

Synthesis and Reactions of 1*H*-4,1,2-Benzothiadiazines, and Observations on the Structure of Hydrazonoyl Sulphides

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Syntheses of 1-acetyl-7- and -8-bromo- and -6,8-dibromo-3-phenyl-4,1,2-benzothiadiazines establish, in conjunction with previous data, the generality of 1*H*-4,1,2-benzothiadiazine synthesis from appropriately substituted *N'*-acetyl-*N'*-arylbenzothiohydrazides. The corresponding 6-nitrobenzothiadiazine is also available by this route, and such cyclizations can proceed by expulsion of a nitro-group, presumably as nitrite ion. These 1*H*-4,1,2-benzothiadiazines undergo electrophilic substitution at positions 6 and 8, are nucleophilic at position 1, and are oxidizable at position 4 to the corresponding sulphone. X-Ray crystallographic studies of bis-[α -(2,6-dibromophenyl)hydrazono]benzyl] sulphide confirm the symmetrical structure of hydrazonoyl sulphides.

WE have developed two methods for the synthesis of simple 1*H*-4,1,2-benzothiadiazines (Scheme 1). The first involves the reaction of suitably substituted hydrazonoyl halides with thioacetate ion, normally in refluxing acetonitrile.¹⁻³ The second involves basic treatment of suitably substituted *N*-acetyl-*N*-aryl-*N'*-thioaroylhydrazines, normally with triethylamine in refluxing acetonitrile.⁴ Other reactions leading to

benzothiadiazines include the preparation of 3-phenylazo-1*H*-4,1,2-benzothiadiazine by refluxing dithizone in acetic acid⁵ and of 1-methyl-3-phenyl-4,1,2-benzothiadiazine by treatment of *N'*-methyl-*N'*-phenylbenzothiohydrazide with iodine in benzene,⁶ but it is not known how general these reactions are. The first method suffers from the drawback that frequently material is diverted to the production of the corresponding

¹ I. T. Barnish and M. S. Gibson, *J. Chem. Soc. (C)*, 1970, 854.

² P. D. Callaghan and M. S. Gibson, *J. Chem. Soc. (C)*, 1970, 2106.

³ I. T. Barnish, P. D. Callaghan, and M. S. Gibson, *J.C.S. Perkin I*, 1974, 215.

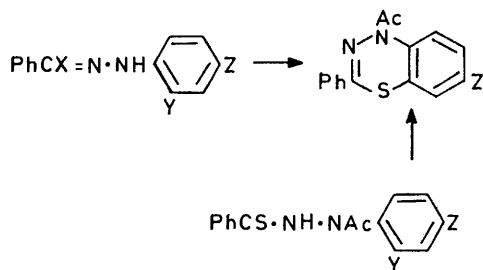
⁴ P. D. Callaghan, M. S. Gibson, and A. J. Elliott, *J.C.S. Perkin I*, 1975, 1386.

⁵ W. S. McDonald, H. M. N. H. Irving, G. Raper, and D. C. Rupainwar, *Chem. Comm.*, 1969, 392; C. H. Carlin and A. H. Corwin, Abstracts, 157th National Meeting of the American Chemical Society, Minneapolis, April 1969.

⁶ D. H. R. Barton, J. W. Ducker, W. A. Lord, and P. D. Magnus, *J.C.S. Perkin I*, 1976, 38.

hydrazonoyl sulphide, $S(\text{CPh}:\text{N}\cdot\text{NH}\cdot\text{C}_6\text{H}_3\text{YZ})_2$. In this respect the second method is more attractive and we have directed our attention to extending its scope.

In our earlier experiments,¹⁻⁴ ring closure had only been effected in cases where the substituent Z was electron-attracting, and then not in all cases. With Y = Br and Z = H or Me, cyclization was not observed. We first considered the question of whether the 2,4-positioning of the substituents Y and Z relative to nitrogen was mandatory, and have studied the behaviour of 2,5- and 2,6-dibromo- and 2,4,6-tribromo-phenylhydrazine derivatives in these reactions. The arylhydrazine was

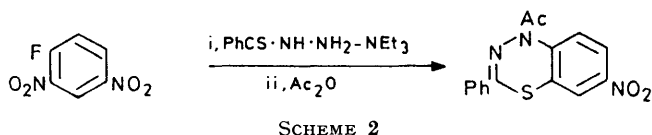


SCHEME 1

benzoylated and the resulting benzohydrazide conveniently converted into the hydrazonoyl chloride by reaction with phosphoroyl chloride. Treatment of the hydrazonoyl chloride with sodium thioacetate in acetonitrile at room temperature (at reflux for the tribromo-compound) gave the anticipated *N'*-acetyl-*N'*-arylbenzothiohydrazide together with the hydrazonoyl sulphide. Each of these benzothiohydrazides was converted into the corresponding 1-acetyl-4,1,2-benzothiadiazine when refluxed with triethylamine in acetonitrile, though the reaction was sluggish with the 2,5-dibromo-compound. The ¹H n.m.r. spectra of the derived thiadiazines are consistent with their structural assignments. For example, relative to 6-bromo-3-phenyl-1*H*-4,1,2-benzothiadiazine, the signal due to the 8-proton appears at considerably lower field in the spectrum of the 7-bromo-isomer, and in that of the 8-bromo-isomer the signal due to the 1-proton (N-H) is considerably further downfield, consistent with the position of the bromine atom adjacent to nitrogen. It is thus clear that these cyclization reactions are not limited to cases in which Z is oriented *para* to nitrogen, but some general electron withdrawal associated with the substituent(s) seems necessary.

In our earlier work, difficulties had been encountered with reactions of thioacetate ion with hydrazonoyl halides in which Y or Z was a nitro-group.³ This problem has been further examined in the context of alternative syntheses of 1-acetyl-6-nitro-3-phenyl-4,1,2-benzothiadiazine. We first prepared *N'*-acetyl-*N'*-(2-bromo-4-nitrophenyl)benzothiohydrazide in the normal way, though it was not obtained pure. Refluxing with acetonitrile-triethylamine gave a mixture from which the thiadiazine was isolated in 26% yield. The same compound was produced by acetylating the product obtained by the reaction of benzothiohydrazide with 1-fluoro-

2,4-dinitrobenzene in acetonitrile-triethylamine (Scheme 2). These experiments established both the compati-

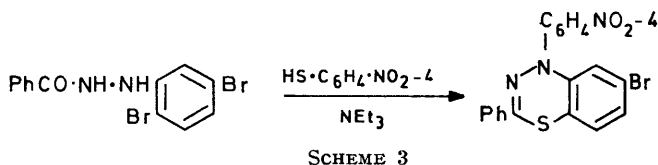


SCHEME 2

bility of the nitro-group with the reaction conditions and its displaceability in ring closure. However the processes are complicated by side reactions and are not synthetically attractive.

We also considered the possibility of avoiding steps involving the hydrazonoyl halide. This approach seemed most feasible with the more stable sulphur nucleophiles. Thus *N'*-(2,5-dibromophenyl)benzohydrazide and 4-nitrobenzenethiol react slowly in boiling acetonitrile-triethylamine to give the benzothiadiazine in a process that may have more generality (Scheme 3).

With a number of benzothiadiazines available, we have undertaken a brief study of their reactions. Acidic hydrolysis of 1-acetyl-4,1,2-benzothiadiazines to 1*H*-4,1,2-benzothiadiazines and their regeneration by acetylation had been noted previously.¹ We have found these reactions, not surprisingly, to be sluggish with the 8-substituted compounds. The 1*H*-compounds are susceptible to electrophilic substitution at positions 6 and 8.



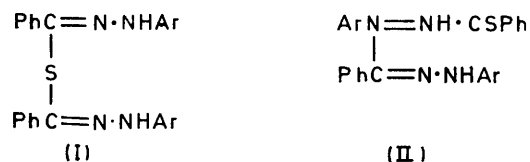
SCHEME 3

Thus pyridinium perbromide converts both 6- and 8-bromo-3-phenyl-1*H*-4,1,2-benzothiadiazines into the 6,8-dibromo-compound.

The 1*H*-4,1,2-benzothiadiazines are feebly nucleophilic at the 1-position (*cf.* acetylation). This position may also be methylated with methyl toluene-4-sulphonate, providing an alternative source of 1-methyl derivatives.⁶ Aryl halides such as 1-fluoro-2,4-dinitrobenzene will similarly arylate the 1-position. A 1-nitroso-derivative was also prepared by using pentyl nitrite, but was unstable and not completely characterized. Lastly, one of the 1*H*-benzothiadiazines was oxidized to the sulphone with hydrogen peroxide in acetic acid.

One problem which had been incompletely resolved in previous work was the structure of the hydrazonoyl sulphides which accompany thiohydrazide derivatives and benzothiadiazines in many of these reactions. These have been formulated throughout as hydrazonoyl sulphides (I), consistent with methods of formation and with spectral data, but the unsymmetrical structure (II), formally derivable by rearrangement of (I), has not been completely dismissed. The question of the correct formulation of these compounds has been resolved by X-ray studies on bis-[α -(2,6-dibromophenylhydrazono)-benzyl] sulphide. The molecules of this material are

required crystallographically to have either C_2 symmetry in space group $Aba2$ or C_{2h} symmetry in space group $Cmca$. That is, the four molecules in the unit cell must occupy the four-fold (4a) positions in $Aba2$, or the 4a or 4b positions in $Cmca$.⁷ The crystallographic requirement for symmetry rules out structure(II), but is consistent with structure(I).



EXPERIMENTAL

¹H N.m.r. spectra were recorded with a Varian A60 instrument (tetramethylsilane as internal reference). Mass spectra were obtained with an A.E.I. MS30 double-beam instrument (heated probe) operating at 70 eV; data are recorded for the lowest mass isotopic species, bromine excepted.

2,5-Dibromophenylhydrazine.—This compound (17.1 g, 90%), prepared from 2,5-dibromoaniline by diazotization and reduction with tin(II) chloride in the normal way,² had m.p. 87–89°.

***N'*-(2,5-Dibromophenyl)benzohydrazide.**—This hydrazide (4.9 g, 71%), from treatment of the hydrazine with benzoyl chloride–triethylamine,² crystallized from ethanol as needles, m.p. 169–170° (Found: C, 41.95; H, 2.8; Br, 43.45. $C_{13}H_{10}Br_2N_2O$ requires C, 42.1; H, 2.95; Br, 43.25%). ***N'*-(2,5-Dibromophenyl)benzothiohydrazide** (1.95 g, 40%), from the hydrazine and carboxymethyl dithiobenzoate–sodium hydroxide^{4,8} at 40–50 °C, crystallized from light petroleum (b.p. 60–90 °C) as yellow prisms, m.p. 149° (Found: C, 40.05; H, 2.55; S, 8.25. $C_{13}H_{10}Br_2N_2S$ requires C, 40.45; H, 2.6; S, 8.3%).

Similarly prepared were *N'*-(2,6-dibromophenyl)benzohydrazide (7.9 g, 66%), m.p. 150–152° (lit.,³ 150–151°); *N'*-(2,6-dibromophenyl)benzothiohydrazide (2.4 g, 82% crude, containing persistent orange by-product), m.p. 156–158°; *N'*-(2,4,6-tribromophenyl)benzohydrazide (13.4 g, 70%), from ethanol as rods, m.p. 172–173° (lit.,⁹ 172°); *N'*-(2,4,6-tribromophenyl)benzothiohydrazide (7.17 g, 78%) [from benzene–light petroleum (b.p. 30–60 °C)] as pale yellow prisms, m.p. 135° (Found: C, 33.85; H, 1.95; N, 6.0. $C_{13}H_9Br_3N_2S$ requires C, 33.55; H, 1.95; N, 6.0%).

Hydrazonoyl Chlorides.—These were prepared from the hydrazides by treating with phosphoryl chloride for (a) 12 h at 60 °C, or (b) 6 h at reflux. When cool, the mixture from (a) was added dropwise to ice-cold sodium hydrogen carbonate solution with stirring, and the product was collected, washed, dried, and crystallized. Alternatively, (b) the mixture was evaporated *in vacuo* and the resulting gum was triturated with ethanol to give a solid product which was crystallized.

(a) *N'*-(2,5-Dibromophenyl)benzohydrazide (10.7 g) and phosphoryl chloride (50 ml) gave *N*- α -chlorobenzylidene-*N'*-(2,5-dibromophenyl)hydrazine (10.5 g, 89%), which crystallized from acetonitrile as needles, m.p. 98–99° (Found: C, 40.1; H, 2.5; N, 7.35. $C_{13}H_9Br_2ClN_2$ requires C, 40.15;

H, 2.3; N, 7.2%). *N'*-(2,6-Dibromophenyl)benzohydrazide (5.40 g) gave *N*- α -chlorobenzylidene-*N'*-(2,6-dibromophenyl)hydrazine (5.22 g, 91%) as cream needles, m.p. 65° (from acetonitrile) (Found: C, 40.25; H, 2.45; N, 7.25%). Similarly prepared were *N*- α -chlorobenzylidene-*N'*-(4-bromophenyl)hydrazine (65%), m.p. 123°, and *N*- α -chlorobenzylidene-*N'*-(4-chlorophenyl)hydrazine (74%), m.p. 106° (lit.,¹⁰ 138–139, 108–110°).

(b) *N'*-(2,4,6-Tribromophenyl)benzohydrazide (8.2 g) gave *N*- α -chlorobenzylidene-*N'*-(2,4,6-tribromophenyl)hydrazine (7.5 g, 88%), m.p. 108–109°, as rods (from acetonitrile) (Found: C, 33.3; H, 1.65; N, 6.15. $C_{13}H_5Br_3ClN_2$ requires C, 33.4; H, 1.7; N, 6.0%).

***N'*-Acetyl-*N'*-arylbenzothiohydrazides and Hydrazonoyl Sulphides.**—General conditions for reaction of hydrazonoyl halides with sodium thioacetate in acetonitrile at room temperature correspond with those previously reported.² Hydrazonoyl sulphides were recovered by virtue of their sparing solubility in hot ethanol; acetyl-thiohydrazides were isolated from the ethanolic extracts by dilution with water, with addition of acetic acid if necessary to induce coagulation. For reference purposes, *N*- α -bromobenzylidene-*N'*-(2,4-dibromophenyl)hydrazine was also treated with sodium thioacetate in acetonitrile–water mixtures of composition 19 : 1 and 9 : 1. Yields of the corresponding acetyl-thiohydrazide and hydrazonoyl sulphide were (a) 83–88 and 10–11%, and (b) 91–95 and 8% respectively.

N- α -Bromobenzylidene-*N'*-(2,4-dibromophenyl)hydrazine (4.33 g) gave the hydrazonoyl sulphide (0.62 g, 9%), m.p. 201–202° (decomp.), as rods (from benzene) [lit.,¹ 200–202° (decomp.)], and *N'*-acetyl-*N'*-(2,4-dibromophenyl)benzothiohydrazide (4.07 g, 90%), m.p. 177–178° (decomp.) as yellow prisms (from ethanol) (Found: C, 42.2; H, 2.75; N, 6.6. Calc. for $C_{15}H_{12}Br_2N_2OS$: C, 42.05; H, 2.8; N, 6.55%).

N- α -Chlorobenzylidene-*N'*-(2,5-dibromophenyl)hydrazine (1.3 g) gave *bis*-[α -(2,5-dibromophenyl)hydrazono]benzyl sulphide (0.12 g, 5.5%), m.p. 210° (decomp.), as rods (from benzene) (Found: C, 42.1; H, 2.5; N, 7.6. $C_{26}H_{18}Br_4N_4S$ requires C, 42.3; H, 2.45; N, 7.6%), and *N'*-acetyl-*N'*-(2,5-dibromophenyl)benzothiohydrazide (0.85 g, 60%), m.p. 146–147°, as yellow needles (from ethanol) (Found: C, 42.2; H, 2.85; N, 6.7%).

N- α -Chlorobenzylidene-*N'*-(2,6-dibromophenyl)hydrazine (8.0 g) gave *bis*-[α -(2,6-dibromophenyl)hydrazono]benzyl sulphide (1.8 g, 12%), m.p. 200–201° (decomp.), as cream needles (from toluene) (Found: C, 42.6; H, 2.5; N, 7.45%), and *N'*-acetyl-*N'*-(2,6-dibromophenyl)benzothiohydrazide (5.5 g, 62%), m.p. 150–151° (decomp.), as yellow prisms (from aqueous ethanol) (Found: C, 42.3; H, 2.85; N, 6.5%). The latter compound was identical (m.p., t.l.c., and i.r. spectrum) with that produced by refluxing *N'*-(2,6-dibromophenyl)benzothiohydrazide with acetic anhydride–acetic acid for 20 min.

N- α -Bromobenzylidene-*N'*-(2-bromo-4-fluorophenyl)hydrazine (5.0 g) gave the hydrazonoyl sulphide (0.82 g, 10%), m.p. 184–186° (decomp.), as blades (from benzene) [lit.,¹ 184–185° (decomp.)], and *N'*-acetyl-*N'*-(2-bromo-4-fluorophenyl)benzothiohydrazide (3.6 g, 72%), m.p. 156–157° (decomp.), as yellow prisms (from ethanol); the latter compound was essentially pure (t.l.c.) and was used directly for conversion into the thiadiazine.

⁵ G. Ponzio and C. Macciotta, *Gazzetta*, 1914, **44**(I), 269.

¹⁰ Cf. A. F. Hegarty, J. A. Kearney, and F. L. Scott, *J.C.S. Perkin II*, 1973, 1422; A. F. Hegarty, personal communication.

⁷ 'International Tables for X-ray Crystallography,' vol. I, Kynoch Press, Birmingham, 1965, pp. 127, 153.

⁸ K. A. Jensen, H. R. Baccaro, O. Buchardt, G. E. Olsen, C. Pedersen, and J. Toft, *Acta Chem. Scand.*, 1961, **15**, 1109.

In the case of *N*- α -chlorobenzylidene-*N'*-(2,4,6-tribromophenyl)hydrazine (6.0 g), the reaction was conducted at reflux for 1 h. The mixture apparently contained no thio-diazine. The normal work-up gave the hydrazonoyl sulphide (1.18 g, 11%), m.p. 198—200° (decomp.), as rods (from benzene) [lit. ³ 196—198° (decomp.)], and *N'*-acetyl-*N'*-(2,4,6-tribromophenyl)benzothiohydrazide (4.12 g, 65%) m.p. 123—125° (decomp.), as yellow prisms (from benzene); essentially pure (t.l.c.); the latter compound was converted directly into the thiadiazine.

Two hydrazonoyl sulphides were prepared from the hydrazonoyl chloride and sodium sulphide nonahydrate in the normal way: ¹ *bis*-[α -(4-bromophenylhydrazono)benzyl] sulphide (50%), m.p. 202° (decomp.), as cream leaves (from benzene) (Found: C, 54.0; H, 3.65; N, 9.4; S, 5.6. C₂₆H₂₀BrClN₄S requires C, 53.8; H, 3.45; N, 9.65; S, 5.5%); and *bis*-[α -(4-chlorophenylhydrazono)benzyl] sulphide (40%), m.p. 199° (decomp.), as cream needles (from benzene) (Found: C, 64.15; H, 4.05; Cl, 14.45; S, 6.2. C₂₆H₂₀Cl₂N₄S requires C, 63.55; H 4.1; Cl 14.45; S 6.5%).

Cyclization of N'-Acetyl-N'-arylbenzothiohydrazides.—The general method was that described previously except where noted otherwise.⁴

N'-Acetyl-*N'*-(2,5-dibromophenyl)benzothiohydrazide (1.0 g) gave, after 20 h under reflux, 1-acetyl-7-bromo-3-phenyl-4,1,2-benzothiadiazine (0.38 g 44%) as cream needles, m.p. 123—125° (from benzene). The compound retained impurities and so a sample (0.6 g) was deacetylated (3 h reflux with ethanol-conc. hydrochloric acid) to give 7-bromo-3-phenyl-1H-4,1,2-benzothiadiazine (0.37 g, 70%), which crystallized from ethanol as long yellow needles, m.p. 149—150° (Found: C, 51.15; H, 2.95; N, 9.05. C₁₃H₉BrN₂S requires C, 51.15; H, 2.95; N, 9.2%); δ (CS₂) 7.82—7.62 (2 H, m), 7.45—7.15 (4 H, m), 7.10—6.76 (2 H, m), and 6.75—6.62 (1 H, distorted d). Acetylation (1 h reflux with acetic anhydride-acetic acid) gave the acetyl derivative, which crystallized from ethanol (charcoal) as needles, m.p. 124—125° (Found: C, 51.85; H, 3.4; N, 7.9. C₁₅H₁₁BrN₂OS requires C, 51.9; H, 3.2; N, 7.9%), identical with the foregoing sample.

N'-Acetyl-*N'*-(2,6-dibromophenyl)benzothiohydrazide (5.1 g) gave, after 8 h under reflux, 1-acetyl-8-bromo-3-phenyl-4,1,2-benzothiadiazine (3.5 g, 85%) as cream prisms, m.p. 127—128° (from benzene) (Found: C, 51.65; H, 3.2; S, 9.2. C₁₅H₁₁BrN₂OS requires C, 51.9; H, 3.2; S, 9.25%). Refluxing this compound (3.4 g) with ethanol-conc. hydrochloric acid for 36 h gave a crude product which was chromatographed (Florisil; benzene-chloroform) to give starting material (1.2 g), an unidentified red product, and 8-bromo-3-phenyl-1H-4,1,2-benzothiadiazine (0.4 g, 13%) as yellow needles, m.p. 75° (from ethanol) (Found: C, 51.15; H, 3.1; N, 9.05%); δ (CS₂) 8.20—7.95br (1 H, s), 7.90—7.67 (2 H, m), 7.45—7.15 (4 H, m), and 7.00—6.60 (2 H, m).

N'-Acetyl-*N'*-(2-bromo-4-fluorophenyl)benzothiohydrazide (3.0 g) gave 1-acetyl-6-fluoro-3-phenyl-4,1,2-benzothiadiazine (1.1 g, 48%), m.p. 173—174° (lit. ¹ 183°). Deacetylation of a sample (1.0 g) gave 6-fluoro-3-phenyl-1H-4,1,2-benzothiadiazine (0.72 g, 81%) as long yellow needles, m.p. 106—107° (from ethanol); an analysed sample had m.p. 107—108° (Found: C, 64.0; H, 3.8; F, 7.9; N, 11.3; S, 13.3. C₁₃H₉FN₂S requires C, 63.9; H, 3.7; F, 7.8; N, 11.5; S, 13.1%).

N'-Acetyl-*N'*-(2,4,6-tribromophenyl)benzothiohydrazide (1.0 g) gave after 6 h under reflux, 1-acetyl-6,8-dibromo-3-phenyl-4,1,2-benzothiadiazine (0.45 g, 55%) as needles, m.p.

129—130° [from benzene (charcoal)], identical with the sample described below.

1-Acetyl-6-nitro-3-phenyl-4,1,2-benzothiadiazine.—Previous attempts to prepare this compound were unsuccessful. The present experiments have been successful, but persistent contaminants have prevented the preparation of samples giving satisfactory analytical figures.

(a) *N*- α -Bromobenzylidene-*N'*-(2-bromo-4-nitrophenyl)hydrazine ¹¹ (5.0 g) and sodium thioacetate (2.5 g) gave, in the normal way, the hydrazonoyl sulphide (0.75 g 10%) as yellow prisms, m.p. 227—228° (decomp.) (from toluene); ν_{\max} (KBr) 3 260 cm⁻¹ (N-H). The reaction liquor yielded a rusty red solid (3.85 g), m.p. 62—66°, containing three components (t.l.c.) of which one appeared to be the desired acetyl-thiohydrazide. The crude product (3.0 g) was boiled under reflux for 4 h in acetonitrile-triethylamine and the product isolated by dilution with water. Chromatography on Florisil gave 1-acetyl-6-nitro-3-phenyl-4,1,2-benzothiadiazine (0.58 g, 24%) as fluorescent golden needles, m.p. 182—183° (from ethanol); ν_{\max} 1 690 cm⁻¹ (C=O); δ (CDCl₃) 8.20—7.85 (5 H, m), 7.65—7.20 (3 H, m), and 2.55 (3 H, s); *m/e* 313 (*M*⁺), 292, 290, 284, 283, 277, 273, 271, 241, 238, 225, 185, 163, 149, 135, 121, 105, 103, 83, 81, 78, and 77. Deacetylation gave a red solid, m.p. 147—155° which contained 6-nitro-3-phenyl-1H-4,1,2-benzothiadiazine. This was established by correlation of i.r. and mass spectra (see below); the mass spectrum showed additional peaks at *m/e* 386, 358, 351, 322, 299, and 284 due to other material.

(b) Benzothiohydrazide ⁸ (1.52 g), 1-fluoro-2,4-dinitrobenzene (1.86 g), acetonitrile (20 ml), and triethylamine (5 ml) were boiled under reflux for 1 h, the solution turning deep red. Chromatography on Florisil gave 6-nitro-3-phenyl-1H-4,1,2-benzothiadiazine (0.49 g, 18%) as fluorescent red needles, m.p. 159—160°; ν_{\max} 3 295 cm⁻¹ (N-H); δ (Me₂SO) 8.33—8.25 (1 H, m), 7.78—7.20 (5 H, m), and 6.71—6.48 (3 H, m); *m/e* 271 (*M*⁺), 255, 241, 237, 225, 195, 187, 177, 165, 149, 138, 135, 123, 122, 121, 105, 103, 78, and 77.

Treatment with acetic anhydride (1 h reflux) gave the 1-acetyl derivative, identical (mixed m.p. and i.r. and ¹H n.m.r. spectra) with the foregoing sample.

7-Bromo-1-(4-nitrophenyl)-3-phenyl-1H-4,1,2-benzothiadiazine.—A mixture of 4-nitrobenzenethiol (0.42 g), *N'*-(2,5-dibromophenyl)benzohydrazide (1.0 g), ethanol (15 ml), and triethylamine (5 ml) was boiled under reflux for 72 h. Solvents were removed *in vacuo*. 7-Bromo-1-(4-nitrophenyl)-3-phenyl-1H-4,1,2-benzothiadiazine (0.46 g, 40%) crystallized from ethanol as orange prisms, m.p. 207—208° (Found: C, 53.55; H, 3.05; N, 9.6. C₁₅H₁₂BrN₃O₂S requires C, 53.5; H, 2.85; N, 9.35%); *m/e* 427/425 (*M*⁺), 411/409, 395/393, 381/379, 346, 324/322, 307, 305, 303, 278/276, 197, 196, 153, 121, 103, 95, and 77.

Reactions of 1H-4,1,2-Benzothiadiazines.—(a) 6- and 8-Substitution. (i) Freshly prepared pyridinium perbromide (1.6 g) and 6-bromo-3-phenyl-1H-4,1,2-benzothiadiazine (1.52 g) were stirred together in glacial acetic acid (50 ml) at room temperature for 2 h. The colour of the mixture changed from dark brown to yellow. The solid was filtered off, washed, and crystallized from ethanol to give 6,8-dibromo-3-phenyl-1H-4,1,2-benzothiadiazine (1.82 g, 95%) as yellow needles, m.p. 108—109° (Found: C, 40.95; H, 2.3; Br, 41.4. C₁₃H₈Br₂N₂S requires C, 40.6; H, 2.1; Br, 41.6%); δ (CCl₄) 7.90 (1 H, s), 7.71—7.59 (2 H, m), 7.29—7.19 (4 H, m), and 7.05—6.98 (1 H, distorted d). The same compound

¹¹ J. M. Burgess and M. S. Gibson, *Tetrahedron*, 1962, **18**, 1001.

was produced under similar conditions from 8-bromo-3-phenyl-1*H*-4,1,2-benzothiadiazine.

The dibromo-compound (0.5 g) was boiled with acetic anhydride (5 ml) for 36 h to give the 1-acetyl derivative (0.52 g, 94%), which crystallized from ethyl acetate as needles, m.p. 129–130°, identical with the foregoing sample (Found: C, 42.4; H, 2.5; N, 6.55%. $C_{15}H_{10}Br_2N_2OS$ requires C, 42.25; H, 2.35; N, 6.55%); $\delta(CS_2)$ 8.00–7.79 (2 H, m), 7.71–7.65 (1 H, distorted d), 7.50–7.25 (4 H, m), and 2.33 (3 H, s).

(ii) 6-Fluoro-3-phenyl-1*H*-4,1,2-benzothiadiazine (1.0 g) similarly gave 8-bromo-6-fluoro-3-phenyl-1*H*-4,1,2-benzothiadiazine (0.85 g, 64%) as pale yellow needles, m.p. 99–100° (from methanol) (Found: C, 48.4; H, 2.45; N, 8.5. $C_{13}H_8BrFN_2S$ requires C, 48.3; H, 2.5; N, 8.65%).

(b) 1-Substitution. (i) A mixture of 6-bromo-3-phenyl-1*H*-4,1,2-benzothiadiazine (1.52 g), methyl toluene-4-sulphonate (0.95 g), and acetonitrile (30 ml) was boiled under reflux for 144 h. Chromatography (Florisil; pentane-chloroform) gave the starting thiadiazine (0.62 g) and 6-bromo-1-methyl-3-phenyl-4,1,2-benzothiadiazine (0.72 g, 45%) as yellow rods, m.p. 63–64° (Found: C, 52.5; H, 3.45; S, 10.0. $C_{14}H_{11}BrN_2S$ requires C, 52.7; H, 3.45; S, 10.05%); $\delta(CCl_4)$ 7.90–7.71 (2 H, m), 7.38–7.12 (5 H, m), 6.61–6.50 (1 H, distorted d), and 3.37 (3 H, s).

(ii) A mixture of 6-bromo-3-phenyl-1*H*-4,1,2-benzothiadiazine⁴ (0.72 g), 1-fluoro-2,4-dinitrobenzene (0.43 g), acetonitrile (15 ml), and triethylamine (5 ml) was boiled under reflux for 6 h; solvents were removed *in vacuo*. Crystallization from ethyl acetate gave 6-bromo-1-(2,4-dinitrophenyl)-3-phenyl-4,1,2-benzothiadiazine as red needles, m.p. 213–214° (Found: C, 48.2; H, 2.35; N, 11.55. $C_{19}H_{11}BrN_4O_4S$ requires C, 48.4; H, 2.35; N, 11.9%); $\delta(Me_2SO)$ 8.17–7.40 (4 H, m), 7.25–6.61 (6 H, m), and 6.21–6.05 (1 H, distorted d).

(iii) Isopentyl nitrite (0.29 g, 1 equiv.) was added during

10 min to a stirred solution of 6-bromo-3-phenyl-1*H*-4,1,2-benzothiadiazine (0.76 g) in ethanol (30 ml) and hydrochloric acid (1 ml) at room temperature. After 2 h, the yellow solid was filtered off, washed, and dried. Crystallization from acetone (at –78 °C) gave the 1-nitroso-derivative (0.45 g, 54%) as yellow needles, m.p. 92–94°, which slowly decomposed at room temperature; $\delta(CDCl_3)$ 8.08–7.81 (2 H, m), 7.72–7.63 (1 H, d), and 7.60–7.20 (5 H, m). Microanalytical figures were discrepant.

(c) Oxidation. A solution of 6-bromo-3-phenyl-1*H*-4,1,2-benzothiadiazine (0.76 g) in acetic acid (30 ml) and 6% hydrogen peroxide (10 ml) was boiled under reflux for 15 min and then cooled. Water (30 ml) was added and the solid was filtered off, and dried. Crystallization from ethanol-ethyl acetate gave 6-bromo-3-phenyl-1*H*-4,1,2-benzothiadiazine 4,4-dioxide (0.55 g, 66%) as pale pink prisms, m.p. 249–250° (Found: C, 46.0; H, 2.85; N, 8.2. $C_{13}H_8BrN_2O_2S$ requires C, 46.3; H, 2.7; N, 8.3%); *m/e* 338/336 (M^+), 293/291, 274/272, 247/245, 243, 235/233, 231, 219, 216, 207, 205, 199, 198, 197, 171, 169, 166, 165, 162, 143, 135, 123, 118, 105, 104, 103, 78, and 77.

X-Ray Crystallographic Studies of Bis- $[\alpha$ -(2,6-dibromo-phenylhydrazono)benzyl] Sulphide.—Crystals of the hydrazonoyl sulphide were examined under a polarizing microscope. A small single crystal was chosen and sealed in a Lindemann capillary tube. Oscillation and Weissenberg photographs were taken with nickel-filtered $Cu-K_\alpha$ radiation. The following orthorhombic unit cell parameters were obtained from these photographs: $a = 6.86$, $b = 15.85$, $c = 24.49$ Å, $D_c = 1.84$, $D_m(\text{floatation}) = 1.88$ g cm⁻³, $Z = 4$, space group $Cmca$ or $Aba2$.

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