# 1,1'-Bis-methyl-3, 3-methylenebisimidazolium dichloride as an efficient phase transfer catalyst for ring opening of epoxides using SCN<sup>-</sup> and N<sub>3</sub><sup>-</sup> in water Soheil Sayyahi<sup>a</sup>\*, Hadis Mohammad Rezaee<sup>b</sup>, Fatemeh Sharifat Khalfabadi<sup>b</sup> and

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An efficient synthesis of  $\beta$ -azido alcohols and  $\beta$ -hydroxy thiocyanates has been achieved by ring opening of epoxides using 1,1'-bis-methyl-3, 3-methylene-bisimidazolium dichloride as a phase transfer catalyst at room temperature in water. The reaction is regioselective and afforded the corresponding products in moderate to excellent yields.

Keywords: ionic liquid, ring opening reaction,  $\beta$ -azido-alcohols,  $\beta$ -hydroxy thiocyanates

In synthetic chemistry, ionic liquids (ILs) or molten salts are an interesting group of chemicals, composed of anions and cations, either of which may interact with solutes and therefore significantly affect the outcome of reactions. They have some special properties, such as low vapour pressure, ability to dissolve a wide range of organic, inorganic and organometallic compounds, thermal stability, non-flammability and wide electrochemical stability.<sup>1-5</sup>

Phase transfer catalysts (PTC) are powerful reagents in chemical transformations, the characteristics of which include mild reaction conditions, safety, operational simplicity and selectivity.<sup>6,7</sup> One of the essential roles of classical PTC is to transfer an inorganic reagent from the aqueous phase into the organic phase, thus enabling the organic substrate to react with the transferred ion and form the product in the organic phase reaction. Recently, ILs have assumed this aspect as a phase transfer or anion exchange catalyst.<sup>8–10</sup>

In continuing our efforts to develop and introduce new phase transfer catalyst for organic transformation,<sup>11-14</sup> we describe here the application of 1,1'-bis-methyl-3,3'-methylene-bisimid-azolium dichloride as a PTC for ring opening of epoxides in aqueous media.

## **Results and discussion**

Nucleophilic addition to epoxides plays a pivotal role in the stereoselective preparation of 1,2-disubstituted products.<sup>15</sup> Azido-alcohols are versatile intermediates in organic synthesis since they are very important precursors of  $\alpha$ -amino alcohols and vicinal diamines in the chemistry of carbohydrates, nucleosides, lactams, and oxazolines.<sup>16,17</sup> Thiocyanates are also useful intermediates in agricultural, pharmaceutical and synthetic chemistry.<sup>18,19</sup> Unfortunately, some of the synthetic methods available for the synthesis of azidohydrins or thiocyanohydrins suffer from disadvantages such as long reaction times, use of volatile organic solvents and expensive reagents, low regioselectivity and high temperature reaction conditions.<sup>14,20,21</sup>

As a starting point, the ionic liquid 1,1'-bis-methyl-3,3methylene-bisimidazolium dichloride was synthesised by microwave irradiation of 1-methylimidazole and dry dichloromethane under reflux condition for 15 min (Scheme 1). This ionic liquid has been investigated for the ring opening of a variety of epoxides with the N<sub>3</sub> and SCN anions, giving  $\beta$ -azido alcohols and  $\beta$ -hydroxy thiocyanates, respectively.

In order to evaluate catalytic activity of 1,1'-bis-methyl-3, 3-methylene-bisimidazolium dichloride, reactions between styrene oxide and ammonium thiocyanate were carried out in water at room temperature. The best results were obtained with 1 mmol of the epoxide, 3 mmol NH<sub>4</sub>SCN and 0.5 g of the ionic liquid. Various aliphatic/aromatic epoxides have been used as substrates to react under the optimised reaction condition. The results are summarized in Table 1, which shows that the ionic liquid operates effectively, with excellent yield for most reactions. In all cases, a very clean reaction was observed and careful examination of the 'H NMR spectra of the crude products clearly indicated the formation of only one regioisomer in each case.

In the <sup>1</sup>H NMR spectra of cyclic epoxides such as cyclohexene oxide, the coupling constant of the ring protons adjacent to the –SCN and –OH groups clearly suggested their trans configuration ( ${}^{3}J_{12} = 15$  Hz).

It is generally accepted that the epoxide ring-opening reaction proceeds under neutral or basic conditions via  $S_N 2$  mechanism giving inversion at the attacked C atom, generally the less substituted one and furnishing 1,2- disubstituted products with a *trans* or *anti* relationship of the nucleophile to the oxygen leaving group (entries 2a–7b). In styrene oxide (entries 1a–1b), the positive charge on the oxygen appears to be localised on the more highly substituted benzylic carbon leading to the major product.

It is noteworthy that no evidence for the formation of sideproduct such as diol or thiirane was observed and the products were obtained in pure form without further purification.

In summary, we have developed a novel, efficient and regioselective ring opening of epoxides that with SCN<sup>-</sup> or  $N_3^-$ 



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Table 1 Ring opening of epoxides with NH<sub>4</sub>SCN and NaN<sub>3</sub>



<sup>a</sup> Products were identified by comparison of their physical and spectroscopic data with those of authentic samples.<sup>11,19,21-23</sup> <sup>b</sup>Isolated yields.

as nucleophiles in the presence of 1,1'-bis-methyl-3, 3'-methylenebisimidazolium dichloride. Shorter reaction times, simplicity in operation, the low cost of reagents and high yields of products can be considered as an advantage of this method.

### Experimental

Chemical were purchased from Aldrich and Merck Chemical companies and used without further purification. The synthesis of the IL was carried out in a microwave oven with a 2500 W power (MicroSynth, Milestone) equiped with a condenser. Products were characterised by comparison of their physical data, IR and 'H NMR spectra with known samples. NMR spectra were recorded in CDCl<sub>3</sub> or DMSO on a Bruker Advance DPX 400 MHz instrument spectrometer using TMS as an internal standard. IR spectra were recorded on a BOMEM MB-Series 1998 FT-IR spectrometer. The purity of the products and reaction monitoring were followed by TLC on silica gel polygram SILG/UV 254 plates.

Synthesis of 1,1'-bis-methyl-3, 3-methylenebisimidazolium dichloride A mixture of 1-methylimidazole (0.06 mol, 5.0 g) and dichloromethane (0.03 mol, 2.54 g) was placed in a 50 mL round-bottomed flask equipped with a magnetic stirrer and subjected to microwave irradiation (200W) under reflux condition for 15 minutes. After cooling to room temperature, the precipitate was filtered off and washed twice with 10 mL of dry THF. After drying for 12 h under vacuum at 80 °C, the expected ionic liquid was obtained as white solid; Yield 48%; m.p. 73–75 °C; <sup>1</sup>H NMR (400 MHz, DMSO- $d_6$ , 25 °C):  $\delta$  3.90 (6H, s, 2NCH<sub>3</sub>), 6.86 (2H, s, NCH<sub>2</sub>), 7.81 (2H, s, 2NCH), 8.22 (2H, s, 2NCH), 9.80 (2H, s, 2NCHN) ppm. <sup>13</sup>C NMR (100 MHz, DMSO- $d_6$ , 25 °C):  $\delta$  36.65 (NCH<sub>3</sub>), 58.04 (NCH<sub>2</sub>N), 122.49 (NCH), 124.64 (NCH) 138.62 (NCHN) ppm. Analyses: Calcd for C<sub>9</sub>H<sub>14</sub>Cl<sub>2</sub>N<sub>4</sub>: C, 43.39; H, 5.66; N, 22.49. Found: C, 43.27; H, 5.70; N, 22.61%.

#### General experimental procedure

 $NH_4SCN$  or  $NaN_3$  (3 mmol)was added to the suspension of an epoxide (1 mmol) and 1, 1'-Bis-methyl-3, 3'-methylene-bisimidazolium dichloride (0.5 g) in water (5.0 mL). The mixture was stirred at room temperature for the time shown in Table 1. The reaction was monitored by TLC (*n*-hexane: ethyl acetate; ratio=5:1). After the reaction was complete, the product was extracted with EtOAc (3 × 10 mL). The organic phase was collected and washed with water; dried over  $Na_2SO_4$ , and evaporated *in vacuo* to give desired product.

2-Azido-2-phenyl-1-ethanol (1a): IR ( $v_{max}$ /cm<sup>-1</sup>): 3373 (OH), 2102 (N<sub>3</sub>). <sup>1</sup>HNMR (400 MHz, CDCl<sub>3</sub>):  $\delta$  = 3.37 (1H, s, OH), 3.74 (2H, m, CH<sub>2</sub>), 4.65–4.69 (1H, m, CH), 7.34–7.44 (5H, m, ArH) ppm. <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>):  $\delta$  = 66.37 (CHN<sub>3</sub>), 68.03 (CH<sub>2</sub>OH), 127.49 (m-CH), 128.46 (*o*-CH), 128.61 (*p*-CH), 136.47 (C) ppm.

2-Hydroxy-1-phenylethyl thiocyannate (**1b**): IR ( $v_{max}$ cm<sup>-1</sup>): 3419 (OH), 2151 (SCN); <sup>1</sup>HNMR (400 MHz, CDCl<sub>3</sub>):  $\delta$  = 4.15–4.32 (1H, m, CHSCN), 4.42 (1H, m, CH<sub>2</sub>), 4.62 (1H, m, CH<sub>2</sub>), 4.85 (1H, s, OH), 7.32–7.52 (5H, m, ArH) ppm. <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>):  $\delta$  = 46.34 (CH), 59.70 (CH<sub>2</sub>OH), 110.58 (SCN), 128.57 (*m*-CH), 129.83 (*p*-CH), 129.94 (*o*-CH), 137.43 (C) ppm.

3-Phenoxy-2-hydroxypropyl thiocyanate (**2b**): IR ( $\nu_{max}$ /cm<sup>-1</sup>): 3435 (OH), 2156 (SCN); <sup>1</sup>HNMR (400 MHz, CDCl<sub>3</sub>):  $\delta$  = 3.30 (2H, d, CH<sub>2</sub>SCN), 3.78 (1H, s, OH), 4.15 (2H, d, OCH<sub>2</sub>), 4.29 (1H, m, CHOH), 6.95 (2H, m, ArH), 7.02 (1H, m, ArH), 7.28 (2H, m, ArH) ppm. <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>):  $\delta$  = 37.4 (CH<sub>2</sub>SCN), 68.1 (CHOH), 69.5 (OCH<sub>2</sub>), 113.0 (SCN), 114.6 (*o*-CH), 121.3 (*p*-CH), 129.9 (*m*-CH), 158.5 (C) ppm.

3-Allyloxy-2-hydroxypropyl thiocyanate (**3b**): IR ( $v_{max}$ /cm<sup>-1</sup>): 3440 (OH), 2156 (SCN); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta = 3.04-3.24$  (3H, m, OH, CH<sub>2</sub>SCN), 3.53 (2H, d, OCH<sub>2</sub>), 4.05 (3H, m, OCH<sub>2</sub>CHOH), 5.19–5.29 (2H, m, =CH<sub>2</sub>), 5.87 (1H, m, =CH) ppm. <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>):  $\delta = 37.3$  (CH<sub>2</sub>SCN), 69.2 (CH<sub>2</sub>O), 71.1 (CHOH), 71.6 (OCH<sub>2</sub>), 113.1 (SCN), 117.5 (CH2=), 133.7 (=CH) ppm.

*1-Azido-3-butoxypropan-2-ol* (**5a**): IR ( $v_{max}$ /cm<sup>-1</sup>): 3445 (OH), 2102 (N<sub>3</sub>); <sup>1</sup>HNMR (400 MHz, CDCl<sub>3</sub>):  $\delta = 0.87$  (3H, t, CH<sub>3</sub>), 1.31–1.35 (2H, m, CH<sub>2</sub>), 1.50–1.53 (2H, m, CH<sub>2</sub>), 3.14 (1H, s, OH), 3.30–3.32 (2H, m, CH<sub>2</sub>N<sub>3</sub>), 3.39–3.44 (4H, m, CH<sub>2</sub>OCH<sub>2</sub>), 3.87 (1H, m, CHOH) ppm. <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>):  $\delta = 13.78$  (CH<sub>3</sub>), 19.16 (CH<sub>2</sub>), 30.74 (CH<sub>2</sub>), 53.52 (CH<sub>2</sub>N<sub>3</sub>), 69.74 (CH<sub>2</sub>O), 70.59 (CHOH), 70.71 (OCH<sub>2</sub>CH) ppm.

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