Vapor-Phase Asymmetric Hydroformylation

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Polystyrene-supported (*R*,*S*)-BINAPHOS–Rh complex was demonstrated to be applicable to the asymmetric hydroformylation of gaseous substrates in a non-solvent system: 3,3,3-trifluoropropene (**2a**) and (*Z*)-2-butene (**2b**) were converted into the corresponding branched aldehydes with 90% and 80% ee, respectively.

In general, heterogeneous catalysis is advantageous due to its high activity, thermal stability, easy recovery and reuse, and thus, vapor-phase reactions over heterogeneous catalysts are most widely used in industrial processes. On the other hand, vapor-phase asymmetric catalysis has no precedents thus far. Substrates for asymmetric catalysis often have rather high boiling points. Above the boiling points, finely tuned chiral catalysts are not stable, in many cases. Furthermore, the use of solvents is considered to be essential in order to keep the reaction conditions uniform throughout by interacting with solutes, via coordination, hydrogen bonding, or dipoles. In order to avoid the use of organic solvents, recent efforts are focused on asymmetric catalysis in environmentally benign solvents, such as supercritical CO_2[1] and water.[2] Here we report that the vapor-phase asymmetric catalysis over a chiral transition metal complex can be carried out without any solvents.[3] Attachment of the complex to a polymer matrix[4] is the key solution for the problematic issues that arise from the absence of solvents.

Asymmetric hydroformylation of olefins is a direct route to optically active aldehydes which are valuable precursors for a variety of pharmaceuticals and agrochemicals. Previously, we developed chiral Rh(I) complex **1a** as the first example of a truly efficient catalyst for asymmetric hydroformylation of various kinds of olefins.[5] Attachment of complex **1a** to polystyrene enabled the recovery and reuse of the catalyst.[6] As is common to the other asymmetric catalysis, the achievements were performed in a homogeneous catalysis style. In this transformation, substrates such as olefins, carbon monoxide, and hydrogen are of high volatility. Thus, the idea that gaseous mixture of all the substrates would be easily available at low temperatures prompted us to examine the vapor-phase asymmetric hydroformylation using a fixed bed illustrated in Figure 1 (apparatus A). Polystyrene-supported catalyst **1b** is placed at the center of a stainless autoclave without touching the liquid phase. As a reference, a homogeneous catalysis style apparatus B was also employed.
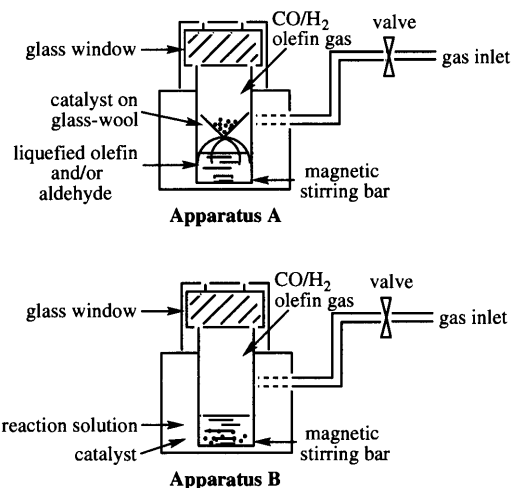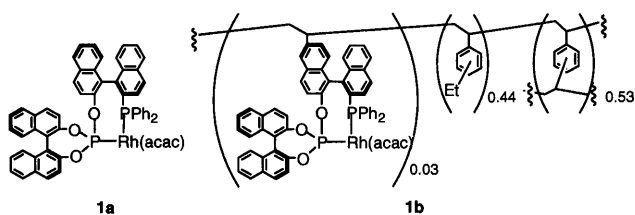

Figure 1. Apparatus A (Top): At the center of a glass-window-equipped autoclave, a stainless steal wire stool was placed, and polymer-supported chiral catalyst **1b** was mounted on the stool with the aid of glass-wool. The autoclave was charged with a substrate olefin and syngas (H_2/CO) and then kept at 40–60 °C. The surface of the liquefied substrate or product does not reach the stool. The shape of the polymer flake was not damaged throughout the reaction. Apparatus B (Bottom): Either **1b** or non-supported catalyst **1a** was used in the liquid phase. During the reaction, **1b** was partially broken mechanically into pieces by stirring.

A volatile substrate, 3,3,3-trifluoropropene (**2a**, saturated vapor pressure 8.5 atm at 40 °C),[7] was first employed. It is well known that aldehyde **3a** is an important intermediate for the synthesis of a fluorinated amino acid, a potential biologically active compound.[5] As the reaction proceeded, the polymer catalyst became wet judged from visual observation. Analysis revealed that **3a** was produced with 114 h^{-1} turnover frequency, 93% regioselectivity, and 90% ee (run 1). Thus, asymmetric hydroformylation was accomplished without any solvents. By ICP emission spectrometry analysis, no Rh was detectable in the product with the experimental error range being less than 0.8% of the initially loaded Rh. This sharply contrasts to the fact that polymer-fragmentation was a significant problem to cause the dissociation of powdery Rh-containing polymer in the sink-in apparatus B.[6b]

So far as polymer-supported **1b** was employed, the performance was maintained in apparatus B, except for the problematic polymer-fragmentation (run 2). Accordingly, it is likely that the reaction in run 1 took place in a maner similar to that in run 2, as realized by adsorption of substrate **2a** on the surface of swollen polymer catalyst **1b**. In contrast, however, drastic loss of catalytic activity was observed with non-supported catalyst **1a** (run 3). Due to the poor solubility of catalyst **1a** in fluorinated substrate **2a**, the catalyst stuck on the bottom of the autoclave during the reaction, without any dispersion. The

Table 1. Asymmetric hydroformylation of alkenes with polymer-supported (**1b**) or non-supported (**1a**) Rh(acac)[(*R,S*)-BINAPHOS] catalyst in the presence or absence of reaction medium[a]

Run	Substrate	Catalyst	Medium	Appar -atus	Appearence	H$_2$/CO atm /atm	Temp /°C	Time /h	TOF /h⁻¹	3/4	%ee
1	CF$_3$CH=CH$_2$ (**2a**)	**1b**	none	A	—	40/40	40	18	114	93/7	90 (*S*)
2		**1b**	none	B	polymer suspension	37/37	40	18	156	91/9	88 (*S*)
3		**1a**	none	B	solid precipitates[b]	40/40	40	18	1.9	85/15	81 (*S*)
4		**1a**	benzene	B	solid precipitates[b,c]	40/40	40	18	64	95/5	93 (*S*)
5	(*Z*)-2-butene (**2b**)	**1b**	none	A	—	16/16	60	8	27	100/0	80 (*S*)
6		**1b**	none	B	polymer suspension	16/16	60	8	24	100/0	80 (*S*)
7		**1a**	none	B	cloudy	16/16	60	8	6.5–31	100/0	80 (*S*)
8		**1a**	benzene	B	clear	16/16	60	8	23	100/0	82 (*S*)
9[d]	styrene (**2c**)	**1b**	none	A	—	37/37	60	6	157	85/15	91 (*R*)
10[d]		**1a**	benzene	B	clear	37/37	60	6	1050[e]	87/13	91 (*R*)

[a]Analysis of the products were reported in Refs. 5 and 6. [b]Complex **1a** was insoluble. [c]Benzene/substrate = 5–10 (vol/vol). [d]Substrate/catalysts = 10000 (50 mmol, 5.8 mL of styrene, Rh = 5 x 10⁻³ mmol). [e]Conversion to aldehydes in 6 h was 63%. The reaction was stopped before completion in order to compare the catalytic activity. The conversion reached 100% after 12 h with substrate/catalyst = 2000, maintaining the high regio- and enantioselectivities. See Refs. 5 and 6.

existence of benzene improved the TOF only to some extent (run 4). Hence, the difference between the results with polymer-supported catalyst **1b** (runs 1 and 2) and that with non-supported **1a** (runs 3 and 4) suggests that the existence of the polymer matrix is essential in providing a phase where the substrate efficiently meets the active center of the catalyst,[8] particularly in the case that the catalyst is insoluble in the substrate.
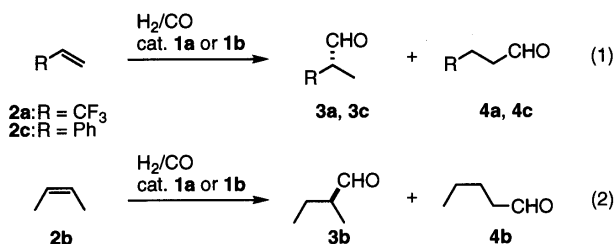
The catalyst system, namely **1b** without solvents, was also applicable to another low-boiling point substrate, (*Z*)-2-butene (**2b**, saturated vapor pressure 9.1 atm at 60 °C)[9] (run 5), the results being comparable to the performance previously attained under homogeneous conditions using **1a** in benzene (run 8). Even a less volatile olefin, styrene (**2c**, 0.092 atm at 60 °C), was successfully hydroformylated by the present process although the TOF was inferior to the homogeneous counterpart (runs 9 and 10).

Thus, the solvent-free asymmetric hydroformylation demonstrates the potential application of this catalyst to continuous use in a flow system. The absence of mechanical breaking of the polymer catalyst prevents the leaching of metals. Meanwhile, the polymer matrixes are presented of potential use as the substitute for organic solvents[10] in asymmetric catalysis.

References and Notes
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