Hydroformylation Reactions with Rhodium-Complexed Dendrimers on Silica

S. Christine Bourque,[†] François Maltais,[†] Wen-Jing Xiao,[†] Olivier Tardif,[†] Howard Alper,*,[†] Prabhat Arya,[‡] and Leo E. Manzer[§]

Contribution from the Department of Chemistry, University of Ottawa, 10 Marie Curie St., Ottawa, Ontario, Canada K1N 6N5, Steacie Institute for Molecular Sciences, National Research Council Canada, 100 Sussex Dr., Ottawa, Ontario, Canada K1A 0R6, and DuPont Central Research & Development, Experimental Station, Wilmington, Delaware 19880-0262

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Abstract: Polyamidoamine dendrimers, constructed on the surface of silica, were phosphonated by using diphenylphosphinomethanol, prepared *in situ,* and complexed to rhodium by use of $[Rh(CO)_2Cl]_2$. Excellent selectivities, favoring the branched aldehydes obtained from aryl olefins and vinyl esters, were observed by using the Rh(I) complex as the catalyst in hydroformylation reactions. The heterogeneous Rh (I) catalyst can also be recycled and reused without significant loss of selectivity or activity.

Introduction

The hydroformylation reaction,[1] a versatile method for the functionalization of carbon−carbon double bonds, is one of the largest industrial catalytic processes producing millions of tons of aldehydes annually. The majority of industrial applications involve the production of linear aliphatic aldehydes such as butanal or nonanal from propene and octene, respectively. The branched aromatic aldehydes are more important from the fine chemicals viewpoint as they provide valuable intermediates for the pharmaceutical industry. For example, the synthesis of ibuprofen and naproxen, common anti-inflammatory agents, can be achieved by the mild oxidation of the branched aldehyde of 4-isobutylstyrene and 6-methoxy-2-vinylnaphthalene, respectively.[2] In both cases, the *S*-enantiomer is the pharmacologically active species while the *R*-enantiomer is benign. However, in the case of ibuprofen an asymmetric synthesis is not crucial since the body efficiently converts the benign *R*-enantiomer into the biologically active *S*-enantiomer.[3]

In recent years, major efforts have been directed toward the development of new catalytic systems that effectively combine the advantages of both heterogeneous and homogeneous catalysis.[4] Such a catalyst would ideally be easily recoverable and potentially recyclable while maintaining high catalytic efficiency. To date, the majority of research in this area has focused on polymer supported catalysts.[4b] Normally, the immobilization of a catalytic species on a polymer support is accompanied by a significant loss in catalytic activity or selectivity. A variation on the polymer support approach is to use a dendrimer that can be easily precipitated out of the reaction solution and recovered with use of microporous membrane filtration.

Dendrimers, being introduced within the last 20 years, are a relatively new class of molecules.[5] The highly branched nature of dendrimers offers many interesting characteristics and applications including multiple sites for metal coordination. In 1994, van Koten and co-workers prepared soluble polycarbosilane dendrimer complexes of nickel(II).[6] The latter effectively catalyzed the addition of polyhaloalkenes to double bonds. In 1997, Reetz and co-workers used a polyaminodiphosphine dendrimer as a support for rhodium and palladium catalysts.[7] We have now developed heterogeneous polyaminoamido diphosphonated dendrimers built on a silica gel core support (PPh_2- $PAMAM-SiO_2$). We were gratified to observe that these dendrimers, when complexed to Rh(I), are excellent catalysts for the hydroformylation reaction.

Results and Discussion

(1) Preparation of PAMAM−SiO₂ Dendrimers. Polyaminoamido (PAMAM) dendrimers, up to the 4th generation, were constructed on the surface of a silica gel particle (35−70 mm), with aminopropyl groups (0.9 mmol/g $\pm$ 0.1) protruding from the surface. Standard dendrimer building methods pioneered by

[†] University of Ottawa.
[‡] National Research Council Canada.
[§] DuPont Central Research & Development.

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Tomalia and co-workers[8] were employed to propagate the dendrimer generation. A Michael-type addition of the preexisting amino group to methyl acrylate forms the amino propionate ester. Subsequent amidation of the ester moieties with ethylenediamine completes the generation. Repetition of these two reactions produces the desired generation of the dendrimer. As a crude purification method, simple vacuum filtration and solvent rinsing served to remove excess reagents.

It must be recognized that the heterogeneity of the dendrimer on silica does not allow for simple proton and carbon NMR characterization. It is conceivable that during the preparation of these dendrimers, several branches may not have reacted completely resulting in amputated versions of the proposed structures. An incomplete reaction at one stage will propagate itself in higher generations.

A recent paper, discovered during the preparation of this manuscript, by Tsubokawa and co-workers[9] explores the grafting of the same PAMAM dendrimers onto a silica core. They concluded that the resulting product was more likely to be a highly branched polymer rather then a true dendrimer especially at higher generations.

(2) Preparation of Phosphonated PAMAM−SiO$_2$ Dendrimer Rhodium Complexes. The dendrimers on silica were phosphonated in order to provide an attractive coordination site for rhodium. Double phosphinomethylation of each terminal amine moiety was carried out with diphenylphosphinomethanol prepared in situ from paraformaldehyde and diphenylphosphine.[7a] The resulting phosphonated dendrimers were characterized by ^{31}P solid-state NMR, with chemical shifts of −27 to −28 ppm for the various generations comparing well with the published result of −28 ppm[7a] for the homogeneous polyamino phosphonated dendrimer. The diphosphonated amino group can act as a bidentate ligand for coordination with many transition metals. One can envision the formation of a six-membered ring upon complexation with the metallic species. The phosphonated dendrimers were readily complexed by reaction with chloro-(dicarbonyl)rhodium(I) dimer in hexanes. The dendrimer complexes are easily isolated by microporous membrane filtration. The resulting complexed dendrimers (see Figure 1) were characterized by ^{31}P solid-state NMR (complexed $\delta = 24$ to 25 ppm, uncomplexed $\delta = -27$ to −28 ppm).

The rhodium-complexed PPh$_2$−PAMAM−SiO$_2$ dendrimers were digested with hydrofluoric acid or *Aqua-Regia* by microwave heating and analyzed for Rh content by ICP analysis. The rhodium content of the various generations is summarized in Table 1. The degree of complexation decreases significantly beyond the second generation. This is believed to be due to incomplete phosphonation reactions arising from steric crowding and ultimately resulting in the threshold of dendrimer growth being reached. The PPh$_2$−PAMAM−SiO$_2$ dendrimers can be handled in air; however, partial oxidation of the phosphine, detected by ^{31}P NMR analysis ($\delta = 30$ ppm), occurs after exposure to atmospheric oxygen for one month. This decomposition is expedited if filtration of the phosphonated dendrimers and complexes is not carried out under a flow of inert gas such as argon or nitrogen. Storage of the dendrimers and complexes under nitrogen is sufficient to avoid oxide formation.
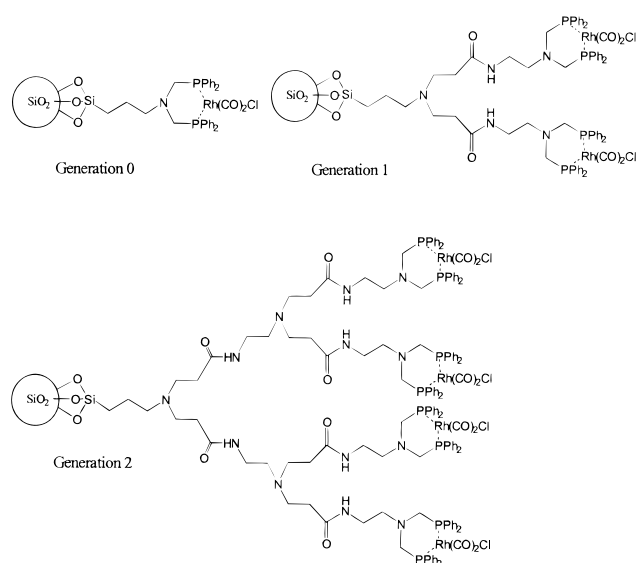
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Figure 1. The proposed structures of the generation 0, 1, and 2 Rh−PPh$_2$−PAMAM−SiO$_2$ complexes.

Table 1. Rhodium Content of the Various PPh$_2$−PAMAM−SiO$_2$ Dendrimers[a]

generation	g of Rh/g of Si	μmol of Rh/25 mg of SiO$_2$
0	0.046	11.2
1	0.029	7.0
2	0.039	9.5
3	0.0018	0.44
4	0.0026	0.63

[a] Average result from two independent laboratories for the same sample.

(3) Catalytic Hydroformylation of Olefins with Rhodium-Complexed Silica-Supported Dendrimers. The catalytic activity of the rhodium-complexed PPh$_2$−PAMAM−SiO$_2$ dendrimers was investigated with regards to the hydroformylation reaction (eq 1) and the results are summarized in Table 2.
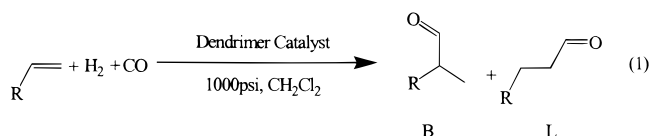
Treatment of styrene with a 1:1 mixture of carbon monoxide and hydrogen (1000 psi total pressure) in dichloromethane, and with Rh-complexed PPh$_2$−PAMAM−SiO$_2$ dendrimer (25 mg), affords aldehydes in nearly quantitative yield with excellent regioselectivity at room temperature for generations 0, 1, and 2. The catalytic activity is significantly less at room temperature when generation 3 and 4 dendrimer complexes are used as catalysts. Raising the reaction temperature to 65 and 75 °C decreases the selectivity for the branched aldehyde and increases the activity of the higher generation catalyst. Decreasing the total pressure of the reaction to 800 and 500 psi also decreases the selectivity for the branched aldehyde.

After the hydroformylation reaction with the generation 0, 1, and 2 catalysts, the product solution is yellow in color suggesting that some leaching of the rhodium metal occurs. This leaching is less evident in the generation 3 and 4 catalysts. The catalyst from the entry 4 reaction was recovered by microporous filtration, washed with distilled hexanes, and reused four times without significant loss of activity or selectivity. The wash solution was colorless after the second cycle, consistent with little, if any, leaching.

Table 2. The Hydroformylation of Styrene with Rh−PPh$_2$−PAMAM−SiO$_2$ Catalysts[a]

entry	catalyst generation	pressure[b] (psi)	temp (°C)	conversion[c] (%)	selectivity[d] B:L
1	0	1000	25	98	25:1
2	1	1000	25	98	27:1
3	2	1200	75	>99	9:1
4	2	1000	75	>99[e]	8:1
5	2	800	75	>99	6:1
6	2	500	75	>99	3:1
7	2	1000	65	>99	13:1
8	2	1000	25	>99	30:1
9	3	1000	75	>99	8:1
10	3	1000	25	5	ND[f]
11	4	1000	75	>99	8:1
12	4	1000	25	2	ND[f]

[a] 2.0 mmol of styrene, 10 mL pf CH$_2$Cl$_2$, 22 h. [b] Total pressure with a 1:1 ratio of CO:H$_2$. [c] Determined by GC. [d] Determined by ^{1}H NMR. [e] Catalyst was recovered by microporous filtration, washed with distilled hexanes, and reused four times without significant loss of activity or selectivity. [f] Not determined.

Table 3. The Hydroformylation of Various Olefins Catalyzed by Rh−PPh$_2$−PAMAM−SiO$_2$ Catalysts

entry	substrate[a]	catalyst generation	temp (°C)	conversion[b] (%)	selectivity[c] B/L ratio
1	isobutylstyrene	2	25	60	26:1
2	4-methoxystyrene	2	75	>99	7:1
3	vinylnaphthalene	3	75	>99	7:1
4	vinyl benzoate	2	75	>99	19:1
5	vinyl benzoate	2	25	29	21:1
6	vinyl benzoate	3	75	>99	18:1
7	vinyl acetate	2	75	>99	7:1
8	vinyl acetate	2	65	>99	13:1
9	vinyl acetate	2	35	96	18:1
10	vinyl acetate	2	25	52	20:1
11	vinyl acetate	2	25	95	18:1
12	vinyl acetate	3	75	>99	9:1
13	allyl phenyl ether	2	75	>99	2:1
14	octene	2	75	>99	1:2
15	octene	2	110	>99	1:2

[a] 2.0 mmol of substrate, 10 mL of CH$_2$Cl$_2$, 1000 psi of total pressure with a 1:1 ratio of CO:H$_2$, 22 h (except 48 h for entry 11). [b] Determined by GC. [c] Determined by ^{1}H NMR.

Table 3 describes the catalytic activity of the generation 2 and 3 dendrimer complexes as catalysts with a variety of olefins. *p*-Isobutylstyrene gives excellent regioselectivity at room temperature; however, the presence of the isobutyl group in the *para* position slows down the reaction compared to styrene. Excellent selectivity was also observed by reaction of vinyl acetate at room temperature with a conversion of 52% (entry 10) with the generation 2 rhodium complex as the catalyst. Increasing the temperature to 35 °C decreases the selectivity slightly; however, the conversion is nearly complete (entry 9). Octene reacts to form the linear aldehyde in slight excess. Increasing the reaction temperature from 75 to 110 °C does not improve the selectivity (entries 14, 15).

Turnover number results for the hydroformylation of styrene with various Rh−PPh$_2$−PAMAM−SiO$_2$ dendrimer complexes as catalysts are presented in Table 4. At room temperature, the turnover numbers for generations 0, 1, and 2 are generally of the order of 10 to 20 mmol of substrate to mmol of Rh/h while generation 3 and 4 afforded 78 and 84/h, respectively. At 70 °C, the generation 3 and 4 dendrimer complexes gave relatively high turnover frequencies of 180 and 200/h while the lower generations are of the order of 100/h. The time dependence of the turnover rate is demonstrated in entries 6−9 where the highest turnover frequency occurs within the first 2 h of the

Table 4. Turnover Numbers for the Hydroformylation of Styrene with Various Rh−PPh$_2$−PAMAM−SiO$_2$ Dendrimer Catalysts[a]

entry	generation	temp[b] (°C)	time (h)	conversion (%)	turnover (/h)
1	0	25	22	32	13
2	0	70	22	92	102
3	1	25	22	15	10
4	1	70	22	60	96
5	2	25	22	37	18
6	2	70[c]	2	44	230
7	2	70[c]	4	74	200
8	2	70[c]	8	88	120
9	2	70	22	82	100
10	3	25	72	25	78
11	3	70[c]	22	18	180
12	4	25	72	38	84
13	4	70[c]	22	28	200

[a] 25 mg of catalyst, 1000 psi of total pressure with a 1:1 ratio of CO:H$_2$. [b] 10.0 mmol of styrene at 25 °C, 25.0 mmol at 70 °C except where indicated. [c] 10.0 mmol.

reaction (entry 6). The turnover frequency drops by half between 4 and 8 h (entries 7 and 8, respectively) of reaction.

Summary

The dendrimer-supported complexes, Rh−PPh$_2$−PAMAM−SiO$_2$, are new and highly active catalysts for the hydroformylation of a variety of olefins. Aryl olefins and vinyl esters afford branched chain aldehydes in high selectivity.

Experimental Section

General. Carbon monoxide, a powerful asphyxiant, should be used with care. To use and work with carbon monoxide safely, reactions must be carried out in a properly working fumehood with CO detectors installed nearby.

General Procedure for the Preparation of the PAMAM−SiO$_2$ Dendrimers. Aminopropyl silica gel (0.018 mmol NH$_2$, 20.0 g) and methyl acrylate (0.18 mol, 15.65 g) were stirred at 50 °C under nitrogen for 3 days in methanol (100 mL). The suspension was cooled and filtered through a medium pore frit, washed first with methanol (3 × 30 mL) and then with ether (3 × 30 mL). The residual solvent was removed in vacuo (96% yield) affording methyl propylaminopropionate silica gel (0.03 mol of ester groups, 20.0 g). The latter was then added to ethylenediamine (100 mL) in methanol (100 mL) and stirred at room temperature under nitrogen for 5 days. The resulting first-generation PAMAM−SiO$_2$ was isolated by filtration, then washed with methanol (3 × 30 mL) and dichloromethane (3 × 30 mL). The residual solvent was removed in vacuo (95% yield).

The second-generation PAMAM−SiO$_2$ can be prepared by following the above procedure starting with the first-generation PAMAM−SiO$_2$ (0.028 mol of NH$_2$ groups, 20.8 g) and methyl acrylate (0.5 mol, 43.0 g), and by changing the reaction time to 5 days. After isolation, the ester was added to ethylenediamine (200 mL) in methanol (100 mL) and stirred at room temperature under nitrogen for 7 days (91% yield).

The third (83% overall yield) and fourth (75% overall yield) generations were prepared in the same manner.

General Procedure for the Phosphonation of PAMAM−SiO$_2$ Dendrimers. Under argon, diphenylphosphine (40.0 mmol) was added to a solution of paraformaldehyde (30.0 mmol) in degassed methanol (40 mL). The mixture was stirred at 70 °C for 30 min and then cooled to room temperature. The PAMAM−SiO$_2$ dendrimer (2.0 mmol with respect to NH$_2$) was added along with degassed methanol (20 mL) and toluene (80 mL). The reaction was stirred at 70 °C for 2 h and then at room temperature overnight. The product was isolated by filtration by using a 0.45 μm membrane filter under a stream of argon and washed with methanol (100 mL). The residual solvent was removed in vacuo and the product was stored under argon.

General Procedure for the Complexation of PPh$_2$−PAMAM−SiO$_2$ with Rhodium. The PPh$_2$−PAMAM−SiO$_2$ (1.0 mmol w.r.t. PPh$_2$)

was added to a solution of [Rh(CO)$_2$Cl]$_2$ (0.25 mmol) in freshly distilled hexanes (40 mL). The mixture was stirred at room temperature overnight under nitrogen. The product was filtered through a 0.45 μm membrane filter under a stream of argon and washed with dry hexanes (50 mL). Residual hexanes were removed in vacuo.

General Procedure for the Hydroformylation Reaction. A glass liner containing the substrate, catalyst (25 mg), and solvent (10 mL) was placed in a 45 mL autoclave equipped with a magnetic stirring bar. The autoclave was flushed three times with carbon monoxide and then pressurized to the desired level. The hydrogen line was then attached to the autoclave and purged before pressuring the autoclave to the desired level. The autoclave was placed in an oil bath preset to the desired temperature on a stirring hot plate. After the appropriate reaction time (see Tables 2−4), the autoclave was removed from the oil bath and cooled to room temperature prior to the release of the excess carbon monoxide − hydrogen. The resulting solution was filtered to remove the catalyst and the solvent was evaporated *in vacuo*. The product aldehydes were analyzed by ^{1}H NMR spectroscopy and gas chromatography and identified by comparison of spectral results with literature data[10] and authentic samples.

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