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A strongly positive dendrimer effect in asymmetric catalysis: allylic aminations with Pyrphos-palladium functionalised PPI and PAMAM dendrimers†

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A remarkable and unprecedented increase in catalyst selectivity in dendrimer catalysis is observed for the Pyrphos-Pd catalysed allylic amination of 1,3-diphenyl-1-acetoxypropene as a function of the dendrimer generation (with up to 64 metal sites). This steady increase in ee-values for the allylic amination is less pronounced for the poly(propyleneimine)-derived catalysts than for the corresponding palladium-PAMAM dendrimer catalysts for which an increase in selectivity from 9% ee for a mononuclear reference system to 69% ee for the Pd_{64}-dendrimer was found.

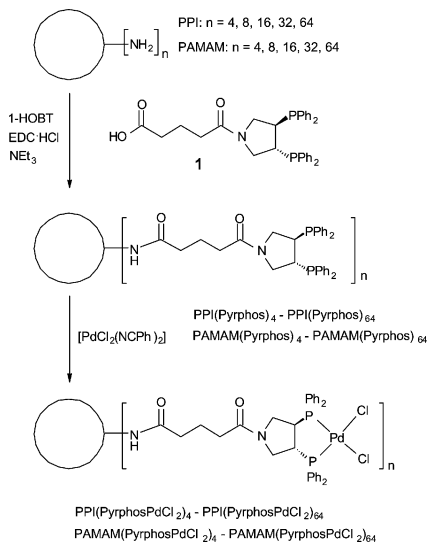
In spite of an ever growing number of examples for the application of metalladendrimers in catalysis[1] there are still only a few reports on applications in asymmetric catalysis to date.[2] On the other hand, enantioselective catalytic conversions should be particularly suited as sensitive probes for "dendrimer effects" in view of the small free activation enthalpy increments which are associated with the catalyst selectivity.[3]

We recently reported the fixation of the Pyrphos ligand[4] to the amino endgroups of poly(propyleneimine) (PPI) dendrimers and the generation of multisite cationic rhodium hydrogenation catalysts bearing up to 32 metal sites.[5] These dendrimer catalysts displayed reduced activity and selectivity, with respect to the mononuclear complexes, in the hydrogenation of several prochiral substrates and thus a pronounced *negative* "dendrimer effect". In this paper we report, for the first time for such Pyrphos-derived species, a strongly positive effect[6] on the selectivity of an asymmetric catalytic transformation upon going to very large multisite chiral dendrimer catalysts. This enhancement of the catalyst selectivity was observed in palladium catalyzed allylic substitutions which are known to be particularly sensitive to small changes in the chemical environment of the active catalyst sites.[7,8]

Several studies on the catalytic properties of palladium dendrimers bearing *achiral* phosphines have been recently reported.[9–11] For the reaction of *trans*-cinnamyl acetate with morpholine van Leeuwen and coworkers, using carbosilane dendrimers, reported a slight increase in the ratio of the branched *vs.* the linear product,[10] while Kaneda *et al.* observed no significant dendrimer effect using these substrates.[11] However, the latter group found an increase in diastereoselectivity of the amination of *cis*-3-acetoxy-5-carbomethoxycyclohex-1-ene upon going to higher dendrimer generations, an observation which they attributed to the increased surface crowding in these macromolecular catalysts. Togni *et al.* reported the application of chiral phosphinepalladium derivatives to dendrimer catalysis.[12] However, this study was limited to low generation dendrimers which did not display a significantly different behaviour in catalysis to that of the mononuclear systems of reference.

The chiral Pyrphos-functionalized dendrimers, which we employed, were both the PPI derivatives mentioned above (containing 4, 8, 16, 32 and 64 metal binding sites) and the analogous poly(amidoamine) (PAMAM) dendrimers (containing 4–64 binding sites) which were synthesized in an analogous way by ethyl-*N*,*N*-dimethylaminopropylcarbodiimide (EDC) induced amide coupling of the ligand-linker unit **1** with the amino end groups of the dendrimer (Scheme 1). Stirring $PPI(Pyrphos)_4$–$PPI(Pyrphos)_{64}$ and $PAMAM(Pyrphos)_4$–$PAMAM(Pyrphos)_{64}$ with $[PdCl_2(NCPh)_2]$ in CH_2Cl_2 at ambient temperature cleanly gave the metallated dendrimers $PPI(PyrphosPdCl_2)_4$–$PPI(PyrphosPdCl_2)_{64}$ and $PAMAM(PyrphosPdCl_2)_4$–$PAMAM(PyrphosPdCl_2)_{64}$, respectively. Their complete metallation was established by their ^{31}P NMR spectra which displayed a single coordination-shifted resonance at δ 42.4–43.0 (δ −11.0 to −12.2 for the non-metallated phosphines).

In contrast to the highly charged cationic Pyrphos-rhodium dendrimers which we previously employed in asymmetric hydrogenations, the neutral dichloropalladium derivatives showed no tendency to aggregate significantly in solution or upon precipitation. This was particularly apparent in preliminary TEM studies performed on samples of both $PPI(PyrphosPdCl_2)_{16}$ and of $PPI(PyrphosPdCl_2)_{32}$ which gave electron micrographs showing the more or less isolated individual



Scheme 1 Synthesis of the Pyrphos-functionalized dendrimers $PPI(Pyrphos)_4$–$PPI(Pyrphos)_{64}$ and $PAMAM(Pyrphos)_4$–$PAMAM(Pyrphos)_{64}$ and their conversion to the metallated dendrimers $PPI(PyrphosPdCl_2)_4$–$PPI(PyrphosPdCl_2)_{64}$ and $PAMAM(PyrphosPdCl_2)_4$–$PAMAM(PyrphosPdCl_2)_{64}$.

† Electronic supplementary information (ESI) available: experimental procedures for the synthesis and metallation of phosphane dendrimers, and catalytic studies. See http://www.rsc.org/suppdata/cc/b3/b302155f/

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metalladendrimers (Fig. 1).‡ The statistical analysis of the diameters of the metallated features observed in the individual samples yielded distribution maxima (2.8 and 4.7 nm, respectively) corresponding exactly to the theoretically predicted values for the two dendrimer generations (Fig. 1b). These values are consistent with the hydrodynamic radii of the phosphine precursors determined in solution (1.6 and 2.8 nm, respectively).

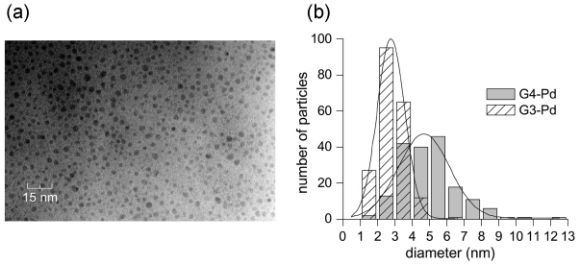
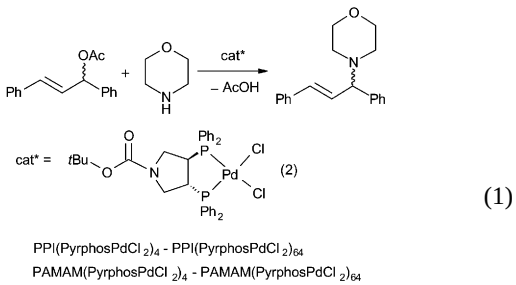


Fig. 1 (a) TEM image of the "fourth-generation" palladadendrimer PPI(PyrphosPdCl$_2$)$_{32}$ displaying features which belong both to individual molecules as well as the superimposition of several dendrimers. (b) Statistical size distribution based on the TEM images of PPI(PyrphosPdCl$_2$)$_{16}$ [3rd generation] and PPI(P$_2$Pd32) [4th generation].

As a test reaction for probing the catalytic performance we chose the well established allylic amination of 1,3-diphenyl-1-acetoxypropene with morpholine [eqn. (1)]. The mononuclear catalyst [(Boc-Pyrphos)PdCl$_2$] (**2**) is very unselective for this transformation (9% ee) which provides the point of reference for the subsequent studies with the dendrimer catalysts. Using complex **2** or the metalladendrimers PPI(PyrphosPdCl$_2$)$_4$–PPI(PyrphosPdCl$_2$)$_{64}$ and PAMAM(PyrphosPdCl$_2$)$_4$–PAMAM(PyrphosPdCl$_2$)$_{64}$ in 0.3 mol% catalyst concentration, the amination of 1,3-diphenyl-1-acetoxypropene was carried out at 45 °C in DMSO. The results of this study (representing the average values for 3 runs) are displayed in Fig. 2.



(1)

A remarkable and unprecedented increase in catalyst selectivity is observed as a function of the dendrimer generation. This steady increase in ee-values for the allylic amination is less pronounced for the PPI-derived catalysts [40% ee for PPI(PyrphosPdCl$_2$)$_{64}$] than for the palladium-PAMAM dendrimer catalysts for which an increase in selectivity from 9% ee for **2** to 69% ee for PAMAM(PyrphosPdCl$_2$)$_{64}$ was found. The variations of these values observed in catalytic runs with different catalyst batches were less than (± 0.5% ee). The same general trend was observed in the asymmetric allylic alkylation of 1,3-diphenyl-1-acetoxypropene with sodium dimethyl malonate which indicates that the results of the amination reaction may be typical for allylic substitutions in general.[13]

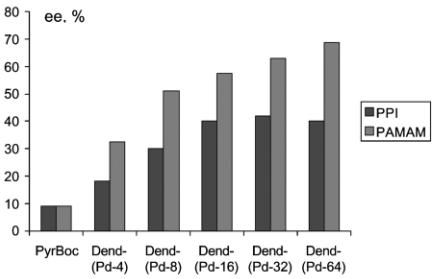


Fig. 2 Dependence of the enantiomeric excesses found for the reaction in eqn. (1) on the dendrimer generation for both precatalyst series PPI(PyrphosPdCl$_2$)$_4$–PPI(PyrphosPdCl$_2$)$_{64}$ and PAMAM(PyrphosPdCl$_2$)$_4$–PAMAM(PyrphosPdCl$_2$)$_{64}$.

We are currently studying the underlying mechanistic reasons for this remarkable "dendrimer effect". It is well known that for C_2-chiral Ph$_2$P-diphosphines the orientation of the phenyl substituents controls the stereoselectivity in the catalytic transformations. Upon going to the higher dendrimer generations with their increasingly crowded diphosphine periphery, the conformational flexibility and preferential orientation of these aryl substituents may be altered which in turn changes their selectivity in the allylic substitutions.

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Notes and references

‡ Powder samples are diluted in dimethyl sulfoxide. A droplet is deposited onto a copper grid (3 mm diameter) and allowed to dry overnight. A film is obtained and ready for observation in a TOPCON 002 transmission electron microscope, operating at a 200 kV accelerating voltage. EDX spectroscopy, coupled to TEM images, allows us to check the presence of Pd in the particles. Distributions in size are measured on numeric images using Analysis software (distributed by Eloise). Counting is performed on 200 particles, for each sample. The distribution is fitted to a Gaussian law centered on 2.8(7) nm, for G3–Pd. For G4–Pd, the distribution is less narrow and centred on 4.7(7) nm. The broadening at larger diameter takes into account the elliptical shape of the objects.

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