THE STRUCTURES AND CHEMISTRY OF THE PRODUCTS FROM THE REACTION OF AMINO ALCOHOLS WITH CARBON DISULPHIDE[1]

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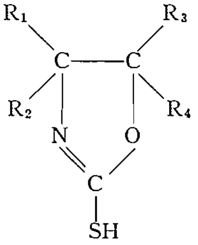
ABSTRACT

A study of the infrared spectra of the oxazoline derivatives, which are formed by the condensation of carbon disulphide with amino alcohols, shows that they possess the oxazolidine-2-thione structure rather than the tautomeric 2-thiol-2-oxazoline structure. 2-Benzylamino-4,4-dimethyl-2-oxazoline was formed by the reaction of benzylamine with 2-methylmercapto-4,4-dimethyl-2-oxazolinium iodide. 5-Diethylaminomethyl-2-oxazolidone and its methylation product also have been prepared.

The structures of the oxygen–nitrogen containing heterocyclics from the reaction of carbon disulphide with amino alcohols have been described previously as either oxazoline-2-thiols (I) (2, 8) or oxazolidine-2-thiones (II) (4, 5). Structure I is encountered most frequently in the literature (8) although Ettlinger (3) describes the infrared spectra of oxazolidine-2-thione and 5,5-dimethyloxazolidine-2-thione in detail. A further study of the infrared spectra (Table I) of several of these heterocyclics and their corresponding methylation products confirms structure II as the correct one for these condensation



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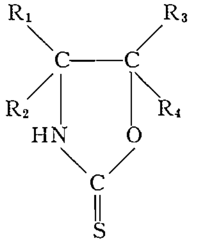

II

TABLE I

INFRARED ABSORPTION BAND OF SUBSTITUTED OXAZOLIDINE-2-THIONES

Compound	N—H stretching	C=N	N—H bending
4-Methyl-4-hydroxymethyloxazolidine-2-thione	3380[a] 3265[a] 3145		1526
4,4-Dimethyloxazolidine-2-thione	3155		1525
5-Diethylaminomethyloxazolidine-2-thione	3140		1546
2-Methylmercapto-4,4-dimethyl-2-oxazolinium iodide	3275 3030	1646	1533
2-Methylmercapto-4-ethyl-2-oxazolinium iodide	3315	1641	1528

[a] *One of these bands may be the result of O—H stretching vibrations.*

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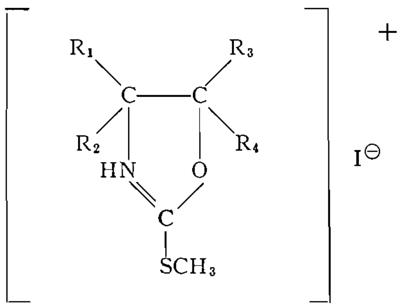
products. The infrared spectra of 4-methyl-4-hydroxymethyloxazolidine-2-thione (II, $R_1 = CH_3$; $R_2 = HOCH_2$; R_3 and $R_4 = H$), 4,4-dimethyloxazolidine-2-thione (II, R_1 and $R_2 = CH_3$; R_3 and $R_4 = H$), and 5-diethylaminomethyloxazolidine-2-thione (II, R_1, R_2, and $R_3 = H$; R_4 = diethylaminomethyl) show the absence of a C=N band and the presence of strong N—H stretching and bending bands. On the other hand 2-methylmercapto-4,4-dimethyl-2-oxazolinium iodide (III, R_1 and $R_2 = CH_3$; R_3 and $R_4 = H$) and 2-methylmercapto-4-ethyl-2-oxazolinium iodide (III, R_1, R_3, and $R_4 = H$; $R_2 = C_2H_5$) do have strong C=N stretching bands at 1646 cm.$^{-1}$ and 1641 cm.$^{-1}$ respectively in agreement with their structure (III).



III

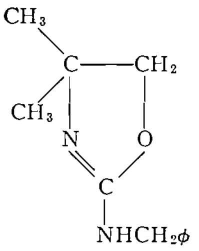
The yields of the substituted oxazolidine-2-thiones with the exception of 4-methyl-4-hydroxymethyloxazolidine-2-thione are based on the following equation:

$$2NH_2CR_1R_2CR_3R_4OH + CS_2 \rightarrow HOCR_3R_4CR_1R_2NHCS_2^{\ominus}\overset{\oplus}{N}H_3CR_1R_2CR_3R_4OH$$

$$\xrightarrow{\Delta} \text{II} + NH_2CR_1R_2CR_3R_4OH + H_2S.$$

The yield of 4-methyl-4-hydroxymethyloxazolidine-2-thione was raised to 84.7% (based on conversion of 1 mole equivalent of amino alcohol into 1 mole equivalent of the substituted oxazolidine-2-thione) by intermittent refluxing of the reaction mixture with additional portions of carbon disulphide.

2-Methylmercapto-4,4-dimethyl-2-oxazolinium iodide was converted into 2-benzylamino-4,4-dimethyl-2-oxazoline (IV) by refluxing with benzylamine in the presence of ethanol. This reaction is similar to the conversion of 2-



IV

methylmercapto-2-imidazolines into 2-substituted amino-2-imidazolines previously (1, 7) described.

During the course of this work 5-diethylaminomethyl-2-oxazolidone (m.p. 51.5–53°C.) and 5-(diethyl methyl ammonium methyl)-2-oxazolidone iodide (m.p. 160.5–161.5°C.) also were prepared.

EXPERIMENTAL[2]

4,4-Dimethyloxazolidine-2-thione (6, 8)

2-Amino-2-methyl-1-propanol (44.6 gm., 0.5 mole) in benzene (150 cc.) was added dropwise to a stirred solution of carbon disulphide (35.3 gm., 0.55 mole) in benzene (150 cc.) at 5°C. over a period of 15 min. The stirring was continued for 30 min. at room temperature after which the yellow crystalline intermediate was recovered by filtration. This dithiocarbamate salt was heated in an oil bath at 105–135°C. until the evolution of hydrogen sulphide ceased. The cooled residue was triturated with water (100 cc.) and the colorless crystals (m.p. 121–123°C.) were removed by filtration, yield 24.7 gm. (75.3%). Two crystallizations from water raised the melting point to 123.5–124°C. Calc. for C_5H_9NOS: C, 45.77; H, 6.91; N, 10.68%. Found: C, 45.58; H, 6.60; N, 10.3%.

2-Methylmercapto-4,4-dimethyl-2-oxazolinium Iodide

4,4-Dimethyloxazolidine-2-thione (20 gm., 0.15 mole) was refluxed in a solution of methyl iodide (23.8 gm., 0.16 mole) in absolute methanol (70 cc.) for 30 min. On cooling in a freezing mixture, colorless crystals (m.p. 80–82°C.) were obtained, yield 25.2 gm. (57.3%). The melting point was raised to a constant value of 84–85°C. by one crystallization from cold absolute methanol. Calc. for $C_6H_{12}INOS$: C, 26.38; H, 4.43; S, 11.74; N, 5.13%. Found: C, 26.67; H, 4.15; S, 11.45; N, 4.94%.

2-Benzylamino-4,4-dimethyl-2-oxazoline

A solution of 2-methylmercapto-4,4-dimethyl-2-oxazolinium iodide (25.15 gm., 0.09 mole) and benzylamine (9.87 gm., 0.09 mole) in ethanol (10 cc.) was refluxed for eight and a half hours. Removal of the ethanol *in vacuo* under an atmosphere of nitrogen gave a turbid oil (yield 30 gm.). A small sample of this oil was converted into its picrate (m.p. 149–150°C.) in the usual manner. Two crystallizations from ethanol raised the melting point to 150–151°C. Calc. for $C_{18}H_{19}N_5O_8$: C, 49.86; H, 4.42; N, 16.15%. Found: C, 49.54; H, 4.39; N, 16.3%.

The major portion (27.76 gm.) of the oily reaction product was dissolved in warm (50°C.) water (500 cc.) and the solution was passed through a column of Amberlite IRA-400 resin (300 cc.) at a rate of 7–8 cc. per min. The column was washed with 8500 cc. of water. Colorless needles (m.p. 73–73.5°C.) were obtained in 55.5% yield (11.5 gm.) from the effluent and washings on evapora-

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[2] *All melting points are uncorrected. Microanalyses were determined by Micro-Tech Laboratories, Skokie, Illinois, and Drs. G. Weiler and F. B. Strauss, Oxford, England.*

tion *in vacuo* under nitrogen. Two crystallizations from carbon tetrachloride raised the melting point of the 2-benzylamino-4,4-dimethyl-2-oxazoline to 79–80.5°C. Calc. for $C_{12}H_{16}N_2O$: C, 70.53; H, 7.89; N, 13.72%. Found: C, 70.81; H, 7.83; N, 13.78%.

4-Ethyloxazolidine-2-thione

4-Ethyloxazolidine-2-thione (m.p. 73–74°C.) (8) was prepared from 2-amino-1-butanol by the method described above for 4,4-dimethyloxazolidine-2-thione. Calc. for C_5H_9NOS: C, 45.77; H, 6.92; N, 10.68; S, 24.44%. Found: C, 45.92; H, 6.47; N, 10.5; S, 24.8%.

2-Methylmercapto-4-ethyl-2-oxazolinium Iodide

A solution of 4-ethyloxazolidine-2-thione (4 gm., 0.03 mole) and methyl iodide (4.33 gm., 0.03 mole) in 35 cc. of absolute methanol was refluxed for 30 min. The residue, after removal of the methanol *in vacuo*, crystallized on standing, yield 3.91 gm. (43.4%). Crystallization from absolute methanol raised the melting point from 83–84.5°C. to 84.5–85.5°C. Calc. for $C_6H_{12}INOS$: C, 26.38; H, 4.43; N, 5.13%. Found: C, 26.27; H, 4.44; N, 5.12%.

4-Methyl-4-hydroxymethyloxazolidine-2-thione

Carbon disulphide (83.75 gm., 1.1 mole) was added to a stirred solution of 2-amino-2-methyl-1,3-propanediol (105.1 gm., 1 mole) in ethanol (750 cc.) at 2–5°C. over a period of 25 min. This solution was refluxed for six hours after which a second portion of carbon disulphide (42 gm., 0.55 mole) was added and the refluxing continued for another 16 hr. Finally a third portion (80 gm., 1.05 moles) of carbon disulphide was added and the solution was refluxed for a further 16 hr. After removal of the excess carbon disulphide and solvent, a brown semicrystalline residue was obtained. It was triturated with acetone and the colorless crystals (m.p. 88–93°C.) were removed by filtration, yield 124.5 gm. (84.7%). The crude material was purified to a constant melting point of 92.5–93.5°C. by several crystallizations from ethyl acetate. Calc. for $C_5H_9NO_2S$: C, 40.79; H, 6.16; N, 9.52; S, 21.79%. Found: C, 40.95; H, 6.73; N, 9.65; S, 21.6%.

A portion (19.5 gm., 0.13 mole) of the 4-methyl-4-hydroxymethyloxazolidine-2-thione was refluxed in absolute methanol (75 cc.) with methyl iodide (20.7 gm., 0.146 mole) for 30 min. Removal of the alcohol *in vacuo* under nitrogen gave a yellow crystalline product (m.p. 112–114.5°C.), yield 13.76 gm. (79.2%). Crystallization from ethyl acetate raised the melting point to 115.5–116.5°C. This material gave a negative qualitative test for sulphur and its analytical values agreed with those calculated for 4-methyl-4-hydroxymethyl-2-oxazolidone. Homeyer (5) reported the melting point of this compound as 115–116.5°C. Calc. for $C_5H_9NO_3$: C, 45.80; H, 6.92%. Found: C, 45.68; H, 6.74%.

5-Diethylaminomethyloxazolidine-2-thione

A solution of 1-amino-3-diethylamino-2-propanol (219.4 gm., 1.5 moles) in 1000 cc. of benzene was added dropwise to a stirred solution of carbon disulphide (125.6 gm., 1.65 moles) in 1750 cc. benzene at 2°C. over a period of four hours. After 15 min., a grayish precipitate formed. The reaction mixture was allowed to stand overnight in the refrigerator after which the solid material was removed by filtration. This solid was suspended in 3000 cc. of ethanol and the solution was refluxed until the evolution of hydrogen sulphide ceased. The resulting brown ethanol solution was filtered to remove sulphur and then treated with Norite A. The filtrate, on evaporation to one-third its original volume and cooling, gave colorless needles. A second crop was obtained from the mother liquor. The total yield of crude product (m.p. 95–97°C.) was 109 gm. (77.2%). This crude material after crystallization from ethanol melted at 96–97°C. Calc. for $C_8H_{16}N_2OS$: C, 51.02; H, 8.57; N, 14.86; S, 17.03%. Found: C, 51.15; H, 8.55; N, 14.70; S, 16.9%.

A picrate formed in the usual manner melted at 154–155°C., yield 77.2%. Calc. for $C_{14}H_{19}N_5O_8S$: C, 40.27; H, 4.58; N, 16.7%. Found: C, 40.33; H, 4.88; N, 16.6%.

A sample (2.8 gm., 0.015 mole) of 5-diethylaminomethyloxazolidine-2-thione in 9 cc. of methanol was treated with hydriodic acid (2.05 cc., $d = 1.7$). On addition of dry ether (150 cc.) to this solution, an oil separated. This oil crystallized (m.p. 113–120°C.) on standing, yield 4.23 gm. (90.0%). Two crystallizations from ethanol raised the melting point of the hydroiodide salt to 124–126°C. Calc. for $C_8H_{17}IN_2OS$: C, 30.39; H, 5.42; N, 8.86%. Found: C, 30.60; H, 5.60; N, 9.0%.

5-Diethylaminomethyl-2-oxazolidone

1-Amino-3-diethylamino-2-propanol (18.31 gm., 0.125 mole) and diethyl carbonate (22 gm., 0.186 mole) were condensed in the presence of sodium methylate catalyst (0.10 gm.) by the method of Homeyer (5). After removal of the excess ethyl carbonate *in vacuo* under nitrogen, an oil was obtained, yield 19.09 gm. (88.5%). This oil crystallized (m.p. 40–43°C.) on standing and two crystallizations from ethanol raised the melting point to 51.5–53°C. Calc. for $C_8H_{16}N_2O_2$: C, 55.80; H, 9.37; N, 16.27%. Found: C, 56.10; H, 9.41; N, 15.9%.

A sample (1.0 gm., 0.0058 mole) of 5-diethylaminomethyl-2-oxazolidone was refluxed with methyl iodide (0.825 gm., 0.0058 mole) in absolute methanol for 30 min. This solution was cooled to room temperature and allowed to stand for 15 hr. Colorless crystals (m.p. 158–161°C.) were deposited from the solution, yield 1.235 gm. (67.7%). Two crystallizations from absolute ethanol raised the melting point to a constant value of 160.5–161.5°C. Calc. for $C_9H_{19}IN_2O_2$: C, 34.41; H, 6.09; I, 40.39; N, 8.92%. Found: C, 34.22; H, 5.94; I, 40.58; N, 9.04%.

Infrared Spectra

The infrared spectra were obtained with a Perkin-Elmer single beam spectrophotometer equipped with a sodium chloride prism. The samples were observed as mulls of the solid in Nujol.

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