Supramolecular Immobilization of a Perfluoro-Tagged Pd-Catalyst with Dendritic Architectures and Application in Suzuki Reactions

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Abstract: A new supramolecular complex of a perfluoro-tagged palladium phosphine catalyst to a dendritic core-shell architecture with a perfluoroalkyl shell was used as recoverable catalyst for Suzuki couplings. This homogeneous complex can also serve as a model for related catalysts adsorbed on fluorous silica gel.

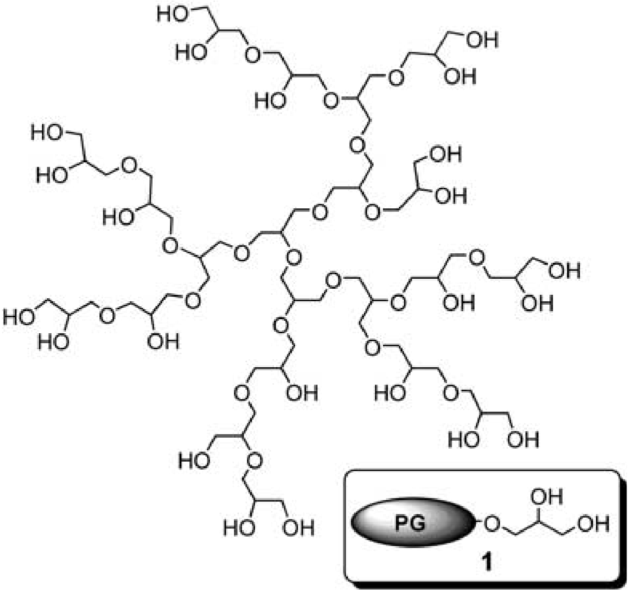
Keywords: dendrimers; fluorinated ligands; ligand recycling; palladium catalysis; supramolecular complex; Suzuki coupling

Introduction

Dendritic core-shell architectures have attracted increasing interest for their ability to act as unimolecular nanocarriers for catalysts, pharmaceuticals and other guest molecules.[1] More recently, such nanostructures have also been prepared with perfluorinated shells[2,3] allowing easy recovery of products and recycling of catalytic nanoparticles in alternative reaction media, such as $scCO_2$ and perfluorinated solvents.[4]

For many applications the difficult accessibility of dendrimers *via* costly multistep syntheses represents a major problem.[5] Hyperbranched polymers that can be obtained in one reaction step from the polymerization of AB_m monomers are currently being discussed as possible alternatives.[6] In contrast to the perfectly branched glycerol dendrimers (DB = 100%),[3,7] hyperbranched polyglycerols (PG) **1** are randomly branched, but well-defined dendritic structures with a degree of branching of approx. 60%. They are prepared in a one-step process and are readily available on a kilogram scale with relatively low molecular weight distributions (typically < 2).[8]

For the covalent immobilization and the recycling of homogeneous catalysts dendritic polymers have been used by many groups.[9] However, only a few examples have been reported for the non-covalent anchoring of catalysts in dendritic architectures by supramolecular interactions.[10] In these cases, the linkage between the transition metal complexes and the dendritic support is based on, e.g., ionic interactions in combination with multiple hydrogen bonds and allows a high degree of flexibility.



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Yet another approach for the non-covalent immobilization of catalysts has been presented by one of our groups who used interactions between fluorous phase silica (FPS) and perfluoro-tagged palladium complexes for the immobilization and recycling of catalysts in organic solvents.[11] In this heterogeneous system the efficient catalysis, the catalytic properties and the quantitative catalyst recovery by simple filtration were demonstrated for various C–C coupling reactions. Due to the heterogenic nature of this system it is quite difficult to analyze the catalytic process in detail. Therefore, a homogeneous analogue of this catalytic system should allow us to get more insight into the active catalytic species and the supramolecular interactions by NMR techniques.

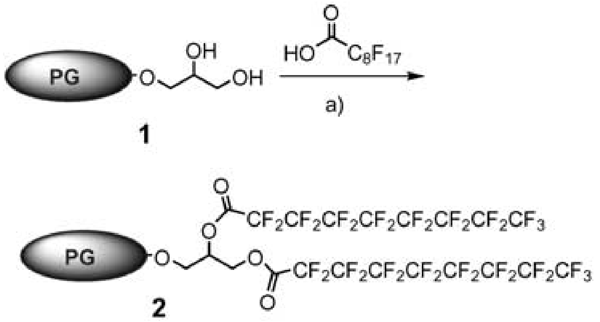
Recently, we have reported on the syntheses of novel dendritic architectures with perfluorinated shells derived from the covalent modification of perfect glycerol dendrimers, hyperbranched polyglycerols and hyperbranched polyethyleneimines.[3] These polymers are soluble in several perfluorinated solvents and can encapsulate ions, polar dyes and metal nanoparticles. However, we were not able to perform catalytic reactions in the presence of these systems. This is probably due to complexation and inactivation of Pd by the presence of chelating S- or N-ligands in these dendritic polymers. Thus, we herein present a nitrogen- and sulfur-free dendritic structure based on a dendritic architecture built from polyglycerol core and a perfluoroalkyl shell. This system was used as supramolecular support to immobilize a perfluoro-tagged catalyst and study its catalytic activity in Suzuki coupling reactions as well as the complex stability.

Results and Discussion

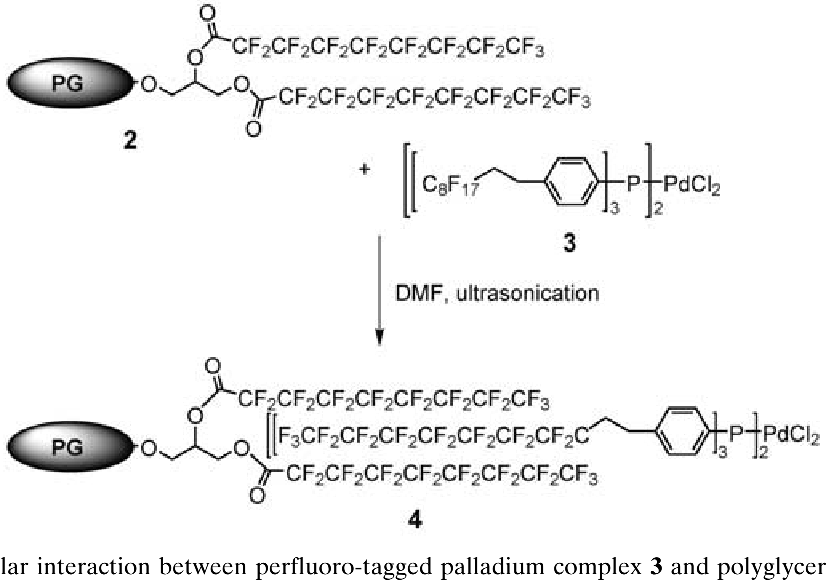
For the preparation of the dendritic core-shell-type architecture, we esterified hyperbranched polyglycerol **1** ($M_n = 5000$ g mol^{-1})[8] with a perfluorinated carboxylic acid by azeotropic distillation (Scheme 1). This fluorophilic nanocarrier was prepared on a multigram scale and was easily purified with a strongly basic anion exchange resin (4 mmol OH$^-$/g) to yield 85% of PG-perfluoroester **2**. The degree of functionalization obtained from ^{13}C NMR (inverse gated) was 47%.

Then the perfluoro-tagged palladium phosphine complex **3**,[12] meanwhile commercially available (Fluka), was immobilized in the perfluorinated shell of the dendritic polyglycerol ester to obtain the supramolecular architecture **4** simply by dissolution of both components in DMF with ultrasonication (Scheme 2).

The strong interaction between the perfluorinated chains in the supramolecular complex **4** was observed by ^{19}F NMR spectroscopy (Figure 1). The spectrum



Scheme 1. Synthesis of dendritic polyglycerol perfluoroalkyl ester **2** from hyperbranched polyglycerol **1**; a) pTSA cat., BTF, azeotropic distillation, 3 days.



Scheme 2. Supramolecular interaction between perfluoro-tagged palladium complex **3** and polyglycerol ester **2**.

shows an isolated CF_3 signal at −83.31 ppm. Upon complex formation a significant amount of the CF_3 signal undergoes a high-field shift of 1.70 ppm to −81.61 ppm. This shift of the CF_3 signal is characteristic for the partial intercalation of perfluoroalkyl chains and has also been observed for other supramolecular aggregates as well as for the self-aggregation of perfluoroalkyl-modified perfect dendrimers.[13] It is noteworthy for the catalytic action of the immobilized catalyst that the fluorous-fluorous interaction is temperature dependent and is reduced significantly at higher temperatures (Figure 2). This will enhance the flexibility of the ligand and hence increase its catalytic activity. This temperature-dependent aggregation might also explain the excellent results of the heterogeneous system consisting of perfluoro-tagged Pd catalysts adsorbed on fluorous silica gel.[11] In this case we now have a strong indication for the formation of a homogeneous catalytic species, which might be due to the temperature-dependent desorption of the catalyst from the solid support at elevated temperature (80 °C), while a strong insoluble complex is present at room temperature.

We also obtained TEM images of the supramolecular aggregate **4** (Figure 3). The image shows spherical particles with a diameter of approx. 3 ± 2 nm. This corresponds to the size expected for single molecules of the dendritic perfluoroalkyl ester **2**, however, a micellar assembly of a few particles cannot be excluded due to the error of the TEM measurement. But the particles are certainly small enough to be homogeneously dissolved in solution.

The catalytic activity of immobilized perfluoro-tagged palladium complex **4** was now studied in homogeneous Suzuki coupling reactions (Scheme 3) and compared to the perfluoro-tagged catalyst itself at different catalyst concentrations (Table 1). For these studies a 1:1 molar ratio of polyglycerol ester **2**/perfluoro-tagged Pd catalyst **3** was used.

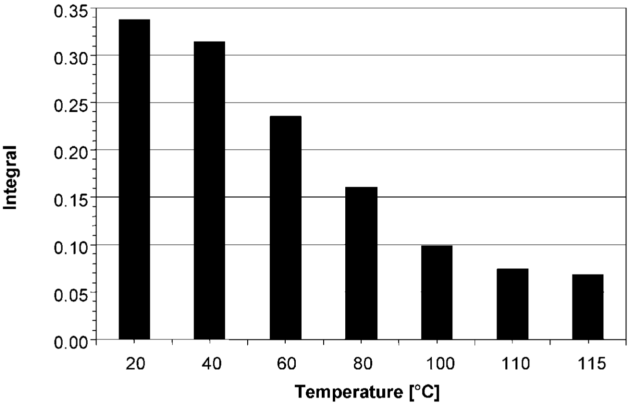


Figure 2. Temperature-dependence of the CF_3-group integral of the complex **4** at −83.31 ppm in DMF.

Initially, we tried to use a mixture of dimethoxyethane (DME) and water as solvent system similar to the heterogeneous FSG-system.[11] However, the supramolecular catalyst **4** was not soluble in this mixture. We only observed homogeneous reaction conditions when using DMF as a solvent. An advantage of this selective solubility is that the supported catalyst **4** can easily be recycled by precipitation in a mixture of DME/water (10% HCl) 2:1, whereas the substrate and product remain soluble in this mixture. The precipitated catalyst complex **4** was filtered and re-used for three consecutive Suzuki coupling reactions. Each reaction series was performed at three different catalyst loadings 0.1, 0.5 and 1 mol %

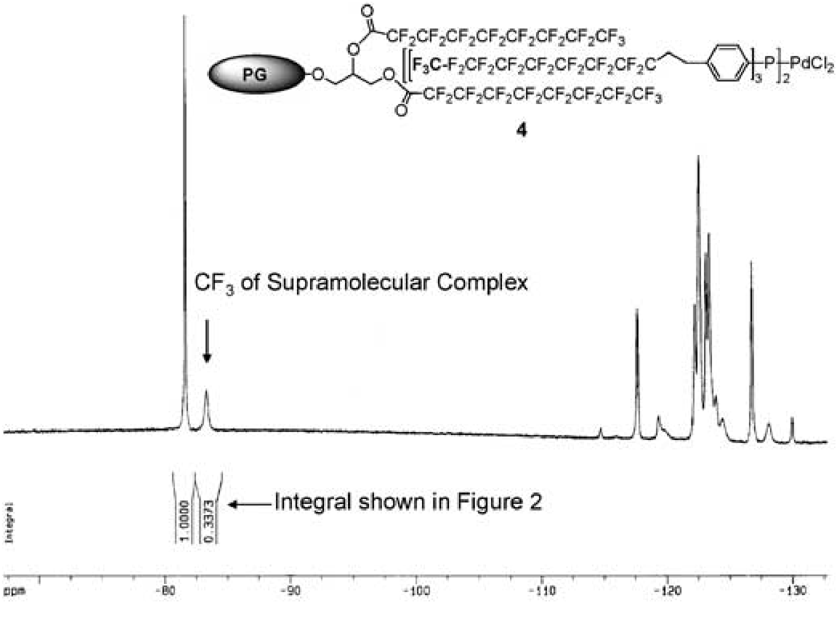


Figure 1. ^{19}F NMR spectra of supramolecular complex **4** in DMF at 20 °C.

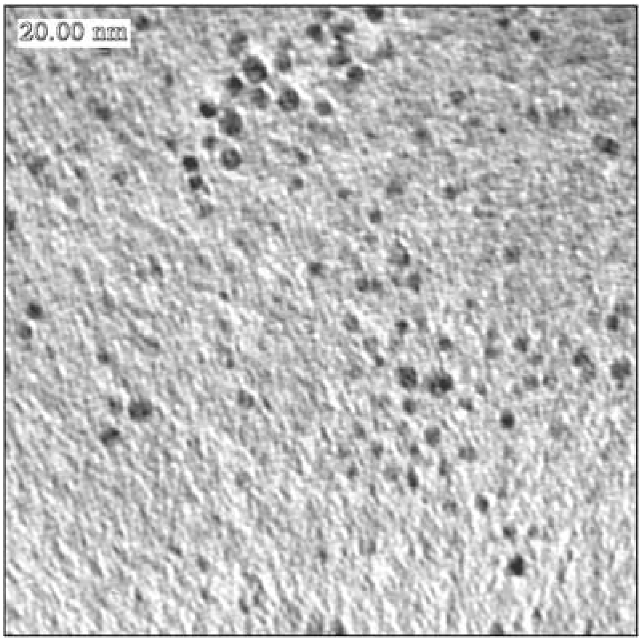
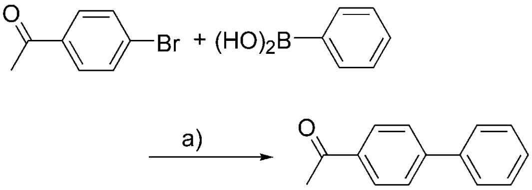


Figure 3. TEM image of the supramolecular complex **4**. The bar in the TEM image is equivalent to 20 nm.



Scheme 3. Suzuki coupling reaction performed with the supramolecular palladium complex **4**. a) 0.1, 0.5 and 1 mol % catalyst (see Table 1), Na_2CO_3, DMF, 80 °C, 20 h.

(Table 1). The pure product can easily be obtained by extraction of the soluble phase with chloroform/water. After concentration of the chloroform layer the conversion yield was determined from the ^1H NMR spectra by integration of the methyl signals.

We have also tested the catalytic activity of the perfluoro-tagged palladium catalyst without the dendritic support **2** under the same conditions (Table 1). While Gladyzs et al. demonstrated that it is possible to use fluorous catalysts in the absence of fluorous solvents provided the perfluoro-tagged catalyst is sufficiently soluble at the reaction temperature,[14] in our case, perfluoro-tagged palladium is also catalytically active in DMF, but the yields without support **2** are significantly lower than the reactions of the supramolecular assembly **4**. This is probably due to the fact that the Pd complex **3** alone is not soluble in DMF, whereas the supramolecular assembly **4** is soluble. It is also noteworthy that a catalyst loading of 0.1 mol % is sufficient for a single run, however, for multiple use higher concentrations of the complex **4** are needed (Table 1). The high catalytic activity of this supramolecular complex **4** can be explained by its relative small particle size (3 ± 2 nm) and the homogeneous reaction conditions. Thus, the dendritic support serves to molecularly disperse the Pd complex in the reaction mixture.

With regard to our earlier experiments with perfluoro-tagged Pd complexes adsorbed on fluorous silica gel, the supramolecular complex **4** can be used as a homogeneous model system to explain the observed reactivity.[11] We assume that the way these two catalytic systems act is similar and in both cases the release of the perfluoro-tagged Pd-catalyst occurs at high temperature, while a strong complex is present at room temperature. Therefore, also the fluorous solid phase acts in the same way as the fluorous dendritic polymer, namely to disperse the perfluoro-tagged catalyst and bring a large portion of it into homogeneous contact with the reaction mixture, in which the heterogeneous FPS remains insoluble.

Conclusion

In summary, we have immobilized a perfluoro-tagged palladium catalyst on a dendritic polyglycerol ester with a perfluorinated shell **2** and investigated its catalytic activity in Suzuki couplings. The supported catalyst **4** can be separated from the product by simple precipitation using a mixture of DME/water. The dendritic support allows for a better solubility of the perfluoro-tagged palladium complex in organic solvents and increases the yield of the reaction significantly. Also, the recycling and multiple use of this supramolecular catalyst **4** is straightforward. This demonstrates a new concept for dissolving perfluoro-tagged catalysts in the usual organic solvents and for allowing their separation and recovery by precipitation. Furthermore, this supramolecular dendritic assembly serves as a valuable soluble model for the interaction of perfluoro-tagged catalysts with insoluble supports such as fluorous silica gel and clearly reveals the ligand diffusion from the complex at elevated tem-

Table 1. Results of consecutive Suzuki couplings.

Catalyst loading [mol%]	Yield [%] (1st run)	Yield [%] (2nd run)	Yield [%] (3rd run)	Yield [%] without support **2**
0.1	>99	29	3	26
0.5	>99	>99	97	29
1	>99	>99	>99	55

peratures. This behavior can also explain the high catalytic activity of the heterogeneous FPS system.

Experimental Section

Synthesis of Polyglycerol Perfluorononanoic Ester (2)

A suspension of hyperbranched polyglycerol ($M_n = 5000$ g mol^{-1}) (0.315 g, 4.3 mmol of hydroxy groups),[8] 2,2,3,3,4,4,5,5,6,6,7,7,8,8,9,9,9-heptadecafluorononanoic acid (2 g, 4.3 mmol) and para-toluenesulfonic acid (pTSA) (0.105 g, 0.7 mmol) in a mixture of toluene (40 mL) and α,α,α-trifluorotoluene (BTF) (20 mL) was heated to reflux for 3 days. The water was removed by azeotropic distillation. After reaction the solvent was removed by evaporation and the residue was redissolved in perfluorobenzene (5 mL). To this solution 1.2 g of basic anion exchange resin, Merck (4 mmol OH^-/g) was added and stirred for 4 hours. The resin was removed by filtration and the solvent was evaporated in vacuum to obtain a brownish viscous polymer **2**, yield: 1.118 g (85%). ^1H NMR (400 MHz, $C_6F_6/CDCl_3$): $\delta = 3.2-5$ (m, CH_2O, CHO), 5.5 (m, CH_2O, CHO); ^{13}C NMR (100 MHz, $C_6F_6/CDCl_3$): $\delta = 65.7$ (m, CH_2O), 67.8 (m, CH_2O), 68.7 (m, CH_2O), 69.7 (m, CH_2O), 72.3 (m, CH_2O), 74.3 (m, CH_2O), 79.6 (m, CH_2O), 106.2 (m, CF_2), 108.2 (m, CF_2), 111.6 (m, CF_2), 113.8 (m, CF_2), 116.3 (t, CF_2, $^1J_{F\text{-}C} = 30$ Hz), 119.2 (t, CF_2, $^1J_{F\text{-}C} = 30$ Hz), 122.0 (m, CF_2), 128.1 (m, CF_2), 130.4 (m, CF_2), 106.2 (m, CF_2), 108.9 (m, CF_2), 111.6 (m, CF_2), 158.6 (m, OCO).

General Procedure for Suzuki Coupling Reactions

A 0.001 M solution of perfluoro-tagged catalyst **3** (10 mg, 0.003 mmol) and the dendritic perfluoroester **2** (60 mg, 0.003 mmol) in 3 mL of absolute DMF was prepared by ultrasonification for 30 min. Then one equivalent 4-bromoacetophenone, 1.1 equivalent of phenylboronic acid and 2.5 equivalent of sodium carbonate were added under argon. The reaction mixture was heated to 80 °C for 20 hours. The solvent was evaporated and the residue was dissolved again with a mixture of dimethoxyethane (DME) and water (10% HCl) (2:1). The insoluble part was filtered, washed with DME/water (2:1) and recycled for the next run (recovery yield ca. 50%). The combined DME/water layers were concentrated in vacuum and extracted three times with chloroform-water. Evaporation of the combined chloroform layers gave the product. The conversion yield was calculated from the methyl signals in the ^1H NMR spectra (product/substrate).

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