

# Dendritic Catalysts and Dendrimers in Catalysis

Didier Astruc\* and Françoise Chardac

Laboratoire de Chimie Organique et Organométallique, UMR CNRS N°5802, Université Bordeaux I, 33405 Talence Cedex, France

Received April 6, 2001

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\* To whom correspondence should be addressed. E-mail: d.astruc@lcoo.u-bordeaux.fr.



Didier Astruc has been a Professor of Chemistry at the University of Bordeaux I since 1984 and a Senior Member of the Institut Universitaire de France since 1995. He studied in Rennes, where he passed his thesis before a post-doc at MIT (Cambridge) with R. R. Schrock. He is the author, inter alia, of *Electron Transfer and Radical Processes in Transition-Metal Chemistry* (VCH, 1995, prefaced by Henry Taube) and *Chimie Organométallique* (EDP Science, 2000). He has been Awarded the Prize of the Coordination Chemistry Division of the French Chemical Society (1981), the German-French Alexander von Humboldt Prize (1989), and the Le Bel Prize of the French Chemical Society (2000). His scientific interests are presently in the field of nanosciences, especially dendrimers, polymers, and colloids, and their applications as sensors, catalysts, and enzyme mimics.



Françoise Chardac (formerly Piscioti) was born in Poitiers and studied in Bordeaux. She passed her Diplôme under the supervision of Professor R. Lalande in terpene chemistry. Then she collaborated with Professor R. Calas and Dr. J. Dunoguès in organosilicon chemistry in the Laboratoire de Chimie Organique et Organométallique of the University of Bordeaux I, where she is doing a literature search at present.

## I. Introduction and Scope

The field of dendrimers<sup>1–5</sup> was developed in the late 1970s<sup>6</sup> and early 1980s<sup>7–11</sup> and has exploded during the past decade.<sup>12–38</sup> This situation is due, beyond the aesthetics appeal, to their great potential of applications in biology and materials science. Among the main potential applications of dendrimers, catalysis stands as one of the most promising ones. Indeed, dendrimers offer a unique opportunity to combine the advantages of homogeneous and heterogeneous catalysis yet keep the well-defined molecular features required for a fully detailed analysis of the catalytic events.<sup>39,40</sup> It is possible to tune the structure, size, shape, and solubility of dendrimers and metallodendrimers at will and to locate catalytic sites at the core or at the periphery.<sup>30,31</sup> A large number and variety

of metallodendrimers are now known, and excellent reviews are available.<sup>25,29–35</sup> It is clear that designs are without frontier in the field. It has been demonstrated that, as expected, it is possible to remove the catalyst from the reaction medium after a reaction carried out in the presence of a metallodendritic catalyst. This is achieved by precipitation or techniques which are familiar to the biochemists, e.g., ultrafiltration or ultracentrifugation. Membrane reactors are presently developed for this purpose. Organometallic and inorganic catalysts<sup>41–45</sup> supported on organic polymers such as polystyrene or inorganic polymers such as silica have been investigated for some time,<sup>46–51</sup> but dendrimers now offer a much better control of the number, shape, and structure of the catalytic sites and of their microenvironment.

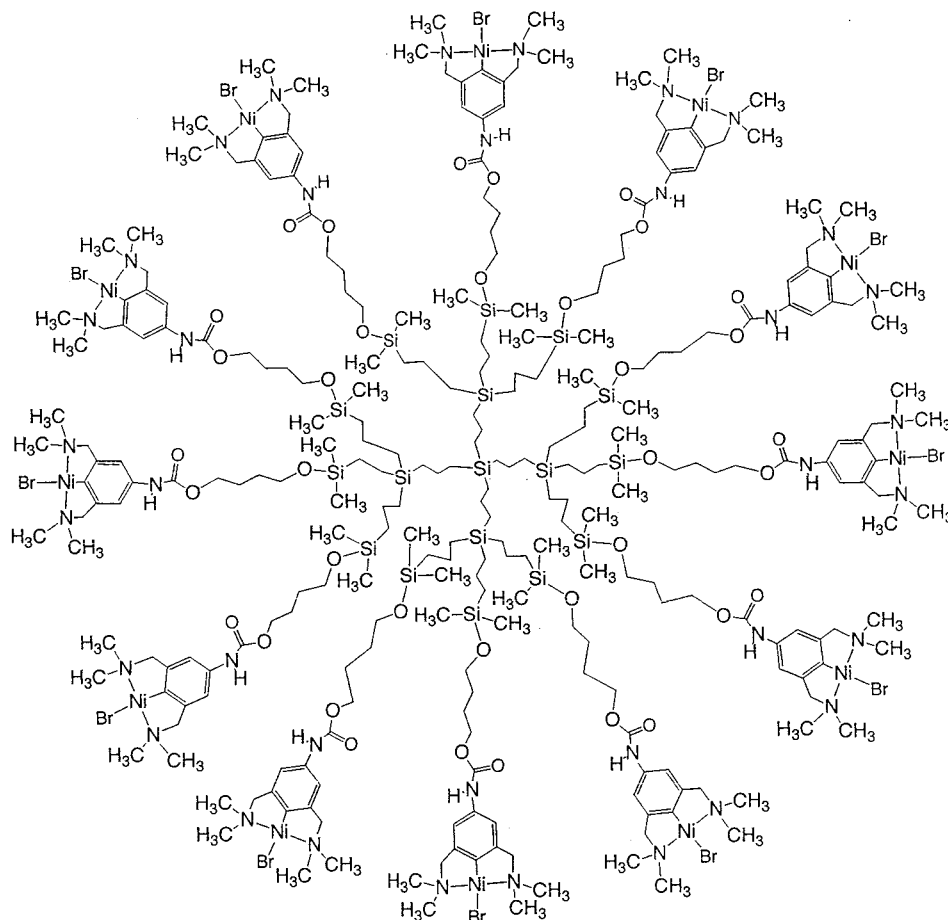
The field of dendrimers has been repeatedly reviewed,<sup>1–4,14–38</sup> and catalytic applications have been frequently mentioned and even the subject of short review sections.<sup>30,31</sup> The field has not yet been the subject of a review per se because most papers on dendritic catalysts have appeared in the last 2 years. Therefore, the present review is timely to detail and discuss the results which have been obtained in the area. Although the first publications appeared in 1994 and despite their promising and pioneering value, few positive dendritic effects were observed in these early studies but appeared recently. Moreover, considerable efforts have been realized in the last 2–3 years to recover the catalyst and reuse it as many times as possible without too much of decrease in efficiency. It is becoming more and more obvious that dendritic catalysts will be applicable in the close future. New classes of nanostructured materials with well-defined porosities have potential applications in catalysis,<sup>46–51</sup> and some of them are made from dendrimers. They will be noted in this review. Dendrimers are often also themselves constructed using catalytic reactions (e.g., hydrosilylation, Pd-catalyzed carbon–carbon coupling), but this classical aspect is not incorporated in this review except a quick journey in the world of polymerization catalysts in section XIV.

The broadest class of dendritic catalysts is related to homogeneous catalysis, although some supported and heterogeneous dendritic catalysts now also appear. Moreover, the field of dendritic catalysts and dendrimers in catalysis spreads into various areas of organic, inorganic, materials, biological, and polymer chemistry, as can be seen above in the Table of Contents.

## II. Homogeneous Catalysis by Non-Chiral Dendritic Transition-Metal Complexes

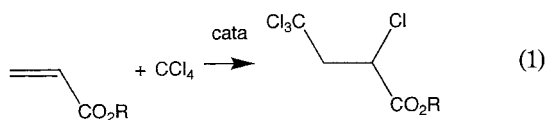
### 1. Kharasch Addition of CCl<sub>4</sub> to Methacrylate Catalyzed by Ni<sup>II</sup>

In their seminal work, van Koten et al. prepared carbosilane dendrimers with, at the periphery, 12 branches containing diaminoaryl nickel(II) groups (Figure 1) that catalyze the Kharasch addition of tetrachloromethane to methacrylate (a classic ex-



**Figure 1.** van Koten's metallodendrimer that catalyzes the Kharasch additions of polyhalogenoalkanes to C=C bonds (eq 1).

ample of anti-Markovnikov addition that follows a radical mechanism, eq 1).<sup>52,53</sup> These dendritic cata-



lysts have turnover frequencies which are 30% lower than those obtained with monomeric or polymer-bound analogues.<sup>54</sup> Possibilities of ultrafiltration were already foreseen at this early stage of the field. Later, these authors disclosed a negative dendritic effect on the atom-transfer radical addition (ATRA) in the case of the Kharasch addition of  $\text{CCl}_4$  to methacrylate catalyzed by dendrimers terminated by  $\text{Ni}^{\text{II}}$  sites with their "pincer" aryldiamino ligand. During the catalytic runs using the metallodendrimers with 12 and 36 branches, purple to brown precipitates formed and they lost catalytic activity. The authors suggested that, in these precipitates, the  $\text{Ni}^{\text{II}}$  sites were partly irreversibly oxidized to  $\text{Ni}^{\text{III}}$  sites, indicating that the back reaction of the  $\text{Ni}^{\text{III}}$  sites with the product radical or with the initial radical  $\text{CCl}_3\cdot$  became less efficient with time. Molecular modeling showed that the Ni-Ni intersite distance was relatively small in the metallodendrimers, causing Cl bridging in mixed-valence intermediates responsible for inhibition in congested metallodendrimers.<sup>55</sup> Preliminary investigations have shown

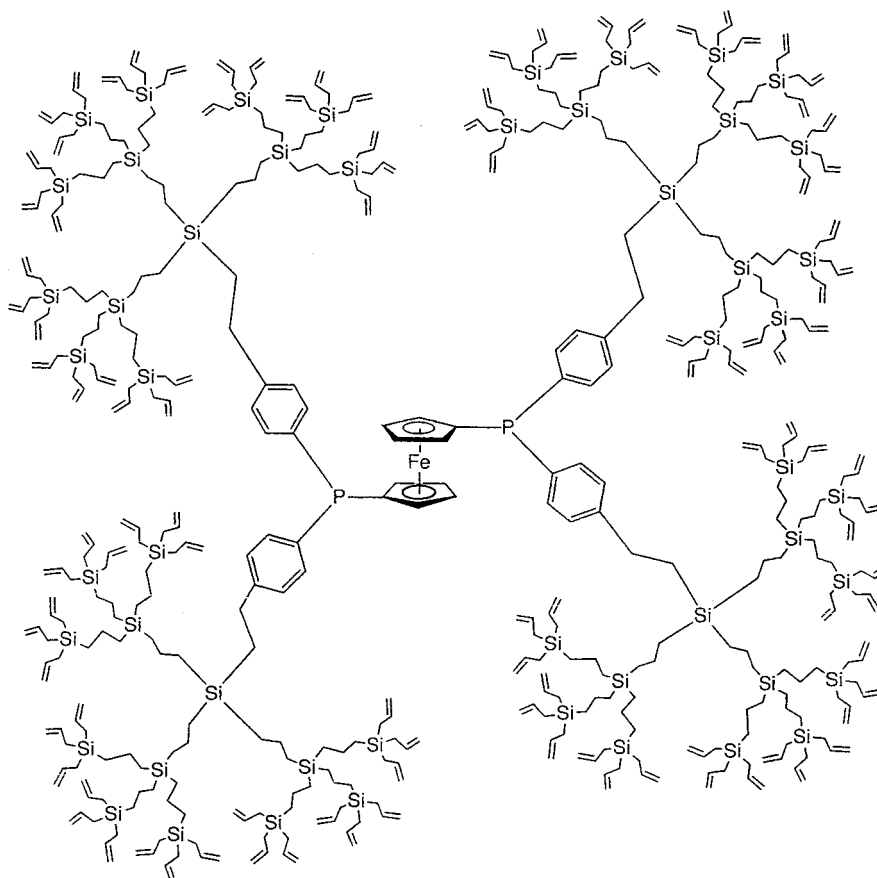
that the application of this catalytic system in a continuous process using a membrane reactor was possible.<sup>56</sup> The van Koten group also described the use of amino acid dendrimers as molecular scaffolds for the attachment of catalytically active organometallic Ni "pincer" complexes via a urea functionality. The activity of these dendritic catalysts in the Kharasch addition of  $\text{CCl}_4$  to methyl methacrylate is comparable to that of their mononuclear analogues  $[\text{NiX}(\text{NCN})]$ , carbosilane dendrimers, or polymer-supported complexes. Hence, the presence of polar functional groups does not adversely influence catalytic performance.<sup>57</sup>

## 2. CO/Alkene Polymerization Catalyzed by $\text{Pd}^{\text{II}}$

van Leeuwen is one of the pioneers of the field of dendrimer catalysis. When he was at Shell, his group reported a star-shaped hexaphosphine-palladium catalyst with a benzene core for polyketone formation from alternating CO/alkene polymerization. While the monometallic catalyst gave 50% fouling (precipitation of the polymer on the wall of the reactor), this star-shaped catalyst gave only 3% fouling, possibly for solubility reasons. This is also a very early "dendritic effect".<sup>58,59</sup>

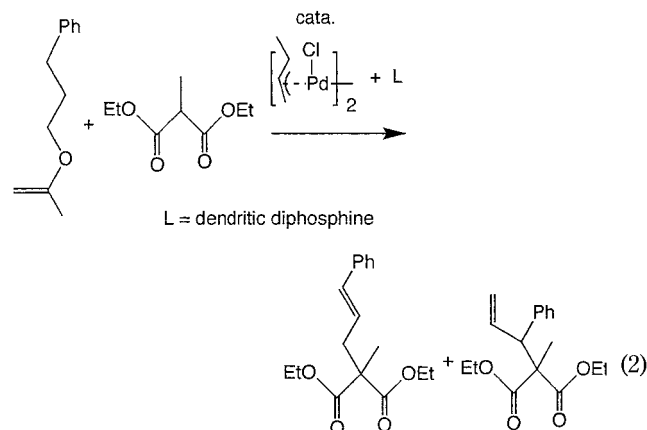
## 3. Palladium-Catalyzed Allylic Alkylation

The van Leeuwen group synthesized a series of diphosphine ligands centered on 1,1'-bis-diphenylphos-



**Figure 2.** van Leeuwen's diphosphine ligands centered on 1,1'-bis-diphenylphosphinoferrocene bearing dendritic carbosilane substituents at the para aryl positions whose palladium complexes catalyze allylic alkylations (eq 2).

phinoferrocene-bearing dendritic carbosilane substituents at the para aryl positions in a divergent manner (Figure 2). Reactions with  $[\text{Pd}(\text{MeCN})_2\text{Cl}_2]$  afforded the ferrocene-centered chelate complexes, and these metallodendrimers were shown to be efficient in palladium-catalyzed allylic alkylation (eq 2). The linear trans product was mainly obtained.



The rate of the reaction decreased, however, as the dendritic generation increased. This negative dendritic effect was attributed to the more difficult mass transport with increasing the steric bulk of the dendritic wedges and was more pronounced when going from generation 2 to 3. Remarkably, the size of the metallodendrimer also determined the selectivity of the allylic alkylation reaction, because the dendritic bulk hindered the attack of the nucleophile

on the Pd-allyl moiety.<sup>59a</sup> Steric interactions between the branches and increase of the P-Pd-P bite angle preferentially lead to the linear product.

van Leeuwen's group has also synthesized functionalized carbosilane dendrimers. Their palladium complexes have been used as catalysts in the allylic alkylation performed in a continuous membrane reactor. The second-generation carbosilane dendrimer served as a starting point. It is a white solid whose X-ray crystal structure could be determined and whose molecular volume of  $2414 \text{ \AA}^3$  was anticipated to be large enough for separation of the catalyst from the reaction mixture by nanofiltration. The phosphine-functionalized dendrimers of generation 0, 1, and 2 were synthesized by hydrosilylation of double bonds with chlorodimethylsilane or dichloromethylsilane followed by reaction with  $\text{Ph}_2\text{PCH}_2\text{-Li/TMEDA}$ . The dendritic phosphine of higher generation such as that with 72 phosphines could not be prepared because of steric congestion. The phosphine dendrimers were allowed to react with  $[\text{PdCl}(\eta^3\text{-C}_3\text{H}_7)]_2$  yielding either bidendate palladium phosphine dendrimers or mixtures when monodentate dendritic phosphines were used as ligands. All the metallodendrimers were used as catalysts in the allylic alkylation of allyl trifluoroacetate and sodium diethyl methyl malonate yielding diethyl allylmethylmalonate. The reaction was first carried out in a batch process, and all the metallodendrimers showed a very high catalytic activity. Using 0.2% of catalyst, the yield was larger than 80% after 30 min and only small differences of reaction rates were observed for

the different catalysts. In a continuous process using a membrane reactor, the metallodendrimer containing 12 chelated palladium atoms with a calculated volume of about 7600 Å<sup>3</sup> was used as the catalyst. The retention of this catalyst in the membrane reactor was determined to be 98.1%, which corresponds to a calculated value of only 25% of decreased activity after flushing the reactor 15 times. Samples taken from the flow were not catalytically active, which confirms that the observed decrease of activity was due to decomposition of the palladium complex and not to loss of the dendritic catalyst.<sup>59b</sup>

#### 4. Hydrogenation of Olefins

Mizugaki et al. examined the selective hydrogenation of conjugated dienes to monoenes using an atmospheric pressure of H<sub>2</sub> at 25 °C by the dendritic catalyst DAB-*dendr*-[N(CH<sub>2</sub>PPh<sub>2</sub>)<sub>2</sub>PdCl<sub>2</sub>]<sub>16</sub> prepared by reaction of Reetz's dendritic phosphine (vide infra) with [PdCl<sub>2</sub>(PhCN)<sub>2</sub>]. The excellent selectivity of the hydrogenation of cyclopentadiene to cyclopentene is remarkable. The catalytic activity was higher than that of the corresponding monomer [PdCl<sub>2</sub>{PhN(CH<sub>2</sub>-PPh<sub>2</sub>)<sub>2</sub>}] and the polystyrene-bound catalyst. The metallodendrimer was less active than Pd/C and Pd/Al<sub>2</sub>O<sub>3</sub>, but these heterogeneous catalysts are not selective contrary to the dendritic catalyst. Another remarkable feature of this system is that the hydrogenation of 1,3-cyclooctadiene by the same dendritic-PdCl<sub>2</sub> complex occurred with much higher rates than by the monometallic catalyst. Interestingly, this reaction was very efficient in ethanol in which the dendritic catalyst was not soluble whereas it was slow in DMF in which it was soluble. Thus, heterogeneization renders the system efficient. Rationalization of all these features would be speculative, but it seems that the active metallic sites are well accessible on the surface of the heterogeneous catalyst. The dendritic catalyst was easily recovered from reaction mixtures by centrifugation and reused without much loss of activity.<sup>67</sup>

#### 5. Rhodium-Catalyzed Hydroformylation

The Reek and van Leeuwen group synthesized diphenylphosphine-functionalized carbosilane dendrimers Si{(CH<sub>2</sub>)<sub>n</sub>Si(CH<sub>3</sub>)<sub>2</sub>(CH<sub>2</sub>PPh<sub>2</sub>)<sub>2</sub>}<sub>4</sub> (*n* = 2, 3; generations 1–3) and Si{(CH<sub>2</sub>)<sub>n</sub>Si(CH<sub>3</sub>)(CH<sub>2</sub>PPh<sub>2</sub>)<sub>2</sub>}<sub>4</sub> (*n* = 2, 3; generation 1, 2), and used these ligands for rhodium-catalyzed hydroformylation of 1-octene. These metallodendrimers gave the same selectivity as their monomer analogues, and activities depended on the size and flexibility of the dendrimers.<sup>59c</sup>

Reetz et al. modified Meijer's 16-branch polypropylene imine dendrimer with chelating diphenylphosphine ligands, which led to a 32-branch phosphine dendrimer. This polyphosphine dendrimer formed complexes with various transition-metal groups such as PdMe<sub>2</sub> or Rh(cod) BF<sub>4</sub> (cod = 1,5-cyclooctadiene) which had catalytic properties.<sup>62</sup> Hydroformylation of 1-octene with the Rh<sup>I</sup> dendritic catalyst showed a turnover number comparable to that of the monomer.<sup>62</sup> It was pointed out that such catalysts could be separable by membrane separation techniques.<sup>63,64</sup>

Gong et al. synthesized four water-soluble dendritic phosphonated ligands based on PAMAM dendrimers

of generation 3 (32 end groups) with the hydrophilic amine or sulfonic acid group on the surface of the dendrimer. For this purpose, the PAMAM dendrimers were allowed to react with [Ph<sub>2</sub>P(CH<sub>2</sub>OH)<sub>2</sub>]Cl and 1,3-propane sultone. The Rh<sup>I</sup> dendritic complexes were used as the catalysts in the two-phase hydroformylation of styrene and 1-octene under mild reaction conditions (40 °C, 20 atm). High catalytic activity for both styrene and 1-octene and high selectivity for the isoaromatic aldehyde were found.<sup>66</sup>

Cole-Hamilton's group reported dendrimers based on polyhedral oligomeric silsesquioxanes cores with 16 PPh<sub>2</sub> arms (Figure 7) that give much higher linear selectivities (14:1) than their small molecule analogues (3–4:1) in the hydroformylation of oct-1-ene catalyzed by the Rh<sup>I</sup> complex. In this metallodendrimer, the phosphorus atoms are separated by five atoms including one silicon atom, i.e., 4–7 Å within one arm, while this distance in the 5–10 Å range between arms (from molecular modeling).<sup>74a,b</sup> Indeed, analogous metallodendrimers containing only one more CH<sub>2</sub> unit between the Si and P atoms showed no special selectivity enhancement over the monometallic catalysts. This positive dendritic effect was explained by the steric crowding and small arm length inducing eight-membered ring bidentate coordination that enhances the linear selectivity. Fluxionality within the complex was also suggested based on <sup>31</sup>P NMR studies.<sup>74a</sup>

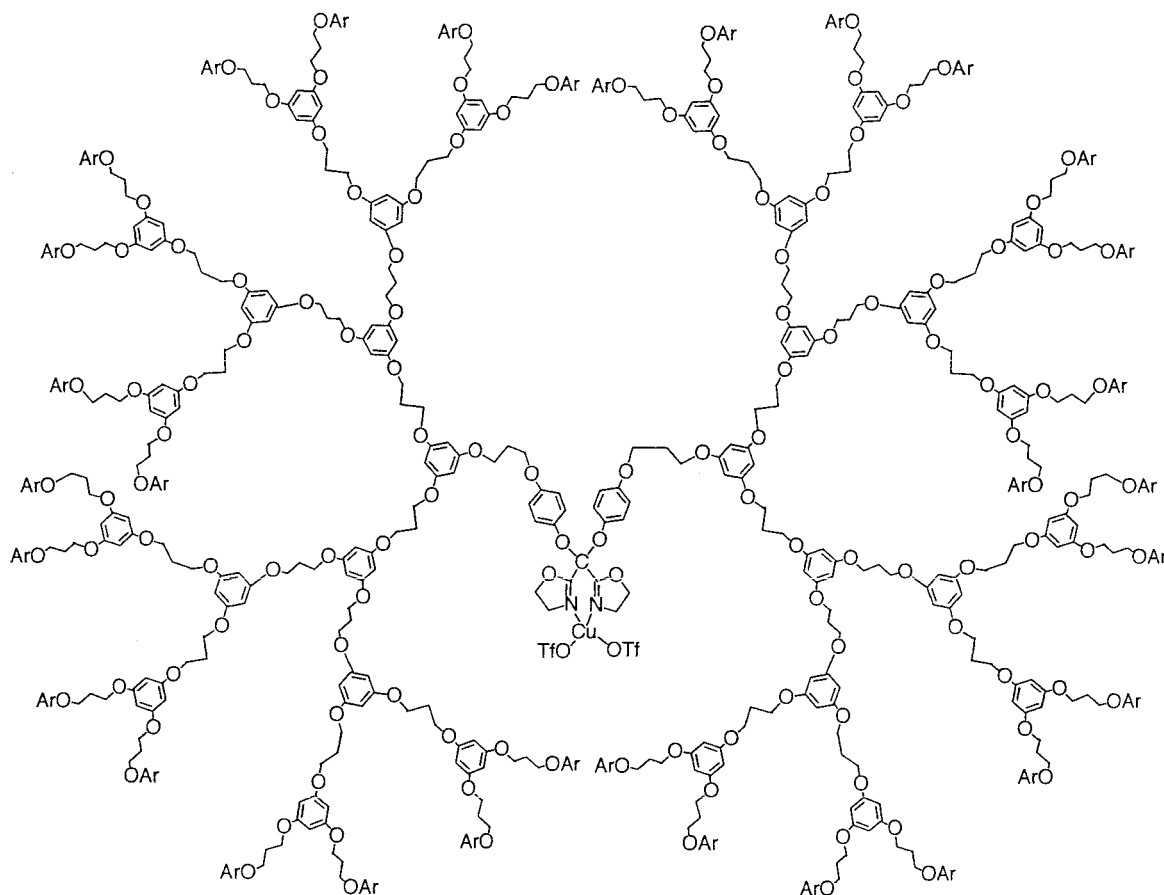
Kakkar's group reported new organophosphine dendrimers with phosphorus atoms at the focal points (Figure 8). The divergent construction involved reaction of (CH<sub>3</sub>)<sub>3</sub>SiNEt<sub>2</sub> with P{(CH<sub>2</sub>)<sub>3</sub>OH}<sub>3</sub>, then sequential reactions of the dendrimer with these two reagents successively up to the P<sub>46</sub> dendrimer. The metallodendrimers containing [RhCl(η<sup>4</sup>-1,5-C<sub>8</sub>H<sub>12</sub>)-PR<sub>3</sub>] moieties were best synthesized by reactions of these phosphorus dendrimers with [Rh(μ-Cl)(η<sup>4</sup>-1,5-C<sub>8</sub>H<sub>12</sub>)<sub>2</sub>] and were shown to catalyze the hydrogenation of 1-decene in a 1:200 metal-to-substrate ratio (25 °C, 20 bar H<sub>2</sub>, 30 min, THF). The catalytic activity (turnover number about 200 mol<sub>prod</sub> (mol<sub>cat</sub>)<sup>-1</sup> and turnover frequency about 400 mol<sub>prod</sub> (mol<sub>cat</sub>)<sup>-1</sup> h<sup>-1</sup>) was found to be similar to that of the monometallic complex. There was a slight decrease in turnover frequencies upon growth of the Rh<sup>I</sup><sub>46</sub> dendrimer. After one such cycle of hydrogenation using the Rh<sub>46</sub> dendritic catalyst, the organic product was extracted into pentane and the Rh<sub>46</sub> dendrimer was recrystallized from THF/hexane mixtures and reused with only 5% decrease in conversion,<sup>75a</sup> which favorably compares with supported catalysts.<sup>75b</sup>

#### 6. Heck Reaction

The Pd<sup>II</sup> complex of Reetz's dendritic polyphosphines (vide supra) catalyzed the Heck reaction with a 4-fold increase in turnover number as compared to the monometallic analogue. This was taken into account in terms of the higher thermal stability of the dendritic catalyst.<sup>62</sup>

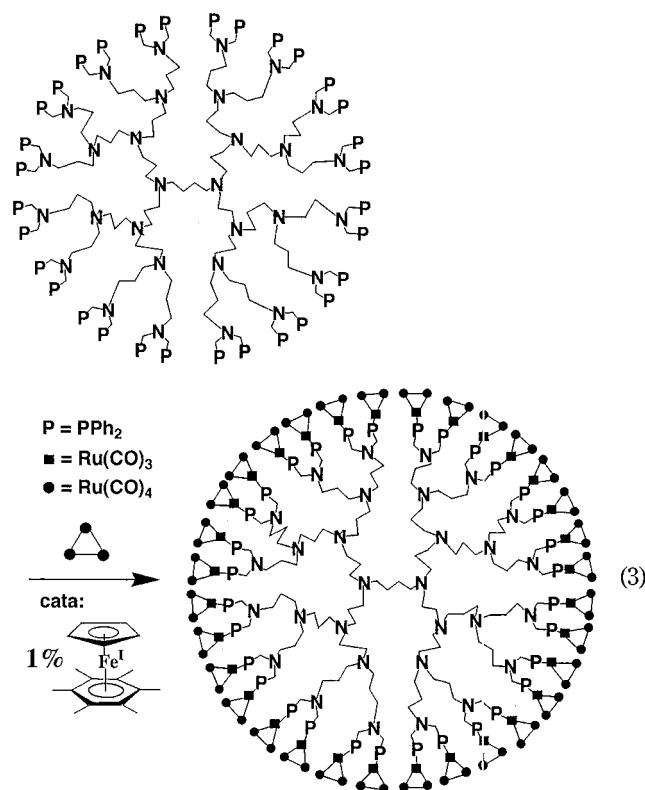
#### 7. Electron-Transfer Chain (ETC) Catalysis

Reetz's polyphosphines were also used by Alonso and Astruc to introduce 32 or 64 [Ru<sub>3</sub>(CO)<sub>11</sub>] cluster



**Figure 3.** Chow's dendritic copper(II)-bis(oxazoline) catalyst for the Diels–Alder reaction between cyclopentadiene and crotonyl imide (see mechanism at the bottom of the figure).

units onto the termini of the phosphine branches (eq 3). These reactions were carried out by electron-transfer chain (ETC) catalysis using the 19-electron



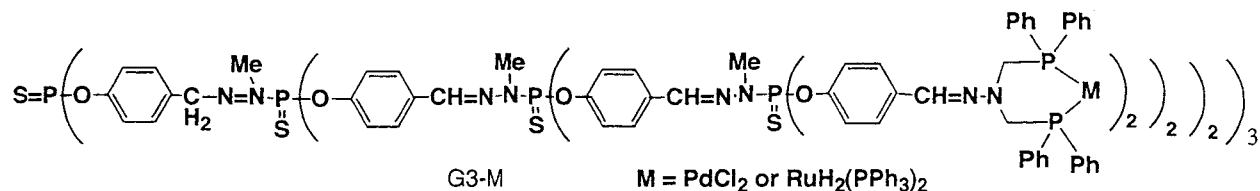
complex [FeCp(C<sub>6</sub>Me<sub>6</sub>)] as the initiator. The selectivities of these reactions were demonstrated by <sup>31</sup>P NMR. Catalytic studies using these first dendrimers decorated at the periphery with clusters containing three metals are underway.<sup>65</sup>

### 8. Diels–Alder Reactions Catalyzed by Cu<sup>II</sup>

Chow reported a dendritic copper(II)-bis(oxazoline) catalyst (Figure 3) for the Diels–Alder reaction between cyclopentadiene and crotonyl imide. These authors identified two essential steps in this Diels–Alder reaction. The constant of formation of the catalyst–dienophile complex, the first reaction step, gradually decreases with dendritic generation. The rate of the Diels–Alder reaction itself remains about the same for the first and second dendritic generation, however, and suddenly decreases for the third dendritic generation. The kinetic studies showed that a larger dendritic sector had a stronger destabilization effect on the binding strength between the catalyst and the dienophile. It was assumed that backfolding of the dendritic branches at this third generation brings about steric bulk at the catalytic site. The result is an exo- to-endo active site transition which hinders the approach of the diene toward the catalyst–dienophile complex.<sup>60,61</sup>

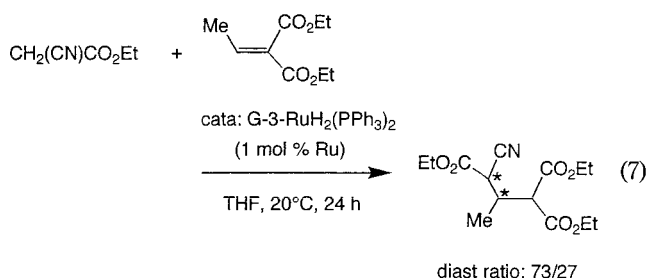
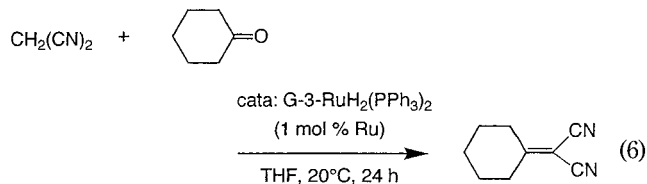
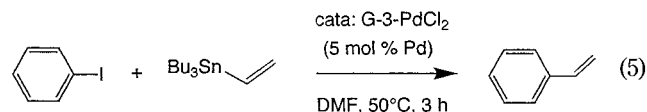
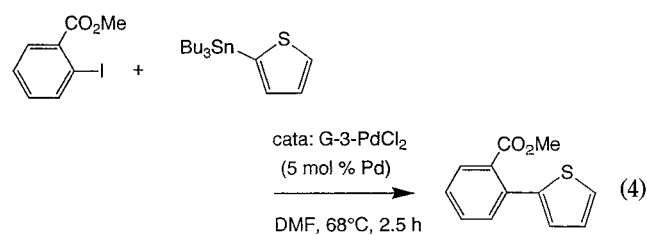
### 9. Knoevenagel and Aldol Condensations and Michael Addition

Majoral's group used generation-3 diphosphine dendrimers containing 24 Pd or Ru (Figure 4) to



**Figure 4.** Majoral's G-3 diphosphine dendrimers containing 24 Pd or Ru atoms that catalyze Stille coupling, Knoevenagel condensation, and Michael addition reactions (eqs 4–7).

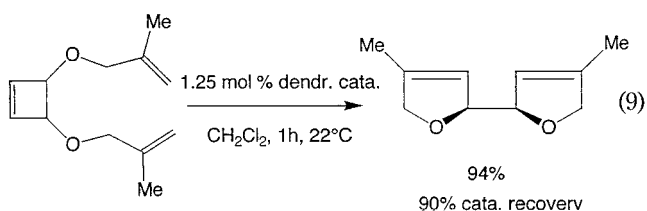
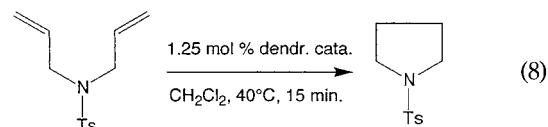
catalyze the Stille coupling reaction of methyl-2-iodobenzoate with 2-(tributylstannyl)thiophene, the Knoevenagel condensation between malononitrile and cyclohexanone leading to the corresponding unsaturated nitrile and the Michael addition between ethyl cyanoacetate and diethylethylidenemalonate (eqs 4–7). The activity can be compared with that of the monomer complexes and is often higher, and recycling is possible without significant loss of activity.<sup>68</sup>



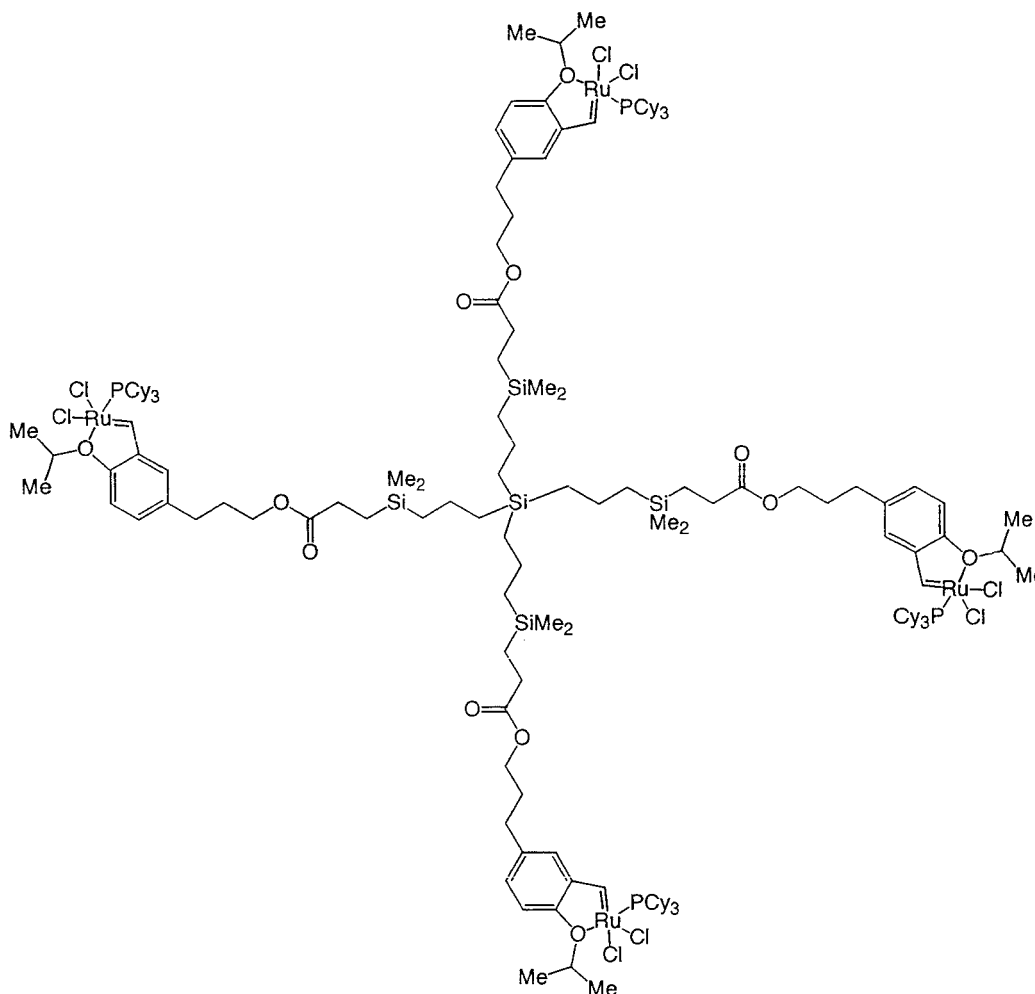
The aldol condensation of benzaldehyde and methylisocyanate yielding oxazolines has been catalyzed by cationic cyclopalladated carbosilane dendrimers acting as Lewis acids. Comparison of the catalytic performance of the dendrimers to that of the parent monometallic catalyst [Pd(C<sub>6</sub>H<sub>3</sub>{CH<sub>2</sub>-NMe<sub>2</sub>}-2-SiMe<sub>3</sub>-5)(py)(H<sub>2</sub>O)][BF<sub>4</sub>] showed that the selectivity was not affected up to the second dendritic generation. The rate of the reaction decreased with increasing steric congestion at the dendrimer periphery, however.<sup>76</sup>

## 10. Olefin Metathesis Catalyzed by Ruthenium Complexes

Hoveyda's group synthesized two efficient and recyclable dendritic Ru-based metathesis catalysts (Figures 5 and 6). Examples involving catalytic ring closing, ring opening, and cross metathesis were shown (eqs 8 and 9) where the metallodendritic catalyst, unlike the monomer, can be recovered. The



structure of the monomeric catalyst differs from Grubbs' catalyst [Ru(PPh<sub>3</sub>)<sub>2</sub>Cl<sub>2</sub>(=CHPh)]<sup>69</sup> in that a chelating carbene (a styrenyl ether) takes the place of the benzylidene and one phosphine. In the 4-branch Si-centered dendrimer, the branches are -(CH<sub>2</sub>)<sub>3</sub>-SiMe<sub>2</sub>(CH<sub>2</sub>)<sub>3</sub>OC(O)(CH<sub>2</sub>)<sub>2</sub>- units connected to the styrenyl ether ligand. The yield of ring-closing metathesis of TsN(CH<sub>2</sub>CH=CH<sub>2</sub>)<sub>2</sub> using 5% mol Ru of the dendritic catalyst was 99%. The catalyst was recovered with 13% vacant styrenyl ligand (i.e., 13% Ru loss). Repeated use of the dendritic catalyst led to complete conversion of TsN(CH<sub>2</sub>CH=CH<sub>2</sub>)<sub>2</sub> with 91% yield. The dendritic catalyst remains active after 6 cycles (although 59% of the Ru content has been depleted), the yield being still 87% in ring-closing metathesis. The authors suggest that the high level of activity may be attributed, at least partially, to the fact that the metallodendrimer releases a highly active monophosphine Ru complex into the solution. It was indicated that the catalytically active Ru species was released from the dendrimer into the reaction mixture and could be trapped again by a styrenyl ether ligand arm of the dendrimer.<sup>70</sup> Another analogous 4-branch metallodendritic catalyst was prepared in which the last phosphine ligand was replaced by the diamino-carbene ligand used by Grubbs for the design of the extremely efficient next-generation metathesis catalyst.<sup>71a</sup> This dendritic catalyst exhibited catalytic activity higher than the first one as it promoted the formation of trisubstituted allylic alcohol and was recovered with only 8%



**Figure 5.** Hoveyda's 4-branch Si-centered dendritic Ru-based metathesis catalysts for ring-closing (eq 8), ring-opening, and cross metathesis reactions.

Ru loss. It also catalyzed tandem ROM/RCM (eq 9) and was easily separable from reaction mixtures because of its polarity and high molecular weight. This very detailed report<sup>70</sup> follows other reports on recyclable Ru-based metathesis catalysts.<sup>71b,72</sup>

RCM reactions of diethyldiallylmalonate to the favored five-membered cyclopentene ring using chelating dendritic ligands coordinated to Ru has also recently been achieved by the van Koten group.<sup>73</sup> Thus, dendrimers containing 4 or 12 branches, i.e.,  $\text{Si}[(\text{CH}_2)_3\text{SiMe}_2\text{-}i\text{-C}_6\text{H}_4\text{CHOH}(\text{CH}_3)\text{py}]_4$  and  $\text{Si}\{(\text{CH}_2)_3\text{-Si}[(\text{CH}_2)_3\text{SiMe}_2\text{-}i\text{-C}_6\text{H}_4\text{CHOH}(\text{CH}_3)\text{py}]_3\}_4$  reacted with  $[\text{Ru}(\text{=CHPh})\text{Cl}_2(\text{PR}_3)_2]$  ( $\text{R} = i\text{-Pr}$  or  $c\text{-Hex}$ ) to give five-coordinate dendritic Ru complexes in which the O,N-chelating ligands were attached to Ru with the alkoxy ligand in equatorial and the pyridyl ligand in axial positions. The RCM reactions were quantitative after 30 min at 80 °C with 1 mol % (based on ruthenium) of either catalyst, as with the monometallic catalyst. In a similar experiment, carried out in which the solution of the catalyst was separated from that containing the substrate by a membrane, conversion did not increase above 20%. Extensive decomposition occurred as a black precipitate formed in the vessel containing the catalyst, presumably because the catalyst was deactivated by the mem-

brane surface. Compatible membranes are now called for.<sup>73</sup> See also sections IV, V, XII, and XIV.

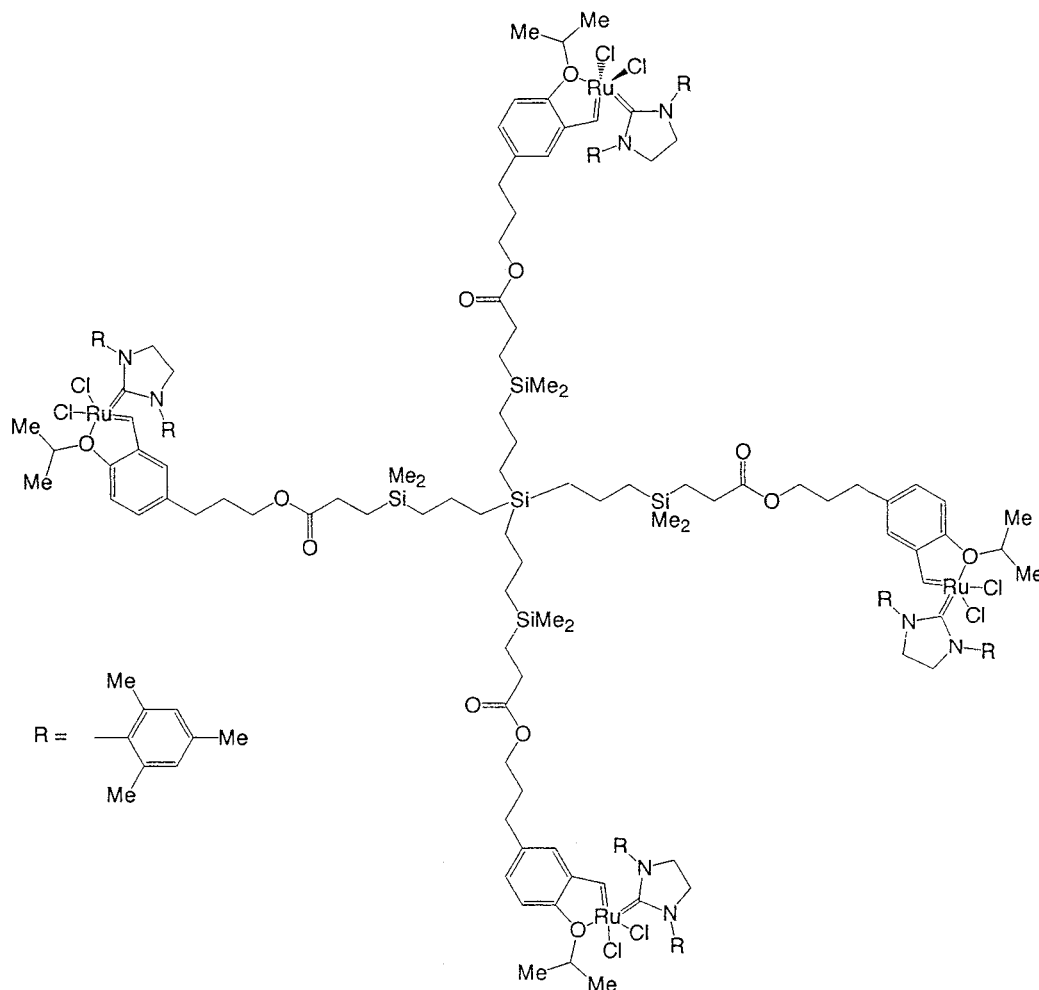
### III. Asymmetric Catalysis by Chiral Metallodendrimers

#### 1. Chiral Centers Located on the Branches of the Dendrimer

##### A. Hydrogenation

The very first attempts to carry out asymmetric catalysis using chiral metallodendrimers were reported by Brunner's group. These reports belong to the pioneering works in catalysis using metallodendrimers that appeared in 1994. Brunner designed dendritic catalysts containing dendritic phosphines which he called "dendrzyme" because of their hoped-for similarities with enzymes (Figure 9).<sup>77</sup> In the "dendrzyme" complexes the Cu(I) center is surrounded by a Schiff base containing a pyridine with (1*S*,2*S*)-2-aminophenyl-1,3-propanediol, (1*R*,2*S*)-ephedrine, or L-aspartic acid units. The first generation of dendrzyme was made in situ by adding copper(I) triflate to the chiral compound.<sup>78</sup> The cyclopropanation of styrene occurs with a maximum of 10% ee (case of L-aspartate). Brunner et al. reported another





**Figure 6.** Hoveyda's 4-branch Si-centered dendritic Ru-based metathesis catalysts for ring-closing, ring-opening, and cross metathesis reactions that also catalyzes tandem ROM/RCM reaction (eq 9).

complex synthesized from a diphosphine core and dendritic branches containing menthyl groups. The ligand was coordinated to  $\text{Rh}^{\text{I}}$  in situ by reaction with  $[\text{Rh}(\eta^4\text{-COD})\text{Cl}]_2$ . Application of the rhodium complex (Rh:substrate ratio 1:50) to the hydrogenation of acetamidocinnamic acid after 20 h at 20 bar  $\text{H}_2$  pressure led the desired product with a small enantioselectivity (enantiomeric ratio of 51:49).<sup>79</sup> A very interesting feature of this early study, however, is that the rate of hydrogenation was higher in the presence of the dendritic diphosphine ligand having the dendritic wedge located at the meta position of the arene rings than with the nondendritic dppe. This spatial arrangement had a crucial role since, on the other hand, hydrogenation with a dendritic diphosphine having dendritic wedges in 2,5-position exhibited a 300-fold rate decrease while the enantioselectivities remained very weak.

#### B. Diethylzinc Addition to Benzaldehyde

Bolm reported the use of Fréchet's dendrons with a chiral pyridyl alcohol at the focal point up to the third generation to catalyze the enantioselective diethylzinc addition to benzaldehyde. Three dendritic generations were compared, but the enantiomeric excess (about 85%) and yields were the same. This

indicated that the dendrimer structure has a negligible influence on the catalytic site.<sup>80</sup>

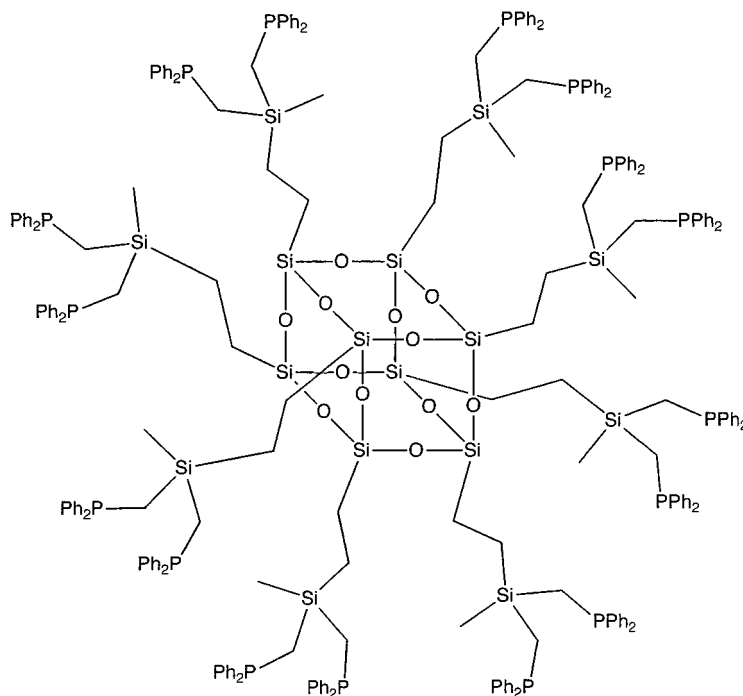
#### C. Cyclopropanations of Styrene

Hirsch's group synthesized fullerene dendrimers with an inherently chiral hexaaddition pattern with  $C_3$ -symmetry. It was revealed that some of these dendritic hexakisadducts, namely, all-*S*- $^f\text{C}$  and all-*S*- $^f\text{A}$ , possess catalytic properties as their Cu-bisoxazoline complexes for stereoselective cyclopropanations of styrene with ethyl diazoacetate. The observed stereoselectivities caused by these first prototypes of fullerene-based *dendrzymes* are lower compared to those obtained with other Cu-bisoxazoline catalysts (low ee values but comparatively high de values were observed).<sup>81</sup>

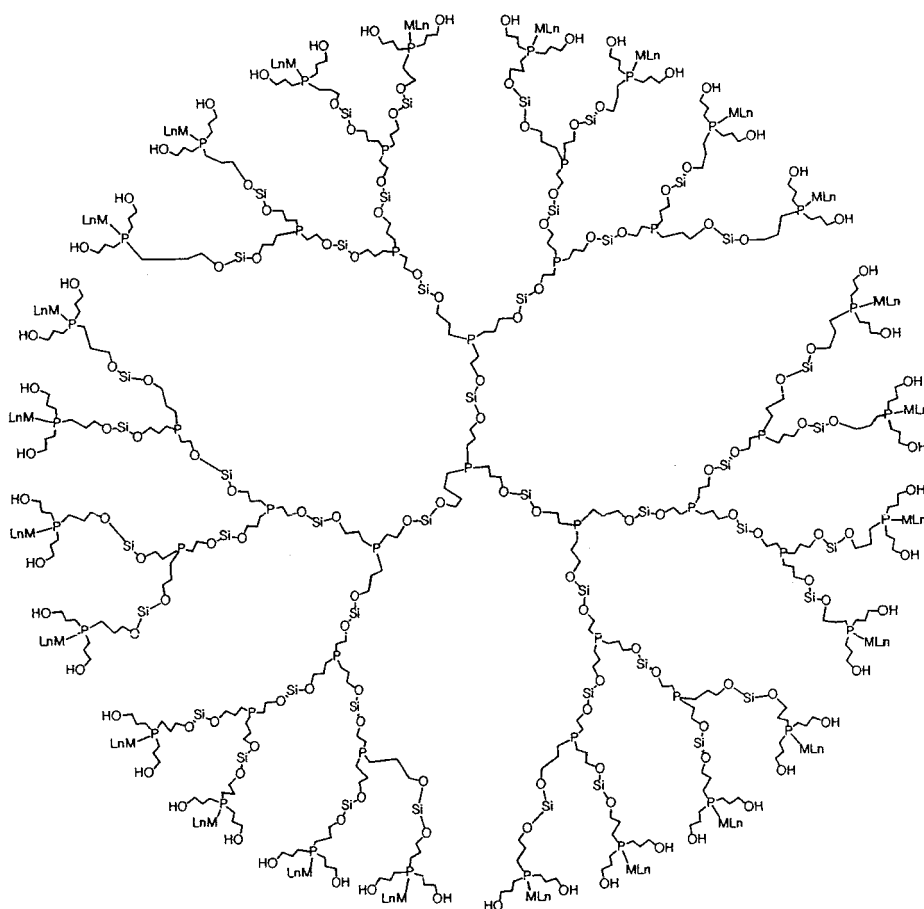
## 2. Chiral Centers Located at the Periphery of the Dendrimer

#### A. Hydrogenation

Togni et al. decorated 8-, 12-, and 16-branch dendrimers with ferrocenyldiphosphine ligands and also synthesized the corresponding rhodium(I) complexes (Figure 11). These ferrocenylphosphine-rhod-



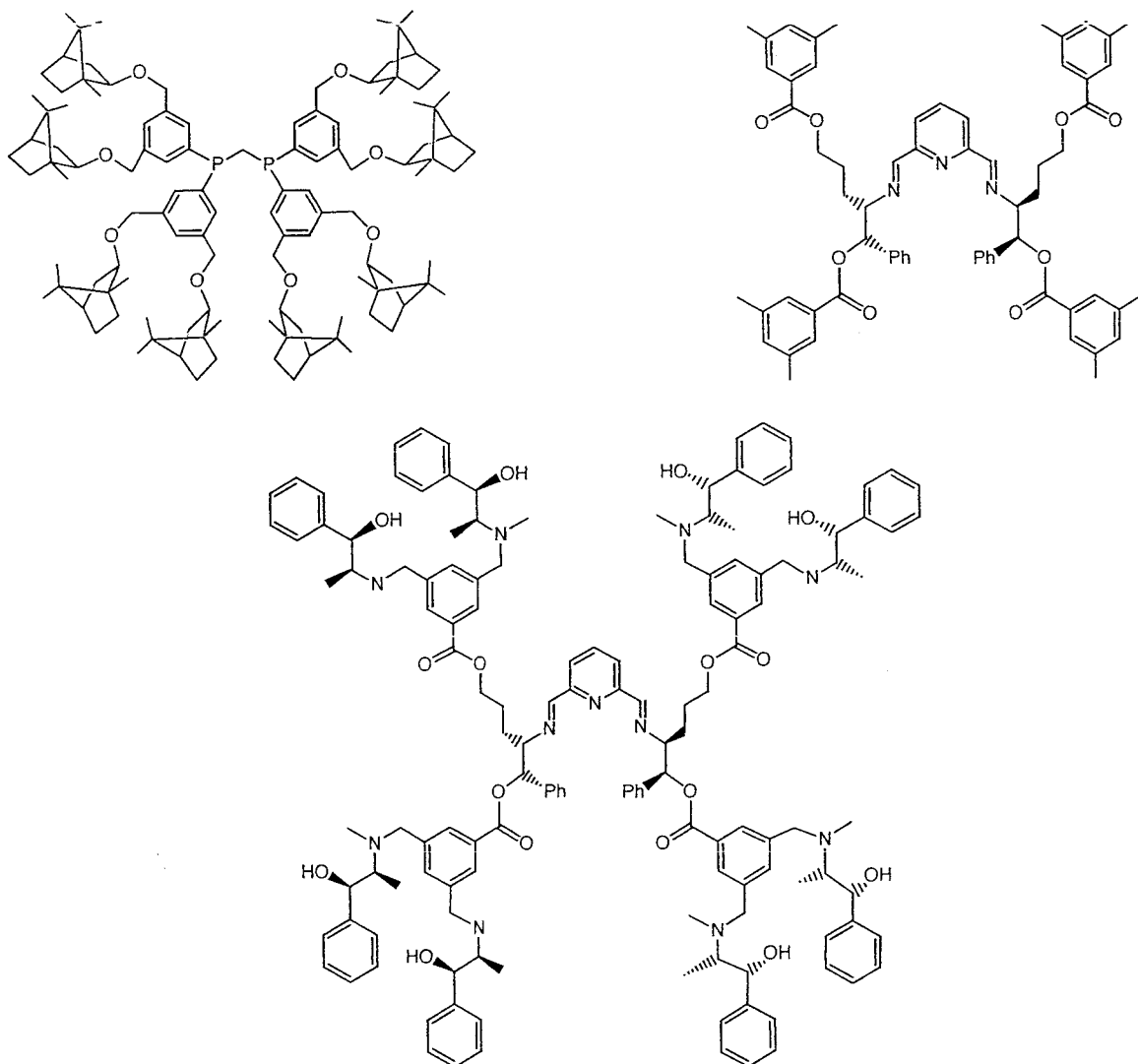
**Figure 7.** Cole-Hamilton's dendrimers based on polyhedral oligomeric silsesquioxanes cores with 16 PPh<sub>2</sub> arms that give high linear selectivities (positive dendritic effect) in the hydroformylation of oct-1-ene catalyzed by the dendritic Rh<sup>I</sup> complex.



**Figure 8.** Kakkar's new organophosphine dendrimers with phosphorus atoms at the focal points (up to P<sub>46</sub> here on the figure) coordinated to [RhCl( $\eta^4$ -1,5-C<sub>8</sub>H<sub>12</sub>)PR<sub>3</sub>] moieties that catalyze the hydrogenation of 1-decene.

ium(I) dendrimers catalyze the hydrogenation of dimethylitaconate (eq 11) with ee of 98%, which compares with the ee of 99% obtained for the mono-

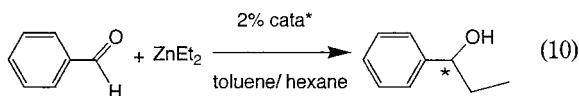
meric Josiphos catalyst. Moreover, the dendritic catalyst can be separated from the reaction mixture using a nanofiltration membrane.<sup>86,87</sup>



**Figure 9.** Brunner's dendrizyme ligands reported in 1994, active for the cyclopropanation of styrene (Cu–dendritic  $N_3$  ligand) and the hydrogenation of acetamidocinnamic acid (Rh–dendritic dppe ligand) and which showed the first positive dendritic effect in catalysis.

### B. Addition of Diethylzinc to Unsaturated Substrates

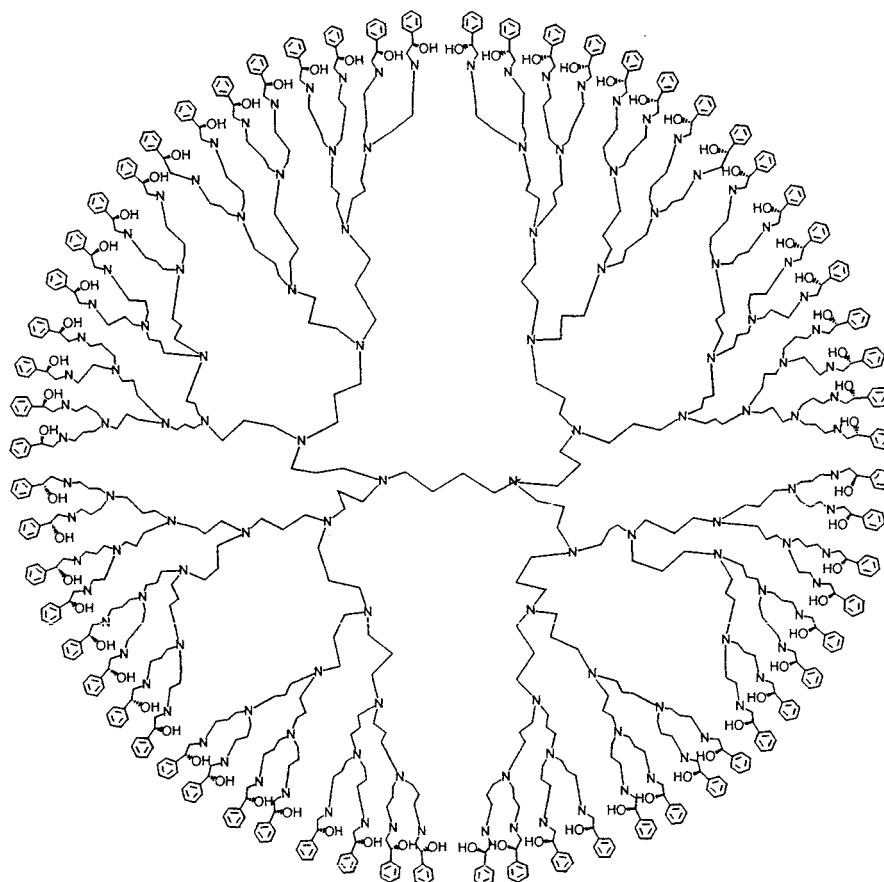
Peerlings and Meijer reported the first catalytic studies with high-generation dendrimers in 1995.<sup>83–85</sup> They studied the increased influence of conformational rigidity as the generation number increases in poly(propylene imine) dendrimers on the asymmetric addition of diethylzinc to benzaldehyde (eq 10) catalyzed by optically active amino–alcohols. This reac-



tion is indeed an ideal test reaction for the induction of asymmetry by amino–alcohol catalysts. Polypropyleneimine dendrimers have been modified with (*R*)-phenyloxirane and their corresponding *N*-methylated derivatives (Figure 10), and these dendritic catalysts have been tested for the addition of diethylzinc to benzaldehyde. The chemical yields and ee drop as the dendritic generation of the catalyst increases (ee drops from 36% for the monofunctional catalyst to the fifth-generation dendritic catalyst).<sup>83,84</sup> Optically

active *R*-styrene oxide was also brought into reaction with the amine-functionalized poly(propylene imine) dendrimer yielding mainly the secondary alcohol–secondary amine functionalities. Reaction of diethylzinc with benzaldehyde using these dendritic catalysts led to a dramatic drop in enantiomeric excess, going from 11% to 0% for catalysts with 1–64 end groups. Thus, the dendritic effect is negative in both of these cases. This negative dendritic effect was attributed to an increase in steric hindrance of the end groups at the periphery of the dendrimer, resulting in an increased difficulty for all end groups to adopt their preferred conformation in order to catalyze the diethylzinc addition. The presence of H-bonds greatly enhances this effect.<sup>85</sup>

Seebach et al. synthesized a hexa-arm dendrimer and attached their ligand of  $C_2$  symmetry, TADDOL ( $\alpha, \alpha', \alpha', \alpha'$ -tetraaryl-1,3-dioxolane-4,5-dimethanol) (Figure 12), and the Ti(OCHMe<sub>2</sub>) group at the periphery. Using this chiral metallodendrimer, they found that the enantiomeric addition of diethyl zinc to benzaldehyde proceeded with the same enantioselectivity (ee, 97%) as the monomeric chiral catalyst. The



**Figure 10.** Peerlings and Meijer's poly(propylene imine) dendrimers modified with (*R*)-phenyloxirane for the catalytic asymmetric addition of diethylzinc to benzaldehyde (eq 10) demonstrating a negative dendritic effect on the enantioselectivity as the dendritic generation increases.

metallodendrimer, with a molecular weight of only 3833 Da, had to be separated by column chromatography rather than by ultrafiltration methods.<sup>88,98</sup>

Soai's group reported the modification of PAMAM dendrimers with ephedrine ligands giving dendritic catalysts for the rarely reported addition of diethylzinc to *N*-diphenylphosphinylimines. For instance, the first- and second-generation dendritic ligands induce low stereoselectivities (*ee* = respectively, 43% and 39%) as compared to 92% for the bifunctional ephedrine ligand.<sup>82</sup> Soai's group also studied the enantioselective addition of diethylzinc to *N*-diphenylphosphinylimines<sup>91a</sup> using dendritic chiral ligands that have rigid hydrocarbon cores and three or six chiral  $\beta$ -amino-alcohol chain ends. These reactions yielded enantiomerically enriched *N*-diphenylphosphinylamines with up to 94% *ee*<sup>91b</sup>

### C. Kinetic Resolution of Terminal Epoxide

Breinbauer and Jacobsen demonstrated the first positive dendritic effect in asymmetric catalysis with dendritic PAMAM-Co(salen) complexes for the hydrolytic kinetic resolution of terminal epoxide. Metallodendrimers with several branch numbers were compared, and it was found that the best results were obtained with the 4-branch metallodendrimer. Efficiency per metal: 4-Co-PAMAM > 8-Co-PAMAM > 16-Co-PAMAM.

It was shown that this very interesting positive dendritic effect was due to the cooperativity in the

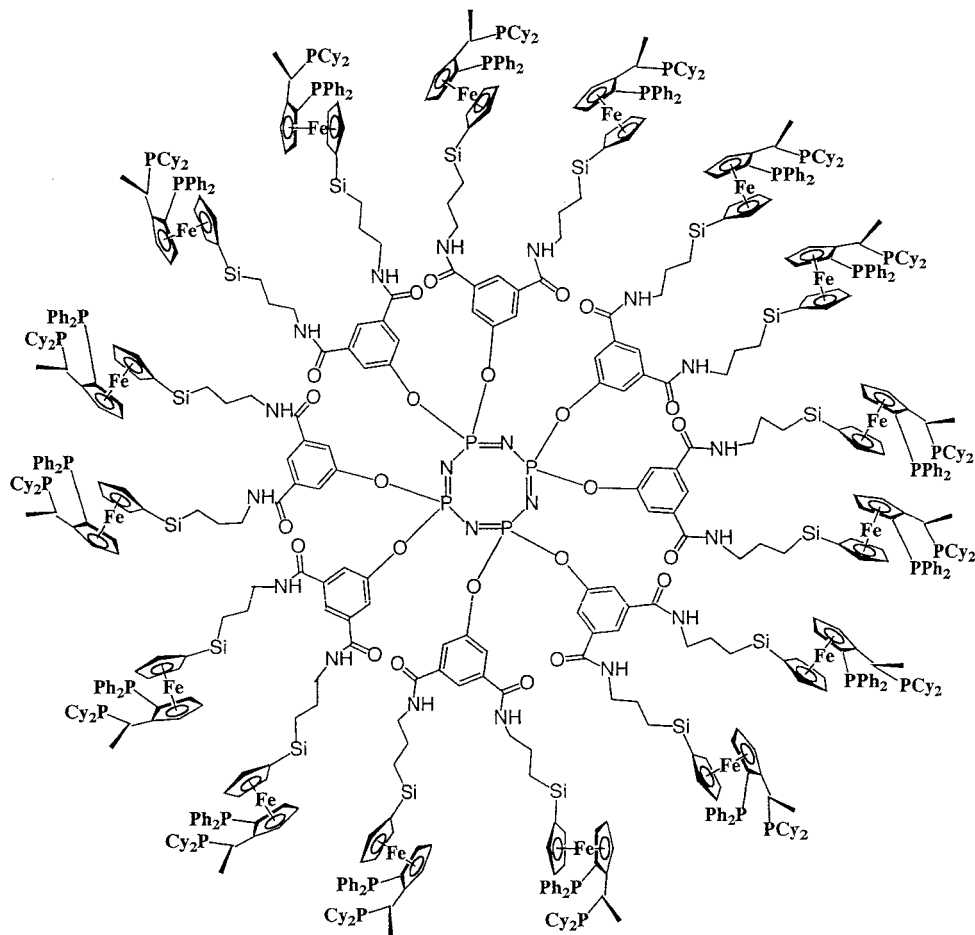
key mechanistic step: the coordinated nucleophile attacks the epoxide that is coordinated to another cobalt atom. Thus, the proximity between two cobalt complexes favors the reaction, and this proximal situation is best encountered in dendrimers with four branches (Figure 13).<sup>89</sup>

Soai's group synthesized chiral dendrimers with rigid backbones containing three or six  $\beta$ -amino-alcohols on the hyperbranched chain ends. These dendrimers could act as chiral catalysts for the enantioselective addition of dialkylzincs to aldehydes, and the secondary alcohols were obtained in enantiomeric excess up to 86%.<sup>90</sup>

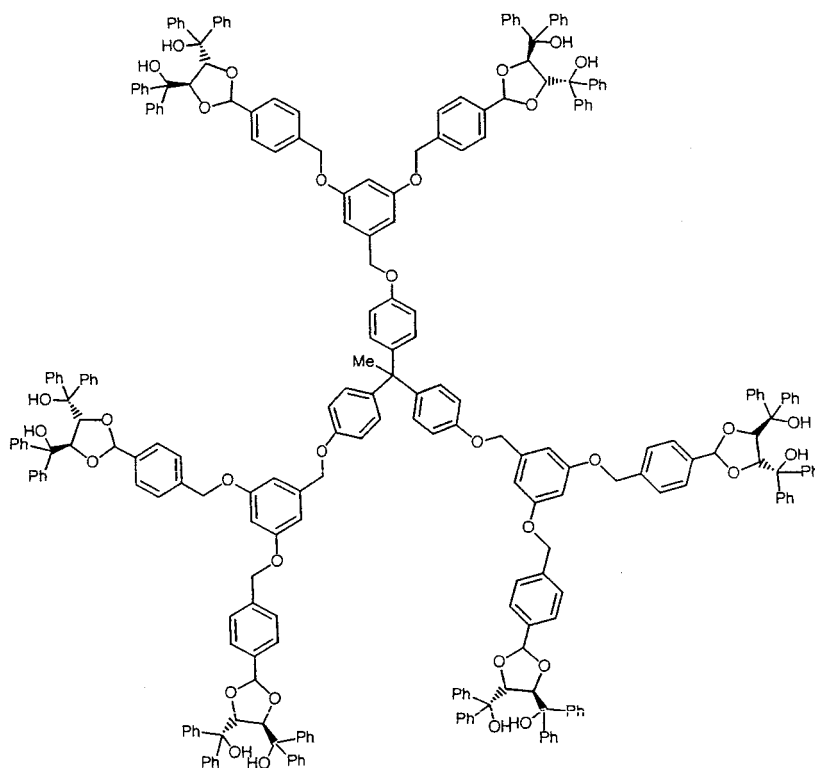
## 3. Chiral Center Located at the Core of the Dendrimer

### A. Protonation Reactions

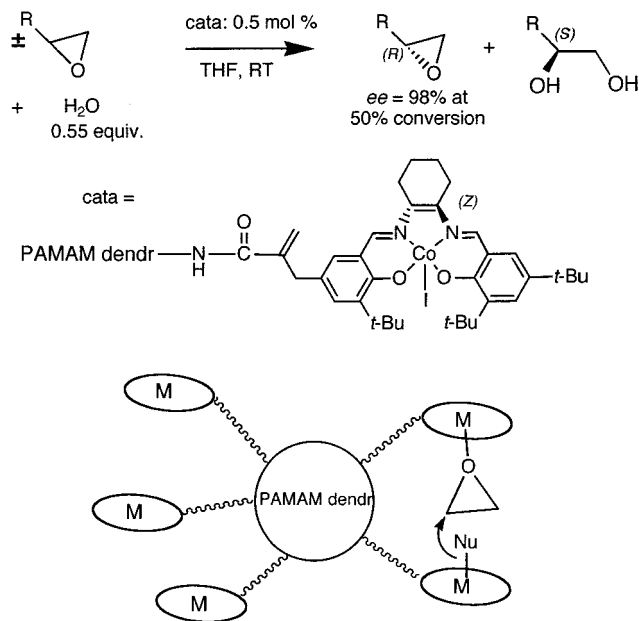
Seebach's group found that chiral dendritically expanded diamines (Figure 15) are catalysts in enantioselective protonation reactions. In such a reaction, any stereoselectivity observed depends primarily on the configuration and active conformation of the proton source. Kinetic control is sufficiently guaranteed by an essentially diffusion-controlled process, and thermodynamic control (product equilibration) is excluded if the acidity of the resulting protonated compound is much lower than that of the proton source applied. The base-catalyzed addition of methanol to methylphenyl ketene (eq 12) was



**Figure 11.** Example of Togni' dendrimers with optically active ferrocenyldiphosphine ligands whose rhodium(I) complexes efficiently catalyze the hydrogenation of dimethylitaconate with very high ee (eq 11).

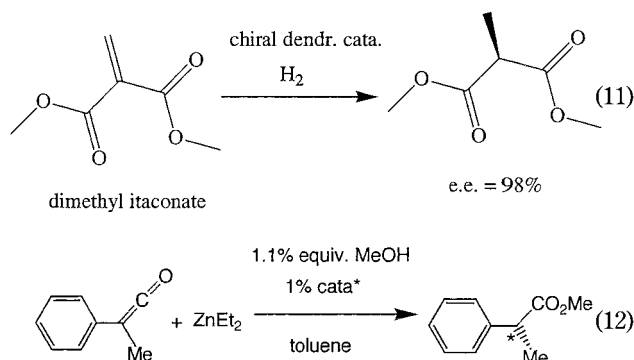


**Figure 12.** Seebach's hexa-arm dendrimer attached to chiral TADDOL whose related metallodendrimer with  $\text{Ti}(\text{OCHMe}_2)$  group at the periphery efficiently catalyzes the enantiomeric addition of diethyl zinc to benzaldehyde.

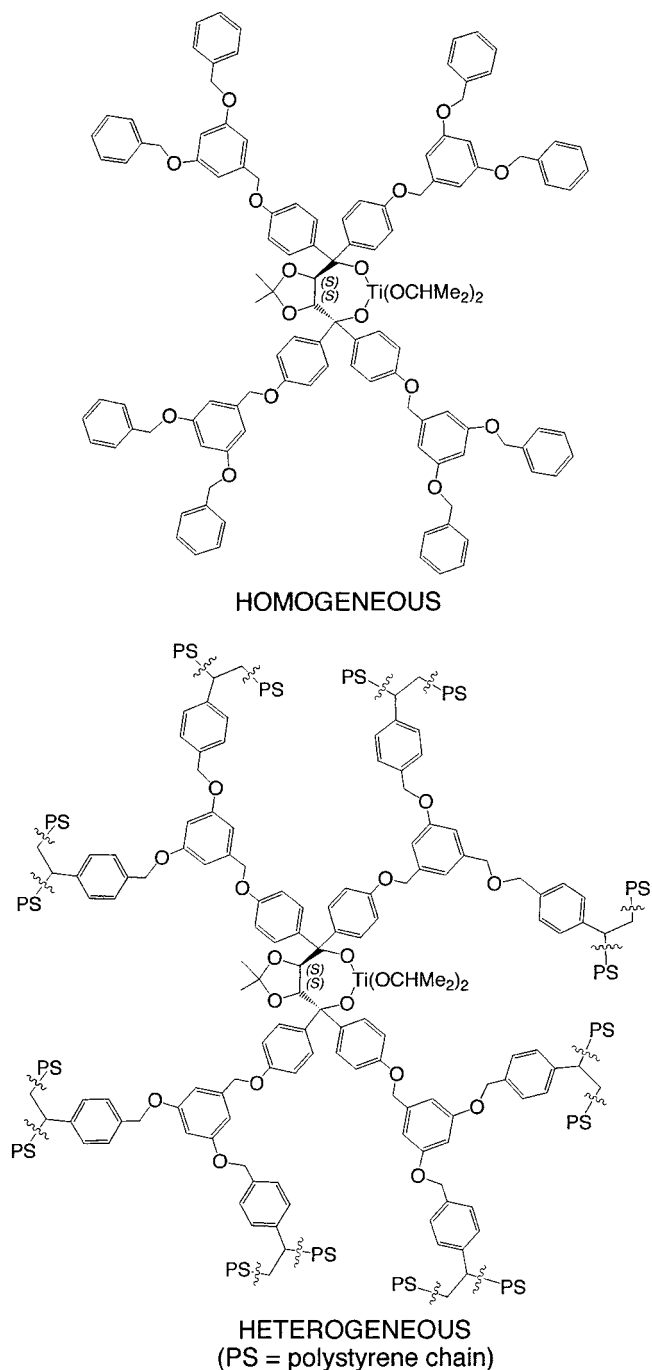


**Figure 13.** Breinbauer and Jacobsen's dendritic PAMAM-Co(salen) complexes catalyzing the hydrolytic kinetic resolution of terminal epoxide and disclosing a positive dendritic effect due to the interbranch cooperativity in the key mechanistic step shown.

tested, and brucine and a dendritic diamine were compared. The dendritic amine had a core resembling



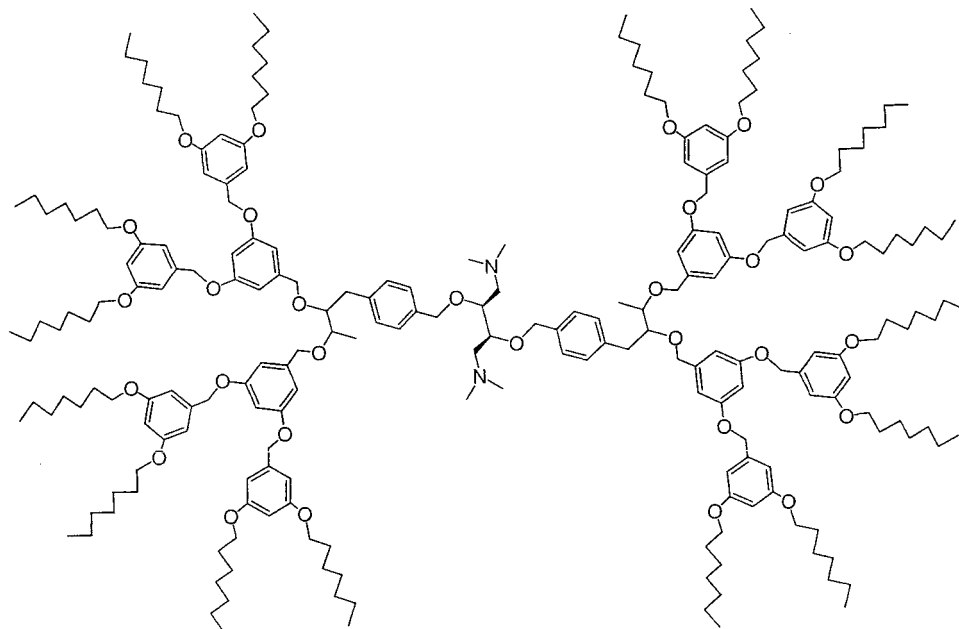
the well-known (*S,S*)-1,4-bis(dimethylamino)-2,3-dimethoxybutane (DDB), which had already been used by Seebach in asymmetric catalysis. The dendritic segments were of the Fréchet type. The Eyring plots of the ee show a remarkable positive dendritic effect when comparing the dendritic diamine with simple DDB and brucine. Other base-catalyzed reactions that do not include an enantioselective protonation step, e.g., the addition of ketene to chloral and the Michael addition of thiophenol to cyclohexenone, showed no effect. The results suggest that at least one of the chiral branching units is adjacent to the trajectory of the proton and shapes the topicity of the reaction (binding geometry of the intermediate enolate). In addition, the nonlinear temperature dependence of the stereoselectivity must be the result of a change in the active conformation of at least one of the chiral branches since the simple DDB gives a linear Eyring diagram contrary to brucine and the DDB-centered dendritic diamine.<sup>97–98b</sup>



**Figure 14.** Seebach's dendritic Ti-TADDOLates coordinated to Ti(IV) with Fréchet-type branches (homogeneous and heterogeneous on polystyrene support) for the enantioselective addition of Et<sub>2</sub>Zn to benzaldehyde with very high enantioselectivities.

### B. Hydrogenation

The Fan and Chan groups reported a series of dendritic BINAP ligands with Fréchet-type polyether wedges and their ruthenium complexes as catalysts in asymmetric hydrogenation of 2-[*p*-(2-methylpropyl)phenyl]acrylic acid in methanol-toluene (1:1, v/v) at 50 °C. The dendritic BINAP-Ru catalysts showed slightly higher enantioselectivity (ee = 92.6% with 100% conversion in 20 h) than Ru-BINAP (ee = 89.8%). The catalyst could be precipitated at the end of the reaction and then reused three times without loss of activity or enantioselectivity.<sup>102</sup>



**Figure 15.** Seebach's chiral dendritic diamine catalyst with a core resembling (*S,S*)-1,4-bis(dimethylamino)-2,3-dimethoxybutane (DDB) and Fréchet-type segments for an enantioselective protonation reaction (the base-catalyzed addition of methanol to methylphenyl ketene, eq 12).

The Deng and Chang groups reported chiral diamine-based dendritic ligands containing Fréchet-type polyether wedges and their ruthenium complexes up to the fourth generation for the catalysis of asymmetric transfer hydrogenation of acetophenone.<sup>103a</sup> The chiral diamine core was recently discovered by Noyori for this reaction, for which  $[\text{RuCl}_2(\eta^6\text{-cymene})]_2$  is the Ru source and is available on the kilogram scale.<sup>103b</sup> The dendrimers rather favorably compare with the parent nondendritic catalyst in terms of activity, and the enantioselectivity was retained. It was remarkable that, upon recycling the dendritic catalyst, the enantioselectivity was retained while the activity only decreased slightly. Further addition of  $[\text{RuCl}_2(\eta^6\text{-cymene})]_2$  could not regain the reactivity and even gave poor selectivity.<sup>103a</sup>

### C. Reduction of Ketones

Bolm et al. investigated the asymmetric reduction of ketones with  $\text{BH}_3\text{:SMe}_2$  and chiral amines *S-p*- $\text{XOC}_6\text{H}_4\text{CH}_2\text{C}(\text{NH}_2)\text{C}(\text{OH})\text{Ph}_2$ . They compared the ee obtained with  $\text{X} = \text{H}$ , a polymer, and Fréchet-type dendrons and observed some advantage of the use of the dendrimeric amines. For instance, the ee for the reduction of acetophenone is 87% with  $\text{X} = \text{H}$ , 91% with the best dendron, and 76% with the polymer. The best results were obtained with the reduction of *p*-chloroacetophenone for which the ee is 96% using  $\text{X} = \text{dendron}$  comparing to 84% using  $\text{X} = \text{polymer}$ .<sup>100</sup>

### D. Addition of $\text{Et}_2\text{Zn}$ to Aldehydes

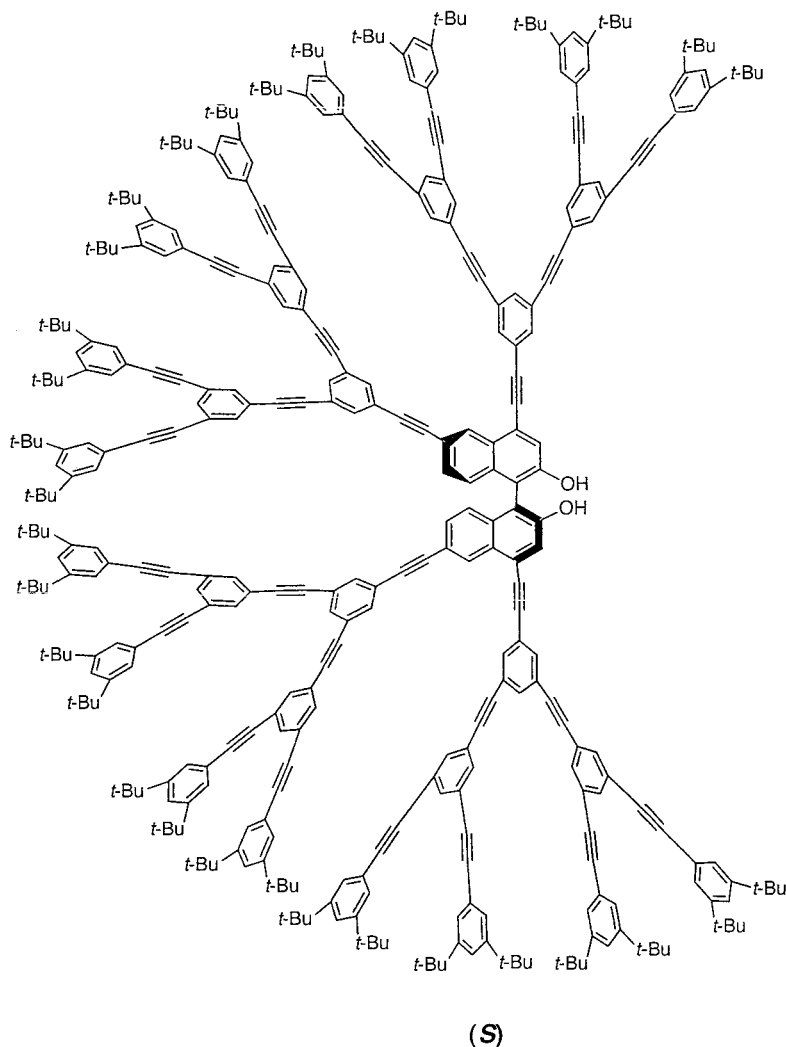
Rheiner and Seebach used dendritic Ti-TADDOLates with Fréchet-type branches up to the fourth generation (64 branches) in the enantioselective addition of  $\text{Et}_2\text{Zn}$  to benzaldehyde. There was no detectable decrease of selectivity (98:2) up to the second generation, and the rates hardly decreased up to the third generation. Enantiomeric branches caused no change for stereoselectivity within experi-

mental error. The authors pointed out that there might be applications for special properties such as high molecular weight, good solubility, and spacing of central sites from cross-linked polymer matrixes.<sup>92a</sup>

Seebach et al. used Fréchet's dendrimers with styryl end groups to cross-link a catalyst to a polystyrene support. The catalyst ligand core, TALDOL, is coordinated to Ti(IV) (Figure 14). It has been used for the enantioselective catalysis of nucleophilic addition to aldehydes. High enantioselectivities were obtained for the addition of diethylzinc to aldehydes. The Ti(IV)-TADDOL dendritic polystyrene catalyst also has a much higher turnover rate than linear polystyrene analogues.<sup>92b,93</sup>

The authors extended their studies to such dendritic catalysts with spacers of variable length and flexibility and found remarkable features: (i) while the enantioselectivity is above 9:1 with all polymers of low loading, only the dendritic polymer gives rise to a constant selectivity of 98:2 in 20 sequential applications; (ii) the catalytic performances drop with increasing the chain length of the spacers between the TADDOL core and polymer backbone; (iii) the low-loaded dendritic catalyst beads with the shortest spacer keep their swelling properties high even after 20 runs, while all others do not swell as well after multiple reuse; (iv) the rate of reaction is the same with and without stirring using the beads of dendritic catalyst that has the shortest spacer filling the whole reaction volume under standard conditions. This means that diffusion of reactants and products to and from the active center is obtained.<sup>94,95</sup>

These authors also investigated the use of membrane reactors in these enantioselective catalytic reactions. Therefore, they synthesized TADDOL-derived dendritic catalysts with a molecular weight high enough to be retained inside a membrane that is impermeable to the catalyst but permeable to reactants and products.<sup>96</sup>



**Figure 16.** Pu's rigid dendrimers constructed around an optically pure diacetate of 4,4',6,6'-tetrabromo-1,1'-bi-2-naphthol which are enantioselective fluorescence sensors and very efficiently catalyze the asymmetric alkylation of benzaldehyde with diethylzinc

Very interesting rigid dendrimers have been constructed by Pu's group around an optically pure diacetate of 4,4',6,6'-tetrabromo-1,1'-bi-2-naphthol (Figure 16). These dendrimers efficiently conduct energy migration from the periphery to the core and are potentially useful in developing an enantioselective fluorescence sensor. The [G-2] dendrimer also catalyzes the asymmetric alkylation of benzaldehyde with diethylzinc with a much higher catalytic activity (98.6% conversion in 24 h at room temperature) than (S)BINOL (37% conversion under these conditions) and also generates the opposite enantiomeric product. Both enantioselectivities of the dendrimer and BINOL are very low. This dramatic difference is due to the fact that the zinc complex formed from the reaction with BINOL is likely to exist as aggregates in solution through intermolecular Zn–O–Zn bonds which should greatly reduce the Lewis-acid activity of the zinc center. Such aggregate is not formed in the case of the dendrimer due to the bulky and rigid dendritic arms, yet the molecular models show that there is enough space allowing the substrate to approach the reaction center. High enantioselectivity in the presence of  $[\text{Ti}(\text{O}-i\text{-Pr})_4]$  was found for the dendrimer (100% conversion, 90% ee) as well as for

BINOL (100% conversion, 89% ee), indicating that the catalytic center must be identical, i.e., monomeric, in both cases. The advantage of the dendrimer over BINOL is that it can be easily removed from the reaction mixture by precipitation with methanol.<sup>101</sup>

Yoshida's group catalyzed the asymmetric allylation of aldehydes using chiral Ti-1,1'-binaphthol metallodendrimers containing poly(benzyl ether) wedges at the 6,6'-positions, whose molecular optical rotation did not change with the generation number. The enantioselectivity remained remarkably stable with increase of the generation number ( $90 \pm 2\%$  ee; nondendritic parent, 87% ee).<sup>103c</sup>

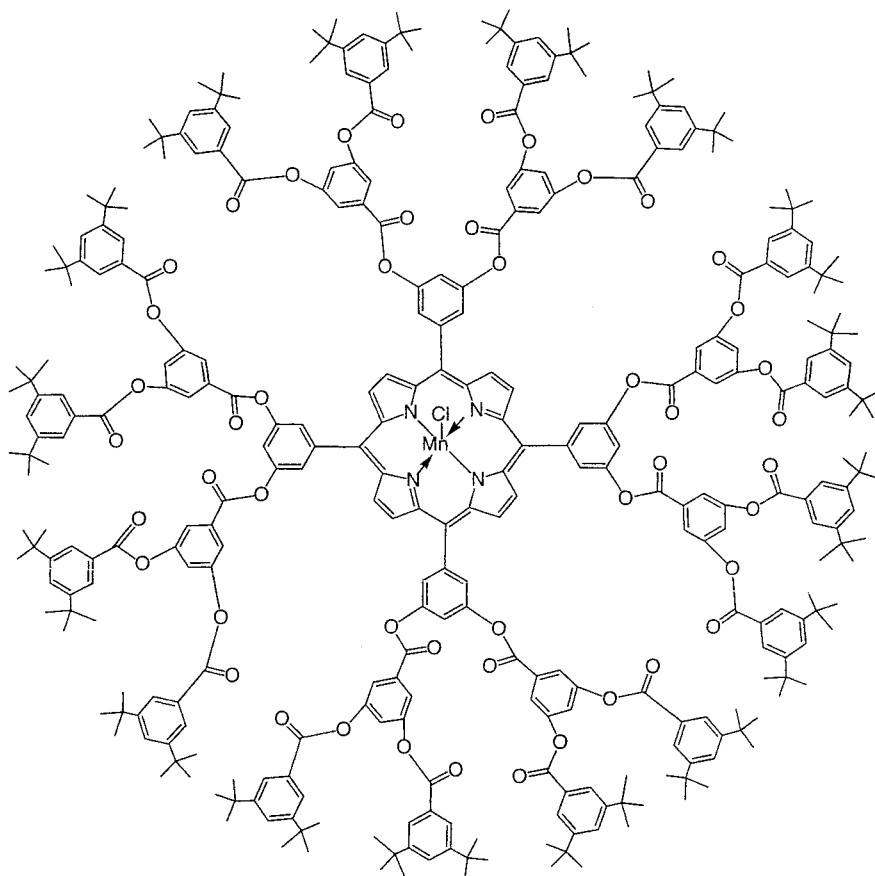
In summary, the first attempts had led to the conclusion that higher dendrimer generations provide a lower enantioselectivity than monomeric or low-generation analogues. Thus, the field had received relatively limited attention, but the more recent excellent results obtained by Seebach, Jacobsen, Togni, Deng, Chan, and Yoshida are now, on the contrary, very promising in terms of applications.

#### E. Cyanosilylation Reaction

A dendritically cross-linked polymer was employed by Seebach's group in the Ti–BINOLate-mediated







**Figure 18.** Suslick's dendritic chloromanganese(III) porphyrins for the catalysis of epoxidation of alkenes with iodosylbenzene.

porphyrin, 5,10,15,20-tetrakis(2',4',6'-triphenylphenylporphyrin).<sup>105,108</sup>

#### 4. Oxidation of Bromide

The Dettu group reported dendritic polyphenylsulfides, polyphenylselenides, and polyphenyltellurides prepared using Fréchet-type wedges and in which the branches are terminated by propyloxyl spacers connected to phenylsulfido (respectively, phenylseleno and phenyltelluro) groups (Figure 19). The selenide and telluride dendrimers catalyze the oxidation of bromide with hydrogen peroxide giving positive bromine species that can be captured by cyclohexene in two-phase systems. The increase in the rate of catalysis follows statistical effects for 1, 6, and 12 phenyltelluro groups. However, the increase in the rate of catalysis exceeds statistical contributions for the first generations with 3, 6, and 12 phenylseleno groups and suggests cooperativity among phenylseleno groups. On the basis of  $O_2$  consumed, the 12-phenylseleno dendrimer has a turnover number of  $>6 \times 10^4$  mol  $H_2O_2$  consumed per mol catalyst.<sup>109</sup>

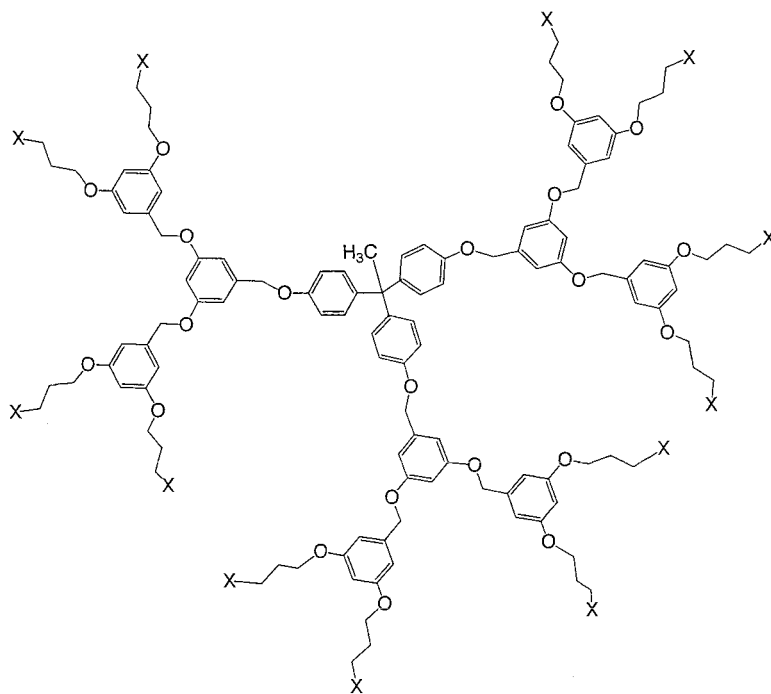
#### 5. Oxidation of Mercaptoethanol by Dioxygen

Kimura et al. synthesized a phthalocyanine-centered dendrimer by means of Newkome's methodology and used the second-generation cobalt-phthalocyanine dendrimer (Figure 20) as a catalyst for the oxidation of mercaptoethanol by dioxygen. These authors noted the high stability of the catalytic site.<sup>110</sup>

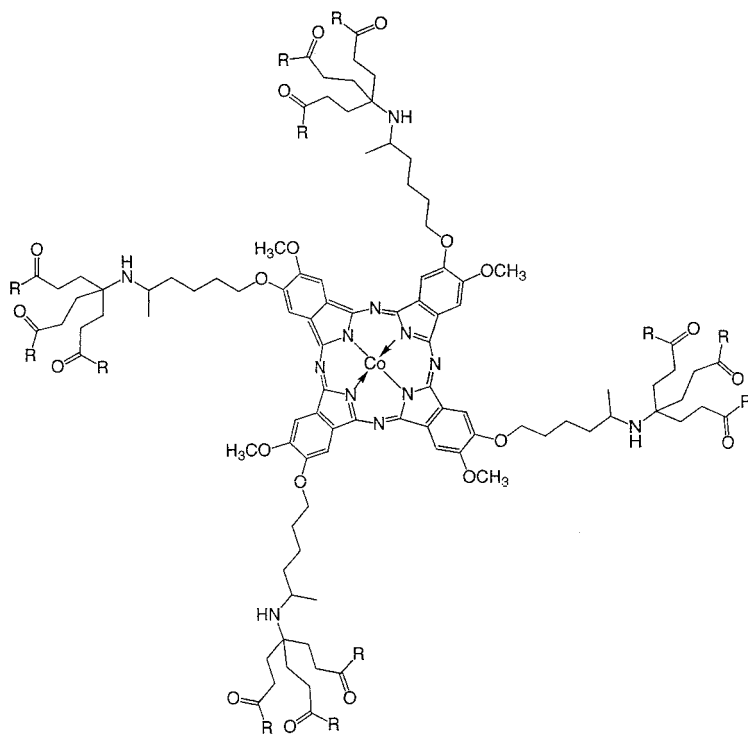
### V. Particle-Dendrimer Assemblies

#### 1. Hydrogenation

Crooks<sup>129</sup> and Tomalia<sup>187</sup> independently showed the formation of colloids inside dendrimers by reduction of metal ions coordinated to the nitrogen ligands located inside the PAMAM dendrimers. Crooks' group indeed reported the synthesis of dendrimer-encapsulated metal particles using PAMAM or poly(propylene)imine dendrimers and their use in homogeneous catalysis.<sup>189</sup> This approach was previously carried out with other polymers, ligands, or surfactants in order to control the size and prevent agglomeration. Dendrimers have a better-defined shape than ordinary polymers or surfactants, however, and were chosen because they were hoped by Crooks to function as "nanoreactors" and nanoporous stabilizers. Polymers previously used to stabilize nanoparticles aggregate in bowls, which increases their adsorption onto metallic sites. This phenomenon is responsible for lowering their catalytic properties. This problem is more limited in dendrimers because of their relative rigidity. Thus, access to the metallic catalytic sites is favored in dendrimers compared to polymers loaded by the same metals. The catalytic reactions were carried out by the Crooks group in organic solvents, water, supercritical  $CO_2$  (sc  $CO_2$ ), or fluoruous/organic biphasic solvents. The success of these experiments shows that the substrate can penetrate into and react in the interior of the metal-particle-loaded dendrimers. Lower generation den-



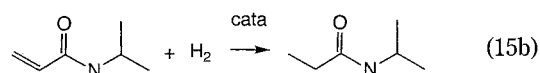
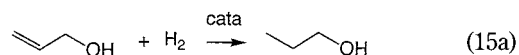
**Figure 19.** DeTTY's dendritic polyphenylselenides/polyphenyltellurides with Fréchet-type wedges that catalyze the oxidation of bromide with hydrogen peroxide with some positive dendritic effect.



**Figure 20.** Kimura's phthalocyanine-centered dendrimer synthesized by means of Newkome's methodology. The second-generation cobalt-phthalocyanine dendrimer is a stable catalyst for the oxidation of mercaptoethanol by dioxygen.

drimers work better than high-generation ones, however, because the porosity is generation-dependent (higher generation are more sterically crowded than lower generation). In this sense, the dendrimer acts as a nanofilter whose "mesh" can be adjusted. The catalytic hydrogenation of allylic alcohol to 1-propanol (eq 15) was carried out by Pd particles encapsulated in OH-terminated dendrimers in water. The turnover frequency calculated from the rate of

hydrogen uptake was  $218 \text{ mol of H}_2 (\text{mol of Pd})^{-1} \text{ h}^{-1}$  at  $20^\circ\text{C}$ .<sup>129</sup>



Crooks' group also prepared ion-paired, self-assembled inverted micelles from PAMAM dendrimers (G4-NH<sub>2</sub>) and decanoic acid in toluene and tested these toluene solutions for catalytic activity toward the same reaction. The strategy consisted of using a PAMAM dendrimer whose aqueous solution was set at pH 2 in order to preferentially protonate the exterior amines and then to add Pd<sup>2+</sup> in order to coordinate the interior amines. Finally, reduction of dendrimer-encapsulated Pd<sup>2+</sup> to Pd<sup>0</sup> particles is effected using NaBH<sub>4</sub>. G4-NH<sub>2</sub>-encapsulated nanoparticles can be quantitatively transported from the aqueous phase into toluene by addition of 10–20% of decanoic acid to the organic phase (which is readily visualized because the dendrimer-encapsulated particles are brown). The catalytic turnover frequency for the olefin reduction was about 760 mol of H<sub>2</sub> (mol of Pd)<sup>-1</sup> h<sup>-1</sup> at 20 °C, which compares favorably with the above value obtained in the preceding experiments.<sup>130</sup>

Crooks also applied the biphasic fluoruous/organic solvent method in order to facilitate recovery and recycling of soluble catalysts. The catalyst must contain fluorinated chains in order to be soluble in the fluoruous solvent that is not miscible with the organic solvent containing the reactants. Stirring the mixture leads to a fine emulsion, and catalysis proceeds at the interface between the two liquids. Alternatively, heating reversibly provokes homogenization of the reaction mixture. After completion of the reaction, the phases are allowed to separate at room temperature and the product is isolated from the organic phase while the catalyst is recovered in the fluoruous layer. Thus, perfluoroether groups were covalently or electrostatically linked to the exterior of dendrimers in order to carry out a carbon-coupling Heck reaction between iodobenzene and *n*-butyl acrylate, giving *n*-butyl*trans*-formylcinnamate. This product was obtained with 100% regioselectivity at 90 °C.<sup>188</sup> The selectivity is lower (74–98%) and the reaction temperatures higher (120–130 °C) in the absence of the dendrimer. Unoptimized yields with the dendrimer-encapsulated catalyst in this biphasic medium ranged between 35% and 85%. Chechik and Crooks also prepared PAMAM dendrimer-encapsulated Pd nanoparticles as fluoruous phase-soluble catalysts. The terminal amino groups of PAMAM dendrimers were allowed to react with the carboxylic end groups of the perfluoropolyethers, and the dark-brown dendrimer-encapsulated Pd nanoparticles prepared therefrom were soluble in fluoruous solvents. These catalysts were active in fluoruous biphasic systems for the hydrogenation of alkenes and for the isomerization of terminal alkenes and were also recycled 12 times without appreciable loss of catalytic activity.<sup>132</sup>

## 2. Heck Reaction

Perfluorinated catalysts also allow the use of sc CO<sub>2</sub> in which they are soluble. The use of this relatively new solvent in catalysis is indeed important for green chemistry, i.e., to avoid toxicity and allow catalyst recovery. Using perfluorinated dendrimer-encapsulated Pd particles, Crooks' group car-

ried out Heck coupling between aryl iodides and methacrylate yielding exclusively the highly unfavored 2-phenylacrylic acid methyl ester isomer at 5000 psi and 75 °C, whereas classical Pd catalysis yields predominantly *trans*-cinnamaldehyde (>97%).<sup>191</sup>

## 3. Anodic Oxidation of Ethanol

Park's group introduced Ni and Ru into PAMAM dendrimers by coordination to nitrogen atoms and prepared nanoparticles by electrodeposition of these metals. The electrochemical and catalytic use of these nanoparticles have been investigated and showed enhancement of the catalytic activities for the oxidation of ethanol compared to bulk metal oxide electrodes.<sup>133</sup> See also the first example of the following section on redox catalysis.

## VI. Redox Catalysis

Redox catalysis is the mediation or catalysis of redox reactions. This broad area spreads to classic chemical systems, electrochemistry, biology, and photochemistry, although the term redox catalysis is usually reserved to the three latter groups.<sup>114,115</sup> Examples involving dendrimers reported for electrochemical reactions are reviewed here. Catalysis of hydrogenation is reviewed in sections II, III, and V, whereas catalysis of oxygenation (oxygen-atom transfer) is reviewed in sections IV and V.

### 1. Anodic Oxygen Reduction

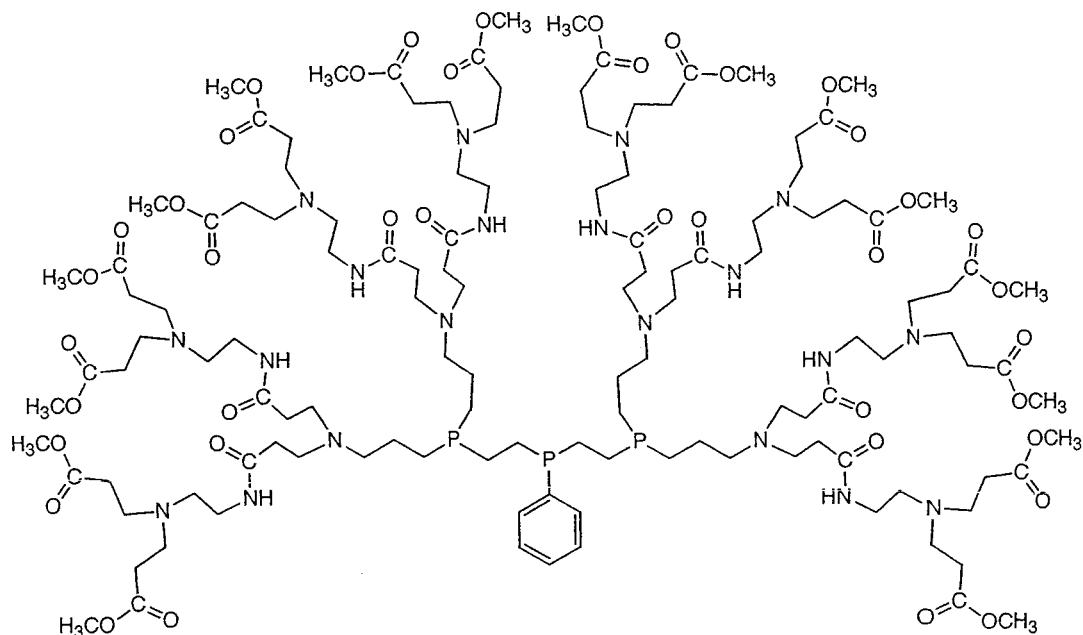
Crooks et al. reported that metallic nanoclusters of 60 Pt atoms can be encapsulated within electrode-confined dendrimers and used as catalytic sites for oxygen reduction. The generation-4 PAMAM dendrimer-encapsulated Pt<sub>60</sub> was attached to the Au macroelectrode using a chemisorption procedure; then the O<sub>2</sub> reduction was compared to that of a Pt-free electrode. Reduction of O<sub>2</sub> on Au (macroscopic electrode) and Pt (particles) are easily distinguished because the reduction potential shifts positive on Pt by 75 mV in this case. The catalytic current is much larger with this Pt additive.<sup>131</sup>

### 2. Cathodic Reduction of CO<sub>2</sub> to CO

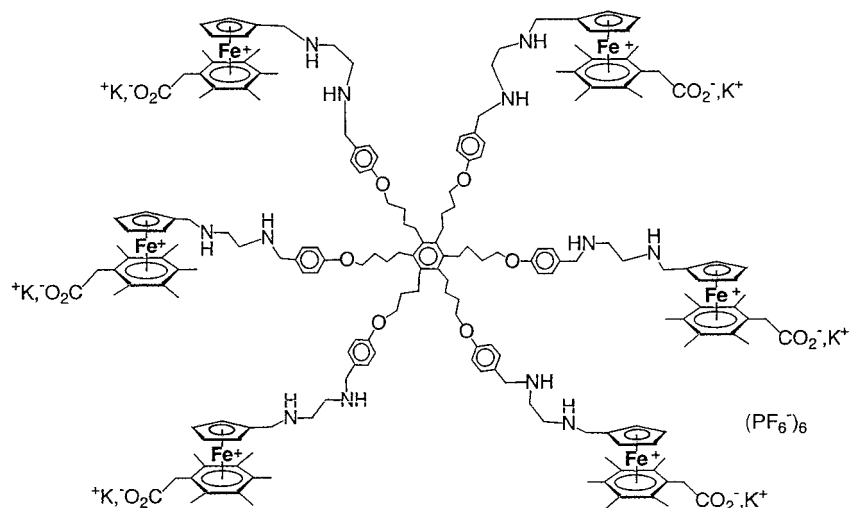
One of the earliest reports on catalysis using metallodendrimers appeared in 1994 from DuBois et al. and concerned a dendrimer containing five planar Pd<sup>II</sup> complexes bearing a triphosphine and an acetonitrile ligand. This metallodendrimer catalyzes the cathodic reduction of CO<sub>2</sub> to CO and appeared to deactivate by formation of Pd–Pd bonds.<sup>126</sup> To overcome this difficulty, DuBois' group prepared organophosphine complexes that are embedded within polyamidoamine dendrimers (Figure 22). In this new dendrimer, phosphorus atoms are located at the core of a Tomalia-type PAMAM frame. Catalytic properties for the CO<sub>2</sub> electroreduction were also found for this 16-branch dendrimer.<sup>127</sup>

### 3. Ferrocenes as Redox Mediators for Glucose Oxidation

Dendrimers containing first-row late-transition-metal sandwich complexes stable in at least two



**Figure 21.** DuBois' triphosphine-centered PAMAM-type dendrimer whose Pd complex redox-catalyzes the cathodic reduction of  $\text{CO}_2$  in which side Pd–Pd bond formation is avoided by the dendritic bulk.



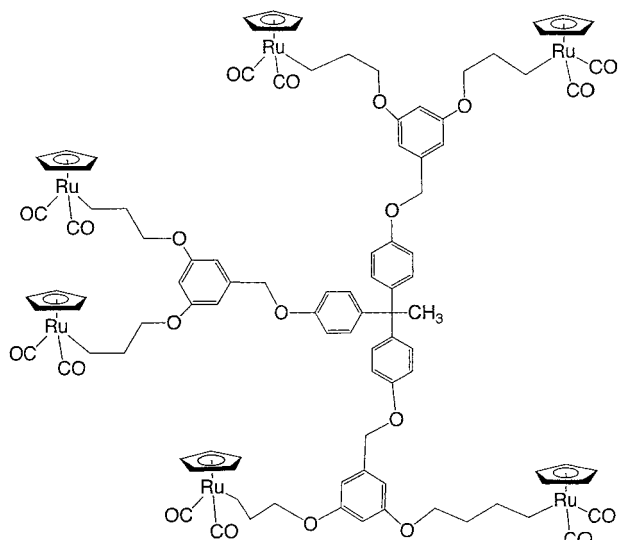
**Figure 22.** Astruc's star-shaped molecules containing six organometallic termini  $[\text{Fe}(\text{core}-\eta^5\text{-Cp})(\eta^6\text{-arene})][\text{PF}_6]$  that were shown to be as active as mononuclear complexes with the same driving force for the redox-catalyzed cathodic reduction of nitrate and nitrite to ammonia in water.

oxidation states are redox catalysts, i.e., they catalyze the anodic oxidation<sup>111,112</sup> or the cathodic reduction<sup>113</sup> of substrates. This area has been reviewed.<sup>114,115</sup> Typically, ferrocene groups are active catalysts ( $\text{Fe}^{\text{II/III}}$ ) on the oxidation side (for instance, for glucose oxidase enzyme catalysis of glucose oxidation).<sup>116</sup>

#### 4. Complexes $[\text{Fe}^{\text{II/III}}\text{Cp}(\eta^6\text{-arene})]^{+/0}$ as Redox Catalysts for the Reduction of $\text{NO}_2^-$ and $\text{NO}_3^-$

The  $[\text{Fe}^{\text{II/III}}\text{Cp}(\eta^6\text{-arene})]^{+/0}$  complexes ( $E^\circ = -1.8$  to  $-2.2$  V vs ferrocene) are active on the reduction side (for instance for the reduction of nitrates and nitrites).<sup>113,115</sup> Metallodendrimers functionalized with these sandwich groups at the core or at the periphery were the first known organometallic dendrimers,<sup>117–123</sup> and their reversible redox activity was shown. Mixed-

valence compounds containing both types of iron sandwiches and their redox chemistry were also reported.<sup>124</sup> They can be catalysts for both oxidation and reduction reactions. Dendritic  $[\text{Fe}(\text{dendr}-\eta^5\text{-Cp})(\eta^6\text{-arene})][\text{PF}_6]$  containing six organometallic termini (Figure 21) were shown to be as active as mononuclear complexes with the same driving force for the redox-catalyzed cathodic reduction of nitrate and nitrite to ammonia, based on rate constants determined by cyclic voltammetry.<sup>113</sup> DAB-polyamino dendrimers were allowed by the Cuadrado group to react with mixtures of ferrocenoyl chloride and cobaltocenoyl chloride. The resulting metallodendrimers contained statistical distributions of both ferrocenoyl and cobaltocenoyl and were reported to be the most stable metallocene dendrimers. They can perform redox-catalytic functions on both the oxidation and reduction sides.<sup>125</sup>



**Figure 23.** Moss' hexabranched ruthenium dendrimer whose silica-supported version was examined as a catalyst of the Fischer–Tropsch synthesis.

## VII. Heterogeneous Catalysis.

### 1. Fischer–Tropsch Catalysis

The Moss group investigated the Fischer–Tropsch synthesis using an hexabranched ruthenium dendrimer supported on silica (Figure 23). The termini of the dendritic branches are 18-electron  $[\text{RuCp}(\text{CO})_2\text{alkyl}]$  groups. Under Fischer–Tropsch conditions, this dendrimer is metastable. The time-on-stream behavior of this catalyst in the CO hydrogenation was compared to an impregnated  $\text{Ru}/\text{SiO}_2$  catalyst and showed no FT-specific product pattern, which is substantiated by the rate of formation of some specific hydrocarbons. This study shows that a single ruthenium site is not sufficient for the Fischer–Tropsch synthesis.<sup>128</sup>

### 2. Insoluble Dendritic Lewis Acids: Mukayama and Friedel–Crafts Reactions

Reetz and Giebel loaded the  $\text{DAB-dendr}(\text{NH}_2)_{32}$  dendrimer with a Lewis acid scandium catalyst by a sulfonylation reaction using  $\text{Ti}_2\text{O}/\text{Et}_3\text{N}$  followed by metalation of the  $-\text{NHSO}_2\text{CF}_3$  functional groups of the dendrimer using  $\text{Sc}(\text{OTf})_3$ , seemingly producing the  $\text{NTf}[\text{Sc}(\text{OTf})_2]$ -terminated dendrimer. The dendritic material was insoluble, however, and cross-linking appeared most probable. Nevertheless, the catalytic activity as a Lewis acid was found in the three-component reaction of benzaldehyde, aniline, and enoxysilane producing a  $\beta$ -aminoketone in the Mukayama reaction and in the Friedel–Crafts acylation of anisole by acetic anhydride affording *p*-methoxyacetophenone. In all these reactions the yields were good and the insoluble dendritic catalyst was simply removed by filtration and reused without loss of catalytic activity. This catalyst is thus heterogeneous and represents the first example of its new class.<sup>134</sup>

## VIII. Supported Dendritic Catalysts

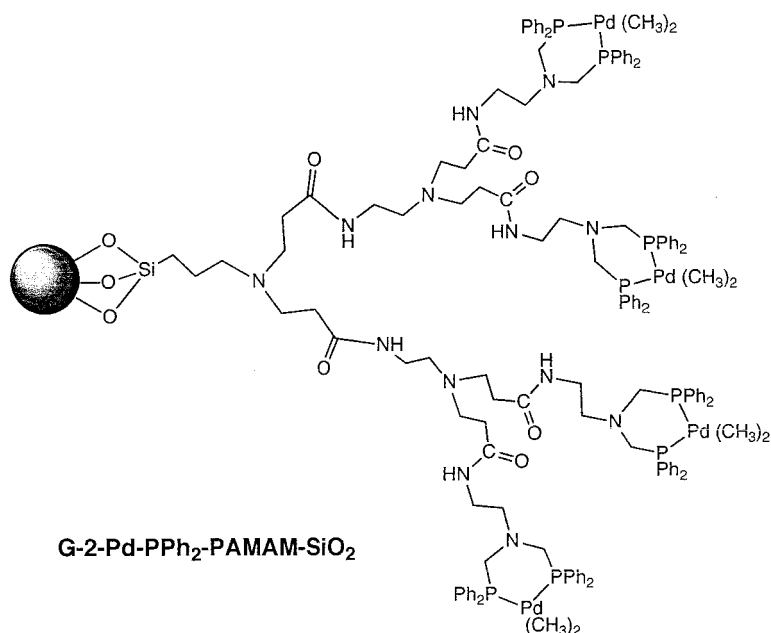
### 1. Heck Reaction

Alper et al. examined the Heck reaction of aryl bromides with both butyl acrylate and styrene by using a palladium catalyst in which palladium was complexed to dendritic phosphines on silica. The silica–PAMAM dendrimers (Figure 24) were synthesized starting from commercial aminopropyl silica gel and further construction involved Michael-type reaction with methyl acrylate followed by amidation of the ester units with ethylenediamine to complete the first generation as in Tomalia's seminal work. The double phosphinomethylation of each terminal amino group was achieved by reaction of the silica–PAMAM dendrimer with diphenylphosphinomethanol, and reaction of the dendritic diphosphine with  $[\text{PdMe}_2(\eta^2\text{-NMe}_2\text{CH}_2\text{CH}_2\text{NMe}_2)]$  led to the substitution of the TMEDA ligand by the dendritic diphosphine. Moderate to good yields in these Heck-type reactions were obtained, and the dendritic palladium- $\text{PPh}_2$ -PAMAM- $\text{SiO}_2$  catalyst could be recycled and reused with only moderate reduction in activity. The yields of stilbene were reduced when generation 3 and 4 dendrimers were used instead of generation 1 and 2 (the latter gave the best yield). The effect of temperature was studied with this generation-2 catalyst, and it was found that the best yields were obtained when the temperature was in the 110 to 140 °C range.<sup>135</sup>

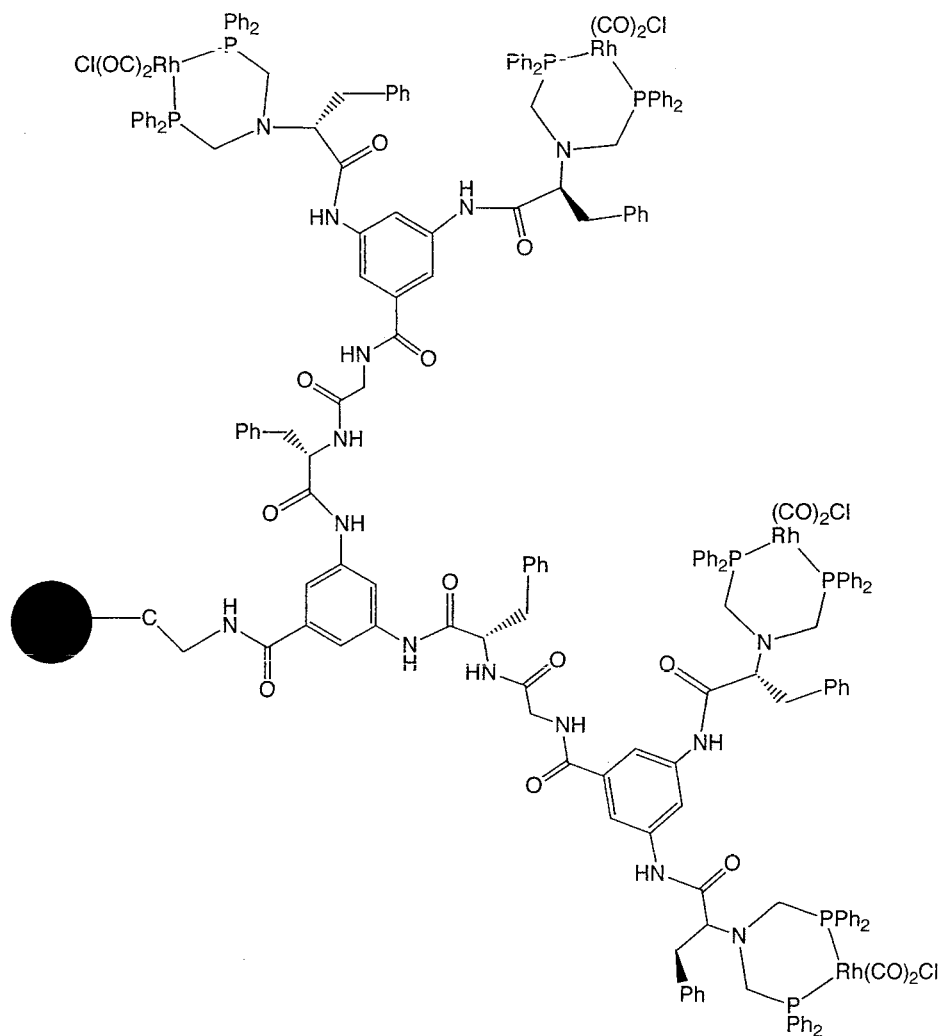
### 2. Hydroformylation

Using a related strategy, the groups of Alper, Manzer, and Arya prepared silica–PAMAM-type dendrimers terminated by bis-diphenylphosphine termini up to the fourth generation (eight branches) using a divergent strategy for the hydroformylation of styrene and vinyl acetate. The hydroformylation of either styrene or vinyl acetate proceeded in up to quantitative yields and in fine regioselectivity. Dendrimers with variable length for the dendritic segments of the PAMAM dendrimers were compared in terms of their catalytic activity, and it was shown that a minimum length of six methylene units between two nitrogen atoms is necessary for optimal catalytic efficiency. This confirms the negative dendritic effect when the dendritic generation increases with a too short dendritic segment because of the increasing bulk around the catalytic coordination sites. After the hydroformylation reactions, the product solution is yellow or orange, evidence of leaching of rhodium from the silica. The carbon monoxide pressure also promotes this leaching but not by the pressure of hydrogen alone.<sup>136</sup>

These authors also reported a solid-phase approach to obtain dendritic ligands onto polystyrene-based beads. The advantages of this second approach are (i) the ease of solid-state synthesis using a building block approach, (ii) the characterization of products anchored onto beads after cleavage, (iii) better swelling properties in most solvents, and (iv) flexible polymeric backbones. A pseudo-peptide-based building block with two Fmoc-protected amino groups and a carboxylic acid were synthesized on large scale;



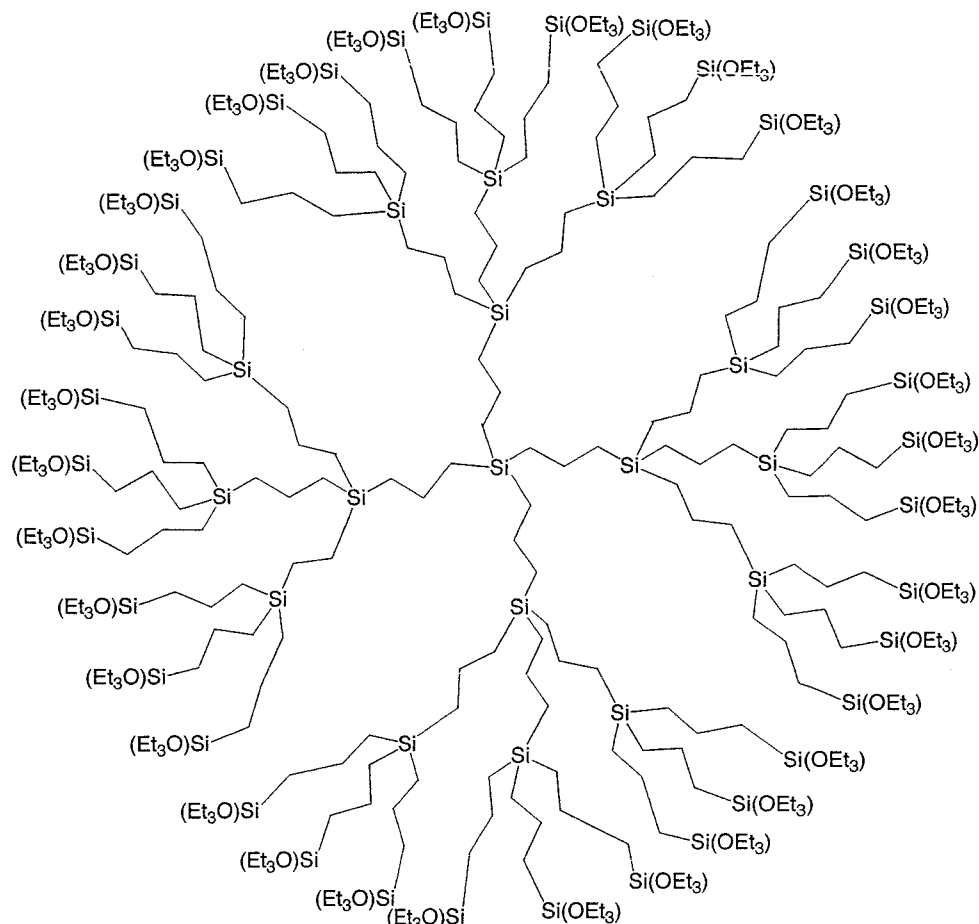
**Figure 24.** Alper's silica-supported PAMAM-type palladium dendrimer used as catalysts for Heck reactions



**Figure 25.** Alper's polystyrene-supported G-2 palladium dendrimer containing amino acid wedges as catalysts for the efficient regioselective hydroformylation of styrene.

then dendritic phosphines (Figure 25) up to eight branches were synthesized therefrom using a divergent scheme. The rhodium complexes were found to

be excellent catalysts for the hydroformylation of several olefins. In particular, the generation-2 catalyst (four branches) is reactive up to five cycles. For



**Figure 26.** Tilley's alkoxy-silyl-terminated carbosilane dendrimers used for the preparation of high-surface xerogels whose Ti complexes efficiently catalyzed the epoxidation of cyclohexene.

instance, the hydroformylation of styrene at 45 °C using this catalyst led to complete conversion with a high selectivity for the branched isomer (branched: linear, 16:1).<sup>137</sup>

The groups of Arya, Alper, and Manzer also designed a biomimetic approach toward supported ligands on dendritic arms to explore recyclable hydroformylation catalysts. They addressed the "leaching problem" by locating the ligand sites along the inner dendritic arms and relied on solid-phase methodology to achieve this goal. They reasoned that the immersion of ligands in dendritic architectures might exhibit a prolonged reactivity by preserving the catalytic sites from the outer environment. They compared the activity of generation-0 and generation-1 dendrons attached to the polymer support and containing  $\text{ArN}(\text{CH}_2\text{PPh}_2)_2\text{Rh}(\text{CO})_2\text{Cl}$  moieties. It was found that both catalysts exhibited >99% conversion of styrene, *p*-methoxystyrene, vinyl acetate, and vinyl benzoate with branch-to-linear ratio of aldehydes ranging from 14:1 to 30:1. Recycling showed that the conversion remained the same even up to six cycles for styrene, but conversion decreased for the other olefins, the larger first-generation catalyst giving better results than the generation-0 catalyst.<sup>138</sup>

### 3. Epoxidation of Cyclohexene

Tilley's group synthesized second- and third-generation alkoxy-silyl-terminated carbosilane den-

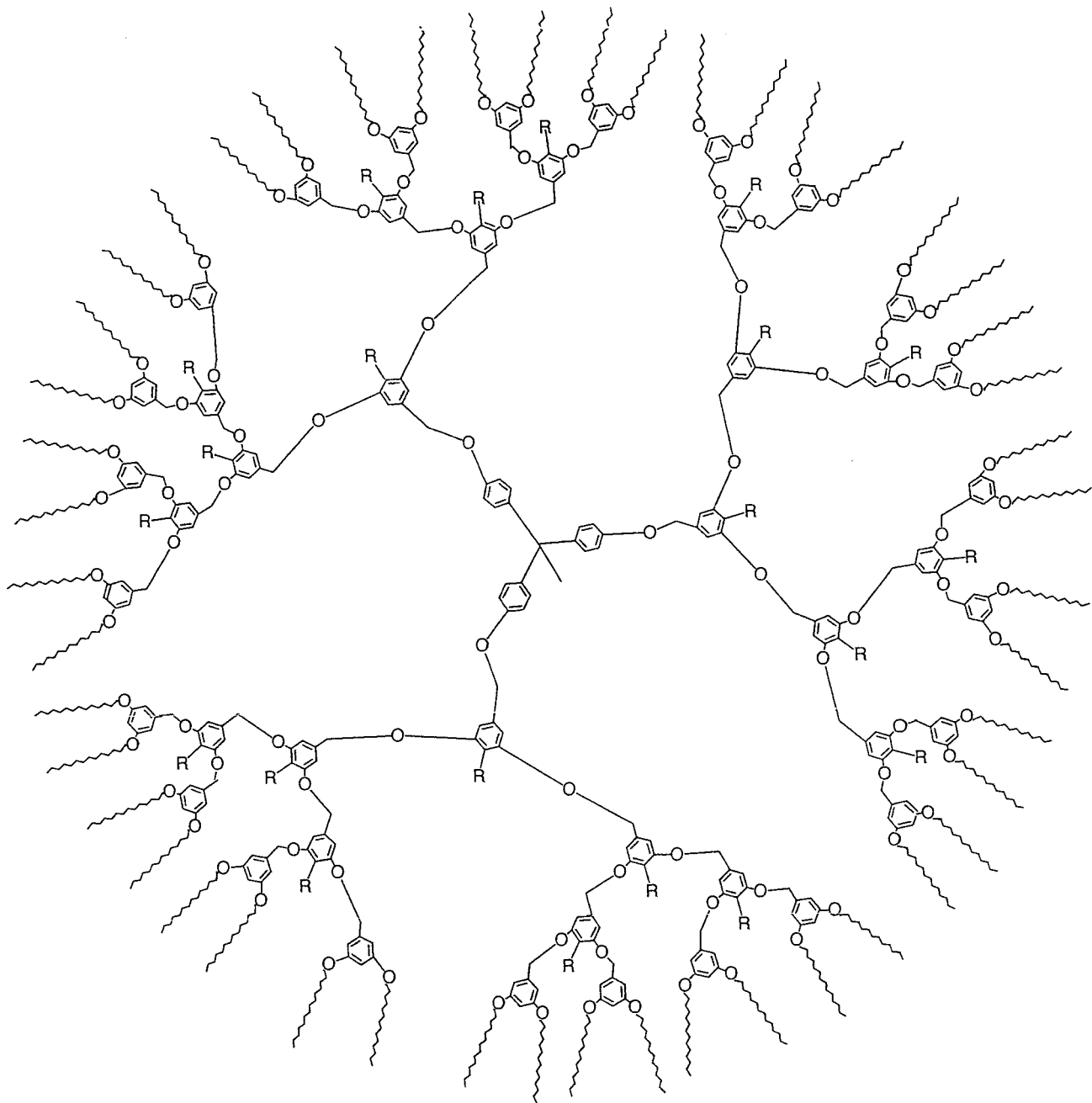
drimers (Figure 26) and used these dendrimers for the preparation of high-surface xerogels. Treatment of these aerogels with  $[\text{Ti}(\text{O}i\text{-Pr})_4]$  or  $[\text{Ti}\{\text{OSi}(\text{O}t\text{-Bu})_3\}_4]$  yielded dendritic Ti-containing catalysts for the epoxidation of cyclohexene which were shown to be very selective and more active in terms of yields and initial rates than the Shell catalyst prepared from silica and  $[\text{Ti}(\text{O}i\text{-Pr})_4]$ .<sup>139</sup> The first hybrid xerogels from Si-containing dendrimers had been reported by Boury, Corriu, and Nuñez.<sup>48</sup> See also the first example of the following section.

## IX. Micellar and Phase-Transfer Catalysis

### 1. Nucleophilic and Electrophilic Substitution

Dendrimers are molecular micelles,<sup>5</sup> and the micellar properties<sup>140</sup> of dendrimers have been exploited.<sup>5</sup> Kenawy attached dendrimers onto polymer-montmorillonite, and the supported dendrimers were modified to produce ammonium and phosphonium salts. The catalytic phase-transfer activities of these supported dendritic systems were investigated, and it was shown that they are highly activating for the nucleophilic substitution reactions of  $\text{Br}^-$  by  $\text{SCN}^-$ ,  $\text{CN}^-$ , or  $\text{NO}_2^-$  in *n*-BuBr. For instance, the yields reach 100% with 10% mol catalyst in a short time at reflux of the toluene/water solvent mixture. Reaction rates were higher with the phosphonium catalyst than with the ammonium catalyst. The recyclability





**Figure 27.** Hawker and Fréchet's micelle-like dendrimers with inner alcohol functionalities ( $R = \text{CH}_2\text{OH}$ ) increasing the hydrophilic character of the dendritic interior that catalyzed dehydrohalogenation of iodoalkanes to olefins.

was checked with excellent results, and the work up was extremely simple, requiring only filtration. No cross-contamination from the catalyst to the organic product was found.<sup>141</sup>

In a patent, De Haén et al. reported the application of polyetheneglycol dendrimers and polypropyleneglycol dendrimers to phase-transfer catalysis of nucleophilic substitution reaction. The benzylation of  $\beta$ -naphthol by benzyl chloride or the conversion of benzyl chloride to benzyl thiocyanate was achieved in the presence of 10–30% dendritic catalyst, the solvent being toluene or dichloromethane. Under these conditions, Tomalia's first-generation PAMAM dendrimers were not active. In addition, an increased yield for classical phase-transfer catalysis reactions could be obtained when dendritic molecules in

amounts greater than 10% of the starting material are present concomitantly with catalysts such as quaternary ammonium salts. The dendrimers could be easily separated by filtration or ultrafiltration at the end of the reactions.<sup>142</sup>

The Hawker and Fréchet groups designed dendrimers that can play the role of reverse micelles with catalytic activity (Figure 27). The dendrimers were constructed by the convergent approach involving tetradecyl-substituted benzyl bromide as the terminal unit and a methyl-ester-functionalized diphenol as the repeat unit. After construction, these ester groups located inside the dendrimer were reduced to the corresponding alcohols in order to increase the hydrophilic character of the dendritic interior and provide hydrogen-bonding sites. These dendrimers

thus have a high inner density of aromatic rings and hydroxy groups affording a suitable environment to stabilize positively charged transition states of reactions as in enzymes. Nonpolar products could have the possibility to migrate from polar interior to the outside medium leading to high turnovers.  $S_N2$  and unimolecular reactions ( $E_1$ ) were examined. The  $E_1$  reaction dehydrohalogenation of 2-iodo-2-methylpropane and 2-iodo-2-methylheptane leading to olefins was catalyzed by 0.01 mol of the dendrimer with ca. 90–99% conversion after 43 h at 70 °C in the presence of a 12-fold excess of sodium bicarbonate in cyclohexane- $d_{12}$  (turnover, 17 400). The olefins obtained were mixtures of internal and terminal olefins whose ratio was catalyst-dependent, a feature that was not rationalized. Decreasing the size of the dendrimer from [G-4] to [G-3] resulted in a 15–20% reduction in both rates and turnover numbers. The  $S_N2$  alkylation of pyridine with  $CH_3I$  at room temperature in cyclohexane was again best promoted by the [G-4] dendrimer. In this case, attempts to perform the reaction at low dendrimer concentration resulted in incomplete conversions, most likely due to product inhibition since polar methyl pyridinium iodide has a high affinity for the dendritic core. Seemingly, the reaction is thus stoichiometric in dendrimer.<sup>145</sup>

## 2. Decarboxylation

Unimolecular micelles, a term first used by Newkome,<sup>5</sup> refers to amphiphilic dendrimers. These dendrimers can catalyze the concerted unimolecular decarboxylation of 6-nitrobenzoxazole-3-carboxylate ion. Indeed, the internal quaternary ammonium ions of such dendrimers can be active sites for phase-transfer or polyelectrolyte catalysis. Hydrogen bonding of solvent to the carboxylate anion reduces the rate, and dipolar aprotic solvents increase the rate of decarboxylation. Thus, the ammonium chloride dendrimers derived from DAB-*dendr*-( $NH_2$ ) $_n$  by sequential amidation and  $LiAlH_4$  reduction increase the decarboxylation rate by 200–500 times in pure water.<sup>143,144</sup>

In another patent, hyperbranched polymers containing polyoxoalkylene chains have been reported by De Haën et al. as catalysts or coadjuvants of phase-transfer catalysis reactions.<sup>146</sup>

## X. Dendritic Organic Catalysts

### 1. Decarboxylation

Ford's group reported a polyether dendrimer with 36 pendant quaternary ammonium ions which accelerates the decarboxylation of 6-nitrobenzoxazole-3-carboxylate (eq 14a) and the bimolecular hydrolysis of *p*-nitrophenol diphenyl phosphate in water in the presence of the *o*-iodosobenzoate ion (eq 14b). The third generation of polycationic dendrimers showed an increase of catalytic activity as compared to the lower generation containing 12 pendant ammonium cations. This rate enhancement was taken into account by the high local concentration of reactants bonded to the dendritic periphery by hydrogen-bonding and hydrophobic interactions.<sup>147</sup> This

phenomenon has already been observed with micelles and lattices bearing quaternary ammoniums.<sup>148</sup> The catalytic activity was lower than with the lattices, however, because the latter are more hydrophobic and have a lower degree of solvation than dendrimers. This work is one of the very first catalytic studies with dendrimers published in 1994. In a related study, Ford's group also studied the catalysis of the same reaction by  $Cu^{II}$ ,  $Zn^{II}$ , and  $Co^{III}$  complexes of DAB-*dendr*-( $NH_2$ ) $_x$  dendrimers<sup>30</sup> having 8, 32, and 64 primary amine end groups. The reactions were carried out at  $pH \leq 8.1$  with relative activities  $Cu^{II} > Zn^{II} > Co^{III}$ . The rates of hydrolysis are faster with sodium perchlorate than with sodium chloride to control ionic strength. With sodium perchlorate and  $Cu^{II}$ , the rate increases with increasing size of the dendrimer. With sodium chloride and  $Cu^{II}$ , it is the opposite. The fastest hydrolysis occurred for a dendrimer-to- $Cu^{II}$  ratio  $\leq 2$ .<sup>149–151</sup>

### 2. Acylation of Alcohols

Marquardt and Lünig synthesized a dendrimer containing up to 12 pendent concave pyridine groups. The acylation of alcohols using diphenylketene was catalyzed by this dendrimer with no decrease of activity for primary, secondary, or tertiary alcohols. This contrasted with the behavior of similar catalysts in linear polymers or coupled to a Merrifield resin. Remarkably, it was also possible to recover the catalyst by nanofiltration in 70–99% yields.<sup>152,153</sup>

### 3. Nitroaldol Reaction

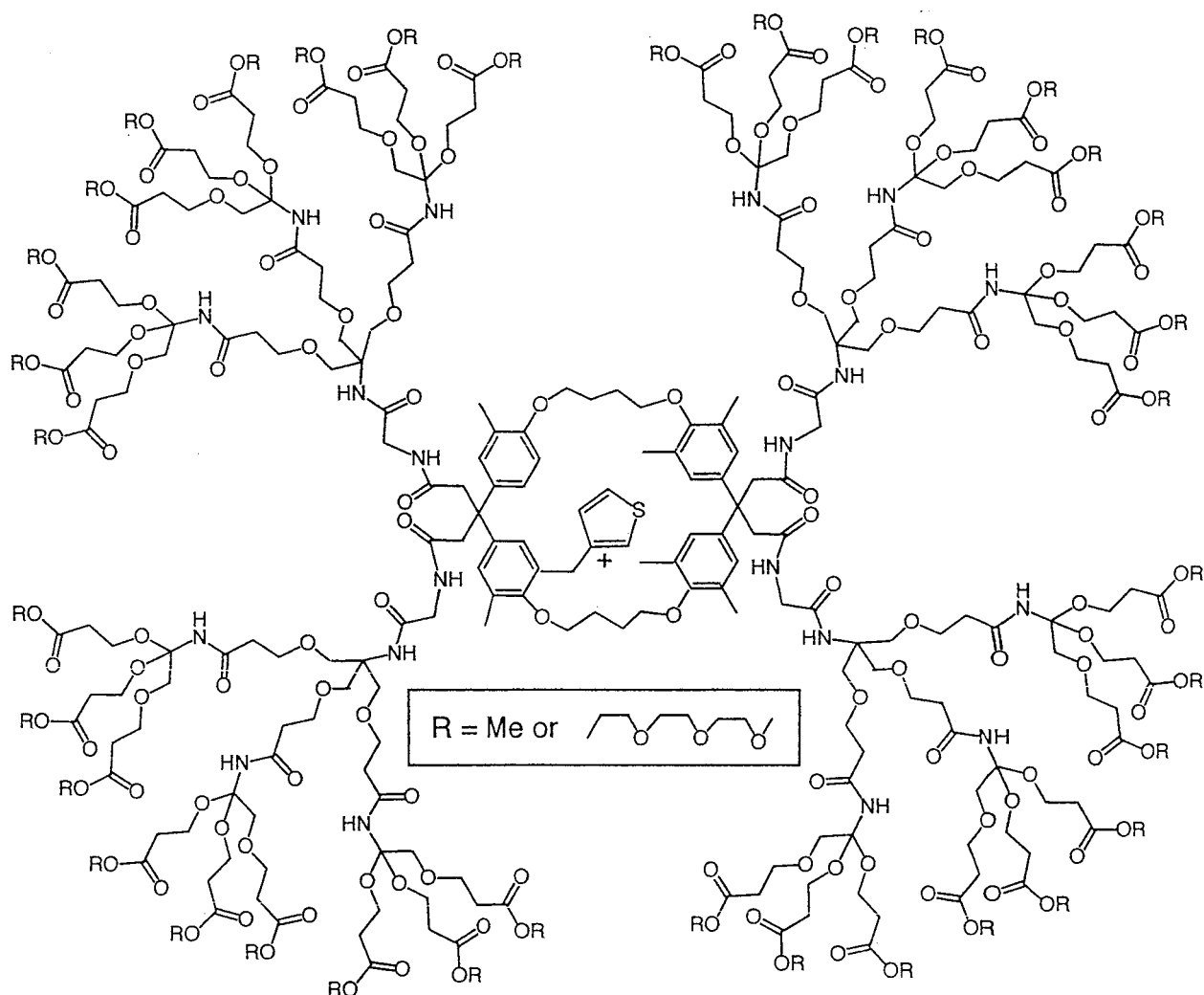
Morao and Cossio attached Fréchet's dendron to triethanolamine in order to catalyze the nitroaldol reaction requiring a base such as a tertiary amine as catalyst. This reaction, called the Henry reaction, couples an aldehyde to a primary nitroalkane to give a nitro alcohol. In this case, the activity of the catalyst decreases as the dendrimer becomes larger and the dendrimer does not impose a stereoselective course for the reaction.<sup>154a</sup>

### 4. Aminolysis

Martin and Twyman reported the acceleration of an aminolysis reaction using a PAMAM dendrimer with 64 terminal amine groups. When compared to an equivalent of *N*-acetythylenediamine, the initial rate of a simple aminolysis reaction in water was found to be greatly enhanced using such a generation-4 PAMAM dendrimer. This initial increase is largely due to the hydrophobic binding of the substrate within the outer region of the dendrimer. As a consequence of this binding, the substrate is held in close proximity to the reactive amine groups on the surface of the dendrimer. It is this increase in effective molarity that results in an increase in the observed initial rate.<sup>154b</sup>

### 5. Asymmetric Reduction of Ketones

The Rico-Lattes and Lattes group used a chiral PAMAM dendrimer containing lactose end groups as an asymmetric reagent for the asymmetric reduction



**Figure 28.** Diederich's catalytic dendrophanes composed of a thiazolio-cyclophane initiator core containing four-generation polyetheramide dendrons that tentatively mimic the thiamine-diphosphate-dependent enzyme pyruvate oxidase

of prochiral ketones by  $\text{NaBH}_4$  in THF (it is likely that the reaction is stoichiometric rather than catalytic, but the concept is elegant). The substrate migrates from the lipophilic dendrimer core to the lactose periphery where the reductant is bound to the lactose OH groups by hydrogen bonding. The reaction is heterogeneous because the lactose-terminated dendrimer- $\text{NaBH}_4$  complex is insoluble in THF. High *ee*'s (between 82% and 100%) were obtained.<sup>154c,d</sup>

### XI. Enzyme Mimics

In his seminal review,<sup>1</sup> Tomalia underlined the comparison between dendrimers and biological systems in terms of construction, shape, topology, and behavior. In a review,<sup>14</sup> Astruc stressed the research avenues on dendrimers toward biology, from biomimeticism to medicinal engineering. Recently, Diederich<sup>26</sup> developed the biological significance of dendrimers in a review article.

Diederich et al. also synthesized catalytic dendrophanes composed of a thiazolio-cyclophane initiator core containing four-generation polyetheramide dendrons (Figure 28) with the aim to mimic the thiamine-diphosphate-dependent enzyme pyruvate oxidase. The low catalytic activity in the interior of

the dendrophanes were explained by the steric hindrance of the reaction transition states by the dendritic branches.<sup>155</sup> See also section VIII.

### XII. Membrane Reactors

The set up of membrane reactors is essential to the application of catalysis to industrial processes.<sup>156</sup> In reactors, membranes are mostly used to separate the reaction components, and nanofiltration membranes to filter small molecules (down to 400 Da) are commercially available. A retention of the catalyst on the order of 99.9% is required in order to use a catalyst that is stable in a reactor over a long time. This area has also spread to the field of metallodendritic catalysts. The use of membranes has been mentioned at various occasions throughout this review. In particular, the groups of Kragl and Reetz described the retention of Meijer's diamino-propyl-type dendrimers modified with palladium phosphine termini by ultra- or nanofiltration membranes. They used these dendritic catalysts for the allylic substitution in a continuously operating chemical membrane reactor. Retention rates are higher than 99.9%, resulting in a 6-fold increase of the total turnover number for the dendritic Pd catalyst of

generation 3 bearing 16 diphosphine–Pd groups at the periphery.<sup>157</sup> The continuous reactor was operated with a conversion of up to 12% for 60 residence times. With the Pd dendrimer of generation 4 bearing 32 diphosphines (as in eq 3), the conversion was 75% after 100 residence times. The product was contaminated with palladium, however. Thus, a positive dendritic effect was obtained, but more experiments are called for in order to draw firm conclusions, also because the experimental conditions were not the same with the metallodendrimers of generations 3 and 4. The investigation of a continuous operating chemical membrane reactor has been an ongoing program in the Kragl laboratory<sup>158</sup> that is now also pursued in Vogt's laboratory.<sup>159</sup> The groups of Kragl, Keim, Vogt, and van Koten achieved the hydrovinyl-ation of styrene in a membrane reactor using carbosilane dendrimers with hemilabile P,O ligands. Isomerization of the chiral product 3-phenylbut-1-ene to internal achiral olefins takes place at high conversion. To avoid this isomerization, the reaction was run continuously at lower conversion. The dendritic catalysts had four branches terminated by a cationic palladium–allyl moiety. Each metal of these dendrimers was also coordinated in a chelating fashion by the terminal phosphanylcarboxylic acid ester, i.e., by the alkylidiphosphino ligand as well as the carbonyl of a benzyl ester group separated from the phosphine by several methylene units. The catalysis in a high-pressure membrane reactor using the metallodendrimer, in which the above number of methylene units is three ( $M_w = 2868 \text{ g mol}^{-1}$ ), led to 85% of retention in the membrane reactor. Although this retention is still far from being sufficient for practical purposes, this result looks promising. The system reaches its maximum productivity ( $2.3 \text{ g L}^{-1} \text{ h}^{-1}$ ) after 9 h, the decrease being most probably accelerated by the formation of Pd (black) on the membrane surface, which can be seen after the reaction. The desired 3-phenylbut-1-ene was produced over a period of 80 h. Gratifyingly, hardly any isomerization or other side products could be detected in the product solution. It was anticipated that the next dendritic generation of this metallodendrimer, i.e., that containing 12 palladium atoms, will already allow enough hold back by a nanofiltration membrane to give efficient catalyst immobilization.<sup>159a,b</sup> The van Leeuwen group also contributed to this field with dendrimers having carbosilane cores and phosphinopalladium–allyl termini as indicated in section II.

A German patent recently appeared concerning the manufacture of compounds in a membrane reactor in the presence of a polymer-supported catalyst or a dendritic polymer-supported catalyst. The inorganic (ceramic) membrane allows the product to permeate and to retain the catalyst in the reactor. The membrane has a pore diameter lower than 200 nm (preferably lower than 1 nm) and consists of a separation layer of  $\text{Al}_2\text{O}_3$  and/or  $\text{SiO}_2$ . The process is illustrated by the continuous reduction of tetralone to tetralol with borane in the presence of polystyrene (molecular weight, 38 000) catalyst containing chemically bonded oxazaborolidine groups, with a residence time of 20 min and a pressure drop of 2 bar across

the membrane. The product contained less than 1 mg/L catalyst.<sup>158e</sup>

### XIII. Computational Analysis

Computational investigations of the structure and conformation of poly(benzyl phenyl ether) dendrimers as supports for organometallic catalysts have been reported by Naidoo, Hughes, and Moss via atomistic molecular dynamics computer simulations. These dendrimers terminated with benzyl groups were compared to their chromium tricarbonyl complexes representing an example of organometallic group functioning as catalyst.<sup>160</sup> The computational results indicate that the chromium carbonyl centers are available to participate in chemical reactions, and the conclusion was valid for all solvent conditions when the course-grain simulation study by Murat and Grest was used.<sup>161</sup> The terminal groups of both the organic and organochromium dendrimers smaller than generation 3 undergo significant backfolding, however. For higher generations, the terminal benzyl–tricarbonyl–chromium groups do not penetrate the core region to the same extent as do terminal benzyl groups of similar generation. This is due to the molecular crowding. The backfolding does not prevent chemical reactions.<sup>160</sup>

### XIV. Catalysis of Dendritic Polymerization

#### 1. Introduction

In this section, we give examples of the use of dendritic initiators or catalysts for polymerization reactions. These polymerization reactions involve the dendrimers themselves, which subsequently become dendritic polymers, dendritic stars, or hyperbranched polymers. There are a number of variations from transition-metal-catalyzed polymerization to nonmetal-initiated hyperbranched polymerization. Thus, we restrict the review to only a few examples because the area is at the borderline of the present scope. The field actually started in the middle of the last century with the pioneering ideas and works by Flory.<sup>162,163</sup> The area did not subsequently attract too much attention during several following decades. It became more popular recently when the term “hyperbranched polymer” was coined<sup>164</sup> and when polydispersities of such hyperbranched polymers could be improved (i.e., diminished).

#### 2. Hyperbranched Polymers

Indeed, it has been shown that much better polydispersities could be obtained by polymerization of an  $\text{AB}_2$  system in the presence of a core, especially if the core is in excess to the slowly added monomer containing the  $\text{AB}_2$  system.<sup>165–168</sup> The access to hyperbranched polymers of low polydispersities is essential because such one-pot polymerization procedures require much less energy than the multistep time-consuming construction of dendrimers whose polydispersity is theoretically 1.0.

Polymerization of dendrons containing polymerizable terminal groups is an alternative to the synthesis of dendritic polymers. For instance, Kaneko et al.

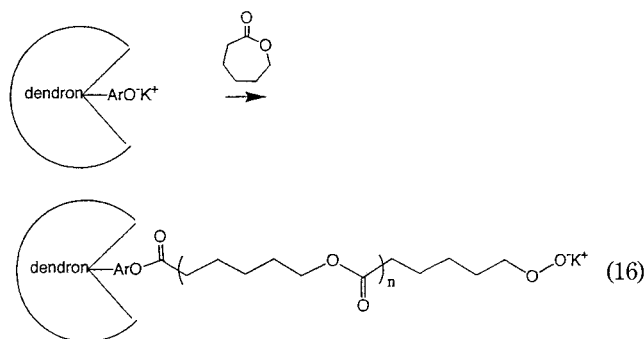
polymerized monodendrons containing acetylenic groups using a rhodium catalyst. The high-molecular weight dendrimers obtained had good membrane-forming ability and were available for oxygen-permeable membranes.<sup>169</sup>

### 3. Atom-Transfer Radical Polymerization (ATRP)

The groups of Hawker and Fréchet involved dendritic initiators for living radical polymerization and synthesized dendritic-linear block copolymers. These authors used dendrons containing either a single benzylic TEMPO or halide functionality at their focal point which have been active for the nitroxide-mediated and atom-transfer radical polymerization (ATRP).<sup>170</sup>

### 4. Ring-Opening Polymerization

Fréchet's group used dendrimers as macroinitiators for anionic ring-opening polymerization of  $\epsilon$ -caprolactone (eq 16). In this strategy, the dendrimer



contains a single reactive group at the focal point (i.e., the dendrimer is a dendron). This anionic polymerization is under kinetic control and forms hybrid linear-globular block copolymers.<sup>171</sup>

Hedrick et al. used a hexahydroxy dendritic core as an initiator for the "living" ring-opening polymerization (ROP) of  $\epsilon$ -caprolactone producing a hydroxy-terminated six-arm star polymer with controlled molecular weight and narrow polydispersities (<1.1). These chain ends were then capped with dendrons containing activated bromide moieties to produce "macro-initiators" for atom-transfer radical polymerization (ATRP). Methyl acrylate was polymerized from these "macro-initiators" in the presence of an organometallic promoter to produce the dendritic star polymers of high molecular weight and low polydispersities. Alternatively, amphiphilic analogues with a hydrophilic outer layer could be synthesized by variation of the polymer layers (methyl methacrylate, hydroxymethacrylate, and methacrylate functional ethylene oxide).<sup>183</sup>

### 5. Star Polymerization

Cloutet et al. used benzene star initiators containing six  $\text{ArCH}_2\text{Cl}$  branches for the living cationic polymerization of styrene in the presence of  $\text{SnCl}_4$  as a Lewis acid. These systems are living with up to 10 styrene units per branch. Such polymer stars

could be functionalized with  $\text{C}_{60}$  or other polymer blocks such as polyoxoethylene.<sup>172-177</sup>

### 6. Lewis-Acid Polymerization

In German patents, Becke et al. and Zahalka et al. disclosed the Lewis acid dendrimers  $[\text{Si}\{(\text{CH}_2)_3\text{B}(\text{C}_6\text{F}_5)_3\}_4]^{4-}[\text{C}_6\text{H}_5\text{NHCH}_2^+]_4$ ,  $\text{Si}[\text{CH}_2\text{CH}_2\text{Si}\{\text{CH}_2\text{CH}_2\text{CH}_2\text{B}(\text{C}_4\text{H}_9)_2\}_2]_4$ , and others of this type as cocatalysts for the polymerization of ethylene, propylene, and 5-ethylidene-2-norbornene and the copolymerization of ethene with propene using  $[\text{ZrCp}_2\text{Me}_2]$ , ethylenebis(indenyl)zirconium dimethyl, dimethylsilylbis(indenyl)zirconium dichloride, and ethylenebis(tetrahydroindenyl)zirconium dichloride as catalysts, respectively.<sup>178</sup>

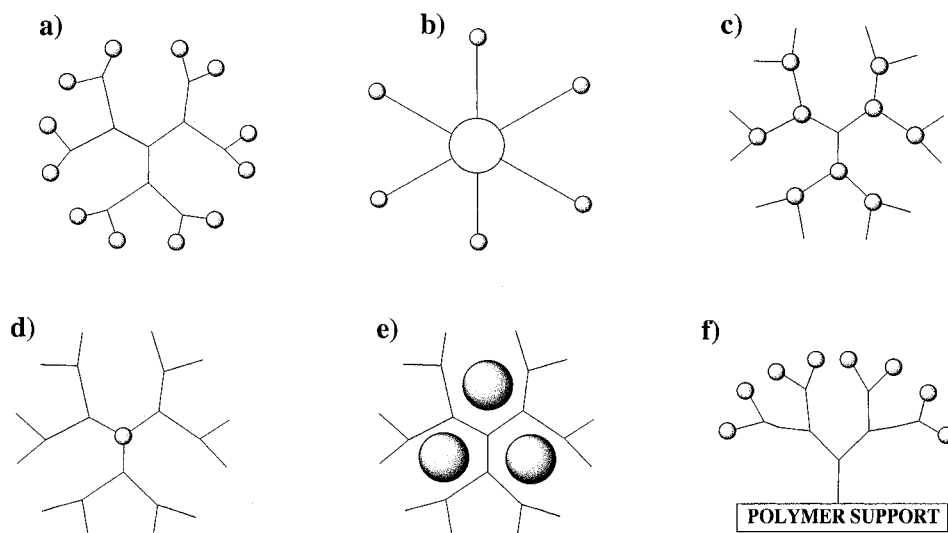
Carbosilane dendrimers with 4, 8, and 12 zirconocene dichloride termini connected to the dendritic branches via dimethylsilylcyclopentadienyl moieties have been synthesized by Seyferth et al. These metallodendrimers were used to polymerize ethylene and to copolymerize ethylene with other olefins. An excellent activity was obtained, but zirconocene dichloride monomers are about 10 times more active than this metallodendrimer.<sup>179a</sup> Hyperbranched polymers containing dimethylvinylsilane units were also synthesized and functionalized with zirconocenes by Seyferth's group. A higher activity in ethylene polymerization for the hyperbranched polymer ( $12\,400\text{ kg mol}^{-1}\text{ h}^{-1}$ ) than for the metallodendrimer ( $5\,760\text{ kg mol}^{-1}\text{ h}^{-1}$ ) was obtained.<sup>179b</sup>

### 7. Polyurethane Catalysts

Froehling and Corstjens examined the use of poly(propylene imine) astromol dendrimers as polyurethane catalysts. To this end, they first converted the primary amines of the first- and second-generation dendrimers into tertiary amines through the Eschweiler-Clarke reductive methylation reaction. The catalytic activity of the dendrimers containing, respectively, 6 and 14 tertiary amine groups was tested in kinetic measurements using the model reaction of 1-butanol with phenylisocyanate in toluene. There is no difference in catalytic activity per N-atom between the dendrimers and the low-molecular weight diamine *N,N,N,N*-tetramethyl-1,3-diaminopropane. The Lewis acid catalyst dibutyltin dilaurate was also used with these tertiary amines as cocatalysts, and again the results were identical with these dendritic amines and the low molecular weight amine. Usually, the conventional amine catalysts are volatile and possess a well-known noxious odor, which presents a problem with respect to safety and health. On the other hand, the high molecular weight dendritic amines have a negligible vapor pressure and odor. In fact, the second-generation dendritic amine is odorless and can be used in processing or in situations where amine emission is a problem.<sup>180</sup>

### 8. Photoinitiating Systems

In the same line, Janssen's group showed the efficient use of high-molecular weight, low volatile astramol poly(propylene imine) dendrimers as Norrish type II amine synergists, i.e., photoinitiating



**Figure 29.** Schematic summary of the various types of metallodendrimers used in catalysis: (a) metals located at the termini of the dendritic branches; (b) metals located at the termini of the star branches in order to avoid the dendritic surface congestion; (c) metal located at or near the focal points on the branches; (d) metal located at the center (core); (e) metal aggregates formed inside the dendrimer by reduction of coordinated metal ions from type c); (f) dendron attached to a polymer support with metals located at the termini of the branches.

systems in UV-curable coatings for various applications were they serve a dual role of initiator and oxygen scavenger.<sup>181</sup>

## 9. Ring-Opening Metathesis Polymerization (ROMP)

Beerens, Verpoort, and Verdonck loaded low-generation polyolefin carbosilane dendrimers with Grubb's ruthenium ring-opening metathesis polymerization catalyst (ROMP) by a stoichiometric metathesis reaction in which 1 equiv of Grubb's ruthenium catalyst is added per dendritic olefin-terminated branch. The product of this reaction is a metallodendrimer in which each dendritic branch is terminated by a ruthenium-carbene group. These metallodendrimers have a high activity for the ROMP of norbornene and can initiate the preparation of multiarm star polymers in a controlled manner.<sup>182</sup> See also section II.10.

## XV. Conclusion and Prospects

Since the first reports that appeared by the groups of van Leeuwen,<sup>58,59</sup> Brunner,<sup>77-79</sup> van Koten,<sup>52</sup> Ford,<sup>147,148</sup> and DuBois,<sup>126,127</sup> dendrimers have been involved in many aspects of catalysis, especially during the last 2 years. There is much more than the aesthetic attraction in the use of dendrimers in the field. The perfect definition of catalytic sites and the clear possibility to recover the dendritic catalysts have been fully demonstrated.

The dendritic topology is very important to define the activity and selectivity of the catalyst. The various possibilities for the location of the metal in a catalytically active metallodendrimer or metallostar are summarized in Figure 29. Catalytic efficiency is very often marred by steric congestion at the metallodendritic surface. The dichotomy between surface-congested metallodendrimers and surface-free metallostars has been stressed.<sup>113b</sup> Steric congestion may

sometimes result in positive dendritic effects in terms of selectivity, however, as shown in Cole-Hamilton's hydroformylation.<sup>74</sup>

Many efforts have recently concentrated on the recovery of the dendritic catalysts using membrane reactors, an area pioneered by Kragl's group.<sup>159,183</sup> Industrial applications with membrane reactors remain to be carried out, however, and this aspect is now becoming a major challenge. In some particular cases, interesting positive dendritic effects in catalysis have been shown by Jacobsen,<sup>45</sup> Cole-Hamilton,<sup>74</sup> and Detty.<sup>109</sup> In most cases, however, what is hoped for is an efficiency in terms of turnover rates, yields, and stereoselectivities which is very close to that of the parent, nondendritic analogous catalysts.

After the seminal ideas by Brunner<sup>77</sup> with dendrizymes in asymmetric catalysis, Seebach<sup>98</sup> was successful in obtaining highly enantioselective reactions with the TALDOL ligand in Lewis-acid-catalyzed reactions. The above properties required for catalysis are usually encountered in relatively small dendrimers in which steric effects between the catalytic sites remain negligible and do not inhibit the approach of the metal coordination, as demonstrated by Meijer's group.<sup>30</sup> While research in catalysis using metallodendrimers is considerably expanding, there is also a noteworthy trend toward supported or heterogeneous dendritic catalysts, an area pioneered by Alper.<sup>135,138</sup> Biological aspects of dendrimers toward enzyme mimics, emphasized by Tomalia,<sup>1</sup> Brunner,<sup>77</sup> and Diederich,<sup>26</sup> should expand especially because our knowledge of dendrimers as molecular micelles or inverted micelles is already now well established after the works by the groups of Newkome,<sup>5</sup> Meijer,<sup>30</sup> and Fréchet.<sup>145</sup> The enzyme mimic is clear when catalysis occurs inside the dendrimer, i.e., at the core or on the branches, and when recognition sites are present nearby in the microenvironment. Obviously, this aspect will attract increasing attention.<sup>184,185</sup>

On the side of materials science, dendritic initiators or catalysts are being scrutinized as polymerization agents, and dendrimers mixed with other materials such as particles have intriguing properties. Composite nanostructures including dendrimers, pioneered by Tomalia<sup>1,186,187</sup> and Crooks,<sup>188,189</sup> will obviously develop in the close future, and their catalytic properties will be awaited. These new materials will be used in "green chemistry" using the biphasic fluoros/organic solvents,<sup>189–194</sup> in aqueous solution,<sup>188</sup> or in supercritical CO<sub>2</sub>.<sup>188,195,196</sup> In addition, combinatorial<sup>197,198</sup> and solid-phase support<sup>199–201</sup> strategies in catalysis with dendrimers and dendrimer–colloid composites will be pursued in the close future.

## XVI. Acknowledgment

Financial support from the Institut Universitaire de France (DA), the CNRS, the University Bordeaux I, the Ministère de l'Enseignement et de la Recherche Scientifique, and the Région Aquitaine is gratefully acknowledged.

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