917. 1,2,3-*Benzothiadiazole. Part II.*[1] *Electrophilic Substitution in* 4- *and* 6-*Amino*-1,2,3-*benzothiadiazoles.*

By E. R. Ward and D. D. Heard.

Chlorination, bromination, iodination, diazo-coupling, and nitration of 4- and 6-amino-1,2,3-benzothiadiazoles, and some of their *N*-acyl derivatives have been studied.

The results, together with previous work on electrophilic substitution in the parent compound and its amino- and hydroxy-derivatives, are reviewed, together with ultraviolet spectral evidence. Electrophilic substitution in this system can be tentatively explained in terms of the powerful deactivating effect of the hetero-ring (most strongly at the 4- and the 6-position) and partial bond fixation in the benzene ring. The latter concept largely accounts for evidence previously held to support the theory that 1,2,3-benzothiadiazole is " naphthalene-like " and it is suggested that this analogy be abandoned.

Differences in the 300—350 mμ region of the spectra of 2- and 4-phenylazo-1-naphthylamines are found in analogous derivatives of 1,2,3-benzothiadiazole and are used to orientate products of diazo-coupling.

Continuing our study of the 1,2,3-benzothiadiazole system [1] we now report some electrophilic substitutions, summarised in Table 1.

[1] Part I, Ward, Poesche, Higgins, and Heard, *J.*, 1962, 2374.

TABLE 1.

Electrophilic substitution in the 4- and 6-amino-1,2,3-benzothiadiazole series.

Subst.	Reaction conditions, product isolation †	Substn. (%) at position * 5	7	5,7
4-NH_2	Br_2, 1 mol., $CHCl_3$, 20°; C	—	—	91 ‡
4-NHAc	Br_2, 1 mol., 85% v/v aq.AcOH, 20°, 24 hr.; HC	—	60	23
4-NH_2-7-Br	Br_2, 20 mol., $CHCl_3$, 20°	—	—	98
4-NH_2	I_2, 1·1 mol., 50% v/v aq. Et_2O. reflux, 8 hr.; C	6·3	85	—
4-NH_2	$PhN_2^+HSO_4^-$, 1·1 mol. ,50% v/v aq. AcOH, 5°; C	—	49	—
4-NH_2	*p*-Cl·C_6H_4·$N_2^+HSO_4^-$, 1·1 mol., 50% v/v aq. AcOH, 5°; C	—	69	—
4-NH_2	*p*-NO_2·C_6H_4·$N_2^+HSO_4^-$, 1·1 mol., 50% v/v aq. AcOH, 5°; C	—	66	—
4-NHTos	HNO_3 (*d* 1·5, 1·05 mol.), AcOH, 65°, 1 hr.; HC	24	45	4·4
4-NHTos	HNO_3 (*d* 1·5, 2·1 mol.), AcOH, 65°, 1 hr.; HC	13	35	10
4-NHTos	HNO_3 (*d* 1·5, 2·1 mol.), BF_3,AcOH, 65°, 1 hr.; HC	9	46	10
6-NH_2	Br_2, 1 mol., $CHCl_3$, 20°; C	—	89	—
6-NH_2	Br_2, 10 mol., $CHCl_3$, reflux, 1 hr.: C	—	40	29
6-NHTos	Br_2, 2 mol., pyridine, 20°, 24 hr.	—	100	—
6-NHTos	Br_2, 10 mol., pyridine, reflux, 3 hr.; HC	—	—	51
6-NH_2-7-NO_2	Br_2, 1 mol., pyridine, reflux, 1 hr.		No reaction	
6-NH_2	I_2, 1·1 mol., 50% v/v aq. Et_2O, reflux, 8 hr.	—	85	—
6-NH_2	$PhN_2^+HSO_4^-$, 1·1 mol., 50% v/v aq. AcOH, 5°; C	—	34	—
6-NH_2	*p*-Cl·C_6H_4·$N_2^+HSO_4^-$, 1·1 mol., 50% v/v aq. AcOH, 5°; C	—	63	—
6-NH_2	*p*-NO_2·C_6H_4·$N_2^+HSO_4^-$, 1·1 mol., 50% v/v aq. AcOH, 5°; C	—	86	—
6-NHTos	HNO_3 (*d* 1·5, 1·2 mol.), AcOH, 90°	—	75	—

* Yield of pure product after allowance for recovered starting material. † C = Chromatography. HC = hydrolysis and chromatography. ‡ 45% of amine recovered. Tos = *p*-C_6H_4Me·SO_2.

Chlorination or nitration of relevant *N*-acetyl derivatives gave no products which could be satisfactorily identified.

Previous work on electrophilic substitution in the parent substance and its derivatives is summarised in Table 2.

TABLE 2.

Electrophilic substitution in the 1,2,3-benzothiadiazole series.

Subst.	Reaction	Positions attacked *
(Parent)	Br_2, hot AcOH	No reaction †
	H_2SO_4, KNO_3, 100°	5 and 7 ‡
5-NH_2	Diazo-coupling	4
5-NH_2-4-Cl	Diazo-coupling	No reaction
5-NH_2,HCl	Cl_2	Addition
5-OH	Br_2, cold AcOH	4
5-OH	HNO_3 (*d* 1·4), hot AcOH	4
6-OH	Br_2, cold AcOH	7
6-OH	Br_2 (excess), AcOH, reflux	5, 7
6-OH	HNO_3 (*d* 1·4), warm AcOH	7
6-OH	Cl_2, hot AcOH	7, then addition and decomp.
6-OH-7-Cl	HNO_3 (*d* 1·52) (large excess), hot AcOH	5

* Ref. 5 unless otherwise stated. † Ref. 4. ‡ Ref. 1.

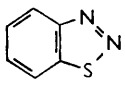
We have also found that 1,2,3-benzothiadiazole is not nitrated by the boron trifluoride–nitrogen tetroxide complex in nitromethane (this dinitrates naphthalene at 80°; [2] cf. Parent [3] who used it to nitrate 2-nitrothiazole).

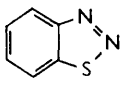
The early suggestion by Fries and his co-workers that 1,2,3-benzothiadiazole and its derivatives closely resemble their naphthalene analogues has often been accepted [4-7] (in one case [7] as " conclusive "). Hodgson and Dodgson [5] tentatively accepted it but pointed

[2] Bachman and Vogt, *J. Amer. Chem. Soc.*, 1958, **80**, 2381; Ward and Johnson, *J.*, 1961, 4314.
[3] Parent, *J. Org. Chem.*, 1962, **27**, 2282.
[4] Fries and Reitz, *Annalen*, 1936, **527**, 38.
[5] Fries, Vorbrodt, and Siebert, *Annalen*, 1927, **454**, 172.
[6] Hodgson and Dodgson, *J. Soc. Dyers and Colourists*, 1948, **64**, 65; Sherman in " Heterocyciic Compounds," ed. Elderfield, Wiley, New York, 1961, Vol. VII, pp. 548—558.
[7] Bambas, " The Chemistry of Heterocyclic Compounds," Interscience Publ., Inc., New York, 1952, pp. 10—30.

out differences in the reactivity of the two systems and suggested, for example, that the reduced reactivity of the parent compound to bromine or nitric acid might be accounted for by salt formation at nitrogen or sulphur in the hetero-ring. We feel that no purpose is served by perpetuating this supposed analogy which was based on only a few electrophilic substitutions. Some of the early evidence is now known to be wrong and in terms of modern knowledge the analogy no longer has even the tentative validity that Hodgson and Dodgson claimed for it.

Compared with naphthalene, 1,2,3-benzothiadiazole is, in fact, extremely unreactive to electrophilic reagents. It is mononitrated only under extreme conditions (which then probably cause more degradation than substitution), whereas naphthalene can be trinitrated even at 0°. This lack of reactivity cannot be accounted for by salt formation since 1,2,3-benzothiadiazole is not particularly basic (*e.g.*, quaternisation is not easy [8] and the amines have low pK_a values), and hence even under extreme conditions the free base is probably still available for substitution. The low reactivity is similarly shown in derivatives, for although *N*-1-naphthyltoluene-*p*-sulphonamide is dinitrated in acetic acid at 0°, the corresponding derivative of 6-amino-1,2,3-benzothiadiazole is mononitrated only at 90° and that of the 4-amino-compound is dinitrated with difficulty at 65°. However, the suggestion of Fries *et al.* can be usefully reinterpreted to account for the valid items of the original supporting evidence (Skraup reactions, for example). We suggest that structures tending towards (I) are favoured over (II) [although probably not so much as in


(I)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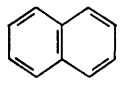
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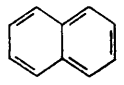
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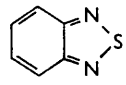

(V)

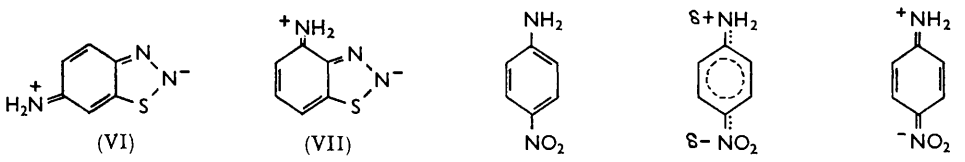
naphthalene where (III) is favoured over (IV)], giving the 5,6-bond in 1,2,3-benzothiadiazole a lower order than that of the 4,5- or 6,7-bond. This result resembles that in naphthalene where the 2,3-bond has a lower order than the 1,2-bond, this being the usual explanation for the normal lack of reactivity of 2-substituted naphthalenes at the 3-position. This tendency will be even greater in the 2,1,3-benzothiadiazoles by virtue of structure (V) and is supported by the fact that the positions attacked in nitration or diazo-coupling of 4- and 5-amino-2,1,3-benzothiadiazole are 7 and 4, respectively.[9]

However, the validity of applying such concepts to compounds containing a heterocyclic ring *ortho*-fused to a benzene ring requires examination. It may indeed be profitable to apply the concept of the aromatic sextet to systems such as the very stable 1,2,3-benzothiadiazole, as did Hodgson and Dodgson,[6] yet diazo-oxides are usually unstable and are not formulated as a bicyclic system though they should gain stability by assuming such a structure. Again, since a sulphur atom can often replace CH=CH in an aromatic ring, one might expect some analogy between cinnoline and 1,2,3-benzothiadiazole; in fact, cinnoline is quaternised readily and is nitrated in the cold. However, the experimental evidence for such systems, even as regards electrophilic substitution, is severely limited.[10] Further general analysis of reactivities in such systems must await more experimental results.

Supplementary evidence on the structure of 1,2,3-benzothiadiazole comes from the studies of our colleague, Dr. B. D. Pearson, on the ultraviolet spectra of the four amino-1,2,3-benzothiadiazoles in cyclohexane and in ethanol.[11] He suggests that, since the value of the maxima for the first absorption band for these amines falls in the order 6 > 4 >

[8] Nunn and Chadbourne, unpublished work.
[9] Pesin, Khaletskii, and Sergeev, *Zhur. obshchei Khim.*, 1962, **32**, 181.
[10] de la Mare and Ridd, "Aromatic Substitution, Nitration and Halogenation," Butterworths, London, 1959.
[11] Pearson, unpublished work.

5 > 7, this is also probably the order of mesomeric interaction between the amino-group and the unsaturated electron-attracting function of the hetero-nucleus. This interpretation is based on the formulation of excited states such as (VI) or (VII), which Dr. Pearson associates with the electronic transition involved with the first absorption band. The order for mesomeric interaction parallels the expected stabilities of the quinonoid structures



(VIII)

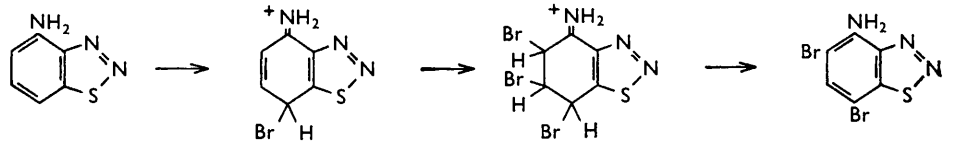
(VI > VII) and is similar to the transition he suggested for *p*-nitroaniline (VIII). Further support comes from the fact that the first absorption band of the aminobenzothiadiazoles is very solvent-dependent, as previously encountered with *o*- or *p*-nitroaniline and the nitronaphthylamines. Dr. Pearson suggests that the $-N{=}N-$ group in the hetero-ring in 1,2,3-benzothiadiazole resembles the nitro-group in its conjugative effects. These ideas would partly account for the relatively low reactivity to electrophiles of 1,2,3-benzothiadiazole and its hydroxy- and amino-derivatives, also for the fact that the parent compound is nitrated with difficulty at positions 5 and 7, these being least deactivated by the hetero-ring. One might expect some resemblance between the reactivity of the amino-derivatives and that of the corresponding nitroanilines. Similarly a chlorine atom at position 6 should be relatively reactive to nucleophilic reagents, as is that in *p*-chloronitrobenzene. We found, however, that 6-chloro-1,2,3-benzothiadiazole was unchanged by refluxing, concentrated, aqueous sodium hydroxide.

Tables 1 and 2 show that the positions and ease of substitution generally agree with the ideas set out above, in particular the suggestion that structure (I) is favoured over (II). The latter suggestion implies that electronic effects in the benzene ring would best be conveyed from the 4- to the 5- or the 7-position (the last most favoured), from the 5- to the 4- (with a much weaker effect possible at 6), from the 6- to the 7- (with a weaker effect possible at 5), and from the 7- to the 6- or the 4-position (the last most favoured). Activating effects from groups such as NH_2 or OH would then compete with the deactivating effect of the hetero-ring, operating strongly at the 4- and even more strongly at the 6-position. As usual, one would expect that in electrophilic substitution the positions attacked would be determined largely by the strongly activating groups. Further reaction factors are the possibility of steric intervention at position 4 or 7 and the interactions that could occur between substituent groups at these positions with the 3-nitrogen or the sulphur atoms (our discussion has tended to ignore the influence of the sulphur atom, a deficiency which we recognise).

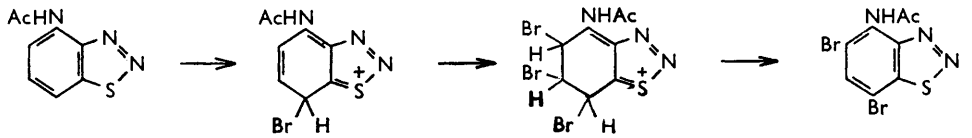
Thus, as one would deduce from the above analysis, 5-hydroxy- and 5-amino-1,2,3-benzothiadiazole are substituted only at position 4; in particular the 5-hydroxy-derivative is only 4-mononitrated, suggesting that the 6-position is not available to even strong electrophiles. In the corresponding 6-derivatives, whilst substitution is easy at position 7, further substitution can occur at the 5-position, where as for the 5-derivative deactivation is expected at position 6 (position 4 is also deactivated but there is strong activation from the amino-group). In the 4-derivatives, substitution is, as expected, at position 5 or 7, the latter being more favoured. Hence, in diazo-coupling the weak electrophile fails to react at position 5 at all. In the bromination of the 4-acetamido-compound the 5-bromo-compound may have been formed but not detected. This is suggested by the formation

of the 5,7-dibromo-compound and oily by-products. In the nitration of the 4-toluene-*p*-sulphonamido-compound the higher proportion of 5-substitution suggests some enhancing effect from the tosyl group (cf. Ward and Marriott [12]).

The fact that 4-amino-1,2,3-benzothiadiazole with 1 mol. of bromine yields the 5,7-dibromo-compound, together with unchanged starting material, but no monobromo-amine, recalls the behaviour of 1-naphthylamine and the nitro-1-naphthylamines, which are brominated similarly under the same conditions. Ward and Wells [13] suggested that this type of reaction proceeds in several stages, namely, monosubstitution by an electrophilic process followed by nucleophilic addition and subsequent loss of hydrogen bromide and a proton. The mechanism in our case, would then be as in the annexed scheme. How-



ever, whereas *N*-acetyl-1-naphthylamine is only monobrominated in aqueous acetic acid at 20°, 4-acetamido-1,2,3-benzothiadiazole is partially dibrominated. If we accept the diminished reactivity of the benzothiadiazole compound relative to its naphthalene analogue, then this again suggests that further substitution is not electrophilic but proceeds by a mechanism similar to that cited above. Here the positive charge is accommodated in the hetero-ring, a stabilisation not possible in the naphthalene series and explaining the different behaviour.



In connexion with this, it is generally accepted that addition processes for halogenation are intrinsically favoured in heterocyclic systems (cf. de la Mare and Ridd [10]), and this may account for our failure to isolate chlorination products by use of chlorine in hot acetic acid or aqueous bleaching powder. Further anomalies in bromination are that whereas the 6-toluene-*p*-sulphonamido-derivative can be only mononitrated (despite the potential enhancing effect of the tosyl group) it can be dibrominated by the potentially weaker electrophile Br_2. This bromination must be classed as " abnormal." Ward and Wells [13] have discussed such reactions and again suggest the intervention of an addition–elimination process, removal of hydrogen bromide being facilitated by the pyridine used as solvent. However, we feel that further detailed general studies of the bromination of toluene-*p*-sulphonamido-derivatives are required. In particular, we are attempting to determine whether the enhancing effect of the tosyl group is specific to aromatic nitration rather than a general effect in aromatic electrophilic substitution (although this alone cannot resolve the substitutions now under review).

The amino-monohalogeno- and -mononitro-1,2,3-benzothiadiazoles were readily orientated by diazotisation and subsequent deamination (the methods of Hodgson and Turner [14] being used), to give known monosubstituted 1,2,3-benzothiadiazoles. Furthermore, the 5-X-4-amino-derivatives were always eluted before the 7-X-4-amino-isomers, as expected from calculated dipole moments, which are lower for the former (cf. Johnson and

[12] Ward and Marriott, *Chem. and Ind.*, 1962, 1760.
[13] Ward and Wells, *J.*, 1961, 4866.
[14] Hodgson and Turner, *J.*, 1942, 748; 1943, 86.

Telesz [15] and ref. 1). That the dibromo-amines obtained from 4- and 6-amino-1,2,3-benzothiadiazole were 4- and 6-amino-5,7-dibromo-1,2,3-benzothiadiazoles followed from the fact that they gave the same dibromo-compound on deamination, which could then only be 5,7-dibromo-1,2,3-benzothiadiazole.

The monoazo-compounds obtained by coupling diazotised aniline to 4- and 6-amino-1,2,3-benzothiadiazoles were reduced to the diamines and identified with 4,7- and 6,7-diamino-1,2,3-benzothiadiazole prepared by reducing 4- and 6-amino-7-nitro-1,2,3-benzothiadiazole. 4-Amino-7-phenylazo-1,2,3-benzothiadiazole was claimed by Fries and Reitz,[4] but as we have stated before [1] it could not have been authentic. 4,5-Diamino-1,2,3-benzothiadiazole was prepared by these workers by reducing the azo-compound obtained by coupling diazotised sulphanilic acid to 5-amino-1,2,3-benzothiadiazole, and we have now obtained it by reducing 4-amino-5-nitro-1,2,3-benzothiadiazole. 6,7-Diamino-1,2,3-benzothiadiazole behaves like *o*-phenylenediamine since it reacts with nitrous acid, formic acid, and 9,10-phenanthraquinone to form the appropriate derivatives.

The structures of the azo-compounds formed by diazotised aniline being established, those of the azo-compounds formed by diazotised *p*-chloro- and *p*-nitro-aniline were readily obtained from their ultraviolet spectra in 95% aqueous ethanol. Ward, Pearson, and Wells [16] found pronounced spectral differences between isomeric 2- and 4-azo-1-naphthylamines, the outstanding feature being that in the region 300—350 mμ the former showed a maximum whereas the latter gave a deep trough. Similar differences are now found between the 6-amino-7-arylazo-1,2,3-benzothiadiazoles (with the *o*-aminoazo-grouping as in the 2-azo-1-naphthylamines) and the 4-amino-7-arylazo-1,2,3-benzothiadiazoles. We are continuing our studies of the ultraviolet spectra of arylazoarylamines.

Since the dinitro-amine arising from the nitration of 4-toluene-*p*-sulphonamido-1,2,3-benzothiadiazole is a minor product in the formation of 5- and 7-mononitro-derivatives it is reasonable to designate it as the 4-amino-5,7-dinitro-compound. This is supported by the elution order for this substance admixed with 4-amino-5- and -7-nitro-1,2,3-benzothiadiazole which is 5- > 5,7- > 7-, in agreement with their decreasing dipole moments.

Experimental [with W. H. Poesche]

The volatility of many derivatives of 1,2,3-benzothiadiazole necessitates precautions in their isolation; in particular, products described here were dried at 50° *in vacuo*. Ultraviolet spectra were recorded with a Unicam S.P. 700 spectrophotometer for 95% v/v aqueous-ethanol solutions. The infrared spectra of most of the compounds described here have been recorded by Dr. K. Morgan (University of Birmingham).

Bromination.—(*a*) *4-Amino-1,2,3-benzothiadiazole.* A solution of the amine (1·51 g., 0·01 mole) in chloroform (45 ml.) was treated with one of bromine (0·53 ml., 0·01 mole) in chloroform (15 ml.) with stirring. The precipitated solids were collected, dried, suspended in hot water, and basified with aqueous ammonia (*d* 0·88). The solids were collected and dried (1·2 g.). Further material (0·96 g.) was obtained by evaporation of the filtrate (water-bath). The combined solids were chromatographed in benzene on alumina (60 × 2 cm.), giving two yellow bands. Elution of the lower one with benzene gave *4-amino-5,7-dibromo-1,2,3-benzothiadiazole* (1·54 g.), yellow needles [from benzene–light petroleum (b. p. 100—120°)], m. p. 176° (Found: C, 23·4; H, 0·9; Br, 49·9. $C_6H_3Br_2N_3S$ requires C, 23·0; H, 1·0; Br, 51·7%). The upper band, removed with 9 : 1 v/v benzene–ethyl acetate, gave 0·68 g. (45%) of starting material. *4-Acetamido-5,7-dibromo-1,2,3-benzothiadiazole* formed yellow needles (from ethanol), m. p. 222° (decomp.) (Found: C, 27·4; H, 1·5; N, 11·8. $C_8H_5Br_2N_3OS$ requires C, 27·4; H, 1·5; N, 12·0%).

The dibromo-amine (0·2 g.) was diazotised and deaminated by the methods of Hodgson and Turner.[14] The mixture was diluted with water (50 ml.), and the solids were collected, dried,

[15] Johnson and Telesz, *J. Soc. Dyers and Colourists*, 1962, **78**, 496.
[16] Ward, Pearson, and Wells, *J. Soc. Dyers and Colourists*, 1959, **75**, 484.

and extracted with hot benzene (2 × 20 ml.). Evaporation of the extract gave crude 5,7-*dibromo*-1,2,3-*benzothiadiazole* (0·137 g., 73%), white needles (from aqueous ethanol), m. p. 103° (Found: C, 24·4; H, 1·2; Br, 53·2. $C_6H_2Br_2N_2S$ requires C, 24·5; H, 0·7; Br, 54·5%).

(*b*) 6-Amino-1,2,3-benzothiadiazole was similarly brominated and on chromatography the product gave one band only. Elution with benzene yielded 6-*amino*-7-*bromo*-1,2,3-*benzothiadiazole* (2 g.), white needles (from benzene), m. p. 168° (Found: C, 31·3; H, 2·0; Br, 35·5. $C_6H_4BrN_3S$ requires C, 31·3; H, 1·8; Br, 34·8%). The amine (0·92 g.) was diazotised by dissolving it in hot hydrobromic acid (45% w/v; 10 ml.), cooling the solution to −5°, and adding, with stirring, a solution of sodium nitrite (0·35 g.) in water (2 ml.). After 15 min., precooled 50% w/v hypophosphorous acid (5·5 ml.) was stirred in and after 24 hr. at 0° the solids were collected. These were dried over sulphuric acid and sublimed at 90°, yielding 7-bromo-1,2,3-benzothiadiazole (0·13 g., 15%), identified by mixed m. p. The bromination was repeated with ten times the quantity of bromine (0·1 mole) and refluxing for 1 hr. After cooling, the precipitated solids were collected, suspended in hot water, basified with aqueous ammonia (*d* 0·88), kept overnight at 0°, and again collected. After drying they were dissolved in benzene (250 ml.) and chromatographed on alumina (60 × 2 cm.). Development by benzene gave three bands. The lowest, eluted with benzene, gave 6-*amino*-5,7-*dibromo*-1,2,3-*benzothiadiazole* (0·924 g.), cream needles (from benzene), m. p. 191° (Found: C, 23·7; H, 1·0; Br, 51·7; N, 13·6%). This was diazotised and deaminated by the methods used for 4-amino-5,7-dibromo-1,2,3-benzothiadiazole, giving 5,7-dibromo-1,2,3-benzothiadiazole (57%). Further elution by 8 : 1 v/v benzene–ethyl acetate removed the lower bands, both of which were 6-amino-7-bromo-1,2,3-benzothiadiazole.

(*c*) 4-*Acetamido*-1,2,3-*benzothiadiazole*. A solution of the amide (0·965 g., 0·005 mole) in cold 85% v/v aqueous acetic acid (0·15M in sodium acetate) was treated with one of bromine (0·27 ml., 0·005 mole) in the same solvent (100 ml.), and the mixture was left overnight. The mixture was evaporated on the water-bath, and the residue refluxed with ethanol (21 ml.), water (11 ml.), and sulphuric acid (*d* 1·84; 5 ml.) for 2 hr. After removal of most of the ethanol, the mixture was poured on ice (100 g.) and neutralised with aqueous ammonia (*d* 0·88), and the solids were collected and dried over sulphuric acid. The filtrate was extracted with benzene (3 × 15 ml.), the extract was dried over anhydrous sodium sulphate, and the above solids were dissolved in it. Chromatography of this solution on alumina (60 × 2 cm.) gave five bands. Elution with benzene removed the top three, but these only gave oils (0·265 g.) which were not further investigated. The fourth band was removed by 7 : 1 v/v benzene–ethyl acetate, giving 4-amino-5,7-dibromo-1,2,3-benzothiadiazole (0·36 g.), and the last by ethyl acetate yielding 4-*amino*-7-*bromo*-1,2,3-*benzothiadiazole* (0·69 g.), yellow needles (from ethanol), m. p. 138° (Found: C, 31·5; H, 2·0; Br, 35·3; N, 18·5. $C_6H_4BrN_3S$ requires C, 31·3; H, 1·8; Br, 34·8; N, 18·3%). The bromo-amine was diazotised, and deaminated, by the methods used for 6-amino-7-bromo-1,2,3-benzothiadiazole, yielding 7-bromo-1,2,3-benzothiadiazole (20%). Bromination in chloroform by the procedure used for the parent amine gave 4-amino-5,7-dibromo-1,2,3-benzothiadiazole (98%).

(*d*) 6-*Toluene*-p-*sulphonamido*-1,2,3-*benzothiadiazole*. A solution of the amide (1·22 g., 0·004 mole) in pyridine (24 ml.) was treated with one of bromine (0·43 ml., 0·008 mole) in pyridine (12 ml.), then set aside overnight and poured on ice (60 g.) and hydrochloric acid (*d* 1·2; 90 ml.). The solids were collected, washed with water and, on drying, yielded almost pure 7-*bromo*-6-*toluene*-p-*sulphonamide*-1,2,3-*benzothiadiazole* (1·6 g., 105% for monobromination). This, when crystallised from acetic acid, had m. p. 225° (Found: C, 40·7; H, 2·7; Br, 21·0; N, 11·0; S, 16·6. $C_{13}H_{10}BrN_3O_2S_2$ requires C, 40·6; H, 2·6; Br, 20·8; N, 11·0; S, 16·7%) and it was hydrolysed to the amine by dissolution in sulphuric acid (*d* 1·84) at 40°, followed by addition to ice. The bromination was repeated with a large excess of bromine (10 mol.) and refluxing for 3 hr. After hydrolysis of the product as above, followed by chromatography, 6-amino-5,7-dibromo-1,2,3-benzothiadiazole was obtained (51%).

(*e*) *Attempted bromination of* 7-*nitro*-6-*toluene*-p-*sulphonamid*-1,2,3-*benzothiadiazole*. Bromination in refluxing pyridine with bromine (1 mol.) for 1 hr. gave 100% of unchanged starting material.

Iodination.—(*a*) 6-*Amino*-1,2,3-*benzothiadiazole*. The amine (1·51 g.) was refluxed with iodine (2·79 g., 0·011 mole; previously ground with calcium carbonate, 2·79 g.) in 50% v/v aqueous ether (10 ml.) for 8 hr., with occasional shaking. The ether was removed and the solids were collected, washed with 10% aqueous sodium thiosulphate (20 ml.) and water, and

dried. The product was refluxed with ethanol (100 ml.), and water was added to the hot filtered extract until a faint turbidity appeared. Cooling gave 6-*amino*-7-*iodo*-1,2,3-*benzothiadiazole* (2·36 g.) that from aqueous ethanol formed white needles, m. p. 161° (Found: C, 26·3; H, 1·3; I, 45·3. $C_6H_4IN_3S$ requires C, 26·0; H, 1·4; I, 45·8%).

(*b*) 4-*Amino*-1,2,3-*benzothiadiazole*. The amine (0·75 g.) was treated as above, the crude product washed and dried as before, then refluxed with benzene (120 ml.), and the cooled extract chromatographed on alumina (60 × 2 cm.). Development with benzene gave two yellow bands. The lower one was eluted with 10 : 1 v/v benzene–ethyl acetate, yielding almost pure 4-*amino*-5-*iodo*-1,2,3-*benzothiadiazole* (0·088 g.), m. p. 137° (from aqueous ethanol) (Found: C, 25·6; H, 1·3; N, 14·7. $C_6H_4IN_3S$ requires C, 26·0; H, 1·5; N, 15·2%). The upper band, removed with 5 : 1 v/v benzene–ethyl acetate, gave almost pure 4-amino-7-iodo-1,2,3-benzothiadiazole (1·175 g.), m. p. 143° (from aqueous ethanol) (Found: C, 26·2; H, 1·5; I, 44·7. Calc. for $C_6H_4IN_3S$: I, 45·8%).

(*c*) *Deamination of amino-iodo*-1,2,3-*benzothiadiazoles*. The iodination products were diazotised and deaminated by the methods of Hodgson and Turner.[14] The deamination products were isolated by diluting the reaction mixture, after deamination, with water and subsequent steam-distillation. Cooling of the distillates in ice gave the corresponding iodo-1,2,3-benzothiadiazoles in *ca.* 25% yield, identified by mixed m. p.s.

Diazo-coupling to 4- *and* 6-*Amino*-1,2,3-*benzothiadiazoles*.—To a solution of the amine (1·0 g.) in 50% v/v aqueous acetic acid (20 ml. for 4-isomer, 28 ml. for 6-isomer) was slowly added, with stirring, below 5°, one of the *pure* solid diazonium sulphate (1·1 mol.) in the same solvent (10 ml.). Stirring was continued for 1 hr. The next day ice (50 g.) was added and the solids were collected, washed with water, and dried. The crude azo-compounds arising from the couplings with diazotised aniline or *p*-chloroaniline (0·25 g. of reaction product) were refluxed with sufficient benzene to ensure complete dissolution on cooling to room temperature (200—500 ml.; a trace of insoluble impurity was filtered off) and chromatographed on alumina (2 × 100 cm.). Development and elution were carried out with benzene, benzene–ethyl acetate, or ethyl acetate, the solvent composition being modified according to observations of the column during the separation (the columns were protected from direct sunlight, to prevent decomposition). The crude azo-products (0·25 g.) arising from coupling with diazotised *p*-nitroaniline were treated similarly but were originally dissolved in a large excess of refluxing ethyl acetate (3 l.), and then the solution was concentrated to *ca.* 300 ml. before chromatography. The strongly coloured eluates containing particular azo-compounds were concentrated by distillation, and the residual solvent (*ca.* 50 ml.) was removed by a current of hot air, affording almost pure *products* whose properties are tabulated.

TABLE 3.

4- and 6-Amino-7-arylazo-1,2,3-benzodithiazoles.

					Found (%)				Required (%)		
No.	Ar	M. p.	Solvent for crystn.	Form *	C	H	N	Formula	C	H	N
4-*Amino-series*											
1	Ph	186°	Aq. EtOH	Needles	57·3	3·8	27·2	$C_{12}H_9N_5S$	56·5	3·5	27·5
2	*p*-Cl·C_6H_4	282 †	Xylene	,,	50·5	3·4	24·7	$C_{12}H_8ClN_5S$	49·9	2·8	24·2
3	*p*-NO_2·C_6H_4	>350	PhCl	Powder ‡	48·1	2·7	27·2	$C_{12}H_8N_6O_2S$	48·0	2·7	27·0
6-*Amino-series*											
4	Ph	208	Aq. EtOH	Prisms	57·0	3·4	28·5	$C_{12}H_9N_5S$	56·5	3·5	27·5
5	*p*-Cl·C_6H_4	233—234	,,	Needles	49·8	2·9	23·9	$C_{12}H_8ClN_5S$	49·9	2·8	24·2
6	*p*-NO_2·C_6H_4	>360	§	,, ¶	48·5	2·8	28·0	$C_{12}H_8N_6O_2S$	48·0	2·7	27·0

* Orange, except nos. 3 and 6. † With decomp. ‡ Purple. § Xylene–light petroleum (b. p. 100—120°). ¶ Red.

No.	Ultraviolet absorption (mμ) ($\log_{10}\varepsilon$)
1	248 (3·82), 268sh (3·65), 299sh (3·33), 420 (4·16)
2	253 (4·08), 267sh (3·98), 290sh (3·70), 435 (4·34)
3	250 (3·90), 267sh (3·81), 298 (3·75), 470 (4·40)
4	244 (3·96), 278sh (3·68), 323 (4·21), 357 (3·90), 448 (4·03)
5	250 (4·05) 325 (4·29), 347 (4·00), 459 (4·15)
6	238sh (3·85) 333 (3·97) 488 (3·94)

Nitration.—(*a*) 4-*Toluene*-p-*sulphonamido*-1,2,3-*benzothiadiazole*. The amide (0·6 g., 0·002 mole) was dissolved in the minimum amount of acetic acid (5·4 ml.) at 60°, a crystal of sodium nitrite added, and at this temperature the mixture was treated, dropwise, with 1·2 ml. (0·0021 mole of HNO_3) of a solution of nitric acid (*d* 1·5; 0·45 ml.) in acetic acid (6 ml.), with stirring. The temperature rose to 65° and after an hour's stirring at 60° the mixture was poured on ice (50 g.), and the solids were collected and dried (0·63 g.). They were hydrolysed by dissolution in sulphuric acid (*d* 1·84; 1·25 ml.), warming to 40° for 3 min., and then pouring on ice. The solids were collected, washed with water, and dried (0·31 g.). The acid filtrate was extracted with ethyl acetate (3 × 25 ml.), the extract was dried (Na_2SO_4), and the solids were dissolved in it. Chromatography of this solution on alumina (90 × 2 cm.) gave three bands on development by benzene. The lowest, removed by 9 : 1 v/v benzene–ethyl acetate, gave 4-*amino*-5-*nitro*-1,2,3-*benzothiadiazole*, m. p. 206° (from acetic acid) (Found: C, 36·9; H, 1·7; N, 27·9; S, 15·8. $C_6H_4N_4O_2S$ requires C, 36·7; H, 2·0; N, 28·6; S, 16·3%). The second band was eluted by 4 : 1 v/v benzene–ethyl acetate, yielding 4-*amino*-5,7-*dinitro*-1,2,3-*benzothiadiazole*, m. p. 280° (from chlorobenzene) (Found: C, 30·9; H, 1·4; N, 28·8; S, 13·2. $C_6H_3N_5O_4S$ requires C, 29·9; H, 1·3; N, 29·0; S, 13·3%). The third band was eluted with ethyl acetate, giving 4-*amino*-7-*nitro*-1,2,3-*benzothiadiazole*, m. p. 291° (from chlorobenzene) (Found: C, 36·9; H, 1·8; N, 28·7; S, 16·4%). Repeating this experiment with 2·1 mol. of nitric acid, with or without addition of boron trifluoride, yielded the same products. Diazotisation and deamination of the mononitro-amines, by the methods of Hodgson and Turner,[14] yielded the corresponding mononitro-1,2,3-benzothiadiazole (*ca.* 25%), identified by mixed m. p.

(*b*) 6-*Toluene*-p-*sulphonamido*-1,2,3-*benzothiadiazole*. The amide (3·05 g., 0·01 mole) was dissolved in the minimum amount of acetic acid at 60° (60 ml.), a crystal of sodium nitrite added, and a solution of nitric acid (0·5 ml., 0·012 mole) in acetic acid (0·5 ml.) stirred in at this temperature. The mixture was heated to 90°, then kept overnight, and the solids were collected, washed with a small amount of acetic acid, and dried (2·92 g.). 7-*Nitro*-6-*toluene*-p-*sulphonamido*-1,2,3-*benzothiadiazole* gave yellow needles, m. p. 223°, from ethanol (Found: C, 44·8; H, 3·1. $C_{13}H_{10}N_4O_4S$ requires C, 44·5; H, 3·1%). Hydrolysis, as in (*a*), gave 6-amino-7-nitro-1,2,3-benzothiadiazole (90%), m. p. 310° (from acetic acid) (decomp.) (Found: C, 37·0; H, 2·5; N, 28·4%). Deamination of this, as above, gave 7-nitro-1,2,3-benzothiadiazole (30%), identified by mixed m. p.

(*c*) 4-*Acetamido*-1,2,3-*benzothiadiazole*. Attempts to nitrate this by a variety of procedures only gave unstable material from which nothing could be identified.

Preparation of 4,5-, 4,7-, *and* 6,7-*Diamino*-1,2,3-*benzothiadiazole*. 4-Amino-5-nitro-, 4-animo-7-nitro-, or 6-amino-7-nitro-1,2,3-benzothiadiazole (0·1 g.) was boiled with stannous chloride dihydrate (0·56 g.) in hydrochloric acid (*d* 1·2; 1 ml.) until dissolution was complete (2—3 min.). After cooling in ice, the solids were collected, dissolved in hot water (1 ml.), and basified at 0° with 40% w/v aqueous sodium hydroxide. The precipitated diamine was collected and dried. The following diamines crystallised from benzene (yields 30—60%): 4,5-, yellow needles, m. p. 160° (Fries and Reitz [4] give 158°), 4,7-, red needles, m. p. 176° (Found: C, 43·2; H, 3·9; N, 33·2. $C_6H_6N_4S$ requires C, 43·4; H, 3·6; N, 33·8%), and 6,7-*diamino*-1,2,3-*benzothiadiazole*, green needles, m. p. 195° (Found: C, 43·8; H, 3·6%). 4- and 6-Amino-7-phenylazo-1,2,3-benzothiadiazole were similarly reduced to the corresponding diamines. On reaction with nitrous acid 6,7-diamino-1,2,3-benzothiadiazole gave 8H-*triazolo*[4,5-*g*]-1,2,3-*benzothiadiazole*, red prisms (from xylene), m. p. 236° (Found: C, 41·7; H, 1·8; N, 38·7; S, 17·5. $C_6H_3N_5S$ requires C, 40·8; H, 1·7; N, 39·6; S, 18·1%). With formic acid the diamine gave 8H-*imidazo*-[4,5-*g*]-1,2,3-*benzothiadiazole*, white needles (from water), m. p. 230° (decomp.) (Found: C, 46·4; H, 2·3; N, 31·0. $C_7H_4N_4S$ requires C, 47·6; H, 2·3; N, 31·8%). It reacted with 9,10-phenanthraquinone to form *dibenzo*[*a*,*c*]-[1,2,3]*thiadiazolo*[5,4-*j*]*phenazine*, yellow needles [from benzene–light petroleum (b. p. 80—100°)] (Found: C, 70·8; H, 2·8. $C_{20}H_{10}N_4S$ requires C, 70·9; H, 3·0%).

Preparation of Monohalogeno-1,2,3-*benzothiadiazoles*.—To a solution of the amino-1,2,3-benzothiadiazole (1·5 g.) in sulphuric acid (*d* 1·84; 20 ml.) was gradually added, with stirring, one of nitrosylsulphuric acid (2M; 5·6 ml.) in sulphuric acid (*d* 1·84) below 10°. After 1 hr. this mixture was poured on ice (80 g.). The diazo-solution was then added to one of potassium iodide (3·3 g.) in water with stirring, kept overnight, and made alkaline with 20% w/v aqueous sodium hydroxide, and 10% w/v aqueous sodium thiosulphate was added (20 ml.). The mixture was steam-distilled until a clear distillate was obtained at 0°; the solids were collected,

dried, and crystallised from aqueous methanol. This procedure gave 4- (45%), m. p. 111° (Found: C, 27·8; H, 1·1; I, 48·7. $C_6H_3IN_2S$ requires C, 27·4; H, 1·2; I, 48·2%), 6- (60%), m. p. 116° (Found: C, 27·6; H, 1·2; I, 48·2%), and 7-*iodo*-1,2,3-*benzothiadiazole* (70%), m. p. 137° (Found: C, 27·3; H, 0·9; I, 49·3%). Addition of the diazo-solution from the 7-isomer to a solution of cuprous bromide (1·5 g.) in hydrobromic acid (45% w/v; 15 ml.) at 0°, followed by steam-distillation gave 7-*bromo*-1,2,3-*benzothiadiazole*, m. p. 77° (from methanol) (Found: C, 31·9; H, 1·1; N, 13·3. $C_6H_3BrN_2S$ requires C, 33·5; H, 1·4; N, 13·0%). Similarly, addition to cuprous chloride (1·5 g.) in hydrochloric acid (*d* 1·2; 15 ml.) gave 7-*chloro*-1,2,3-*benzothiadiazole* (47%), m. p. 78° (from aqueous methanol) (Found: C, 42·0; H, 2·1. $C_6H_3ClN_2S$ requires C, 42·3; H, 1·8%), thus completing the preparation of all the mono-chloro-, -bromo-, and -iodo-1,2,3-benzothiadiazoles. All these diazo-decompositions gave large amounts of azo-compounds as by-products.

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