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Regioselective ring-opening of aziridines with potassium thiocyanate and thiols using sulfated zirconia as a heterogeneous recyclable catalyst ☆, ☆☆

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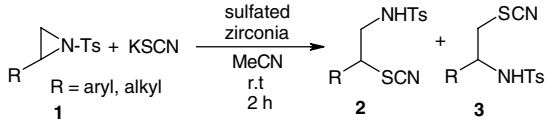
Abstract—Ring-opening of aziridines with potassium thiocyanate and thiols has efficiently been carried out at room temperature in the presence of sulfated zirconia to give the corresponding β-aminothiocyanates and β-aminosulfides, respectively, in high yields within 2 h and with high regioselectivity. The catalyst, a solid acid, functions under heterogeneous conditions.

Aziridines are important precursors for the synthesis of various nitrogen-containing bioactive molecules, such as heterocycles,[1a,b] alkaloids[1c] and amino acids.[1d,e] They behave as carbon electrophiles capable of reacting with different nucleophiles and their ability to undergo regioselective ring-opening reactions contributes mainly to their synthetic utility.[2] Thus, several methods have been developed for the regioselective ring-opening of aziridines with various nucleophiles.[3] While we were developing a novel procedure for cleaving aziridines with KSCN, two methods for such a conversion were reported using $LiClO_4$[4a] and β-cyclodextrin.[4b] The first method required 4–8 h while the second method took 26 h to form the products. The recovery and recycling of the catalysts in these processes were not discussed.

We have observed that the aziridine ring can be opened smoothly with KSCN in the presence of sulfated zirconia to give the corresponding β-aminothiocyanates in high yields (Scheme 1).



Scheme 1.

β-Aminothiocyanates are utilized for the synthesis of thiazoles and benzothiazoles having pesticidal properties.[5] A series of such compounds were prepared[6] using various *N*-tosyl-2-aryl(alkyl) aziridines (Table 1). The conversion required only 2 h at room temperature and the ring-opening of the aziridines took place regioselectively. With *N*-tosyl-2-arylaziridines, products **2** resulting from cleavage at the benzylic position, and with *N*-tosyl-2-alkylaziridines, products **3** resulting from the cleavage at the terminal position were formed predominantly along with minor amounts of the other regioisomers. The ratios of **2** and **3** was determined from ^{1}H NMR spectra of the crude products and the pure compounds were fully characterized from their ^{1}H NMR and mass spectra.[6]

In the case of the symmetrical bicyclic aziridines **4** only products **5** were formed (Scheme 2), the stereochemistry of which were found to be *trans* from ^{1}H NMR spectra.[6]

Sulfated zirconia was also found to be an efficient catalyst for ring-opening of aziridines with thiols to form β-aminosulfides (Schemes 3 and 4).

β-Aminosulfides are useful precursors for the synthesis of various bioactive compounds.[7] Several methods were

Keywords: Aziridine; Ring-opening; Potassium thiocyanate; Thiol; Sulfated zirconia; Regioselectivity.
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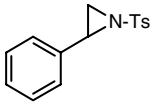
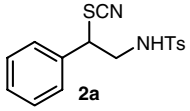
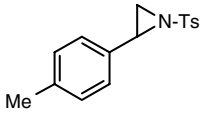
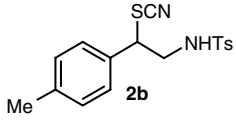
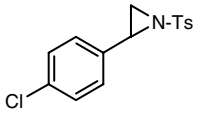
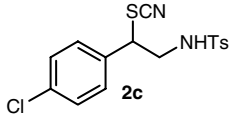
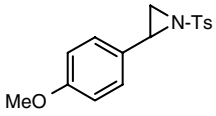
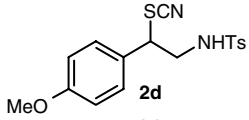
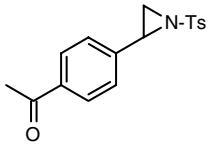
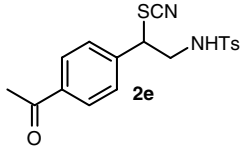
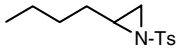
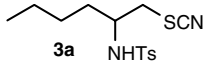
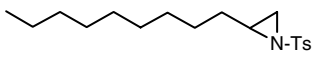
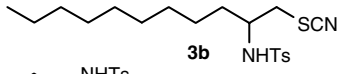
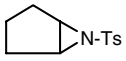
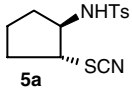
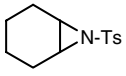
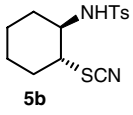
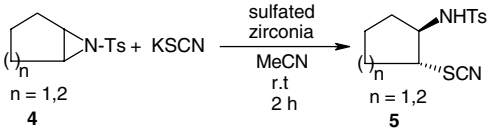
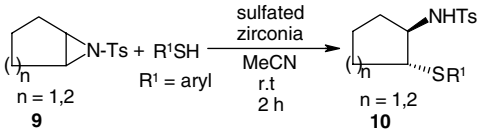
Table 1. Synthesis of β-aminothiocyanates from aziridines using sulfated zirconia[a]

Entry	Aziridine	Product	Isolated yield (%)[b]
1		 **2a**	91 (5)
2		 **2b**	89 (7)
3		 **2c**	84 (9)
4		 **2d**	86 (6)
5		 **2e**	82 (8)
6		 **3a**	85 (9)
7		 **3b**	83 (10)
8		 **5a**	89
9		 **5b**	87

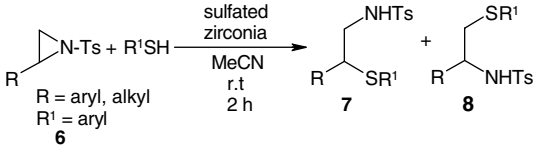
[a] All the products were characterized from spectral (^{1}H NMR and MS) data.
[b] Yields reported in parentheses are for the other regioisomer.



Scheme 2.



Scheme 4.

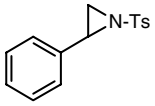
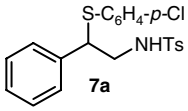
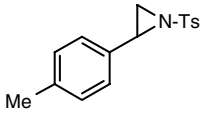
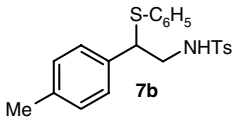
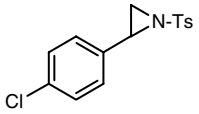
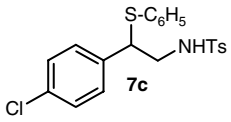
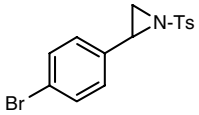
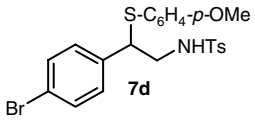
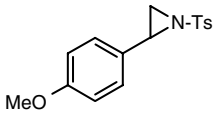
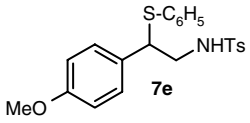
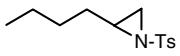
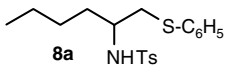
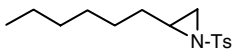
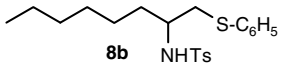
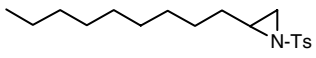
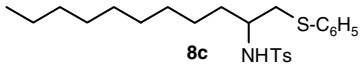
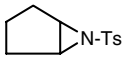
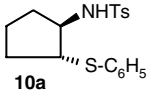
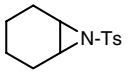
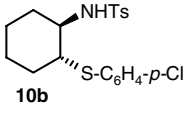


Scheme 3.

developed earlier for the preparation of β-aminosulfides by ring-opening of aziridines with thiols using protic and Lewis acids and bases.[8] However, many of these methods required large excesses of thiols, more than stoichiometric amounts of the catalysts and harsh reaction conditions. The recovery of the catalyst was also a problem.

A series of β-aminosulfides was prepared[6] from different *N*-tosyl-2-aryl(alkyl) sulfides by treatment with various thiophenols in the presence of sulfated zirconia (Table 2). The conversion took place at room temperature and the products were formed in high yields within 2 h. Here also, the ring-opening of the aziridines

Table 2. Synthesis of β-aminosulfides from aziridines using sulfated zirconia[a]

Entry	Aziridine	Product	Isolated yield (%)[b]
1		 **7a**	90 (5)
2		 **7b**	92 (7)
3		 **7c**	89 (9)
4		 **7d**	87 (6)
5		 **7e**	93 (8)
6		 **8a**	84 (7)
7		 **8b**	85 (10)
8		 **8c**	81 (12)
9		 **10a**	91
10		 **10b**	88

[a] All the products were characterized from spectral (^{1}H NMR and MS) data.
[b] Yields reported in parentheses are for the other regioisomer.

occurred with high regioselectivity. *N*-tosyl-2-arylaziridines afforded predominantly products **7** (formed by cleavage at the benzylic position) while *N*-tosyl-2-alkylaziridines gave products **8** (formed by cleavage at the terminal position). The ratios of **7** and **8** were again determined from the ^{1}H NMR spectra of the crude products.

Ring-opening of symmetrical bicyclic aziridines **9** with a thiol afforded only **10** as the products (Scheme 4). The stereochemistry of the products were also found to be *trans* from the ^{1}H NMR spectra.

The catalyst, sulfated zirconia,[9] a solid acid, works under heterogeneous conditions. Over the past few years this catalyst has gained significant attention in laboratories and industry due to its excellent catalytic activity over a wide range of organic syntheses and transformations.[9] The use of conventional protic and Lewis acids pose significant risks in handling, disposal and regeneration. Sulfated zirconia can be easily handled and removed from the reaction mixture. In the case of ring-opening of aziridines with KSCN and thiols the catalyst was recycled three times, its activity gradually decreased for ring-opening with KSCN while no appreciable change in activity was observed for ring-opening with thiols. In the absence of this catalyst cleavage of aziridines did not take place.

In conclusion, we have developed a novel and efficient method for ring-opening of aziridines with KSCN and thiols for the preparation of β-aminothiocyanates and β-aminosulfides using sulfated zirconia under very mild

conditions. The operational simplicity, high yields and regioselectivity and reusability of the catalyst are notable advantages of this method.

Acknowledgement

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6. General procedure for the preparation of β-aminothiocyanates and β-aminosulfides: A mixture of *N*-tosylaziridine (5 mmol), KSCN or thiol (7.5 mmol) and sulfated zirconia (100 mg) was taken in MeCN (10 mL). The mixture was stirred at room temperature (complete conversion was indicated by TLC) and after 2 h the reaction was filtered. The residue was washed with MeCN (2×5 mL) and the catalyst was recovered. The filtrate was concentrated and subjected to column chromatography over silica gel using hexane–EtOAc (4:1) to afford pure β-aminothiocyanate or β-aminosulfide.
The spectral (^{1}H NMR and MS) data of some representative β-aminothiocyanates and β-aminosulfides are given below.
Compound **2c**:[5] ^{1}H NMR (200 MHz, $CDCl_3$): δ 7.75 (2H, d, $J = 8.0$ Hz), 7.34–7.17 (6H, m), 5.12 (1H, m), 4.65 (1H, dd, $J = 8.5$, 5.0 Hz), 3.38 (1H, m), 3.19 (1H, m), 2.46 (3H, s); FABMS: *m*/*z* 369, 367 ($M^{+\cdot}+1$).
Compound **3b**:[4a] ^{1}H NMR (200 MHz, $CDCl_3$): δ 7.78 (2H, d, $J = 8.0$ Hz), 7.42 (2H, d, $J = 8.0$ Hz), 4.62 (1H, d, $J = 7.0$ Hz), 3.31–3.13 (3H, m), 2.41 (3H, s), 1.92–1.83 (2H, m), 1.54–1.28 (14H, m), 0.92 (3H, t, $J = 7.0$ Hz); FABMS: *m*/*z* 383 ($M^{+\cdot}+1$).
Compound **5a**:[4a] ^{1}H NMR (200 MHz, $CDCl_3$): δ 7.73 (2H, d, $J = 8.0$ Hz), 7.29 (2H, d, $J = 8.0$ Hz), 4.55 (1H, br s), 3.19 (1H, ddd, $J = 10.0$, 9.0, 4.0 Hz), 3.01 (1H, ddd, $J = 10.5$, 9.0, 4.0 Hz), 2.42 (3H, s), 1.93–1.78 (2H, m), 1.42–1.35 (2H, m), 1.32–1.22 (2H, m); FABMS: *m*/*z* 297 ($M^{+\cdot}+1$).
Compound **7a**:[8d] ^{1}H NMR (200 MHz, $CDCl_3$): δ 7.64 (2H, d, $J = 8.0$ Hz), 7.38–7.02 (11H, m), 4.60 (1H, t, $J = 7.0$ Hz), 4.14 (1H, t, $J = 7.0$ Hz), 3.30 (2H, t, $J = 7.0$ Hz), 2.42 (3H, s); FABMS: *m*/*z* 420, 418 ($M^{+\cdot}+1$).
Compound **8a**:[8d] ^{1}H NMR (200 MHz, $CDCl_3$): δ 7.62 (2H, d, $J = 8.0$ Hz), 7.28–7.15 (7H, m), 4.68 (1H, d, $J = 7.0$ Hz), 3.30 (1H, m), 3.12 (1H, dd, $J = 10.0$, 4.0 Hz), 2.71 (1H, dd, $J = 10.0$, 7.0 Hz), 2.40 (3H, s), 1.46–1.08 (6H, m), 0.96 (3H, t, $J = 7.0$ Hz); FABMS: *m*/*z* 364 ($M^{+\cdot}+1$).
Compound **10a**:[8e] ^{1}H NMR (200 MHz, $CDCl_3$): δ 7.68 (2H, d, $J = 8.0$ Hz), 7.28–7.19 (7H, m), 5.01 (1H, br s), 3.38 (1H, ddd, $J = 10.5$, 9.5, 4.0 Hz), 3.26 (1H, ddd, $J = 10.0$, 9.5, 4.0 Hz), 2.44 (3H, s), 2.19–2.08 (2H, m), 1.88–1.67 (2H, m), 1.62–1.42 (2H, m); FABMS: *m*/*z* 348 ($M^{+\cdot}+1$).
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