

[Bmim]PF₆: A Novel and Recyclable Ionic Liquid for Conversion of Oxiranes to Thiiranes in Aqueous Media

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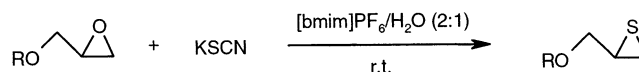
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Abstract: A variety of epoxides respond rapidly with potassium thiocyanate in [bmim]PF₆-H₂O (2:1) solvent system at room temperature under mild and convenient conditions to produce the corresponding thiiranes in high to quantitative yields. Enhanced rates, improved yields, and recyclability of ionic liquids are the remarkable features observed in ionic liquids (ILs). The use of ionic liquids for this transformation avoids the use of heavy metal halides as promoters and chlorinated hydrocarbons as solvents. The ionic liquid was recycled in five to six subsequent runs with gradual decrease in activity.

Epoxides are well-known carbon electrophiles capable of reacting with various nucleophiles, and their ability to undergo regioselective ring-opening reactions contributes largely to their synthetic value.¹ The epoxide ring opening with certain nucleophiles is generally carried out using either acid or base catalysis to produce ring-opened products. A variety of methods have been developed for the preparation of thiiranes.² One of the most straightforward synthetic procedures for the preparation of thiiranes is the condensation of oxiranes with inorganic thiocyanates such as potassium and ammonium thiocyanates³ or thiourea in water or in aqueous alcohols.⁴ Potassium thiocyanate has been the most widely used reagent for this transformation. Other reagents such as phosphine sulfide,⁵ 3-methylbenzothiazol-2-thione,⁶ and dimethylthioformamide⁷ in the presence of trifluoroacetic acid have been reported to produce thiiranes from oxiranes. However, many of these methods often involve the use of strongly acidic or oxidizing conditions, extended reaction times, and high-temperature reaction conditions

SCHEME 1



and also entail undesirable side reactions due to the rearrangement or polymerization of oxiranes, resulting in low yields of thiiranes especially in case of cyclohexene episulfide, styrene episulfide, and other higher thiiranes. Furthermore, most of these methods are of limited synthetic scope when applied to multifunctional compounds. Since organic sulfur compounds have become increasingly useful and important in organic synthesis, the development of convenient and practical methods for the preparation of thiiranes, especially those that carry acid-labile functional groups, are desirable.

The toxic and volatile nature of many organic solvents, particularly chlorinated hydrocarbons, that are widely used in organic synthesis have posed a serious threat to the environment. Consequently methods that successfully minimize their use are the focus of much attention. In this respect, ionic liquids are attracting growing interest as alternative reaction media for various chemical and biotransformations.⁸ Ionic liquids have emerged as a set of green solvents with unique properties such as tunable polarity, high thermal stability, immiscibility with a number of organic solvents, negligible vapor pressure, and recyclability. Their high polarity and ability to solubilize both inorganic and organic compounds can result in enhanced rates of chemical processes and can provide higher selectivities compared to conventional solvents. Room temperature ionic liquids, especially those based on the 1-*n*-alkyl-3-methylimidazolium cation, have shown great promise as an attractive alternative to conventional solvents. One of several advantages of ionic liquids is that they are environmentally benign since they have no detectable vapor pressure. As a result of their green credentials and potential to enhance rates and selectivities, ionic liquids are finding increasing applications in organic synthesis.^{9,10} Furthermore, there are no examples on the use of ionic liquids for the conversion of epoxides to episulfides.

We herein report the use of ionic liquids for the synthesis of episulfides from oxiranes and potassium thiocyanate under mild and neutral conditions. Initially, we have carried out the experiment with 2-phenoxy-methyloxirane and potassium thiocyanate for 2 h in 1-butyl-3-methylimidazolium hexafluorophosphate-water (2:1) solvent system to afford the corresponding episulfide in 95% yield (Scheme 1). The product was obtained after simple extraction with ether. The remaining ionic liquid was further washed with ether and recycled in subsequent runs without further purification. These results prompted us to extend this process for

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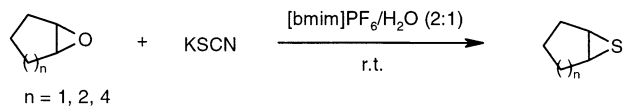
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SCHEME 2



various epoxides. Interestingly, aryl, alkyl, and sterically hindered epoxides reacted smoothly with potassium thiocyanate under these reaction conditions to produce corresponding thiiranes in excellent yields. Similarly, cycloalkyl oxiranes such as cyclopentyl, cyclohexyl, and cyclooctyl oxiranes were converted into the corresponding cycloalkyl thiiranes in high to quantitative yields by using this procedure (Scheme 2). The reaction conditions are mild enough not to induce isomerization of C–C multiple bonds during the preparation of thiiranes bearing allylic and propargylic functionalities and are selective enough to convert oxiranes to thiiranes in the presence of acid-sensitive groups, which are difficult to achieve under conventional conditions where protic acids such as trifluoroacetic acid or strong Lewis acids are employed. Moreover, the reactions are clean and high yielding while no side products or decomposition of the products are observed. Ammonium thiocyanate also works equally well for this conversion. The scope and generality of this process is illustrated with respect to various epoxides and potassium thiocyanate, and the results are presented in the Table 1. Compared to conventional methods, enhanced reaction rates, improved yields, and high selectivity are the remarkable features observed in these ionic liquids. However, in the absence of either ionic liquid or water, the reaction did not yield any product even after a long reaction time. Addition of 1 equiv of water dramatically improved the reaction rates as well as yields. This is probably due to the higher solubility of potassium thiocyanate in water. The solubility of potassium thiocyanate in ionic liquid is very poor, and hence the addition of water increases the solubility of potassium thiocyanate. The reaction, however, was unsuccessful in water alone. Thus, the combination of ionic liquid and water was found to be an efficient reaction media for this transformation. Furthermore, we have performed the reactions in DMF/H₂O and HPF₆/H₂O solvent systems to compare the efficiency of ionic liquids. Although, the reactions did not occur in DMF/H₂O solvent system even under heating conditions, they worked well in HPF₆/H₂O solvent system to produce thiiranes. In this reaction, the efficiency of the ionic liquid was strongly influenced by the nature of the anion. The reactions of various epoxides with thiocyanates were examined in hydrophilic [bmim]-BF₄ and hydrophobic [bmim]PF₆ ionic liquids. Among these ionic liquids, [bmim]PF₆ was found to be superior in terms of conversion. Since the ionic liquids were insoluble in diethyl ether, the products were easily isolated by simple extraction with ether. The rest of the ionic liquid was further washed with diethyl ether and recycled in five to six subsequent runs with gradual decrease in activity. For example, the treatment of styrene oxide with potassium thiocyanate in [bmim]PF₆ ionic liquid afforded 2-phenylthiirane in 93%, 89%, 85%, 81%, and 78% yields over five cycles.¹¹ Even though yields were gradually decreased in runs carried out using recovered ionic liquid, the products obtained were of the same purity as in the first run. In further reactions, the

efficiency of various quaternary ammonium salts was tested. The reactions, however, did not take place at room temperature either in *n*-tetrabutylammonium chloride and water (2:1) or in 1-*n*-butyl-3-methylimidazolium chloride and water (2:1) solvent system; they proceeded at 85 °C under thermal conditions. The lowering of the reaction temperature was detrimental to the efficiency of this procedure. Furthermore, the epoxides did not react with water to produce *vic*-diols under these reaction conditions. The purity of the ionic liquids was determined by comparing their ¹H NMR spectra with commercial samples obtained from Fluka. The purity of [bmim]PF₆ ionic liquid is ≥97.0% (NMR). Although ionic liquids are expensive commercially, they can easily be prepared from an inexpensive and readily available *N*-methyl imidazole, 1-chlorobutane, and hexafluorophosphoric acid or sodium tetrafluoroborate.

In this paper, [bmim]PF₆-H₂O or [bmim]BF₄-H₂O solvent system was proved to be a useful and alternative reaction medium for the synthesis of episulfides from epoxides, avoiding the use of environmentally unfavorable volatile chlorinated hydrocarbons by playing a dual role of solvent as well as catalyst. The substrates show significant increase in reactivity, reducing the reaction times and improving the yields substantially. The simple experimental and product isolation procedures combined with ease of recovery and reuse of this novel reaction media is expected to contribute to the development of green strategy for the preparation of episulfides from epoxides. The use of ionic liquids as reaction media for this transformation avoids the use of moisture-sensitive and heavy metal Lewis acids and also eliminates routine aqueous workup procedures for the isolation of products.

Experimental Section

General Methods. Melting points are uncorrected. TLC was performed using precoated silica gel 60 F₂₅₄ (0.25 mm) glass plates. Chromatography was performed using silica gel (100–200 mesh). IR spectra were recorded neat on a refractive spectrophotometer. ¹H NMR spectra were recorded in CDCl₃ at 200 MHz. Chemical shifts are given in ppm with respect to internal TMS, and *J* values are quoted in Hz. Mass spectra were recorded at 70 eV. Epoxides were either purchased commercially or synthesized as reported in the literature.¹² 1-Butyl-3-methylimidazolium tetrafluoroborate ([bmim]BF₄) and 1-butyl-3-methylimidazolium hexafluorophosphate ([bmim]PF₆) ionic liquids were prepared according to the procedures reported previously in the literature.¹³







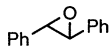
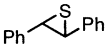




General Procedure for Conversion of Epoxide to Episulfide. Epoxide (1 mmol) and potassium thiocyanate (1 mmol) in 1-butyl-3-methylimidazolium hexafluorophosphate (2 mL) and water (1 mL) were stirred at room temperature for an appropriate time (see Table 1). After completion of the reaction, as indicated by TLC, the reaction mixture was washed with diethyl ether (3 × 10 mL). The combined ether extracts were concen-

(11) The continual reuse of [bmim]BF₄ and [bmim]PF₆ ionic liquids may cause the liberation of most hazardous HF. Therefore, these BF₄ and PF₆ ionic liquids should be recycled with the utmost care. After three to four subsequent runs, the ionic liquid was diluted with water and extracted with ethyl acetate and the extracts were dried at 80 °C under reduced pressure for reuse in further reactions.

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TABLE 1. Conversion of Oxiranes to Thiiranes in 1-Butyl-3-methylimidazolium Ionic Liquids

entry	epoxide 1	product ^a 2	Conversion (%) ^b	[bmim]PF ₆ -H ₂ O		[bmim]BF ₄ -H ₂ O	
				Time (h)	Yield (%) ^c	Time (h)	Yield (%) ^c
a			98	3.0	95	4.5	87
b			95	5.0	87	6.0	81
c			97	3.5	90	5.5	85
d			100	4.0	92	5.0	88
e			99	3.0	93	5.0	89
	R = phenyl	R = Phenyl					
f	R = CH ₂ Cl	R = CH ₂ Cl	97	3.5	91	4.5	80
g	R = n-hexyl	R = n-hexyl	99	4.0	92	6.5	87
h			100	3.5	95	4.5	91
	R = phenyl	R = Phenyl					
i	R = allyl	R = allyl	99	3.0	92	5.0	85
j	R = n-butyl	R = n-butyl	97	4.5	90	6.0	87
k	R = p-tert-Bu-phenyl	R = p-tert-Bu-phenyl	100	4.0	89	5.5	83
l	R = p-Cl-phenyl	R = p-Cl-phenyl	100	3.5	96	4.0	85
m	R = p-MeO-phenyl	R = p-MeO-phenyl	100	3.0	92	5.5	89
n	R = benzoyl	R = benzoyl	99	5.0	85	7.0	85
o	R = p-Me-phenyl	R = p-Me-phenyl	100	4.5	95	5.5	90

^a All products were reported previously in the literature.¹⁴ ^b Conversions were determined by GC analysis. ^c Yield refers to the isolated pure products after column chromatography.

trated in vacuo, and the resulting product was directly charged on a small silica gel column and eluted with a mixture of ethyl acetate and *n*-hexane (2:8) to afford pure episulfide. The rest of the ionic liquid was further washed with ether and recycled in subsequent runs. The products were characterized by comparison of their NMR, IR, MS, TLC, mixed TLC analysis, and physical data with authentic samples. The spectral data of all products other than **2n** were identical with those of authentic samples.¹⁴ Spectroscopic data for the product 2-phenylcarbonyloxymethylthiirane (**2n**): liquid; IR (KBr) ν 2927, 1720, 1606, 1450, 1316, 1271, 1160, 1109, 1027, 711 cm⁻¹; ¹H NMR (200 MHz, CDCl₃) δ 2.38 (d, 1H, *J* = 6.5 Hz), 2.58 (d, 1H, *J* = 6.5 Hz), 3.20–3.29 (m, 1H), 4.29–4.50 (m, 2H), 7.40–7.60 (m, 3H), 8.10 (d, 2H, *J* = 8.0 Hz); ¹³C NMR (50 MHz, CDCl₃) δ 23.8, 30.8,

68.8, 128.4, 129.8, 133.1, 165.9; EIMS *m/z* 194 M⁺, 170, 154, 139, 133, 117, 103, 80, 69, 56, 44. Anal. Calcd for C₁₀H₁₀O₂S (194.25): C, 61.83; H, 5.19; S, 16.50. Found: C, 61.85; H, 5.20; S, 16.51.

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