

Chemoselective Transfer Hydrogenation of α,β -Unsaturated Aldehydes to Allylic Alcohols Using Formic Acid Catalyzed by Polymer-Bound Rh Carbonyl Clusters

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Chemoselective hydrogenation of α,β -unsaturated carbonyl compounds to the corresponding allylic alcohols has been continuously studied due to the high potential utility of allylic alcohols.¹ We have already reported that the catalyst system consisting of $\text{Rh}_6(\text{CO})_{16}$ and amines had high activities for the hydrogenation of α,β -unsaturated aldehydes under the water-gas shift reaction conditions² or in the presence of hydrogen and carbon monoxide.³ Using aminated polystyrenes, the above catalyst system could be heterogenized to form polymer-bound Rh cluster complexes that showed high performances of recoverable and reusable catalysts.^{4,5}

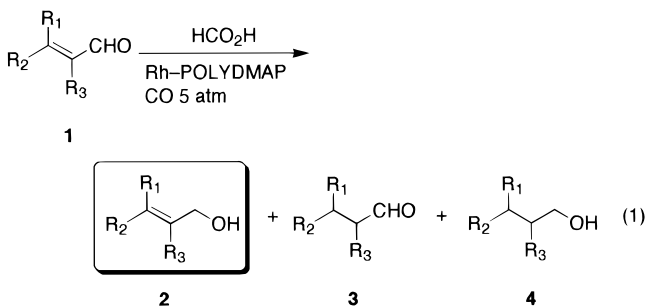
In the case of hydrogenations of carbonyl compounds to alcohols, formic acid or 2-propanol as a hydrogen source⁶ has been interesting from the standpoint of safety and using environmentally benign reagents.⁷ In this paper, we used the Rh-amine catalyst system in the

Table 1. Effect of Solvents on the Homogeneous and Heterogeneous Hydrogenations of Cinnamaldehyde (1) Using $\text{Rh}_6(\text{CO})_{16}$ ^{a,b}

solvent	DS ^c	convn of 1 ^d (%)	selectivity ^d (%)		
			2	3	4
THF	2.7	91 (86)	91 (89)	1 (1)	8 (10)
1,4-dioxane	1.8	99 (89)	82 (85)	1 (2)	17 (13)
THP	1.5	95 (88)	82 (87)	2 (1)	16 (12)
toluene	2.1	99 (0)	66 (–)	2 (–)	32 (–)
MeOH	1.2	10 (0)	72 (–)	24 (–)	4 (–)

^a Reaction conditions: **1** (1.0 mmol), $\text{Rh}_6(\text{CO})_{16}$ (0.005 mmol), formic acid (2.0 mmol), 4-DMAP (2.0 mmol), solvent (3.0 mL), $P_{\text{CO}} = 5$ atm, 30 °C, 5 h. ^b Values in parentheses are for the heterogeneous system; POLYDMAP (100 mg, 0.14 mmol equiv of DMAP) was used. ^c Degree of swelling of the POLYDMAP. DS: degree of swelling, Swollen resin volume/dry resin volume. ^d Determined by GC using internal standard technique. **2**, unsaturated alcohol; **3**, saturated aldehyde; **4**, saturated alcohol.

transfer hydrogenation of α,β -unsaturated aldehydes to allylic alcohols using formic acid, where higher catalytic activities were obtained than when H_2O or H_2 was the hydrogen source.^{2,3} The homogeneous catalyst system could be heterogenized with POLYDMAP as an aminated polystyrene support⁸ to form a catalyst that could be recycled without loss of high activities and selectivities for the above hydrogenations (eq 1).



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1. Homogeneous Hydrogenations. In order to attain highly chemoselective reductions of aldehyde functions in the presence of formic acid as a reductant, various reaction conditions (*e.g.*, CO pressures, additives, reaction temperatures, and solvents) were scrutinized in the homogeneous hydrogenation of cinnamaldehyde as a model substrate. This selective hydrogenation needed base additives as was also found in our previous hydrogenations using H_2O or H_2 as a hydrogen source.^{2,3} 4-(Dimethylamino)pyridine (4-DMAP) was found to be the best additive, while diamines as bases were effective in the case of H_2O or H_2 .^{2,3} Further CO was essential for the hydrogenation, and at least 5 atm of CO was necessary for the efficient formation of cinnamyl alcohol. Hardly any hydrogenation occurred under a nitrogen atmosphere without any CO. The highest selectivity for the unsaturated alcohol was attained at 30 °C, and hydrogenations at higher temperatures resulted in poor selectivity to allylic alcohols. Table 1 shows the effect of solvents on the homogeneous hydrogenation using formic acid together with that of the corresponding heteroge-

(8) POLYDMAP is *ca.* 4% cross-linked gel beads with particle sizes between 30 and 80 U.S. mesh (>80%). The 4-DMAP equivalence of this polymer is 1.4 mmol equiv/g (dry polymer).

Table 2. Chemoselective Hydrogenation of α,β -Unsaturated Aldehydes to Unsaturated Alcohols Using Formic Acid^{a,b}

entry	substrate	time (h)	convn ^c (%)	selectivity ^c (%)			Yield of 2 ^d (%)
				2	3	4	
1		8 (12)	97 (97)	91 (90)	0 (0)	9 (10)	87
2		10 (24) ^e	98 (89)	94 (94)	0 (1)	6 (5)	78
3 ^f		10 ^e (24) ^e	92 (86)	100 (100)	0 (0)	0 (0)	80
4		10 (24)	83 (76)	100 (100)	0 (0)	0 (0)	70
5		5 (20)	92 (72)	52 (57)	0 (8)	48 (35)	
6		5 (20)	89 (90)	88 (97)	9 (1)	3 (2)	79
7		5 (20)	92 (78)	89 (91)	4 (1)	7 (8)	67
8 ^g		20 (20)	92 (68)	95 (90)	0 (5)	5 ^h (5) ^h	
9		20 (24)	92 (90)	96 (99)	0 (0)	4 (1)	81
10		5 (24)	99 (92)	100 ^h (100) ^h	-	0 (0)	87
11		5 (14)	96 (98)	100 ⁱ (100) ⁱ	0 (0)	0 (0)	93

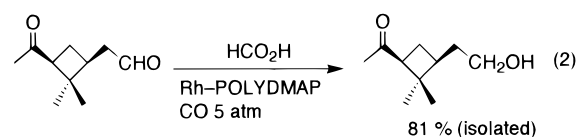
^a Reaction conditions: substrate (1.0 mmol), Rh₂(CO)₁₆ (0.005 mmol), 4-DMAP (2.0 mmol), formic acid (2.0 mmol), THF (3.0 mL), P_{CO} = 5 atm, 30 °C. ^b Values in parentheses are for the heterogeneous system, where the POLYDMAP (100 mg, 0.14 mmol eq. of 4-DMAP) was used in place of 4-DMAP. ^c Determined by GC using internal standard technique. 2, Unsaturated alcohol; 3, saturated aldehyde; 4, saturated alcohol. ^d Isolated yields. See in experimental section about the isolation procedures. ^e Formic acid (3.0 mmol) was used. ^f Mixture of regio isomers. ^g E/Z = 2.6. ^h Mixture of regio isomers. E/Z = 2.0. ⁱ Citronellol. The isolated olefinic bond is intact. ^j 3-Cyclohexene-1-methanol.

neous Rh system. Cyclic ether solvents, *e.g.*, THF, 1,4-dioxane, and tetrahydropyran, were effective, while methanol and toluene were poor solvents, respectively. Among the cyclic ether solvents, the highest selectivity for cinnamyl alcohol (91%) was obtained with THF.

Results of the homogeneous hydrogenation of various α,β -unsaturated aldehydes using 4-DMAP and THF as a solvent are shown in Table 2 together with those obtained in the heterogeneous system (*vide infra*). Methyl-substituted cinnamaldehydes of 2-methyl-3-phenylpropenal and 3-phenyl-2-butenal showed high selectivities for the corresponding unsaturated alcohols, respectively (Table 2, entries 2 and 3). In the case of phenyl-substituted cinnamaldehydes, the chemoselective hydrogenation of 3,3-diphenyl-2-propenal occurred to give 3,3-diphenyl-2-propen-1-ol as the sole product (Table 2, entry 4), while *trans*-2,3-diphenyl-2-propenal showed a poor selectivity for the corresponding unsaturated alcohol (Table 2, entry 5). Either an electron-donating or -withdrawing substituent in the para position of cinnamaldehydes did not significantly influence the chemoselectivity (Table 2, entries 6 and 7). Under these reaction conditions, dechlorination of 3-(4-chlorophenyl)-2-propenal did not occur (Table 2, entry 6). Further, citral and 3-methyl-2-butenal, typical aliphatic α,β -unsaturated aldehydes, gave the corresponding allylic alcohols in high yields, respectively (Table 2, entries 8 and 9). The isolated olefinic bond in citral remained intact under the above reaction conditions. This high chemoselectivity for the aldehyde functions in the presence of nonconjugated

olefinic bonds could be observed also in citronellal and cyclohexene-4-carboxaldehyde (Table 2, entries 10 and 11). The hydrogenations of 3-phenyl-2-butenal and citral used as mixtures of geometrical isomers (*E/Z* = 2.6 and 2.0) proceeded with high retention of the olefinic configuration, respectively.

In an intermolecular competitive reaction between benzaldehyde and acetophenone, benzyl alcohol was only hydrogenation product without formation of 1-phenylethanol from acetophenone. High aldehyde chemoselectivity was also confirmed in the intramolecular competitive hydrogenation of *cis*-3-acetyl-2,2-dimethylcyclobutaneacetaldehyde. Only the formyl function could be reduced to afford *cis*-3-acetyl-2,2-dimethylcyclobutaneethanol in 92% yield (81% isolated). No products were obtained from reduction of the ketone group (eq 2).



2. Heterogeneous Hydrogenations. It is well known that use of polymer-bound metal complex catalysts can simplify the process of purification of products. In order to heterogenize the above homogeneous Rh-amine system by using polymer supports, POLYDMAP was used in place of 4-DMAP as a base additive. POLYDMAP has a 4-(dimethylamino)pyridino moiety on the

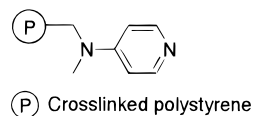


Figure 1. Structure of the POLYDMAP.

para position of styrene unit in the cross-linked polystyrene support (Figure 1). As shown in Table 1, THF was also an effective solvent in the heterogeneous system, but the effects of solvent (except for cyclic ethers) were much different from those in homogeneous systems. The degree of swelling of POLYDMAP (DS) in every solvent used in Table 1 was obtained by measurement of both dry and swollen polymer volumes in each solvent. Use of THF or toluene showed a high DS value, but the hydrogenation did not occur with toluene. In the heterogeneous systems, it seemed that the DS in the cyclic ether solvents did not strongly affect the hydrogenation rate and product selectivity. In the above homogeneous hydrogenation, a large amount of 4-DMAP was necessary to obtain unsaturated alcohols in good yields. Typically, 2 equiv was used. On the other hand, the heterogeneous hydrogenations smoothly proceeded with POLYDMAP having a much lower amino content, even 7% of that in the homogeneous system. This phenomenon might be due to the concentration effect of amino moieties within the polymer beads. The concentration of DMAP within the swollen volume of the beads in THF was 0.70 mmol/mL, which was similar to the value in the homogeneous reaction (0.67 mmol/mL). A very low conversion of cinnamaldehyde was obtained in the homogeneous hydrogenation with 0.14 mmol of 4-DMAP, the same amount as in the heterogeneous system. No influence on the hydrogenation rate was observed when ground POLYDMAP was used under the model reaction conditions using cinnamaldehyde.⁹ Results of the heterogeneous hydrogenations of various α,β -unsaturated aldehydes using POLYDMAP are also shown in Table 2. Generally, high chemoselectivity for the hydrogenation of various aldehydes could be obtained in spite of lower hydrogenation rates than those in the homogeneous system.

As expected, use of POLYDMAP could make the workup procedures very simple. The polymer-bound Rh catalysts were easily separated from the reaction mixture by filtration, and then the filtrate was concentrated, followed by column chromatography on silica gel with hexane/AcOEt (10/1 v/v) to give pure allylic alcohols. Furthermore, we recycled the polymer-bound Rh catalyst in the hydrogenation of 3-methyl-2-butenal (shown in Table 3). The high catalytic activity of the polymeric complexes and high chemoselectivity for 3-methyl-2-buten-1-ol were maintained even after the fourth recycle.

This Rh-amine catalyst system with formic acid as a hydrogen source shows higher activity than those under the similar reaction conditions with H₂O or H₂ as hydrogen sources.^{2,3} We think that Rh hydride species could be generated at faster rate under the reaction conditions using formic acid; 4-DMAP or POLYDMAP forms salts with formic acid and also acts as counterions of the hydride Rh carbonyl cluster anions, which is similar to the case of hydrogenation with H₂O and CO.^{5e}

(9) POLYDMAP beads were ground at liquid nitrogen temperature, and the resulting powder was used in a hydrogenation of cinnamaldehyde.

Table 3. Recycling the Polymer-Bound Rh Catalyst in the Hydrogenation of 3-Methyl-2-butenal (1)^a

recycle no.	convn of 1 ^b (%)	selectivity ^b (%)		
		2	3	4
fresh	90	99	0	1
1	93	99	0	1
2	90	99	0	1
3	88	99	0	1
4	88	99	0	1

^a Reaction conditions: 1 (1.0 mmol), Rh₆(CO)₁₆ (0.005 mmol), POLYDMAP (100 mg), THF (3.0 mL), formic acid (3.0 mmol), P_{CO} = 5 atm, 30 °C, 24 h. ^b Determined by GC using internal standard technique. 2, unsaturated alcohol; 3, saturated aldehyde; 4, saturated alcohol.

In conclusion, the Rh₆(CO)₁₆/4-DMAP catalyst system was found to be efficient for the chemoselective hydrogenation of α,β -unsaturated aldehydes to allylic alcohols with formic acid. The use of formic acid as the hydrogen source gave higher catalytic activities with this catalyst than those with H₂O or H₂. The above Rh cluster catalyst could be heterogenized to form a recoverable and reusable polymer-bound Rh complex when POLYDMAP was employed.

Experimental Section

General Procedures. Aldehyde compounds, amines, and solvents were purified by the standard procedures before use.¹⁰ 3-Phenyl-2-butenal, *trans*-3-(4-chlorophenyl)-2-propenal, *trans*-3-(4-methoxy-phenyl)-2-propenal, 3,3-diphenyl-2-propenal, and (*Z*)-2,3-diphenyl-2-propenal were synthesized according to the literature.¹¹ *cis*-3-Acetyl-2,2-dimethylcyclobutaneacetaldehyde was obtained by ozonolysis of α -pinene.¹² All of the substrates and products were characterized by comparison with the literature data. POLYDMAP was obtained from Reilly Industries and dried in vacuo prior to use. Formic acid (99%) was purchased from Wako Pure Chemicals and used as received. Rh₆(CO)₁₆ was prepared according to the method of Chini.¹³ GC analysis was performed by Shimadzu GC-8A with FID detector and a 2 m column (Silicone UC W-98). ¹H NMR spectra were obtained on JEOL GSX-270 or JNM-AL400 spectrometers at 270 or 400 MHz in CDCl₃ with TMS as an internal standard. Infrared spectra were recorded on a JASCO FT/IR 410.

General Procedure for the Homogeneous Hydrogenation. To a glass liner containing formic acid (2 mmol) and 4-DMAP (2 mmol) was added Rh₆(CO)₁₆ (0.005 mmol), followed by a THF (3.0 mL) solution of an aldehyde (1.0 mmol) under a nitrogen atmosphere. The glass liner was set in a stainless steel autoclave and then flushed three times and pressurized to 5 atm with CO. After the reaction mixture was stirred at 30 °C for an appropriate time, the solution obtained was subjected to GC analysis.

Measurement of the Degree of Swelling of the POLYDMAP. The dry resin beads (0.2 mL) were filled in a graduated cylinder, to which was added 1 mL of solvent. The polymer was treated with ultrasonication for 1 min to remove air and was then placed for 2 h. The degree of swelling of the POLYDMAP (DS) was calculated as the swollen resin volume over the dry one (0.2 mL). These procedures were carried out using every solvent used in Table 1.

General Procedure for the Heterogeneous Hydrogenation with POLYDMAP. POLYDMAP (100 mg, 0.14 mmol equiv of 4-DMAP) was used in place of 4-DMAP. To a glass liner

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containing formic acid (2 mmol) and the POLYDMAP (100 mg) was added $\text{Rh}_6(\text{CO})_{16}$ (0.005 mmol), followed by a THF (3.0 mL) solution of an aldehyde (1.0 mmol) under a nitrogen atmosphere. The glass liner was set in a stainless steel autoclave and then flushed three times and pressurized to 5 atm with CO. After the reaction mixture was stirred at 30 °C for an appropriate time, the polymer-bound Rh complexes were removed by filtration and washed three times with THF. The combined filtrate was concentrated and subjected to column chromatography on silica gel (Wako gel C-200) with a mixture of hexane and ethyl acetate (10:1), which afforded pure allylic alcohols. The polymer was initially golden amber, which became reddish brown after the filtration. The IR adsorptions of the reddish brown polymer-bound Rh complexes in the carbonyl stretching region were observed at 2078, 2037, 2000, and 1819 cm^{-1} .

Recycling of the Polymer-Bound Rh Catalyst in the Hydrogenation of 3-Methyl-2-butenal. The first run using 3-methyl-2-butenal (1.0 mmol) was carried out in using the same procedure as described in the above heterogeneous hydrogenation. After the reaction mixture was stirred at 30 °C for 24 h, the reactor was cooled and the pressure was slowly released. The supernatant in the glass liner was withdrawn using a syringe under a nitrogen atmosphere. The residual polymeric catalyst was washed with three 5 mL aliquats of THF, followed by addition of formic acid and THF solution of the substrate, flushed three times and pressurized to 5 atm with CO, and stirred at 30 °C for 24 h. These recycling procedures were repeated four times in the same manner as in the first recycle.

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