Communication

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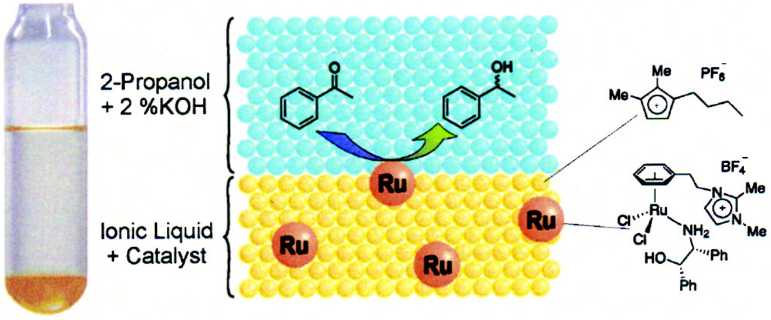

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A Versatile Ruthenium Precursor for Biphasic Catalysis and Its Application in Ionic Liquid Biphasic Transfer Hydrogenation: Conventional vs Task-Specific Catalysts

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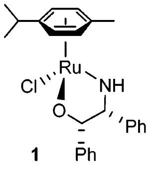
Ionic liquids are receiving growing attention as a means to immobilize catalysts, facilitating product isolation and offering an opportunity to reuse the catalyst, with their potential already demonstrated in numerous catalytic processes.[1] Modification of known catalysts may, however, be necessary to obtain a catalytic system which combines high activity with good catalyst retention. Phosphine ligands containing ionic groups such as $-SO_3^-$ or $-NR_3^+$ probably represent the most common approach to alter the solubility of a complex to match ionic liquids.

Since the introduction of highly active and selective ruthenium catalysts based on chiral diamine or amino alcohol ligands, e.g. **1** and **2**, transfer hydrogenation has attracted considerable interest.[2] Immobilization of the chiral catalyst onto a solid support often affords good recyclability, but the obtained ee is usually lower than in the homogeneous or biphasic case.[3] Examples for aqueous biphasic transfer hydrogenation are rare,[4] and to date only two reports on transfer hydrogenation in ionic liquids exist. One describes microwave-assisted reduction with palladium on charcoal and formate salts,[5] and the other reports on the rhodium-catalyzed hydrogenation of acetophenone in phosphonium tosylates with 2-propanol as proton source.[6] Catalyst recycling is possible in both cases, but yields decrease considerably with each cycle in the first example, whereas the high reaction temperatures, viz. 120−150 °C, in the second case are somewhat problematic and conversion is usually below 50%. The scarcity of transfer hydrogenation in ionic liquids might to some extent be due to the fact that only few will form a separate phase with the common proton source 2-propanol. In addition, the presence of strong base—often essential for the reaction—further limits the solvent choice.



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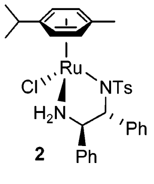

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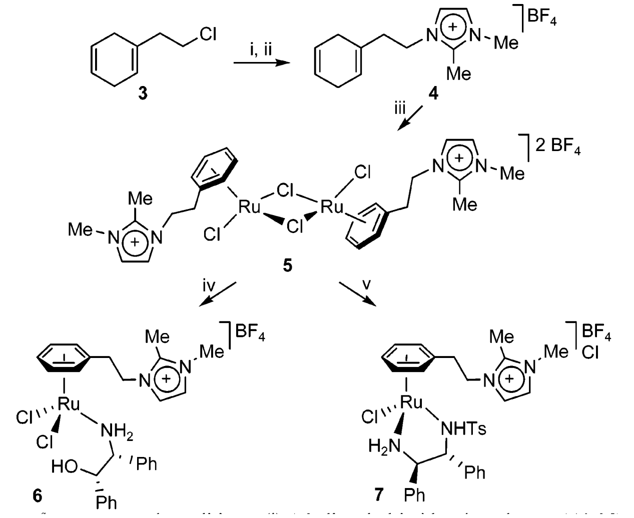
In most examples of ruthenium-catalyzed transfer hydrogenation, the active catalyst is a neutral 16-electron complex, which is usually formed in situ from precursors such as **1** and **2** by reaction with base.[2g] Hence, the presence of charged ligands may be required to adequately immobilize the catalyst in an ionic liquid phase. Herein, we report the synthesis of new ruthenium catalysts with attached imidazolium tags and compare their performance to well-established complexes using both 2-propanol and formic acid as the proton source in the presence of ionic liquids.

The route to the new complexes, bearing η^6-arenes with pending imidazolium tags is depicted in Scheme 1. Starting from phenylethanol, Birch reduction and subsequent chlorination affords chloroethyl cyclohexadiene **3**. Quaternization of 1,2-dimethylimidazole with **3** and subsequent anion exchange with $NaBF_4$ yields the functionalized imidazolium salt **4**, which itself can be classified as an ionic liquid (mp = 85 °C). The latter step is necessary to increase the solubility for the remaining transformations. Reduction of $RuCl_3$ with three equivalents of **4** (excess diene is easily reclaimed after the reaction) in methanol under reflux conditions leads to the dinuclear complex **5** in good yield.

Scheme 1[a]



[a] Reagents and conditions: (i) 1,2-dimethyl imidazole, toluene, 110 °C; (ii) $NaBF_4$, CH_2Cl_2; (iii) $RuCl_3$, MeOH, 80 °C; (iv) (1*S*,2*R*)-2-amino-1,2-diphenylethanol, DMF, rt; (v) (1*R*,2*R*)-*N*-tosyl-1,2-diphenylethylenediamine, DMF, rt.

This methodology offers a significant advantage in that **5** can be regarded as a versatile starting material for the synthesis of a wide range of catalysts and conventional, easily accessible ligands can be used without necessitating further modification. Depending on the nature of the anion, **5** is insoluble in most common organic solvents but is highly soluble in water and ionic liquids. As numerous ruthenium-based catalysts are derived from such dimers,[7] it represents an ideal precursor for both aqueous and ionic liquid biphasic catalysis. To the best of our knowledge, this is the first time that charged moieties on a complexed arene have been used to alter the solubility properties of a complex, although ruthenium dimers with functionalized arenes have been recently synthesized by other groups.[8]

Addition of (1*S*,2*R*)-2-amino-1,2-diphenylethanol or (1*R*,2*R*)-*N*-tosyl-1,2-diphenylethylenediamine to **5** in DMF affords the cationic complexes **6** and **7**, respectively, in near quantitative yield. Both complexes have been tested in the biphasic, enantioselective transfer hydrogenation of acetophenone and the results compared with those of the pre-catalysts **1** and **2**.

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Table 1. Asymmetric Transfer-hydrogenation of Acetophenone in 2-propanol/KOH Catalyzed by Ruthenium Complexes **1**, **2**, **6** and **7**[a]

entry	cat.	run	% conv[b]	% ee[c]	% leaching[d]
1	**1**	1	97	58	61
2		2	1		
3	**2**	1	95	98	63
4		2	5		
5	**6**	1	95	27	5
6		2	15		
7	**7**	1	80	98	8
8		2	66		
9		3	57		
10		4	21		

[a] Reaction at 35 °C, 24 h in a 0.1 M solution of acetophenone in 2-propanol/KOH (2 mol %) and S/C = 200; catalyst immobilized in 1.5 mL of $[C_4C_1C_1Im]PF_6$. [b] Determined by GC. [c] Determined by GC using a Chromapack CP-Cyclodex B column. [d] Determined by ICP-OES.

Table 2. Performance and Recycling of Catalysts **2** and **7** in the Reduction of Acetophenone with Formic Acid/Triethylamine Azeotrope as Proton Source; ee ≥ 99 % in all cases[a]

	2[b], %	**2**[b], %	**7**[b], %	**7**[c], %
cycle 1	>99	>99	>99	>99
cycle 2	>99	>99	68	>99
cycle 3	>99	80	19	80
cycle 4	99	45	1	52
cycle 5	96			

[a] Reaction at 40 °C for 24 h in a 1.5 M solution of acetophenone in formic acid/triethylamine azeotrope and S/C = 200; catalyst immobilized in 0.5 mL of $[C_4C_1C_1Im]PF_6$. [b] Product extracted with hexane, ionic liquid washed with H_2O, and dried in vacuo. [c] Product extracted with hexane and ionic liquid dried in vacuo.

In 2-propanol with 5 mol % KOH and in the absence of an ionic liquid phase, **6** and **7** afford results comparable to those from their *p*-cymene analogues, albeit **6** and **7** are slightly less active. However, the obtained ee with **6** is significantly lower than for its neutral counterpart **1** (25 vs 58%), which is in accordance with previous findings that for these amino alcohol complexes, enantioselectivity is highly dependent on the arene substitution pattern.[2f]

After screening numerous ionic liquids, 1-butyl-2,3-dimethylimidazolium hexafluorophosphate, $[C_4C_1C_1Im]PF_6$, was chosen for the immobilization of the catalysts as it forms a phase separate from 2-propanol and appears to be stable toward base. At the beginning of the reaction, **6** and **7** are found exclusively in the ionic liquid, whereas the neutral complexes **1** and **2** are present in both phases. However, during the course of the reaction, leaching does occur, probably due to base-induced catalyst degradation. Accordingly, when the amount of base is reduced from five to two equivalents, catalyst loss is markedly reduced (i.e. from 22 to 5% for **6**), and enantioselectivities increase slightly, although at the cost of reduced activity. Relative to the neutral complexes **1** and **2**, catalyst loss is up to 10 times lower in the cationic analogues **6** and **7**, demonstrating the positive effect of the imidazolium tag. Yet, even under these milder, less basic conditions, **1** and **6** appear to become deactivated quickly, and reuse of the ionic liquid phase is not viable, see Table 1. In contrast, **7** is stable for at least 72 h and recycling of the ionic liquid phase is feasible, although limited, as conversion drops from 80% in the first cycle to 21% in the fourth cycle.

As these results, although promising, are not satisfactory in terms of catalyst reuse, formic acid/triethylamine azeotrope was used as a proton source. Complexes bearing amino alcohol ligands are known to be inactive with this reagent;[8b] thus, the screening was restricted to **2** and **7,** and both compounds afforded essentially quantitative conversion and excellent enantioselectivity (>99%). As this reagent forms a homogeneous phase together with $[C_4C_1C_1Im]PF_6$, a product extraction step with hexane or Et_2O is necessary. The remaining solution can be recharged with ketone and formic acid and reused. However, this gradually leads to increasing reaction volume and thus decreased turnover frequency due to dilution. Accordingly, the solution containing the catalyst was washed with water after product extraction and dried in vacuo prior to the next catalytic cycle. In this manner, an ionic liquid solution containing **2** could be used five times without significant decrease in activity, see Table 2. Furthermore, a range of different substrates including cyclic ketones and aldehydes can be reduced using the same ionic liquid/catalyst solution (see Supporting Information). The catalyst solution could be stored for days without any effect on activity or enantioselectivity, although this procedure is not applicable to complex **7**, which is too soluble in water and consequently extracted from the ionic liquid.

In the course of the recycling experiments, the color of the solution changes from orange to deep red which probably indicates some decomposition of the catalyst. This is, however, not reflected in the enantioselectivity, which remains above 99% throughout all catalytic cycles.

In conclusion, a versatile precursor for aqueous and ionic liquid biphasic catalysis has been synthesized and tested in biphasic ionic liquid transfer hydrogenation. With 2-propanol/KOH, the beneficial effect of additional charged groups in terms of catalyst retention and recycling was demonstrated. With formic acid, conventional catalysts afford better results due to a necessary extraction step with water. Studies to further optimize the reaction conditions and to apply **5** to other catalytic reactions such as, for example, biphasic olefin metathesis are currently underway.

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Supporting Information Available: Experimental procedures, additional catalysis experiments, and characterization data. This material is available free of charge via the Internet at http://pubs.acs.org.

References

(1) (a) Wasserscheid, P., Welton, T., Eds. *Ionic Liquids in Synthesis*; Wiley-VCH: Weinheim, 2002. (b) Dupont, J.; de Souza, R. F.; Suarez, P. A. Z. *Chem. Rev.* **2002**, *102*, 3667. (c) Gordon, C. M. *Appl. Catal., A* **2001**, *222*, 101. (d) Seddon, K. R., Ed. *Ionic Liquids as Green Solvents*; ACS Symposium Series 856; American Chemical Society: Washington, DC, 2003.

(2) (a) Noyori, R. *Angew. Chem., Int. Ed.* **2002**, *41*, 2008. (b) Rautenstrauch, V.; Hoang-Cong, X.; Churlaud, R.; Abdur-Rashid, K.; Morris, R. H. *Chem. Eur. J.* **2003**, *9*, 4954. (c) Ell, A. H.; Johnson, J. B.; Bäckvall, J. E. *Chem. Commun.* **2003**, 1652. (d) Yi, C. S.; He, Z. J.; Guzei, I. A. *Organometallics* **2001**, *20*, 3641. (e) Henning, M.; Püntener, K.; Scalone M. *Tetrahedron: Asymmetry* **2000**, *11*, 1849. (f) Takehara, J.; Hashiguchi, S.; Fujii, A.; Inoue, S.; Ikariya, T.; Noyori, R. *Chem. Commun.* **1996**, 233. (g) Haack, K.-J.; Hashiguchi, S.; Fujii, A.; Ikariya, T.; Noyori, R. *Angew. Chem., Int. Ed. Engl.* **1997**, *36*, 285.

(3) (a) Saluzzo, C.; Lemaire, M. *Adv. Synth. Catal.* **2002**, *344*, 915. (b) Bianchini, C.; Barbaro, P. *Top. Catal.* **2002**, *19*, 17.

(4) (a) Benyei, A.; Joo, F. *J. Mol. Catal.* **1990**, *58*, 151. (b) Sánchez-Delgado, R. A.; Medina, M.; López-Linares, F.; Fuentes, A. *J. Mol. Catal. A: Chem.* **1997**, *116*, 167. (c) Dwars, T.; Oehme, G. *Adv. Synth. Catal.* **2002**, *344*, 239. (d) Ogo, S.; Abura, T.; Watanabe, Y. *Organometallics* **2002**, *21*, 2964.

(5) Berthold, H.; Schotten, T.; Honig, H. *Synthesis* **2002**, 1607.

(6) Comyns, C.; Karodia, N.; Zeler, S.; Andersen, J. A. *Catal. Lett.* **2000**, *67*, 113.

(7) Bennet, M. A. In *Comprehensive Organometallic Chemistry II*; Wilkinson, G., Stone, F. G. A., Abel, E. W., Eds.; Pergamon: Oxford, 1995; Vol. 7, p 549.

(8) (a) Soleimannejad, J.; Sisson, A.; White, C. *Inorg. Chim. Acta* **2003**, *352*, 121. (b) Hannedouche, J.; Clarkson, G. J.; Wills, M. *J. Am. Chem. Soc.* **2004**, *126*, 986. (c) Marconi, G.; Baier, H.; Heinemann, F. W.; Pinto, P.; Pritzkow, H.; Zenneck, U. *Inorg. Chim. Acta* **2003**, *352*, 189.

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