COMMUNICATION

ChemComm
www.rsc.org/chemcomm

Catalytic asymmetric hydrogenation in a room temperature ionic liquid using chiral Rh-complex of ionic liquid grafted 1,4-bisphosphine ligand†

Sang-gi Lee,*[a] Yong Jian Zhang,[ab] Jing Yu Piao,[a] Hyeon Yoon,[c] Choong Eui Song,[a] Jung Hoon Choi[b] and Jongki Hong[c]

[a] *Life Sciences Division, Korea Institute of Science and Technology, P.O. Box 131, Cheongryang, Seoul 130-650, Korea. E-mail: sanggi@kist.re.kr*

[b] *Department of Chemistry, Hanyang University, Seoul 133-791, Korea*

[c] *Hazardous Substance Research Team, Korea Basic Science Institute, Seoul 136-701, Korea*

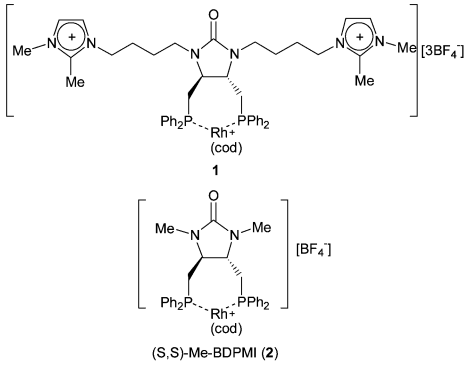
Received (in Cambridge, UK) 6th August 2003, Accepted 5th September 2003
First published as an Advance Article on the web 23rd September 2003

Introduction of imidazolium ionic liquid pattern to the catalyst not only avoided catalyst leaching but also increased the stability of catalyst in ionic liquid, and thus, the Rh-complex of 1,4-bisphosphine bearing two imidazolium salt moieties was successfully immobilized in an ionic liquid and reused several times for the hydrogenation of an enamide without significant loss of catalytic efficiency.

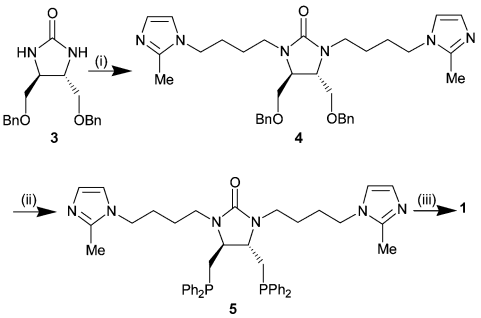
To facilitate the separation and subsequent reuse of chiral catalysts, methods for immobilizing homogeneous catalysts have been pursued for decades.[1] One of the promising approaches is the use of two-phase systems, in which the phase of preference of the catalyst differs from that of the substrate, allowing facilitation of catalyst recovery from products by phase-separation.[2] In this context, much attention has recently been devoted to room temperature ionic liquids (ILs), in particular, consisting of 1-butyl-3-methylimidazolium (bmim) cations and their counter anions.[3] In many cases, the catalysts can be easily immobilized in ILs, and thus, separated by simple phase-separation and recycled. In spite of their high potential as vehicles for catalyst immobilization, relatively few examples on the utilization of ILs in asymmetric catalytic hydrogenation have been reported.[4–7] The chiral Ru complexes of BINAP or BINAP analogs were efficiently immobilized in ILs and reused several times in the hydrogenation of olefins and ketones without significant loss of catalytic efficiencies.[5,6] In contrast to Ru-complexes, the catalytic activity of air-sensitive chiral Rh-bisphosphine catalysts such as the Rh-(*R*,*R*)-Me-DuPhos complex was largely decreased after first run.[7] Therefore, the problems associated with leaching and/or stability of the reactive chiral Rh-complex in ILs still remained to be solved.

Recently it has been clearly demonstrated that attachment of imidazolium salts to achiral Rh-[8]and Ru-catalysts[9] increased the preferential solubility of the catalysts to IL, and the catalysts were successfully reused without significant loss of catalytic efficiency. During our ongoing efforts on the utilization of ionic liquids for catalysis,[10] we decided to apply this ionic tag strategy to Rh-catalyzed asymmetric hydrogenation in ILs. Herein we report ionic liquid grafted chiral Rh-complexes of 1,4-bisphosphine ligand **1** having two 1,2-dimethylimidazolium salt tags resembling closely the IL reaction medium and its catalytic efficiency and reusability in asymmetric hydrogenation of an enamide in an IL.

The route for the synthesis of the chiral Rh-complex **1** is illustrated in Scheme 1.† The 2-methylated imidazolium moiety has been chosen because of the lability of the C(2)-methine proton in imidazolium salt toward transition metals.[11] The bisphosphine **5**, a precursor for **1**, can easily be prepared from **3** which is obtained from tartaric acid as described previously.[12a] The *N*,*N*′-dialkylation of **3** with 1-bromo-4-chlorobutane followed by reaction with 2-methylimidazole afforded bis(imidazole) **4**. After deprotection of the O-benzyl groups, the resulting diol was mesylated, then reacted with potassium diphenylphosphide to give the bisphosphine **5**. All initial attempts to obtain the imidazolium salt from **5** were unsuccessful due presumably to P-methylation, and provided complicated products. Eventually, it was found that the use of the Rh-complex of bisphosphine **5** could protect the P atoms during *N*-methylation of imidazole moieties with $Me_3O^+BF_4^-$ to give **1**.[13] Thus, bisphosphine **5** was first mixed with $[Rh(cod)_2][BF_4]$ in methylene chloride for 30 min, and then treatment with trimethyloxonium tetrafluoroborate at room temperature for 2 h afforded the Rh-complex **1**. In ^{31}P NMR, the singlet P signal (−10.1 ppm) of **5** was shifted down field (32.6 ppm, d, J_{Rh-P} = 139.2 Hz) indicating the formation of the C_2-symmetric Rh-complex **1**.



The catalytic efficiencies of **1** and Me-BDPMI **2** (for comparison), which exhibited excellent catalytic efficiency in organic solvent,[12] were examined in $[bmim][SbF_6]$/*i*PrOH two-phase system for the hydrogenation of an enamide (Table 1).‡ As expected, the ionic liquid grafted Rh-complex **1** was successfully immobilized in the IL, which can be reused three times without any loss of catalytic efficiency (entries 1 ~ 3). In the fourth run, the catalytic activity was slightly decreased

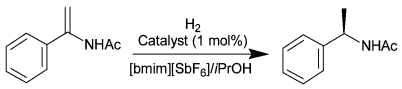


Scheme 1 Synthesis of **1**. (i) (a) NaH/THF/$Br(CH_2)_4Cl$, reflux, 12 h (91%), (b) NaH/DMF, 2-methylimidazole, rt, 40 h (90%). (ii) (a) $Pd(OH)_2$/cyclohexene/EtOH, reflux, 10 h (85%), (b) MsCl/Et_3N, rt, 4 h (94%), (c) $KPPh_2$/THF–DMF(v/v = 10/1), rt, 8 h (48%). (iii) $[Rh(cod)_2]BF_4$/MC , rt, 30 min then $Me_3{}^+OBF_4{}^-$ rt, 2 h.

† Electronic supplementary information (ESI) available: experimental details. See http://www.rsc.org/suppdata/cc/b3/b309304b/

DOI: 10.1039/b309304b

Table 1 Rh-Catalyzed asymmetric hydrogenation of *N*-acetylphenylethenamine using **1** and Me-BDPMI **2** in [bmim][SbF_6]/iPrOH two-phase solvent systems[a]



Entry	Cat	Run	Time (h)	Conv.(%)[b]	%ee[c]
1	1	1	1	100	97.0
2		2	1	100	96.6
3		3	1	100	96.2
4		4	1	82	95.4
5		4	8	100	95.4
6	2	1	1	100	95.8
7		2	1	100	95.1
8		3	1	78	94.2
9		4	1	51	91.4
10		4	12	85	88.0
11[d]	2	1	1	100	95.6

[a] Cat :substrate = 0.01 :1; [bmim][SbF_6]/iPrOH = 1/2 (v/v); Reaction temperature: 20 °C; H_2 Pressure: 1 atm. [b] Determined by NMR and GC. [c] Determined by chiral GC using CP-Chirasil Dex CB column. [d] Reaction carried out in the presence of 0.5 mol% of **2**.

(entry 4), but the reaction was completed when the reaction time was prolonged to 8 h (entry 5). Moreover, the enantioselectivity was also not much decreased. However, the catalytic efficiency of Rh-Me-BDPMI complex **2** dropped significantly after two cycles. Thus, the conversions and enantioselectivities were decreased in the third (entry 8) and fourth (entry 9) runs. The reactions did not complete even with prolonged reaction time (entry 10).§

In ICP-AES analysis of the *i*PrOH layer separated from the first run (entry 1) with **1**, no Rh (< 1 ppm) and phosphorus (< 3 ppm) were found within the detection limits. Whereas 2% of Rh and 6% of phosphorus atom were leached out to the *i*PrOH layer during the phase-separation of the first run (entry 6). These results clearly indicate that attachment of an imidazolium ionic tag could increase the preferential solubility to ILs. However, catalyst leaching is not the only reason for the decreased catalytic activity of catalyst **2** upon recycling – the complete conversion of the reaction carried out in the presence of 0.5 mol% of **2** (entry 11) supports this.

Taken all together, it could be concluded that an introduction of imidazolim salt moieties on the ligand backbone not only avoids the problem of catalyst leaching from the IL layer but also increases the catalyst stability. Studies on the imidazolium ionic tag strategy to increase the reusability and stability of the other chiral catalysts in environmentally benign ionic liquids will surely be continued.

This work was supported by NCCP, KIST, NRL program from MOST and CMDS at KAIST

Notes and references

‡ A mixture of **5** (2.8 mg, 3.7×10^{-3} mmol) and added [$Rh(cod)_2$]BF_4 (1.3 mg, 3.1×10^{-3} mmol) in methylene chloride (1 mL) was stirred for 30 min at rt, and then, trimethyloxonium tetrafluoroborate (1.1 mg, 7.4×10^{-3} mmol) was added and the mixture was stirred for 2 h. After evaporation of the volatiles, an ionic liquid, [bmim][SbF_6](1 mL) and a solution of substrate (50 mg, 3.1×10^{-1} mmol) in *i*PrOH (2 mL) were added. The mixture was hydrogenated under 1 atm. H_2 at rt for 1 h. To determine the conversion and enantioselectivity, the iPrOH layer was separated, and subjected without any purification into GC equipped with CP-Chirasil-Dex-CB chiral column and ^{1}H NMR. For catalyst recycling, a degassed solution of enamide in *i*PrOH was added again to the ionic liquid layer remaining in the reaction vessel.

§ We also examined the catalytic activity of **2** in other ionic liquids such as [bmim][PF_6] (1st run: 100% conv., 2nd run: 100% conv., 3rd run: 78% conv., 4th run: 51% conv.), [bmim][BF_4] (1st run: 100% conv. 2nd run: 80% conv., 3rd run: 50% conv. 4th run: 20% conv.).

1 (*a*) C. E. Song and S.-g. Lee, *Chem. Rev.*, 2002, **102**, 3495; (*b*) Q.-H. Fan, Y. M. Li and A. S. C. Chan, *Chem. Rev.*, 2002, **102**, 3385.

2 (*a*) W. A. Hermann and C. W. Kohpainter, *Angew. Chem., Int. Ed. Engl.*, 1993, **32**, 1524; (*b*) *Aqueous-Phase Organometallic Catalysis*, ed. B. Cornils, W. A. Hermann, Wiley-VCH, Weinheim, 1998; (*c*) B. E. Hanson, in *Chiral Catalyst Immobilization and Recycling*, ed. D. E. De Vos, I. F. J. Vankelecom, P. A. Jacobs, Wiley-VCH, Weinheim, 2000, p. 8196.

3 (*a*) P. Wasserscheid and W. Keim, *Angew. Chem. Int. Ed.*, 2000, **39**, 3772; (*b*) T. Welton, *Chem. Rev.*, 1999, **99**, 2071; (*c*) K. R. Seddon, *J. Chem. Tech. Biotechnol.*, 1997, **68**, 351; (*d*) J. Dupont, R. F. de Souza and P. A. Z. Suarez, *Chem. Rev.*, 2002, **102**, 3667.

4 Y. Chauvin, L. Mussmann and H. Olivier, *Angew. Chem., Int. Ed. Engl.*, 1995, **34**, 2698.

5 (*a*) A. L. Monterio, F. K. Zim, R. F. de Souza and J. Dupont, *Tetrahedron: Asymmetry*, 1997, **8**, 177; (*b*) A. Berger, R. F. de Souza, M. R. Delgado and J. Dupont, *Tetrahedron: Asymmetry*, 2001, **12**, 1825.

6 (*a*) R. A. Brown, P. Pollet, E. McKoon, C. A. Eckert, C. L. Liotta and P. G. Jessop, *J. Am. Chem. Soc.*, 2001, **123**, 1254; (*b*) P. G. Jessop, R. R. Stanly, R. A. Brown, C. A. Eckert, C. L. Liotta, T. T. Ngo and P. Pollet, *Green Chem.*, 2003, **5**, 123; (*c*) H. L. Ngo, A. Hu and W. Lin, *Chem. Commun.*, 2003, 1912.

7 S. Guernik, A. Wolfson, M. Herskowitz, N. Greenspoon and S. Geresh, *Chem. Commun.*, 2001, 2314.

8 (*a*) J. Sirieix, M. Ossberger, B. Betzemeier and P. Knochel, *Synlett*, 2000, 1613; (*b*) C. C. Brasse, U. Englert, A. Salzer, H. Waffenschmidt and P. Wasserscheid, *Organometallics*, 2000, **19**, 3818; (*c*) F. Favre, H. Olivier-Bourbigou, D. Commereuc and L. Saussine, *Chem. Commun.*, 2001, 1360; (*d*) P. Wasserscheid, H. Waffenschmidt, P. Machnitzki, K. W. Kottsieper and O. Stelzer, *Chem. Commun.*, 2001, 451; (*e*) R. P. J. Bronger, S. M. Silva, P. C. J. Kamer and P. W. N. M. van Leeuwen, *Chem. Commun.*, 2002, 3044.

9 During preparation of this manuscript, ionic liquid supported Ru-carbene complex has been reported. See (*a*) Q. Yao and Y. Zhang, *Angew. Chem. Int. Ed.*, 2003, **42**, 3395; (*b*) N. Audic, H. Clavier, M. Mauduit and J.-C. Guillemin, *J. Am. Chem. Soc.*, 2003, **125**, 9248.

10 (*a*) S.-g. Lee, J. H. Park, J. Kang and J. K. Lee, *Chem. Commun.*, 2001, 1698; (*b*) C. E. Song, W. H. Shim, E. J. Rho, S.-g. Lee and J. H. Choi, *Chem. Commun.*, 2001, 1122; (*c*) C. E. Song, D.-u. Jung, E. J. Rho, S.-g. Lee and D. Y. Chi, *Chem. Commun.*, 2002, 3038; (*d*) S.-g. Lee and J. H. Park, *Bull. Korean. Chem. Soc.*, 2002, **23**, 1367; (*e*) S.-g. Lee and J. H. Park, *J. Mol. Cat. A: Chem.*, 2003, **33**, 2301.

11 D. Bourissou, O. Guerret, F. P. Gabbaï and G. Bertrand, *Chem. Rev.*, 2000, **100**, 39.

12 (*a*) S.-g. Lee, Y. J. Zhang, C. E. Song, J. K. Lee and J. H. Choi, *Angew. Chem. Int. Ed.*, 2002, **41**, 847; (*b*) S.-g. Lee and Y. J. Zhang, *Org. Lett.*, 2002, **4**, 2429.

13 The protection of phosphine group by a catalytically active Rh metal has been utilized in the synthesis of a Rh-complex of tetrahydroxy bisphosphine: See, J. Holz, D. Heller, R. Stürmer and A. Börner, *Tetrahedron Lett.*, 1999, **40**, 7059.