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Phosphorus-Containing Dendrimers: Chemoselective Functionalization of Internal Layers

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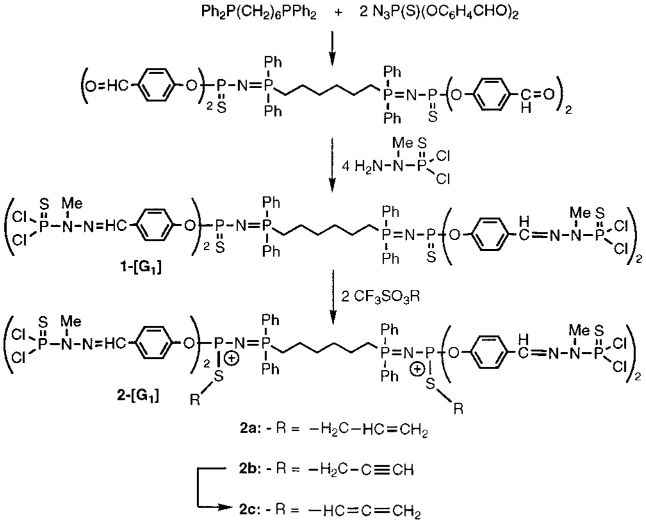
Some of the most fascinating properties of dendrimers are due to the presence of a large number of functional groups on the surface.[1] Reactive sites can also be present at the center of a dendrimer, i.e., at the core,[2] and much more rarely within the cascade structure.[1,3,4] In the latter case functionalities are introduced either during the construction of these macromolecules[1] or through a postmodification of the dendrimer backbone and can be found on each monomer unit constituting a generation. Up to now very few examples of selective introduction of functional groups in a *given* generation, where and when required in the internal layers, are reported despite the interest of having reactive groups in a well-determined location.[3−6]

We report here the chemoselective grafting of up to 18 allyl or propargyl groups on the core and within the cascade structure of a dendrimer of generation 4. X-ray crystallographic studies of the first generation of two dicationic dendrimers are also reported.

The strategy used for the synthesis of phosphorus-containing dendrimers offers the possibility to incorporate in the framework of the macromolecule strongly polarized $P^+—N═P—S^-$ groups. These fragments can be included in the backbone any time during the construction as is illustrated in Scheme 1 where incorporation of two P═N—P(S) moieties on a core of the dendrimer of generation 1, **1-[G$_1$]** is shown.[7] Such a methodology can also be applied to introduce 18 of these linkages (2 on the core, 16 on generation 3, i.e., within the cascade structure) in the internal layers of the dendrimer of generation 4, **1-[G$_4$]** (Scheme 2).

Treatment of the dendrimer **1-[G$_1$]** with two equiv of allyl trifluoromethane sulfonate allows the chemoselective allylation on the sulfur atom of both −P═N—P(S) internal groups, and the formation of the dication **2a-[G$_1$]**. This reaction can be easily monitored by ^{31}P NMR since the disappearance of the two doublets due to the P═N—P(S) fragments (**1-[G$_1$]**, δ = 20.1 (CH_2—P—N) and 51.9 (N—P(S)) ppm, $^2J_{PP}$ = 35 Hz) on behalf of two new doublets (**2a-[G$_1$]**, δ = 20.4 (P—S—$CH_2CH═CH_2$) and 26.9 (CH_2—P—N) ppm, $^2J_{PP}$ = 17 Hz) due to the two cationic linkages $[P═N═P—(SCH_2CH═CH_2)]^+$ can be observed.

Scheme 1



Similarly addition of propargyl triflate to **1-[G$_1$]** leads to the selective functionalization on the sulfur atom of the two P═N—P(S)═ fragments, with the quantitative formation of the dicationic species **2b-[G$_1$]**. The ^{31}P NMR spectrum exhibits, beside the signal due to $P(S)Cl_2$ chain ends, two doublets at 18.8 (P—S—CH_2—C≡C—H) and 27.5 (CH_2—P) ppm with $^2J_{PP}$ = 13 Hz for **2b-[G$_1$]**. This ^{31}P NMR spectrum shows also without any ambiguity that no reaction on the terminal $P(S)Cl_2$ takes place: chemical shifts of these groups remain unchanged after addition of the alkylating reagent. Structures of **2a-[G$_1$]** and **2b-[G$_1$]** are corroborated by ^{1}H and ^{13}C NMR while X-ray crystallography studies confirm the structure of **2a-[G$_1$]**.[8] The CAMERON drawing of **2a-[G$_1$]** is depicted in Figure 1 together with significant bond lengths and angles.

Remarkably **2b-[G$_1$]** is slowly and quantitatively transformed (CH_2Cl_2 solution, 0 °C, three months) into the new functionalized macromolecule **2c-[G$_1$]** incorporating two allenic systems instead of the two propargylic ones.

Such an isomerization can be followed by ^{1}H NMR: the disappearance of the doublet of doublets due to the methylene groups at 4.22 ($^4J_{HH}$ = 2.6 Hz, $^2J_{HP}$ = 19.0 Hz) ppm and of the triplet due to the ≡CH groups at 3.20 ($^4J_{HH}$ = 2.6 Hz) ppm on behalf of a doublet at 6.3 ($^4J_{HH}$ = 6.5 Hz) ppm for the ═CH_2 groups can be observed. The ^{13}C NMR spectrum also shows the disappearance of the signals due to the propargylic carbon atoms at 20.9 (d, $^2J_{CP}$ = 5 Hz, CH_2—S), 76.0 (s, *C*≡C—H), and 77.7 (d, $^4J_{CP}$ = 6 Hz, ≡C—H) ppm on behalf of new signals at 92.6 (s, ═CH_2), 106.1 (s, CH═), and 203.0 (s, ═C═) ppm characteristic of allenic systems. The molecular structure of **2c-[G$_1$]** is confirmed by X-ray crystallographic analysis.[8]

Selective functionalization with allyl and propargyl triflates was attempted also with the dendrimer **1-[G$_4$]** possessing 18 P═N—P(S) units (Scheme 2). The reaction proceeds instantaneously when allyl or propargyl triflates are used and gives quantitatively the polycationic dendrimer **2a-[G$_4$]** or **2b-[G$_4$]** incorporating 18 allyl or propargyl fragments in the internal generations. Again ^{31}P

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(1) For reviews see: (a) Tomalia, D. A.; Durst, H. D. In *Topics in Current Chemistry, Vol. 165; Supramolecular Chemistry I: Directed Synthesis and Molecular Recognition*; Weber, E., Ed.; Springer-Verlag: Berlin, Heidelberg, 1993; pp 193−313. (b) Issberner, J.; Moors, R.; Vögtle, F. *Angew. Chem., Int. Ed. Engl.* **1994**, *33*, 2413. (c) Newkome, G. R.; Moorefield, C. N.; Vögtle, F. In *Dendritic Molecules*; VCH: Weinheim, Germany, 1996.

(2) See for example: Fréchet, J. M. J. *Science* **1994**, *263*, 1710 and references therein.

(3) For a pioneering work see for example: (a) Newkome, G. R.; Moorefield, C. N. *Polym. Prepr.* **1993**, *34*, 75. (b) Newkome, G. R.; Moorefield, C. N. *Macromol. Symp.* **1994**, *77*, 63. (c) Newkome, G. R.; Moorefield, C. N.; Keith, J. M., Baker, G. R.; Escamilla, G. H. *Angew. Chem., Int. Ed. Engl.* **1994**, *33*, 666.

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(7) Larré, C.; Caminade, A.-M.; Majoral, J.-P. *Angew. Chem., Int. Ed. Engl.* **1997**, *36*, 596.

(8) Crystal data for **2a-[G$_1$]**: triclinic, $P\bar{1}$, a = 13.229(2) Å, b = 14.056(2) Å, c = 16.938(2) Å, α = 83.47(1)°, β = 67.96(1)°, γ = 73.44(1)°, V = 2798.2 Å^3, Z = 1, μ = 5.88 cm^{-1}, Mo Kα radiation (λ = 0.710 73 Å), colorless crystals (0.60 × 0.40 × 0.25). Crystal data for **2c-[G$_1$]**: triclinic, $P1$, a = 13.290(2) Å, b = 14.060(2) Å, c = 17.048(2) Å, α = 83.13(1)°, β = 68.44 (1)°, γ = 73.21 (1)°, V = 2798.2, Z = 1, μ = 6.11 cm^{-1}, Mo Kα radiation (λ = 0.710 73 Å), colorless crystals (0.60 × 0.35 × 0.20).

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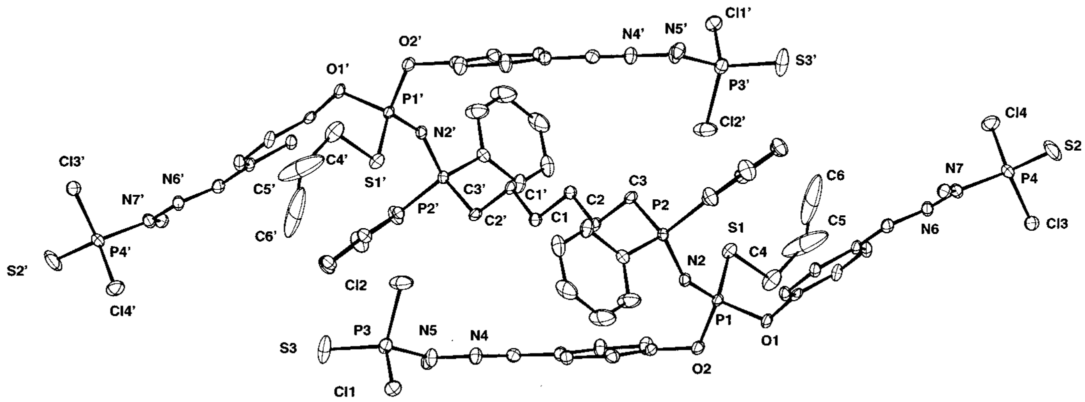


Figure 1. Crystal structure of **2a-[G$_1$]**. Selected bond lengths (Å) and angles (deg): P(1)−S(1) = 2.038(2), S(1)−C(4) = 1.830(8), C(4)−C(5) = 1.52(3), C(5)−C(6) = 1.30(3), C(4)−C(5)−C(6) = 130(2).

Scheme 2

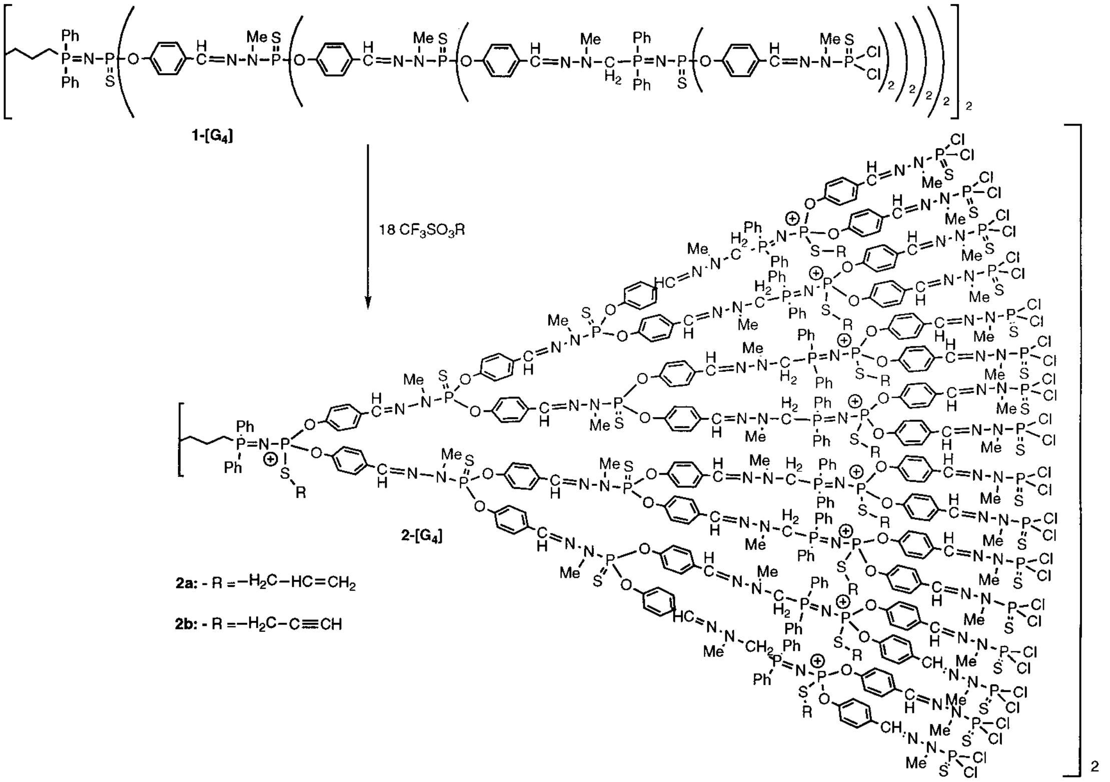
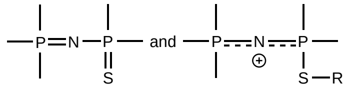
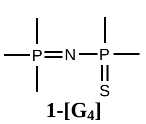
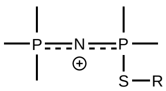


Table 1. Selected ^{31}P NMR Data for



$-\mathrm{P{=}N{-}P({=}S)}-$ and $-\mathrm{P{\cdots}\overset{\oplus}{N}{\cdots}P(S{-}R)}-$

Units for Dendrimers **1-[G$_4$]**, **2a-[G$_4$]**, and **2b-[G$_4$]**[a]

			
	1-[G$_4$]	**2a-[G$_4$]** R = $CH_2{-}CH{=}CH_2$	**2b-[G$_4$]** R = $CH_2{-}C{\equiv}CH$
core	20.4 (34.6)	26.7 (15)	27.4 (12)
	52.5 (34.6) [P(S)]	20.5 (15) (PSR)	18.8 (12) (PSR)
generation 3	13.5 (31.7)	19.7 (11)	20.5 (8)
	52.5 (31.7) [P(S)]	21.3 (11) (PSR)	19.6 (8) (PSR)

[a] $^2J_{PP}$ values are given in parentheses.

NMR is a useful tool to follow the evolution of the reaction and the formation of the resulting dendrimers **2a-[G$_4$]** and **2b-[G$_4$]** (Table 1).

Preliminary results show that such a selective reaction can be extended to a number of other triflates. As an example,2 or 18 phosphonate groups can be grafted on dendrimer **1-[G$_1$]** or **1-[G$_4$]**, respectively, using the phosphonate triflate $(EtO)_2P(O)CH_2OSO_2CF_3$.

In conclusion these first achievements in the preparation of multifunctionalized phosphorus-containing dendrimers with precisely placed functional groups, where and when wanted, in the internal layers open new avenues for the preparation of well-defined molecular objects and devices for a number of applications.

Acknowledgment. Thanks are due to CNRS for financial support.

Supporting Information Available: Detailed spectroscopic data for compounds **2a-[G$_1$]**, **2b-[G$_1$]**, **2c-[G$_1$]**, **2a-[G$_4$]**, and **2b-[G$_4$]** and further details of the crystal structure of **2a-[G$_1$]** and **2c-[G$_1$]** (33 pages, print/PDF). See any current masthead page for ordering information and Web access instructions.

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