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Phosphorus-Containing Dendrons: Synthesis, Reactivity, Properties, and Use as Building Blocks for Various Dendritic Architectures

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Dendrons, also called dendritic wedges, are a special variety of dendrimers possessing one or two functional groups at the core, in addition to the numerous functional end groups. This review is focused on phosphorus-containing dendrons, which are dendrons built with one phosphorus atom at each branching point. Their synthesis, reactivity and properties are described, with emphasis on their use as building blocks for the elaboration of very complex and original dendritic architectures. Electrochemical and catalytic properties, as well as examples in the field of materials are also given.
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Introduction

Dendritic macromolecules constitute the fourth class of macromolecular architectures discovered about two decades ago,[1–3] after the linear, cross-linked, and branched polymers.[4] These hyperbranched architectures are expected to produce new properties and behaviours, and arouse an ever-increasing interest, with more than one thousand publications and more than one hundred patents per year over the last four years. Most of the work concerning hyperbranched architectures is focussed on the most structurally controlled compounds, i.e. dendrimers and dendrons,[5,6] which are

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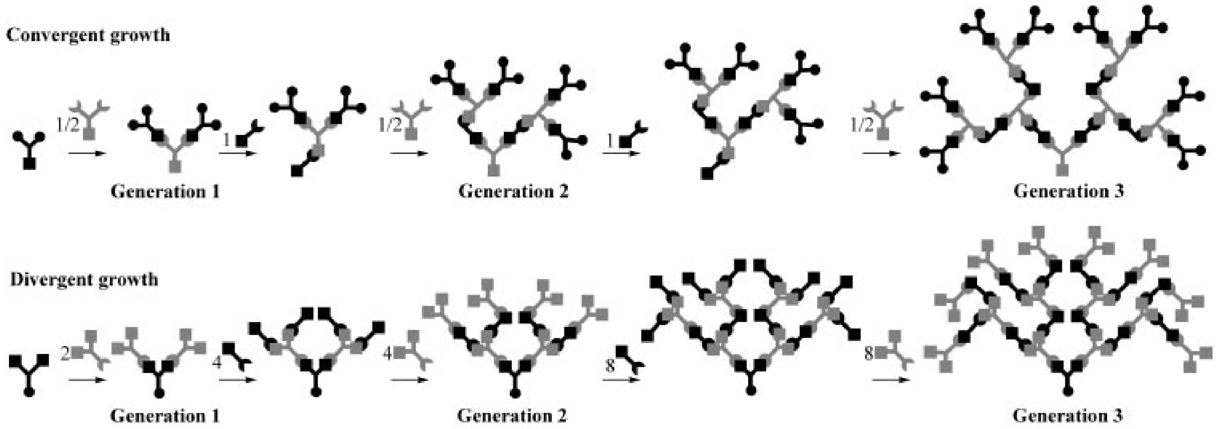
MICROREVIEWS: This feature introduces the readers to the authors' research through a concise overview of the selected topic. Reference to important work from others in the field is included.



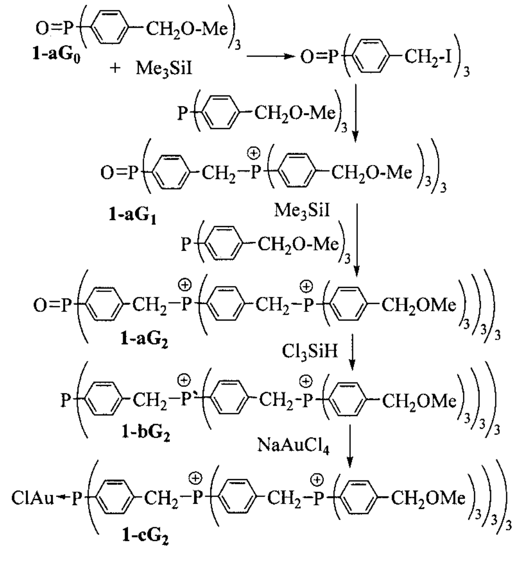
Scheme 1.

synthesised step-by-step (generation after generation) and not with polymerisation reactions. Dendrons,[7] also called dendritic wedges,[8] differ from dendrimers by the presence of one (or a few) functional group(s) located at the core, which are different from the other functional groups located at the periphery; their structure is very reminiscent of that of trees, the function at the core playing the role of the trunk. They are synthesised either by a convergent or a divergent process, generally using two types of monomers, one linear and one branched. In a convergent process, the periphery of the dendron never reacts, and only one reaction occurs at the level of the core; each generation is created by the association of two dendrons with a small molecule. In the divergent process, the periphery reacts at each step, whereas no reaction occurs at the core; each generation is created by the association of several small molecules with one dendron (Scheme 1). In both cases, the main problem is to find five types of functional groups among which one does not react with any of the other four, and four of the functional groups react specifically two-by-two.

The chemical composition of dendrimers and dendrons may be varied infinitely. We proposed about ten years ago a method of synthesis,[9,10] based on the reactivity of phosphorus derivatives, which afforded the highest well-defined generation described to date for any type of dendrimer (generation 12).[11] This method consists of condensation reactions of aldehydes with a phosphorhydrazide, and nucleophilic substitutions of Cl by hydroxybenzaldehyde under basic conditions. This method and its variants are so powerful that we have already published more than 130 papers in this field,[12] and the same method and its variants are also useful for the synthesis of dendrons. The aim of this microreview is to focus on the synthesis, reactivity, properties and use of complex architectures elaborated from dendrons possessing phosphorus at each branching point. Dendrons possessing phosphorus only at the core[13] are considered to be out of the scope of this review.

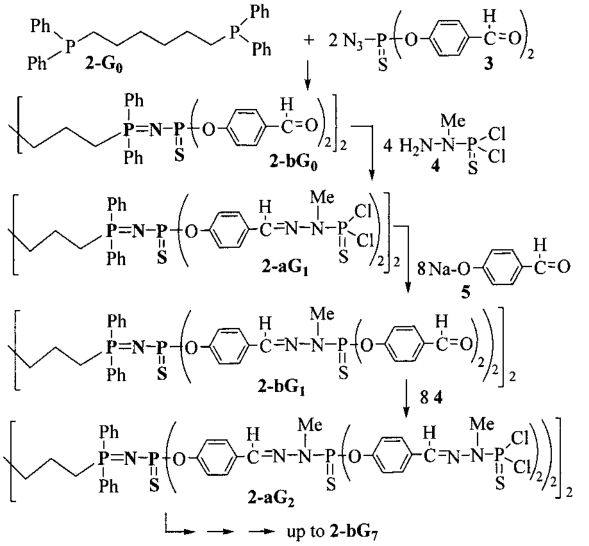
Synthesis of Phosphorus-Containing Dendrons

The first phosphorus-containing dendrons **1-G*n*** (*n* = 0–2, corresponding to the generation) were synthesised in 1993 by Engel et al.,[14] but they were not recognised as dendrons but classed as dendrimers at that time. The function located at the core is a phosphane oxide, and the growing process consists of an iodination, followed by the quaternarisation of a phosphane. The phosphane oxide can be considered a masked phosphane, thus the dendrimer **1-aG*n*** can be transformed into the dendron **1-bG*n*** by reduction with a chlorosilane (Scheme 2). The phosphane located at the core of **1-bG*n*** is different from all the other functional groups in the molecule, and is truly reactive, as shown by the complexation of gold.



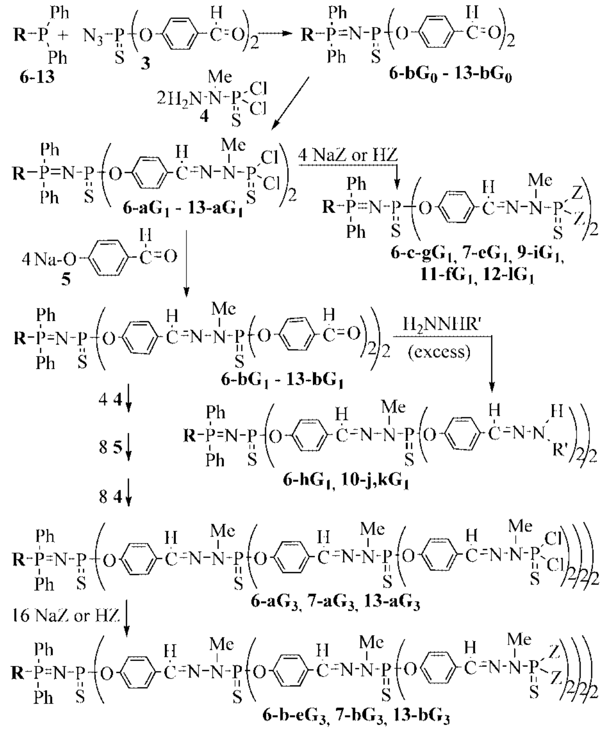
Scheme 2.

We described the second type of phosphorus-containing dendron **2-G*n*** (*n* = 0–7), which were also called dendrimers, but they possessed two functional groups at the core, which was different from the others (Scheme 3).[15] Indeed, the P=S groups included in P=N–P=S linkages behave differently from all the other P=S groups, and react easily with electrophiles[16] as will be illustrated later. These linkages are created by a Staudinger reaction between a phosphane such as **2-G$_0$** and a phosphorus azide such as **3**. Then the dendron is grown from the aldehydes with our classical method of synthesis of dendrimers, using the phosphorhydrazide **4** in condensation reactions and hydroxybenzaldehyde sodium salt **5** for nucleophilic substitutions.[9–11] It must be emphasised that both reactions can easily be performed at a multi-gram scale. The reiteration of both steps has been carried out up to the obtaining of the seventh generation.



Scheme 3.

The use of Staudinger reactions allowed us to synthesise various types of dendrons possessing an R–PPh$_2$=N–P=S group at the core, starting from variously functionalised phosphanes (Scheme 4). The most often used R substituent is the vinyl group **6**,[17] but an allyl **7**,[18] a styryl **8**,[18] a methyl **9**,[19] a protected benzaldehyde **10**,[19] a triethoxysilane **11**,[20] and a diethoxyphosphonate **12**[21] have also been used as the core of these dendrons (Scheme 4 and Table 1). In addition, dendrons were built by the same process with the bis diphenylphosphanyl ferrocene **13** used as the core.[22] In most cases, the synthesis of the corresponding dendrons has been carried out up to generation 3, using the method already shown in Scheme 3, with the phosphorhydrazide **4** and hydroxybenzaldehyde **5**. Obviously, dendron growth could have been pursued up to higher generations. However, the process was voluntarily stopped at the third generation so as to be able to detect changes that occur at core level when some of these dendrons are used as building blocks for the elaboration of more complex structures. The ^{31}P NMR spectrum of the third generation dendron **6-aG$_3$** shows that even the phosphorus atoms located at the core are clearly distinguishable (Figure 1). The synthetic process affords directly as end groups P(S)Cl$_2$ (case a; see Scheme 4 and Table 1) and CHO (case b); various functionalised end groups have also been grafted starting from these functions. The most widely used method for the last step of the synthetic process is the substitution reaction of Cl using phenols (case e)[23] generally functionalised by nitrile (case c),[17] dimethylamine (case d),[17] diphenylphosphane (case f),[20,23] trifluoromethane (case g),[24] and free or complexed iminophosphane (cases l, m).[21] The reaction of a diamine has also been used (case i).[19] In a few cases, condensation reactions of hydrazines with the aldehyde end groups allowed the grafting of other functional groups that were either charged (case h)[25] or not (cases j, k).[19]



Scheme 4.

With aldehydes being one of the repetitively used units in the classical synthesis of our dendrimers and dendrons, any type of compound having at least one aldehyde and another functional group can be used as the core of dendrons, applying the same method. For instance, 4-acetoxybenzaldehyde,[26] pyridine-2,6-dicarboxaldehyde,[18] and ferrocene dicarboxaldehyde[27] have been used as cores of dendrons built by the successive reactions of the phosphorhydrazide and hydroxybenzaldehyde, affording in the final step dendrons **14-bG$_1$**, **15-bG$_2$** and **16-bG$_4$**, respectively (Scheme 5). However, this method of synthesis is not compatible with some kinds of functional groups; in particular for those sensitive to water, the condensation step must be avoided, thus we had to design alternative methods of synthesis.

For instance, the Si(OEt)$_3$ group is readily hydrolysed by traces of moisture, and the dendron **11-aG$_1$** cannot be grown by our traditional method of synthesis. Thus, the sodium salt **17** (NaOC$_6$H$_4$PPh$_2$) is used instead of NaOC$_6$H$_4$CHO (**5**), then the azide **18** is reacted in a Staudinger reaction, affording directly the third generation **19-aG$_3$** with P(S)Cl$_2$ end groups. Aldehydes were grafted in the last step using the salt **5** (Scheme 6).[20] This method, based on the Staudinger reaction, was also found to be useful for the grafting of other functional groups, such as a pyrene derivative (see for instance dendron **20-G$_2$** in Scheme 6).[20]

Table 1. Functional groups located at the core (R) and on the periphery of the most external PS group (X) of dendrons shown in Scheme 4.

Number	R	X	Highest generation	Ref.
6-a	$CH_2=CH$	Cl	3	[17]
6-b	$CH_2=CH$	O–C_6H_4–*p*-CHO	3	[17]
6-c	$CH_2=CH$	O–C_6H_4–*p*-CN	3	[17]
6-d	$CH_2=CH$	O–C_6H_4–*m*-NMe_2	3	[17]
6-e	$CH_2=CH$	O–C_6H_5	3	[23]
6-f	$CH_2=CH$	O–C_6H_4–*p*-PPh_2	3	[23]
6-g	$CH_2=CH$	O–C_6H_4–*p*-CF_3	1	[24]
6-h	$CH_2=CH$	O–C_6H_4–*p*-$CH=NNHC(O)CH_2NMe_3^+$	2	[25]
7-a	$CH_2=CH–CH_2$	Cl	3	[18]
7-b	$CH_2=CH–CH_2$	O–C_6H_4–*p*-CHO	3	[18]
7-e	$CH_2=CH–CH_2$	O–C_6H_5	2	[18]
8-a	$CH_2=CH$–*p*-C_6H_4	Cl	1	[18]
8-b	$CH_2=CH$–*p*-C_6H_4	O–C_6H_4–*p*-CHO	1	[18]
9-a	Me	Cl	1	[19]
9-i	Me	$NHCH_2CH_2NHEt_2^+$	1	[19]
10-a	$[–CH_2O–]_2CH$–*p*-C_6H_4	Cl	1	[19]
10-b	$[–CH_2O–]_2CH$–*p*-C_6H_4	O–C_6H_4–*p*-CHO	1	[19]
10-j	$[–CH_2O–]_2CH$–*p*-C_6H_4	O–C_6H_4–*p*-$CH=NNH_2$	1	[19]
10-k	$[–CH_2O–]_2CH$–*p*-C_6H_4	O–C_6H_4–*p*-$CH=NN(CH_2PPh_2)_2$	1	[19]
11-a	$(EtO)_3SiCH_2CH_2CH_2$	Cl	1	[20]
11-b	$(EtO)_3SiCH_2CH_2CH_2$	O–C_6H_4–*p*-CHO	1	[20]
11-f	$(EtO)_3SiCH_2CH_2CH_2$	O–C_6H_4–*p*-PPh_2	1	[20]
12-a	$(EtO)_2P(O)CH=CH$–*p*-C_6H_4	Cl	1	[21]
12-b	$(EtO)_2P(O)CH=CH$–*p*-C_6H_4	O–C_6H_4–*p*-CHO	1	[21]
12-l	$(EtO)_2P(O)CH=CH$–*p*-C_6H_4	O–C_6H_4–*p*-N=CH–*o*-C_6H_4–PPh_2	1	[21]
12-m	$(EtO)_2P(O)CH=CH$–*p*-C_6H_4	O–C_6H_4–*p*-N=CH–*o*-C_6H_4–PPh_2PdCl_2	1	[21]
13-a	½$[(PPh_2Cp)_2Fe]$	Cl	4	[22]
13-b	½$[(PPh_2Cp)_2Fe]$	O–C_6H_4–*p*-CHO	4	[22]

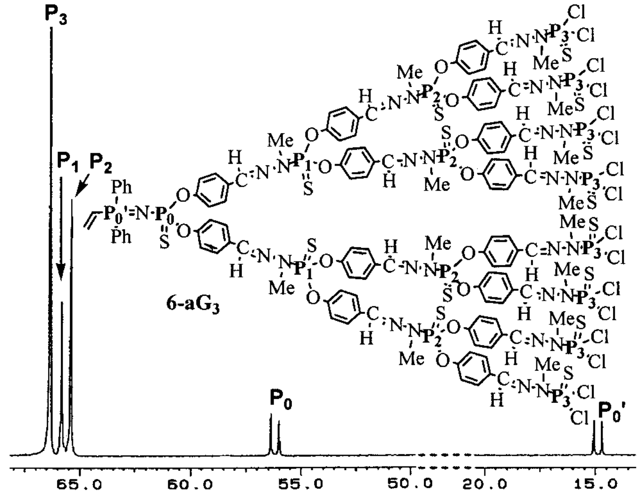
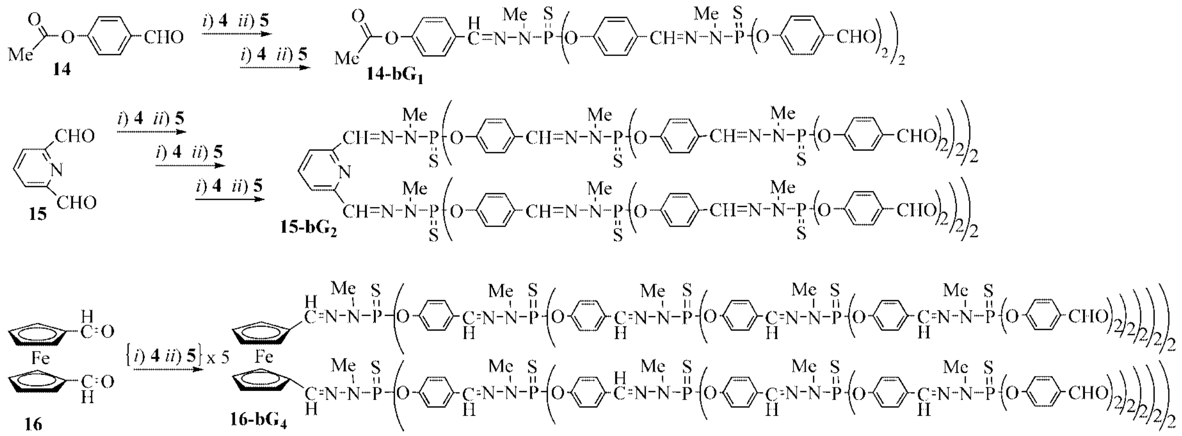


Figure 1. ^{31}P NMR spectrum of the third generation dendron **6-aG$_3$**.

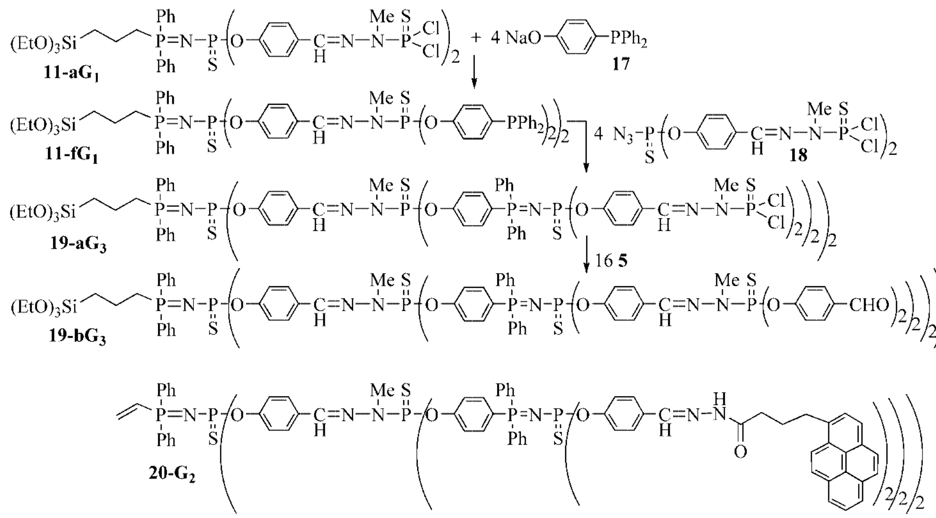
On the other hand, the presence of chlorine at the core of dendrons is incompatible both with our traditional method of synthesis, in particular with the use of the strong nucleophile **5**, and with the method shown in Scheme 6, because of the use of the salt **17**. Thus, the dendron grown from the chloromethyl phosphane oxide derivative **20-bG$_0$** is built using the repetition of three steps. The first one is the condensation reaction of methylhydrazine with aldehyde; the second is another condensation reaction, between Ph_2PCH_2OH and the secondary hydrazone. The third and last step before the repetition of the three steps is the Staudinger reaction of the phosphane end groups with the azide **3**, which again affords aldehyde end groups. This dendron was grown to the fourth generation **21-bG$_4$** (Scheme 7).[18]

Reactivity at the Core of Phosphorus-Containing Dendrons

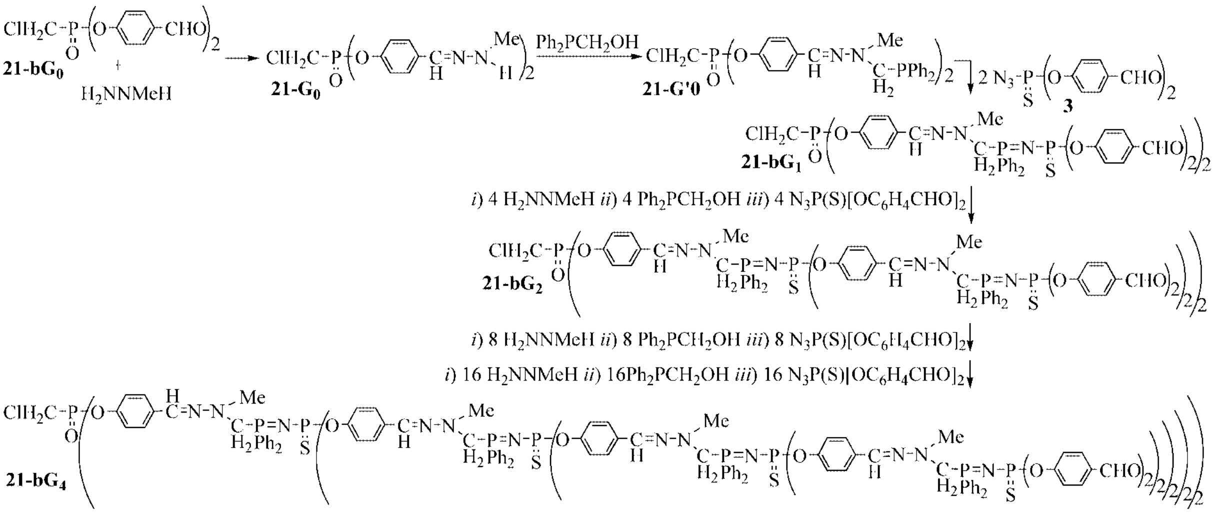
The reactivity at the core of most of the dendrons we have synthesised is related to the presence of a P=N–P=S group. In addition to its own reactivity this group may also enhance the reactivity of other functional groups linked to it. The mesomeric form of the P=N–P=S linkage has a high electron density on sulfur ($P^+–N=P–S^–$) which allows the regiospecific complexation of gold, whereas the other P=S groups do not react in this way (Scheme 8).[30] The existence of this mesomeric form also allows the reaction of the P=N–P=S linkage with electrophiles such as methyl triflate. The reaction was first applied to small molecules,[28] then to dendrons.[15] Various functionalised triflates such as allyl or propargyl triflate have also been used.[29] These reactions are easily monitored by ^{31}P NMR spectroscopy. Indeed, the P=N–P=S linkages give two very characteristic doublets at $\delta \approx 20$ ppm (P=N) and $\delta \approx 52$ ppm (P=S), which move upon *S*-alkylation to $\delta \approx 28$ ppm and $\delta \approx 33$ ppm, respectively. It should be noted that this reaction at the core occurs even for the seventh generation, illustrating the high porosity of these dendrimers, and the specificity of this reaction.[15] Indeed, the numerous other P=S groups consti-



Scheme 5.



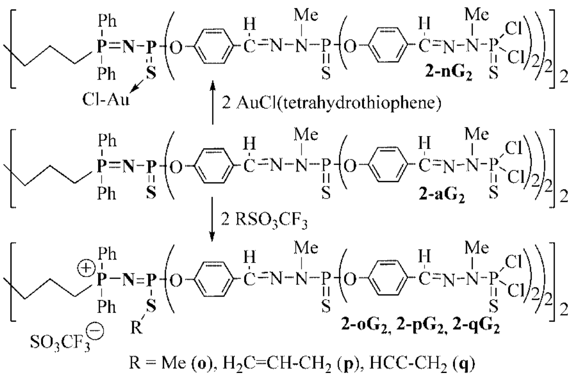
Scheme 6.



Scheme 7.

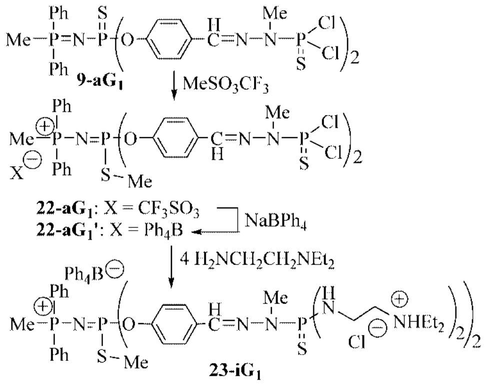
tuting the points of divergence of these dendrons are not alkylated, as shown for one example in Scheme 8, but this type of reaction has been carried out with numerous dendrons.

The alkylation of sulfur is compatible with further modifications of the periphery of the dendrons. In particular, we tried to graft water-solubilising end groups to the cationic dendron **22-aG$_1$**. In order to avoid the formation of triflic



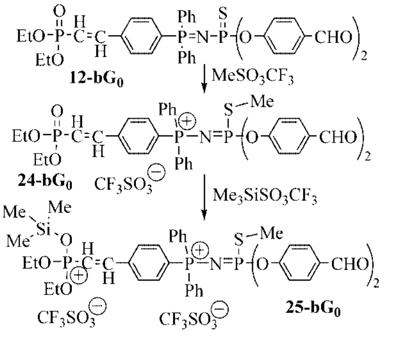
Scheme 8.

acid, which is potentially aggressive for the hydrazone linkage, the triflic counterion of **22-aG$_1$** was first replaced by tetraphenylborane. Then the reaction of 4 equiv. of *N,N*-diethylethylenediamine affords cleanly the pentacationic dendron **23-iG$_1$** (Scheme 9).[19]



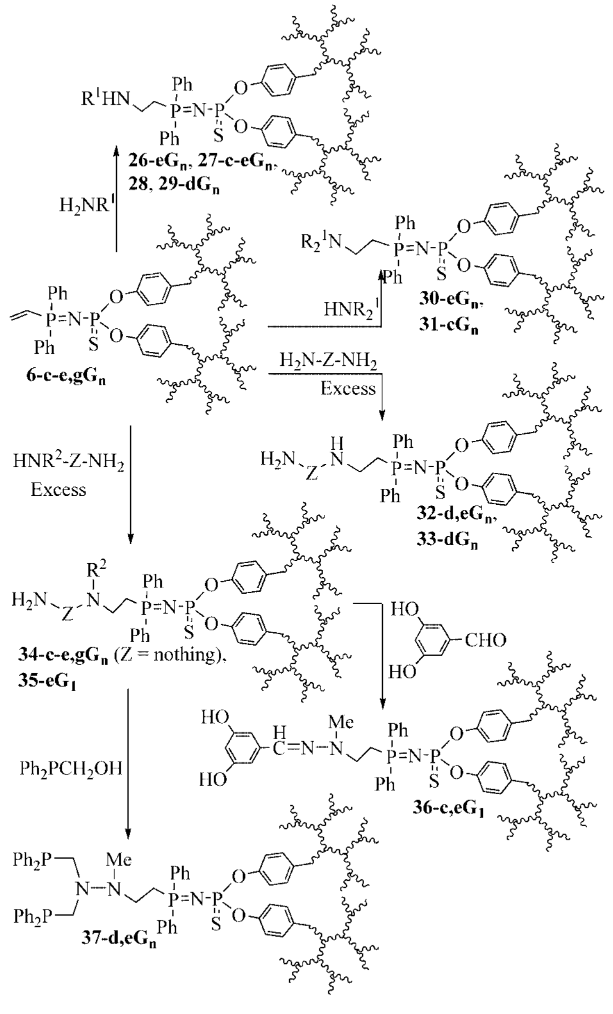
Scheme 9.

Another illustration of the specificity of the reactivity of the P=N–P=S linkages with alkyl triflates is given by the small dendron **12-bG$_0$** in which only the P=S bond is alkylated by methyl triflate, leading to **24-bG$_0$**. The conjugated P=O bond does not react with methyl triflate, but it reacts with trimethylsilyl triflate, because of the oxophilicity of silicon to afford the dicationic compound **25-bG$_0$** (Scheme 10).[21]



Scheme 10.

The P=N–P=S linkage also induces an electron-withdrawing effect on the functional group linked to the phosphazene, which we exploited particularly when a vinyl group is linked to this phosphorus (series of dendrons **6-G$_n$**). We demonstrated the possibility of performing Diels–Alder additions on this vinyl group,[26] but most of the reactions we carried out were Michael type additions of primary and secondary amines. They were first tested with small compounds possessing one CH_2=CH–PPh_2=N–PR_2=X (X = O, S) linkage,[31] then applied to dendrons. In all cases, we used functionalised amines. The reaction works nicely with primary amines (compounds **26**–**29**) and gave at the core a secondary amine together with an alkyne,[23] a triethoxysilyl group,[20,31] or even a phenol[23] (Scheme 11 and Table 2). In the latter case, the reaction of the amine is specific, no addition of the phenol is observed. Analogous reactions are obtained with secondary amines, such as diallylamine **30** and thiomorpholine **31**.[23] The reactions are carried out either at room temperature or by heating, depending on the rate of the addition, and using either a stoichiometric amount or a slight excess of reagent. The reactions are easily monitored by ^{31}P NMR, with a deshielding effect on the signal of the P=N group from δ = 10–12 ppm for **6-G$_n$** to δ = 17–18 ppm after addition.



Scheme 11.

Table 2. Functional groups linked to the CH_2CH_2 group located at the core (R′) and on the periphery of the most external PS groups (X) of dendrons shown in Scheme 11.

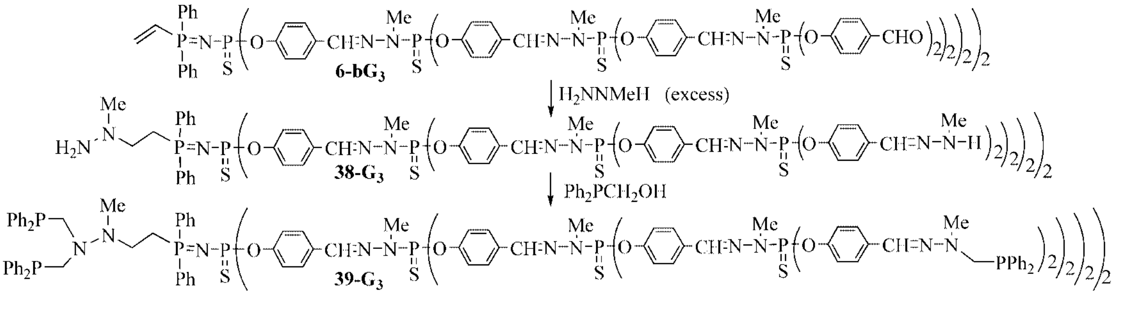
Number	R′	X	Highest generation	Ref.
26-e	$NHCH_2C{\equiv}CH$	$O–C_6H_5$	3	[23]
27-c	$NH(CH_2)_3Si(OEt)_3$	$O–C_6H_4$–*p*-CN	3	[20]
27-d	$NH(CH_2)_3Si(OEt)_3$	$O–C_6H_4$–*m*-NMe_2	3	[20]
27-e	$NH(CH_2)_3Si(OEt)_3$	$O–C_6H_5$	1	[31]
28	$NH(CH_2)_3Si(OEt)_3$	pyrene[a]	2	[20]
29-d	$NH(CH_2)_2$–*p*-C_6H_4–OH	$O–C_6H_4$–*m*-NMe_2	3	[23]
30-e	$N(CH_2CH{=}CH_2)_2$	$O–C_6H_5$	3	[23]
31-c	$N[–CH_2–CH_2–]_2S$	$O–C_6H_4$–*p*-CN	3	[23]
32-d	$NH–CH_2–CH_2–NH_2$	$O–C_6H_4$–*m*-NMe_2	3	[17]
32-e	$NH–CH_2–CH_2–NH_2$	$O–C_6H_5$	3	[23]
33-d	NH–*o*-$C_6H_{10}–NH_2$	$O–C_6H_4$–*m*-NMe_2	2	[23]
34-c	$NMeNH_2$	$O–C_6H_4$–*p*-CN	3	[17]
34-d	$NMeNH_2$	$O–C_6H_4$–*m*-NMe_2	3	[17]
34-e	$NMeNH_2$	$O–C_6H_5$	3	[23]
34-g	$NMeNH_2$	$O–C_6H_4$–*p*-CF_3	1	[24]
35-e	$N[(CH_2)_3NH_2]_2$	$O–C_6H_5$	1	[31]
36-c	$NMeN{=}CH–C_6H_3(OH)_2$	$O–C_6H_4$–*p*-CN	1	[31]
36-e	$NMeN{=}CH–C_6H_3(OH)_2$	$O–C_6H_5$	1	[31]
37-d	$NMeN(CH_2PPh_2)_2$	$O–C_6H_4$–*m*-NMe_2	3	[17]
37-e	$NMeN(CH_2PPh_2)_2$	$O–C_6H_5$	1	[19]

[a] from **20-G*n***.

A large excess of reagents must be used with diamines. Two cases can be distinguished: either the diamine possesses two identical primary amino groups, or it possesses one primary and one secondary amino group. In the former case, the use of several hundreds of equivalents prevents the coupling of two dendrons (cases **32** and **33** in Scheme 11 and Table 2), as shown by the loss of symmetry of the diamine, evidenced by ^1H and ^{13}C NMR spectroscopy.[17,23] The reaction is expected to be more complicated when using nonsymmetrical diamines that have two types of amino groups (primary and secondary). Indeed, besides avoiding the association of two dendrons as for symmetrical diamines, a regiospecific reaction of only one type of amine must be obtained. Such specificity was expected with methylhydrazine (considered to be a special nonsymmetrical diamine), in which the most substituted nitrogen is generally more reactive. The reaction proceeds rapidly at room temperature with an excess of methylhydrazine (30 equiv.) leading to a single product, **34-G*n***, corresponding to the exclusive addition of the NMeH group.[17,23,24] The same specificity for the secondary amine is observed with the diamine **35**.[31]

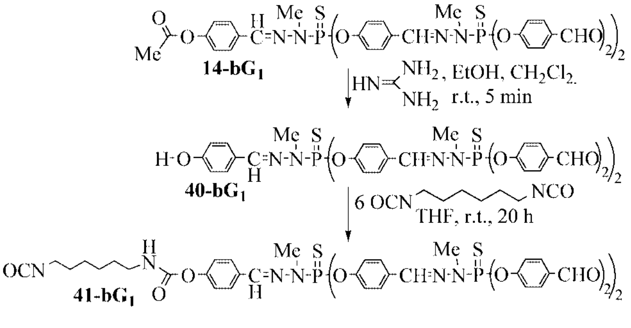
The series of compounds **34-G*n*** is particularly interesting, due to the wide range of reactions available starting from a NH_2 group, which may enlarge the scope of functional groups located at the core of dendrons. It may afford stable hydrazones by condensation reactions with aldehydes, as shown by the synthesis of **36-c,eG$_1$**[31] (Scheme 11). We have also grafted a diphosphane group by reaction with Ph_2PCH_2OH (compounds **37-G*n***),[17,19] a type of condensation that we have already used on the periphery of dendrimers.[32,33] A particular case of the reactions shown in Scheme 11 is afforded by dendrons possessing as end groups functions able to react with amines, because both the core and the periphery will react. An example of such a compound is provided by the dendrons **6-bG*n***, in which the vinyl group at the core reacts in a Michael type addition, whereas the aldehyde end groups react via condensation reactions. The use of a large excess of methylhydrazine, necessary to prevent a polymerisation reaction between the NH_2 of the core and the aldehydes, affords the dendrons **38-G*n***. Their subsequent reaction with Ph_2PCH_2OH affords the dendrons **39-G*n*** that possess a diphosphane at the core and monophosphanes as end groups (Scheme 12).[17]

However, the presence of aldehydes as end groups does not necessarily preclude a specific reaction at the core, as shown by dendrons **14-bG$_1$**. The deprotection of the acetyl



Scheme 12.

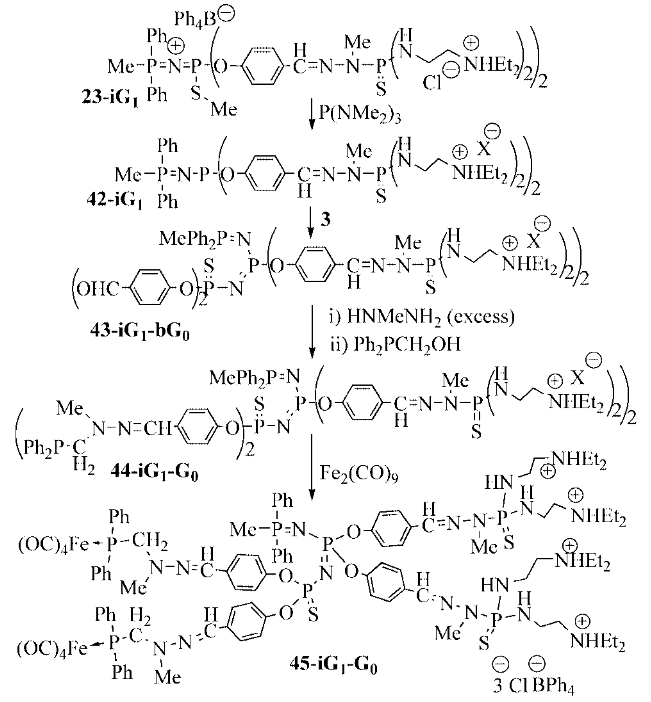
group by guanidine occurs cleanly and under very mild conditions to afford the phenol group of **40-bG$_1$**. This phenol is potentially useful for a number of subsequent reactions; we tested the reactivity of diisocyanatohexane, whose addition gives the dendron **41-bG$_1$**, functionalised by an isocyanate and a carbamate at the core (Scheme 13).[26]



Scheme 13.

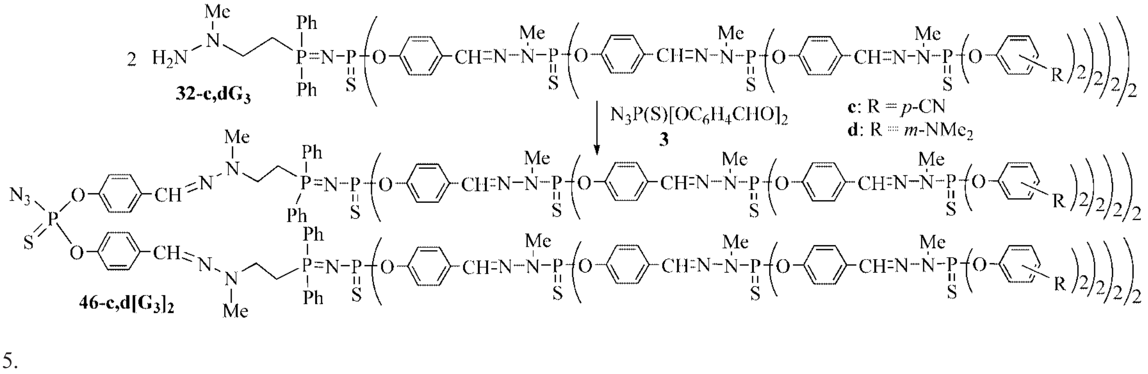
Use of Phosphorus-Containing Dendrons for the Elaboration of Complex Dendritic Architectures

Most of the reactions at the core of dendrons described above can be applied to the elaboration of special dendritic architectures. We have been interested in this field for a long time; an example of our work being the growth of dendritic branches inside a pre-existing dendrimer.[34] In most cases, the dendrons used for building special architectures are those issued from the vinyl group at the core, but in one case the alkylated P=N–P=S core of dendron **23-iG$_1$** was used for such a purpose. Indeed, the alkylation of sulfur induces a weakening of the strength of the PS bond, which can be easily cleaved using a nucleophilic phosphane such as P(NMe$_2$)$_3$.[34,35] The dendron **42-iG$_1$** is too sensitive to oxidation to be fully isolated, but it can be directly reacted with the azide **3** to afford the small diblock dendrimer **43-iG$_1$–bG$_0$**, which possesses two types of end groups. The aldehydes can be used to afford other end groups: their reaction with methylhydrazine followed by Ph$_2$PCH$_2$OH affords **44-iG$_1$–G$_0$**, whose phosphane can be used for complexation, as illustrated by the reaction with iron, leading to the cationic complex **45-iG$_1$–G$_0$** (Scheme 14).[19]



Scheme 14.

Besides this example using the reactivity of the P=N–P=S group, all the other examples of special dendritic architectures that we have described develop from dendrons possessing an amine or phosphane at the core. The simplest type of association consists of using 2 equiv. of dendrons with 1 equiv. of a small molecule. If this molecule possesses another functional group, the resulting bis dendron is itself a dendron, as shown for instance by the condensation of 2 equiv. of the dendrons **32-c,dG$_3$** with 1 equiv. of the azidodialdehyde **3**. The azide remaining at the core of **46-c,d[G$_3$]$_2$** (Scheme 15 and Figure 2)[17] will be used later to afford more elaborate structures. The same methodology was applied to the dendron **32-gG$_1$**, which reacts with the special tetraphosphazene **47**, which possesses four types of functional groups. The reaction occurs as expected only with the aldehydes, leading to the novel type of dendrimeric species **48-g[G$_1$]$_2$**. This compound possesses several types of functional groups at the core constituted by the oligophosphazene linkage, as well as other functional groups within the branches and on the periphery (Scheme 16 and Figure 2).[24]



Scheme 15.

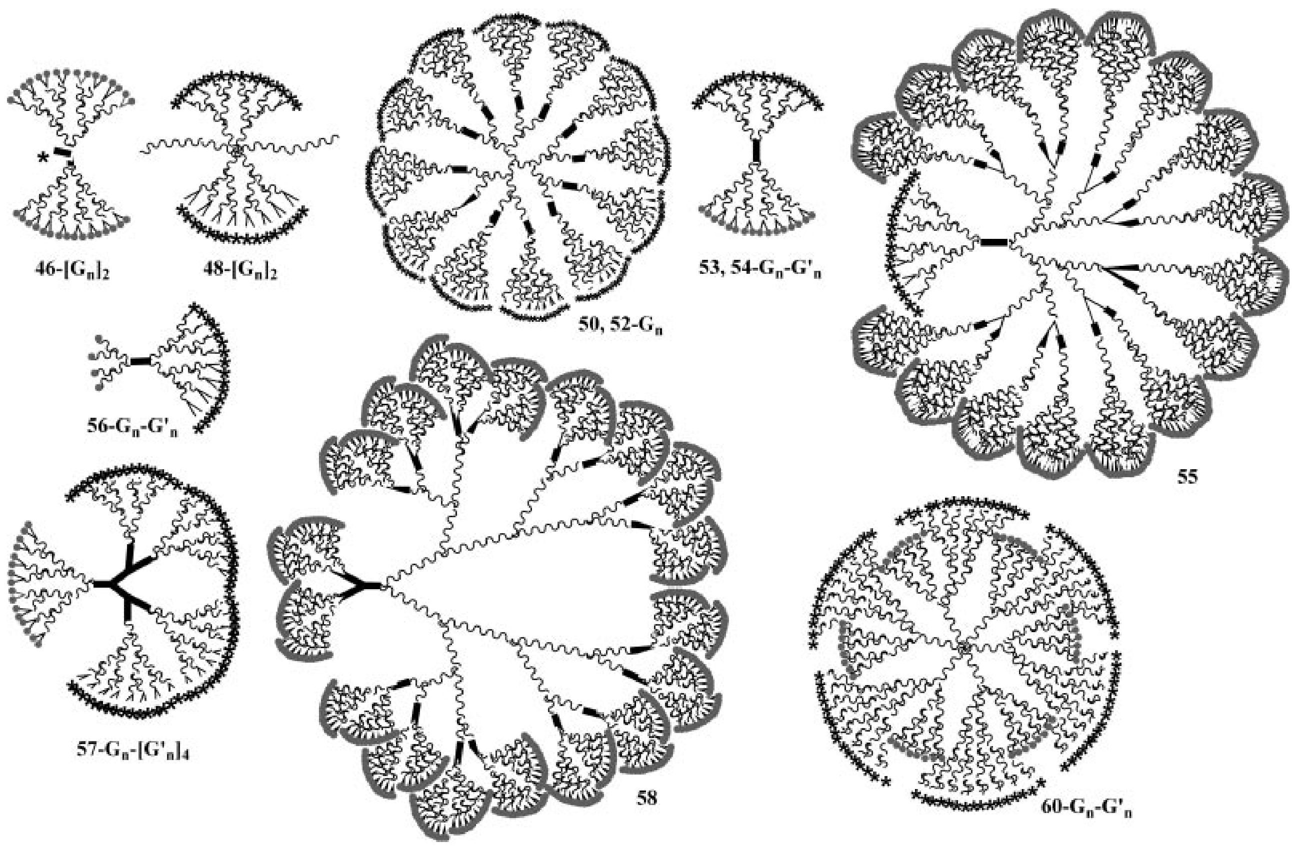
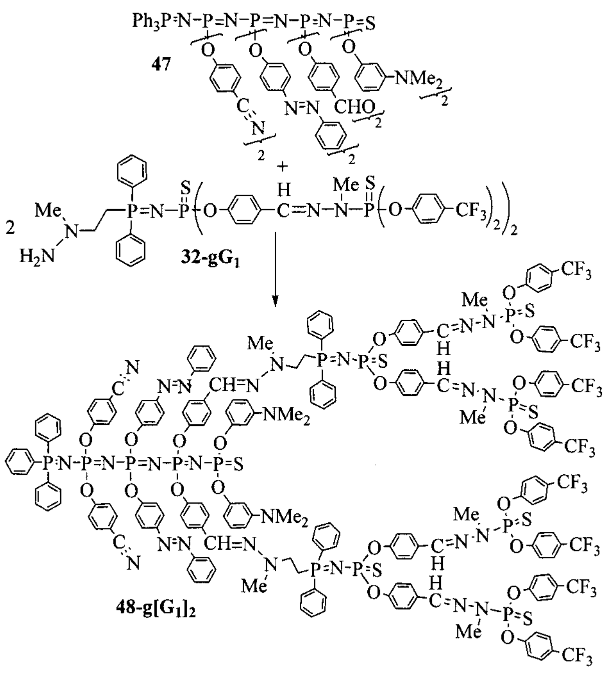


Figure 2. Various schematised special dendritic architectures elaborated from dendrons.

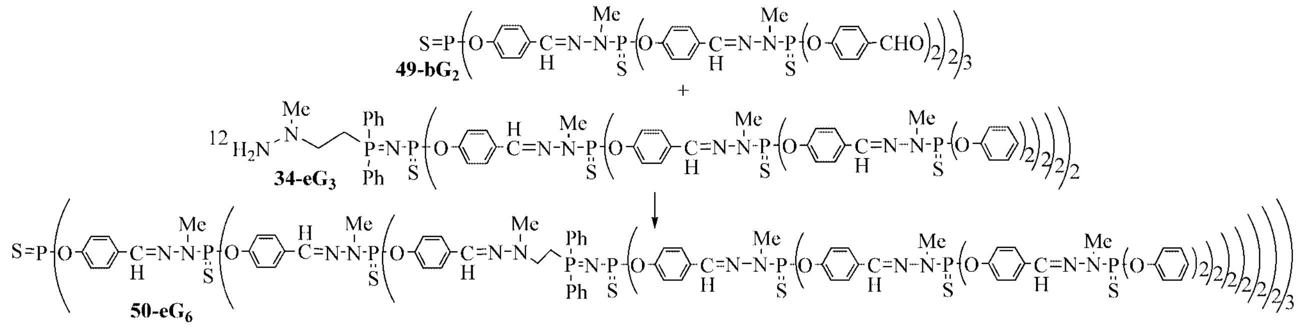


Scheme 16.

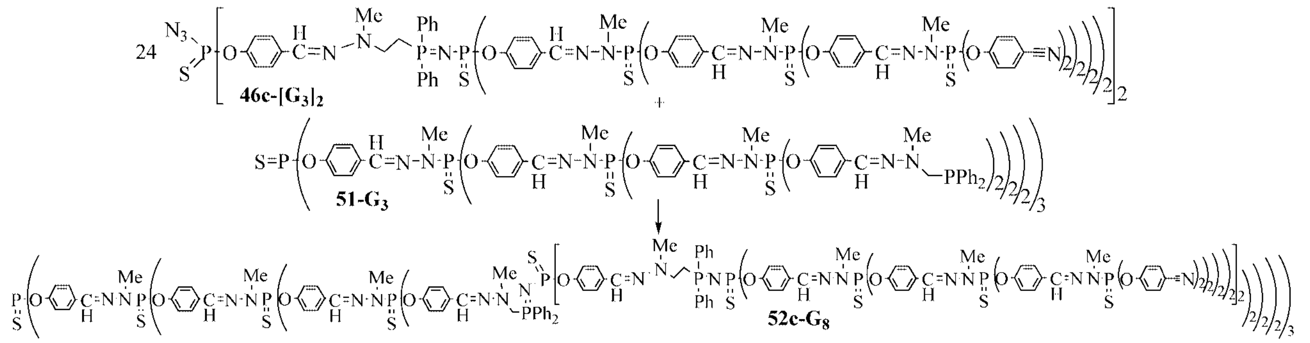
Such methodology has been extended to the synthesis in only one step of high generation layered dendrimers. Indeed, the hydrazine function located at the core of the third generation dendron **34-eG$_3$** reacts with the aldehyde end groups of the second generation dendrimer **49-bG$_2$**. The reaction is slow despite the use of an excess of dendrons, and went to completion only after 18 days, as shown with ^{1}H NMR data by the disappearance of the aldehydes. Despite its length, this reaction is interesting because it affords the sixth generation of the layered dendrimer **50-eG$_6$** in only one step from the second generation (Scheme 17 and Figure 2).[23] It should be noted that an analogous reaction carried out with the third generation dendrimer **49-bG$_3$** did not continue to completion, even after 40 days. The steric hindrance precludes the insertion of approximately 1 equiv. of dendron among 24, despite the fact that the seventh generation dendrimer, and even higher generations, can be obtained step-by-step using sequentially small molecules instead of dendrons.[11]

However, the type of reaction used for connecting the dendrons to the dendrimer also has an influence on the highest generation of dendrimer usable. Indeed, the Staudinger reaction of the dendritic azide **46-b[G$_3$]$_2$** with the third generation dendrimer **51-G$_3$** affords the eighth generation of the layered dendrimers **52-cG$_8$** in one step. The P=N–P=S linkages are present only at the level of the fourth and fifth generation (Scheme 18 and Figure 2).[17]

Despite their original dendritic architectures, the compounds shown in the previous schemes possess only one type of end group. However, we have in hand all the tools necessary for synthesising large "Janus" dendrimers that are dendrimers possessing two types of end groups located in

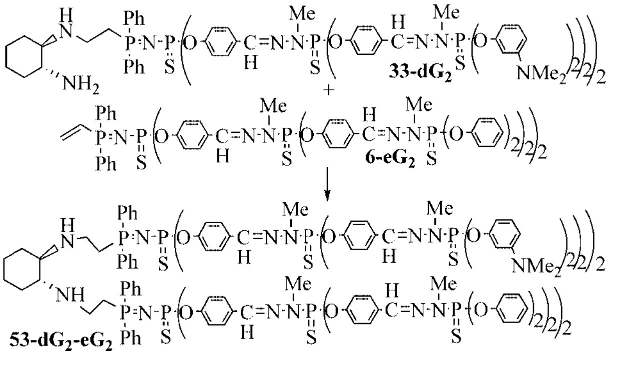


Scheme 17.



Scheme 18.

two different areas of the periphery, obtained in particular by grafting two different dendrons by their core. The first attempt involves the second generation dendrons **6-eG$_2$** and **33-dG$_2$**, which react in a Michael type addition. The resulting unsymmetrical compound **53-dG$_2$–eG$_2$** can also be viewed as a dendron, because of the presence of two NH groups at the centre of the molecule (Scheme 19 and Figure 2).[23]

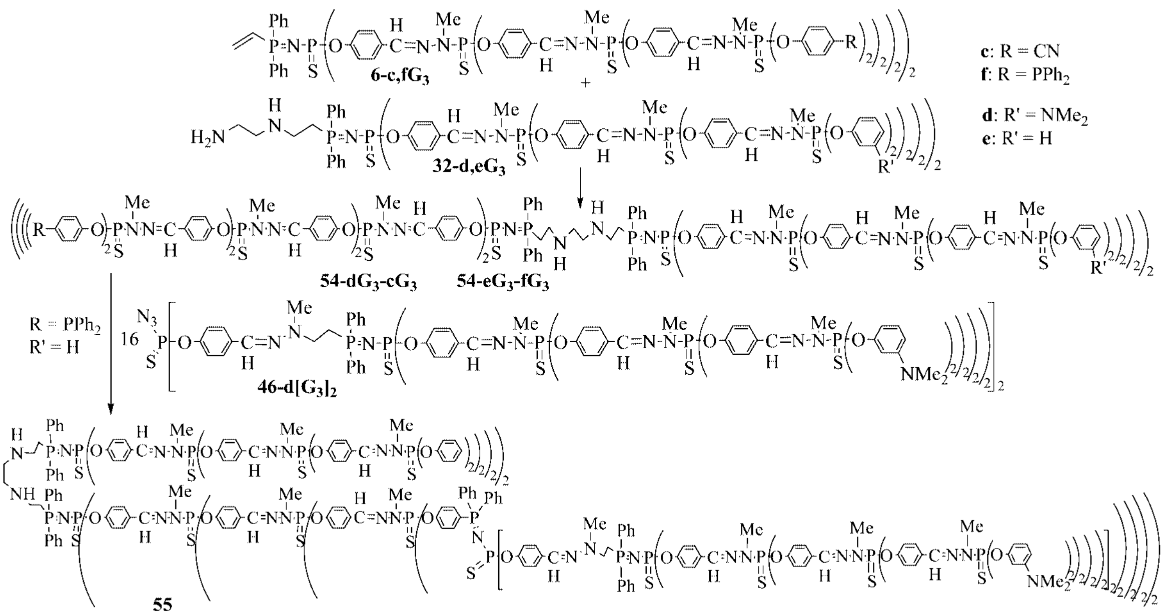


Scheme 19.

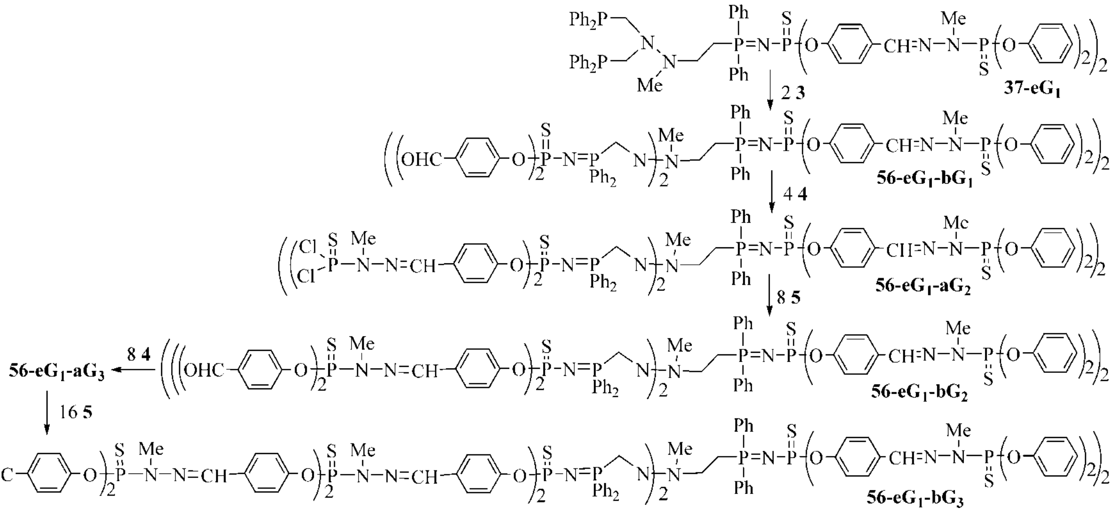
Such methodology using Michael type additions can be applied to larger generations. We decided to use compounds no higher than the third generation, in order to be able to detect the modification of the core with a sufficient intensity by NMR spectroscopy. The reaction was carried out with compounds **6-G$_3$** and **32-G$_3$**, leading to compound **54-G$_3$-G$_3$** (Scheme 20 and Figure 2).[17,23] This reaction is compatible with several types of end groups on the periphery of the dendrons, and in particular with phosphanes. This compound (**54-eG$_3$–fG$_3$**) is the precursor of the very special "fish-like" dendritic species **55**. This compound is obtained by the grafting, via a Staudinger reaction, of dendrons **46-d[G$_2$]$_2$** on only half of the periphery of **54-eG$_3$–fG$_3$**, i.e. the face that possesses phosphanes (Scheme 20 and Figure 2).[23] This unsymmetrical compound has 16 phenoxy groups as end groups on one side, two NH "central" functions, 50 P=N–P=S linkages located at four different levels in the ratio 32:16:1:1, and 512 NMe$_2$ as end groups on the other side.

As illustrated above the synthesis of complex dendritic species from dendrons can necessitate several steps, in particular to extend the number of functional groups that are usable. The reaction of the bisaldehyde azide **3** with the core of a dendron such as **37-eG$_1$** affords the possibility of growing new dendritic branches at the core of the dendron; this also allows us to multiply the possible types of functionalisation on one side of this new "Janus" dendritic molecule. Starting from the four aldehyde groups of **56-eG$_1$–bG$_1$**, we applied our classical method for the synthesis of dendrimers, using alternately the phosphorhydrazide **4** and the sodium salt of hydroxybenzaldehyde (**5**). This dendritic species has been grown up to the third generation on one side (compound **56-eG$_1$–bG$_3$**), but it could have been continued to higher generations (Scheme 21 and Figure 2).[19] This compound possesses four end groups on one side and 16 on the other.

However, the shortest method to obtain a different ratio of two types of end group obviously consists of using dendrons that have a different number of end groups. For instance, the reaction of 2 equiv. of **46-c[G$_3$]$_2$** with **37-dG$_3$** af-



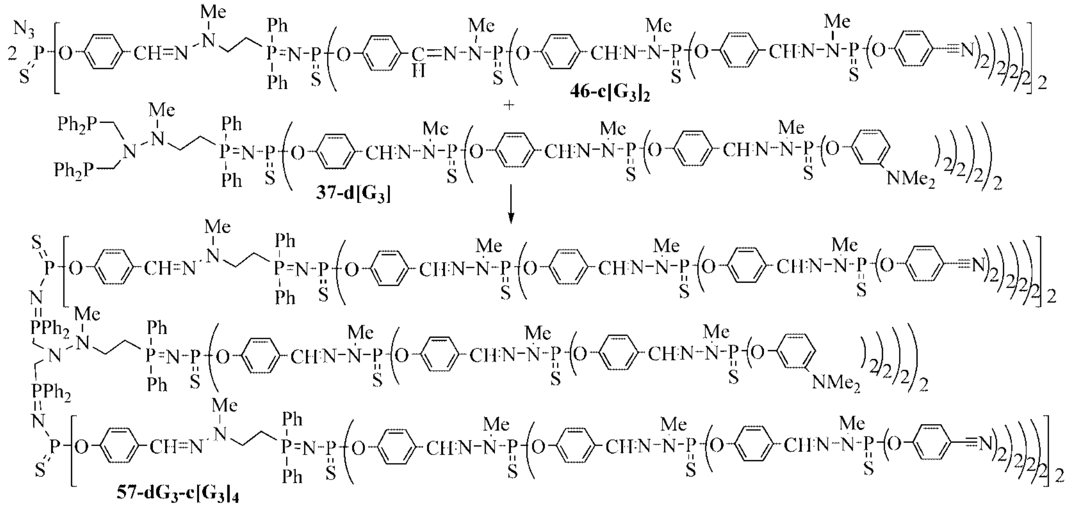
Scheme 20.



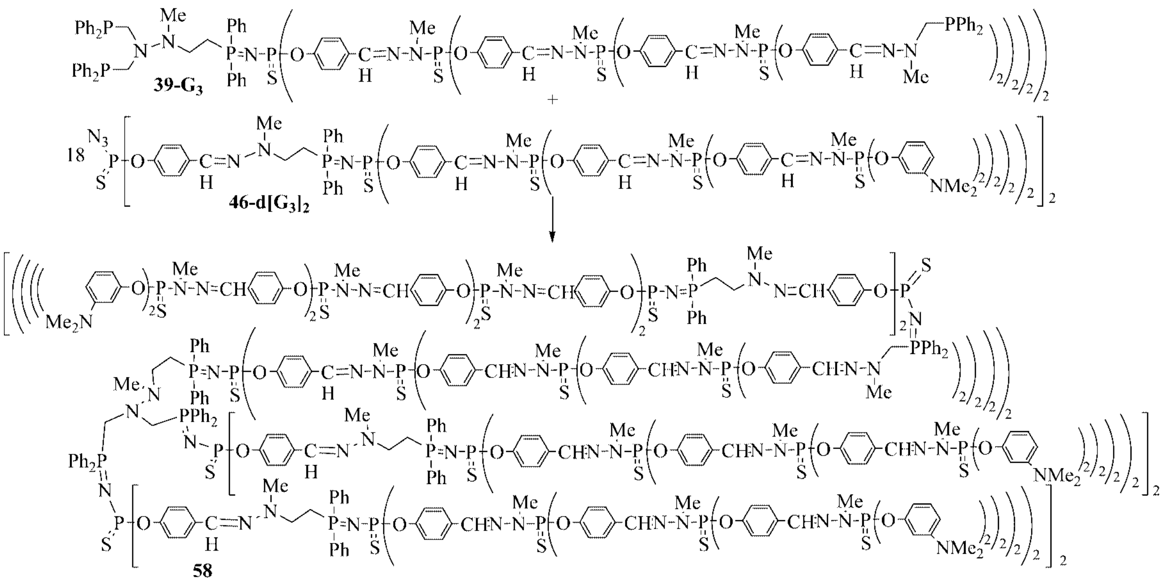
Scheme 21.

fords the straightforward compound **57-dG$_3$-c[G$_3$]$_4$**, in which the ratio of the end groups is 1:4, i.e. 16 NMe$_2$ and 64 cyano groups (Scheme 22, Figure 2).[17] The same methodology can be envisaged starting from dendron **39-G$_3$** instead of **37-dG$_3$**. The former possesses phosphanes both at the level of the core (2 P^{III}) and on the periphery (16 P^{III}), which will react in Staudinger reactions with the dendron **46-d[G$_3$]$_2$**. The result is the complex dendritic structure **58**, which is relatively reminiscent of the structure of compound **55**. However, despite its nonsymmetrical internal structure, compound **58** possesses only one type of end group (576 dimethylamino groups). Compound **58** is a kind of layered segment-block dendrimer (Scheme 23 and Figure 2).[17]

A very original distribution of two types of end groups is also obtainable from dendrons. It necessitates a dendrimer possessing reactive internal functions such as **59-eG$_3$–bG$_0$**.[34] The NH$_2$ group located at the core of dendron **34-cG$_2$** is used to react with the internal aldehydes of **59-eG$_3$–bG$_0$**. Obviously, the problem of steric hindrance evoked previously for the layered dendrimer **50-eG$_7$** might be more crucial here, where the reactions must occur inside the dendrimer and not on its periphery. The condensation is relatively slow and requires 10 days to go to completion, but it finally affords compounds **60-eG$_3$–c–G$_4$** (Scheme 24 and Figure 2),[23] confirming the high porosity of our phosphorus dendrimers, already demonstrated by NMR[15] and



Scheme 22.



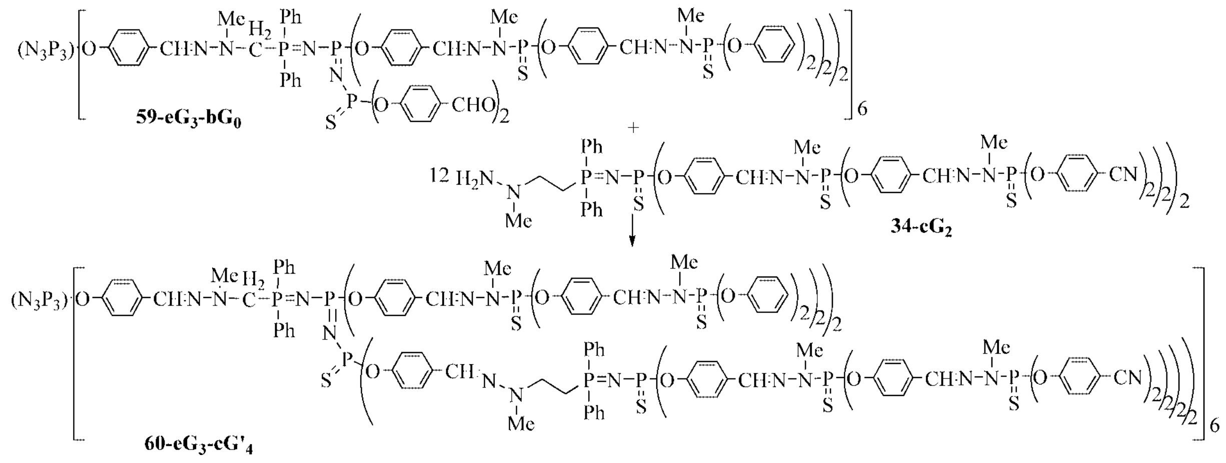
Scheme 23.

fluorescence.[36] However, **34-cG$_2$** is the largest dendron that can be accommodated inside **59-eG$_3$–bG$_0$**; indeed, the reaction of **34-cG$_3$** failed to go to completion.

Other Properties and Uses of Phosphorus-Containing Dendrons

Besides their usefulness for the synthesis of complex dendritic architectures, dendrons offer other possible uses such as in characterising the special properties of the "dendritic state", for catalysis, or for elaborating new materials, depending on the function located at the core. Dendrons possessing a ferrocene at the core were elaborated with the aim of measuring the influence of the encapsulation of an electroactive function on the electrochemical properties. Dendrons **13-G$_n$** were relatively deceptive, because the wave detected in electrochemistry did not correspond to the oxidation of the ferrocene but of the P=N–P=S linkages. This oxidation is not reversible and induces a polymerisation of the dendron.[22] On the other hand, dendrons **16-G$_n$** do not possess any P=N–P=S linkage, and are usable, therefore, for the detection of any influence on the electrochemical properties, depending on the generation and thus the size of the dendron. Compound **16-bG$_0$** shows the characteristic quasi reversible (Ipc/Ipa ≅ 1) single electron oxidation process, whereas **16-bG$_1$** exhibits a slightly more irreversible process (Ipc/Ipa = 0.88). This trend is confirmed by the pronounced irreversibility observed for **16-bG$_2$**, which gives a very weak and poorly resolved signal (Figure 3).[27] The core is undetectable presumably because it cannot approach the electrode closely enough because of the steric hindrance induced by the dendritic branches.

The presence of a diphosphanyl group at the core of dendron **37-dG$_3$** prompted us to use it as a ligand for transition metal complexes, in particular for ruthenium. Most ruthenium complexes possess catalytic properties, thus it was



Scheme 24.

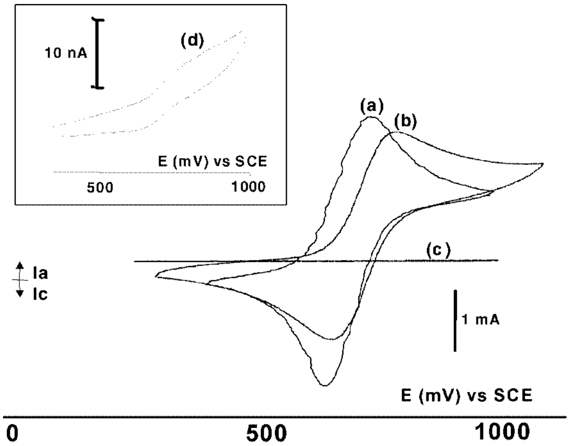
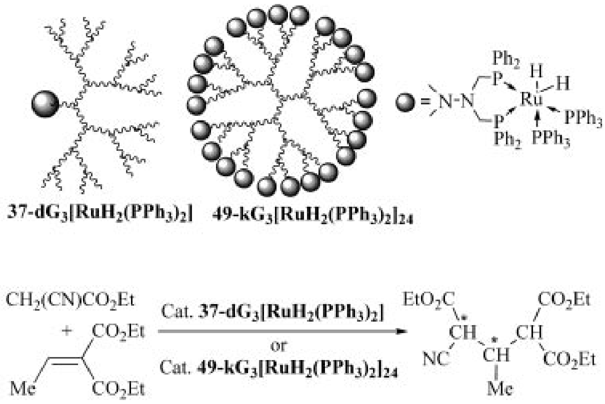


Figure 3. Cyclic voltammograms (scan rate 100 mV·s^{-1}) obtained for dendrimers **16-bG$_0$** (a), **16-bG$_1$** (b), **16-bG$_2$** (c), and enlargement for **16-bG$_2$** (d).

tempting to use dendron **37-dG$_3$[RuH$_2$(PPh$_3$)$_2$]** as a catalyst. Indeed, the use of dendritic complexes in catalysis is an area of intense activity, especially for those possessing phosphane complexes,[12b] mainly because of the possibility of recovering the catalyst simply by precipitation or ultra-filtration. Dendron **37-dG$_3$[RuH$_2$(PPh$_3$)$_2$]** was tested in catalysed diastereoselective Michael additions (Scheme 25). The activity of this dendron was compared to that of a third generation dendrimer possessing the same complex as end groups, **49-kG$_3$[RuH$_2$(PPh$_3$)$_2$]$_{24}$**. It was shown that both compounds have the same efficiency at the same mol-% in ruthenium (1 %), and that both can be recovered by precipitation and reused twice. It was expected that the steric hindrance around the metallic centre induced by the dendrons might modify the diastereoselectivity of such a reaction, but no change was observed (Table 3).[37]

The triethoxysilyl group connected to the core of dendrons **11-G$_n$**, **27-G$_n$**, and **28-G$_n$** was used for the elaboration of new hybrid organic–inorganic materials. Indeed, the cohydrolysis of these dendrons with Si(OEt)$_4$ (TEOS) in a sol-gel process generally affords the expected functionalised silica.[20] However, the nature of the material and its porosity is highly dependant on the initial ratio of dendron/TEOS, the generation of the dendron, and the length of the linker between the Si(OEt)$_3$ group and the first branching point. It appears that the higher the dendron generation, the greater the required quantity of TEOS for the gelation. Dendron **11-bG$_0$** requires at least 10 equiv. of TEOS, whereas dendron **19-bG$_3$** requires 140 equiv. of TEOS. ^{29}Si MAS NMR shows that the dendrons are covalently linked to the silica. The porosity of these materials was measured by nitrogen adsorption. Some materials were found to be mesoporous with a narrow or large pore size distribution, others were found to be macroporous or microporous, depending on the length of the linker, the generation of the dendron, the nature of its end groups, and the initial ratio of dendron/TEOS. Elemental and thermal analyses of the materials show that the percentage representing the organic part incorporated in the silica is always high, but inferior to the theoretical percentage.



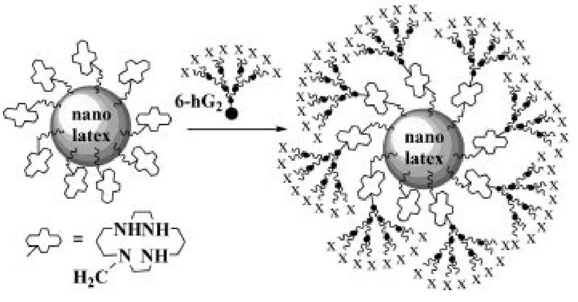
Scheme 25.

Another way to use dendrons in materials chemistry consists of grafting them to the surface of a pre-existing material, in order to modify its properties. We have used this approach with dendrons **6-hG$_n$**, which has ammonium end groups, to modify by Michael type additions the surface of nanolatexes previously covered by cyclam (Scheme 26). A full coverage of the nanolatexes by the dendrons is observed

Table 3. Percentage of conversion and diastereoisomeric ratio for the reaction shown in Scheme 25, using two types of dendritic catalysts (1 mol-% in Ru in all cases). This shows the influence of the recovery and reuse of the catalyst on the efficiency.

Catalyst	Conversion [%]	Diastereomeric ratio	Catalyst	Conversion [%]	Diastereomeric ratio
37-dG$_3$[RuH$_2$(PPh$_3$)$_2$] first run	100	72:28	**49-kG$_3$[RuH$_2$(PPh$_3$)$_2$]$_{24}$** first run	100	73:27
37-dG$_3$[RuH$_2$(PPh$_3$)$_2$] second run	100	72:28	**49-kG$_3$[RuH$_2$(PPh$_3$)$_2$]$_{24}$** second run	100	73:27
37-dG$_3$[RuH$_2$(PPh$_3$)$_2$] third run	89	72:28	**49-kG$_3$[RuH$_2$(PPh$_3$)$_2$]$_{24}$** third run	90	73:27

in all cases. The number of dendron per nanolatex depends on the generation, but the total number of ammonium groups is practically the same (approximately 600 to 800 ammonium end groups per nanolatex). Interestingly, the suspensions of these modified nanolatexes are stable in water without any surfactant, in contrast to the initial nanolatex. Furthermore, the "dendrigrafted" nanoparticles can be redispersed in water after drying, which is not the case for the initial nanolatex. The dendritic shell also offers a higher thermal stability, and induces the gelation of the water solution after one week at room temperature; about 345000 water molecules were estimated to be gelled by each grafted molecule of **6-hG$_2$**.[25]



Scheme 26.

Conclusion

This micro-review has demonstrated that phosphorus-containing dendrons are important building blocks for the elaboration of very complex and original dendritic macromolecules. Emphasis has so far been placed on fundamental research, but these dendrons and peculiar dendritic architectures have the potential for development in more applied research. Obviously, there is still considerable work to be done to determine any practical uses of phosphorus-containing dendrons, but some areas of application can be foreseen. For instance, one may consider the modification of the surface of materials, the targeted delivery of drugs, and other types of application in which the presence of two different types of function in a tailored ratio is important.

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