Synthesis and Kinetics of the Formation of N-Substituted Cyclic Sulfinamides from Secondary Amine Disulfides

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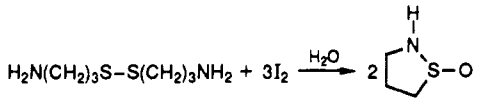
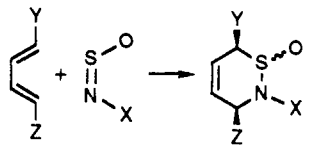
N-substituted cyclic saturated sulfinamides were prepared from two secondary amine disulfides, 3-[(1-phenylethyl)amino]propyl disulfide and 3-(cyclohexylamino)propyl disulfide, and two bicyclic sulfinamides were made from 2-(2-piperidyl)ethyl disulfide and 2-(2-pyrrolidyl)ethyl disulfide by aqueous iodine oxidation. The rates of the oxidative cyclization of iodine oxidation of 3-[(1-phenylethyl)amino]propyl disulfide and of the two benzimidazole-substituted disulfides 2-(2-benzimidazolyl)ethyl disulfide and 3-(2-benzimidazolyl)propyl disulfide were accelerated. The secondary amine disulfide is oxidized about 10^6 times as fast as the quaternary amine disulfide, twice as fast as the tertiary amine disulfide, and about 100 times faster than the primary amine disulfide. Thus, a variety of N-substituted sulfinamides can be formed rapidly. The benzimidazolyl group also facilitates the oxidative cleavage reaction. The relative rate ratio for oxidative cleavage of 3-(3-benzimidazolyl)propyl disulfide, 2-(2-benzimidazolyl)ethyl disulfide, and quaternary ammonium disulfide is 3000:1000:1. Different oxidants were used for the oxidative cleavage of secondary amine disulfides $[RNH(CH_2)_3S]_2$. In all cases the corresponding cyclic sulfinamide was isolated. Aqueous iodine gave the highest yield of the cyclic sulfinamide. When *N*-bromosuccinimide or iodine and triethylamine were used, the cyclic sulfonamide was isolated in addition to the sulfinamide. Trichlorosilane was shown to cause the reduction of the sulfinamide to the sulfenamide.

Introduction

Cyclic sulfinamides are the sulfur analogues of lactams, but little research on the formation of this functional group has been reported. Several years ago we[1] reported that the unsubstituted, saturated cyclic sulfinamide isothiazolidine 1-oxide could be prepared rapidly and under mild conditions by the oxidative cleavage of the alkyl disulfides. A five-membered ring sulfinamide had never been isolated before.



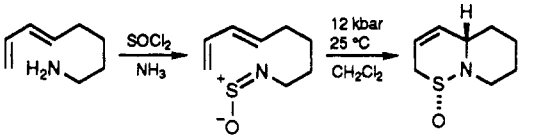
Wichterle and Rocek[2] reported a Diels–Alder reaction between *N*-sulfinylaniline and dienes to give *N*-sulfinyl-3,6-dihydro-1,2-thiazine 1-oxides. These reactions are



X = Ar, COR, CO_2R, SO_2R, H; Y, Z = H, CH_3

highly stereoselective and give syn addition products; however, varying mixtures of sulfur epimers are obtained. This $4\pi-2\pi$ cycloaddition is quite general and occurs at or below room temperature as long as the *N*-sulfinyl compound bears an electron-withdrawing group on the nitrogen.[3] Wucherpfennig[4,5] prepared the parent compound (X = H) by hydrolysis of the sulfinamide on which X = $C(O)OCH_2CCl_3$. He also prepared a series of thermally unstable four-membered ring derivatives by reactions of the *N*-sulfinyl-*p*-toluenesulfonamide with vinyl ethers.[6]

Unsaturated bicyclic sulfinamides have also been obtained by an intramolecular cyclization.[7]



We have now extended the series of saturated sulfinamides to include the monocyclic N-substituted derivatives made from secondary amine disulfides 3-[(1-phenylethyl)amino]propyl disulfide and 3-(cyclohexylamino)-propyl disulfide and bicyclic sulfinamides made from 2-(2-piperidyl)ethyl disulfide and 2-(2-pyrrolidyl)ethyl disulfide by aqueous iodine oxidation.

Under certain conditions, the rate of iodine oxidation of 3-(*N*,*N*-dimethylamino)propyl disulfide occurred 10^6 times faster than that of a simple disulfide.[1] In order to determine how this acceleration varies with the structure of the amine disulfide, we have studied the rates of the oxidative cyclization of 3-[(1-phenylethyl)amino]propyl disulfide and of two benzimidazole-substituted disulfides 2-(2-benzimidazolyl)ethyl disulfide and 3-(2-benzimidazolyl)propyl disulfide.

Results

Synthesis. Usually when secondary amines are prepared by alkylation, the primary amine has to be protected but in this case protection was not necessary and the reaction of either 1-phenylethylamine or cyclohexylamine with 3-chloropropanol proceeded smoothly to give the secondary amino alcohols.[8] The alcohols were then converted to the thiols by reaction with thiourea and hydrobromic acid to produce the isothiouronium salts, which were hydrolyzed with aqueous sodium hydroxide. The thiols were oxidized to the disulfides with aqueous hydrogen peroxide/ferrous sulfate.

The bicyclic sulfinamides were prepared from the corresponding monocyclic amine disulfides. The amine disulfide 2-(2-piperidyl)ethyl disulfide was easily prepared in a manner analogous to the methods previously described above since the amine alcohol was available commercially and could be converted to the thiol in the usual way. The

(1) Doi, J. T.; Musker, W. K. *J. Org. Chem.* **1985**, *50*, 1.
(2) Wichterle, O.; Rocek, J. *Collect. Czech., Chem. Commun.* **1954**, *19*, 282.
(3) Kresze, G. In *1,4-Cycloaddition Reactions, The Diels-Alder Reaction in Heterocyclic Syntheses*; Hamer, J., Ed.; Academic: New York, 1967; pp 453-471.
(4) Wucherpfennig, W. *Liebigs Ann. Chem.* **1971**, *746*, 16.
(5) Wald, L.; Wucherpfennig, W. *Liebigs Ann. Chem.* **1971**, *746*, 28.
(6) Wucherpfennig, W. *Tetrahedron Lett.* **1971**, *22*, 1891.
(7) Bell, S. I.; Weinreb, S. M. *Tetrahedron Lett.* **1988**, *29*, 4233.
(8) Bottini, A. T.; Roberts, J. D. *J. Am. Chem. Soc.* **1958**, *80*, 5203.

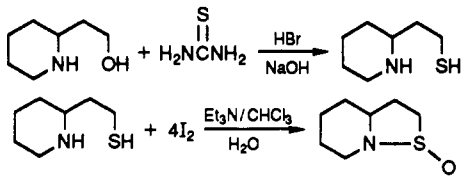
0022-3263/90/1955-4156$02.50/0

Table I. Rate Constants for the Aqueous I_2 Reactions of [3-[(1-Phenylethyl)amino]propyl] Disulfide[a]

run	10^4[RSSR]	[KI]	[buffer]	pH_f	10^3k_{obsd}	k_2
1	12.2	0.80	0.05 a	4.63	4.9 ± 0.3	4.0
2	8.13	0.80	0.05 a	4.63	3.7 ± 0.1	4.6
3	4.07	0.80	0.05 a	4.65	1.7 ± 0.1	4.2
4	12.2	0.50	0.05 a	4.92	7.4 ± 0.5	6.1
5	12.2	0.40	0.05 a	4.90	8.6 ± 0.2	7.0
6	12.2	0.20	0.05 a	4.70	14 ± 1	11
7	12.2	0.10	0.05 a	4.90	22 ± 1	18
8	12.2	0.80	0.03 a	4.69	4.0 ± 0.1	3.3
9	12.2	0.80	0.01 a	4.64	3.9 ± 0.1	3.2
10	12.2	0.80	0.05 a	3.95	1.1 ± 0.02	0.90
11	12.2	0.80	0.05 p	5.27	15 ± 1	12.3
12	12.2	0.80	0.05 a	5.53	28 ± 4	23
13	12.2	0.80	0.05 p	6.25	110 ± 10	90

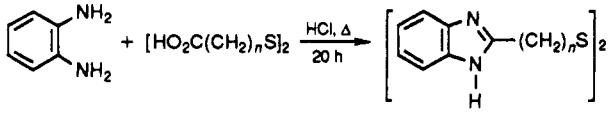
[a] Key: a = acetate buffer; p = phosphate buffer. Units: k_{obsd}, s^{-1}; k_2, M^{-1} s^{-1}. Conditions: T = 26.0 °C; [KI] + [KCl] = 1.0 M.

thiol was then oxidized to the disulfide; however, higher yields of the sulfinamide were achieved by iodine oxidation of the thiol directly to the sulfinamide.

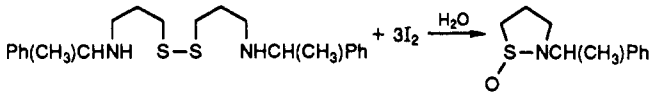


Preparation of the related amine disulfide 3-(2-pyrrolidyl)ethyl disulfide was a bit more complicated due to the fact that the amine alcohol had to be synthesized. The first step involves the synthesis of dimethyl γ-nitropimelate by treatment of methyl 4-nitrobutyrate with methyl acrylate. The nitropimelate was then hydrogenated to the pyrrolidinyl propionate, which was reduced with lithium aluminum hydride to the amine alcohol.

The benzimidazole disulfide salts were prepared by a Phillips condensation of *o*-phenylenediamine with a carboxylic acid disulfide.[9]



I_2 Oxidation. The product of the reaction of 3-[(1-phenylethyl)amino]propyl disulfide with aqueous iodine is a mixture of the two diastereomeric sulfinamides, 2-(1-phenylethyl)isothiazolidine 1-oxide.



The kinetics were followed by monitoring triiodide absorbance at 353 nm at 26.0 °C. Within a given run, the pH remained invarient due to acetate or phosphate buffer and the disulfide concentration was more than 10 times that of the initial triiodide. In Table I are listed the rate data for 3-[(1-phenylethyl)amino]propyl disulfide. The reaction is first-order in disulfide concentration (runs 1–3, log k_{obs} vs log [RSSR], slope 0.98, r = 0.99). There is an inverse first-order dependence on iodide ion concentration (runs 1 and 4–7, log k_{obs} vs log [KI], slope −0.71, r = 1.00). There is no buffer dependence (runs 1, 8, and 9), and there is a linear relationship between log k_{obs} and pH (runs 1 and 10–13, log k_{obs} vs pH, slope 0.86, r = 1.00; runs 1, 10, and 12 in acetate, slope 0.89, r = 0.999). In these solutions, the pH ranges from 3.9 to 6.2 and the amine is substantially protonated; thus, each successive increase of 1 pH unit corresponds to a 10-fold increase in the concentration of the free base. In accordance with the observed first-order dependence on disulfide concentration, values of the second-order rate constants k_2 equal to k_1/[RSSR] were calculated.

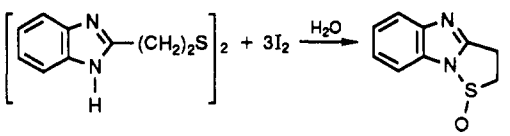
(9) Phillips, M. A. *J. Chem. Soc.* **1928**, 2393.

Table II. Rate Constants for Aqueous I_2 Reactions of [(2-Benzimidazoyl)alkyl] Disulfides[a]

run	10^4[RSSR]	[KI]	[acetate buffer]	pH	10^4k_{obsd}	k_2
			(2-Benzimidazolyl)-2-ethyl Disulfide			
1	2.79	0.00625	0.05	4.90	28 ± 0.1	10
2	2.09	0.00625	0.05	4.88	23 ± 2	11
3	1.395	0.00625	0.05	4.81	14 ± 0.1	10
4	1.045	0.00625	0.05	4.88	11 ± 0.4	10.5
5	2.08	0.00625	0.225	4.60	10 ± 1	4.8
6	2.08	0.00625	0.1125	4.68	11 ± 0.1	5.3
			(2-Benzimidazolyl)-3-propyl Disulfide			
1	5.00	0.00625	0.05	3.82	15 ± 2	3.0
2	3.33	0.00625	0.05	3.83	11 ± 0.03	3.0
3	3.135	0.00625	0.05	3.85	10 ± 1	3.2
4	2.25	0.00625	0.05	3.83	7.6 ± 0.3	3.4
5	1.665	0.00625	0.05	3.83	5.1 ± 0.5	3.1
6	2.08	0.10	0.05	4.13	1.4 ± 0.1	0.67
7	2.08	0.05	0.05	4.22	2.6 ± 0.04	1.25
8	2.08	0.025	0.05	4.15	5.1 ± 0.5	2.4
9	2.08	0.0175	0.05	4.14	6.6 ± 0.1	3.2
10	2.08	0.20	0.05	5.18	6.3 ± 0.2	3.0
11	2.08	0.10	0.05	5.15	10 ± 0.2	4.8
12	2.08	0.05	0.05	5.16	17 ± 0.01	8.2
13	2.08	0.025	0.05	5.11	35 ± 2	17
14	2.08	0.0175	0.05	5.09	56 ± 6	27
15	2.08	0.00625	0.05	5.15	92 ± 1	44
16	2.08	0.00625	0.225	4.64	33 ± 2	16
17	2.08	0.00625	0.1125	4.73	38 ± 0.2	18

[a] Units: k_{obsd}, s^{-1}; k_2, M^{-1} s^{-1}. Conditions: T = 26.0 °C; [KI] + [KCl] = 1.0 M.

On the basis of the identical rate law, rate acceleration, and product of the oxidation of 3-[(1-phenylethyl)amino]propyl disulfide, the product of the reaction of 2-(2-benzimidazolyl)ethyl disulfide with aqueous iodine is the tricyclic sulfinamide



The product was identified by the position of the S–O stretching frequency in the FTIR and by the multiplicity of the diastereotopic CH_2 protons in the ^1H NMR although it was not isolable in pure form. Table II lists the rate data for the aqueous iodine oxidation of 2-(2-benzimidazolyl)-ethyl disulfide. The reaction is first-order in disulfide concentration (runs 1–4) as shown in Table II (log k_{obs} vs log [RSSR], slope 0.99, r = 1.00); thus, values of the second-order rate constant k_2 equal to k_1/[RSSR] were calculated. There is no buffer dependence (runs 5 and 6).

On the basis of the identical rate law, rate acceleration, and product of the oxidation of 3-[(1-phenylethyl)-amino]propyl disulfide, the product of the reaction of 3-(2-benzimidazolyl)propyl disulfide with aqueous iodine should be the tricyclic sulfinamide.

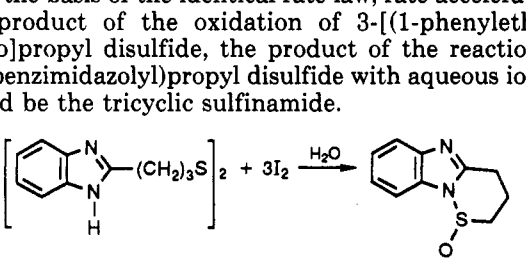
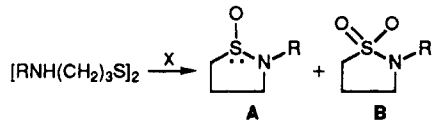


Table III. Disulfide Oxidation Reactions with Various Oxidants



X	R	% A isolated	% B isolated
iodine, water	1-phenylethyl	73	
iodine, water	cyclohexyl	73	
1-chlorobenzotriazole	1-phenylethyl	39	
N-chlorosuccinimide	1-phenylethyl	25	
N-bromosuccinimide	1-phenylethyl	38	26
iodine, triethylamine	1-phenylethyl	40	19

The product was not isolable but was identified by the FTIR and ^{1}H NMR as before.

The rate data for the aqueous iodide oxidation of 3-(benzimidazolyl)propyl disulfide are given in Table II. There is a first-order dependence on disulfide concentration (runs 1–5, log k_{obs} vs log [RSSR], slope 0.96, r = 1.00); thus, values of the second-order rate constant k_2 equal to k_1/[RSSR] were calculated. The reaction is inverse first-order in iodide ion concentration at pH 4 (runs 6–10, log k_{obs} vs log [KI], slope −0.83, r = 1.00) and pH 5 (runs 11–16, log k_{obs} vs log [KI], slope −0.81, r = 0.99). There is a linear relationship between log k_{obs} and pH (runs 4 and 16 and runs 10 and 15 have an average slope of 1.0); again, there is no buffer dependence (runs 17 and 18).

Other Oxidants. Table III lists the different oxidants used for the oxidative cleavage of secondary amine disulfides $[RNH(CH_2)_3S]_2$ and the yield of products. In all cases some of the corresponding cyclic sulfinamide was isolated. Aqueous iodine gave the highest yield of the cyclic sulfinamide. When *N*-bromosuccinimide or iodine and triethylamine were used, the cyclic sulfonamide was isolated in addition to the sulfinamide.

Oxidation of the sulfinamide 2-(1-phenylethyl)isothiazolidine 1-oxide to the sulfonamide 2-(1-phenylethyl)isothiazolidine 1,1-dioxide was achieved by reaction with 3-chloroperoxybenzoic acid in the usual way.[10] Reduction of 2-(1-phenylethyl)isothiazolidine 1-oxide to the corresponding sulfenamide 2-(1-phenylethyl)isothiazolidine with trichlorosilane was also investigated.[11]

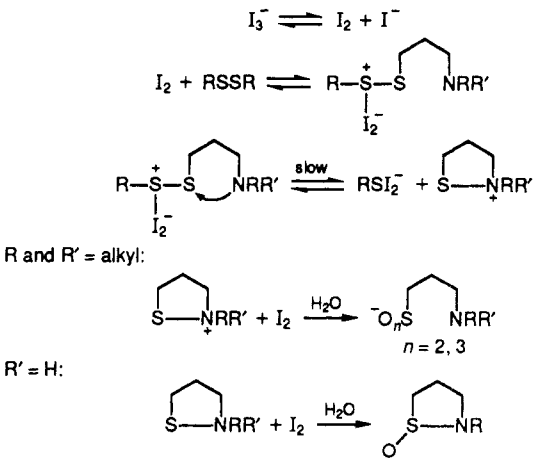
Discussion

When amine disulfides are cleaved by aqueous iodine, neighboring group participation facilitates the rate of reaction and formation of cyclized products. We[12] have shown that there is a factor of ~10^6 enhancement in the rate of reaction of the tertiary amine disulfide 3-(dimethylamino)propyl disulfide with aqueous iodine over that of the quaternary ammonium iodide salt 3-(trimethylammonio)propyl disulfide.[1] The rate law for the reaction at a given pH was

$$d[I_3^-]/dt = -k_{obsd}[I_3^-][RSSR][I^-]^{-1} \quad (1)$$

Furthermore, the value of k_{obsd} was proportional to $K_a/(K_a + [H^+])$, where K_a = 9.5 and corresponded to the dissociation constant of the tertiary amine in the intermediate. On the basis of these observations, we proposed attack of iodine on one of the sulfur atoms of the unprotonated

Scheme I. Aqueous Iodine Oxidation of Amine Disulfides



amine disulfide followed by a rate-determining cleavage of the disulfide bond by attack of the amine group on the distal sulfur atom, as shown in Scheme I. Both the resulting intermediate, cyclic N-alkylated sulfenamide and the thiolate/iodine complex are subsequently oxidized further to give a mixture of acyclic sulfinic and sulfonic acids.

The primary amine disulfides 3-aminopropyl disulfide and 4-aminobutyl disulfide also cyclized. Here the intermediate is a cyclic sulfenamide that does not cleave but is oxidized further to the sulfinamide.[1] Further oxidation to the sulfonamide does not occur with iodine. The maximum anchimeric assistance by the primary amine is ca. 10^4, or a factor of roughly 10^2 less than that of the tertiary amine. The rate law for the primary amine-assisted reaction was the same as that for the tertiary amine.

As an extension of this work,[1,12] the reaction of a secondary amine disulfide with aqueous iodine was studied and its rate was compared with those of the primary, tertiary, and quaternary amine disulfides. The rate law for the reaction of 3-[(1-phenylethyl)amino]propyl disulfide with aqueous iodine is the same as the tertiary amine disulfide and the primary amine disulfides given in eq 1; thus, the rate expression for the oxidation of 3-[(1-phenylethyl)amino]propyl disulfide is also consistent with the mechanism given in Scheme I where R = $Ph(CH_3)CH$ and R′ = H. The intermediate thiolate/iodine complex must also cyclize to the sulfenamide and further to the cyclic sulfinamide because the yield of cyclic sulfinamide is greater than 50%.

The kinetics for the reaction of the tertiary amine disulfide 3-(dimethylamino)propyl disulfide with aqueous iodine were carried out in solutions of pH 5.6–10 with the aid of stopped-flow techniques. For practical reasons, the reactions of the primary and the secondary amines were carried out only at the lower pHs. In order to determine to what extent the rate of reaction has been accelerated, we can refer to compounds in which there is no anchimeric assistance such as 3-(trimethylammonio)propyl disulfide and 3-hydroxypropyl disulfide.[12,13] Both of these compounds are cleaved by aqueous iodine via rate-determining attack of iodide ion on the disulfide–iodine complex. The rates of these reactions are little affected by the pH of the solution or by the concentration of iodide ion in the solution, and values of k_2 range from 0.12 to 0.33 M^{-1} s^{-1} for the quaternary ammonium salt and 0.22 to 0.59 M^{-1} s^{-1} for the alcohol disulfide in spite of changes in the pH and the

(10) Siegel, W. O.; Johnson, C. R. *J. Org. Chem.* **1970**, *35*, 3657.
(11) Benn, F. R.; Briggs, J. C.; McAuliffe, C. A. *J. Chem. Soc., Dalton Trans.* **1984**, 293.
(12) Doi, J. T.; Musker, W. K. *J. Am. Chem. Soc.* **1984**, *106*, 1887.
(13) Doi, J. T.; Luehr, G. W.; Musker, W. K. *J. Org. Chem.* **1985**, *50*, 5716.

Table IV. Effect of N-Substitution on Oxidative Cleavage of 3-Aminopropyl Disulfides at pH 5.85 and 26 °C

	NH_2–	RNH–[a]	$(CH_3)_2N$–	$(CH_3)_3N^+$–
k_2(calcd),[b] M^{-1} s^{-1}	1.65	138	68.1	0.122
k_{rel}	14	1100	560	1.0

[a] R ≡ $Ph(CH_3)CH$. [b] $k_2(calcd) = k_{obsd}/[RSSR]$.

iodide ion concentration. Thus, by comparing values of k_2 for a given run, one can judge the amount of anchimeric assistance occurring in that reaction.

Using this criterion, the effects of N-substitution on the oxidative cleavage of amine disulfides have been determined and are listed in Table IV. The related secondary amine disulfide is oxidized about twice as fast as the tertiary amine disulfide, and both oxidations occur about ~100 times faster than the rate of oxidation of the primary amine disulfide.[1] The effect of changing substituents at nitrogen from a hydrogen to an alkyl group is thought to be due to differences in solvation. The amine end of the primary amine disulfide is highly solvated. This phenomenon creates a solvent-induced barrier that can retard the reaction in two different ways. Initially the water prevents the hydrophobic disulfide group and iodine molecules from coordinating to each other, and finally the water must be stripped away from the amine when it attacks the disulfide–iodine complex in the rate-determining step. Evidence for this hypothesis is derived from the fact that many S_N2 reactions proceed considerably faster in aprotic than in protic solvents. Thus, solvation, along with the fact that tertiary and secondary amines are more nucleophilic than primary amines, may account for the factor of $\sim 10^2$ difference in reactivity. The order secondary, tertiary > primary amine is easier to explain than the order secondary, primary > tertiary, which we observed in the transannularly assisted thioether oxidations in the N-substituted 5-aminothiocanes we examined earlier.[14]

Along with the study of the effects of N-substitution on neighboring group participation in the aqueous iodine oxidation of amine disulfides, two other structural features were examined: benzimidazole vs amine nuclei and participation via a five- and six-membered ring in the benzimidazole series. The kinetic data for the benzimidazole disulfide 3-(2-benzimidazolyl)propyl disulfide indicate that its mechanism is identical with that of the secondary amine disulfide. Comparative data are listed in Table IV. The relative rates for 3-(3-benzimidazolyl)propyl disulfide and 2-(2-benzimidazolyl)ethyl disulfide are 3:1. The benzimidazole that can form a six-membered ring sulfinamide is oxidized at a rate approximately 3 times as fast as the benzimidazole that can form a five-membered ring sulfinamide. This is in contrast to unsubstituted primary amine disulfides where the five-membered ring sulfinamide is formed faster than the six-membered ring sulfinamide,[1] but it is the same result we observed for formation of imidazole sulfoxides by way of five-membered ring interactions and (benz)imidazole sulfoxides from the corresponding thioethers by way of five- and six-membered rings.[15] The rigidity of the benzimidazole moiety reduces the entropic disadvantages for participation for both five- and six-membered rings from what it would be in the analogous acyclic cases. In order for neighboring group participation to occur for the benzimidazole disulfides, the σ^* orbital of the sulfur–sulfur bond must align with the sp^2 hybrid orbital on the nitrogen. The formation of a six-membered ring allows easier alignment of the sulfur with the nitrogen because of the angular constraints imposed by the sp^2-hybridized atoms in the benzimidazole ring, and therefore the six-membered ring benzimidazole sulfinamide is formed faster than the five-membered ring benzimidazole sulfinamide.

The benzimidazole group is a less effective neighboring group in disulfide cleavage, even though a considerably larger fraction of the benzimidazole moieties ($pK_a = 6.5$)[14] are in the free base form than the secondary amine ($pK_a = 9.5$)[1] in solutions of pH 4–6 used in the oxidation reactions in Tables I and II.[15] Thus, the secondary and tertiary amine groups are the most effective neighboring groups in the iodine oxidation of amine disulfides that cleave via a transition state in which a five-membered ring is formed. The amines are easily compared because all the substituted disulfides have the same rate laws and their relative rates are secondary > benzimidazolyl > tertiary > primary ≫ quaternary at pH 5.85, but secondary, tertiary > primary > benzimidazolyl ≫ quaternary when the numbers are corrected for the fraction of free base (Table IV).

The products of the cyclization reactions of the secondary amine disulfides are mono- and bicyclic N-alkylated sulfinamides. No sulfinamides were isolable in pure form when benzimidazole was the neighboring group although there was kinetic evidence for N–S interaction during the cleavage reaction and both the ^1H NMR and FTIR provided evidence that cyclized sulfinamides had formed in solution. The reactions were carried out in aqueous buffer, and presumably, the benzimidazole may be a sufficiently good leaving group that hydrolysis occurs.

No methods for the reduction of sulfinamides could be found in the literature; however, several procedures for the reduction of sulfoxides have appeared. Many of these methods take advantage of the strong affinity of phosphorus or silicon toward oxygen.[16] Triphenylphosphine/iodine/sodium iodide reagent has been used for the deoxygenation of sulfoxides,[17] and several methods have appeared in which either hexachlorodisilane[18] or trichlorosilane[19] was used to reduce phosphine oxides. The use of trichlorosilane seemed ideal since bridged cyclic phosphine oxides were reduced without ring opening and loss of the phosphorus bridge. After the reaction, low-resolution GC/MS showed one major peak in the gas chromatogram with the correct mass to charge ratio for the sulfenamide and a base peak due to loss of the 1-phenylethyl group on the nitrogen. It appears that reduction had occurred; however, the sulfenamide must be somewhat unstable since attempted purification of the material resulted in decomposition.

Experimental Section

Iodine Oxidation of Disulfides. The kinetic data for the iodine oxidations of the disulfides were obtained on a Beckmann DU quartz spectrophotometer equipped with a Gilford Instrument Laboratories, Inc., 2415A automatic cuvette positioner, 252 photometer, and 6051 recorder and a Brinkman Instrument Lauda K2/R constant-temperature bath.

All solutions used were first thermostated to 26.0 °C. Equal volumes of iodine stock solutions and buffer solutions were premixed on the same day that they were used. When the concentration of potassium iodide was varied, the ionic strength was

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maintained such that [KI] + [KCl] = 1.0 M. Equal volumes of the buffered triiodide solutions and disulfide solutions in doubly deionized water were then simultaneously injected into a 1-cm quartz cell in the spectrophotometer.

The decay of triiodide absorbance at 353 nm was recorded vs time for at least 2 half-lives. First-order treatment of this data resulting from a linear regression of ln (absorbance) vs time generally gave correlation coefficients greater than 99.9%. All reactions were run at least two times.

Monocyclic Sulfinamides and Precursors. Columns for column chromatography were prepared with J. T. Baker 60–200-mesh silica gel. Columns for flash chromatography were prepared with EM Science 230–400-mesh silica gel. C, H, and N analyses were performed by Microanalytical Laboratories, University of California, Berkeley, CA. The purity of other title compounds was judged to be ≥90% by ^{13}C or ^{1}H NMR spectral determinations. ^{1}H NMR were recorded on a General Electric QE-300 FT or a Varian EM-390 spectrometer, and ^{13}C NMR spectra were recorded on the General Electric QE-300 FT spectrometer. ^{31}P broad-band proton-decoupled NMR spectra were obtained on a Nicolet NT-200 FT spectrometer operating at 80.99 MHz. The low-resolution GC/MS were recorded on a Finnigan 1020. The FTIR spectra were obtained by using an IBM System 9000 spectrometer. High-resolution GC/MS were obtained on a Hewlett-Packard gas chromatograph with a DB-1 column and a Vacuum Gauge mass spectrometer.

3-[(1-Phenylethyl)amino]propanol was prepared by a modification of the method of Bottini and Roberts.[8] 3-Choropropanol (9.75 g, 103 mmol) was added dropwise into a 250-mL flask containing a stirred mixture of 1-phenylethylamine (25.00 g, 206 mmol) and 3 mL of water. The reaction mixture was stirred on a steam bath for 5.5 h, cooled in an ice bath for 3 h, and extracted (4 × 40 mL) with benzene. Concentration of the organic layer under reduced pressure yielded a thick yellow liquid. Vacuum distillation yielded 1-phenylethylamine (bp 36–37 °C (0.10 mm)) and the clear, colorless 3-[(1-phenylethyl)amino]-propanol (17.21 g (93.2%); bp 111–112 °C (0.10 mm); n^{20}_D 1.5307).

^{1}H NMR ($CDCl_3$, 300 M Hz) δ 7.30 (m, 5 H, aromatic H), 3.75 (m, 3 H, OCH_2, CH), 3.15 (br, 1 H, NH), 2.70 (m, 2 H, NCH_2), 1.65 (m, 2 H, CCH_2C), 1.35 (d, 3 H, CH_3); ^{13}C NMR ($CDCl_3$, 75.61 MHz, ^{1}H decoupled) δ 144.87 (C-1 ring), 128.54 (C-3 ring), 127.06 (C-2 ring), 126.46 (C-4 ring), 64.01 ($HOCH_2$), 58.60 (CH), 47.58 (NCH_2), 31.34 (CCH_2C), 24.19 (CH_3).

3-[(1-Phenylethyl)amino]propanethiol was prepared by a modification of the method of Frank and Smith.[21] A 300-mL flask containing 3-[(1-phenylethyl)amino]propanol (16.50 g, 92.9 mmol) was equipped with a stir bar and a reflux condenser. A solution of 48% hydrobromic acid (46.52 g, 276 mmol) and thiourea (7.00 g, 92.9 mmol) was added slowly through the top of the condenser (exothermic) and the resultant mixture refluxed for 12 h. The reaction mixture was cooled in an ice bath, and sodium hydroxide (11.04 g, 276 mmol) in 11 mL of water was added dropwise through the top of the condenser. After approximately half the aqueous sodium hydroxide had been added, the clear, colorless solution became pink; after all the aqueous sodium hydroxide solution had been added, the cloudy pink solution was then refluxed with stirring for 4 h. When stirring was stopped, the solution separated into a thin pink layer on top of a cloudy white aqueous layer. The solution was made basic, as necessary, to pH 9–10 with aqueous sodium hydroxide and extracted (3 × 50 mL) with ether. The ether solution was dried with magnesium sulfate (pink impurity stays on magnesium sulfate), filtered, and concentrated under reduced pressure. A continuous extraction of the aqueous layer was performed with ether for 8 h. The extractant was dried with magnesium sulfate, combined with previous extracts and concentrated under reduced pressure to yield a foul-smelling, clear liquid that gave a positive nitroprusside test for thiols.[21] The thiol was purified by column chromatography with 30% ethanol/chloroform (R_f = 0.56) to give 16.62 g (92%) of the pure thiol.

^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.30 (m, 5 H, aromatic H), 3.75 (q, 1 H, CH), 2.55 (m, 4 H, NCH_2, SCH_2), 1.70 (m, 2 H, CCH_2C), 1.35 (m, 5 H, CH_3, NH, SH); ^{13}C NMR ($CDCl_3$, 75.61 MHz, ^{1}H decoupled) δ 145.57 (C-1 ring), 129.93 (C-3 ring), 128.43 (C-2 ring), 126.53 (C-4 ring), 58.36 (CH), 46.05 (NCH_2), 35.80 (CCH_2C), 24.38 (CH_3), 22.52 (SCH_2).

3-[(1-Phenylethyl)amino]propyl disulfide was prepared by a modification of the method of Cecil and McPhee.[23] Ice-cold 30% aqueous hydrogen peroxide (12.36 g, 109 mmol) was added dropwise to an ice-cold, stirred mixture of 3-[(1-phenylethyl)-amino]propanethiol (42.58 g, 218 mmol), 200 mL of water, and a trace of ferrous sulfate in a 500-mL flask. A rubber septum cap with a disposable glass pipet tip through the top was used to stopper the flask. The mixture was allowed to warm to room temperature and was then shaken vigorously on a wrist-action shaker until a negative nitroprusside test for thiol[22] was obtained (approximately 12 h). The milky tan solution was extracted (4 × 50 mL) with chloroform. The chloroform extract was dried with magnesium sulfate, filtered, and concentrated under reduced pressure to give a thick yellow liquid. The product was purified by flash chromatography with 30% ethanol/chloroform (R_f = 0.53) to give 39.25 g (92.7%) of disulfide.

^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.30 (m, 5 H, aromatic H), 3.70 (q, 1 H, CH), 2.60 (m, 4 H, NCH_2, SCH_2), 1.90 (br, 1 H, NH), 1.80 (m, 2 H, CCH_2C), 1.35 (d, 3 H, CH_3); ^{13}C NMR ($CDCl_3$, 75.61 MHz, ^{1}H decoupled) δ 145.64 (C-1 ring), 128.41 (C-3 ring), 126.88 (C-2 ring), 126.53 (C-4 ring), 58.29 (CH), 46.30 (NCH_2), 36.79 (CH_2S), 29.79 (CCH_2C), 24.42 (CH_3). Anal. Calcd for $(C_{11}H_{16}NS)_2$: C, 67.99; H, 8.30; N, 7.21. Found: C, 67.80; H, 8.24; N, 7.12.

2-(1-Phenylethyl)isothiazolidine 1-oxide was prepared by a modification of the procedure of Doi and Musker.[1] Bis[3-[(1-phenylethyl)amino]propyl] disulfide (1.01 g, 2.60 mmol) was dissolved in 75 mL of doubly deionized water with vigorous shaking. The mixture was attached to an autotitrator containing 1.0 M potassium hydroxide, with the end point set to pH 7.00. A solution of iodine (1.98 g, 7.80 mmol) in 30 mL of methanol was added dropwise with stirring over 5 h at room temperature. Excess iodine was removed by shaking with a small amount of solid sodium thiosulfate, and methanol was removed under reduced pressure. The aqueous solution was extracted (3 × 35 mL) with chloroform. The chloroform layer was dried with magnesium sulfate, filtered, and concentrated under reduced pressure. Column chromatography with 20% ethanol/chloroform (R_f = 0.65) yielded 0.42 g (77.1%) of a diastereomeric mixture of sulfinamides.

^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.32 (m, 5 H, aromatic H), 4.56, 4.36 (2 q, 1 H, CH), 3.43, 3.29 (2 m, 1 H, SCH), 3.00 (m, 3 H, SCH, NCH_2), 2.62, 2.20 (2 m, 2 H, CCH_2C), 1.72, 1.66 (2 d, 3 H, CH_3); FTIR (neat) 1074, 1028 cm^{-1} (S–O str); MS, m/e 209.2, base peak at 105.2 ($CH[CH_3]Ph$), calcd 209.3. Anal. Calcd for $C_{11}H_{15}NSO$: C, 63.12; H, 7.22; N, 6.69. Found: C, 63.10; H, 7.30; N, 6.51.

3-(*N*-Cyclohexylamino)propanol was prepared as described for 3-[(1-phenylethyl)amino]propanol. Removal of benzene under reduced pressure yielded a yellow solid. After the solid was rinsed with *n*-hexane, yellow impurities were washed into the mother liquor, leaving shiny white flakes (85.1%; mp 69–70 °C).

^{1}H NMR ($CDCl_3$, 90 MHz) δ 3.80 (t, 2 H, OCH_2), 3.10 (br, 1 H, OH), 2.85 (t, 2 H, NCH_2), 2.45 (m, 1 H, C-1 ring), 1.70, 1.05 (m, 13 H, ring H {except C-1}, CCH_2C, NH).

3-(*N*-Cyclohexylamino)propanethiol was prepared as described for 3-[(1-phenylethyl)amino]propanethiol except that the alcohol, 48% hydrobromic acid, and thiourea were refluxed for 9 h. Addition of aqueous sodium hydroxide was followed by 3 h of reflux. Simple extraction of the basic solution with ether yielded a foul-smelling white solid (54.7%; mp 61–63.5 °C). Continuous extraction of the aqueous layer with ether did not improve the yield.

^{1}H NMR ($CDCl_3$, 90 MHz) δ 2.70 (m, 5 H, C-1 ring, NCH_2, SCH_2), 1.40 (m, 14 H, ring H {except C-1}, CCH_2C, NH, SH).

3-(*N*-Cyclohexylamino)propyl disulfide was prepared as described for 3-[(1-phenylethyl)amino]propyl disulfide. Column chromatography with 20% ethanol/chloroform (R_f = 0.16) gave 49.0% of the pure yellow liquid product.

^{1}H NMR ($CDCl_3$, 300 MHz) δ 2.67 (q, 4 H, NCH_2, SCH_2), 2.35 (m, 1 H, C-1 ring), 1.40 (m, 13 H, ring H {except C-1}, NH, CCH_2C); ^{13}C NMR ($CDCl_3$, 75.61 MHz) δ 56.73 (C-1 ring), 45.73 (NCH_2),

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36.83 (SCH_2), 33.54 (C-2 ring), 29.88 (CCH_2C), 26.10, 25.01 (C-3, C-4 ring). Anal. Calcd for $(C_9H_{18}NS)_2$: C, 62.73; H, 10.53; N, 8.13. Found: C, 62.85; H, 10.53; N, 8.13.

2-Cyclohexylisothiazolidine 1-oxide was prepared as described for 2-(1-phenylethyl)isothiazolidine 1-oxide. Flash chromatography with 10% ethanol/chloroform (R_f = 0.51) yielded the liquid sulfinamide (72.9%).

^1H NMR ($CDCl_3$, 300 MHz) δ 3.53 (m, 1 H, SCH), 3.22 (m, 2 H, SCH, NCH), 2.87 (m, 2 H, NCH, CCHC), 2.61 (m, 1 H, C-1 ring), 1.70 (m, 11 H, ring H [except C-1], CCHC). FTIR (neat) 1073, 1040 cm^{-1} (S–O str); MS, *m/e* 187, base peak 55, calcd 187. Anal. Calcd for $C_9H_{17}NSO$: C, 57.71; H, 9.15; N, 7.48. Found: C, 57.46; H, 9.12; N, 7.37.

Benzimidazole Sulfinamides and Precursors. 2-(2-Benzimidazolyl)ethyl disulfide dihydrochloride was prepared by a modification of the method of Phillips.[9] To a stirred solution of 20 mL of water, *o*-phenylenediamine (6.59 g, 36.4 mmol), and 3,3′-dithiodipropanoic acid (3.82 g, 18.2 mmol) was added 20 mL of concentrated hydrochloric acid dropwise. The reaction mixture was refluxed 18 h. Upon cooling, green crystals came out of solution. Recrystallization from 50% ethanol/water yielded light green crystals (2.91 g (33.2%); mp 190–191.5 °C).

^1H NMR (CD_3OD, 300 MHz) δ 7.76 (q, 2 H, aromatic H), 7.58 (q, 2 H, aromatic H), 3.65 (t, 2 H, CCH_2), 3.33 (t, 2 H, SCH_2). Anal. Calcd for $(C_9H_{10}N_2SCl)_2 \cdot 3H_2O$: C, 44.91; H, 5.44; N, 11.64. Found: C, 44.75; H, 5.05; N, 11.43.

2-(2-Benzimidazolyl)ethyl disulfide dihydrochloride consumed only the 3 equiv of iodine needed to produce the cyclic sulfinamide. However, when the reaction mixture was worked up in the usual way, the expected sulfinamide could not be isolated in pure form. The spectral properties of the unpurified product are consistent with those of a sulfinamide.

FTIR (neat) 997, 1117 cm^{-1} (S–O str); ^1H NMR (CD_3OD, 300 MHz) δ 7.50 (m, 2 H, aromatic H), 7.20 (m, 2 H, aromatic H), 3.20–3.60 (m, 4 H, SCH_2CH_2N).

3-(2-Benzimidazolyl)propyl disulfide dihydrochloride was prepared as described for 2-(2-benzimidazolyl)ethyl disulfide dihydrochloride. Recrystallization from 50% ethanol/water yielded white solid (49.5%; mp 42–43 °C).

^1H NMR (CD_3OD, 300 MHz) δ 7.77 (m, 2 H, aromatic H), 7.56 (m, 2 H, aromatic H), 3.34 (t, H, CCH_2), 2.89 (t, 2 H, SCH_2), 2.38 (m, 2 H, CCH_2C); Anal. Calcd for $(C_{10}H_{12}N_2SCl)_2 \cdot 2H_2O$: C, 48.87; H, 5.74; N, 11.40. Found: C, 48.84; H, 5.66; N, 11.05.

3-(2-Benzimidazolyl)propyl disulfide dihydrochloride consumed only the 3 equiv of iodine needed to produce the cyclic sulfinamide. However, when the reaction mixture was worked up in the usual way, the expected sulfinamide could not be isolated in pure form. The spectral properties of the unpurified product are consistent with those of a sulfinamide.

^1H NMR ($CDCl_3$, 300 MHz) δ 7.55 (m, 2 H, aromatic H), 7.22 (m, 2 H, aromatic H), 3.11 (t, 2 H, CCH_2), 2.78 (m, 2 H, SCH_2), 2.30 (m, 2 H, CCH_2C).

Bicyclic Sulfinamides and Precursors. 2-(2-Piperidyl)-ethanethiol was prepared as described for 3-[(1-phenylethyl)-amino]propanethiol with 2-(2-piperidyl)ethanol as starting material. At the end of the reaction, water was removed by freeze-transfer and the resulting slush was extracted with ether and chloroform. The extracts were combined and dried with magnesium sulfate, and the solvent was removed under reduced pressure. The thiol was purified by column chromatography with 20% ethanol/chloroform (R_f = 0.39) to yield 71.6% of the foul-smelling thiol (bp 54–55 °C (0.20 mm); n^{20}_D 1.5121).

^1H NMR ($CDCl_3$, 300 MHz) δ 3.05, 2.74 (m, 2 H, NCH_2), 2.60 (m, 3 H, SCH_2, NCH), 1.65 (m, 7 H, N*H*, NCH_2CH_2, SCH_2CH_2, ring $CHCH_2$), 1.37 (m, 2 H, ring CH_2CH_2CH), 1.08 (m, 1 H, SH); ^{13}C NMR ($CDCl_3$, 75.61 MHz, ^1H decoupled) δ 55.57 (CHN), 47.02 (NCH_2), 36.74, 35.47 (CH_2CH_2SH), 32.81 (CH_2CH), 26.55, 24.69 (CCH_2CH_2C).

9-Thia-1-azabicyclo[4.3.0]nonane 9-oxide was prepared by dissolving 2-(2-piperidyl)ethanethiol (0.50 g, 3.44 mmol) in 45 mL of chloroform and iodine (1.75 g, 6.88 mmol) in 45 mL of chloroform. These solutions were simultaneously added through separate addition funnels to a stirred solution of triethylamine (0.70 g, 6.88 mmol) in 25 mL of chloroform over a 5-h period. After all the thiol and iodine solutions had been added to the triethylamine solution, additional triethylamine (0.35 g, 3.44 mmol) in 10 mL of water was added and the solution was allowed to stir vigorously for 2 h. Excess iodine was removed by shaking with a small amount of sodium thiosulfate. The chloroform layer was washed with water (20 mL) and 10% hydrochloric acid (2 × 20 mL) and dried with magnesium sulfate, followed by removal of solvent under reduced pressure. Column chromatography with 20% ethanol/chloroform (R_f = 0.80, 0.68) yielded 0.26 g (47.3%) of a diastereomeric mixture of sulfinamides.

^1H NMR ($CDCl_3$, 300 MHz) δ 3.85 (m, 1 H), 3.53 (m, 2 H), 3.28 (m, 1 H), 2.73 (m, 8 H), 1.62 (m, 14 H); ^1H NMR (D_2O, 300 MHz) δ 3.75 (m, 1 H), 3.46 (m, 2 H), 3.25 (m, 1 H), 2.90 (m, 5 H), 2.55 (m, 2 H), 2.17, 2.02, 1.78 (m, 9 H), 1.34 (m, 6 H); ^{13}C NMR ($CDCl_3$, 75.61 MHz, ^1H decoupled) δ 62.78, 59.94 (SCH_2), 54.71, 54.09 (NCH), 46.74, 45.23 (NCH_2), 34.71, 31.89 (SCH_2CH_2), 30.15, 29.97 (CH_2CH), 26.67, 25.39 (CCH_2CH_2C), 23.93, 23.39 (CCH_2CH_2C); FTIR (neat) 1050, 1076 cm^{-1} (S–O str); high-resolution GC/MS (CH_2Cl_2), *m/e* for $C_7H_{13}NSO$, calcd 159.071, found two GC peaks of equal area at 159.072, base peak at 131 (CH_2CH_2), and 159.073, base peak at 131 (CH_2CH_2).

Dimethyl γ-Nitropimelate. A solution of methyl 4-nitrobutyrate (5.31 g, 28.9 mmol), benzyltrimethylammonium hydroxide (0.97 g, 2.31 mmol), and 10 mL of 1,4-dioxane was added together in a 50-mL flask equipped with a stir bar and an addition funnel and cooled in an ice bath. Methyl acrylate (2.49 g, 28.9 mmol) was added dropwise through the addition funnel, and the reaction mixture was allowed to stir at room temperature overnight. Trifluoroacetic acid (0.26 g, 2.31 mmol) in 1 mL of 1,4-dioxane was then added to the ice-cooled reaction flask. Vacuum distillation yielded 4.95 g (73.5%) of the pure product (bp 123–127 °C (0.20 mm)).

^1H NMR ($CDCl_3$, 300 MHz) δ 4.66 (septet, 1 H, $CHNO_2$), 3.68 (s, 6 H, 2 OCH_3), 2.40, 2.22 (2 m, 8 H, 2 CH_2CH_2); ^{13}C NMR ($CDCl_3$, 75.61 MHz, ^1H decoupled) δ 172.45 (CO), 86.63 ($CHNO_2$), 51.93 (OCH_3), 29.86, 28.60 (CH_2CH_2).

Methyl β-(5-oxo-2-pyrrolidyl)propionate was prepared by modification of the method of Leonard et al.[24] Dimethyl γ-nitropimelate (17.01 g, 72.9 mmol) was dissolved in 40 mL of methanol and the resultant mixture hydrogenated at 3 atm at 23 °C over platinum oxide catalyst (0.50 g). After 52 h, approximately 170 mmol of hydrogen was absorbed. No further absorption of hydrogen was observed after 52 h. The catalyst was removed by suction filtration through sintered glass, and the solvent was removed under reduced pressure. Vacuum distillation yielded 9.53 g (76.3%) of the pure product (bp 148–152 °C (0.20 mm) [lit.[24] bp 150–160 °C (0.5 mm)]).

^1H NMR ($CDCl_3$, 300 MHz) δ 7.35 (br, 1 H, NH), 3.68 (m, 1 H, CH), 3.64 (s, 3 H, OCH_3), 2.50 (m, 6 H, CH_2CH_2, CH_2CO_2), 1.77 (m, 2 H $CHCH_2$); ^{13}C NMR ($CDCl_3$, 75.61 MHz) δ 178.66 (CON), 173.24 (CO_2), 54.24 (CH), 53.40 (OCH_3), 31.36 (CH_2CO_2), 30.21 (CH_2CON), 30.05 (ring CH_2CH), 26.70 ($CHCH_2$).

3-(2-Pyrrolidyl)propanol was prepared by modification of the procedure of Doyle et al.[25] Lithium aluminum hydride (2.52 g, 66.4 mmol) was placed in a 100-mL three-neck flask equipped with a stir bar, condenser, and an addition funnel and flushed with nitrogen. Dry tetrahydrofuran (16 mL) and dry ether (16 mL) were syringed into the flask. Methyl β-(5-oxo-2-pyrrolidyl)propionate (3.70 g, 21.6 mmol) in 16 mL of dry tetrahydrofuran was added dropwise through the addition funnel over 1 h. The reaction mixture was allowed to stir overnight at room temperature and then gently refluxed for 1 h. Water (approximately 20 mL) was carefully added dropwise to the cooled solution to decompose excess lithium aluminum hydride. After suction filtration to remove lithium and aluminum salts, solvents were evaporated and the residue was distilled to yield 1.96 g (70.3%) of the pure product (bp 106–110 °C (4 mm) [lit.[25] bp 118 °C (4.5 mm)]).

^1H NMR ($CDCl_3$, 300 MHz) δ 3.95 (br, 2 H, NH, OH), 3.33 (m, 2 H, OCH_2), 2.67 (m, 3 H, CH_2NHCH), 1.47 (m, 8 H, ring CH_2CH_2, CH_2CH_2); ^{13}C NMR ($CDCl_3$, 75.61 MHz, ^1H decoupled) δ 62.18 ($HOCH_2$), 58.83 (CH), 45.87 ($NHCH_2$), 33.27 (CH_2CH_2OH), 31.63 (ring CH_2CH), 30.34 (CH_2CH), 25.33 (ring NCH_2CH_2).

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3-(2-Pyrrolidyl)propyl disulfide was prepared from 3-(2-pyrrolidyl)propanethiol. The thiol was prepared as described for 3-[(1-phenylethyl)amino]propanethiol except that the alcohol, 48% hydrobromic acid, and thiourea were refluxed for 50 h. Addition of aqueous sodium hydroxide was followed by 22 h of reflux. The aqueous solution was extracted with chloroform, water was removed by freeze-transfer, and the resulting solid was Soxhlet extracted with chloroform for 22 h. Extracts were combined and dried with magnesium sulfate, and the solvents were removed under reduced pressure. Column chromatography with 20% ethanol/chloroform (R_f = 0.41) yielded 95.6% of the pure, foul-smelling thiol.

^{1}H NMR ($CDCl_3$, 300 MHz) δ 3.85 (br, 1 H, NH), 3.40 (m, 3 H, $CHNCH_2$), 2.60 (m, 2 H, SCH_2), 1.35–2.35 (m, 9 H, ring CH_2CH_2, CH_2CH_2, SH); ^{13}C NMR ($CDCl_3$, 75.61 MHz, ^{1}H decoupled) δ 59.97 (CH), 46.19 (NCH_2), 30.81, 30.25 (ring $CHCH_2$, $CHCH_2$), 24.30, 23.84, 23.23 (SCH_2CH_2, ring $NCHCH_2$).

The 3-(2-pyrrolidyl)propyl disulfide was prepared as described for 3-[(1-phenylethyl)amino]propyl disulfide. Water was removed under vacuum, and the resulting thick liquid was extracted with chloroform to yield 52.6% of the pure disulfide.

^{1}H NMR ($CDCl_3$, 300 MHz) δ 5.05 (br, 1 H, NH), 3.30 (m, 3 H, $CHNCH_2$), 2.65 (m, 2 H, SCH_2), 1.30–2.10 (m, 8 H, ring CH_2CH_2); ^{13}C NMR ($CDCl_3$, 75.61 MHz, ^{1}H decoupled) δ 56.82 (CH), 46.24 (NCH_2), 38.47 (SCH_2), 32.72, 29.85 (ring $CHCH_2$, $CHCH_2$), 25.71, 23.61 (SCH_2CH_2, ring NCH_2CH_2).

2-Thia-1-azabicyclo[4.3.0]nonane 2-oxide was prepared as described for 2-(1-phenylethyl)isothiazolidine 1-oxide. Column chromatography with 15% ethanol/chloroform (R_f = 0.49, 0.55) yielded 23% of a diastereomeric mixture of sulfinamides.

^{1}H NMR ($CDCl_3$, 300 MHz) δ 3.35 (m, 2 H), 3.15 (m, 1 H), 3.00 (m, 1 H), 2.85 (m, 1 H), 2.60 (m, 1 H), 1.50–2.20 (m, 10 H), 1.00–1.45 (m, 7 H), 0.80 (m, 3 H); ^{13}C NMR ($CDCl_3$, 75.61 MHz, ^{1}H decoupled) δ 61.49, 50.73, 48.61, 48.15, 48.09, 44.41, 32.18, 31.16, 31.09, 29.04, 23.64, 21.60, 20.91, 14.90. FTIR (neat) 1039, 1057 cm^{-1} (S–O str); high-resolution GC/MS (CH_2Cl_2) m/e for $C_7H_{13}NSO$, calcd 159.072, found one GC peak (diastereomers may be unresolved) at 159.071, base peak at 83 [$-(CH_2)_2SO$ or $-NS(O)CH_2$].

Reduction of Sulfinamide with Trichlorosilane. Modification of the procedure of Benn et al.[20] was used to reduce the sulfinamide. 2-(1-Phenylethyl)isothiazolidine 1-oxide (0.056 g, 0.268 mmol) was dissolved in 4 mL of dry toluene in a 50-mL three-neck flask equipped with a stir bar, an addition funnel, a nitrogen inlet and outlet needle, and a reflux condenser. Triethylamine (0.726 mL, 5.21 mmol) in 3 mL of dry toluene was added to the reaction flask through a syringe, and trichlorosilane (0.145 g, 1.07 mmol) in 3 mL of dry toluene was added dropwise through the addition funnel under a nitrogen atmosphere. The reaction mixture was refluxed for 2.5 h and cooled in an ice bath. The toluene layer was syringed off into a separatory funnel, washed with (2 × 3 mL) water, and filtered through glass wool, and the toluene was removed under reduced pressure. Attempts to isolate the sulfenamide were unsuccessful; however, low-resolution GC/MS showed one major peak at m/e 193.2 (calcd 193.3), base peak at 105.2 ($CH(CH_3)Ph$).

Oxidation of Sulfinamide with 3-Chloroperoxybenzoic Acid. The sulfinamide 2-(1-phenylethyl)isothiazolidine 1-oxide was oxidized to the sulfonamide 2-(1-phenylethyl)isothiazolidine 1,1-dioxide with 3-chloroperoxybenzoic acid by modification of the procedure of Siegel and Johnson.[10] 2-(1-Phenylethyl)isothiazolidine 1-oxide (0.48 g, 2.29 mmol) was dissolved in 27 mL of dichloromethane and the resultant mixture cooled to 0 °C. 3-Chloroperoxybenzoic acid (0.48 g, 2.29 mmol) in 10 mL of dichloromethane was added dropwise with stirring, and the reaction mixture was allowed to stir 19 h at 0 °C. The solution was washed (2 × 5 mL) with 5% aqueous sodium bicarbonate and (2 × 20 mL) saturated sodium bicarbonate and dried with magnesium sulfate, and the solvent was removed under reduced pressure. Column chromatography with 20% ethanol/chloroform (R_f = 0.72) yielded 0.49 g (94.2%) of the pure product.

^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.25 (s, 5 H, aromatic H), 4.65 (q, 1 H, CH), 3.00 (m, 4 H, SCH_2, NCH_2), 2.20 (quintet, 2 H, CCH_2C), 1.60 (d, 3 H, CH_3); FTIR (neat) 1192, 1119, 1308 cm^{-1}. Anal. Calcd for $C_{11}H_{15}NSO_2$: C, 58.64; H, 6.71; N, 6.22. Found: C, 58.77; H, 6.79; N, 5.96.

Supplementary Material Available: ^{1}H and/or ^{13}C NMR spectra for new title compounds (18 pages). Ordering information is given on any current masthead page.