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# 2-Hydroxy-*N*,*N*,*N*-tributylethanaminium thiocyanate as solvent and reagent for the preparation of alkyl thiocyanates

Farajollah Mohanazadeh[a,*] and Magid Aghvami[b]

[a] *Department of Chemistry, Iranian Research Organization for Science and Technology, Tehran, Iran*
[b] *Department of Chemistry, Tarbiat Moalem University, Tehran, Iran*

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**Abstract**—2-Hydroxy-*N*,*N*,*N*-tributylethanaminium thiocyanate was utilized as both solvent and reagent for the conversion of alkyl halides to the corresponding alkyl thiocyanates in good yields under mild conditions.

Alkyl thiocyanates[1] have found a wide variety of applications as insecticides,[2] biocidal,[3] antiasthmatic,[4] vulcanization accelerators,[5] and starting materials for the preparation of heterocycles.[6] Moreover, thiocyanates isomerize on warming to isothiocyanates. A number of methods are available for the preparation of alkyl thiocyanates, such as, displacement of leaving groups with thiocyanate ions (KSCN,[7] NaSCN,[7] $Zn(SCN)_2$,[7] $NH_4SCN$,[8] $Me_3SiNCS$,[9] $Me_3SiNCS/TiCl_4$,[10] $Me_3SiNCS/Bu_4NF$.[11]). Thiocyanates can also be obtained from alcohols,[12] silyl ethers[13], or amines.[14] As the thiocyanate anion is ambidentate, the reaction can give mixtures of thiocyanates and isothiocyanates, or can proceed selectively to either isomer. Though some of the above mentioned methods provide good yields of alkyl thiocyanates, they also involve the use of hazardous or explosive[15] reagents. Additionally, the thiocyanate group is unstable when heated or submitted to acidic conditions. Thus, the development of an efficient, safe, and environmentally friendly method for the preparation of alkyl thiocyanates is an important challenge.

Ionic liquids have attracted extensive research interest in recent years as environmentally benign solvents due to their favorable properties like non-flammability, negligible vapor pressure, reusability, and high thermal stability.[16] Another important feature of ionic liquids is their design, miscibility with water or organic solvents can be tuned through side-chain length on the cation and choice of anion. Furthermore, they can be functionalized to act as acids, bases or ligands. Their high polarity and ability to solubilize both organic and inorganic compounds can result in enhanced reaction rates and can provide higher selectivity compared to conventional solvents.

In this Letter, we report the use of a new task-specific ionic liquid, 2-hydroxy-*N*,*N*,*N*-tributylethanaminium thiocyanate **1**, for the synthesis of alkyl thiocyanates from alkyl halides under mild and neutral conditions (Scheme 1). 2-Hydroxy-*N*,*N*,*N*-tributylethanaminium bromide **2**[17] (Scheme 1) was obtained quantitatively from reaction of tributylamine and 2-bromoethanol at 120 °C for 6 h. 2-Hydroxy-*N*,*N*,*N*-tributylethanaminium thiocyanate[18] (Scheme 1, **1**) was prepared by reaction of compound **2** and KSCN in acetone. Ionic liquid **1** is soluble in chloroform, dichloromethane, acetone, and ethanol, but is not soluble in water, ether, and hexane. It is very stable at room temperature and can be stored as a bench top reagent for months without any appreciable change in its reactivity.

In a typical procedure, alkyl halide (10 mmol) and ionic liquid (13 mmol) were mixed at room temperature or at

$$n\text{-Bu}_3\text{N} + \text{BrCH}_2\text{CH}_2\text{OH} \xrightarrow[6\ \text{h}]{120\ ^{\circ}\text{C}} n\text{-Bu}_3\text{N}^+\text{CH}_2\text{CH}_2\text{OH Br}^- \quad \mathbf{2}$$

$$n\text{-Bu}_3\text{N}^+\text{CH}_2\text{CH}_2\text{OH Br}^- \xrightarrow[\text{acetone}]{\text{KSCN}} n\text{-Bu}_3\text{N}^+\text{CH}_2\text{CH}_2\text{OH NCS}^- \quad \mathbf{1}$$

**Scheme 1.** Preparation of ionic liquid 1.

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*Keywords*: Ionic liquids; Alkyl thiocyanates; Alkyl halides.

[*] Corresponding author. Tel.: +98 21 88838324; fax: +98 21 88212026; e-mail: mohannazadeh@irost.org

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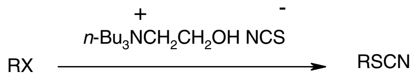
**Table 1.**



$$RX \xrightarrow{n\text{-}Bu_3\overset{+}{N}CH_2CH_2OH\ \overset{-}{NCS}} RSCN$$

| Entry | Alkyl halide | Product | Time (min) | Yield[a] (%) |
|---|---|---|---|---|
| 1 | Benzyl bromide | Benzyl thiocyanate | 45 | 99[b] |
| 2 | Benzyl chloride | Benzyl thiocyanate | 60 | 96[b] |
| 3 | 4-Cyanobenzyl bromide | 4-Cyanobenzyl thiocyanate | 45 | 98[b] |
| 4 | 4-Methylbenzyl bromide | 4-Methylbenzyl thiocyanate | 60 | 95[b] |
| 5 | 1-Phenylethyl bromide | 1-Phenylethyl thiocyanate | 60 | 95[b] |
| 6 | Phenacyl bromide | Phenacyl thiocyanate | 45 | 99[b] |
| 7 | 2-*iso*-Pentenyl bromide | 2-*iso*-Pentenyl thiocyanate | 120 | 92[b] |
| 8 | *n*-Propyl bromide | *n*-Propyl thiocyanate | 180 | 95[c] |
| 9 | *n*-Pentyl bromide | *n*-Pentyl thiocyanate | 180 | 96[c] |
| 10 | 2-Hydroxyethyl bromide | 2-Hydroxyethyl thiocyanate | 180 | 81[c] |
| 11 | 2-Propyl bromide | 2-Propyl thiocyanate | 240 | 91[c] |
| 12 | 2-Cyclohexenyl bromide | 2-Cyclohexenyl thiocyanate | 360 | 58[c] |
| 13 | Cyclohexyl bromide | Cyclohexyl thiocyanate | 360 | 41[c] |

[a] Comparison of spectral data (IR, NMR) and thin layer chromatography with authentic samples confirmed the structures and purities of the reported thiocyanates.

[b] Reaction conducted at room temperature.

[c] Reaction conducted at 45 °C.

45 °C for the time specified in Table 1. On completion, ether (20 mL) was added, the ethereal layer separated, washed with water (10 mL), dried over $Na_2SO_4$, and filtered. The filtrate was evaporated to leave the crude product. In most cases (Table 1, entries 1–11), the crude product was highly pure (>98% as confirmed by GC). When necessary purification by column chromatography was undertaken (Table 1, entries 12, 13). The bromide salt of the ionic liquid was generated by mixing the separated ionic liquid with 5% HBr for 20 min and then decanting and heating at 80 °C under vacuum for 60 min. Hence, ionic liquid **1** could be recycled following reaction with KSCN/ acetone.

All the reactions reported here were clean as judged by GC, TLC, and NMR analysis of the crude reaction mixture. Although incomplete reactions were observed, analysis of the crude reaction mixtures revealed no by-products other than the desired product and unreacted starting material.

In conclusion, a new procedure using the easily accessible and inexpensive ionic liquid, 2-hydroxy-*N*,*N*,*N*-tributylethanaminium thiocyanate, as reagent and solvent for the preparation of alkyl thiocyanates from alkyl halides has been described. This method offers marked improvements with regard to operational simplicity, high isolated yields of products, and mild and neutral reaction conditions.

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17. 2-Hydroxy-*N*,*N*,*N*-tributylethanaminium bromide **2**: Tributylamine (9.25 g, 0.05 mol) and 2-bromoethanol (6.25 g, 0.05 mol) were mixed at 120 °C for 6 h. The reaction

mixture was washed with ether (2 × 30 mL) and dried in a vacuum oven at 80 °C for 30 min. $^1$H NMR (500 MHz, $CDCl_3$) $\delta$ 0.83 (t, $J = 7.1$ Hz, 9H), 1.3 (m, 6H), 1.5 (m, 6H), 3.2 (m, 6H), 3.4 (t, $J = 7.2$ Hz, 2H), 3.8 (t, $J = 7.2$ Hz, 2H), 6.1 (s, 1H).

18. 2-Hydroxy-*N*,*N*,*N*-tributylethanaminium thiocyanate **1**: 2-Hydroxy-*N*,*N*,*N*-tributylethanaminium bromide **2** (15.5 g, 0.05 mol) and potassium thiocyanate (4.85, 0.05 mol) were mixed in acetone (80 mL). The mixture was stirred at room temperature for 3 h. The precipitated potassium bromide was filtered off and washed with acetone. Evaporation of the combined filtrates under vacuum gave an oily liquid, which was dissolved in $CH_2Cl_2$ (60 mL). The organic layer was washed with water (20 mL), dried over sodium sulfate and the solvent was evaporated under reduced pressure. Ionic liquid **1** was obtained (13.68 g, 95%) as a colorless oily liquid. Anal. Calcd for $C_{15}H_{32}N_2OS$: C, 62.45; H, 11.18; N, 9.71; S, 11.1. Found: C, 62.01; H, 10.42; N, 10.12; S, 10.3. $^1$H NMR (500 MHz, $CDCl_3$) $\delta$ 0.9 (t, $J = 7.2$ Hz, 9H), 1.35 (m, 6H), 1.6 (m, 6H), 3.29 (m, 6H), 3.44 (t, $J = 7.3$ Hz, 2H), 3.9 (t, $J = 7.3$ Hz, 2H), 5.8 (s, 1H).