Unusual Cycloaddition Reactions of Substituted-*N*-(arylsulfonyl)aziridines with Aryl and Alkyl Isothiocyanates in the Presence of Sodium Iodide as Catalyst

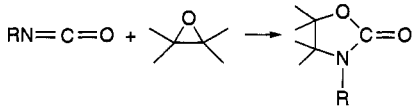
Upender K. Nadir* and Nupur Basu

Department of Chemistry, Indian Institute of Technology Delhi, Hauz Khas, New Delhi 110016, India

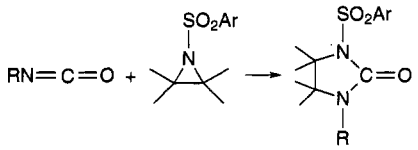
Received March 14, 1994

Introduction

In the reactions of aryl and alkyl isocyanates with oxiranes[1–3] and aziridines[4–7] in the presence of catalysts studied so far, the three-membered ring has been reported to add to the carbon–nitrogen double bond of the isocyanate moiety to give oxazolidones and imidazolidones (eqs 1 and 2).

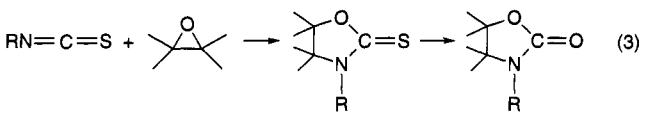


(1)

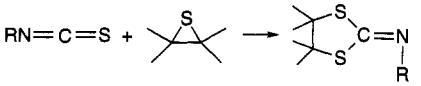


(2)

Interestingly, for reactions of a related heterocumulene system, namely, isothiocyanates, with three-membered heterocyclic ring systems, conflicting behavior has been reported. With oxiranes, addition of the three-membered ring to the carbon–nitrogen double bond results in the formation of an intermediate 2-oxazolidinethione, which in turn gets hydrolyzed to 2-oxazolidone[1] (eq 3). In contrast, with thiiranes the three-membered ring cyclo adds to the terminal carbon–sulfur double bond of the isothiocyanate moiety[8] (eq 4).

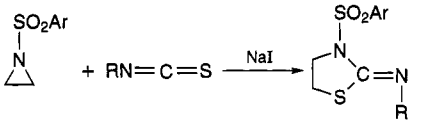


(3)



(4)

However, ring expansion reactions of aziridines with isothiocyanates have received little attention. The only such report,[5] which concerns ring expansion reactions of unsubstituted *N*-(arylsulfonyl)aziridines with isothiocyanates, shows that the three-membered ring adds to the carbon–sulfur double bond of the isothiocyanate moiety (eq 5) to give 2-iminothiazolidines **1**. As substituted aziridines have not been subjected to this type of reaction, it was considered desirable to allow various substituted *N*-(arylsulfonyl)aziridines to react with aryl and alkyl isothiocyanates to determine the exact course of the reaction, to gain an insight into the mechanism of the reaction, and to understand the scope and limitations of the procedure.

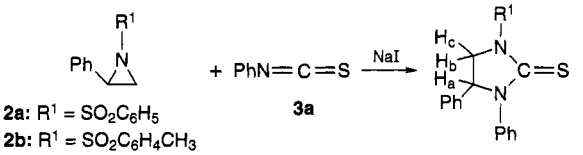


(5)

1

Results and Discussion

The aziridines chosen were *N*-(benzenesulfonyl), *N*-(*p*-toluenesulfonyl), and *N*-(*p*-chlorobenzenesulfonyl)-2-phenylaziridines (**2a–c**) and *trans*-2,3-diphenyl-*N*-(benzenesulfonyl)aziridine (**2d**). The arylsulfonyl group attached to the nitrogen makes these aziridines highly electrophilic, so that attack by the nucleophile is favored.[9] The aziridines were prepared by means of a British patented procedure.[10] These aziridines have been allowed to react with aryl and alkyl isothiocyanates in the presence of sodium iodide as a catalyst. Reactions of phenyl isothiocyanate (**3a**) with aziridines **2a**, **2b**, and **2c** have given 1-(arylsulfonyl)-3,4-diphenyl-2-imidazolidinethiones **4a–c** (eq 6).



(6)

2a: $R^1 = SO_2C_6H_5$
2b: $R^1 = SO_2C_6H_4CH_3$
2c: $R^1 = SO_2C_6H_4Cl$

4a: $R^1 = SO_2C_6H_5$
4b: $R^1 = SO_2C_6H_4CH_3$
4c: $R^1 = SO_2C_6H_4Cl$

The addition of *N*-(arylsulfonyl)-2-phenylaziridines appears to take place at the carbon–nitrogen double bond of the aryl isothiocyanate. The structures proposed for **4a–c** have been established on the basis of IR and ^1H NMR and ^{13}C NMR spectral data, as well as elemental analysis results.

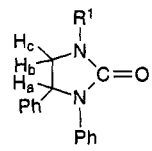
It is worthwhile to mention that on the basis of IR absorptions in the 1632 cm^{-1} region, characteristic of C=N bond, Markov et al.[5] inferred that the reactions of 2,3-unsubstituted 1-(arylsulfonyl)aziridines with phenyl isothiocyanate in the presence of sodium iodide gave 2-iminothiazolidines **1** and suggested that the addition had taken place at the carbon–sulfur double bond (eq 5). The products obtained by us (**4a–c**) however, gave no IR absorption at 1632 cm^{-1}; instead strong absorptions were observed at 1025–1030 and at 1470–1485 cm^{-1}. It is well documented in the literature[11] that for substituted imidazolidinethiones the absorption for C=S appears at 1020–1250 cm^{-1} and that for RN(C=S) appears at 1470–1530 cm^{-1}. The absence of absorption at 1632 cm^{-1} in the spectral data of compounds **4a–c** produced by the

(1) Dyen, M. E.; Swern, D. *Chem. Rev.* **1967**, *67*, 197.
(2) Herweh, J. E.; Foglia, T. A.; Swern, D. *J. Org. Chem.* **1968**, *33*, 4029.
(3) Baba, A.; Fujiwara, M.; Matsuda, H. *Tetrahedron Lett.* **1986**, *27*, 77.
(4) Gulbins, E.; Morlock, R.; Hamann, K. *Liebigs Ann. Chem.* **1966**, *696*, 180.
(5) Markov, V. I.; Daneleiko, D. A. *Zh. Org. Khim.* **1974**, *10*, 1269.
(6) Nadir, U. K.; Basu, N. *Tetrahedron Lett.* **1992**, *33*, 7949.
(7) Nadir, U. K.; Basu, N. *Tetrahedron* **1993**, *49*, 7787.
(8) Ueno, Y.; Nakai, T.; Okawara, M. *Bull. Chem. Soc. Jpn.* **1970**, *43*, 162.
(9) Kozikowski, A. P.; Ishida, H.; Isobe, K. *J. Org. Chem.* **1979**, *44*, 2788. Tseng, C.; Terashima, S.; Yamada, S. *Chem. Pharm. Bull.* **1977**, *25*, 29. Tseng, C.; Terashima, S.; Yamada, S. *Ibid.* **1977**, *25*, 166.
(10) I. C. I. Ltd., B. P. I., 1969, 544, 970; *Chem. Abstr.* **1970**, *72*, 12545q.
(11) Kohn, H.; Cravey, M. J.; Arceneaux, J. H.; Cravey, R. L.; Willcott, M. R. *J. Org. Chem.* **1977**, *42*(6), 941.

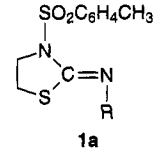
0022-3263/95/1960-1458$09.00/0

reactions of substituted *N*-(arylsulfonyl)aziridines with phenyl isothiocyanate is indeed interesting. That the IR absorption spectrum of the 2-iminothiazolidine **1a**, prepared by us by means of Markov's procedure, did agree with the reported values[5] indicates that substituted and unsubstituted *N*-(arylsulfonyl)aziridines respond differently to treatment with phenyl isothiocyanate in the presence of sodium iodide.

In the ^{13}C NMR spectra, the chemical shifts of the nonaromatic carbon atoms of **4a–c** are nearly identical to those of corresponding carbon atoms of 2-imidazolidinones **5a–c** prepared previously by us.[6] The same is true for the chemical shifts of H_a, H_b, and H_c protons. These results indicate that these carbon and hydrogen atoms are in a similar type of chemical environment in both the cases, which in turn suggests that compounds **4a–c** are 2-imidazolidinethiones rather than 2-iminothiazolidines.



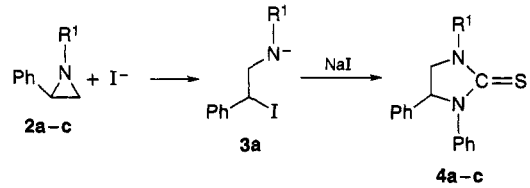
5a: $R^1 = SO_2C_6H_5$
5b: $R^1 = SO_2C_6H_4CH_3$
5c: $R^1 = SO_2C_6H_4Cl$



1a

It is proposed that in this reaction, as in the reaction of *N*-(arylsulfonyl)-2-phenylaziridines with phenyl isocyanate in presence of sodium iodide catalyst,[6] the attack of iodide ion precedes cycloaddition. It has also been established by us that for 2-arylaziridines the iodide attack occurs exclusively at the substituted carbon center of the aziridine ring.[6] On the basis of these facts, a mechanism (Scheme 1) that explains the formation of structures **4a–c** has been proposed.

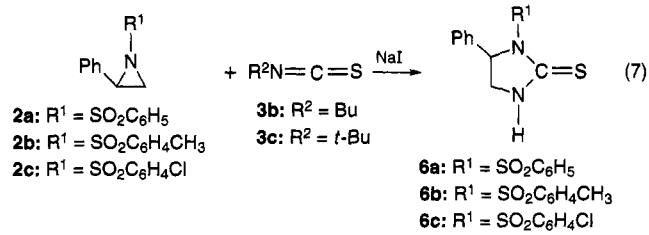
Scheme 1



2a–c **3a** **4a–c**

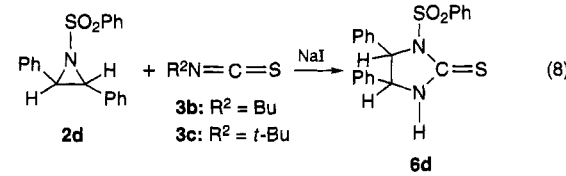
Interestingly, reactions of the same set of aziridines (**2a–c**) with alkyl isothiocyanates in the presence of sodium iodide catalyst gave rise to products that suggested an altogether different mechanism. Reactions of aziridine **2a** with butyl (**3b**) and *tert*-butyl isothiocyanate (**3c**) yielded identical products, 3-(benzenesulfonyl)-4-phenyl-2-imidazolidinethione (**6a**). Similarly, when allowed to react with either isothiocyanate **3b** or **3c**, aziridines **2b** and **2c** gave product **6b** or **6c**, respectively (eq 7). Reaction of **2d** with **3b** or **3c** also gave the same product, **6d** (eq 8).

The structural assignment of compounds **6a–c** was done on the basis of spectral data and elemental analysis results. The data obtained for a typical compound **6c** are discussed below: (i) The ^1H NMR spectrum of **6c** showed three triplets, at δ 3.48 (2H), 4.92 (1H), and 5.1 (1H), as well as aromatic signals at δ 7.30–7.82 (9H). On D_2O exchange, the triplet at δ 3.48 (2H) was reduced to a doublet, and the proton integration remained the same; the signal at δ 4.92 (1H) remained unchanged; and the



2a: $R^1 = SO_2C_6H_5$
2b: $R^1 = SO_2C_6H_4CH_3$
2c: $R^1 = SO_2C_6H_4Cl$
3b: R^2 = Bu
3c: R^2 = *t*-Bu
6a: $R^1 = SO_2C_6H_5$
6b: $R^1 = SO_2C_6H_4CH_3$
6c: $R^1 = SO_2C_6H_4Cl$

(7)



2d **3b**: R^2 = Bu **3c**: R^2 = *t*-Bu **6d**

(8)

signal at δ 5.1 (1H) disappeared. These observations indicate that the compound has an NH group adjacent to a methylene center and that there is a methine center adjacent to a methylene but away from NH. That the off resonance decoupled ^{13}C NMR spectrum showed a doublet and a triplet in the nonaromatic region suggests the presence of methine and methylene carbon centers.

(ii) The ^1H and ^{13}C NMR data of **6c** indicated the absence of either a butyl or a *tert*-butyl group. The fact that reactions of both isothiocyanates **3b** and **3c** with aziridine **2c** gave rise to the same product (**6c**) also suggests that the alkyl group present in the isothiocyanate moiety is displaced in the reaction process.

(iii) The IR spectrum showed absorption at 1350 and 1160 cm^{-1} ($\nu(SO_2)$) and at 3130 cm^{-1} (ν(NH)). These data together with the aromatic proton integration values in the ^1H NMR spectrum indicate that the compound contains both an *N*-arylsulfonyl group and an NH group. Strong absorptions at 1025 and 1475 cm^{-1} indicate the presence of a C=S group and an RN(C=S) linkage, respectively.

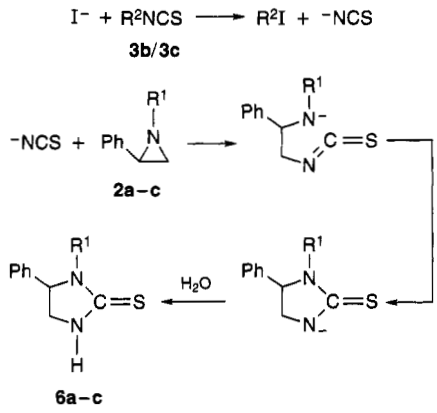
(iv) Mass spectral data and elemental analysis for compound **6c** supported the molecular formula ($C_{15}H_{13}ClN_2O_2S_2$) proposed for the same.

It has already been established by us that the iodide ion opens up 2-arylaziridines at the more substituted carbon atom.[6] The structures of compounds **6a–c** suggest that in this case the 2-arylaziridine (**2a–c**) rings are opened up at the unsubstituted carbon. The obvious conclusion is that they are opened up by a nucleophile other than iodide ion. Since the products indicate the total absence of an alkyl group, it is possible that the isothiocyanate ion generated from reaction of sodium iodide and alkyl isothiocyanate is the only other nucleophilic species available to open the aziridine ring.

To verify this proposition, alkyl isothiocyanates **3b** and **3c** were stirred in THF with sodium iodide. That fractional distillation of the liquid obtained after workup gave butyl iodide, leaving much of alkyl isothiocyanate unreacted, confirmed the generation of isothiocyanate ions. It is well documented[12] that isothiocyanate ions once formed can act as ambident nucleophiles, i.e., that the nucleophile may attack an electrophilic center with either end. On the basis of these observations, a mechanism is proposed in Scheme 2. In support of this mechanism, it was found that aziridine **2a**, when stirred with sodium thiocyanate without sodium iodide catalyst

(12) Fava, A. In *The Chemistry of Organic Sulfur Compounds*; Kharasch, N., Meyers, C. Y., Eds.; Pergamon Press: Norwich, Great Britain, 1996; Vol. 2, Chapter 3.

Scheme 2



or alkyl isothiocyanate, gave, on workup, 2-imidazolidinethione **6a** along with some unreacted aziridine.

Similarly, for reaction with 2,3-diphenylaziridine (**2d**), the isothiocyanate ion, once formed, can attack at any one of the two identically substituted carbon atoms of the aziridine ring and give rise to product **6d**.

However, the reaction of an iodide ion with PhNCS to generate PhI and $^-$NCS is unlikely. Thus, for reactions with PhNCS, aziridine rings **2a–c** are opened up by iodide ion rather than $^-$NCS ion (Scheme 1).

Experimental Section[13,14]

Reaction of Isothiocyanates with Aziridines (General Method). To a stirred solution of aziridine **2** (0.002 mol) and sodium iodide (0.002 mol) in THF was added isothiocyanate **3** (0.002 mol) by syringe at rt. The reaction mixture was stirred at rt for 10 h when **3a** was used ans for 18 h when **3b** and **3c** were used. The solvent was then removed under reduced pressure, and the residue was poured into water and extracted with benzene. The organic layer was washed with 1% $Na_2S_2O_3$(aq) and water and then dried over anhydrous Na_2SO_4. The solvent was evaporated, and the residue was subjected to silica gel column chromatography. Elution with benzene–hexane followed by recrystallization from benzene–petroleum ether gave pure imidazolidinethione. Ether can also be used as the extracting solvent in place of benzene.

1-(Benzenesulfonyl)-3,4-diphenyl-2-imidazolidinethione (4a): yield 41%; mp 166–168 °C; IR (KBr) 1470, 1375, 1340, 1160, 1025 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 3.80 (dd, 1H, J = 5, 9 Hz), 4.30 (t, 1H, J = 9 Hz), 5.20 (dd, 1H, J = 5, 9 Hz), 7.32–8.00 (m, 15H); ^{13}C NMR ($CDCl_3$) δ 49.0 (t), 57.8 (d), 124.2, 126.0, 127.1, 127.9, 132.2, 132.4, 133.8, 135.0, 135.8, 136.5, 137.2, 138.0. Anal. Calcd for $C_{21}H_{18}N_2O_2S_2$: C, 63.95; H, 4.56; N, 7.10. Found: C, 64.15; H, 4.79; N, 7.18.

1-(*p*-Toluenesulfonyl)-3,4-diphenyl-2-imidazolidinethione (4b): yield 39%; mp 176–178 °C; IR (KBr) 1485, 1360, 1340, 1160, 1030 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 2.44 (s, 3H), 3.88 (dd, 1H, J = 5, 9 Hz), 4.31 (t, 1H, J = 9 Hz), 5.20 (dd, 1H, J = 5, 9 Hz), 7.18–8.00 (m, 14H); ^{13}C NMR ($CDCl_3$) δ 21.0 (q), 49.8 (t), 57.8 (d), 124.0, 125.8, 127.3, 127.9, 132.4, 132.6, 133.7, 135.2, 135.6, 136.8, 137.5, 138.0. Anal. Calcd for $C_{22}H_{20}N_2O_2S_2$: C, 64.70; H, 4.90; N, 6.86. Found: C, 64.77; H, 5.15; N, 6.92.

1-(*p*-Chlorobenzenesulfonyl)-3,4-diphenyl-2-imidazolidinethione (4c): yield 38%; mp 182–184 °C; IR (KBr) 1480, 1375, 1350, 1160, 1030 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 3.80 (dd, 1H, J = 5, 9 Hz), 4.32 (t, 1H, J = 9 Hz), 5.22 (dd, 1H, J = 5, 9 Hz), 7.20–7.98 (m, 14H); ^{13}C NMR ($CDCl_3$) δ 49.8 (t), 57.0 (d), 124.4, 125.9, 127.0, 127.6, 131.9, 132.2, 133.5, 135.0, 135.5, 136.7, 137.7, 138.8. Anal. Calcd for $C_{21}H_{17}ClN_2O_2S_2$: C, 58.80; H, 3.96; N, 6.53. Found: C, 59.08; H, 4.07; N, 6.32.

3-(Benzenesulfonyl)-4-phenyl-2-imidazolidinethione (6a): yield 38% when isothiocyanate **3b** was used, 40% when isothiocyanate **3c** was used; mp 112–114 °C; IR (KBr) 3140, 1485, 1350, 1275, 1160, 1028 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 3.48 (t, 2H, J = 7 Hz; on D_2O exchange became d, 2H, J = 6 Hz), 4.92 (distorted t, 2H; on D_2O exchange became sharp t, 1H), 7.32–7.88 (m, 10H); ^{13}C NMR ($CDCl_3$) δ 49.8 (t), 61.0 (d), 127.4, 128.3, 129.4, 130.4, 131.2, 136.2, 137.5, 138.0. Anal. Calcd for $C_{15}H_{14}N_2O_2S_2$: C, 56.60; H, 4.40; N, 8.80. Found: C, 56.58; H, 4.49; N, 8.88.

3-(*p*-Toluenesulfonyl)-4-phenyl-2-imidazolidinethione (6b): yield 39% when isothiocyanate **3b** was used, 42% when isothiocyanate **3c** was used; mp 123–125 °C; IR (KBr) 3130, 1490, 1355, 1160, 1025 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 2.43 (s, 3H), 3.44 (t, 2H, J = 7 Hz; on D_2O exchange became d, 2H, J = 6 Hz), 4.88 (distorted t, 2H; on D_2O exchange became sharp t, 1H), 7.24–7.80 (m, 9H); ^{13}C NMR ($CDCl_3$) δ 21.4 (q), 50.2 (t), 61.8 (d), 127.4, 128.1, 129.3, 130.1, 131.6, 136.8, 137.7, 138.8. Anal. Calcd for $C_{16}H_{16}N_2O_2S_2$: C, 57.83; H, 4.81; N, 8.43. Found: C, 58.09; H, 4.77; N, 8.19.

3-(*p*-Chlorobenzenesulfonyl)-4-phenyl-2-imidazolidinethione (6c): yield 39% when isothiocyanate **3b** was used, 41% when isothiocyanate **3c** was used; mp 130–133 °C; IR (KBr) 3130, 1475, 1350, 1160, 1025 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 3.48 (t, 2H, J = 7 Hz; on D_2O exchange became d, 2H, J = 6 Hz), 4.92 (t, 1H, J = 7 Hz), 5.1 (t, 1H, disappeared on D_2O exchange), 7.30–7.82 (m, 9H); ^{13}C NMR ($CDCl_3$) δ 49.8 (t), 61.8 (d), 128.0, 129.1, 130.6, 131.2, 131.9, 136.6, 137.3, 138.8; MS *m/z* (rel intensity) 352 (M^+), 293, 175, 118 (100), 91, 77. Anal. Calcd for $C_{15}H_{13}ClN_2O_2S_2$: C, 51.06; H, 3.68; N, 7.94. Found: C, 51.28; H, 3.44; N, 7.71.

3-(Benzenesulfonyl)-4,5-diphenyl-2-imidazolidinethione (6d): yield 32% when isothiocyanate **3b** was used, 35% when isothiocyanate **3c** was used; mp 198–200 °C; IR (KBr) 3138, 1475, 1355, 1166, 1028 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 4.84 (dd, 1H, J = 5, 9 Hz; on D_2O exchange became d, 1H, J = 5 Hz), 5.20 (d, 1H, J = 5 Hz), 5.32 (d, 1H, J = 9 Hz, disappeared on D_2O exchange), 7.28–7.88 (m, 15H); ^{13}C NMR ($CDCl_3$) δ 63.8 (d), 66.2 (d), 127.4, 128.1, 128.4, 128.7, 133.5, 137.5, 138.8. Anal. Calcd for $C_{21}H_{18}N_2O_2S_2$: C, 63.95; H, 4.56; N, 7.10. Found: C, 63.69; H, 4.64; N, 7.28.

(13) For details of analytical instruments used, spectral calibrations, and general experimental information, see ref 7.

(14) Benzene and aziridines are potent carcinogens.

JO940408C