

Heterogeneous and solid supported dendrimer catalysts

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- 1 Introduction
- 2 Heterogeneous and solid supported peripherally functionalised dendrimers in catalysis
- 3 Internally functionalised dendrimers in catalysis
- 4 Conclusion
- 5 References

1 Introduction

In recent years, considerable attention has been directed toward the attachment of homogenous catalysts to insoluble supports in an attempt to combine the practical advantages of heterogeneous catalysis with the efficiency of homogenous systems.^{1–4} Heterogenisation allows for the easy separation and recycling of the catalyst from the reaction mixture, which opens up the possibility of recycling and simpler reaction procedures. However, due to the heterogeneous nature of these catalysts, there can be problems with the accessibility of the catalytic sites by the reagents in solution. Homogenous catalysts are typically more difficult to recover but generally offer greater specificity and higher catalytic activity because the catalytic groups are more available to the substrates when the catalyst is completely soluble in the reaction media.

Complex ligands and homogenous metal catalysts have become very expensive so there is an increasing need for recycling. However, the problematic separation of homogenous catalysts from reaction products in solution has hampered the commercialisation of many excellent homogenous catalysts. This is despite the recent developments in polymeric based homogenous catalysis whereby large catalysts can be removed by ultrafiltration techniques or precipitation.^{5,6} For industrial catalytic processes, there is a need for the development of systems that function like homogenous catalysts (*i.e.* high reactivity) and are also easy to separate from the reaction mixture. To date, the majority of research in this area has focused on polymer-supported catalysts and in most cases, the immobilisation of a catalytic species on a polymer support is accompanied by a significant loss in catalytic activity and/or selectivity. Polymer based catalysts are often ineffective, due to leaching of the catalytic groups, or the unavailability of the catalytic sites (owing to uncontrollable polymer conformations) and indefinable incorporation of catalysts within the polymer chain.

In several areas of chemistry, dendrimers are becoming increasingly important as an alternative (or complementary) macromolecular architecture to classical polymers; catalysis is an example of one such field where dendrimers are emerging as important materials. Due to the statistical nature of the syntheses used to prepare polymers, a wide distribution of molecular weights is typically isolated. In contrast, dendrimers are monodisperse, highly symmetrical macromolecules whose tree-like complexity is created by a series of iterative chemical changes resulting in a star-shaped configuration (Fig. 1). Each successive layer of repeat units is referred to as a generation. Dendrimers have unique properties, which are quite different

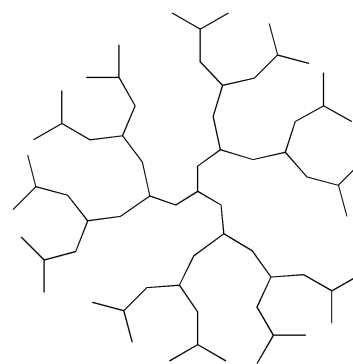
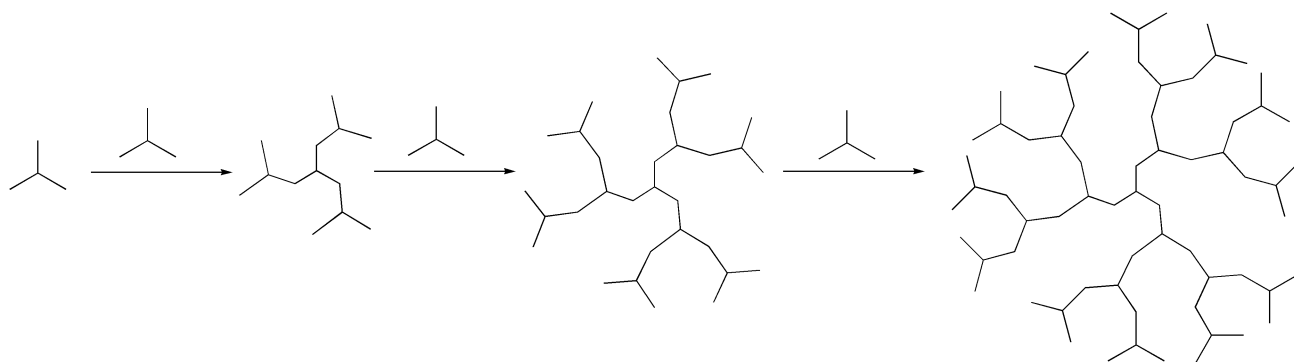


Fig. 1 Schematic representation of a dendrimer.

from those of classical polymers. One important property of dendrimers, with respect to catalysis, is that they are generally highly soluble in organic media. This, combined with the fact that catalytic groups can be appended to specific sites on a dendrimer, gives an important advantage over the typically insoluble polymers with random arrangements of catalytic sites (which are often severely sterically hindered). Thus catalytically active species are potentially more available in the reaction media with dendrimers than with polymeric catalysts. Dendrimer catalysts also have the advantage that, if large enough, they can be recovered *via* ultrafiltration techniques, whereas polymeric materials tend to be sticky and therefore difficult to remove and handle. On the other hand, dendrimer synthesis is usually significantly more time consuming and expensive than preparation of conventional polymers (dendrimer synthesis requires a stepwise approach, described below, and polymer synthesis is a one step process), so this is the principal drawback for the use of these highly ordered and soluble molecules in catalysis.

Dendrimers date back to 1985, when Newkome⁷ and Tomalia⁸ and their co-workers independently published their results on a series of branched molecules, which they respectively termed as *arborols* and *dendrimers* (*dendrimer* has now become the accepted name). There are two main approaches to dendrimer synthesis. The first method developed was the divergent approach (Scheme 1). As the name implies, the divergent strategy involves assembling repeat units around a core through successive chemical reactions at the periphery of the growing macromolecule. A monomer unit with at least two masked terminal groups is added to the initiator core, then the terminal groups are deprotected or activated and a second layer of protected monomer units is added to give the second generation dendrimer, and so on. Each repetitive sequence forms a generation, which is denoted by a repeating pattern in the structure. Relatively large dendrimers can be synthesised quickly using the divergent approach (but there are often problems with purification and monodispersity). The second main approach to dendrimer synthesis, developed by Hawker and Fréchet,^{9,10} is based on a convergent strategy, whereby dendron wedges are



Scheme 1 Divergent synthesis of a third generation dendrimer.

built up separately and then anchored to the core in a final step. With AB_2 type monomers, this process involves attaching two terminal moieties to one terminal group that has a masked functional group, affording the first generation. Deprotection and treatment with half an equivalent of masked monomer gives the next generation and so on. Other approaches to dendrimer synthesis, based on variations or combinations of these two methods, have also been developed, for example the double stage convergent method also developed by Fréchet and co-workers.¹¹

There are many types of dendrimers comprised of repeat units such as amines, amides, carbosilanes, siloxanes, esters, ethers, acetylenes, amino acids, organometallics and nucleic acids.¹² Other functionalities can be incorporated into dendrimers including porphyrins, phthalocyanines and chromophores.¹² The uniqueness of these 3-dimensional polymers, added to the unprecedented ability to control their shape, size, molecular weight, topology and surface chemistry, makes the investigation of dendrimers an exciting and rapidly expanding area of research. The applications of dendrimers are diverse and examples include encapsulation and solubilisation, chemotherapy, contrast reagents for MRI, DNA transfection vectors, light harvesting and the area that this review is concerned with; *catalysis*.

In an attempt to overcome the problems associated with polymer-based catalysts, chemists inevitably turned their attention to dendrimers. Catalytic groups can be added to specific sites at the *surface*, *core*, or the *interior branches* of the dendrimer in a controlled manner (Fig. 2); this gives a significant advantage over the uncontrollable and indefinite incorporation of catalysts within conventional polymers. Catalytic groups at the surface of a dendrimer are readily available for reaction, especially in larger dendrimers, which adopt a globular conformation with most terminal groups located on the surface. The loading on these systems is extremely high due to the inherent nature of dendritic structures and dendrimer synthesis. High catalyst loading is an important aspect economically, and in combination with the fact that many of the common classes of dendrimer are relatively simple to prepare (as well as being available commercially), this has important implications for their use as catalysts. Alternatively, when a catalytic site is anchored to the core of a dendrimer, the catalyst loading is low but complete control over the micro-environment around the catalytic group is possible. This can lead to significant advantages with respect to selectivity and solvent choice. Also, there is the potential for shape and size selective catalysis when the catalytic site is at the core. Catalytic groups can be incorporated at the branching points within the dendrimer to give catalysts with both high loading of catalytic sites and control of the microenvironment around the catalyst.

Several groups around the world have utilised the highly branched nature of dendrimeric materials to obtain multivalent ligands for use in homogenous catalysis. There are many examples of the use of peripherally and internally functionalised dendrimers in *homogenous* catalysis of reactions including

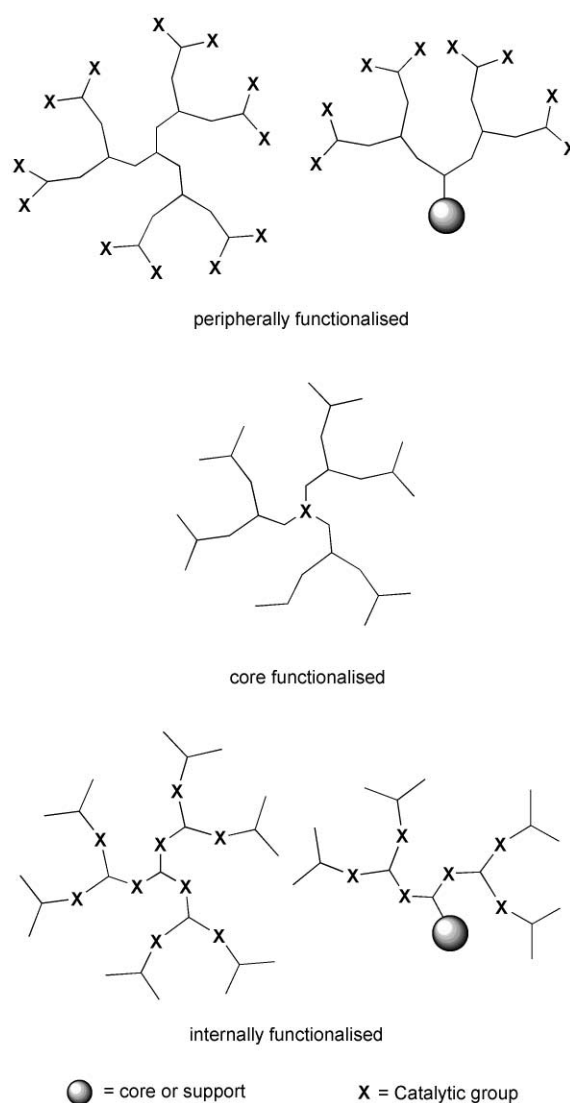


Fig. 2 Functionalised dendrimer catalysts.

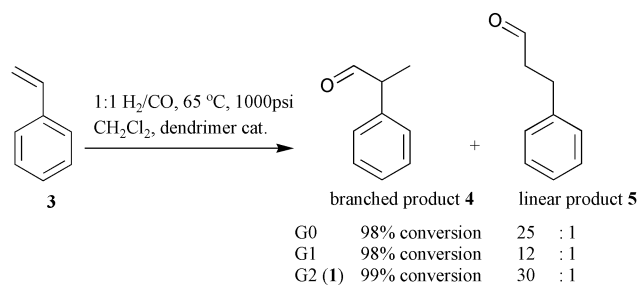
the Kharash addition,¹³ hydroformylation,⁵ hydrolysis,¹⁴ Heck couplings,⁵ oxidation,^{15,16} allylic alkylation,^{6,17} Stille couplings, Knoevenagel condensations and Michael additions,¹⁸ nucleophilic additions,¹⁹ asymmetric hydrogenations,²⁰ and so on. This is a broad and rapidly expanding subject, which we and others have recently reviewed.^{21–25} However, little attention has been paid to the use of dendrimers in heterogeneous catalysis. This review is therefore going to concentrate on the significant achievements within the new and exciting area of *heterogeneous* dendrimer supports for catalysis. In contrast to heterogeneous polymer catalysts, research to date on heterogeneous and solid supported dendrimeric catalysts has been limited, and examples of such systems in the recent literature date back to 1999.

The aim of this review is to discuss the key examples in *heterogeneous–solid supported dendrimeric catalysis* and, where possible, provide a comparison with homogenous dendrimer catalysts and classical polymers (in terms of catalytic activity, selectivity and recyclability *etc.*). However, there is some overlap with homogenous dendrimer catalysts with respect to the types of reaction that can be catalysed and the supporting dendrimer structure.

The majority of this review is concerned with solid supported dendrimer catalysts; a variation on the polymer support approach to catalysis is to use soluble dendrimers functionalised with catalytically active species attached to insoluble supports such as silica residues or polymer beads. Most dendrimer catalysts of this type are functionalised at the periphery with catalytic groups, however, core and inner branch functionalised solid supported dendrimer catalysts have also been developed. Dendrimer supported catalysts have the added advantage that the active catalyst and dendrimer are solvated, making the catalytic sites more available in solution (relative to polymers). Insoluble supported dendrimers are easy to remove from solutions as precipitates or *via* filtration. Another approach to dendritic catalysis is the use of truly heterogeneous (insoluble) dendrimer catalysts (although examples in the literature are extremely limited).

2 Heterogeneous and solid supported peripherally functionalised dendrimers in catalysis

So far, the main area of interest for supported dendrimeric catalyst ligands is in hydroformylation catalysis. The hydroformylation reaction²⁶ (Scheme 2) is a versatile method for



Scheme 2 Hydroformylation of styrene catalysed by rhodium complexed PAMAM dendrimers.

the functionalisation of C–C bonds, and is one of the largest industrial catalytic processes, producing millions of tons of aldehydes annually. The majority of industrial applications involve the production of linear aliphatic aldehydes, however, branched aromatic aldehydes are more important from the fine chemicals point of view as they provide valuable intermediates for the pharmaceutical industry (*e.g.* in the synthesis of Ibuprofen and Naproxen).^{27,28} Hence, there is a need for inexpensive and effective ways of producing branched aldehydes on an industrial scale. Some homogeneous dendrimeric hydroformylation catalysts were already known⁵ and these formed the basis for the development of solid supported systems.

Alper *et al.*²⁶ have recently developed heterogeneous diphosphonated polyamidoamine (PAMAM) derivatives adhered to a silica gel support and observed that when complexed to rhodium(I), these are excellent catalysts for the hydroformylation of aryl olefins and vinyl esters with the branched aldehydes being highly favoured over the linear analogues (as with the homogenous dendrimeric catalysts)⁵ (Scheme 2). The heterogeneous Rh(I) catalysts can be reused without noticeable loss of activity.

The PAMAM dendrimers up to generation 4 (2, 4, 8 and 16 terminal amines) were grown out divergently from protruding aminopropyl groups on the silica gel particles using the

standard method developed by Tomalia and co-workers⁸ (*i.e.* a repetitive sequence of Michael addition and amidation). The dendrimers on silica were phosphonated at the terminal amine groups and then complexed by reaction with a (dicarbonyl)-rhodium(I) chloride dimer to give the catalytic dendrimers (Fig. 3). Analysis revealed that the degree of rhodium complexation decreases significantly beyond the second generation, due to incomplete phosphonation arising from steric crowding of the terminal amine groups.

The catalytic activity of the supported dendrimers was studied using styrene, vinyl acetate, vinyl naphthalene and octene. Catalytic hydroformylation of styrene with G0, 1 and 2 catalysts at room temperature afforded the aldehydes in quantitative yields with high regioselectivity in favour of the branched product (Scheme 2). The G3 and G4 dendrimer complexes are significantly less active. Raising the reaction temperature to 65 °C substantially increases the activity of the higher generation catalysts but decreases the selectivity, for example, vinyl benzoate was converted to the branched product in 99% conversion and only a 18 : 1 ratio with the G3 catalyst. The turnover rates for the hydroformylation of styrene with the Rh–PPh₂–PAMAM–SiO₂ catalysts were in the order of 100–200 h⁻¹ for G0, 1, and 2, and 78 and 84 h⁻¹ for G3 and G4 at 25 °C. These silica supported PAMAM dendrimer–rhodium catalysts represent a novel and highly active class of catalysts for the hydroformylation of alkenes. The observed lower activity of the third and fourth generation catalysts was attributed to the effective low rhodium loading caused by steric effects. The catalysts can be removed by microporous filtration and washing with hexanes, and in some cases reused four times without significant loss in reactivity and selectivity.

Over the past 20 years the palladium catalysed Heck reaction, used in the coupling of aryl halides with vinylic substrates, has proved to be a versatile tool which allows easy access to often complex products from relatively simple substrates.^{29,30} Despite the practical ease of reaction and the reliably good yields, the Heck reaction has rarely developed past the laboratory method.³¹ This is primarily due to the expense of the palladium catalysts and high catalyst loadings required,³² and with homogenous systems, the removal of the catalyst is time consuming and costly. So, large-scale Heck reactions are only viable when the products are of high commercial value. However, homogenous dendrimeric catalysts for the Heck reaction have been developed recently, which overcome some of these problems. For example, Reetz and co-workers⁵ reported the use of a poly(propylene imine) dendrimer with 16 palladium complexed phosphino groups used to catalyse the Heck coupling of bromobenzene and styrene, affording (*E*)-stilbene in 90% yield. The catalyst was recovered by precipitation and reused several times without noticeable loss of activity.

Recently, in an attempt to extend the Heck reaction to the bulk chemical sector, several groups have developed non-polymeric heterogeneous catalytic systems,^{33,34} designed to reduce the cost and technical problems associated with the catalysts. For example, Ying *et al.*³⁵ developed a palladium(0) complex on silica that shows very high turnover rates, especially for activated bromoarenes, but the catalyst preparation requires specialist techniques. Most other examples in the literature use iodoarenes, but they are the most expensive and least available halides. Heterogeneous *polymer* supported metal complexes for catalysis of the Heck reaction have also attracted interest recently^{36,37} but despite advances in terms of increased turnovers and catalyst stability, there is still a lack of suitable systems for industrial use. Zhang *et al.*³⁷ used a polymer supported phenanthroline palladium catalyst for the arylation of acrylamide and found that catalytic activity decreased significantly with the use of tributylamine as the base, and catalyst preparation was complicated.

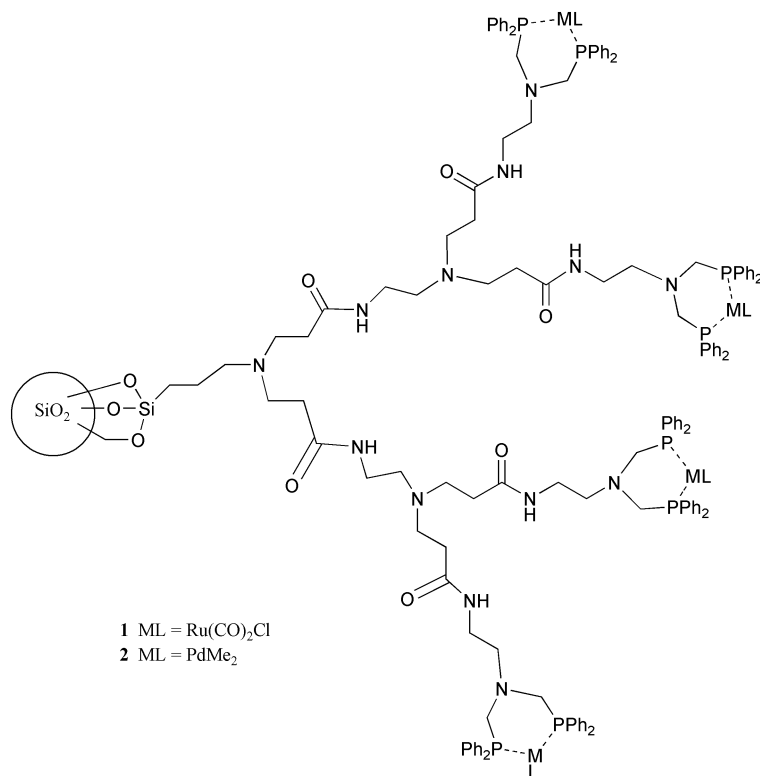
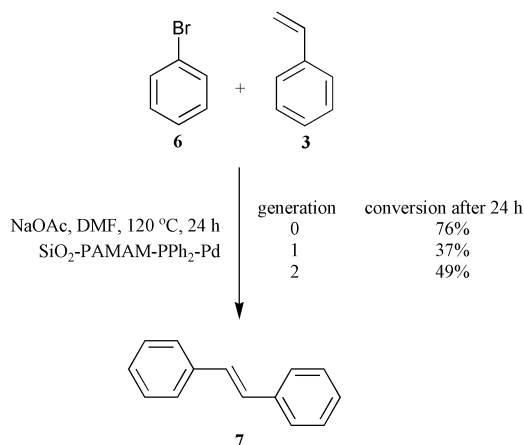


Fig. 3 Second generation PAMAM dendrimer–metal complex.

Alper *et al.*³⁸ extended the application of silica supported phosphine–rhodium terminated PAMAM dendrimers, to the use of palladium complexes for the catalysis of the Heck reaction. These catalysts are effective in the Heck reaction of aryl bromides with a range of alkenes (including styrene and butyl acrylate), affording coupling products in moderate to good yields. The palladium complexed dendrimers (Fig. 3) were prepared by reaction between palladium complex ([Me₂NCH₂CH₂NMe₂]PdMe₂) and the supported phosphine dendrimers (G0–4) and the products were isolated by microporous membrane filtration. As with the rhodium analogues, it was observed that the degree of complexation to palladium decreases significantly with dendrimer generation from G0 to G4. The utility of these Heck catalysts was assessed using the reaction between bromobenzene and styrene in the presence of sodium acetate (*i.e.* the same conditions as applied by Reetz and co-workers⁵ for their homogenous dendritic Heck system) and high yields of (*E*)-stilbene **7** were obtained using generation 0, 1 and 2 catalysts (Scheme 3) (although the yields were very low with generation 3 and 4 catalysts). The second generation catalyst **2** gives the highest turnover rate (81 h⁻¹). The effect of



Scheme 3 Heck coupling catalysed by solid supported dendrimer catalysts.

temperature was studied with the generation 2 catalyst and the best yields were obtained in the temperature range 110–140 °C; above 140 °C, catalyst deactivation occurs with noticeable formation of palladium black. The nature of the base used with this catalytic system is important and the inorganic bases potassium carbonate and sodium acetate give the best yields.

This second generation catalyst was also shown to be active in the Heck reaction for a wide range of substrates, and bromo and iodo reagents with similar yields (although no reaction occurs with the less reactive aryl chlorides). This is an important feature, as there is demand for effective Heck couplings using the cheaper and more available bromides. The yields achieved tend to be lower when the aryl halide has a *para*-electron withdrawing group, which is unusual and implies that the oxidative addition step is facile, with the alkene insertion or reductive elimination being the rate limiting step. The catalyst system was also found to be active for thiophenes with no catalyst poisoning.

Subsequent work³⁹ was carried out in an attempt to overcome the problems with steric crowding at the surface in higher generations, as described above. The chain length of the repeat units within the PAMAM dendrimer component was extended to relieve the steric crowding and congestion at the surface and therefore facilitate increased catalyst loading at higher generations. This was accomplished by the replacement of the ethylenediamine linker with 1,4-diaminobutane, 1,6-diaminohexane and 1,12-diaminododecane. Again, palladium complexed PAMAM dendrimers up to the fourth generation were constructed on the surface of aminopropyl silica.

Results from the catalytic hydroformylation of styrene and vinyl acetate showed that all generations and chain lengths of dendrimeric catalysts gave quantitative yields and high regioselectivity. As the chain length increased from C2 to C4 to C6 there was a massive increase in catalytic activity and recyclability (for any given generation), but there was no significant activity difference between the 6 and 12 carbon chain dendrimers. In contrast to the previous example,³⁸ the third and fourth generation dendrimers with C4, C6 and C12 spacers exhibited a similar degree of activity and regioselectivity as the smaller second generation dendrimer (Scheme 2). This was attributed

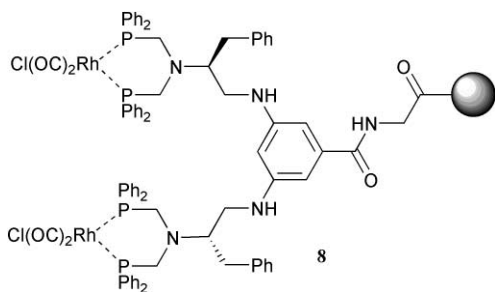
Table 1 Hydroformylation of styrene with SiO₂-PAMAM-Rh-PPh₂ catalysts

Generation	Spacer group	Temperature/°C	Conversion (%)	Branched-linear ratio
3	C-2	75	99	8 : 1
3	C-4	65	99	9 : 1
3	C-6	65	99	10 : 1
3	C-12	65	99	8 : 1
4	C-2	65	99	8 : 1
4	C-4	65	99	10 : 1
4	C-6	65	99	8 : 1
4	C-12	65	99	12 : 1

to the decreased crowding at the dendrimer surface resulting in higher (quantitative) rhodium loading. For example, 99% conversion and an 8 : 1 ratio in favour of the branched product was achieved with the fourth generation C6 linker catalyst (Table 1). This demonstrates the importance of the length of the spacer chain on catalytic activity and the potential of selectively synthesising branched phenyl propionaldehydes.

An alternative approach to catalytic hydroformylation by heterogeneously bound dendrimeric catalysts was reported in 2000⁴⁰ and represents the first solid phase synthetic approach to polystyrene supported dendrimers with surface phosphine groups capable of metal complexation. Polystyrene beads were used as the solid support in this case, but otherwise the strategy used is similar to the earlier example.⁵ There are several advantages to the use of polystyrene beads as a solid support *e.g.* the ease of solid phase synthesis using the building block approach, easy characterisation of the products after cleavage from the beads, and better swelling properties.

The repeat building block was synthesised in 3 steps from 3,5-diaminobenzoic acid. Dendrimer generations 1, 2 and 3 (with 2, 4 and 8 amino groups respectively) were assembled using solid phase synthesis on to FmocNH functionalised polystyrene beads. The Fmoc-Rink-amide MBHA (*p*-methylbenzhydrylamine) resin was treated with piperidine in DMF to deprotect the Fmoc group, the protected dendrimer repeat unit was then coupled to the free amine. Deprotection gave the supported first generation dendrimer with surface amine groups. The reaction sequence was then repeated to give the second and third generation supported dendrimers. All generations were subsequently phosphonated and reacted with chloro(dicarbonyl)rhodium(I) dimer to produce the corresponding rhodium complexes (Fig. 4).

**Fig. 4** First generation aromatic polyamide dendrimer-rhodium(I) complex.

The rhodium complexed dendrimers were tested as hydroformylation catalysts with a variety of olefins including styrene and vinyl acetate. As observed with the silica gel supported systems discussed previously, these bead supported aromatic polyamide dendrimer-rhodium complexes were highly active and regioselective (in favour of the branched products). Using the second generation catalyst at 45 °C, under standard hydroformylation conditions, complete conversion to the product occurred with high selectivity for the branched isomer (Scheme 2). In contrast to the previous examples, the second and third generation catalysts were found to be more active

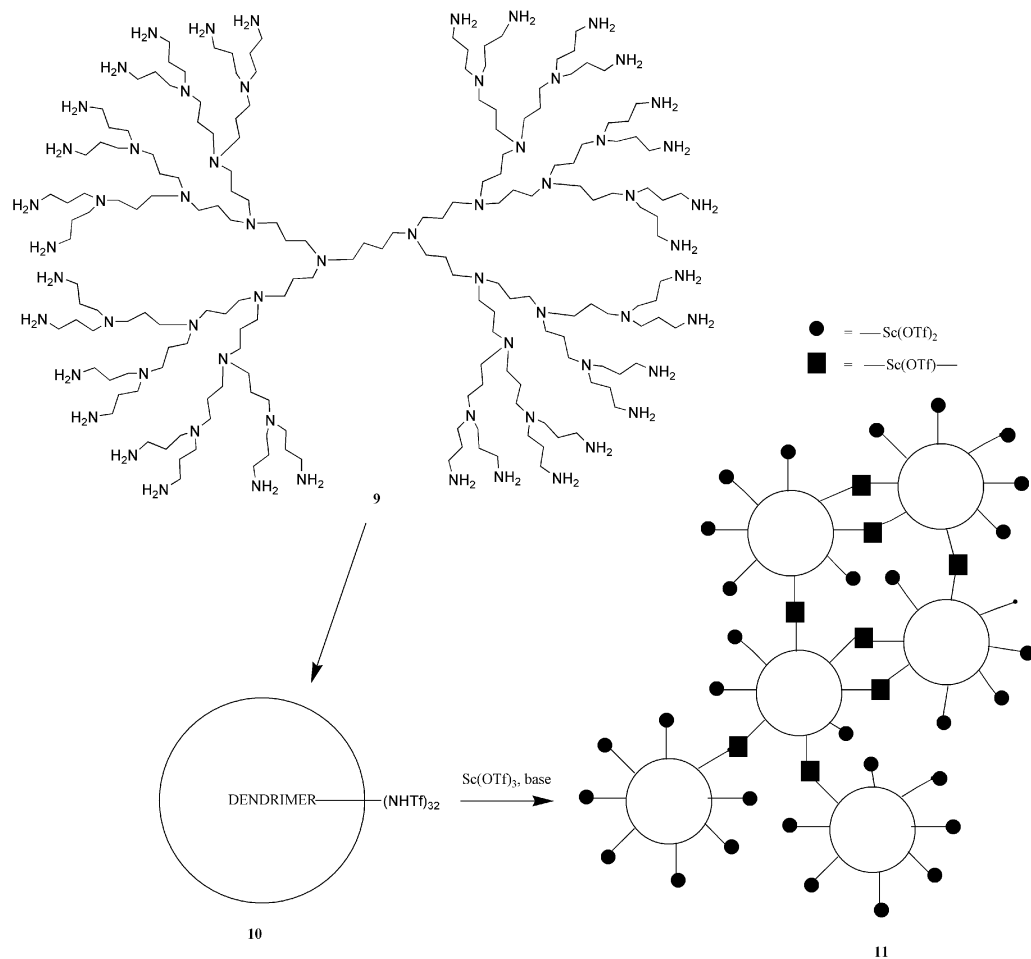
than the first generation, and the catalytic activity remained virtually unchanged up to the fifth cycle.

An example of heterogeneous dendrimeric catalysis involving the use of scandium containing cross linked dendrimers was reported by Reetz and Giebel.⁴¹ It was already established that scandium complexes containing withdrawing ligands such as Sc(OTf)₃, ScCl₃, Sc(PF₆)₃ or the polymer polyallyl scandium triflamide ditriflate (PA-Sc-TAD, triflic acid = trifluoromethanesulfonic acid) have useful catalytic properties (as Lewis acids) and are effective catalysts in a variety of reactions including Mukaiyama Aldol additions, Diels-Alder reactions, Michael additions and Friedel-Crafts acylations.^{42,43} Reetz and Giebel extended this principle to the use of dendrimers.

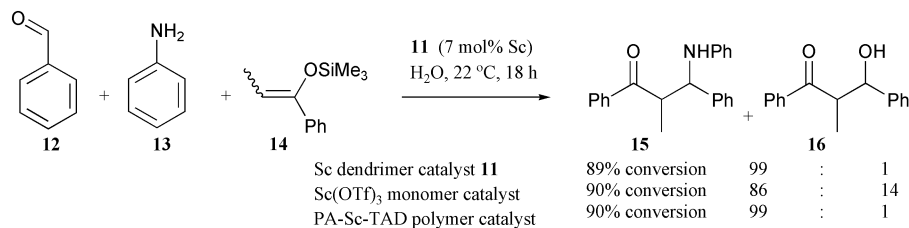
The commercially available poly(propylene imine) dendrimer with 32 surface amino groups **9** was subjected to sulfonylation using triflic anhydride and triethylamine to produce a poorly soluble solid, shown to be the fully functionalised product **10** by IR spectroscopy. Compound **10** was then treated with the cross linking agent Sc(OTf)₃ in the presence of base (to give nucleophilic substitution of Sc(OTf)₃ by either 1, 2 or 3 NH groups) which resulted in the formation of an insoluble, completely amorphous solid with a 40% scandium loading (represented by **11** in Scheme 4). In contrast to the examples described above, these heterogeneous materials are insoluble due to a scandium promoted cross linking of individual (soluble) dendrimer units, rather than an insoluble support attached to a soluble dendrimer.

Despite the amorphous, non-porous nature of the scandium containing cross-linked dendrimer **11**, initial investigations into the catalytic activity revealed that it is a highly chemoselective catalyst that can be recycled repeatedly without loss of activity or leaching of scandium. The 3-component reaction of benzaldehyde, aniline and the silane **14** with formation of the β -aminoketone **15** was tested first (Scheme 5). Scandium catalyst (7 mol%) was used and added to a two-phase system composed of water and the reagents. During the reaction a swelling of the solid catalyst occurred and it is thought likely that it is this that allows efficient transport of the reagents and therefore enables access to the catalytically active scandium centres in the interior of the material. The β -aminoketone **15** was isolated as the only product in 90% yield, and the recycled catalyst showed identical performance even after 3 runs.

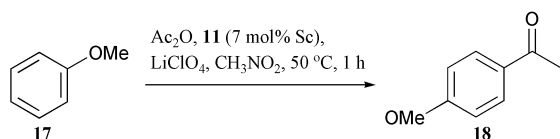
As illustrated in Scheme 5, the dendrimeric catalyst has similar catalytic properties to the related polymeric material PA-Sc-TAD,^{42,43} which also gives exclusive formation of the β -aminoketone **15**, whereas use of the monomeric catalyst scandium(III) triflate (10 mol%) gives rise to a mixture of **15** and **16**. The authors proposed that this trend is probably due to the influence of ligands rather than a *polymeric* or *dendrimeric effect*. In terms of practicality, the heterogeneous dendrimeric catalyst is easier to remove and recycle than the rubbery polymeric material. It was also demonstrated that dendrimer catalyst **11** could be used in organic solvents in the catalysis of a Diels-Alder reaction between vinyl ketone and a pentadiene derivative to form the *endo* product predominantly, and also in the catalysed acylation of anisole with acetic anhydride and LiClO₄ additive, to produce 4-methoxyacetophenone **18** in 73% yield (Scheme 6). This is the first example in the literature



Scheme 4 Synthesis of catalytic scandium containing cross-linked dendrimers.



Scheme 5 Catalysis of the Mukaiyama reaction by scandium containing dendrimer catalyst **11**.



Scheme 6 Acylation of anisole catalysed by scandium containing dendrimer catalyst **11**.

of a Friedel–Crafts acylation induced by a dendrimeric catalyst. In summary, it has been shown that scandium containing dendrimers of type **11** are stable, effective and environmentally benign heterogeneous catalysts with Lewis acid properties. They can be handled in air, used in organic or aqueous media and are easily recycled and reused without any appreciable loss of catalytic activity.

A somewhat different approach to heterogeneous dendrimeric catalysis was developed by Tilley *et al.*^{44,45} and involved the use of dendrimer based xerogels as catalyst supports. The use of the corresponding polymer gels in catalysis is already known, so this methodology was extended to the assembly of dendrimers into network structures by covalently linking the macromolecules together *via* a sol–gel protocol. In

principle, using spherical dendrimers in this way could lead to materials with well defined pore sizes and high surface areas, and furthermore, using dendrimers of various generations should allow the ultimate pore sizes and volumes of the product materials to be tailored for specific applications.

The dendrimeric starting materials used here were carbosilanes of various generations with trialkoxysilyl terminal groups. The second and third generations (with 36 and 108 terminal ethoxy groups) were hydrolysed, and then the resulting hydroxy functionalised dendrimers were left in solution with either benzene or THF for several days. The sols formed were solvent processed by washing with solvents of decreasing relative permittivities or with hot toluene, and air dried to give the xerogels as powders. These xerogels were found to be highly porous with relatively high surface areas and large pore volumes (although the surface areas varied depending on the method of solvent processing used). As expected, the sol–gel derived materials were useful catalysts and this was attributed to their high surface areas, ease of functionalisation and modifiable porosities. Various soluble metal complexes have been grafted onto these dendrimer based gels; for example, treatment of the second and third generation gels (with the highest surface

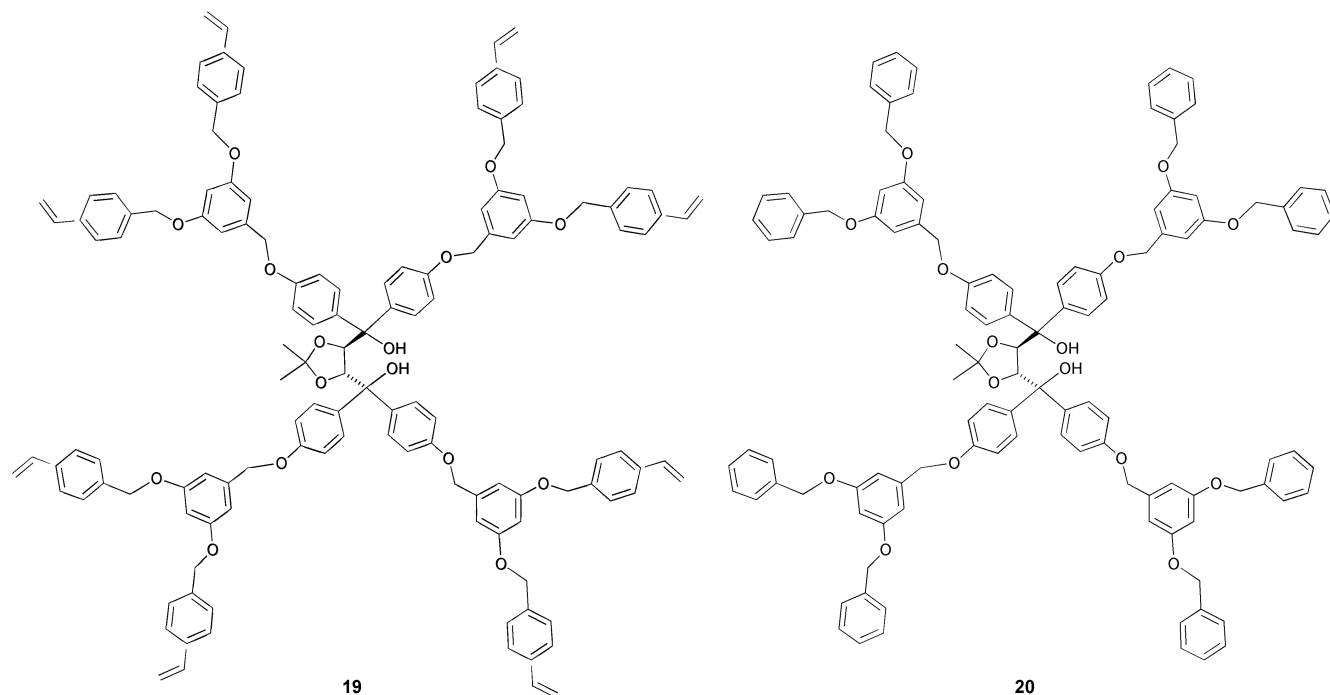


Fig. 5 Chiral TADDOL dendrimers with (19) and without (20) polymerisable surface groups.

areas) with soluble titanium complexes (e.g. $\text{Ti}(\text{O}^i\text{Pr})_4$ and $\text{Ti}[\text{O}(\text{Si}(\text{O}^i\text{Bu})_3)_4]$ provided heterogeneous catalysts for the epoxidation of alkenes). Catalytic epoxidation of cyclohexene was carried out, with cumene hydroperoxide as the oxidant, and all titanium catalysts were found to be highly active with no leaching of the grafted metal complexes from the gel supports. In all the titanium grafted dendrimer gels used, the selectivity (in terms of cyclohexene oxide) was 100% and the yields of product obtained after 2 hours were very high (76–97%), especially compared to that of the industrially used Shell catalyst (a polymer gel), which gave 23% conversion under the same conditions. In addition, high turnover numbers and initial rates ($5.3\text{--}9.1 \text{ mmol min}^{-1}(\text{g cat})^{-1}$) were achieved with the dendrimer gel catalysts.

3 Internally functionalised dendrimers in catalysis

Seebach and co-workers have recently described how a known *homogenous* dendritic catalyst can be incorporated within a polymer bead and used to great effect as a *heterogeneous* catalyst.⁴⁶ The dendrimer **19** (Fig. 5) contains vinyl groups on the surface, which were used as cross linkers during the copolymerisation of styrene to yield polystyrene beads [incorporating the (*R,R*)- $\alpha,\alpha,\alpha',\alpha'$ -tetraaryl-1,3-dioxolane-4,5-dimethanol (TADDOL)-functionalised dendrimers] with a diameter of about 400 μm (in their non-swollen state). The resulting polymer was then complexed with $\text{Ti}(\text{OCHMe}_2)_4$ to give the required Ti–TADDOLate catalyst. The catalysts were tested using the enantioselective addition of diethylzinc to benzaldehyde. Surprisingly, these polymerised heterogeneous catalysts seemed to outperform the equivalent non-polymerised dendritic catalyst **20** in terms of rate. It can be hypothesised that this increase in rate is due to control of the polar environment around the catalyst (*i.e.* the change in local polarity around the catalyst stabilises the transition state).

It can also be argued that the rigid and open structure around the catalyst enables reactants and products to diffuse freely in and out of the polymer, thus increasing the rate of reaction. Another advantage of these polymeric dendritic catalysts is that they can easily be recovered *via* filtration and used again. Seebach and co-workers report that no drop in enantioselectivity occurred after 20 reaction cycles.

In 2001, Alper *et al.*⁴⁷ reported the use of an improved solid supported dendrimer catalyst for hydroformylation reactions (Scheme 2). Previously, the main drawback with heterogenised catalysts has been leaching of the metals (e.g. rhodium) and this has negative implications for the lifetime and recycling potential of a catalyst. Alper *et al.* extended the basic principle demonstrated in their previous example²⁹ to design catalysts with reduced metal leaching and therefore prolonged lifetime and recyclability. The catalysts were designed according to the biomimetic based hypothesis that ‘ligands emerged in dendritic architectures may exhibit a prolonged reactivity by preserving the catalytic sites from the outer environment, and it may prevent the leaching of the metal’.⁴⁷ The key difference here relative to the hydroformylation catalysts described earlier is that the catalytic sites are located in the inner branches of the dendrimer. Heterogenised catalytic systems **21** and **22** were synthesised (Fig. 6), and although both of them contain two catalytic groups, they are exposed to very different environments. It was envisaged that the catalytic sites in **21** would be more exposed than those in **22**, and therefore **22** should exhibit better recycling behaviour (providing it is not too hindered to exhibit any reactivity).

The catalytic and recycling behaviour of catalysts **21** and **22** was examined. It was found that both catalysts were very reactive in the hydroformylation of styrene, *p*-methoxystyrene, vinyl acetate and vinyl benzoate and, as expected, the ligands **21** and **22** behaved differently in terms of recyclability. With all the examples studied, no reduction in reactivity was observed for **22** compared to **21**, although the larger more hindered catalyst **22** was found to have prolonged reactivity over several cycles. For example, with *p*-methoxystyrene, both catalysts were reactive up to the fourth cycle (>99%, 17 : 1 branched–linear), but the reactivity of **21** decreased significantly on the fifth cycle, whereas catalyst **22** was equally reactive up to the sixth cycle. Both catalysts were highly active in the hydroformylation of styrene and gave >99% conversion to the product (14 : 1 branched–linear) up to the sixth cycle.

Another example involving a dendrimer containing catalyst prepared by the sol–gel method was reported by Juwiler and Neumann in 2001.⁴⁸ The catalyst preparation involved the functionalisation of dendritic silanol **23** with bis(cyclopentadienyl)metal dichlorides [$\text{M} = \text{Ti}(\text{IV}), \text{Mo}(\text{VI}), \text{V}(\text{V}), \text{W}(\text{VI})$] to give **24** with isolated metal centres (Scheme 7). The metal

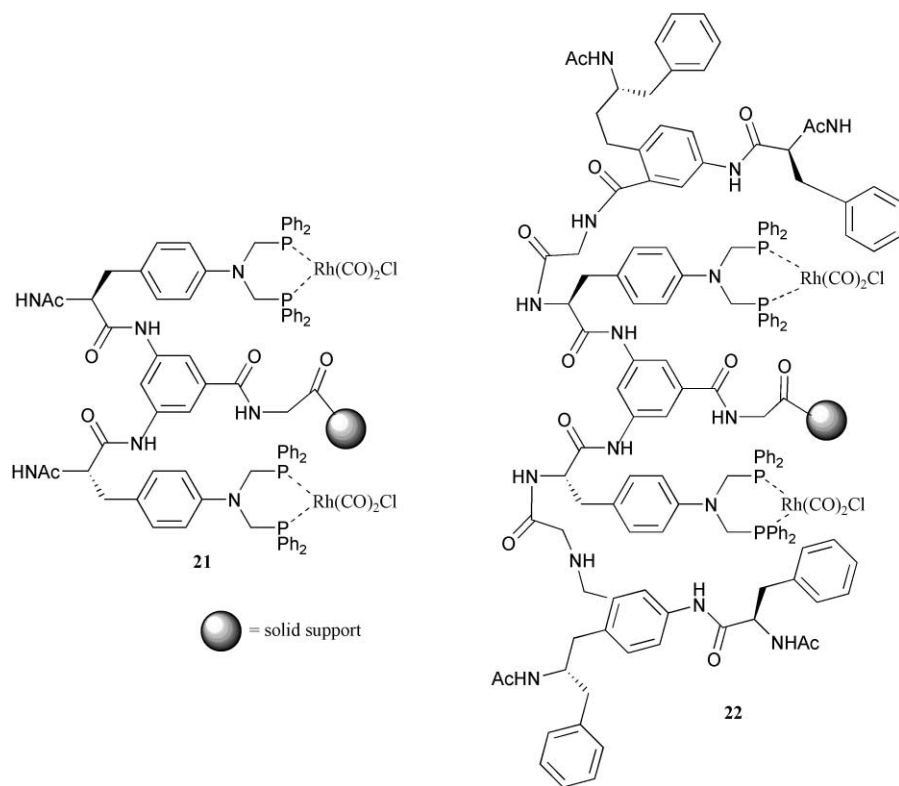
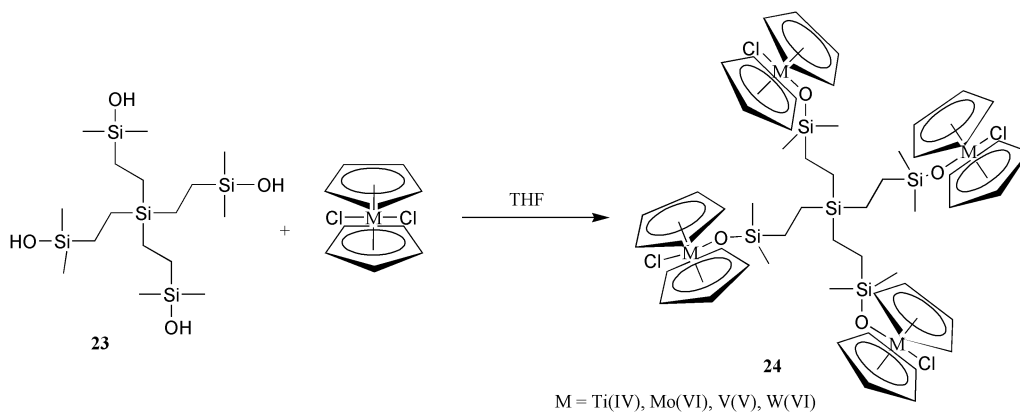


Fig. 6 Solid supported internally functionalised dendrimer catalysts for hydroformylation.



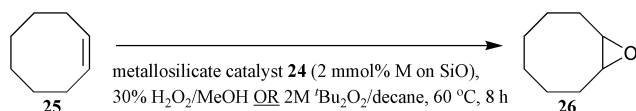
Scheme 7 Preparation of dendrimeric silane precursors for formation of metasilicate catalysts.

functionalised dendrimers were then encapsulated in the silicate sol-gel matrix and activated by calcination to produce heterogeneous catalysts. Non-dendritic amorphous catalytic silicates containing metal oxides are commonly synthesised by the sol-gel procedure,⁴⁹ but the main difficulty with this technique is in homogeneously dispersing the metal centres in the silica matrix. In contrast, the silicate matrix derived from **24** has a high dispersion of metal oxides and it has been shown that these catalysts have high activity for alkene epoxidation with *tert*-butyl hydroperoxide.

All catalysts investigated were active in the epoxidation of alkenes, and maximum activity was observed for the molybdenum containing material. The preliminary determination of catalytic activity was carried out using the highly active alkene, cyclooctene (Scheme 8). The order of metal activity was found to be Mo > Ti > V > W, and leaching

was negligible when the more highly active molybdenum and titanium catalysts were used under anhydrous conditions. The activity of the molybdenum catalyst was as good as that for other amorphous silicates; for example, >99% conversion of cyclooctene was achieved with the molybdenum dendritic silicate. The titanium catalyst was also highly active, giving 95% conversion of cyclooctene to cyclooctane oxide (Table 2).

As well as being highly active, the titanium and molybdenum catalysts were also relatively stable to the reaction conditions used, so given their success in the epoxidation of cyclooctene, these materials were tested with a range of alkenes. As expected, the reactivity depended on the nucleophilicity of the alkene, e.g. the less reactive terminal alkenes dec-1-ene and oct-1-ene gave 61% and 56% conversion respectively with the molybdenum catalyst. 2-Methylhept-2-ene was more active and was epoxidised in 90% conversion with the molybdenum catalyst. Further optimisation of the catalyst was carried out by changing the loading of the transition metal in the silicate. For the molybdenum and titanium catalysts, it was found that 2 mol% metal gives optimum catalytic activity. This indicates that at this concentration, most metal sites are isolated and accessible to the oxidant and substrate, whereas at higher



Scheme 8 Oxidation of cyclooctene catalysed by dendrimeric metasilicates.

Table 2 Epoxidation of cyclooctene catalysed by dendrimeric metallosilicates

Metallosilicate	Conversion (selectivity) %	Conversion (selectivity) %
	30% hydrogen peroxide oxidant	6 M <i>tert</i> -butyl peroxide oxidant
Ti(IV)	39 (98)	95 (99)
V(V)	12 (94)	81 (95)
Mo(VI)	46 (99)	>99 (99)
W(VI)	51 (85)	20 (99)

loadings accessibility and site isolation are probably more limited.

4 Conclusion

Catalysis using *homogenous* metallo dendrimers has received considerable attention over the last 6–7 years, the aim of this review however has been to demonstrate that there is also a noticeable trend toward *supported* or *heterogeneous* dendritic catalysts. Supported and heterogeneous dendrimers have been involved in several aspects of catalysis over the last 3 years. The high definition and regular distribution of catalytic sites and the clear possibility to recover and recycle the dendritic catalysts has been fully demonstrated. Numerous examples of dendritic transition metal catalysts based on different dendrimer backbones functionalised at various locations have been described.

Before the advent of dendrimeric catalysts, immobilisation of a catalytic species on a solid bead or polymer support typically resulted in a significant decrease in the activity of a catalyst. However, with the incorporation of dendrimers into solid supported and heterogeneous catalysts, the situation has improved. Several examples have been highlighted in which high activity and prolonged catalyst lifetimes are achieved. In many of these cases the dendrimer containing structures have commonly outperformed their analogous homogenous or polymer supported systems. For example, the silica supported dendrimeric palladium complex developed by Alper and co-workers³⁸ for Heck reactions proved to be highly active for a variety of substrates and the catalyst could be removed easily and recycled without loss of activity. In contrast, the corresponding polystyrene–palladium catalyst became deactivated quickly under the same reaction conditions. Reetz and Giebel⁴¹ reported the use of a scandium containing cross linked dendrimer as a heterogeneous Lewis acid catalyst. The dendrimeric catalyst was equally active and selective compared to the corresponding polymeric catalyst for the Mukaiyama Aldol addition. In terms of practicality, it was much easier to handle and recycle than the rubbery polymeric material.

Some of the more recent examples described in this review involve the incorporation of internally functionalised dendrimers into solid supported and heterogeneous catalysts. The ability to mimic enzymes is clear when catalysis occurs inside a dendrimer. For example, Seebach and co-workers⁴⁶ described how a known homogenous dendritic catalyst can be incorporated within a polymer (*via* copolymerisation of the vinyl terminated dendrimer with styrene) and used as a heterogeneous catalyst. The resulting catalyst is superior to the homogenous analogue (in terms of rate), the difference being attributed to the polar environment around the catalytically active sites in the heterogeneous material.

The examples described above strongly support the possibility of achieving high reactivities in heterogeneous and solid supported systems. The origin of this high reactivity is thought to be due to the presence of well exposed ligands, which are more accessible compared to the catalytic sites in irregular shaped polymeric materials. Cooperativity may be the other factor playing a role in the higher reactivities. It is clear that this is a rapidly expanding area of chemistry that is still in its infancy and has great potential for future applications, both industrially and on a laboratory scale.

5 References

- D. A. Annis and E. N. Jacobson, *J. Am. Chem. Soc.*, 1999, **121**, 707.
- N. Moszner, T. Volkel and V. Rheinberger, *Macromol. Chem. Phys.*, 1996, **197**, 621.
- N. S. Clair, Y. F. Wang and A. L. Margolin, *Angew. Chem., Int. Ed.*, 2000, **39**, 380.
- S. J. Fritschel, J. J. H. Ackerman, T. Keyer and J. K. Stille, *J. Org. Chem.*, 1979, **44**, 3152.
- M. T. Reetz, G. Lohmer and R. Schwickardi, *Angew. Chem., Int. Ed.*, 1997, **36**, 1526.
- D. Degroot, E. B. Eggeling, J. C. De Wilde, H. Kooijman, R. J. Van Haaren, A. W. Van der Made, A. L. Spek, D. Vogt, J. N. H. Reek, P. C. J. Kramer and P. W. N. M. Van Leeuwen, *Chem. Commun.*, 1999, 1623.
- G. R. Newkome, Z. Q. Yao, G. R. Baker and V. K. Gupta, *J. Org. Chem.*, 1985, **50**, 2003.
- D. A. Tomalia, H. Baker, J. Dewald, M. Hall, G. Kallos, S. Martin, J. Roeck, J. Ryder and P. Smith, *Polym. J.*, 1995, **17**, 117.
- C. Hawker and J. M. J. Fréchet, *J. Chem. Soc., Chem. Commun.*, 1990, 1010.
- C. Hawker and J. M. J. Fréchet, *J. Am. Chem. Soc.*, 1990, **112**, 7638.
- K. L. Wooley, C. J. Hawker and J. M. J. Fréchet, *J. Am. Chem. Soc.*, 1991, **113**, 4252.
- G. R. Newkome, C. N. Moorefield and F. Vögtle, *Dendritic molecules*, VCH, Weinham, 1996.
- G. Van Koten and J. T. B. H. Jastrzebski, *J. Mol. Catal. A: Chem.*, 1999, 317.
- C. Hawker and J. M. J. Fréchet, *J. Chem. Soc., Chem. Commun.*, 1990, 1010.
- C. Francavilla, F. W. Bright and M. R. Detty, *Org. Lett.*, 1999, **1**, 1043.
- P. Bhyrappa, J. K. Young, J. S. Moore and K. S. Suslick, *J. Am. Chem. Soc.*, 1996, **118**, 5708.
- G. E. Oosterom, R. J. van Haaren, J. N. H. Reek, P. C. J. Kramer and P. W. N. M. van Leeuwen, *Chem. Commun.*, 1999, 1119.
- V. Maraval, R. Laurent, A. M. Caminade and J. P. Marjoral, *Organometallics*, 2000, **19**, 4025.
- P. B. Rheiner and D. Seebach, *Chem. Eur. J.*, 1999, **5**, 3221.
- H. Brunner and S. Altmann, *Chem. Ber.*, 1994, **127**, 2285.
- G. van Koten and J. T. B. H. Jastrzebski, *J. Mol. Catal. A: Chem.*, 1999, **146**, 317.
- G. E. Ooestrom, J. N. H. Reek, P. C. J. Kramer and P. W. N. M. van Leeuwen, *Angew. Chem., Int. Ed.*, 2001, **40**, 1828.
- L. J. Twyman, A. S. H. King and I. K. Martin, *Chem. Soc. Rev.*, 2002, **31**, 69.
- D. Astruc and F. Chardac, *Chem. Rev.*, 2001, 2991.
- L. J. Twyman and A. S. H. King, *J. Chem. Res.*, 2002, 43.
- S. C. Bourque, F. Maltais, W. J. Xiao, A. Tardif, H. Alper, P. Arya and L. E. Manzer, *J. Am. Chem. Soc.*, 1999, **121**, 3035.
- B. G. Reuben, H. Wittcoff, *Pharmaceutical chemicals in perspective*, Wiley, New York, 1989.
- K. Tamao, K. Sumitami, Y. Kiso, M. Zembayashi, A. Fujioka, S. Kodama, I. Nakajima, A. Minato and M. Kumada, *Bull. Chem. Soc. Jpn.*, 1976, **49**, 1958.
- R. F. Heck, *Comprehensive organic synthesis*, eds. B. M. Trost and I. M. Fleming, Pergamon, Oxford, 1991, 883.
- A. de Meijer and F. E. Meyer, *Angew. Chem., Int. Ed.*, 1994, **33**, 2379.
- B. Cornils, W. A. Herrmann, *Applied homogenous catalysis with organometallic compounds*, VCH, Weinham, 1996.
- R. F. Heck, *Acc. Chem. Res.*, 1979, **12**, 146.
- M. T. Reetz and G. Lohmer, *Chem. Commun.*, 1996, 1921.
- M. Beller, H. Fisher, K. Kuhlein, C. P. Reisinger and W. A. Herrmann, *J. Organomet. Chem.*, 1996, **520**, 257.
- C. P. Mehnert and J. Y. Ying, *J. Am. Chem. Soc.*, 1998, **120**, 12288.
- M. K. Terasawa, T. Kanda, Y. Imanaka and S. Ternashi, *J. Organomet. Chem.*, 1978, **162**, 403.
- Z. Zang, Y. Pan, H. W. Hu and T. Y. Kao, *Synthesis*, 1991, 539.

- 38 H. Alper, P. Arya, S. C. Bourque, G. R. Jefferson and L. E. Manzer, *Can. J. Chem.*, 2000, **78**, 920.
- 39 S. C. Bourque and H. Alper, *J. Am. Chem. Soc.*, 2000, **122**, 956.
- 40 P. Arya, N. V. Rao, J. Singkhonrat, S. C. Bourque and H. Alper, *J. Org. Chem.*, 2000, **65**, 1881.
- 41 M. T. Reetz and D. Giebel, *Angew. Chem., Int. Ed.*, 2000, **39**, 2498.
- 42 S. Kobayashi, *Eur. J. Org. Chem.*, 1999, 15.
- 43 S. Kobayashi and S. Nagayama, *Synlett*, 1997, 653.
- 44 J. W. Kriesel and T. D. Tilley, *Polym. Prepr.*, 2000, **41**, 566.
- 45 J. W. Kriesel and T. D. Tilley, *Chem. Mater.*, 2000, **12**, 1171.
- 46 D. Seebach, A. K. Beck and A. Heckel, *Angew. Chem., Int. Ed.*, 2001, **40**, 92.
- 47 P. Arya, G. Panda, N. V. Rao, H. Alper, S. C. Bourque and L. E. Manzer, *J. Am. Chem. Soc.*, 2001, **123**, 2889.
- 48 D. Juwiler and R. Neumann, *Catal. Lett.*, 2001, **72**, 241.
- 49 C. J. Brinker, G. W. Scherer, *Sol-Gel Science*, Academic Press, Boston, 1990.