that transient formation of phosphodihydrazides 17 can be detected by low-temperature ^{31}P NMR experiments when 1,2-, 1,3-, or 1,4-dialdehydes are reacted with phosphodihydrazides 9 or 10.[6] But until now all attempts to isolate such new ligands have failed.

In contrast, addition of the *m,m'*- or the *p,p'*-dialdehyde 2 or 3 (1 equiv) in THF to a THF solution of 2 equiv of phosphodihydrazides 9 or 10 led to the new ligands 18–20 obtained in 80% yield after workup (Scheme III). The IR NH_2 stretching frequencies were observed at ca. 3320 and 3180 cm^{-1} for each derivative, indicating the presence of free NH_2. ^{31}P NMR spectra consist of two singlets (18, δ = 143.8 (O–P–N), 81.6 (S=P–N–N) ppm; 19, δ = 141.5 (O–P–N), 81.2 (S=P–N–N) ppm; 20, δ = 143.7 (O–P–N), 26.4 (O=P–N–N) ppm). The low-field signal strongly suggests a cis configuration relative to the diazadiphosphetidine ring for all these species. In the ^1H NMR spectra, two doublets in the 2.7–3.2 ppm region show that two types of N–CH_3 groups are present: the doublet centered at 2.7 (18, $^3J_{PH}$ = 12 Hz) or 2.8 (19, $^3J_{PH}$ = 10 Hz; 20, $^3J_{PH}$ = 9 Hz) ppm can be attributed to methyl groups owing to the free hydrazino linkages –N(CH_3)NH_2 while the doublet centered at 3.1 (18, $^3J_{PH}$ = 8 Hz; 20, $^3J_{PH}$ = 6 Hz) or 3.2 (19, $^3J_{PH}$ = 8.7 Hz) ppm is due to the methyl groups of the –N(CH_3)–N=CH– fragments. ^1H NMR spectra show also broad resonances for the two NH_2 groups. ^{13}C NMR, mass spectrometry, and analysis confirm the structure of compounds 18–20.

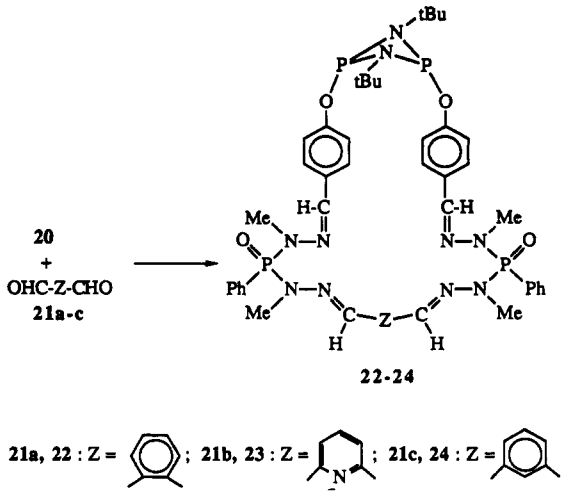
Compounds 18–20 are suitable ligands for other target molecules, viz. asymmetric macrocycles.

Indeed, reaction of the phosphodihydrazide 20 with 1,2-benzenedicarboxaldehyde affords the first macrocycle 22 with a total annular size of 29 ring atoms in 75% yield (Scheme IV).

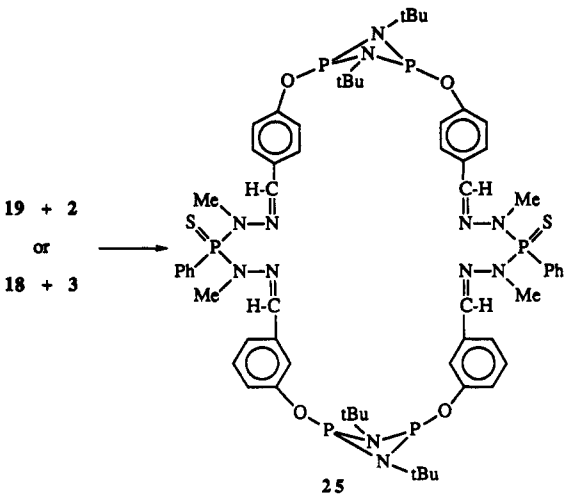
Similarly, addition of 2,6-pyridine dicarboxaldehyde or 1,3-benzene dicarboxaldehyde to 20 leads to the corresponding asymmetric 30-membered rings 23 or 24 possessing four phosphorus atoms.

Fast atom bombardment mass spectrometry clearly indicates that only compounds resulting from [1 + 1] cyclocondensation are observed here. No traces of 58- (in the case of 22) or 60- (in the case of 23 or 24) membered

Scheme IV



Scheme V



rings arising from [2 + 2] cyclocondensation have been detected. ^{31}P NMR spectra show that, as expected, no isomerization of the diazadiphosphetidine ring occurs (δ = 141.8 to 141.9 ppm).

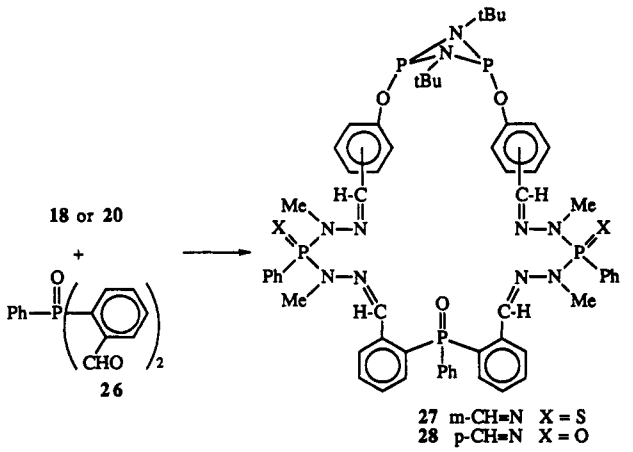
Asymmetry can also be introduced by using ligands which only differ in the position of either aldehyde or imine functions (i.e., meta or para position on the aromatic ring). Two approaches are possible. Indeed, treatment of the phosphodihydrazide **19** (imino function in para position) with the diazadiphosphetidine dialdehyde **2** (aldehyde function in meta position) or reaction of the phosphodihydrazide **18** (imino function in meta position) with the diazadiphosphetidine dialdehyde **3** (aldehyde function in para position) lead via a [1 + 1] cyclocondensation to the asymmetric 38-membered ring **25** (70% yield) (Scheme V).

NMR data of the resulting macrocycles prepared by the two methods are rigorously identical.

Note that macrocyclization with the phosphodihydrazide **20** and the dialdehyde **3** affords the expected 40-membered ring **13** ([1 + 1] cyclocondensation) which was prepared as reported above via a [2 + 2] cyclocondensation involving the dialdehyde **3** and the phosphodihydrazide **10**.

When reacted with the phosphorus dialdehyde **26**, phosphodihydrazide **18** or **20** affords the asymmetric derivative **27** or **28**, a 30- or 32-membered ring incorporating for the first time five phosphorus atoms with three different types of phosphorus environments, viz. C–P–C, N–P–N and O–P–N (Scheme VI). ^{31}P NMR spectra

Scheme VI



corroborate such a structure. Indeed three singlets in the expected region are observed at δ 24.6 or 78.0 (P_{IV-N}) 34.6 or 32.1 (P_{IV-C}) and 144.8 or 142.4 (P_{III}) ppm (see Experimental Section).

All attempts at growing X-ray quality crystals have, so far, been unsuccessful.

Conclusion

Attention can be focused on the remarkable advantages of the proposed method of preparation of original phosphorus macrocycles. This method implies mild conditions and furnishes very good yields of easily isolable macrocyclic species. This approach is not limited to one type of ligand or to one type of macrocycle. It allows (i) the preparation of macrocycles with an odd or even number of links, (ii) the multiplication of the possibilities of complexation by introducing four, five, or six phosphorus atoms, (iii) the introduction of phosphorus atoms with different coordination modes, and (iv) the easy alteration of the environment around phosphorus.

The design of building blocks for macrocyclic synthesis, i.e., the diphosphorus 1,11- or 1,13-dialdehydes **2–7** or the tetraphosphodihydrazides **18–20** allows us to direct the reactions leading to macrocycles toward the formations of species arising either from [1 + 1] or [2 + 2] cyclocondensations.

It has been demonstrated that the tetraphosphorus acyclic derivatives **18–20** are exceptionally good ligands for the preparation of asymmetric phosphorus macrocycles. Of note is the formation of pentaphosphorus macrocycles, **27** and **28**, possessing both N–P–N, N–P–O, and C–P–C endocyclic linkages.

In some cases, various approaches to a given macrocycle are proposed. Taking into account the geometry of the starting diazadiphosphetidine, all the reactions giving rise to macrocycles are found to be stereospecific.

Experimental Section

General. All manipulations were carried out with standard high vacuum or dry argon atmosphere techniques. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker AC80 spectrometer. ^{31}P NMR chemical shifts are reported in ppm relative to 85% H_3PO_4. Mass spectra were obtained by methane desorption. Melting points were obtained on an Electrothermal apparatus. Due to space consumption, only a few representative systematic names are given.[14]

Synthesis of Dialdehydes 2 and 3. Triethylamine (0.02 mol, 2.023 g) was added at rt to a solution of hydroxybenzaldehyde (0.02 mol, 2.442 g) in 50 mL of THF. The mixture was stirred for 15 min. This solution was added dropwise to a solution of dichlorodiazadiphosphetidine (0.01 mol, 2.750 g) in 50 mL of THF at 0 °C. The mixture was stirred for 5 h at rt during which time a precipitate of triethylamine hydrochloride was formed. The solution was filtered and the precipitate washed with 2 × 15 mL of THF. The solution was concentrated to 2 mL. If the ^{31}P NMR spectrum exhibited only one signal (cis isomer) at this step, the solution was evaporated to dryness and the residue was extracted with pentane. If the ^{31}P NMR spectrum indicated the presence of both cis and trans isomers, the solution was evaporated to dryness, the residue was dissolved in 50 mL of toluene and heated for 5 h under reflux. Evaporation of toluene and extraction of the residue with pentane gave **2** or **3** (cis isomers) as pale yellow thick oil.

2: pale yellow thick oil; yield 4.017 g, 90%; $^{31}P\{^1H\}$ NMR (CH_2Cl_2) δ 142.9 (s); ^1H NMR ($CDCl_3$) δ 1.32 (s, 18 H, *t*-Bu), 7.41 (m, 8 H, C_6H_4), 9.93 (s, 2 H, CHO); $^{13}C\{^1H\}$ NMR ($CDCl_3$) δ 30.6 (t, $^3J_{CP}$ = 6 Hz, CCH_3), 51.5 (t, $^2J_{CP}$ = 11.8 Hz, CCH_3), 114.8–153.3 (m, C_6H_4) 191.0 (s, CHO); IR (neat) 1700 cm^{-1} ($\nu_{C=O}$); MS 447 $[M + 1]^+$. Anal. Calcd for $C_{22}H_{28}N_2O_4P_2$: C, 59.17; H, 6.32; N, 6.28. Found: C, 59.26; H, 6.24; N, 6.01.

3: pale yellow thick oil; yield 4.017 g, 90%; $^{31}P\{^1H\}$ NMR ($CDCl_3$) δ 144.7 (s); ^1H NMR ($CDCl_3$) δ 1.20 (s, 18 H, *t*-Bu), 7.1 and 7.7 (AB dd, $^3J_{AB}$ = 8.5 Hz, 8 H, C_6H_4), 9.74 (s, 2 H, CHO); $^{13}C\{^1H\}$ NMR ($CDCl_3$) δ 30.4 (t, $^3J_{CP}$ = 6 Hz, CCH_3), 51.4 (t $^2J_{CP}$ = 11 Hz, CCH_3), 115.6–157.9 (m, C_6H_4), 189.9 (s, CHO); IR (Nujol) 1690 cm^{-1} ($\nu_{C=O}$); MS 447 $[M + 1]^+$. Anal. Calcd for $C_{22}H_{28}N_2O_4P_2$: C, 59.17; H, 6.32; N, 6.28. Found: C, 59.29; H, 6.42; N, 6.16.

Synthesis of Dialdehyde 4. To a solution of dialdehyde **2** (0.002 mol, 0.893 g) in 40 mL of THF was added powdered sulfur (0.002 mol, 0.064 g). The mixture was stirred for 4 h under reflux. The solution was evaporated to dryness and the residue extracted with pentane.

4: pale yellow thick oil: yield 0.813 g, 85%; $^{31}P\{^1H\}$ NMR ($CDCl_3$) δ 54.9 (d, $^2J_{PP}$ = 19 Hz, P_{IV}), 107.9 (d, $^2J_{PP}$ = 19 Hz, P_{III}); ^1H NMR ($CDCl_3$) δ 1.32 (s, 18 H, *t*-Bu), 7.36 (m, 8 H, C_6H_4), 9.81 (s, 2 H, CHO); IR (neat) 1700 cm^{-1} ($\nu_{C=O}$). Anal. Calcd for $C_{22}H_{28}N_2O_4P_2S$: C, 55.22; H, 5.91; N, 5.86. Found: C, 55.03; H, 5.78; N, 5.80.

Synthesis of Dialdehydes 6 and 7. To a solution of dialdehyde **2** or **3** (0.002 mol, 0.893 g) in 40 mL of THF was added powdered sulfur (0.004 mol, 0.128 g). The mixture was stirred for ten days under reflux. The solution was evaporated to dryness and the residue extracted with pentane. Evaporation of pentane gave **6** (or **7**) as a pale yellow powder.

6: pale yellow powder: yield 0.867 g, 85%; mp 101 °C; $^{31}P\{^1H\}$ NMR (THF) δ 45.6 (s); ^1H NMR ($CDCl_3$) δ 1.62 (s, 18 H, *t*-Bu), 7.61 (m, 8 H, C_6H_4), 9.90 (s, 2 H, CHO), $^{13}C\{^1H\}$ NMR ($CDCl_3$) δ 29.4 (t, $^3J_{CP}$ = 4.5 Hz, CCH_3), 57.1 (s, $-CCH_3$), 114.6–151.2 (m, C_6H_4), 190.2 (s, CHO); IR (KBr) 1700 cm^{-1} ($\nu_{C=O}$); MS 511 $[M + 1]^+$. Anal. Calcd for $C_{22}H_{28}N_2O_4P_2S_2$: C, 51.76; H, 5.53; N, 5.49. Found: C, 51.58; H, 5.48; N, 5.32.

7: pale yellow powder; yield 0.857 g, 84%; $^{31}P\{^1H\}$ NMR (toluene) δ 44.5 (s); ^1H NMR ($CDCl_3$) δ 1.62 (s, 18 H, *t*-Bu), 7.3 and 7.8 (AB dd, $^3J_{AB}$ = 7.7 Hz, 8 H, C_6H_4), 9.91 (s, 2 H, CHO); $^{13}C\{^1H\}$ NMR ($CDCl_3$) δ 29.4 (t, $^3J_{CP}$ = 5 Hz, CCH_3), 57.2 (s, CCH_3), 115.4–155.0 (m, C_6H_4), 189.9 (s, CHO); IR (KBr) 1704 cm^{-1} ($\nu_{C=O}$). MS 511 $[M + 1]^+$. Anal. Calcd for $C_{22}H_{28}N_2O_4P_2S_2$: C, 51.76; H, 5.53; N, 5.49. Found: C, 51.41; H, 5.82; N, 5.24.

Synthesis of Macrocycles 11–13, 15, and 16. To a solution of dialdehyde **2**, **3**, **6**, or **7** (0.002 mol, 0.893 g (**2**, **3**), 1.021 g (**6**, **7**)) in 50 mL of THF was added at rt powdered phosphodihydrazide, **9** or **10** (0.002 mol, 0.460 g (**9**), 0.428 g (**10**)). The mixture was stirred for 20 h (**12**, **13**, **16**) or 45 h (**11**, **15**). The solution was evaporated to dryness. The resulting powder was washed with methanol (2 × 15 mL).

11: white powder; yield 1.088 g, 85%; mp 130 °C dec; $^{31}P\{^1H\}$ NMR ($CDCl_3$) δ 79.12 (s, P_{IV}), 143.9 (s, P_{III}); ^1H NMR ($CDCl_3$) δ 1.24 (s, 36 H, *t*-Bu), 3.22 (d, $^3J_{HP}$ = 9.6 Hz, 12 H, N-CH_3), 7.50 (m, 30 H, C_6H_5, C_6H_4, HC=N); $^{13}C\{^1H\}$ NMR ($CDCl_3$) δ 30.4 (m, CCH_3, NCH_3), 51.3 (t, $^2J_{CP}$ = 11.4 Hz, CCH_3), 115.3–153.3 (m, C_6H_5, C_6H_4), 136.5 (d, $^3J_{CP}$ = 13.1 Hz, HC=N); MS 1281 $[M + 1]^+$. Anal. Calcd for $C_{60}H_{78}N_{12}O_4P_6S_2$: C, 56.23; H, 6.14; N, 13.12. Found: C, 55.78; H, 6.19; N, 13.26.

12: yellow powder; yield 0.960 g, 75%; $^{31}P\{^1H\}$ NMR (THF) δ. 78.3 (s, P_{IV}), 142.3 (s, P_{III}); ^1H NMR ($CDCl_3$) δ 1.31 (s, 36 H, *t*-Bu), 3.22 (d, $^3J_{HP}$ = 9.6 Hz, 12 H, NCH_3), 7.41 (m, 30 H, C_6H_5, C_6H_4, HC=N); $^{13}C\{^1H\}$ NMR ($CDCl_3$) δ 30.7 (m, CCH_3, NCH_3), 51.3 (t, $^2J_{CP}$ = 11.4 Hz, *C*-CH_3), 114.9–153.6 (m, C_6H_5, C_6H_4), 136.5 (d, $^3J_{CP}$ = 13.4 Hz, HC=N); MS 1281 $[M + 1]^+$. Anal. Calcd for $C_{60}H_{78}N_{12}O_4P_6S_2$: C, 56.23; H, 6.14; N, 13.12. Found: C, 56.19; H, 6.12; N, 13.02.

13: white powder; yield 0.998 g, 80%; mp 130 °C dec; $^{31}P\{^1H\}$ NMR (THF) δ 22.3 (s, P_{IV}), 141.8 (s, P_{III}); ^1H NMR ($CDCl_3$) δ 1.21 (s, 36 H, *t*-Bu), 3.13 (d, $^3J_{HP}$ = 7 Hz, 12 H, NCH_3), 7.37 (m, 30 H, C_6H_5, C_6H_4, HC=N); $^{13}C\{^1H\}$ NMR ($CDCl_3$) δ 30.6 (t, $^3J_{CP}$ = 6 Hz, C-CH_3), 32.0 (d, $^2J_{CP}$ = 8.6 Hz, NCH_3), 51.3 (t, $^2J_{CP}$ = 11 Hz, *C*-CH_3), 115.1–153.6 (m, C_6H_5, C_6H_4), 136.0 (d, $^3J_{CP}$ = 14.1 Hz, HC=N); IR (KBr) 1687 (w) cm^{-1} ($\nu_{C=N}$); MS 1249 $[M + 1]^+$. Anal. Calcd for $C_{60}H_{78}N_{12}O_6P_6$: C, 57.67; H, 6.30; N, 13.46. Found: C, 57.50; H, 6.15; N, 13.15.

15: pale yellow powder; yield 1.155 g, 82%; $^{31}P\{^1H\}$ NMR ($CDCl_3$) δ 45.8 (s, PO), 79.2 (s, PPh); ^1H NMR ($CDCl_3$) δ 1.40 (s, 36 H, *t*-Bu), 3.21 (d, $^3J_{HP}$ = 9 Hz, NCH_3), 7.43 (m, 30 H, C_6H_5, C_6H_4, HC=N); $^{13}C\{^1H\}$ NMR ($CDCl_3$) δ 30.5 (t, $^3J_{CP}$ = 4.6 Hz, CCH_3), 31.7 (d, $^2J_{CP}$ = 9.8 Hz, NCH_3), 56.77 (s, CCH_3), 118.6–151.0 (m, C_6H_5, C_6H_4), 136.5 (d, $^3J_{CP}$ = 13.4 Hz, HC=N); MS 1409 $[M + 1]^+$. Anal. Calcd for $C_{60}H_{78}N_{12}O_4P_6S_6$: C, 51.12; H, 5.57; N, 11.92. Found: C, 51.06; H, 5.45; N, 11.60.

16: yellow powder; yield 0.845 g, 60%; $^{31}P\{^1H\}$ NMR ($CHCl_3$) δ 46.3 (s, PO), 78.9 (s, PPh); ^1H NMR ($CDCl_3$) δ 1.51 (s, 36 H, *t*-Bu), 3.23 (d, $^3J_{HP}$ = 9 Hz, 12 H, NCH_3), 7.41 (m, 30 H, C_6H_5, C_6H_4, HC=N); MS 1409 $[M + 1]^+$. Anal. Calcd for $C_{60}H_{78}N_{12}O_4P_6S_6$: C, 51.12; H, 5.57; N, 11.92. Found: C, 51.07; H, 5.49; N, 11.78.

Template Reaction: Synthesis of Macrocycles 11 and 12. To a solution of dialdehyde **2** or **3** (0.003 mol, 1.339 g) in 25 mL of methanol was added powdered lead perchlorate (1.5×10^{-5} mol). After complete solubilization, a solution of phosphodihydrazide **9** (0.003 mol, 0.690 g) in 25 mL of methanol was added at rt. After 5 min of stirring **11** or **12** precipitated. The mixture was stirred for 2 additional h then filtrated. The resulting precipitate was washed with methanol (2 × 15 mL).

11: 3.687 g, yield 96%.

12: 3.533 g, yield 92%.

Synthesis of Tetraphosphodihydrazides 18–20. To a solution of dialdehyde **2** or **3** (0.002 mol, 0.893 g) in 50 mL of THF was added at rt powdered phosphodihydrazide **9** or **10** (0.004 mol, 0.921 g (**9**), 0.856 g (**10**)). The mixture was stirred for 40 h. The solution was concentrated to 4 mL and the compound precipitated by adding pentane.

18: white powder; yield 1.392 g, 80%; $^{31}P\{^1H\}$ NMR ($CDCl_3$) δ 81.6 (s, P_{IV}), 143.8 (s, P_{III}); ^1H NMR ($CDCl_3$) δ 1.24 (s, 18 H, *t*-Bu), 2.70 (d, $^3J_{HP}$ = 12 Hz, 6 H, CH_3NNH_2), 3.10 (d, $^3J_{HP}$ = 8 Hz, 6 H, $CH_3NN{=}C$), 4.41 (br s, 4 H, NH_2), 7.72 (m, 20 H, C_6H_5, C_6H_4, HC=N); $^{13}C\{^1H\}$ NMR ($CDCl_3$) δ 30.7 (t, $^3J_{CP}$ = 6 Hz, CH_3C), 31.2 (d, $^2J_{CP}$ = 9.9 Hz, $CH_3NN{=}C$), 39.3 (d, $^2J_{CP}$ = 8 Hz, CH_3NNH_2), 51.4 (t, $^2J_{CP}$ = 11.5 Hz, CCH_3), 115.6–153.4 (m, C_6H_5, C_6H_4), 136.9 (d, $^3J_{CP}$ = 11.4 Hz, HC=N); IR (KBr) 3180 (vw), 3320 (vw) (ν_{NH_2}) cm^{-1}; MS 871 $[M + 1]^+$. Anal. Calcd for $C_{38}H_{54}N_{10}O_2P_4S_2$: C, 52.41; H, 6.25; N, 16.08. Found: C, 52.19; H, 6.20; N, 16.01.

19: pale yellow powder; yield 1.392 g, 80%; $^{31}P\{^1H\}$ NMR (THF) δ 81.2 (s, P_{IV}), 141.5 (s, P_{III}); ^1H NMR ($CDCl_3$) δ 1.31 (s, 18 H,

(14) Some representative names: **13**, 2,6,22,26-tetraoxa-4,12,13,15,16,24,32,33,35,36,45,50-dodecaaza-3,5,14,23,25,34-hexaphosphaheptacyclo[36.2.2.2^{7,10}.2^{18,21}.2^{27,30}.1^{3,5}.1^{23,25}]pentaconta-7,9,11,16,18,20,27,29,31,36,38,40,41,43,46,48-hexadecaene, 4,24,45,50-tetrakis(1,1-dimethylethyl)-13,15,33,35-tetramethyl-14,34-diphenyl-, 14,34-dioxide; **15**, 2,6,24,28-tetraoxa-4,13,14,16,17,26,35,36,38,39,47,50-dodecaaza-3,5,15,25,27,37-hexaphosphaheptacyclo[39.3.1.1^{3,5}.1^{7,11}.1^{19,23}.1^{25,27}.1^{29,33}]pentaconta-1(45),7,9,11(49),12,17,19,21,23(48),29,31,33-(46),34,39,41,43-hexadecaene, 4,26,47,50-tetrakis(1,1-dimethylethyl)-14,16,36,38-tetramethyl-15,37-diphenyl-, 3,5,15,25,27,37-hexasulfide; **27**, 7*H*,19*H*-18,20-imino-12,16:22,26-dimetheno-16*H*,18*H*-dibenzo[*r*,*u*][1,5,3,12,13,15,16,24,25,27,28,2,4,14,20,26]dioxanonaazapentaphosphacyclotetratriacontine, 19,40-bis(1,1-dimethylethyl)-8,9,29,30,31,38-hexahydro-7,9,29,31-tetramethyl-8,30,38-triphenyl-, 38-oxide 8,30-disulfide.

t-Bu), 2.87 (d, $^3J_{HP}$ = 10 Hz, 6 H, CH_3NNH_2), 3.24 (d, $^3J_{HP}$ = 8.7 Hz, CH_3NN=C), 3.60 (br s, 4 H, NH_2), 9.51 (m, 20 H, C_6H_5, C_6H_4, HC=N); $^{13}C\{^1H\}$ NMR ($CDCl_3$) δ 30.7 (m, CH_3C, CH_3NN=C), 39.2 (d, $^2J_{CP}$ = 8 Hz, CH_3NNH_2), 51.4 (t, $^2J_{CP}$ = 11.4 Hz, CCH_3), 115.3–153.7 (m, C_6H_5, C_6H_4), 137.0 (d, $^3J_{CP}$ = 11.5 Hz, HC=N); IR (KBr) 3180 (vw), 3320 (vw) (ν_{NH_2}) cm^{-1}; MS 871 $[M + 1]^+$. Anal. Calcd for $C_{38}H_{54}N_{10}O_2P_4S_2$: C, 52.41; H, 6.25; N, 16.08. Found: C, 52.66; H, 6.17; N, 16.05.

20: white powder; yield 1.341 g, 80%; mp 130 °C dec; $^{31}P\{^1H\}$ NMR (THF) δ 26.4 (s, P_{IV}), 143.7 (s, P_{III}); ^1H NMR ($CDCl_3$) δ 1.31 (s, 18 H, *t*-Bu), 2.84 (d, $^3J_{HP}$ = 9 Hz, 6 H, H_3CNNH_2), 3.12 (d, $^3J_{HP}$ = 6 Hz, 6 H, H_3CNN=C), 3.96 (br s, 4 H, NH_2), 7.5 (m, 20 H, C_6H_5, C_6H_4, HC=N); $^{13}C\{^1H\}$ NMR ($CDCl_3$) δ 30.6 (m, CH_3C, CH_3NN=C), 39.6 (d, $^2J_{CP}$ = 9 Hz, H_3CNNH_2), 51.4 (t, $^2J_{CP}$ = 11 Hz, CCH_3), 115.3–153.6 (m, C_6H_5, C_6H_4), 135.8 (d, $^3J_{CP}$ = 12.9 Hz, HC=N); IR (KBr) 3194 (vw), 3325 (vw) (ν_{NH_2}) cm^{-1}. MS 839 $[M + 1]^+$. Anal. Calcd for $C_{38}H_{54}N_{10}O_4P_4$: C, 54.39; H, 6.49; N, 16.70. Found: C, 54.25; H, 6.38; N, 16.48.

Synthesis of Macrocycles 22–25, 27, and 28. A solution of dialdehyde **21a–c** (0.008 mol, 0.107 g (**21a,c**), 0.108 g (**21b**)) in 10 mL of THF was added at rt to a solution of tetraphosphodihydrazide **18**, **19**, **20** (0.008 mol, 0.696 g (**18**, **19**), 0.671 g (**20**)) in 10 mL of THF. The mixture was stirred for 6 h. The solution was then evaporated to dryness. The resulting powder was washed with 2 × 10 mL of methanol.

22: white powder; yield 0.582 g, 75%; mp 163 °C dec; $^{31}P\{^1H\}$ NMR (THF) δ 21.9 (s, P_{IV}), 141.9 (s, P_{III}); ^1H NMR ($CDCl_3$) δ 1.23 (s, 18 H, *t*-Bu), 3.1 (m, 12 H, NCH_3), 7.4 (m, 26 H, C_6H_5, C_6H_4, HC=N); $^{13}C\{^1H\}$ NMR ($CDCl_3$) δ 30.5 (m, CH_3C, CH_3N), 51.3 (t, $^2J_{CP}$ = 11.2 Hz, CH_3C), 115.1–153.6 (m, C_6H_5, C_6H_4), 135.6 (m, HC=N); IR (KBr) 1690 (vw), ($\nu_{C=N}$) cm^{-1}; MS 937 $[M + 1]^+$. Anal. Calcd for $C_{46}H_{56}N_{10}O_4P_4$: C, 58.95; H, 6.03; N, 14.96. Found: C, 58.53; H, 5.98; N, 14.79.

23: white powder; yield 0.562 g, 75%; mp 140 °C dec; $^{31}P\{^1H\}$ NMR (THF) δ 22.3 (s, P_{IV}), 141.9 (s, P_{III}); ^1H NMR ($CDCl_3$) δ 1.24 (s, 18 H, *t*-Bu), 3.11 (m, 12 H, NCH_3), 7.41 (m, 25 H, C_6H_5, C_6H_4, C_5H_3N, HC=N); $^{13}C\{^1H\}$ NMR ($CDCl_3$) δ 30.6 (m, CCH_3, NCH_3), 51.3 (t, $^2J_{CP}$ = 11 Hz, CCH_3), 115.1–153.6 (m, C_6H_5, C_6H_4, C_5H_3N), 136.6 (m, HC=N). MS 938 $[M + 1]^+$. Anal. Calcd for $C_{45}H_{55}N_{11}O_4P_4$: C, 57.61; H, 5.91; N, 16.43. Found: C, 57.55; H, 5.69; N, 16.20.

24: pale yellow powder; yield 0.487 g, 65%; $^{31}P\{^1H\}$ NMR (THF) δ 22.6 (s, P_{IV}), 141.8 (s, P_{III}); ^1H NMR ($CDCl_3$) δ 1.33 (s, 18 H, *t*-Bu), 3.16 (m, 12 H, NCH_3), 7.54 (m, 26 H, C_6H_5, C_6H_4, HC=N); $^{13}C\{^1H\}$ NMR ($CDCl_3$) δ 30.6 (m, CCH_3, NCH_3), 51.3 (t, $^2J_{CP}$ = 11 Hz, CCH_3), 115.1–153.5 (m, C_6H_5, C_6H_4), 135.6 (m, HC=N); MS 937 $[M + 1]^+$. Anal. Calcd for $C_{46}H_{56}N_{10}O_4P_4$: C, 58.95; H, 6.03; N, 14.96. Found: C, 58.86; H, 5.98; N, 14.76.

25: white powder; yield 0.717 g, 70%; mp 145 °C dec; $^{31}P\{^1H\}$ NMR (THF) δ 78.2 (s, P_{IV}), 142.3 (s, P_{III}); ^1H NMR ($CDCl_3$) δ 1.31 (s, 36 H, *t*-Bu), 3.24 (m, 12 H, NCH_3), 7.41 (m, 30 H, C_6H_5, C_6H_4, HC=N); $^{13}C\{^1H\}$ NMR ($CDCl_3$) δ 30.6 (m, CCH_3, NCH_3), 51.3 (t, $^2J_{CP}$ = 11 Hz, CCH_3), 114.9–153.3 (m, C_6H_5, C_6H_4), 136.6 (m, HC=N); MS 1281 $[M + 1]^+$. Anal. Calcd for $C_{60}H_{78}N_{12}O_4P_6S_2$: C, 56.23; H, 6.14; N, 13.12. Found: C, 56.03; H, 6.07; N, 12.97.

27: white powder; yield 0.710 g, 76%; $^{31}P\{^1H\}$ NMR (THF) δ 32.1 (s, $P_{IV}C$), 78.0 (br s, $P_{IV}N$), 142.4 (br s, P_{III}); ^1H NMR ($CDCl_3$) δ 1.21 (s, 18 H, *t*-Bu), 2.84 (br s, 6 H, *o*-Ar CH=NNCH_3), 3.14 (br s, 6 H, *m*-ArCH=NNCH_3), 7.61 (m, 35 H, C_6H_5, C_6H_4, HC=N); $^{13}C\{^1H\}$ NMR ($CDCl_3$) δ 30.7 (m, NCH_3 CCH_3, 51.5 (t, $^2J_{CP}$ = 11 Hz, CCH_3), 109.3–157.7 (m, C_6H_5, C_6H_4, CH=N); MS 1169 $[M + 1]^+$. Anal. Calcd for $C_{58}H_{65}N_{10}O_3P_5S_2$: C, 59.57; H, 5.60; N, 11.98. Found: C, 59.21; H, 5.40; N, 12.13.

28: white powder; yield 0.709 g, 78%; $^{31}P\{^1H\}$ NMR ($CHCl_3$) δ 24.6 (s, $P_{IV}N$), 34.6 (br s, $P_{IV}C$), 144.8 (br s, P_{III}); ^1H NMR ($CDCl_3$) δ 1.30 (s, 18 H, *t*-Bu), 2.71 (br s, 6 H, *o*-Ar CH=NNCH_3), 3.00 (br s, 6 H, *p*-ArCH=NNCH_3), 7.61 (m, 35 H, C_6H_5, C_6H_4, HC=N); MS 1137 $[M + 1]^+$. Anal. Calcd for $C_{58}H_{65}N_{10}O_5P_5$: C, 61.26; H, 5.76; N, 12.31. Found: C, 61.14; H, 5.23; N, 12.70.

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Registry No. **1**, 24335-35-1; *cis*-**2**, 137918-40-2; *trans*-**2**, 137918-41-3; *cis*-**3**, 138008-30-7; *trans*-**3**, 137918-42-4; **4**, 137918-45-7; **5**, 137918-60-6; **6**, 137918-43-5; **7**, 137918-44-6; **9**, 54529-68-9; **10**, 54529-67-8; **11**, 137918-46-8; **12**, 137918-47-9; **13**, 137918-48-0; **15**, 137918-49-1; **16**, 137918-50-4; **18**, 137918-51-5; **19**, 137918-52-6; **20**, 137918-53-7; **21a**, 643-79-8; **21b**, 5431-44-7; **21c**, 626-19-7; **22**, 137918-54-8; **23**, 137918-55-9; **24**, 137918-56-0; **25**, 137918-57-1; **26**, 65654-65-1; **27**, 137918-58-2; **28**, 137918-59-3; HO-*m*-C_6H_4-CHO, 100-83-4; HO-*p*-C_6H_4-CHO, 123-08-0.