Hydrazides and Thiohydrazides as Sources of Condensed Oxadiazines and Thiadiazines, Including Novel Azo Derivatives Based on Dithizone

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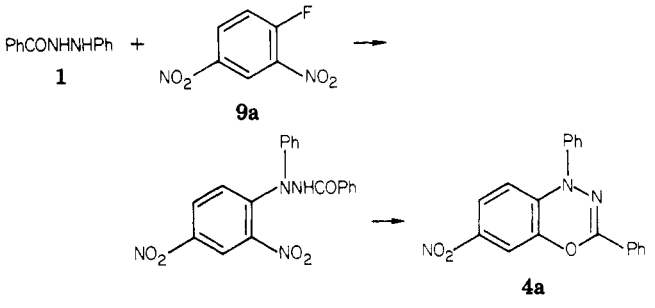
Condensation reactions of *N'*-phenylbenzohydrazide, *N'*-phenylbenzothiohydrazide, and dithizone with a variety of activated aromatic and heteroaromatic 1,2-dihalogeno and 1-halogeno-2-nitro compounds are described in which the hydrazide or thiohydrazide functions as a bidentate nucleophile. These reactions lead to derivatives of the 4*H*-1,3,4-benzoxadiazines and 4*H*-1,3,4-benzothiadiazines and analogous pyrimido-, pyrazino-, and quinoxalinooxadiazines and -thiadiazines which are representative of new ring systems. The corresponding reaction of *N'*-phenylbenzothiohydrazide with chloranil proceeds with expulsion of sulfur. The mechanism of this reaction is discussed.

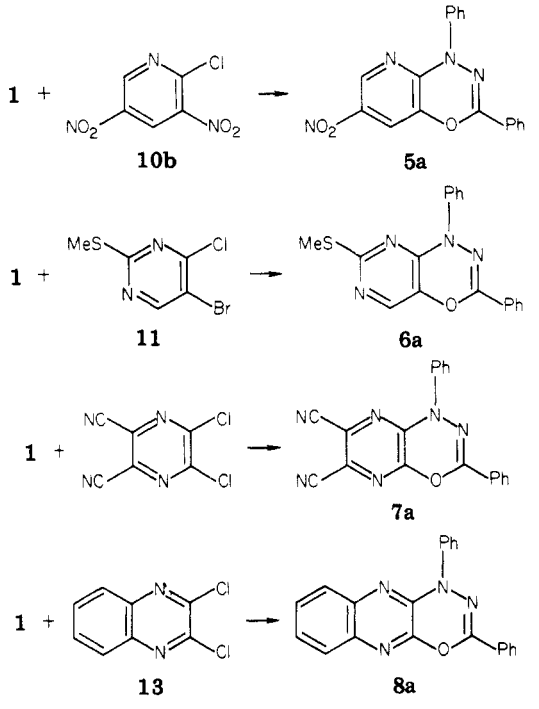
The syntheses and reactions of 4*H*-1,3,4-benzothiadiazines have been of recent interest to a number of research groups, including our own. We have used two general approaches to syntheses, one based on hydrazonoyl halides and the other on *N'*-arylbenzothiohydrazides. In each case the N'-aryl group becomes incorporated in the benzothiadiazine ring system, and the synthesis leads to 2-aryl-4-acyl- and 2,4-diaryl-4*H*-1,3,4-benzothiadiazines.[1] Two other approaches provide examples of syntheses of two separate 2-(arylazo)-4*H*-1,3,4-benzothiadiazines.[2] Further syntheses provide 2-alkyl-4-aryl derivatives,[3] a 2-alkyl-4*H* derivative,[4] the 4-methyl-2-phenyl derivative,[5] and ethyl 4*H*-1,3,4-benzothiadiazine-2-carboxylate.[6] More recently, Ames and co-workers have reported syntheses of a number of 4*H*-1,3,4-benzothiadiazines and related 1,1-dioxides, including a new source of the latter group typified by diazotization of ethyl [(2-aminophenyl)sulfonyl]glyoxylate phenylhydrazone.[7] We have been interested in developing syntheses of new condensed 4*H*-1,3,4-thiadiazines and related oxadiazines in which the precursory benzothiohydrazide or benzohydrazide functions as a bidentate nucleophile. The chosen *N'*-aryl substituent would thus become the 4-substituent in the resulting thiadiazine or oxadiazine, rather than becoming incorporated as part of the fused-ring system. We now report experiments to this end in which *N'*-phenylbenzohydrazide (**1**), *N'*-phenylbenzothiohydrazide (**2**), and 1,5-diphenyl-3-mercaptoformazan (dithizone, **3**) have been used as nucleophiles.

We first gave attention to the synthesis of fused oxadiazine systems. Compound **1** was found to condense smoothly with 2,4-dinitrofluorobenzene (**9a**) in the presence of triethylamine (TEA) at room temperature to give the N'-substituted hydrazide (Scheme I). The structure of the latter product follows from microanalysis and the presence of a band at 1660 cm^{-1} (C=O) in the IR spectrum. This compound, when heated with sodium hydroxide and TEA in dimethylformamide (DMF), eliminated the 2-nitro group and gave the oxadiazine **4a** in 82% yield. Structure **4a** is supported by the ^1H NMR spectrum (upfield proton at C-5 observed as a doublet, ortho coupled) and is consistent with previous work.[8]

Scheme I



Scheme II



(1) (a) Vukov, D. J.; Gibson, M. S.; Lee, W. E.; Richardson, M. F. *J. Chem. Soc., Perkin Trans 1* **1977**, 192 and references cited therein. (b) Elliott, A. J.; Callaghan, P. D.; Gibson, M. S.; Nemeth, S. T. *Can. J. Chem.* **1975**, *53*, 1484 and references cited therein.

(2) (a) McDonald, W. S.; Irving, H. M. N. H.; Raper, G.; Rupainwar, D. C. *J. Chem. Soc. D* **1969**, 392. Carlin, C. H.; Corwin, A. H. "Abstracts of Papers", 157th National Meeting of the American Chemical Society Minneapolis, MN, Apr 1969; American Chemical Society: Washington, DC, 1969, Abstract no. 123. (b) Kiwan, A. M.; Kassim, A. Y. *J. Chem. Soc., Perkin Trans. 2*, **1977**, 1118.

(3) Shawali, A. S.; Hassaneen, H. M. *Bull. Chem. Soc. Jpn.*, **1977**, *50*, 2827.

(4) Spitulnik, M. J. *J. Heterocycl. Chem.*, **1977**, *14*, 1073.

(5) Barton, D. H. R.; Ducker, J. W.; Lord, W. A.; Magnus, P. D. *J. Chem. Soc., Perkin Trans. 1* **1976**, 38.

(6) Garanti, L.; Scandroglio, A.; Zecchi, G. *J. Heterocycl. Chem.* **1976**, *13*, 1339.

(7) Ames, D. E.; Chandrasekhar, S.; Hansen, K. J. *J. Chem. Soc., Perkin Trans. 1*, **1978**, 539.

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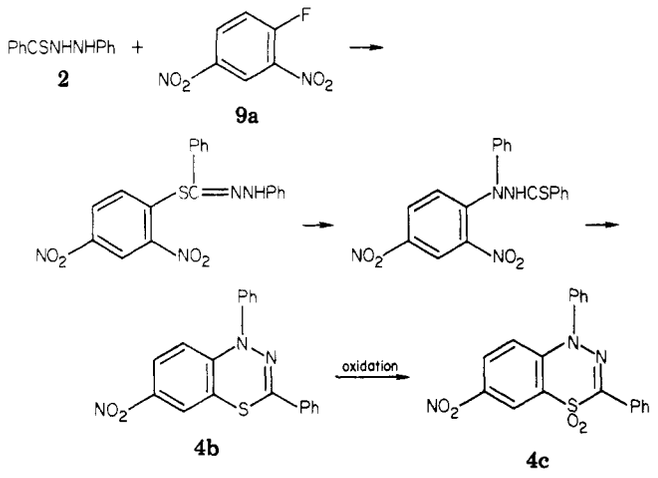
Scheme III

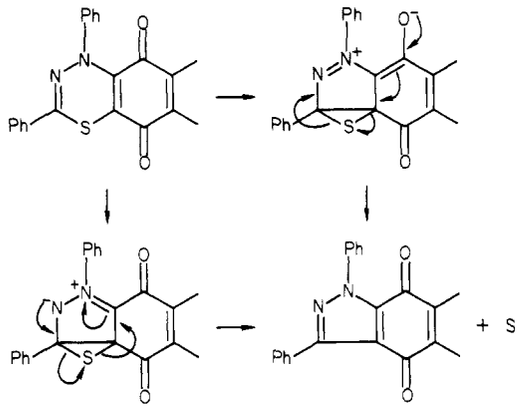


A similar sequence was attempted with 1 and 2-chloro-3-nitropyridine (**10a**), but condensation was not achieved at room temperature, and use of DMF at reflux gave only gummy mixtures. However, 1 and 2-chloro-3,5-dinitropyridine (**10b**) readily gave the corresponding hydrazide, which in turn was transformed into the oxadiazine **5a** (Scheme II) under conditions analogous to those used for preparation of **4a**. The latter conditions sufficed to convert 1 and 5-bromo-4-chloro-2-methylthiopyrimidine (**11**) directly to the oxadiazine **6a**, but 1 and the more reactive 2,3-dichloro-5,6-dicyanopyrazine (**12**) gave **7a** under milder conditions. Finally, 1 and 2,3-dichloroquinoxaline (**13**) were refluxed with TEA in DMF to give the oxadiazine **8a** in 82% yield.

Our next move was to extend these experiments to a parallel series using N′-phenylbenzothiohydrazide (**2**). The latter compound, when stirred with **9a** in acetonitrile/TEA at room temperature, gave a yellow product which was shown by thin-layer chromatography (TLC) to consist of a major component and a fluorescent minor component. This material was readily transformed into the thiadiazine **4b** by boiling in ethanol/TEA (Scheme III). The composition of the yellow product was not unequivocally established since the mass spectrum recorded under normal conditions was coincident with that of **4b**. When recorded at a 20-eV ionizing voltage and 120–150 °C, the mass spectrum contained an additional peak of low intensity, *m/e* 394 (M^+, $C_{19}H_{14}N_4O_4S$), but the intensities were too low to observe the characteristic fragmentation pattern of aryl thiohydrazonates which would permit distinction from the isomeric thiohydrazide.[2] Attempted oxidation with hydrogen peroxide in acetic acid, which converts simpler thiohydrazides to hydrazonyl disulfides,[9] left the material unchanged while potassium ferricyanide/sodium bicarbonate led directly to **4b**. We favor a thiohydrazonate formulation with rearrangement to the thiohydrazide and ring closure to the thiadiazine.[2] The structure (**4b**) of the resulting thiadiazine follows from oxidation with hydrogen peroxide in acetic acid to the corresponding 1,1-dioxide.[1,7] The ^1H NMR signal for the C-8 proton in the dioxide is seen as a doublet (meta coupled) considerably downfield, under the influence of the SO_2 group, of that for the C-8 proton in the thiadiazine, while that for the C-6 proton is seen as a quartet at slightly lower field than that for the C-6 proton in the thiadiazine. These observations are only consistent with formulas **4b** and **4c** for the thiadiazine and

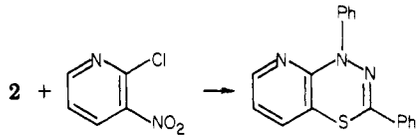
(8) Elliott, A. J.; Gibson, M. S. *Can. J. Chem.* **1975**, *53*, 2534.
(9) Wolkoff, P.; Hammerum,, S.; Callaghan, P. D.; Gibson, M. S. *Can. J. Chem.* **1974**, *52*, 879. Cf. ref 5.

Scheme IV



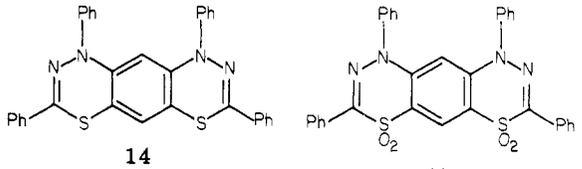
derived 1,1-dioxide, respectively.

In subsequent reactions with **2**, condensation with the second reactant to give the corresponding thiadiazine was normally achieved directly by boiling in acetonitrile/TEA.



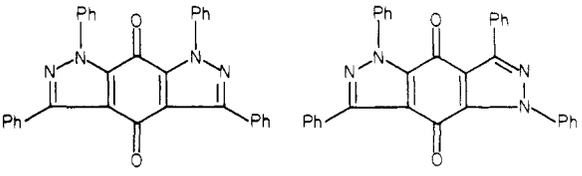
10a 5b

Thus **10a** was converted to **5b**, **11** to **6b**, and **13** to **8b**; the more reactive **12** gave **7b** under milder conditions. The series was extended to 1,5-difluoro-2,4-dinitrobenzene (**9b**) which condensed with two molecules of **2** to give **14**; the latter, oxidized in the normal way, gave **15**. While **14** was too sparingly soluble for direct ^1H NMR study, the ^1H NMR spectrum of **15** shows the central ring protons as two singlets each of relative intensity 1 rather than one singlet of relative intensity 2. This confirms the structures of **14** and **15** as assigned.



14 15

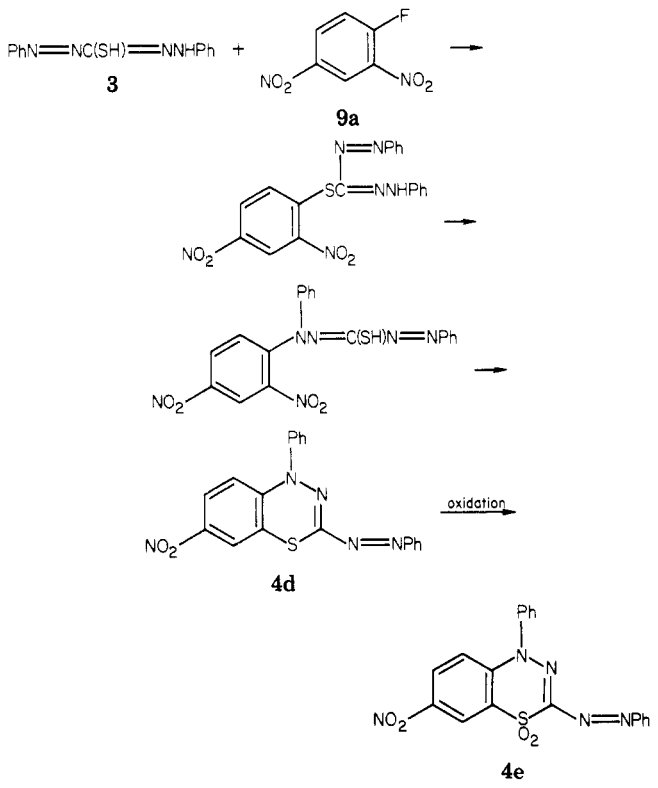
We finally examined the reaction of **2** with tetrachloro-1,4-benzoquinone (chloranil) under reflux in DMF/TEA. In all of the foregoing cases, the thiadiazine ring being formed in the cyclization reaction is fused to an aromatic system whereas in the present case the corresponding ring is quinonoid. The product of this reaction ($C_{32}H_{20}N_4O_2$) is a very sparingly soluble material containing no sulfur, and it is not at present clear whether this is **16a**, **16b**, or a mixture of these two isomers. The for-



16a 16b

mation of this product can be seen in terms of formation of (two) thiadiazine rings with subsequent extrusion of sulfur as shown in the partial formulas in Scheme IV. Extrusion of sulfur has not been observed in syntheses of 4*H*-1,3,4-thiadiazines in which the ring is fused to an aromatic system, e.g., in 4*H*-1,3,4-benzothiadiazines. Nor have such condensed thiadiazines been found to undergo

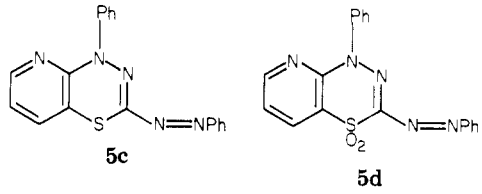
Scheme V



extrusion of sulfur during reactions. This is understandable in terms of the above mechanistic considerations. However, a variety of simple substituted 1,3,4-thiadiazines have been found to undergo sulfur-extrusion reactions to give the corresponding pyrazoles with relative ease,[10] and it has been suggested that the presence of a proton at the 4-position is necessary for these contractions (extrusions) to occur.[10c] Although this condition was met in the work cited, our own results, as well as the interpretation of the course of the reaction of 1-(diethylamino)-1-propyne with dehydrodithizone (where the 4-nitrogen in the proposed thiadiazine intermediate carried a phenyl substituent),[11] suggest that this condition is not necessary in all cases of sulfur extrusion. This area seems to warrant further study.

Our last series of experiments focussed on dithizone (**3**) as a source of condensed 4*H*-1,3,4-thiadiazines bearing a 2-(phenylazo) substituent, some of which might have a potential for dyestuffs applications. Initially, we noted the rapid formation of a yellow material, evidently a 1:1 condensation product, from reaction of **3** with **9a** in acetonitrile/TEA at 0 °C, while the same ingredients at room temperature for an extended time were transformed into the purple thiadiazine **4d** (Scheme V). With respect to this yellow product, we faced a problem analogous to that of formulating the primary product from the reaction of **2** with **9a** and on the evidence available have reached similar conclusions. We formulate the reaction sequence as shown in Scheme V. The structure (**4d**) of the resulting thiadiazine follows from oxidation to the corresponding 1,1-dioxide **4e** and correlation of the ^{1}H NMR spectra of the two compounds with each other and with the pair of compounds **4b** and **4c**. Heating **3** in acetonitrile/TEA with 1-chloro-2-nitro-4-(trifluoromethyl)benzene (**9c**) and with 4-chloro-3-nitrobenzenesulfonamide (**9d**) gave analogous thiadiazines **4f** and **4g**, respectively.

We next condensed **3** with **10a** in refluxing acetonitrile/TEA and obtained a purple pyridothiadiazine which we formulate as **5c**. The ^{1}H NMR spectra of **5c**



and the derived 1,1-dioxide **5d** are consistent with these structures and with an interpretation involving Smiles-type rearrangement which parallels that for the formation of **4d** from **3** and **9a** above. Compound **3** was similarly condensed with **11** to give **6c**, with **13** to give **8c**, and under milder conditions with **12** to give **7c**. In each case, we view the formation of these brilliantly colored thiadiazines as involving formation of a thiohydrazonate, its rearrangement, and subsequent ring closure, as in corresponding sequences based on **2**.

The above results show that **1**, **2**, and **3** can behave as bidentate nucleophiles in a wide variety of condensation reactions which lead to fused 4*H*-1,3,4-oxadiazines and -thiadiazines. We believe the compounds within the sets **5**–**8** to be representative of the new ring systems.

Experimental Section

TLC was performed on Kieselgel GF (Merck) slides with toluene as eluant. IR data are reported for Nujol mulls unless otherwise stated. ^{1}H NMR spectra were determined at 60 MHz in dimethyl sulfoxide (Me_2SO-d_6) or trifluoroacetic acid (TFA) with tetramethylsilane as internal standard unless otherwise stated; the instruments used were Varian A-60, T-60, and HA-100 and Bruker WP-60 spectrometers. Mass spectra were recorded on Hitachi Perkin-Elmer, CEC 21-100 and 110B, and AEI MS-30 spectrometers; *m/e* values are quoted for the lowest isotopic species.

Most of the starting materials used were stock or commercially available chemicals; 4-chloro-3-nitrobenzenesulfonamide was prepared from the commercially available sulfonyl chloride and ammonia.

***N'*-(2,4-Dinitrophenyl)-*N'*-phenylbenzohydrazide and 2,4-Diphenyl-7-nitro-4*H*-1,3,4-benzooxadiazine (4a).** TEA (5 mL) was added to a stirred mixture of **1** (4.24 g, 0.02 mol) and **9a** (3.72 g, 0.02 mol) in acetonitrile (35 mL) at room temperature. After 2 h, the solvent was removed in vacuo, and the residue was washed with water and dried. Crystallization from benzene gave the hydrazide as yellow needles: 5.8 g (74%); mp 159–160 °C; IR 1660, 1605, 1535, 1385, 1340, 694 cm^{-1}.

Anal. Calcd for $C_{19}H_{14}N_4O_5$: C, 60.32; H, 3.70; N, 14.82. Found: C, 60.31; H, 3.59; N, 14.74.

A mixture of the hydrazide (3.78 g, 0.01 mol), sodium hydroxide (0.4 g, 0.01 mol), DMF (25 mL), and TEA (5 mL) was boiled under reflux for 4 h, cooled, and poured into 5% aqueous acetic acid (500 mL). The solid was filtered off, washed with water, and dried. Crystallization from benzene gave **4a** as red needles: 2.7 g (82%); mp 178–179 °C; IR 1505, 1430, 1320, 1300, 763, 689 cm^{-1}; ^{1}H NMR (100 MHz, Me_2SO-d_6) δ 6.60 (1 H, d, J = 9.5 Hz), 7.40–7.59 (8 H, m), 7.75–7.96 (4 H, m); mass spectrum, *m/e* 331 (M^+).

Anal. Calcd for $C_{19}H_{13}N_3O_3$: C, 68.89; H, 3.93; N, 12.69. Found: C, 68.72; H, 3.85; N, 12.89.

***N'*-(3,5-Dinitro-2-pyridyl)-*N'*-phenylbenzohydrazide and 2,4-Diphenyl-7-nitro-4*H*-1,3,4-pyrido[3,2-*e*]oxadiazine (5a).** TEA (5 mL) was added to a stirred mixture of **1** (2.12 g, 0.01 mol) and **10b** (2.03 g, 0.01 mol) in methanol (30 mL) at room temperature. After 2 h, the mixture was poured into ice-cold water (500 mL) containing acetic acid (20 mL), and the solid was filtered off, washed well with water, and dried. Crystallization from toluene gave the hydrazide as yellow needles: 2.7 g (71%); mp 231–232 °C; IR 1665, 1590, 1530, 1340, 1271, 1142, 831, 768, 728, 624 cm^{-1}.

(10) (a) Beyer, H.; Honeck, H.; Reichelt, L. *Justus Liebigs Ann. Chem.* **1970**, *741*, 45. (b) Schmidt, R. R.; Huth, H. *Tetrahedron Lett.* **1975**, 33. (c) Naka, T.; Furukawa, Y. *Chem. Pharm Bull.* **1979**, *27*, 1965.

(11) Boyd, G. V.; Norris, T.; Lindley, P. F. *J. Chem. Soc., Chem. Commun.* **1974**, 639.

Anal. Calcd for $C_{18}H_{13}N_5O_5$: C, 56.99; H, 3.43; N, 18.47. Found: C, 57.25; H, 3.26; N, 18.43.

A mixture of the hydrazide (3.80 g, 0.01 mol), sodium hydroxide (0.4 g, 0.01 mol), DMF (25 mL), and TEA (5 mL) was boiled under reflux for 4 h, cooled, and poured into 5% aqueous acetic acid (500 mL). The solid was filtered off, washed with water, and dried. Crystallization from toluene gave **5a** as matted red needles: 2.8 g (85%); mp 180 °C; IR 1515, 1455, 1440, 1345, 1308, 746, 690 cm^{-1}; ^1H NMR (Me_2SO-d_6) δ 7.36–7.66 (5 H, m), 7.74–7.96 (5 H, m), 8.57 (1 H, s), 8.61 (1 H, s); mass spectrum, m/e 332 (M^+).

Anal. Calcd for $C_{18}H_{12}N_4O_3$: C, 65.06; H, 3.61; N, 16.87. Found: C, 65.31; H, 3.60; N, 16.82.

2,4-Diphenyl-6-(methylthio)-4*H*-1,3,4-pyrimido[4,5-*e*]oxadiazine (6a). Compound **1** (2.12 g, 0.01 mol), **11** (2.39 g, 0.01 mol), DMF (100 mL), TEA (10 mL), and powdered sodium hydroxide (0.5 g, 12.5 mmol) were boiled together under reflux for 4 h, and the mixture was cooled and poured into water (1 L) containing acetic acid (20 mL). The solid was filtered off, dried, and crystallized from ethanol to give **6a** as bright yellow needles: 1.3 g (39%); mp 165–166 °C; IR 1580, 1555, 1370 cm^{-1}; ^1H NMR (TFA) δ 2.28 (3 H, s), 7.4–8.0 (11 H, m).

Anal. Calcd for $C_{18}H_{14}N_4OS$: C, 64.12; H, 4.31; N, 16.09. Found: C, 64.14; H, 4.22; N, 16.13.

6,7-Dicyano-2,4-diphenyl-4*H*-1,3,4-pyrazino[2,3-*e*]oxadiazine (7a). Compound **1** (2.12 g, 0.01 mol), **12** (1.99 g, 0.01 mol), and DMF (90 mL) were stirred together at room temperature, and TEA (10 mL) was added. The mixture was stirred for 3 h and poured into water (750 mL) containing acetic acid (30 mL). The solid was filtered off and dried. Crystallization from a large volume of ethanol gave **7a** as yellow-orange prisms: 1.8 g (53%); mp 250–253 °C; IR 2250 (C≡N), 1650, 1560 cm^{-1}; ^1H NMR (Me_2SO-d_6) δ 7.4–7.9 (m).

Anal. Calcd for $C_{19}H_{10}N_6O$: C, 67.45; H, 2.98; N, 24.84; mol wt 338.0915. Found: C, 67.19; H, 3.36; N, 24.88; mol wt (mass spectrometry) 338.0867.

2,4-Diphenyl-4*H*-1,3,4-quinoxalino[2,3-e]oxadiazine (8a). A mixture of **1** (2.12 g, 0.01 mol), **13** (1.99 g, 0.01 mol), DMF (50 mL), and TEA (10 mL) was boiled under reflux for 12 h, cooled, and poured into 5% aqueous acetic acid (750 mL). The solid was filtered off, washed well with water, and dried. The crude product was chromatographed (Florisil/toluene), the yellow fluorescent fraction being collected and evaporated. Crystallization from toluene gave **8a** as yellow needles: 2.8 g (82%); mp 241–242 °C; IR 1495, 1448, 1380, 1304, 1148, 762, 699 cm^{-1}; ^1H NMR (Me_2SO-d_6) δ 7.20 (2 H, br s), 7.45–7.52 (7 H, m), 7.60–7.86 (5 H, m); mass spectrum, m/e 338 (M^+).

Anal. Calcd for $C_{21}H_{14}N_4O$: C, 74.56; H, 4.14; N, 16.57. Found: C, 74.43; H, 4.16; N, 16.58.

2,4-Diphenyl-7-nitro-4*H*-1,3,4-benzothiadiazine (4b). Compound **2** (2.28 g, 0.01 mol), **9a** (1.86 g, 0.01 mol), and acetonitrile (30 mL) were stirred together at 0 °C, and TEA (5 mL) was added. After 10 min, the mixture was poured into iced water (500 mL) containing acetic acid (20 mL). The solid was filtered off, washed well with water, and dried. The product (3.7 g) consisted of a yellow major component and a yellow fluorescent minor component (TLC): IR 3280 (w), 1600, 1530, 1380, 1340, 1264, 1051, 692 cm^{-1}.

The product (1.9 g), ethanol (15 mL) and TEA (15 mL) were boiled together under reflux for 30 min. When the mixture was cool, the solvent was evaporated in vacuo, and the residue was washed with water and dried. Crystallization from DMF gave **4b** as red needles: 1.4 g (82% based on the thiohydrazide); mp 158–159 °C; IR 1490, 1390, 1340, 1314, 1300, 1259, 1147, 1130, 769, 757, 739, 687 cm^{-1}; ^1H NMR (100 MHz, Me_2SO-d_6) δ 6.71 (1 H, d, J = 8.7 Hz), 7.32–7.64 (8 H, m), 7.84–7.95 (2 H, m), 8.01 (1 H, q, J_{ortho} = 8.7 Hz, J_{meta} = 2.4 Hz), 8.14 (1 H, d, J = 2.4 Hz); mass spectrum, m/e 347 (M^+).

Anal. Calcd for $C_{19}H_{13}N_3O_2S$: C, 65.71; H, 3.75; N, 12.10. Found: C, 65.49; H, 3.73; N, 11.90.

The yellow product was unaffected by brief boiling with acetic acid and 6% hydrogen peroxide. Attempted oxidation with potassium ferricyanide/sodium bicarbonate in a two-phase chloroform/water system gave **4b**.

Oxidation of 4b to 4c. Compound **4b** (0.7 g, 2.0 mmol), acetic acid (30 mL), and 6% hydrogen peroxide (10 mL) were boiled under reflux for 15 min. When the mixture was cool, the solid was filtered off, washed with water, and dried. Crystallization from ethanol/ethyl acetate gave **4c** as yellow needles: 0.5 g (69%); mp 202–204 °C after blackening at ca. 195 °C; IR 1520, 1470, 1340, 1309, 1295, 1159, 1116, 768, 697 cm^{-1}; ^1H NMR (100 MHz, Me_2SO-d_6) δ 7.08 (1 H, d, J = 9.5 Hz), 7.49–7.79 (8 H, m), 7.85–7.99 (2 H, m), 8.37 (1 H, q, J_{ortho} = 9.5 Hz, J_{meta} = 2.5 Hz), 8.75 (1 H, d, J = 2.5 Hz); mass spectrum, m/e 379 (M^+).

Anal. Calcd for $C_{19}H_{13}N_3O_4S$: C, 60.16; H, 3.43; N, 11.08. Found: C, 59.97; H, 3.45; N, 11.22.

2,4-Diphenyl-4*H*-1,3,4-pyrido[3,2-*e*]thiadiazine (5b). Compound **2** (2.28 g, 0.01 mol), **10a** (1.58 g, 0.01 mol), acetonitrile (70 mL), and TEA (10 mL) were boiled together under reflux for 40 min. Water (10 mL) was added, and the solution was allowed to cool. The solid was filtered off, washed well with water, and dried to give **5b** as yellow needles: 2.3 g (70%); mp 99–100 °C; IR 1550, 1490, 1405 cm^{-1}; ^1H NMR (TFA) δ 7.4–8.0 (m).

Anal. Calcd for $C_{18}H_{13}N_3S$: C, 71.26; H, 4.32; N, 13.85. Found: C, 70.95; H, 4.30; N, 13.62.

2,4-Diphenyl-6-(methylthio)-4*H*-1,3,4-pyrimido[4,5-*e*]thiadiazine (6b). Compound **2** (2.28 g, 0.01 mol), **11** (2.39 g, 0.01 mol), acetonitrile (70 mL), and TEA (10 mL) were boiled together under reflux for 45 min, and the mixture was allowed to cool. The solid was filtered off, washed well with water, and dried to give **6b** as yellow needles: 2.3 g (66%); mp 126 °C; IR 1560, 1535, 1500, 1365, cm^{-1}; ^1H NMR (TFA) δ 2.29 (3 H, s), 7.4–8.0 (11 H, m).

Anal. Calcd for $C_{18}H_{14}N_4S_2$: C, 61.69; H, 4.03; N, 15.99; mol wt 350.0659. Found: C, 61.45; H, 4.11; N, 16.08; mol wt (mass spectrometry) 350.0659.

6,7-Dicyano-2,4-diphenyl-4*H*-1,3,4-pyrazino[2,3-*e*]thiadiazine (7b). Compound **2** (2.28 g, 0.01 mol), **12** (1.99 g, 0.01 mol), and acetonitrile (70 mL) were stirred together at room temperature, and TEA (10 mL) was added. There was an immediate reaction and a red precipitate appeared. The product was filtered off, washed well with water, and dried to give **7b** as red needles: 2.9 g (83%); mp 246 °C; IR 2260 (C≡N), 1600, 1530 cm^{-1}; ^1H NMR (Me_2SO-d_6) δ 7.4–7.9 (m).

Anal. Calcd for $C_{19}H_{10}N_6S$: C, 64.40; H, 2.84; N, 23.71; mol wt 354.0687. Found: C, 64.20; H, 3.22; N, 23.92; mol wt (mass spectrometry) 354.0698.

2,4-Diphenyl-4*H*-1,3,4-quinoxalino[2,3-*e*]thiadiazine (8b). Compound **2** (2.28 g, 0.01 mol), **13** (1.99 g, 0.01 mol), acetonitrile (70 mL), and TEA (10 mL) were boiled together under reflux for 30 min, and the mixture was allowed to cool. The yellow solid was filtered off, washed well with water, and dried to give **8b** as yellow needles: 2.5 g (72%); mp 196 °C; IR 1530, 1490, 1395 cm^{-1}; ^1H NMR (TFA) δ 7.3–8.0 (m).

Anal. Calcd for $C_{21}H_{14}N_4S$: C, 71.17; H, 3.98; N, 15.81; mol wt 354.0938. Found: C, 70.85; H, 4.26; N, 16.10; mol wt (mass spectrometry) 354.0986.

Reaction of 2 with 9b to Give 14. Compound **2** (2.28 g, 0.01 mol), **9b** (Aldrich; 1.02 g, 0.005 mol), DMF (150 mL), and TEA (20 mL) were boiled together under reflux for 16 h. The mixture was poured onto ice–water (1 L) containing acetic acid (20 mL). The precipitate was filtered off and dried. Crystallization from DMF gave **14** as brown needles: 0.3 g (14%); mp 185 °C; IR 1590, 1490 cm^{-1}; mass spectrum, m/e 526 (M^+).

Anal. Calcd for $C_{32}H_{22}N_4S_2$: C, 72.98; H, 4.21; N, 10.64. Found: C, 72.62; H, 4.42; N, 10.43.

Oxidation of 14 to 15. Compound **14** (1.0 g, 1.9 mmol), acetic acid (50 mL), and 6% hydrogen peroxide (20 mL) were heated to reflux, and then, after the addition of water (30 mL), the mixture was allowed to cool. The solid was filtered off and dried. Crystallization from ethanol gave **15** as yellow needles: 0.68 g (60%); mp 133–134 °C; IR 1590, 1500, 1380 cm^{-1}; ^1H NMR (Me_2SO-d_6) δ 6.52 (1 H, s), 7.3–8.2 (20 H, m), 9.08 (1 H, s); mass spectrum, m/e 590 (M^+).

Anal. Calcd for $C_{32}H_{22}N_4O_4S_2$: C, 65.07; H, 3.75; N, 9.49. Found: C, 65.25; H, 3.97; N, 9.47.

Reaction of 2 with Chloranil to Give 16a and/or 16b. Compound **2** (2.28 g, 0.01 mol), chloranil (1.23 g, 0.005 mol), DMF (100 mL), and TEA (10 mL) were boiled together under reflux for 30 min, and the mixture was then filtered while hot. The solid was washed with DMF and then with water and finally dried. Crystallization from a large volume of dimethylacetamide gave **16a** and/or **16b** as bright yellow needles: 1.1 g (40%); mp 440 °C; IR 1680, 1620, 1600, 1490 cm^{-1}; mass spectrum, m/e 492 (M^+).

Anal. Calcd for $C_{32}H_{20}N_4O_2$: C, 78.03; H, 4.09; N, 11.38. Found: C, 77.99; H, 4.02; N, 11.45.

7-Nitro-4-phenyl-2-(phenylazo)-4*H*-1,3,4-benzothiadiazine (4d). Dithizone (5.12 g, 0.02 mol), **9a** (3.72 g, 0.02 mol), and acetonitrile (40 mL) were stirred together at room temperature, and TEA (10 mL) was added. After 2 h, the solid was filtered off, and the filtrate was diluted with water, after which more solid separated and was filtered off. The combined solids were dried and crystallized from benzene to give **4d** as dark purple needles: 6.8 g (79%); mp 259–260 °C; IR 1560, 1500, 1335, 1270, 1090, 772 cm^{-1}; ^1H NMR (100 MHz, Me_2SO-d_6) δ 6.44 (d, J = 9.25 Hz), 7.40–7.65 (m), 7.73–7.87 (m), 7.94 (d, J = 2.5 Hz); mass spectrum, m/e 375 (M^+).

Anal. Calcd for $C_{19}H_{13}N_5O_2S$: C, 60.80; H, 3.47; N, 18.67. Found: C, 60.65; H, 3.54; N, 18.50.

When this reaction was conducted at 0 °C for 5 min, a yellow 1:1 condensation product (80%) was obtained which could be crystallized from chloroform/hexane but not obtained pure. At ca. 170 °C, the compound was transformed into the thiadiazine (TLC and subsequent melting point). The mass spectrum of the compound as normally determined was identical with that of the thiadiazine, although at a 20-eV ionizing voltage a low-intensity peak at m/e 422 (M^+) was observed.

Anal. Calcd for $C_{19}H_{14}N_6O_4S$: C, 54.03; H, 3.32; N, 19.91. Found: C, 53.02; H, 3.39; N, 19.46.

This 1:1 condensation product was not affected by brief boiling with acetic acid and 6% hydrogen peroxide. Extended boiling (4 h) with acetic acid or attempted oxidation with potassium ferricyanide/sodium bicarbonate in a two-phase chloroform/water system gave **4d**.

Oxidation of 4d to 4e. Compound **4d** (2.0 g, 5.3 mmol), acetic acid (50 mL), and 6% hydrogen peroxide (10 mL) were boiled under reflux for 20 min. When the mixture was cool, the precipitate was filtered off. Crystallization from acetic acid gave **4e** as orange needles: 1.7 g (78%); mp 243–247 °C after darkening at 225 °C; IR 1520, 1380, 1345, 1302, 1155, 1121, 688 cm^{-1}; ^1H NMR (100 MHz, Me_2SO-d_6) δ 7.08 (d, 1 H, J = 9.5 Hz), 7.51–7.92 (10 H, m), 8.35 (1 H, q, J_{ortho} = 9.5 Hz, J_{meta} = 2.5 Hz), 8.75 (1 H, d, J = 2.5 Hz); mass spectrum, m/e 407 (M^+) [a small peak was noted at m/e 423 ($C_{19}H_{13}N_5O_5S$), possibly due to an azoxy compound as a contaminant].

Anal. Calcd for $C_{19}H_{13}N_5O_4S$: C, 56.02; H, 3.19; N, 17.20. Found: C, 56.06; H, 3.16; N, 17.32.

4-Phenyl-2-(phenylazo)-7-(trifluoromethyl)-4*H*-1,3,4-benzothiadiazine (4f). Dithizone (5.12 g, 0.02 mol), **9c** (4.50 g, 0.02 mol), acetonitrile (120 mL), and TEA (30 mL) were warmed on a steam bath for 30 min, and then the mixture was stirred at room temperature for 4 h. The solid was filtered off, washed with a little acetonitrile and water, and dried to give **4f** as purple needles: 5.7 g (71%); mp 199 °C; IR 1600, 1560, 1495 cm^{-1}.

Anal. Calcd for $C_{20}H_{13}F_3N_4S$: C, 60.30; H, 3.29; N, 14.06. Found: C, 60.15; H, 3.63; N, 13.82.

4-Phenyl-2-(phenylazo)-4*H*-1,3,4-benzothiadiazine-7-sulfonamide (4g). Dithizone (5.12 g, 0.02 mol), **9d** (4.72 g, 0.02 mol), acetonitrile (130 mL), and TEA (20 mL) were boiled together under reflux for 2 h, and the mixture was then concentrated to approximately half its volume. The solid was filtered off, washed well with water, and dried to give **4g** as purple needles: 5.1 g (63%); mp 259 °C; IR 3450, 3330, 1600, 1560 cm^{-1}.

Anal. Calcd for $C_{19}H_{15}N_5O_2S_2$: C, 55.73; H, 3.69; N, 17.10. Found: C, 56.06; H, 3.83; N, 17.36.

4-Phenyl-2-(phenylazo)-4*H*-1,3,4-pyrido[3,2-*e*]thiadiazine (5c). Dithizone (2.56 g, 0.01 mol), **10a** (1.58 g, 0.01 mol), acetonitrile (20 mL), and TEA (10 mL) were boiled under reflux for 4 h. When the mixture was cool, the solution was poured into water (700 mL) containing acetic acid (20 mL). The solid was filtered off, dried, and crystallized from ethanol to give **5c** as purple needles: 2.5 g (75%); mp 164 °C; IR 1585, 1415, 1380, 1259, 1127, 1120, 686 cm^{-1}; ^1H NMR (100 MHz, Me_2SO-d_6) δ 6.99 (1 H, q, J = 7.5 Hz, J' = 4.7 Hz), 7.45–7.65 (9 H, m), 7.77–7.91 (3 H, m); mass spectrum, m/e 331 (M^+).

Anal. Calcd for $C_{18}H_{13}N_5S$: C, 65.26; H, 3.93; N, 21.15; S, 9.67. Found: C, 65.44; H, 3.81; N, 21.08; S, 9.76.

Oxidation of 5c to 5d. Compound **5c** (1.65 g, 0.005 mol), acetic acid (60 mL), and 6% hydrogen peroxide (10 mL) were boiled under reflux for 30 min. When the mixture was cool, the solid was filtered off, washed well with water, and dried. Crystallization from acetic acid gave **5d** as orange needles: 1.1 g (61%); mp 227–229 °C after darkening at ca. 220 °C; IR 1575, 1540, 1425, 1310, 1161, 1139, 1073, 751, 683 cm^{-1}; ^1H NMR (100 MHz, Me_2SO-d_6) δ 7.52–7.78 (ca. 11 H, m), 7.81–7.93 (2 H, m), 8.63 (1 H, q, J = 4 Hz, J' = 1.5 Hz), 8.69 (1 H, s); mass spectrum, m/e 363 (M^+) [a small peak was noted at m/e 379 ($C_{18}H_{13}N_5O_3S$), possibly due to an *N*-oxide or azoxy compound as a contaminant].

Anal. Calcd for $C_{18}H_{13}N_5O_2S$: C, 59.50; H, 3.58; N, 19.28. Found: C, 58.93; H, 3.60; N, 19.19.

6-(Methylthio)-4-phenyl-2-(phenylazo)-4*H*-1,3,4-pyrimido[4,5-*e*]thiadiazine (6c). Dithizone (5.12 g, 0.02 mol), **11** (4.78 g, 0.02 mol), acetonitrile (90 mL), and TEA (20 mL) were boiled together under reflux for 2 h, and the mixture was cooled and filtered. The solid was washed well with water and dried to give **6c** as purple needles: 6.3 g (83%); mp 208–209 °C; IR (KBr) 1575, 1515, 1390 cm^{-1}

Anal. Calcd for $C_{18}H_{14}N_6S_2$: C, 57.12; H, 3.73; N, 22.21; mol wt 378.0720. Found: C, 57.06; H, 3.73; N, 22.16; mol wt (mass spectrometry) 378.0703.

6,7-Dicyano-4-phenyl-2-(phenylazo)-4*H*-1,3,4-pyrazino[2,3-e]thiadiazine (7c). Dithizone (2.56 g, 0.01 mol), **12** (1.99 g, 0.01 mol), and acetonitrile (40 mL) were stirrred together at room temperature, and TEA (10 mL) was added. The mixture was stirred for 2 h and then filtered. The product was washed with methanol and water and dried in air to give **7c** as scarlet needles: 3.21 g (84%); mp 298–301 °C dec; IR (KBr) 2230 (C≡N), 1585, 1480, 1395, 1370 cm^{-1}.

Anal. Calcd for $C_{19}H_{10}N_8S$: C, 59.68; H, 2.64; N, 29.30; mol wt 382.0805. Found: C, 59.49; H, 2.80; N, 28.95; mol wt (mass spectrometry) 382.0805.

4-Phenyl-2-(phenylazo)-4*H*-1,3,4-quinoxalino[2,3-*e*]thiadiazine (8c). Dithizone (2.56 g, 0.01 mol), **13** (1.99 g, 0.01 mol), DMF (50 mL), and TEA (10 mL) were boiled under reflux for 4 h, and then the mixture was allowed to cool. The solid was filtered off, washed well with water, and dried to give **8c** as red needles: 2.7 g (71%); mp 313 °C; IR 1570, 1395, 1380, 1360, 1242, 1133, 688 cm^{-1}; mass spectrum, m/e 382 (M^+).

Anal. Calcd for $C_{21}H_{14}N_6S$: C, 65.97; H, 3.67; N, 21.99. Found: C, 66.12; H, 3.85; N, 22.04.

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Registry No. **1**, 532-96-7; **2**, 13437-75-7; **3**, 60-10-6; **4a**, 74298-39-8; **4b**, 74298-40-1; **4c**, 74298-41-2; **4d**, 74298-42-3; **4e**, 74298-43-4; **4f**, 74298-44-5; **4g**, 74298-45-6; **5a**, 74298-46-7; **5b**, 63810-94-6; **5c**, 74298-47-8; **5d**, 74298-48-9; **6a**, 74298-49-0; **6b**, 63810-92-4; **6c**, 74298-50-3; **7a**, 74298-51-4; **7b**, 63810-91-3; **7c**, 74298-52-5; **8a**, 74298-53-6; **8b**, 63811-31-4; **8c**, 74298-54-7; **9a**, 70-34-8; **9b**, 327-92-4; **9c**, 121-17-5; **9d**, 97-09-6; **10a**, 5470-18-8; **10b**, 2578-45-2; **11**, 63810-78-6; **12**, 56413-95-7; **13**, 2213-63-0; **14**, 74298-55-8; **15**, 74298-56-9; **16a**, 74298-57-0; **16b**, 74298-58-1; benzoic acid 2-(2,4-dinitrophenyl)-2-phenylhydrazide, 74298-59-2; benzoic acid 2-(3,5-dinitropyridin-2-yl)-2-phenylhydrazide, 74298-60-5.