

## Substituent Effects in Synthesis of 4*H*-1,3,4-Benzothiadiazines from Hydrazonyl Halides and Thioacetate Ion

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The reactions of a number of new hydrazonyl halides, mainly of the type  $\text{PhCBr:N}\cdot\text{NH}\cdot\text{C}_6\text{H}_3\text{BrZ}(2,4-)$ , with potassium thioacetate in boiling acetonitrile have been examined. 4-Acetyl-2-phenyl-7-*Z*-4*H*-1,3,4-benzothiadiazines were isolated where  $Z = \text{CN}$  or  $\text{CF}_3$ , but apart from these and previously reported cases ( $Z = \text{halogen}$ ), the synthesis seems not to be generally extendable to other substituents  $Z$ . Also described are 4-acetyl-2-phenyl-4*H*-1,3,4-benzothiadiazine (from  $\text{PhCCl:NNHC}_6\text{H}_4\text{F-}o$ ) and 4-acetyl-9-bromo-2-phenyl-4*H*-naphtho[1,2-*e*][1,3,4]thiadiazine [from  $\text{PhCBr:N}\cdot\text{NH}\cdot\text{C}_{10}\text{H}_5\text{Br}_2(2,4-)$ ].

VARIOUS preparations of the four halogeno-substituted 4*H*-1,3,4-benzothiadiazines (IV;  $Z = \text{F, Cl, Br, or I}$ ) from hydrazonyl halides (I;  $X = \text{Cl or Br}$ ) and potassium thioacetate in boiling acetonitrile have been described.<sup>1,2</sup>

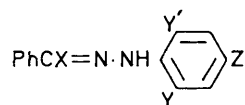
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In most preparations, the corresponding hydrazonyl sulphide (II), the *N'*-acetyl-*N'*-arylbenzothiohydrazide (III), and decomposition products are also obtained.

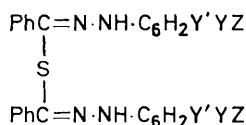
<sup>1</sup> I. T. Barnish and M. S. Gibson, *J. Chem. Soc. (C)*, 1970, 854.

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

The thiadiazine synthesis is successful where  $Y = F$ ,  $Br$ , or  $I$ , but fails where  $Y = Cl$ , and fails also where  $Y = Br$  and  $Z = H$ . We now describe the behaviour of the hydrazone halides (Ia—i) and (V) in this reaction. Compounds (Ia—g) were chosen to investigate the influence of the *para*-substituent  $Z$  on thiadiazine formation.<sup>2</sup> Compound (Ih) was chosen to determine whether the limitation<sup>1</sup> observed for the case  $Y = Br$ ,  $Z = H$  would extend to the case  $Y = F$ ,  $Z = H$ , compound (Ii) to examine the effect of further substitution in the *N*-aryl ring, and compound (V) to establish whether the synthesis could be extended to naphthothiadiazines.



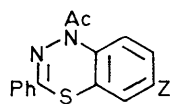
(I)



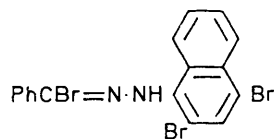
(II)



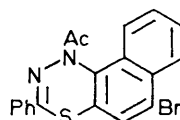
(III)



(IV)



(V)



(VI)

- a;  $X = Y = Br$ ,  $Z = CN$       e;  $X = Y = Br$ ,  $Z = SCN$   
 b;  $X = Y = Br$ ,  $Z = CF_3$       f;  $X = Cl$ ,  $Y = Br$ ,  $Z = Me$   
 c;  $X = Y = Br$ ,  $Z = SO_2 \cdot NMe_2$       g;  $X = Br$ ,  $Y = Z = F$   
 d;  $X = Y = Br$ ,  $Z = CO_2Et$       h;  $X = Cl$ ,  $Y = F$ ,  $Z = H$
- a—h inclusive;  $Y' = H$   
 i;  $X = Y = Y' = Z = Br$

The required hydrazone halides were obtained by standard methods. Compounds (Ia—e) were prepared by brominating the corresponding hydrazone ( $PhCH=N \cdot NH \cdot C_6H_4Z$ ), a small excess of bromine normally being employed. Compounds (Ig) and (V) were similarly prepared from benzaldehyde 2,4-difluorophenylhydrazone and benzaldehyde 1-naphthylhydrazone, respectively. Compound (Ii) was prepared by brominating benzaldehyde 2,4,6-tribromophenylhydrazone and (incidentally) from attempted monobromination of benzaldehyde 2,6-dibromophenylhydrazone, indicating that there is little difference in reactivity towards bromine at the  $\alpha$ - and the 4-positions. Overbromination was also noted in the case of benzaldehyde *p*-tolylhydrazone; accordingly hydrazone chlorides were prepared in two cases (If and h) by reaction of the

<sup>3</sup> Cf. R. Huisgen, M. Seidel, G. Wallbillich, and H. Knapfer, *Tetrahedron*, 1962, **17**, 3.

<sup>4</sup> A. J. Elliott, M. S. Gibson, M. M. Kayser, and G. A. Pawelchak, *Canad. J. Chem.*, in the press.

corresponding hydrazone ( $PhCO \cdot NH \cdot NH \cdot C_6H_3YZ$ ) with phosphorus pentachloride.<sup>3</sup>

Hydrazone sulphides (II) were prepared from most of the hydrazone halides (Ia—i) by reaction with sodium sulphide<sup>1</sup> or, in one or two cases, potassium thioacetate in acetonitrile at room temperature. The latter procedure leads to (II) and (III), but separation of the sulphide (II) normally poses no problem.<sup>2</sup>

The reactions of compounds (Ia—i) with potassium thioacetate in boiling acetonitrile display considerable differences. Compound (Ia) gave the thiadiazine (IVa), but in only 7% yield; an unidentified by-product was also formed, but the bulk of the products were apparently derived from decomposition of (IIIa). Compound (Ib) gave (IVb) (12%) together with an unidentified by-product and decomposition products of (IIIb). The two by-products from the foregoing reactions do not correspond in structural type, and similar by-products were not observed in the following reactions. Compounds (Ic and d) gave only tarry products and the thiadiazines, if present, could not be isolated; compound (Id) has incidentally been converted into a benzothiadiazine by reactions related to those under discussion, but in low yield.<sup>4</sup> Compound (Ie) gave a mixture of products which presented the striking feature of the absence of thiocyanato-groups (i.r. spectrum). A similar mixture (t.l.c., i.r. spectrum) was obtained from the corresponding reaction at room temperature, indicating ready reaction of the thiocyanato-group with thioacetate ion. From studies with simpler model systems<sup>5</sup> it is thought that the reaction products may include (II and III;  $Y = Br$ ,  $Z = SAc$ ), though these were not characterised, together with decomposition products. Compound (If) gave (IIIf) together with tarry products; this reaction resembled that of (I;  $X = Cl$ ,  $Y = Br$ ,  $Z = H$ ) reported previously.<sup>1</sup>

These results show that extension of the benzothiadiazine synthesis to other substituents  $Z$  is not straightforward. The substituent  $Z$  should preferably be electron-attracting, but this alone provides no guarantee of success.

The conversion (Ig)  $\rightarrow$  (IVg) was predictably one with a good chance of success;<sup>1</sup> indeed (IVg) was easily isolated (67% yield) with minimal production of by-products. Compound (Ih), in which the ease of displacement of fluorine relative to bromine might be expected to outweigh the absence of an electron-attracting substituent  $Z$  such as halogen, gave (IVh) (14%), together with a substantial amount of (IIIh), though the latter was not obtained pure. The thiadiazine (IVh), on hydrolysis, gave 2-phenyl-4*H*-1,3,4-benzothiadiazine; the compound to which this structure had previously been assigned<sup>6</sup> is now recognised as 2-phenylbenzothiazole.<sup>1,7</sup>

<sup>5</sup> M. M. Kayser and M. S. Gibson, *Canad. J. Chem.*, in the press.

<sup>6</sup> P. C. Guha and T. N. Ghosh, *J. Indian Inst. Sci.*, 1929, **12A**, 31.

<sup>7</sup> G. Corsi, *Ann. Chim. (Italy)*, 1966, **56**, 1203.

Of the remaining compounds, (Ii) gave a small amount of (Iii), together with tarry decomposition products. However, (V) gave the naphthothiadiazine (VI) in 76% yield. This presumably reflects the stabilisation of the transition state, in which one of the naphthalene rings remains benzenoid, relative to the cases of ring closure to form benzothiadiazines.

These results substantiate previous views of this reaction, but indicate that the effectiveness of the synthesis (I)  $\rightarrow$  (IV) is likely to be limited to (a) cases in which Z is halogen or one of a small number of other electron-attracting groups, and (b) polycyclic examples typified by the synthesis of the naphthothiadiazine (VI).

#### EXPERIMENTAL

Mass spectra were determined on an A.E.I. MS-902 instrument, samples being introduced by means of a high temperature probe (200–300°). Results are quoted as *m/e* values for the lowest isotopic species except in the case of bromo-compounds when values for <sup>79</sup>Br and <sup>81</sup>Br are given.

*o*-Fluorophenylhydrazine and 1-naphthylhydrazine were available as commercial samples. Other arylhydrazines were prepared as described; physical properties (m.p.) corresponded with data reported.<sup>8</sup>

*Arylhydrazines.*—2,4-Difluoroaniline (10.0 g) in concentrated hydrochloric acid (200 ml) was diazotised at –2 to 0° with sodium nitrite (5.89 g, 1.1 equiv.) in water (50 ml). Excess of urea was then added. The solution was cooled to –4° and reduced by rapidly adding anhydrous tin(II) chloride (36.82 g, 1.25 equiv.) in concentrated hydrochloric acid (70 ml), previously cooled to –50°. After 1 h the mixture was worked up in the normal way<sup>2</sup> to give 2,4-difluorophenylhydrazine (11.4 g, ca. 100%), which crystallised from light petroleum (b.p. 60–80°) as needles, m.p. 64–64.5° (Found: C, 50.2; H, 4.3; N, 19.2. C<sub>6</sub>H<sub>6</sub>F<sub>2</sub>N<sub>2</sub> requires C, 50.0; H, 4.2; N, 19.4%). The *benzylidene derivative* crystallised from light petroleum (b.p. 60–80°) as lilac prisms, m.p. 84.5–85.5° (Found: C, 67.0; H, 4.2; N, 12.0. C<sub>13</sub>H<sub>10</sub>F<sub>2</sub>N<sub>2</sub> requires C, 67.2; H, 4.3; N, 12.1%); the *m-nitrobenzylidene derivative* crystallised from ethanol as orange needles, m.p. 163.5–164° (Found: C, 56.5; H, 3.4; N, 14.9. C<sub>13</sub>H<sub>9</sub>F<sub>2</sub>N<sub>3</sub>O<sub>2</sub> requires C, 56.3; H, 3.2; N, 15.2%).

The remaining arylhydrazines were similarly prepared, except for *p*-dimethylsulphamoylphenylhydrazine, in which case the whole reaction mixture was basified prior to extraction of the hydrazine.

*Benzaldehyde p-cyanophenylhydrazone* crystallised from benzene as buff plates, m.p. 149.5–150.5° (Found: C, 76.2; H, 5.0; N, 18.8. C<sub>14</sub>H<sub>11</sub>N<sub>3</sub> requires C, 76.0; H, 5.0; N, 19.0%).

*Hydrazonyl Bromides.*—A slight excess of bromine (1, 2, or 3 mol. equiv., as required) in glacial acetic acid was added to a stirred suspension of the hydrazone in acetic acid at room temperature. After reaction, the product was filtered off, washed with water, dried, and crystallised.

<sup>8</sup> (a) A. Weissberger, H. D. Porter, and W. A. Gregory, *J. Amer. Chem. Soc.*, 1944, **66**, 1851; (b) E. J. Forbes, M. Stacey, J. C. Tatlow, and R. T. Wragg, *Tetrahedron*, 1960, **8**, 70; (c) A. Lespagnol, D. Bar, Mme. Erb-Debruyne, and Mme. Delhomenie-Sauvage, *Bull. Soc. chim. France*, 1960, 490; (d) H. Thoms and K. Ritsert, *Ber. deut. pharm. Ges.*, 1921, **31**, 65; (e) Z. Horü, *J. Pharm. Soc. Japan*, 1935, **55**, 880.

Typically, benzaldehyde *p*-ethoxycarbonylphenylhydrazone<sup>8d</sup> (23.8 g) and bromine (9.2 ml) in acetic acid (400 ml) gave *N*- $\alpha$ -bromobenzylidene-*N'*-(2-bromo-4-ethoxycarbonylphenyl)hydrazine (Id) (26.9 g, 71%), which crystallised from ethanol (charcoal) as needles, m.p. 130–131° (Found: C, 44.9; H, 3.3; Br, 37.6; N, 6.4. C<sub>16</sub>H<sub>14</sub>Br<sub>2</sub>N<sub>2</sub>O<sub>2</sub> requires C, 45.1; H, 3.3; Br, 37.6; N, 6.6%);  $\nu_{\max}$  (Nujol) 1720 cm<sup>-1</sup> (C=O).

Similarly prepared were *N*- $\alpha$ -bromobenzylidene-*N'*-(2-bromo-4-cyanophenyl)hydrazine (Ia) (69%), m.p. 167–168° (needles, from ethyl acetate) (Found: C, 44.6; H, 2.5; Br, 42.0; N, 11.0. C<sub>14</sub>H<sub>9</sub>Br<sub>2</sub>N<sub>3</sub> requires C, 44.3; H, 2.4; Br, 42.2; N, 11.1%); *N*- $\alpha$ -bromobenzylidene-*N'*-(2-bromo-4-trifluoromethylphenyl)hydrazine (Ib) (57%), m.p. 108.5–109.5° (needles, from ethanol) (Found: C, 40.1; H, 2.3; Br, 38.0; N, 6.8. C<sub>14</sub>H<sub>9</sub>Br<sub>2</sub>F<sub>3</sub>N<sub>2</sub> requires C, 39.8; H, 2.1; Br, 37.9; N, 6.6%); *N*- $\alpha$ -bromobenzylidene-*N'*-(2-bromo-4-dimethylsulphamoylphenyl)hydrazine (Ic) (52%), m.p. 159–160.5° (needles, from ethanol) (Found: C, 39.3; H, 3.3; Br, 34.8; N, 9.3; S, 6.7. C<sub>15</sub>H<sub>15</sub>Br<sub>2</sub>N<sub>3</sub>O<sub>2</sub>S requires C, 39.0; H, 3.3; Br, 34.7; N, 9.1; S, 6.9%); *N*- $\alpha$ -bromobenzylidene-*N'*-(2-bromo-4-thiocyanatophenyl)hydrazine (Ie) (53%), m.p. 130.5–131.5° (needles, from ethanol-ethyl acetate) (Found: C, 41.0; H, 2.1; Br, 38.7; N, 10.0; S, 7.5. C<sub>14</sub>H<sub>9</sub>Br<sub>2</sub>N<sub>3</sub>S requires C, 40.9; H, 2.2; Br, 38.9; N, 10.2; S, 7.8%); *N*- $\alpha$ -bromobenzylidene-*N'*-(2,4-difluorophenyl)hydrazine (Ig) (75%), m.p. 77.5–78.5° (needles, from acetic acid) (Found: C, 50.4; H, 3.0; Br, 25.5; N, 9.2. C<sub>13</sub>H<sub>9</sub>BrF<sub>2</sub>N<sub>2</sub> requires C, 50.2; H, 2.9; Br, 25.7; N, 9.0%); and *N*- $\alpha$ -bromobenzylidene-*N'*-(2,4-dibromo-1-naphthyl)hydrazine (V) (29%), m.p. 142–143° (needles, from ethyl acetate) (Found: C, 42.2; H, 2.3; N, 5.8. C<sub>17</sub>H<sub>11</sub>Br<sub>2</sub>N<sub>2</sub> requires C, 42.2; H, 2.3; N, 5.8%).

Compound (Ii) was prepared both by bromination of benzaldehyde 2,4,6-tribromophenylhydrazone and by attempted monobromination of benzaldehyde 2,6-dibromophenylhydrazone;<sup>9</sup> needles, m.p. 112–113° (from ethanol) (lit.,<sup>10</sup> 113°).

*Hydrazonyl Chlorides.*—Benzoyl chloride (17.22 g) in dry ether (32 ml) was added during 15 min to a stirred solution of *o*-fluorophenylhydrazine (15.5 g, 1 equiv.) and triethylamine (25.6 ml, 1.5 equiv.) in ether cooled to –50°. After 75 min, work-up in the normal way<sup>2</sup> gave *N*-benzoyl-*N'*-*o*-fluorophenylhydrazine (26.95 g, 95%), which crystallised from benzene as needles, m.p. 151–152° (Found: C, 68.0; H, 5.1; N, 12.1. C<sub>13</sub>H<sub>11</sub>FN<sub>2</sub>O requires C, 67.8; H, 4.8; N, 12.2%). A mixture of the hydrazide (26.9 g) and phosphorus pentachloride (29.1 g) in dry ether (275 ml) was refluxed for 8 h 15 min. The normal procedure for isolation<sup>2</sup> gave a viscous oil from which no solid separated on cooling to 0 to –20°. Ethanol (30 ml) was added and the solution was cooled to –78°, whereupon *N*- $\alpha$ -chlorobenzylidene-*N'*-*o*-fluorophenylhydrazine (Ih) slowly crystallised; yield (including crop from mother liquor) 16.05 g (55%). Crystallisation from ethanol gave prisms, m.p. 56–56.5° (Found: C, 63.1; H, 4.1; N, 11.2. C<sub>13</sub>H<sub>10</sub>ClFN<sub>2</sub> requires C, 62.8; H, 4.0; N, 11.3%).

*N*- $\alpha$ -Chlorobenzylidene-*N'*-(2-bromo-4-methylphenyl)hydrazine (If) (22%), prepared from the corresponding hydrazide,<sup>11</sup> crystallised from ethanol as prisms, m.p.

<sup>9</sup> E. Votoček and R. Lukes, *Bull. Soc. chim. France*, 1924, **35**, 868.

<sup>10</sup> J. E. Humphries, E. Bloom, and R. Evans, *J. Chem. Soc.*, 1923, **123**, 1766.

<sup>11</sup> F. D. Chattaway and G. D. Hodgson, *J. Chem. Soc.*, 1916, **109**, 582.

66—67° (Found: C, 52.0; H, 3.85; N, 8.5.  $C_{14}H_{12}BrClN_2$  requires C, 51.9; H, 3.7; N, 8.7%).

*N-Benzoyl-N'-(2,6-dibromophenyl)hydrazine* (74%), prepared from benzoyl chloride and 2,6-dibromophenylhydrazine,<sup>9</sup> crystallised from benzene as needles, m.p. 150—151° (Found: C, 42.2; N, 3.8; Br, 43.5; N, 7.3.  $C_{13}H_{10}Br_2N_2O$  requires C, 42.2; H, 2.7; Br, 43.2; N, 7.6%). This compound was recovered in diminished amount from attempted reaction with phosphorus pentachloride.

*Hydrazonyl Sulphides*.—(i) A number of these compounds were prepared from the hydrazonyl halide and hydrated sodium sulphide in acetonitrile at room temperature (reaction time 2—4 h).<sup>1</sup> These include: bis- $[\alpha$ -(2-bromo-4-cyanophenylhydrazono)benzyl] sulphide (IIa) (59%), m.p. 225—226° (cream needles, from toluene) (Found: C, 53.6; H, 3.0; Br, 25.3; N, 13.3; S, 4.7.  $C_{28}H_{18}Br_2N_6S$  requires C, 53.3; H, 2.9; Br, 25.4; N, 13.3; S, 5.1%); compound (IIc) (43%), m.p. 203.5—205° (needles, from toluene) (Found: C, 45.8; H, 3.8; Br, 20.3; N, 10.4.  $C_{30}H_{30}Br_2N_6O_4S_3$  requires C, 45.3; H, 3.8; Br, 20.2; N, 10.6%); compound (IIe) (41%), m.p. 182—183° (decomp.) [cream leaves, from light petroleum (b.p. 80—100°)] (Found: C, 55.5; H, 4.1; Br, 26.2; N, 9.2; S, 5.2.  $C_{28}H_{24}Br_2N_4S$  requires C, 55.3; H, 3.95; Br, 26.3; N, 9.2; S, 5.3%); compound (IIg) (61%), m.p. 191—192° (needles, from benzene) (Found: C, 63.7; H, 3.8; F, 15.4; N, 11.2.  $C_{26}H_{18}F_4N_4S$  requires C, 63.2; H, 3.6; F, 15.4; N, 11.3%); compound (IIh) (52%), m.p. 184—185° (needles, from benzene) (Found: F, 8.2; N, 11.9; C, H discrepant.  $C_{26}H_{20}F_2N_4S$  requires F, 8.3; N, 12.2%).

(ii) Some hydrazonyl sulphides were prepared from the hydrazonyl halide and potassium thioacetate.<sup>2</sup> Compound (Ib) (4.22 g), potassium thioacetate (2.30 g), and acetonitrile (120 ml) were stirred together at room temperature for 105 min. The solid was filtered off, washed with water, and dried to give bis- $[\alpha$ -(2-bromo-4-trifluoromethylphenylhydrazono)benzyl] sulphide (IIb) (0.5 g, 14%), which crystallised from benzene as needles, m.p. 178—179° (Found: C, 47.1; H, 2.6; Br, 22.1; N, 7.8.  $C_{28}H_{18}Br_2F_6N_4S$  requires C, 46.9; H, 2.5; Br, 22.3; N, 7.8%). The reaction filtrate contained compound (IIIb), but this was not isolated in analytically pure condition.

Similarly prepared were compound (IIe) (24%), m.p. 173° [rods, from light petroleum (b.p. 100—120°)] (Found: C, 52.8; H, 3.6; Br, 22.0; N, 7.4; S, 4.2.  $C_{32}H_{28}Br_2N_4O_4S$  requires C, 53.0; H, 3.9; Br, 22.1; N, 7.7; S, 4.4%); and compound (IIi) (15%), m.p. 196—198° (decomp.) (cream rods, from benzene) (Found: C, 35.1; H, 2.1; Br, 53.6; N, 6.5; S, 4.1.  $C_{26}H_{16}Br_6N_4S$  requires C, 34.8; H, 1.8; Br, 53.6; N, 6.25; S, 3.6%).

*Formation of Thiadiazines from Hydrazonyl Halides and Thioacetate Ion*.—(i) Compound (Ia) (7.58 g, 0.02 mol) was added to a refluxing mixture of potassium thioacetate (4.60 g, 0.04 mol) and acetonitrile (240 ml). After 4 h at reflux, the hot mixture was filtered and the solid (water-soluble) was discarded. The cooled solution was poured into an excess of water containing glacial acetic acid (30 ml) and the precipitate (6.1 g) was collected and dried *in vacuo*. Trituration with cold acetonitrile left a cream solid (0.65 g) which was a mixture of two compounds (t.l.c.). This solid was dissolved in a minimum of boiling ethanol. On cooling slowly, pale yellow needles (0.18 g; fraction A), m.p. 231—233°, were deposited and were filtered off. The filtrate was chilled (ice-salt) yielding a

white precipitate which was filtered off and augmented by solid obtained from the ethanolic mother liquor (fraction B). The total fraction B was crystallised from ethyl acetate to give 4-acetyl-2-phenyl-4H-1,3,4-benzothiadiazine-7-carbonitrile (IVa) (0.45 g, 7%) as needles, m.p. 188—188.5° (Found: C, 65.3; H, 4.1; N, 14.5.  $C_{16}H_{11}N_3OS$  requires C, 65.5; H, 3.8; N, 14.3%);  $\nu_{max}$  2225 (C≡N) and 1695  $cm^{-1}$  (C=O);  $m/e$  293 ( $M^+$ ), 251 ( $M - CH_2CO$ ), 250 (251 - H), 190 ( $M - PhCN$ ), 148 (251 - PhCN), 121 (PhCS/148 - HCN), 104, 103, 94 (121 - HCN), 77, 69, 51, and 43.

Fraction A was not identified;  $\nu_{max}$  2225  $cm^{-1}$  (C≡N);  $m/e$  428/426/424, 427/425/423, 314/312, 266, 234, 214/212, 165, 133, 94, 82, and 69. The bulk of the reaction products, present in the acetonitrile trituration liquors, appeared to contain (IIIa) and various decomposition products (t.l.c.).

(ii) Compound (Ib) (4.22 g) and potassium thioacetate (2.30 g), treated as in (i), gave a thick red oil which, after drying *in vacuo*, became a red solid (2.5 g). Trituration with cold acetonitrile left a yellow solid (0.5 g). Crystallisation of this from ethyl acetate gave orange prisms (0.25 g; fraction C). The mother liquor from the crystallisation, when cooled to -78°, gave the benzothiadiazine (IVb) (0.25 g, 12%) as needles, m.p. 123—124.5° raised to 125—125.5° by crystallisation from ethanol (Found: C, 57.2; H, 3.2; N, 8.3; S, 9.7.  $C_{16}H_{11}F_3N_3OS$  requires C, 57.1; H, 3.3; N, 8.3; S, 9.5%);  $m/e$  336 ( $M^+$ ), 294 ( $M - CH_2CO$ ), 293 (294 - H), 275, 233, 191 (294 - PhCN), 171 (191 - HF), 164 (191 - HCN), 121, 104, 103, 77, 69, 51, and 43.

Fraction C was crystallised from ethyl acetate to give an unidentified compound, m.p. 191.5—193° (Found: C, 47.4; H, 2.9; N, 6.1; S, 13.3. Calc. for  $C_{18}H_{12}BrF_3N_2S_2$ : C, 47.3; H, 2.6; N, 6.1; S, 14.0%);  $m/e$  458/456, 377, 355/353, 345, 290/288, 201, 144, 121, 103, 59, and 54.

The acetonitrile trituration liquors apparently contained (IIIb) and decomposition products.

(iii) Compound (Ic) (3.11 g) and potassium thioacetate (2.30 g), treated as in (i), gave a hot reaction filtrate which deposited benzothiadiazine (IVg) (1.87 g), m.p. 176—177°, identical with an authentic sample,<sup>2</sup> on cooling; the mother liquor provided a further crop; total yield 1.92 g (67%). The final reaction filtrate apparently contained some (IIIg) (t.l.c.).

(iv) Compound (Ih) (1.0 g) and potassium thioacetate (0.93 g), treated as in (i), gave a hot reaction filtrate which was cooled and poured into water. The yellow solid (0.19 g; fraction D) was collected and dried *in vacuo*; acetic acid was added to the opalescent liquor and coagulation occurred to give a yellow solid (0.5 g; fraction E), which was collected and dried.

Fraction D crystallised from ethanol to give benzothiadiazine (IVh) (0.14 g, 13%) as needles, m.p. 123—126°, not further purified in order to conserve material for hydrolysis studies;  $\nu_{max}$  1695  $cm^{-1}$  (C=O);  $m/e$  268 ( $M^+$ ), 226 ( $M - CH_2CO$ ), 225 (226 - H), 165 ( $M - PhCN$ ), 123 (226 - PhCN), 121, 103, 96 (123 - HCN), 77, 76, 69, 57, 55, and 43;  $\delta$  (CDCl<sub>3</sub>) 8.15—7.10 (8H, m) and 2.53 (3H, s).

Fraction E was trituated with boiling light petroleum (b.p. 60—80°) and then crystallised from benzene to give *N'*-acetyl-*N'*-*o*-fluorophenylbenzothiohydrazide (IIIh) (0.3 g, ca. 26%) as yellow prisms, m.p. 151.5—152.5° (decomp.); analytical figures were discrepant, possibly owing to occlusion of benzene;  $m/e$  288 ( $M^+$ ), 270 ( $M - H_2O$ ), 269 (270 - H), 251 (270 - F), 246 ( $M - CH_2CO$ ), 212, 167

(270 — PhCN), 161, 153 ( $M$  — PhCNS), 148 (251 — PhCN), 140, 135 (PhCNS), 121, 111 (153 —  $\text{CH}_2\text{CO}$ ), 109, 103, 95, 83, 82, 78, 77, 76, 75, 64, 63, 58, 57, 51, 50, 46, and 43.

Compound (IVh) (50 mg) was hydrolysed by refluxing with ethanol and concentrated hydrochloric acid for 20 min. The solution was cooled and poured into water. The precipitate was filtered off, washed with water, and crystallised from aqueous ethanol to give 2-phenyl-4H-1,3,4-benzothiadiazine as yellow needles, m.p. 84—85° (insufficient for analysis);  $m/e$  226 ( $M^+$ ), 225 ( $M - H$ ), 194, 165, 149, 123 ( $M - \text{PhCN}$ ), 122, 113, 104, 103, 96 (123 — HCN), 77, 69, 63, and 51.

(v) Compound (V) (4.83 g) and potassium thioacetate (2.30 g), treated as in (i), gave a hot reaction filtrate which, when cooled to  $-78^\circ$ , deposited the crude 4-acetyl-9-bromo-2-phenyl-4H-naphtho[1,2-e][1,3,4]thiadiazine (VI) (2.63 g) as a brown solid. The mother liquor was poured into water and the sticky solid (1.24 g) was collected, dried, and chromatographed on alumina (benzene as eluant) to give more naphthothiadiazine (0.41 g; total 3.04 g, 76%). Crystallisation from ethanol containing a little benzene gave yellow needles, m.p. 179—180° (Found: C, 57.7; H, 3.4; Br, 20.4; N, 6.8; S, 7.8.  $\text{C}_{19}\text{H}_{13}\text{BrN}_2\text{OS}$  requires C, 57.4; H, 3.3; Br, 20.2; N, 7.1; S, 8.1%).

*Reactions of Other Hydrazone Halides with Thioacetate Ion.*—Under the conditions employed in the foregoing synthesis of benzothiadiazines, none of the other hydrazone halides examined yielded benzothiadiazines.

In two cases, hydrazone sulphides were isolated. Compound (If) (3.25 g) and potassium thioacetate (2.30 g), refluxed for 4 h in acetonitrile and filtered whilst hot, gave a solid which was not completely soluble in water. The insoluble portion (0.23 g, 11%) was compound (IIIf), m.p. 182—183° (decomp.) (after crystallisation), identical with the foregoing sample. The reaction filtrate contained (IIIf) and other materials, but apparently no thiadiazine.

Compound (Ii) (4.30 g) similarly gave compound (IIi) (0.25 g, 7%), m.p. 196—198° (decomp.) (after crystallisation), identical with the foregoing sample.

Compounds (Ic and d), (I;  $X = Y = \text{Br}$ ,  $Z = \text{NO}_2$ ), and (I;  $X = Z = \text{Br}$ ,  $Y = \text{NO}_2$ ) gave mixtures rendered intractable by extensive decomposition.

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