

LXXII.—*Bromination of some 5-Substituted 1-Phenylbenzthiazoles.*

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THE bromination of 1-phenylbenzthiazole has been investigated by Bogert and Abrahamson (*J. Amer. Chem. Soc.*, 1922, **44**, 826), who obtained a red unstable tetrabromo-additive compound, to which they assigned the constitution (I), which on boiling with dilute acetic acid yielded 5-bromo-1-phenylbenzthiazole.

The tetrabromide thus prepared gradually loses bromine on exposure to air, becoming almost colourless, and is instantaneously reduced to 1-phenylbenzthiazole by sulphurous acid and sodium bisulphite (compare J., 1925, **127**, 1319, 1488, 2023). The compound must therefore be a *perbromide*; and may have the constitution (I) or (II), the latter being analogous to that of the tetrabromides of pyridine and quinoline (Trowbridge, *J. Amer. Chem. Soc.*, 1897, **19**, 558; Grimaux, *Bull. Soc. chim.*, 1882, **38**, 124).

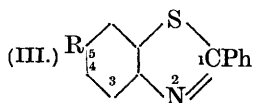


The formation of a *di-iodo*-additive compound and not a *tetraiodo*-derivative by 1-phenylbenzthiazole (*loc. cit.*) is in favour of the formula (I); the slight ionisation of 1-phenylbenzthiazole tetrabromide in glacial acetic acid solutions is, moreover, in accordance with the presence of a "thiazonium" sulphur atom as in (I), but the question cannot be fully discussed until the behaviour of substances such as dimethyl sulphide dibromide (Cahours, *Annalen*, 1865, **135**, 355) has been thoroughly reinvestigated.

The passage of phenylbenzthiazole tetrabromide into 5-bromo-1-phenylbenzthiazole (Bogert and Abrahamson, *loc. cit.*) suggests that there is probably an intimate connexion between the ring nitrogen atom (2) of the fused thiazole nucleus and the carbon atom (5) of the homocyclic ring of the benzthiazole system. The transformation is indeed a sort of "para-migration," and no doubt takes

place by way of a para-bridged intra-annular phase of the benzene ring. It might be expected, therefore, that the substitution of groups of varying polar character on the carbon atom (5) would have a profound effect on the unsaturation of the nitrogen atom (2) as exhibited by a tendency towards the formation of bromo-additive compounds (compare also Fries, *Annalen*, 1906, **346**, 128). It is, moreover, clear that this effect will manifest itself whether the tetrabromide has the constitution (I) or (II), for in the former case the effect on the nitrogen atom (2) will be communicated to the sulphur atom (7) by way of the well-known alternation of affinity effect in carbon chains.

Actually, it was found in connexion with the 5-substituted 1-phenylbenzthiazoles (III) that the electro-polar character of the 5-substituent has a remarkable effect on the tendency of these bases to form bromo-additive compounds.



Thus the negative nitro-group ($\text{R} = \text{NO}_2$) in 5-nitro-1-phenylbenzthiazole depresses the unsaturation of the thiazole system to such an extent as to render the formation of bromo-additive compounds impossible in acetic acid solutions, and to allow the formation only with considerable difficulty of the dibromide (IV) in chloroform. The less negative bromine atom in 5-bromo-1-phenylbenzthiazole ($\text{R} = \text{Br}$), on the other hand, allows the formation of a very unstable tetrabromo-additive compound with difficulty; whilst the positive amino-group ($\text{R} = \text{NH}_2$) enhances unsaturation of the thiazole system in 5-amino-1-phenylbenzthiazole to such an extent as to cause the immediate formation of a stable tetrabromide in the case of the latter benzthiazole derivative.

Bromination of 1-phenylbenzthiazole in chloroform gave rise to two isomeric forms of the tetrabromo-additive compound (m. p. 126° and 153°), just as di- β -naphthylthiocarbamide yields two forms of the hexabromide of 2- β -naphthylamino- α -naphthathiazole (Hunter, J., 1925, **127**, 2273). Both forms of the tetrabromide were reduced by sulphurous acid and passed into the substitution derivative on boiling with dilute alcohol and acetic acid (*loc. cit.*). It is highly probable that the lower-melting tetrabromide is identical with that formed in the bromination of the phenylbenzthiazole in glacial acetic acid solution, which usually commences to sinter at about 130° .

The bromo-additive compounds of the benzthiazole series, like the *p*-bromophenyltrimethylammonium perhalides (Reade, J.,

1924, **125**, 150), decompose rapidly at the temperature of fusion (and frequently below this : J., 1925, **127**, 2026), and therefore the melting point is not a real criterion of purity. For this reason, too much stress cannot be laid on the isolation of isomeric forms of the compounds, for the melting point (which is also the decomposition point) is appreciably affected by the crystalline form of the compound.* It is hoped to investigate this question more fully at an early date.

EXPERIMENTAL.

1-Phenylbenzthiazole was prepared from benzylideneaniline by Bogert and Abrahamson's method (*loc. cit.*). The finely crushed melt was added in a slow stream to boiling 60% sulphuric acid, and the resulting mixture boiled for an hour (water being added to make up for that lost by evaporation). The acid extract was filtered into cold water (10 vols.), and the precipitated base was washed, dried at 70°, dissolved in the minimum of boiling alcohol (to remove resinous material), and the filtered solution poured into cold water. The product, after drying, crystallised from light petroleum-alcohol (3 : 1) in pale yellow prisms, m. p. 114°, having the odour of geraniums and other properties described by Hofmann (*Ber.*, 1879, **12**, 2359).

Bromination. (A). Phenylbenzthiazole (2 g.) dissolved in glacial acetic acid was gradually treated with bromine (Bogert and Abrahamson, *loc. cit.*). The tetrabromide separated in red needles or prisms, which were dried in a vacuum over potassium hydroxide; m. p. 137° after sintering at 130° (Found : Br, 60.6. Calc., Br, 60.3%). On boiling with dilute acetic acid or alcohol, 5-bromo-1-phenylbenzthiazole was produced which crystallised from glacial acetic acid in shining prisms, m. p. 152°.

Since this method of preparing the tetrabromide invariably gave resinous products, the bromination of 1-phenylbenzthiazole in chloroform was examined.

(B). Phenylbenzthiazole (2 g.) dissolved in chloroform (30 c.c.) was gradually treated with bromine (2 c.c.), and the resulting solution boiled, and cooled in ice. On scratching, reddish-brown needles of phenylbenzthiazole tetrabromide separated which were dried in a vacuum over potassium hydroxide; m. p. 126° (decomp.) (Found : Br, 60.6. $C_{13}H_9NBr_4S$ requires Br, 60.3%). The filtrate from this compound, on concentration and cooling, furnished slender, orange needles of a second *tetrabromide*, which were dried as before; m. p. 153° (decomp.) (Found : Br, 59.8%).

* Thus specimens of 1-anilinobenzthiazole tetrabromide crystallised from chloroform under different conditions may have melting points anywhere between 112° and 117° (Hunter, J., 1925, **127**, 2025).

5-Nitro-1-phenylbenzthiazole was obtained by the direct nitration of phenylbenzthiazole with nitric acid (*d* 1.5) and by nitration with a mixture of sulphuric acid and nitric acid (*d* 1.4) as described in the literature (*loc. cit.*). After two crystallisations from glacial acetic acid, the nitrobenzthiazole was obtained in small, orange prisms, m. p. 188°. In both cases the yield exceeded 90%.

5-Nitro-1-phenylbenzthiazole Dibromide.—*5-Nitro-1-phenylbenzthiazole* was recovered unchanged after a saturated solution of the compound in glacial acetic acid had been treated with bromine. The nitrophenylbenzthiazole (2 g.) suspended in chloroform (40 c.c.) was gradually treated with bromine (2 c.c.); after $\frac{1}{2}$ hour, the mixture was boiled and filtered, and the filtrate kept over-night. The somewhat pasty precipitate of the *dibromide* was collected and agitated with an ethereal solution of bromine, when vermilion prisms were obtained which were dried in the usual way. They softened at 120° and melted at 144° (Found: Br, 37.8. $C_{13}H_8O_2N_2Br_2S$ requires Br, 38.5%). The dibromide lost bromine on exposure to air and was reduced by sulphurous acid in the usual way. On boiling with dilute acetic acid, bromine was evolved with regeneration of the original nitrobenzthiazole.

5-Bromo-1-phenylbenzthiazole Tetrabromide.—When *5-bromo-1-phenylbenzthiazole* (1 g.) in chloroform (12 c.c.) was gradually treated with bromine (1.6 c.c.), a dark red solution was obtained which deposited red prisms of a tetrabromo-additive compound, m. p. 206—208° (decomp.) (Found: Br, 64.8. $C_{13}H_8NBr_5S$ requires Br, 65.6%). This compound was most unstable and lost bromine immediately on exposure to air; bromine was also eliminated with regeneration of the original *5-bromo-substitution derivative* by boiling with dilute acetic acid, or by treating with sulphurous acid. By using a smaller quantity of bromine, red needles of another bromide were obtained which changed colour at 85°, became orange at 110°, and showed signs of loss of bromine at 175°; m. p. 208° (decomp.). The bromine content was that of a tribromo-additive compound [Found: Br, 60.9. $(C_{13}H_8NBr_4S)_2$ requires Br, 60.4%]. This bromide had similar properties to the tetrabromide already described; it was converted into *5-bromo-1-phenylbenzthiazole* by sulphurous acid or by boiling dilute acetic acid.

5-Amino-1-phenylbenzthiazole, prepared by reduction of the *5-nitro-derivative* (*loc. cit.*), on repeated crystallisation from boiling aniline or toluene, was obtained in small prisms, m. p. 208°, as recorded. In cases where the reduction had proceeded too vigorously, the product after crystallisation was very dark and resinous; attempts were therefore made to work up the base by way of the benzyldene derivative (*loc. cit.*). The product separated from

alcohol in pale yellow plates, m. p. 190° (39° above the recorded temperature); the m. p. was unaltered by recrystallisation. 5-Benzylideneamino-1-phenylbenzthiazole prepared from pure 5-amino-1-phenylbenzthiazole had the melting point of 151° recorded in the literature. The nature of the high-melting product has not yet been investigated.

5-Amino-1-phenylbenzthiazole Tetrabromide.—5-Amino-1-phenylbenzthiazole (1 g.) suspended in chloroform (30 c.c.) was gradually treated with bromine (1.1 c.c.) dissolved in a small amount of the same solvent; an ochre-coloured precipitate of the bromo-additive compound appeared on the addition of the first drop of halogen. The mixture was boiled and filtered, the residue digested with dry ether containing bromine, and the product dried in the usual way. A dark brown, microcrystalline powder was thus obtained which melted at 216° after showing colour change between 180° and 190° (Found: Br, 60.1. $C_{13}H_{10}N_2Br_4S$ requires Br, 58.6%). The filtrate from this bromide, on slight concentration, furnished red prisms of another *tetrabromide*, m. p. 210 — 211° , which were dried in a vacuum as before (Found: Br, 60.3%). The brown tetrabromide was remarkably stable to air and in this respect resembled the dibromide of 4'-amino-1-phenyl-5-methylbenzthiazole (J., 1925, **127**, 1318). On boiling with acetic acid a red solution was obtained which deposited prisms of the second tetrabromide, m. p. 210° . Both bromides were reduced in the usual way by sulphurous acid, etc. On boiling the red crystals with dilute acetic acid, a dark product was obtained; this was digested with dilute alkali, dried, and repeatedly extracted with boiling alcohol, which removed a purple impurity. The brown residue was washed with ether and dried. It appeared to be an impure bromo-substitution product and softened at about 170° ; its analysis corresponded most closely with a *dibromo*-derivative (Found: Br, 39.3. $C_{13}H_9N_2Br_2S$ requires Br, 41.8%). The purple alcoholic extracts on evaporation furnished a quantity of dark-coloured product insufficient for investigation.

The experiments here described were commenced early in 1924 with the object of studying the effect of the substitution of groups of varying polar and spatial character on the unsaturation of the fused thiazole nucleus. Since the work has been temporarily abandoned, it has seemed desirable to publish the results so far obtained.

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