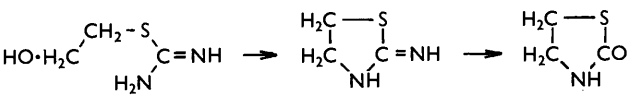
1026. *Some Derivatives of* S-(2-*Hydroxyethyl*)*thiourea.*

By L. A. Cort.

The hydrobromide of *S*-(2-hydroxyethyl)thiourea decomposes above its melting point to yield 1,4-dithian, as do also the hydrobromides of the *O*-formyl and the *O*-acetyl derivative. The picrate can be titrated with alkali hydroxides. Attempted preparation of the hydriodide of the *O*-formyl compound led to tetrathiourea hydriodide.

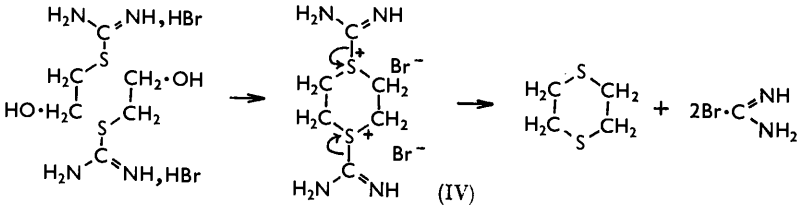
The melting behaviour [1] of the picrate of *S*-(2-hydroxyethyl)thiourea (I) suggests that ring-closure might be occurring to give the picrate of 2-iminothiazolidine (II) (or of the tautomer, 2-amino-2-thiazoline). However, the action of heat on the picrate, on the one gram scale, did not lead to the known thiazolidine picrate; only ammonium picrate



(I) (II) (III)

was isolated. It is possible that the water produced in the condensation (I) ⟶ (II) effects hydrolysis to give thiazolid-2-one (III) and ammonia, but since it did not appear practicable to increase the scale of the experiment attention was directed to other salts.

The hydrobromide of *S*-(2-hydroxyethyl)thiourea (I) behaved like the picrate in that after melting it re-solidified as the temperature was raised. However, in this case there is clearly no scheme of reaction (I) ⟶ (II) ⟶ (III); no 2-iminothiazolidine, thiazolid-2-one, or derivative thereof could be isolated; instead the products were 1,4-dithian and polymeric material.



(IV)

It is likely that the first step in this reaction is dimerisation to give a diquaternary salt (IV), and that this then undergoes dissociation. It would be expected that the bromoformamidine formed would rearrange to cyanamide hydrobromide, which would polymerise to dicyanamide and melamine, as is known [2] to be the case with chloroformamidine.

After removal of the 1,4-dithian, the residue was largely soluble in both hot dilute acid

[1] Cort and Pearson, *J.*, 1960, 1686.
[2] Johnson and Sprague, *J. Amer. Chem. Soc.*, 1939, **61**, 176; Mulder and Smit, *Ber.*, 1874, **7**, 1634.

and alkali, but no derivatives of 2-mercaptoethylamine could be isolated from these solutions (cf. acid hydrolysis [3] of thiazolines), confirming that there has been no condensation (I) ⟶ (II).

The hydrobromide *S*-(2-formyloxyethyl)thiourea and that of the *O*-acetate also decomposed above the melting point, and both gave 1,4-dithian, but in very much lower yield.

On treatment with dilute aqueous sodium hydroxide and benzoyl chloride, *S*-(2-hydroxyethyl)thiourea hydrobromide yielded benzoylthioethyl benzoate (as would be expected), but when sodium hydrogen carbonate was used in place of the hydroxide, the tribenzoyl derivative of the free base was obtained.

The picrate of the thiourea (I) could be titrated with 0·1N-sodium hydroxide, to give the molecular weight within ±3%; this is expected to be capable of useful extension.

In one experiment, for the attempted preparation of the hydriodide of *S*-(2-formyloxyethyl)thiourea, a product was isolated which analysed satisfactorily for tetrathiourea hydriodide. This is the first reported case of a compound of this type with acids, such compounds usually having the formula $(H_2N{\cdot}CS{\cdot}NH_2)_2,HX$, although tetrathiourea complexes are known with salts.

Experimental

M. p.s are corrected.

S-(2-*Hydroxyethyl*)*thiouronium Bromide*.—Prepared in the usual manner (in acetone) from ethylene bromohydrin, the bromide (77%) crystallised after 72 hr. It had m. p. 73—80° and was hygroscopic (some preparations were deliquescent; Olin and Dains [4] record the salt as an oil). Treatment with benzoyl chloride and 2N-sodium hydroxide gave the dibenzoyl derivative (m. p. 39°; prisms from methanol) of 2-mercaptoethanol (lit.,[5] m. p. 39°) (Found: C, 67·1; H, 4·6; S, 11·5. Calc. for $C_{16}H_{14}O_3S$: C, 67·1; H, 4·9; S, 11·2%).

Use of 0·1N-sodium hydrogen carbonate in place of the hydroxide led to the isolation of NN′-*dibenzoyl*-S-(2-*benzoyloxyethyl*)*thiourea*, m. p. 156°, needles from acetone–methanol (Found: C, 67·7; H, 4·75; N, 6·6; S, 7·4. $C_{24}H_{20}N_2O_4S$ requires C, 66·7; H, 4·6; N, 6·5; S, 7·4%).

It did not prove possible to isolate a salt from the hydrobromide, with trichloroacetic, benzoic, or 3,5-dinitrobenzoic acids, but the picrate [1] was readily obtained.

Titration of the Picrate.—Titration with 0·1N-sodium hydroxide was possible provided that attention was paid to the following points: aqueous acetone (1 : 2) was a suitable solvent; ethyl bis-2,4-dinitrophenylacetate was a suitable indicator (as used similarly [6] with picrates of hydrocarbons); it was necessary to add the alkali dropwise throughout, never to let it accumulate in local excess, and never to add further alkali when some previously added remained unneutralised. Titration to the stable end-point was a slow procedure, up to 5 hr. for 0·8 g. of picrate, but results were usefully reproducible (Found: *M*, 359, 353, 349, 341, 347. $C_9H_{11}N_5O_8S$ requires *M*, 349).

S-(2-*Formyloxyethyl*)*thiouronium Bromide*.—Prepared (in acetone) from 2-bromoethyl formate, the crude bromide (84%) was hygroscopic (m. p. 90—95°). It failed to yield a picrate in methanol, but after several days the solution deposited *S*-(2-hydroxyethyl)thiouronium picrate, m. p. and mixed m. p. 154—158°, re-solidifies 162°, re-melts 239—243° (decomp.) (Found: C, 31·2; H, 2·9; N, 20·0; S, 8·9. Calc. for $C_9H_{11}N_5O_8S$: C, 31·0; H, 3·2; N, 20·1; S, 9·2%).

S-(2-*Acetoxyethyl*)*thiouronium Bromide*.—The hygroscopic bromide was obtained (62%) from 2-bromoethyl acetate. Crystallisation from acetone–light petroleum (b. p. 60—80°) gave needles, m. p. 92—95° (lit.,[4] m. p. 99°) (Found: C, 24·7; H, 4·3; Br, 32·8; N, 11·3; S, 13·3. Calc. for $C_5H_{11}BrN_2O_2S$: C, 24·7; H, 4·6; Br, 32·9; N, 11·6; S, 13·2%). This salt behaved, as regards picrate formation, like the *O*-formyl compound.

Action of Heat on the Salts.—(*a*) *S*-(2-Hydroxyethyl)thiouronium picrate (1·0 g.) was heated from 150° to 180° during 8 min., then held at 180° for 3 min. After melting it slowly resolidified

[3] Crawhall and Elliott, *J.*, 1952, 3094; 1951, 2071.
[4] Olin and Dains, *J. Amer. Chem. Soc.*, 1930, **52**, 3322.
[5] Fromm and Jörg, *Ber.*, 1925, **58**, 306.
[6] " Organic Reagents for Organic Analysis," Hopkin and Williams, Ltd., 2nd edn., 1950, p. 112.

(with considerable effervescence at 170°). Crystallisation from aqueous acetone gave deep yellow prisms (0·3 g.), m. p. 258—275° (decomp.) (ammonium picrate?), which liberated ammonia with cold 0·1N-sodium hydroxide. (The picrates of 2-amino-2-thiazoline and 2-mercaptoethylamine have m. p. 235° and 126°, respectively.[7,8])

(*b*) *S*-(2-Hydroxyethyl)thiouronium bromide (10 g.) was melted and heated to 170°; it re-solidified with effervescence at *ca.* 160°. Treatment of a methanol extract with picric acid gave ammonium picrate (1·1 g.), orange-red orthorhombic biprisms (from acetone–benzene), m. p. 287—290° (decomp.) (Found: C, 29·35; H, 2·6; N, 22·8. Calc. for $C_6H_6N_4O_7$: C, 29·3; H, 2·5; N, 22·8%). The residue from the methanol extract was almost completely insoluble in cold dilute acid and alkali.

The product from 15 g. of bromide was extracted with carbon disulphide, to give 1,4-dithian (0·8 g., 18%), hexagonal plates, m. p. 110—111° (from acetone) (lit.,[9] m. p. 111°) (Found: C, 40·0; H, 6·6; S, 53·4. Calc. for $C_4H_8S_2$: C, 40·0; H, 6·7; S, 53·3%). (Thiazolid-2-one [10] has m. p. 52°, from carbon disulphide.)

The product from 20 g. of bromide was boiled with 2N-potassium hydroxide in 80% ethanol (300 ml.); some material (2·1 g.) did not dissolve during 1 hr. The action of benzoyl chloride on the filtrate yielded no solid derivative.

A similar hydrolysis by 3N-sulphuric acid also gave a solid residue (1·7 g.). Half of the filtrate yielded no solid derivative with benzoyl chloride and alkali; the other half with picric acid yielded yellow prisms (50 mg.) which did not melt below 360°, and did not liberate ammonia with alkali. No derivatives of 2-mercaptoethylamine (cf. ref. 8) were obtained. The solid residues were soluble in cold concentrated sulphuric acid; dilution produced amorphous material only.

(*c*) *S*-(2-Formyloxyethyl)thiouronium bromide (5 g.) gave a clear melt. Effervescence commenced at *ca.* 160°, and the material slowly (15 min.) solidified when held at 200°. Extraction by carbon disulphide gave 1,4-dithian (120 mg.), m. p. 104—107°, m. p. and mixed m. p. 111° after crystallisation from acetone. The residue was almost completely soluble in hot water (20 ml.); the solution yielded, with picric acid, only ammonium picrate [2·9 g.; m. p. and mixed m. p. 285—290° (decomp.)].

(*d*) With *S*-(2-acetoxyethyl)thiouronium bromide effervescence commenced in the molten bromide at *ca.* 150°. There was considerable darkening and the material appeared to have resolidified after 30 min. at 200°. Extraction by carbon disulphide gave 1,4-dithian (210 mg. from 20 g. of bromide), m. p. 100—107°, m. p. and mixed m. p. 111° after crystallisation.

Attempted Preparation of S-(2-*Formyloxyethyl*)*thiouronium Iodide.*—2-Chloroethyl formate (12·5 g.), sodium iodide (17·4 g.), and thiourea (12·1 g.) were boiled together in acetone (50 ml.) during 8 hr. After a further 12 hr. the deposited sodium chloride (8·7 g.) was removed and the solution set aside for 7 days. The crystals which separated (3·2 g.) had m. p. 170—180° (decomp.). Recrystallisation from acetone–benzene (poor recovery) furnished felted needles of *tetrathiourea hydriodide*, m. p. 193° [Found: C, 11·2; H, 4·3; I, 28·8; N, 26·3; S, 29·35. $(H_2N{\cdot}CS{\cdot}NH_2)_4$,HI requires C, 11·1; H, 4·0; I, 29·35; N, 25·9; S, 29·7%].

Attempts to obtain this compounds by saturating a solution of thiourea in acetone with hydrogen iodide were unsuccessful; thiourea was recovered (m. p. and mixed m. p. 179°).

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[7] Schöberl, Kawohl, and Hamm, *Chem. Ber.*, 1951, **84**, 571.
[8] Gabriel and Colman, *Ber.*, 1912, **45**, 1643.
[9] Masson, *J.*, 1886, **49**, 234.
[10] Michels and Gever, *J. Amer. Chem. Soc.*, 1956, **78**, 5350.