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Using Geminal Dicationic Ionic Liquids as Solvents for High-Temperature Organic Reactions

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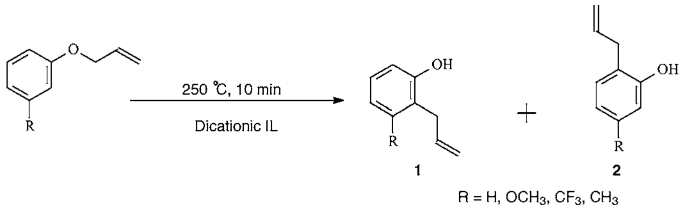
ABSTRACT



Several organic reactions conducted at high temperatures, including the isomerization reaction, the Claisen rearrangement, and the Diels–Alder reaction, were investigated in three geminal dicationic ionic liquids with high thermal stability. High to moderate yields of the products for most entries were obtained. Advantages of these approaches are discussed. These ionic liquids were shown to be recyclable. The utility of these ionic liquid solvents for high-temperature organic reactions was demonstrated.

Room-temperature ionic liquids (ILs) have been touted as replacements for traditional molecular solvents in synthesis because of their nonvolatility, nonflammability, stability, and ease of recyclability.[1] In recent years, numerous applications of room-temperature ionic liquids have been investigated in organic,[1a,d,2] organometallic,[1−3] and enzymatic synthesis[1d,3b,4] as well as in chemical analysis.[5] Presumably, due to their high stability and low volatility, ionic liquids are promising solvents for organic reactions carried out at high temperatures. Surprisingly, there are few reports on high-temperature organic reactions in these new solvents.[6] Zulfiqar and Kitazume reported a sequential reaction which involved a Claisen rearrangement and cyclization reaction catalyzed by anhydrous scandium trifluoromethanesulfonate at 200 °C in ionic liquids to obtain dihydrobenzo[*b*]furan derivatives.[6a] With microwave heating, high-speed Heck reactions were done in [bmim][PF_6] at 180 or 220 °C.[6b] To our knowledge, no other synthetic organic reactions in ionic liquids at temperature above 200 °C have been reported.

It has been reported that the decomposition/volatilization temperatures of monocationic ionic liquids is high in most cases.[7] Recent research indicated that the thermal stability of these ionic liquids has been overestimated.[8,5e] Inverse gas chromatographic tests showed that thermal degradation of imidazolium-based ionic liquids occur at temperatures below

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200 °C.[5e] Similar conclusions were reached by Scott and coworkers using "precise thermogravimetric analysis (TGA) measurements".[8a] It was found that degradation of ionic liquids occurred at temperatures much lower than the ones reported previously. Organic reactions done at temperatures above 200 °C require ionic liquid solvents with higher thermal stability. Most recently, a series of geminal dicationic ionic liquids with high thermal stabilities was prepared by our group.[9] The degradation/volatization onset temperatures of these geminal dicationic ionic liquids ranged from 330 to >400 °C. These high-stability ionic liquids are promising solvents for high-temperature organic reactions. In this communication, the utility of three high-stability ionic liquid solvents (Figure 1) for high-temperature organic reactions, including the isomerization reaction, the Claisen rearrangement, and the thermo-induced Diels–Alder reaction, were investigated. The effects of temperature and type of dicationic ionic liquid on the reaction times and yields are discussed.

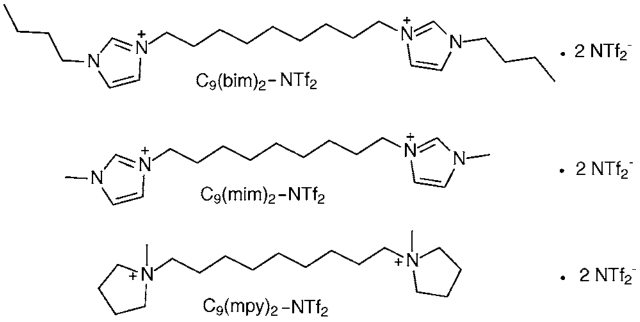
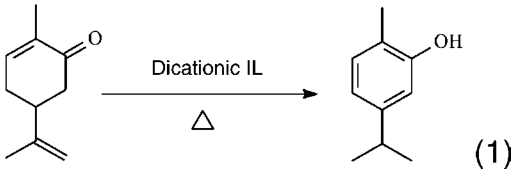


Figure 1. Structure of the dicationic ionic liquid used in this paper.

The first thermal reaction investigated was the isomerization of carvone to carvacrol (Table 1). After carvone was dissolved in the dicationic ionic liquids, the temperature was kept at 250 °C and the reaction was finished in 3–4 h (monitored by TLC, see the Supporting Information), the product was extracted with ethyl ether, and moderate yields of carvacrol were obtained. When the reaction was done at 300 °C, both the reaction rate and yield increased. The increase in reaction rate was expected, while the enhanced yield was an added benefit. The nature/type of ionic liquid also affects this isomerization reaction. At 300 °C, the yield of the carvone isomerization in $C_9(mpy)_2$–NTf_2 was higher than those in $C_9(bim)_2$–NTf_2 and $C_9(mim)_2$–NTf_2. In this case, the aliphatic ionic liquid solvent produced higher yields than did the aromatic–imidazolium-based dicationic ionic liquids. Compared to Strauss's method,[10] in which the isomerization of carvone is done in water at 250 °C, the optimum yield of this method is slightly lower. However, this procedure has the advantage that the reaction in ionic liquid can be done at atmospheric pressure, thus avoiding the use of a more complex high-pressure reactor.

Table 1. Isomerization of Carvone in Dicationic Ionic Liquids

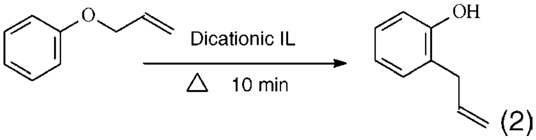


entry	ionic liquid	T (°C)	time (h)	yield[a] (%)
1	$C_9(bim)_2$–NTf_2	250	3	52
2		300	0.5	58
3	$C_9(mim)_2$–NTf_2	250	4	43
4		300	0.5	68
5	$C_9(mpy)_2$–NTf_2	250	4	49
6		300	0.5	75

[a] Isolated yield.

The second reaction investigated was the Claisen rearrangement of allyl phenyl ether (Table 2). The reaction was complete in 10 min in these ionic liquids. In contrast to the isomerization of carvone, the yield was much higher at 250 °C than at 300 °C. Further, increasing the reaction time resulted in side reactions and decreasing yields of the expected product. One of the side products was very difficult to separate from the rearrangement product by flash chromatography, which made the isolation and purification process difficult. In addition, low yields of 2-methyl-2,3-dihydrobenzo[*b*]furan were obtained when the reaction time

Table 2. Claisen Rearrangement of Allyl Phenyl Ether in Dicationic Ionic Liquids



entry	ionic liquid	T (°C)	yield[a] (%)
7	$C_9(bim)_2$–NTf_2	250	63
8		300	10
9	$C_9(mim)_2$–NTf_2	250	75
10		300	20
11	$C_9(mpy)_2$–NTf_2	250	35
12		300	18

[a] Isolated yield.

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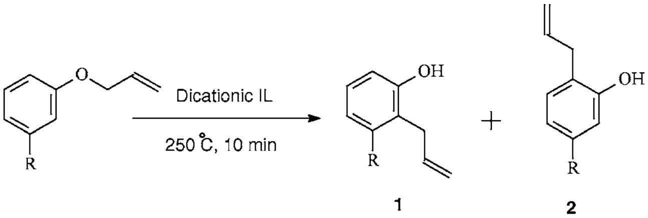
was increased to 60 min at 250 °C in the $C_9(mpy)_2-NTf_2$ ionic liquid. Different ionic liquids also affected the reaction. In this case, much better yields were obtained in the imidazolium-based $C_9(mim)_2-NTf_2$ and $C_9(bim)_2-NTf_2$ ionic liquids than in the $C_9(mpy)_2-NTf_2$ ionic liquid.

The Claisen rearrangements of three meta-substituted allyl phenyl ethers in the dicationic ionic liquids at 250 °C were investigated. The results are shown in Table 3. The nature of the ionic liquid had a substantial effect on both the yield and the product ratio. The reactions were negligible in the $C_9(bim)_2-NTf_2$ IL (i.e., none of the products were the expected rearrangements products). Only cyclization dihydrobenzo[*b*]furan products and decomposition products, *m*-trifluoromethylphenol, were obtained with low yields for the rearrangement of *m*-trifluoromethyl allyl phenyl ether in this ionic liquid. The pyrrolidinium-based $C_9(mpy)_2-NTf_2$ IL is only a moderately effective solvent for these Claisen rearrangements. Modest yields for the reaction of *m*-methoxy allyl phenyl ether and *m*-methyl allyl phenyl ether were obtained. However, a good yield for the rearrangement of *m*-trifluoromethyl allyl phenyl ether was observed. The best IL solvent for these reactions was $C_9(mim)_2-NTf_2$. The reaction was quite clean, and high yields of the expected Claisen rearrangement products were attained for all of the substituted allyl phenyl ethers. Also, no significant side reaction products were found in this ionic liquid. In addition, clean Claisen rearrangement products only were obtained in the $C_9(mim)_2-NTf_2$ ionic liquid. Some unidentified side products, which are difficult to separate from the expected product by flash chromatography, were observed for the reactions in the other two dicationic ionic liquids. The explanation for this phenomenon is not yet clear.

Table 3. Claisen Rearrangement of Meta-Substituted Allyl Phenyl Ether in Dicationic Ionic Liquids



(3-5)

entry	R	ionic liquid	1/2	yield[a] (%)
13	OMe	$C_9(bim)_2-NTf_2$		
14		$C_9(mim)_2-NTf_2$	1:1.8	82
15		$C_9(mpy)_2-NTf_2$	1:2.4	34
16	Me	$C_9(bim)_2-NTf_2$		
17		$C_9(mim)_2-NTf_2$	4:5	87
18		$C_9(mpy)_2-NTf_2$	1:1	44
19	CF_3	$C_9(bim)_2-NTf_2$		
20		$C_9(mim)_2-NTf_2$	1:1.2	77
21		$C_9(mpy)_2-NTf_2$	1:1	74

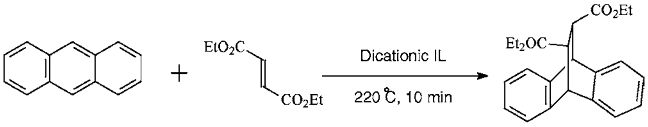
[a] Isolated yield.

No significant regioselectivity for these reactions was observed when different dicationic ionic liquid were used. Similar ratios of the two isomeric products were observed for all the rearrangements in $C_9(mim)_2-NTf_2$ and $C_9(mpy)_2-NTf_2$. The rearrangement of *m*-methoxy allyl phenyl ether shows the highest regioselectivity in the $C_9(mpy)_2-NTf_2$ ionic liquid. The ratio of the two isomers was 1:2.4.

The Claisen rearrangement in $C_9(mim)_2-NTf_2$ has significant advantages over the reaction in traditional monocationic ionic liquids.[6] First, there is no need for a Lewis acid catalyst. Second, the reaction time decreases greatly (10 min vs 10 h). Claisen rearrangement products are obtained in the dicationic ionic liquid while the products obtained in the monocationic ionic liquid under Lewis acid catalysis are dihydrobenzo[*b*]furan derivatives.[6] Compared to the analogous Claisen rearrangement performed in superheated water,[10] the reaction for this IL method was done at atmosphereic pressure (i.e., no autoclaves are needed).

The last reaction investigated was a thermally induced Diels−Alder reaction of anthracene with diethyl fumarate (Table 4). In these three dicationic ionic liquids, the reaction was finished in 10 min at 220 °C. Reasonable yields were obtained in the $C_9(mim)_2-NTf_2$ (51%) and $C_9(mpy)_2-NTf_2$ (47%) ionic liquids. Increasing reaction time or temperature resulted in the volatilization of the anthracene; therefore, the equilibrium moved to the left and the conversion decreased. The low isolated yield of this reaction is due to the high solubility of the product in these ionic liquids. Even after five equal-volume extractions by ethyl ether, a relatively large amount of product still stayed in the ionic liquids (from TLC).

Table 4. Diels−Alder Reaction of Anthracene and Diethyl Fumarate in Dicationic Ionic liquids



(6)

entry	ionic liquid	conversion[a,b] (%)
22	$C_9(bim)_2-NTf_2$	45
23	$C_9(mim)_2-NTf_2$	71
24	$C_9(mpy)_2-NTf_2$	66

[a] Although a reasonable conversion of starting materials to products is obtained in 10 min, the product is difficult to remove from the IL by simple solvent extraction using ether; for example, five extractions of 23 removed 72% of the product. [b] Conversion was determined by HPLC (C18, ACN/water = 50:50, detection wavelength = 254 nm, flow rate = 1.0 mL/min) analysis of the IL solution based on diethyl fumarate.

Although the dicationic liquid used for the reaction darkened somewhat after exposure to high temperatures, they still can be recycled and used for additional runs. $C_9(mim)_2-NTf_2$ and $C_9(mpy)_2-NTf_2$ were chosen to investigated the recyclability of these solvents for the Claisen rearrangement of allyl phenyl ether and the isomerization of carvone, respectively. Table 5 shows that these two ionic liquids can be reused without significant decreases in the conversion or yield.

Table 5. Reaction Conversions and Yields with Reused/Recycled Dicationic IL Solvents

reaction	ionic liquid	cycle	conversion[a] (%)	yield[a] (%)
1	$C_9(mpy)_2-NTf_2$	1	99	74
		2	99	81
		3	98	79
2	$C_9(mim)_2-NTf_2$	1	93	80
		2	87	77
		3	88	75

[a] Conversion and yield were determined by HPLC (C18, ACN/water = 50:50, detection wavelength = 254 nm, flow rate = 1.0 mL/min) analysis of the mixtures extracted from IL solution by ether.

In summary, three classes of high-temperature organic reactions were investigated in three geminal dicationic ionic liquids. The results showed that the application of these new thermal stable IL solvents for high-temperature organic synthesis is promising and that these dicationic ILs can be reused/recycled. Differences in the structure of the cation affects the reaction significantly. Generally, for the isomerization of carvone, $C_9(mpy)_2-NTf_2$ was the optimum solvent, while for the Claisen rearrangement and the Diels−Alder reactions in this work, $C_9(mim)_2-NTf_2$ produced the best results.

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Supporting Information Available: Details of the experiments, characterization of the products, and NMR spectra. This material is available free of charge via the Internet at http://pubs.acs.org.

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