Note

Synthesis of 2-iminothiazolidines through reaction of N-arylsulphon酰aziridines with isothiocyanates in the presence of iodide ions

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Reaction of 2-substituted N-arylsulphonylaziridines with isothiocyanates using lithium iodide as a catalyst yields iminothiazolidines. Besides the spectral and analytical data, the structure is also confirmed by X-ray crystallographic data. The amount of recovered aziridines decreased by use of DMF and DMSO, instead of acetone, as solvents. The reaction works well also with benzylic isothiocyanates.

Aziridines, like other three-membered ring heterocycles, are highly strained. As a result, they are susceptible to ring opening reactions, which makes them useful as synthetic intermediates. However their potential for elaboration to five membered heterocycles like imidazolidinones and thiazolidinones etc. has not been studied adequately. In our continuing programme to use aziridines for making four and five membered heterocycles, we have shown that the reaction of 2-substituted N-arylsulphonylaziridines with isocyanates in the presence of iodide ion leads to the formation of the corresponding imidazolidinethiones. With isothiocyanates, imidazolidinethiones are obtained. The regio- and stereo-chemical course of this reaction has been delineated. In the present communication we report the results of our studies to improve the yields of reaction of 2-substituted N-arylsulphonylaziridines with isothiocyanates and to extend its generality.

Results and Discussion

We have previously reported that the reaction of 2-substituted N-arylsulphonylaziridines with phenyl isothiocyanates in the presence of sodium iodide led to the formation of imidazolidinethiones in modest yields. In these reactions about 50% of aziridines remained unreacted. In order to improve yield of imidazolidinethiones, we decided to carry out the reaction in the presence of lithium, potassium and cesium iodides. The recovered unreacted aziridine depended on the type of iodide salt used in these reactions (Table I).

Thus Lil is found to be an efficient catalyst for the above reaction. However the products, formed in 62-68% yield, in case of lithium iodide were found to be the imidazolidinethiones 2a-c rather than the thiazolidinimines 3a-c. The structural assignment was based on spectral data and analytical data (see Experimental Section). The above structure was assigned by converting the aziridines into β-iodophenyl

<table>
<thead>
<tr>
<th>Iodide salts</th>
<th>Yield of unreacted aziridine (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lithium iodide</td>
<td>0</td>
</tr>
<tr>
<td>Sodium iodide</td>
<td>50</td>
</tr>
<tr>
<td>Potassium iodide</td>
<td>65</td>
</tr>
<tr>
<td>Cesium iodide</td>
<td>100</td>
</tr>
</tbody>
</table>

Table I—Reaction of 2-substituted N-arylsulphonylaziridines phenyl isothiocyanates in the presence of lithium, potassium and cesium iodides

\[
\begin{align*}
\text{Ph}_2\text{S} & \xrightarrow{\text{Lil}} \text{PhNS} = \text{N}_2 \text{Ph} \\
\text{a, Ar}= \text{Ph} & \\
\text{b, Ar}= -\text{OCH}_3 & \\
\text{c, Ar}= -\text{Cl} & \\
1 \text{a-c} & \rightarrow 2 \text{a-c} & \rightarrow 3 \text{a-c}
\end{align*}
\]
ethylaryl sulfonamides by treatment with trimethylsilyl iodide and their reaction with phenyl isothiocyanate to give products identical with that derived from the direct reaction.

In this case the reaction gives 2a-c as evidenced by X-ray crystal analysis. Single crystal X-ray diffraction was done. A single crystal of dimensions 1.7x1.5x0.4 mm$^3$ was used for data collection. The intensity data and unit cell parameter were measured on Enraf Nonius CAD4 diffractometer using CuK$\alpha$ (\(\lambda = 0.7093\) Å).

The Figure 1 shows ortep diagram and Figure 2

unit cell packing diagram of 2c.

The effect of the solvent on the reaction was also studied by reacting 2c with phenyl isothiocyanate in the presence of lithium iodide in various solvents. The results are shown in Table II.

This result is as expected since the reaction involves nucleophilic attack of the iodide ion on the aziridine carbon and this is favoured by polar aprotic solvents like DMSO and DMF.

With benzoyl isothiocyanates also, 1a-c were transformed smoothly into the benzoyl derivatives 4a-c. Surprisingly, in this case the reaction in the presence
of sodium iodide led to the same product albeit in diminished yield (Table III).

Experimental Section

General. Melting points and boiling points are uncorrected. IR spectra (KBr pellets or liquid film) were recorded on a Nicolet 5DX FTIR Instrument and NICOLET PROTEGE 460 FTIR Instrument; 1H NMR and 13C NMR spectra (CDCl3, internal standard TMS) on a JEOL FX-100 machine at 100 MHz and DPX-300 Bruker Machine at 300 MHz and mass spectra (70 eV) on a JMS 300 (JEOL) GC/MS Spectrometer. Microanalyses were carried out on a Perkin Elmer 240 CHN Elemental Analyser.

General procedure for the preparation of 2-alkyl- or 2-aryl-iminothiazolidines. To a solution of the pertinent aziridine (1-2 mmoles) in dry tetrahydrofuran (30 mL) was added sodium iodide or lithium iodide (1-2 mmoles) under an atmosphere of nitrogen and the solution stirred for 10 to 15 min. The pertinent isothiocyanate (1-2 mmoles) was then added dropwise through a syringe. The reaction mixture was stirred for 6 to 14 hr (in some cases refluxing for 2 to 10 hr prior to stirring at room temperature was required). The progress of the reaction was monitored by TLC. After completion of the reaction the solvent was distilled off, the residue was diluted with cold water (25 mL) and extracted with ethyl acetate (3 x 25 mL). The ethyl acetate extracts were washed with 10% sodium thiosulphate (3 x 25 mL), water (3 x 25 mL) and dried over anhydrous sodium sulphate. The solvent was distilled off and the crude product purified by column chromatography on silica gel to obtain the corresponding 2-alkyl or 2-aryliminothiazolidine.
General procedure for reaction of iodotrimethylsilane with aziridines. According to a modified literature procedure, chlorotrimethylsilane (3-6 mmoles) in dry acetonitrile (15 mL) was kept in a 100 mL three-necked round bottomed flask fitted with a dropping funnel and a nitrogen inlet and the apparatus flushed with nitrogen. Sodium iodide (3-6 mmoles) in dry acetonitrile was added to it and the temperature lowered to 5°C. After stirring for 15 minutes at -5°C, the aziridine (1.5-3 mmoles) dissolved in acetonitrile (20 mL) was added dropwise and stirring continued for 3 to 18 hr at room temperature. The reaction mixture was poured into 10% sodium thiosulphate solution (100 mL) and extracted with ether (3 x 25 mL). The ether extracts were washed with water, dried over anhydrous sodium sulphate and the solvent distilled off to give the β-iodoethyrylsulphonamide which was purified by crystallisation from benzene-petroleum ether.

General procedure for the preparation of iminothiazolidines from substituted β-idoethyrylsulphonamides. A 100 mL three-necked round bottomed flask fitted with a dropping funnel, a nitrogen inlet and a condenser was charged with sodium hydride (0.3-2 mmoles), as a 50 % dispersion in oil. The oil was washed off by swirling with dry hexane under nitrogen and decanting the solvent. The whole setup was evacuated with the help of a vacuum pump until the last traces of hexane were removed. Dry nitrogen was allowed in and dry powdered mono- or di-substituted β-idoethyrylsulphonamide (0.3-2 mmole) introduced into the flask. The system was again evacuated and filled with nitrogen (a positive pressure of nitrogen was maintained throughout the course of the reaction). Dry THF (20 mL) was added through the dropping funnel and the mixture stirred for 2 hr. To this was added the isothiocyanate (0.3-2 mmoles) in dry THF (10 mL) rapidly with constant stirring. The mixture was stirred additionally for 3 to 18 hr at room temperature. The solvent was then evaporated and cold water (25 mL) added to it. The aqueous solution was extracted with ether. The combined ether extracts were washed successively with 10% sodium thiosulphate (3 x 25 mL) and water (3 x 25 mL) and then dried over anhydrous sodium sulphate. Ether was distilled off and the residue purified either by crystallisation from benzene-petroleum ether or by column chromatography on silica gel to give the 2-alkyl- or 2-aryl-iminothiazolidine.

Preparation of 3-benzenesulphonyl-5-phenyl-2-phenyliminothiazolidine 2a. Typical procedure. Phenyl-N-benzenesulphonylaziridine (2 mmoles) was reacted with phenyl isothiocyanate (2 mmoles) in the presence of lithium iodide (2 mmoles) according to the general procedure and the reaction mixture stirred for 12 hr at room temperature and then refluxed for 3 hr. Workup afforded a solid, which was purified by column chromatography on silica gel (eluent: benzene-petroleum ether), yield 63%; m.p. 102-3°C; IR: 1644 (vC=N), 1168, 1350 (vSO2) cm⁻¹; ¹H NMR (CDCl3): δ 4.08 (dd, J=8 and 10Hz, 1H), 4.58 (dd, J=6.5 and 10Hz, 1H), 4.79 (dd, J=6.5 and 8Hz, 1H), 6.71-8.1 (m, 15H); ¹³C NMR (CDCl3): δ 45.58 (d), 54.30 (t), 120.0-140 (aromatic carbons), 149 (s), 152 (s); MS: m/z 394 (M⁺). Anal. Found (Calcd) %: C, 64.15 (63.96); H, 4.79 (4.56); N, 7.18 (7.10).

5-Phenyl-3-(p-toluenesulphonyl)-2-phenyliminothiazolidine 2b: Yield 62%; m.p. 132-3°C; IR: 1644 (vC=N), 1168, 1350 (vSO2) cm⁻¹; ¹H NMR (CDCl3): δ 2.48 (s, 3H), 4.04 (dd, J=8 and 10Hz, 1H), 4.59 (dd, J=6.5 and 8Hz, 1H), 4.79 (dd, J=6.5 and 8Hz, 1H), 6.71-8.1 (m, 15H); ¹³C NMR (CDCl3): δ 21.4 (q), 45.58 (d), 54.30 (t), 120.0-140 (aromatic carbons), 149 (s), 152 (s); MS: m/z 428 (M⁺). Anal. Found (Calcd) %: C, 64.15 (63.96); H, 4.79 (4.56); N, 7.18 (7.10).

3-(p-Chlorobenzenesulphonyl)-5-phenyl-2-phenyliminothiazolidine 2c: Yield 67%; m.p. 126-27°C; IR: 1644 (vC=N), 1168, 1350 (vSO2) cm⁻¹; ¹H NMR (CDCl3): δ 4.09 (dd, J=8 and 10Hz, 1H), 4.58 (dd, J=6.5 and 8Hz, 1H), 4.85 (dd, J=6.5 and 8Hz, 1H), 6.71-8.1 (m, 15H); ¹³C NMR (CDCl3): δ 45.58 (d), 54.30 (t), 120-135 (aromatic carbons), 149 (s), 152 (s); MS: m/z 428 (M⁺). Anal. Found (Calcd) %: C, 59.08 (58.80); H, 4.07 (3.96); N, 6.32 (6.53).

4-Methyl-3-(p-toluenesulphonyl)-2-phenyliminothiazolidine: Yield 55%; IR: 1644 (vC=N), 1168, 1350 (vSO2) cm⁻¹; ¹H NMR (CDCl3): δ 1.83 (d, J=6Hz, 3H), 2.44 (s, 3H), 3.75 (d, J=9Hz, 1H), 4.1 (m, 1H), 4.35 (dd, J=5.6 and 9Hz, 1H), 6.7-8 (aromatic protons, 9H); ¹³C NMR (CDCl3): δ 18.9 (q), 22.4 (q), 50.2 (d), 52.6 (t), 124.4-138 (aromatic carbons), 149 (s), 152 (s).

3-Benzensulphonyl-5-phenyl-2-benzyliminothiazolidine 4a: Yield 61%; m.p. 140-42°C; IR: 1658 (vC=O), 1616 (vC=N), 1356, 1160 (vSO2) cm⁻¹; ¹H NMR (CDCl3): δ 4.17 (dd, J=8.5 and 10.5Hz, 1H), 4.67 (dd, J=7.2 and 10.5Hz, 1H), 4.8 (distorted triplet, J=7.2 and 8.5Hz, 1H), 6.71-8.1 (m, 15H); ¹³C NMR (CDCl3): δ 46.06 (d), 54.94 (t), 126.97-137.13 (aromatic carbons), 167.08 (s), (C=N), 170.57 (s).
(C=O); MS: m/z 105 (PhCO); Anal. Found (Caled) %: C, 63.06 (62.56), H, 4.20 (4.26), N, 6.69 (6.63).

3-p-Toulenesulphonyl-5-phenyl-2-benzoyliminothiazolidine 4b: Yield 60%; m.p. 138-40°C; IR: 1658 (vC=O), 1616 (vC=N), 1160, 1356 (vSO₂) cm⁻¹; ¹H NMR (CDCl₃): δ 2.48 (s, 3H), 4.17 (dd, J=8.5 and 10.5Hz, 1H), 4.69 (dd, J=7.2 and 8.5Hz, 1H), 4.82 (dd, J=7.2 and 8.5Hz, 1H), 6.71-8.1 (m, 15H); ¹³C NMR (CDCl₃): δ: 21.688 (q), 46.53 (d), 55.58 (t) 127.60-145.60 (aromatic carbons), 167.92 (s, C=N), 176.17 (s, C=O); MS: Base peak at m/z 105 (PhCO); Anal. Found (Caled) %: C, 58.76 (57.89); H, 3.70 (3.72); N, 6.20 (6.14).

3 (p-Chlorobenzenesulphonyl)-5-phenyl-2-benzoyliminothiazolidine 4c: Yield 65%; m.p. 180-82°C; IR: 1658 (vC=O), 1616 (vC=N), 1160, 1356 (vSO₂) cm⁻¹; ¹H NMR (CDCl₃): δ 4.23 (dd, J=8.5 and 10.5Hz, 1H), 4.7 (dd, J=7.2 and 8.5Hz, 1H), 4.85 (distorted triplet, J=7.2 and 8.5Hz, 1H), 6.71-8.1 (m, 15H); ¹³C NMR (CDCl₃): δ 46.59 (d), 55.47 (t), 127.49-141.01 (aromatic carbons), 167.61 (s, C=N), 176.02 (s, C=O); MS: Base peak at m/z 105 (PhCO); Anal. Found (Caled) %: C, 63.9 (63.3); H, 4.35 (4.58); N, 6.58 (6.42).

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References