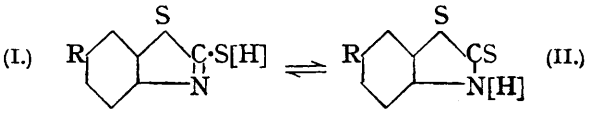
370. *The Unsaturation and Tautomeric Mobility of Heterocyclic Compounds. Part IX. The Methylation of 5-Substituted 1-Thiolbenzthiazoles, and the Ultra-violet Absorption of Mobile and Static Derivatives of 1-Thiolbenzthiazole.*

By CHIRAGH HASAN and ROBERT F. HUNTER.

THE triad system [H]N·C:S ⇌ N:C·S[H] in 5-substituted 1-thiolbenzthiazoles (I ⇌ II) exhibits certain interesting features when contrasted with the semi-cyclic amide-imidol system of the 1-hydroxybenzthiazoles (Hunter and Parken, J., 1935, 1755). The covalent form of the molecule is reactive towards alkylating agents, and methylation takes place readily in the absence of alkali catalysts with the production of *S*-methyl ethers.



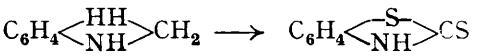
Methylation of 1-thiol-5-methylbenzthiazole, which was synthesised from 1-chloro-5-methylbenzthiazole and sodium hydrosulphide (cf. Hofmann, *Ber.*, 1887, **20**, 1788), in methyl alcohol yielded *1-methylthiol-5-methylbenzthiazole*, unaccompanied by any detectable amount of *1-thio-2 : 5-dimethyl-1 : 2-dihydrobenzthiazole*, which was synthesised from 1-nitrosoimino-2 : 5-dimethyl-1 : 2-dihydrobenzthiazole and phosphorus pentasulphide by the method of Mills, Clark, and Aeschlimann (J., 1923, **123**, 2363). Under similar conditions, *5-bromo-1-thiolbenzthiazole* (I ⇌ II; R = Br), however, gave rise to a small quantity (*ca.* 4—5%) of *5-bromo-1-thio-2-methyl-1 : 2-dihydrobenzthiazole* (III), in addition to the S-*methyl* derivative (IV) which constitutes the bulk of the product.

5-Nitro-1-thiolbenzthiazole (I ⇌ II; R = NO_2) obtained from 1-chloro-5-nitrobenzthiazole and sodium hydrosulphide proved identical with the product obtained by nitration of 1-thiolbenzthiazole (Teppema and Sebrell, *J. Amer. Chem. Soc.*, 1927, **49**, 1780). Part of the 5-nitro-derivative initially formed in the former reaction undergoes reduction with the production of 5-amino-1-thiolbenzthiazole. On methylation, 5-nitro-1-thiolbenthiazole yielded a methyl derivative, whose constitution as *5-nitro-1-methylthiolbenzthiazole* follows from its synthesis from 1-methylthiolbenzthiazole by nitration.

In methyl-alcoholic solution, 1-thiol-5-methylbenzthiazole showed an ultra-violet absorption which was strikingly similar to that of 1-thio-2 : 5-dimethyl-1 : 2-dihydrobenzthiazole, and quite different from that of 1-methylthiol-5-methylbenzthiazole (Fig. 1). It therefore follows that the thiolbenzthiazole has the thiodihydro-structure (II). The curves belong to the same family as those of the hydroxybenzthiazole derivatives studied earlier (*loc. cit.*). In the *S*-methyl ether there occur two maxima at about the same wavelength (3000 A.) as in the case of 1-methoxy-5-methylbenzthiazole, in addition to a subsidiary maximum at about 3300 A., where the other curves have a maximum.

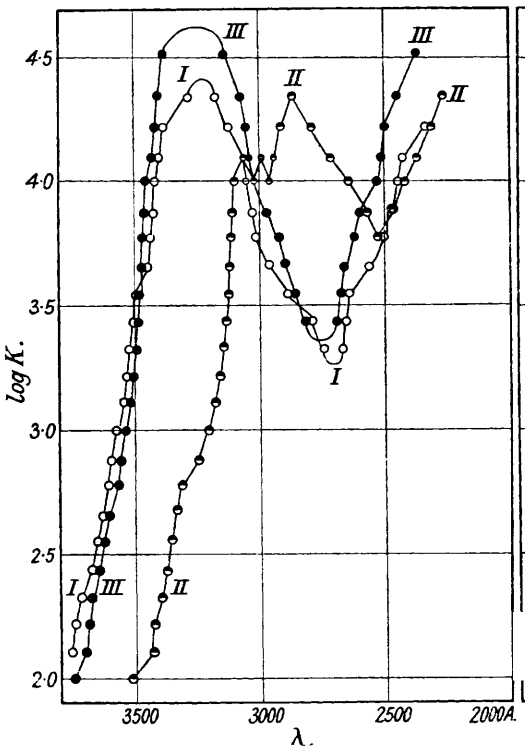
The absorption spectrum of 1-thiol-5-methylbenzthiazole in ethyl-alcoholic sodium ethoxide and in aqueous sodium hydroxide was also examined. In both of these curves there is a shift to the left (Fig. 2), suggesting deformation in the Fajans sense, which is greater in aqueous sodium hydroxide solution.

Mills, Clark, and Aeschlimann's picture (J., 1923, **123**, 2363) of Mohlau's synthesis of benzthiazole from dimethylaniline (*Ber.*, 1888, **21**, 59) suggests a synthesis of 1-thiolbenzthiazole by thionation of methylaniline:



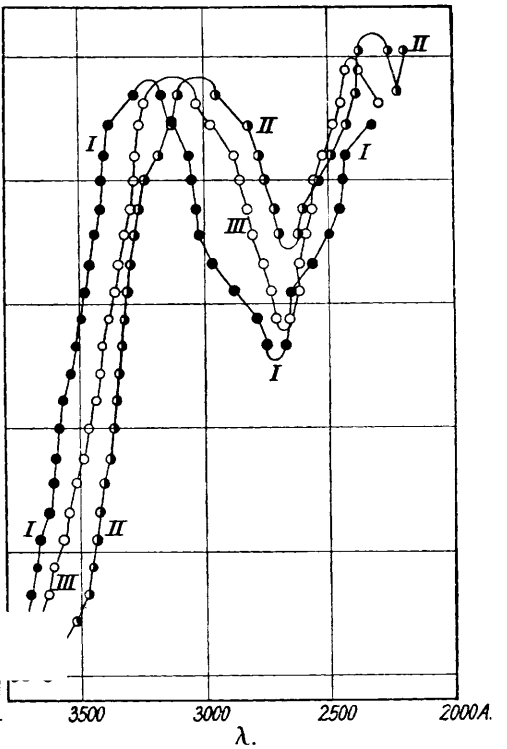
1-Thiolbenzthiazole was actually prepared by this reaction, but the yield was very poor (*ca.* 10%) and attempts to improve it by the use of zinc oxide as a catalyst were unsuccessful.

FIG. 1.



I = 1-*Thiol*-5-*methylbenzthiazole*.
II = 1-*Methylthiol*-5-*methylbenzthiazole*.
III = 1-*Thio*-2 : 5-*dimethyl*-1 : 2-*dihydrobenzthiazole*.

FIG. 2.



I = 1-*Thiol*-5-*methylbenzthiazole in* MeOH.
II = 1-*Thiol*-5-*methylbenzthiazole in* NaOH.
III = 1-*Thiol*-5-*methylbenzthiazole in* NaOEt.

EXPERIMENTAL.

1-Chloro-5-methylbenzthiazole, obtained from 1-amino-5-methylbenzthiazole by means of the Sandmeyer reaction (Hunter and Jones, J., 1930, 2207), crystallised from alcohol in needles, m.p. 49—50°. 1-Thiol-5-methylbenzthiazole was obtained by evaporating a mixture of 1-chloro-5-methylbenzthiazole (4 g.), sodium hydrosulphide (5 g.), and alcohol (20—25 c.c.) to dryness on a water-bath. The residue was treated with dilute hydrochloric acid and dissolved in aqueous sodium hydroxide, and the thiolbenzthiazole isolated by reprecipitation with dilute sulphuric acid. On recrystallisation from alcohol, 1-thiol-5-methylbenzthiazole was obtained in long needles, m. p. 181°. The disulphide obtained by oxidation of this had m. p. 201° (cf. Sebrell and Boord, *J. Amer. Chem. Soc.*, 1923, **45**, 2397).

Methylation of 1-*Thiol*-5-*methylbenzthiazole*.—A mixture of 1-thiol-5-methylbenzthiazole (1 g.) and methyl sulphate (3 c.c.) in methyl alcohol was heated under reflux on a water-bath for an hour, and the excess of methyl sulphate was destroyed with aqueous ammonia (*d* 0·880). On crystallisation from methyl alcohol, 1-*methylthiol*-5-*methylbenzthiazole* was obtained in broad thin plates, m. p. 48° (Found : C, 55·2; H, 4·7; S, 33·0. $C_9H_9NS_2$ requires C, 55·4; H, 4·65; S, 32·8%). This methyl derivative was very soluble in methyl alcohol and was accompanied by a gum which became crystalline on being rubbed, and proved identical with the thin plates already described.

1-*Thio*-2 : 5-*dimethyl*-1 : 2-*dihydrobenzthiazole*.—1-Nitrosoimino-2 : 5-dimethyl-1 : 2-dihydrobenzthiazole (1 g.) was ground with an equal weight of phosphorus pentasulphide. When the mixture was heated at 120°, a violent reaction occurred. Heating was continued for a few minutes, the product extracted with boiling benzene, and the brown gum obtained by removal

of this solvent dissolved in methyl alcohol. A small black precipitate which separated overnight was removed, and the filtrate kept; 1-*thio*-2 : 5-*dimethyl*-1 : 2-*dihydrobenzthiazole* crystallised in yellow plates, m. p. 138° (Found : S, 33·2. $C_9H_9NS_2$ requires S, 32·8%). The thiodimethyldihydro-derivative was also prepared by fusion of 1-keto-2 : 5-dimethyl-1 : 2-dihydrobenzthiazole (Hunter and Parken, *loc. cit.*) with phosphorus pentasulphide.

5-*Bromo*-1-*thiolbenzthiazole*.—4 G. of 1-chloro-5-bromobenzthiazole (obtained in 25—30% yield from 5-bromo-1-aminobenzthiazole by means of the Sandmeyer reaction; m. p. 101—102° after recrystallisation from alcohol) were heated with sodium hydrosulphide (4 g.) in alcohol (25 c.c.); the crystals of the chlorothiazole gradually disappeared with separation of a granular precipitate of sodium chloride. The *thiolbenzthiazole*, isolated as in the previous case, separated from alcohol in long, woolly, hair-like crystals, which subsequently changed to small thick needles, m. p. 272° (Found : S, 26·1. $C_7H_4NBrS_2$ requires S, 26·0%).

Methylation of 5-*Bromo*-1-*thiolbenzthiazole*.—A mixture of 5-bromo-1-thiolbenzthiazole (1 g.), methyl sulphate (3 c.c.), and methyl alcohol (5 c.c.) was heated on a water-bath for 1½ hours and thereafter on a wire gauze for 10 minutes. The cooled mixture was treated with aqueous ammonia (*d* 0·880) and kept overnight and the precipitate which separated was fractionally crystallised from methyl alcohol. 5-*Bromo*-1-*methylthiolbenzthiazole* separated in plates and thereafter in needles, m. p. 102° (Found : C, 37·0; H, 2·4; S, 24·7. $C_8H_6NBrS_2$ requires C, 36·9; H, 2·3; S, 24·6%). This constituted by far the bulk of the methylation product, but the mother-liquors on concentration furnished, after the separation of further crops of needles of the methylthiol derivative, two small clusters of brown prisms (*ca.* 0·04 g.) of 5-bromo-1-thio-2-methyl-1 : 2-dihydrobenzthiazole, m. p. 119° crude, 134° after recrystallisation from benzene, and 135° when mixed with the specimen described below.

5-*Bromo*-1-*thio*-2-*methyl*-1 : 2-*dihydrobenzthiazole*.—A mixture of 5-bromo-1-nitrosoimino-2-methyl-1 : 2-dihydrobenzthiazole (1 g.) and phosphorus pentasulphide (1·1 g.) was heated in an oil-bath, a violent reaction occurring at 110°; heating was continued up to 150°. The product, isolated by benzene, was recrystallised from a mixture of methyl and ethyl alcohols and thereafter from methyl alcohol, 5-*bromo*-1-*thio*-2-*methyl*-1 : 2-*dihydrobenzthiazole* being obtained in yellow needles and also in aggregates of brown prisms, m. p. 135° (Found : S, 24·85. $C_8H_6NBrS_2$ requires S, 24·6%).

5-*Nitro*-1-*thiolbenzthiazole*.—(i) To 1-thiolbenzthiazole (2·5 g.) in concentrated sulphuric acid (16 c.c.) cooled in a freezing mixture was added a mixture of fuming nitric acid (3 c.c.) and concentrated sulphuric acid (5 c.c.) drop by drop with stirring. The whole was kept for an hour and poured into ice-water, the precipitate extracted with boiling aqueous ammonia, and the filtered extract acidified. On recrystallisation from glacial acetic acid 5-nitro-1-thiolbenzthiazole was obtained in small yellow needles, m. p. 256°, undepressed by the specimen described below. (ii) 1·5 G. of 1-chloro-5-nitrobenzthiazole (Farooq and Hunter, *J. Indian Chem. Soc.*, **1933**, **10**, 563) and sodium hydrosulphide (1·5 g.) in alcohol (15 c.c.) were heated on a water-bath and the residue obtained by evaporation of the alcohol was treated with dilute hydrochloric acid, sulphur dioxide being evolved. The product was extracted with aqueous sodium hydroxide and the nitrothiolbenzthiazole obtained by precipitation with dilute sulphuric acid was crystallised from boiling alcohol, forming yellow needles, m. p. 260—261°. The alcoholic mother-liquors on concentration furnished 5-amino-1-thiolbenzthiazole, m. p. 260°, which was identified by diazotisation and coupling with β-naphthol to give a red azo-dye and by oxidation to 5 : 5-diaminobenzthiazolyl disulphide, m. p. 235° (Teppema and Sebrell, *loc. cit.*).

Methylation. A mixture of 5-nitro-1-thiolbenzthiazole (0·5 g.), methyl sulphate (1·5 c.c.), and methyl alcohol (2·5 c.c.) was heated on a water-bath until the nitro-compound dissolved. The solution was treated with excess of ammonia, and the product crystallised from alcohol, 5-*nitro*-1-*methylthiolbenzthiazole* separating in small pink-brown needles, m. p. 126° (Found : C, 43·0; H, 2·8; S, 28·6. $C_8H_6O_2N_2S_2$ requires C, 42·5; H, 2·7; S, 28·3%). The same compound, obtained by the gradual addition of 1-methylthiolbenzthiazole to fuming nitric acid in a freezing mixture (cf. Hunter, J., 1930, 143), crystallised from alcohol in small salmon-pink needles, m. p. 128°, and 126—127° when mixed with the preceding specimen.

Synthesis of 1-*Thiolbenzthiazole*.—(i) A solution of 1-chlorobenzthiazole (2·5 g.) in alcohol was heated under reflux with an alcoholic solution of sodium hydrosulphide (4·5 g.) for 2 hours. The residue obtained on removal of the solvent was treated with dilute sulphuric acid; the yellow precipitate of the thiolbenzthiazole crystallised from alcohol in cubes, m. p. 179°. (ii) A mixture of methylaniline (15 g.) and sulphur (20 g.) was heated at its b. p., under reflux, for 2 hours, hydrogen sulphide being evolved. Yellow needles separated on keeping overnight; the mixture was extracted with aqueous sodium hydroxide, and the extract acidified,

1-thiolbenzthiazole contaminated with sulphur being obtained. This was purified by extraction with hot aqueous ammonia and subsequent acidification, but the yield was only about 10% and was lowered by more prolonged heating.

Absorption Spectra Measurements (with ABDUL AZIZ FIRDAUS).—The measurements were made with a Carl Leiss spectrograph (type C), quartz absorption cells and a Wellington anti-screen plate being used. A hydrogen tube which gave a constant source of light enabled constant comparison spectra to be inserted between successive exposures, with various cell thicknesses of solution. Juxtaposition was secured by means of a Hartman diaphragm, and from the density matchpoints, molecular extinction coefficients followed.

An M/1000-solution of 1-thiol-5-methylbenzthiazole in absolute methyl alcohol was first examined, and thereafter diluted to M/10,000 and then to M/100,000 with the same solvent. A similar procedure was observed with M/1000-solutions of 1-thio-2 : 5-dimethyl-1 : 2-dihydrobenzthiazole and 1-methylthiol-5-methylbenzthiazole in methyl alcohol. M/1000-Solutions of 1-thiol-5-methylbenzthiazole in N/100-aqueous sodium hydroxide and N/100-ethyl-alcoholic sodium ethoxide were also examined, the solutions being subsequently diluted to M/10,000 and M/100,000 with water and alcohol respectively.

THE MUSLIM UNIVERSITY, ALIGARH, INDIA. [*Received, October 5th*, 1936.]