Synthetic, Mechanistic, and Structural Studies Related to 1,2,4-Dithiazolidine-3,5-dione

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Reaction of *O*-ethyl thiocarbamate (**4**) with (chlorocarbonyl)sulfenyl chloride (**5**) gives 3-ethoxy-1,2,4-dithiazolin-5-one (**2**) and 3,5-diethoxy-1,2,4-thiadiazole (**3**), with the relative amounts of **2** and **3** formed depending very much on the solvent (e.g., diethyl ether favors **2**; chloroform favors **3**). The effects of added base, order of addition, concentration, and temperature were also studied. Mechanisms for the observed transformations have been proposed and are supported by the characterization of relatively unstable acyclic intermediates, e.g., formimidoyl(chlorocarbonyl)-disulfane **8**, symmetrical bis(formimidoyl)disulfane **10**, and ethoxythiocarbonyl imidate **11**, which are obtained under alternative conditions. Compound **2** is converted with concentrated aqueous hydrochloric acid upon short reflux to 1,2,4-dithiazolidine-3,5-dione (**1**), rearranges upon prolonged melting to give principally *N*-ethyl-1,2,4-dithiazolidine-3,5-dione (**13**), and is desulfurized with various trivalent phosphorus compounds to yield *O*-ethyl cyanate (**15**) plus carbonyl sulfide. X-ray crystallographic structures of **1** and **2** have been solved; the planarity and aromatic character of these molecules help to explain some of their reactions.

Recent work from our laboratory[2] has shown that 1,2,4-dithiazolidine-3,5-dione (**1**), a compound first prepared by German scientists several decades ago,[3−5] is a highly effective sulfurization reagent that provides access to phosphorothioate analogues of DNA and phosphopeptides. In addition, **1** represents a protected form[6] of ammonia and may be useful for mild homologation of the classical Gabriel synthesis.[7] The present contribution reports an efficient, optimized two-step procedure for the preparation of **1**, via the key intermediate 3-ethoxy-1,2,4-dithiazolin-5-one (**2**),[8] and also describes how the reaction designed to give **2** provides entry to another heterocycle, 3,5-diethoxy-1,2,4-thiadiazole (**3**).[9] In addition, X-ray crystallographic analyses of **1** and **2** confirm the planar aromatic character of each heterocycle and facilitate the understanding of some reactions of the title heterocycles **1** and **2**.

Results and Discussion

Reaction of *O*-Ethyl Thiocarbamate (4) with (Chlorocarbonyl)sulfenyl Chloride (5). With the goal to prepare alkyl-free heterocyclic disulfide **1**, reaction of **4**[10] with **5**[11] was found to stop at heterocycle **2** (Scheme 1).[3a,c] A second isolable product from the reaction was 3,5-diethoxy-1,2,4-thiadiazole (**3**, Scheme 1),[9] and the

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(2) (a) Xu, Q.; Musier-Forsyth, K.; Hammer, R. P.; Barany, G. In *Peptides: Chemistry, Structure & Biology. Proceedings of the 14th American Peptide Symposium*; Kaumaya, P. T. P.; Hodges, R. S. Eds.; Mayflower Scientific: Kingswinford, England, 1996; pp 123−124. (b) Xu, Q.; Musier-Forsyth, K.; Hammer, R. P.; Barany, G. *Nucleic Acids Res.* **1996**, *24*, 1602−1607.

(3) (a) Review: Zumach, G.; Kühle, E. *Angew Chem., Int. Ed. Engl.* **1970**, *9*, 54−63. (b) Dahms, G.; Haas, A.; Klug, W. *Chem. Ber.* **1971**, *104*, 2732−2742. (c) The method sketched in ref 3a was described more exactly in a letter dated Dec 19, 1973, from G. Zumach to G. Barany: 31% yield for reaction in diethyl ether of **4** and **5** in the presence of Et_3N (1 equiv) to give **2**, mp 56−57 °C (iPrOH); 30% yield for conversion **2** to **1**, mp 142−144 °C (toluene). (d) The present work describes substantially improved yields of **1** or **2** over those reported in ref 3c, defines an alternative product **3**, and indicates that the presence of base is not critical to achieve good yields and purities of **2**. The initial reaction of **4** and **5** does not give any ^{13}C NMR-detectable **1**, regardless of the presence or absence of base. The ether needs to be reasonably dry to minimize the formation of the hydrolysis product *O*-ethyl carbamate [^1H NMR ($CDCl_3$) δ 4.12 (q, 2 H), 1.24 (t, 3 H); ^{13}C NMR ($CDCl_3$) δ 157.3, 60.9, 14.4].

(4) Compound **1** is also claimed in two patents, but as stated in a review (ref 3a), the methods that are general for *N*-R-1,2,4-dithiazolidine-3,5-diones (R = alkyl, aryl) fail for the special case R = H. The patents referred to describe the following. (a) R′O(C=S)NHR + Cl(C=O)SCl: Zumach, G.; Weiss, W.; Kühle, E., Belgian Patent 682,-991, June 23, 1966; British Patent 1,136,737, June 21, 1966; *Chem. Abstr.* **1969**, *70*, 77951p. (b) H(C=O)NHR + 2 Cl(C=O)SCl: Zumach, G.; Weiss, W.; Kühle, E., Farbenfabriken Bayer AG. Belgian Patent 682,820, June 20, 1966; *Chem. Abstr.* **1968**, *68*, 105203a. For a comprehensive description of this and the related patent literature, see ref 3a and the following: (d) Kühle, E. *The Chemistry of the Sulfenic Acids*; Georg Thieme: Stuttgart, Germany, 1973.

(5) Previous preparative and mechanistic studies from our laboratory related to *N*-R-1,2,4-dithiazolidine-3,5-diones [R = H, alkyl, and H_2N-R' corresponding to amino acids and peptides] are described in the following: (a) Barany, G.; Merrifield, R. B. *J. Am. Chem. Soc.* **1977**, *99*, 7363−7365. (b) Słomczyńska, U.; Barany, G. *J. Heterocycl. Chem.* **1984**, *21*, 241−246. (c) Barany, G.; Słomczyńska, U.; Mott, A. W. *Abstracts of Papers*, 187th National Meeting of the American Chemical Society, St. Louis, MO, April 8−13, 1984; American Chemical Society: Washington, DC, 1984; ORG 32. (d) Zalipsky; S.; Albericio, F.; Słomczyńska, U.; Barany, G. *Int. J. Pept. Protein Res.* **1987**, *30*, 740−783. (e) Hammer, R. P.; Barany, G. *Abstracts of Papers*, 195th National Meeting of the American Chemical Society, Toronto, Canada, June 5−10, 1988; American Chemical Society: Washington, DC, 1988; ORG 137.

(6) The dithiasuccinoyl (Dts) amino protecting group, removable by thiolysis and other reductive methods, was described first in ref 5a and has been applied in numerous other papers from our laboratories, e.g.: (a) Barany, G.; Merrifield, R. B. *J. Am. Chem. Soc.* **1980**, *102*, 3084−3095. (b) Barany, G.; Albericio, F. *J. Am. Chem. Soc.* **1985**, *107*, 4936−4942. (c) Albericio, F.; Barany, G. *Int. J. Pept. Protein Res.* **1987**, *30*, 177−205. (d) Hammer, R. P.; Albericio, F.; Gera, L.; Barany, G. *Int. J. Pept. Protein Res.* **1991**, *36*, 31−45. (e) Jensen, K. J.; Hansen, P. R.; Venugopal, D.; Barany, G. *J. Am. Chem. Soc.* **1996**, *118*, 3148−3155 and references cited in all of these papers.

(7) For a review of Gabriel synthesis of amines (alkylation of phthalimide salts, followed by dephthaloylation), see: Gibson, M. S.; Bradshaw, R. W. *Angew. Chem., Int. Ed. Engl.* **1968**, *7*, 919−930.

(8) Compound **2** also has attractive properties for efficient sulfurization (see ref 2b and Scheme 4 of the present paper) and in Gabriel-like syntheses: Chen, L.; Hammer, R. P.; Barany, G., work in progress.

(9) Compound **3** has been described previously: (a) Holmberg, B. *Chem. Zentralbl.* **1930**, 1925−1926. (b) Kresze, G.; Horn, A.; Philippson, R.; Trede, A. *Chem. Ber.* **1965**, *98*, 3401−3409. The paper by Kresze and co-workers includes some interesting mechanistic experiments, including crossover studies.

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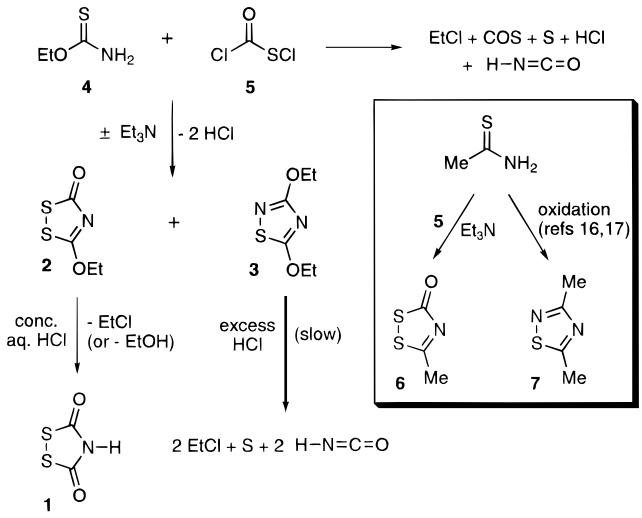
Scheme 1



relative amounts of **2** and **3** formed depended on solvent in a striking fashion (Table 1). In addition, the absolute amounts of **2** and/or **3** formed were influenced markedly by the presence or absence of a tertiary amine base (Scheme 1, Table 1) and somewhat by the concentrations and order of addition of reactants.

Reactions of equimolar amounts of **4** with **5** in chloroform ($CHCl_3$ or $CDCl_3$) at 0−25 °C were rapid, with immediate transformation of **4** to final products and the absence of intermediates that might have been detectable by *in situ* ^1H and ^{13}C NMR monitoring. When no base was present, the principal products were the volatile ethyl chloride (EtCl), cyanic acid (HN═C═O),[12] hydrogen chloride (HCl), and carbonyl sulfide (COS), as well as insoluble elemental sulfur ($^1/_8$ S_8); no **1** and negligible amounts of **2** or **3** were formed. The same reaction carried out in anhydrous diethyl ether (Et_2O)[3d] at 10 °C (external cooling to control the spontaneous exotherm) provided a crude product mixture that comprised principally dithiazoline **2** in 78% absolute yield (52% after recrystallization), as well as **3**, at 5% of the molar amount of **2** (Table 1, entry 1).

Addition of an ethereal mixture of **4** (1 equiv) and triethylamine (Et_3N, 1 equiv)[13] to a solution of **5** (1 equiv) in Et_2O (Table 1, entry 2) again gave **2** as the predominant product in initial purity and overall yield (75% crude, 63% after recrystallization) comparable to those of the base-free reaction.[3c,d] In contrast, when the reaction was carried out in $CHCl_3$ (opposite order of addition, i.e., **5** to a mixture of **4** and Et_3N), the major product was **3**, with only a minor amount of **2**. In this latter case, the purified yield of **5** was 54%, taking into account that 2 molecules of **4** are required to form the product (Table 1, entry 16). Results upon addition of a second equivalent of base[13] were solvent-dependent: in Et_2O, yields of **2** were only slightly worse than optimal (entries 10 vs 8 vs 6), while in $CHCl_3$, the extra base contributed to formation of a complicated mixture of acyclic products and recovered starting material (Table 1, entry 15 and footnote *c*).

As could be predicted, the relative amount of "dimer-like" **3** with respect to "monomer-like" **2** increased at higher concentration of starting reactants (Table 1, entries 3 and 4 vs 8 and 9 in Et_2O; entries 11 vs 14 in $CHCl_3$) and was somewhat higher when the order of addition was sulfenyl chloride **5** to the mixture of **4** and Et_3N (entries 4 vs 3 and 9 vs 8 in Et_2O; entries 14 vs 13 in $CHCl_3$).

The differences observed in product distribution between Et_2O and $CHCl_3$ do not appear to be a simple solvent polarity effect, as the respective dielectric constants[14] and solvent parameters[14] are not widely different (Et_2O, $\epsilon_r = 4.20$, $E_T^N = 0.117$; $CHCl_3$, $\epsilon_r = 4.80$, $E_T^N = 0.259$). As a measurement of the sensitivity of this reaction to solvent polarity, several other solvents were

Table 1. Product Distribution from Reaction of *O*-Ethyl Thiocarbamate (4) and (Chlorocarbonyl)sulfenyl Chloride (5) under Various Conditions[a]

		concentration (M)				conv of **4** (%)	
entry	solvent	**4**	Et_3N	**5**	order of addition	**2**	**3**
1[b]	Et_2O	2	0	0.2	**4** to **5**	78	5
2[b]	Et_2O	2	2	0.2	(**4** + Et_3N) to **5**	75	9
3	Et_2O	1	1	1	(**4** + Et_3N) to **5**	46	12
4	Et_2O	1	1	1	**5** to (**4** + Et_3N)	35	24
5	Et_2O	1	0	1	**4** to **5**	67	18
6	Et_2O	0.4	0	0.4	**4** to **5**	80	6
7	Et_2O	0.4	0	0.4	**5** to **4**	68	10
8	Et_2O	0.4	0.4	0.4	(**4** + Et_3N) to **5**	84	5
9	Et_2O	0.4	0.4	0.4	**5** to (**4** + Et_3N)	75	9
10	Et_2O	0.4	0.8	0.4	(**4** + 2 × Et_3N) to **5**	75	13
11	$CHCl_3$	1	1	1	**5** to (**4** + Et_3N)	3	52
12	$CHCl_3$	0.4	0	0.4	**5** to **4**	1	32
13	$CHCl_3$	0.4	0.4	0.4	(**4** + Et_3N) to **5**	14	41
14	$CHCl_3$	0.4	0.4	0.4	**5** to (**4** + Et_3N)	5	63
15	$CHCl_3$	0.4	0.8	0.4	**5** to (**4** + 2 × Et_3N)	<1	*c*
16[b]	$CHCl_3$	0.2	0.2	0.2	**5** to (**4** + Et_3N)	7	69

[a] Unless indicated otherwise, experiments were carried out in the indicated solvent on 2 mmol scales [each of **4** and **5** in a 1:1 molar ratio, and (as needed) Et_3N]. Two stock solutions at the indicated concentrations were combined in the indicated order of addition, at a rate to maintain the temperature at 10 ± 5 °C. Results were qualitatively the same, except for slightly lower absolute conversions, in those cases where experiments were carried out at ambient temperature without cooling. Each completed reaction mixture was diluted as necessary with additional solvent (to ~0.1 M product), washed with 1 N aqueous HCl (3×), dried ($MgSO_4$), and concentrated. The residue was then taken up in CH_2Cl_2, filtered to remove elemental sulfur, and evaporated. Product yields and distributions reflect conversion of starting **4**, e.g., when 10 mmol of **4** gives 2 mmol of **2** and 3 mmol of **3**, this is reported as 20% of **2** and 60% of **3**. Compound **1** was not detected (≤3%) in any of these reactions. [b] Larger scale, see Experimental Section for full procedure directed toward pure **2** or **3**. [c] Based on starting **4**, 85% mass recovery; complicated spectrum with multiple ethyl-containing products, the major one of which was **4**, formed by decomposition of the actual products upon workup. ^1H and ^{13}C NMR spectra of the reaction product mixture, taken before workup, showed unreacted **4**, intermediate **11**, and EtCl as the three major products, accounting respectively for 21, 56, and 6% of the ethyl groups. The expected **2** and **3** were not formed to any appreciable extent, as revealed by spectroscopic examination both before and after workup.

(10) (a) Blankenhorn, E. *J. Prakt. Chem.* **1877**, *16*, 358−384. (b) Wheeler, H. L.; Barnes, B. *Am. Chem. J.* **1899**, *22*, 141−151. (c) Davies, W.; MacLauren, J. A. *J. Chem. Soc.* **1951**, 1434−1438. (d) Goerdeler, J.; Schulze, A. *Chem. Ber.* **1982**, *115*, 1252−1255.

(11) (a) Weiss, W. German Patent 1,224,720, Nov 11, 1966; *Chem. Abstr.* **1966**, *65*, 12112h. (b) Barany, G.; Schroll, A. L.; Mott, A. W.; Halsrud, D. A. *J. Org. Chem.* **1983**, *48*, 4750−4761.

(12) Cyanic acid (bp 23.5 °C) readily trimerizes to cyanuric acid (2,4,6-trihydroxy-1,3,5-triazine), a material with limited or negligible solubility in organic solvents that decomposes prior to melting. Review: Smolin, E. M.; Rapoport, L. In *The Chemistry of Heterocyclic Compounds*; Weissberger, A. Ed.; Wiley Interscience: New York, 1959; Vol. 13, pp 17−48. Some of the reactions described in this work gave a byproduct, which, on the basis of solubility properties and mass spectrometry, is assigned as cyanuric acid.

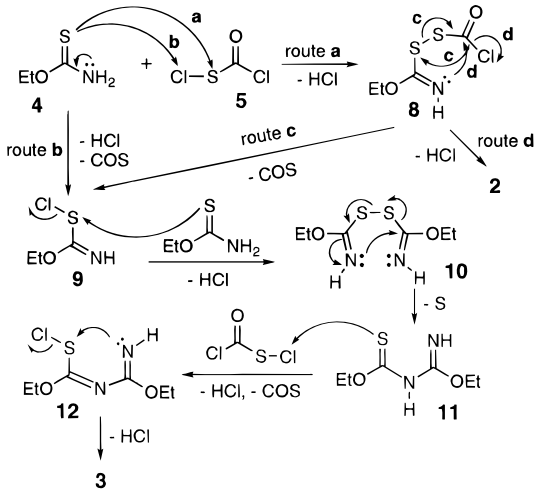
(13) Balanced equations for reactions of **4** and **5** to give either **2** *or* **3** nominally show formation of 2 equiv of HCl, which may need to be neutralized by Et_3N. As shown in the text, a full 2 equiv of Et_3N has little effect on the outcome when the reaction is conducted in Et_2O, whereas when $CHCl_3$ (or $CDCl_3$) is the solvent, the major product appears to be **11** (Scheme 2), which decomposes upon workup back to starting material **4**.

tested: 1,2-dimethoxyethane ($\epsilon_r = 7.20$, $E_T^N = 0.231$) and methyl *tert*-butyl ether ($\epsilon_r = 4.5$, $E_T^N = 0.148$) gave results comparable to those with Et_2O, toluene ($\epsilon_r = 2.38$, $E_T^N = 0.099$) gave results comparable to those with $CHCl_3$, and results with dioxane ($\epsilon_r = 2.21$, $E_T^N = 0.164$) and tetrahydrofuran ($\epsilon_r = 7.58$, $E_T^N = 0.231$) were intermediate. Thus, the observed results are likely to reflect other factors, such as the solubility of intermediates, e.g., **8**, in the particular solvent (see discussion of mechanism that follows, as well as Scheme 2).

Mechanisms of Dithiazolinone and Thiadiazole Formation. Insights into the mechanisms of the aforementioned transformations came, in part, from experiments generating the same *core* heterocyclic systems, e.g., 3-methyl-1,2,4-dithiazolin-5-one (**6**)[15] by the reaction of thioacetamide with (chlorocarbonyl)sulfenyl chloride (**5**), and 3,5-dimethyl-1,2,4-thiadiazole (**7**)[16,17] by the oxidation of thioacetamide with appropriate reagents (see Scheme 1, inset). A relevant precedent is the formation of *N*,*N*′-dialkyl-1,2,4-thiadiazolidine-3,5-diones as side products during the preparation of *N*-alkyl-1,2,4-dithiazolidine-3,5-diones from **5** and the appropriate *O*-alkyl′, *N*-alkyl thiocarbamate.[18] The bis-ethoxy-substituted thiadiazole **3** encountered in the present work (optimized yield 69%; see Table 1, entry 16) was prepared previously by oxidation of thiocarbamate **4** with hydrogen peroxide[9a] (25% yield) or *N*-sulfinyl-*p*-toluenesulfonamide[9b] (61% yield). These precedents raise the relatively straightforward explanation that formation of **3** is due to the action of **5** as an oxidizing agent, a role it is known to take in other reactions [Cl(C═O)SCl ≡ "Cl_2" + COS].[19]

While it is difficult to predict which product should be preferred depending on whether Et_2O or $CHCl_3$ is the reaction solvent, we are able to propose a mechanism for formation of **2** as well as **3** that involves as the common initial step an electrophilic attack on the sulfur of the thiocarbamate **4** (Scheme 2). Thus, reactions of the thiocarbonyl moiety of **4** with either the sulfur (Scheme 2, route a) or chlorine (Scheme 2, route b) atoms of

Scheme 2



sulfenyl chloride **5** generate respectively the formimidoyl(chlorocarbonyl)disulfane **8**[20] or the formimidoylsulfenyl chloride **9**. In our proposed mechanism, route a predominates in Et_2O, and route b is preferred in $CHCl_3$. Alternatively, disulfane **8** may be formed initially in either of these solvents, but we would postulate that, in $CHCl_3$, **8** rearranges readily to sulfenyl chloride **9** (Scheme 2, route c) before it can collapse and cyclize to dithiazolinone **2** (Scheme 2, route d, the preferred pathway in Et_2O). The proposal continues with the bimolecular reaction of **9** with a second equivalent of **4**, providing symmetrical bis(formimidoyl)disulfane **10**.[21] Subsequently, **10** rearranges, with loss of elemental sulfur, via a six-membered transition state to give acyclic intermediate **11**, in analogy to the rearrangement of *N*,*N*′-dialkylbis(formimidoyl)disulfanes studied by Barrett.[21b] In the final step of our proposed mechanism, the thiocarbonyl of **11** is activated[22] with a second equivalent of **5** to give the sulfenyl chloride **12**, which then closes rapidly to provide thiadiazole **3**.

We have been able to isolate several of the proposed intermediates, i.e., **8**, **10**, and **11**, and have shown that their chemistry is consistent with Scheme 2. Authentic disulfide **10** was prepared by reaction of **4** (2 equiv) and iodine (1 equiv) in the presence of Et_3N (2 equiv); the reaction was cleanest with Et_2O as solvent (salts removed by filtration).[21b] Compound **10** in $CDCl_3$ rearranged to **11** upon addition of trifluoroacetic acid (partial decomposition to **4** occurred under the same conditions), again in analogy to reactions observed by Barrett.[21b] Interestingly, the rather unstable **11** is the major component detected directly in the complicated product mixture from reaction in $CDCl_3$ of **4** and **5** (1 equiv each) in the presence of Et_3N (2 equiv),[13] and **10** is formed (present along with unreacted starting material) from reaction in

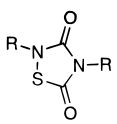
(14) Data taken from the following: Reichardt, C. *Solvents and Solvent Effects in Organic Chemistry*; VCH Verlagsgesellschaft: Weinheim, 1988; pp 408−410.

(15) This general class of compounds has been mentioned in a review article (ref 3a) and a book (ref 4d), without any experimental documentation (e.g., yield, mp). See the present paper for our procedure to prepare **6** (due to the low solubility of thioacetamide in both Et_2O and $CHCl_3$, the results are not strictly comparable to our observations on the reactions of **4** and **5**). Physical and spectral properties of **6** are also reported herein.

(16) Literature routes to **7**, and some mechanistic proposals, are described in ref 9b and the following: (a) Walter, W. *Justus Liebigs Ann. Chem.* **1960**, *633*, 49−55. (b) El-Wassimy, M. T. M.; Jorgensen, K. A.; Lawesson, S.-O. *Tetrahedron* **1983**, *39*, 1729−1734. (c) Hu, N. K.; Aso, Y.; Otsubo, T.; Ogura, F. *Chem. Lett.* **1985**, 603−606.

(17) In ref 16c, it was shown that oxidation of thioamides R(C═S)-NH_2 with polystyrene-bound selenoxide in acetic acid produced exclusively dialkythiadiazoles (e.g., **7** for R = Me), while reactions in other solvents such as EtOH, benzene, and CH_3CN produced only the corresponding nitriles, RC≡N.

(18) I.e., for R ≠ H, the reaction of R'O(C═S)NHR + Cl(C═O)SCl (compare to refs 3a and 4a) gives rise to low levels of carbamoylsulfenyl chlorides ClS(C═O)NHR, which cyclodimerize with loss of HCl + $^1/_2$S to provide the heterocycle drawn below; see ref 5b for detailed mechanistic studies including crossover experiments.



(19) As an example where **5** acts merely as an oxidant, in ref 3a, Zumach and Kühle report that Cl(C═O)SCl (**5**) reacts with thiophenol (PhSH) to give diphenyl disulfide (PhSSPh) plus COS and HCl. A more complicated further example is given in ref 5c.

(20) The reactions of thiocarbamates with sulfenyl chlorides to provide formimidoyldisulfanes were described first by Harris: Harris, J. F., Jr. *J. Am. Chem. Soc.* **1960**, *82*, 155−158. They are supported by ample examples and mechanistic studies from Kühle (refs 3 and 4) and us (ref 5 and herein). See text for experimental evidence supporting the structure of intermediate **8** and studies of its further transformations.

(21) Symmetrical disulfanes of this type are well known and are generally prepared by slow addition of 0.5 equiv of an oxidant, e.g., I_2, to thiocarbamates or thioamides. For examples, see: (a) McGowan, G. *J. Chem. Soc.* **1886**, 190−196. (b) Barrett, A. G. M.; Barton, D. H. R.; Colle, R. *J. Chem. Soc., Perkin Trans 1* **1980**, 665−671.

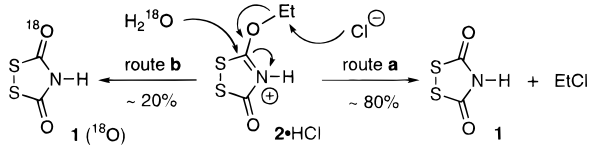
(22) An analogue of **11** with ethoxy groups replaced by phenyl groups has been isolated and subsequently converted to a thiadiazole by oxidation, see ref 9b.

Table 2. Electron Impact Mass Spectra of 1,2,4-Dithiazolidine-3,5-dione (1) Prepared under Various Conditions[a]

		$S_2^{\bullet+}$ [b]	$HNCOS_2^+$ [b]		$M^{\bullet+}$ of **1** [b]		$(M+2)/[(M)+(M+2)]$ [c]	
entry	reaction conditions	64	107	109	135	137	$HNCOS_2^+$	$M^{\bullet+}$
1	1,2,4-dithiazolidine-3,5-dione (**1**)	100	14	1	52	5	0.07	0.09
2	**1** + HCl/$^{18}OH_2$, 1 h, 100 °C	100	14	3	41	9	0.17	0.18
3	**2** + HCl/$^{18}OH_2$ → **1**, 15 min, 100 °C	100	12	4	27	10	0.25	0.27
4	**2** + HCl/$^{18}OH_2$ → **1**, 1 h, 100 °C	100	12	5	29	15	0.29	0.34

[a] See text for procedure, specifically with regard to entry 3; 83% yield for **1**. For the control experiment on entry 2, on same scale but with a 4-fold longer reaction time, the recovery of **1** was 64%, indicating that some hydrolysis had taken place (the recovered **1** had the same mp as the pure starting **1**). The experiment on entry 4, with the longer reaction time, was worked up less efficiently, i.e., crystals were collected directly rather than evaporating to dryness. Therefore, the isolated yield of 30% cannot be compared to the other, more quantitative, experiments. Entry 1 is a standard of **1**, and the (M + 2) peaks reported are due to the natural abundance of ^{34}S. [b] Intensities of the mass of this ion are indicated as percent of the most intense ion. [c] Ratios of the intensities of indicated species.

Scheme 3



$CDCl_3$ of **4** (2 equiv) and **5** (1 equiv) in the presence of Et_3N (2 equiv).

As already described, the reaction of **4** and **5** in Et_2O in the absence of tertiary amine eventually gives heterocycle **2**, which is soluble in Et_2O. However, a white precipitate was observed to form shortly after both reactants had been combined, and this highly unstable solid was isolated by rapid filtration under suction. The observed mass (CIMS) and ^1H NMR ($CDCl_3$) spectra were consistent with the structure of the intermediate formimidoyl(chlorocarbonyl)disulfane **8** (or its hydrochloride salt, **8**·HCl).[23] After 30 min in $CDCl_3$ solution, **8** had completely disappeared and showed EtCl (85% of ethyl groups) as the main product (presumed coproducts COS and elemental S; only small amounts of **2** and **11** formed), in accord with results in $CHCl_3$ in the absence of external base (Scheme 1, Table 1, entry 12). Rapid addition of freshly collected solid **8** to a $CDCl_3$ solution containing Et_3N (~1 equiv) showed the major product to be again EtCl (50% of ethyl groups), but **2** (15% of ethyl groups) and **11** (27% of ethyl groups) also formed. Again, these results with isolated **8** mirror the ultimate solvent-dependent product distribution from the reactions of **4** and **5** in the absence and in the presence of tertiary amine.

Conversion of 3-Ethoxy-1,2,4-dithiazolin-5-one (2) to 1,2,4-Dithiazolidine-3,5-Dione (1). The desired title heterocycle **1** was obtained by heating **2** with concentrated aqueous hydrochloric acid at reflux. Two plausible pathways for this transformation involve protonation of heterocycle **2**, followed by attack of chloride on the ethyl group, to give **1** and EtCl (Scheme 3, route a) or, alternatively, nucleophilic addition of water to the imino carbon with ultimate loss of ethanol (Scheme 3, route b). Conversion of **2** to **1** was carried out in HCl−$H_2{}^{18}O$ (Table 2, entries 3 and 4) and found to give product of both *m*/*z* 135 and 137 (EIMS), indicating significant incorporation of ^{18}O in **1**. Taking into account the ^{34}S contribution to *m*/*z* 137 in dithiazolidine **1** (Table 2, entry 1), as well as background oxygen exchange of **1** under the reaction conditions (Table 2, entry 2), we conclude that route a is favored over route b by a factor of approximately 4:1. Route a is directly analogous to a process which otherwise (R ≠ H) occurs essentially spontaneously.[3a,4,5a] In the special case of interest here, reaction at 25 °C in $CDCl_3$ solution of **2** (0.6 M) saturated with anhydrous HCl was shown to give EtCl and **1**, albeit *very* slowly (5% conversion after 12 h), and hence not of any preparative value.

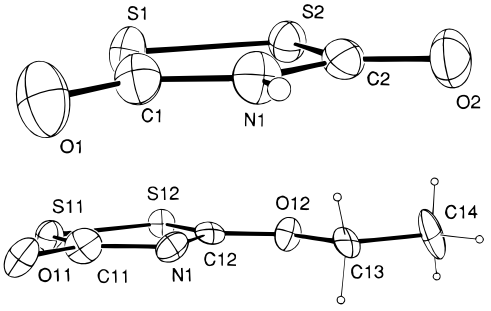


Figure 1. ORTEP representations of **1** and **2** (40% ellipsoids, H atoms in idealized positions). Selected bond distances, bond angles, and torsion angles are listed in Table 3.

X-ray Crystallographic Structures of 1,2,4-Dithiazolidine-3,5-dione (1) and 3-Ethoxy-1,2,4-dithiazolin-5-one (2), and Mechanistic Implications. Structures of **1** and **2** were solved (Figure 1, Table 3),[24] showing the planar, aromatic structure of both heterocycles.[25] Bond lengths and angles of **1** and **2** were typical for five-membered cyclic disulfides with aromatic character.[25] Whereas the preferred bond angle (C−S−S) and torsion angle (C−S−S−C) in acyclic disulfides are around 105° and ±90°, respectively, the heterocycles **1** and **2** have corresponding bond angles of 90−95° and torsion angles of 0 ± 5°. These values help to account for the facile desulfurization reactions (Scheme 4 and ref 2) of **1** and **2**. Thus, addition of a soft nucleophile, e.g., a phosphorus(III) species, to one of the sulfur atoms in the rings is an enthalpically favorable processes (loss of strain energy), accentuated by favorable entropic components (three molecules formed from two molecules). However, under acidic or neutral conditions and over long-term ambient storage, both **1** and **2** are kinetically stable for weeks or even years. Finally, the fact that the basic imino nitrogen of **2** is coplanar with the ethoxy group is

(23) The fact that the compound precipitates from Et_2O suggests strongly that it is **8**·HCl (ammonium chlorides have very low solubility in Et_2O). The δ = 4.92 ppm for the methylene protons of the Et group indicates a strongly electropositive center and is also consistent with an ammonium form [in contrast, bis(formimidoyl)disulfane **10** has δ = 4.29 ppm for the methylene protons of the Et group].

(24) The authors have deposited atomic coordinates for the structures of compounds **1** and **2** with the Cambridge Crystallographic Data Centre. The coordinates can be obtained, on request, from the Director, Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge, CB2 1EZ, UK.

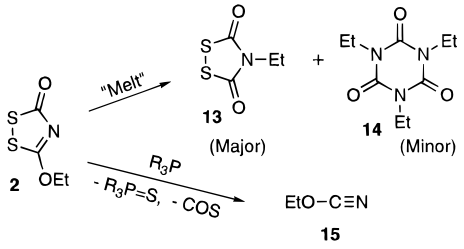
(25) Barany, G. *Cryst. Struct. Commun.* **1982**, *11*, 913−928 and references cited therein. This work provides a relevant discussion of planarities, bond lengths, bond angles, and dihedral angles in a number of five-membered heterocyclic disulfides.

Table 3. X-ray Crystallographic Parameters and Selected Bond Lengths, Bond Angles, and Torsion Angles for 1,2,4-Dithiazolidine-3,5-dione (1) and 3-Ethoxy-1,2,4-dithiazolin-5-one (2)

compound	**1**	**2**[a]
M_w	135.16	163.21
space group	$I4_1/a$	*Pc* (No. 7)
a, Å	19.556(6)	3.939(2)
b, Å	19.556(6)	35.84(1)
c, Å	4.996(2)	18.789(4)
α	90	90
β	90	90.81(3)
γ	90	90
V, Å^3	1910.6(11)	2652(3)
Z	16	16
temp (K)	297	172
ρ_{calcd}, g/cm^3	1.880	1.635
radiation	Mo *K*α = 0.710 73 Å	Mo *K*α = 0.710 73 Å
crystal shape	prism	needle
size (mm)	0.60 × 0.45 × 0.35	0.60 × 0.20 × 0.15
total reflections	3297	6067
unique reflections	1088	5968
obsd reflections	1088	5753
R_1 (on *F*)	0.032	0.087
ωR_2 (on F^2)	0.080	0.181
	Selected Bond Lengths (Å)	
N1−C1/N1−C11	1.367(2)	1.36(2)
C1−O1/C11−O11	1.208(2)	1.23(2)
C1−S1/C11−S11	1.764(2)	1.81(2)
S1−S2/S11−S12	2.0584(8)	2.053(6)
S2−C2/S12−C12	1.761(2)	1.76(2)
C2−N1/C12−N1	1.369(2)	1.26(2)
C2−O2/C12−O12	1.208(2)	1.31(2)
	Selected Bond Angles (deg)	
N1−C1−S1/N1−C11−S11	113.5(1)	116(1)
C1−S1−S2/C11−S11−S12	95.42(5)	93.3(5)
S1−S2−C2/S11−S12−C12	95.45(6)	91.9(5)
S2−C2−N1/S12−C12−N1	113.6(1)	123(1)
	Selected Torsion Angles (deg)	
S1−S2−C2−O2/S11−S12−C12−O12	−179.6(1)	175(1)
S1−S2−C2−N1/S11−S12−C12−N1	1.5(1)	−2(2)
S1−C1−N1−C2/S11−C11−N1−C12	−1.7(2)	6(2)
S2−S1−C1−O1/S12−S11−C11−O11	−177.8(2)	180(2)
S2−S1−Cl−N1/S12−S11−C1l−N1	2.3(1)	−4(2)
S2−C2−N1−C1/S12−C12−N1−C11	−0.1(2)	−5(3)
N1−C12−O12−C13	[b]	−7(3)

[a] The asymmetric unit contains eight chemically identical molecules that are not crystallographically equivalent. Pseudotranslations between the eight molecules render much of the data weak, and the noncentrosymmetric nature of the structure also limits the data: parameter ratio. [b] Not applicable.

Scheme 4



consistent with the major proposed pathway for conversion of **2** to **1** (Scheme 3, route a).

Other Transformations of 3-Ethoxy-1,2,4-dithiazolin-5-one (2) (Scheme 4). When heated past the melting point, **2** undergoes (most likely bimolecular) rearrangement to give *N*-ethyl-1,2,4-dithiazolidine-3,5-dione (**13**).[5b] A minor byproduct of this reaction is 1,3,5-triethyl-2,4,6-trioxohexahydro-*s*-triazine (triethyl isocyanurate) (**14**),[26a,c] the trimer of ethyl isocyanate (EtN═C═O). The rapid desulfurization of **2** by a variety of phosphines in chloroform or acetonitrile provides a novel entry to *O*-ethyl cyanate (**15**).[2,8,27]

Experimental Section

General. ^{1}H, ^{13}C, and ^{31}P NMR spectra were observed in the indicated deuterated solvents with IBM NR 200 AF or NR 300 AF or Varian VXR 300 instruments. Resonances are expressed as ppm downfield from TMS; coupling constants of ethyl groups were approximately 7.1 Hz and are not specified. Exchangable protons are not reported. IR spectra were obtained on a Perkin Elmer 1600 Series FTIR spectrophotometer. Electron ionization mass spectra were obtained on a Finnigan MAT 95 instrument at the indicated eV and a source temperature of 200 °C. Positive and negative methane chemi-

(26) (a) The reference spectral positions for isocyanurate **14** were established on a reasonably pure crystalline sample, mp 75−88 °C, which was obtained from the residue of a redistillation of the contents of an old bottle of ethyl isocyanate (EtN═C═O). (b) The corresponding cyanurate isomer, 2,4,6-triethoxy-*s*-triazine, was made by reaction of cyanuric chloride with NaOH (3 equiv in EtOH), as outlined in the following: Dudley, J. R.; Thurston, J. T.; Schaefer, F. C.; Holm-Hansen, D.; Hull, C. J.; Adams, P. *J. Am. Chem. Soc.* **1951**, *73*, 2986−2990. The cyanurate was readily distinguishable [^{1}H NMR ($CDCl_3$) δ 4.31 (q, 2 H), 1.28 (t, 3 H); ^{13}C NMR ($CDCl_3$) δ 172.9, 64.1, 14.1]. (c) Literature mp's: 95 °C for **14**; 30 °C for the cyanurate isomer; see: *Dictionary of Organic Compounds*, 5th ed.; Chapman & Hall: New York, 1982; C-10334 and T-02371, pp 131 and 5388.

(27) For relatively complicated routes to EtOC≡N, see: (a) Jensen, K. A.; Holm, A. *Acta Chem. Scand.* **1964**, *18*, 826−828. (b) Martin, D.; Mucke, W. *Chem. Ber.* **1965**, *98*, 2059−2062. For alkyl cyanate chemistry, see: (c) Jensen, K. A.; Due, M.; Holm, A.; Wentrup, C. *Acta Chem. Scand.* **1966**, *20*, 2091−2106.

cal ionization mass spectra were recorded under the specified conditions on the Finnigan MAT 95 instrument. Low-resolution fast atom bombardment mass spectroscopy (FABMS) was carried out on a VG Analytical 707E-HF low-resolution double-focusing mass spectrometer equipped with a VG 11/250 data system, operated at a resolution of 2000. Elemental analyses were performed by M-H-W Laboratories (Phoenix, AZ).

X-ray Data Collection, Solution, and Refinement (Table 3). Crystals were mounted in an Enraf-Nonius CAD4 diffractometer. Intensity data for independent reflections ($0° < 2\theta < 60°$) were collected at the indicated temperature (Table 3) by the ω scan technique. Data reduction was performed on a PDP 11/34 computer using an Enraf-Nonius SDP program library. The structures were solved by direct methods (MULTAN) and refined by full-matrix least-squares with SHELXTL (version 5) program on a Pentium PC using all measured data. The final R values based on data having $I > 2\sigma|I|$ are given in Table 3.

1,2,4-Dithiazolidine-3,5-dione (1). A stirred suspension of recrystallized 3-ethoxy-1,2,4-dithiazolin-5-one (**2**)[28] (13.9 g, 85 mmol) in concentrated aqueous HCl (80 mL) was brought over 45 min to 110 °C and 10 min later passed while hot through a glass fritted funnel to remove elemental sulfur. The filtrate was concentrated to dryness to provide a solid, which was crystallized from toluene: yield, 8.5 g (74%), mp 141−143 °C (lit. mp[3b] 141 °C; lit. mp[3c] 142−144 °C); ^{13}C NMR ($CDCl_3$) δ 167.7; ^{13}C NMR (CD_3CN) δ 168.7; IR ($CDCl_3$) 3360 (w), 1735 (s), 1700 (vs), 1683 (s, sh), 1287 (m) cm^{-1}; methane CIMS (source 160 °C, solid probe 60 °C, 0.1 mm) m/z 136 [(M + H)$^+$, 100), 108 [(M + H)$^+$ − CO, 29], 93 (14), 64 (S_2^+, 19).

Anal. Calcd for $C_2HNO_2S_2$ (MW 135.16): C, 17.77; H, 0.74; N, 10.36; S, 47.44. Found: C, 17.91; H, 0.84; N, 10.44; S, 47.31.

Samples of crystalline **1** were maintained under ambient conditions for 2 years or more without any signs of decomposition as judged by ^{13}C NMR, repeat elemental analysis, and mp redetermination; routine storage is carried out at −20 °C.

Conversion of 3-Ethoxy-1,2,4-dithiazolin-5-one (2) to 1,2,4-Dithiazolidine-3,5-dione (1) by Hydrogen Chloride in [^{18}O]Water (Table 2). $H_2{}^{18}O$ (∼0.5 mL) was placed in an open 7-mL screw-cap tube and saturated for 1 h with dry HCl gas (produced[29] by slowly dropping 50 mL of concentrated sulfuric acid onto 100 g of NaCl). Compound **2** (100 mg) was added, and after bubbling had subsided (15 min), the tube was sealed and brought to 100 °C for 15 min reaction. Next, the still-hot reaction mixture was filtered through glass wool, and evaporation provided white crystals (76 mg, 83%): mp 136−139 °C, mass spectral data in Table 2, entry 3.

3-Ethoxy-1,2,4-dithiazolin-5-one (2). Method A. A mixture of *O*-ethyl thiocarbamate (**4**) (21.0 g, 0.2 mol) and Et_3N (28 mL, 0.2 mol) in Et_2O (100 mL) was added dropwise over 1 h into a stirred and externally chilled solution of (chlorocarbonyl)sulfenyl chloride (**5**) (16.8 mL, 0.2 mol) in ethyl ether (1 L), at a rate to maintain the reaction temperature below 10 °C. After an additional 4.5 h of stirring, the precipitated $Et_3N{\cdot}HCl$ (30.2 g, quantitative) was removed by filtration. The filtrate was concentrated to provide a light-yellow solid (26.8 g, 91% purity by ^{1}H NMR with the remainder being **3**). Recrystallization from ether (100 mL) at −20 °C gave off-white needles (16.4 g), mp 51−53 °C (lit.[3c] mp 56−57 °C). The mother liquor provided an additional portion of light yellow needles (4.1 g): mp 42−46 °C; total yield, 20.5 g (63%).

Method B. A solution of thiocarbamate **4** (5.25 g, 50 mmol) in Et_2O (25 mL) was added dropwise over 40 min into a stirred and externally chilled solution of **5** (4.2 mL, 50 mmol) in Et_2O (250 mL), at a rate to maintain the reaction temperature below 10 °C. A white precipitate formed[20] but disappeared as the reaction progressed with an additional 1.5 h of stirring at 25 °C. Solvent was evaporated at reduced pressure, and the residue was redissolved in CH_2Cl_2 (100 mL), filtered to remove an insoluble white solid (0.4 g) believed to be cyanuric acid (2,4,6-trihydroxy-1,3,5-triazine),[12] and reconcentrated to provide a light-yellow solid (7.22 g, 89% purity by ^{1}H NMR with the remainder being **3**). Recrystallization from Et_2O (15 mL) at −20 °C gave off-white needles (3.6 g). The mother liquor provided an additional portion of light yellow needles (0.6 g): total yield, 4.2 g (52%); ^{1}H NMR ($CDCl_3$) δ 4.68 (q, 2 H), 1.47 (t, 3 H); ^{13}C NMR ($CDCl_3$) δ 187.3, 179.6, 73.5, 14.1; IR ($CDCl_3$) 2990 (w), 1705 (s), 1541 (vs), 1470 (m), 1393 (w), 1365 (w), 1297 (w), 1259 (s), 1239 (m), 1153 (w), 1004 (w) cm^{-1}; positive methane CIMS (source 160 °C, solid probe 20 °C, 0.1 mm) m/z 164 [(M + H)$^+$, 100], 136 [(M + H)$^+$ − CO, 67]; negative methane CIMS m/z 162 [(M − H)$^-$, 59], 133 (14), 102 [(M − H)$^-$ − COS, 100]; EIMS (source 200 °C, solid probe 30 °C) m/z 163 (M$^{\bullet+}$, 24), 135 (M$^{\bullet+}$ − CO, 13), 131 (M$^{\bullet+}$ − S, 10), 107 (M$^{\bullet+}$ − CO − C_2H_4, 18), 103 (M$^{\bullet+}$ − COS, 8), 70 (79), 64 (29), 60 (21), 29 ($C_2H_5^+$, 100).

Anal. Calcd for $C_4H_5NO_2S_2$ (MW 163.22): C, 29.44; H, 3.09; N, 8.58; S, 39.29. Found: C, 29.23; H, 3.14; N, 8.68; S, 39.41.

Samples of crystalline **2** were maintained under ambient conditions, exposed to open atmosphere, for up to 2 years without any signs of decomposition as judged by ^{1}H NMR, ^{13}C NMR, and mp redetermination; routine storage is carried out at −20 °C.

Thermal Decomposition and Rearrangement of 3-Ethoxy-1,2,4-dithiazolin-5-one (2). Title substrate **2** (89 mg, 0.53 mmol) was melted and heated at 100 °C in a closed 7-mL screw-cap tube with a Teflon-lined cap. After 5 days, the tube was cooled, vented, taken up in $CDCl_3$, and filtered to provide an insoluble residue (6 mg, 0.2 mmol assuming elemental sulfur) and a soluble portion (66 mg) that, according to ^{1}H and ^{13}C NMR, was devoid of starting material and comprised *N*-ethyl-1,2,4-dithiazolidine-3,5-dione (**13**)[5b] (0.28 mmol, 53%) [^{1}H NMR ($CDCl_3$) δ 3.81 (q, 2 H), 1.23 (t, 3 H); ^{13}C NMR ($CDCl_3$) δ 167.3, 41.5, 12.7], 1,3,5-triethyl-2,4,6-trioxohexahydro-*s*-triazine (triethyl isocyanurate, **14**)[26a,c] (0.03 mmol, 16% of ethyl groups) [^{1}H NMR ($CDCl_3$) δ 3.88 (q, 2 H), 1.18 (t, 3 H); ^{13}C NMR ($CDCl_3$) δ 148.6, 38.1, 13.1], and an unknown *N*-ethyl derivative (0.09 mmol, 17%) [partial ^{1}H NMR ($CDCl_3$) δ 4.09 (q) (corresponding triplet not resolved); ^{13}C NMR ($CDCl_3$) δ 160.4, 40.5, 30.0].

In a separate experiment, substrate **2** (89 mg, 0.55 mmol) in $CDCl_3$ (0.5 mL) was refluxed for 7 days and shown by ^{1}H and ^{13}C NMR to be a 19:1 mixture of unchanged **2** (major) plus rearrangement product **13** (minor).

3,5-Diethoxy-1,2,4-thiadiazole (3). A solution of (chlorocarbonyl)sulfenyl chloride (**5**) (6.25 mL, 75 mmol) in $CHCl_3$ (375 mL) was added over 30 min into a stirred and externally chilled mixture of *O*-ethyl thiocarbamate (**4**) (7.88 g, 75 mol) and Et_3N (10.7 mL, 75 mmol) in $CHCl_3$ (375 mL), at a rate to maintain the reaction temperature at 5−10 °C. After a further 15 min, the reaction mixture was washed with 1 N aqueous HCl (2 × 1 L) and water (2 × 1 L), dried ($MgSO_4$), concentrated, taken up in $CHCl_3$ (50 mL), filtered to remove a substantial mass of elemental sulfur, and concentrated again. The crude product (5.4 g) comprised title product (52 mmol, 69% of ethyl groups in starting **4**) and **2** (5.5 mmol, 7%); extrapolating from results of a small-scale reaction in $CDCl_3$, EtCl (17%) and *O*-ethyl carbamate (3%) also were formed but were removed in the workup [the NMR study also showed that **3** decomposed at 25 °C on a time scale of days to EtCl, ^{1}H NMR δ 3.56 (q), 1.48 (t), ^{13}C NMR δ 40.2, 18.8, and COS, ^{13}C NMR δ 153.1; see Scheme 1]. A portion of the crude material (3.5 g) was subjected to careful short-path distillation, bp 68−71 °C (0.2 mm) or bp 50−53 °C (0.1 mm), leaving **2** and some sulfur in the residue and providing analytically pure title product (2.3 g, extrapolated yield 54% based on ethyl groups in starting **4**), which solidified in the receiver, mp 41−43 °C (lit.[9a,b] mp 48−49 °C); ^{1}H NMR ($CDCl_3$) δ 4.52 (q, 2 H), 4.38 (q, 2 H), 1.45 (t, 3 H), 1.41 (t, 3 H); ^{13}C NMR ($CDCl_3$) δ 189.7, 165.5, 69.8, 64.8, 14.2, 14.1; IR ($CDCl_3$) 2985 (w), 1542 (vs), 1512 (s), 1476 (w), 1377 (m), 1328 (vs), 1252 (m), 1228 (w), 1078 (w), 1013 (w) cm^{-1}; positive methane CIMS (source 160 °C, solid probe 50 °C, 0.1 mm) m/z 175 [(M + H)$^+$, 100], 147 [(M + H)$^+$ − C_2H_4, 90], 72 (27); EIMS (source 200 °C, solid

(28) On a 20 mmol scale, *crude* **2** from the reaction of **4** and **5** was treated as described in the text with concentrated aqueous HCl. Surprisingly, relatively little **1** was isolated (∼15% based on **4**), and the main product (∼40% of the crude product) was cyanuric acid (compare to ref 12).

(29) *The Merck Index*, 11th ed.; Budavari, S., Ed.; Merck & Co.: Rahway, NJ 1989; No. 4721, p 759.

probe 50 °C, 30 eV) *m*/*z* 174 ($M^{\bullet+}$, 28%), 146 ($M^{\bullet+} - C_2H_4$, 30%), 118 ($M^{\bullet+} - 2C_2H_4$, 100), 75 (47), 72 (25), 70 (29), 57 (14), 44 (19), 43 (20), 29 ($C_2H_5^+$, 71).

Anal. Calcd for $C_6H_{10}N_2O_2S$ (MW 174.22): C, 41.36; H, 5.79; N, 16.08; S, 18.40. Found: C, 41.11; H, 5.86; N, 15.97; S, 18.23.

***O*-Ethyl Thiocarbamate (4).** Following the method of Davies and MacLauren,[10c] solutions of potassium ethyl xanthate (192 g, 1.2 mol) in water (500 mL) and chloroacetic acid (113 g, 1.2 mol) plus sodium hydroxide (48 g, 1.2 mol) in water (450 mL) were combined and stirred at 25 °C throughout a full working day, following which concentrated ammonium hydroxide (100 mL, ~1.5 mol) was added, and stirring continued overnight. The product was then extracted into Et_2O (2 × 500 mL), and the organic phase was washed with equal volumes of H_2O and 1 N aqueous HCl, dried ($MgSO_4$), and concentrated. The resultant oil was placed under petroleum ether at −20 °C, providing a white solid. The purification process removed the *S*-ethyl isomer, which was present as a 7% contaminant in the crude product: yield, 78.5 g (62%); mp 36−38 °C (lit.[10c] mp 40−41 °C; lit.[10d] mp 38−39 °C); ^{1}H NMR ($CDCl_3$) δ 4.48 (q, 2 H), 1.34 (t, 3 H) [no δ 2.90, diagnostic of *S*-ethyl isomer]; ^{13}C NMR ($CDCl_3$) δ 192.0, 67.3, 13.8.

3-Methyl-1,2,4-dithiazolin-5-one (6). A solution of thioacetamide (0.73 g, 10 mmol) and Et_3N (2.8 mL, 20 mmol) in 1,2-dimethoxyethane (5 mL) was added dropwise over 20 min to a stirred and externally chilled solution of (chlorocarbonyl)-sulfenyl chloride (**5**) (0.84 mL, 10 mmol) in 1,2-dimethoxyethane (50 mL), at a rate to maintain the reaction temperature below 10 °C. After an additional 1 h of stirring, the precipitated Et_3N·HCl was removed by filtration. The filtrate was concentrated at reduced pressure to provide a dark-brown solid (0.9 g), which was dissolved in ethyl acetate (6 mL). Two-thirds of this solution was applied to flash chromatography (hexane−ethyl acetate = 4:1) to produce an off-white solid: yield, 0.29 g (29%, extrapolated to purification of all of the crude material); mp 64−67 °C; ^{1}H NMR ($CDCl_3$) δ 2.73 (s, 3 H); ^{13}C NMR δ 192.7, 188.0, 23.1.

Anal. Calcd for $C_3H_3NOS_2$ (MW 103.18): C, 27.06; H, 2.27; N, 10.52; S, 48.14. Found: C, 26.88; H, 2.20; N, 10.66; S, 48.12.

Formimidoyl(chlorocarbonyl)disulfane (8)[20] and Its Chemistry. A solution of *O*-ethyl thiocarbamate (**4**) (0.21 g, 2 mmol) in Et_2O (5 mL) was added dropwise over 5 min into a stirred and externally chilled solution of (chlorocarbonyl)-sulfenyl chloride (**5**) (168 mL, 2 mmol) in Et_2O (5 mL), at a rate to maintain the reaction temperature below 10 °C. A white precipitate formed instantaneously, and after another 5 min stirring while ice-bath-chilled, the **8** was collected by rapid filtration and drying under aspirator suction (essentially quantitative formation of solid; the filtrate was concentrated and shown to comprise <5% of the total mass). Spectral data were recorded immediately: ^{1}H NMR (<5 min in $CDCl_3$) δ 4.92 (q, 2 H), 1.54 (t, 3 H); ^{13}C NMR ($CDCl_3$) unable to detect **8** because of decomposition during acquisition; positive isobutane CIMS (source 160 °C, solid probe 25 °C, 0.1 mm) *m*/*z* 200 ($M + H^+$).

Solid compound **8** decomposed within 10 min upon standing at 25 °C to give heterocycle **2**, hydrolysis product *O*-ethyl carbamate, gaseous byproducts (COS, EtCl), and a significant insoluble fraction, which was presumably elemental sulfur. A solution of **8** in $CDCl_3$ was re-examined by ^{1}H NMR after 30 min at 25 °C, showing **2** (~5%), **11** (10%), *O*-ethyl carbamate (3%), and EtCl (81%). In a separate experiment, freshly prepared **8** from the same scale reaction was divided into equal portions. One portion was added to a solution of Et_3N (0.14 mL, ~1 equiv) in $CDCl_3$ (4 mL). After 30 min of stirring, the distribution of major compounds was **2** (~16%), **11** (27%), *O*-ethyl carbamate (5%), and EtCl (50%). The other portion was treated with twice the amount of Et_3N, and the distribution of major compounds was **2** (~16%), **11** (17%), **4** (6%), *O*-ethyl carbamate (5%), and EtCl (50%).

Bis(ethoxyformidoyl) Disulfane (10) and Its Chemistry. Modeled after the procedure of Barrett et al.,[21b] a solution of iodine (635 mg, 2.5 mmol) in Et_2O (15 mL) was added dropwise over 5 min to an ice-bath-chilled solution of *O*-ethyl thiocarbamate (**4**) (535 mg, 5 mmol) and Et_3N (0.7 mL, 5 mmol) in Et_2O (5 mL). Slightly more iodine (~20 mg) was added to get a brown endpoint. After 10 min, the reaction mixture was filtered to remove salts and concentrated at reduced pressure to provide semisolid **10** (>90% pure by ^{1}H NMR): yield, 0.47 g (90%); ^{1}H NMR ($CDCl_3$) δ 4.29 (q, 2 H), 1.26 (t, 3 H); ^{13}C NMR ($CDCl_3$) δ 161.8, 66.8, 14.2; FABMS [3-nitrobenzyl alcohol (MNBA) matrix] *m*/*z* 209 ($M + H^+$), and some peaks with one or two additional sulfurs.

Neat compound **10** decomposed upon overnight standing at 4 °C to give a complicated mixture, of which the main identifiable components were thiocarbamate **4** and (to a lesser extent) isocyanurate **14**, as well as a significant yellow insoluble fraction, which was presumably elemental sulfur. In an NMR tube experiment, freshly prepared **10** in $CDCl_3$ was treated with a drop of trifluoroacetic acid. An immediate exotherm was observed, along with intense coloration and precipitation of sulfur. Spectral examination indicated formation in a 2:1 molar ratio of **4** and a new species assigned to ethoxythiocarbonyl *O*-ethyl imidate (**11**): ^{1}H NMR ($CDCl_3$) δ 4.46 (q, 2 H), 4.32 (q, 2 H), 1.42 (t, 3 H), 1.35 (t, 3 H); ^{13}C NMR ($CDCl_3$) δ 190.1, 165.6, 70.5, 65.6, 14.2, 14.0; FABMS [3-nitrobenzyl alcohol (MNBA) matrix] *m*/*z* 177 ($M + H^+$).

***O*-Ethyl Cyanate (15) by Desulfurization of 3-Ethoxy-1,2,4-dithiazolin-5-one (2).** A solution of **2** in $CDCl_3$ (0.2 M) was treated with ~1 equiv of triphenyl phosphite, and spectra were recorded shortly thereafter: ^{1}H NMR ($CDCl_3$) δ 4.49 (q, 2 H), 1.40 (t, 3 H); ^{13}C NMR ($CDCl_3$) δ 188.1, 70.8, 13.5; ^{31}P NMR ($CDCl_3$) δ 54.9 (triphenyl thiophosphate). Similar results were obtained with other trivalent phosphorus compounds, e.g., triphenylphosphine and trimethyl phosphite, and with the solvent CD_3CN.

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