

# Isothiocyanates. XLII.

## Synthesis of 3-isothiocyanatophenyl alkyl sulfides and sulfones

M. UHER, P. ZÁLUPSKÝ, and A. MARTVOŇ

*Department of Organic Chemistry, Slovak Technical University,  
880 37 Bratislava*

Received 21 January 1974

A series of 3-isothiocyanatophenyl alkyl sulfides and sulfones has been prepared from the appropriate ammonium salts by thiophosgene method. Their infrared and ultraviolet spectra have been recorded and are interpreted in this work.

In our previous works [1–3], dealing with isothiocyanates containing in addition to the functional group another sulfur atom, we synthesized a series of 4-substituted phenyl isothiocyanates.

In the present work we describe the synthesis of 3-NCS-C<sub>6</sub>H<sub>4</sub>-Y-R, where Y = S, SO<sub>2</sub> and R = methyl, ethyl, *n*-hexyl, and *n*-octyl. The choice of these alkyls was motivated by the possible steric interaction of the terminal carbon with NCS group [1] as well as by the effect of the aliphatic residue on the value of distribution coefficient and, consequently, on the biological activity of the compound.

3-Nitrobenzenesulfonyl chloride was used as starting compound to prepare the mentioned derivatives. This was reduced by red phosphorus and iodine in a mixture of acetic acid and water [4] to bis(3-nitrophenyl) disulfide. Reduction of this product by sodium sulfide in alkaline medium gave the sodium salt of 3-nitrobenzenethiol which was alkylated by alkyl halides affording the appropriate sulfides [1]. Their physicochemical constants corresponded to those given in the literature.

In such a way prepared 3-nitrophenyl alkyl sulfides were further reduced with tin(II) chloride and converted into salts of 3-aminophenyl alkyl sulfides by gaseous hydrogen chloride or oxidized with 30% hydrogen peroxide in glacial acetic acid to 3-nitrophenyl alkyl sulfones and subsequently reduced similarly as sulfides.

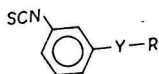
Isothiocyanates were prepared from the appropriate ammonium salts by thiophosgene method in a modified thiophosgenating reactor [10].

All the synthesized isothiocyanates of the sulfidic series were liquids and the sulfones solids (Table 1) contrary to 4-isothiocyanatophenyl alkyl sulfides which were either liquids or solids and to 4-isothiocyanatophenyl alkyl sulfones which had significantly higher melting points [1].

Infrared spectra of the prepared isothiocyanates revealed medium intense bands at 951–957 cm<sup>-1</sup> belonging to  $\bar{\nu}_s(\text{NCS})$ . The spectra of all the compounds investigated showed very intense bands belonging to asymmetric stretching vibrations of the NCS group in the 2000–2200 cm<sup>-1</sup> range. The most intense band on the spectra of 3-isothiocyanatophenyl alkyl sulfides appeared at 2100 cm<sup>-1</sup> and on the spectra of the corresponding sulfones at ~2050 cm<sup>-1</sup>. Lengthening of the alkyl chain did not influence the location of maximum of the  $\bar{\nu}_{as}(\text{NCS})$  absorption band; it was in accordance with small differences in the inductive effects of *n*-alkyl groups. With increasing alkyl residues the stretching vibrations of C–H bonds were shifted only insignificantly to lower wavenumbers.

Table 1

The synthesized 3-isothiocyanatophenyl alkyl sulfides and sulfones



| Com-<br>pound | R               | Y               | Formula               | M     | Calculated/found |              |                | Yield<br>[%] | B.p.<br>[°C/torr]<br>M.p.<br>[°C] | 23.5°<br>$n_D$ |
|---------------|-----------------|-----------------|-----------------------|-------|------------------|--------------|----------------|--------------|-----------------------------------|----------------|
|               |                 |                 |                       |       | % H              | % C          | % S            |              |                                   |                |
| <i>I</i>      | Methyl          | S               | $C_8H_7NS_2$          | 181.3 | 52.93<br>52.84   | 3.87<br>3.99 | 35.40<br>35.31 | 67.0         | 130/1                             | 1.6888         |
| <i>II</i>     | Ethyl           | S               | $C_9H_9NS_2$          | 195.2 | 55.30<br>55.41   | 4.61<br>4.72 | 32.80<br>32.96 | 63.0         | 115/2                             | 1.6632         |
| <i>III</i>    | <i>n</i> -Hexyl | S               | $C_{13}H_{17}NS_2$    | 251.4 | 62.20<br>62.11   | 6.78<br>6.69 | 25.60<br>25.76 | 42.6         | 136/1.5                           | 1.6069         |
| <i>IV</i>     | <i>n</i> -Octyl | S               | $C_{15}H_{21}NS_2$    | 279.5 | 64.20<br>64.09   | 7.52<br>7.43 | 22.90<br>22.98 | 37           | 140/1.5                           | 1.5915         |
| <i>V</i>      | Methyl          | SO <sub>2</sub> | $C_8H_7NO_2S_2$       | 213.3 | 44.90<br>44.82   | 3.28<br>3.31 | 30.00<br>30.11 | 61           | 70                                | —              |
| <i>VI</i>     | Ethyl           | SO <sub>2</sub> | $C_9H_9NO_2S_2$       | 227.3 | 47.60<br>47.51   | 3.96<br>4.08 | 28.25<br>28.18 | 54           | 50                                | —              |
| <i>VII</i>    | <i>n</i> -Hexyl | SO <sub>2</sub> | $C_{13}H_{17}NO_2S_2$ | 283.4 | 55.20<br>55.33   | 6.00<br>6.14 | 22.65<br>22.53 | 35           | 190/1.5                           | —              |
| <i>VIII</i>   | <i>n</i> -Octyl | SO <sub>2</sub> | $C_{15}H_{21}NO_2S_2$ | 311.5 | 57.80<br>57.95   | 6.40<br>6.59 | 20.45<br>20.58 | 30           | 25                                | —              |

Table 2

Infrared and ultraviolet spectra of 3-isothiocyanatophenyl alkyl sulfides and sulfones

| Com-<br>pound | $\tilde{\nu}_s(\text{NCS})$<br>[cm <sup>-1</sup> ] | $\tilde{\nu}_s(\text{S=O})$<br>[cm <sup>-1</sup> ] | $\tilde{\nu}_{as}(\text{S=O})$<br>[cm <sup>-1</sup> ] | $\tilde{\nu}_{as}(\text{NCS})$<br>[cm <sup>-1</sup> ] | $\lambda_{\max I}$<br>[nm]<br>log $\epsilon$ | $\lambda_{\max II}$<br>[nm]<br>log $\epsilon$ |
|---------------|--|--|---|---|--|---|
| <i>I</i>      | 951  | —  | —   | 2060, 2115, 2205                                      | 220<br>4.90                                  | 259<br>4.68<br>4.38                           |
| <i>II</i>     | 966  | —  | —   | 2060, 2114, 2205                                      | 218<br>4.78                                  | 260<br>4.50<br>4.25                           |
| <i>III</i>    | 961  | —  | —   | 2060, 2150, 2198                                      | 218<br>4.99                                  | 262<br>4.75<br>4.48                           |
| <i>IV</i>     | 952  | —  | —   | 2060, 2120, 2195                                      | 219<br>5.00                                  | 262<br>4.74<br>4.46                           |
| <i>V</i>      | 955  | 1156   | 1333<br>1308  | 2047, 2095, 2202,<br>2221                             | 216<br>4.68                                  | 281<br>4.34                                   |
| <i>VI</i>     | 960  | 1147   | 1327<br>1311  | 2052, 2110, 2212                                      | 214<br>5.06                                  | 278<br>4.56                                   |
| <i>VII</i>    | 970  | 1146   | 1331  | 2045, 2115, 2207                                      | 213<br>4.97                                  | 280<br>4.43                                   |
| <i>VIII</i>   | 971  | 1147   | 1331<br>1307  | 2054, 2102, 2216                                      | 214<br>4.68                                  | 279<br>4.12                                   |

sh — shoulder.

The u.v. spectra of 3-isothiocyanatophenyl alkyl sulfides revealed two important maxima at 218–220 and 259–262 nm the last having a shoulder at ~280 nm (Table 2). The corresponding 4-isothiocyanatophenyl alkyl sulfides showed two maxima at 291–292 and 302–303 nm; their intensities were only slightly different from those of 3-substituted derivatives [5]. This spectrum was a modification of the spectrum of phenyl isothiocyanate. The NCS in *para* position was apparently the determining group enabling mesomeric interactions with the ring and the free electron pairs on the sulfidic sulfur. In *meta* position, where the NCS group could not form mesomeric structures, S-alkyl was the determining group modifying the spectrum of benzene by its free electron pairs. This was supported also by the  $-I$  effect of the NCS group in *meta* position. The small influence of NCS group in *meta* position was also evident from bathochromic effect on the spectra of phenyl alkyl sulfides (5–8 nm only, while with *para* derivatives ~50 nm).

The u.v. spectra of 3-isothiocyanatophenyl alkyl sulfones showed two maxima  $\lambda = 213-216$  nm and  $\lambda = 278-281$  nm. Contrary to unsubstituted phenyl methyl sulfone, the maximum at lower wavenumbers was more intense by order. The band at higher wavenumbers was bathochromically shifted by 16 nm which was less than with 4-isothiocyanatophenyl alkyl sulfones where the NCS group interacted with SO<sub>2</sub> group [6] and its intensity again increased ( $\log \epsilon = 3 \rightarrow 4.6$ ). While the bathochromic effect was unimportant with 3-isothiocyanatophenyl alkyl sulfones, the hyperchromic effect was very significant with regard to phenyl isothiocyanate, phenyl alkyl sulfone, and 4-isothiocyanatophenyl alkyl sulfones.

### Experimental

3-Nitrobenzenesulfonyl chloride was prepared according to [7], bis(3-nitrophenyl) disulfide according to [4], methyl, ethyl, and *n*-hexyl iodides according to [8], and *n*-octyl bromide according to [9].

Infrared spectra were measured on a double-beam UR-20 (Zeiss, Jena) spectrophotometer in the 800–3000 cm<sup>-1</sup> range in NaCl cells 1.04 mm in width; concentration  $2.5 \times 10^{-2}$  M in chloroform. Ultraviolet spectra were recorded on a Specord UV-VIS instrument in the 200–350 nm region in 10-mm cells; concentration  $1.1 \times 10^{-5} - 2.0 \times 10^{-5}$  M in ethanol. The synthesized isothiocyanates are characterized in Tables 1 and 2.

#### *3-Nitrophenyl n-octyl sulfone*

3-Nitrophenyl *n*-octyl sulfide (8.9 g; 0.03 mole) was dissolved in glacial acetic acid (100 ml) under stirring and 30% hydrogen peroxide (0.12 mole) was added. The obtained solution was stirred and heated in a boiling water bath for 3 hours. After cooling the solution to laboratory temperature, the precipitated sulfone was sucked off and dried over potassium hydroxide in a desiccator. Yield 8.3 g (92.5%), m.p. 35°C.

For C<sub>14</sub>H<sub>21</sub>NO<sub>4</sub>S (299.2) calculated: 56.10% C, 7.02% H, 10.68% S; found: 56.17% C, 7.13% H, 10.72% S.

The other nitro sulfones were prepared similarly. Their physicochemical constants corresponded to those given in the literature.

#### *3-Aminophenyl n-octyl sulfone*

Tin(II) chloride (200 g) in glacial acetic acid (400 ml) and ethanol (400 ml) was saturated by gaseous hydrogen chloride under vigorous stirring until the solution was clear (3–4 hours).

3-Nitrophenyl *n*-octyl sulfone (3.0 g; 0.01 mole) dissolved in glacial acetic acid was added under stirring into a solution of reducing agent containing tin(II) chloride (0.05 mole). The reducing mixture was further refluxed for 4 hours under stirring, cooled, made alkaline by aqueous solution of sodium hydroxide, and the amine was extracted with ether. The extracts were dried, ether was distilled off at reduced pressure, and the salt of the amine was precipitated with gaseous hydrogen chloride. Yield 2.01 g (66%), m.p. 145°C.

For  $C_{14}H_{24}ClNO_2S$  (305.7) calculated: 55.0% C, 7.87% H, 11.60% Cl, 10.45% S; found: 54.78% C, 7.79% H, 11.79% Cl, 10.60% S.

### *3-Isothiocyantophenyl alkyl sulfides and sulfones*

The appropriate ammonium chloride (1 mole) was dissolved in the least amount of water and added to a chloroform solution of thiophosgene (1.05 mole) in the thiophosgenating reactor during 10 minutes [10]. The reaction was slightly exothermic; when the temperature exceeded 30°C, cooling was necessary. Sodium hydrogen carbonate (2 moles at the beginning) was added to release the amine. In the course of reaction, the addition of sodium hydrogen carbonate was regulated so that the pH of the reaction mixture after 2-hour stirring was neutral or slightly alkaline. Then the chloroform layer was removed and the water layer was washed with chloroform. The chloroform solutions were given back to the reactor, washed with diluted hydrochloric acid (0.1 N), and dried with sodium sulfate. Chloroform was distilled off at reduced pressure and isothiocyanates were isolated either by distillation *in vacuo* or by crystallization from petroleum ether or benzene.

### References

1. Uher, M., Kristian, P., Antoř, K., and Drobnica, L., *Chem. Zvesti* **21**, 44 (1967).
2. Uher, M., Antoř, K., Martvoň, A., and Sticzay, T., *Chem. Zvesti* **27**, 403 (1973).
3. Uher, M. and Jendrichovský, J., *Collect. Czech. Chem. Commun.* **38**, 289 (1973).
4. Kawahara, K., *J. Pharm. Soc. Jap.* **77**, 959 (1957); *Chem. Abstr.* **52**, 2791 (1958).
5. Uher, M., Kristian, P., Sticzay, T., and Antoř, K., *Collect. Czech. Chem. Commun.* **34**, 4005 (1969).
6. Uher, M., Kristian, P., Antoř, K., and Sticzay, T., *Zborník prác Chemickotechnologickej fakulty SVŠT*. (Collection of Communications, Section Chemistry, Slovak Technical University.) P. 50. Bratislava, 1968.
7. *Preparativnaya organicheskaya khimiya*. (Preparative Organic Chemistry.) P. 279. Goschimizdat, Moscow, 1959.
8. Marko, M. and Krasnec, L., *Základy preparatívnej organickej chémie I*. (Principles of Preparative Organic Chemistry.) P. 221. Slovenské vydavateľstvo technickej literatúry. (Slovak Publishing House of Technical Literature.) Bratislava, 1962.
9. Vogel, A. I., *A Textbook of Practical Organic Chemistry*, p. 281. Longmans, London, 1954.
10. Fľoch, L., *Thesis*, p. 27. Slovak Technical University, Bratislava, 1973.

Translated by A. Kardořová