

Chemistry of Sulfonyl Isocyanates and Sulfonyl Isothiocyanates. XII. Cyclizations with Epoxides

J. W. McFarland*, J. J. Beaulieu [1], L. N. Arrey [2], and L. M. Frey [2]

Department of Chemistry, DePauw University,
Greencastle, Indiana 46135
Received March 1, 1988

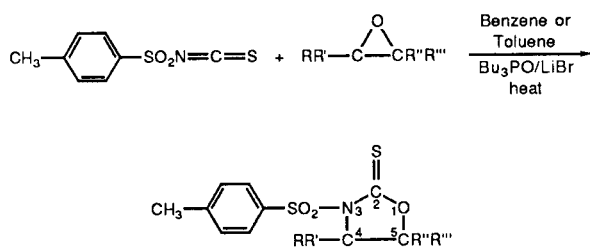
4-Toluenesulfonyl isothiocyanate reacted with 1,2-epoxy-3-phenoxypropane and 2,3-epoxypropyl 4-methoxyphenyl ether to give, respectively, 3-(4-toluenesulfonyl)-5-phenoxyethylene-2-oxazolidinethione (**I**) and 3-(4-toluenesulfonyl)-5-(4-methoxyphenoxyethylene)-2-oxazolidinethione (**II**) in high yields. The sulfonyl isothiocyanate reacted further with styrene oxide to give a mixture of oxazolidinethiones from which a solid **III** was isolated. The structure of **III** is either the 4- or 5-phenyl derivative of 3-(4-toluenesulfonyl)-2-oxazolidinethione. Reactions of the isothiocyanate with 3-chloro-1,2-epoxypropane and 1,2-epoxybutane afforded, respectively, 3-(4-toluenesulfonyl)-5-chloromethyl-2-oxazolidinethione (**IV**) and 3-(4-toluenesulfonyl)-4-ethyl-2-oxazolidinethione (**V**). Evidence for structures was by pmr, ir, and elemental analyses.

J. Heterocyclic Chem., **25**, 1435 (1988).

It was shown by McFarland and co-workers that 2-oxazolidinethiones may be prepared from chloro alcohols and sulfonyl isothiocyanates by a two-step procedure [3,4]. Sulfonyl isothiocyanates have also been shown to be useful in cyclization reactions to give imidazolidinethione and hexahydropyrimidinethiones [5]. The success from the cyclization of sulfonyl isocyanates with epoxides [6,7] has prompted us to study the cyclizations from sulfonyl isothiocyanates with epoxides. The sulfonyl isothiocyanates are known to be less reactive than are the sulfonyl isocyanates. In reactions with amino alcohols, the isothiocyanates selectively reacted with the amino group, whereas the isocyanates usually react with both functional groups [5].

The reactions of five epoxides, containing both aromatic and aliphatic groups, with 4-toluenesulfonyl isothiocyanate are reported in this paper.

Scheme 1

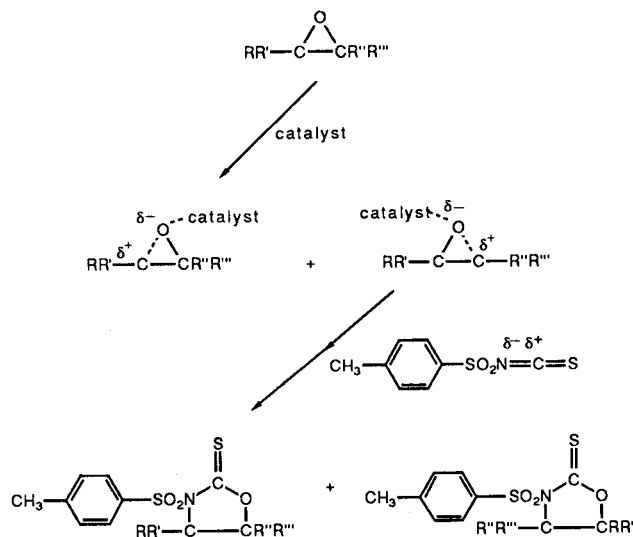


- | | |
|-----|---|
| I | R = H, R' = H, R'' = H, R''' = -CH ₂ OC ₆ H ₅ |
| II | R = H, R' = H, R'' = H, R''' = -CH ₂ OC ₆ H ₄ -OCH ₃ -4 |
| III | R = H, R' = C ₆ H ₅ , R'' = H, R''' = H |
| IV | R = H, R' = H, R'' = H, R''' = CH ₂ Cl |
| V | R = H, R' = C ₂ H ₅ , R'' = H, R''' = H |

1,2-Epoxy-3-phenoxypropane and 2,3-epoxypropyl 4-methoxyphenyl ether reacted with 4-toluenesulfonyl isothiocyanate in refluxing toluene to afford 90% and

84%, respectively, of 3-(4-toluenesulfonyl)-5-phenoxyethylene-2-oxazolidinethione (**I**) and 3-(4-toluenesulfonyl)-5-(4-methoxyphenoxyethylene)-2-oxazolidinethione (**II**). Final purification of **II** was by silica gel column chromatography. The fact that the yields were high indicates that essentially one isomer was obtained in each case. If the course of the reaction follows the mechanism shown below [6], the 5-isomer would predictably predominate.

Scheme 2



The reaction of styrene oxide with 4-toluenesulfonyl isothiocyanate gave an oil which, from pmr and ir analyses, appeared to be a mixture of oxazolidinethione 4- and 5-isomers. Solid **III** was obtained by the use of column chromatography.

3-Chloro-1,2-epoxypropane and 1,2-epoxybutane also gave rise to substituted sulfonyl oxazolidinethiones **IV** and **V**, respectively. The assignments are tentative. Fur-

ther investigations are underway to determine structures of the products. The purity of product was found to be dependent upon the purity of the isothiocyanate. When the isothiocyanate was not freshly-distilled the products were contaminated by elemental sulfur.

EXPERIMENTAL

4-Toluenesulfonyl isothiocyanate was prepared by the procedures of McFarland and Houser [3] and of Dickore and Kuehle [8]. The epoxides, lithium bromide, and tributylphosphine oxide were purchased from the Aldrich Chemical Company, Inc. and used without further purification. The ir spectra were recorded on a Nicolet 5DXB Fourier Transform Spectrometer and the pmr spectra on a Varian EM360L Nuclear Magnetic Resonance Spectrometer. Melting points were obtained on a Mel-Temp apparatus and are uncorrected. Elemental analyses were by the Midwest Microlab, Inc., Indianapolis, Indiana.

3-(4-Toluenesulfonyl)-5-phenoxyethylene-2-oxazolidinethione (I).

To a mixture of 7.0 g (0.033 mole) of 4-toluenesulfonyl isothiocyanate, 0.1 g of lithium bromide, and 0.35 g of tributylphosphine oxide in 35 ml of sodium-dried toluene was added 4.95 g (0.033 mole) of (\pm)-1,2-epoxy-3-phenoxypropane in 10 ml of dry toluene. The mixture was heated under reflux during 8 hours. Removal of solvent *in vacuo* afforded an oil which solidified on standing. Trituration with petroleum ether gave 10.8 g (90%) of solid, mp 106-114°. Trituration with diethyl ether resulted in pure I, mp 120-122°; pmr (deuteriochloroform): δ 2.30 (s, 3H), 3.45 (d, 2H), 4.1 (d, 2H), 4.95 (m, 1H), 6.8 (d, 2H), 7.2 (m, 5H), 7.75 (d, 2H); ir (potassium bromide): 3000, 2900, 1600, 1518, 1318, 1153 cm^{-1} .

Anal. Calcd. for $\text{C}_{17}\text{H}_{17}\text{NO}_4\text{S}_2$: C, 56.14; H, 4.73; N, 3.85; S, 17.67. Found: C, 56.31; H, 4.81; N, 4.04; S, 17.38.

3-(4-Toluenesulfonyl)-5-(4-methoxyphenoxyethylene)-2-oxazolidinethione (II).

The above procedure was used with 5.10 g (0.024 mole) of 4-toluenesulfonyl isothiocyanate, 4.32 g (0.024 mole) of 2,3-epoxypropyl 4-methoxyphenyl ether, 0.1 g of lithium bromide and 0.35 g of tributylphosphine oxide in 50 ml of refluxing toluene for 6 hours. Removal of solvent followed by trituration with petroleum ether afforded 9.4 g (100%) of slightly greasy solid. Trituration with 25 ml of ethyl ether gave 7.89 g (84%), mp 87-89°. A pure sample of II was obtained by passing a chloroform solution through a silica gel column and eluting with acetone, mp 84-86°; pmr (deuteriochloroform): δ 2.4 (s, 3H), 3.55 (d, 2H), 3.75 (s, 3H), 4.20 (d, 2H), 5.05 (m, 1H), 6.8 (s, 4H), 7.30 (d, 2H), 7.85 (d, 2H); ir (potassium bromide): 3003, 2937, 1556, 1509, 1310, 1151 cm^{-1} .

Anal. Calcd. for $\text{C}_{18}\text{H}_{19}\text{NO}_5\text{S}_2$: C, 54.96; H, 4.83; N, 3.56; S, 16.28. Found: C, 54.64; H, 4.87; S, 16.40.

3-(4-Toluenesulfonyl)phenyl-2-oxazolidinethione (III).

The procedure employed was that for preparing I and II, except 7.09 g (0.03 mole) of 4-toluenesulfonyl isothiocyanate and 3.96 g (0.03 mole) of styrene oxide were heated with catalyst in refluxing dry benzene for 2.5 hours. Removal of solvent gave a wax which was trituated with diethyl ether. The remaining 3.26 g (30%) melted 94-116°. A 1.0 g fraction was

chromatographed using a silica gel column and eluting successively with chloroform and acetone. The oxazolidinethione fraction amounted to 0.34 g, mp 94-101°. **No further purification was attempted**; pmr (deuteriochloroform): δ 2.35 (s, 3H), 4.55 (m, 2H), 5.0 (m, 1H), 7.18 (d, 2H), 7.28 (s, 5H, slight overlap with doublet), 7.8 (d, 2H); ir (potassium bromide): 3031, 2924, 1602, 1543, 1324, 1164 cm^{-1} .

Anal. Calcd. for $\text{C}_{16}\text{H}_{15}\text{NO}_3\text{S}_2$: C, 57.65; H, 4.50; N, 4.20; S, 19.22. Found: C, 56.50; H, 4.78; N, 4.14; S, 19.22.

3-(4-Toluenesulfonyl)-5-chloromethyl-2-oxazolidinethione (IV).

4-Toluenesulfonyl isothiocyanate (7.0 g, 0.033 mole), 3-chloro-1,2-epoxypropane (3.05 g, 0.033 mole), and catalyst were heated under reflux in 50 ml of dry toluene for 2 hours. After removal of solvent 10.0 g (100%) of wax remained and was trituated with diethyl ether to afford 4.64 g (46%) of solid. A 1.0 g sample was chromatographed as above. A fraction (0.47 g) had mp 92-94°; pmr (deuteriochloroform): δ 2.30 (s, 3H); 3.45 (dd, 2H), 3.80 (d, 2H), 4.90 (m, 1H), 7.25 (d, 2H), 7.86 (d, 2H); ir (potassium bromide): 3023, 2964, 1609, 1556, 1330, 1151 cm^{-1} .

Anal. Calcd. for $\text{C}_{11}\text{H}_{12}\text{ClNO}_3\text{S}_2$: C, 43.16; H, 3.96; N, 4.58; S, 20.99; Cl, 11.61. Found: C, 43.43; H, 3.55; N, 4.97; S, 21.19; Cl, 11.33.

3-(4-Toluenesulfonyl)-4-ethyl-2-oxazolidinethione (V).

A mixture of 6.78 g (0.032 mole) of 4-toluenesulfonyl isothiocyanate, 2.29 g (0.032 mole) of 1,2-epoxybutane, 0.1 g of lithium bromide, and 0.35 g of tributylphosphine oxide in 50 ml of dry benzene was heated under reflux during 4 hours. Work-up in the usual way afforded 8.44 g of yellow oil. Addition of 30 ml of diethyl ether and filtration gave 0.62 g of sulfur, mp 115-116°. After standing overnight white crystals had precipitated from the diethyl ether filtrate, weight 2.17 g (24%), mp 73-75°; pmr (deuteriochloroform): δ 0.95 (t, 3H), 1.75 (m, 2H), 2.4 (s, 3H), 2.85-3.6 (m, 2H-overlap of hydrogens on ring- CH_2), 3.70 (m, 1H), 7.23 (d, 2H), 7.84 (d, 2H); ir (potassium bromide): 2977, 2917, 1603, 1570, 1311, 1164 cm^{-1} .

Anal. Calcd. for $\text{C}_{12}\text{H}_{15}\text{NO}_3\text{S}_2$: C, 50.53; H, 5.26; N, 4.91; S, 22.45. Found: C, 50.65; H, 5.22; N, 4.72; S, 22.15.

Acknowledgements.

We are grateful to Mr. Wilbert B. McCluer, The Dow Chemical Company Foundation, and The Charles A. Dana Foundation for partial support of this work.

REFERENCES AND NOTES

- [1] Dow Chemical Foundation Scholar, Summer, 1987; McCluer Scholar, 1987-88.
- [2] Charles A. Dana Foundation Intern, Summer, 1987.
- [3] J. W. McFarland and R. W. Houser, *J. Org. Chem.*, **33**, 340 (1968).
- [4] J. W. McFarland, C. E. Hayes, E. B. Blair, and K. R. Stuhlman, *J. Heterocyclic Chem.*, **17**, 271 (1980).
- [5] J. W. McFarland, T. H. Kozel, K. R. Stuhlman, and T. S. Chevalier, *J. Heterocyclic Chem.*, **17**, 273 (1980).
- [6] J. W. McFarland, J. J. Beaulieu, L. M. Frey, and L. N. Arrey, *J. Heterocyclic Chem.*, **25**, 1431 (1988).
- [7] J. E. Herweh and W. J. Kauffman, *J. Heterocyclic Chem.*, **8**, 983 (1971); *Tetrahedron Letters*, 809 (1971).
- [8] K. Dickore and E. Kuehle, German Patent 1,183,492 (Dec. 17, 1964); *Chem. Abstr.*, **62**, 7691 (1965).