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Lithium perchlorate-catalyzed regioselective ring-opening of aziridines with potassium thiocyanate

J. S. Yadav,* B. V. Subba Reddy, B. Jyothirmai and M. S. R. Murty

Division of Organic Chemistry, Indian Institute of Chemical Technology, Hyderabad 500 007, India

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Abstract—Aziridines react smoothly with potassium thiocyanate in the presence of a catalytic amount of lithium perchlorate in acetonitrile under mild reaction conditions to afford the corresponding β-aminothiocyanates in high yields and with high regioselectivity. The combination of lithium perchlorate and acetonitrile provides a convenient catalytic medium to perform the reactions under neutral conditions.

Aziridines are well-known carbon electrophiles capable of undergoing reactions with various nucleophiles; this ability to undergo regioselective ring-opening reactions contributes largely to their synthetic value.[1] They are useful precursors for the synthesis of many biologically interesting molecules such as amino acids,[2] heterocycles[3] and alkaloids.[4] In consequence, several methods have been reported for the regioselective ring-opening of aziridines with nucleophiles such as organometallic reagents,[5] silyl nucleophiles,[6] Wittig reagents,[7] amines,[8] halides[9] and alkenes.[10] However, there are no reports on the regioselective ring-opening of aziridines with thiocyanates.

In recent years, $LiClO_4$ in diethyl ether (LPDE) has been utilised as a mild Lewis acid imparting high regio-, chemo- and stereos-selectivity in various organic transformations.[11] $LiClO_4$ in acetonitrile provides a convenient reaction medium to perform reactions under neutral conditions. Furthermore, lithium perchlorate is found to retain its activity even in the presence of amines and also effectively activates nitrogen-containing compounds such as imines.[12]

Aminothiocyanates are used as chiral nitrogen, sulfur chelate aprotic ligands in the enantioselective synthesis of optically active alcohols,[13,14] and are widely used for the synthesis of thiazole and benzothiazole heterocycles[15] which exhibit potent pesticidal action.[16]

In this letter, we describe a simple and convenient method for the synthesis of β-aminothiocyanates from aziridines using 10 mol% of lithium perchlorate in acetonitrile under mild reaction conditions (Scheme 1).

In a typical procedure, *N*-tosyl-2-phenylaziridine was treated with potassium thiocyanate in the presence of 10 mol% $LiClO_4$ in acetonitrile at ambient temperature. After completion of the reaction as indicated by TLC, the reaction mixture was quenched with water, extracted with ethyl acetate and purified by column chromatography to afford the corresponding β-aminothiocyanate **2d** in 87% yield. In a similar fashion, several other *N*-tosyl-2-arylaziridines reacted smoothly with potassium thiocyanate to afford the corresponding β-aminothiocyanates in high yields.[17] The *N*-tosyl-2-arylaziridines underwent cleavage by thiocyanate ions with preferential attack at the benzylic position resulting in the formation of products **2** with only trace amounts of **3** (Table 1, entries d–i). However, *N*-tosyl-2-alkylaziridines

Scheme 1.

Keywords: Lithium perchlorate; Aziridines; Potassium thiocyanate; β-Aminothiocyanates.
* Corresponding author. Tel.: +91 40 27193030; fax: +91 40 7160512; e-mail: yadavpub@iict.res.in

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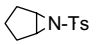
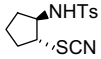
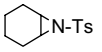
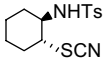
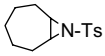
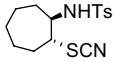
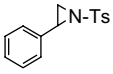
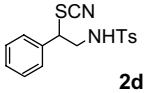
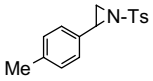
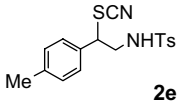
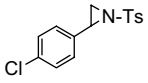
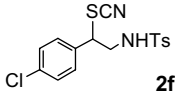
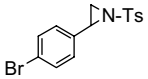
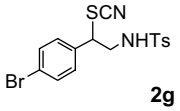
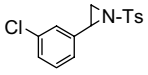
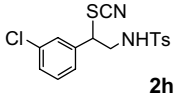
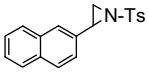
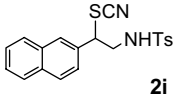
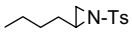
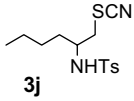
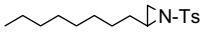
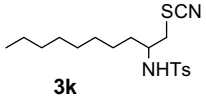
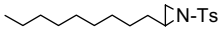
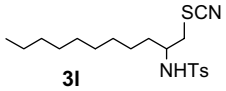
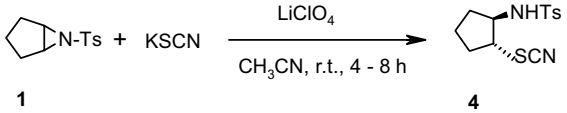
Table 1. $LiClO_4$-catalyzed synthesis of β-aminothiocyanates from aziridines

Entry	Aziridine	Product	Reaction time (h)	Yield[a] (%)	Ratio **2**:**3**
a		 **4a**	6.0	85	—
b		 **4b**	5.0	82	—
c		 **4c**	6.5[d]	75	—
d		 **2d**	4.5	87	92:8[b]
e		 **2e**	5.0	85	90:10[b]
f		 **2f**	5.5	82	87:13[b]
g		 **2g**	6.0	86	85:15[b]
h		 **2h**	5.5	84	89:11[b]
i		 **2i**	6.0	79	85:15[b]
j		 **3j**	7.0	81	16:84[c]
k		 **3k**	8.0	83	18:82[c]
l		 **3l**	7.5	78	20:80[c]

[a] Isolated and unoptimized yield.
[b] Ratio of products from internal attack versus terminal attack.
[c] Ratio of products from terminal attack versus internal attack.
[d] Reaction was carried out at reflux.

afforded predominantly the ring-opened products **3** along with minor amounts of **2** (Table 1, entries j–l). The ratios of products **2** and **3** were determined from the ^1H NMR spectra of the crude products. In all cases, the reactions proceeded efficiently in high yields at ambient temperature. In further reactions, treatment of bicyclic-*N*-tosylaziridines with potassium thiocyanate afforded the corresponding β-aminothiocyanates in good yields (Scheme 2).

Since the bicyclic aziridines were symmetrical, no regioisomers were formed. In the case of bicyclic aziridine **1b**, the stereochemistry of the ring product **4b** was determined as trans from the ^1H NMR coupling constants of the ring hydrogens at δ 3.00 (ddd, $J = 10.0$, 9.5, 4.0 Hz, 1H) for (–CHN) and δ 3.15 (ddd, $J = 9.5$, 9.5, 3.8 Hz, 1H) for (–CHSCN). The two large coupling con-



Scheme 2.

stant values are in accordance with trans-stereochemistry and the small coupling constant values are due to cis-stereochemistry. The method is clean and highly regioselective, affording β-aminothiocyanates in excellent yields. The reaction conditions are mild and no side products or decomposition of the products was observed. All the products were fully characterized by ^{1}H NMR, IR and mass spectroscopic data. In the absence of a catalyst, the reaction did not proceed even at reflux. The efficacy of other Lewis acids such as $Sc(OTf)_3$, $InCl_3$, YCl_3 and $YbCl_3$ was studied for this reaction. Among these catalysts, lithium perchlorate/acetonitrile was found to be an efficient catalytic system in terms of conversion and reaction rates. This is because of the mild Lewis acidity of the lithium ion, which activates the nitrogen atom of the aziridine and facilitates the ring-opening by thiocyanate ions. The scope and generality of this process was illustrated with respect to various aziridines.

In summary, we have described a novel and efficient method for the preparation of β-aminothiocyanates from aziridines and potassium thiocyanate using a catalytic amount of lithium perchlorate under neutral reaction and work-up conditions.

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17. Experimental procedure: a mixture of *N*-tosylaziridine (5 mmol), potassium thiocyanate (7.5 mmol) and $LiClO_4$ (10 mol%) in acetonitrile (10 mL) was stirred at ambient temperature for the appropriate length of time (Table 1). After completion of the reaction as indicated by TLC, the reaction mixture was quenched with water (10 mL) and extracted with ethyl acetate (2×15 mL). The combined organic layers were dried over anhydrous Na_2SO_4, concentrated in vacuo and purified by column chromatography on silica gel (Merck, 100–200 mesh, ethyl acetate–hexane, 2:8) to afford the pure β-aminothiocyanate. Spectroscopic data for product **4b**: liquid, IR (KBr): ν 3260, 2938, 2151, 1598, 1450, 1330, 1160, 1092, 758 cm^{-1}. ^{1}H NMR ($CDCl_3$): 1.25–1.40 (m, 4H), 1.60–1.85 (m, 2H), 2.10–2.38 (m, 2H), 2.43 (s, 3H), 3.00 (ddd, 1H, $J = 10.0$, 9.5, 4.0 Hz), 3.15 (ddd, 1H $J = 9.5$, 9.5, 3.8 Hz), 5.20 (d, $J = 9.5$ Hz, NH), 7.30 (d, 2H, $J = 8.0$ Hz), 7.80 (d, 2H, $J = 8.0$ Hz). EIMS: *m*/*z*: 310 M$^+$, 252, 210, 155, 111 and 91. Anal. Calcd for $C_{14}H_{18}N_2O_2S_2$ (310.43): C, 54.17; H, 5.84; N, 9.02. Found: C, 54.35; H, 5.80; N, 8.93. ^{13}C NMR (proton decoupled, 75 MHz, $CDCl_3$): δ 21.4, 23.4, 23.7, 30.1, 32.2, 56.6, 63.5, 127.0, 129.5, 137.6 and 143.3. Compound **2d**: liquid, IR (KBr): ν 3255, 2095, 1654, 1551, 1152, 1088, 815, 755 cm^{-1}. ^{1}H NMR ($CDCl_3$): δ 2.40 (s, 3H), 3.05–3.10 (m, 1H), 3.15–3.30 (m, 1H), 4.50–4.60 (dd, 1H, $J = 8.5$ and 5.0 Hz), 4.80–4.90 (m, 1H), 7.10–7.35 (m, 7H), 7.80 (d, 2H, $J = 8.0$ Hz). EIMS: *m*/*z*: 332 M$^+$, 260, 184, 155, 135, 104, 91 and 65. Anal. Calcd for $C_{16}H_{16}N_2O_2S_2$ (332.44): C, 57.81; H, 4.85; N, 8.43. Found: C, 57.45; H, 4.92; N, 8.32. ^{13}C NMR (proton decoupled, 75 MHz, $CDCl_3$): δ 21.6, 58.4, 65.4, 127.3, 127.9, 128.6, 128.9, 129.7, 134.1, 136.5 and 145.1. Compound **3l**: liquid, IR (KBr): ν 3306, 2924, 2155, 1613, 1344, 1165, 1090, 837 cm^{-1}. ^{1}H NMR ($CDCl_3$): δ 0.90 (t, 3H, $J = 7.0$ Hz), 1.25–1.50 (m, 14H), 1.80–1.90 (m, 2H), 2.40 (s, 3H), 3.25–3.35 (m, 3H), 4.60 (d, 1H, $J = 9.0$ Hz), 7.40 (d, 2H, $J = 8.0$ Hz), 7.80 (d, 2H, $J = 8.0$ Hz). EIMS: *m*/*z* : 382 M$^+$, 205, 191, 155 and 91. Anal. Calcd for $C_{19}H_{30}N_2O_2S_2$ (382.58): C,59.65; H, 7.90; N, 7.32. Found: C, 59.58; H, 7.85; N, 7.37. ^{13}C NMR (proton decoupled, 75 MHz, $CDCl_3$): δ 14.0, 21.4, 22.5, 25.8, 29.0, 29.1, 29.3, 29.4, 31.7, 31.9, 33.2, 63.5, 127.5, 129.7, 136.0, 144.8.