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# Thermal Behaviors of Ionic Liquids Under Microwave Irradiation and Their Application on Microwave-Assisted Catalytic Beckmann Rearrangement of Ketoximes

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# Thermal Behaviors of Ionic Liquids Under Microwave Irradiation and Their Application on Microwave-Assisted Catalytic Beckmann Rearrangement of Ketoximes

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## ABSTRACT

Microwave-assisted Beckmann rearrangements of ketoximes in room temperature ionic liquids have been accomplished successfully using only 5 mol% of H<sub>2</sub>SO<sub>4</sub> as a catalyst.

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Microwave-assisted organic reactions have been recently received a great deal of attention and are quickly developing area in synthetic chemistry.<sup>[1]</sup> The reactions under microwave irradiation sometimes proceeded much faster with higher yields compared to the conventional heating. Despite of several advantages of this technology, one of the drawbacks is its limitation to the use of harmful organic solvents. Moreover, explosions caused by irradiation of microwave to organic solvent are sometimes unavoidable. Therefore, the finding of ideal replacements, less toxic, and environmentally benign, for conventional solvent offers new opportunities in microwave-assisted organic reactions. In this context, room temperature ionic liquids may have a great potential for attaining this goal. Ionic liquids, particularly those based on 1-n-butyl-3-methylimidazolium salts, [bmim] [X] where  $X = BF_4$ , PF<sub>6</sub>, SbF<sub>6</sub>, and OTf, have received recently much attention as novel green solvents.<sup>[2]</sup> During our on going study on organic reaction using ionic liquids,<sup>[3]</sup> we interested in the combination of ionic liquids with microwave (MW)-assisted organic reactions. Ionic liquids consisting entirely of ions could absorb the microwave energy efficiently. Moreover, the risk of an explosion caused by rapid increase of vapor pressure of the solvent can be avoided since the ionic liquids have no measurable vapor pressure. Very recently, upon taking advantage of these properties, we<sup>[4]</sup> and others<sup>[5]</sup> utilized the ionic liquids for microwave-assisted organic reactions. Here we wish to report the extension of utility of ionic liquids as reaction medium for microwave-assisted organic reaction to the catalytic Beckmann rearrangement of ketoximes.

Beckmann rearrangement of a ketoxime to the corresponding amide is an important synthetic method. Generally the reaction requires a large amount of Brønsted acids such as sulfuric acid, which cause a serious drawback by forming ammonium sulfate as a by product.<sup>[6]</sup> To overcome this, various catalytic systems for liquid-phase Beckmann rearrangement of ketoximes have been developed.<sup>[7]</sup> However, the efficiency is not very high, and the turn over number (TON) based on acid catalysts is generally less than 5. The application of ionic liquids in Beckmann rearrangements of ketoximes may provide a beneficial effect on stabilization of the positively charged iminium intermediates. Acidity of the Brønsted acid may be enhanced due to the solvophobicity of ionic liquids, and thus, the reactivity of the reaction could be increased. Recently, it has been reported that the Beckmann rearrangements of ketoximes in ionic liquids using 10–20 mol% of PC<sub>15</sub> by Peng and Deng<sup>[8]</sup> and 10 mol% of P<sub>2</sub>O<sub>5</sub> or Eaton's reagent by Ren et al.<sup>[9]</sup> However, to our best knowledge, there is no report on microwave-assisted Beckmann rearrangement of ketoximes in ionic liquids.

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*Figure 1.* TGA (thermogravimetric analysis) of ionic liquids, [bmim][X], and DMF (10°C/min, N<sub>2</sub>).

It is generally known that the ionic liquids are thermally stable. However, there is no reported data on the thermal stability of ionic liquids in the literature. Therefore, the thermal stability of the ionic liquids, [bmim] [X], has been investigated first using thermogravimetric analysis (TGA) (Fig. 1). The TGA showed that all of the ionic liquids exhibited similar thermal stability regardless of the counter anion and decomposed drastically in the temperature range  $380-400^{\circ}$ C. We also examined the thermal behaviors of the ionic liquids under microwave irradiation. The heating rates of the ionic liquids, [bmim] [X], are faster than DMF, and largely affected by the counter anion, X. The [bmim] [OTf] showed the fastest heating rate, thus, the temperature reached  $200^{\circ}$ C after 2 min. An interest finding is that the temperature of [bmim] [PF<sub>6</sub>] and [bmim] [BF<sub>4</sub>] were reached thermal stationary states after 100 s (ca. 115–120°C) (Fig. 2).

With these thermal data in hand, we examined the utility of ionic liquids as solvents for microwave-assisted catalytic Beckmann rearrangements of ketoxime using  $H_2SO_4$  as a catalyst.  $H_2SO_4$  is one of the most commonly used Brønsted acid catalysts, but normally required excess amounts. In the first time, the effects of counter anion of [bmim] [X] on the reactivity have been examined using 25 mol% of  $H_2SO_4$ . To prevent the localized superheating and improve the homogeneity of the reaction mixture, we conducted the reaction with intermittent heating and mixing at a full power of domestic oven (2450 MHz, 850 W). Thus, a 1 M solution of propiophenone oxime in [bmim] [X] in the presence of 25 mol% of  $H_2SO_4$  was irradiated for 20 s, then the reaction mixture was

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*Figure 2.* Thermal behaviors of ionic liquids and DMF under MW irradiation. Temperature is the mean average  $(\pm 5^{\circ}C \text{ error range})$  of three measurements.

taken out, mixed again for 5 s and then irradiated again for 20 s. This step was repeated until completion of the reaction. The results are summarized in Table 1.

As shown in Table 1, all of the reactions using 25 mol% of  $H_2SO_4$  were completed within 60 s to give phenyl group migrated product quantitatively indicating that the rearrangements were not much affected on the counter anion of ionic liquids. The hydrophobic ionic liquids, [bmim] [SbF<sub>6</sub>], [bmim] [BF<sub>4</sub>], [bmim] [PF<sub>6</sub>] was almost retained even in using 5 mol% of catalyst (Entries 1–3). In contrast with microwave irradiation, the rearrangements of propiophenone oxime under conventional heating condition using 25 mol% of H<sub>2</sub>SO<sub>4</sub> were not efficient. After 3 h heating at 120°C, 76% yield of the phenyl group migrated product was obtained by using [bmim] [PF<sub>6</sub>] as a solvent, however, less than 30% of product was formed in other ionic liquids.

The efficiency of this novel protocol consisting of  $H_2SO_4$  catalystionic liquid-microwave for Beckmann rearrangement were tested for other ketoximes using 5 mol% of  $H_2SO_4$  in [bmim] [PF<sub>6</sub>] and the results are summarized in Table 2. All of the acyclic ketoximes rearranged highly efficiently within 60 s microwave irradiation (Entries 1–5). However, the cyclic ketoxime,  $\alpha$ -tetralone oxime, was not rearranged effectively, thus, only 30% of the rearranged product was formed under 120 s microwave irradiation (Entry 6).

In summary, the utility of environmentally benign room temperature ionic liquids as solvents for microwave-assisted catalytic Beckmann rearrangement of ketoximes has been proved. The ketoximes were

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rearranged in the presence of only 5 mol% of  $H_2SO_4$  in hydrophobic ionic liquids such as [bmim] [PF<sub>6</sub>] to give the corresponding amides in high yields within 60s microwave irradiation. Further application

*Table 1.* The effect of counter anion of [bmin] [X] on Beckmann rearrangement of ketoxime.



|       |                            | Yield (%) <sup>a</sup>                       |   |  |  |
|-------|----------------------------|--|---|--|--|
| Entry | Ionic liquid               | MW<br>25 mol% H <sub>2</sub> SO <sub>4</sub> | MW<br>5 mol% H <sub>2</sub> SO <sub>4</sub> | Thermal heating<br>(120°C)<br>25 mol% H <sub>2</sub> SO <sub>4</sub> |  |
| 1     | [bmin] [SbF <sub>6</sub> ] | >99 (60 s)                                   | >99 (100 s)                                 | 25 (3 h)   |  |
| 2     | [bmin] [BF <sub>4</sub> ]  | >99 (60 s)                                   | >99 (60 s)                                  | <5 (3 h)   |  |
| 3     | [bmin] [PF <sub>6</sub> ]  | >99 (40 s)                                   | >99 (60 s)                                  | 76 (3 h)   |  |
| 4     | [bmin] [OTF]               | >99 (60 s)                                   | >99 (120 s)                                 | 30 (3 h)   |  |

<sup>a</sup>Isolated yield.

*Table 2.* Microwave-assisted Beckmann rearrangement of ketoximes in [bmin]  $[PF_6]$  using 5 mol% H<sub>2</sub>SO<sub>4</sub>.

|       | R <sup>OH</sup> 5 mol<br>R <sup>B</sup> R' [bmim][F<br>MW ir |          |          |                        |
|-------|--|----------|----------|------------------------|
| Entry | R  | R'       | Time (s) | Yield (%) <sup>a</sup> |
| 1     | $4-Cl-C_6H_4$  | $C_2H_5$ | 60       | 81                     |
| 2     | $4-Me-C_6H_4$  | $C_2H_5$ | 40       | 91                     |
| 3     | 4-MeO-C <sub>6</sub> H <sub>4</sub>                          | $C_2H_5$ | 60       | 80                     |
| 4     | $C_6H_5$   | $C_6H_5$ | 60       | 99                     |
| 5     | 4-MeO-C <sub>6</sub> H <sub>4</sub>                          | $C_6H_5$ | 60       | 99                     |
| 6     | $C_2H_5$   | $C_2H_5$ | 60       | 99                     |
| 7     | $\alpha$ -Tetralone oxime                                    |          | 120      | 30                     |

<sup>a</sup>Isolated yield.

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of ionic liquids as solvents for microwave-assisted organic reactions are under investigation.

# **EXPERIMENTAL**

# Synthesis of [bmim] [X]

All ionic liquids were prepared from [bmim] [Cl].<sup>[10]</sup> Thus, to a solution of [bmim] [C1] (1 equiv.) in anhydrous acetone at room temperature was added 1 equiv. of sodium hexafluorophosphate for [bmim] [PF6], sodium tetrafluoroborate for [bmim] [BF<sub>4</sub>] or sodium hexafluoroantimonate for [bmim] [SbF<sub>6</sub>]. The reaction mixture was stirred for 24 h at  $20^{\circ}$ C and was then filtered through a plug of Celite. The volatile was removed in vacuo, and the residue was dissolved in methylene chloride and washed with water several times. After evaporation of the methylene chloride, ionic liquid was vacuum dried for 2 days and stored under an atmosphere of dry argon. All ionic liquids contained less than 10 ppm of chlorine in chlorine analysis at Analysis Center in Korea Institute of Science and Technology and less than 15 ppm of water in Karl Fischer analysis (Metrolm Model: 756KF Coulometer).

## **Thermal Behavior of Ionic Liquid**

Thermographic analyses, (TGA) with  $10^{\circ}$ C/min heating rate have been carried out using TGA 2050 model from TA instrument Inc. under N2 atmosphere. For thermal behavior of ionic liquids under microwave irradiation, an ionic liquid (1 mL) in a Pyrex vessel (10 mL) was irradiated in the absence of insulation during given period of time and the temperature was measured using digital thermometer equipped with type K-2 thermocouple.

#### General Procedure for Beckmann Rearrangement

A solution of a ketoxime (1 mmol) and catalytic amount of  $H_2SO_4$ (0.5 mmol) in an ionic liquid (1 mL) was placed in a flat bottom flask and mixed thoroughly on a vortex mixer (Scientific Inc., Model G-560). The mixture was irradiated intermittently in an unmodified domestic microwave oven for 60 s (20 + 20 + 20 s), and loaded on silica column chromatography directly to isolate product.

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