Room temperature ionic liquids: new solvents for Schrock's catalyst and removal using polydimethylsiloxane membranes†

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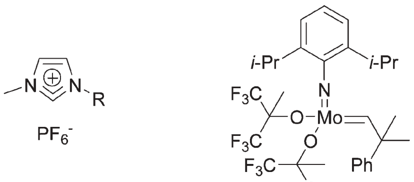
A room temperature ionic liquid was used as the solvent for metathesis reactions with the Schrock catalyst and a new method to facilitate separation between small molecules and ionic liquids using polydimethylsiloxane thimbles is reported.

The incorporation of potentially recyclable, green solvents in organic synthesis is a critical target of industrial and academic research.[1] Much research in this field has focused on room temperature ionic liquids (RTILs) as alternate solvents for transition metal catalyzed reactions. RTILs have found applications in catalysis reactions such as hydrogenations, hydroformylations, and Heck reactions among many others and have been found to alter the course of some reactions.[2,3] Recent work has demonstrated the importance of olefin metathesis in organic chemistry to construct both small molecules and polymers by Grubbs' and Schrock's catalysts in organic solvents.[4] Although the Schrock catalyst is very active towards metathesis and chiral versions have been synthesized that catalyze highly enantioselective reactions, no reports of the use of these catalysts in a RTIL have been published. This omission is most likely due to the extreme sensitivity of Schrock's catalyst to dioxygen and many polar functional groups that leads one to believe they will not be active in RTIL.

We herein report a new method for utilizing Schrock's catalyst, **2**, for olefin ring-closing and cross metathesis reactions using 1-butyl-3-methylimidazolium hexafluorophosphate, (BMIM) **1a**, as solvent (Fig. 1). Several olefin ring-closing and cross metathesis reactions were carried out in this RTIL to approximately 100% conversion by ^{1}H NMR spectroscopy. In the course of this work, we developed a new method for removal of the RTIL from the small molecules by performing Soxhlet extractions using polydimethylsiloxane (PDMS) thimbles.



1a R=$(CH_2)_3CH_3$
1b R=$(CH_2)_7CH_3$

2

Fig. 1 Room temperature ionic liquids **1a** and **1b** and Schrock's catalyst **2**.

We began with the preparation of BMIM, as previously described in the literature,[5] to yield a slightly yellow, viscous liquid following removal of residual organic starting materials. We placed this solvent under vacuum at 100 °C for 24 h to dry it of water. The solvent was stored under a N_2 atmosphere in a glove box prior to use.

It is known that **2** catalyzes both olefin ring-closing[4,6] and cross metathesis[4b,6b,7] reactions in organic solvents at room temperature in good yields. We set out to develop a method to catalyze these same reactions in BMIM by investigating the reactions of olefins containing various functional groups. In a typical experiment, 1 mL of BMIM was mixed with Schrock's catalyst (25 mg) and placed in a 75 °C oil bath for 10 minutes. The olefin was subsequently added under N_2 and allowed to stir at 75 °C for 1–3.5 h.‡ Before addition of the olefin, the catalyst was sparingly soluble in BMIM, but after addition the catalyst fully dissolved. Reactions were found to proceed to approximately 100% conversion by ^{1}H NMR spectroscopy with 5 mol% catalyst per diene as shown in Table 1.

These reactions were notable because they went to high conversions with modest catalyst loadings, as compared to similar reactions in methylene chloride. For instance, we reacted **5**, **9**, and **13** with Schrock's catalyst in methylene chloride at room temperature. These reactions were complete in less than 3 h, similar to reactions in BMIM at 75 °C.

It is well known that these catalysts are quickly poisoned by carboxylic acids, and when we studied the ring closing of a dicarboxylic acid (**20**) we observed a similar result. No product was observed under any conditions that we attempted.

Schrock's catalyst is also active towards the living ring-opening metathesis polymerization (ROMP) of strained cyclic olefins.[8] Based on the success of our ring-closing and cross metathesis reactions, we investigated whether the Schrock catalyst would catalyze the ROMP of strained norbornene derivatives. Polymerizations were attempted using either BMIM or 1-octyl-3-methylimidazolium hexafluorophosphate, **1b**, as solvent with monomers **3** and **4** (Fig. 2). These monomers were chosen because they have been polymerized by Schrock's catalyst in organic solvents to yield well-defined, narrow molecular weight polymers. The ROMP of **3** was performed with a monomer to catalyst ratio of 100 : 1 in BMIM at both room temperature and at 50 °C for 17 h, but no polymer was obtained. When the solvent was changed to **1b**, a small amount of white, polymer-like material was obtained following precipitation into methanol. The isolated material would not re-dissolve in any solvent for analysis by size exclusion

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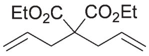
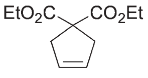
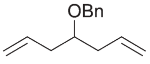
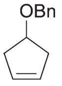
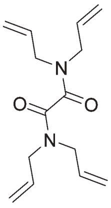
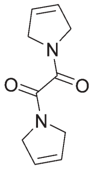
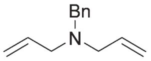
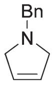
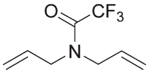
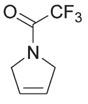
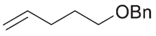
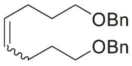
† Electronic supplementary information (ESI) available: Detailed experimental protocol for PDMS thimble fabrication and ^{1}H and ^{13}C NMR spectroscopy data for formation of compounds **6**, **8**, **10**, **12**, **14**, and **16**, as well as for compounds **5**, **7**, **17**, **18**, and **19** following Soxhlet extraction. See DOI: 10.1039/b618341g

Table 1 Metathesis reactions in BMIM with Schrock's catalyst **2**[a]

Substrate	Product	Time/h	Conversion[b]	Yield[c]
 **5**	 **6**	1	>97%	84%
 **7**	 **8**	3.5	>97%	94%
 **9**	 **10**	3	>97%	39%[d]
 **11**	 **12**	3.5	>97%	61%[e]
 **13**	 **14**	1	>97%	NA[f]
 **15**	 **16**	3	>97%	87%[g]

[a] Catalyst loading is 5 mol% per diene for all substrates. [b] Conversion determined by ^{1}H NMR spectroscopy. [c] Isolated yield following Soxhlet extraction and column chromatography. [d] 96% when extracted from RTIL with 80% hexane–20% CH_2Cl_2. [e] Low yield due to low boiling point of product. [f] Product too volatile to isolate. [g] E : Z ratio of 3.7 : 1.

chromatography or ^{1}H NMR spectroscopy. We investigated the ROMP of **4** in BMIM at room temperature and in **1b** at room temperature and 50 °C. White polymer-like materials were obtained in all three cases but were not isolable. Thus, although the catalyst is active towards ROMP in these solvents, the polymerizations were not controlled.

Following the ring-closing and cross metathesis reactions, removal of BMIM from the product was found to be problematic with certain substrates. We are certainly not the first to have this problem as it is a limitation when working with RTILs, particularly for small scale reactions where little product (less than one gram) is synthesized. Distillation is a common method to separate small molecules from ionic liquids, but distillations on small sample sizes, such as found in our experiments, is very challenging to carry out in high yields. We found that BMIM could be separated from small molecules by column chromatography in certain cases, when used with an eluent of 30% ethyl acetate–70% hexane. This method worked well for products **6**, **8**, and **16**, but was unsatisfactory for other substrates that are more polar or contain an amine such as **10**, **12**, and **14**. For these molecules, separation was poor and the product was contaminated with significant amounts of BMIM. Use of an eluent with more than 30% ethyl acetate allowed BMIM to move down the column and little to no separation of product from the BMIM was observed. Liquid–liquid extraction was also attempted using hexane as a second phase. This method also proved to be unsuccessful with polar molecules as the product must be soluble in hexane. Because of these limitations, we set out to develop a new method to easily separate small molecules from BMIM that would not be labor intensive and would allow small amounts (less than one gram) to be separated.

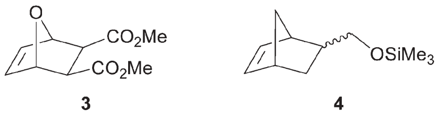


Fig. 2 Monomers **3** and **4** used for ROMP.

Our method for separation utilizes a PDMS thimble inside a Soxhlet extraction apparatus. The thimble was fabricated using commercially available, un-crosslinked PDMS. We weighed the two components of PDMS in a 10 : 1 ratio (by mass) and thoroughly mixed them. This mixture was subsequently poured into a mold consisting of a hollow cylindrical drying tube (1.59 cm diameter) that contained a cylindrical stainless steel rod (1.27 cm diameter). The PDMS was cured for 12 h at room temperature and then transferred to an oven and heated at 65 °C for at least 4 h to completely cure. The mold was removed from the drying tube by cutting the tube off and from the steel rod by swelling in hexane. The PDMS thimble was dried under vacuum. The PDMS thimbles were cylindrical in shape, with an average length of 11.4 cm, an inside diameter of 1.27 cm, and a wall thickness of 0.16 cm.

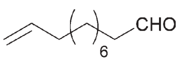
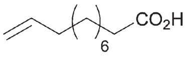
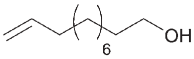
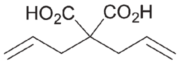
The PDMS thimbles were used to perform Soxhlet extractions with methanol. In a typical experiment, a small molecule was dissolved in 1 mL of BMIM and 5 mL of methanol. This mixture was added to the PDMS thimble and the thimble was placed in the Soxhlet apparatus. A cap was placed on the thimble to prevent methanol from the reflux condenser dripping into the thimble and overflowing its contents.

The concept behind these experiments is simple. Small molecules will diffuse through the PDMS thimble into bulk methanol, while BMIM will remain encapsulated within the PDMS thimble. PDMS is a hydrophobic polymer that is flexible and allows small molecules and gasses to readily diffuse through it. We based our work on a critical experiment by Crespo *et al.* who showed that RTILs do not diffuse through PDMS because they are too polar.[9] Thus, we hypothesized that we could extract small molecules from BMIM while it remained behind in the thimble.

Small molecules containing various functional groups were added to a PDMS thimble in BMIM–methanol and subjected to a Soxhlet extraction (Table 2). Each extraction was run for 6 days with 0.5 g of the small molecule. At the completion of each experiment, the methanol outside the PDMS thimble was evaporated and the remaining materials were studied by ^{1}H NMR spectroscopy. No BMIM was seen in the ^{1}H NMR spectrographs, which demonstrated that it remained encapsulated within the PDMS thimble.

Yields obtained varied from 66% for molecule **18** with a polar carboxylic acid functional group, to 98% for both **5** and **19**. Entries

Table 2 Removal of small molecules using PDMS for Soxhlet extraction

Entry	Small molecule	Yield
1	**5**	98%
2	**7**	86%
3	 **17**	79%[a]
4	 **18**	66%
5	 **19**	98%
6	 **20**	0%

[a] Isolated as a mixture of acetal–aldehyde (9 : 1 molar ratio).

1–5 in Table 2 were successfully extracted from BMIM using this method; these molecules are also mostly insoluble in water. Their solubility in water is important because PDMS is hydrophobic and polar molecules diffuse through it at slower rates than apolar molecules.[9–11] To test the limit of this method, we attempted to extract the water soluble diacid, **20**, using a PDMS thimble. After 6 days, methanol outside the thimble was evaporated to dryness and only a trace amount of **20** was observed by ^{1}H NMR spectroscopy. Thus, one limitation of this method is that the most polar substrates will not readily diffuse through PDMS under these conditions. Because of this limitation, this method could potentially be used to separate apolar and polar molecules.

Soxhlet extractions were also performed following the metathesis reactions of all substrates listed in Table 1 in order to obtain isolated yields on smaller scale reactions (approximately 100 mg for each reaction in Table 1). The extractions were successful for separating the ionic liquid from the products. Small contaminants due to decomposed Schrock's catalyst also escaped the PDMS membrane in each case, so the products were purified by subsequent column chromatography to obtain the isolated yields as shown in Table 1.

In summary, BMIM is an attractive new solvent for both olefin ring-closing and cross metathesis reactions using Schrock's catalyst. These reactions were comparable to the same reactions in methylene chloride, and proceeded to $\sim$100% conversion at 75 °C for molecules containing a variety of functional groups. In a second important extension, we developed a new method to extract small amounts of organic products from BMIM by carrying out a Soxhlet extraction using PDMS thimbles. This method is general and should work well for all but the most polar of substrates and, importantly, can be carried out on small amounts of materials. The thimbles were easy to fabricate from cheap, commercially available starting materials and the extractions were not labor intensive. Although we did not explore it, after extraction the RTIL could be recycled for further reactions.

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Notes and references

‡ *Olefin ring-closing metathesis with Schrock's catalyst in RTIL.* In a glove box, Schrock's catalyst (25 mg, 0.033 mmol) and BMIM (1 mL) were added to a Schlenk flask. The flask was sealed and removed from the glove box and attached to a Schlenk manifold. The Schlenk flask was placed in a 75 °C oil bath for 10 minutes. Diethyl diallylmalonate, **5**, (151 µL, 0.63 mmol) was added to the Schlenk flask under N$_2$ and stirred for 1 h. The reaction was cooled to room temperature and the ionic liquid was subsequently removed by Soxhlet extraction. The product was cleaned by subsequent column chromatography (10% ethyl acetate–90% hexane) to yield a clear liquid **6** (111 mg, 84% yield). The ^{1}H and ^{13}C NMR data correlate with those reported in the literature.[11]

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