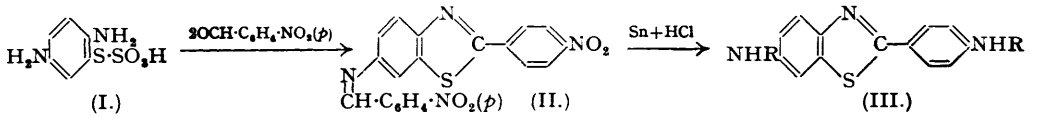
652. *Some Potential Trypanocidal and Antibacterial Compounds in the Heterocyclic Series. Part I. Benzthiazoles.*

By F. F. Stephens and D. G. Wibberley.

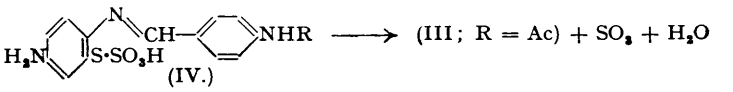
Several benzthiazole compounds, mostly prepared from diaminophenylthiosulphuric acids, have been synthesized for antibacterial and trypanocidal examination. One of these compounds, 6-amidino-2-*p*-amidinophenylbenzthiazole, revealed interesting trypanocidal action.

It is well known that aromatic diamidines exhibit considerable antibacterial activity (*e.g.*, Ashley, Barber, Ewins, Newbery, and Self, *J.*, 1942, 103; Wien, Harrison, and Freeman, *Brit. J. Pharmacol.*, 1948, **3**, 211) and that trypanocidal action has been demonstrated in the benzthiazole field (Browning, Cohen, Ellingworth, and Gulbransen, *Proc. Roy. Soc.*, 1931, *B*, **108**, 119). For these reasons, among others, it was decided to prepare 6-amidino-2-*p*-amidinophenylbenzthiazole and to examine its parasiticidal properties.

6-Amino-2-*p*-aminophenylbenzthiazole (III; R = H), a suitable intermediate in the preparation of this diamidine, has already been reported by Bogert and Taylor (*Coll. Czech. Chem. Comm.*, 1931, **3**, 480), who obtained it in poor yield by reaction of "*p*-phenylenediaminemonothiosulphuric acid" (2 : 5-diaminophenylthiosulphuric acid) (I) (Bernthsen, *Annalen*, 1889, **251**, 1) with *p*-nitrobenzoyl chloride (followed by reduction) and also by condensation of one mole of this thiosulphuric acid with two moles of *p*-nitrobenzaldehyde. In the latter reaction, the primary product was considered to be 6-(*p'*-nitrobenzylideneamino)-2-*p*-nitrophenylbenzthiazole (II) and this was converted into the diamine (III; R = H) by acid reduction :



We have found that a far better yield of the diamine (III; R = H) is obtained if the thiosulphuric acid (I) is treated with an equimolecular amount of *p*-acetamidobenzaldehyde. In this case the initial product is the Schiff's base 2-(*p*-acetamidobenzylideneamino)-5-aminophenylthiosulphuric acid (IV; R = Ac)*, and this is quantitatively cyclised to (III; R = Ac) by boiling it under reflux with acetic acid and ammonium acetate :

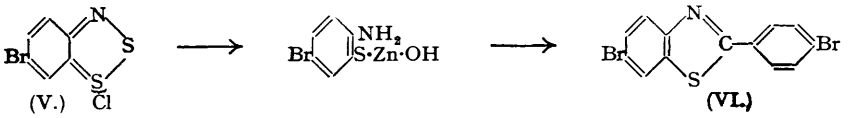


p-Aminobenzaldehyde is conveniently prepared by Beard and Hodgson's method (*J.*, 1944, 4), and we have shown that the unacetylated Schiff's base (IV; R = H) may be obtained without isolation of this aldehyde (see Experimental). Cyclisation of (IV; R = H), by the method referred to above, gave 6-acetamido-2-*p*-acetamidophenylbenzthiazole (III; R = Ac) which yielded the required diamine (III; R = H) by acid hydrolysis. 6-Cyano-2-*p*-cyanophenylbenzthiazole was obtained by tetrazotisation of (III; R = H) followed by Sandmeyer reaction. It was also prepared by reaction of 6-bromo-2-*p*-bromophenylbenzthiazole (VI) with cuprous cyanide, (VI) having been obtained from the corresponding diamine (III; R = H) by Sandmeyer reaction, and also by application of the Herz reaction (G.P. 360,690; König, *Ber.*, 1928, **61**, 2065; Hixson and Cauwenberg, *J. Amer. Chem. Soc.*, 1930, **52**, 2118; Ast and Bogert, *Rec. Trav. chim.*, 1935, **54**, 917; Fox and Bogert, *J. Amer. Chem. Soc.*, 1939, **61**, 2013; Blomquist and Diuguid, *J. Org. Chem.*, 1947, **12**, 718) in which *p*-bromoaniline was converted by reaction with sulphur monochloride into its thiazathionium chloride (V) (cf. Bezzubets, *J. Gen. Chem. Russia*, 1947, **17**, 681; *Chem. Abs.*, 1948, **42**, 6807). Ring opening with alkali led to the zinc salt of 2-amino-5-bromothiophenol, which produced the desired dibromo-compound on condensation with *p*-bromobenzoyl chloride.

6-Cyano-2-*p*-cyanophenylbenzthiazole was converted into the corresponding diamidine dihydrochloride by the usual Pinner method (see Ashley, Barber, *et al.*, *loc. cit.*), dioxan or nitrobenzene being used as solvent. Opportunity was taken to bring about reaction between

* For note on the structure of the Schiff's bases, see p. 3336.

the intermediate di-imino-ether hydrochloride and alcoholic hydrazine to obtain the diamidrazone (cf. Taylor and Baker, " The Organic Chemistry of Nitrogen," 1937, p. 399).



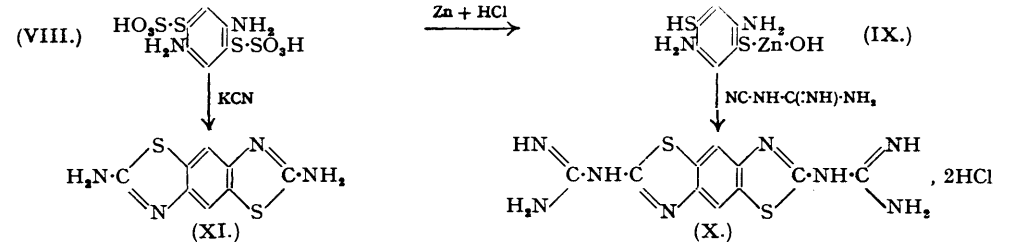
(V.) (VI.)

In view of the considerable trypanocidal activity shown by phenanthridinium compounds (review by Walls, *J. Soc. Chem. Ind.*, 1947, **66**, 182) 6-amino-2-*p*-aminophenylbenzthiazole methochloride (VII) was prepared : its similarity to one of the phenanthridinium compounds (VII*a*) is clear.

(VII.) (VII*a*.)

By reaction of *m*-nitrobenzaldehyde with (I) and cyclisation of the resulting Schiff's base (or, better, by reaction of equimolecular amounts in acetic acid–ammonium acetate medium) 6-acetamido-2-*m*-nitrophenylbenzthiazole was prepared. This was converted into 6-cyano-2-*m*-cyanophenylbenzthiazole by conventional reactions and thence into the corresponding diamidine. The quaternary salt 6-amino-2-*m*-aminophenylbenzthiazole methochloride was also synthesized.

The work of Browning *et al.* (*loc. cit.*) was concerned in part with the trypanocidal action of certain styryl-benzthiazoles and we originally intended to prepare 6-amidino-2-*p*-amidinostyrylbenzthiazole. The dinitrile corresponding to this substance is described (see p. 3340), but the final stage could not be attained before the work had to be abandoned. 6-Cyano-2-methylbenzthiazole, required for this preparation, was obtained by two routes : (*a*) from 2-methylbenzthiazole (Kiprianov *et al.*, *J. Gen. Chem. Russia*, 1936, **6**, 232 ; *Chem. Abs.*, 1936, **30**, 4859) by nitration, reduction (Browning *et al.*, *loc. cit.*), and Sandmeyer reaction ; and (*b*) from 2 : 5-diaminophenylthiosulphuric acid by reaction with acetic anhydride to give 6-acetamido-2-methylbenzthiazole, followed by hydrolysis and Sandmeyer reaction (cf. Green and Perkin, *J.*, 1903, **83**, 1201).



(VIII.) (IX.) (XI.) (X.)

In view of the known antibacterial action of guanidines and, further, of the statement (Safin, Kushner, Brancone, and Subbarow, *J. Org. Chem.*, 1948, **13**, 924) " that *p*-phenylenediguanidine possesses curative properties against *Trypanosoma equiperdum* in mice," we prepared some guanidines in the benzthiazole series. Acid reduction of 2 : 5-diaminophenylmonothiosulphuric acid (I) gave 2 : 5-diaminothiophenol (isolated as the zinc salt) (Green and Perkin, *loc. cit.*). On condensation of this compound with dicyandiamide (Smith *et al.*, *J. Amer. Chem. Soc.*, 1931, **53**, 4103) 6-amino-2-guanidinobenzthiazole was obtained. A similar reduction of 2 : 5-diaminophenyl-1 : 4-bisthiosulphuric acid (VIII) (Green and Perkin, *loc. cit.*) gave the zinc salt (IX) of 2 : 5-diaminodithioquinol from which, by reaction with dicyandiamide, 2′ : 2″-diguanidinodithiazolo(4′ : 5′-1 : 2)(4″ : 5″-4 : 5)benzene (X) was obtained. The bisthiosulphuric acid (VIII) also treated with potassium cyanide to give 2′ : 2″-diaminodithiazolo-(4′ : 5′-1 : 2)(4″ : 5″-4 : 5)benzene (XI) (cf. Heller, *J. pr. Chem.*, 1924, **108**, 257).

Note on the Structure of the Schiff's Bases (IV.)—In agreement with Bogert and Taylor (*loc. cit.*) we have assigned formulæ of type (IV) to the Schiff's bases obtained by reaction of *p*-phenylenediaminemonothiosulphuric acid with *p*-acetamido- or *p*-amino-benzaldehyde. A referee has expressed the opinion that anil condensation may occur initially on the unhindered

amino-group, the benzylidene group then being transferred during treatment with glacial acetic acid and ammonium acetate, *e.g.*, by intermolecular rather than intramolecular reaction, to the *o*-thiol-amino-system. It should be pointed out, however, that precisely similar results are obtained from aromatic aldehydes and 4-dimethylaminoaniline-2-thiosulphuric acid (*idem*, *loc. cit.*; Bogert and Updike, *J. Amer. Chem. Soc.*, 1927, **49**, 1373; see also Heller, *loc. cit.*). We suggest that in compounds of this type neither of these formulæ is correct and that the thiosulphuric acid moiety may be involved in the condensation or reaction with aldehydes. Some evidence for this view is provided by the following: (*a*) analysis of the compound (IV; R = Ac) and others of the same type not reported here indicates addition of the components rather than condensation with elimination of water; (*b*) whereas 4-dimethylaminoaniline-2-thiosulphuric acid reacts immediately with aromatic aldehydes to produce coloured products, yet the methyl ester of this acid (Heller, *loc. cit.*) will not so react; (*c*) cyclisation of the so-called Schiff's bases (IV) may be effected by boiling them with aniline, *p*-toluidine or diphenyl ether; (*d*) *s*-dimethyl-*p*-phenylenediaminemonothiosulphuric acid was prepared and also gave coloured products with aldehydes; (*e*) during potentiometric titration of the compound from *p*-dimethylaminobenzaldehyde and the thiosulphuric acid (I) (dissolved in sodium hydroxide solution) by 0·1N-sulphuric acid, the pH increases sharply in the range 8—9 with slow addition of acid, giving a curve very similar to that obtained in the titration of puberulonic acid (Corbett, Hassall, Johnson, and Todd, *J.*, 1950, 1).

Experimental.

(See also B.P. Appln. 8,680/49.)

2-(p-*Acetamidobenzylideneamino*)-5-*aminophenylthiosulphuric Acid.*—2 : 5-Diaminophenylthiosulphuric acid (110 g.), dissolved in water (1500 ml.) at 90°, was treated with *p*-acetamidobenzaldehyde (81·5 g.) dissolved in alcohol (500 ml.), and the mixture heated with stirring on the steam-bath for 15 minutes. After cooling, the bright red *acid* (182 g.; m. p. 260°) was filtered off, washed first with spirit and then with water, and dried. A little of the product was purified by successive extractions with acetone, ethanol, and water, the m. p. rising to 265—266° (Found: C, 47·0; H, 4·5; N, 10·7. $C_{15}H_{15}O_4N_3S_2,H_2O$ requires C, 47·0; H, 4·45; N, 10·9%).

6-*Acetamido*-2-p-*acetamidophenylbenzthiazole.*—(*a*) The above acid (180 g.) was boiled under reflux for 5 hours with glacial acetic acid (1200 ml.) and ammonium acetate (600 g.). The mixture was cooled and poured into an excess of water, and the crude benzthiazole (120 g.; m. p. 285°) filtered off, washed, and dried. Recrystallisation from glacial acetic acid gave pale yellow crystals (m. p. 318—319°) (Found: N, 12·5. $C_{17}H_{15}O_2N_3S$ requires N, 12·9%).

(*b*) *p*-Nitrotoluene (100 g.) was converted into *p*-aminobenzaldehyde by Beard and Hodgson's method (*loc. cit.*). The mixture was filtered immediately after steam-distillation, and to the hot filtrate was added 2 : 5-diaminophenylthiosulphuric acid (110 g.) dissolved in boiling water (1200 ml.). The mixture was made acid with acetic acid and allowed to cool overnight, and the bright red Schiff's base (IV; R = H) (147 g.; m. p. 274°) which separated was removed, washed, and dried. This was cyclised and 6-*acetamido*-2-p-*acetamidophenylbenzthiazole* (111 g.; m. p. 302—304°) isolated as described under (*a*) above.

6-*Amino*-2-p-*aminophenylbenzthiazole.*—The above diacetamido-compound (32·5 g.), water (360 ml.), and sulphuric acid (140 ml.; *d* 1·84) were heated together in an open beaker until complete solution was obtained. On pouring the cooled solution into water (2 l.) the sulphate of the base (28 g.; m. p. >360°), $C_{13}H_{11}N_3S,H_2SO_4$, was precipitated. The free base, liberated from the sulphate by alkali, was purified by co-distillation under vacuum with liquid paraffin and was a pale yellow solid (m. p. 258°) (Found: N, 17·2. Calc. for $C_{13}H_{11}N_3S$: N, 17·4%). It is convenient to keep this compound as the sulphate because, unless purified as described above, the free base rapidly turns dark green in moist air. A solution of the base in aqueous alcohol showed strong fluorescence in ultra-violet light.

6-*Bromo*-2-p-*bromophenylbenzthiazole.*—(*a*) *By Sandmeyer reaction.* 6-Acetamido-2-*p*-acetamidophenylbenzthiazole (3·25 g.) was brought into solution by heating with dilute sulphuric acid as described above. The cold solution was diluted with water (25 ml.), cooled further by addition of ice, and the base tetrazotised at 0—5° by addition of sodium nitrite (1·5 g.) (the total volume of the tetrazo-solution being 95 ml.). This was added to a solution of cuprous bromide (15 g.) in hydrobromic acid (70 ml.; *d* 1·5) and water at 0°. The resulting mixture was kept overnight, then gradually warmed to 90° on the steam-bath, and diluted with water, and the solid removed by filtration. Vacuum sublimation of the dry residue (5·1 g.) gave pale yellow crystals (2·5 g.; m. p. 213—214°) which, after recrystallisation from dioxan, were obtained as white needles (m. p. 217—218°) (Found: Br, 42·7. $C_{13}H_7NBr_2S$ requires Br, 43·4%).

(*b*) *By Herz reaction.* Sulphur monochloride (80 ml.) was run slowly on to *p*-bromoaniline (10 g.) with stirring; a vigorous reaction ensued and hydrogen chloride was copiously evolved. The mixture was stirred for 3 hours at room temperature and then for 2 hours at 60—70° (by this time the rapid evolution of gas had ceased). After cooling, an equal volume of dry benzene was added, and the dark green product filtered off, washed with dry benzene, and dried *in vacuo*. The solid was added to a solution of sodium hydroxide (25 g.) and sodium hydrosulphite (dithionite) (10 g.) in aqueous alcohol (500 ml.; 30% EtOH); the bulk dissolved, and the resulting clear solution was decanted from a small amount of tar. Addition of a slight excess of a concentrated aqueous solution of zinc sulphate, followed

by sufficient acetic acid to give slight acidity, precipitated the zinc salt of 2-amino-5-bromothiophenol (10 g.), which was collected, washed with water and then alcohol, and dried at 110°. This was suspended in glacial acetic acid (400 ml.) and treated with *p*-bromobenzoyl chloride (10·5 g.), and the mixture boiled for 5 minutes. After cooling and pouring into water, 6-*bromo*-2-p-*bromophenylbenzthiazole* separated, and was collected, washed first with dilute sodium hydroxide solution then with water, and dried at 110° (m. p. 212—214°; yield 12·4 g.). Recrystallisation from dioxan raised the m. p. to 217—218°, undepressed when mixed with the product from (*a*).

6-*Cyano*-2-p-*cyanophenylbenzthiazole*.—(*a*) The sulphate (28 g.) of the diamino-compound was suspended in water (200 ml.), concentrated hydrochloric acid (40 ml.) added, and the mixture cooled to 0°. Tetrazotisation was effected by addition of sodium nitrite (11 g.), after which the solution was neutralised (Congo-red) by cautious addition of 50% sodium hydroxide solution (the temperature being kept below 10°). The neutral tetrazo-solution was slowly added to a boiling solution of cuprous cyanide (15 g.) and sodium cyanide (30 g.) in water (400 ml.), boiling being continued for 10 minutes after the addition was complete. The brown solid so obtained was filtered off, washed, dried, and vacuum sublimed (290—300°/1 mm.) to give long lemon-yellow needles of 6-*cyano*-2-p-*cyanophenylbenzthiazole* (6·5 g.) which, after recrystallisation from nitrobenzene, melted at 288—289° (Found: C, 69·0; H, 2·9; N, 16·0. $C_{15}H_7N_3S$ requires C, 69·0; H, 2·7; N, 16·1%).

(*b*) 6-Bromo-2-*p*-bromophenylbenzthiazole (9 g.) was treated with cuprous cyanide (4·35 g.) in quinoline (36 ml.) according to the procedure of Barber *et al.* (*J.*, 1947, 84). The yield of vacuum-sublimed dinitrile (m. p. 288—289°) was 3 g.; it was white, and never yellow as prepared by method (*a*)

6-*Amidino*-2-p-*amidinophenylbenzthiazole Dihydrochloride*.—The above dinitrile (3 g.) was suspended in a mixture of nitrobenzene (60 ml.) and ethanol (6 ml.), and dry hydrogen chloride was passed through the mixture (cooled with ice-water) for 9 hours (the apparatus being protected from moisture by means of a calcium chloride tube). By this time the solid had passed into solution, and this was kept at room temperature for 3 days. The crystalline precipitate of imino-ether hydrochloride which had formed was filtered off and treated with saturated alcoholic ammonia (60 ml.) for 24 hours. The crude *diamidine* was precipitated by addition of dry ether, filtered off, and purified by dissolution in dilute hydrochloric acid followed by precipitation with an excess of acetone. The product (2·5 g.) was dissolved in the minimum quantity of water and again precipitated by addition of acetone (m. p. >300°; pale yellow) (Found: N, 17·4; S, 7·8. $C_{15}H_{13}N_5S,2HCl,2H_2O$ requires N, 17·3; S, 7·9%). It was also possible to recrystallise the compound from 3N-hydrochloric acid. For pharmacological purposes a solution of the di-isethionate (assayed spectroscopically) was prepared essentially by the method described in B.P. 559,015 (dioxan being used as solvent). Ultra-violet absorption of the dihydrochloride (in water) showed a maximum at 3070 A. (ε = 30,300).

6-*Amidrazono*-2-p-*amidrazonophenylbenzthiazole Dihydrochloride*.—6-Cyano-2-*p*-cyanophenylbenzthiazole (1 g.) was converted into its di-imino-ether hydrochloride as described above, and this was treated for 3 hours with ethanol (15 ml.) containing hydrazine hydrate (3 ml.; 100%). The *product* was precipitated by addition of ether and recrystallised from dilute hydrochloric acid. The yield was 1 g. (m. p. >360°) (Found: N, 22·5. $C_{15}H_{15}N_7S,2HCl,2H_2O$ requires N, 22·6%).

6-*Amino*-2-p-*aminophenylbenzthiazole Methochloride Hydrochloride*.—6-Acetamido-2-*p*-acetamidophenylbenzthiazole (10 g.) was added to nitrobenzene (150 ml.) at 185°, the mixture allowed to cool to 175°, and methyl toluene-*p*-sulphonate (7·2 g.) added. The temperature was kept at 170—180° for 30 minutes, the solution allowed to cool overnight, excess of dry benzene added, and the crude metho-toluene-*p*-sulphonate removed and washed with benzene. Traces of solvent were removed from the product by steam-distillation, after which it was hydrolysed by being refluxed for 2 hours with concentrated hydrochloric acid (35 ml.) and water (35 ml.). On cooling the reddish-brown *metho-chloride hydrochloride* (3·5 g.; m. p. 332°) crystallised (Found: N, 12·9; Cl, 20·8. $C_{14}H_{14}N_3ClS,HCl$ requires N, 12·8; Cl, 21·6%).

6-*Acetamido*-2-m-*nitrophenylbenzthiazole*.—*m*-Nitrobenzaldehyde (36 g.), 2 : 5-diaminophenylthiosulphuric acid (52·8 g.), ammonium acetate (240 g.), and glacial acetic acid (480 ml.) were boiled under reflux for 6½ hours, and the mixture allowed to cool. It was then poured into water (1 l.), and crude 6-*acetamido*-2-m-*nitrophenylbenzthiazole* (60 g.; m. p. 195—200°) was precipitated; on recrystallisation from acetic acid, it was obtained as pale-yellow needles (37 g.; m. p. 206—208°) (Found: N, 13·4. $C_{15}H_{11}O_3N_3S$ requires N, 13·4%).

6-*Amino*-2-m-*nitrophenylbenzthiazole*.—Hydrolysis of the above acetamido-compound (3 g.) by heating with sulphuric acid (14 ml.; *d* 1·84) and water (36 ml.) gave, after recrystallisation from nitrobenzene, 6-*amino*-2-m-*nitrophenylbenzthiazole* (1·5 g.) as orange-coloured needles (m. p. 230°) (Found: N, 15·3. $C_{13}H_9O_2N_3S$ requires N, 15·5%).

6-*Amino*-2-m-*aminophenylbenzthiazole*.—The above nitro-amine (5 g.) was dissolved in hot dioxan (100 ml.), and the solution stirred for 10 minutes with a little Raney nickel catalyst. The catalyst was removed by filtration, fresh Raney nickel added to the filtrate, and the nitro-group reduced by hydrogen (initial pressure 50 lb./sq. in.) at room temperature. The catalyst was removed, and the fluorescent dioxan solution diluted with water to 500 ml. to precipitate the *diamine*. Recrystallisation of the white solid (becoming pale yellow in the air) from dilute ethanol gave pale yellow needles (3·4 g.; m. p. 210°) (Found: N, 17·2. $C_{13}H_{11}N_3S$ requires N, 17·4%). The *diacetyl* derivative melted at 292° (Found: N, 12·8. $C_{17}H_{15}O_2N_3S$ requires N, 12·9%).

6-*Cyano*-2-m-*cyanophenylbenzthiazole*.—The above diamine (3 g.) in water (35 ml.) and concentrated hydrochloric acid (8 ml.) was tetrazotised at 0—5° by addition of sodium nitrite (1·75 g.), and the resulting solution added to cuprous cyanide (3 g.) and sodium cyanide (4 g.) in water (60 ml.) at 20°. The mixture was kept for 2 hours, then slowly raised to the boil; the crude *dinitrile* was removed, and

purified by two vacuum sublimations to give pale yellow needles (0·5 g.; m. p. 226—227°) (Found: N, 15·9. $C_{15}H_7N_3S$ requires N, 16·05%).

6-*Amidino*-2-m-*amidinophenylbenzthiazole Dihydrochloride.*—The foregoing dinitrile was converted into the diamidine dihydrochloride by the general method used for the *p*-isomer (but with dioxan as solvent for formation of the imino-ether), but the salt was not obtained analytically pure.

6-*Amino*-2-m-*aminophenylbenzthiazole Methochloride Hydrochloride.*—6-Acetamido-2-*m*-acetamidophenylbenzthiazole (3 g.) was methylated with methyl toluene-*p*-sulphonate (2·16 g.) in nitrobenzene (45 ml.) at 180—190° (1 hour). After cooling and addition of benzene, the crystalline methotoluene-*p*-sulphonate was isolated and dissolved in boiling water (70 ml.), and traces of solvent removed by steam-distillation. Concentrated hydrochloric acid (20 ml.) was added to the solution, which was then evaporated to 40 ml., cooled, and treated with ammonia solution (*ca.* 11 ml.; *d* 0·88) until it gave a faintly acid reaction (Congo-red). On being kept, the *methochloride hydrochloride* (1·2 g.) crystallised, and was recrystallised from methanol to give dark green needles (1·0 g.; m. p. 307—308°) (Found: N, 12·9; Cl, 20·7. $C_{14}H_{14}N_3ClS,HCl$ requires N, 12·8; Cl, 21·6%).

6-*Cyano*-2-*methylbenzthiazole.*—2 : 5-Diaminophenylthiosulphuric acid (22 g.), acetic anhydride (20 ml.), and acetic acid (50 ml.) were boiled under reflux for 7 hours, the mixture was diluted and neutralised, and the product so precipitated recrystallised from water to give 6-acetamido-2-methylbenzthiazole (9·7 g.), m. p. 154°. Hydrolysis of this with 20% sulphuric acid gave 6-amino-2-methylbenzthiazole (5·8 g.), m. p. 127—128°, identical with that prepared by nitration and then reduction of 2-methylbenzthiazole. The amino-compound (5 g.) was dissolved in a mixture of concentrated hydrochloric acid (10 ml.) and water (25 ml.), and diazotised with sodium nitrite (2·2 g.) in water (10 ml.). The clear diazo-solution was neutralised and added to a solution of cuprous cyanide (2·5 g.) and sodium cyanide (3·4 g.) in water (60 ml.) at room temperature, after which the mixture was heated for 30 minutes on the steam-bath. In this way a black solid (6 g.) was obtained, giving 6-cyano-2-methylbenzthiazole (3 g.) on vacuum sublimation. This formed white needles, m. p. 144°, from ethanol (Kiprianov *et al.*, *J. Gen. Chem. Russia*, 1945, **15**, 200; *Chem. Abstr.*, 1946, **40**, 2309, give m. p. 135°) (Found: N, 16·2. Calc. for $C_9H_6N_2S$: N, 16·1%).

6-*Cyano*-2-p-*cyanostyrylbenzthiazole.*—6-Cyano-2-methylbenzthiazole (0·87 g.) and *p*-cyanobenzaldehyde (0·66 g.) were heated under reflux in boiling acetic anhydride (2 ml.) for 6 hours. The mixture was cooled and diluted with ethanol, and the pale yellow solid removed by filtration. Recrystallisation from ethyl benzoate gave pale yellow needles (*ca.* 1 g.) of the *dinitrile* (m. p. 281—283°) (Found: N, 14·5. $C_{17}H_9N_3S$ requires N, 14·6%).

Zinc Salt of 2 : 5-*Diaminothiophenol.*—2 : 5-Diaminophenylthiosulphuric acid (10 g.), dissolved in water (200 ml.), was treated at 25° with concentrated hydrochloric acid (46 ml.) and zinc dust (12 g.). When effervescence had ceased, the mixture was heated for 30 minutes in a boiling-water bath, filtered, and the *zinc* salt precipitated from the filtrate by addition of concentrated aqueous sodium acetate solution. The product (9·2 g.) was isolated by filtration, washed, and dried to give a white powder becoming blue in moist air (Found: N, 12·0; Zn, 26·6. $C_6H_7N_2S,ZnOH,\frac{1}{2}H_2O$ requires N, 12·2; Zn, 28·2%).

6-*Amino*-2-*guanidinobenzthiazole.*—The above zinc salt (3·4 g.) was dissolved in a mixture of spirit (30 ml.) and concentrated hydrochloric acid (8 ml.), and to the solution was added finely powdered dicyandiamide (1·8 g.). The mixture was vigorously stirred and heated for 15 minutes on the steam-bath. The solid passed into solution and then a heavy white precipitate appeared, which was removed from the cold mixture and recrystallised from N-hydrochloric acid (50 ml.) to give 6-*amino*-2-*guanidinobenzthiazole dihydrochloride* (2·5 g.) as white needles (m. p. 317°) (Found: N, 25·2; Cl, 24·2. $C_8H_9N_5S,2HCl$ requires N, 25·0; Cl, 25·3%). The free *base*, obtained from an aqueous solution of the dihydrochloride by precipitation with alkali, recrystallised from dioxan as white needles (m. p. 260—261°) (Found: N, 33·5. $C_8H_9N_5S$ requires N, 33·8%).

2′ : 2″-*Diguanidinodithiazolo*(4′ : 5′-1 : 2)(4″ : 5″-4 : 5)*benzene Dihydrochloride.*—The zinc salt of 2 : 5-diaminodithioquinol (IX; Green and Perkin, *loc. cit.*) (1·2 g.), spirit (20 ml.), concentrated hydrochloric acid (5 ml.), and dicyandiamide (0·85 g.) were treated as described above for the monoguanidino-compound. The *dihydrochloride* (X) recrystallised from water as greenish-yellow needles (m. p. >360°; 0·6 g.) (Found: N, 27·1; Cl, 17·3. $C_{10}H_{10}N_8S_2,2HCl,2H_2O$ requires N, 26·96; Cl, 17·1%).

2′ : 2″-*Diaminodithiazolo*(4′ : 5′-1 : 2)(4″ : 5″-4 : 5)*benzene Sulphate.*—The potassium salt of 2 : 5-diaminophenyl-1 : 4-bisthiosulphuric acid (8 g.) was dissolved in water (12 ml.), and to the solution was added recrystallised potassium cyanide (4 g.) in water (6 ml.). The mixture was stirred for one hour, kept for 2 hours, and filtered, and the residue washed with water and dried to give the pale yellow 2 : 2′-diaminodithiazolobenzene (3 g.; m. p. >360°). Recrystallisation from 3N-sulphuric acid gave the *sulphate* (m. p. >360°) (Found: C, 29·9; H, 2·2; N, 17·7. $C_8H_6N_4S_2,H_2SO_4$ requires C, 30·0; H, 2·5; N, 17·5%).

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