Synthesis of 1*H*-4,1,2-Benzothiadiazines † from Substituted *N*-Acetyl-*N*-aryl-*N'*-thioaroylhydrazines

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Treatment of *N*-acetyl-*N*-aryl-*N'*-thioaroylhydrazines, in which the *N*-aryl group is 2,4-disubstituted, with triethylamine in refluxing acetonitrile gives 6-substituted 1-acetyl-3-aryl-1*H*-4,1,2-benzothiadiazines in cases where the displaceable 2-substituent is bromine, fluorine, or iodine and the 4-substituent is electron-attracting; the synthesis fails when the 2-substituent is chlorine.

Two problems recur in the synthesis of 1*H*-4,1,2-benzothiadiazines from appropriately substituted hydrazonoyl halides and thioacetate ion at elevated temperatures. First, the intermediate hydrazonoyl thioacetate may undergo deacylation, followed by further reaction with hydrazonoyl halide, to give the hydrazonoyl sulphide [equation (i)]. Second, isomerisation of the hydrazonoyl thioacetate to the *N*-acetyl-*N*-aryl-*N'*-thiobenzoylhydrazine leads, under the reaction conditions, to accumulation of the latter compound and its decomposition products [equation (ii)]. Other side reactions occur in some cases, further reducing the yield of

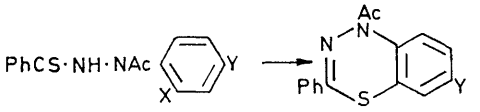
$$AcSCPh{=}N{\cdot}NHAr \longrightarrow {}^{-}SCPh{=}N{\cdot}NHAr \longrightarrow S(CPh{=}N{\cdot}NHAr)_2 \quad (i)$$

$$AcSCPh{=}N{\cdot}NHAr \longrightarrow SCPh{\cdot}NH{\cdot}NAcAr \quad (ii)$$

† The Editor regrets that this ring system was incorrectly named as 4*H*-1,3,4-benzothiadiazine in refs. 1—3, and apologises for any confusion caused.

[1] I. T. Barnish, P. D. Callaghan, and M. S. Gibson, *J.C.S. Perkin I*, 1974, 215.
[2] P. D. Callaghan and M. S. Gibson, *J. Chem. Soc.* (*C*), 1970, 2106.
[3] I. T. Barnish and M. S. Gibson, *J. Chem. Soc.* (*C*), 1970, 854.

thiadiazine.[1] These difficulties are largely circumvented in a synthesis of 1*H*-4,1,2-benzothiadiazines from *N*-acetyl-*N*-aryl-*N'*-thiobenzoylhydrazines described here.



(1) (2)

Two methods were employed for the preparation of the desired acetyl-thiohydrazides, but both methods gave products that were difficult to purify. Treatment of hydrazonoyl halides with thioacetate ion in acetonitrile at room temperature gave the hydrazonoyl sulphide and the *N*-acetyl-*N*-aryl-*N'*-thiobenzoylhydrazine in variable amounts, but the more soluble acetyl-thiohydrazide could normally be separated from the hydrazonoyl sulphide (and halide) without great difficulty.[2] Alternatively, the arylhydrazine was treated with carboxymethyl dithiobenzoate in alkaline solution to yield the *N'*-thiobenzoyl derivative,[4] which was then acetylated. The arylhydrazines of interest were mostly 2,4-disubstituted and it was often necessary to conduct thiobenzoylation in warm or hot solution. Although yields were good, the thiohydrazides were sometimes difficult to purify,[4] because of the persistence of coloured impurities. Acetylation gave *N*-acetyl derivatives which were identified with the corresponding products from the hydrazonoyl halide–thioacetate ion reactions in a number of cases. All these *N*-acetyl derivatives showed (amide) carbonyl i.r. absorption near 1 670 cm^{-1}. By contrast, acetic anhydride–triethylamine converted *N*-methyl-*N*-phenyl-*N'*-thiobenzoylhydrazine into a labile acetyl derivative showing carbonyl i.r. absorption at 1 710 cm^{-1}; this compound was readily deacetylated to the original thiohydrazide in warm ethanol and is presumably the *S*-acetyl derivative (hydrazonoyl thioacetate), acetylation having occurred at the more nucleophilic sulphur atom. In one experiment an *N*-acetyl-thiohydrazide was readily hydrolysed under alkaline conditions, possibly owing to deprotonation, equilibration with the hydrazonoyl thioacetate, and rapid hydrolysis of the latter.

The mass spectra of *N*-acetyl-*N*-aryl-*N'*-thiobenzoylhydrazines show molecular ion peaks of low intensity, with the main features of the spectra derived from fragmentation of a dehydration product which is probably produced thermally. Significant fragmentations of the molecular ions corresponding to loss of PhCNS or of the substituent X (when X is bromine or iodine) are also apparent. For *N*-acetyl-*N*-aryl-*N'*-benzoylhydrazines, major fragmentations of the molecular ions correspond to loss of PhCO or of CH_2CO; dehydration is of minor significance.

In seeking conditions for cyclization to thiadiazines, compound (1; X = Y = Br) was first treated with potassium thioacetate in boiling acetonitrile, *i.e.* under conditions used previously with hydrazonoyl halides. The thiadiazine was formed, but only in 15% yield. However, use of triethylamine in acetonitrile boosted this yield to 68%. Similar conversions were carried out to give the thiadiazines (2; Y = F, I, CF_3, SO_2·NMe_2, or CN) in yields which in all cases were higher than those obtained from corresponding reactions of hydrazonoyl halides with thioacetate ion; indeed compound (2; Y = SO_2·NMe_2) was not available by the latter method. No thiadiazine was produced from compound (1; X = Cl, Y = I); instead, the triethylammonium salt was formed. A similar limitation has been noted in the hydrazonoyl halide–thioacetate route for cases where the 2-substituent is chlorine.[3]

The option of eliminating the penultimate step in this thiadiazine synthesis by acetylating the thiohydrazide in the presence of triethylamine was finally considered. Thiohydrazide anion should be converted into the hydrazonoyl thioacetate and thence by *S*→*N*-acetyl migration and ring closure into the thiadiazine. Compounds (2; Y = Br or I) were prepared in moderate yield in this way; uncyclized acetyl-thiohydrazides were present in the reaction mixtures.

The new methods offer alternative modes of 1*H*-4,1,2-benzothiadiazine synthesis. The choice of displaceable halogen appears less crucial than in the previous method, but the presence of a second, electron-attracting substituent (at C-4) still seems to be required.

EXPERIMENTAL

Mass spectra were measured on an A.E.I. MS-902 instrument at 70 eV and source temperature 150—200 °C; samples were introduced on direct insertion probes.

Because of purification problems, all the *N*-acetyl-*N*-aryl-*N'*-thioaroylhydrazines were identified by reference to i.r. and mass spectral data and were correlated (m.p., t.l.c.), where possible, with previously prepared samples; all known thiadiazines were correlated with authentic samples.

Light petroleum refers to the fraction b.p. 60—90°.

Anilines.—(i) Bromine (20.0 g) in glacial acetic acid (50 ml) was added during 70 min to a stirred suspension of *p*-dimethylsulphamoylaniline [5] (25.0 g) in acetic acid (300 ml) at 16 °C (external cooling). Stirring was continued for 90 min and the precipitate (7.0 g, 16%) was collected; crystallization from ethanol gave *2,6-dibromo-4-dimethylsulphamoylaniline* as needles, m.p. 185—186° (Found: C, 27.0; H, 2.9; Br, 44.9; N, 7.6. $C_8H_{10}Br_2N_2OS$ requires C, 26.8; H, 2.8; Br, 44.7; N, 7.8%). The filtrate was poured into water (600 ml) and the solid (20.5 g, 59%) was collected; crystallization from ethanol gave *2-bromo-4-dimethylsulphamoylaniline* as needles, m.p. 151—152° (Found: C, 34.7; H, 4.2; Br, 28.8; N, 9.7. $C_8H_{11}BrN_2O_2S$ requires C, 34.4; H, 3.9; Br, 28.7; N, 10.0%).

(ii) Sodium hydroxide (2.0 g) in water (10 ml) was added during 4 h to a refluxing mixture of 3-bromo-4-nitrophenol [6] (8.53 g), n-butanol (40 ml), ethyl iodide (10 ml), and water (10 ml). Refluxing was continued for a further 4 h and the orange solution was then poured into hot water with vigorous

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

[5] K. Ganapati, *J. Indian Chem. Soc.*, 1938, **15**, 525.

[6] H. H. Hodgson and F. H. Moore, *J. Chem. Soc.*, 1926, 155.

stirring; ethanol (20 ml) was added as the solution cooled to prevent the nitro-ether separating as an oil. Crystallization of the solid from aqueous ethanol containing a small amount of sodium hydroxide gave cream needles (8.65 g, 90%), m.p. 46.5—48°.

The nitro-ether (4.96 g) in ethanol (30 ml) and concentrated hydrochloric acid (1 ml) was stirred and refluxed with iron powder (3.0 g) for 4.5 h. The mixture was basified with aqueous sodium hydroxide and then distilled in steam, the initial ethanol-rich distillate being discarded. 2-Bromo-4-ethoxyaniline was obtained as an oil (3.8 g, 88%); a sample treated with acetic anhydride gave the *acetyl derivative* as prisms, m.p. 94—95° (from aqueous ethanol) (Found: C, 46.5; H, 4.6; N, 5.4. $C_{10}H_{12}BrNO_2$ requires C, 46.5; H, 4.7; N, 5.4%).

5-Bromo-2-nitrophenol,[6] similarly treated, gave the nitro-ether (78%; phenol recovered, 15%), m.p. 80—81.5° (lit.,[7] 79.5—80.5°), and thence the aniline (90%); acetyl derivative, m.p. 120—120.5° (lit.,[7] 118—119°).

Arylhydrazines.—These were prepared by diazotization of the aniline and reduction with tin(II) chloride in the usual way.[1]

2-Bromo-4-dimethylsulphamoylaniline (20.5 g) gave (2-*bromo-4-dimethylsulphamoylphenyl)hydrazine* (18.0 g, 83%) as prisms, m.p. 167—168° (from ethanol) (Found: C, 32.9; H, 4.1; Br, 27.2; N, 14.0. $C_8H_{12}BrN_3O_2S$ requires C, 32.7; H, 4.1; Br, 27.2; N, 14.3%); m-*nitrobenzylidene derivative*, orange-yellow needles, m.p. 225.5—226° (from benzene–dimethylformamide) (Found: C, 42.4; H, 3.6; Br, 18.8; N, 13.0. $C_{15}H_{15}BrN_4O_4S$ requires C, 42.2; H, 3.5; Br, 18.7; N, 13.1%).

2-Bromo-4-ethoxyaniline (6.3 g) gave the hydrazine as needles (3.45 g, 49%), m.p. 81—82° (from cyclohexane); p-*nitrobenzylidene derivative*, orange prisms, m.p. 143—145° (from ethanol–ethyl acetate) (Found: C, 49.4; H, 3.9; Br, 21.9. $C_{15}H_{14}BrN_3O_3$ requires C, 49.5; H, 3.9; Br, 22.0%).

4-Bromo-2-ethoxyaniline (5.7 g) gave the hydrazine as buff needles (4.5 g, 73%), m.p. 106—107° (from cyclohexane); p-*nitrobenzylidene derivative*, maroon needles, m.p. 186—187° (from ethanol–ethyl acetate) (Found: C, 49.2; H, 3.8; N, 11.6%); *acetyl derivative*, prisms, m.p. 170—172° (from aqueous ethanol) (Found: C, 43.8; H, 4.7; N, 10.5. $C_{10}H_{13}BrN_2O_2$ requires C, 44.0; H, 4.8; N, 10.3%).

N-*Acetyl*-N-*aryl*-N′-*thioaroylhydrazines* (*from Hydrazonoyl Halides*).—The hydrazonoyl halide was treated with potassium thioacetate (2 equiv., except where noted below) in acetonitrile at room temperature in the manner previously described;[2] reference samples of hydrazonoyl sulphides were prepared, as required, from the hydrazonoyl halide and sodium sulphide nonahydrate in acetonitrile.[3]

N-α-Bromobenzylidene-*N*′-(2,4-difluorophenyl)hydrazine (3.11 g) gave the hydrazonoyl sulphide (0.08 g, 3%) and, from the reaction liquor, N-*acetyl*-N-(2,4-*difluorophenyl*)-N′-*thiobenzoylhydrazine* (2.5 g, 82%), which crystallized from benzene as yellow prisms, m.p. 152—153° (decomp.) (Found: C, 59.3; H, 4.1; N, 9.1. $C_{15}H_{12}F_2N_2OS$ requires C, 58.8; H, 3.9; N, 9.2%); *m/e* 306 (M^+, 2%), 288 (306 − H_2O; 92), 287 (19), 269 (100), 264 (306 − CH_2CO, 2), 185 (32), 171 (306 − PhCNS, 35), 166 (13); 153 ($F_2C_6H_3NC_2H_2$, 13), 140 ($F_2C_6H_3NCH$, 42), 139 ($F_2C_6H_3NC$, 14), 135 (PhCNS, 21), 129 (67), 127 ($F_2C_6H_3N$, 88), 113 ($F_2C_6H_3$, 25), 112 ($F_2C_6H_2$, 6), 103 (PhCN, 65), 102 ($C_5H_4F_2$, 25), and 76 (C_6H_4; 88); metastable ions corresponding to the transitions 288 ⟶ 287 (loss of H); 288 ⟶ 269 (loss of F) and 269 ⟶ 166 (loss of PhCN), 288 ⟶ 185 (loss of PhCN); 288 ⟶ 135 (PhCNS), 135 ⟶ 103 (loss of S), and 103 ⟶ 76 (loss of HCN); 171 ⟶ 129 (loss of CH_2CO) and 129 ⟶ 102 (loss of HCN); 139 ⟶ 112 (loss of HCN).

N-α-Bromobenzylidene-*N*′-(2-bromo-4-trifluoromethylphenyl)hydrazine (4.2 g) gave, after separation of the hydrazonoyl sulphide, N-*acetyl*-N-(2-*bromo-4-trifluoromethylphenyl*)-N′-*thiobenzoylhydrazine* (2.05 g, 49%) as yellow needles, m.p. 152—153° (decomp.) (from benzene) (Found: Br, 19.2; N, 6.7; C, H discrepant. $C_{16}H_{12}BrF_3N_2OS$ requires Br, 19.2; N, 6.7%).

N-α-Chlorobenzylidene-*N*′-(2-fluorophenyl)hydrazine (5.0 g) gave the hydrazonoyl sulphide (50 mg, 1%) and the acetyl-thiohydrazide (5.06 g, 93%), identical with reference samples.

N-α-Chlorobenzylidene-*N*′-phenylhydrazine (2.3 g) gave the acetyl-thiohydrazide (1.76 g, 56%) as yellow prisms, m.p. 147—149° (decomp.) (from benzene) [lit.,[8] 154° (decomp.)]. The mother liquors contained traces of hydrazonoyl sulphide, identified by correlation (t.l.c.) with a reference sample, m.p. 168—169°.

N-α-Bromobenzylidene-*N*′-(2,4-dibromophenyl)hydrazine (5.0 g) gave the acetyl-thiohydrazide (2.85 g, 58%); crystallization from benzene gave yellow needles, m.p. 161—162° (decomp.), but the compound could not be obtained analytically pure. The hydrazonoyl sulphide was present in the mother liquors.

In the following cases, sodium thioacetate (1 equiv.) replaced the potassium salt.

N-(α-Bromo-*p*-chlorobenzylidene)-*N*′-(2,4-dibromophenyl)hydrazine (4.67 g) gave the *acetyl-thiohydrazide* (3.9 g, 84%) as yellow needles, m.p. 168° (decomp.) (from benzene) (Found: C, 39.0; H, 2.6; N, 5.9. $C_{15}H_{11}Br_2ClN_2OS$ requires C, 38.9; H, 2.4; N, 6.1%).

N-(α-Bromo-*p*-methoxybenzylidene)-*N*′-(2,4-dibromophenyl)hydrazine (4.6 g) gave, in dimethylformamide (30 ml) as solvent, the acetyl-thiohydrazide (4.0 g, 87%); crystallization from benzene gave yellow prisms, m.p. 160—161° (reddening above 120°), but the compound could not be obtained analytically pure.

N-*Acetyl*-N-*aryl*-N′-*thiobenzoylhydrazines* (*from Arylhydrazines*).—The arylhydrazine was added to a stirred solution of carboxymethyl dithiobenzoate (1 equiv.) in M-sodium hydroxide, the pH being maintained in the range 9—10 throughout the reaction. Of the compounds examined, those bearing an *o*-fluoro-substituent reacted satisfactorily at room temperature; otherwise reaction was effected at 40 °C for 1 h, or on a steam-bath for 10 min, followed by gradual cooling to room temperature, after which the product was precipitated by addition of acetic acid to pH 7. The crude thiohydrazides (90—95%), though reasonably pure (t.l.c.), were contaminated with coloured impurities which were very difficult to remove. In two cases, analytical samples were prepared. Otherwise, for economy, the crude thiohydrazides were treated with acetic anhydride in acetic acid or acetonitrile at room temperature for 20 min (or shorter time if warmed); precipitation with water then gave the acetyl derivatives (75—85%), which were found to retain impurities after crystallization (t.l.c.). The slightly impure acetyl derivatives were converted into thiadiazines as described later.

Thus 2-bromo-4-ethoxyphenylhydrazine (3.35 g) gave

[7] A. Mangini, *Gazzetta*, 1936, **66**, 675.
[8] G. Corsi, *Ann. Chim.* (*Italy*), 1966, **56**, 1203.

N-(*2-bromo-4-ethoxyphenyl*)-N′-*thiobenzoylhydrazine* (4.85 g), which crystallized from benzene–light petroleum as pale yellow needles (3.46 g), m.p. 106—108° (Found: C, 51.2; H, 4.2; S, 9.2. $C_{15}H_{15}BrN_2OS$ requires C, 51.3; H, 4.3; S, 9.1%); *acetyl derivative*, yellow needles, m.p. 173—174° (decomp.) (from ethanol) (Found: C, 51.8; H, 4.5; Br, 20.8. $C_{17}H_{17}BrN_2O_2S$ requires C, 51.9; H, 4.3; Br, 20.4%).

4-Bromo-2-ethoxyphenylhydrazine (4.2 g) similarly gave the *thiohydrazide* (5.3 g), which crystallized from benzene–light petroleum as pale yellow needles (3.2 g), m.p. 145—146° (decomp.) (Found: C, 51.2; H, 4.3; N, 7.9%); *acetyl derivative*, yellow needles, m.p. 153—157° (decomp.) (from benzene–light petroleum) (Found: C, 51.7; H, 4.3; N, 7.2%).

Similarly prepared were *N*-acetyl-*N*-(2,4-difluorophenyl)-*N*′-thiobenzoylhydrazine, m.p. 149—152° (decomp.) (from benzene–light petroleum); *N*-acetyl-*N*-(2,4-dibromophenyl)-*N*′-thiobenzoylhydrazine, m.p. 164—165° (decomp.) (from benzene); *N*-acetyl-*N*-(2,4-di-iodophenyl)-*N*′-thiobenzoylhydrazine, m.p. 160—161° (decomp.) (from benzene) [lit.,[2] 158.5—160.5° (decomp.)]; *N*-acetyl-*N*-(2-chloro-4-iodophenyl)-*N*′-thiobenzoylhydrazine, m.p. 173—175° (decomp.) (from ethanol) [lit.,[2] 175—176° (decomp.)]; *N*-acetyl-*N*-(2-bromo-4-iodophenyl)-*N*′-thiobenzoylhydrazine, m.p. 176—177° (decomp.) (from benzene) [lit.,[2] 174—176° (decomp.)]; *N*-acetyl-*N*-(2-bromo-4-dimethylsulphamoylphenyl)-*N*′-thiobenzoylhydrazine, m.p. 100—105° (decomp.) (crude).

Compound (1; X = Y = F) (1.0 g) was refluxed with ethanol (10 ml) and 40% sodium hydroxide solution (2 ml) for 1 h. When cool, the solution was poured into water and acidified with acetic acid. The precipitated solid (0.45 g, 52%), m.p. 126—130°, was identified (i.r. spectrum, t.l.c.) as *N*-(2,4-difluorophenyl)-*N*′-thiobenzoylhydrazine.

N-*Methyl*-N-*phenyl*-N′-*thiobenzoylhydrazine*.— *N*-Methyl-*N*-phenylhydrazine (10.6 g) was added to a stirred solution of carboxymethyl dithiobenzoate (10.6 g) in M-potassium hydroxide solution (75 ml) during 10 min at room temperature; gradual addition of M-potassium hydroxide maintained the pH near 10. The mixture was warmed to 70 °C and allowed to cool slowly. The pH was adjusted to 6 (acetic acid) and the mixture was extracted with ether. The ether solution was washed with sodium hydrogen carbonate solution and water, dried, and evaporated to give the thiohydrazide as an oil which crystallized from hexane as yellow needles (6.1 g, 50%), m.p. 94—95° (lit.,[9] 95.5—96.5°).

The thiohydrazide (1.0 g) was boiled with acetic anhydride (15 ml) and triethylamine (15 ml) for 10 min. Isolated with ether, the acetyl derivative was obtained as an orange-yellow gum which could not be crystallized; treatment with warm ethanol discharged the orange colour, regenerating the thiohydrazide (t.l.c.).

N-*Acetyl*-N′-*benzoyl*-N-(*4-bromo-2-iodophenyl*)*hydrazine*.— This acetyl-hydrazide, prepared from the hydrazonoyl chloride (4.35 g) and anhydrous sodium acetate (1.64 g) in acetonitrile (120 ml) (4 h reflux), crystallized from ethanol as prisms (3.2 g, 70%), m.p. 184.5—185.5° (Found: C, 39.4; H, 2.5; N, 6.2. $C_{15}H_{12}BrIN_2O_2$ requires C, 39.2; H, 2.6; N, 6.1%); *m/e* 460/458 (M^+), 418/416 ($M^+ - CH_2CO$), 341/339 ($BrIC_6H_3NHAc$), 332/330 ($M^+ - HI$), 299/297 ($BrIC_6H_3NH_2$), 290/288, 214/212, 172/170 ($BrC_6H_3NH_2$), 105 (PhCO), 103 (PhCN), and 77; low intensity peaks were discernible at 442/440 ($C_{15}H_{10}BrIN_2O$).

Preparation of Benzothiadiazines from N-*Acetyl*-N-*aryl*-N′-*thioaroylhydrazines*.—As general procedure, the acetyl derivative was refluxed with triethylamine (3.6 g) in acetonitrile (15 ml) for 2—4 h. In some cases the thiadiazine crystallized on cooling and was supplemented by concentrating the reaction liquor; otherwise the reaction mixture was diluted with water and the product was collected and crystallized.

N-Acetyl-*N*-(2,4-dibromophenyl)-*N*′-thiobenzoylhydrazine (1.0 g) gave the 6-bromothiadiazine (0.55 g, 68%), m.p. 180—182° (lit.,[3] 181—183°).

N-Acetyl-*N*-(2,4-difluorophenyl)-*N*′-thiobenzoylhydrazine (0.72 g) gave the 6-fluorothiadiazine (0.56 g, 83%), m.p. 178—179° (lit.,[3] 183°).

N-Acetyl-*N*-(2,4-di-iodophenyl)-*N*′-thiobenzoylhydrazine (1.22 g) gave the 6-iodothiadiazine (0.83 g, 90%), m.p. 169—171° (lit.,[2] 170—171°).

N-Acetyl-*N*-(2-bromo-4-trifluoromethylphenyl)-*N*′-thiobenzoylhydrazine (1.06 g) gave after 2 h, the 6-trifluoromethylthiadiazine (0.39 g, 43%), m.p. 125—125.5° (lit.,[1] 125—125.5°); some starting material was detected (t.l.c.) in mother liquors.

N-Acetyl-*N*-(2-bromo-4-dimethylsulphamoylphenyl)-*N*′-thiobenzoylhydrazine (1.07 g) gave 1-*acetyl*-6-*dimethylsulphamoyl*-3-*phenyl*-1H-4,1,2-*benzothiadiazine* (0.70 g, 80%) as cream prisms, m.p. 227—230° (from acetonitrile) (Found: C, 54.7; H, 4.7; N, 11.3. $C_{17}H_{17}N_3O_3S$ requires C, 54.4; H, 4.5; N, 11.2%).

N-α-Bromobenzylidene-*N*′-(2-bromo-4-cyanophenyl)-hydrazine (1.90 g), potassium thioacetate (0.98 g), and acetonitrile (50 ml) were stirred together at −5 °C for 1.25 h. The solid was filtered off, washed with water, and dried to give the hydrazonoyl sulphide (0.32 g, 20%), m.p. 224—225° (from benzene), identical with a reference sample. The filtrate, which contained the needed acetyl derivative (t.l.c.) although it could not be obtained crystalline, was diluted with triethylamine (15 ml) and refluxed for 3 h to give the thiadiazine-6-carbonitrile (0.45 g, *ca.* 31%), m.p. 190—191° (lit.,[1] 188—188.5°).

N-Acetyl-*N*-(2-chloro-4-iodophenyl)-*N*′-thiobenzoylhydrazine (1.0 g) deposited the triethylammonium salt (0.45 g), m.p. 121—125° (decomp., with evolution of triethylamine), under the above conditions; crystallization from ethanol regenerated the acetyl derivative. No thiadiazine was apparently formed (t.l.c.).

In the following experiments, the acetyl derivative was refluxed with triethylamine (15 ml) and acetonitrile (15 ml) for 2 h; the mixture was poured into 5% acetic acid and the product filtered off.

N-Acetyl-*N*-(2,4-dibromophenyl)-*N*′-*p*-methoxythiobenzoylhydrazine (2.3 g) gave 1-*acetyl*-6-*bromo*-3-p-*methoxyphenyl*-1H-4,1,2-*benzothiadiazine* (1.7 g, 90%) as needles, m.p. 199—200° (from acetonitrile) (Found: C, 51.0; H, 3.4; Br, 21.2. $C_{16}H_{13}BrN_2O_2S$ requires C, 50.9; H, 3.5; Br, 21.2%). The thiadiazine (3.77 g), ethanol (100 ml), and concentrated hydrochloric acid (50 ml) were refluxed for 2 h and the mixture was then poured into water. The precipitated solid was dried and crystallized from hexane–toluene to give the 1-*unsubstituted thiadiazine* as yellow plates (1.4 g, 42%), m.p. 157° (Found: C, 50.4; H, 3.3. $C_{14}H_{11}BrN_2OS$ requires C, 50.3; H, 3.3%).

N-Acetyl-*N*′-*p*-chlorothiobenzoyl-*N*-(2,4-dibromophenyl)-hydrazine (4.62 g) gave the corresponding *thiadiazine* (2.5 g, 66%), m.p. 176—179°; a yellow trace impurity could not be removed by chromatography or crystallization from ethanol–ethyl acetate or hexane–toluene (Found: C, 47.2; H, 2.6;

[9] W. Walter and M. Radke, *Annalen*, 1970, **739**, 201.

N, 7.3. $C_{15}H_{10}BrClN_2OS$ requires C, 47.2; H, 2.6; N, 7.3%). Acidic hydrolysis of the thiadiazine, as above, gave the 1-*unsubstituted thiadiazine* (48%) as pale green needles, m.p. 145—147° (Found: C, 46.6; H, 2.5; N, 8.5. $C_{13}H_8BrClN_2S$ requires C, 46.0; H, 2.4; N, 8.3%).

N-Acetyl-*N*-(2-fluorophenyl)-*N'*-thiobenzoylhydrazine was recovered from this treatment, contaminated with decomposition products and the thiadiazine (t.l.c., i.r.); *N*-acetyl-*N*-(2-bromo-4-ethoxyphenyl)-*N'*-thiobenzoylhydrazine and the 4-bromo-2-ethoxy-isomer were more extensively decomposed, though t.l.c. showed that each compound was still present.

Preparation of Benzothiadiazines from N-*Aryl*-N'-*thiobenzoylhydrazines*. Acetic anhydride (0.68 g) was added to a boiling solution of *N*-(2-fluoro-4-iodophenyl)-*N'*-thiobenzoylhydrazine (1.5 g) and triethylamine (0.82 g) in acetonitrile (5.5 ml). After 45 min the solution was cooled, and the iodothiadiazine (0.9 g) crystallized; recrystallization from ethanol gave needles (0.62 g, 38%), m.p. 166—169°. The reaction liquor contained the acetyl derivative of the thiohydrazide, and decomposition products.

N-(2,4-Dibromophenyl)-*N'*-thiobenzoylhydrazine (2.0 g), triethylamine (0.53 g), acetonitrile (6 ml), and acetic anhydride (1.06 g) similarly gave a crystalline deposit (0.95 g) which on fractional crystallization from ethanol gave the bromothiadiazine (0.15 g, 8%), m.p. 176—178°, and the acetyl derivative of the thiohydrazide (0.8 g, *ca.* 36%); the reaction liquor contained more of this acetyl derivative, and decomposition products.

N-(2,4-Di-iodophenyl)-*N'*-thiobenzoylhydrazine was recovered almost quantitatively, though in slightly less pure condition, from a similar experiment from which acetic anhydride was omitted; acetylation then gave the acetyl derivative, containing possibly (t.l.c.) a trace of the thiadiazine (2; X = I).

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