

# Ionic liquids as powerful media in scandium triflate catalysed Diels–Alder reactions: significant rate acceleration, selectivity improvement and easy recycling of catalyst

Choong Eui Song,<sup>\*a</sup> Woo Ho Shim,<sup>b</sup> Eun Joo Roh,<sup>a</sup> Sang-gi Lee<sup>a</sup> and Jung Hoon Choi<sup>\*b</sup>

<sup>a</sup> Life Sciences Division, Korea Institute of Science and Technology, PO Box 131, Cheongryang, Seoul, 130-650, Korea. E-mail: s1673@kist.re.kr

<sup>b</sup> Department of Chemistry, Hanyang University, Seoul, 133-791, Korea

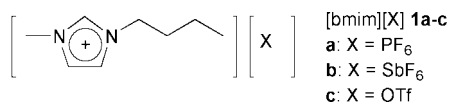
Received (in Cambridge, UK) 2nd February 2001, Accepted 8th May 2001

First published as an Advance Article on the web 31st May 2001

Ionic liquids act as powerful media (or additives) in scandium triflate catalysed Diels–Alder reactions not only for facilitating of catalyst recovery but also for accelerating reaction rate and improving selectivity.

Scandium triflate catalysed C–C bond formation reactions, pioneered by Kobayashi, have recently been received considerable attention due to their broad synthetic utility.<sup>1</sup> However, there are limitations to performing these catalytic reactions on a large scale due to their low turnover numbers (TONs are usually < 10–20). To explore the possibility of repetitive use of catalyst, several polymer- or dendrimer-bound scandium catalysts have very recently been employed.<sup>2</sup> However, most supported scandium catalysts require complicated synthetic manipulations and, moreover, their catalytic activity still remains far from satisfactory. Recently, a new approach has been adopted for catalyst separation and recycling in a few types of catalytic reaction involving the use of room-temperature ionic liquids,<sup>3</sup> *i.e.* a salt mixture with a melting point below ambient. Air- and moisture-stable room-temperature ionic liquids consisting of 1,3-dialkylimidazolium cations and their counter anions, in particular, have attracted growing interest in the last few years. In these solvents, catalysts having polar or ionic character can be immobilised without additional structural modification and thus the ionic solutions containing the catalyst can be easily separated from reagents and products.

Herein, we report that ionic liquids [bmim][X] **1a–c** ([bmim]<sup>+</sup> = 1-butyl-3-methylimidazolium cation; **1a**: X = PF<sub>6</sub>; **1b**: X = SbF<sub>6</sub>; **1c**: X = OTf)<sup>4</sup> act as powerful media (or additives) in scandium triflate catalysed Diels–Alder reactions<sup>5</sup> not only for facilitating of catalyst recovery but also for accelerating reaction rate and improving selectivity.



In a preliminary study, 1,4-naphthoquinone dissolved in [bmim][PF<sub>6</sub>] **1a** was treated with 3.0 equiv. of 1,3-dimethylbutadiene in the presence of 10 mol% of Sc(OTf)<sub>3</sub>, the amount used usually in conventional organic solvents.<sup>6</sup> Surprisingly, under such conditions, the reaction proceeded in seconds with sudden generation of heat and color change of the reaction mixture to dark brown. This observation may suggest that the reaction using 10 mol% of catalyst was too fast to control. Therefore, we reduced the amount of catalyst gradually to 0.2 mol%, for which the reaction was completed smoothly within 2 h at room temperature whereas the same reaction in CD<sub>2</sub>Cl<sub>2</sub> is extremely sluggish (compare Table 1, entries 5 and 1). Even use of only 0.1 mol% of Sc(OTf)<sub>3</sub> catalyst in ionic liquid **1a** was sufficient to complete the reaction. It was found that the catalytic activity was not much affected by the counter ions of ionic liquids **1a–c** employed in this work (Table 1, entries 5–7). Moreover, very interestingly, the use of only 1 equiv. of the ionic liquid **1a** as an additive in CH<sub>2</sub>Cl<sub>2</sub> solvent gave a

Table 1 Sc(OTf)<sub>3</sub> catalyzed Diels–Alder reactions<sup>a</sup>

Entry	Solvent	Yield(%) <sup>b</sup>
1	CD <sub>2</sub> Cl <sub>2</sub>	22
2	<b>1a</b> (0.1 equiv.) + CD <sub>2</sub> Cl <sub>2</sub>	46
3	<b>1a</b> (0.5 equiv.) + CD <sub>2</sub> Cl <sub>2</sub>	85
4	<b>1a</b> (1 equiv.) + CD <sub>2</sub> Cl <sub>2</sub>	> 99
5	<b>1a</b>	> 99
6	<b>1b</b>	> 99
7	<b>1c</b>	> 99

<sup>a</sup> Reaction conditions: 3 mmol of 2,3-dimethylbuta-1,3-diene, 1 mmol of 1,4-naphthoquinone, 0.2 mol% of Sc(OTf)<sub>3</sub>, 1 mL of solvent, 20 °C, 2 h.  
<sup>b</sup> Estimated by <sup>1</sup>H NMR spectroscopy.

satisfactory rate acceleration effect (entry 4, Table 1). A kinetic study clearly illustrates the remarkable difference in reaction rate in ionic liquid **1a** and in CH<sub>2</sub>Cl<sub>2</sub> (Fig. 1).

We next examined Diels–Alder reactions of other substrates in the presence of 0.2 mol% of Sc(OTf)<sub>3</sub> at 20 °C. As shown in Table 2, in all cases the reactions proceeded with increased reaction rate and were complete within 4 h. Similar rate acceleration effects have been observed in Diels–Alder reactions using water or LiClO<sub>4</sub> in diethyl ether as reaction medium.<sup>7</sup> It should be also noted here that the rate acceleration effect of ionic liquids have been observed by us in other catalytic reactions, *e.g.*, (salen)Mn catalysed asymmetric epox-

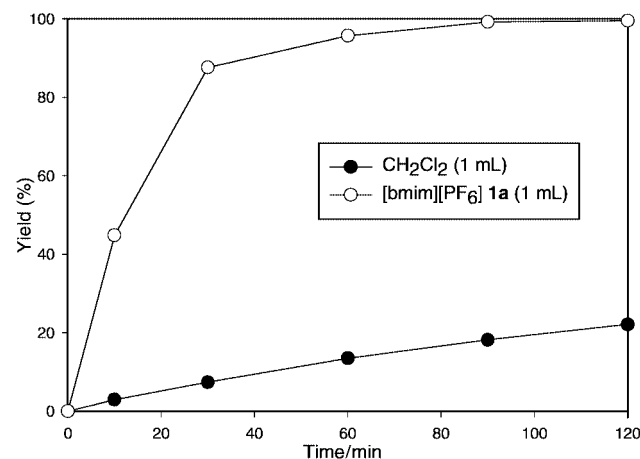


Fig. 1 Kinetic studies in the reaction of 1,4-naphthoquinone (1 mmol) with 2,3-dimethylbuta-1,3-diene (3 mmol) in the presence of 0.2 mol% of Sc(OTf)<sub>3</sub> at 20 °C.

**Table 2** Sc(OTf)<sub>3</sub> catalyzed Diels–Alder reactions in ionic liquid **1a**<sup>a</sup>

Entry	Dienophile	Diene	Product	Endo:exo <sup>b</sup>	Yield (%) <sup>c</sup>
1				>99:1 (94:6)	94
2				—	88
3				>99:1 (95:5)	96
4				—	80
5				>99:1	84
6				>99:1	71

<sup>a</sup> Reaction conditions: 3 mmol of diene, 1 mmol of dienophile, 0.2 mol% of Sc(OTf)<sub>3</sub>, 1 mL of **1a**, 20 °C, 4 h. <sup>b</sup> Endo/exo selectivities were estimated by <sup>1</sup>H NMR spectroscopy; endo/exo selectivity obtained in CH<sub>2</sub>Cl<sub>2</sub> shown in parentheses; see ref. 6. <sup>c</sup> Isolated yield.

idation of olefins,<sup>8</sup> Sc(OTf)<sub>3</sub> catalysed Friedel–Crafts alkylation of arenes,<sup>9</sup> and Sc(OTf)<sub>3</sub> catalysed Friedel–Crafts alkenylation of arenes.<sup>10</sup> Another exciting point of the use of ionic liquids is the improvement of the endo/exo selectivity in the studied reactions. In ionic liquid **1a**, reaction proceeded with endo selectively (endo:exo = >99:1, Table 2, entries 1, 3, 5 and 6). This compares to 94:6 (entry 1) in CH<sub>2</sub>Cl<sub>2</sub>.<sup>6</sup>

Finally, upon completion of the reaction, the ionic liquid phase containing **1c** and Sc(OTf)<sub>3</sub> was almost quantitatively recovered by simple extraction of product with Et<sub>2</sub>O. The recovered ionic liquid phase containing the catalyst was reused several times without any loss of activity even after the eleventh use (Table 3).

In conclusion, we have demonstrated that ionic liquids act as powerful media (or additives) not only for facilitating catalyst recycling but also for accelerating reaction rate and selectivity enhancement in scandium triflate catalysed Diels–Alder reactions. Therefore, this novel immobilisation methodology involving the use of ionic liquids can be expected to have great

**Table 3** Recovery and reuse of the ionic liquid phase containing Sc(OTf)<sub>3</sub><sup>a</sup>

Run	1	2	3	4	5	6	7	8	9	10	11
Yield (%) <sup>b</sup>	94	86	81	88	86	85	83	87	89	91	90

<sup>a</sup> Reaction conditions: 3 mmol of 2,3-dimethylbuta-1,3-diene, 1 mmol of methyl vinyl ketone, 0.2 mol% of Sc(OTf)<sub>3</sub>, 1 mL of **1c**, 20 °C, 2 h. <sup>b</sup> Isolated yield.

potential ability to solve the intrinsic problems (decrease of catalytic activity and selectivity, and complicated structural modification of catalysts) of the conventional immobilisation methodology of homogeneous catalysts. Further applications of this methodology to other catalytic reactions are under investigations in our laboratory.

This research was supported by a grant from the Ministry of Science and Technology in Korea.

## Notes and references

- For a review, see: S. Kobayashi, *Synlett*, 1994, 689.
- K. Manabe, Y. Mori, T. Wakabayashi, S. Nagayama and S. Kobayashi, *J. Am. Chem. Soc.*, 2000, **122**, 7202; M. T. Reetz and D. Giebel, *Angew. Chem., Int. Ed.*, 2000, **39**, 2498; S. Nagayama and S. Kobayashi, *Angew. Chem., Int. Ed.*, 2000, **39**, 567; S. Kobayashi and S. Nagayama, *J. Am. Chem. Soc.*, 1998, **120**, 2985; S. Kobayashi and S. Nagayama, *J. Am. Chem. Soc.*, 1996, **118**, 8977; S. Kobayashi and S. Nagayama, *J. Org. Chem.*, 1996, **61**, 2256.
- P. Wasserscheid and W. Keim, *Angew. Chem., Int. Ed.*, 2000, **39**, 3772; T. Welton, *Chem. Rev.*, 1999, **99**, 2071 and references therein.
- Ionic liquids **1a–c** were prepared according to the reported procedures; P. A. Z. Suarez, J. E. L. Dullius, S. Einloft, R. F. de Souza and J. Dupont, *Polyhedron*, 1996, **15**, 1217; P. Bonhôte, A.-P. Dias, N. Papageorgiou, K. Kalyanasundaram and M. Grätzel, *Inorg. Chem.*, 1996, **35**, 1168.
- Diels–Alder reactions in ionic liquids have been recently carried out without any catalysts; M. J. Earle, P. B. McCormac and K. R. Seddon, *Green Chem.*, 1999, **1**, 23; C. W. Lee, *Tetrahedron Lett.*, 1999, **40**, 2461; T. Fischer, A. Sethi, T. Welton and J. Woolf, *Tetrahedron Lett.*, 1999, **40**, 793; J. Howarth, K. Hanlon, D. Fayne and P. McCormac, *Tetrahedron Lett.*, 1997, **38**, 3097; F. Zufigat and T. Kitazume, *Green Chem.*, 2000, **2**, 137.
- S. Kobayashi, I. Hachiya, M. Araki and H. Ishitani, *Tetrahedron Lett.*, 1993, **34**, 3755.
- P. A. Grieco, *Aldrichim. Acta*, 1991, **24**, 59.
- C. E. Song and E. J. Roh, *Chem. Commun.*, 2000, 837.
- C. E. Song, W. H. Shim, E. J. Roh and J. H. Choi, *Chem. Commun.*, 2000, 1695.
- (a) Our unpublished results: Friedel–Crafts alkenylation of benzene with phenylacetylene was complete within 12 h at 20 °C in the presence of 10 mol% of Sc(OTf)<sub>3</sub> in the SbF<sub>6</sub> salt **1b**, whereas the same reaction without the ionic liquid **1b** did not occur at all. To obtain similar conversion without an ionic liquid, much more severe reaction conditions are needed (170 h at 85 °C);<sup>10b</sup> (b) T. Tsuchimoto, T. Maeda, E. Shirakawa and Y. Kawakami, *Chem. Commun.*, 2000, 1573.