Grafting of water-soluble phosphines to dendrimers and their use in catalysis: positive dendritic effects in aqueous media†

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Generations 1 to 3 of dendrimers ended by water-soluble phosphines are synthesized and their ruthenium complexes are used as catalysts in aqueous media; a slightly positive dendritic effect on the regioselectivity is observed for hydration of alkynes and a large positive dendritic effect is observed in the biphasic (water/heptane) catalysed isomerisation of allylic alcohols to ketones where the products are easily isolated and the catalyst can be reused several times, even the first generation.

Catalysis is a unique tool to carry out chemical transformations, and it is well established that subtle changes in experimental parameters could have a dramatic effect on the outcome of catalytic reactions. A relatively large number of dendritic catalysts have been proposed already, illustrating the growing importance of this field of research.[1] However, whole sections of catalysis have been scarcely explored up to now using dendritic catalysts; this is in particular the case for catalyses performed in aqueous media.[2] This fact might appear surprising since water is abundant, cheap, non-toxic and environment friendly, often able to induce dramatic improvements of the catalytic efficiency;[3] it is presumably due to the difficulty to have dendritic organometallic catalysts soluble in water (or even compatible with water). Water-solubility of dendrimers is generally obtained by introducing charges (positive or negative) on the terminal groups. In the case of dendritic catalysts, the catalytic entities often constitute the terminal groups, and the presence of charges might totally modify the catalytic properties. In a first attempt to solve this dilemma, charges and phosphino complexes were randomly grafted to the surface of PAMAM dendrimers,[4] but this method do not afford well-defined catalysts. To the best of our knowledge, we report here the first examples of dendrimers bearing both an organometallic complex and a permanent positive charge on each terminal group, enough remote from the catalytic centers to preserve their catalytic properties.

PTA (1,3,5-triaza-7-phosphaadamantane)[5] is known both to afford water-soluble complexes and to be easily alkylated at one nitrogen, introducing a positive charge able to enhance the solubility in water without killing the catalytic properties. Thus, the grafting of PTA to the terminal groups of dendrimers might lead to water-soluble organometallic dendritic catalysts. The type of internal structure of dendrimers we decided to use is built from a cyclotriphosphazene core, with phenoxy hydrazino thiophosphate branches (**1-G*n***,[6] from generation 1 to 3 ($n = 1$–3)). Such type of internal structure was previously shown compatible with catalytic experiments in several organic solvents, and even able to favour them.[7] Furthermore, it was shown that the presence of positive (or negative) charges on each terminal groups induces the solubility in water, or at least in aqueous media for this type of skeleton.[8] The grafting of PTA necessitates the presence of potentially alkylating groups on the surface of dendrimers; benzylchlorides are known to be good alkylating groups of amines, thus they were our first targets.

Starting from the aldehyde terminal groups of dendrimers **1-G*n***, the first reaction we carried out to obtain benzyl chloride terminal groups is the reduction, to afford the benzylic alcohols **2-G*n***. In first attempts, $NaBH_4$ was used, but the reaction was slow and the work-up tedious, thus BH_3,SMe_2 was preferred. The completion of the reaction is shown in particular by ^1H NMR, with the disappearance of the signal corresponding to the aldehyde at 9.9 ppm on behalf of CH_2 groups (4.4 ppm). Compounds **2-G*n*** are isolated in 72% (**2-G$_3$**) to 80% yield (**2-G$_1$**). Then the benzyl alcohol terminal groups are transformed into benzylic chlorides **3-G*n*** by reaction with $SOCl_2$, under anhydrous conditions. The completion of the reaction is shown in particular by ^1H NMR, which displays a shift of the signal corresponding to the CH_2 groups from 4.4 ppm for **2-G*n*** to 4.6 ppm for **3-G*n***, but also by ^{13}C NMR (shift from 63 ppm for **2-G*n*** to 45 ppm for **3-G*n***, also for the CH_2 groups). Dendrimers **3-G*n*** were isolated in 80–85% yield. Reaction with PTA affords cleanly the phosphino dendrimers **4-G*n***; neither dialkylation on two nitrogen atoms of PTA, nor alkylation of the phosphine was observed, as expected. The grafting of PTA induces an important deshielding of its signal in the ^{31}P NMR spectra, from −99 ppm for PTA alone to −80 ppm when grafted to the dendrimer in **4-G*n***. The completion of the reaction is in particular shown in ^1H NMR spectra by the shielding of the signal corresponding to the CH_2 benzyl group from 4.6 ppm for **3-G*n*** to 4.1 ppm for **4-G*n***. These PTA-dendrimers were isolated in very good yields (from 97% for **4-G$_1$** to 88% for **4-G$_3$**).

At this step, several types of metals could be complexed by the PTA terminal groups, but we decided to choose the ruthenium derivative $[Ru(p\text{-cymene})Cl_2]_2$, due to the versatility of the type of reactions this metal is able to catalyse. The complexation at room temperature affords cleanly the ruthenium complexes **5-G*n***

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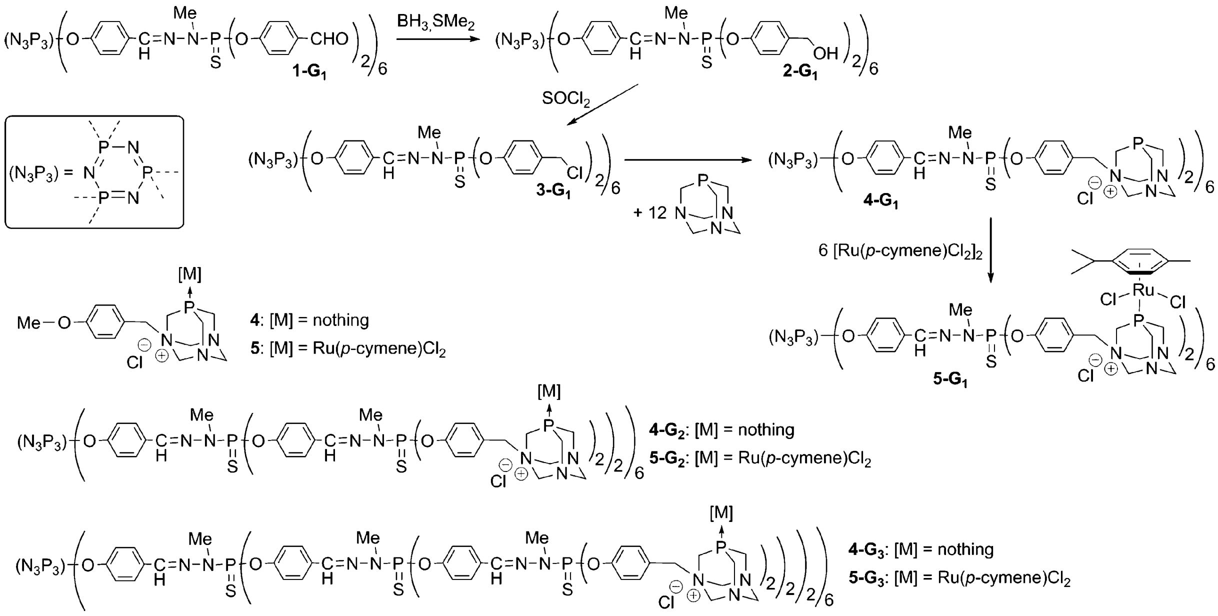

Scheme 1 The 3 or 4 steps needed for the synthesis of dendrimers terminated by PTA (**4-G*n***) or PTA-Ru(*p*-cymene)Cl$_2$ groups (**5-G*n***), starting from aldehyde terminal groups (**1-G*n***). All steps are shown only with the first generation dendrimers, but were carried out also with generations two and three, and with the model compound.

(Scheme 1). ^{31}P NMR shows unambiguously the complexation of PTA which induces a very large deshielding of the corresponding signal from −80 ppm for **4-G*n*** to −14 ppm for **5-G*n***.[9] All complexes were isolated in moderate yields after work-up (52% to 68% yield). The solubility in pure water of compounds **5-G*n*** is high for **5**, moderate for **5-G$_1$** but very poor for **5-G$_2$** and **5-G$_3$**, at room temperature. Nevertheless, catalytic experiments are often performed at high temperature, and only low quantities of catalysts are needed, thus the poor solubility should not hamper the catalytic experiments.

Compounds **5-G*n*** have a hydrophilic surface and a hydrophobic interior, thus these dendritic complexes should be particularly useful for catalytic reactions performed in mixtures of water–organic solvent. Metal-catalysed hydration of alkynes provides an important route to carbonyl compounds,[10] with complete atom economy, thus it appeared particularly interesting to study in a first attempt. In general, addition of water to terminal alkynes follows Markovnikov's rule, leading mainly to ketones. We have used 5 mol% of Ru-catalysts to perform the hydration of phenylacetylene in water–isopropanol (1 : 3 in volume, one phase) mixtures. The percentage of catalysts refers to the number of ruthenium groups; it means that for comparing the efficiency of the monomer and of the first generation, 12 equivalents of **5** are compared with 1 equivalent of **5-G$_1$**. The percentages of conversion, measured by relative integration of the ^{1}H NMR signals after 48 h at 90 °C, are average: the first generation is better than the monomer, but a decreasing efficiency is observed with generations 2 and 3. On the other hand, the selectivity for the ketone increases from the monomer to the third generation from 91 to 98%, showing a slightly positive dendritic effect (Fig. 1). In view of these average results, we did not try to modify the reaction conditions, and we did not attempt to recover and reuse these dendritic catalysts for this type of reactions.

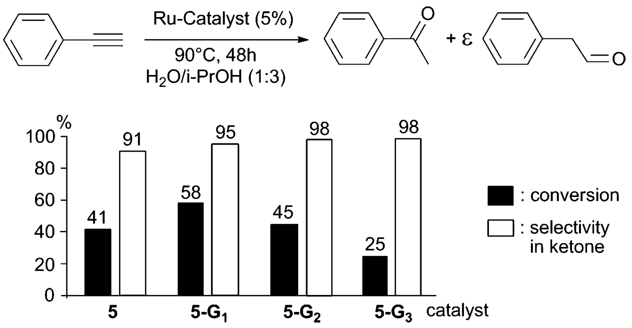

Fig. 1 Hydration of phenylacetylene using monomer **5** and dendrimers **5-G*n*** (*n* = 1–3) as catalysts; % of conversion and selectivity (a slightly positive dendritic effect is observed on the selectivity).

The second type of catalysed reaction in aqueous media we studied is the isomerisation of allylic alcohols. Without catalyst, such reaction necessitates two steps (reduction of alkene and oxidation of alcohol), whereas it is performed one-pot with an organometallic catalyst.[11] The isomerisation of 1-octen-3-ol into octan-3-one is carried out using 1 mol% of Ru-catalysts and 2% of Cs$_2$CO$_3$ as co-catalyst,[12] in mixtures water–heptane (1 : 1) at 75 °C and under vigorous stirring (no reaction occurs in the absence of water). Before stirring, analysis of both phases and of the inter-phase indicates that octanol is in the organic phase, the co-catalyst in water, and the dendrimer both in the aqueous phase and at the interface. Upon vigorous stirring both phases mix, but they are rapidly recovered by decantation. Such system should allow catalyst recycling, as we will see later. The reactions are monitored by gas chromatography (GC) on the organic phase, and are stopped after 8 h. A clearly positive dendritic effect is observed in this case for the conversion, on going from 38% with the monomer **5** to 98% with the third generation **5-G$_3$** (Fig. 2, left part).

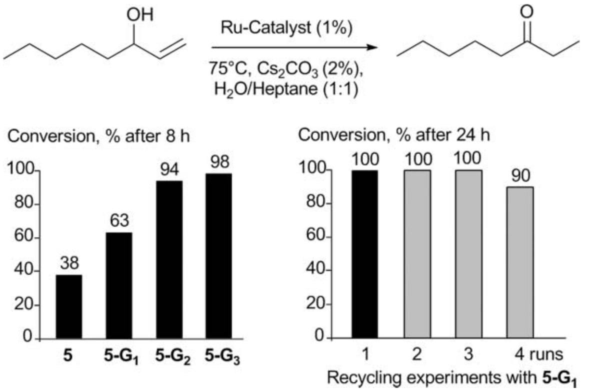

Fig. 2 Isomerisation of 1-octan-3-ol using the monomer **5** and dendrimers **5-G*n*** ($n = 1–3$) as catalysts, showing a clear positive dendritic effect. On the right: recycling experiments with **5-G$_1$**; the second run (first grey bar) is the first reuse.

In view of these interesting results, we decided to study the possibility to recycle the catalyst. We choose the smallest dendrimer (**5-G$_1$**) to perform these experiments; indeed the first generation is generally the most difficult to recycle in catalysis experiments. However, **5-G$_1$** gave the worst results of all dendrimers in terms of efficiency after 8 h, thus we increased the reaction time, and we choose to stop the reactions after 24 h; in these conditions a 100% conversion is attained. The recycling is performed very simply by decantation and removal of the organic phase, followed by addition of heptane and 1-octan-3-ol. In the first three catalytic runs the percentage of conversion remains 100%, whereas it begins slightly to decrease at the fourth run (Fig. 2, right part).

In conclusion, the grafting of a water-solubilising phosphine (PTA) affords special dendrimers having a hydrophilic surface and a hydrophobic interior. Their complexation with Ru derivatives affords catalysts usable for the hydration of acetylenes, but also for the isomerisation of allylic alcohols. In this later case, the catalytic efficiency increases as the generation of the dendritic catalysts increases, inducing a clearly positive dendritic effect. Such positive effect was very rarely observed previously for catalytic entities linked to the surface of dendrimers,[7a,13] and never in aqueous media, to the best of our knowledge.

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9 Selected ^{31}P NMR data in ppm (the numbering refers to the generation, P_1 is the closest to the N_3P_3 core): **4**: −81.8; **5**: −27.6; **4-G$_1$**: −80.6 (PTA), 11.3 (N_3P_3), 64.8 (P_1); **5-G$_1$**: −14.6 (PTA), 11.4 (N_3P_3), 64.8 (P_1); **4-G$_2$**: −80.7 (PTA), 11.7 (N_3P_3), 65.3 (P_1 and P_2); **5-G$_2$**: −14.6 (PTA), 11.2 (N_3P_3), 64.8 (P_2), 65.0 (P_1); **4-G$_3$**: −79.5 (PTA), 12.1 (N_3P_3), 66.4 (P_1, P_2 and P_3); **5-G$_3$**: −12.8 (PTA), 14.0 (P_0), 68.7 (P_3), 68.9 (P_1 and P_2). See ESI† for more details.

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