



Number of terminal groups versus generation of the dendrimer, which criteria influence the catalytic properties?

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ABSTRACT

We report the synthesis of a dense dendrimer ended by the PTA ligand (1,3,5-triaza-7-phosphaadamantane), and the use of the corresponding Rh and Ru complexes for catalysis. The catalytic properties of these dendrimers are compared with those of two other dendrimers: a dendrimer of the same generation but having half the number of ligands, and a dendrimer of the next generation, but having the same number of ligands. The positive influence of the density of catalytic sites on the surface of these dendrimers for alcohol isomerization in water has been evidenced.

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Introduction

Dendrimers¹ are at the forefront of polymer researches since two decades, because of their exceptional characteristics compared to conventional polymers, such as a precisely defined and mono-disperse structure, due to their step-by-step repetitive synthesis, and a large number of terminal groups, the nature of which governs the interactions of the dendrimer with its environment. Among many different uses, catalysis with dendrimers occupies an important place since the first example in 1994.² Several reviews have covered this topic,³ but a lot of questions remain unsolved, in particular the reasons of the so-called dendritic effect, positive or negative, that is to say a difference in the efficiency when catalytic entities are linked to the terminations of dendrimers. One of the parameters that may influence the catalytic properties is the density of the terminal groups. However, in the case of dendrimers, the influence of this parameter is difficult to assess since the modifications of density are correlated (not linearly) with the modification of size (generation) in homogeneous families of dendrimers.

We have been interested since a long time in studying the influence of an increase of the internal density on the properties

of dendrimers,⁴ but also in the study of the catalytic properties of the phosphorus dendrimers that we synthesize.⁵ In this communication, we report our attempts to determine if the density of terminal groups may have some influence on the catalytic properties of a dendrimer.

Results and discussion

Among the numerous types of ligands that could be used for testing the influence of the density of terminal groups of dendrimers, we chose PTA (1,3,5-triaza-7-phosphaadamantane),⁶ which is easy to graft to dendrimers (Fig. 1) thanks to its specific alkylation on one nitrogen atom, affording in addition a certain solubility in neat water or in aqueous media, due to the presence of charges.⁷

Synthesis of dendrimers

We have already reported the synthesis of dendrimers **1-G₁** and **1-G₂**⁸ from dendrimers ended by aldehydes. For the synthesis of the dense dendrimer, we have elaborated another synthetic route. The starting compound is dendrimer **2-G₁**,⁹ which possesses 12 Cl terminal groups. This dendrimer is reacted with twelve equivalents of 5-hydroxy-dimethylisophthalate in the presence of 24 equiv of cesium carbonate in THF at room temperature (Scheme 1). This

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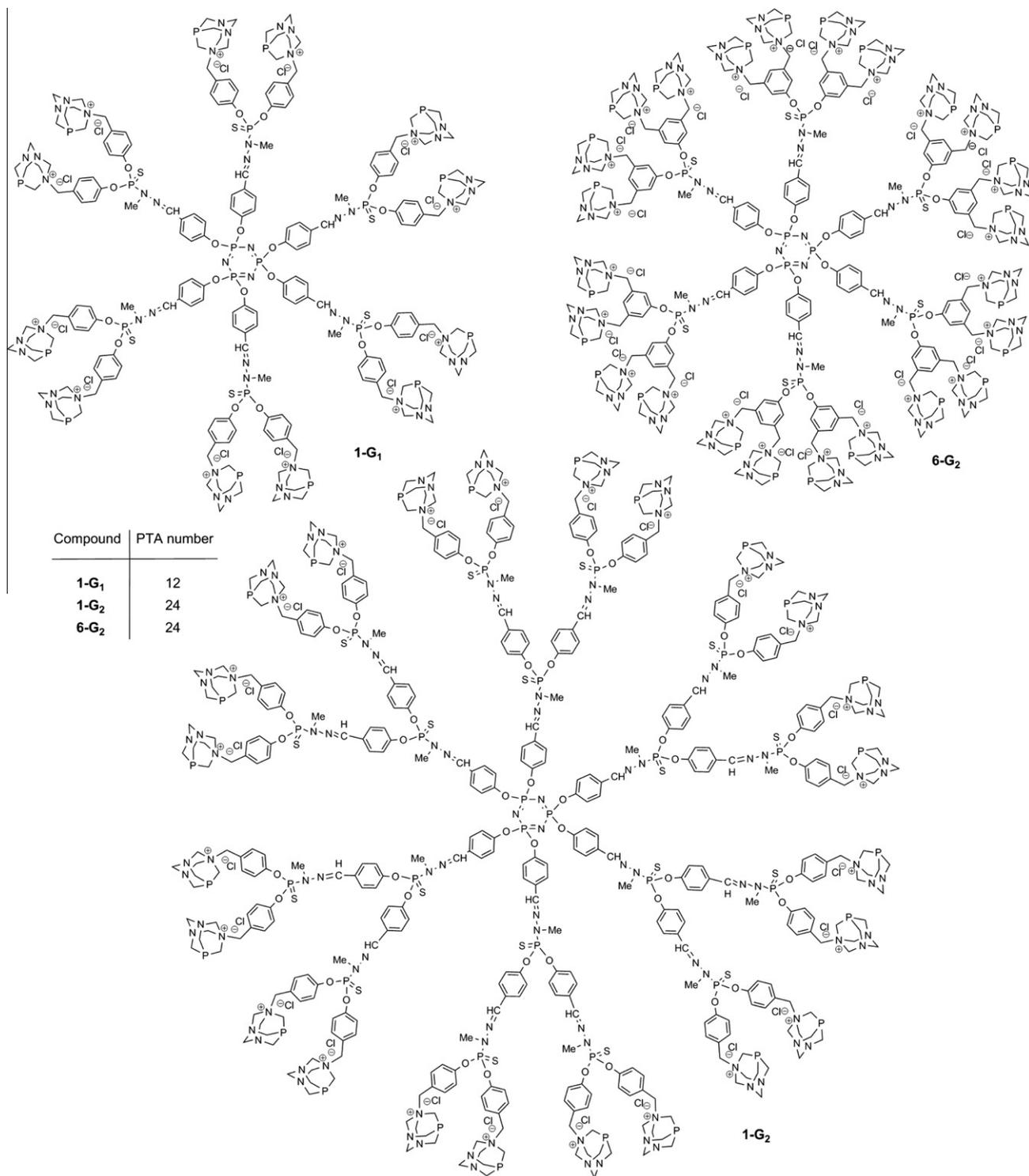
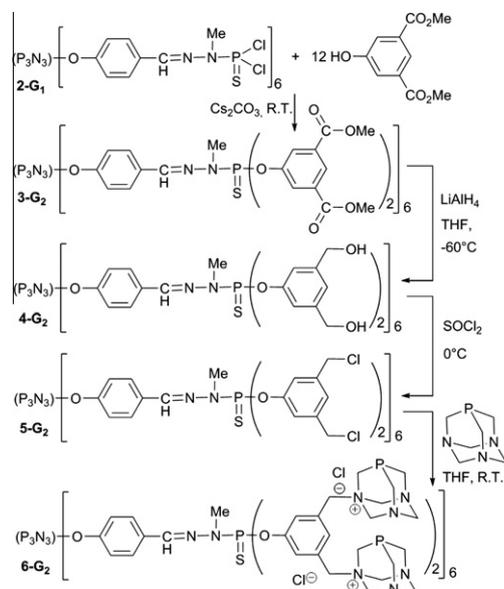


Figure 1. Chemical structure of dendrimers **1-G₁**, **1-G₂**, and **6-G₂**, allowing the comparison between their size and their number of terminal groups.

reaction doubles the number of terminal functions, thus affording the second generation of the dendrimer, **3-G₂** which possesses 24 ester terminal groups. The completion of the reaction is easily monitored by ^{31}P NMR, which displays the disappearance of the signal at 65.85 ppm for compound **2-G₁** first on behalf of an intermediate signal at ca. 72 ppm, which disappears whereas a signal at 66.22 ppm, appears, corresponding to **3-G₂**.¹⁰

The next step is the reduction of the ester functions of **3-G₂**, which is carried out with LiAlH_4 at low temperature for 2 h (the mixture is cooled with acetone/liquid N_2). Longer reaction

times lead to a partial destruction of the dendrimer (detected by ^{31}P NMR). The completion of the reaction affording dendrimer **4-G₂**¹¹ is monitored by ^1H NMR, which displays the disappearance of the signal corresponding to the methoxy group of the ester at 3.83 ppm and the appearance of the signal for $\text{CH}_2\text{-OH}$ at 4.51 ppm. The reaction also modifies the ^{13}C NMR spectra, with the disappearance of the signal for the methoxy groups at 52.58 ppm as well as for the carboxyl at 165.06 ppm and the appearance of the signal for the $\text{CH}_2\text{-OH}$ groups at 63.12 ppm.



Scheme 1. Synthesis of the dense second generation dendrimer ended by 24 PTA ligands.

Then SOCl_2 is added to dendrimer **4-G₂** until its total dissolution (without solvent). The resulting solution is cooled with an ice bath overnight under stirring to afford dendrimer **5-G₂**.¹² A shift of the benzyl group in ^1H NMR is observed from 4.51 ppm ($\text{CH}_2\text{-OH}$) to 4.44 ppm ($\text{CH}_2\text{-Cl}$) for the chlorinated product. In the ^{13}C NMR spectra, the CH_2 alcohol signal was at 63.12 ppm whereas CH_2 chloride appears at 45.11 ppm.

In the last step, 24 equiv of PTA are reacted with dendrimer **5-G₂** in THF at room temperature. A shift of PTA phosphorus from -99.0 ppm to -76.4 ppm for dendrimer **6-G₂**¹³ is observed in ^{31}P NMR. This compound dissolved in water gives a ^{31}P NMR spectrum in D_2O which displays the phosphorus atoms of the surface and of the branches, but the core cannot be seen since that part of the dendrimer is too hydrophobic for the water to enter. By addition of acetonitrile the internal structure of dendrimer **6-G₂** is better dissolved, thus the signal of the core can be seen. We have already observed such phenomenon for another type of water-soluble phosphorus-containing dendrimer.¹⁴

Having in hand dendrimer **6-G₂**, the next step is the comparison of its catalytic properties with that of dendrimer **1-G₁** (same size, but half the number of PTA ligands) and dendrimer **1-G₂** (same number of PTA ligands, but larger size) (Fig. 1).

Catalysis experiments

In order to allow a fair comparison between the properties of various dendrimers, the number of catalytic sites (i.e. in general the number of terminal functions) is always kept constant. For instance, if one equivalent of dendrimer **6-G₂** is used, it will be compared with one equivalent of dendrimer **1-G₂**, but with two equivalents of dendrimer **1-G₁**. We have tested the three dendrimers as ligands in two different types of catalytic experiments.

The isomerization of allylic alcohols is a reaction that proceeds with atom economy, if it is catalyzed. Indeed, without a catalyst, this reaction necessitates two steps (reduction of alkene and oxidation of alcohol), whereas it is performed one-pot with a catalyst. This reaction is of current interest, as emphasized by a recent theoretical and experimental investigation upon the use of ruthenium catalysts for such purpose.¹⁵ We have previously reported the isomerization of allylic alcohol with Ru complexes of dendrimeric

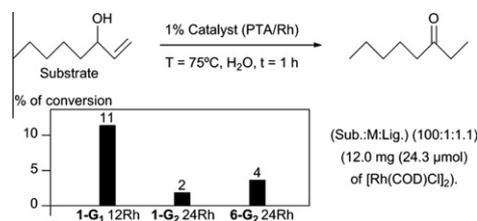


Figure 2. Alcohol isomerization in water using Rh complexes of the dendrimers shown in Figure 1 as catalysts.

PTA **1-G_n** ($n = 1-3$) in mixtures $\text{H}_2\text{O}/\text{heptane}$, for which we have observed a positive dendritic effect, that is an increase of the catalytic efficiency when the generation of the dendrimer increases.⁸ However, ruthenium is not the sole metal that could be used, and rhodium has also given interesting results for allylic alcohol isomerization.¹⁶ Thus we decided to test the rhodium dimer $[\text{Rh}(\text{COD})\text{Cl}]_2$ for complexing the PTA terminal groups of our dendrimers. The complexation is carried out in situ in water: the dendrimers and the rhodium complex (Rh/PTA 1:1.1) are left reacting for 15 minutes before the substrate was added and the heating was started. The reactions are left stirring vigorously for one hour, then the results are monitored by gas chromatography (GC). The reaction seems to have favoured the smallest dendrimer since the 1st generation dendrimer **1-G₁** with only 12 PTA complexes shows the best results, and when considering 24 PTA complexes, the smaller compound **6-G₂** is slightly better than **1-G₂**. However, none of these results are good enough, presumably because of the poor solubility in water of the complexes, the one of **1-G₂** being the least soluble (Fig. 2). Thus we moved to study another reaction, the hydration of alkynes.

The hydration of alkynes is formally the addition of water to a triple bond, providing an important route to carbonyl compounds.¹⁷ In general, addition of water to terminal alkynes follows the Markovnikov's rule, leading mainly to ketones. In a previous attempt, we have used $\text{Ru}(\text{p-cymene})\text{Cl}_2$ complexes of dendrimers **1-G₁** and **1-G₂** for catalyzing such reaction in mixtures $\text{H}_2\text{O}/i\text{PrOH}$ at 90°C for 48 h (5% of catalyst); the percentage of conversion was respectively 58% and 45%, with a selectivity to ketone of 95% and 98%.⁸ Here we have modified the experimental conditions by decreasing the % of catalyst (1% instead of 5%), by decreasing the time of reaction (17 h instead of 48 h), and by adding a co-catalyst (10% of H_2SO_4). Under this case as previously, the complexes are generated in situ. In these improved conditions, the catalysis proceeds more rapidly, as displayed in Figure 3, and the selectivity in ketone is 100% with all dendrimers. A decrease of the efficiency is observed when the generation of the dendrimer increases in the homogeneous series **1-G_n** ($n = 1, 2$), whereas the more dense

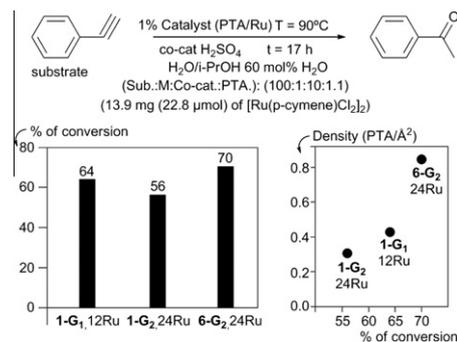


Figure 3. Hydration of alkyne using Ru complexes of the dendrimers shown in Figure 1 as catalysts.

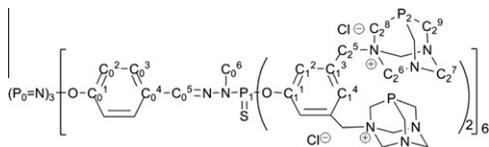


Figure 4. Numbering scheme used for NMR assignment.

dendrimer **6-G₂** gives the best results. An estimation of the density of the terminal groups was obtained assuming a spherical shape for the dendrimers. A correlation between the density and the catalytic efficiency is observed; increasing the local density of catalytic entities increases the catalytic efficiency (right part of Fig. 3).

In conclusion, by using three dendrimers related either by the number of terminal groups or by the size, our experiments, and more precisely the catalyzed hydration of alkynes, have demonstrated for the first time the importance, and the positive influence of the density of the catalytic entities on the efficiency of the catalysis. We intend to expand the scope of this study to other dendrimers and other catalyzed reactions.

Acknowledgments

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- Synthesis of dendrimer **3-G₂**. 0.500 g (274 μmol) of **2-G₁**, 0.747 g (3.56 mmol) of 5-hydroxy-dimethylisophthalate, and 2.32 g (7.11 mmol) of C₂O₃ were dissolved in 50 mL distilled THF. The reaction mixture was left stirring overnight and two filtrations over celite were made and an evaporation. **3-G₂** was obtained as a white powder in 60% yield. **3-G₂**: ³¹P {¹H} NMR (81 MHz, CDCl₃), 11.2 (s, P₀), 66.2 (s, P₁). ¹H NMR (200 MHz, CDCl₃), 3.31 (d, ³J_{HP} = 10.7 Hz, 18 H, C₀⁶H), 3.83 (s, 72 H, CH₃O), 7.09 (d, ³J_{HH} = 8.4 Hz, 12 H, C₀²H), 7.62 (d, ³J_{HH} = 8.4 Hz, 12 H, C₀³H), 7.67 (s, 6 H, C₀⁵H), 8.02 (s, 24 H, C₁²H), 8.45 (s, 12 H, C₁⁴H). ¹³C {¹H} NMR (50 MHz, CDCl₃), 32.92 (d, ²J_{CP} = 12.8 Hz, C₀⁶H), 52.58 (s, CH₃O), 121.12 (s, C₀²), 126.78 (d, ³J_{CP} = 4.3 Hz, C₁²), 127.69 (s, C₁⁴), 128.45 (s, C₀³), 131.65 (s, C₀⁴), 132.12 (s, C₁³), 139.98 (d, ³J_{CP} = 14.3 Hz, C₀⁵), 150.49 (d, ²J_{CP} = 7.1 Hz, C₁¹), 151.41 (d, ²J_{CP} = 6.8 Hz, C₀¹), 165.06 (s, C=O). The numbering used for the assignment of NMR signals for this compound and others is displayed in Figure 4.
- Synthesis of dendrimer **4-G₂**. **3-G₂** (1.04 g, 266 μmol) was dissolved in distilled THF (100 mL). The solution was cooled by acetone/N₂(liquid). A 1 M solution of LiAlH₄ in THF (5.3 mL, 5.3 mmol) was added to the cooled solution, and the reaction was left stirring for 2 hours. The reaction was quenched by the addition of a few drops of H₂O and then aqueous HCl to correct the pH. A filtration was made and the residual solid was freeze-dried. **4-G₂** was obtained as a white powder in 31% yield. **4-G₂**: ³¹P {¹H} NMR (81 MHz, CD₃OD), 12.4 (s, P₀), 65.6 (s, P₁). ¹H NMR (200 MHz, CD₃OD), 3.29 (d, ³J_{HP} = 10.5 Hz, 18 H, C₀⁶H), 4.51 (s, 48 H, C₂⁵H), 6.94 (d, ³J_{HH} = 8.6 Hz, 12 H, C₀²H), 7.13 (s, 36 H, C₁²H + C₁⁴H), 7.60 (d, ³J_{HH} = 8.6 Hz, 12 H, C₀³H), 7.70 (s, 6 H, C₀⁵H). ¹³C {¹H} NMR (63 MHz, CD₃OD), 32.26 (d, ²J_{CP} = 11.32 Hz, C₀⁶), 63.12 (s, C₂⁵), 117.91 (d, ³J_{CP} = 4.4 Hz, C₁²), 120.99 (br s, C₀²), 121.50 (s, C₁⁴), 128.19 (s, C₀³), 132.56 (s, C₀⁴), 139.29 (d, ³J_{CP} = 14.5 Hz, C₀⁵), 143.57 (s, C₁³), 151.06 (br d, ²J_{CP} = 7.6 Hz, C₀¹ + C₁¹). See Figure 4 for the numbering used.
- Synthesis of dendrimer **5-G₂**. 6 mL of SOCl₂ were added to 0.178 g (54 μmol) of **4-G₂**. The mixture was cooled by means of ice-bath and left stirring overnight. To evaporate the excess SOCl₂, toluene was used for co-evaporation. **5-G₂** was obtained as a white powder in 79% yield. **5-G₂**: ³¹P {¹H} NMR (81 MHz, CDCl₃), 11.4 (s, P₀), 65.3 (s, P₁). ¹H NMR (200 MHz, CDCl₃), 3.27 (d, ³J_{HP} = 10.7 Hz, 18 H, C₀⁶H), 4.44 (s, 48 H, C₂⁵H), 7.03 (d, ³J_{HH} = 8.5 Hz, 12 H, C₀²H), 7.18 (br s, 36 H, C₁²H + C₁⁴H), 7.56 (br d, ³J_{HH} = 8.5 Hz, 18 H, C₀⁵H + C₀³H). ¹³C {¹H} NMR (63 MHz, CDCl₃), 33.01 (d, ²J_{CP} = 12.5 Hz, C₀⁶), 45.11 (s, C₂⁵), 121.36 (s, C₁²), 121.43 (s, C₀²), 125.46 (s, C₁⁴), 128.34 (s, C₀³), 131.88 (s, C₀⁴), 139.22 (d, ³J_{CP} = 14.2 Hz, C₀⁵), 139.62 (s, C₁³), 150.81 (d, ²J_{CP} = 7.30 Hz, C₁¹), 151.33 (br s, C₀¹). See Figure 4 for the numbering used.
- Synthesis of dendrimer **6-G₂**. 0.127 g (34 μmol) of **5-G₂** and 0.144 g (891 μmol) of PTA were dissolved in distilled THF (20 mL). The reaction was left stirring overnight and then filtered. After evaporation of the solution, four washings with THF were made. **6-G₂** was obtained as a white powder in 38% yield. **6-G₂**: ³¹P {¹H} NMR (81 MHz, D₂O/CD₃CN), –76.4 (s, P₂), 14.4 (s, P₀), 70.6 (m, P₁). ¹H NMR (200 MHz, D₂O/CD₃CN), 3.43–3.72 (br m, 18 H, C₀⁶H), 3.80–5.28 (br m, 36 H, C₂⁵H + C₂⁷H + C₂⁸H + C₂⁹H), 6.43–8.15 (br m, 66 H, C₀²H + C₀³H + C₀⁵H + C₁²H + C₁⁴H). See Figure 4 for the numbering used.
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