Unexpected chemoselectivity in the rhodium-catalyzed transfer hydrogenation of α,β-unsaturated ketones in ionic liquids

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Chalcone and some other α,β-unsaturated ketones were subjected to transfer hydrogenation catalyzed by the dimer $[Rh(cod)Cl]_2$ and the Wilkinson's catalyst in imidazolium-, ammonium- and phosphonium-based ionic liquids. In certain ionic liquids, the reduction of chalcone gave 1,3-diphenylpropan-1-one chemoselectively, in contrast with molecular solvents, which resulted in the formation of 1,3-diphenylpropan-1-ol. An accelerated reaction rate was observed in $[emim][BuSO_4]$ and $[emin][HeSO_4]$. The observed chemoselectivity could be maintained applying a 5 molar equivalent excess of $[bmim][BF_4]$ to chalcone in 2-PrOH. This phenomenon suggests that there is an interaction between the chalcone carbonyl group and the ionic liquid which prevents reduction of the carbonyl group. The catalyst $[Rh(cod)Cl]_2$ dissolved in an ionic liquid was successfully recycled at least three times, in contrast with Wilkinson's catalyst, which lost its activity on recycling.

Introduction

In recent years, ionic liquids have attracted considerable attention as green, efficient and environmentally friendly reaction media for the future.[1] This is due mainly to their appreciable advantages, such as extremely low vapor pressure, good solvent power, high thermal stability and tunable physical properties. Accordingly, it is not surprising that a wide range of organic chemical reactions have recently been successfully performed in ionic liquids.[2]

Catalytic transfer hydrogenation is a well-known protocol whereby organic compounds can be hydrogenated without the use of special equipment or molecular hydrogen gas. The combination of transfer hydrogenation with non-volatile, non-flammable ionic liquids furnishes an environmentally safe and friendly alternative to classical hydrogenation.[3-10]

We earlier successfully achieved the transfer hydrogenation of α,β-unsaturated carboxylic acids over Pd catalysts in the presence of HCO_2NH_4 as hydrogen donor in imidazolium-based ionic liquids.[7] A new Pd/MgLa mixed oxide catalyst was also effectively used in this type of transfer hydrogenation.[11] The transfer hydrogenolysis of some halogenated aromatic compounds has also been examined in ionic liquids with this new Pd/MgLa catalyst.[11]

Table 1 Transfer hydrogenation of chalcone in $[bmim][BF_4]$ with $Pd(OAc)_2$ or $RhCl(PPh_3)_3$ as catalyst[a]

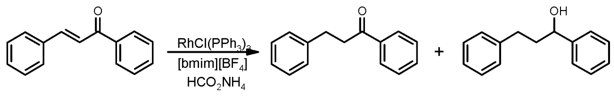
Entry	Catalyst	Conversion%	
		2a	**3a**
1	2 mol% $Pd(OAc)_2$	57	2
2	5 mol% $Pd(OAc)_2$	85	5
3	10 mol% $Pd(OAc)_2$	70	30
4	2 mol% $RhCl(PPh_3)_3$	15	0
5	5 mol% $RhCl(PPh_3)_3$	16	0
6	10 mol% $RhCl(PPh_3)_3$	74	0

[a] Reaction conditions: **1a** (0.2 mmol), HCO_2NH_4 (0.8 mmol), $[bmim][BF_4]$ (1 ml), 60 °C, 3 h.

Results and discussion†‡

In the present paper we report our results relating to the chemoselective rhodium-catalyzed transfer hydrogenation of α,β-unsaturated ketones, with different ionic liquids as solvent. For the initial investigation, we selected chalcone **1a** as a model compound under similar reaction conditions applied earlier for the transfer hydrogenation of cinnamic acid derivatives.[7]

Under these conditions, the transfer hydrogenation of chalcone was examined over $Pd(OAc)_2$ and Wilkinson's catalyst in $[bmim][BF_4]$ (Scheme 1). Over $Pd(OAc)_2$, a mixture of 1,3-diphenylpropan-1-one **2a** and 1,3-diphenylpropan-1-ol **3a** was obtained (Table 1, entries 1–3). Surprisingly, in the case of Wilkinson's catalyst, the transfer hydrogenation was chemoselective, but **2a** was formed in only a moderate conversion (entries 4 and 5).



1a 2a 3a

Scheme 1

Since the conversion of the chemoselective transfer hydrogenation was merely moderate, even with 10 mol% Wilkinson's catalyst (entry 6), we increased the reaction temperature to 90 °C. Practically 100% conversion could be achieved within 30 min at this temperature (Table 2, entry 1).

We also screened some other hydrogen donors in $[bmim][BF_4]$ ionic liquid, but only relatively low chemoselective conversions were observed in 30 min (Table 2). As concerns the tested formate

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Table 2 Transfer hydrogenation of chalcone in [bmim][BF_4] in the presence of different hydrogen donors[a]

Entry	Hydrogen donor	Conversion%	
		2a	**3a**
1	HCO_2NH_4	>99	0
2	HCO_2Na	64	0
3	HCO_2K	54	0
4	$HCO_2H : Et_3N$ 1 : 1	40	0
5	$HCO_2H : Et_3N$ 2 : 1	45	0
6	$HCO_2H : Et_3N$ 5 : 2	37	0
7	2-propanol (Na_2CO_3)	55	0

[a] Reaction conditions: **1a** (0.2 mmol), $RhCl(PPh_3)_3$ (0.02 mmol), H-donor (0.8 mmol), [bmim][BF_4] (1 ml), 90 °C, 30 min.

Table 3 Transfer hydrogenation of chalcone in molecular solvents[a]

Entry	Molecular solvent	Conversion%	
		2a	**3a**
1	EtOH	88	12
2	DMF	69	31
3	DMSO	92	8
4	THF	69	31
5	hexane	86	14
6	2-PrOH (Na_2CO_3)	0	>99
7[b]	2-PrOH (Na_2CO_3)	70	30

[a] Reaction conditions: **1a** (0.2 mmol), $RhCl(PPh_3)_3$ (0.02 mmol), HCO_2NH_4 (0.8 mmol), [bmim][BF_4] (1 ml), 90 °C, 30 min. [b] 0.004 mmol of $RhCl(PPh_3)_3$.

Table 4 Transfer hydrogenation of chalcone in ionic liquids[a]

Entry	Ionic liquid	Reaction time (min)	Conversion%	
			2a	**3a**
1	[emim][$EtSO_4$]	90	84	0
2	[emim][$BuSO_4$]	15	>99	0
3	[emim][$HeSO_4$]	15	>99	0
4	[bmim][BF_4]	30	>99	0
5	[bmim]Cl	240	74	26
6	[bmim][$AlCl_4$]	240	0	0
7	[emim][PF_6]	240	88	3
8	[bmim][PF_6]	240	93	6
9	[hmim][PF_6]	240	60	0
10	ECOENG-500™	15	>99	0
11	[$P_{14,6,6,6}$][Cl	30	>99	0
12	[$P_{14,6,6,6}$][PF_6]	240	55	0
13	[$P_{14,6,6,6}$][BF_4]	240	>99	0
14	[$P_{4,4,4,4}$][BF_4]	90	>99	0
15	[$P_{1,i4,i4,i4}$][TsO]	240	0	0

[a] Reaction conditions: **1a** (0.2 mmol), $RhCl(PPh_3)_3$ (0.02 mmol), NH_4CO_2H (0.8 mmol), ionic liquid (1 ml), 90 °C.

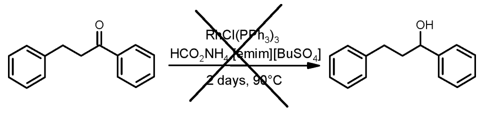
salts and 2-PrOH as hydrogen donors, mixtures of HCO_2H and Et_3N were found to be too reactive, resulting in intensive gas formation and the reaction became uncontrollable. An attempt was made to decrease this hyperactivity of the hydrogen donor by applying lower reaction temperatures, but without any success.

The chemoselective rhodium-catalyzed transfer hydrogenation at 90 °C for 30 min was studied in different molecular solvents (Table 3) and ionic liquids (Table 4) to clarify the effects of the reaction medium on the chemoselectivity. In these investigations HCO_2NH_4 was utilized as hydrogen donor. In the molecular solvents under these conditions, a mixture of **2a** and **3a** was obtained in all cases (Table 3, entries 1–5). When 2-PrOH was applied as solvent and hydrogen donor, the reduction was quicker, and **3a** resulted in high conversion (entry 6). When the amount of the catalyst was reduced to 2 mol%, the reaction rate decreased and a mixture of **2a** and **3a** was obtained (entry 7).

In addition, the transfer hydrogenation of chalcone **1a** was investigated in different ionic liquids (Table 4).

No transfer hydrogenation occurred in [bmim][$AlCl_4$] or [$P_{1,i4,i4,i4}$][TsO] (Table 4, entries 6 and 15), and no chemoselectivity was observed in [bmim]Cl, [emim][PF_6] or [bmim][PF_6] (entries 5, 7 and 8). In contrast with imidazoliun-based ionic liquids containing $[PF_6]^-$ and a shorter alkyl chain (entries 7 and 8), chemoselective transfer hydrogenation was observed in [hmim][PF_6] with a lower reaction rate (entry 9). A higher reaction rate and chemoselectivity were observed in the ionic liquids involving $[emim]^+$ and $[BuSO_4]^-$ or $[HeSO_4]^-$ (entries 2 and 3), furthermore in ECOENG-500™, an ammonium-based ionic liquid (entry 10). Chemoselectivity was also achieved in the phosphonium-based ionic liquids (entries 11–14). It is interesting that the phosphonium-based ionic liquid containing Cl^- afforded **2a** chemoselectively with a high reaction rate (entry 11), whereas no chemoselectivity was previously observed in [bmim]Cl (entry 5).

For the further investigation of the chemoselectivity attained in the ionic liquids, we attempted to reduce the previously prepared **2a** under the same conditions in one of the most active ionic liquids (Scheme 2). No further hydrogenation of **2a** to **3a** was observed in [emim][$BuSO_4$] even within 2 days, which confirmed the chemoselectivity previously experienced in this ionic liquid.



2a **3a**

Scheme 2

For a better understanding we decided to investigate the chemoselectivity in different mixtures of the molecular solvent 2-PrOH and the ionic liquid [bmim][BF_4] (Table 5). In the pure ionic liquid (entry 1), HCO_2NH_4 was applied as hydrogen donor, in all other cases, 2-PrOH was used. When the volumetric ratio was 2 : 8 the amount of 2-PrOH was not sufficient to serve adequately as hydrogen donor (entry 2). When the volumetric ratio of 2-PrOH was increased, the reaction resulted chemoselectively in **2a** (entries 3–5). When there was less than 10 vol% ionic liquid in the mixture, the chemoselectivity was lost and **3a** also appeared (entries 6 and 7). The product distribution was inverted when the amount of ionic liquid was decreased further (entry 8).

The molar ratio of the ionic liquid present in the solvent mixture to chalcone **1a** indicated that ~ 5 molar equivalents of ionic liquid (20 vol%, entry 5) shoud be present in the solution to maintain chemoselective reduction. When the amount of ionic

Table 5 Transfer hydrogenation of chalcone in 2-PrOH + [bmim][BF$_4$] mixtures[a]

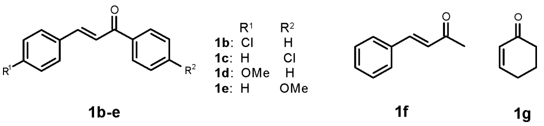
Entry	Molar ratio [bmim][BF$_4$] : **1a**	Volumetric ratio 2-PrOH : [bmim][BF$_4$]	Conversion%	
			2a	**3a**
1	~ 27 : 1	0 : 10	>99	0
2	~ 21 : 1	2 : 8	0	0
3	~ 16 : 1	4 : 6	40	0
4	~ 10 : 1	6 : 4	45	0
5	~ 5 : 1	8 : 2	64	0
6	~ 2.5 : 1	9 : 1	71	4
7	~ 1.3 : 1	9.5 : 0.5	81	4
8	~ 0.5 : 1	9.8 : 0.2	4	96
9	0 : 1	10 : 0	0	>99

[a] Reaction conditions: **1a** (0.2 mmol), RhCl(PPh$_3$)$_3$ (0.02 mmol), NH$_4$CO$_2$H (0.8 mmol), [bmim][BF$_4$] (1 ml), 90 °C, 30 min.

liquid was only ~ 0.5 equivalents relative to chalcone **1a** (2 vol%, entry 8), the reaction selectivity was lost, and mainly **3a** was obtained.

In light of these results, we assume that ionic liquids participate in a specific interaction with chalcone **1a** that prevents reduction of the carbonyl group if sufficient ionic liquid (~5 molar equivalents) is present in the solvent mixture (entry 5). This interaction is still predominant when the ionic liquid is present in a molar ratio of ~1.3–2.5, **2a** being the main component in the reaction mixtures (entries 6 and 7). Further decrease of the molar ratio of the ionic liquid in the mixture, however resulted in loss of the chemoselectivity (entry 8).

As regards the ionic liquids tested, one of the best results was achieved in [bmim][BuSO$_4$], which has very similar physicochemical properties (density, viscosity and polarity) to those of [bmim][BF$_4$] (Table 4, entry 2). As the reaction took place chemoselectively within 15 min we examined the effect of reducing the amount of catalyst applied. When the quantity of catalyst was halved to 0.01 mmol (5 mol%), no significant changes were observed relative to 10 mol% within 15 min. In the transfer hydrogenation of other chalcone derivatives, this reduced amount of Wilkinson's catalyst was used in [bmim][BuSO$_4$] ionic liquid.



Scheme 3

The results of the transfer hydrogenation of chalcone derivatives are listed in the Table 6 (Scheme 3). The aromatic substituted chalcones **1b–g** (entries 1–4) were chemoselectively hydrogenated within 15 min, similarly to chalcone. In the case of **2b**,**c** no dehydrohalogenation was observed. Benzylideneacetone **1f** (entry 5) and cyclohexen-2-one **1g** (entry 6) were also chemoselectively hydrogenated. For benzylideneacetone, a reaction time of 30 min was required to achieve good conversion.

Table 6 Transfer hydrogenation of chalcone in [bmim][BuSO$_4$][a]

Entry	Derivative	Conversion%	
		2b–g	**3b–g**
1	4-chlorochalchone **1b**	>99	0
2	4′-chlorochalchone **1c**	>99	0
3	4-methoxychalcone **1d**	>99	0
4	4′methoxychalcone **1e**	>99	0
5[b]	benzylideneacetone **1f**	98	0
6	cyclohexene-2-one **1g**	>99	0

[a] Reaction conditions: **1b–g** (0.2 mmol), RhCl(PPh$_3$)$_3$ (0.01 mmol), NH$_4$CO$_2$H (0.8 mmol), [bmim][BuSO$_4$] (1 ml), 90 °C, 15 min. [b] Reaction time of 30 min was needed.

Table 7 Transfer hydrogenation of chalcone in ionic liquids with [Rh(cod)Cl]$_2$ catalyst[a]

Entry	Ionic liquid	Reaction time (min)	Conversion%	
			2a	**3a**
1	[emim][EtSO$_4$]	240	73	0
2	[emim][BuSO$_4$]	90	84	0
3	[emim][HeSO$_4$]	90	82	0
5	[bmim][BF$_4$]	90	>99	0
6	[bmim]Cl	240	89	4
7	[emim][PF$_6$]	240	75	0
8	[bmim][PF$_6$]	240	91	0
9	[hmim][PF$_6$]	240	70	0
10	ECOENG-500™	90	89	11
11	[P$_{14,6,6,6}$][Cl	240	0	>99
12	[P$_{14,6,6,6}$][PF$_6$]	240	>99	0
13	[P$_{14,6,6,6}$][BF$_4$]	240	91	9
14	[P$_{4,4,4,4}$][BF$_4$]	90	68	32
15	[P$_{1,i4,i4,i4}$][TsO]	240	50	50

[a] Reaction conditions: **1a** (0.2 mmol), [Rh(cod)Cl]$_2$ (0.02 mmol), HCO$_2$H (0.8 mmol Et$_3$N (0.32 mmol), ionic liquid (1 ml), 90 °C.

The possibility of recycling Wilkinson's catalyst was examined with chalcone **1a** in [bmim][BF$_4$] in the presence of HCO$_2$NH$_4$. The product could be extracted with 2-PrOH from this ionic liquid. Ionic liquid containing the catalyst was dried under vacuum and further chalcone **1a** and HCO$_2$NH$_4$ as hydrogen source were added. In this second use of the system, a conversion of only 35% was achieved within 4 h.

We also tested the applicability of [Rh(cod)Cl]$_2$ in this chemoselective transfer hydrogenation. The same chemoselectivity was observed in most of the ionic liquids as with Wilkinson's catalyst, but a longer reaction period (90 min) and a more active hydrogen source (mixture of HCO$_2$H and NEt$_3$) were necessary (Table 7). The following differences were observed: in contrast to Wilkinson's catalyst, chemoselectivity occurred also in all ionic liquids containing [PF$_6$]$^-$ anion (enties 7–9, and 12), while no chemoselectivity took place in ECOENG-500^{TM}, and phosphonium based ionic liquids, except [P$_{14,6,6,6}$][PF$_6$] (entries 10, 11, 13–15). This catalyst likewise worked well with all of the previously tested chalcone derivatives in [bmim][BF$_4$].

The possibility of recycling was examined in a similar way as with Wilkinson's catalyst (though in more cycles); the results are presented in Table 8.

On extraction with 2-PrOH, a decrease in catalytic activity was observed in each recycling cycle since the reaction time required to reach 90% conversion increased, first to 6 h and then to 11 h, (entries 2 and 3). Better results were obtained with toluene extraction. The catalyst activity was found to be decreased only in the second cycle, with a necessary reaction time of 4 h (entry 4). In the subsequent cycles involving toluene extraction, the

Table 8 Recycling of [bmim][BF$_4$] + [Rh(cod)Cl]$_2$ system in chalcone hydrogenation[a]

Entry	Extraction solvent	Cycle	Reaction time (h)	Conversion **2a**
1	2-PrOH	1	1.5	>90
2	2-PrOH	2	6	>90
3	2-PrOH	3	11	>90
4	toluene	1	1.5	>90
5	toluene	2	4	>90
6	toluene	3	4	>90
7	toluene	4	4	>90

[a] Reaction conditions: **1a** (0.2 mmol), [Rh(cod)Cl]$_2$ (0.02 mmol), HCO$_2$H (0.8 mmol), Et$_3$N (0.32 mmol), [bmim][BF$_4$] (1 ml), 90 °C.

catalytic activity was stabilized at this decreased level (entries 5–7). Under these conditions, the system was successfully recycled three times.

Conclusions

Chemoselective rhodium-catalyzed transfer hydrogenation of chalcone and some other α,β-unsaturated ketones was achieved in certain ionic liquids in contrast with molecular solvents. An accelerated reaction rate was observed in [emim][BuSO$_4$] and [emin][HeSO$_4$]. In a mixture of molecular solvent (2-PrOH) and ionic liquid ([bmim][BF$_4$]), an excess of at least 5 molar equivalents of the ionic liquid relative to the substrate was found to be essential to ensure the chemoselectivity. Whereas recycling of Wilkinson's catalyst in an ionic liquid was unsuccessful, the system involving [Rh(cod)Cl]$_2$ as catalyst could be successfully recycled at least three times when the product was extracted with toluene.

Acknowledgements

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Notes and references

† General procedure: 0.2 mmol of substrate was added to a previously prepared solution of 1 ml ionic liquid and 0.02 mmol of catalyst. 0.8 mmol of hydrogen source was added to the mixture, which was then heated and stirred at 90 °C. The reaction mixture was analyzed by HPLC with reference substances to determine the reaction time and conversion. The product was isolated by toluene extraction. Imidazolium-based ionic liquids were purchased from Solvent-Innovation GmbH, and all others from Sigma-Aldrich. The ionic liquids were used without further purification.

‡ ECOENG-500™:PEG-5 cocomonium methylsulfate, product of Solvent-Innovation GmbH.

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