The Chemistry of 1,2,5-Thiadiazoles. III. [1,2,5]Thiadiazolo[3,4-c][1,2,5]thiadiazole[1]

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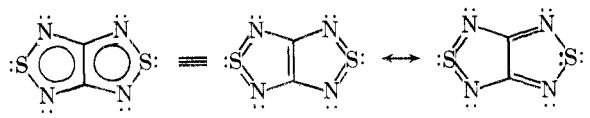
The stable new heteroaromatic compound, [1,2,5]thiadiazolo[3,4-c][1,2,5]thiadiazole (1), was synthesized by three routes. Ring closure of 2 with *excess* sulfur mono- or dichloride in DMF gave 1. The aminoamidine 9a was isolated from the reaction of 2 with only 1 mol of sulfur dichloride. Diamine 3 could be cyclized to 1 with either thionyl chloride in pyridine or with sulfur monochloride in DMF. Oxamide dioxime (4) closed to 1 when treated with sulfur dichloride in DMF. Hydrolysis of 1 gave 3, which on further hydrolysis gave oxamide.

We report the synthesis of a new bicyclic heteroaromatic compound, [1,2,5]thiadiazolo[3,4-c][1,2,5]thiadiazole (1),



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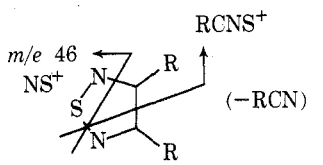
by three independent methods. This ring system represents a unique extension of the isoelectronic replacement of all peripheral atoms of naphthalene with hetero equivalents. A symmetrical and relatively stable ring system results which has only sulfur and nitrogen atoms in exterior positions, with no substituents except unshared electron pairs. The new ring system can be regarded as aromatic by the criteria of planarity, shortened bond lengths, and chemical stability. It shares with the thieno[3,4-c]thiophene series the characteristic that the uncharged resonance contributors contain at least one tetravalent sulfur;[2] yet it appears to possess much greater stability than the thieno[3,4-c]thiophene family. It is the first in a series of bicyclic, tricyclic, and tetracyclic aromatic compounds, with only hetero elements in the periphery, which we shall describe in later papers of this series.[3,4]

Properties of 1. Pure [1,2,5]thiadiazolo[3,4-c][1,2,5]-thiadiazole (1) is a white, crystalline solid, mp 115.7–116°. Trace contaminants (often sulfur) give it a faint yellow color. Although small samples of 1 could be obtained by preparative GLC on an SE-30 column, purification was best accomplished by recrystallization from methanol, vacuum sublimation, or column chromatography on silica gel, or combinations of the three methods.

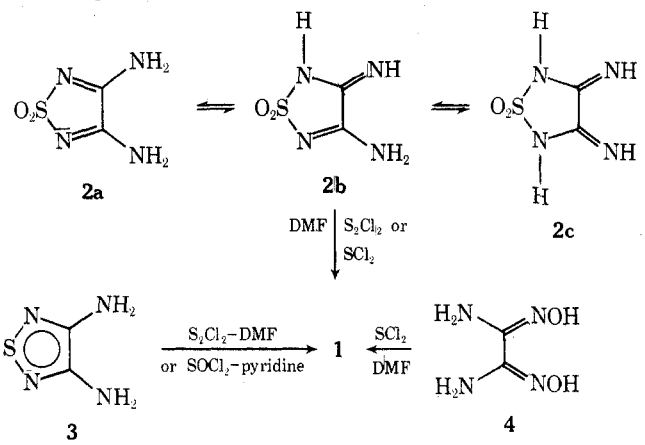
The physical properties of 1 resemble those of naphthalene: it is a planar,[5] nonpolar, volatile, and only very weakly basic white solid, soluble in organic solvents and only very slightly soluble in water.

The molecular formula of 1 was established to be $C_2N_4S_2$ by elemental analysis. A high degree of symmetry for 1 was indicated by the simple infrared spectrum, which contained only four absorptions at 10.9, 12.3, 18.5, and 23 μm. Maxima occurred at 215 and 317 m in the ultraviolet spectrum. The ^{13}C NMR spectrum in chloroform showed a single line at 169.4 ppm from Me_4Si for the two identical carbons. [For comparison, the carbons of 1,2,5-thiadiazole appear at 149.1 ppm ($CHCl_3$), and the ring fusion carbons of 2,1,3-benzothiadiazole appear at 154.2 ppm ($CHCl_3$).][6] An X-ray structural analysis confirmed the planar structure of 1.[5]

In addition to confirming the formula $C_2N_4S_2$ by exact mass measurement of the molecular ion *m/e* 143.9563 (100%), the mass spectrum of 1 showed three major fragment ions: *m/e* 78, 72, and 46. The ion at *m/e* 77.94708 (NS_2, 34%) must result from an ion rearrangement in which the two sulfur atoms are brought into close proximity. The ion at *m/e* 72 (CN_2S, 37%, metastable ion at *m/e* 36.0) corresponds to cleavage of the molecular ion in half. The ion at *m/e* 46 (NS, 63%) arises from both the molecular ion and CN_2S^+, with metastable ions at *m/e* 14.7 and 29.4, respectively. The formation of the ions NS^+ and CN_2S^+ can be compared with two major fragmentation pathways we have found for monocyclic 1,2,5-thiadiazoles; simple cleavage to form NS^+, and loss of RCN (with charge retention on the fragment $RCNS^+$).



Synthesis of 1. Method I. The first synthesis of 1 resulted from work on substituted 1,2,5-thiadiazole 1,1-dioxides.[1] Reaction of 3,4-diamino-1,2,5-thiadiazole 1,1-dioxide (2) with excess sulfur monochloride in *N,N*-dimethylformamide (DMF) gave 1 in 59% yield.[7] Subsequently, it was found that cyclization of 2 with excess sulfur dichloride in DMF improved the yield of 1 to 75%.

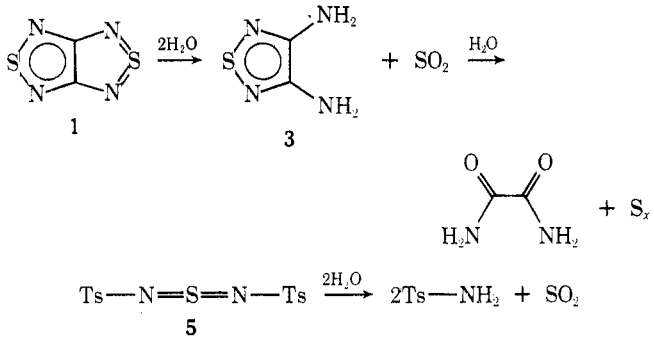


Method II. The second synthesis of 1, a structure proof, was accomplished by cyclization of authentic 3,4-diamino-1,2,5-thiadiazole (3)[4] by two methods known to form a 1,2,5-thiadiazole ring from α-diamines.[8,9] A good yield of 1 (81.5%) was obtained by heating a pyridine solution of 3 during the addition of 2 mol of thionyl chloride in portions. Cyclization of 3 to 1 was also accomplished in 83% yield with sulfur monochloride in DMF.

Method III. The most convenient synthesis of 1 was accomplished by the sulfur dichloride cyclization of oxamide dioxime (4) in DMF at 55°, a reaction which proceeds in 66% yield. On the other hand, cyclization of 4 with sulfur monochloride in DMF gave 1 in yields of less than 10%, even though the reagent has been used successfully in the

synthesis of other 1,2,5-thiadiazoles from α-diamines and α-dioximes.[8,10]

Reactions of 1. In contrast to 2,1,3-benzothiadiazole, which steam distils cleanly, only a small portion of **1** was recovered from steam distillation. Examination of the undistilled portion showed only oxamide with no remaining **1**. In a similar fashion, **1** was suspended in water at 75° for 12 hr to give a mixture of **3**, oxamide,and elemental sulfur.



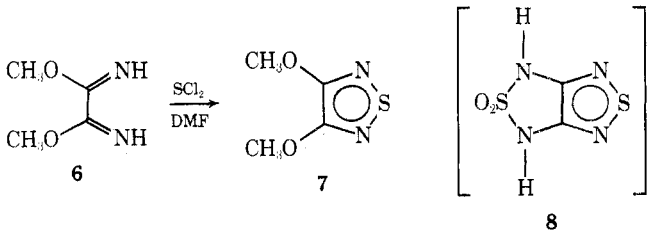
1 **3**

5

This indicated that the hydrolysis of **1** to oxamide proceeded via **3**, yet an authentic sample of **3** heated in water at 75° for 12 hr was recovered unchanged. The sulfur dioxide generated by the hydrolysis of **1** to **3** appears to be required for the subsequent hydrolysis of **3**. Indeed, when **3** was heated for 8 hr at 75° in aqueous sulfur dioxide, it was completely hydrolyzed to oxamide and elemental sulfur. Thus, neutralization of the sulfur dioxide formed during the hydrolysis of **1** should halt the hydrolysis at the stage of diamine **3**. This was found to be true, for when **1** was refluxed for 20 min in dilute ammonium hydroxide, **3** was obtained in nearly quantitative yield without oxamide or elemental sulfur.

The hydrolysis of **1** to **3** is analogous to the rapid hydrolysis of bis(*p*-toluenesulfonyl)sulfodiimide (**5**).[11] Both **1** and **5** contain the sulfodiimide linkage (RN=S=NR) with electron-withdrawing substituents on the nitrogens, yet the hydrolysis of **1** is slower than that of **5** because of its aromatic stabilization and the milder electron-withdrawing effect of the 1,2,5-thiadiazole ring compared with the two tosyl groups of **5**.

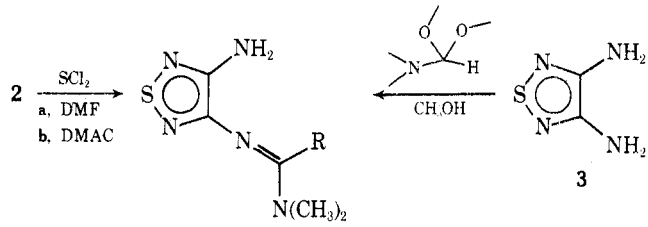
Studies Related to the Ring Closure Reactions Leading to 1. Method I. In an effort to learn more about the sulfur dichloride cyclization of **2** to **1** in DMF, a DMF solution of **2** was treated dropwise with only 1 mol of sulfur dichloride in DMF. This is in contrast to the usual reaction conditions requiring addition of **2** to a large excess of sulfur dichloride. The closure of dimethyl oxaldiimidate (**6**) with 1 mol of sulfur dichloride in DMF proceeded very well to give 3,4-dimethoxy-1,2,5-thiadiazole (**7**) in 94% yield. We



6 **7** **8**

had anticipated analogous sulfur dichloride bridging of the exocyclic nitrogens of **2**[12] to give the bicyclic intermediate **8**. The reaction of **2** did not, however, lead to the analogous product **8** but on aqueous work-up[13] gave a white solid with the molecular formula $C_5H_9N_5S$ (*m/e* calcd 171.0579; found 171.0579). This material was shown to bear two exchangeable hydrogens as evidenced by the increase in mass to *m/e* 173 after equilibration with D_2O. In view of the elemental composition, this result was interpreted as the presence of a primary amino function.

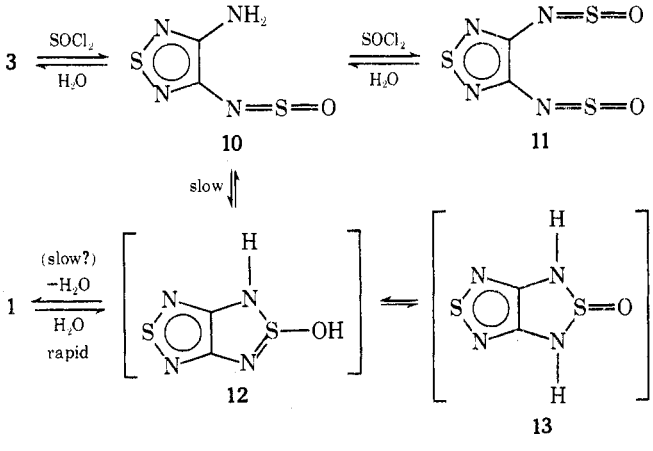
A similar reaction of **2** with 1 mol of sulfur dichloride carried out in *N,N*-dimethylacetamide (DMAC), in place of DMF, gave a compound with its molecular ion at *m/e* 185. These data suggested the formation of amidine functions involving the solvents. On this basis, the structure proposed for the product from cyclization of **2** in DMF and DMAC were **9a** and **9b**, respectively, implicating a Vilsmeier-type intermediate derived from sulfur dichloride and the reaction solvent.[14]



9a, R = H
b, R = CH_3

The structure of **9a** was confirmed by independent synthesis. Aminoamidine **9a** was isolated as a white solid, mp 124.5–125°, upon slow treatment of **3** with 1 mol of dimethylformamide dimethyl acetal in methanol.[15] The 220-MHz NMR spectrum of **9a** ($CDCl_3$) showed a singlet at δ 8.31, a broad singlet at 4.85, and two singlets at 3.07 and 3.03, in a 1:2:3:3 ratio; and corresponding to the imine proton, the amino protons, and the two nonequivalent *N*-methyl groups, respectively.[16] Aminoamidine **9a** prepared from **3** was spectroscopically identical with material from the reaction of **2** with sulfur dichloride in DMF.

Method II. The mechanism for the thionyl chloride cyclization of *o*-phenylenediamine to 2,1,3-benzothiadiazole in the presence of tertiary amines has been reported.[17] In the present reaction scheme, pyridine may assist in two places: by removing the 2 mol of hydrogen chloride formed in generation of intermediate **10**, which allows free **10** to cyclize to **12**, and by aiding in the dehydration of **12** to **1**.[18] It

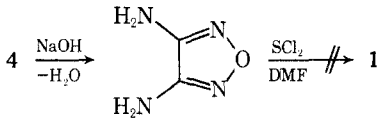


10 **11** **12** **13**

was found that, even in pyridine solution, **3** treated with excess thionyl chloride gave poor yields (0–59%) of **1**. In order to obtain **1** in good yield, it was necessary to maintain at least a catalytic concentration of **10** throughout the reaction. This was done by initially adding only 1.9 mol (of required 2.0 mol) of thionyl chloride, followed by the slow addition of the remaining thionyl chloride. Evidently, the cyclization of **10** to **12** is much slower than the same process for the benzene analog of **10**,[17,19] owing to the powerful deactivation of the amino group by the 1,2,5-thiadiazole ring. Thus, in the presence of excess thionyl chloride, the red compound **10** is rapidly trapped as the yellow bis-*N*-

sulfinyl compound 11 (aqueous work-up of such a reaction gave mostly starting material 3 by hydrolysis of 11 via 10, and yielded very little 1).

Method III. In view of the obscure mechanism for the cyclization of α-dioximes to 1,2,5-thiadiazoles[8] and 1,2,5-thiadiazole *N*-oxides,[10a] the possible intermediacy of 3,4-diamino-1,2,5-oxadiazole (14) was considered. When 14 (obtained by base-catalyzed dehydration of 4)[20] was treated with sulfur dichloride in DMF under conditions identical with those which convert 4 to 1, no trace of 1 was observed. This rules out 14 as an intermediate. Dehydration



14

of 4 by sulfur dichloride in DMF is probably a competing reaction leading to a less than optimum yield of 1, in analogy to the partial dehydration of dimethylglyoxime to 3,4-dimethyl-1,2,5-oxadiazole by sulfur monochloride in DMF.[8]

Experimental Section

General. Melting points (uncorrected) were determined in a Mel-Temp apparatus in open capillary tubes. Elemental analyses were performed by Midwest Microlab, Indianapolis, Ind., unless otherwise indicated. Infrared spectra were recorded on Perkin-Elmer 137 or 621 spectrometers. Ultraviolet spectra were recorded on methanol solutions using a Cary 14 spectrometer. Low-resolution mass spectra (70 eV) were obtained on a Varian MAT CH-7 instrument. High-resolution mass spectra (70 eV) were determined with an AEI MS-9 spectrometer. Proton NMR spectra were obtained on a Varian HR-220 spectrometer. The ^{13}C NMR spectra were recorded on a Varian XL-100 instrument operating in FT mode.[6] *N,N*-Dimethylformamide (DMF) was distilled successively from phosphorus pentoxide and calcium hydride. *N,N*-Dimethylacetamide (DMAC) was distilled from calcium hydride. Anhydrous magnesium sulfate was routinely used as a drying agent.

1 from 2 with Sulfur Monochloride (Method I). A solution of sulfur monochloride (12.0 ml, 150 mmol) in 50 ml of DMF was cooled on ice with stirring while 4.00 g (27.0 mmol) of 2[1] was added in portions over 20 min. After the mixture had been stirred at room temperature for 2.5 hr, it was poured onto 120 g of ice and extracted with ether (4 × 80 ml). The combined ether extracts were washed with water (2 × 25 ml), dried, and evaporated to dryness, yielding 2.74 g of crude 1 as yellow-white plates. It was then chromatographed on 75 g of silica gel. A small amount of elemental sulfur was eluted with 2% ether in hexane, followed by 2.30 g (59%) of 1 eluted with 4–8% ether in hexane. The colorless prisms, mp 115.2–116°, were sublimed at 50–60° (3 mm): mp 115.7–116° (Hershberg apparatus); ir (KBr, recorded between 2.5 and 25 μm) 10.9, 12.3, 18.5, and 23 μm; uv λ_{max} (log ε) 215 nm (3.17), 317 (4.32); ^{13}C NMR ($CHCl_3$) 169.4 ppm;[6] mass spectrum *m/e* (rel intensity) 144 (100, M^+), 104 (2, CN_2S_2), 98 (1, C_2N_3S), 78 (34, NS_2), 72 (37, CN_2S), 64 (2, S_2), 58 (2, CNS), 52 (2, C_2N_2), 46 (63, NS), 40 (0.5, CN_2), 38 (0.5, C_2N), and 32 (9, S); metastable ions 42.2 (144 → 78), 36.0 (144 → 72), 29.4 (72 → 46), and 14.7 (144 → 46).

Exact Mass. Calcd for $C_2N_4S_2$: 143.9564. Found: 143.9563. Calcd for NS_2: 77.94722. Found: 77.94708.

Anal. Calcd for $C_2N_4S_2$: C, 16.66; H, 0.00; N, 38.86; S, 44.48. Found: C, 16.78; H, 0.00; N, 38.87; S, 44.27 (A. Bernhardt).

1 from 2 with Sulfur Dichloride (Method I). A solution of sulfur dichloride (1.4 ml, 22 mmol) in 8 ml of DMF was cooled on ice while 2 (592 mg, 4.00 mmol) was added in portions over 10 min. After the mixture had been stirred at room temperature for 3 hr, it was cooled to 0°, poured onto 20 g of ice, and extracted with ether (4 × 20 ml). The combined ether extracts were washed with water (4 × 5 ml), dried, and evaporated to dryness to give 430 mg (74.6%) of 1.

3,4-Dimethoxy-1,2,5-thiadiazole (7). The procedure is an improvement on the sulfur dichloride cyclization of diethyl oxaldiimidate in refluxing benzene yielding 3,4-diethoxy-1,2,5-thiadiazole in 66% yield.[21] Sulfur dichloride (51.0 g, 495 mmol) in 250 ml of DMF was cooled to −30°. Dimethyl oxaldiimidate[22] (6, 52.2 g, 450 mmol) in 75 ml of DMF was added dropwise over 20 min at −30°. After the mixture had been stirred for 4 hr at room temperature, it was treated with 600 ml of water and steam distilled. The organic layer was separated and the aqueous layer was extracted with methylene chloride (2 × 40 ml.) The combined organic extracts were dried and fractionated to give 61.8 g (94.1%) of colorless 7: mp 33–34°; bp 90° (~20 mm); NMR ($CDCl_3$) δ 4.01 (s); ir (neat) 5.99, 6.47, 6.59, 6.90, 6.95, 7.10, 7.22, 7.30, 7.83, 8.02, 8.44, 10.10, 11.41, and 13.00 μm; mass spectrum *m/e* (rel intensity) 146 (100), 145 (11) 131 (7), 117 (21), 116 (6), 103 (16), 89 (31), 85 (7), 74 (27), 61 (34), 58 (32), 54 (7) 46 (76), and 15 (39).

Exact Mass. Calcd for $C_4H_6N_2O_2S$: 146.0150. Found: 146.0156.

Anal. Calcd for $C_4H_6N_2O_2S$: C, 32.87, H, 4.14. Found: C, 32.97; H, 4.20.

9a from 2. Freshly distilled sulfur dichloride (60 μl, 0.95 mmol) was added slowly at 0° to 148 mg (1.00 mmol) of 2 in 1 ml of DMF. After the red reaction mixture had been stirred for 10 min, half of it was evaporated to dryness under high vacuum. A mass spectral analysis of the crude solid showed molecular ions at *m/e* 171 (**9a**) and 126.[13] The remaining half of the reaction mixture was stirred with 5 ml of water and extracted twice with ether. No material was present in the ether extract. The aqueous layer was neutralized with excess sodium bicarbonate and extracted three times with ether. The combined ether extracts were dried and evaporated under high vacuum to give crystals of **9a**, spectroscopically identical with **9a** prepared from 3.

Exact Mass. Calcd for $C_5H_9N_5S$: 171.0579. Found: 171.0579.

Solid **9a** dissolved in ether was stirred vigorously with D_2O for 30 min. The ether layer was separated, dried, and evaporated to give dideuterated **9a**: mass spectrum *m/e* 173, 158, 131, 129, 109, 99, 83, 76, 57, 44, 43, 42, 30, 28, and 15.

9b from 2. A sulfur dichloride cyclization of 2 was conducted in DMAC rather than DMF. A mass spectrum of the crude mixture prior to work-up showed a larger molecular ion at *m/e* 140 than *m/e* 185 (**9b**).[13]

Exact Mass. Calcd for $C_6H_{11}N_5S$: 185.0735. Found: 185.0737.

9a from 3. *N,N*-Dimethylformamide dimethyl acetal (232 mg, 2.00 mmol) in 2 ml of methanol was added over 10 min to a refluxing solution of 3 (232 mg, 2.00 mmol) in 3 ml of methanol. After the colorless solution had been refluxed for an additional 30 min, it was cooled on ice and filtered to give white **9a**: mp 124.5–125° (methanol); ir (KBr) 2.89, 2.99, 3.09, 3.39, 6.16, 6.55, 6.67, 6.82, 7.01, 7.12, 7.46, 7.98, 8.17, 8.99, 9.42, 11.65, 11.96, and 12.87 μm; NMR ($CDCl_3$) δ 8.31 (s, 1), 4.85 (broad s, 2), 3.07 (s, 3), and 3.03 (s, 3); mass spectrum *m/e* (rel intensity) 171 (100), 156 (16), 129 (20), 127 (16), 108 (21), 98 (19), 83 (30), 74 (13), 57 (12), 44 (67), 43 (17), 42 (40), 30 (14), 28 (16), and 15 (10).

Exact Mass. Calcd for $C_5H_9N_5S$: 171.0579. Found: 171.0578.

Anal. Calcd for $C_5H_9N_5S$: C, 35.07; H, 5.30. Found: C, 35.23; H, 5.55.

Aminoamidine **9a** could also be synthesized from 3 by treatment with thionyl chloride in DMF.

1 from 3 with Thionyl Chloride (Method II). Thionyl chloride (550 μl 7.57 mmol) was added dropwise to a solution of 3,4-diamino-1,2,5-thiadiazole (3,[4] 468 mg, 4.00 mmol) in 4 ml of pyridine (exothermic). After the red solution had been heated for 15 min (oil bath 125°), thionyl chloride (30 μl, 0.4 mmol) was added dropwise and heating was continued for 30 min before a final portion of thionyl chloride (30 μl, 0.4 mmol, total ~8.4 mmol) was added dropwise. After being heated for 30 min, the brownish solution was cooled on ice and stirred briefly with 10 ml of ice water. The solid was filtered, washed well with water, and air dried to give 470 mg (81.5%) of 1.

Similar experiments, in which the entire quantity of thionyl chloride was added at the onset, gave lower yields (0–59% depending on the addition rate). The product from rapid addition, **11**, was obtained as an extremely moisture-sensitive pale yellow solid: mass spectrum *m/e* 208, 120, and 46. Even during transfer to the mass spectrometer in a glove bag under dry nitrogen, **11** frequently hydrolyzed partly to a red solid (**10**), mass spectrum *m/e* 162, 120, 74, and 46, and some 1. When solid **11** was treated with catalytic amounts of water, sulfur dioxide was evolved and variable yields of 1 were produced.

1 from 3 with Sulfur Monochloride (Method II). A solution of 3 (116 mg, 1.00 mmol) in 1 ml of DMF was cooled to −15° and added to sulfur monochloride (325 μl, 4.0 mmol) in 2 ml of DMF at −15°. The red mixture was stirred at room temperature for 1.5 hr, poured onto 20 g of ice, and extracted with ether (4 × 50 ml). The combined ether extracts were washed with water (3 × 15 ml) and dried. Evaporation of the ether left 120 mg (83.3%) of 1.

1 from 4 (Method III). A solution of oxamide dioxime (4,[23] 11.8

g, 100 mmol) in 150 ml of DMF was added dropwise over 40 min to a stirred solution of sulfur dichloride (38.2 ml, 600 mmol) in 250 ml of DMF at 0–10°. After the mixture had been heated at 55° for 8 hr, it was cooled to 5° and poured onto 400 g of ice. The product was extracted with ether (7 × 150 ml). The combined ether extracts were washed with water (3 × 25 ml), dried, and evaporated to dryness under vacuum to give 15.9 g of yellow solid. After standing overnight, the product was dissolved in 100 ml of boiling methanol, decanted from 2.3 g of elemental sulfur, treated with carbon, and filtered hot. The methanolic filtrate was cooled on Dry Ice and the resulting white plates of 1 were collected on a cold filter. After air drying, the product weighed 9.50 g (66%).

Similar experiments using sulfur monochloride in place of sulfur dichloride gave low yields (<10%) of 1.

14 from 4. The procedure of Coburn was altered slightly to improve safety and yield.[20] Oxamide dioxime (6, 11.8 g, 100 mmol) was added to a solution of sodium hydroxide (4 g in 40 ml of water) in a 300-ml Pyrex-lined autoclave. The autoclave was heated at 160–185° for 2 hr, then cooled on ice and the white solid was filtered, washed with ice water (2 × 20 ml), and dried (7.0 g, 70%). The solid was dissolved in hot water and filtered. After the filtrate had been cooled, pure white 14 was collected, mp 178.5–180.5° (lit.[20] mp 180°). Mass spectral and infrared analyses showed the product to be free of starting material.

Exact Mass. Calcd for $C_2H_4N_4O$: 100.0385. Found: 100.0386.

Reaction of 14 with Sulfur Dichloride. A solution of 14 (1.0 g, 10 mmol) in 15 ml of DMF was added over 15 min to a stirred solution of sulfur dichloride (3.8 ml, 60 mmol) in 25 ml of DMF at 0–5°. After the mixture had been heated for 8 hr at 55°, it was cooled to 0°, poured onto 40 g of ice, and extracted with ether (6 × 20 ml). The combined ether extracts were washed with water (2 × 10 ml), dried, and evaporated to dryness to give only a small amount of yellow solid shown to be elemental sulfur by its mass spectrum. No trace of 1 was detected in this and two additional experiments.

Hydrolysis of 1. A. In Water. A suspension of 1 (72 mg, 0.50 mmol) in water was heated at 75°. After 1 hr, the solid had dissolved to give a light yellow solution, and after 12 hr, a precipitate had formed. The water was removed by lyophilization to give an off-white solid. Mass spectral analysis showed 3, oxamide, and elemental sulfur.

B. In Dilute Ammonium Hydroxide. A suspension of 1 (1.44 g, 10.0 mmol) in 30 ml of 3 *M* ammonium hydroxide was refluxed until all of the solid had dissolved (20 min or less). The colorless solution was lyophilized to give 3 in nearly quantitative yield. After recrystallization (water), the melting point, ir, and mass spectra of 3 were identical with those of an authentic sample.[4]

In other experiments, mixtures of 1 and 3 were found to give a pale lavender color.

Hydrolysis of 3. A. In Water. A 58-mg sample of 3 was dissolved in water and heated at 75° for 12 hr. The solution was lyophilized to give recovery of the starting material.

B. In Water with Sulfur Dioxide. A 58-mg sample of 3 was dissolved in water and bubbled with sulfur dioxide for several seconds. After the solution had been heated 8 hr at 75° (precipitate present), it was lyophilized to give a mixture of oxamide and elemental sulfur by mass spectral analysis.

15.[16] Aminopyrazine (Aldrich, 9.51 g, 100 mmol) was suspended in 20 ml of ethanol and heated to reflux. Dimethylformamide dimethyl acetal (14.0 g, 117 mmol) was added dropwise over 10 min and the solution was refluxed for an additional 3 hr. After the solvent and excess reagent had been distilled under vacuum, the faintly yellow amidine 15 (14.73 g, 98.2%) was vacuum distilled: mp slightly above room temperature; bp 84–85° (0.04 mm); NMR (15° probe temperature) ($CDCl_3$) δ 8.37 (s, 1), 8.23 (narrow m, 1), 8.04 (m, 2), and 3.07 (s, 6); NMR (CCl_4) δ 8.39 (s, 1), 8.13 (narrow m, 1), 7.96 (m, 2), 3.00 (s, 3), and 2.99 (s, 3); NMR (C_6D_6) δ 8.65 (narrow m, 1), 8.38 (s, 1), 8.00 (m, 2), 2.63 (s, 3), and 2.18 (s, 3); NMR (C_5D_5N) δ 8.60 (m, 2), 8.24 (m, 2), 2.95 (s, 3), 2.81 (s, 3); ir (neat) 3.23, 3.38, 3.53, 6.15, 6.35, 6.66, 6.83, 6.94, 7.21, 7.43, 7.88, 8.04, 8.47, 8.72, 9.02, 9.42, 9.87, 10.13, 11.64, 11.87, and 13.10 μm; mass spectrum *m/e* (rel intensity) 150 (100), 149 (50), 135 (28), 134 (8), 108 (15), 94 (27), 82 (11), 81 (10), 80 (30), 79 (32), 71 (10), 57 (50), 53 (9), 52 (29), 44 (71), 43 (8), 42 (45), 40 (9), 30 (21), 28 (25), 26 (8), and 15 (19).

Exact Mass. Calcd for $C_7H_{10}N_4$: 150.0905. Found: 150.0905.

16.[16] An experiment similar to the above was carried out on 2-amino-3-chloropyrazine to give 16: NMR (CCl_4) δ 8.33 (s, 1), 7.87 (d, J = 2.6 Hz, 1), 7.73 (d, J = 2.6 Hz, 1), 3.12 (s, 3), and 3.11 (s, 3); ir (neat) 6.15, 6.44, 6.71, 6.89, 7.04, 7.26, 8.03, 8.62, 8.96, 9.18, 9.44, 10.16, 11.50, 11.85, and 13.49 μm; mass spectrum *m/e* (rel intensity, ^{35}Cl ions only) 184 (44), 169 (8), 168 (6), 149 (84), 133 (12), 128 (12), 113 (11), 108 (12), 79 (18), 57 (54), 52 (19), 44 (100), 42 (69), 30 (26), 28 (19), and 15 (23).

Exact Mass. Calcd for $C_7H_9{}^{35}ClN_4$: 184.0516. Found: 184.0514.

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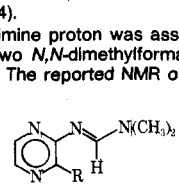
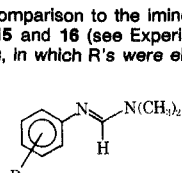
Registry No.—**1,** 55904-34-2; **2,** 55904-35-3; **3,** 55904-36-4; **4,** 2580-79-2; **6,** 30986-09-5; **7,** 55904-37-5; **9a,** 55904-38-6; **9b,** 55904-39-7; **14,** 17220-38-1; **15,** 51519-09-6; **16,** 55904-40-0; sulfur monochloride, 10025-67-9; sulfur dichloride, 10545-99-0; *N,N*-dimethylformamide dimethyl acetal, 4637-24-5; thionyl chloride, 7719-09-7; aminopyrazine, 5049-61-6; 2-amino-3-chloropyrazine, 6863-73-6.

References and Notes

(1) For part II in this series see R. Y. Wen, A. P. Komin, R. W. Street, and M. Carmack, preceding paper in this issue.
(2) M. P. Cava, M. Behforouz, G. E. Husbands, and M. Srinivasan, *J. Am. Chem. Soc.*, **95,** 2561 (1973).
(3) Part IV: A. P. Komin and M. Carmack, *J. Heterocycl. Chem.*, in press.
(4) The synthesis of **3** by three routes will appear in part V: *J. Heterocycl. Chem.*, submitted for publication.
(5) An X-ray structure analysis by Professor Riley Schaeffer showed **1** to be planar, with the following dimensions: bond angles: NSN 103.2°, SNC 104.4°, and NCC 114°; bond lengths: NS 1.62 Å, NC 1.35 Å, and CC 1.44 Å.
(6) The chemical shifts with respect to chloroform were converted to Me_4Si by adding 77.2 ppm.
(7) (a) M. Carmack, R. W. Street, and R. Y. Wen, Abstracts, 158th National Meeting of the American Chemical Society, New York, N.Y., Sept 1969, No. ORGN-54; (b) R. W. Street, M.S. Dissertation, Indiana University, 1968.
(8) L. M. Weinstock, P. Davis, B. Handelsman, and R. Tull, *J. Org. Chem.*, **32,** 2823 (1967).
(9) (a) A. M. Khaletskii, V. G. Pesin, and C.-C. Chao, *Dokl. Akad. Nauk SSSR*, **106,** 88 (1956); *Chem. Abstr.*, **50,** 13885*c* (1956); (b) D. Picher and R. N. Castle, *J. Heterocycl. Chem.*, **8,** 441 (1971).
(10) (a) K. Pilgram, *J. Org. Chem.*, **35,** 1165 (1970). (b) Reactions of dioximes with selenium monochloride: C. L. Pedersen, *J. Chem. Soc., Chem. Commun.*, **17,** 704 (1974).
(11) G. Kresze and W. Wucherpfenning, *Angew. Chem., Int. Ed. Engl.*, **6,** 149 (1967).
(12) Compound **2** has considerable imino character, i.e., **2b** and **2c** are prevalent.[1]
(13) Mass spectral examination of the crude reaction mixture, prior to water work-up, showed an additional compound with a molecular ion at *m/e* 126 (fragment at *m/e* 99, $M^{\cdot+}$ − HCN). The analogous reaction with DMAC as solvent gave a corresponding molecular ion at *m/e* 140 (fragment at *m/e* 99, $M^{\cdot+}$ − CH_3CN). On this basis, the compounds are probably the imidazole derivatives obtained by elimination of dimethylamine from **9a** and **9b,** respectively. Neither of the imidazoles was isolated.
(14) There is good evidence for a Vilsmeier-type reagent prepared from sulfur dichloride and DMF: U. Hasserodt, *Chem. Ber.*, **101,** 113 (1968).
(15) H. Brederick, F. Effenberger, and A. Hofmann, *Chem. Ber.*, **97,** 61 (1964).
(16) The imine proton was assigned by comparison to the imine protons of the two *N,N*-dimethylformamidines, **15** and **16** (see Experimental Section). The reported NMR of **17** (C_6D_6), in which R's were electron-withdrawing groups, showed nonequivalence of the two *N*-methyl groups: J. P. Marsh, Jr., and L. Goodman, *Tetrahedron Lett.*, 683 (1967).



15, R = H
16, R = Cl



17

(17) H. Beecken, *Chem. Ber.*, **100,** 2170 (1967).
(18) The dehydration of **12** to **1** may be slow, since it was shown that the reverse reaction, hydrolysis of **1** to **3** via **12,** is faster than that of any known 1,2,5-thiadiazole. The hydrolysis of **1** to **12** is similar to the covalent hydration observed for pyrazino[2,3-*b*]pyrazine: W. L. F. Armarego, *J. Chem. Soc.*, 4304 (1963).
(19) W. Wucherpfennig, *Chem. Ber.*, **101,** 371)1968).
(20) M. D. Coburn, *J. Heterocycl. Chem.*, **5,** 83 (1968).
(21) R. Y. Wen, Ph.D. Dissertation, Indiana University, 1962; University Microfilms, Ann Arbor, Mich., Order No. 63-3859; *Diss. Abstr.*, **23,** 4121 (1963).
(22) H. Weldinger and J. Kranz, *Chem. Ber.*, **97,** 1599 (1964).
(23) H. E. Ungnade, L. W. Kissinger, A. Narath, and D. C. Barham, *J. Org. Chem.*, **28,** 134 (1963).