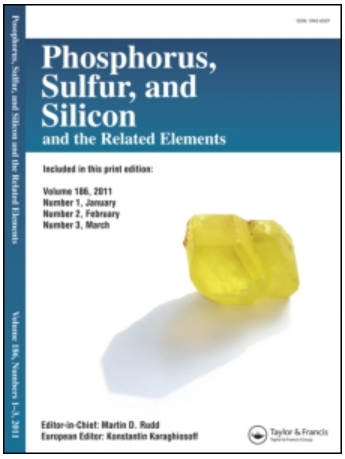

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SYNTHESIS AND REACTIVITY OF DENDRIMERS BASed ON PHOSPHORYL (P=O) GROUPS

Marie-Laure Lartigue[a]; Anne-Marie Caminade[a]; Jean Pierre Majoral[a]
[a] Laboratoire de chimie de Coordination du, CNRS, TOULOUSE Cedex 4, France

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SYNTHESIS AND REACTIVITY OF DENDRIMERS BASED ON PHOSPHORYL (P=O) GROUPS*

MARIE-LAURE LARTIGUE, ANNE-MARIE CAMINADE† and JEAN PIERRE MAJORAL†

Laboratoire de Chimie de Coordination du CNRS, 205 route de Narbonne, 31077 TOULOUSE Cedex 4, France

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The synthesis of phosphoryl-based dendrimers is described, using the reiteration of a two-steps process which gives alternatively aldehyde and $P(O)Cl_2$ end groups. The synthesis has been carried out up to the third generation, to give a compound which bears 24 chlorine atoms on the surface. Preliminary experiments on the first generation of the dendrimer possessing either 6 CHO or 6 Cl groups show that these compounds display a versatile reactivity. For instance, α, β-unsaturated esters, crown ethers, chiral phosphine sulfides or diallylamine are grafted on the surface, and the resulting dendrimers are isolated in good to nearly quantitative yields.

Keywords: dendrimer; highly branched compounds; phosphoryl; ester; crown ether; diallylamine

INTRODUCTION

The synthesis of highly branched polymers of defined structure, namely dendrimers, gives rise to a growing interest in organic chemistry[1] since the pioneering works by Vögtle in 1978[2], Tomalia[1a,3] and Newkome[4]. In phosphorus chemistry, the first dendrimer, based on phosphonium salts, was described by Engel in 1990[5]. For our part, we described in 1994 the first neutral phosphorus dendrimer, based on thio phosphoryl (P=S) groups[6] ; then we studied some examples of reactivity[7] and other ways of synthesis of dendrimers[8]. Other examples of phosphorus dendrimers were also described by DuBois (based on phosphines[9]) and Labarre (based on cyclotriphosphazene[10]).

* Dedicated to Dr. Robert Wolf on the occasion of his 70th birthday

† Corresponding authors. Fax: +33 61 55 30 03; E-mail: majoral@lcc-toulouse.fr or caminade@lcc-toulouse.fr

We report here the synthesis up to the third generation (24 end groups) of a new family of dendrimers based on phosphoryl (P=O) groups, as well as preliminary reactivity studies.

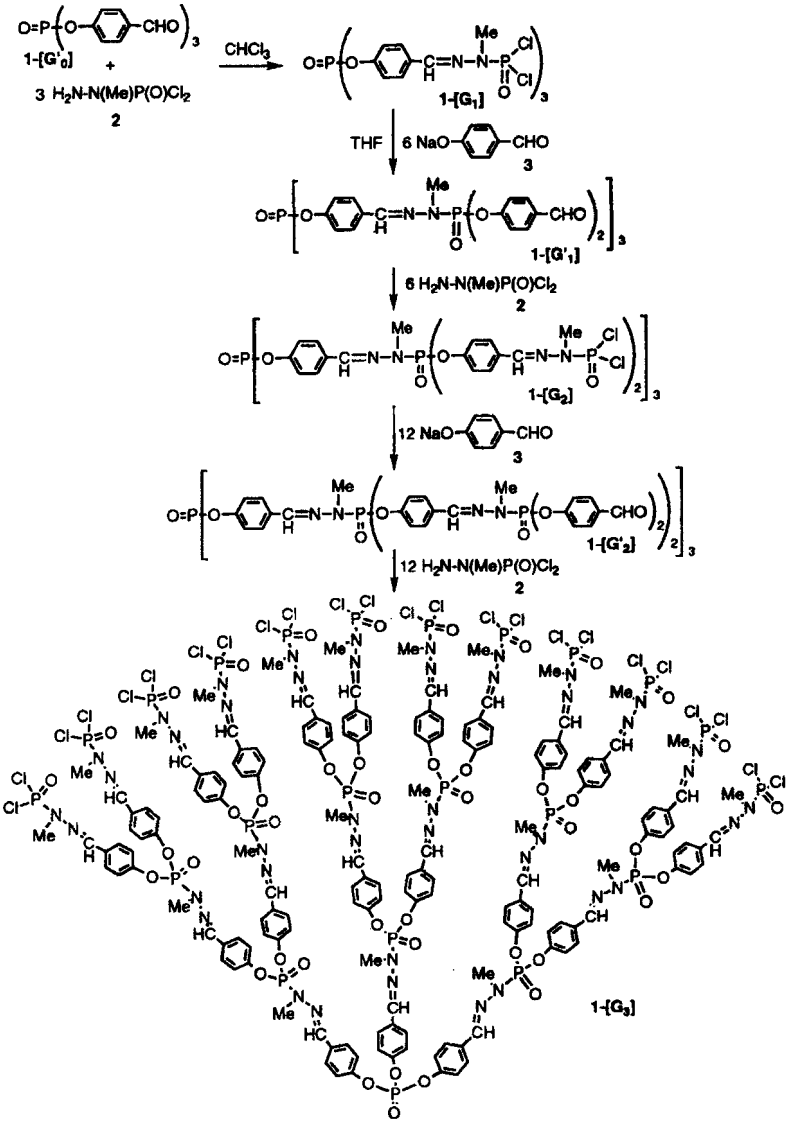
RESULTS AND DISCUSSION

The synthesis of the phosphoryl-based dendrimers **1-[G_n]** is derived from the two-steps process we experimented for the P=S analogues[6], using H_2N-N(Me)P(O)Cl_2 **2** instead of H_2N-N(Me)P(S)Cl_2. The first step consists of the synthesis of the trialdehyde **1-[G'$_0$]** from $POCl_3$ and hydroxybenzaldehyde sodium salt. The second step is a condensation reaction between this trialdehyde **1-[G'$_0$]** and the dichlorophosphorhydrazide **2**, obtained by reaction of $POCl_3$ with methylhydrazine (Scheme 1). This condensation affords in nearly quantitative yield the first generation of the dendrimer with 6 chlorine end groups, **1-[G_1]**. Addition of a stoechiometric amount of hydroxybenzaldehyde sodium salt **3** affords the first generation of the dendrimer with 6 CHO end groups, **1-[G'$_1$]**, also in nearly quantitative yield. The successive and alternative addition of dichlorophosphorhydrazide **2** and hydroxybenzaldehyde sodium salt **3** allows the isolation of the second generation (**1-[G_2]**: 12 Cl end groups; **1-[G'$_2$]**: 12 CHO end groups) and finally the third generation of the dendrimer(**1-[G_3]**: 24 Cl end groups) (Scheme 1).

TABLE I ^{31}P NMR values (ppm) for dendrimers **1-[G_n]** and **1-[G'$_n$]**

Compound	*Number of end groups*	P_0	P_1	P_2	P_3
1-[G'$_0$]	3 CHO	- 19,9			
1-[G_1]	6 Cl	- 18,4	18,5		
1-[G'$_1$]	6 CHO	- 18,6	- 7,1		
1-[G_2]	12 Cl	- 18,0	- 6,2	18,5	
1-[G'$_2$]	12 CHO	- 18,4	- 6,3	- 7,1	
1-[G_3]	24 Cl	- 17,8	-5 ,7	- 6,2	18,5

All the reactions are monitored by ^{31}P NMR (Table I, see experimental part for the numbering used). In all cases, the condensation reaction induces a slight



SCHEME 1

deshielding of the signal of the phosphorus which bears the hydroxy benzaldehyde groups (**1-[G'$_0$]** → **1-[G$_1$]**: from - 19.9 to - 18.4 ppm for the core phosphorus P_0; **1-[G'$_1$]** → **1-[G$_2$]** or **1-[G'$_2$]** → **1-[G$_3$]**: from - 7.1 to - 6.2 ppm for the phosphorus of the first layer P_1 or the phosphorus of the second layer P_2, respectively). A shielding of the phosphorhydrazide part is also observed in this con-

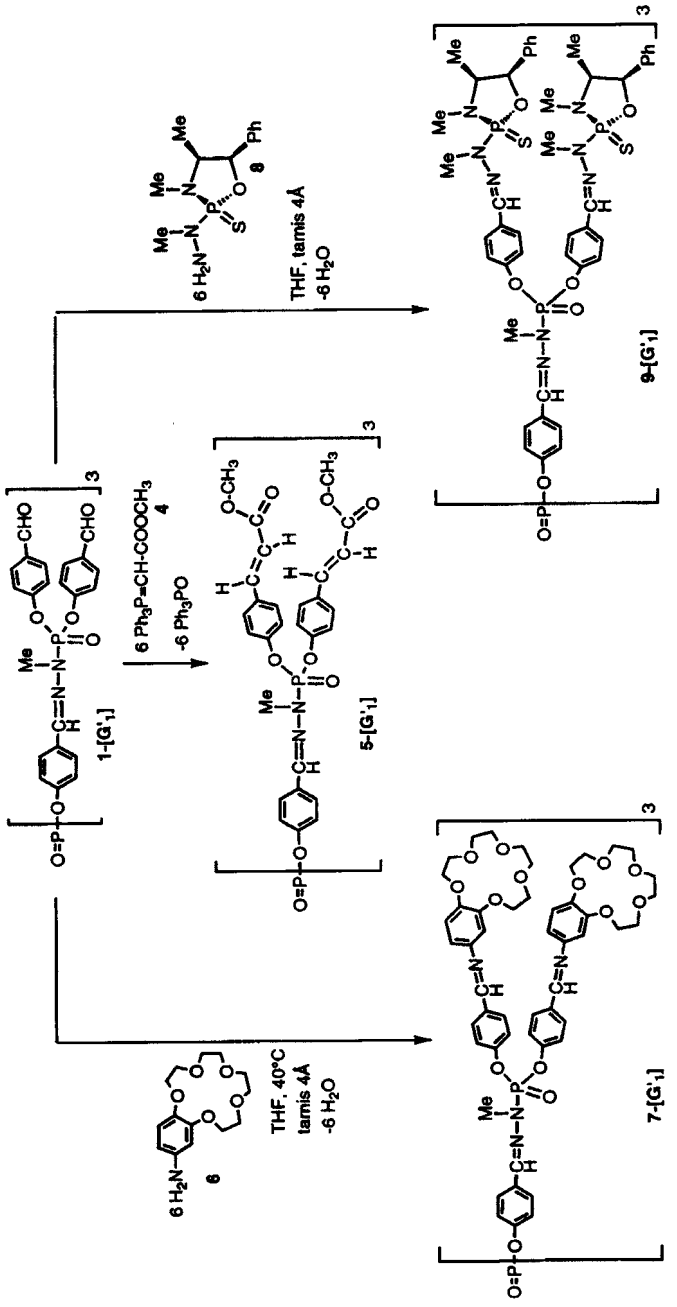
densation reaction (δ = 23 ppm for **2**, δ = 18.5 ppm for P_1, P_2 or P_3 in **1-[G_1]**, **1-[G_2]** or **1-[G_3]**, respectively). The substitution of chlorine by hydroxy benzaldehyde is also monitored by ^{31}P NMR: the transformation **1-[G_n]** $\rightarrow$ **1-[G'_n]** induces a shielding of the signal corresponding to the phosphorus concerned by the substitution, from + 18.5 to - 7.1 ppm.

All compounds are also characterised by ^1H NMR, which shows in particular the total disappearance of aldehyde groups during the condensation **1-[G'_n]** $\rightarrow$ **1-[G_{n+1}]**, as well as ^{13}C NMR and IR spectroscopy. The reaction of all the terminal functions at each step of the synthesis is also proved by mass spectrometry (FAB) which shows, up to dendrimer **1-[G'_2]**, the unique presence of the expected molecular ion with the correct isotopic repartition (*m/z*: 3255 $[M+1]^+$for **1-[G'_2]**).

All these experimental data prove that the synthesis of dendrimers with P=O junctions occurs in the same conditions and as easily as the synthesis of the analogous dendrimers with P=S junctions. However, the **1-[G_n]** dendrimers appear to be slightly more sensitive toward moisture than the P=S analogues. Thus we decided to stop the construction of the P=O dendrimers after the synthesis of the third generation **1-[G_3]**, and we begun to test their reactivity, in particular to check if the presence of phosphoryl groups could induce some changes when compared to the thiophosphoryl analogues. Experiments are carried out with the first generation dendrimers **1-[G_1]** and **1-[G'_1]** as models.

We studied first the reactivity of the aldehyde functions of **1-[G'_1]** toward an ylide and primary amines (Scheme 2). The Wittig reaction of 6 equivalents of carboxymethylene triphenylphosphorane **4** with one equivalent of **1-[G'_1]** needs one week at room temperature to go to completion, as shown by ^{31}P NMR. The signals at δ = 17.4 and - 7.1 ppm, corresponding to the ylide **4** and P_1 in **1-[G'_1]** gradually disappear, on behalf of two new signals at δ = 23.1 and - 6.6 ppm, corresponding to Ph_3P=O and P_1 in **5-[G'_1]**, respectively. ^1H NMR shows the total disappearance of aldehyde functions on behalf of α,β-unsaturated esters. The presence of only one doublet for the HC=C<u>H</u>-COO fragment indicates that this Wittig reaction is stereospecific; furthermore, the large value of the coupling constant ($^3J_{HH}$ = 16.0 Hz) correspond to a trans configuration of the double bond, as generally expected for stabilised ylides such as **4**.

The condensation reaction of all the aldehyde functions of **1-[G'_1]** with the crown ether substituted primary amine **6** occurs after one week in THF at 40°C (Scheme 2). The monitoring of the reaction by ^{31}P NMR indicates the diminishing of the signal at δ = - 7.1 ppm (P_1 in **1-[G'_1]**) on behalf, first, of a singlet at δ = - 6.9 ppm, corresponding to an intermediate monocondensation reaction. Both signals diminish, then disappear on behalf of a singlet at δ = - 6.7 ppm, corresponding to P_1 in **7-[G'_1]**. This reaction is slightly more rapid than the analo-



SCHEME 2

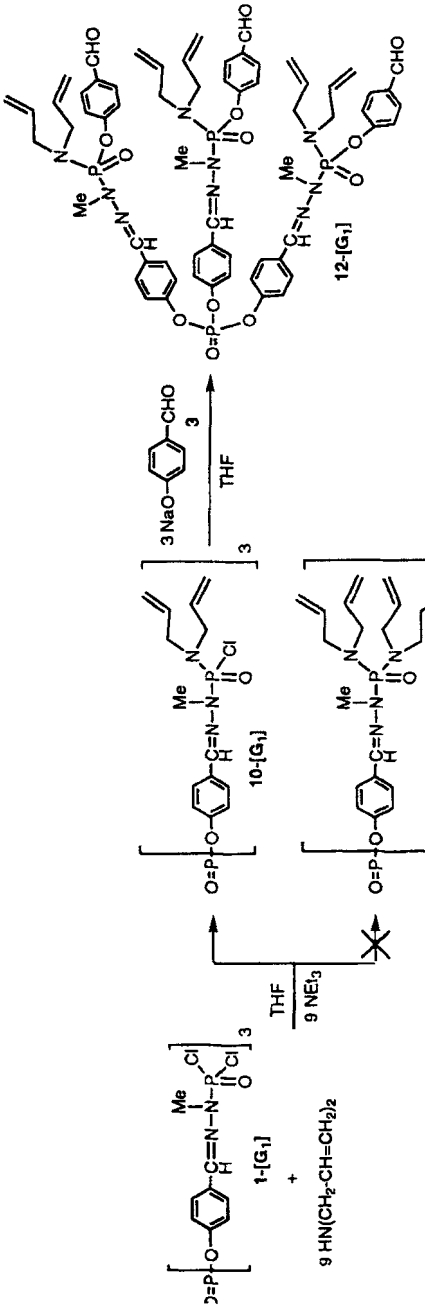
gous one for the P=S-based dendrimer, which needed one week in refluxing THF to go to completion[7c].

The condensation reaction is much more rapid when nucleophilic amines are used. Indeed, the reaction of **8**, the methylhydrazine derivative of oxazaphospholidine, with **1-[G'$_1$]** is complete after only one hour at room temperature (Scheme 2). The oxazaphospholidine **8** is easily obtained by reaction of methylhydrazine with (2R,4R,5S)-(+)2-chloro-2-thio-3,4-dimethyl-5-phenyl-1,3,2-oxazaphospholidine, presumably with retention of configuration, according to literature results for analogous substitution reactions with amines[11]. The condensation reaction of **8** with **1-[G'$_1$]** induces in ^{31}P NMR a slight deshielding of the signal of P_1, as already seen for the previous condensation reaction, but also a shielding of the signal corresponding to P=S: δ = 85.0 ppm for **8** and δ = 80.1 ppm for **9-[G'$_1$]**. Dendrimer **9-[G'$_1$]** is interesting, taking into account that very few dendrimers possessing chiral groups on the surface are known until now[12].

The slight increase in reactivity observed for the synthesis of **7-[G'$_1$]** when compared to the P=S analogues, and the slightly increased sensitivity to moisture of derivatives **1-[G$_n$]** incited us to check the reactivity of the $P(O)Cl_2$ functions of **1-[G$_1$]**. We choose the substitution reaction with diallylamine, which gave after one week only a monosubstitution reaction on each $P(S)Cl_2$ end groups for the P=S-based dendrimers[7a,7c]. The reaction of **1-[G$_1$]** is carried out with an excess of allylamine and in the presence of triethylamine, at room temperature. After 12 hours, the ^{31}P NMR spectrum of the reaction mixture shows that the signal at δ = 18.5 ppm corresponding to P_1 in **1-[G$_1$]** has disappeared on behalf of a new signal at δ = 19.8 ppm. A longer reaction time and heating the mixture to reflux do not induce the appearance of another signal, thus indicating that the reaction is finished. However, the data obtained by ^{1}H NMR spectroscopy, and above all, mass spectrometry (*m/z*: 1026 $[M+1]^+$ for Cl = 35) imply the formation of the monosubstituted compound **10-[G$_1$]**, which possess three $P(O)Cl(N(allyl)_2)$ end groups instead of the fully substituted compound **11-[G$_1$]** (Scheme 3). Thus, the reaction of the P=O-based dendrimer is more rapid than for the P=S analogue, even though it does not lead to the full substitution.

However, the P-Cl functions of **10-[G$_1$]** remain reactive, for example toward hydroxy benzaldehyde sodium salt **3.** Indeed, the reaction has gone to completion after 4 hours at room temperature to afford compound **12-[G$_1$]** in nearly quantitative yield, as shown by ^{31}P NMR, with the disappearance of the singlet at δ = 19.8 ppm (P_1 in **10-[G$_1$]**) on behalf of a new singlet at δ = 5.8 ppm, corresponding to P_1 in **12-[G$_1$]**. Such a reaction does not occur with the thiophosphoryl-based dendrimers.

This fact confirms that phosphoryl-based dendrimers are more reactive than the thiophosphoryl analogues. This will be a factor to take into account when

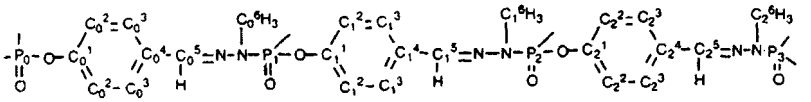


SCHEME 3

designing dendrimers for some specific purposes which imply the use of poorly reactive reagents. Furthermore, the known better complexation ability of P=O groups in comparison with P=S groups towards cations could find some applications in the future for dendrimer chemistry.

EXPERIMENTAL SECTION

General. All manipulations were carried out with standard high vacuum or dry argon atmosphere techniques. ^{1}H, ^{13}C and ^{31}P NMR spectra were recorded on a Bruker AC 200 spectrometer. ^{31}P NMR chemical shifts were reported in ppm relative to 85% H_3PO_4. Mass spectra were obtained by Fast atom bombardment on Finnigann MAT TSQ 700 spectrometer. The numbering used for ^{31}P and ^{13}C NMR is depicted in the following scheme :



Synthesis of the dichlorophosphorhydrazide 2 :

To a solution of trichlorophosphine oxide (1.2 mL, 12.90 mmol) in chloroform (40 mL) was slowly added monomethylhydrazine (1.3 mL, 25.70 mmol) in solution in 20 ml of chloroform at - 60°C and under stirring. The mixture was left overnight under stirring while the temperature raise slowly to room temperature. Then methylhydrazine hydrochloride was eliminated by filtration and centrifugation. Compound **2** is left in solution and used *in situ*. ^{31}P $\{^{1}H\}$ NMR ($CHCl_3$): δ = 23.0 (s) ppm.

Synthesis of compound 1-[G'$_0$] :

To a suspension of hydroxybenzaldehyde sodium salt (13.18 g, 96.44 mmol) in 300 mL of THF was added trichlorophosphine oxide (3 mL, 32.14 mmol) at room temperature. The mixture was stirred for 2 hours, then filtered, centrifuged and evaporated to dryness. The resulting powder was washed with ether (3×30mL).

1-[G'$_0$]: white powder. 90 % yield. Melting point: 97 °C

^{31}P $\{^{1}H\}$ NMR (THF): δ = -19.8 (s, P_0) ppm. ^{1}H NMR ($CDCl_3$): δ = 7.40 (d, $^{3}J_{HH}$ = 8.8 Hz, 6H, C_6H_4), 7.90 (d, $^{3}J_{HH}$ = 8.8 Hz, 6H, C_6H_4), 9.93 (s, 3H, CHO)

ppm. ^{13}C {^1H} NMR ($CDCl_3$): δ = 119.9 (d, $^3J_{CP}$ = 5.0 Hz, C_0^2), 131.2 (s, C_0^3), 133.6 (s, C_0^4), 153.7 (d, $^2J_{CP}$ = 7.0 Hz, C_0^1), 189.6 (s, CHO) ppm. IR (KBr): 1700 (νC=O) cm^{-1}. Anal Calc for $C_{21}H_{15}O_7P$: C, 61.46; H, 3.68. Found: C, 61.55; H, 3.75.

General procedure for the synthesis of dendrimers with P(O)Cl_2 end groups, 1-[G_n] :

To a solution of dichlorophosphorhydrazide **2** in chloroform obtained as described above, was added a stoechiometric amount of dendrimer **1-[G'$_{n-1}$]** in solution in chloroform, at room temperature and in the presence of molecular sieve (4Å). The mixture was stirred for 2 hours, then filtered, centrifuged and evaporated to dryness. The resulting powder was washed with ether.

General procedure for the synthesis of dendrimers with CHO end groups, 1-[G'$_n$]:

To a suspension of hydroxybenzaldehyde sodium salt in THF was added a stoechiometric amount of dendrimer **1-[G$_n$]** in solution in THF, at room temperature. The mixture was stirred for 2 hours, then filtered, centrifuged and evaporated to dryness. The resulting powder was washed with ether.

1-[G_1]: white powder. 97 % yield. Melting point: 127 °C.

^{31}P {^1H} NMR ($CHCl_3$): δ = -18.4 (s, P_0), 18.5 (s, P_1) ppm. ^1H NMR ($CDCl_3$): δ = 3.32 (d, $^3J_{HP}$ = 11.0, 9H, $C_0^6H_3$), 7.28 (d, $^3J_{HH}$ = 7.9 Hz, 6H, C_6H_4), 7.48 (d,$^3J_{HH}$ = 7.9 Hz, 6H, C_6H_4), 7.65 (s, 3H, HC_0^5=N). ^{13}C {^1H} NMR ($CDCl_3$): δ = 30.6 (d, $^2J_{CP}$ = 10.5 Hz, C_0^6), 119.8 (d, $^3J_{CP}$ = 5.1 Hz, C_0^2), 128.3 (s, C_0^3), 131.1 (br s, C_0^4), 140.1 (d, $^3J_{CP}$ = 20.5 Hz, C_0^5), 150.8 (d, $^2J_{CP}$ = 7.5 Hz, C_0^1) ppm. Mass spec. *m/z*: 843 $[M+1]^+$

1-[G'$_1$]: white powder. 97 % yield. Melting point: 91 °C.

^{31}P {^1H} NMR (THF): δ = -18.5 (s, P_0), -7.1 (s, P_1) ppm. ^1H NMR ($CDCl_3$): δ = 3.23 (d, $^3J_{HP}$ = 8.2 Hz, 9H, $C_0^6H_3$), 7.55 (m, 36H, C_6H_4), 7.78 (s, 3H, HC_0^5=N), 9.90 (s, 6H, CHO) ppm. ^{13}C {^1H} NMR ($CDCl_3$): δ = 31.6 (d, $^2J_{CP}$ = 10.6 Hz, C_0^6), 119.8 (d, $^3J_{CP}$ = 5.0 Hz, C_0^2), 120.5 (d, $^3J_{CP}$ = 5.2 Hz, C_1^2), 127.8 (s, C_0^3), 130.9 (s, C_1^3), 131.5 (br s, C_0^4), 133.1 (d, $^5J_{CP}$ = 1.7 Hz, C_1^4), 138.4 (d, $^3J_{CP}$ = 15.5 Hz, C_0^5), 150.5 (d, $^2J_{CP}$ = 7.4 Hz, C_0^1), 154.2 (d, $^2J_{CP}$ = 6.7 Hz, C_1^1), 189.8 (s, CHO) ppm. IR (KBr): 1704 (ν C=O) cm^{-1}. Mass spec. *m/z*: 1359 $[M+1]^+$

1-[G_2]: white powder. 96 % yield. Melting point: 158 °C.

^{31}P {^1H} NMR ($CHCl_3$): δ = -17.9 (s, P_0), -6.3 (s, P_1), 18.5 (s, P_2) ppm. ^1H NMR ($CDCl_3$): δ = 3.19 (d, $^3J_{HP}$ = 6.8 Hz, 9H, $C_0{}^6H_3$), 3.28 (d, $^3J_{HP}$ = 10.1Hz, 18H, $C_1{}^6H_3$), 7.50 (m, 45H, C_6H_4 and CH=N). ^{13}C {^1H} NMR ($CDCl_3$): δ = 30.5 (d, $^3J_{CP}$ = 10.8 Hz, $C_1{}^6$), 31.6 (d, $^3J_{CP}$ = 12.6 Hz, $C_0{}^6$), 119.8 (d, $^3J_{CP}$ = 4.0 Hz, $C_0{}^2$), 120.3 (d, $^3J_{CP}$ = 4.0 Hz, $C_1{}^2$), 128.0 (s, $C_1{}^3$), 128.2 (s, $C_0{}^3$), 130.5 (br s, $C_1{}^4$), 131.1 (br s, $C_0{}^4$), 139.8 (d, $^3J_{CP}$ = 20.8 Hz, $C_0{}^5$), 140.2 (d, $^2J_{CP}$ = 18.8 Hz, $C_1{}^5$), 150.9 (d, $^2J_{CP}$ = 5.7 Hz, $C_0{}^1$, $C_1{}^1$) ppm.

1-[G'$_2$] : white powder. 95 % yield. Melting point: 109 °C.

^{31}P {^1H} NMR (THF): δ = -18.4 (s, P_0), -7.0 (s, P_2), -5.1 (s, P_1) ppm. ^1H NMR ($CDCl_3$): δ = 3.19 (d, $^3J_{HP}$ = 8.3 Hz, 27H, CH_3), 7.57 (m, 93H, C_6H_4 and CH=N), 9.87 (s, 12H, CHO) ppm. ^{13}C {^1H} NMR ($CDCl_3$): δ = 31.6 (d, $^2J_{CP}$ = 10.4 Hz, $C_1{}^6$), 31.7 (d, $^2J_{CP}$ = 11.0 Hz, $C_0{}^6$), 119.8 (d, $^3J_{CP}$ = 5.0 Hz, $C_0{}^2$), 120.3 (d, $^3J_{CP}$ = 5.0 Hz, $C_1{}^2$), 120.5 (d, $^3J_{CP}$ = 5.0 Hz, $C_2{}^2$), 127.6 (s, $C_1{}^3$), 127.8 (s, $C_0{}^3$), 130.9 (s, $C_2{}^3$), 131.5 (br s, $C_1{}^4$), 131.9 (br s, $C_0{}^4$), 133.1 (s, $C_2{}^4$), 138.5 (d, $^3J_{CP}$ = 14.6 Hz, $C_0{}^5$), 138.7 (d, $^3J_{CP}$ = 15.3 Hz, $C_1{}^5$), 150.4 (d, $^2J_{CP}$ = 10.4 Hz, $C_0{}^1$), 150.7 (d, $^2J_{CP}$ = 6.7 Hz, $C_1{}^1$), 154.2 (d, $^2J_{CP}$ = 6.7 Hz, $C_2{}^1$), 189.8 (s, CHO) ppm. IR (KBr): 1704 (ν C=O) cm^{-1}. Mass spec. *m/z*: 3255 $[M+1]^+$

1-[G_3]: white powder. 95 % yield. Melting point: 128 °C.

^{31}P {^1H} NMR ($CHCl_3$): δ = -17.8 (s, P_0), -6.1 (s, P_2), -5.7 (s, P_1), 18.5 (s, P_3) ppm. ^1H NMR ($CDCl_3$): δ = 3.17 (d, $^3J_{HP}$ = 7.3 Hz, 27H, $C_0{}^6H_3$, $C_1{}^6H_3$), 3.29 (d, $^3J_{HP}$ = 11.14 Hz, 36H, $C_2{}^6H_3$), 7.44 (m, 105H, C_6H_4 and CH=N) ppm. ^{13}C {^1H} NMR ($CDCl_3$): δ = 31.6 (d, $^2J_{CP}$ = 10.5 Hz, $C_2{}^6$), 31.7 (d, $^2J_{CP}$ = 10.5 Hz, $C_0{}^6$, $C_1{}^6$), 119.8 (d, $^3J_{CP}$ = 5.6 Hz, $C_0{}^2$), 120.4 (d, $^3J_{CP}$ = 5.0 Hz, $C_1{}^2$, $C_2{}^2$), 127.7 (s, $C_1{}^3$), 127.8 (s, $C_0{}^3$), 128.1 (s, $C_2{}^3$), 130.6 (m, $C_2{}^4$), 131.4 (m, $C_1{}^4$), 131.9 (br s, $C_0{}^4$), 137.8 (d, $^3J_{CP}$ = 15.9 Hz, $C_0{}^5$), 138.1 (d, $^3J_{CP}$ = 15.3 Hz, $C_1{}^5$), 140.3 (d, $^3J_{CP}$ = 20.7 Hz, $C_2{}^5$), 150.3 (d, $^2J_{CP}$ = 6.8 Hz, $C_0{}^1$), 150.5 (d, $^2J_{CP}$ = 6.8 Hz, $C_1{}^1$), 151.1 (d, $^2J_{CP}$ = 7.0 Hz, $C_2{}^1$) ppm.

Synthesis of compound 5-[G'$_1$]:

To a solution of compound **1-[G'$_1$]** (0.19 g, 0.14 mmol) in solution in THF (5 mL) was added at room temperature the ylide **4** (0.28 g, 0.84 mmol) in solution in THF (10 mL). The mixture was stirred for one week, then evaporated to dryness. The white powder thus obtained was dissolved in a minimun amount of THF (*c.a.* 4 mL) then pentane (10 mL) and ether (10 mL). Compound **5-[G'$_1$]**

precipitated as a white powder, whereas triphenyl phosphine oxide remained in solution.

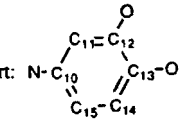
5-[G'$_1$]: white powder. 92 % yield.

^{31}P {^1H} NMR (THF): δ = -18.6 (s, P_0), -6.6 (s, P_1) ppm. ^1H NMR ($CDCl_3$): δ = 3.16 (d, $^3J_{HP}$ = 7.90 Hz, 9H, $C_0{}^6H_3$), 3.68 (s, 18H, CH_3-O), 6.28 (d, $^2J_{HH}$ = 16.00 Hz, =CH-COO), 7.41 (m, 45H, C_6H_4, CH=N,-O-C_6H_4-C<u>H</u>=) ppm. ^{13}C {^1H} NMR ($CDCl_3$): δ = 31.6 (d, $^3J_{CP}$ = 10.8 Hz, $C_0{}^6$), 50.9 (s, CH_3-O), 117.4 (s, C_6H_4-<u>C</u>H=), 119.8 (d, $^3J_{CP}$ = 5.6Hz, $C_0{}^2$), 120.4 (d, $^3J_{CP}$ = 4.9 Hz, $C_1{}^2$), 127.8 (s, $C_0{}^3$), 128.9 (s, $C_1{}^3$), 131.1 (br s, $C_1{}^4$), 131.7 (d, $^4J_{CP}$ = 2.6 Hz, $C_0{}^4$), 138.0 (d, $^3J_{CP}$ = 14.7 Hz, $C_0{}^5$), 142.7 (s, -<u>C</u>H-COO), 150.4 (d, $^2J_{CP}$ = 7.2 Hz, $C_0{}^1$), 151.0 (d, $^2J_{CP}$ = 7.1 Hz, $C_1{}^1$), 166.4 (s, -COO) ppm.

Synthesis of compound 7-[G'$_1$]:

A mixture of crown ether **6** (0.27 g, 0.97 mmol) and compound **1-[G'$_1$]** (0.22 g, 0.16 mmol) in solution in THF (20 mL), was heated for one week at 40 °C in the presence of molecular sieve (4Å). The solution was then filtered, centrifuged and evaporated to dryness. The resulting powder was washed with ether.

Numbering used for the aromatic ring of the crown ether part:



7-[G'$_1$]: brown powder. 72 % yield.

^{31}P {^1H} NMR (THF): δ = -18.6 (s, P_0), -6.7 (s, P_1). ^1H NMR ($CDCl_3$): δ = 3.18 (d, $^3J_{HP}$ = 7.6 Hz, 9H, $C_0{}^6H_3$), 3.72 (m, 96H, -CH_2-O-), 6.45 (m, 18H, C_6H_3), 7.53 (m, 45H, C_6H_4 and CH=N) ppm. ^{13}C {^1H} NMR ($CDCl_3$): δ = 31.6 (d, $^2J_{CP}$ = 15.4 Hz, $C_0{}^6$), 68.2, 68.7, 69.7 and 70.2 (s, CH_2-O-), 107.1 (s, C_{11}), 112.4 (s, C_{14}), 113.9 (s, C_{15}), 119.6 (d, $^2J_{CP}$ = 4.9 Hz, $C_0{}^2$), 120.3 (d, $^2J_{CP}$ = 5.0 Hz, $C_1{}^2$), 127.8 (s, $C_0{}^3$), 129.5 (s, $C_1{}^3$), 131.8 (br s, $C_0{}^4$), 133.1 (br s, $C_1{}^4$), 138.0 (d, $^3J_{CP}$ = 13.5 Hz, $C_0{}^5$), 144.8 (s, C_{10}), 147.1 and 148.8 (s, C_{12}, C_{13}), 150.3 (d, $^2J_{CP}$ = 7.5 Hz, $C_0{}^1$), 151.8 (d, $^2J_{CP}$ = 6.7 Hz, $C_1{}^1$), 156.4 (s, $C_1{}^5$).

Synthesis of compound 8:

To a solution of monomethylhydrazine (0.41 mL, 7.65 mmol) in THF (5 mL) was added a solution of (2R,4R,5S)-(+)2-chloro-2-thio-3,4-dimethyl-5-phenyl-1,3,2-oxaza phospholidine (1 g, 3.82 mmol) in THF (10 mL) at 0°C. This mix-

ture was stirred overnight, then filtered, centrifuged and evaporated to dryness. The resulting powder was washed with acetonitrile/ether.

8: white powder. 96 % yield.

^{31}P {^{1}H} NMR (THF): δ = 85.8 (s) ppm. ^{1}H NMR($CDCl_3$): δ = 0.78 (d, $^{3}J_{HH}$ = 6.58 Hz, 3H, $C\underline{H}_3$-CH-), 2.63 (d,$^{3}J_{HH}$ = 11.64 Hz, 3H, $C\underline{H}_3$-N-CH-), 3.13 (d, $^{3}J_{HH}$ = 9.75 Hz, 3H, CH_3-N-N-), 3.69 (m, 3H, NH_2 and CH_3-C$\underline{H}$-N-), 5.63 (d, $^{3}J_{HH}$ = 7.4Hz, 1H, -C$\underline{H}$-C_6H_5), 7.29 (m, 5H, C_6H_5) ppm. ^{13}C {^{1}H} NMR ($CDCl_3$): δ = 14.5 (d, $^{3}J_{CP}$ = 1.2 Hz, $\underline{C}H_3$-CH-N-), 29.4 (d, $^{2}J_{CP}$ = 7.2 Hz, $\underline{C}H_3$-N-CH-), 40.1 (d, $^{2}J_{CP}$ = 15.0, CH_3-N-N-), 58.5 (d, $^{2}J_{CP}$ = 10.3 Hz, $\underline{C}H$-CH_3), 78.2 (d, $^{2}J_{CP}$ = 1.0 Hz, -$\underline{C}H$-C_6H_5), 125.3 (s, *o*-C_6H_5), 127.3 (s, *p*-C_6H_5), 127.6 (s, *m*-C_6H_5), 135.5 (s, *i*-C_6H_5).

Synthesis of compound 9-[G'$_1$]:

To a solution of compound **1-[G'$_1$]** (0.67g, 0.49 mmol) in solution in THF (15 mL) was added at room temperature and in the presence of molecular sieve (4 Å) a solution of compound **8** (0.81 g, 2.98 mmol) in THF (15 mL). The mixture was stirred for 1 hour, then filtered, centrifuged and evaporated to dryness. The resulting powder was washed with ether.

9-[G'$_1$]: white powder. 90 % yield. Melting point: 129°C.

^{31}P {^{1}H} NMR (THF): δ = -18.4 (s, P_0), -6.4 (s, P_1), 80.1 (s, P(S)) ppm. ^{1}H NMR ($CDCl_3$): δ = 0.87 (d, $^{3}J_{HH}$ = 6.27 Hz, 18H, $C\underline{H}_3$-CH-), 2.62 (d, $^{3}J_{HH}$ = 11.3 Hz, 18H, CH_3-N-P(S)), 3.20 (d, $^{3}J_{HP}$ = 7.64 Hz, 9H, $C_0{}^6H_3$), 3.42 (d, $^{3}J_{HH}$ = 10.1 Hz, 18H, CH_3-N-N-), 3.68 (d, $^{3}J_{HH}$ = 6.29 Hz, 6H, -C$\underline{H}$-CH_3), 5.69 (d, $^{3}J_{HH}$ = 6.31 Hz, 6H, -C$\underline{H}$-C_6H_5), 7.38 (m, 75H, C_6H_4, C_6H_5 and CH=N-). ^{13}C {^{1}H} NMR ($CDCl_3$): δ = 14.4 (s, $\underline{C}H_3$-CH), 28.9 (d, $^{2}J_{CP}$ = 7.9 Hz, CH_3-N-P(S)), 31.8 (d, $^{2}J_{CP}$ = 11.2 Hz, $C_0{}^6$), 32.4 (d, $^{2}J_{CP}$ = 14.8 Hz, $C_1{}^6$), 59.5 (d, $^{3}J_{CP}$ = 11.1 Hz, -$\underline{C}H$-CH_3), 79.5 (br s, -$\underline{C}H$-C_6H_5), 119.5 (d, $^{3}J_{CP}$ = 4.9 Hz, $C_0{}^2$), 120.2 (d, $^{3}J_{CP}$ = 5.0 Hz, $C_1{}^2$), 125.4 (s, *o*-C_6H_5), 127.5 (m, $C_0{}^3$, $C_1{}^3$ and *m*-C_6H_5, *p*-C_6H_5), 132.1 (m, $C_0{}^4$, $C_1{}^4$), 135.8 (d, $^{3}J_{CP}$ = 9.4 Hz, *i*-C_6H_5), 137.5 (d, $^{3}J_{CP}$ = 13.1 Hz, $C_1{}^5$), 150.2 (m, $C_0{}^1$, $C_1{}^1$).

Synthesis of compound 10-[G$_1$]:

To a solution of compound **1-[G$_1$]** (0.30 g, 0.35 mmol) in solution in THF (15 mL) was added at room temperature a mixture of diallylamine (0.39 mL, 3.19

mmol) and triethylamine (0.49 mL, 3.50 mmol). The resulting mixture was stirred for 12 hours, then filtered, centrifuged and evaporated to dryness to obtain an oil. This oil was dissolved in acetonitrile (4 mL) then ether (10 mL) was added to "precipitate" a pale yellow oil.

10-[G_1]: pale yellow oil. 95 % yield.

^{31}P {^1H} NMR (THF): δ = -18.2 (s, P_0), 19.8 (s, P_1). ^1H NMR ($CDCl_3$): δ = 3.09 (d, $^3J_{HP}$ = 9.8 Hz, 9H, $C_0{}^6H_3$), 3.72 (m, 12H, -N-CH_2-), 5.08 (m, 12H, CH_2 =), 5.64 (m, 6H, -CH=), 7.35 (m, 12H, C_6H_4), 7.47 (s, 3H, $HC_0{}^5$=N). ^{13}C {^1H} NMR ($CDCl_3$): δ = 31.0 (d, $^2J_{CP}$ = 8.5 Hz, $C_0{}^6$), 48.1 (d, $^2J_{CP}$ = 3.6 Hz, -CH_2-N-), 117.7 (s, CH_2=), 119.6 (d, $^3J_{CP}$ = 5.0 Hz, $C_0{}^2$), 127.6 (s, $C_0{}^3$), 132.0 (br s, $C_0{}^4$), 132.6 (d, $^3J_{CP}$ = 2.6 Hz, -CH=), 137.5 (d, $^3J_{CP}$ = 16.9 Hz, $C_0{}^5$), 150.1 (d, $^2J_{CP}$ = 7.7 Hz, $C_0{}^1$). Mass spec. *m/z*: 1026 $[M+1]^+$ (Cl = 35)

Synthesis of compound 12-[G_1]:

To a suspension of hydroxybenzaldehyde sodium salt (0.13 g, 0.87 mmol) in THF (10 mL)was added a solution of compound **10-[G_1]** (0.30 g, 0.29 mmol) in THF (15 mL) at room temperature. The mixture was stirred for 4 hours, then filtered, centrifuged and evaporated to dryness. The resulting powder was washed with ether.

12-[G_1]: white powder. 96 % yield. Melting point: 59°C.

^{31}P {^1H} NMR (THF): δ = -18.4 (s, P_0), 5.8 (s, P_1). ^1H NMR ($CDCl_3$): δ = 3.11 (d, $^3J_{HP}$ = 7.4 Hz, 9H, $C_0{}^6H_3$), 3.74 (m, 12H, -N-CH_2-), 5.09 (m, 12H, -CH_2=), 5.54 (m, 6H, -CH=), 7.54 (m, 27H, C_6H_4 and CH=N), 9.84 (s, 3H, CHO) ppm. ^{13}C {^1H} NMR ($CDCl_3$): δ = 31.5 (d, $^2J_{CP}$ = 9.1 Hz, $C_0{}^6$), 47.8 (d, $^2J_{CP}$ = 3.8 Hz, -CH_2-N-), 117.3 (s, CH_2=), 119.7 (d, $^3J_{CP}$ = 5.0 Hz, $C_0{}^2$), 120.4 (d, $^3J_{CP}$ = 5.2 Hz, $C_1{}^2$), 127.3 (s, $C_0{}^3$), 130.8 (s, $C_1{}^3$), 131.5 (s, $C_0{}^4$), 132.4 (s, $C_1{}^4$), 133.4 (d, $^3J_{CP}$ = 2.4 Hz, -CH=), 135.7 (d, $^3J_{CP}$ = 15.2 Hz, $C_0{}^5$), 149.9 (d, $^2J_{CP}$ = 7.3 Hz, $C_0{}^1$), 155.1 (d, $^2J_{CP}$ = 6.8 Hz, $C_1{}^1$), 190.0 (s, -CHO).

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