Noncovalently Functionalized Dendrimers as Recyclable Catalysts

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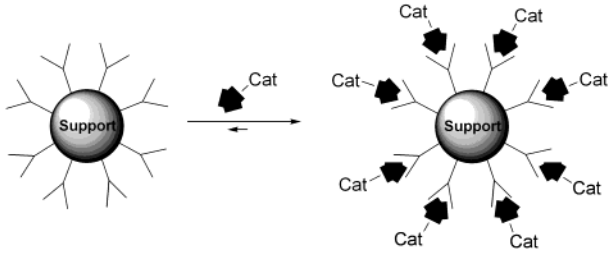
Abstract: The efficient reversible functionalization of the periphery of urea adamantyl poly(propylene imine) dendrimers with catalytic sites using noncovalent interactions is described. Phosphine ligands equipped with urea acetic groups, a binding motive complementary to that of the dendrimer host, have been prepared and assembled to the dendrimer support. The resulting supramolecular complex has been used as a multidentate ligand system in the palladium-catalyzed allylic amination reaction in a batch process and in a continuous-flow membrane reactor. We found that the activity and selectivity of the dendrimeric complex is similar to that of the monomer complex, which indicates that the catalytic centers act as independent sites. The size of the supramolecular system is sufficiently large and the binding of the guests is strong enabling a good separation of the catalyst components from the reaction mixture using nanofiltration techniques.

Introduction

The immobilization of transition metal catalysts by anchoring them to organic or inorganic solid supports combines the good catalytic performance of a tailor-made system with a facile separation of the catalyst from the product phase.[1] Disadvantages of these heterogenized systems include a decreased activity due to mass transfer limitations, lowered selectivity, and metal leaching. Metal leaching can be suppressed by using properly chosen ligands that coordinate strongly to the metal center. The use of soluble supports such as small (hyperbranched) polymers,[2] dendrimers,[3−5] and hybride materials[6] result in homogeneous, immobilized catalysts that do not suffer from mass transfer limitations. In most systems reported so far the catalyst was covalently linked to the support or via ionic interactions. An interesting alternative approach would be the noncovalent anchoring of the catalyst to the soluble support using well-defined binding sites. The reversible nature of this type of anchoring allows controlled de- and re-functionalization of the support, which enables the easy reuse of the support and simplifies the variation of catalyst loading even during catalysis. Furthermore, using a noncovalent approach, multicomponent assemblies can be envisaged that are interesting for tandem reactions and combinatorial techniques. To achieve the supramolecular anchoring of catalysts, a soluble support must contain well-defined binding sites to which the tailor-made transition metal catalysts with a complementary binding motive can be assembled (Scheme 1). Another requirement is that the dimension of the support allows the use of nanofiltration techniques. Dendrimers are excellent supports for developing this type of material because of their well-defined size and structure.

Scheme 1. The Concept of Supramolecular Anchoring of Catalysts to a Soluble Support



Recently, a fifth generation poly(propylene imine) dendrimer functionalized with urea adamantyl units at the periphery (**1**) has been reported.[7] This dendrimer provided directional binding

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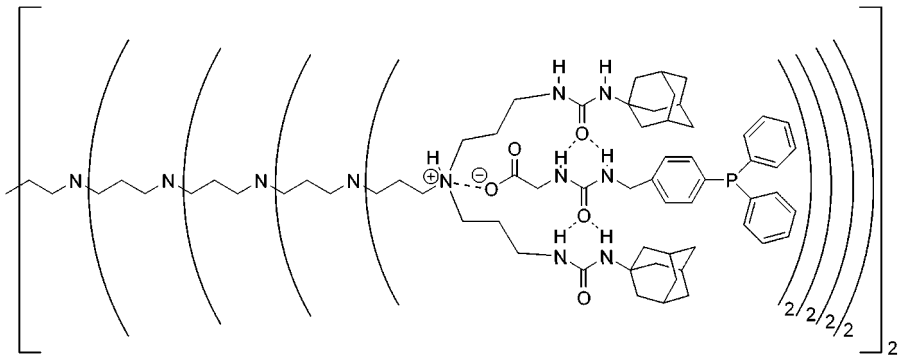
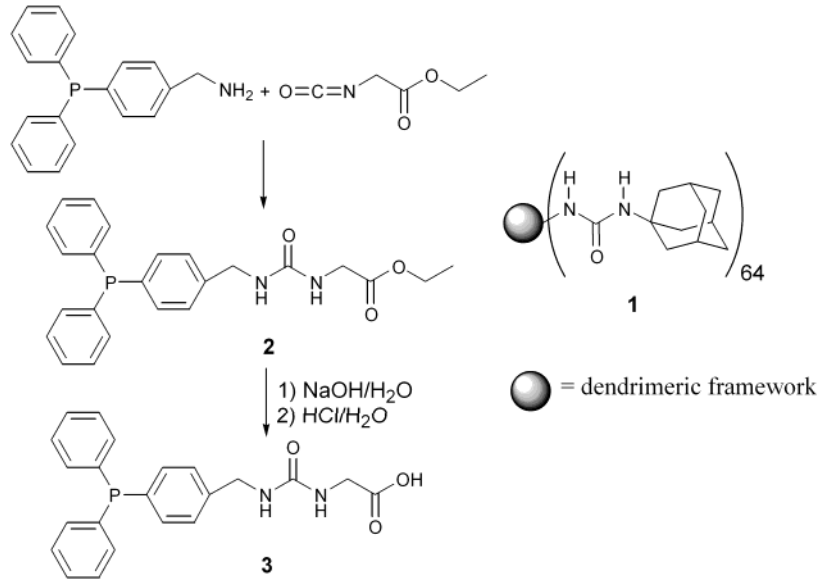


Figure 1. Phosphine ligands assembled to the periphery of a urea adamantyl functionalized poly(propylene imine) dendrimer (**1**).

Scheme 2. Synthesis of a Phosphine-Containing Guest Molecule (**3**) in Two Steps and the Structure of the Schematic Structure of the Urea Adamantly Functionalized Dendrimeric Host (**1**)



sites for the strong but reversible binding of 32 guest molecules functionalized with the complementary binding motive. The binding is based on a combination of ionic interactions and the formation of multiple hydrogen bonds. Here we report for the first time the noncovalent anchoring of phosphine ligands and their transition metal complexes, which can be used as catalysts, to the periphery of a soluble dendrimeric support (Figure 1). The resulting recyclable homogeneous supramolecular complex is used in the palladium-catalyzed allylic amination reaction in a batch process and in a continuous-flow membrane reactor.

Results and Discussion

Synthesis and Complex Formation. It was previously found that both the urea and the carboxylic acid functionality must be present in the guest molecules to achieve the required strong binding to the dendrimeric host **1**.[7,8] We also anticipated that the introduction of the binding motive in a ligand system must be straightforward to have a general strategy that can also be used for more complicated ligand systems. A reaction of *p*-(diphenylphosphino)benzylamine with commercially available ethyl isocyanatoacetate yielded ester derivative **2** (Scheme 2). After hydrolysis of the ester and recrystallization from chloroform pure **3** was isolated as a white powder. Phosphine guest **3** is thus prepared in two simple reaction steps.

The binding of the guest molecule into the periphery of **1** was studied by NMR spectroscopy. In contrast to acid ligand **3**, ester ligand **2** showed no affinity for the binding motive of the dendrimer. Addition of 32 equiv of acid(**3**) to **1** (in $CDCl_3$) resulted in a shift of the urea protons of the dendrimer from 6.20 and 5.43 ppm to 6.34 and 5.64 ppm, respectively. This shift is similar to that previously reported for other guest molecules.[7] Addition of an extra portion of dendrimer (1 equiv) resulted in a random distribution of the guest molecules over the dendrimers and average signals for the urea protons of the dendrimer were observed in the ^{1}H NMR spectrum at 6.30 and 5.57 ppm, respectively. This clearly shows that the exchange between the bound and unbound species is rapid on the NMR time scale. In a ^{1}H-NOE NMR experiment of the dendrimer with 32 equiv of acid(**3**) the aromatic protons of the guest were selectively irradiated and a NOE effect was observed for the adamantyl protons. This shows that the diphenylphosphine groups of the guest and the adamantyl endgroups of the dendrimer are in close proximity. A 2D-NOESY NMR spectrum

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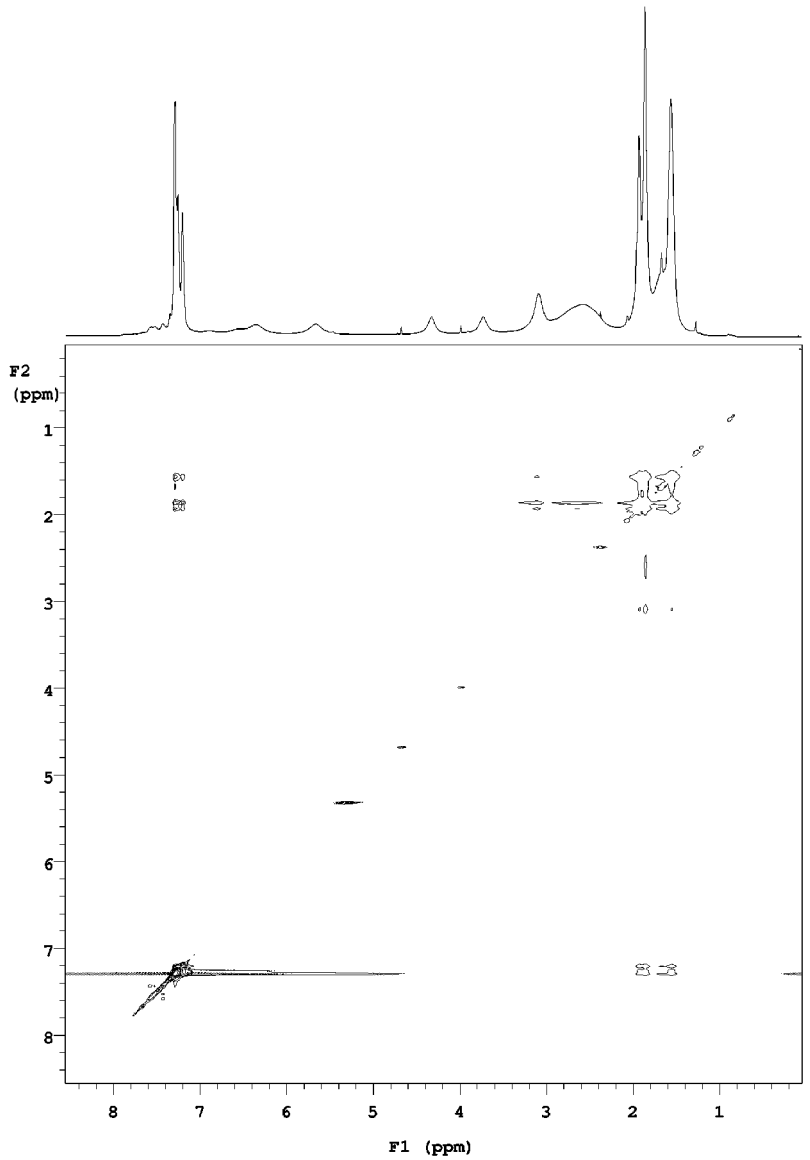


Figure 2. 2D-NOESY NMR spectrum of guest ligands acid(**3**) assembled to the periphery of urea adamantyl poly(propylene imine) dendrimers (**1**).

also shows the interaction of the aromatic protons of the guest molecule with the protons of the adamantyl groups (Figure 2). These experiments suggest that, as a result of the multiple hydrogen bond interactions, the guest molecule is positioned in the periphery of the dendrimeric host in a well-defined way, as is shown schematically in Figure 1.

After the guest ligands were bound into the periphery of the dendrimer they were complexed to palladium by addition of Pd(COD)MeCl or $[(\text{crotyl})\text{PdCl}]_2$ (Scheme 3a). A second approach toward the formation of metal functionalized systems involves the synthesis of the metal complex of acid(**3**) prior to the noncovalent anchoring of the complex to the periphery of the dendrimer, leading to the same product (Scheme 3b). Upon the addition of 0.5 equiv of (COD)PdMeCl with respect to the phosphine ligand, trans complexes are formed. In the $^{31}\text{P}-\{^1\text{H}\}$ NMR spectrum a broad singlet at 30.4 ppm is observed, which is comparable to the 30.7 ppm found for the model compound *trans*-$(\text{PPh}_3)_2\text{PdMeCl}$. The PdMe signal in the ^{1}H NMR spectrum is at -0.04 ppm, compared to -0.03 ppm for *trans*-$(\text{PPh}_3)_2\text{PdMeCl}$. Importantly, the ^{1}H NMR spectrum shows that the guest molecules and the dendrimeric host are still assembled after metal complexation; the signals for the urea protons of the dendrimer have broadened significantly and are shifted with respect to the free dendrimeric host.

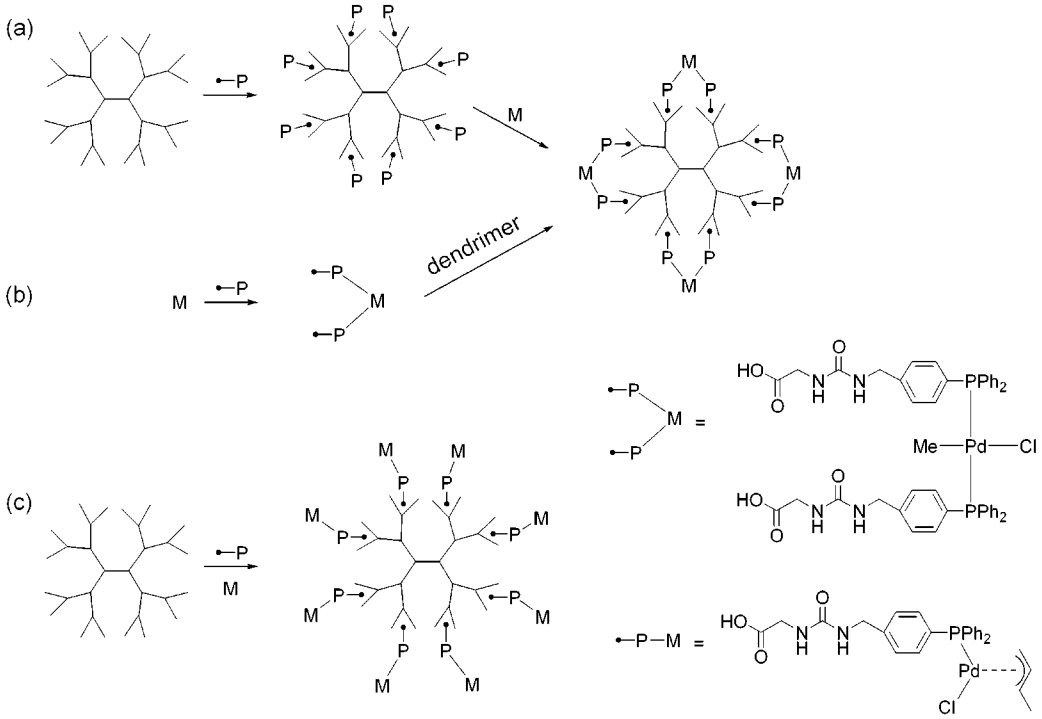
A third route toward Pd-functionalized dendrimers involves the mixing of all the reactants simultaneously (Scheme 3c). In this way we have prepared $[\{\text{acid}(\mathbf{3})\}\text{Pd}(\text{crotyl})\text{Cl}]_{32}-$dendrimer complex, which gives a characteristic broad singlet in the $^{31}\text{P}-\{^1\text{H}\}$ NMR spectrum at 24.4 ppm and $[\{\text{acid}(\mathbf{3})\}_2\text{Pd}(\text{crotyl})\text{Cl}]_{16}-$dendrimer complex (broad singlet at 24.9 ppm). These complexes were used for catalysis (vide supra).

Size exclusion chromatography (SEC) was used to check the stability of the acid(**3**)$-$Pd$-$dendrimer complex. NMR showed that the $[\{\text{acid}(\mathbf{3})\}_2\text{Pd}(\text{allyl})\text{Cl}]_{16}-$dendrimer complex remained intact after SEC, in contrast to the $\{\text{ester}(\mathbf{2})\}_2\text{Pd}-$dendrimer mixture. This indicates that the binding constant of the acid(**3**)$-$PdCl(allyl)$-$complex to the periphery of the dendrimer as well as that of the Pd to the ligand is very high. This is in line with the high binding constants (10^4 M^{-1}) that were found previously for similar supramolecular systems.[8]

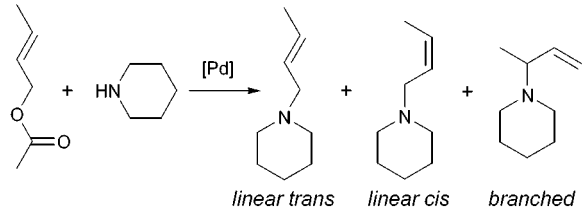
Catalysis

The dendrimeric host containing 32 phosphine ligands assembled to the periphery of **1** was used as a multidentate

Scheme 3. Schematic Presentation of the Preparation of Transition Metal Complexes Using Ligands Noncovalently Anchored to the Periphery of a Dendrimer



Scheme 4. Allylic Amination of Crotyl Acetate and Piperidine



ligand in the Pd-catalyzed allylic amination[9] with crotyl acetate and piperidine as the substrate molecules (Scheme 4). The reaction has been performed under various conditions with [{acid(**3**)}$_2$Pd(crotyl)Cl]$_{16}$−dendrimer (P/Pd = 2) and [{acid(**3**)}Pd(crotyl)Cl]$_{32}$−dendrimer (P/Pd = 1) as a catalyst. The reaction was started by mixing the substrates and the catalyst solution and appeared to be fast; using the [{acid(**3**)}$_2$Pd(crotyl)Cl]$_{16}$−dendrimer (P/Pd = 2) and a substrate/palladium ratio of 100 the conversion was 91% after 5 min. Approximately the same rate was observed for the Pd complex of ester(**2**) in the absence of the dendrimer (Table 1). This indicates that every active site on the dendrimer acts as an independent catalyst.[10] These experiments show clearly that the supramolecular anchoring of the catalysts does not decrease the activity, which generally is observed for catalysts immobilized on an insoluble support. Moreover, the product selectivity generated by the {acid(**3**)}$_2$−Pd−dendrimer complex is the same as that induced by the {ester(**2**)}$_2$−Pd complex. The noncovalently functionalized dendrimeric catalyst used in these batchwise reactions was recycled by using SEC. The conversion measured after 1 h, however, was lower in the second run, suggesting that the catalyst partly decomposed during the recycling procedure.

Table 1. Results of the Pd-Catalyzed Allylic Amination of Crotyl Acetate and Piperidine, Comparing the Supramolecular Dendrimeric Catalyst with the Monomer[a]

catalyst	P/Pd	conversion[b] (%)	trans (%)	cis (%)	branched (%)
{ester(**2**)}$_2$Pd(crotyl)Cl[a]	2	89	38	14	48
{acid(**3**)}$_2$Pd(crotyl)Cl-dendrimer[a]	2	91	37	15	48
{ester(**2**)}Pd(crotyl)Cl[c]	1	80	33	6	61
{acid(**3**)}Pd(crotyl)Cl-dendrimer[c]	1	72	33	6	61

[a] Room temperature; solvent, CH_2Cl_2; volume, 5 mL; [crotyl acetate] = 0.2 M, [piperidine] = 0.4 M, [Pd] = 0.002 M. [b] Conversion after 5 min. [c] Room temperature; solvent, CH_2Cl_2; volume, 5 mL; [crotyl acetate] = 0.12 M, [piperidine] = 0.24 M, [Pd] = 0.0040 M.

Upon using the [{acid(**3**)}Pd(crotyl)Cl]$_{32}$−dendrimer complex (P/Pd = 1) as a catalyst, a similarly fast reaction was observed (Table 1).[11] Again the results for the {acid(**3**)}Pd(crotyl)Cl−dendrimer complex are similar to those for the {ester(**2**)}Pd(crotyl)Cl complex. The selectivity is slightly different from that obtained with a P/Pd ratio of 2.[12]

Optimal advantage of dendrimers as soluble supports for catalysts can be obtained when they are applied in a continuous-flow membrane reactor.[10,13,14] For this purpose we used a Koch MPF-60 NF membrane (molecular weight cutoff = 400 dalton) that was placed in a homemade reactor. The retention measured for the ester complex (**2**)Pd(crotyl)Cl (MW = 617.4) in the

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(11) Since the reaction conditions are different, these results cannot be compared to the results of Table 1.

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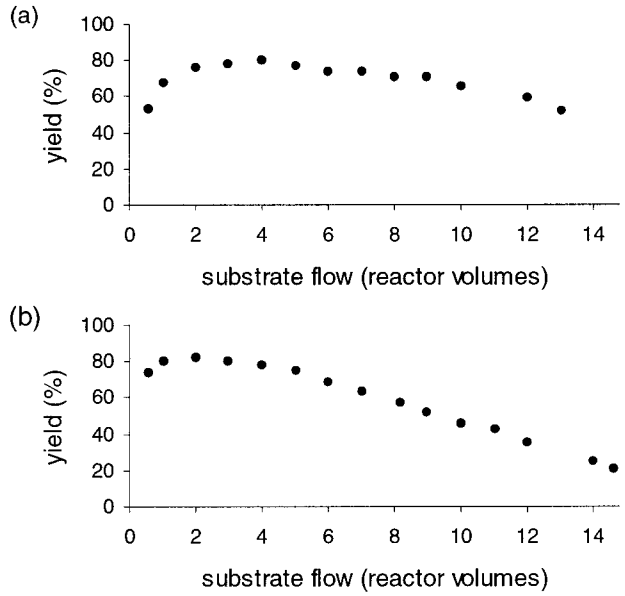

Figure 3. Application of noncovalently functionalized dendrimers in a continuous-flow membrane reactor using acid(**3**) as a ligand (a) and using ester(**2**) as a ligand (b).

presence of the host dendrimer is 97%, which is too low for practical application since one-third of the ligand will be washed out of the reactor after 13 reactor volumes of solvent have been pumped through. In contrast, the supramolecular acid−dendrimer complex [(**3**)Pd(crotyl)Cl]$_{32}$−dendrimer has a retention as high as 99.4%. Interestingly, upon using a lower palladium loading (P/Pd = 2) the retention further increased to 99.9%, suggesting that the palladium diphosphine complexes are bound more strongly due to cooperative effects. These results indicate that this type of supramolecular complexe will be efficiently separated from smaller compounds such as the reactants and products in a continuous-flow membrane reactor. The application in catalysis was studied by using the allylic amination reaction.

A solution of crotyl acetate and piperidine in dichloromethane (including *n*-decane as an internal standard) was pumped through the reactor. The Pd complex of acid(**3**) assembled to the dendrimer was used as a catalyst and compared to the Pd complex of ester(**2**) in the presence of the dendrimer.[15]

In Figure 3 the conversion is plotted as a function of the substrate flow.[16] In both experiments the conversion has increased to its maximum (ca. 80%) after approximately 1 h (which is equivalent to 1−2 reactor volumes of substrate solution pumped through the reactor). Upon using acid(**3**) the conversion remains fairly constant during the first 10 h of the experiment (Figure 3a).[17] The slight decrease observed is presumably a result of slow deactivation of the catalyst, which has also been observed using covalently functionalized dendrimers.[10,14] Upon using ester(**2**) the activity of the catalytic system drops more rapidly, since ester(**2**), which is not bound to the dendrimer, is washed out of the reactor (retention = 97%). In this experiment slow deactivation of the catalyst occurs as well. Although these deactivation processes slightly obscure the results, the differences observed between ligands ester(**2**) and acid(**3**) clearly demonstrate that the noncovalently functionalized dendrimers are suitable as soluble and recyclable supports for catalysts. We are currently studying the potential of the concept in other reactions.

(15) Room temperature; reactor volume, 5 mL; solvent, CH_2Cl_2; [crotyl acetate] = 0.1 M, [piperidine] = 0.2 M, [Pd] = 0.004 M; flow rate, 9 mL/h.

(16) The selectivity observed during these continuous experiments is similar to that of the batch processes.

(17) The activity of the catalyst observed in the continuous process cannot be compared directly to that observed in the batch reaction because of the large differences in the reactor setup.

Conclusions

In conclusion, we have developed a new homogeneous catalyst that is anchored to a soluble dendrimer support using supramolecular interactions. The catalytic system is noncovalently attached to the periphery of a urea adamantyl poly(propylene imine) dendrimer by ionic interactions in combination with multiple hydrogen bonds, which positions the guest ligand at the periphery of the dendrimer in a well-defined way. The supramolecular dendrimeric system shows the same activity and selectivity in the Pd-catalyzed allylic amination as its unbound monomeric analogue, which indicates that every active site on the dendrimer acts as an independent catalyst and is easily accessible to the substrate. Moreover, the catalyst is strongly bound such that the system can be operated in a continuous setup, which results in efficient separation of the catalyst from the reaction mixture. Employing the concept of noncovalent anchoring simplifies the route toward sophisticated dendrimeric catalysts since ligand modification with the binding motive is straightforward. One of the limitations in dendrimeric catalysis is the troublesome synthesis of functionalized dendrimers, since quantitative coupling of ligands to the periphery is not always possible. With this strategy these problems are circumvented. Moreover, this approach opens the way toward the use of multipurpose supports, not only for dendrimers but also other supports, which can be functionalized and refunctionalized with multiple complex catalytic systems containing a relatively simple binding motive.

Experimental Section

General Data. All reactions were carried out under an atmosphere of purified nitrogen with standard Schlenk techniques. Solvents were distilled under N_2 from sodium/benzophenone (THF, hexane) or calcium hydride (dichloromethane) prior to use. Water and $CDCl_3$ were degassed and stored under nitrogen. Chemicals were purchased from Aldrich Chemical Co. and Acros Chimica and were used without further purification. The piperidine was filtered over neutral alumina prior to use. For the size exclusion chromatography Bio-Beads S-X1 Beads (Gel Permeation Gel 200−400 mesh, Bio-Rad Laboratories, Hercules, USA) were used. *p*-(Diphenylphosphino)benzylamine,[18] (COD)PdMeCl,[19] [(allyl)PdCl]$_2$,[20] and [(crotyl)PdCl]$_2$[20] were prepared according to literature procedures. ^{1}H− and ^{31}P−{^{1}H} NMR spectra were recorded on a Varian Mercury 300. ^{13}C−{^{1}H} NMR spectra were recorded on a Varian Inova 500. The chemical shifts are given in ppm relative to TMS for ^{1}H and ^{13}C NMR and relative to H_3PO_4 for ^{31}P NMR. Fast Atom bombardment (FAB) mass spectrometry was carried out using a JEOL SX/SX 102A (Tokyo, Japan) four-sector tandem mass spectrometer ($B_1E_1B_2E_2$ geometry), coupled to a JEOL MS/MP9021D/UPD data system. Gas chromatography was performed on an Interscience HR GC Mega 2 apparatus (split/splitless injector, J&W Scientific, DB1 30 m column, film thickness 3.0 mm, carrier gas: 70 kPa He, F.I.D. detector).

Synthesis of the phosphine ligands. (a) Ester(2). To a solution of 0.4417 g of (diphenylphosphino)benzylamine (1.516 mmol) in 5 mL of dichloromethane was added 0.17 mL of ethyl isocyanatoacetate (1.515 mmol). After the mixture was stirred for 2 h at room temperature the solvent was evaporated. The product was recrystallized from dichloromethane/hexane and obtained as a white solid in 89% yield

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(0.5690 g, 1.353 mmol). Mp: 100−101 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.4−7.2 (m, 14H, ArH), 5.0 (s (br.), 2H, NH), 4.36 (d, 2H, ArCH_2N, $^3J_{HH}$ = 5.7 Hz), 4.15 (q, 2H, OCH_2CH$_3$, $^3J_{HH}$ = 7.2 Hz), 3.97 (d, 2H, NCH_2CO, $^3J_{HH}$ = 5.1 Hz), 1.23 (t, 3H, OCH$_2$CH_3, $^3J_{HH}$ = 7.2 Hz). ^{31}P−{^{1}H} NMR (121.5 MHz, $CDCl_3$): δ −5.59 (s). ^{13}C−{^{1}H} NMR (125.8 MHz, $CDCl_3$): δ 171.4 (s, *C*OOEt), 157.8 (s, NH*C*ONH), 140.0 (s, *ipso*-PhCH$_2$N), 137.4 (d, *ipso*-PhP, $^1J_{CP}$ = 10.6 Hz), 136.4 (d, *ipso*-PhP, $^1J_{CP}$ = 10.6 Hz), 134.3 (d, *m*-PhCH$_2$N, $^2J_{CP}$ = 19.4 Hz), 133.9 (d, *o*-PhP, $^2J_{CP}$ = 19.4 Hz), 128.9 (s, *p*-PhP), 128.7 (d, *m*-PhP, $^3J_{CP}$ = 6.7 Hz), 127.7 (d, *o*-PhCH$_2$N, $^3J_{CP}$ = 7.2 Hz), 61.6 (s, O*C*H$_2$CH$_3$), 44.5 (s, Ar*C*H$_2$N), 42.5 (s, N*C*H$_2$CO), 14.4 (s, CH$_3$). IR (KBr) υ (cm^{-1}) 3338 (NH), 3052 (CH, arom.), 2982 (CH, alif.), 1748 (CO), 1630 (CO), 1576 (CO). FAB-MS *m*/*z* 437.2 ([M + O + H]$^+$), HRMS (FAB$^+$) *m*/*z* calcd for $C_{24}H_{26}O_4N_2P$ [M + O + H]$^+$ 437.1630. Found: 437.1619. Anal. Calcd for $C_{24}H_{25}N_2O_{3.25}P$ (partly oxidized): C 67.92; H 5.94; N 6.60. Found: C 67.85; H 5.82; N 6.45.

(b) Acid(3). A solution of 0.0233 g of NaOH (0.583 mmol) in 4 mL of water was added to a solution of 0.2197 g of **2** (0.5225 mmol) in 5 mL of THF. After overnight stirring the THF was evaporated and the reaction mixture was neutralized by addition of 1 mL of 0.58 M aqueous HCl. The solvent was decanted and the crude product was washed with water. After recrystallization from chloroform a white powder was obtained in 40% yield (0.0824 g, 0.210 mmol). Mp: 129−130 °C. ^{1}H NMR (300 MHz, DMSO-d_6): δ 7.5−7.2 (m, 14H, ArH), 6.88 (t, 1H, NH, $^3J_{HH}$ = 6 Hz), 6.20 (t, 1H, NH, $^3J_{HH}$ = 6 Hz), 4.22 (d, 2H, ArCH_2N, $^3J_{HH}$ = 5.7 Hz), 3.69 (d, 2H, NCH_2CO, $^3J_{HH}$ = 5.4 Hz). ^{31}P−{^{1}H} NMR (121.5 MHz, DMSO-d_6): δ −2.26 (s). ^{13}C−{^{1}H} NMR (125.8 MHz, DMSO-d_6): δ 172.5 (s, *C*OOH), 158.0 (s, N−*C*O−N), 142.0 (s, *ipso*-PhCH$_2$N), 136.8 (d, *ipso*-PhP, $^1J_{CP}$ = 9.7 Hz), 134.4 (d, *ipso*-PhP, $^1J_{CP}$ = 10.2 Hz), 133.4 (d, *m*-PhCH$_2$N, $^2J_{CP}$ = 21.1 Hz), 133.1 (d, *o*-PhP, $^2J_{CP}$ = 19.4 Hz), 128.9 (s, *p*-PhP), 128.7 (d, *m*-PhP, $^3J_{CP}$ = 6.8 Hz), 127.4 (d, *o*-PhCH$_2$N, $^3J_{CP}$ = 5.9 Hz), 42.6 (s, Ar*C*H$_2$N), 41.6 (s, N*C*H$_2$CO). IR (KBr) υ (cm^{-1}) 3412 (OH), 3376 (NH), 3052 (CH), 2924 (CH), 1724 (CO), 1624 (CO), 1575 (CO). FAB-MS *m*/*z* 409.1 ([M + O + H]$^+$) HRMS (FAB$^+$) *m*/*z* calcd for $C_{22}H_{22}O_4N_2P$ [M + O + H]$^+$ 409.1317. Found: 409.1240. Anal. Calcd for $C_{22}H_{21}N_2O_{3.6}P$ (partly oxidized): C 65.73; H 5.27; N 6.97. Found: C 65.63; H 5.52; N 7.04.

Binding of the Guest into the Periphery of the Dendrimer. (a) {Acid(3)}$_{32}$-Dendrimer. A solution of 0.0198 g of **3** (50.5 μmol) in 1 mLof $CDCl_3$ was added to a solution of 0.0297 g of fifth generation adamantyl−urea functionalized poly(propylene imine) dendrimer (**1**) (1.60 μmol) in 1 mL of $CDCl_3$. The resulting mixture was analyzed by ^{1}H− and ^{31}P−{^{1}H} NMR. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.6−7.2 (m, 448H, ArH of guest ligand), 6.5 (broad shoulder, NH of guest), 6.34 (s (br), 64H, CH$_2$N*H*CONH of dendrimer), 5.64 (s (br), 64H, CH$_2$-NHCON*H* of dendrimer), 4.32 (s (br), 64H, ArCH_2N of guest), 3.73 (s (br), 64H, NCH_2CO of guest), 3.07 (s (br), 128H, CH_2NHCONH of dendrimer), 2.2−2.8 (br, 372H, NCH_2CH$_2$CH$_2$NHCO {128H} + NCH_2-CH$_2$CH_2N {240H} + NCH_2CH$_2$CH$_2$CH_2N {4H}), 1.93 (s (br), 192H, adamantyl), 1.86 (s (br), 384H, adamantyl), 1.56 (m, 636H, adamantyl {384H} + NCH$_2$CH_2CH$_2$NHCO {128H} + NCH$_2$CH_2CH$_2$N {120H} + NCH$_2$CH_2CH_2CH$_2$N {4H}). ^{31}P−{^{1}H} NMR (121.5 MHz, $CDCl_3$): δ −5.73 (s).

(b) {Acid(3)}$_{16}$−Dendrimer. Half of the {acid(**3**)}$_{32}$−dendrimer solution (25.2 μmol of **3**, 0.802 μmol of dendrimer) was added to 0.0147 g of dendrimer (**1**) (0.794 μmol). The mixture was analyzed by ^{1}H NMR. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.5−7.1 (m, 224H, ArH of guest ligand), 6.30 (s (br), 64H, CH$_2$N*H*CONH of dendrimer), 5.57 (s (br), 64H, CH$_2$NHCON*H* of dendrimer), 4.65 (s (br), 32H, ArCH_2N of guest), 3.74 (s (br), 32H, NCH_2CO of guest), 3.08 (s (br), 128H, CH_2NHCONH of dendrimer), 2.2−2.8 (br, 372H, NCH_2CH$_2$CH$_2$NHCO {128H} + NCH_2CH$_2$CH_2N {240H} + NCH_2CH$_2$CH$_2$CH_2N {4H}), 1.98 (s (br), 192H, adamantyl), 1.91 (s (br), 384H, adamantyl), 1.60 (m, 636H, adamantyl {384H} + NCH$_2$CH_2CH$_2$NHCO {128H} + NCH$_2$CH_2CH$_2$N {120H} + NCH$_2$CH_2CH_2CH$_2$N {4H}).

(c) [{Acid(3)}$_2$−PdMeCl]. A solution of 3.371 mg of (COD)-PdMeCl (12.7 μmol) in 0.7 mL of $CDCl_3$ was added to a solution of 0.0098 g of **3** (25 μmol) in 0.3 mL of $CDCl_3$. After being stirred for 3 h the mixture was analyzed by ^{1}H− and ^{31}P−{^{1}H} NMR. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.8−7.1 (m, 8H, ArH), 6.56 (s (br), 1H, NH), 6.24 (s (br), 1H, NH), 5.58 (s, 4H, COD), 4.18 (s (br), 2H, ArCH_2N), 3.68 (s (br), 2H, NCH_2CO), 2.36 (s, 8H, COD). ^{31}P−{^{1}H} NMR (121.5 MHz, $CDCl_3$): δ 32.3 (s), 30.4 (s).

(d) [{Acid(3)}$_2$−PdMeCl]$_{32}$−Dendrimer. Method A. A solution of 3.352 mg of (COD)PdMeCl (12.6 μmol) in 1 mL of $CDCl_3$ was added to a solution of {acid(**3**)}$_{32}$−dendrimer (25.2 μmol of **3** + 0.802 μmol of dendrimer (**1**)) in 1 mL of $CDCl_3$. After overnight stirring the mixture was analyzed by ^{1}H− and ^{31}P−{^{1}H} NMR.

Method B. A solution of 0.0146 g of dendrimer (0.789 μmol) in 0.5 mL of $CDCl_3$ was added to a solution of [{acid(**3**)}$_2$−PdMeCl] (12.7 μmol of Pd, 25 μmol of **3**) in 1 mL of $CDCl_3$. After stirring for 15 min the mixture was analyzed by ^{1}H− and ^{31}P−{^{1}H} NMR.

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.8−7.0 (m, 448H, ArH of guest ligand), 6.34 (br, 64H, CH$_2$N*H*CONH of dendrimer), 5.69 (br, 64H, CH$_2$NHCON*H* of dendrimer), 5.59 (s, 128H, COD), 4.4 (br, 64H, ArCH_2N of guest), 3.7 (br, 64H, NCH_2CO of guest), 3.08 (s (br), 128H, CH_2NHCONH of dendrimer), 2.2−2.8 (br, 372H, NCH_2CH$_2$CH$_2$NHCO {128H} + NCH_2CH$_2$CH_2N {240H} + NCH_2CH$_2$CH$_2$CH_2N {4H}), 2.37 (s, 256H, COD), 1.96 (s (br), 192H, adamantyl), 1.90 (s (br), 384H, adamantyl), 1.59 (m, 636H, adamantyl {384H} + NCH$_2$CH_2CH$_2$NHCO {128H} + NCH$_2$CH_2CH$_2$N {120H} + NCH$_2$CH_2CH_2CH$_2$N {4H}), −0.04 (br, 192H, PdMe). ^{31}P−{^{1}H} NMR (121.5 MHz, $CDCl_3$): δ 30.5 (br).

Retention Measurements. A solution of 0.0231 g of fifth generation adamantyl−urea functionalized poly(propylene imine) dendrimer (**1**) (1.25 μmol), 15.692 mg of **3** (40.0 μmol) or 16.812 mg of **2** (40.0 μmol), and 7.879 mg of [(crotyl)PdCl]$_2$ (20.0 μmol) in 2 mL of dichloromethane was stirred overnight. The membrane was cut to the correct size for the reactor and stored in acetone during one night before storing it in methanol (for at least one night). When it was adjusted in the membrane reactor, the membrane was flushed overnight with dichloromethane. The ligand−Pd−dendrimer mixture was transferred into the reactor and the solvent was pumped through for 25 h at a flow rate of 6 mL/h to flush the reactor 30 times. The solvent was evaporated from both the contents of the reactor and the solution that had been pumped through the membrane. The residue was weighed and analyzed by NMR.

Catalysis. The allylic amination experiments were performed under N_2 atmosphere at room temperature.

Batch Process. The catalyst solution of the model compound was prepared by overnight stirring of a mixture of the fifth generation of adamantyl−urea functionalized poly(propylene imine) dendrimer, the ligand, and [(crotyl)PdCl]$_2$ in 2 mL of dichloromethane. To the catalyst solution were added 2.0 mL of CH_2Cl_2 and 1.0 mL of substrate solution. The reaction was monitored in time by quenching samples in DBA/Et_2O solution (DBA = dibenzylideneacetone). Conversions and product distribution were determined by using GC analysis.

Continuous Process. The catalyst solutions were prepared similar to those for the batch reactions. For the model reaction 0.0117 g of dendrimer (0.632 μmol), 8.408 mg of **2** (20.0 μmol), and 3.915 mg of [(crotyl)PdCl]$_2$ (9.94 μmol, 19.9 μmol of Pd) were stirred overnight in 2 mL of dichloromethane. For the dendrimeric catalyst solution 0.0116 g of dendrimer (0.627 μmol), 7.836 mg of **3** (20.0 μmol), and 3.905 mg of [(crotyl)PdCl]$_2$ (9.91 μmol, 19.8 μmol of Pd) were stirred overnight in 2 mL of dichloromethane. The membrane was cut to the correct size for the reactor, stored in acetone for one night, and then stored in methanol (for at least one night). After it was transferred into the membrane reactor, the membrane was first flushed overnight with CH_2Cl_2 and then with substrate solution (approximately two reactor volumes). The substrate solution was prepared by mixing 1.5 mL of crotyl acetate, 2.47 mL of piperidine, and 2.44 mL of *n*-decane (as internal standard) in CH_2Cl_2 (total volume = 100 mL) and was pumped through the reactor with a flow rate of 9 mL/h. The reaction was started by transferring the catalyst solution in the membrane reactor. Samples of the solution coming out of the reactor were quenched in DBA/Et_2O and analyzed by GC.

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