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Heck Reactions Catalyzed by PAMAM-Dendrimer Encapsulated Pd(0) Nanoparticles

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ABSTRACT

The behavior of PAMAM-dendrimer encapsulated palladium nanoparticles as catalysts for the Heck reaction has been examined, and it has been demonstrated that this simple system is a very efficient catalyst giving good yields under phosphine-free conditions and with 200–400 times less Pd than usual.

Dendrimers are a family of highly branched well-defined macromolecules, which have attracted increasing interest in recent years.[1−5] Dendrimers are a fascinating class of molecules, because they are synthetic objects available in the nanometer size, their properties can be changed by modifying the surface, while having a well-defined nanoenvironment in the interior of the dendrimer.

Supramolecular guest−host chemistry in dendrimers[6] has been a central topic in dendrimer chemistry since the early theoretical works by Maciejewski,[7] who suggested the existence of a dense shell at the surface in large dendrimers and an interior with voids. The formation of host−guest complexes with dendrimers was first demonstrated by the groups of Tomalia[8,9] and Newkome[10] and later came the famous dendritic box by the Meijer group,[11] where the guest molecules are topologically trapped inside a dendrimer glazed with a hydrogen bonded shell. One of the interesting aspects of dendrimer guest−host complexes is their potential use in homogeneous catalysis, where the size of the dendrimer will facilitate the easy recovery or removal of the catalyst from the products formed.

The encapsulation of metal nanoparticles inside a dendrimer was first demonstrated by the groups of Tomalia[12] and Crooks,[13] who showed that Cu(0) clusters could be formed inside hydroxy-terminated PAMAM dendrimers, and that the dendritic host stabilized the clusters against aggregation and precipitation as bulk metal, and more recently the preparation of Pt(0)- and Pd(0)-clusters stabilized as guests in PAMAM dendrimers were reported.[14,15]

The most important palladium-catalyzed reaction in organic chemistry, apart from catalytic hydrogenation, is the Heck reaction.[16−19] The reaction allows the preparation of substituted alkenes by alkylation or arylation of alkenes with vinyl or aryl halides. The classical conditions for performing Heck reactions involve the use of a Pd(0) complex or a Pd(II) salt (which is reduced in situ to Pd(0)) and a phosphine ligand, which stabilizes Pd(0) as PdL_4 or PdL_3 complexes. In recent years, efforts have been made to develop phosphine-free systems for Heck couplings[18] due to chemical and economical reasons. Many phosphines are toxic as well as expensive, seen from an industrial point of view.

The exact nature of the catalytically active Pd in the phosphine-free systems is not known, and one of the problems encountered upon switching from classical conditions to phosphine-free conditions is the loss of catalytic activity by the precipitation of Pd(0) in the form of Pd black. However, two recent results point toward Pd nanoparticles as catalytically active species: Reetz and co-workers[20] saw the formation of Pd clusters in the highly active phosphine-free catalytic system that they have developed,[21] and Crooks and Yeung[22] demonstrated fluorous-phase catalysis of Heck reactions with Pd(0) complexes of modified PPI dendrimers, although with moderate yields apart from two examples.

Since we were interested in the applications of dendrimers, we decided to investigate the possible use of PAMAM-dendrimer Pd(0) complexes as catalysts for the Heck reaction, but taking into consideration what is known about the reaction mechanism.

It is generally believed that there are at least two different mechanisms for the Heck reaction[23−25] and that the mechanism operating in the underligated/phosphine-free systems is a cationic mechanism.[19] A polar solvent should favor a polar pathway, and because the PAMAM dendrimers contain

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Scheme 1

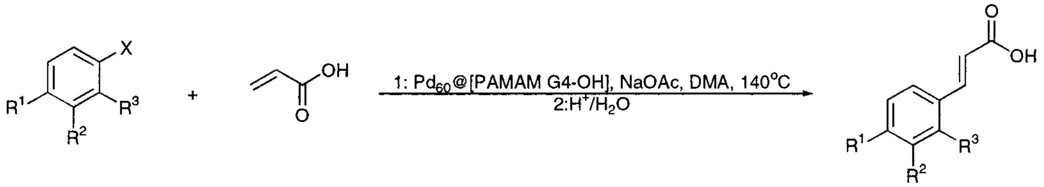

Table 1: Results from the Heck Reaction between Aryl Halides and Acrylic Acid Catalyzed by Pd_{60}@[PAMAM G4-OH]

entry	compound	R^1	R^2	R^3	X	yield (%)	TON	TOF (hr^{-1})
1	1	H	H	H	Cl	≈0	≈0	≈0
2	1	H	H	H	Br	35	14000	1166
3	1	H	H	H	I	75	30000	2500
4	2	H	H	Br	I	92	36800	3066
5	3	H	H	$COCH_3$	I	80	32000	2666
6	4	Br	H	H	I	67	26800	2233
7	5	H	CH_3	CH_3	I	78	31200	2600
8	1	H	H	H	I	24	1920	160
9	2	H	H	Br	I	58	4640	386
10	1	H	H	H	I	70	28000	2333
11	1	H	H	H	I	20	8000	666
12	1	H	H	H	I	10	4000	333

amide-groups, they could be expected to provide the necessary polar nanoenvironment. The choice of solvent was made for two reasons: (1) salts are formed during the reaction, and they have to be transported out of the polar dendrimer, and (2) the tertiary structure of the hydroxy-terminated PAMAM dendrimer could be expected to depend on the polarity of the solvent, and in this case, a polar solvent should favor a more open structure of the dendrimer, thus giving easier access to the reactants to the interior of the dendrimer. (For a very recent paper describing solvent effects on the tertiary structure of a dendrimer see ref 26). This led us to use the classical conditions as shown in Scheme 1, where acrylic acid is arylated with an aryl halide catalyzed by Pd in DMA or DMF.

Typically Heck reactions are performed with between 1 and 10 mol % of Pd and a phosphine ligand, Crooks and Yeung used between 3 and 5 mol % Pd and no phosphine. In our case, also phosphine-free conditions, we found that as little as 0.025 mol % Pd in the form of Pd_{60}@[G4 PAMAM-OH][13] were sufficient to give the isolated yields shown in Table 1. Changing the catalyst to Pd_{40}@[G4 PAMAM-OH][13] did not affect the yields appreciably. We did not see any aging effect on the catalyst either.

The results for a variety of aryl halides are shown in Table 1.[27] In all cases, the product was the trans-cinnamic acid and the yields refer to isolated material. Table entries 1−3 show the effect of the halogen (X), and only marginal reaction takes place with X = Cl. The effect of the substituents on the aryl halide was examined (entries 4−7), and introduction of electron withdrawing groups gives higher yields. The turnover numbers (TONs) and the turn over frequencies (TOFs), which are defined as mol product/mol catalyst and mol product/mol catalyst/hour, were calculated from the isolated yield, the amount of Pd used, and the reaction time. Reduction of the amount of catalyst from 0.025 mol % to 0.005 mol % gave a decrease in yield as seen from entries 8−9.

Finally, in entries 10−12, we examined the reaction using a primitive membrane reactor made out of a bag of dialysis tubing containing the catalyst. In this case, the solvent was changed to DMF and we used triethylamine as base. This system was used for 3 runs (entries 10−12), and as can be seen, the catalyst loses activity upon reuse. In contrast to the other experiments (entries 1−9), we did see leaching of Pd upon reuse of the catalyst, which was evidenced by contamination of the product with Pd black. The loss of catalytic activity is most likely due to a gradual thermal degradation of the dendrimer, and it is likely that a more robust dendrimer would extend catalyst lifetime.

In summary, we have shown that Pd-nanoparticles encapsulated in a simple dendrimer, are very efficient catalysts for the Heck reaction, giving yields fully comparable to those that can be obtained under the standard conditions involving Pd and phosphines. However, the amount of Pd necessary in our system is a factor 200−400 smaller than in a classical system. The lifetime of the catalyst system is not yet satisfactory, but we think that our results, together with the work by Crooks and Yeung, clearly point toward a bright future for dendrimers in catalysis.

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(27) Experimental conditions: aryl halide (10 mmol), acrylic acid (10 mmol), sodium acetate (20 mmol), Pd_{60}@[PAMAM G4-OH] (0.50 mL containing 0.5 mmol Pd in H_2O), DMA (10 mL). Heated at 140 °C for 12 hours under N_2. Aqueous acidic workup.

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