

## Isothiazoles VI: 4,5-Dihaloisothiazolidin-3-one 1-Oxides

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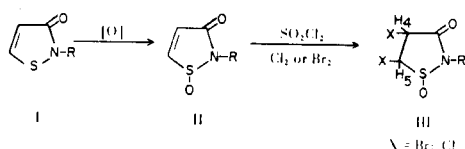
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A useful and facile procedure for preparing 4,5-dihaloisothiazolidin-3-one 1-oxides is reported. Chlorination or bromination of various 4-isothiazolin-3-one 1-oxides yielded the title compounds.

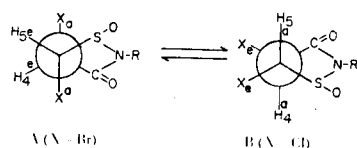
*J. Heterocyclic Chem.*, 13, 1095 (1976).

Previous publications (1,2) describe the synthesis of a series of 4-isothiazolin-3-ones (I) and their oxidation to a variety of 4-isothiazolin-3-one 1-oxides (II). We now wish to report the facile preparation of 4,5-dihaloisothiazolidin-3-one 1-oxides (III) by halogen addition to II.



The 4,5-dihaloisothiazolidin-3-one 1-oxides were isolated in good yield (33-62%). Crude products were readily purified by recrystallization or column chromatography. Compounds III were identified by elemental analyses, ir and nmr spectral data.

The nmr spectra were not immediately reconcilable with the anticipated *trans* addition products. The bromo derivatives exhibited singlets for H<sub>4</sub> and H<sub>5</sub>, whereas the chloro derivatives showed well defined spectra in which H<sub>4</sub> and H<sub>5</sub> were doublets. Derivatives III likely exist as several conformers and the Newman projections A and B best illustrate the two of the probable conformations.



Bromine-bromine interactions favor conformation A by allowing the bromine atoms to be as far apart as possible. Models show the vicinal dihedral angle, H<sub>4</sub>-H<sub>5</sub>, close to 90° and consequently no vicinal coupling would be expected (3) for conformation A. Chlorine addition should provide the thermodynamically most favored diequatorial conformer B. This H<sub>4</sub>-H<sub>5</sub> vicinal dihedral angle approaches 170°. The calculated coupling constant of 10 Hz for B is in agreement with the observed value of 10 Hz.

## EXPERIMENTAL

Melting points were determined using a Thomas-Hoover capillary melting point apparatus, and are uncorrected. Nmr spectra were recorded on a Varian T-60 Spectrometer. The multiplicity of the absorption is shown in brackets: s, singlet, d, doublet, t, triplet and m, multiplet. Elemental analyses were performed by the analytical department of the Research Division of the Rohm and Haas Company. The following experiments illustrate the general reaction procedures employed.

## 4,5-Dichloroisothiazolidin-3-one 1-Oxide.

To a solution of 2.3 g. (0.02 mole) of 4-isothiazolin-3-one 1-oxide in 80 ml. of ethylene dichloride was slowly added 2.7 g. (0.02 mole) of sulfonyl chloride. The solution was stirred overnight, during which time a heavy white precipitate formed. This solid was filtered, washed with ethylene dichloride and dried under vacuum to yield 2.0 g. (54%) of product, m.p. 172-174° from ethyl acetate; nmr (DMSO-d<sub>6</sub>): δ 5.44 (d, J<sub>4,5</sub> = 10 Hz, 4H), 5.84 (d, J<sub>5,4</sub> = 10 Hz, 5H), 11.80 (m, NH).

*Anal.* Calcd. for C<sub>3</sub>H<sub>3</sub>Cl<sub>2</sub>NO<sub>2</sub>S: C, 19.16; H, 1.61; N, 7.45; S, 17.05; Cl, 37.71. Found: C, 19.46; H, 1.64; N, 7.30; S, 17.64; Cl, 37.85.

## 4,5-Dichloro-2-n-octylisothiazolidin-3-one 1-Oxide.

To a solution of 2.29 g. (0.01 mole) of 2-n-octyl-4-isothiazolin-3-one 1-oxide in 3 ml. of ethylene dichloride was slowly added 1.4 g. (0.01 mole) of sulfonyl chloride in 3 ml. of ethylene dichloride. The solution was stirred at room temperature over a weekend. The solution was filtered to remove traces of a solid and concentrated to give an oil. This oil was purified *via* column chromatography (100% benzene:silica) to give 1.0 g. (33%) of the desired product, m.p. 47-48° from ether/pentane; nmr (DMSO-d<sub>6</sub>): δ 5.63 (d, J<sub>4,5</sub> = 10 Hz, 4H), 5.96 (d, J<sub>5,4</sub> = 10 Hz, 5H), 0.86 (t, 3, CH<sub>3</sub>), 1.0-2.0 (m, 12, C<sub>6</sub>H<sub>12</sub>), 3.53 (t, 2, NCH<sub>2</sub>).

*Anal.* Calcd. for C<sub>11</sub>H<sub>19</sub>Cl<sub>2</sub>NO<sub>2</sub>S: C, 44.00; H, 6.38; N, 4.66; S, 10.68; Cl, 23.62. Found: C, 44.11; H, 6.56; N, 4.55; S, 10.81; Cl, 23.85.

## 4,5-Dibromoisothiazolidin-3-one 1-Oxide.

To a solution of 2.2 g. (0.02 mole) of 4-isothiazolin-3-one 1-oxide in 50 ml. of ethylene dichloride was added a solution of 10 ml. of ethylene dichloride containing 3.5 g. (0.022 mole) of bromine. The solution was stirred overnight at room temperature.

The white precipitate which separated was filtered, washed with ethylene dichloride and dried under vacuum to afford 3.2 g. (58%) of product, m.p. 149-151° from ethyl acetate; nmr (DMSO- $d_6$ ):  $\delta$  5.30 (s, 4H), 5.84 (s, 5H), 8.48 (s, NH).

*Anal.* Calcd. for  $C_3H_3Br_2NO_2S$ : C, 13.01; H, 1.09; N, 5.05; S, 11.58; Br, 57.71. Found: C, 13.20; H, 1.30; N, 4.93; S, 11.26; Br, 57.44.

#### 4,5-Dibromo-2-*n*-octylisothiazolidin-3-one 1-Oxide.

To a solution of 2.2 g. (0.01 mole) of 2-*n*-octyl-4-isothiazolin-3-one 1-oxide in 15 ml. of ethylene dichloride was added a solution of 15 ml. of ethylene dichloride containing 1.76 g. (0.011 mole) of bromine. The clear solution was stirred overnight at room temperature. The solution was filtered and concentrated to give

2.4 g. (62%) of the desired product, amber oil; nmr (deuteriochloroform):  $\delta$  4.77 (s, 4H), 5.14 (s, 5H), 0.87 (t, 3  $CH_3$ ), 1.1-2.1 (m, 12,  $C_6H_{12}$ ), 3.74 (t, 2,  $NCH_2$ ).

#### REFERENCES

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