

## A novel task-specific ionic liquid for Beckmann rearrangement: a simple and effective way for product separation

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**Abstract**—Under mild conditions and without any additional organic solvents, Beckmann rearrangement of ketoximes was performed in a novel task-specific ionic liquid consisting sulfonyl chloride. Especially for the conversion of cyclohexanone oxime to  $\epsilon$ -caprolactam,  $\epsilon$ -caprolactam has good solubility in water while the task-specific ionic liquid is immiscible with water, therefore,  $\epsilon$ -caprolactam could be easily separated from the reaction system by water extraction.

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The rearrangement of a ketoxime to the corresponding amide, known as Beckmann rearrangement, is a powerful method both in organic synthesis and chemical manufacturing, particular for the preparation of  $\epsilon$ -caprolactam from cyclohexanone oxime in industry. This reaction, however, generally requires high reaction temperature (approximately 130 °C) and large amount of strong Brønsted acid such as sulfuric acid, phosphorous pentachloride in ether, or hydrogen chloride in a mixture of acetic acid and acetic anhydride in a non-catalytic fashion. The use of excessive amount of such chemicals, the large amount of by-products, and the corresponding problem of corrosion make this process environmentally questionable.<sup>1</sup> In order to overcome these problems, a few examples of catalytic Beckmann rearrangement, proceed either in the vapor-phase process or in the liquid-phase process, have been reported.<sup>2</sup>

Room temperature ionic liquids have received recognition as novel and promising solvents for synthetic chemistry. They have also been refereed to as ‘designer solvents’ as their chemical and physical properties could be adjusted by a careful choice of cation/anion. Recent

advance in ionic liquids research provided another route for achieving task-specific ionic liquids (TSILs) in which a functional group is covalently tethered to the cation or anion of the ionic liquid, especially to the two N atoms of the imidazole ring. It was expected that these TSILs may further enlarge the application scope of ionic liquids in chemistry.<sup>3</sup>

Deng et al. have recently reported a new approach for catalytic Beckmann rearrangement involving using ionic liquids as reaction medium in the presence of  $\text{PCl}_5$ .<sup>4</sup> A following work by Ren et al. showed that  $\text{P}_2\text{O}_5$  or Eaton’s reagent is also a suitable catalyst for this reaction in ionic liquid.<sup>5</sup> In both cases, cyclohexanone oxime was converted to  $\epsilon$ -caprolactam with satisfactory conversion rate and selectivity. This may be contributed to the stabilization of cyclic iminium intermediate and the enhancement of the acidity of Brønsted acids in the ionic liquid media. One of the most serious shortcoming concerning the catalytic Beckmann rearrangement, not only in ionic liquids but also in the industry manufacturing and other catalytic system, is that there is no an effective way to separate the  $\epsilon$ -caprolactam product from the catalysts. This is why ammonia is used to neutralize the sulfuric acid in industry and therefore produce ammonium sulfate as a by-product. It is also inevitable to produce volatile hydrogen chloride as by-product when  $\text{PCl}_5$  and  $\text{P}_2\text{O}_5$  are used as catalysts in ionic liquids. Meanwhile, the oximes investigated as substrates are restricted within a narrow scope and the

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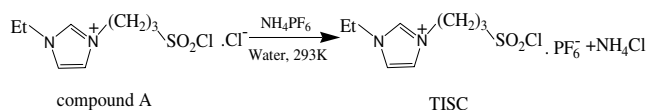
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results are always unsatisfactory except for cyclohexanone oxime. Therefore, further investigation is necessary to elucidate the merits of using ionic liquids for catalytic Beckmann rearrangement.

Based on the designable properties of TSILs, a novel TSIL consisting sulfonyl chloride (TISC, Scheme 1) was synthesized.<sup>6</sup> This TISC has been demonstrated to be both stable in hot water (80 °C)<sup>7</sup> and highly active for Beckmann rearrangement. The synthesis of compound A could be found in previous literature.<sup>8</sup>

In a typical experiment, cyclohexanone oxime and TISC were charged into a 25 mL round-bottom flask with the molar ratio of TISC/cyclohexanone oxime ranged from 1 to 0.2. Then the reactions were allowed to proceed for 1–5 h at the desired temperature. The whole reaction was monitored by a MAT-90 GC/MS. The concentration of the reactant and the product was directly given by the system of GC/MS chemstation according to the area of each chromatograph peak.

The results of rearrangement of cyclohexanone oxime to  $\epsilon$ -caprolactam were summarized in Table 1. We can see that TISC is of very high activity for the Beckmann rearrangement. Cyclohexanone oxime was smoothly transformed to  $\epsilon$ -caprolactam in high yield (Table 1, entry 2) at ca. 80 °C. Increasing the reaction temperature (e.g., to 100 °C) and reaction time did not offer significant advantages (Table 1, entry 4), although the conversion of cyclohexanone oxime would slightly increase with higher temperature (Table 1, entries 1, 2 and 4).



**Scheme 1.** A novel task-specific ionic liquid consisting sulfonyl chloride.

**Table 1.** Beckmann rearrangement of cyclohexanone oxime in TISC

Entry	TISC (g)	TISC/substrate (mol/mol)	T (°C)	t (h)	Con. (%)	Sel. (%)
1	2.0	1:1	60	3	82.3	76.5
2	2.0	1:1	80	2	99.2	98.3
3	2.0	1:5	80	2	98.0	98.1
4	2.0	1:1	100	5	~100	97.8

The best reaction temperature was ca. 80 °C for achieving a maximum selectivity for  $\epsilon$ -caprolactam. Reduce the molar ratio of TISC/cyclohexanone oxime to 0.2 resulted no significant decrease in either conversion or selectivity (Table 1, entries 2 and 3). This indicated that TISC is an effective catalyst for Beckmann rearrangement.

In order to investigate the scope and limitation of such TISC catalyst for the Beckmann rearrangement, other ketoximes substrates were also tested. The results are summarized in Table 2. In each case, oximes were smoothly transformed to the corresponding amine or cyanide after 3–6 h reaction with moderate to high yields. The results are much better than those have been previously reported in ionic liquid systems,<sup>4,5</sup> suggesting that TISC would be a more suitable catalytic system for Beckmann rearrangement.

Once the reaction is complete, more attention is paid to isolate the product and recycle the catalyst. Separation of  $\epsilon$ -caprolactam from the reaction system is always a serious problem in chemical industry so an ionic liquid/aqueous system separation of  $\epsilon$ -caprolactam would offer a very attractive option. Even though previous works had demonstrated the feasibility of catalytic conversion of cyclohexanone oxime to  $\epsilon$ -caprolactam in ionic liquids, there is yet no effective way to separate the product from ionic liquids.  $\epsilon$ -Caprolactam has good solubility in water while TISC is immiscible with water. Therefore,

**Table 2.** Catalytic Beckmann rearrangement of oxime in TISC<sup>a</sup>

Entry	Substrate	t (h)	Product	Yield (%)
1		6		72
2		6		80
3		5		86
4		5		78
5		3		90

<sup>a</sup> Yields are based on GC/MS, reaction temperature 80 °C.

$\epsilon$ -caprolactam could be easily separated from the reaction mixture by water extraction. We believe it is the first example of an easy separation of  $\epsilon$ -caprolactam in ionic liquids. The reaction mixture was extracted thrice with water (5 mL  $\times$  3) after the reaction (Table 1, entry 3) to give  $\epsilon$ -caprolactam at a total yield of 83%. This product contains a very small amount of TISC due to the TISC having a 0.86 g/100 mL in water.<sup>9</sup> It is no doubt that a further refine of the primary product is needed. The remaining TISC was vacuumized for 2 h at 100 °C, in hoping that it could be used for another cycle. Repeating the Beckmann rearrangement reaction of cyclohexanone oxime with the recycled TISC under the same reaction conditions gives, however, a remarkable drop of conversion (34%). In order to study the change of TISC during the process, the pH value of the extractive water (the first 5 mL) was examined. The pH value of 4.7 indicated that some TISC was transformed into sulfonic acid in the reaction. The mechanism study is now undergoing.

In conclusion, TISC has demonstrated to be a suitable catalyst for catalytic Beckmann rearrangement. Owing to the good solubility of  $\epsilon$ -caprolactam in water and the immiscibility of TISC with water,  $\epsilon$ -caprolactam could be extracted by water. This offers an attractive route for  $\epsilon$ -caprolactam manufacturing. To our knowledge, this should be the first report concerning the Beckmann rearrangement of cyclohexanone oxime in TSILs under mild conditions and without any additional organic solvents and an easy separation of product.

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6. A typical procedure: 9.5 g (34.8 mmol) compound A and 5.67 g (34.8 mmol)  $\text{NH}_4\text{PF}_6$  (commercial grade) were dissolved in 30 mL water. The mixture was stirred for 24 h at room temperature. The upper aqueous phase was decanted and the ionic liquid was washed several times with 10 mL water, up to the point where the washing water was chloride-free (tested with  $\text{AgNO}_3$ ). The residual water was removed under vacuum for 6–8 h at 100 °C and 10.0 g (26.1 mmol) of the dark brown ionic liquid was obtained, which corresponds to 75% of the theoretical yield. NMR spectrum of the ionic liquid recorded on a Bruker AM-400:  $^1\text{H}$  NMR (400 MHz, acetone- $d_6$ );  $\delta$  = 8.94 (s, 1H), 7.53 (s, 1H), 7.45 (s, 1H), 4.23 (t,  $J$  = 7, 2H), 4.12 (q,  $J$  = 7, 2H), 2.82 (t,  $J$  = 7.8, 2H), 2.10–2.21 (m, 2H), 1.46 (t,  $J$  = 7, 3H). Furthermore, the thermal decomposition point of the ionic liquid was determined by TGA (Perkin–Elmer TGA Pyris1 instrument, 10 °C min<sup>−1</sup> heating rate under nitrogen) to be 235 °C.
7. (a) Wasserscheid, P.; Van Hal, R.; Bösmann, A. *Green Chem.* **2002**, *4*, 400–404; (b) To confirm the hydrolysis stability of TISC, 5 g of TISC and 5 g of water were heated to 80 °C. Sample was taken at 15 min intervals and the pH value of the solution was checked with a pH indicator from Shanghai. No decrease of pH value was determined during 6 h, indicating that TISC did not hydrolyze.
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