CCLXVII.—*Studies in the Benzothiazole Series. Part II. Thio-2-methylbenzothiazolone and its Oxidation Products.*

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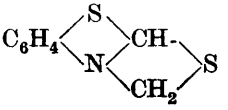
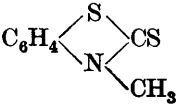
IN preparing benzothiazole for use in various investigations, the method described by Möhlau and Krohn (*Ber.*, 1888, **21**, 59) of heating dimethylaniline with sulphur was employed. Our attention thus became directed to a crystalline by-product of the composition $C_8H_7NS_2$ which is produced in this reaction in very considerable quantity and is of interest since it forms an intermediate stage in the production of benzothiazole, for it was shown by Möhlau and Krohn to give benzothiazole when further heated with sulphur.

Möhlau and Krohn assigned to it the constitution I, and this formulation was retained, after further discussion, by Möhlau and Klopfer (*Ber.*, 1898, **31**, 3164). The substance was again investigated by Rassow, Döhle, and Reim (*J. pr. Chem.*, 1916, [ii], **93**, 183). They also regarded their results as harmonising with Möhlau's ormula, and they named the substance benzothiazolmethensulfid.

(I.) 

 (II.)

In view, however, of the properties of the compound and of the manner in which it is formed such a constitution is manifestly improbable. It seemed to us that the substance was much more likely to be thio-2-methylbenzothiazolone (II).

This view of its constitution proved to be correct, for we find that it can be synthesised in a simple manner which leaves no doubt as to its structure. It is formed by the interaction of *o*-methylaminophenyl mercaptan and thiocarbonyl chloride. The formation of a substance of the formula $C_8H_7NS_2$ from these reagents can only take place as follows :

$$C_6H_4\langle\begin{matrix}SH\\NMeH\end{matrix} + \begin{matrix}Cl\\Cl\end{matrix}\rangle CS \longrightarrow \text{(II.)} + 2HCl.$$

This proof of the constitution is confirmed by another method of formation. The compound is obtained when 1-nitrosoimino-2-methylbenzothiazoline (which, heated in an indifferent solvent, gives nitrogen and the thiazolone) is heated with phosphorus pentasulphide :

$$C_6H_4\langle\begin{matrix}S---\\NMe\end{matrix}\rangle C{:}N{\cdot}NO \xrightarrow{P_2S_5} \text{(II.)} + N_2.$$

It is also formed by the action of phosphorus pentasulphide on 2 : 2′-diformylmethylaminodiphenyl disulphide.

The reactions of the substance further confirm this view of its constitution. When the more mobile of the two sulphur atoms which it contains is replaced by oxygen, as can be done, either by heating the alcoholic solution with mercuric oxide, or by treating the substance with bromine water (compare Rassow and Reim, *J. pr. Chem.*, 1916, [ii], **93**, 232), 2-methylbenzothiazolone results :

$$\text{(II.)} \longrightarrow C_6H_4\langle\begin{matrix}S---\\NMe\end{matrix}\rangle CO.$$

Now that the constitution of this product is known the action of sulphur on dimethylaniline can be very simply represented. Writing dimethylaniline in the form III, it is seen that the formation of the thiothiazolone consists in the replacement of each of the two pairs

$$C_6H_4\langle\begin{matrix}\mathbf{HH}\text{-}\\NMe\end{matrix}\rangle \mathbf{CH_2} \xrightarrow{S} C_6H_4\langle\begin{matrix}\mathbf{S}---\\NMe\end{matrix}\rangle \mathbf{CS} \qquad C_6H_4\langle\begin{matrix}S\\N\end{matrix}\rangle CH\text{-}CH_2$$

(III.) (IV.)

of hydrogen atoms shown in clarendon type by an atom of sulphur.

This formula also enables the oxidation of the substance, which was studied by Möhlau and Rassow and their pupils, to be simply interpreted. Möhlau and Krohn (*loc. cit.*) found that the thiothiazolone was easily oxidised by nitric acid. One atom of sulphur

was removed as sulphuric acid and the nitrate of a base was formed. They were unable to obtain the base from this nitrate, but they prepared and analysed the chloroplatinate and found that their analytical results were in agreement with those which would be required by the chloroplatinate of a base of the formula IV. They accordingly assigned this formula to the base, naming it *iso*-μ-methylbenzothiazole. Möhlau and Klopfer (*loc. cit.*) re-examined the salts obtained by oxidation of the thiothiazolone. By treating the sulphate in alcoholic solution with the equivalent quantity of potassium hydroxide, they succeeded in isolating a very small quantity of a base melting at 202° and giving analytical results in accordance with formula IV. This base, *iso*-μ-methylbenzothiazole, was also prepared by Rassow, Döhle, and Reim (*loc. cit.*), who succeeded in obtaining it in considerable quantity.

We had concluded from the difficulty which Möhlau and his pupils had experienced in isolating a base corresponding with the salts which they had obtained that these must be derived from a quaternary base and that the base which they actually isolated was only a subsidiary product. Investigation showed that this conclusion was correct.

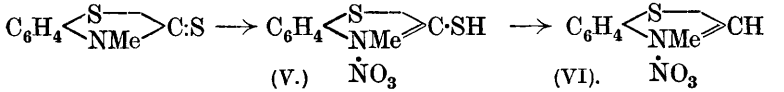
The product obtained by oxidising the thiothiazolone with dilute nitric acid consists, at any rate to a very large extent, of the methonitrate of benzothiazole (VI) mixed with a smaller quantity of the corresponding bisulphate. The chloroplatinate which this product gives is identical with benzothiazole methochloroplatinate, $\left(C_6H_4\langle^{S}_{NMe}\rangle CH\right)_2PtCl_6$—this has the same composition as the chloroplatinate of a base of the formula suggested by Möhlau, $\left(C_6H_4\langle^{S}_{N}\rangle CH\cdot CH_2\right)H_2PtCl_6$, would have—and the picrate and the perchlorate precipitated from the aqueous solution of the product are the methopicrate and the methoperchlorate of benzothiazole. The oxidation of the thiothiazolone can be carried out even more smoothly with hydrogen peroxide. The product is then pure benzothiazole methyl hydrogen sulphate.

The product obtained by Rassow, Döhle, and Reim was probably a mixture, for, when treated with ammonia, it deposited an oil from which *iso*-μ-methylbenzothiazole could be isolated. The greater part, however, consisted of methylbenzothiazolonium salts, for they state that it dissolved in ammonia and the solution on keeping slowly deposited 2 : 2′-diformylmethylaminodiphenyl disulphide. It was thus that Rassow, Döhle, and Reim discovered this compound. Evidently the ammonia con-

verted the quaternary salts into the ammonium salt of the thiophenolic ψ-base, as we have shown in the preceding paper, and this was then gradually oxidised to the disulphide by atmospheric oxygen.

The way in which the thiothiazolone on oxidation yields benzothiazole methyl salts and sulphuric acid can be readily explained. The thiothiazolone has distinct, although very weak, basic properties; it forms a chloroplatinate (Möhlau and Klopfer, *loc. cit.*), a methiodide, and an ethiodide (Rassow, Döhle, and Reim, *loc. cit.*).

On treatment with nitric acid, it must therefore form a salt which, from analogy with the evident constitution of the alkiodides, will have the formula V.



(V.) (VI.)

The action of nitric acid accordingly consists in the replacement of the thiol group in this salt by hydrogen.

The thiol group in the complex VII thus shows the same behaviour when oxidised with nitric acid as is characteristic of this group when present in the somewhat similar complex VIII.

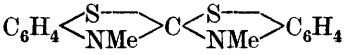
(VII.) (VIII.)

The property of a thiol group, in the latter complex, of being eliminated by oxidation with dilute nitric acid was discovered by Wohl and Marckwald (*Ber.*, 1889, **22**, 575), who found that phenyliminazolyl mercaptan could be converted in this manner into phenyliminazole, and it has since been not infrequently employed for eliminating this group from heterocyclic compounds (*Ber.*, 1889, **22**, 1359; 1892, **25**, 2361; 1893, **26**, 2204; *Annalen*, 1904, **331**, 68).

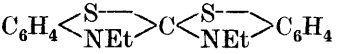
The discovery of the true nature of "benzothiazolmethensulphid" and its oxidation products removes most of the difficulties which Rassow, Döhle, and Reim, and also Rassow and Reim, found in interpreting the behaviour of the sulphonic acids derived from these compounds and of the corresponding derivatives of tolu-thiazole.

We have also obtained further information respecting *iso*-μ-methylbenzothiazole. We have been able to identify it with a base melting at 204° which we have obtained in various ways from compounds containing the grouping $\overset{(1)}{S}\cdot C_6H_4\cdot\overset{(2)}{N}Me$. This base has the formula $C_{15}H_{14}N_2S_2$. Its composition thus differs somewhat from that assigned by Möhlau and Rassow and their pupils to *iso*-

μ-methylbenzothiazole (C_8H_7NS). It is most easily prepared by heating 2 : 2′-diformylmethylaminodiphenyl disulphide with phenylhydrazine. This reaction involves the elimination of one of the two formyl groups from the disulphide, for the phenylhydrazine is converted into its formyl derivative. Since, in addition to the two residues ·NMe·C_6H_4·S·, the molecule of the base contains only a single carbon atom, it can scarcely have any other constitution than that represented by the formula IX.

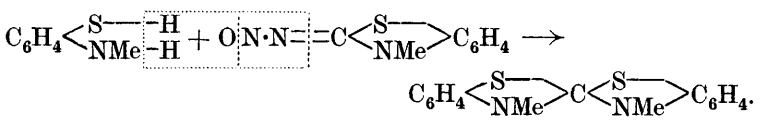


(IX.)



(X.)

We have been able to confirm this constitution by synthesising the compound from 1-nitrosoimino-2-methylbenzothiazoline (Besthorn, *Ber.*, 1910, **43**, 1523) and *o*-aminophenyl mercaptan, condensation taking place very readily when the two substances are heated together :



The product is probably a racemic form, since a spirocyclic compound of this structure should exist in two enantiomorphous modifications (compare Mills and Nodder, T., 1921, **119**, 2094).

The corresponding diethyl derivative (X) has been prepared in a similar manner by heating the diethyl disulphide with phenylhydrazine.

Experimental.

Synthesis of Thio-2-methylbenzothiazolone from o-Methylaminophenyl Mercaptan and Thiocarbonyl Chloride.—*o*-Methylaminophenyl mercaptan (Harries and Löwenstein, *Ber.*, 1894, **27**, 861) (1·95 grams) was dissolved in chloroform (10 c.c.) and treated with a solution of thiocarbonyl chloride (0·6 c.c.) in chloroform (5 c.c.) at 0°. The mixture, after standing for sixteen hours, was warmed for one hour and then washed with dilute hydrochloric acid. After being shaken with warm sodium hydroxide solution to destroy unchanged thiocarbonyl chloride, the solution was dried, and the crystalline residue left after evaporation of the solvent recrystallised several times from alcohol. It was thus obtained in colourless needles, m.p. 90°. The " benzothiazolmethensulfid " of Möhlau and Krohn was described as melting at 89°, but by recrystallisation the melting point can be raised to 90°, and a mixture of the purified substance with the synthesised thiothiazolone melted also at this temperature.

Thio-2-methylbenzothiazolone from 1-Nitrosoimino-2-methylbenzothiazoline.—The nitroso-compound (10 grams) was mixed with phosphorus pentasulphide (10 grams) and heated at 110—120°, when a vigorous reaction began and was completed in a few moments. The product was extracted with benzene and the solution digested with copper powder. After removal of the benzene and crystallisation from alcohol, pure thio-2-methylbenzothiazolone was obtained melting at 90° (Found: S = 35·1, 35·33. $C_8H_7NS_2$ requires S = 35·36 per cent.).

Thio-2-methylbenzothiazolone from 2 : 2′-Diformylmethylaminodiphenyl Disulphide.—A mixture of the disulphide (1 gram) with phosphorus pentasulphide (1 gram) was heated at 100°. When fusion began, a vigorous reaction started and was completed by heating for several minutes. The product was extracted with benzene and purified as before. The melting point and the "mixed melting point" with purified "benzothiazolmethensulfid" were 90° (Found: C = 52·5; H = 3·96; N = 7·72; S = 35·4, 35·36. $C_8H_7NS_2$ requires C = 53·04; H = 3·87; N = 7·9; S = 35·36 per cent.).

Conversion of Thio-2-methylbenzothiazolone into 2-Methylbenzothiazolone.—(*a*) *By Mercuric Oxide.* The thiothiazolone (10 grams), dissolved in boiling absolute alcohol (200 c.c.), was digested with freshly precipitated mercuric oxide for four hours. The solution was concentrated and unchanged thiothiazolone allowed to crystallise. The filtrate was evaporated and the residue distilled in steam. A small quantity of 2-methylbenzothiazolone crystallised from the distillate. Recrystallised from light petroleum, it melted at 76°, and the mixture with pure 2-methylbenzothiazolone (Besthorn, *loc. cit.*) melted at the same temperature (Found: S = 19·7. Calc., S = 19·4 per cent.).

(*b*) *By Bromine Water.* Finely powdered 2-methylbenzothiothiazolone (5 grams) was shaken with bromine water, addition of bromine being continued until it persisted after standing for half an hour. The slightly red solid thus formed was freed from excess of bromine with sulphur dioxide and then treated with hydrochloric acid (*d* 1·18), which dissolved the thiazolone and left the thiothiazolone. The solution was precipitated by dilution with water and the product crystallised from aqueous alcohol and then from light petroleum. It melted at 75° and after mixture with pure 2-methylbenzothiazolone (m. p. 76°) at 75—76° (Found: C = 58·2; H = 4·2. Calc., C = 57·9; H = 4·2 per cent.).

Oxidation of Thio-2-methylbenzothiazolone.—The thiothiazolone (10 grams) was added gradually to a mechanically stirred mixture of nitric acid (*d* 1·4; 20 c.c.) and water (10 c.c.), the temperature

being kept below 12°. Crystals separated towards the end of the reaction and after keeping at 0° for two hours the mixture became semi-solid. The solid collected, washed with ether-alcohol, and dried, weighed 12·1 grams. It was found to be a mixture of benzothiazole methonitrate with a little benzothiazole methobisulphate. This was established by the preparation from it of a number of characteristic methylbenzothiazolonium salts.

Picrate.—Precipitated by a saturated aqueous solution of picric acid. M. p. 155—157°. Mixed m. p. with pure benzothiazole methopicrate 155—157°.

Chloride.—The picrate was decomposed with hydrochloric acid and the picric acid removed by extraction with amyl alcohol and then with ether. The aqueous solution was evaporated and the dried residue crystallised from ether-alcohol (Found : Cl = 19·14. Calc., Cl = 19·13 per cent.).

Chloroplatinate.—Prepared from the chloride. M. p. 257° (Found : Pt = 27·39. $C_{16}H_{16}N_2S_2,PtCl_6$ requires Pt = 27·54 per cent.) (Compare Möhlau and Klopfer, *loc. cit.*).

Iodide.—Prepared by precipitation from the chloride by addition of potassium iodide. M. p. 209°. A mixture with pure benzothiazole methiodide (m. p. 210°) melted 209—210° (Found : I = 46·0. Calc., I = 45·85 per cent.).

The oxidation product was recrystallised from ether–alcohol and analysed. The results were in accordance with those which would be required for a mixture of 96·4 per cent. of benzothiazole methonitrate and 3·6 per cent. of benzothiazole metho-hydrogen sulphate (Found : NO_3 = 28·5; SO_4 = 1·44. Calc., NO_3 = 28·2; SO_4 = 1·40 per cent.). These analyses were confirmed by titrating the substance with sodium hydroxide and phenolphthalein, and then with iodine, when the behaviour characteristic of the alkyl benzothiazolonium salts (see preceding communication) was observed (Found : 0·2236 required 21·5 c.c. of 0·1*N*-sodium hydroxide solution and 10·25 c.c. of 0·1*N*-iodine solution. Calc., 21·3 c.c. of sodium hydroxide and 10·5 c.c. of iodine solution).

Oxidation of Thio-2-methylbenzothiazolone with Hydrogen Peroxide.—The thiothiazolone (4 grams) was dissolved in acetone and to the warm solution 28 per cent. hydrogen peroxide (2·8 c.c.) was added. A colourless oil separated which was removed after twenty-four hours. This was dissolved in alcohol, and the solution, on standing, deposited benzothiazole metho-hydrogen sulphate in colourless needles, m. p. 167—168°. Yield 1 gram (Found : C = 38·9; H = 3·7; N = 5·74; S = 26·2. $C_8H_8NS{\cdot}HSO_4$ requires C = 38·9; H = 3·6; N = 5·66; S = 25·9 per cent. 0·2272 required 5·60 c.c. of 0·5*N*-sodium hydroxide. Calc., 5·52

c.c.). There was recovered from the acetone solution 1·5 grams of unchanged thiothiazolone.

Bis-2-ethylbenzothiazoline-1 : 1-spiran.—2 : 2′-Diformylethylaminodiphenyl disulphide (10 grams) and phenylhydrazine (6 grams) were heated together at 100° for ten hours, when ammonia was evolved. The residue, which solidified on standing, was distilled with steam to remove unchanged phenylhydrazine. From the aqueous layer in the distillation flask colourless crystals, m. p. 144°, separated on cooling. These were shown to be formylphenylhydrazine (Found : N = 20·3. Calc., N = 20·6 per cent.). The melting point of a mixture of this substance with pure formylphenylhydrazine, prepared as described by Just (*Ber.*, 1886, **19**, 201), was 144° and the characters of the two substances were identical.

The oily residue from the steam distillation crystallised from alcohol in colourless plates, m. p. 136° (Found : C = 64·66, 64·99; H = 5·81, 5·89; N = 9·19. $C_{17}H_{18}N_2S_2$ requires C = 64·97; H = 5·73; N = 8·92 per cent.). The substance is insoluble in water, but dissolves readily in dilute hydrochloric acid.

Bis-2-methylbenzothiazoline-1 : 1-spiran.—2 : 2′-Diformylmethylaminodiphenyl disulphide (10 grams) and phenylhydrazine (7 grams) were heated together at 100° for six hours. Ammonia was evolved and after two hours the melt had become solid. The product was extracted with boiling water, which removed formylphenylhydrazine (identified by the m. p. and mixed m. p. [144°] as already described). The residue was crystallised from alcohol and thus obtained as colourless, iridescent platelets, m. p. 204° (Found : C = 63·1; H = 4·99; N = 9·85. $C_{15}H_{14}N_2S_2$ requires C = 62·9; H = 4·89; N = 9·79 per cent.).

Methiodide. The spiran (1 gram) was heated with methyl iodide (2·1 grams) in a sealed tube for twenty-four hours at 60°. The solid product, crystallised from alcohol, gave the pure mono-methiodide as clusters of fine needles, m. p. 186° (Found : I = 29·50, 29·58. $C_{16}H_{17}N_2S_2I$ requires I = 29·7 per cent.).

Methocamphorsulphonate. Prepared in the usual way from the methiodide and silver camphorsulphonate and crystallised from ethyl acetate, this salt formed colourless needles, m. p. 147—148° (Found : C = 59·0; H = 6·12; S = 17·7. $C_{26}H_{32}O_4N_2S_3$ requires C = 58·55; H = 6·20; S = 18·0 per cent.).

Methobromocamphorsulphonate. Similarly prepared and crystallised from ethyl acetate, it formed colourless platelets, m. p. 164—165° (Found : Br = 13·21; S = 16·08. $C_{26}H_{31}O_4N_2S_3Br$ requires Br = 13·10; S = 15·71 per cent.).

Synthesis of Bis-2-methylbenzothiazoline-1 : 1-spiran.—*o*-Methylaminophenyl mercaptan (1·9 grams) was heated at 100° in hydrogen

and 1-nitrosoimino-2-methylbenzothiazoline (2·51 grams) was added in small quantities, each addition being followed by a very vigorous reaction. The heating was continued for three hours, the mixture gradually solidifying. The product, crystallised from alcohol, gave 1·54 grams of the spiran, m. p. 203·5—204°. A mixture with the spiran prepared from the disulphide and phenylhydrazine melted at the same temperature (Found: C = 63·4; H = 4·93; N = 9·74. Calc., C = 62·9; H = 4·89; N = 9·79 per cent.).

Identity of Bis-2-methylbenzothiazoline-1 : 1-spiran with iso-μ-Methylbenzothiazole.—In carrying out the oxidation of thio-2-methylbenzothiazolone with nitric acid as described by Rassow, Döhle, and Reim (*loc. cit.*), we always got good yields of benzothiazole metho-nitrate and -bisulphate, but only once obtained "*iso*-μ-methylbenzothiazol," and then only in small quantity, when the crude salt was treated with ammonia.

The *iso*-μ-methylbenzothiazole melted at 202—204° (the German investigators give the m. p. as 202°) and a mixture with the spiran synthesised from *o*-methylaminophenyl mercaptan and nitrosoimino-methylbenzothiazoline melted at the same temperature.

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