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Rh(I)-catalyzed intramolecular hydroacylation in ionic liquids

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Abstract—Rh(I)-catalyzed hydroacylation of 4-alkenal or 4,6-dienal using ionic liquids (ILs) as reaction media proceeded smoothly, giving cyclopentanone or cycloheptenone derivatives in good yields. It was found that the IL recovered after the reaction, which should contain the Rh(I) catalyst, could be recycled 5–10 times without the loss of catalytic activity and enantioselectivity (in the case of asymmetric hydroacylation).

Ionic liquids (ILs) are receiving much attention as reaction media in synthetic organic chemistry because they have some unique properties such as a wide liquid range with a melting point around room temperature, negligible vapor pressure, high polarity, and thermal stability.[1] Furthermore, ILs are known to dissolve charged species such as organometallic compounds more readily than non-charged species, including most organic compounds, via ionic interactions. This property of ILs might enable easy separation of the catalyst and organic compounds by simple phase separation and recycling of the catalyst remaining in ILs. In recent years, from the viewpoint of green chemistry, various reactions catalyzed by transition metal complexes have been extensively examined using ILs as the reaction media. For Rh chemistry, although there are several reports on recycling of catalysts using ILs,[1,2] there has been no report on the hydroacylation of 4-alkenals,[3,4] which is one of the important Rh(I)-mediated C–C bond forming reactions.[5] Herein, we report the use of ILs as the reaction media for Rh(I)-catalyzed intramolecular hydroacylation with the aim of developing environmentally benign chemical processes.

Initially, we investigated the intramolecular hydroacylation of 4-alkenal **1a** using a cationic Rh(I) complex, [Rh(dppe)]ClO_4, generated in situ from [Rh(nbd)(dppe)]ClO_4 under an atmosphere of hydrogen,[4d] in various ILs (Table 1).[6] As a control experiment, the cyclization of **1a** was carried out in dichloroethane at room temperature in the presence of 10 mol % [Rh(dppe)]ClO_4, and cyclic compound **2a** was obtained in 79% yield. In reactions using various ILs **3** based on the butylmethylimidazolium cation $[BMI]^+$ (runs 2–4), it was found that the hydroacylation of **1a** proceeded to give cyclopentanone derivative **2a** in higher yield than that in dichloroethane, although the reaction time varied depending on the counter anion of BMI. On the other hand, in the case of ILs **4** based on the butyldimethylimidazolium cation $[BDMI]^+$, the completion of the reaction needed a longer time than that in ILs **3** regardless of the counter anions (runs 5–7). These results indicate that Rh(I)-catalyzed hydroacylation proceeds at room temperature even using ILs as the reaction media.

Encouraged by these results, Rh(I)-catalyzed hydroacylation of various 4-alkenals using [BMI][NTf_2] as the reaction medium was investigated (Table 2). The reaction of **1b**, having a phenyl group at the C3 position, gave cyclopentanone **2a** in 94% yield. In the reaction of **1c**, having a 1,1-disubstituted alkene, the corresponding cyclized product **2c** was produced in 91% yield. The cyclizations of **1d** and **1e**, having a conjugated alkene, gave the desired products **2d** and **2e** in quantitative yield, respectively.

Having established the intramolecular hydroacylation of a 4-alkenal in ILs, the hydroacylation of a 4,6-dienal affording a seven-membered ring compound[7] in ILs was examined (Scheme 1). It was found that the hydroacylation of 4,6-dienal was greatly accelerated by the use of IL as a reaction medium, and the reaction of **5** in

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Keywords: Rhodium; Hydroacylation; Ionic liquid; Green chemistry; Diene; Aldehyde.

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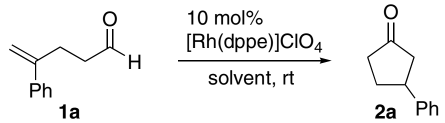
Table 1. Rh(I)-catalyzed hydroacylation of **1a** in various ILs[a]



1a **2a**

Run	Solvent	Time (h)	Yield (%)
1	$ClCH_2CH_2Cl$	5	79
2	[BMI][BF$_4$] (**3a**)	20	95
3	[BMI][PF$_6$] (**3b**)	144	90[b]
4	[BMI][NTf$_2$] (**3c**)	48	>99
5	[BDMI][BF$_4$] (**4a**)	168	>99[b]
6	[BDMI][PF$_6$] (**4b**)	144	93[b]
7	[BDMI][NTf$_2$] (**4c**)	120	>99[b]

[a] All reactions (except for run 1) were carried out in a mixed solvent of $ClCH_2CH_2Cl$ and IL (ratio of 1.0:3.2).

[b] GC yield.

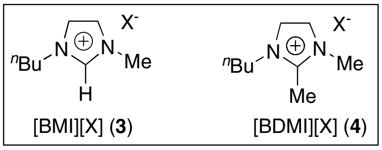
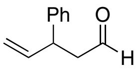
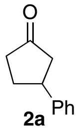
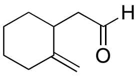
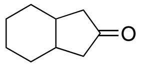
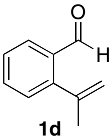
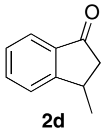
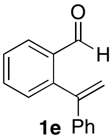
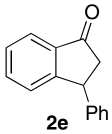


Table 2. Rh(I)-catalyzed hydroacylation of various substrates in [BMI][NTf$_2$][a]

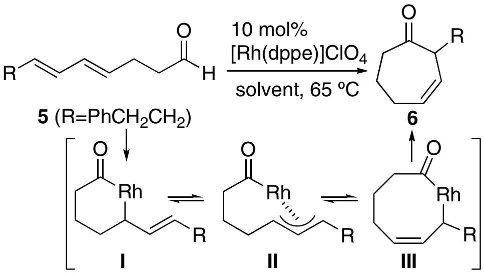
Run	Substrate	Time (h)	Product	Yield (%)
1	 **1b**	8	 **2a**	94
2	 **1c**	8	 **2c**	91[b]
3	 **1d**	1	 **2d**	>99
4	 **1e**	1	 **2e**	>99

[a] All reactions were carried out in the presence of 10 mol % [Rh(dppe)]ClO$_4$ in a mixed solvent of [BMI][NTf$_2$] and $ClCH_2CH_2Cl$ (ratio of 3.2:1.0) at room temperature.

[b] Cis:trans = 43:57.

[BMI][NTf$_2$] (**3c**) was completed within 3 h to give cycloheptenone derivative **6** in 68% yield.

Next, we turned our attention to recycling of the catalyst remaining in the IL (Table 3). The first reaction was carried out under the same conditions as those for run 3 in Table 2. After the reaction had been completed, the reaction mixture was extracted with Et$_2$O, from which cyclic compound **2d** was obtained in quantitative yield after the usual work-up (Table 3, cycle 1). On the other hand, the IL solution that remained after extraction was reused for the next cycle of hydroacylation, and product **2d** was obtained again in an almost quantitative yield after work-up similar to that obtained in the first run (cycle 2). In this manner, the IL recovered after the reaction could be used 10 times without a significant decrease in the catalytic activity. Similarly, recycling of the IL solution that remained after the reaction using 1 mol % [Rh(dppe)]ClO$_4$ catalyst was investigated. It was found that the IL could be repeatedly recycled regardless of the decrease in the amount of the Rh(I) catalyst.



run	solvent	time (h)	yield (%)
1	$ClCH_2CH_2Cl$	18	62
2	[BMI][NTf$_2$]	3	68

Scheme 1. Synthesis of cycloheptenone via hydroacylation of 4,6-dienal **5** in [BMI][NTf$_2$].

Table 3. Recycling of IL containing cationic Rh$^+$-dppe catalyst[a]

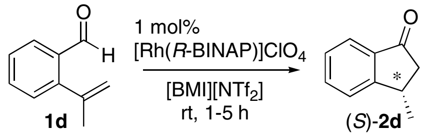
$$\mathbf{1d} \xrightarrow[\text{[BMI][NTf}_2\text{]}\ \text{rt, 1-5 h}]{\text{Rh catalyst}} \mathbf{2d}$$

Rh catalyst (mol %)	Cycle	Yield (%)
[Rh(dppe)]ClO$_4$ (**10**)	1	>99
	2	97
	3	>99
	4	99
	5	98
	6	99
	7	>99
	8	>99
	9	98
	10	>99
[Rh(dppe)]ClO$_4$ (**1**)	1	>99
	2	98
	3	>99
	4	>99

[a] All reactions were carried out in [BMI][NTf$_2$].

Subsequently, the recycling of IL in asymmetric intramolecular hydroacylation[4e–m,8] was examined (Table 4). Treatment of **1d** with 1 mol % of [Rh(R-BINAP)]ClO$_4$ in [BMI][NTf$_2$] at room temperature for 1 h gave cyclopentanone **2d** in >99% yield and 99% ee. It is noteworthy that the IL solution that remained after the asymmetric hydroacylation could also be recycled five times, affording (*S*)-**2d** in an almost quantitative yield and an excellent enantiomeric excess on each cycle.

Table 4. Recycling of IL containing cationic Rh^{+}-(*R*)-BINAP catalyst



Cycle	1	2	3	4	5
Yield (%)	>99	>99	>99	99	99
ee[a] (%)	99	99	99	99	99

[a] Ee was determined by HPLC.

In summary, we have succeeded in developing Rh(I)-catalyzed hydroacylation using ILs as reaction media for the first time. It has been proven that the IL recovered after the reaction could be used repeatedly without a significant decrease in either catalytic activity or enantioselectivity (in the case of asymmetric hydroacylation). These results indicate that the cationic [Rh(dppe)] catalyst can be immobilized in ILs via ionic interactions. Further studies along this line are in progress.

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Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2007.08.061.

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