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Synthesis of small phosphorus dendrimers from (S)P[N(Me)-NH_2]$_3$

Nathalie Launay, Christophe Galliot, Anne-Marie Caminade, Jean-Pierre Majoral*

Laboratoire de chimie de coordination du CNRS, 205, route de Narbonne, 31077 Toulouse Cedex, France

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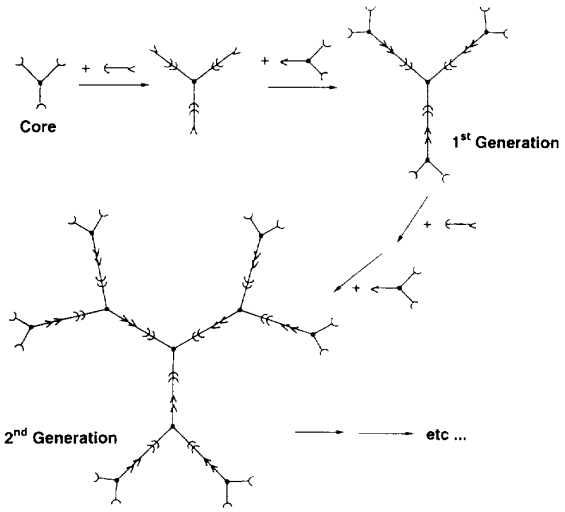
Summary – Three different methods for the synthesis of small phosphorus dendrimers are described. These species are obtained up to the first or second generation using the phosphotrihydrazide (S)P[N(Me)-NH_2]$_3$. These multifunctionalized species have aldehyde, primary amine, phenoxy, phosphine, or P-Cl functions (up to 12 for the largest compound) on the periphery.

dendrimer / multifunctionalization / phosphine / phosphorhydrazone / multi-step synthesis

Introduction

Dendrimers, a new class of fractal and monodisperse polymers with a highly branched architecture of defined structure have attracted considerable attention in the past few years [1]. These 'dream molecules' [2] might offer potential applications in diverse areas such as pharmaceutical and medical applications [3], liquid crystals [4], photo- and electrochemical properties [5] or catalysis [6]. Dendrimers are made step-by-step, by the repetition of a sequence of reactions which creates a new generation at the end of each sequence (scheme 1).



Scheme 1

Dendrimers can be built from virtually any material, provided that the yield of each individual reaction is quantitative, in order to obtain high generations. The first dendrimers were organic compounds [7]; dendrimers containing metals [5,8] or heteroatoms such as silicon [1c,9] and phosphorus [1c,6d-e,10] have since been designed. For our part, we described the first method for the synthesis of neutral phosphorus dendrimers [11] up to the tenth generation and a second method up to the third generation [12]. These two methods are actually the best we have found to date, but we have also tried several other reactions which gave small dendrimers of the first or second generation.

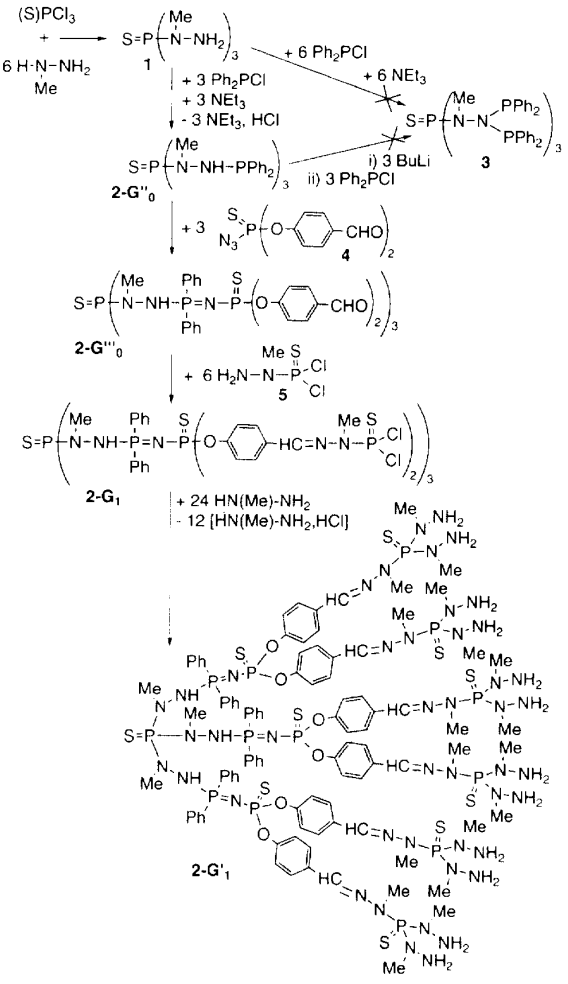
We describe here three different methods for the synthesis of these small dendrimers, obtained by the repetition of sequences of four, three or two reactions using the phosphotrihydazide (S)P[N(Me)-NH_2]$_3$ **1**.

Results and discussion

In a first attempt to synthesize phosphorus dendrimers, we chose a sequence of four reactions, the first step being the formation of (S)P[N(Me)-NH_2]$_3$ **1** from (S)PCl_3 and methylhydrazine [13]. We tried to directly graft phosphorus on each N-H function of **1**, using 6 equiv of chlorodiphenylphosphine, with triethylamine as a base (scheme 2). The reaction was monitored by ^{31}P NMR, which showed the evolution of the singlet corresponding to **1** (δ = 84.6 ppm). This signal first turned into a doublet, then a triplet and finally a quartet (δ = 84.1 ppm, $^3J_{PP}$ = 18.5 Hz) after 2 h at room temperature, whereas the signal corresponding to the PPh_2 moiety was a doublet (δ = 42.0 ppm, $^3J_{PP}$ = 18.5 Hz). These changes correspond to the

* Correspondence and reprints

successive grafting of one PPh_2 group on each hydrazine function in the core to give the triphosphine **2-G$_0''$**. This is confirmed by the fact that 3 equiv of unreacted Ph_2PCl remains in solution. Heating this mixture for 2 h in refluxing THF led only to degradation and we did not observe the formation of any compounds corresponding to the grafting of two PPh_2 groups on one nitrogen such as **3**. This result is surprising since the *gem* substitution of several hydrazines with phosphines is known from the literature [14]. We again tried to obtain the hexaphosphine **3** by first using only 3 equiv of Ph_2PCl to isolate the triphosphine **2-G$_0''$**. Addition of 3 equiv of butyllithium followed by the addition of 3 equiv of Ph_2PCl could give the hexaphosphine **3**, but only results in degradation.



Scheme 2

However, the presence of one phosphine group on each hydrazine function is sufficient to go further in the synthesis of the dendrimer. We use a Staudinger reaction for this third step. The dialdehyde azide **4** [15] reacts readily with the triphosphine **2-G$_0''$** at 0°C to give the hexaaldehyde **2-G$_0'''$** in near quantitative yield (scheme 2). After total evolution of nitrogen, the ^{31}P NMR spectrum of the solution shows the disappearance of the doublet corresponding to the phosphine groups of **2-G$_0''$** (δ = 42.0 ppm) and the singlet corresponding to **4** (δ = 57.7 ppm), and the appearance of a doublet of doublets (δ = 19.3 ppm, $^2J_{PP}$ = 38.2 Hz, $^3J_{PP}$ = 19.0 Hz) and a doublet (δ = 48.2 ppm, $^2J_{PP}$ = 38.2 Hz). Both sets of signals correspond to the formation of the iminophosphorane thiophosphine linkage P=N-P(S) of **2-G$_0'''$**.

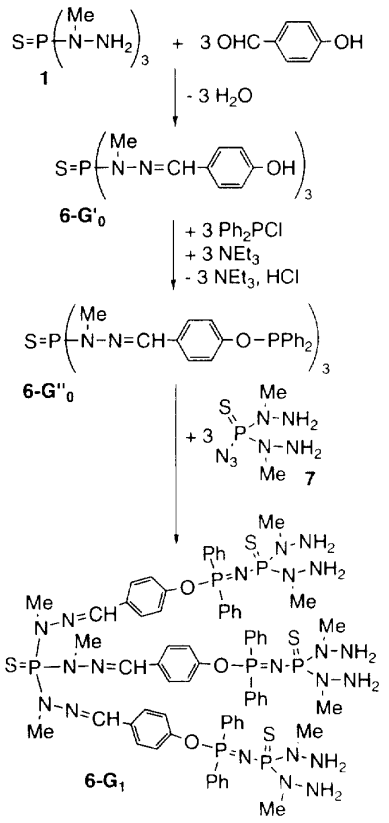
The fourth and final step for the synthesis of the first generation of the dendrimer **2-G$_1$** is a condensation reaction between the aldehyde functions of **2-G$_0'''$** and the dichlorophosphomonohydrazide **5** [11] (scheme 2). The reaction is complete after 3 h at room temperature and **2-G$_1$** is isolated in near quantitative yield. The ^{31}P NMR spectrum shows the expected shielding of the singlet corresponding to the $P(S)Cl_2$ functions (δ = 69.7 ppm for **5**, δ = 62.9 ppm in **2-G$_1$**). The condensation is also indicated by the disappearance of signals corresponding to the aldehyde functions in ^1H and ^{13}C NMR and infrared spectroscopy, and the appearance of a doublet in the ^{13}C NMR spectrum (δ = 140.1 ppm, $^3J_{CP}$ = 18.3 Hz) corresponding to the presence of hydrazone functions (HC=N-N). Furthermore, the formation of the first generation of the dendrimer **2-G$_1$** is proved by the unique presence of the signal with isotopic repartition of the molecular ion (m/z: 2 668 (^{35}Cl) $[M + 1]^+$) in the FAB MS spectrum.

Thus, starting from $P(S)Cl_3$, we have isolated the first generation of the dendrimer **2-G$_1$** after four steps: i) addition of monomethylhydrazine on P-Cl functions; ii) monosubstitution of primary amine functions with diphenylphosphine; iii) Staudinger reaction of the phosphine groups with the dialdehyde azide **4**; and iv) condensation between the aldehyde functions and the dichlorophosphorhydrazide **5**. This sequence of four reactions is rather long, but it is interesting since it allows us to multiply by four the number of P-Cl functions (3 for the core, 12 for **2-G$_1$**).

We tried to obtain the second generation of the dendrimer by repeating the same sequence of four reactions, starting with the addition of monomethylhydrazine on the P-Cl functions of **2-G$_1$**. We experimented with several different combinations of temperature, solvent and dilution. The best results were obtained by a very slow addition of **2-G$_1$** in chloroform solution to methylhydrazine also in chloroform, at −50°C. However, the expected dendrimer **2-G$_1'$** is never obtained in pure state, as shown by ^{31}P NMR. Indeed, besides a singlet at δ = 80.8 ppm, corresponding to P-N-NH_2 in **2-G$_1'$**, we observed a small singlet at δ = 76.5 ppm (intensity less than 10% of the other). Washing with several solvents and column chromatography on silica gel could not induce disappearance of this small signal, which is presumably due either to the grafting of methylhydrazine by the NH_2 group rather than by the MeNH group on one P-Cl function of a few dendrimers, or to cross-linking reactions. Dendrimer **2-G$_1'$** was also characterized by ^1H and ^{13}C NMR, but we decided to stop the synthesis of this family of dendrimers at this step and develop a different strategy using compound **1**.

This new sequence of reactions is simpler than the previous one, since it necessitates only three steps from the trihydrazide **1** to build a generation. The first step

is a condensation reaction with 4 hydroxybenzaldehyde, which gave the triphenol **6-G'$_0$** in nearly quantitative yield [16] (scheme 3).



Scheme 3

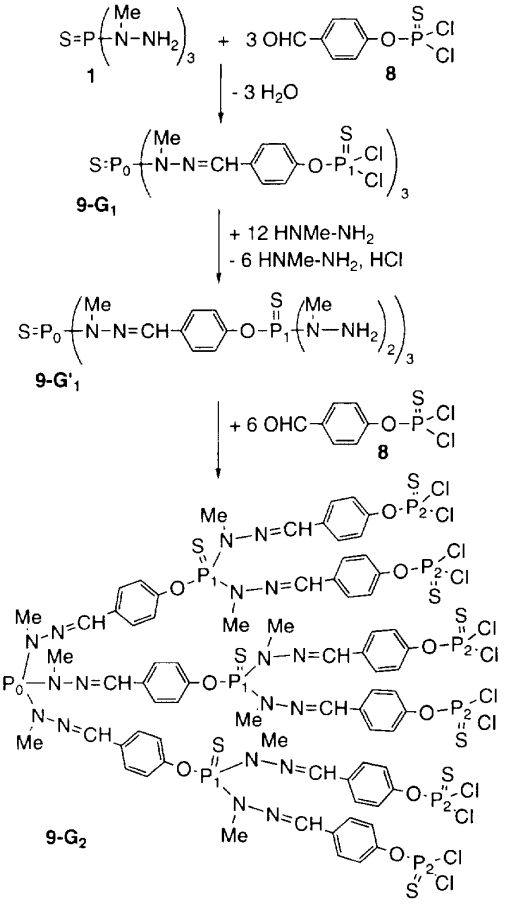
The second step consists of the grafting of phosphine functions on the phenoxy groups of **6-G'$_0$** in the presence of triethylamine as a base. The corresponding triphosphine **6-G''$_0$** was easily obtained, but was very sensitive to moisture. It was characterized in the ^{31}P NMR spectra by the presence of two singlets in a 1:3 ratio at δ = 73.1 and 110.6 ppm for the P^{IV} and P^{III} groups, respectively. The third and final step of this sequence of reactions must give phosphorhydrazide functions on the periphery of the dendrimer. For this purpose, we again used a Staudinger reaction between **6-G''$_0$** and the dihydrazide azide **7** [15]. However, this reaction proceeded very slowly even in refluxing THF and it was impossible to avoid partial degradation and oxidation of some phosphine groups. Therefore, the first generation of the dendrimer **6-G$_1$** was only characterized by ^{31}P NMR. The spectrum consists of three sets of signals: two doublets at δ = 19.8 ppm ($^2J_{PP}$ = 12.5 Hz) and δ = 68.8 ppm ($^2J_{PP}$ = 12.5 Hz), corresponding to the Ph_2P and P(S) groups of the P=N-P(S) linkage respectively, and a singlet at δ = 73.0 ppm, corresponding to the phosphorus of the core.

The difficulties encountered in this third step and the fact that this sequence of three reactions only multiplies the number of terminal functions by two (3 NH_2 for **1**, 6 NH_2 for **6-G$_1$**) prompted us to develop another new strategy, which is inspired by both former sequences of reactions.

The last strategy was the simplest, since it necessitates only two steps: the formation of **1**; and a condensation reaction between **1** and the dichloroaldehyde **8** (scheme 4). The condensation occurred readily to give the first generation of the dendrimer **9-G$_1$** whose ^{31}P NMR spectrum consists of two singlets in a 1:3 ratio at δ = 73.3 and 53.9 ppm, corresponding to P_0-N and P_1-Cl, respectively. The formation of hydrazone functions was clearly indicated in the ^{13}C NMR spectrum by the appearance of a doublet of doublets at δ = 134.6 ppm corresponding to the coupling of CH= N-N both with P_0 ($^3J_{CP0}$ = 12.3 Hz) and P_1 (long distance coupling: $^6J_{CP1}$ = 1.7 Hz).

Thus, this very simple sequence of two reactions (addition of monomethylhydrazine on P-Cl functions and Schiff reaction with **8**) creates a new generation and multiplies the number of terminal functions by two. The repetition of this sequence of reactions is effected starting from the first generation **9-G$_1$**.

A very slow addition of **9-G$_1$** in chloroform solution to methylhydrazine also in chloroform, at −50°C resulted in the near quantitative formation of the hexahydrazide **9-G'$_1$** (scheme 4). The ^{31}P NMR spectrum of **9-G'$_1$** consists of two singlets: the one corresponding to P_0 remains unchanged (δ = 73.4 ppm) whereas



Scheme 4

the one corresponding to P_1 is shielded (δ = 81.4 ppm, $\Delta\delta$ = 27.5 ppm). The ^1H NMR spectrum clearly shows the presence of two doublets in a 1:2 ratio (δ = 3.3 ppm, $^3J_{HP0}$ = 9.3 Hz and δ = 2.9 ppm, $^3J_{HP1}$ = 11.1 Hz) corresponding to two types of Me-N groups, Me-N-P_0 and Me-N-P_1, respectively. The same phenomenon was observed in the ^{13}C NMR spectrum (δ = 31.8 ppm, $^2J_{CP0}$ = 8.7 Hz; CH_3-N-P_0 and δ = 40.1 ppm, $^2J_{CP1}$ = 8.8 Hz; CH_3-N-P_1).

The second generation of the dendrimer **9-G$_2$** was easily obtained after the condensation of **9-G$'_1$** with the aldehyde **8**. The ^{31}P NMR spectrum of **9-G$_2$** consists of three singlets in a 1:3:6 ratio at δ = 72.1, 66.5 and 52.0 ppm corresponding to P_0, P_1 and P_2, respectively. The P_2 signal of **9-G$_2$** appears in the area where P_1 appeared for **9-G$_1$**. In addition to NMR characterization, the formation of the second generation of the dendrimer **9-G$_2$** was proved by the unique presence of the signal with isotopic repartition of the molecular ion (m/z: 2 382 (^{35}Cl) $[M + 1]^+$) in the FAB MS spectrum.

Dendrimer **9-G$_2$** was easy to isolate in good yields, but we found that this compound was not perfectly stable after several days in solution. It means that this family of compounds will not be useful for practical purposes. Thus, we decided not to proceed further in the synthesis, even if the obtention of the second generation of the dendrimer **9-G$_2$** has proved the theoretical viability of this sequence of synthesis of dendrimer up to high generations. However, we have demonstrated that the phosphotrihydrazide $(S)P[N(Me)-NH_2]_3$ **1** is a useful and versatile precursor of a series of multifunctionalized compounds with three to twelve P-Cl, aldehyde, primary amine, phenoxy or phosphine functions.

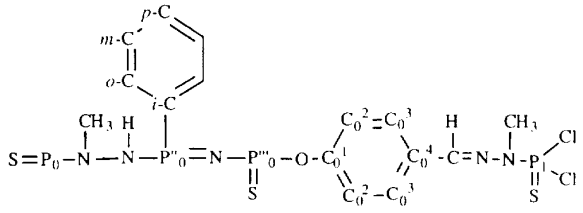
Experimental section

General

All manipulations were carried out with standard high vacuum or dry argon atmosphere techniques. ^1H, ^{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 recorded on a Finniganmat TSQ 700 or 95 spectrometer (FAB). Melting points were measured on an Electrothermal digital melting point. Elemental analyses were obtained in our laboratory or in the Service Central d'Analyse CNRS.

Synthesis of dendrimers **2-G$_n$**

The numbering used for ^{31}P and ^{13}C NMR is as follows:



• *Synthesis of the triphosphine* **2-G$''_0$**

To a solution of triethylamine (1.12 mL, 8 mmol) and diphenylchlorophosphine (1.6 mL, 7 mmol) in THF (15 mL), was added powdered phosphotrihydrazide **1** [13] (0.396 g, 2 mmol). The mixture was stirred for 2 h at room temperature, and then filtered to eliminate the precipitate of triethylamine hydrochloride. After evaporation of the solvent, **2-G$''_0$** was obtained as a yellow oil, purified by washing with pentane (2 × 10 mL).

2-G$''_0$: yellow oil. 70% yield.

^{31}P $\{^1H\}$ NMR (C_6D_6): δ = 42.0 (d, $^3J_{P0P''0}$ = 18.5 Hz, P''_0): 84.1 (q, $^3J_{P0P''0}$ = 18.5 Hz, P_0) ppm.

^1H NMR (C_6D_6): δ = 3.1 (d, $^3J_{HP0}$ = 9.8 Hz, 9H, P_0-N-CH_3); 4.8 (d, $^2J_{HP1}$ = 7.8 Hz, 3H, P''_0-N-H); 7.0–8.0 (m, 30H, C_6H_5) ppm.

^{13}C $\{^1H\}$ NMR (C_6D_6): δ = 42.7 (d, $^2J_{CP0}$ = 9.7 Hz, P_0-N-CH_3); 129.2 (d, $^3J_{CP''0}$ = 6.7 Hz, *m*-C); 129.7 (s, *p*-C); 132.1 (d, $^2J_{CP''0}$ = 13.1 Hz, *o*-C); 142.4 (d, $^1J_{CP''0}$ = 14.6 Hz, *i*-C) ppm.

• *Synthesis of the hexaaldehyde* **2-G$'''_0$**

To a freshly prepared solution of compound **2-G$''_0$** (2 mmol) in THF (7 mL), was added dropwise at 0°C a solution of the azide **4** [15] (2.08 g, 6 mmol) in THF (7 mL). This mixture was stirred for 1 h at room temperature, and then the solvent was evaporated to give a yellow oil. This oil was dissolved in chloroform (15 mL), and then ether was added to precipitate a pale yellow paste. The solution was eliminated *via* cannula and the precipitate was dried under vacuum to give **2-G$'''_0$** as a powder.

2-G$'''_0$: pale yellow powder. 85% yield. Melting point: 98–100°C (decomp).

$^{31}P\{^1H\}$ NMR ($CDCl_3$): δ = 19.3 (dd, $^2J_{P''0P'''0}$ = 38.2 Hz, $^3J_{P0P''0}$ = 19.0 Hz, P''_0); 48.2 (d, $^2J_{P''0P'''0}$ = 38.2 Hz, P'''_0): 87.9 (q, $^3J_{P0P''0}$ = 19.0 Hz, P_0) ppm.

^1H NMR ($CDCl_3$): δ = 2.7 (d, $^3J_{HP0}$ = 9.6 Hz, 9H, P_0-N-CH_3); 5.7 (br d, 3H, P''_0-N-H); 6.9–7.9 (m, 54H, C_6H_5, O-C_6H_4); 9.9 (s, 6H, CHO) ppm.

^{13}C $\{^1H\}$ NMR ($CDCl_3$): δ = 41.7 (d, $^2J_{CP0}$ = 9.6 Hz, P_0-N-CH_3); 121.3 (d, $^3J_{CP'''_0}$ = 5.4 Hz, C^2_0); 128.0 (d, $^2J_{CP''0}$ = 13.6 Hz, *o*-C); 130.5 (s, C^3_0); 132.1 (s, *p*-C); 132.4 (d, $^3J_{CP''0}$ = 11.5 Hz, *m*-C); 132.7 (s, C^4_0); 155.6 (d, $^2J_{CP'''_0}$ = 9.0 Hz, C^1_0); 190.1 (s, CHO) ppm.

IR (KBr): 1 700 (ν_{CHO}) cm^{-1}.

MS m/z: 1 708 $[M + 1]^+$.

Anal calc for $C_{81}H_{72}N_9O_{12}P_7S_4$: C, 56.95; H, 4.24; N, 7.38. Found: C, 56.50; H, 4.11; N, 7.23.

• *Synthesis of compound* **2-G$_1$**

To a solution of phosphomonohydrazide **5** (0.300 g, 1.68 mmol) in chloroform (7 mL), was added powdered hexaaldehyde **2-G$'''_0$** (0.477 g, 0.28 mmol) in the presence of molecular sieve (4 Å). This mixture was stirred for 3 h, and then filtered over Celite to eliminate molecular sieve. After evaporation of the solvent, **2-G$_1$** was obtained as a powder which was washed with ether (15 mL).

2-G$_1$: pale pink powder. 87% yield. Melting point: 139–140°C (decomp).

^{31}P $\{^1H\}$ NMR ($CDCl_3$): δ = 19.0 (dd, $^2J_{P''0P'''0}$ = 37.5 Hz, $^3J_{P0P''0}$ = 20.7 Hz, P''_0); 49.4 (d, $^2J_{P''0P'''0}$ = 37.5 Hz, P''_0); 62.9 (s, P_1); 87.6 (q, $^3J_{P0P''0}$ = 20.6 Hz, P_0) ppm.

^1H NMR ($CDCl_3$): δ = 2.7 (br s, 9H, P_0-N-CH_3); 3.4 (d, $^3J_{HP1}$ 13.9 Hz, 18H, P_1-N-CH_3); 5.5 (br d, 3H, P''_0-N-H); 7.0–8.0 (m, 60H, C_6H_5, O-C_6H_4, CH=N) ppm.

^{13}C $\{^1H\}$ NMR ($CDCl_3$): δ = 31.2 (d, $^3J_{CP1}$ = 13.1 Hz, P_1-N-CH_3); 41.8 (d, $^3J_{CP0}$ = 3.7 Hz, P_0-N-CH_3); 121.3 (d, $^3J_{CP'''0}$ = 5.0 Hz, C^2_0); 127.8 (s, C^3_0); 128.1 (d, $^2J_{CP''0}$ = 11.0 Hz, *o*-C); 129.8 (s, C^4_0); 132.3 (s, *p*-C); 132.6 (d, $^3J_{CP''0}$ = 10.3 Hz, *m*-C); 140.1 (d, $^3J_{CP1}$ = 18.3 Hz, CH=N); 155.6 (d, $^2J_{CP'''_0}$ = 9.0 Hz, C^1_0) ppm.

MS m/z: 2668 $[M + 1]^+$ (Cl=35) (isotopic repartition: 2674: 100%).

Anal calc for $C_{87}H_{90}Cl_{12}N_{21}O_6P_{13}S_{10}$: C, 36.08; H, 3.39; N, 11.00. Found: C, 35.75; H, 3.23; N, 11.13.

• *Synthesis of compound* **2-G'$_1$**

To a solution of methylhydrazine (0.056 mL, 1.05 mmol) in chloroform (2.5 mL) at −50°C (cold bath) was added very slowly a solution of **2-G$_1$** (0.100 g, 0.0374 mmol) in chloroform (2.5 mL). The temperature was allowed to rise slowly to room temperature overnight. Then the mixture was filtered and the solvent was evaporated. Several washings with different solvents and column chromatography on silica gel did not permit to perfectly purify this product (maximum purity: 95%).

2-G'$_1$: pale pink powder.

^{31}P $\{^1H\}$ NMR ($CHCl_3$): δ = 18.7 (dd, $^2J_{P''0P'''0}$ = 36.8 Hz, $^3J_{P0P''0}$ = 19.6 Hz, P''_0); 49.6 (d, $^2J_{P''0P'''0}$ = 36.8 Hz, P''_0); 80.8 (s, P_1); 87.6 (q, $^3J_{P0P''0}$ = 19.6 Hz, P_0) ppm

^1H NMR ($CDCl_3$): δ = 2.7 (br s, 9H, P_0-N-CH_3); 2.9 (d, $^3J_{HP1}$ = 10.6 Hz, 36H, P_1-N-CH_3NH$_2$); 3.2 (d, $^3J_{HP1}$ = 8.5 Hz, 18H, P_1-N-CH_3); 5.5 (br d, 3H, P''_0-N-H); 7.0–8.0 (m, 60H, C_6H_5, O-C_6H_4, CH=N) ppm.

^{13}C $\{^1H\}$ NMR ($CDCl_3$): δ = 32.4 (d, $^3J_{CP1}$ = 7.6 Hz, P_1-N-CH_3-NH$_2$); 40.9 (d, $^3J_{CP1}$ = 8.8 Hz, P_1-N-CH_3); 42.1 (br d, $^3J_{CP0}$ = 5.0 Hz, P_0-N-CH_3); 121.7 (br d, C_0^2); 127.1 (s, C_0^3); 128.4 (d, $^2J_{CP''0}$ = 14.0 Hz, *o*-C); 130.0 (s, C_0^4); 132.9 (s, *p*-C); 133.0 (d, $^3J_{CP''0}$ = 9.1 Hz: *m*-C); 136.6 (d, $^3J_{CP1}$ = 13.0 Hz; CH=N); 151.9 (d, $^2J_{CP''0}$ = 8.2 Hz; C_0^1) ppm.

Synthesis of dendrimer **6-G''$_0$**

To a solution of phosphotrihydrazone **6-G'$_0$** [16] (0.51 g, 1 mmol) in THF (30 mL) was added triethylamine (0.418 mL, 3 mmol). The mixture was stirred for 30 min, then chlorodiphenylphosphine (0.540 mL, 3 mmol) was added. The mixture was stirred for 2 h, filtered, and the solvent was evaporated under vacuum. Washing with ether gave **6-G''$_0$** as a powder.

6-G''$_0$: white powder. 82% yield.

^{31}P $\{^1H\}$ NMR ($CDCl_3$): δ = 73.1 (s, P=S); 110.6 (s, Ph_2P-O) ppm.

^1H NMR ($CDCl_3$): δ = 3.30 (d, $^3J_{HP}$ = 9.0 Hz, 9H, N-CH_3); 6.9–7.8 (m, 45H, C_6H_4, C_6H_5, N=CH) ppm.

^{13}C $\{^1H\}$ NMR ($CDCl_3$): δ = 32.5 (d, $^2J_{CP}$ = 8.5 Hz, N-CH_3); 118.2–135.7 (m, C_6H_4, C_6H_5), 140.8 (d, $^3J_{CP}$ = 14.0 Hz, N=CH), 157.5 (d, $^2J_{CP}$ = 10.0 Hz, P-O-C) ppm.

Synthesis of the O-*(4-formylphenyl)phosphorodichloridothioate* **8**

To a solution of 4-hydroxybenzaldehyde (3.66 g, 30 mmol) in THF (80 mL), was added dropwise triethylamine (4.18 mL, 30 mmol). The mixture was stirred for 30 min at room temperature, and then added very slowly to a solution of (S)PCl_3 (1.52 mL, 15 mmol) in THF (50 mL) at −78°C (cold bath). The temperature was allowed to rise slowly to room temperature overnight. Then the mixture was filtered, and the solvent was evaporated to give **8** as an oil.

8: yellow oil. 88% yield.

IR (THF): 1707 (ν_{CHO}) cm^{-1}.

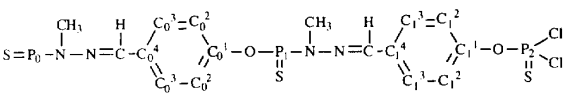
^{31}P $\{^1H\}$ NMR ($CDCl_3$): δ = 52.0 (s) ppm.

^1H NMR ($CDCl_3$): δ = 7.3 (dd, $^3J_{HH}$ = 7.9 Hz, $^4J_{HP}$ = 2.2 Hz, 2H, C^2-H); 8.2 (d, $^3J_{HH}$ = 7.9 Hz, 2H, C^3-H); 10.1 (s, 1H, CHO) ppm.

^{13}C $\{^1H\}$ NMR ($CDCl_3$): δ = 121.5 (d, $^3J_{CP}$ = 5.8 Hz, C^2); 131.0 (d, $^4J_{CP}$ = 2.3 Hz, C^3); 134.2 (d, $^5J_{CP}$ = 2.9 Hz, C^4); 153.3 (d, $^2J_{CP}$ = 9.3 Hz, C^1); 189.7 (d, $^6J_{CP}$ = 1.1 Hz; CHO) ppm.

Synthesis of dendrimers **9-G$_n$**

Dendrimers **9-G$_n$** were named according to the nomenclature of reference [17]. The numbering used for ^{31}P and ^{13}C NMR is as follows:



• *6-Cascade: phosphorothioic [3]: [4-(3-methyl-2,3-diazaprop-2-enyl))phenoxythiophosphinylidène]^1: chloride* **9-G$_1$**

To a solution of aldehyde **8** (0.765 g, 3 mmol) in THF (10 mL) was added powdered phosphorothioic trihydrazide **1** (0.186 g, 1 mmol), in the presence of molecular sieve (4 Å). The mixture was stirred for 24 h at room temperature and then filtered over Celite. Evaporation of the solvent gave **9-G$_1$** as a powder which was washed with ether (2 × 10 mL).

9-G$_1$: pale yellow powder. 84% yield. Melting point: 95°C (decomp).

^{31}P $\{^1H\}$ NMR ($CDCl_3$): δ = 53.9 (s, P_1); 73.3 (s, P_0) ppm.

^1H NMR ($CDCl_3$): δ = 3.3 (d, $^3J_{HP0}$ = 9.3 Hz, 9H, P_0-N-CH_3); 6.8 (dd, $^3J_{HH}$ = 8.6 Hz, $^4J_{HP1}$ = 2.5 Hz, 6H, C_0^2-H); 7.6 (s, 3H, CH=N); 7.7 (dd, $^3J_{HH}$ = 8.6 Hz, $^5J_{HP1}$ = 1.1 Hz, 6H, C_0^3-H) ppm.

^{13}C $\{^1H\}$ NMR ($CDCl_3$): δ = 31.8 (d, $^2J_{CP0}$ = 9.4 Hz, P_0-N-CH_3); 120.8 (d, $^3J_{CP1}$ = 5.8 Hz, C_0^2); 127.3 (d, $^4J_{CP1}$ = 2.9 Hz, C_0^3); 133.9 (d, $^5J_{CP1}$ = 3.6 Hz, C_0^4); 134.6 (dd, $^6J_{CP1}$ = 1.7 Hz, $^3J_{CP0}$ = 12.3 Hz, CH=N); 149.6 (d, $^2J_{CP1}$ = 14 Hz, C_0^1) ppm.

Anal calc for $C_{24}H_{24}Cl_6N_6O_3P_4S_4$: C, 31.71; H, 2.66; N, 9.24. Found: C, 31.86; H, 2.76; N, 9.19.

• *6-Cascade: phosphorothioic [3]: [4-(3-methyl-1,3-diazaprop-2-enyl)phenoxythiophosphinylidène]^1: 2-methylhydrazine* **9-G'$_1$**

To a solution of methylhydrazine (0.149 mL, 2.8 mmol) in chloroform (7 mL) at −50°C was slowly added a solution of **9-G$_1$** (0.182 g, 0.2 mmol) in chloroform (5 mL). The mixture was stirred for 1 h at −40°C, and then the temperature was allowed to rise slowly to room temperature overnight. The mixture was filtered and then solvent was evaporated to give **9-G'$_1$** as a powder which was washed with ether (2 × 15 mL).

9-G'$_1$: white powder. 80% yield. Melting point: 83°C (decomp).

^{31}P $\{^1H\}$ NMR: δ = 73.4 (s, P_0); 81.4 (s, P_1) ppm.

^1H NMR ($CDCl_3$): δ = 2.9 (d, $^3J_{HP1}$ = 11.1 Hz, 18H, P_1-N-CH_3); 3.3 (d, $^3J_{HP0}$ = 9.3 Hz, 9H, P_0-N-CH_3); 3.8 (br s, 12H, NH_2); 6.6 (dd, $^3J_{HH}$ = 8.5 Hz, $^4J_{HP1}$ = 1.2 Hz, 6H, C_0^2-H); 7.5 (s, 3H, CH=N); 7.7 (d, $^3J_{HH}$ = 8.5 Hz, 6H, C_0^3-H) ppm.

^{13}C $\{^1H\}$ NMR ($CDCl_3$): δ = 31.8 (d, $^2J_{CP0}$ = 8.7 Hz, P_0-N-CH_3); 40.1 (d, $^2J_{CP1}$ = 8.8 Hz, P_1-N-CH_3); 120.3 (d, $^3J_{CP1}$ = 4.1 Hz, C_0^2); 127.1 (s, C_0^3); 131.9 (s, C_0^4); 135.2 (d, $^3J_{CP0}$ = 14 Hz, CH=N); 150.1 (d, $^2J_{CP1}$ = 7 Hz, C_0^1) ppm.

MS m/z: 967 $[M + 1]^+$.

Anal calc for $C_{30}H_{54}N_{18}O_3P_4S_4$: C, 37.27; H, 5.63; N, 26.07. Found: C, 37.36; H, 5.72; N, 25.96.

• *12-Cascade: phosphorothioic [3]: [4-(3-methyl-2,3-diazaprop-2-enyl)phenoxythiophosphinylidène]^2: chloride* **9-G$_2$**

To a solution of aldehyde **8** (0.255 g, 1 mmol) in THF (10 mL) was added powdered **9-G$'_1$** (0.161 g, 0.17 mmol), in the presence of molecular sieve (4 Å). The mixture was stirred for 4 h at room temperature, and then filtered over Celite. Evaporation of the solvent gave **9-G$_2$** as a powder which was washed with ether (2 × 10 mL).

9-G$_2$: pale orange powder. 85% yield. Melting point: 90°C (decomp).

^{31}P {^{1}H} NMR (C_6D_6): δ = 52.0 (s, P_2); 66.5 (s, P_1); 72.1 (s, P_0) ppm.

^{1}H NMR (C_6D_6): δ = 3.0 (d, $^3J_{HP0}$ = 10.0 Hz, 9H, P_0-N-CH_3); 3.2 (d, $^3J_{HP1}$ = 9.5 Hz, 18H, P_1-N-CH_3); 6.8–7 (m, 45H, C_6H_4, CH=N) ppm.

^{13}C {^{1}H} NMR (C_6D_6): δ = 32.7 (d, $^2J_{CP0-1}$ = 9.7 Hz, P_{0-1}-N-CH_3); 121.7 (d, $^3J_{CP1-2}$ = 5.6 Hz, C_0^2, C_1^2); 128.5 (d, $^4J_{CP1-2}$ = 2.5 Hz, C_0^3, C_1^3); 133.6 (s, C_0^4); 135.4 (d, $^5J_{CP2}$ = 2.5 Hz, C_1^4); 136.0–137.4 (m, CH=N); 150.7 (d, $^2J_{CP1-2}$ = 10.5 Hz, C_0^1, C_1^1) ppm.

MS m/z: 2 382 $[M + 1]^+$ (Cl = 35) (isotopic repartition: 2 389: 100%).

Anal calc for $C_{72}H_{72}Cl_{12}N_{18}O_9P_{10}S_{10}$: C, 36.20; H, 3.04; N, 10.55. Found: C, 36.33; H, 3.11; N, 10.45.

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