

J. W. McFarland (2), C. E. Hayes, E. B. Blair and K. R. Stuhlmacher (3)

Department of Chemistry, DePauw University, Greencastle, Indiana 46135

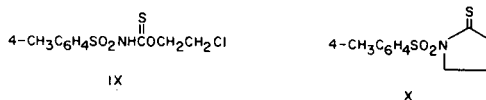
Received July 16, 1979

4-Chlorobenzenesulfonyl isocyanate (I) reacted with 2-chloroethanol and 1-chloro-2-propanol to give, respectively, 2-chloroethyl 4-chlorobenzenesulfonyl carbamate (III) and 1-chloro-2-propyl 4-chlorobenzenesulfonyl carbamate (VI). The carbamates III and VI cyclized under the influence of pyridine to afford, respectively, 3-(4-chlorobenzenesulfonyl)oxazolidin-2-one (IV) and 3-(4-chlorobenzenesulfonyl)-5-methyloxazolidin-2-one (VII). The oxazolidin-2-ones were stable toward hydrochloric acid but hydrolyzed in 2*M* sodium hydroxide solution to *N*-(2-hydroxyethyl)-4-chlorobenzenesulfonamide (V) and *N*-(2-hydroxy-1-propyl)-4-chlorobenzenesulfonamide (VIII), respectively. 4-Toluenesulfonyl isothiocyanate (II) reacted with 2-chloroethanol to give 2-chloroethyl 4-chlorobenzenesulfonyl thiocarbamate (IX), which was converted by pyridine to 3-(4-toluenesulfonyl)oxazolidine-2-thione (X).

*J. Heterocyclic Chem.*, 17, 271 (1980).

The reactions of alcohols with sulfonyl isocyanates have been extensively studied in this laboratory (4-8). McFarland and Houser (9) first reported the reaction of benzenesulfonyl isothiocyanate with 2-chloroethanol and cyclization of the resultant product. It has now been shown that 2-chloroethanol reacts with 4-chlorobenzenesulfonyl isocyanate (I) to afford in 70% yield 2-chloroethyl 4-chlorobenzenesulfonyl carbamate (III). Compound III cyclized to 3-(4-chlorobenzenesulfonyl)oxazolidin-2-one (IV) when heated with pyridine in benzene solution. Evidence for the structure of IV was obtained from ir and nmr analyses, and from the hydrolysis product. The oxazolidin-2-one IV was completely stable toward boiling 6*M* aqueous hydrochloric acid solution. Heating IV with boiling 2*M* aqueous sodium hydroxide solution caused ring opening, and upon neutralization *N*-(2-hydroxyethyl)-4-chlorobenzenesulfonamide (V) resulted. 1-Chloro-2-propanol reacted with I to afford (1-chloro-2-propyl) 4-chlorobenzenesulfonyl carbamate (VI). The carbamate was converted in 65% yield to 3-(4-chlorobenzenesulfonyl)-5-methyloxazolidin-2-one (VII). The latter was hydrolyzed (76.9%) by 2*M* sodium hydroxide solution to *N*-(2-hydroxy-1-propyl)-4-chlorobenzenesulfonamide (VIII).

4-Toluenesulfonyl isothiocyanate (II) reacted with 2-chloroethanol to give 2-chloroethyl 4-toluenesulfonyl thiocarbamate (IX). The thiocarbamate readily cyclized when heated in the presence of pyridine to 3-(4-toluenesulfonyl)oxazolidine-2-thione (X).



## EXPERIMENTAL

4-Chlorobenzenesulfonyl isocyanate (I) was purchased from the Upjohn Co., Carwin Organic Chemicals, and used without further purification. 4-Toluenesulfonyl isothiocyanate (II) was prepared by the methods of McFarland and Houser (9) and of Dickore and Kuehle (10). The ir spectra, using potassium bromide pellets, were recorded on a Perkin-Elmer 137 Spectrophotometer and the nmr spectra on a Hitachi HR-20 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.

### 2-Chloroethyl 4-Chlorobenzenesulfonyl Carbamate (III).

To a solution of 22.0 g. (0.10 mole) of 4-chlorobenzenesulfonyl isocyanate (I) in 50 ml. of anhydrous ether was added dropwise with stirring in a dry nitrogen atmosphere 9.6 g. (0.12 mole) of 2-chloroethanol during 30 minutes. The ether was removed *in vacuo* leaving a soft solid which was recrystallized from benzene/petroleum ether to give 20.9 g. (70%) of white solid (III), m.p. 106-108°; ir: 3150 (N-H), 3000, 2950, 1745 (C=O), 1600, 1360 (SO<sub>2</sub>), 1140 (SO<sub>2</sub>) cm<sup>-1</sup>; nmr (deuteriochloroform): δ 3.65 (2H triplet, CH<sub>2</sub>Cl), δ 4.3 (2H triplet, -OCH<sub>2</sub>-), δ 7.6 (2H doublet, aromatic), δ 8.0 (2H doublet, aromatic), δ 8.1 (1H broad, SO<sub>2</sub>NHC=O).

*Anal.* Calcd. for C<sub>9</sub>H<sub>9</sub>Cl<sub>2</sub>NO<sub>4</sub>S: C, 36.24; H, 3.03. Found: C, 36.10; H, 3.23.

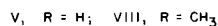
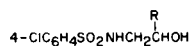
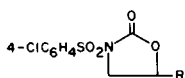
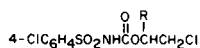
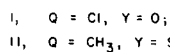
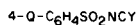
### 3-(4-Chlorobenzenesulfonyl)oxazolidin-2-one (IV).

A solution of 24.8 g. (0.083 mole) of III, 100 ml. of dry benzene, and 15 ml. of pyridine was heated under reflux for 4 hours and then allowed to stand at RT for 3 days. The precipitated crystals (15.5 g., 71%) were collected by suction filtration and washed with benzene, m.p. 148-152°. Recrystallization from ethanol/petroleum ether afforded IV with m.p. 153-155°; ir: 3000, 2900, 1770, 1600, 1360, 1140 cm<sup>-1</sup>; nmr (deuteriochloroform): δ 4.3 (2H triplet, N-CH<sub>2</sub>-), δ 4.55 (2H triplet, O-CH<sub>2</sub>-), δ 7.75 (2H doublet), δ 8.25 (2H doublet).

*Anal.* Calcd. for C<sub>9</sub>H<sub>8</sub>ClNO<sub>4</sub>S: C, 41.30; H, 3.06; Cl, 13.58. Found: C, 41.65; H, 3.18; Cl, 13.40.

### *N*-(2-Hydroxyethyl)-4-chlorobenzenesulfonamide (V).

Compound IV (1.0 g., 0.0038 mole) was heated with 100 ml. of boiling aqueous 2*M* sodium hydroxide solution until all solid went into solution.



Neutralization of the cooled solution with 6*M* aqueous hydrochloric acid solution caused precipitation of white crystals (0.50 g., 56%) of *N*-(2-hydroxyethyl)-4-chlorobenzenesulfonamide (V), m.p. 101-103°; ir: 3500 (O-H), 3200 (-N-H), 3000, 2900, 1600, 1340, 1160  $\text{cm}^{-1}$ ; nmr (deuteriochloroform):  $\delta$  2.2 (1H broad, -NH),  $\delta$  3.4 (2H multiplet, N-CH<sub>2</sub>),  $\delta$  4.0 (2H multiplet, -CH<sub>2</sub>-O-),  $\delta$  5.45 (1H broad, -O-H),  $\delta$  7.8 (2H doublet),  $\delta$  8.15 (2H doublet).

*Anal.* Calcd. for C<sub>8</sub>H<sub>10</sub>ClNO<sub>3</sub>S: C, 40.76; H, 4.25; N, 5.94; S, 13.60. Found: C, 40.78; H, 4.48; N, 5.93; S, 13.42.

(1-Chloro-2-propyl) 4-Chlorobenzenesulfonyl Carbamate (VI).

1-Chloro-2-propanol (12.7 g., 0.13 mole) was added dropwise with stirring under nitrogen to a solution of 22.0 g. (0.10 mole) of I in 50 ml. of dry ether during 30 minutes. The exothermic reaction produced a white solid contaminated with 1-chloro-2-propanol upon removal of ether under reduced pressure. Recrystallization from benzene gave 19.0 g. (61%) of white crystalline VI, m.p. 102-103°; ir: 3160 (N-H), 1740, etc.  $\text{cm}^{-1}$ ; nmr (perdeuterioacetone):  $\delta$  1.35 (3H doublet, CH<sub>3</sub>),  $\delta$  3.7 (2H doublet, -CH<sub>2</sub>Cl),  $\delta$  5.05 (1H multiplet, -O-CH-),  $\delta$  7.71 (2H doublet),  $\delta$  8.15 (2H doublet).

*Anal.* Calcd. for C<sub>10</sub>H<sub>11</sub>Cl<sub>2</sub>NO<sub>3</sub>S: C, 38.47; H, 3.53. Found: C, 38.79; H, 3.61.

3-(4-Chlorobenzenesulfonyl)-5-methyloxazolidin-2-one (VII).

A solution of 10.0 g. (0.032 mole) of VI, 100 ml. of dry benzene, and 15 ml. of pyridine was heated under reflux for 20 hours. Upon cooling a white solid (5.73 g., 65%) precipitated. Recrystallization from ethanol gave VII with m.p. 98-100°; ir: 3000, 2900, 1775, 1600, 1370, 1140  $\text{cm}^{-1}$ ; nmr (perdeuterioacetone):  $\delta$  1.45 (3H doublet, -CH<sub>3</sub>),  $\delta$  3.7 (1H triplet),  $\delta$  4.35 (1H triplet),  $\delta$  4.75 (1H multiplet),  $\delta$  7.65 (2H doublet),  $\delta$  8.05 (2H doublet). (Together the triplets at  $\delta$  3.7 and  $\delta$  4.35 are assigned to the -CH<sub>2</sub>- group of the ring.)

*Anal.* Calcd. for C<sub>10</sub>H<sub>10</sub>ClNO<sub>3</sub>S: C, 43.56; H, 3.63. Found: C, 43.02. H, 3.61.

*N*-(2-Hydroxy-1-propyl)-4-chlorobenzenesulfonamide (VIII).

Cyclic compound VII (2.0 g., 0.0073 mole) was heated under reflux with 50 ml. of 2*M* aqueous sodium hydroxide solution for 1 hour. The cooled solution was neutralized with concentrated sulfuric acid to afford 1.4 g. (76.9%) of VIII, m.p. 51-52°.

*Anal.* Calcd. for C<sub>9</sub>H<sub>12</sub>ClNO<sub>3</sub>S: C, 43.28; H, 4.81; N, 5.61; S, 12.82. Found: C, 43.47; H, 4.98; N, 5.50; S, 12.94.

2-Chloroethyl 4-Toluenesulfonyl Thiocarbamate (IX).

To a solution of 8.52 g. (0.040 mole) of 4-toluenesulfonyl isothiocyanate (II) in 20 ml. of dry ether was added dropwise with stirring under nitrogen a solution of 3.22 g. (0.040 mole) of 2-chloroethanol during 15 minutes. The solution was stirred an additional 1 hour at ambient temperature and then allowed to stand overnight. Removal of ether *in vacuo* gave 11.92 g. of waxy material, which after trituration with two 25-ml. portions of petroleum ether and recrystallization from benzene afforded 5.08 g. (41%) of IX, m.p. 79-82°. Further attempts at purification were unsuccessful; ir: 1390 (C=S), 1300 (C=S)  $\text{cm}^{-1}$ ; nmr (deuteriochloroform):  $\delta$  2.4 (3H singlet, CH<sub>3</sub>),  $\delta$  3.7 (2H triplet, -CH<sub>2</sub>Cl),  $\delta$  4.6 (2H triplet, -O-CH<sub>2</sub>),  $\delta$  7.3 (2H doublet, aromatic),  $\delta$  7.9 (2H doublet,

aromatic),  $\delta$  9.3 (1H broad, -SO<sub>2</sub>NH-C-).

3-(4-Toluenesulfonyl)oxazolidine-2-thione (X).

A solution of 1.39 g. (0.0047 mole) of IX, 20 ml. of pyridine, and 40 ml. of dry benzene was stirred and heated under reflux for 1.5 hours. The addition of petroleum ether to the cooled solution gave 1.14 g. (94%) of X, m.p. 114-124°. Recrystallization from chloroform/petroleum ether afforded product with m.p. 131-134°; ir: 1400 (C=S), 1295 (C=S)  $\text{cm}^{-1}$ ; nmr (perdeuterioacetone):  $\delta$  2.4 (3H singlet, CH<sub>3</sub>),  $\delta$  3.6 (2H triplet, -N-CH<sub>2</sub>-),  $\delta$  4.6 (2H triplet, -CH<sub>2</sub>-O-),  $\delta$  7.3 (2H doublet),  $\delta$  7.8 (2H doublet).

*Anal.* Calcd. for C<sub>10</sub>H<sub>11</sub>NO<sub>3</sub>S<sub>2</sub>: C, 46.69; H, 4.28; N, 5.45. Found: C, 46.64; H, 4.20; N, 5.44.

REFERENCES AND NOTES

- For part VIII, see J. W. McFarland and S. P. Gaskins, *J. Org. Chem.*, **37**, 99 (1972).
- Author to whom correspondence should be addressed. Recipient of DuPont Research Grant, Summer, 1979.
- McCluer Scholar, Summer, 1975.
- J. W. McFarland and J. B. Howard, *J. Org. Chem.*, **30**, 957 (1969).
- J. W. McFarland, D. E. Lenz, and D. J. Grosse, *ibid.*, **31**, 3798 (1966); *ibid.*, **33**, 3514 (1968).
- J. W. McFarland and D. Thoennes, *ibid.*, **35**, 704 (1970).
- J. W. McFarland, D. Green and W. Hubble, *ibid.*, **35**, 702 (1970).
- J. W. McFarland, *Int. J. Sulfur Chem., B*, **7**, 319 (1972).
- J. W. McFarland and R. W. Houser, *J. Org. Chem.*, **33**, 340 (1968).
- K. Dickore and E. Kuehle, German Patent 1, 183, 492 (Dec. 17, 1964); *Chem. Abstr.*, **62**, 7691 (1965).