Nitrile Sulfides. Synthesis of 2-(1,2,4-Thiadiazolyl)benzoates and 2-(1,2,4-Thiadiazolyl)benzonitriles

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1,3-Dipolar cycloadditions of aromatic nitrile sulfides to methyl *o*-cyanobenzoate and to phthalonitrile gave methyl 2-(3-aryl-1,2,4-thiadiazol-5-yl)benzoates **6a–c** and 2-(3-phenyl-1,2,4-thiadiazol-5-yl)benzonitrile (**7**). Cycloaddition of 2-cyanobenzonitrile sulfide to aromatic nitriles gave 2-(5-aryl-1,2,4-thiadiazol-3-yl)benzonitriles **11a,b**, which were converted to methyl 2-(5-aryl-1,2,4-thiadiazol-3-yl)benzoates **13a,b**. Yields of the cycloadducts are increased by dilution of the reaction mixtures with a nonpolar solvent.

Although considerable attention has been focused recently on several classes of 2-(heteroaryl)benzoates,[1-4] including 2-(1,3,4-thiadiazolyl)benzoates,[3] as potential herbicides and plant growth regulators, the two isomeric classes of the 2-(1,2,4-thiadiazolyl)benzoates have not been prepared. We report here the synthesis of 2-(1,2,4-thiadiazolyl)benzoates via application of nitrile sulfide[5,6] cycloaddition chemistry.

Thermolysis of 5-aryl-1,3,4-oxathiazol-2-ones (**1**) in aromatic nitriles produces 3,5-disubstituted-1,2,4-thiadiazoles **5** (Scheme I).[5] The reaction proceeds by way of 1,3-dipolar cycloaddition of an intermediate nitrile sulfide[6] **2** to the nitrile **3**. The substitution pattern in the thiadiazole **5** is determined by the choice of starting materials and is unambiguous.[5]

Addition of 5-phenyl-1,3,4-oxathiazol-2-one (**1a**) in three portions at 5-min intervals to 30 equiv of methyl *o*-cyanobenzoate at 195 °C gave methyl 2-(3-phenyl-1,2,4-thiadiazol-5-yl)benzoate (**6a**, Scheme II) in 12% yield only (Table I). Under very similar conditions, oxathiazolone **1a** and benzonitrile produced 3,5-diphenyl-1,2,4-thiadiazole in 50% yield.[5] Usually, electronegative substitutents in the nitrile result in greater yields of thiadiazole.[5] The low yield of **6a** from methyl *o*-cyanobenzoate thus indicates a significant steric hindrance effect in the cycloaddition. In order to determine conditions to increase the yield, we examined in greater detail the thermolysis of **1a** in the presence of nitriles. Several experimental results are summarized in Table I.

Previous work[5] had shown the remarkable dependence of yield upon the molar ratio of nitrile to oxathiazolone (Table I, lines 3–5). The yield of thiadiazole depends on the relative rates with which the intermediate nitrile sulfide cycloadds to nitrile **3** and decomposes to nitrile **4** and sulfur (Scheme I). Higher concentrations of nitrile should lead to higher yields of thiadiazole **5**. If decomposition of the nitrile sulfide were to occur only by a unimolecular process, eq 1–3 would provide appropriate

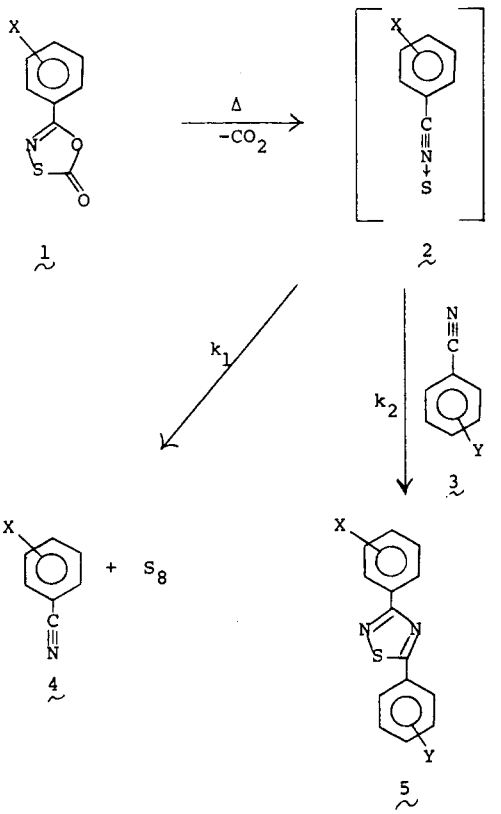
$$d[5]/dt = k_2[2][3] \quad (1)$$

$$d[4]/dt = k_1[2] \quad (2)$$

$$d[5]/d[4] = k'[3] \quad (3)$$

kinetic expressions for the reactions in Scheme I. *The observed dramatic increases of thiadiazole yields with increased number of equivalents of nitrile 3* (14, 39, and 74% yields with 10, 35, and 100 equiv, respectively) *are not consistent with a unimolecular process as the sole mechanism for decomposition of the nitrile sulfide.* In these experiments, **3** was the solvent, and changes from 10 to 35 to 100 equiv of **3** could not significantly change the molar concentration of **3** and thus the yield of thiadiazole.

Scheme I



Under conditions of high dilution (10^{-6}–10^{-5} M) in ethanol, nitrile sulfides decompose with pseudo-first-order kinetics; the observed activation entropies are consistent with bimolecular reactions involving ethanol in the transition state.[7] In the nonpolar solvent carbon tetrachloride, however, decomposition of nitrile sulfides gave deviations from first-order kinetics.[7] Holm, Christiansen, and Lohse[7] pointed out that scavenging of nitrile sulfides with sulfur atoms would clearly give rise to kinetics of higher order than unity.

Our reactions were carried out at much higher concentrations than 10^{-5} M so that higher order reactions were not suppressed. The marked dependence of yield of **5** on the number of equivalents of **3** is consistent with decom-

(1) A. L. Johnson and P. B. Sweetser, *J. Org. Chem.*, **41**, 110 (1976).
(2) A. L. Johnson, *J. Org. Chem.*, **41**, 1320 (1976).
(3) R. L. N. Harris and J. L. Huppatz, *Aust. J. Chem.*, **30**, 2225 (1977).
(4) R. L. N. Harris, J. L. Huppatz, and T. Teitei, *Aust. J. Chem.*, **32**, 669 (1979).
(5) R. K. Howe and J. E. Franz, *J. Org. Chem.*, **39**, 962 (1974).
(6) R. K. Howe, T. A. Gruner, L. G. Carter, L. L. Black, and J. E. Franz, *J. Org. Chem.*, **43**, 3736 (1978), and references therein.
(7) A. Holm, J. J. Christiansen, and C. Lohse, *J. Chem. Soc., Perkin Trans. 1*, 960 (1979).

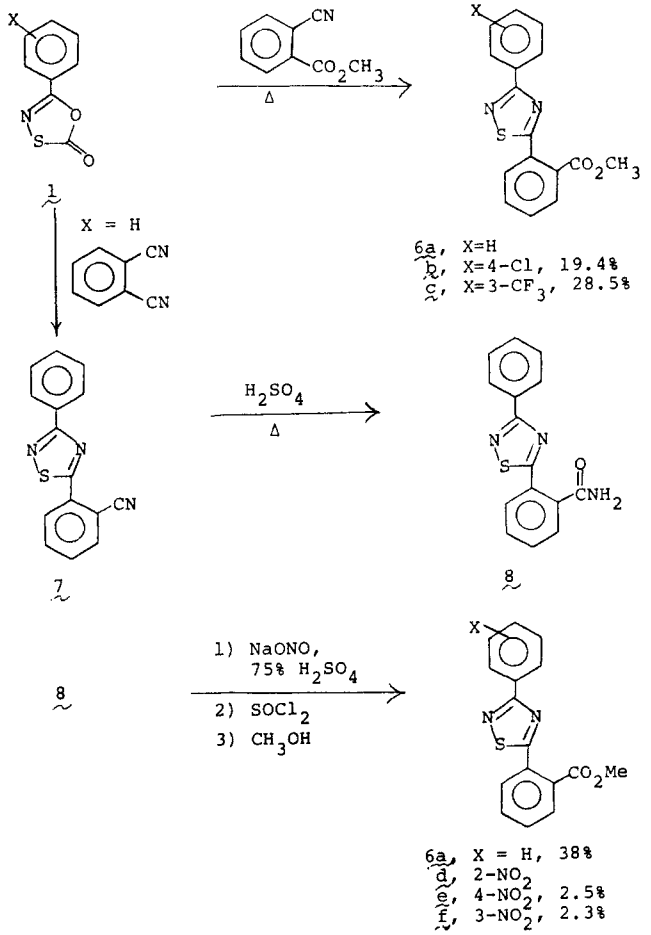
0022-3263/81/1946-0771$01.00/0

Table I.[a] Reactions of 5-Phenyl-1,3,4-oxathiazol-2-one (1, X = H) with Ortho-Substituted Nitriles 3 (NCC_6H_4-o-Y)

Y	molar ratio of 3/1	[1], mol/L	solvent	time of addn of 1[b]	temp, °C	product[c]	% yield[d]
CO_2CH_3	30	0.21	3	10 min[e]	195	6a	12
H	35	0.28	3	10 min[e]	190	5	50[f]
H	10	0.98	3	~1 s	190	5	14[f]
H	35	0.28	3	~1 s	190	5	39[f]
H	100	0.098	3	~1 s	190	5	74[f]
H	8.67	0.28	dodecane	~1 s	190	5	28
CO_2CH_3	1	~6	3	4 min	180-190	6a	≤1
CO_2CH_3	1	0.75	dodecane	4 min	195-205	6a	6
CO_2CH_3	1	0.75	1,2,4-$Cl_3C_6H_3$	4 min	195-205	6a	≤1
CO_2CH_3	1	0.75	$C_6H_5NO_2$	4 min	195-205	6a	<1
CO_2CH_3	5	0.067	dodecane	1-2 min	180-185	6a	16
CN	5	0.067	dodecane	1-2 min	180-185	7	49
CN	5	0.067	dodecane	5 min	180-185	7	71

[a] See Schemes I and II. [b] All reactions were heated another 15 min after addition of 1 was complete (>10 half-lives of 1). Products were shown to be stable under the reaction conditions. [c] For 5, X = Y = H. [d] Yields were determined by GC on a 0.25 in. × 2 ft column packed with 10% OV-17 on Chromosorb W, with internal standards and calibration mixtures. [e] Added in three portions at 5-min intervals. [f] Reference 5.

Scheme II



position of the nitrile sulfide by reaction with short sulfur chains;[8] the sulfur chains grow both by reaction with 2 and by combination with other sulfur chains. Chain growth terminates in cyclic S_8 molecules (eq 4). This mechanism

$$2 \xrightarrow[(x = 1\text{-}7)]{S_x} 4 + S_{x+1} \rightarrow S_8 \qquad (4)$$

involves a series of bimolecular reactions whose rates, and thus the rate of formation of 4, would be slowed to a greater extent by dilution than the rate of a unimolecular decomposition of 2 to 4 and sulfur atoms. Since the sulfur species arise from 2 formed from oxathiazolone 1, a decrease in the concentration of 1 relative to 3 will give lower concentrations of sulfur chains relative to 3 and will result in greater yields of 5, in accordance with the experimental results. Slow or portionwise addition of 1 to 3 results in increased yields (Table I) by allowing a greater percentage of the sulfur chains to form nonreactive S_8 molecules. Whether a unimolecular sulfur extrusion from 2 occurs or not is uncertain; Holm and co-workers[7] have addressed this point in detail. It is quite possible that initial sulfur formation from 2 occurs by combination of two molecules of nitrile sulfide to form 4 and an $ArCNS_2^-$ species (which then generates sulfur) and/or by reaction of a solvent impurity with 2. We found previously that commercial samples of nitriles 3 contained impurities that lowered thiadiazole yields, so we employed purified nitriles in all cases.[5] Further, we employed, insofar as was possible, the same batches of purified nitriles for comparison of yields under different experimental conditions.

The rates of 1,3-dipolar cycloaddition reactions increase with decreased solvent polarity[9,10] because of charge dispersion and partial charge neutralization in going to the transition state. We very briefly surveyed the effect of solvents on the reaction of 1a with benzonitrile and with methyl o-cyanobenzoate. Use of dodecane as solvent and diluent gives increased yields of thiadiazoles relative to excess nitrile (which is polar) (see Table I, lines 3 and 6–8), to trichlorobenzene, or to nitrobenzene as solvent.

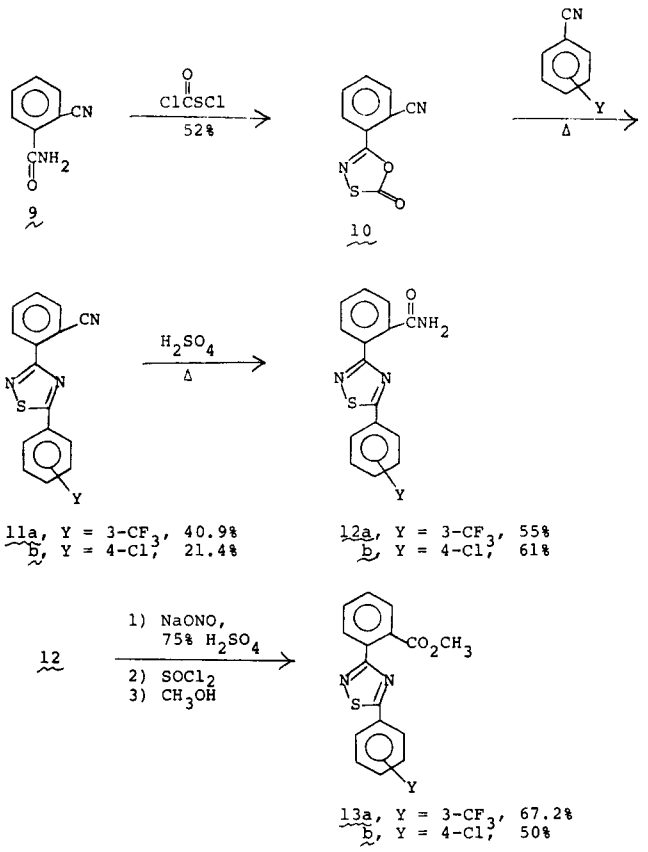
The yield of thiadiazolylbenzoate 6a was still only 16% from reaction of 1a with 5 equiv of methyl o-cyanobenzoate in dilute solution in dodecane. Since phthalonitrile offers less steric hindrance to cycloaddition and possesses a statistical factor advantage, we decided to use it to prepare thiadiazolylbenzonitrile 7, a reasonable precursor of the benzoate 6a. Under the same conditions in which methyl o-cyanobenzoate gave 6a in 16% yield, phthalonitrile gave 7 in 49% yield. Addition of the oxathiazolone 1a over a longer time, 5 min instead of 1 or 2 min, increased the yield of 7 to 71%; 7 was isolated in pure form in 53% yield. Use of an addition time of 9 min allowed isolation of pure 7 in 60.6% yield.

Base hydrolysis of 7 resulted in mixtures of amide, acid, and hydrogen sulfide (after acidification) from thiadiazole

(8) The bimolecular mechanism of nitrile sulfide decomposition was first suggested to us by Professor R. F. Hudson in 1974 (private communication).

(9) R. Huisgen and H. Gotthardt, *Chem. Ber.*, **101**, 1059 (1968).
(10) Y.-M. Chang, J. Sims, and K. N. Houk, *Tetrahedron Lett.*, 4445 (1975).

Scheme III



ring destruction; one basic hydrolysis mixture gave 7% of amide **8**, 40% of thiadiazolylbenzoic acid, and 46% of phthalic acid (crude yields). Treatment of **7** with *p*-toluenesulfonic acid monohydrate in ethanol at reflux[11] for 4 h gave no detectable reaction to form either the ethyl ester or the amide. Use of hot, concentrated sulfuric acid[12] allowed nearly quantitative conversion of nitrile **7** to amide **8**. Nitrosative deamination with sodium nitrite in 75% sulfuric acid[12] of **8** gave 27% concomitant nitration under the mildest conditions under which the deamination would occur. The resultant mixture of acids was converted to a mixture of methyl esters. GC and GC/MS analyses revealed that the ester mixture consisted of 73% of the desired ester **6a**, 7% of *o*-nitro product **6d**, and 20% total of *p*- and *m*-nitro products **6e** and **6f**. Kugelrohr distillation and crystallization gave pure methyl 2-(3-phenyl-1,2,4-thiadiazol-5-yl)benzoate (**6a**) in 38% yield (from **8**), pure *p*-nitro ester **6e** in 2.5% yield, and pure *m*-nitro ester **6f** in 2.3% yield.

Thiadiazolylbenzoates **6b** and **6c** were prepared directly from methyl *o*-cyanobenzoate. Addition of 5-(4-chlorophenyl)-1,3,4-oxathiazol-2-one over a 30-min period to 5 equiv of methyl *o*-cyanobenzoate in dodecane solution gave **6b** in 23% yield (GC analysis); **6b** was isolated in 19.4% yield. Similarly, 5-[3-(trifluoromethyl)phenyl]-1,3,4-oxathiazol-2-one gave **6c** in 28.5% yield (isolated). The chloro and trifluoromethyl substituents were employed to increase the yield of the cycloaddition reaction, on the basis of previously reported[5] substituent effects on nitrile sulfide cycloadditions.

The methyl 2-(5-aryl-1,2,4-thiadiazol-3-yl)benzoates **13a** and **13b** were prepared as shown in Scheme III by starting from 2-(2-oxo-1,3,4-oxathiazol-5-yl)benzonitrile (**10**). Again, the trifluoromethyl and chloro substituents were chosen to increase the cycloaddition yields and also to deactivate the aryl ring toward nitration in the nitrosative deamination step.

The herbicide and plant growth regulator activities of the 2-(1,2,4-thiadiazolyl)benzoates were less than those observed for analogous compounds, e.g., the 2-(1,2,4-oxadiazolyl)benzoates.

Experimental Section

Melting points were taken in open capillaries in a Mel-Temp apparatus and are corrected; boiling points are uncorrected. All reactant nitriles were distilled under vacuum; the center cuts were retained.

2-(3-Phenyl-1,2,4-thiadiazol-5-yl)benzonitrile (7). To a stirred solution of 33.3 g (0.26 mol) of redistilled phthalonitrile in 780 mL of dodecane at 180–185 °C was added 9.32 g (0.052 mol) of 5-phenyl-1,3,4-oxathiazol-2-one[6,13] (0.2 g at a time) during 5 min. The reaction mixure was stirred at 180–185 °C for another 15 min, cooled, concentrated under vacuum, and distilled in a Kugelrohr apparatus. Excess phthalonitrile was removed at 100–130 °C (0.05 mm), and 8.55 g (62%) of solid product was collected at 160 °C (0.05 mm). Crystallization of the solid from ethanol gave 7.30 g (53%) of beige needles: mp 138–140 °C; IR (Nujol) 2220 cm^{-1} (CN).

Anal. Calcd for $C_{15}H_9N_3S$: C, 68.42; H, 3.45; N, 15.96. Found: C, 68.51; H, 3.48; N, 15.94.

In a repeat of this reaction, the oxathiazalone was added portionwise during 9 min. An identical workup gave **7** as white needles: mp 138.5–140 °C; 60.6% yield.

2-(3-Phenyl-1,2,4-thiadiazol-5-yl)benzamide (8). A solution of 8.3 g (0.0315 mol) of 2-(3-phenyl-1,2,4-thiadiazol-5-yl)benzonitrile in 75 mL of concentrated sulfuric acid was heated on a steam bath for 40 min, cooled, and then poured into 600 mL of ice–water with stirring. The resultant solid was collected, washed with water, and air-dried to give 8.68 g (98%) of white solid, mp 171–172 °C. Recrystallization of the solid from 65% aqueous ethanol gave 7.36 g (83%) of white solid: mp 173–174 °C; IR (Nujol) 3370, 3150, 1640 cm^{-1}.

Anal. Calcd for $C_{15}H_{11}N_3OS$: C, 64.04; H, 3.94. Found: C, 64.05; H, 3.97.

Methyl 2-(3-Phenyl-1,2,4-thiadiazol-5-yl)benzoate (6a), Methyl 2-[3-(4-Nitrophenyl)-1,2,4-thiadiazol-5-yl]benzoate (6e), and Methyl 2-[3-(3-Nitrophenyl)-1,2,4-thiadiazol-5-yl]benzoate (6f). To a solution of 7.55 g (0.0268 mol) of 2-(3-phenyl-1,2,4-thiadiazol-5-yl)benzonitrile in 150 mL of 75% H_2SO_4 was added portionwise 11.1 g (0.161 mol) of sodium nitrite at 60–63 °C (mild exotherm) during 15 min with stirring. The solution was stirred another 3 min and then was poured into 700 mL of ice–water. The resultant solid was collected; mp 135–145 °C. The solid was treated with 700 mL of 10% NaOH. The mixture was filtered, and the undissolved solid (mainly sodium carboxylate salted out by excess NaOH) was stirred with 700 mL of water; almost all the solid dissolved. The mixture was filtered, and the two filtrates were combined and acidified. The resultant solid was collected and air-dried to give 6.95 g of solid, mp 145–155 °C (prior softening).

The solid was heated with 22 mL of thionyl chloride at reflux on a steam bath for 30 min. The resultant orange solution was concentrated under vacuum. The residue was heated in 75 mL of methanol at reflux for 15 min. This solution was concentrated under vacuum to 6.5 g of viscous oil. GC and GC/MS analyses showed this oil to consist of 73% of **6a**, 7% of *o*-nitro product, and 20% of *m*- plus *p*-nitro products. Kugelrohr distillation of the oil gave a small forerun up to 130 °C (0.03 mm), ~3.6 g of 96.6% pure **6a** at 140 °C (0.03 mm), 1.54 g of 43% **6a** and 57% higher boilers at 140 °C (0.03 mm), and then 0.43 g of a mixture of the nitrated products at 170–200 °C (0.03 mm).

The 96.6% pure **6a** was Kugelrohr distilled to give 3.05 g (38%) of 100% pure product (mp 60.5–62.5 °C) at 130–135 °C (0.03 mm). Crystallization of 2.85 g of this material from methanol gave 2.50

(11) F. L. James and W. H. Bryan, *J. Org. Chem.*, **23**, 1225 (1958).
(12) S. Sarel and M. S. Newman, *J. Am. Chem. Soc.*, 78, 5416 (1956).
(13) A. Senning and P. Kelly, *Acta Chem. Scand.*, **21**, 1871 (1967).

g of white solid, methyl 2-(3-phenyl-1,2,4-thiadiazol-5-yl)benzoate: mp 61–63 °C; IR (film of melt) 1723 cm^{-1}; NMR ($CDCl_3$) δ 8.43–8.27 (m, 2, Ar H), 7.93–7.35 (m, 7, Ar H), 3.80 (s, 3, OCH_3).

Anal. Calcd for $C_{16}H_{12}N_2O_2S$: C, 64.85; H, 4.08; S, 10.82. Found: C, 64.91; H, 4.10; S, 10.89.

The 0.26 g of pot residue from this last Kugelrohr distillation (consisting of 36% **6a** and 64% nitrated esters) was combined with the 1.54 g of ester mixture from the first Kugelrohr distillation. Crystallization of this 1.80 g of material from 75 mL of methanol gave 0.24 g of **6e**, a pale yellow solid (mp 144–147 °C), as the first crop and 0.29 g of solid (mp <110 °C) as the second crop. Similarly, crystallization of the 0.43 g of material from the first Kugelrohr distillation from methanol gave 0.09 g of pale yellow solid **6e** (mp 145–148 °C) as the first crop and 0.19 g of solid (mp <120 °C) as the second crop. The two first-crops were combined and crystallized from methanol to give 0.23 g (2.5%) of methyl 2-[3-(4-nitrophenyl)-1,2,4-thiadiazol-5-yl]benzoate (**6e**) as a pale yellow solid: mp 151–152 °C; IR (Nujol) 1721, 1510, 1345 cm^{-1}; NMR ($CDCl_3$) δ 8.67–8.27 (AA'BB' m, 4, Ar H), 8.07–7.57 (AA'BB' m, 4, Ar H), 3.83 (s, 3, OCH_3).

Anal. Calcd for $C_{16}H_{11}N_3O_4S$: C, 56.30; H, 3.25. Found: C, 56.09; H, 3.31.

The two second crops (0.48 g total, mp <120 °C) were combined and crystallized twice from methanol to give 0.21 g (2.3%) of methyl 2-[3-(3-nitrophenyl)-1,2,4-thiadiazol-5-yl]benzoate (**6f**): mp 125–126 °C; IR (Nujol) 1701, 1512, 1350 cm^{-1}; NMR ($CDCl_3$) δ 9.20 (t, 1, $J + J' \simeq 3.8$ Hz, H-2 of 3-$NO_2C_6H_4$), 8.67 (d of small t, 1, $J = 8$, 1.3 Hz, H-4 of 3-$NO_2C_6H_4$), 8.37 (d of small q, 1, $J = 8$, $J + J' \simeq 3.8$ Hz, H-6 of 3-$NO_2C_6H_4$), 8.07–7.53 (m, 5, H-5 of 3-$NO_2C_6H_4$ plus all H's of the other ring), 3.88 (s, 3, OCH_3).

Anal. Calcd for $C_{16}H_{11}N_3O_4S$: C, 56.30; H, 3.25. Found: C, 56.30; H, 3.29.

Methyl 2-[3-(4-Chlorophenyl)-1,2,4-thiadiazol-5-yl]benzoate (6b). To a solution of 7.54 g (0.0468 mol) of methyl *o*-cyanobenzoate in 150 mL of dodecane stirred at 180–190 °C was added 2.00 g (0.00936 mol) of powdered 5-(4-chlorophenyl)-1,3,4-oxathiazol-2-one[6,13] 0.1 g at a time during 30 min. The solution was stirred at 190 °C for another 25 min (GC analysis of an aliquot dissolved in acetone showed that **6b** had formed in 23% yield), cooled, and concentrated under oil pump vacuum to 7.24 g of brown residue. Further concentration of the residue in a Kugelrohr apparatus at 85 °C (0.35 mm) gave 1.35 g of brown pot residue. Chromatography of this residue on a 1 in. × 13 in. column of silica gel with toluene gave 0.65 g of product (mp 75.5–80 °C) which was heated in a Kugelrohr apparatus at 140 °C (0.2 mm) to give 0.60 g (19.4%) of solid product (mp 74.5–77 °C) as the pot residue. Crystallization of this solid from methanol gave 0.41 g of **6b**: mp 75.5–77.5 °C; NMR ($CDCl_3$) δ 8.4–7.4 (m, 8), 3.8 (s, 3); IR (Nujol) 1720 cm^{-1}.

Anal. Calcd for $C_{16}H_{11}ClN_2O_2S$: C, 58.10; H, 3.35; N, 8.47. Found: C, 57.98; H, 3.40; N, 8.47.

Methyl 2-[3-[(3-Trifluoromethyl)phenyl]-1,2,4-thiadiazol-5-yl]benzoate (6c). Powdered 5-[3-(trifluoromethyl)-phenyl]-1,3,4-oxathiazol-2-one[6] (6.67 g, 0.027 mol) was added 0.2 g at a time over a 30-min period to a solution of 21.76 g (0.135 mol) of methyl *o*-cyanobenzoate in 540 mL of dodecane stirred at 185–190 °C. The solution was stirred at 190 °C for another 20 min, cooled, and concentrated under oil pump vacuum to 5.3 g of residue. This material was chromatographed on a high-pressure LC unit using a 1 in. × 13 in. scrubber column and a E. M. Lobar size C column, both packed with silica gel. After elution with 1800 mL of toluene, further elution with 10% ether in toluene gave 2.8 g (28.5%) of **6c**, mp 68–70.5 °C. Crystallization of the solid from hexane gave 1.95 g (20%) of **6c**: mp 71–72 °C; NMR ($CDCl_3$) δ 8.6 (m, 2), 8.0–7.5 (m, 6), 3.8 (s, 3); IR (Nujol) 1705 cm^{-1}.

Anal. Calcd for $C_{17}H_{11}F_3N_2O_2S$: C, 56.04; H, 3.04; N, 7.69. Found: C, 56.07; H, 3.05; N, 7.71.

2-(2-Oxo-1,3,4-oxathiazol-5-yl)benzonitrile (10). A mixture of 10.34 g (0.0707 mol) of *o*-cyanobenzamide, 27.80 g (0.212 mol) of (chlorocarbonyl)sulfenyl chloride,[14] and 250 mL of toluene was stirred at 100 °C for 21 h (IR was used to monitor the disappearance of the amide peaks). The solution was allowed to cool; 8.98 g of light yellow solid (mp 158–164 °C dec) was collected and recrystallized from toluene to give 7.33 g (52% yield) of light yellow solid, mp 162–163 °C dec. Recrystallization of a small amount gave an analytical sample: mp 167–168 °C (lit.[15] mp 166–169 °C dec); IR (Nujol) 2220, 1845, 1780–1660 cm^{-1} (br); NMR ($CDCl_3$) δ 8.1–7.7 (m).

Anal. Calcd for $C_9H_4N_2O_2S$: C, 52.94; H, 1.97; N, 13.72. Found: C, 52.95; H, 1.99; N, 13.73.

2-[5-[3-(Trifluoromethyl)phenyl]-1,2,4-thiadiazol-3-yl]benzonitrile (11a). To a solution of 83.8 g (0.489 mol) of *m*-(trifluoromethyl)benzonitrile in 800 mL of decalin stirred at reflux was added slowly 10.0 g (0.0489 mol) of powdered 2-(2-oxo-1,3,4-oxathiazol-5-yl)benzonitrile over a period of 40 min. This mixture was held at reflux for another 40 min, cooled, concentrated under vacuum, and Kugelrohr distilled up to 100 °C (0.07 mm) to give 10.4 g of black residue in the pot. The residue was boiled with methanol, and the hot mixture was filtered free of a little insoluble solid. The filtrate gave 4.42 g of brown needles (mp 116–117 °C) upon cooling; an additional 1.50 g of product (mp 113–115 °C) was obtained from the filtrate (40.9% total yield). A 1.0-g sample of product was recrystallized twice from cyclohexane (charcoal) to give 0.42 g of analytically pure **11a**: mp 117.5–118.5 °C; IR (Nujol) 2230, 1608, 1590 cm^{-1}.

Anal. Calcd for $C_{16}H_8F_3N_3S$: C, 58.00; H, 2.43. Found: C, 58.00; H, 2.41.

2-[5-(4-Chlorophenyl)-1,2,4-thiadiazol-3-yl]benzonitrile (11b). To a solution of 67.9 g (0.494 mol) of *p*-chlorobenzonitrile in 700 mL of decalin stirred at 180–190 °C was added 10.1 g (0.0494 mol) of powdered 2-(2-oxo-1,3,4-oxathiazol-5-yl)benzonitrile during 40 min. The mixture was stirred at 190 °C for another 20 min, cooled, and filtered to give 49.5 g of a mixture of product and *p*-chlorobenzonitrile. This mixture was subjected to Kugelrohr distillation up to 125 °C (0.07 mm) to give 4.7 g of fairly pure (GC assay) solid product. One crystallization of this solid from methylcyclohexane (charcoal) gave 3.15 g (21.4%) of pure **11b**: mp 172–173 °C; IR (Nujol) 2225 cm^{-1}.

Anal. Calcd for $C_{15}H_8ClN_3S$: C, 60.51; H, 2.71. Found: C, 60.61; H, 2.77.

2-[5-[3-(Trifluoromethyl)phenyl]-1,2,4-thiadiazol-3-yl]benzamide (12a). A solution of 3.73 g of **11a** in 40 mL of concentrated sulfuric acid was heated on a steam bath for 35 min, cooled, and poured into 300 mL of ice–water with stirring. The resultant solid was collected, washed with water and recrystallized from ethanol to give 2.16 g (55%) of white solid, mp 217–218 °C. A small amount was recrystallized for an analytical sample: mp 217.5–218.5 °C; IR (Nujol) 3270, 3190, 1640 cm^{-1}.

Anal. Calcd for $C_{16}H_{10}F_3N_3OS$: C, 55.01; H, 2.89. Found: C, 54.82; H, 2.91.

2-[5-(4-Chlorophenyl)-1,2,4-thiadiazol-3-yl]benzamide (12b). A solution of 3.04 g of **11b** in 30 mL of concentrated sulfuric acid was heated on a steam bath for 30 min, cooled, and poured into 300 mL of ice–water with stirring. The resultant solid was collected, washed with water, and crystallized from ethanol to give 1.97 g (61%) of amide **12b**, mp 181.5–184.5 °C. A small sample was recrystallized for analysis: mp 188.5–190 °C; IR (Nujol) 3380, 3190, 1640 cm^{-1}.

Anal. Calcd for $C_{15}H_{10}ClN_3OS$: C, 57.05; H, 3.19. Found: C, 56.51; H, 3.03.

Methyl 2-[5-[3-(Trifluoromethyl)phenyl]-1,2,4-thiadiazol-3-yl]benzoate (13a). To a solution of 2.15 g of **12a** in 45 mL of 75% sulfuric acid at 60–80 °C was added portionwise 3.5 g of sodium nitrite with swirling. The mixture was cooled, poured into 250 mL of ice–water, and filtered. The resultant solid was collected and dissolved in ether. The ether solution was dried ($CaSO_4$) and concentrated under vacuum to a white solid. A mixture of the solid and 10 mL of thionyl chloride was held at reflux for 30 min and then concentrated under vacuum. The residue was heated with 10 mL of methanol at reflux for 30 min. The solution was filtered and concentrated under vacuum to 1.51 g (67.2%) of ≥99% pure **13a** (GC, IR, and NMR analyses) as a viscous oil. This oil was Kugelrohr distilled at 125 °C (0.04 mm)

(14) (a) British Patent 1 079 348 (1966); (b) E. Kühle, *Synthesis*, 617 (1971).

(15) A. Senning and J. S. Rasmussen, *Acta Chem. Scand.*, **27**, 2161 (1973).

to give a center cut of 1.11 g (49%) of **13a** as a clear, viscous oil (pure by GC analysis): NMR ($CDCl_3$) δ 8.3–8.0 (m, 3), 7.85–7.45 (m, 5), 3.8 (s, 3); IR (film) 1725 cm^{-1}.

Anal. Calcd for $C_{17}H_{11}F_3N_2O_2S$: C, 56.04; H, 3.04. Found: C, 55.94; H, 3.05.

Methyl 2-[5-(4-Chlorophenyl)-1,2,4-thiadiazol-3-yl]-benzoate (13b). The above procedure was applied, with 3.5 g of sodium nitrite added during 1 h to 1.95 g of **12b** in 40 mL of 75% sulfuric acid at 70–80 °C. The crude acid (1.93 g, mp 171–174 °C) was converted to 1.80 g of crude ester. Kugelrohr distillation of the ester at 120–140 °C (0.04 mm) gave 1.01 g (50%) of clear viscous oil that crystallized after 1 week: mp 84–85 °C; IR (melt) 1722 cm^{-1}; NMR ($CDCl_3$) δ 8.2–7.4 (m, 8), 3.8 (s, 3).

Anal. Calcd for $C_{16}H_{11}ClN_2O_2S$: C, 58.09; H, 3.35. Found: C, 57.95; H, 3.39.

Registry No. 6a, 76010-55-4; **6b**, 76010-56-5; **6c**, 76010-57-6; **6d**, 76010-58-7; **6e**, 76010-59-8; **6f**, 76010-60-1; **7**, 76010-61-2; **8**, 76010-62-3; **9**, 17174-98-0; **10**, 52059-77-5; **11a**, 76010-63-4; **11b**, 76010-64-5; **12a**, 76010-65-6; **12b**, 76010-66-7; **13a**, 76010-67-8; **13b**, 76010-68-9; phthalonitrile, 91-15-6; 5-phenyl-1,3,4-oxathiazol-2-one, 5852-49-3; methyl *o*-cyanobenzoate, 6587-24-2; 5-(4-chlorophenyl)-1,3,4-oxathiazol-2-one, 17452-79-8; 5-[3-(trifluoromethyl)phenyl]-1,3,4-oxathiazol-2-one, 57459-15-1; (chlorocarbonyl)sulfenyl chloride, 2757-23-5; *m*-(trifluoromethyl)benzonitrile, 368-77-4; 2-(2-oxo-1,3,4-oxathiazol-5-yl)benzonitrile, 52059-77-5; *p*-chlorobenzonitrile, 623-03-0; 2-[5-(4-chlorophenyl)-1,2,4-thiadiazol-3-yl]benzoic acid, 76010-69-0.

Electrochemical Reduction of Carbon Disulfide. Synthesis of Carbon Sulfide Heterocycles[1]

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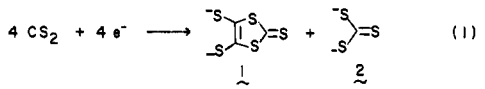
Detailed procedures for the electrochemical reduction of carbon disulfide in *N,N*-dimethylformamide and acetonitrile are given. The synthetic utility of the method is demonstrated by the preparation of several thio-substituted derivatives of tetrathiafulvalene. Cyclic voltammograms of the tetrapotassium salt of the tetrathio anion of tetrathiafulvalene indicate four successive electron-transfer steps and in situ formation of a C_6S_8 species. Oxidation of the CS_2 electrolysis solutions produces a compound which is tentatively identified as [1,3]dithiolo[4,5-*d*]-1,2,3-trithiole-5-thione.

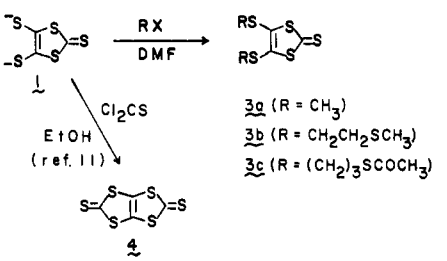
The reduction of carbon disulfide in aprotic media provides synthetic entry into multisulfur species based on the 1,3-dithiole ring structure. Although the sodium amalgam reduction of CS_2 was studied 50 years ago,[2] only recently was the structure of the key product, the 4,5-dimercapto-1,3-dithiole-2-thione dianion (**1**), elucidated by Wawzonek and Heilmann.[3] Under suitable conditions this species can be prepared in close to stoichiometric amounts either by active metal[4] or electrochemical reduction according to eq 1. We and others have exploited this



(1)

chemistry for the synthesis of multisulfur electron donors in the tetrathioethylene series.[5-14] The yields in the electrochemical reduction of CS_2 can be low, because at intermediate stages of these electrolyses, complex mixtures of anionic multisulfur species are produced which are potential, concentration, and time dependent.[15,16] However, essentially stoichiometric yields of **1** can be obtained by electrochemical reduction of CS_2 in either DMF or CH_3CN. The procedures, which are relatively simple, do not require high-purity solvents or electrolytes and can be performed without sophisticated electrochemical gear. These procedures are reported in this paper along with the synthesis of several new carbon–sulfur compounds.

Scheme I



Following the chemistry of Engler and Schumaker[17] and Krug et al.,[11] we have used these procedures to prepare the 1,3,5,7-tetrathiapentalene ring system and derivatives of tetrathiotetrathiafulvalene. The cyclic voltammetry of these compounds is also reported in this paper.

Results and Discussion

The electrochemical reduction of CS_2 provides a convenient synthetic entry into the 1,3-dithiole ring system via the dianion **1** as shown in Scheme I. Alkylation yields thiones such as **3a–c**, while treatment of **1** with thio-

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