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Non-flammable and reusable hydrogenation of aromatic ketones in ionic liquid

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ABSTRACT

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Keywords: Ionic liquid Hydrogenation Aromatic ketones Non-flammability Reuse A novel method of hydrogenation of aromatic ketones in the ionic liquid [BHEA][HCO₂] was developed; this method is more enhanced in terms of flammability and reusability as compared to the conventional method (H_2 and Pd/C). The reductive selectivities of aromatic and aliphatic ketones in this method were observed.

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Typical method for the synthesis of alcohols by hydrogenation of aromatic ketones using Pd and H_2 is widely carried out even now for convenient experimental procedures and/or to induce green reactions.^{1–9} However, this method experiences unavoidable problems with respect to flammability and reusability. While reduction with Pd and ammonium formate is also known well, there are few examples of application to aromatic ketones.^{10,11} In order to solve these problems, we tried to use the ionic liquid.

Ionic liquid is a new type of compound that has been extensively researched since the last decade.^{12,13} This compound is used mainly as a solvent because of its unique polarity and solubility.^{14–17} We think that the problems of hydrogenation using Pd/C with H₂ can be solved if the ionic liquid is used not only as a solvent but also as a reagent. That is, an ionic liquid that contains formate as the counter anion can certainly serve as a hydrogen source (Fig. 1).

Acetophenone (1) was selected as the substrate in order to afford 1-phenylethanol (2) by hydrogenation using Pd/C with H₂ (Table 1, entry 5). Ionic liquids containing formate and hydroxye-thylammonium moiety were selected as the solvent and reagent for a convenient extraction after the reaction (Fig. 2).¹⁵⁻¹⁸

All reactions of **1** with $PdCl_2$ (10 mol %) for 2 h at room temperature in four types of ionic liquids produced **2**, whose yields in the reaction in the ionic liquids [HEPA][HCO₂] and [BHEA][HCO₂] containing secondary ammonium were high (Table 1). The advantage in this reaction is use of Pd^{II} as a stable palladium source. We decided to use [BHEA][HCO₂] as the most suitable ionic liquid in the next research.

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Figure 1. Hydrogenation in ionic liquid with formate.

The quantity of PdCl₂ to afford a hydrogenation product in good yield within a practical time period should be more than 10 mol % (Table 2, entries 1-4 and 14).¹⁹ However, the addition of heat in this reaction decreased the yield (Table 2, entries 3 and 5–7). We reason that this result can be attributed to the heat-induced degradation of formate in the ionic liquid. Although we attempted this reaction using various Pd sources, no other Pd source was found to give a higher yield than PdCl₂ (Table 2, entries 3 and 8–13).

The reuse reactions of Pd and the ionic liquid continued without the addition of formic acid (Table 3).²⁰ Although the reaction time had to be extended in order to obtain a yield higher than 70%, the product was successfully afforded even in the fifth cycle of the reaction. Furthermore, this reaction solution did not ignite even when PdCl₂ was introduced in the middle of the reaction under a condition that would have certainly ignited the reaction solution





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Table 1Screening of ionic liquid

	Ph Me	PdCl ₂ (10 mol%) ionic liquid (40 eq.) r.t., 2 h	Ph 2	H `Me	
Entry	Ionic liquid		Yield ^a (%)		
			2	1	
1	[HEA][HCO ₂]	57	21	
2	[HEP	A][HCO ₂]	73	19	
3	[BHEA][HCO ₂]		81	5	
4	[DEH	EA][HCO ₂]	20	56	
5 ^b	-		80	0	

^a Isolated yield.

^b 10 wt % Pd/C (ca. 5 mol % of Pd metal) in MeOH.



Figure 2. Selected ionic liquids.

in the case of Pd/C with H_2 . Herein, the new method of reusable and non-flammable hydrogenation was thus established. Recycling experiments were attempted by addition of formic acid to the collected ionic liquid containing Pd. However, the remarkable effect of the yield or reaction time was not observed as compared with the case of reuse.

The reductive ability of ketones in this method was strongly dependent on the solubility of the substrate and the electronic character of the substituent. Addition of the co-solvent (DMF) to the ionic liquid system involving a solid substrate made the yield increase (Table 4, entries 7–18 and 21–24). Ketones adjoining a benzene ring that contained an electron donating group at the *ortho* or *para* position afforded the reductive product in poor yield (Table 4, entries 1, 2, 5–8, 15 and 16). On the other hand, ketones adjoining a benzene ring that contained an electron withdrawing

Table 2Study on the quantity, temperature, and kind of Pd

O Pd OH [BHEA][HCO ₂] (40 eq.)							
	Ph Me		P	h Me			
	1			2			
Entry	Entry Pd		Time (h)	Yield ^a (%)			
				2	1		
1	PdCl ₂ (1 mol %)	rt	24	12	76		
2	PdCl ₂ (5 mol %)	rt	24	68	26		
3	PdCl ₂ (10 mol %)	rt	2	83 (81)	13 (5)		
4	PdCl ₂ (10 mol %)	rt	2	98 (90)	2 (0)		
5	PdCl ₂ (10 mol %)	60 °C	2	35	55		
6	PdCl ₂ (10 mol %)	80 °C	2	29	49		
7	PdBr ₂ (10 mol %)	100 °C	2	20	71		
8	PdI ₂ (10 mol %)	rt	2	13	77		
9	PdCl ₂ (10 mol %)	rt	2	-	71		
10	Pd(OAc)2 (10 mol %)	rt	2	5	78		
11	Pd(OCOCF3)2 (10 mol %)	rt	2	7	85		
12	Pd(NO ₃) ₂ (10 mol %)	rt	2	16	64		
13	PdSO ₄ (10 mol %)	rt	2	26	63		
14	PdCl ₂ (20 mol %)	rt	2	99	1		

 $^{\rm a}$ Determined by $^1\!{\rm H}$ NMR analysis of the crude reaction mixture; isolated yields are shown in parentheses.

Table 3

Reuse experiments

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^a Determined by ¹H NMR analysis of the crude reaction mixture.

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Table 4

		5						
. (\sim R^2	PdCl ₂ [BHEA][H	(20 mol%) ICO ₂] (40 eq.)		OH R ²			
R ¹		CO-	co-solvent		J			
v r.t v								
Entry	R ¹	R ²	Co-solvent	Time (h)	Yield ^a (%)			
1	o-Me	Me	_	24	8			
2	o-Me	Me	DMF	24	0			
3	<i>m</i> -Me	Me	-	24	85			
4	<i>m</i> -Me	Me	DMF	24	71			
5	p-Me	Me	-	24	40			
6	<i>p</i> -Me	Me	DMF	24	27			
7	p-OMe	Me	_	24	4			
8	p-OMe	Me	DMF	24	10			
9	p-CF ₃	Me	_	24	10			
10	p-CF ₃	Me	DMF	2	94 (91)			
11	p-CO ₂ Me	Me	_	24	86			
12	p-CO ₂ Me	Me	DMF	0.25	96 (96)			
13	Н	Ph	-	24	36			
14	Н	Ph	DMF	24	76 (70)			
15	0)	_	24	3			
16			DMF	24	9			
		Me						
17	()	_	8	92 (95)			
18		Me	DMF	8	>99 (>99)			
19	0		-	24	67			
20			DMF	24	31			
21	0		_	24	20			
22	Ph P	h	DMF	24	88 (88)			
23	Ö			72	0			
24		آم	DMF	72	0			

^a Determined by ¹H NMR analysis of the crude reaction mixture; isolated yields are shown in parentheses.

group afforded the corresponding alcohol in excellent yield within a short span of reaction time (Table 4, entries 10 and 12). Although the reduction of aryl ketone proceeded, aliphatic ketone did not produce the corresponding alcohol (Table 4, entry 23, 24). These findings were applied to the selective reduction among carbonyl groups, which cannot occur by NaBH₄ reduction (Scheme 1).

We developed the new hydrogenation system of aromatic ketones in the ionic liquid for giving alcohols with the regioselectivity. Since this method includes the advantage in the solvent, the



Scheme 1. Selective hydrogenation.

reagent, and the catalyst, we are sure that the conventional system has been improved.

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- [HEA][HCO₂] 2-Hydroxyethylammonium formate; [HEPA][HCO₂] 2-Hydroxy ethylpropylammonium formate; [BHEA][HCO₂] Bis(2-hydroxyethyl)ammo nium formate; [DEHEA][HCO₂] Diethyl(2-hydroxyethyl)ammonium formate.
- 19. (Table 2, entry 4): To a solution of acetophenone (1) (120 mg, 1.00 mmol) in [BHEA][HCO₂] (5.00 mL, 39.7 mmol) was added PdCl₂ (17.7 mg, 10.0 mol%) at rt and the mixture was stirred at the same temperature for 6 h under argon atmosphere. The mixture was poured into brine (10 mL) and extracted with EtOAc (10 × 10 mL). The organic layer was washed with brine (100 mL) and dried with MgSO₄. After removal of the solvent, the residue was subjected to column chromatography (Merck kieselgel 60, $\varphi = 2.0$ cm, l = 11.5 cm; EtOAc-hexane, 1:5) to give 1-phenylethanol (2) as colorless oil; yield: 110 mg (90%).
- 20. Typical experimental procedure for the reuse experiments (Table 3): To a solution of acetophenone (120 mg, 1.00 mmol) in [BHEA][HCO₂] (5.00 mL, 39.7 mmol) was added PdCl₂ (35.5 mg, 20.0 mol %) at rt and the mixture was stirred at the same temperature for 2 h under argon atmosphere. The mixture was extracted with Et₂O (20 × 10 mL). The organic layer was washed with brine (200 mL) and dried with MgSO₄. The solvent was directly determined by ¹H NMR spectroscopy. The remaining [BHEA][HCO₂] was used in the next reaction without further purification.