The Rearrangement of Aryl Thiohydrazonates

ARTHUR J. ELLIOTT
Department of Chemistry, McMaster University, Hamilton, Ontario L8S 4M1
AND
PATRICK D. CALLAGHAN, MARTIN S. GIBSON, AND STEVEN T. NEMETH
Department of Chemistry, Brock University, St. Catharines, Ontario L2S 3A1[1]

ARTHUR J. ELLIOTT, PATRICK D. CALLAGHAN, MARTIN S. GIBSON, and STEVEN T. NEMETH. Can. J. Chem. **53**, 1484 (1975).

Rearrangement and cyclization of a series of *p*-nitrophenyl and heteroaryl thiohydrazonates ArSCAr′ = $NNHC_6H_3XY(2,4)$, where the displaced substituent X is Br or F and the remaining substituent Y is Br or NO_2, occurs under suitable basic conditions to the corresponding 7-substituted 2-aryl-4-*p*-nitrophenyl- and -4-heteroaryl-4*H*-1,3,4-benzothiadiazines, *e.g.* **13** → **19**. Under these or suitable acidic conditions, the 4,6-dimethyl-2-pyrimidinyl thiohydrazonate rearranges to the thiohydrazide $Ar'CSNHNArC_6H_3XY(2,4)$, apparently the first case of thiohydrazonate-thiohydrazide rearrangement; such acidic treatment produces cleavage of some other heteroaryl thiohydrazonates.

Independent syntheses of two of the 4-heteroaryl-substituted benzothiadiazines are reported.

ARTHUR J. ELLIOTT, PATRICK D. CALLAGHAN, MARTIN S. GIBSON et STEVEN T. NEMETH. Can. J. Chem. **53**, 1484 (1975).

Le réarrangement et la cyclisation d'une série de thiohydrazonates de *p*-nitrophényles et d'hétéroaryles ArSCAr′ = $NNHC_6H_3XY(2,4)$ dans lesquels le substituant déplacé X est Br ou F et l'autre substituant Y est Br ou NO_2 se produit dans des conditions basiques appropriées pour conduire aux aryl-2 *p*-nitrophényl-4 et aux hétéroaryl-4 4*H*-benzothiadiazines-1,3,4 substituées en position 7, *e.g.* **13** donne **19**. Dans ces conditions et/ou dans des conditions acides appropriées, le thiohydrazonate de diméthyl-4,6 pyrimidinyle-2 se réarrange pour fournir le thiohydrazide $Ar'CSNHNArC_6H_3XY(2,4)$ et ceci est apparamment le premier cas d'un réarrangement thiohydrazonate en thiohydrazide; un tel traitement acide produit généralement une coupure d'autres thiohydrazonates d'hétéroaryles.

On rapporte des synthèses indépendantes de deux des benzothiadiazines substitués par des hétéroaryles-4. [Traduit par le journal]

Huisgen *et al.* (1) have noted that whereas thermolysis of 2,5-diphenyltetrazole in phenol gave *N′*,*N′*-diphenylbenzohydrazide, the corresponding reaction in thiophenol gave phenyl *N*-phenyl(thiobenzohydrazonate) (**1**); the corresponding *p*-tolyl thiohydrazonate was prepared similarly. Both thiohydrazonates were stable under the conditions of formation at 160–170°. Thermal rearrangement of **1** to *N′*,*N′*-diphenyl-(thiobenzohydrazide) (**2**) under conditions where oxygen analogs (aryl hydrazonates) rearrange satisfactorily to *N′*,*N′*-diarylhydrazides was attempted later by Hegarty *et al.* (2) but without success.

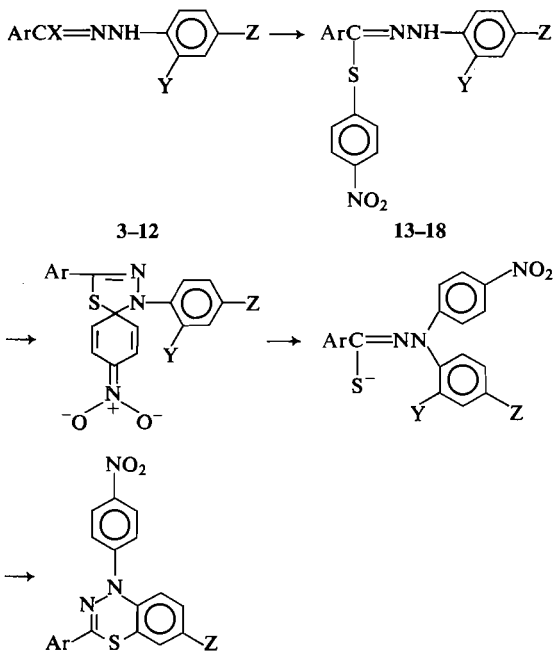
PhC(SPh)=NNHPh — **1**

$PhCSNHNPh_2$ — **2**

Our approach to the problem of rearrangement of aryl thiohydrazonates has involved two considerations: (*i*) the *S*-aryl ring should be made electron deficient by substitution and/or incorporation of heteroatom(s); (*ii*) rearrangement should be further facilitated by employing basic conditions to increase the nucleophilicity of the terminal nitrogen of the hydrazonyl system or, where the *S*-aryl group is basic, by employing acidic conditions to increase the electrophilicity of that group. In most cases substituents in the *N*-aryl group were chosen with a view to synthesis of 4*H*-1,3,4-benzothiadiazine derivatives as indicated below.

Initially the hydrazonyl bromide **3** was treated with *p*-nitrothiophenol in ethanol (EtOH) in presence of triethylamine (NEt_3) to give the thiohydrazonate **13**. By contrast with the corresponding reaction of **3** with thioacetate ion, there was apparently no conversion of **3** to hydrazonyl sulfide (3); also, neither *p*,*p*-dinitrodiphenyl sulfide nor *p*,*p*-dinitrodiphenyl disulfide was detected in the reaction mixture. Other

[1]Address for correspondence.



3, 13, 19	Ar = Ph; X = Z = Br; Y = F
4, 14	Ar = Ph; X = Y = Z = Br
5, 15, 20	Ar = *p*-$CH_3OC_6H_4$; X = Y = Z = Br
6, 16, 21	Ar = *p*-ClC_6H_4; X = Y = Z = Br
7, 17	Ar = Ph; X = Cl; Y = Br; Z = H
8	Ar = Ph; X = Y = Br; Z = SCN
9, 18, 22	Ar = 5-Bromo-2-thienyl; X = Y = Z = Br
10, 23	Ar = Ph; X = Y = Br; Z = NO_2
11	Ar = Ph; X = Cl; Y = Z = Br
12	Ar = Ph; X = Cl; Y = Z = H

SCHEME 1

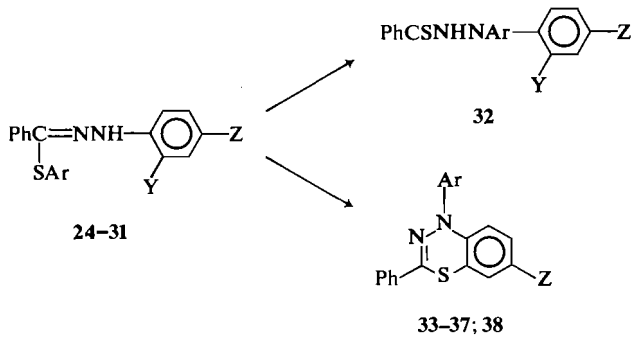
hydrazonyl halides were similarly converted to corresponding *p*-nitrophenyl thiohydrazonates **14–18**, except in the case of **8** where competing reaction of *p*-nitrothiophenoxide ion with the thiocyanato group occurred leading to a complex mixture, possibly containing disulfides (4), from which a small yield of **17** was isolated (Scheme 1). The structures of the thiohydrazonates were confirmed by examination of mass spectra which revealed characteristic loss of the elements of *p*-nitrothiophenol from the molecular ions (5).

When the thiohydrazonate **13** was treated with EtOH–NEt_3 at reflux, the product isolated was not the isomeric *N'*,*N'*-diaryl(thiobenzohydrazide) (product of rearrangement) but the thiadiazine **19** (product of rearrangement and cyclization). Thiohydrazonates **15**, **16**, and **18** similarly gave thiadiazines **20**, **21**, and **22**, respectively, but no thiadiazine was obtained from **17**, a result consistent with earlier observations (3). The primary product from **10** and *p*-nitrothiophenol, presumably the thiohydrazonate, similarly was converted to **23**, whilst the conversion of **14** to **19**, sluggish in EtOH–NEt_3, was achieved readily by employing the perhaps unnecessarily forcing conditions of reflux with sodium hydroxide and NEt_3 in dimethylformamide (DMF).

These reactions differ from the rearrangement of aryl hydrazonates which lead to *N'*,*N'*-diarylhydrazides (2, 5) and resemble rather those reactions of hydrazonyl halides with thioacetate ion in which a hydrazonyl thioacetate, presumed as intermediate, undergoes rearrangement and cyclization by displacement of transiently activated *o*-halogen to a 4-acetyl-4*H*-1,3,4-benzothiadiazine (3). In the absence of definite evidence for involvement of an intermediate *N'*,*N'*-diaryl(thiobenzohydrazide) in thiadiazine formation, it is reasonable to assume that such an intermediate is consumed as it is formed.

A group of heteroaryl thiohydrazonates (**24–29**, **30***a*, and **31***a*) was next prepared by treatment of **4** with (*i*) the appropriate thiol in EtOH–NEt_3 or (*ii*) the sodium salt of the thiol; **30***b* and **31***b* were prepared similarly from the appropriate thiols and hydrazonyl halides **3** and **12**, respectively (Scheme 2). As in the above preparations of *p*-nitrophenyl thiohydrazonates, no hydrazonyl sulfides were detected in the reaction mixtures. Also, as with the *p*-nitrophenyl analogs, loss of the elements of the heterocyclic thiol from the molecular ions was a characteristic feature of the mass spectra of these heteroaryl thiohydrazonates.

It had been reported that **1** undergoes hydrolysis to PhCONHNHPh in concentrated hydrochloric acid – methanol (1) and that the analogous hydrazonate behaves similarly (2). Such conditions should presumably be avoided for the heteroaryl thiohydrazonates if rearrangement is desired. After experimentation, it was noted that **16** and an analogous hydrazonate (**14**; O instead of S in formula) were stable in concentrated hydrochloric acid – benzene under certain conditions and this system was adopted for the work in hand. When the pyrimidinyl thiohydrazonate **24** was so treated, the isomeric thiohydrazide **32** was obtained in 55% yield, providing the first instance in this work of a

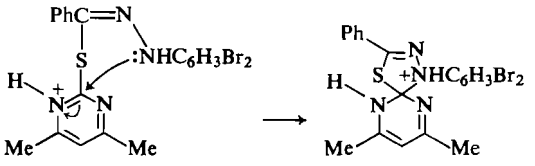


Y = Z = Br except for **30***b* (Y = F; Z = Br) and **31***b* (Y = Z = H)
24, **32** Ar = 4,6-Dimethyl-2-pyrimidinyl
25 Ar = 1-Phenyl-5-tetrazolyl
26, **33** Ar = 2-Quinoxalinyl
27, **34** Ar = 5-Nitro-2-pyridinyl
28 Ar = 2-Pyridinyl
29, **35** Ar = 4-Methyl-2-quinolinyl
30, **36** Ar = 2-Benzothiazolyl
31, **37** Ar = 2-Benzoxazolyl
38 Ar = H

SCHEME 2

thiohydrazonate → thiohydrazide rearrangement which was not complicated by subsequent reactions. However, with the tetrazolyl thiohydrazonate **25**, it was noted that acidic cleavage supervened to give the corresponding thiol and hydrazonyl chloride **11**, providing incidentally further evidence for structural assignment **25**; the presence of the hydrazide ($PhCONHNHC_6H_3Br_2$) was also indicated (t.l.c.), suggesting that some hydrolysis was occurring. Compound **25** could be reconstructed from the component thiol and **11** in EtOH–NEt_3. Acidic cleavage was also implicated in the more complex reaction of the quinoxalinyl thiohydrazonate **26** from which **11** was obtained, although none of the corresponding thiol was isolated. Compound **27** also gave a complex mixture under these conditions; no single product was isolated but there was some indication (p.m.r.) that the isomeric thiohydrazide was present. Compounds **28** and **29** were stable under these conditions.

The acid-catalyzed hydrolysis of hydrazonates has been interpreted in terms of protonation of the hydrazonate oxygen atom (2) and similar considerations can be applied to acidic cleavage and hydrolysis of thiohydrazonates, *i.e.* protonation of the thiohydrazonate sulfur atom and subsequent reaction involving chloride ion or water. However, with the present cases, alternative protonation of heteroatom(s) of the heteroaryl ring may occur, some of which would create a situation conducive to rearrangement, and the reaction course is presumably regulated by competition between these possibilities. The acid-catalyzed rearrangement **24** → **32** would thus proceed as follows:



Attention was next turned to the behavior of heteroaryl thiohydrazonates under basic conditions. In view of the above results with *p*-nitrophenyl analogs, it was considered likely that thiadiazines would result if S → N heteroaryl migration occurred. When the heteroaryl thiohydrazonates were treated with EtOH–NEt_3 at reflux, the corresponding thiadiazines were obtained in the following cases: **26** → **33**, **27** → **34**, **29** → **35**, **30***a* and *b* → **36**. With **30***a* there was evidence (t.l.c.) for the involvement of an intermediate, possibly the isomeric thiohydrazide, in the conversion to **36**. Under these reaction conditions, **24** rearranged to the thiohydrazide **32** after which decomposition slowly set in, whilst **25** was decomposed extensively. Unlike **27**, no reaction was observed with **28** and no reaction was observed with **31***a* or *b*, the latter having been chosen as a case where

any rearrangement could not be followed by thiadiazine formation. When treated with sodium hydroxide and NEt_3 in DMF, however, **31***a* gave **37** but the yield was poor owing to hydrolysis of the benzoxazole ring. Finally, the structures of two of the thiadiazines (**33** and **34**) were confirmed by alternative syntheses from **38** and 2-chloroquinoxaline and 2-chloro-5-nitropyridine, respectively.

It is interesting that so few instances of simple rearrangement of aryl thiohydrazonates to thiohydrazides have been observed but it would seem likely that more examples could be found along the lines of this work. It may be that in many cases equilibrium favors the aryl thiohydrazonate (unlike similar aryl hydrazonates) rather than the thiohydrazide under the conditions which have been employed and that thiadiazine formation constitutes a process for displacement of equilibrium. Regardless, however, of whether the thiohydrazide is involved as intermediate, the S → N aryl migration taking place in formation of thiadiazines can be seen as a Smiles-type rearrangement. For migrating heterocyclic rings, such rearrangements have been studied principally in the pyridine (6) and *s*-triazine (7) series, although there are clearly many other possibilities.

Experimental

Proton magnetic resonance spectra ($CDCl_3$) were recorded on Varian A-60 and T-60 spectrometers using tetramethylsilane as internal standard; the presence of exchangeable protons was confirmed by use of D_2O. Mass spectra were recorded on Hitachi Perkin-Elmer RMU-6A and AEI-MS902 spectrometers; data are quoted as *m/e* values for the lowest isotopic species, bromine excepted (^{81}Br and ^{79}Br).

Hydrazonyl halides were prepared by published methods (3, 5, 8), as were 4,6-dimethylpyrimidine-2-thiol (9), quinoxaline-2-thiol (10) (from 2-chloroquinoxaline (11)), and 5-nitropyridine-2-thiol (12).

DMF and NEt_3 were stored over NaOH for at least 4 days before use.

Preparation of p-Nitrophenyl Thiohydrazonates

As general procedure, the hydrazonyl halide (0.01 mol) and *p*-nitrothiophenol (0.01 mol) were stirred together in EtOH (25 ml) and NEt_3 (1 ml) at room temperature for 2 h; for **3** and **4** the quantities of EtOH and NEt_3 were 40 ml and 3 ml, respectively, and reaction time was 1 h. The product was filtered off, washed, dried, and purified by crystallization.

Compound **3** gave *p-nitrophenyl N-4-bromo-2-fluorophenyl(thiobenzohydrazonate)* (**13**) (3.0 g, 67%) as orange prisms, m.p. 153–155° (from benzene–ethanol); i.r. (Nujol) 3280 cm^{-1} (NH).

Anal. Calcd. for $C_{19}H_{13}BrFN_3O_2S$: C, 51.12; H, 2.91; Br, 17.94; N, 9.42. Found: C, 51.4; H, 3.1; Br, 18.0; N, 9.1.

Compound **4** gave **14** (4.5 g, 90%) as yellow plates, m.p. 173–175° (from benzene–ethanol).

Anal. Calcd. for $C_{19}H_{13}Br_2N_3O_2S$: C, 44.97; H, 2.56; N, 8.28; S, 6.31. Found: C, 45.23; H, 2.79; N, 8.56; S, 6.16.

Compound **5** gave **15** (3.1 g, 57%) as yellow needles, m.p. 164° (from ethanol); p.m.r. δ 9.1 (s, NH), 8.0 (A), and 7.0 (B) (A_2B_2q, J = 9.0 Hz), 8.25–7.3 (m, 7H), and 3.9 (s, 3H); mass spectrum (70 eV) *m/e* 539/537/535 (M^+), 457/455 (M^+ − HBr), 384/382/380 (M^+ − $NO_2C_6H_4SH$), 304/302, 278/276, 277/275, 252/250/248 ($Br_2C_6H_3NH$), 225/223/221, 198/196, 171/169, 170/168, 155 ($NO_2C_6H_4SH$), 151, 133, 90, and 63.

Anal. Calcd. for $C_{20}H_{15}Br_2N_3O_3S$: C, 44.70; H, 2.79; Br, 29.80. Found: C, 44.52; H, 2.68; Br, 29.83.

Compound **6** gave **16** (3.4 g, 63%) as yellow needles, m.p. 158–160° (from benzene–hexane).

Anal. Calcd. for $C_{19}H_{12}Br_2ClN_3O_2S$: C, 42.11; H, 2.22; N, 7.76. Found: C, 42.27; H, 2.25; N, 7.69.

Compound **7** gave **17** (2.62 g, 62%) as yellow needles, m.p. 159° (from ethanol).

Anal. Calcd. for $C_{19}H_{14}BrN_3O_2S$: C, 53.27; H, 3.27; N, 9.81. Found: C, 53.7; H, 3.4; N, 10.0.

Compound **8** (2.09 g, 0.005 mol) reacted under the normal conditions with evolution of HCN to give an orange-yellow solid. Chromatography on Florisil and elution with hexane–ether (4:1) gave **17** which crystallized from EtOH as yellow needles (0.4 g, 18%), m.p. 159°, identical with the foregoing sample of **17**. Further elution gave yellow tarry material from which no solid product was obtained.

Compound **9** gave **18** (2.8 g, 55%) as yellow needles, m.p. 170° (from ethanol).

Anal. Calcd. for $C_{17}H_{10}Br_3N_3O_2S_2$: C, 34.46; H, 1.69; Br, 40.54; N, 7.09. Found: C, 34.68; H, 1.74; Br, 40.51; N, 6.99.

Rearrangement of p-Nitrophenyl Thiohydrazonates and Formation of Substituted 4H-1,3,4-Benzothiadiazines

Compound **13** (1.0 g), EtOH (15 ml), and NEt_3 (15 ml), were boiled under reflux for 2.75 h. *7-Bromo-4-p-nitrophenyl-2-phenyl-4H-1,3,4-benzothiadiazine* (**19**) crystallized slowly from the reaction mixture and was isolated, after cooling, as orange prisms (0.75 g, 79%), m.p. 228–229°.

Anal. Calcd. for $C_{19}H_{12}BrN_3O_2S$: C, 53.52; H, 2.82; Br, 18.78; N, 9.86. Found: C, 53.3; H, 2.9; Br, 18.8; N, 9.8.

Compound **14** (1.0 g), NaOH (0.1 g), DMF (10 ml), and NEt_3 (2.5 ml) were boiled under reflux for 2 h. When cool, the crystalline precipitate (0.77 g, 90%) m.p. 225–227°, was collected; crystallization from benzene gave **19** as orange prisms, m.p. 227–229°, identical with the previous sample of **19**.

Compound **15** (2.0 g), EtOH (20 ml), and NEt_3 (20 ml) were boiled under reflux for 2 h. The solution was concentrated *in vacuo* and the orange solid was collected, washed, and dried. Crystallization from benzene gave the *thiadiazine* (**20**) (1.2 g, 74%) as orange prisms, m.p. 217° (dec.).

Anal. Calcd. for $C_{20}H_{14}BrN_3O_3S$: C, 52.63; H, 3.07; Br, 17.54. Found: C, 52.54; H, 2.97; Br, 17.65.

Compound **16** (2.0 g), treated as for **15** above, gave

21 (0.7 g, 40%) as orange-yellow needles, m.p. 253–254° (dec.) (from benzene).

Anal. Calcd. for $C_{19}H_{11}BrClN_3O_2S$: C, 49.51; H, 2.39; N, 9.12. Found: C, 49.47; H, 2.41; N, 8.96.

Compound **17** (0.5 g), treated as for **15** above, gave a yellow gum which contained at least four components (t.l.c.), none of which was **17** or was fluorescent. Attempts to isolate solid products were unsuccessful.

Compound **18** (1.5 g), EtOH (15 ml), and NEt_3 (15 ml) were boiled under reflux for 4 h, cooled, and the product was filtered off. Compound **22** (0.8 g, 64%) crystallized from benzene–hexane as orange-brown prisms, m.p. 213°.

Anal. Calcd. for $C_{17}H_9Br_2N_3O_2S_2$: C, 39.92; H, 1.76; Br, 31.31; S, 12.52. Found: C, 39.62; H, 1.75; Br, 31.50; S, 12.65.

Compound **10** (3.10 g) was treated with *p*-nitrothiophenol in the manner described above for **5**. A sample (1.0 g) of the crude product was boiled under reflux with EtOH (10 ml) and NEt_3 (10 ml) for 4 h and the solution was then concentrated. The solid was collected, triturated with boiling acetone and benzene, and then crystallized from dioxan to give **23** as red prisms (0.37 g, 45% overall from **10**), m.p. 274° (dec.).

Anal. Calcd. for $C_{19}H_{12}N_4O_4S$: C, 58.16; H, 3.06; N, 14.29. Found: C, 58.6; H, 3.1; N, 14.0.

Preparation of Heteroaryl Thiohydrazonates

(i) The hydrazonyl halide (0.01 mol) and the thiol (0.01 mol) were stirred together in EtOH (30 ml) and NEt_3 (1 ml) at room temperature for 2 h; for preparations of **30** (*a* and *b*) and **31** (*a* and *b*), reaction times were 1 and 3 h, respectively, and the quantity of NEt_3 was increased to 3 ml. The product was filtered off (after dilution with water in the case of **27**), washed, dried, and purified by crystallization.

Compound **4** and quinoxaline-2-thiol gave the *thiohydrazonate* (**26**) (3.2 g, 63%) as yellow prisms, m.p. 142–143° (from hexane–toluene); p.m.r. δ 9.18 (s, NH), 8.52 (s, 1H) ,and 8.1–7.1 (m, 12H); mass spectrum *m/e* 516/514/512 (M^+), 435/433, 434/432, 381/379/377 ($Br_2C_6H_3NHC_8H_5N_2$), 354/352/350 ($M^+ - C_8H_5N_2SH$), 300/298, 251/249/247, 219, 170/168, 162 ($C_8H_5N_2SH$), 129, 121, 118, 103, and 91.

Anal. Calcd. for $C_{21}H_{14}Br_2N_4S$: C, 49.03; H, 2.72; Br, 31.13. Found: C, 49.01; H, 2.63; Br, 31.35.

Compound **4** and 5-nitropyridine-2-thiol gave **27** (3.4 g, 83%) as yellow plates, m.p. 144–145° (from ethanol – ethyl acetate). Analytical figures were discrepant. Proton magnetic resonance δ 9.25 (s, NH), 9.25 (d, 1H, $J = 2.5$ Hz), 8.4–7.98 (m, 3H), and 7.65–7.3 (m, 7H); mass spectrum *m/e* 510/508/506 (M^+), 477/475/473, 429/427, 428/426, 376/374/372 ($Br_2C_6H_3NC_5NH_3NO_2$), 354/352/350 ($M^+ - NO_2C_5H_3NSH$), 347, 309/307/305, 305/303, 295/293/291, 251/249/247 ($Br_2C_6H_3N$), 241, 198, 170/168, 155 ($NO_2C_5H_3NS$), 121, 103, and 76.

Compound **4** and benzothiazole-2-thiol gave **30***a* (4.8 g, 93%) as cream prisms, m.p. 128–130° (from benzene–ethanol).

Anal. Calcd. for $C_{20}H_{13}Br_2N_3S_2$: C, 46.24; H, 2.50; Br, 30.83; N, 8.09. Found: C, 46.5; H, 2.7; Br, 30.6; N, 8.0.

Compound **3** and benzothiazole-2-thiol gave **30***b* (1.4 g, 31%) as cream prisms, m.p. 100–102° (from ethanol).

Anal. Calcd. for $C_{20}H_{13}BrFN_3S_2$: C, 52.40; H, 2.84; N, 9.17; S, 13.97. Found: C, 52.1; H, 2.6; N, 8.9; S, 14.0.

Compound **4** and benzoxazole-2-thiol gave **31***a* (3.5 g, 69%) as reddish prisms, m.p. 136–138° (from benzene–hexane).

Anal. Calcd. for $C_{20}H_{13}Br_2N_3OS$: C, 47.71; H, 2.58; N, 8.35. Found: C, 48.27; H, 2.87; N, 8.20.

Compound **12** and benzoxazole-2-thiol gave **31***b* (2.5 g, 72%) as yellowish prisms, m.p. 116–117° (from benzene–hexane).

Anal. Calcd. for $C_{20}H_{15}N_3OS$: C, 69.57; H, 4.35; N, 12.17. Found: C, 59.76; H, 4.47; N, 12.03.

(ii) Sodium salts of thiols were prepared by addition of 1 equiv. of sodium to the thiol in EtOH and were then precipitated by addition of dry ether, collected, and stored *in vacuo*. The hydrazonyl halide **4** (0.01 mol) and the sodium salt of the thiol (0.01 mol) were stirred together in dry acetonitrile (30 ml) for 2 h, and the product was then filtered off, washed, dried and purified by crystallization. For preparation of **25**, EtOH (30 ml) was used as solvent and the product was collected after pouring the reaction mixture into water.

The sodium salt of 4,6-dimethylpyrimidine-2-thiol gave the *thiohydrazonate* (**24**) (3.7 g, 75%) as colorless needles, m.p. 118° (from hexane); i.r. (Nujol) 3280 cm^{-1} (NH); p.m.r. δ 9.15 (s, NH), 8.1–7.95 (m, 2H), 7.55–7.1 (m, 6H), 6.62 (s, 1H) and 2.32 (s, 6H); mass spectrum *m/e* 494/492/490 (M^+), 461/459/457, 413/411, 359/357/355 ($Br_2C_6H_3NHC_6H_7N_2$), 354/352/350 ($M^+ - C_6H_7N_2SH$), 310/308, 278/276, 251/249/247, 225, 170/168, 140 ($C_6H_7N_2SH$), 121, 103, 82, 77, and 67.

Anal. Calcd. for $C_{19}H_{16}Br_2N_4S$: C, 46.34; H, 3.25; Br, 32.52; N, 11.38. Found: C, 46.4; H, 3.4; Br, 32.6; N, 11.7.

The sodium salt of 1-phenyltetrazole-5-thiol gave **25** (4.7 g, 89%) as fawn needles, m.p. 171–172° (dec.) (from hexane–toluene); p.m.r. δ 9.05 (s, NH) and 7.9–7.25 (m, 13H).

Anal. Calcd. for $C_{20}H_{14}Br_2N_6S$: C, 45.28; H, 2.64; N, 15.85. Found: C, 45.53; H, 2.61; N, 15.75.

The sodium salt of pyridine-2-thiol gave **28** (3.5 g, 76%) as colorless needles, m.p. 131° (from hexane–toluene).

Anal. Calcd. for $C_{18}H_{13}Br_2N_3S$: C, 46.65; H, 2.81; Br, 34.56; N, 9.07. Found: C, 47.0; H, 3.1; Br, 34.8; N, 8.8.

The sodium salt of 4-methylquinoline-2-thiol gave **29** (3.8 g, 73%) as pale yellow prisms, m.p. 117–118° (from hexane–toluene).

Anal. Calcd. for $C_{23}H_{17}Br_2N_3S$: C, 52.37; H, 3.23; Br, 30.36; N, 7.97. Found: C, 52.3; H, 3.4; Br, 30.3; N, 7.9.

Behavior of Heteroaryl Thiohydrazonates under Acidic Conditions

(i) Compound **24** (1.0 g) was dissolved in warm benzene (30 ml) and concentrated HCl (10 ml) was added. The two-phase mixture was heated without agitation on a steam bath for 1 h and then cooled. The benzene layer was separated, washed with aqueous $NaHCO_3$ solution and water, and then dried and evaporated *in vacuo*. Crystallization from hexane–toluene gave the *thiobenzohydrazide* (**32**) (0.55 g, 55%) as bright yellow prisms, m.p. 142°; i.r. (Nujol) 3340 cm^{-1} (NH); p.m.r. δ 9.7 (s, NH), 8.1–7.15 (m, 8H), 6.47 (s, 1H), and 2.3 (s, 6H); mass

spectrum *m/e* 494/492/490 (M^+), 461/459/457, 413/411, 359/357/355, 310/308, 278/276, 251/249/247, 225, 197, 170/168, 121, 103, 77, and 67.

Anal. Calcd. for $C_{19}H_{16}Br_2N_4S$: C, 46.34; H, 3.25; Br, 32.52; N, 11.38. Found: C, 46.4; H, 3.2; Br, 32.5; N, 11.6.

(ii) Compound **25** (2.0 g) in benzene (50 ml) and concentrated HCl (20 ml) was treated as above. The benzene layer was washed with 2 *M* NaOH (50 ml) and the alkaline solution was acidified with concentrated HCl to precipitate a white solid which was filtered off and dried *in vacuo*. Crystallization from toluene gave 1-phenyltetrazole-5-thiol (0.4 g, 60%) as needles, m.p. 157° (dec.) (lit. (13) m.p. 147–150° (dec.)).

Anal. Calcd. for $C_7H_6N_4S$: C, 47.19; H, 3.37; N, 31.46; S, 17.98. Found: C, 47.38; H, 3.24; N, 30.98; S, 17.98.

The benzene solution was evaporated and the residue chromatographed on Florisil (toluene as eluant) to give **11** (0.6 g, 41%) as needles, m.p. 105–108° (from hexane) (lit. (3) m.p. 109–110°); p.m.r. δ 8.05 (s, NH), 7.6–7.4 (m, 2H), and 7.2–6.85 (m, 6H); mass spectrum *m/e* 390/388/386 (M^+), 354/352/350 (M^+ − HCl), 273/271, 251/249/247, 237/235/233, 225/223/221, 171/169, 170/168, 143/141, 119/117, 103, 89, 77.

Thin-layer chromatography indicated that the only other product from the reaction was almost certainly $PhCONHNHC_6H_3Br_2$.

Compound **11** (0.38 g) and 1-phenyltetrazole-5-thiol (0.18 g) isolated from the above reaction were stirred together with EtOH (5 ml) and NEt_3 (0.2 ml) for 2 h at room temperature and the mixture was then poured into water. Isolated by means of ether, compound **25** (0.05 g) crystallized from toluene as needles, m.p. and mixture m.p. 171–172° (dec.).

(iii) Compound **26** (2.0 g) in benzene (50 ml) and concentrated HCl (20 ml), treated as above, gave a mixture of at least eight components (t.l.c.); compound **11**, separated by chromatography (Florisil, hexane–toluene), crystallized from hexane as needles (0.2 g, 13%), m.p. 104–108°, identical with the previous sample.

(iv) Compound **27** (2.0 g), treated with concentrated HCl as above, gave a mixture of at least eight components, none of which could be separated in crystalline form. The product had the following spectral characteristics; i.r. (CCl_4) 3320 cm^{-1} (NH); p.m.r. δ 9.9 (s, NH), 9.02 (d, 1H, J = 2.5 Hz), 8.4–7.25 (m, *ca.* 10H), and 6.7 (d, 1H, J = 9.0 Hz).

The following compounds were unaffected by treatment with concentrated HCl – benzene under the above conditions: **28** and **29**, and **16** and an analogous hydrazonate (**14**; O instead of S).

Behavior of Heteroaryl Thiohydrazonates under Basic Conditions; Formation of Substituted 4H-1,3,4-Benzothiadiazines

(i) Compound **27** (2.0 g), EtOH (10 ml), and NEt_3 (10 ml) were boiled under reflux for 2 h, cooled, and the product was filtered off, washed, and dried. Crystallization from benzene gave *7-bromo-4-(5-nitro-2-pyridinyl)-2-phenyl-4H-1,3,4-benzothiadiazine* (**34**) (1.31 g, 79%) as yellow needles, m.p. 223°.

Anal. Calcd. for $C_{18}H_{11}BrN_4O_2S$: C, 50.59; H, 2.58; N, 13.11. Found: C, 50.8; H, 2.8; N, 12.9.

Compound **26** (2.57 g), EtOH (10 ml), and NEt_3 (10 ml) were boiled under reflux for 2 h. The solution was cooled, poured into 5% acetic acid (700 ml), and the product was filtered off, washed, and dried. Crystallization from benzene gave **33** (2.03 g, 94%) as yellow needles, m.p. 211–212°.

Anal. Calcd. for $C_{21}H_{13}BrN_4S$: C, 58.20; H, 3.00; Br, 18.48. Found: C, 58.05; H, 2.92; Br, 18.66.

Compound **29** (2.0 g), EtOH (10 ml), and NEt_3 (10 ml) were boiled under reflux for 2 h, cooled, and the product was filtered off, washed, and dried. The product was chromatographed on Florisil and the fraction containing the yellow fluorescent component (eluted with $CHCl_3$) was collected and evaporated. Crystallization from benzene gave **35** (0.2 g, 16%) as yellow needles, m.p. 204°; mass spectrum *m/e* 447/445 (M^+), 348, 315, 284, 283, 278, 263, 223, 177/175, 176/174, 159, 149, 142, 140, 130, 115, 103, 89, and 79.

Anal. Calcd. for $C_{23}H_{16}BrN_3S$: C, 61.88; H, 3.59; Br, 17.94; N, 9.42. Found: C, 61.6; 59.0; H, 4.2, 3.6; Br, 17.8, 18.0; N, 8.5.

Compound **30***a* (1.0 g), EtOH (20 ml), and NEt_3 (20 ml) were boiled under reflux for 3.5 h, cooled, and the product was collected. Crystallization from benzene gave **36** as yellow needles (0.43 g, 51%), m.p. 196–197°; compound **30***b* similarly gave **36** (80%), m.p. and mixture m.p. 196–197°.

Anal. Calcd. for $C_{20}H_{12}BrN_3S_2$: C, 54.79; H, 2.74; Br, 18.26; N, 9.59. Found: C, 54.9; H, 2.6; Br, 18.1; N, 9.7.

Compounds **28**, and **31***a* and *b* were unaffected after 2 h under the above conditions, whilst **25** was extensively decomposed. Compound **24** rearranged to **32**, reaction being virtually complete after 30 min (t.l.c.); the product (**32**) isolated after 2 h was contaminated with at least three other substances (t.l.c.) and could not be obtained pure.

(ii) Compound **31***a* (2.0 g), NaOH (0.2 g), DMF (15 ml), and NEt_3 (2.5 ml) were boiled under reflux for 3 h. The dark mixture was concentrated *in vacuo* to half bulk, chilled, and the brown solid was collected, washed with EtOH, and dried. After crystallization from cyclohexane, **37** (0.4 g, 24%) was obtained as pale green prisms, m.p. 158–161°.

Anal. Calcd. for $C_{20}H_{12}BrN_3OS$: C, 56.87; H, 2.84; N, 9.95. Found: C, 57.02; H, 2.94; N, 9.76.

Alternative Syntheses of Thiadiazines 33 and 34

Compound **38** (3) (1.02 g), 2-chloroquinoxaline (0.54 g), acetonitrile (20 ml), and NEt_3 (3 ml) were boiled under reflux for 4 h. Solvent was removed *in vacuo* and the solid was washed with water and dried. Crystallization from benzene gave **33** (0.9 g, 62%), m.p. and mixture m.p. 211–212°.

Compound **38** (1.02 g) and 2-chloro-5-nitropyridine (0.53 g) similarly gave **34** (1.1 g, 76%), m.p. and mixture m.p. 223°.

Under these conditions, **38** did not react with 2-chloro-4,6-dimethylpyrimidine or with 2-chloropyridine.

We thank the National Research Council of Canada for financial support, and Imperial Chemical Industries Ltd. for samples of pyridine-2-thiol and 4-methylquinoline-2-thiol.

1. R. HUISGEN, J. SAUER, and M. SEIDEL. Chem. Ber. **94**, 2503 (1961).
2. A. F. HEGGARTY, J. A. KEARNEY, and F. L. SCOTT. J. Chem. Soc. Perkin II, 1422 (1973).
3. I. T. BARNISH and M. S. GIBSON. J. Chem. Soc. C, 854 (1970).
4. M. M. KAYSER and M. S. GIBSON. Can. J. Chem. **51**, 3499 (1973).
5. A. J. ELLIOTT, M. S. GIBSON, M. M. KAYSER, and G. A. PAWELCHAK. Can. J. Chem. **51**, 4115 (1973).
6. Y. MAKI, M. SUZUKI, and T. MASUGI. Chem. Pharm. Bull. **16**, 559 (1968); O. R. RODIG, R. E. COLLIER, and R. K. SCHLATZER. J. Org. Chem. **29**, 2652 (1964).
7. S. TSUNODA, T. SHIOJIMA, Y. HASHIDA, S. SEKIGUCHI, and K. MATSUI. Bull. Chem. Soc. Jap. **46**, 3499 (1973).
8. I. T. BARNISH, P. D. CALLAGHAN, and M. S. GIBSON. J. Chem. Soc. Perkin I, 215 (1974).
9. R. R. HUNT, J. F. W. MCOMIE, and E. R. SAYER. J. Chem. Soc. 525 (1959).
10. F. J. WOLF, R. M. WILSON, and M. TISHLER. J. Am. Chem. Soc. **76**, 2266 (1954).
11. A. H. GOWENLOCK, G. T. NEWBOLD, and F. S. SPRING. J. Chem. Soc. 622 (1945).
12. A. R. SURREY and H. G. LINDWALL. J. Am. Chem. Soc. **62**, 1697 (1940); W. T. CALDWELL and E. C. KORNFELD. J. Am. Chem. Soc. **64**, 1695 (1942).
13. M. FREUND and H. HEMPEL. Ber. **28**, 74 (1895).