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In Situ Activation of a Latent Ruthenium–Carbene Complex in Ionic Liquid and Its Application in Ring-Closing Metathesis

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Catalytically inactive, latent Ru–carboxylate complex **2**, which was recently serendipitously isolated, can be activated in situ efficiently in ionic liquids (ILs) with the aid of imidazolium halides or tetrabutylammonium halides. The activity of the in situ activated catalyst was largely dependent on IL anions, imidazolium halides, and terabutylammonium halides. Under the optimal condition of 1.0 mol-% of [bmim][Br] in CH_2Cl_2/[bmim][SbF_6] (1:1), latent Ru complex **2** was activated in situ to catalyze the ring-closing metathesis of various dienes with conversions of up to >99 %.

Introduction

Ruthenium-catalyzed olefin metathesis is one of the most powerful methods to construct carbon–carbon double bonds and is widely employed in a variety of chemistry fields, including natural products, pharmaceuticals, and polymer chemistry. The spectacular progress of olefin metathesis is largely due to the evolutionary development of active, well-defined catalysts such as Grubbs- and Hoveyda-type complexes and Ru–alkylidene complexes.[1] Much effort has also been devoted to solving the difficulty in the recovery and reuse of the expensive ruthenium catalysts, and in the product contamination caused by metal leaching. Of the various methods that have been employed to recover and reuse ruthenium catalysts,[2] one of the most promising strategies has been the use of ionic liquids (ILs).[3] During our ongoing study on the development of recoverable ruthenium catalysts for ring-closing metathesis (RCM),[4] we recently attempted the incorporation of imidazolium salt tag onto the chelating ester of "scorpio catalyst" **1a**[5] for the synthesis of imidazolium-tagged Ru complex **1b**, with which we hope that the RCM reactions would be possible in ILs for catalyst recovery. Unfortunately, we only isolated the ester cleaved, chelating carboxylate-bearing, Ru complex **2**. Grela and coworkers also recently reported the serendipitous finding of the same, catalytically inactive, Ru complex **2**, which can be elegantly activated by treatment with Brønsted acids such as HCl to form Ru–dichloride complex **1c** as a catalyst precursor.[6,7] In this communication, we report our successful and efficient, in situ activation of latent Ru complex **2** in an IL with the aid of imidazolium halide or tetrabutylammonium halide **3** (Figure 1).

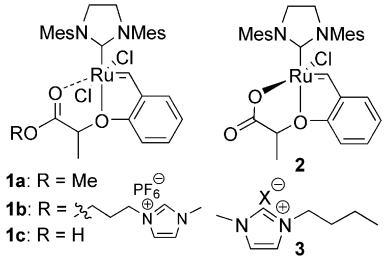

Figure 1. Structures of ruthenium complexes **1a**–**c**, latent ruthenium complex **2**, and imidazolium halide **3**.

Results and Discussion

Initially, we carried out the RCM reactions in IL under the simple assumption that the chelating carboxylate group in **2** could be dissociated effectively in polar ILs. Ru complex **2** for this study was separately synthesized according to the reported procedure by Grela et al.[6] The RCM of the benchmark substrate, *N*,*N*-bisallyl *p*-toluenesulfonamide (**4a**), was carried out at room temperature first with **2** (1.0 mol-%) in CH_2Cl_2/[bmim][SbF_6] (1:1) (bmim = 1-butyl-3-methylimidazolium). After 2 h reaction, less than 10% conversion was observed (Table 1, Entry 1). To our delight, latent Ru complex **2** could be activated thermally in IL, and this activity was dependent on the IL counteranion. Thus, the RCM at 40 °C in [bmim][SbF_6] showed the highest catalytic activity with 94% conversion after 2 h (Table 1, Entry 2). In other ILs such as [bmim][PF_6], [bmim][NTf_2], and [bmim][BF_4], only moderate conversions were obtained (Table 1, Entries 3–5). On the basis of these results, we hy-

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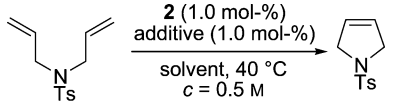
pothesized that the addition of imidazolium halide, [bmim][X] (where X = Cl, Br, I), could lead to a more reactive Ru–dihalide precursor through exchange of the carboxylate group to X.[8] To test this hypothesis, the RCM reactions were carried out in the presence of [bmim][X] (1.0 mol-%), and the results and reaction profiles are summarized in Table 1 and Figure 2. As we expected, when the imidazolium halide (1.0 mol-%) was added, the catalyst was dramatically activated and exhibited anion dependency (Table 1, Entries 6–9), in which [bmim][Br] was the most effective activator with 96% conversion after 30 min (Table 1, Entry 7; Figure 2a). However, only 23% conversion was observed at room temperature (Table 1, Entry 8). The addition of [bmim][Cl] and [bmim][I] achieved 68% (Table 1, Entry 6; Figure 2e) and 21% (Table 1, Entry 9; Figure 2g) conversions, respectively. Similar additive effects were also observed with tetrabutylammonium halides (Table 1, Entries 10–13). However, the anion dependency was slightly different to that observed from the imidazolium halides, and $[Bu_4N][Cl]$ achieved the highest conversion (Table 1, Entry 11; Figure 2b), closely followed by $[Bu_4N][Br]$ (Table 1, Entry 12; Figure 2c) and $[Bu_4N][I]$ (Table 1, Entry 13; Figure 2d). The addition of $[Bu_4N][F]$ achieved the lowest conversion (Table 1, Entry 10; Figure 2f). In contrast, no additive effects were observed in CH_2Cl_2; when the RCM was conducted in CH_2Cl_2 only, less than 10% conversion was observed after 1 h (Table 1, Entry 14). These results clearly indicated efficient transformation of latent Ru complex **2** into the catalytically active Ru species in IL with the aid of additives such as [bmim][X] or $[Bu_4N][X]$.

Table 1. RCM reactions of *N*,*N*-bisallyl *p*-toluenesulfonamide by using Ru complex **2** in ILs.[a]



4a **5a**

Entry	Solvent	Additive	Time	Conv. [%][b]
1[c]	CH_2Cl_2/[bmim][SbF_6]	–	2 h	<10
2	CH_2Cl_2/[bmim][SbF_6]	–	2 h	94
3	CH_2Cl_2/[bmim][PF_6]	–	2 h	68
4	CH_2Cl_2/[bmim][NTf_2]	–	2 h	70
5	CH_2Cl_2/[bmim][BF_4]	–	2 h	44
6	CH_2Cl_2/[bmim][SbF_6]	[bmim][Cl]	30 min	68
7	CH_2Cl_2/[bmim][SbF_6]	[bmim][Br]	30 min	96
8[c]	CH_2Cl_2/[bmim][SbF_6]	[bmim][Br]	30 min	23
9	CH_2Cl_2/[bmim][SbF_6]	[bmim][I]	30 min	21
10	CH_2Cl_2/[bmim][SbF_6]	$[Bu_4N][F]$	30 min	37
11	CH_2Cl_2/[bmim][SbF_6]	$[Bu_4N][Cl]$	30 min	93
12	CH_2Cl_2/[bmim][SbF_6]	$[Bu_4N][Br]$	30 min	82
13	CH_2Cl_2/[bmim][SbF_6]	$[Bu_4N][I]$	30 min	80
14	CH_2Cl_2	[bmim][Br]	1 h	<10
15[d]	CH_2Cl_2/[bmim][SbF_6]	[bmim][Br]	30 min	85
			30 min	31

[a] CH_2Cl_2/[bmim][SbF_6], 1:1. [b] Determined by GC analysis. [c] The reaction was carried out at room temperature. [d] IL layer recovered from Entry 7 was reused.

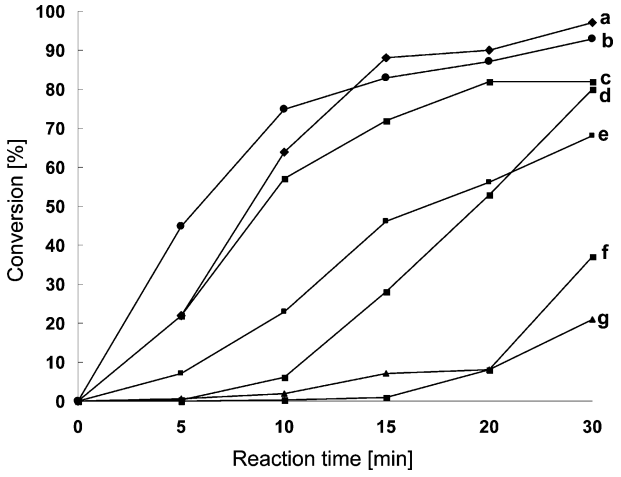


Figure 2. Reaction profiles for the reactions in Table 1, Entries (a) 7, (b) 11, (c) 12, (d) 13, (e) 6, (f) 10, and (g) 9.

In order to elucidate the role of [bmim][Br] additive in the activation of the catalyst, we monitored the reaction by ^1H NMR spectroscopy at room temperature by using equivalent amounts of **2** and [bmim][Br] in CD_2Cl_2. After 5 h, the resonance signal for the benzylidene moiety in **2** (δ = 16.44 ppm) decreased and a new signal (δ = 16.30 ppm) was observed with a 10:4 ratio. The rate of change was accelerated almost twofold by the addition of 100 equivalents of [bmim][SbF_6], so that the ratio of the two signals increased to almost 10:8 (Figure S2, Supporting Information). Interestingly, these ratios were invariant thereafter, suggesting that the mixture of **2** and [bmim][Br] had reached equilibrium. As the amount of [bmim][Br] was increased to 50 equivalents, the new signal at δ = 16.30 ppm became increasingly intense, and with 100 equivalents of [bmim][Br], the resonance signal at δ = 16.44 ppm in **2** had completely disappeared and a new signal was observed after 5 h (Figure 3). In contrast, no signal change was observed from an equivalent mixture of **2** and [bmim][Cl] for 24 h, but in the presence of 100 equivalents of [bmim][Cl], a new downfield-shifted signal (δ = 17.22 ppm in $CDCl_3$) was detected (Figure S3, Supporting Information). In the presence of [bmim][I], the rate of change was increased, and thus, in the presence of 50 equivalents of [bmim][I], the signal at δ = 16.52 ppm ($CDCl_3$) in **2** was upfield shifted to δ = 15.88 ppm after 5 h (Figure S4, Supporting Information). Unfortunately, all attempts to isolate the newly formed Ru complexes responsible for the new signals were unsuccessful. Nevertheless, these observations suggested that in the presence of an equivalent amount of [bmim][Br], the chelating carboxylate group in **2** can be exchanged to form a more pliable Ru complex precursor. In an IL, the exchange rate was increased and the equilibrium was shifted to the new ruthenium species. The exact nature of the in situ activated Ru complexes remains to be elucidated. We next investigated the recyclability of the in situ activated Ru complex with one equivalent of [bmim][Br] in [bmim][SbF_6] (Table 1, Entry 7). After evaporation of CH_2Cl_2, the product was extracted with dry toluene (3 × 5 mL), and the remaining IL

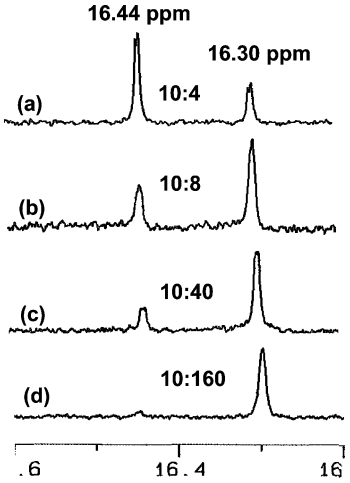
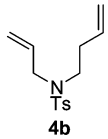
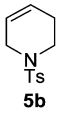
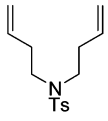
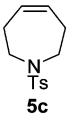
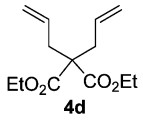
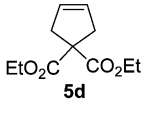
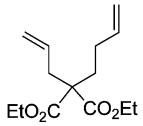
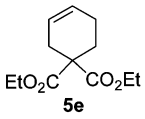
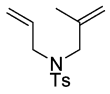
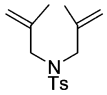


Figure 3. The benzylidene region of the ^{1}H NMR spectra (CD_2Cl_2) of **2** obtained in the presence of (a) 1.0, (b) 10, (c) 50, and (d) 100 equivalents of [bmim][Br] after 5 h at room temperature.

Table 2. RCM reactions of various dienes by using in situ activated Ru complex **2** with an equivalent amount of [bmim][Br] in [bmim][SbF_6].[a]

Entry	Substrate	Product	Time	Conv.[%][b]
1	 **4b**	 **5b**	30 min	>99 (98)
2	 **4c**	 **5c**	30 min	>99 (97)
3	 **4d**	 **5d**	1 h	94 (92)
4	 **4e**	 **5e**	30 min	>99 (98)
5	 **4f**	 **5f**	3.5 h	96 (93)
6	 **4g**	 **5g**	72 h	>5

[a] Reactions carried out at 40 °C with diene **4** (0.32 mmol), Ru complex **2** (1.0 mol-%), [bmim][Br] (1.0 mol-%) in a mixture of [bmim][SbF_6] (0.3 mL) and CH_2Cl_2 (0.3 mL). [b] Determined by GC; isolated yield in parentheses.

layer containing the catalyst was reused in the next runs. However, the catalytic activity of the recovered catalyst immobilized in the IL layer rapidly decreased with repeated use to conversions of 85% in the second run and 31% in the third run (Table 1, entry 15). The decreased catalytic activity could be ascribe to the leaching of **2** and the newly formed Ru complex. Both of these Ru complexes (ca. 1:0.9 ratio) and IL were detected in the toluene layer used for product extraction.

Finally, we investigated the substrate scope of this in situ activated catalyst. As shown in Table 2, dienes **4b–e** were ring-closed efficiently to afford the corresponding cyclic olefins **5b–e** in high yields (Table 2, Entries 1–4). Interestingly, the RCM reactions forming six-and seven-membered rings proceeded more efficiently than those forming the five-membered ring products. Diene **4f** was also effectively ring-closed to afford trisubstituted cyclic olefin **5f** in 96% yield (Table 2, Entry 5). However, the RCM reaction for substrate **4g** to afford tetrasubstituted cyclic olefin **5g** was not successful, and after 72 h, less than 5% conversion was observed (Table 2, Entry 6). Nevertheless, the catalytic activity of the in situ activated ruthenium complex in IL was quite comparable or superior to those of the reported ruthenium complexes activated by using Brønsted acids.[6]

Conclusions

We serendipitously isolated latent ruthenium complex **2** bearing a chelating carboxylate ligand, which can be activated in situ thermally in the IL [bmim][SbF_6]. The efficiency of the in situ activation can be improved further by the addition of one equivalent of [bmim][Br]. ^{1}H NMR spectroscopic studies suggested that the chelating carboxylate ligand in **2** exchanged with [bmim][Br] to form a more pliable ruthenium complex. Although the exact nature of the active ruthenium species formed in the IL remains to be elucidated, the in situ activated ruthenium catalyst exhibited high catalytic efficiency in RCM reactions of dienes. The present method for the activation of latent ruthenium complexes by using ILs promises to offer new opportunities for the design of novel, latent initiators.

Experimental Section

Typical Procedure for Ring-Closing Metathesis by using 2 in Ionic Liquid: To a solution of **2** (2.0 mg, 3.2×10^{-3} mmol) in anhydrous CH_2Cl_2 (0.3 mL) was added a solution of [bmim][Br] (0.7 mg, 3.2×10^{-3} mmol) in [bmim][SbF_6] (0.3 mL) and *N*,*N*-bisallyl *p*-toluenesulfonamide (**4a**; 80.9 mg, 3.2×10^{-1} mmol) successively at room temperature. The reaction was carried out at 40 °C. To follow the reaction, a sample of the reaction mixture, taken every 5 min and quenched with ethyl vinyl ether, was subjected to GC analysis. For catalyst recycling, volatile CH_2Cl_2 was evaporated, and then the IL layer was extracted with anhydrous toluene (3×2 mL) to separate the product. The IL layer containing the catalyst was reused for the next run.

Supporting Information (see footnote on the first page of this article): Experimental details; ^{1}H and ^{13}C NMR spectra of **2**; ^{1}H NMR spectra for ligand exchange studies.

Acknowledgments

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[1] For selected reviews on olefin metathesis, see: a) R. R. Schrock, A. H. Hoveyda, *Angew. Chem. Int. Ed.* **2003**, *42*, 4592–4633; b) T. M. Trnka, R. H. Grubbs, *Acc. Chem. Res.* **2001**, *34*, 18–29; c) P. H. Deshmukh, S. Blechert, *Dalton Trans.* **2007**, 2479–2491; d) A. H. Hoveyda, A. R. Zhugralin, *Nature* **2007**, *450*, 243–251.

[2] For a review on supported Ru catalysts, see H. Clavier, K. Grela, A. Kirschning, M. Mauduit, S. P. Nolan, *Angew. Chem. Int. Ed.* **2007**, *46*, 6786–6801.

[3] a) R. C. Buijsman, E. van Vuuren, J. G. Sterrenburg, *Org. Lett.* **2001**, *3*, 3785–3787; b) D. Semeril, H. Olivier-Bourbigou, C. Bruneau, P. H. Dixneuf, *Chem. Commun.* **2002**, 146–147; c) K. G. Mayo, E. H. Nearhoof, J. J. Kiddle, *Org. Lett.* **2002**, *4*, 1567–1570; d) S. Csihony, C. Fischmeister, C. Bruneau, I. T. Horváth, P. H. Dixneuf, *New J. Chem.* **2002**, *26*, 1667–1670; e) Q. Yao, Y. Zhang, *Angew. Chem. Int. Ed.* **2003**, *42*, 3395–3398; f) Q. Yao, M. Sheets, *J. Organomet. Chem.* **2005**, *690*, 3577–3584; g) N. Audic, H. Clavier, M. Mauduit, J.-C. Guillemin, *J. Am. Chem. Soc.* **2003**, *125*, 9248–9249; h) H. Clavier, N. Audic, M. Mauduit, J.-C. Guillemin, *Chem. Commun.* **2004**, 2282–2283; i) H. Clavier, N. Audic, J.-C. Guillemin, M. Mauduit, *J. Organomet. Chem.* **2005**, *690*, 3585–3599; j) D. Rix, F. Caïjo, I. Laurent, Ł. Gułajski, K. Grela, M. Mauduit, *Chem. Commun.* **2007**, 3771–3773; k) C. Thurier, C. Fischmeister, C. Bruneau, H. Olivier-Bourbigou, P. H. Dixneuf, *J. Mol. Catal. A* **2007**, *268*, 127–133; l) C. Thurier, C. Fischmeister, C. Bruneau, H. Olivier-Bourbigou, P. H. Dixneuf, *ChemSusChem* **2008**, *1*, 118–122; m) P. Śledź, M. Mauduit, K. Grela, *Chem. Soc. Rev.* **2008**, *37*, 2433–2442.

[4] a) B. S. Lee, S. K. Namgoong, S.-g. Lee, *Tetrahedron Lett.* **2005**, *46*, 4501–4503; b) S.-W. Chen, J. H. Kim, C. E. Song, S.-g. Lee, *Org. Lett.* **2007**, *9*, 3845–3848; c) S.-W. Chen, J. H. Kim, H. Shin, S.-g. Lee, *Org. Biomol. Chem.* **2008**, *6*, 2676–2678.

[5] M. Bieniek, R. Bujok, M. Cabaj, N. Lugan, G. Lavigne, D. Arlt, K. Grela, *J. Am. Chem. Soc.* **2006**, *128*, 13652–13653.

[6] R. Gawin, A. Makal, K. Woźniak, M. Mauduit, K. Grela, *Angew. Chem. Int. Ed.* **2007**, *46*, 7206–7209.

[7] For other latent catalysts and activation, see: a) P. A. van der Schaaf, R. Kolly, H.-J. Kirner, F. Rime, A. Mühlebach, A. Hafner, *J. Organomet. Chem.* **2000**, *606*, 65–74; b) T. Ung, A. Hejl, R. H. Grubbs, Y. Schrodi, *Organometallics* **2004**, *23*, 5399–5401; c) C. Slugovc, D. Burtscher, F. Stelzer, K. Mereiter, *Organometallics* **2005**, *24*, 2255–2258; d) M. Barbasiewicz, A. Szadkowska, R. Bujok, K. Grela, *Organometallics* **2006**, *25*, 3599–3604; e) A. Hejl, M. W. Day, R. H. Grubbs, *Organometallics* **2006**, *25*, 6149–6154; f) X. Gstrein, D. Burtscher, A. Szadkowska, M. Barbasiewicz, F. Stelzer, K. Grela, C. Slugove, *J. Polym. Sci., Part A: Polym. Chem.* **2007**, *45*, 3494–3500; g) T. Kost, M. Sigalov, I. Goldberg, A. Ben-Asuly, N. G. Lemcoff, *J. Organomet. Chem.* **2008**, *693*, 2200–2203; h) A. Ben-Asuly, E. Tzur, C. E. Diesendruck, M. Sigalov, I. Goldberg, N. G. Lemcoff, *Organometallics* **2008**, *27*, 811–813.

[8] Anionic ligands can be exchanged between Hoveyda's Ru complexes, see: K. Tanaka, V. P. W. Böhm, D. Chadwick, M. Roeper, D. C. Braddock, *Organometallics* **2006**, *25*, 5696–5698.

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