

477. *Thiazolid-2:5-dione*.

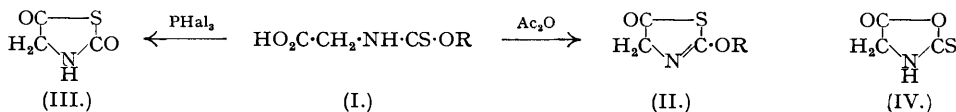
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It is shown that the product obtained by treating *N*-thiocarbethoxyglycine (I) (see previous paper) with phosphorus trihalides is thiazolid-2:5-dione (III). It is also obtained by the dealkylation of 2-ethoxythiazol-5-one with phosphorus trihalides in moist benzene. It readily polymerises on heating its aqueous solution to give what is believed to be a polyglycine. The attempted cyclodealkylation of *N*-thiocarbethoxysarcosine (VI) and *N*-thiocarbethoxy-DL-alanine (VII) did not give solid reaction products.

In the preceding paper it was observed that whereas the cyclodehydration of *N*-thiocarbethoxyglycine (I; R = Et) with acetic anhydride gave the expected 2-ethoxythiazol-5-one (II; R = Et), treatment of (I; R = Et) with phosphorus trihalides gave a product which was not the expected hydrobromide of (II; R = Et). This behaviour was unexpected in that, as Cook, Harris, Heilbron, and Shaw (*J.*, 1949, 1056) have shown, the related *N*-dithiocarbonylbenzyloxyglycine readily gives 2-benzylthiothiazol-5-one hydrobromide on treatment with phosphorus tribromide.

That the reaction involved the loss of the alkyl group (R) was shown by the fact that the same product resulted from (I) irrespective of the nature of R. It could be recrystallised from water in inch-long laths, m. p. 110°, but if the solution was heated for too long or at too high a temperature an inflammable gas was evolved which had the odour of hydrogen sulphide and

contained labile sulphur. Prolonged heating in dilute solution, or shorter heating in more concentrated solution, resulted in the precipitation of an insoluble white powder containing

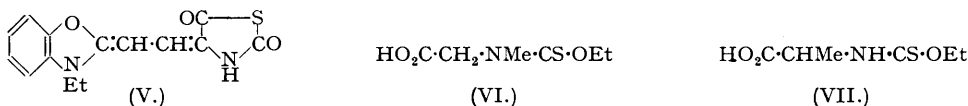


nitrogen and a trace of sulphur. It dissolved in aqueous sodium carbonate with evolution of carbon dioxide. The presence of a reactive methylene group was indicated by the development of colour with triethylamine-alcohol solutions of 2-acetanilidovinyl derivatives of heterocyclic quaternary salts.

Analysis indicated an empirical formula $\text{C}_3\text{H}_3\text{O}_2\text{NS}$ (no halogen) which corresponds to loss of a molecule of water from the acid (I; $\text{R} = \text{H}$). The substance was thus formulated as thiazolid-2:5-dione (III) or (since ethyl chloride may be eliminated from the intermediate acid chloride) 2-thio-oxazolid-5-one (IV).^{*} The preferential formation of an oxazolidine ring seemed, however, unlikely. Proof of the correctness of the formulation (III) was then obtained by dealkylation of 2-ethoxythiazol-5-one (II; $\text{R} = \text{Et}$) by phosphorus trihalides in moist benzene giving, in high yield, the identical product of m. p. 110° . This ready loss of the alkyl group, presumably by acid hydrolysis, appears to be analogous to the formation of 2-hydroxythiazoles instead of the expected ethers on condensation of ethyl thioncarbamates with α -halogeno-ketones (Hantzsch and Hubacher, *Annalen*, 1890, **259**, 250; Knott, *J.*, 1947, 1656).

The synthesis of this compound has been attempted by Cook, Heilbron, and Hunter (*J.*, 1949, 1443), who thought that it might possess a stability intermediate between that of oxazolid-2:5-dione (anhydro-*N*-carboxyglycine) and 2-thiothiazolid-5-one and would thus be a more useful reagent than either of these compounds. Although (III) has not been exploited at all fully it would appear that their expectation is realized in that it is fairly stable (when pure) towards moist air and yet readily polymerises on heating. It gives salt-like compounds on treatment with morpholine or triethylamine which may be analogous to the products obtained by Cook and Levy (*J.*, 1950, 646) from 2-thiothiazolid-5-one.

The condensation of (III) with 2-2'-acetanilidovinylbenzoxazole ethiodide in boiling alcoholic triethylamine gave a dye, the magenta solutions of which in methanol slowly faded. Analysis indicated an empirical formula of $\text{C}_{16}\text{H}_{18}\text{O}_4\text{N}_2\text{S}$ which corresponds to the addition of a molecule of ethanol to the expected [2-(3-ethylbenzoxazole)] [4-thiazolid-2:5-dione]dimethinmerocyanine (V). The latter dye, giving yellow solutions in methanol, was obtained by the cold reaction of the above components.



The condensation of ethyl ethoxydithioformate with sarcosine and DL-alanine gave *N*-thioncarbethoxysarcosine (VI) and *N*-thioncarbethoxy-DL-alanine respectively. Attempts to effect cyclodealkylation of these compounds gave oils which have not been investigated.

EXPERIMENTAL.

Analyses are by Drs. Weiler and Strauss, Oxford.

Thiazolid-2:5-dione (III).—(a) *N*-Thioncarbethoxyglycine (5 g.) (preceding paper) was covered with benzene (15 c.c.), and phosphorus trichloride (3 c.c., 1.1 mols.) was added. The flask was warmed gently on the steam-bath until the glycine commenced to liquefy. The flask was swirled until the contents were completely molten (ca. 40°). Crystallisation then set in rapidly. The solid *dione* was collected immediately (if it is left overnight some liquefaction occurs) and washed with benzene, then ice-cold water (20 c.c.) to remove a slight stickiness. The colourless crystals (2.7 g., 75%) were dissolved cautiously in the minimum of warm water and chilled. Long laths, m. p. 110° , separated. Alternatively small crystals were obtained by ice-cooling of its alcoholic solution (Found: C, 31.2; H, 2.65; N, 11.6; S, 27.1. $\text{C}_3\text{H}_3\text{O}_2\text{NS}$ requires C, 30.75; H, 2.55; N, 11.95; S, 27.4%). The yield does not vary very much if the amount of phosphorus trichloride is increased to 2.2 mols. or reduced to 0.33 mol. The use of phosphorus tribromide gives similar yields. If dioxan-benzene is used as the solvent the yields are lower.

^{*} Since this paper was written Bailey (*J.*, 1950, 3461) has synthesised (I; $\text{R} = \text{Me}$) by an alternative method and cyclised it with thionyl chloride-pyridine. He formulates his product as (IV), presumably assuming that direct elimination of methyl chloride has occurred from the intermediate acid chloride as is known to occur in the synthesis of anhydro-*N*-carboxyglycine. It has now been found, however, that his product, m. p. 108° , is identical (mixed m. p.) with our product.

(b) 2-Ethoxythiazol-5-one (5 g.) was dissolved in benzene (15 c.c.), and phosphorus tribromide (3 c.c.) added. Addition of water (0.6 c.c.) caused immediate precipitation of an oil which rapidly crystallised. It (2.9 g.) formed long laths, m. p. 110°, from water and was identical (mixed m. p.) with the product obtained as in (a).

[2-(3-Ethylbenzoxazole)][4-(thiazolid-2:5-dione)]dimethinmerocyanine (V).—2'-Acetanilidovinylbenzoxazole ethiodide (2.2 g.) was dissolved in ethanol (150 c.c.), the solution was cooled to 30°, and triethylamine (0.5 c.c.) and the dione (0.6 g.) were added. After 2 hours the dye which had separated was collected, boiled out with ethanol, and obtained as orange leaflets, m. p. 248°, from pyridine-benzene (Found: N, 9.65. $C_{14}H_{12}O_3N_2S$ requires N, 9.7%). If the above components were refluxed in ethanol (10 c.c.) for 15 minutes the yellow solution became deep crimson, and a dye separated. It imparted a pink colour to water and was insoluble in benzene. It gave a magenta solution in cold alcohols or nitrobenzene (red when hot), and a yellow solution in acetone. It formed sepia leaflets, m. p. 257°, from nitrobenzene (Found: C, 58.0; H, 5.0; N, 8.35; S, 8.9. $C_{16}H_{18}O_4N_2S$ requires C, 57.5; H, 5.4; N, 8.4; S, 9.6%). It is a weak photographic sensitizer.

Polyglycylglycine.—The dione (1 g.) was dissolved in water (15 c.c.) and heated on the steam-bath. The polymer separated after 1 minute. The white amorphous solid was repeatedly boiled out with water. It darkened slightly at about 300° (Found: N, 21.5; S, 0.65%).

N-Thioncarbethoxy-DL-alanine (VII).—Ethyl ethoxydithioformate (35 g.) in alcohol (40 c.c.) was added to a solution of DL-alanine (20.8 g.) and potassium hydroxide (12.1 g.) in water (40 c.c.) and refluxed on the steam-bath for 24 hours. The solution was concentrated to half volume and acidified with concentrated hydrochloric acid. The solid *ester* (21 g.) formed white prisms, m. p. 103.5°, from water (Found: S, 17.8. $C_8H_{11}O_3NS$ requires S, 18.1%).

N-Thioncarbethoxysarcosine (VI).—Ethyl ethoxydithioformate (8.5 g.) in alcohol (10 c.c.) was added to a solution of sarcosine (5.0 g.) and potassium hydroxide (3.2 g.) in water (10 c.c.), and the whole refluxed on the steam-bath for 24 hours. After concentration to half volume the clear solution was acidified with concentrated hydrochloric acid and after chilling in ice the solid *product* (9.5 g.) was obtained as a colourless powder, m. p. 86°, from aqueous ethanol (Found: S, 18.3. $C_8H_{11}O_3NS$ requires S, 18.1%).

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