107. *Reactions of Benzthiazole Derivatives. Part I. The Reactivity of the Methylthiol Group in Quaternary Salts of* 1-*Methylthiobenzthiazole.*

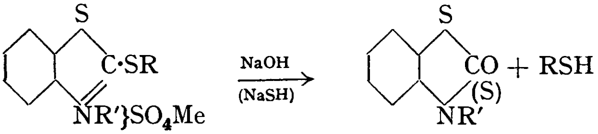
By Wilfred Archibald Sexton.

The methosulphate of 1-methylthiobenzthiazole reacts with aqueous sodium hydroxide, giving 2-methylbenzthiazolone. It reacts with aqueous sodium sulphide, giving 1-thio-2-methyl-1 : 2-dihydrobenzthiazole in good yield. The reaction has also been applied to some derivatives substituted in the benzene ring. In the action of ethyl iodide upon 1-methylthiobenzthiazole a quaternary salt is formed in which the alkyl groups have been interchanged.

1-β-*Hydroxyethylthiobenzthiazole* is changed on heating to 1-hydroxybenzthiazole.

A new example of the reactivity of the methylthiol group in quaternary salts of 1-methylthiobenzthiazole is provided when the methosulphate of 1-methylthiobenzthiazole is treated with aqueous sodium hydroxide or carbonate at room temperature, methylthiol being evolved and 2-methylbenzthiazolone obtained in good yield. In the reaction of the same quaternary salt with an aqueous solution of sodium sulphide or sodium hydrogen sulphide, methylthiol was again evolved and the 1-thio-2-methyl-1 : 2-dihydrobenzthiazole produced, identified by the absence of depression of melting point when mixed with authentic material prepared by heating dimethylaniline with sulphur (Rassow, Döhle, and Reim, *J. pr. Chem.*, 1916, **93**, 183; Mills, Clark, and Aeschliman, J., 1923, **123**, 2353). The yield was excellent.

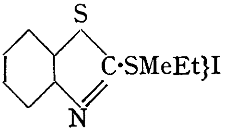
The quaternary ethosulphate of 1-methylthiobenzthiazole on treatment with sodium sulphide gave rise similarly to 1-thio-2-ethyl-1 : 2-dihydrobenzthiazole, and the quaternary methosulphate of 1-ethylthiobenzthiazole was converted similarly into 1-thio-2-methyl-1 : 2-dihydrobenzthiazole :

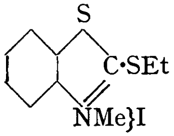


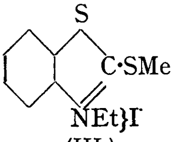
This reaction (which has also been applied to the following substituted derivatives of the original salt : 4-chloro, 4 methyl, and 3 : 4-benzo) recalls the experiment of Fischer

(*Ber.*, 1902, **35**, 3674) in which the methiodide of thio-*N*-methyl-α-pyridone was treated with sodium hydroxide, giving rise to methylthiol.

When the methiodide of 1-methylthiobenzthiazole was treated with sodium hydroxide and with sodium sulphide, the expected thiazolone and thio-dihydrothiazole respectively were obtained. When, however, 1-methylthiobenzthiazole was treated with ethyl iodide, a quaternary salt (II) was obtained which, on treatment with sodium sulphide, gave 1-thio-2-methyl-1 : 2-dihydrobenzthiazole. Treatment of 1-ethylthiobenzthiazole with methyl iodide gave rise to the same quaternary salt. From this it was inferred that either (i) the supposed quaternary iodide was in reality the sulphonium iodide (I), or (ii) during


(I.)


(II.)


(III.)

the reaction of 1-methylthiobenzthiazole with ethyl iodide a rearrangement of alkyl groups had occurred, leading to the quaternary ammonium iodide (II). Support for the latter alternative was found in the preparation of the ethiodide of 1-methylthiobenzthiazole (III) by reaction of the ethosulphate with potassium iodide. Its identity was established by its reaction with sodium sulphide, which gave rise to 1-thio-2-ethyl-1 : 2-dihydrobenzthiazole.

Rassow, Döhle, and Reim (*loc. cit.*) describe a quaternary iodide prepared by the action of ethyl iodide on 1-thio-2-methyl-1 : 2-dihydrobenzthiazole. Their preparation has been repeated, and the salt identified with the quaternary iodide (II) by its reaction with aqueous sodium sulphide to give 1-thio-2-methyl-1 : 2-dihydrobenzthiazole.

1-β-*Hydroxyethylthiobenzthiazole* was readily obtained by the reaction of ethylene chlorohydrin with sodio-1-thiolbenzthiazole. A crude quaternary methosulphate was obtained from this, which on treatment with sodium hydrogen sulphide gave 1-thio-2-methyl-1 : 2-dihydrobenzthiazole. An attempt to prepare the ethiodide of 1-β-hydroxyethylthiobenzthiazole by boiling the substance in ethyl iodide gave rise, surprisingly, to 1-hydroxybenzthiazole. Subsequent investigation showed that the conversion into hydroxybenzthiazole proceeded by the action of heat alone, and a good yield could thus be obtained. A small amount of crystalline material isolated as a by-product of the reaction had the correct m. p. for dithian, but the compound was not definitely identified. The main bulk of the by-product was of a resinous nature.

EXPERIMENTAL.

The methylthiol derivatives of 1-thiolbenzthiazole and its substituted derivatives were all prepared by reaction of methyl sulphate with the sodium salt of the thiol in aqueous solution. The compounds were purified, where this was necessary, by distillation in a vacuum or by crystallisation. 1-Ethylthiobenzthiazole was conveniently obtained by the reaction of ethyl chloride with alcoholic sodio-1-thiolbenzthiazole in an autoclave at 65—70°. The yield was good and the product was purified by distillation in a vacuum (m. p. 29°, b. p. 170°/12 mm.).

Reactions of 1-*Methylthiobenzthiazole and* 1-*Ethylthiobenzthiazole*.—(1) A mixture of 1-methylthiobenzthiazole (100 g.) and methyl sulphate (83 g.) was warmed gently; it became solid on cooling. This crude methosulphate was used in the following experiments: (a) The methosulphate was dissolved in water and treated with concentrated sodium hydroxide solution until the liquor was alkaline to litmus; methylthiol was evolved and an oil separated. On cooling, this solidified and was purified by washing with ligroin. It had m. p. 74—75° and was identified as 2-methylbenzthiazolone by mixed m. p. with authentic material (m. p. 76°) obtained by methylation of 1-hydroxybenzthiazole (Hunter, J., 1930, 125) (Found: C, 58·05; H, 4·2; N, 8·65; S, 19·8. Calc. for C_8H_7ONS: C, 58·2; H, 4·2; N, 8·5; S, 19·4%). The yield was 64% of the theoretical. Sodium carbonate or a suspension of lime gave the same compound.

(b) The quaternary methosulphate from 100 g. of 1-methylthiobenzthiazole was dissolved in water (200 g.) at about 50°, and a solution of crystalline sodium sulphide (133 g.) in water (100 c.c.) added during 5 minutes. The temperature rose to 66° and methylthiol was evolved.

The mixture was stirred for ½ hour and allowed to cool and the solid was separated, washed, and crystallised from alcohol (420 c.c.). The product was identified by m. p. 90—91° and mixed m. p. with authentic material as 1-thio-2-methyl-1 : 2-dihydrobenzthiazole. Sodium hydrogen sulphide was substituted for sodium sulphide and gave the same result. The yield of recrystallised material was 71% of the theoretical.

(2) 1-Methylthiobenzthiazole (50 g.) was treated with ethyl sulphate (50·7 g.) under similar conditions to those used in the reaction with methyl sulphate. The resulting crude quaternary salt was dissolved in water (100 c.c.) at 50° and treated with a solution of crystalline sodium sulphide (66·5 g.). The temperature rose to 62° and was subsequently held at 60—65° for ½ hour. On cooling, the 1-thio-2-ethyl-1 : 2-dihydrobenzthiazole was separated and purified by distillation in a vacuum (yield, 81% of the theoretical), followed by crystallisation from alcohol; m. p. 77° (Hunter, J., 1930, **145**, gives m. p. 75°).

(3) A crude methosulphate of 1-ethylthiobenzthiazole, treated in aqueous solution with sodium sulphide, gave 1-thio-2-methyl-1 : 2-dihydrobenzthiazole (yield, 96%). The m. p. after crystallisation was 88—89°.

(4) 1-Methylthiobenzthiazole (30 g.) was boiled overnight with methyl iodide (30 g.) and methanol (100 c.c.). The resulting quaternary salt (5 g.) was dissolved in water (100 c.c.), and treated at room temperature with 28% sodium hydrosulphide solution (5 c.c.). 1-Thio-2-methyl-1 : 2-dihydrobenzthiazole was precipitated almost quantitatively (m. p. 88—89°).

(5) 1-Methylthiobenzthiazole (36·2 g.) was boiled overnight with ethyl iodide (40 g.), and the resulting quaternary salt (II) crystallised twice from alcohol. It then had m. p. 138—140°. When the quaternary salt (10 g.) was treated in aqueous solution with crystalline sodium sulphide (12 g.), 1-thio-2-methyl-1 : 2-dihydrobenzthiazole was precipitated.

(6) 1-Ethylthiobenzthiazole (39 g.) was boiled for 3 hours with methyl iodide (40 g.). The resulting quaternary salt, m. p. 138—140°, gave no depression of m. p. when mixed with the quaternary salt (II) described under (5). Their identity was checked by reaction with aqueous sodium sulphide, which gave 1-thio-2-methyl-1 : 2-dihydrobenzthiazole.

(7) The crude ethosulphate of 1-methylthiobenzthiazole was treated with a concentrated solution of potassium iodide, and the resulting quaternary iodide (III) crystallised from alcohol. It had m. p. 131°, which was not depressed by admixture with the quaternary iodide (II), m. p. 138—140°, formed from ethyl iodide and 1-methylthiobenzthiazole. This new quaternary iodide was treated with sodium sulphide in the usual way, giving 1-thio-2-ethyl-1 : 2-dihydrobenzthiazole.

(8) 1-Thio-2-methyl-1 : 2-dihydrobenzthiazole was treated with ethyl iodide, and the product purified exactly as described by Rassow, Döhle, and Reim (*loc. cit.*). It had m. p. 131° (lit. 132°). It was recrystallised once from alcohol and once from alcohol–acetone; its m. p. was then 140°, both alone and in admixture with the product (II) of (5) and (6). Its identity was checked by reaction with sodium hydrogen sulphide, which gave 1-thio-2-methyl-1 : 2-dihydrobenzthiazole.

The values for the m. p.'s of the quaternary iodides described above vary with the rate of heating. The above figures were obtained under comparable conditions.

Reactions of Substituted Derivatives of 1-*Methylthiobenzthiazole*.—(1) 4-Chloro-1-methylthiobenzthiazole (43 g.), m. p. 65°, prepared from the thiol of Teppema and Sebrell (*J. Amer. Chem. Soc.*, 1927, **49**, 1754), was heated on a steam-bath for several hours with methyl *p*-toluenesulphonate (37·2 g.). The resulting quaternary salt was extracted with water (600 c.c.), and the aqueous extract divided into two parts.

(a) One portion was rendered alkaline with 30% sodium hydroxide solution (12 c.c.). Methylthiol was evolved, and 4-*chloro*-2-*methylbenzthiazolone* was precipitated (yield, 71%), m. p. 109—110° after crystallisation (Found : N, 7·3; Cl, 18·0. C_8H_6ONClS requires N, 7·0; Cl, 17·8%).

(b) The other portion was treated with sodium hydrosulphide solution until precipitation was complete. 4-*Chloro*-1-*thio*-2-*methyl*-1 : 2-*dihydrobenzthiazole* was obtained in 68% yield, m. p. 169° after crystallisation from alcohol (Found : N, 6·6; Cl, 16·6. $C_8H_6NClS_2$ requires N, 6·5; Cl, 16·5%).

(2) 1-*Methylthio*-4-*methylbenzthiazole* (19·5 g., m. p. 52—54°) was converted into its quaternary methosulphate in the usual way. The salt was dissolved in water (200 c.c.), and the solution divided into two parts.

(a) One part was made alkaline with sodium hydroxide. 2 : 4-*Dimethylbenzthiazolone* was obtained in 92—93% yield, m. p. 121° after two crystallisations from alcohol (Found : N, 7·8; S, 17·1. C_9H_9ONS requires N, 7·8; S, 17·4%).

(b) The other portion was treated in the usual way with sodium hydrosulphide, 1-*thio*-2 : 4-*dimethyl*-1 : 2-*dihydrobenzthiazole* being obtained almost quantitatively. Crystallised from benzene, it had m. p. 190° (Found : N, 7·2; S, 33·3. $C_9H_9NS_2$ requires N, 7·2; S, 32·8%).

(3) The methosulphate from 1-methylthio-β-naphthathiazole was treated in the usual way with caustic akali, giving 2-methyl-β-naphthathiazolone, m. p. 146° after crystallisation from alcohol (Desai, Hunter, and Kureishy, J., 1936, 1668, give m. p. 153°).

Similarly, treatment with aqueous sodium sulphide gave 1-thio-2-methyl-1 : 2-dihydro-β-naphthathiazolone, m. p. 173° after crystallisation from alcohol (Kendall, B.P. 475,647, gives 173°).

1-β-*Hydroxyethylthiobenzthiazole*.—1-Thiolbenzthiazole (50·1 g.) was dissolved together with sodium hydroxide (13·8 g.) in water (200 c.c.). The solution was heated to 60°, and 30% aqueous ethylene chlorohydrin (89 g.) added during ½ hour with agitation, which was continued for 3 hours. The oil which separated was washed by decantation with warm water, allowed to solidify, and crystallised from benzene; m. p. 56—58° (Found : C, 51·2; H, 4·05; N, 6·6; S, 30·1. $C_9H_9ONS_2$ requires C, 51·2; H, 4·25; N, 6·6; S, 30·4%).

1-β-*Hydroxyethylthiobenzthiazole* (30 g.) was heated under reflux for 2½ hours at 125—130°. When the temperature was slowly raised to 200°, a small quantity of oily liquid came over and a white crystalline solid (0·3 g.) collected in the neck of the flask. This had m. p. 107—110°, raised to 110—112° by crystallisation from benzene (dithian ?). The residue in the flask was extracted repeatedly with 2N-sodium hydroxide, and the extracts acidified. The precipitated 1-hydroxybenzthiazole (12·8 g.) was identified by mixed m. p. with authentic material, and also by conversion by means of methyl sulphate into 2-methylbenzthiazolone.

The author wishes to express his thanks to Imperial Chemical Industries Limited, Dyestuffs Group, for permission to publish these results.

(*Note added in proof*). The results given in this paper contradict the statement of Beilenson and Hamer (this vol., p. 143) that the anomalous behaviour which they have observed on treating 2-methylthiolquinoline with ethyl iodide " has no parallel in the case of 1-methylthiolbenzthiazole and ethyl iodide."

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