108. *Reactions of Benzthiazole Derivatives. Part II. The Conversion of* 1-*Alkylthiobenzthiazoles into* 1-*Thio*-2-*alkyl*-1 : 2-*dihydrobenzthiazoles.*

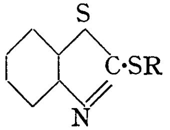
By Firmin P. Reed, Alexander Robertson, and Wilfred Archibald Sexton.

When heated with a trace of iodine, 1-methylthiobenzthiazole is transformed into 1-thio-2-methyl-1 : 2-dihydrobenzthiazole. This reaction has been applied to some homologues and substitution products. 1-Thio-2-alkyl-1 : 2-dihydrobenzthiazoles can also be obtained by heating suitable quaternary iodides obtained from 1-alkylthiobenzthiazoles.

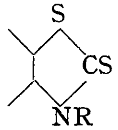
Benzyl chloride reacts with 1-thiolbenzthiazole and its *S*-methylated derivative, giving rise to 1-*thio*-2-*benzyl*-1 : 2-*dihydrobenzthiazole*. This reaction has been investigated in the case of 4-chloro-1-thiolbenzthiazole and 2-thiol-β-naphthathiazole. The S-*benzyl* derivative of the latter thiol reverts to the thiol on heating, and stilbene has been isolated as a by-product.

By analogy with the well-known conversion of alkyl thiocyanates into the isomeric *iso*thiocyanates, the thermal rearrangement of the readily accessible *S*-alkyl compounds (type I) appeared to offer a feasible method for the production of 1-thio-2-alkyldihydrothiazoles (type II), which would be of general application. Unlike the thiocyanates, however, (I, R = Me) and (I, R = Et), on being heated at 200—220°, furnished only traces of the expected isomerides, but when a crystal of iodine was employed as a catalyst, the use of which was suggested by the rearrangement of alkyl groups observed in the formation of the methiodide of 1-ethylthiobenzthiazole (Part I; preceding paper), satisfactory yields of the thio-dihydrothiazoles (type II) were obtained. Bromine also had a catalytic effect, but was much less efficient than iodine.

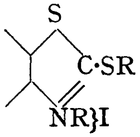
This catalysed reaction has been successfully applied to the 4-methyl-, 4-chloro-, 5-chloro-, and 5-methoxy-derivatives of (I, R = Me), to (I, R = CH_2:CH·CHMe) and to (I, R = CH_2Ph). It appeared to proceed extremely slowly when applied to 5-chloro-1-methylthio-3-methylbenzthiazole, and failed entirely in the case of 2-methylthio-β-naphthathiazole. The structure of the product (II, R = CH_2:CH·CHMe) depends on analogy and on the fact that it is insoluble in concentrated hydrochloric acid, a property which appears to be common to the *N*-alkyl compounds of type (II), and is not possessed by compounds of type (I). It must be noted, however, that migration of the alkenyl group may have been accompanied by a shift of the double bond.



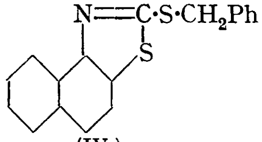
(I.)



(II.)



(III.)



(IV.)

Although the thermal rearrangement of thiazoles (I) proved to be unsatisfactory, decomposition of their quaternary iodides (type III) by heat gave satisfactory yields of the corresponding thio-dihydrothiazoles (II) (compare the behaviour of 4-allyloxyquinaldine methiodide; Maunder-Jones and Trikojus, *Chem. Abst.*, 1933, 1350). Small amounts of the quaternary iodides exerted a similar catalytic effect to that obtained when iodine was used in the conversion of (I) into (II). With the quaternary salt obtained from 1-methylthiobenzthiazole and ethyl iodide, this reaction furnished (II, R = Me), a result in accordance with the rearrangements recorded in Part I.

An attempt to obtain a quaternary salt by the action of benzyl chloride on 1-methylthiobenzthiazole resulted in evolution of methyl chloride and formation of 1-*thio*-2-*benzyl*-1 : 2-*dihydrobenzthiazole* (II, R = CH_2Ph) in good yield. The substance was identified by the absence of m. p. depression on admixture with material prepared by isomerisation of 1-benzylthiobenzthiazole with iodine. By treating benzyl chloride with 1-thiolbenzthiazole in the absence of alkali, 1-thio-2-benzyl-1 : 2-dihydrobenzthiazole was similarly obtained in good yield with elimination of hydrogen chloride.

Reaction of benzyl chloride with an aqueous solution of sodio-2-thiol-β-naphthathiazole gave a benzyl derivative which from its method of formation is believed to be the *S*-substituted derivative, 2-*benzylthio*-β-*naphthathiazole* (IV). The same compound was obtained by the action of excess of benzyl chloride on the thiol in the absence of alkali. Similarly, benzylation of 4-chloro-1-thiolbenzthiazole either in the presence or in the absence of alkali gave 4-*chloro*-1-*benzylthiobenzthiazole*. This derivative was isomerised under the influence of iodine to the higher-melting 4-*chloro*-1-*thio*-2-*benzyl*-1 : 2-*dihydrobenzthiazole*. Thus the point of attack of benzyl chloride in the absence of alkali is the nitrogen atom in the case of the unsubstituted benzene ring, but the sulphur atom where the substituent is 4-chloro- or 3 : 4-benzo (compare Hunter, J., 1930, 125; Hasan and Hunter, J., 1936, 1672, in which it is shown that methylation of 1-thiolbenzthiazole and its 5-methyl, 5-bromo- or 5-nitro-derivative in the absence of alkali occurs in each case on the sulphur atom). We have observed that in the preparation of (I, R = Me) by methylation of 1-thiolbenzthiazole with methyl sulphate and aqueous sodium hydroxide under the usual conditions, the crude product is usually contaminated by about 2—3% of (II, R = Me) (compare Hunter, J., 1930, 129, who obtained only the *S*-isomeride by this method). By a modification of the conditions, yields of about 15% of (II, R = Me) can be obtained.

An attempt was made to isomerise 2-benzylthio-β-naphthathiazole (IV) by heating it in the presence of a trace of iodine. Instead of isomerisation, 2-thiol-β-naphthathiazole was regenerated in substantial yield; stilbene was isolated from the by-products. The failure of this particular benzylthio-derivative to isomerise under the influence of iodine accords with the failure to bring about smooth isomerisation of the corresponding methylthio-derivative. The rupture of the C–S link in the benzylthio-residue recalls the formation of stilbene by the action of heat on dibenzyl sulphide (Fromm and Achert, *Ber.*, 1903, **36**, 538).

EXPERIMENTAL.

Where necessary in the following experiments advantage was taken of the insolubility of the thio-dihydrothiazoles (II) in concentrated hydrochloric acid to remove the soluble unchanged thiazoles (I).

1-*Thio*-2-*methyl*-1 : 2-*dihydrobenzthiazole* (II, R = Me).—(A) A solution of 1-thiolbenzthiazole (1 mol.) in 10% aqueous sodium hydroxide (1·2 mols.) was added with stirring to methyl sulphate (1·2 mols.) at 40—45°, and the mixture kept at this temperature for 3 hours. The product was isolated by means of chloroform, washed with aqueous sodium hydroxide, distilled in a vacuum, and resolved into (I, R = Me), m. p. 50° (yield, 62·9%), and (II, R = Me), m. p. 90° (yield, 15·5%), by means of concentrated hydrochloric acid.

(B) A theoretical yield of this compound was obtained by heating (I, R = Me) (5 g.) with a crystal of iodine at 210—215° for 3 hours. After purification from alcohol it had m. p. 90—91° and was identical with an authentic specimen.

(C) The quaternary salt formed by warming (I, R = Me) (5 g.) with excess of methyl iodide was kept at 180° for 10 minutes, and the thio-dihydrothiazole (II, R = Me) (3·7 g.) isolated with concentrated hydrochloric acid and purified from alcohol. The same product (4·1 g.) was obtained when the methyl iodide was replaced by ethyl iodide, and the experiment carried out at 190°.

(D) When the thiazole (I, R = Me) (5 g.) was heated with about 15% of the amount of methyl iodide (*ca.* 0·3 c.c.) required for complete conversion into the quaternary salt in a sealed tube at 155—160°, 3·7 g. of (II, R = Me) were formed. Distillation of the methosulphate from (I, R = Me) (Part I) (5 g.) at 180—190°/1 mm. gave (II, R = Me) (2·23 g.).

1-Thio-2-ethyl-1 : 2-dihydrobenzthiazole (II, R = Et) was prepared by the foregoing iodine method from (I, R = Et) in good yield; it formed colourless stout prisms, m. p. 75—76°, from alcohol, identical with an authentic specimen. Decomposition of the salt (III, R = Et) (5 g.) at 190° for 15 minutes gave the same substance (1·2 g.).

1-*Thio*-2-n-*propyl*-1 : 2-*dihydrobenzthiazole*.—2-*n*-Propylthiobenzthiazole (b. p. 177—178°/14 mm.) (5 g.) and *n*-propyl iodide (5 c.c.) were heated on a water-bath for 15 minutes and then at 190—200° for 15 minutes. The product was treated with concentrated hydrochloric acid, and the 1-*thio*-2-n-*propyl*-1 : 2-*dihydrobenzthiazole* (1·5 g.) crystallised from alcohol, forming colourless prisms, m. p. 74° (Found : N, 6·4. $C_{10}H_{11}NS_2$ requires N, 6·7%).

1-*Thio*-2-iso*amyl*-1 : 2-*dihydrobenzthiazole*.—2-*iso*Amylthiobenzthiazole (b. p. 186—187°/14 mm.) (12 g.) and *iso*amyl iodide (13 c.c.) were heated on a water-bath for 2 hours and then at 215° for 2 hours. The product was treated with an excess of concentrated hydrochloric acid. The dark brown, semi-solid mass (4 g.) was pressed on a tile, and the 1-*thio*-2-iso*amyl*-1 : 2-*dihydrobenzthiazole* crystallised from alcohol, forming stout colourless rectangular prisms, m. p. 54—55° (Found : N, 6·1. $C_{12}H_{15}NS_2$ requires N, 5·9%).

1-*Thio* 2-α-*methylallyl*-1 : 2-*dihydrobenzthiazole* (II, R = CH_2:CH·CHMe).—Prepared by the interaction of sodiothiolbenzthiazole and excess of α-methylallyl chloride in boiling alcohol, the thiazole (I, R = CH_2:CH·CHMe) (oil, b. p. 186—188°/15 mm.) (5 g.), on being heated with a crystal of iodine at 220° for 3 hours, gave the *thio-dihydrothiazole*, m. p. 115° after two crystallisations from light petroleum (Found : N, 6·4; S, 29·0. $C_{11}H_{11}NS_2$ requires N, 6·3; S, 29·1%).

5-*Chloro*-1-*thio*-2-*methyl*-1 : 2-*dihydrobenzthiazole*.—The methylthio-compound (m. p. 98°) was prepared by methylation of 5-chloro-1-thiolbenzthiazole (U.S.P. 1,788,585) with methyl sulphate and aqueous sodium hydroxide and transformed into the *thio-dihydrothiazole* in the usual manner; m. p. 130° after purification from alcohol (Found : N, 6·6; S, 16·8. $C_8H_6NClS_2$ requires N, 6·5; S, 16·5%).

Similarly, 1-methylthio-5-methoxybenzthiazole (oil, b. p. 280°/20 mm.) gave 1-*thio*-5-*methoxy*-2-*methyl*-1 : 2-*dihydrobenzthiazole*, m. p. 87° after crystallisation from methyl alcohol (Found : N, 6·3; S, 29·6. $C_9H_9ONS_2$ requires N, 6·6; S, 30·3%).

1-Thio-2 : 4-dimethyl- and 4-chloro-1-thio-2-methyl-1 : 2-dihydrobenzthiazole were prepared from the corresponding isomeric methylthiobenzthiazoles (type I) by the iodine method and identified by comparison with authentic specimens (Part I).

1-*Thio*-2-*benzyl*-1 : 2-*dihydrobenzthiazole* (II, R = CH_2Ph).—(A) Sodio-1-thiolbenzthiazole was treated with benzyl chloride in boiling alcohol, giving 1-benzylthiobenzthiazole, m. p. 41—42°. This compound was converted, by heating with a trace of iodine at 200° for 17 hours, into 1-*thio*-2-*benzyl*-1 : 2-*dihydrobenzthiazole*, m. p. 149° after purification from benzene (Found : C, 65·5; H, 4·2; N, 5·5; S, 25·6. $C_{14}H_{11}NS_2$ requires C, 65·4; H, 4·3; N, 5·5; S, 24·9%).

(B) A solution of 1-methylthiobenzthiazole (54 g.) in *o*-dichlorobenzene (100 c.c.) was boiled with benzyl chloride (42 g.) for 10 hours, a gas (presumably methyl chloride) being evolved. On cooling, crystalline 1-thio-2-benzyl-1 : 2-dihydrobenzthiazole separated; yield, 18 g. after washing with light petroleum and drying; m. p. 149°, not depressed by material prepared as in (A).

When the two reactants were boiled for 6 hours without a solvent, the yield was 62%; m. p. 150°.

(C) Equimolecular amounts of benzyl chloride and 1-thiolbenzthiazole were heated at 200° until evolution of hydrogen chloride ceased (1 hr.). The solid product, crystallised from benzene, had m. p. 149—150°, not depressed by material prepared as in (A).

2-*Benzylthio*-β-*naphthathiazole* (IV).—(A) 2-Thiol-β-naphthathiazole (21·8 g.) was dissolved, together with sodium hydroxide (4 g.), in ethyl alcohol (100 c.c.), benzyl chloride (12·7 g.) added to the boiling solution during ½ hour, and boiling continued for 5 hours, sodium chloride separating. The mixture was poured into water, and the 2-*benzylthio*-β-*naphthathiazole* collected and crystallised from alcohol; m. p. 85—86° (Found : N, 4·7; S, 20·1. $C_{14}H_{13}NS_2$ requires N, 4·6; S, 20·8%).

(B) 2-Thiol-β-naphthathiazole (30 g.) was heated under reflux for 6 hours with benzyl chloride (30 g.). On cooling, 2-*benzylthio*-β-*naphthathiazole* separated; after recrystallisation from alcohol it had m. p. 85—86°, not depressed by material prepared as in (A).

(C) 2-Benzylthio-β-naphthathiazole (5 g.) was heated at 220° for 3 hours in the presence of a crystal of iodine. The product was extracted with 2N-sodium carbonate, and the extract acidified with hydrochloric acid. This gave 2-thiol-β-naphthathiazole (2·1 g.; 35%), m. p. 235—237°, raised by recrystallisation from toluene to 248—250°; this was not depressed by authentic material. The residue from the sodium carbonate extraction was treated with warm ethyl alcohol–light petroleum, and the extract allowed to cool. The resulting gummy crystals were washed with concentrated hydrochloric acid and crystallised from light petroleum. The substance was then identified as stilbene by m. p. (125—126°) and mixed m. p. with material prepared by the action of heat on benzylideneazine.

4-*Chloro*-1-*thio*-2-*benzyl*-1 : 2-*dihydrobenzthiazole*.—4-Chloro-1-thiolbenzthiazole was benzylated in alcoholic sodium hydroxide solution in the usual way. The resulting 4-*chloro*-1-*benzylthiobenzthiazole* was crystallised from alcohol; m. p. 73—75°. The same compound was obtained by boiling equal weights of the thiol with benzyl chloride under reflux for 6 hours (Found : N, 5·3; Cl, 12·2. $C_{14}H_{10}NClS_2$ requires N, 4·8; Cl, 12·1%).

The above benzylthio-compound (7 g.) was heated at 220° for 3 hours in the presence of a little iodine. Isomerisation to 4-*chloro*-1-*thio*-2-*benzyl*-1 : 2-*dihydrobenzthiazole* occurred, m. p. 184—185° after crystallisation from benzene (Found : N, 4·8; S, 21·8. $C_{14}H_{10}NClS_2$ requires N, 4·8; S, 21·9%).

The authors thank Imperial Chemical Industries Ltd. (Dyestuffs Group) for permission to publish these results

THE UNIVERSITY, LIVERPOOL.
RESEARCH LABORATORIES, I.C.I. (DYESTUFFS GROUP), LTD.,
BLACKLEY, MANCHESTER.

[*Received, November 25th,* 1938.]