for Ac-*syn*-3-MeProNHMe. The predicted population is greater than that observed in chloroform for the latter peptide. This overprediction could be due to underestimation of steric interactions. Perhaps for Ac-*syn*-3-MeProNHMe, peptide–solvent interactions shift the conformational distribution in chloroform relative to that in carbon tetrachloride or cyclohexane. Peptides can interact strongly with such solvents. For example, the solvation energy of *N*-butylacetamide in carbon tetrachloride is −14 kcal/mol.[22] The solvation enthalpy of Ac-*anti*-3-MeProNHMe is −4 kcal/mol in chloroform relative to carbon tetrachloride.[23] The ability of polar solvents to attenuate intramolecular electrostatic interactions can be qualitatively considered by comparing the total and steric energies. The predictions from the steric energy are in qualitative agreement with observations in aqueous solution. Nevertheless, consideration of the conformational distributions in the full range of solvents shows that polar solvents have effects in addition to attenuation of intrapeptide electrostatic interactions. Polar, aprotic acetonitrile stabilizes the α_R conformer by dipolar interactions of the peptide with bulk solvent. Water, which is more polar, does not simply increase the population of α_R via stronger dipolar interactions with the peptide. Rather, the P_{II} conformer is populated due to the preferential binding of water to the peptide in this conformation.

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Registry No. AcMeProNHMe, 82320-42-1; Ac-L-2-MeProNHMe, 83365-32-6; Ac-*anti*-3-MePrNHMe, 83365-33-7; Ac-L-*anti*-3-MePrNHMe, 83434-50-8; Ac-*syn*-3-MeProNHMe, 82320-41-0; Ac-D-*syn*-3-MeProNHMe, 83434-51-9; racemic *N*-Ts-*syn*-3-MePro, 33443-67-3; *N*-Ts-D-*syn*-3-MePro·quinine, 83434-80-4; (+)-*N*-Ts-D-*syn*-3-MePro, 83434-52-0; (−)-*N*-Ts-L-*syn*-3-MePro, 83434-53-1; D-*syn*-3-MePro·HBr, 83434-81-5; D-*syn*-3-MePro, 10512-88-6.

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One-Electron Oxidation of Trialkylsulfenamides

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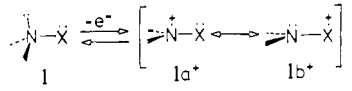
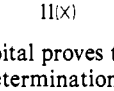
Abstract: Trialkylsulfenamides give long-lived enough radical cations for their cyclic voltammograms to be electrochemically reversible at fast enough scan rates. Radical cation lifetimes are increased by α branching in the nitrogen substituent, decreased by replacing a methyl sulfur substituent by *tert*-butyl, and decreased when pyridine is added and at higher sulfenamide concentration. For the five compounds for which hydrazine analogue (S replaced by NMe) data are available, $(CH_2)_4NSMe$ (**1**), $(CH_2)_5NSMe$ (**2**), *i*-Pr_2NSMe (**3**), 9-SMe-9-ABN (**4**), and Me_2NS-*t*-Bu (**5**), $E^{\circ\prime}$ values are 0.72, 0.81, 0.77, 0.69, and 0.95 V vs. SCE (acetonitrile), respectively, 0.45–0.58 eV more positive than $E^{\circ\prime}$ for the analogous hydrazine. The IP_1 values of **1–5** are 8.47, 8.42, 7.71, 7.82, and 8.34, respectively, 0.06–0.45 eV greater than for the analogous hydrazines. The nitrogen inversion barrier $\Delta G^{\ddagger}$ (T_c) for **4** is 8.7_0 (−84 °C) kcal/mol and that of 9-Et-9-ABN is 7.1_3 (−118 °C). $\mathbf{1}^{+\cdot}$ has ESR splittings of 21.7 (2 H), 18.2 (2 H), 13.8 (N), and 8.5 (3 H) G and that of $\mathbf{4}^{+\cdot}$ 14.1 (N) and 8.3 (3 H) G. The significance of these data is discussed.

Electron loss from nonconjugated amino nitrogen compounds has unusual properties because a large geometry change takes place during the electron transfer. Tetraalkylhydrazines (I, X = NR_2) have received much study.[1] Neutral hydrazines prefer



conformations with the lone-pair axes approximately perpendicular and the nitrogens approximately tetrahedral and prove to have a nitrogen inversion barrier that is very sensitive to the NN rotation angle.

Hydrazine radical cations prefer to have planar nitrogens (but their bending force constants are low) and have a two-atom, three-electron π bond (shown as two resonance forms, $Ia^{+\cdot}$ and $Ib^{+\cdot}$ in eq 1). The equilibrium constant for electron transfer (relative values conveniently determined by measuring the formal potential, $E^{\circ\prime}$ (I, $I^{+\cdot}$), by cyclic voltammetry, CV) does not depend principally upon ionization potential but on the difference in strain energy between I and $I^{+\cdot}$. The rate of electron transfer is sensitive to NN rotation angle, and the electron transfer shows non-Brønsted behavior in that a plot of $\Delta G^{\ddagger}$ vs. ΔG° for electron loss has a slope greater than one.[1c] A study of electron loss from other nonconjugated amino nitrogen compounds is plagued by short radical cation lifetimes. Loss of a proton from a carbon attached to nitrogen is so rapid that $E^{\circ\prime}$ usually cannot be measured by CV. A solution to this kinetic problem has been to use "Bredt's rule protected" R_2N groups such as the 9-azabicyclo[3.3.1]nonyl group II(X).[2] Holding the α-hydrogens in the nodal plane of



II(X)

the cation's nitrogen p orbital proves to provide powerful kinetic stabilization, allowing determination of $E^{\circ\prime}$ for X groups as noncation stabilizing as *tert*-butyl and as thermodynamically cation destabilizing as Cl and NMe_3^+. Disappointingly however, II(O-CH_3) proved to give a cation radical so short-lived that no re-

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duction peak could be observed by CV, precluding $E^{\circ\prime}$ measurement, dispite the fact that the methoxy group should be more cation stabilizing by resonance than either *tert*-butyl or chlorine.

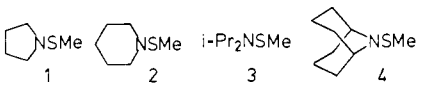
In this work we have investigated the second-row-analogue thioalkoxy for attachment to the amino nitrogen in a study of the electron transfer of eq 1. Because of the well-known diagonal relationship,[3] which is based on a similarity in ionization potentials for the element one column to the right and one row down in the periodic table, one expects a closer match in lone-pair energies of N and S than N and O and hence larger lone-pair–lone-pair interaction in NS than in NO bonds. However, the question of whether S or O is more cation stabilizing is a complex one, to which we hoped our experiments might contribute. In the study of three-electron σ bonds, Musker's group has shown that the bridgehead bicyclo[3.3.0]octyl $(S\cdots N)^+$ example is long-lived[4] like its $(S\cdots S)^+$ analogue,[5] while Alder's group[6] showed that holding the nitrogens together in propellane structures (bis(bridgehead) diaza medium-sized tricyclic systems) is necessary for long lifetimes of $(N\cdots N)^{+\cdot}$ three-electron σ bonds. Our work was undertaken to explore possible analogies in SN three-electron π-bond radical cations.

Sulfenamides (III, R_2NSR', thiohydroxylamine derivatives in *Chemical Abstracts* nomenclature) have attracted some interest as accelerators of the vulcanization of rubber and as plant and animal poisons for complex aryl derivatives.[7] The NS rotational barriers of *S*-aryl-, *N*-sulfonyl-, and *N*-carbonyl-substituted examples have been extensively studied, generating considerable discussion of why the rotational barrier increases as the *S*-aryl group becomes more electron withdrawing.[8] The reported chemistry of sulfenamides has almost exclusively involved N–S bond cleavage,[9] and sulfenamides have attracted some interest as sulfenyl-group transfer reagents in synthesis.[9]

In this work electron-transfer equilibria are studied for seven trialkylsulfenamides.

Compound Preparation

Sulfenamides having sulfur substituents lacking α-hydrogens are readily made by a variety of methods, including reacting dialkylamines with sulfenyl chlorides or the more easily stored *N*-thioalkylamides.[9] There are definite problems, however, with using such routes when α-hydrogens are present, as shown by Armitage and Clark's study of the reaction of dimethylamine with methylsulfenyl chloride.[10] We were surprised not to find literature references for the preparation of *S*-methylsulfenamides by the obvious route of displacing thiomethyl anion from dimethyl disulfide using lithium dialkylamides until we tried the reaction. We found ourselves incapable of detecting **1–3** in the product



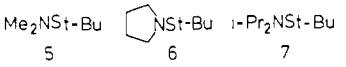
1 2 3 4

mixtures resulting from adding dimethyl disulfide to lithium pyrrolidide, piperidide, or diisopropylamide in THF at various temperatures, except for one tantalizing experience in which some **3** was found in one experiment but could not be found again. One the other hand, the 9-ABN (II) derivative **4** was prepared smoothly under these conditions. Our success in making **4** suggested to us that the problem might be that electron transfer was faster than S_N2 displacement, for electron transfer would be expected to generate an $R_2N\cdot,\cdot SR$ radical pair, which might well principally result in transfer of a labile hydrogen α to nitrogen of the amino radical. Similar electron-transfer problems seem likely to be involved in the failure of ordinary S_N2 alkylation conditions for O-alkylation of dialkylhydroxylamine anions, a problem that can be solved by using phase-transfer alkylation conditions,[2,11] presumably causing the reaction to occur in a nonpolar medium where electron transfer is less favorable. Whether this speculation is correct or not, simply switching the solvent from THF to pentane proved to make the preparations of **1–3** from dimethyl disulfide and lithium dialkylamide reliable. The *S-tert*-butyl compounds **5–7** were prepared from the sulfenyl halides and also studied.

Table I. Electrochemical Data for Some Sulfenamides

compound	$E^{\circ\prime}$, V ($E_p^{ox} - E_p^{red}$,V)[a]	scan rate for reversibility, V/s[b]
1 $(CH_2)_4NSMe$	0.72 (0.067)	5
2 $(CH_2)_5NSMe$	0.81 (0.067)	10
3 *i*-Pr_2NSMe	0.77 (0.061)	0.2
4 9-SMe-9-ABN	0.69 (0.065)	<0.05
5 Me_2NS-*t*-Bu	0.95 (0.082)[c]	~100
6 $(CH_2)_4NS$-*t*-Bu	0.85 (0.083)	5
7 *i*-Pr_2NS-*t*-Bu	0.87 (0.080)	0.5

[a] Conditions: 2–3 mM sulfenamide in CH_3CN containing 0.1 M *n*-$Bu_4N^+ClO_4^-$ at a gold electrode vs. SCE at 0.2 V/s scan rate except where noted. [b] Scan rate where $i_p^{red}/i_p^{ox} > 0.9$. [c] At a 5 V/s scan rate; the reduction peak could not be seen at 0.2 V/s.



5 6 7

Results

Trialkylsulfenamides. Cyclic voltammograms for trialkylsulfenamides **1–7** show a one-electron oxidation at 0.7–1.0 V vs. SCE (Table I). The CV curve for each is nearly electrochemically reversible ($i_p^{red}/i_p^{ox} \sim 1$, $E_p^{ox} - E_p^{red}$ near the value of 57 mV for fast heterogeneous electron-transfer rate) at fast enough scan rates, but several of the compounds show increasingly smaller reduction waves at slower scan rates, indicating that the radical cations decompose during slower scans. The oxidation–reduction peak separations of 0.06–0.09 V are comparable to those observed for tetraalkylhydrazines.[1] Also included in Table I are the scan rates required for oxidation and reduction waves to be about the same size. This allows ordering the compounds as to lifetime for decomposition; the faster the scan rate required for reversibility, the less persistent the radical cation. The observed order is seen to depend principally on the amino alkyl groups and is 9-ABN > *i*-Pr_2N > $(CH_2)_5N \approx (CH_2)_4N$ > Me_2N. This order suggested to us that deprotonation at carbon α to nitrogen is involved in the decomposition, since we expected that alignment of the $H_\alpha C,N(p$ orbital) would be important. The 9-ABN group holds its α-hydrogens in the nodal plane of the cation radical nitrogen p orbital and ought not to lose these hydrogens; an isopropyl group has poor $H_\alpha C,N(\pi)$ overlap for conformational reasons and is also more hindered for approach of base than the primary alkyl compounds. The dimethyl-substituted compound has no alignment problem and also the smallest alkyl groups; its radical cation is the least persistent. In agreement with the α-deprotonation decomposition hypothesis, added base does accelerate radical cation decomposition. Addition of 6.8 mM of pyridine to the CV solution of **1** resulted in a decrease of the size of the reduction wave relative to the oxidation wave, and no reduction peak at all could be observed at a 0.5 V/s scan rate (at which i_p^{red}/i_p^{ox} was about 0.5 with no added pyridine), while i_p^{red}/i_p^{ox} was only about 0.7 at a 10 V/s scan rate. If pyridine is a strong enough base to destroy the radical cation, neutral sulfenamide ought also to destroy it.

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(13) Nelsen, S. F.; Weisman, G. R.; Clennan, E. L.; Peacock, V. E. *J. Am. Chem. Soc.* **1976**, *98*, 6893.

Table II. Lone-Pair Ionization Potentials for Trialkylsulfenamides and Their Tetraalkylhydrazine Analogues (S Replaced by NMe)

sulfenamide	IP_v, eV	hydrazine	IP_v, eV[a]	ΔIP_v, eV[b]
1 $(CH_2)_4NSMe$	8.47	$(CH_2)_4NNMe_2$	8.11, 8.71	+0.36
2 $(CH_2)_5NSMe$	8.42, 8.64	$(CH_2)_5NNMe_2$	8.09, 8.63	+0.33
3 *i*-Pr_2NSMe	7.71, 8.37	*i*-Pr_2NNMe_2	7.65, 8.37	+0.06
4 9-SMe-9-ABN	7.82, 8.45	9-NMe_2-9-ABN	7.53, 8.42	+0.29
5 Me_2NS-*t*-Bu	8.34	Me_2NNMe-*t*-Bu	7.89, 8.48	+0.45

[a] From ref 12. [b] IP(sulfenamide) − IP_1(hydrazine).

Table III. Nitrogen Inversion Barriers[a] for Some 9-Substituted 9-Azabicyclo[3.3.1]nonane Derivatives (II(X))

	4[a]	8[a]	9[b]	10[b]
II(X), X =	SCH_3	CH_2CH_3	CH_3	NH_2
$\Delta G^{\ddagger}_c$, kcal/mol	8.70 (2)	7.13 (2)	8.11 (4)	9.19 (4)
T_c, °C	−84	−118	−90	−90
$\Delta H^{\ddagger}$, kcal/mol	7.6 (2)	7.8 (2)	9.7 (5)	8.6 (5)
$\Delta S^{\ddagger}$, cal/deg·mol	−6 (1)	+4 (2)	+8 (3)	−3 (3)

[a] Determined by dynamic ^{13}C NMR in CD_2Cl_2–Freon 12 mixtures. The numbers in parentheses are statistical errors in the last place quoted. [b] From ref 13.

Although pK_a values have not been reported for protonated sulfenamides (sulfenamides cleave in acid), they are almost certainly more basic than pyridine. Shorter radical cation lifetimes at higher sulfenamide concentrations were also observed. i_p^{red}/i_p^{ox} values for **2** at 0.5, 1.2, and 2.4 mM concentration and 0.2 V/s scan rates were 0.6, 0.4, and 0.3, respectively.

The structural analogy between hydrazines and sulfenamides suggests that a comparable geometry change to that established for hydrazines ought to occur when an electron is removed from sulfenamides. To establish conformational similarities between the two types of systems more fully, we have gathered photoelectron (PE) spectral data, determined the nitrogen inversion barrier by NMR for one example, and obtained ESR data for two of the cations.

The lone-pair-region PE results for five sulfenamides are summarized in Table II. Only one lone-pair ionization peak was observed for **1** and **5**, and the peak separations are rather small for the other examples. For **2**, a single rather flat-topped peak was observed, but it was better simulated by using two closely spaced peaks ($\Delta IP = 0.2_2$) than a single peak. Because lone-pair ionizations are rather sensitive to alkyl-group substitution changes, we believe our data establish that for **1** and **5**, the N and S π lone pair have quite similar energies ($\Delta IP <$ about 0.1_5 eV).

Nitrogen inversion barriers have apparently not been previously measured for sulfenamides. We were able to measure this barrier for **4** and its amine model (S replaced by CH_2) **8** and report these data along with those for the *N*-methyl- and *N*-amino-9-ABN in Table III.

The ESR spectra of the radical cations of **1** and **4**, prepared by oxidation with tris(*p*-bromophenyl)aminium hexachloroantiminate in methylene chloride, were determined at room temperature. As expected, the spectrum of $\mathbf{4}^{+\cdot}$ has exceedingly poor resolution because of a large number of unresolved long-range splittings. (Each observed line is, in principle, a 2916-line pattern!) The observed spectrum was reasonably well simulated by using a(N) = 14.1 G, a(3H) = 8.3 G, and a "line width" of 4 G. We failed to resolve the long-range "γ-hydrogen" splittings for $\mathbf{1}^{+\cdot}$, but the observed spectrum was reasonably well simulated by using a(N) = 13.8 G, a(3 H) = 8.5 G, a(2 H) = 21.7 G, and a(2 H) = 18.2 G, with an apparent line width of 1.5 G.[35]

Discussion

Neutral Sulfenamide Conformations and Vertical Ionization Potentials. Gauche-effect[14] considerations and the obvious analogy with hydrazines lead to the expectation that the nitrogen lone pair and the sulfur π-lone-pair[15] axes should be perpendicular for

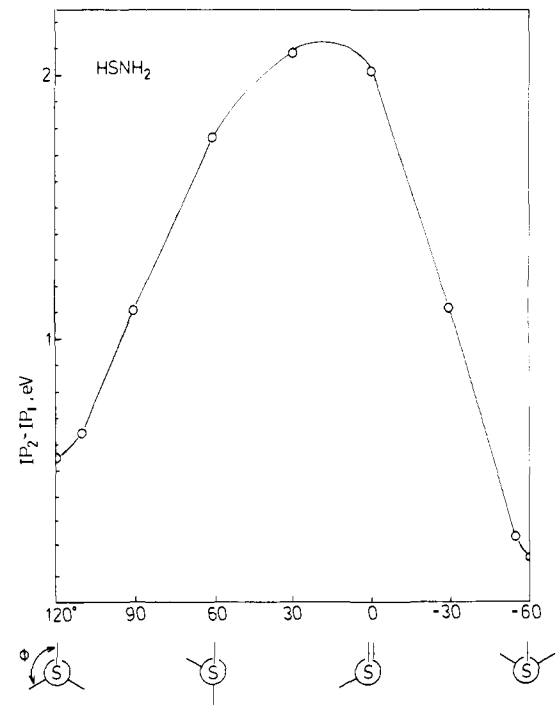
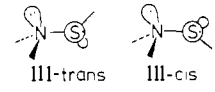


Figure 1. Plot of MINDO/3 $IP_2 - IP_1$ values for H_2NSH as a function of NS rotational angle.

sulfenamides (HS, NH dihedral angle ϕ = 120° and −60°, respectively, for tetrahedral nitrogen compounds), giving conformations III(trans) and III(cis) as the energy minima. This result



is given by both MINDO/3 and INDO calculations and also by an ab initio calculation (in which only III(trans) was apparently considered[16]) on the parent compound, H_2NSH. Although MINDO/3 and INDO agree in predicting III(cis) to be the stablest conformation (by 2.4 and 2.9 kcal/mol relative to III(trans), respectively), this result seems clearly an artifact of the INDO calculation method. NH_2OH is also predicted by INDO to be more stable in the cis form than the trans form by 2.3 kcal/mol (the energy curve reported[17] has the angle scale off by π radians). More accurate ab initio calculations give *trans*-NH_2OH stabler than *cis*-NH_2OH by 8.0 kcal/mol.[18] The cis form is destabilized relative to trans by N,O s-rich lone-pair dipole–dipole interaction, a factor that is mostly ignored by INDO-level calculations. The cis form is stablized relative to trans because it has a larger N lone-pair–σ^* (SH) stabilizing interaction. Lone-pair–σ^* interactions appear to be rather overestimated in importance by INDO-level calculations.

For hydrazines, the difference in the first two ionization potentials is sensitive to the lone-pair–lone-pair dihedral angle, being large when the lone pairs are coplanar. Both INDO and MINDO/3 calculations give similar plots for the difference in these ionization potentials vs. dihedral angle, which have proven useful for estimation of dihedral angle from PE spectroscopic ionization potentials.[19] Calculated ionization potentials for NH_2SH vs.

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(15) Although the lone pairs on bivalent oxygen or sulfur are sometimes considered as two approximate sp^3 hybrids, because the energies of the lone pairs are important in relation to their interaction with the nitrogen atom, they should properly be considered as a high energy π lone pair and a more stabilized S-rich lone pair: Jorgensen, W. L.; Salem, L. "The Organic Chemists Book of Orbitals"; Academic Press: New York, 1973; p 42.

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dihedral angle show a similar large splitting when the N lone pair and the S π lone pair are coplanar, but the appearance of the INDO and MINDO/3 curves is rather different. INDO predicts the nitrogen and sulfur lone-pair energies to be unreasonably different; for NH_3 and H_2S in idealized geometrics, IP_1 values of 14.02 and 10.07 eV (difference 3.95 eV) are obtained, but experimentally, the values are 10.85 and 10.48 eV, respectively (difference 0.33 eV). MINDO/3 gives much more reasonable ionization potentials, NH_3 9.74 eV, H_2S 10.01 eV (difference −0.27 eV), and successfully predicts a smaller $IP_2 - IP_1$ value for *cis*- and *trans*-NH_2SH.[20] The MINDO/3-predicted $IP_2 - IP_1$ curve for NH_2SH is shown in Figure 1.

The observed small $IP_2 - IP_1$ values for the trialkylsulfenamides studied therefore demonstrate that they are present in the expected perpendicular lone-pair conformations. Both steric and the electronic considerations discussed above favor the trans form. Because $IP_2 - IP_1$ for a sulfenamide must be at least equal to the N–S π lone-pair energy gap, the matching of S and N lone-pair energies in these systems is closer than might have been anticipated. Indeed, the observed $IP_2 - IP_1$ difference for sulfenamides is smaller than that observed for hydrazines, where both lone pairs are centered at nitrogen and the rotational angle is known to minimize lone-pair–lone-pair interaction. Both hydrazine lone pairs are approximately sp^3 hybrids that significantly mix with the σ framework. The lone-pair crossing ($IP_2 - IP_1 = 0$ eV) near a 90° lone-pair–lone-pair dihedral angle that is predicted by INDO-level calculations for hydrazines has been found empirically not to occur. Acyclic hydrazines with a wide variety of alkyl substituents give the same $IP_2 - IP_1$ value of 0.52 ± 0.02 eV,[20a] which would require an unreasonable constancy of rotational angle if the predicted crossing actually occurred. The minimum $IP_2 - IP_1$ value for sulfenamides is clearly much smaller. The lone-pair ionization bands for sulfenamides resemble those for hydrazines in being extremely broad (fit by Gaussians with 0.5–0.7 eV half-width at half-height), indicating very different geometry for the neutral species and the relaxed cation radical, as in the case of hydrazines. A comparison of sulfenamide lone-pair IP values with their hydrazine analogues (S replaced by NMe) is shown in Table II. The sulfenamide IP_1 values are only 0.06–0.45 V higher than those of their hydrazine analogues, and because sulfenamide $IP_2 - IP_1$ differences are smaller, the sulfenamide average-lone-pair energies are only 0.03–0.21 eV larger than for their hydrazine analogues.

Sulfenamide Nitrogen Inversion Barrier. Another conformational similarity between sulfenamides and hydrazines appears in the nitrogen inversion barrier data of Table III. Both sulfenamide **4** and hydrazine **10**[13] show higher N_9 inversion barriers than their amine models. Replacement of the 9-CH_2 group of the 9-ethyl compound by S raises $\Delta G^{\ddagger}_c$ by 1.6 kcal/mol, while replacing that of the 9-methyl compound by NH raises $\Delta G^{\ddagger}_c$ by 1.1 kcal/mol. We note that our line-shape analysis says that for both $CH_2 \rightarrow S$ and $CH_2 \rightarrow N$ replacement, the increase in $\Delta G^{\ddagger}_c$ is caused by a decrease in entropy, not an increase in enthalpy. $\Delta S^{\ddagger}$ determinations by NMR have a large enough absolute error that even we do not feel constrained to believe this result, which we cannot rationalize. It is no longer surprising that the *N*-ethyl compound **8** has a 1 kcal/mol lower barrier than *N*-methyl compound **9**, for Katritzky and co-workers have provided abundant examples for such a barrier change in comparing *N*-ethyl with *N*-methyl six-membered rings;[21] the reason for the barrier change appears not, however, to be known. The result of $CH_2 \rightarrow S$ α to nitrogen raising $\Delta G^{\ddagger}_c$ more than $CH_2 \rightarrow N$ is also analogous to the Katritzky group's finding a larger barrier increase when O replaces CH_2 next to N than when N replaces CH_2 next to N.[21]

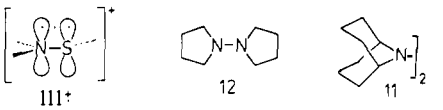
Table IV. Comparison of $E^{\circ\prime}$ Values for Trialkylsulfenamides and Hydrazine Analogues (S Replaced by NCH_3)

sulfenamide	hydrazine analogue	$E^{\circ\prime}$ (hydrazine)[a]	$\Delta E^{\circ\prime}$
1	$(CH_2)_4NNMe_2$	0.17	0.55
2	$(CH_2)_5NNMe_2$	0.36	0.45
3	*i*-Pr_2NNMe_2	0.29	0.48
4	9-ABN-NMe_2	0.11	0.58
5	Me_2NNMe-*t*-Bu	0.49	0.46

[a] Data from ref 12, referred to *n*-Bu_4NClO_4 supporting electrolyte by adding +0.05 V. [b] $E^{\circ\prime}$(sulfenamide) − $E^{\circ\prime}$(hydrazine).

In any analysis of these $\Delta G^{\ddagger}_c$ values, both N and S heteroatom substitution for CH_2 next to nitrogen raises the inversion barrier, another similarity between sulfenamides and hydrazines.

ESR Spectra of Trialkylsulfenamide Radical Cations. The ESR data are completely consistent with the expected three-electron π-bonded geometry III$^{+\cdot}$, analogous to hydrazine radical cations.



III$^{+\cdot}$ 12 11

The nitrogen splitting for the 9-ABN derivative **4**$^{+\cdot}$ is 1.07 times as large as that for the cation of hydrazine **11** (a(2 N) = 13.5 G[22]), which has a formal π spin density at nitrogen of 0.5, suggesting that the formal π spin density at nitrogen for **1**$^{+\cdot}$ is about 0.54. The methyl splitting of 8.3 G requires a substantial sulfur π spin density and would be consistent with a 0.46 ρ^{π}_S value if Q_{MeS} were 18.0 G, which is not an unreasonable size for this parameter (see the last section of the Discussion). The observation of two different two-hydrogen methylene splittings for **1**$^{+\cdot}$ is consistent with conformation III$^{+\cdot}$ and an NS rotational barrier that is high on the ESR time scale. Comparing once again with the symmetrical hydrazine analogue **12**, we find that **1**$^{+\cdot}$ has a nitrogen splitting 1.07 times as large as that for **12**$^{+\cdot}$, and its average NCH_2 splitting is 1.08 times as large as that for **12**$^{+\cdot}$.[23] The SCH_3 splittings of **1**$^{+\cdot}$ and **4**$^{+\cdot}$ are very similar, implying similar sulfur π spin densities. From these results, the III$^{+\cdot}$ singly occupied MO is almost equally distributed between N and S, with a slightly larger coefficient at N. As in the PE results (which refer to a very different geometry, that of the ground state), the matching of sulfur π-lone-pair and nitrogen-lone-pair effects is surprisingly close.

***E*°′ Values for Sulfenamides.** All of our information is consistent with a trialkylsulfenamide going from neutral geometry III(trans) to the radical cation geometry III$^{+\cdot}$ upon electron removal, making these electron-transfer equilibria very analogous to those for tetraalkylhydrazines. Both systems will show an increase in eclipsing strain upon electron removal, but this strain increase must be smaller for sulfenamides than for hydrazines, both because the NS and CS bond lengths are larger than NN and CN bond lengths and because there is only one alkyl group on the sulfenamide sulfur atom. A trend to smaller $E^{\circ\prime}$(sulfenamide) − $E^{\circ\prime}$(hydrazine) values with bulkier alkyl groups might be present in these data, but more and differently chosen examples would be required to establish this fully. Both systems flatten at nitrogen, and although the energy to flatten at a sulfenamide nitrogen is slightly larger than at hydrazine nitrogen, a hydrazine must flatten at two nitrogens and the sulfenamide only at one, so the energy cost of flattening should also favor electron loss from a sulfenamide relative to a hydrazine of similar substitution. The higher IP_1 for a sulfenamide than for a hydrazine will cause a higher $E^{\circ\prime}$ for the sulfenamide relative to the hydrazine, but the difference in IP_1 is rather small (+0.06–0.45 eV for the examples of Table IV), and for isosteric hydrazines, a plot of $E^{\circ\prime}$ vs. IP_1 has a slope of only 0.15,[12a] corresponding to an effect of IP_1 on

(19) We thank Professor A. J. Ardengo, III, for supplying the SN bond parameters use in the MINDO/3 program, β = 0.313 17 and α = 1.878 176 in data block 40.

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Table V. Comparison of ESR Splitting Constants for Methyl-Substituted One π-Electron Radicals

radical	a (Me), G	radical	A, (Me), G
$Me_2CH\cdot$	24.7[a]	$Me_2NH^{+}\cdot$	34.3[d]
$Me_2N\cdot$	27.4[b]	$Me_2O^{+}\cdot$	43[e]
$MeO\cdot$	52[c]	$Me_2S^{+}\cdot$	20.4[f]

[a] Reference 25. [b] Reference 26. [c] Reference 27. [d] Reference 28. [e] Reference 29. [f] Reference 30.

$E^{\circ\prime}$ of under 0.07 V. As discussed previously,[12b] because the major IP_1 differences are caused by differences in alkyl-group polarizability, most of the decrease in ease of electron removal as alkyl groups are made larger disappears in solution. Despite these considerations, $\Delta E^{\circ\prime}$ for the sulfenamide and hydrazine of Table IV is 0.45 − 0.58 V ($\Delta\Delta G^{\circ}$ = 10.4 − 13.4). The geometry changes that actually occur upon electron loss ought to favor electron removal from sulfenamides over hydrazines. The ESR experiments suggest that odd-electron delocalization in sulfenamide and hydrazine radical cations are very similar (about 54:46 vs. 50:50 spin distribution). Why, then, is it 12 kcal/mol harder to remove an electron from a sulfenamide than from a hydrazine? We suggest that the principal reasons are a substantially lower sulfenamide radical cation resonance energy and greater inductive destabilization by *S*-alkyl than by *N*-dialkyl substituents. Following our work on other 9-ABN derivatives, in which steric differences were ignored and it was assumed that σ_I values actually do give a valid measure of inductive effects on cation stabilization for II(X) derivatives in solution, one finds that the difference in resonance stabilization between a neutral compound and its radical cation (ΔRS) is given by deviation of the observed $E^{\circ\prime}$ from the line in an $E^{\circ\prime}$ vs. σ_I(X) plot for examples having no significant resonance stabilization.[2] With $\sigma_I(SCH_3) = 0.25 \pm 0.05$,[24] the $E^{\circ\prime}$ of **4** (II(X = SMe)) gives a ΔRS value of 11.8 ± 1.5 kcal/mol, which is 7.7 kcal/mol less than the 19.5 kcal/mol estimated in the same way for the hydrazine II(X = NMe_2). This admittedly crude estimation assigns a 0.25-V increase in $E^{\circ\prime}$ for **4** compared to its hydrazine analogue because σ_I(SMe) is larger than the $\sigma_I(NMe_2)$ of 0.06 and attributes the remaining 0.33 V of the $\Delta E^{\circ\prime}$ observed to lower resonance stabilization for a sulfenamide than a hydrazine radical cation. It is obvious that ignoring solvation and steric effects makes this assignment of the factors involved qualitative.

Stabilities of Sulfenamide and Hydroxylamine Cation Radicals. The short lifetime of the hydroxylamine cation II(X = $OCH_3)^{+}\cdot$, less than the 10 ms required for observation of a CV reduction wave,[2] is a striking contrast to the long lifetime of **4**$^{+}\cdot$ (II(X = $SCH_3)^{+}\cdot$), for which no decomposition is noticeable in the tens of seconds involved in a slow-scan CV experiment. The short lifetime of the hydroxylamine radical cation cannot reasonably arise from a thermodynamic effect. The vertical IP of II(X = OCH_3), 7.79 eV,[2] is experimentally indistinguishable from that of **4**, and its irreversible CV oxidation wave peaks at 0.73 V vs. SCE (200 mV/s scan rate), rather close to $E^{\circ\prime}$ for the sulfenamide (0.69 V). Inductive destabilization effects on the cations ought to be similar for OMe and SMe (σ_I of OCH_3 and SCH_3 are 0.30 ± 0.04 and 0.25 ± 0.05, respectively[24]), and INDO calculations predict similar destabilization upon twisting $(H_2NSH)^{+}\cdot$ and $(H_2NOH)^{+}\cdot$ 90° and breaking their three-electron π bond. Why, then, is the hydroxylamine cation short-lived compared to the sulfenamide cation? We will argue that the answer lies in the amount of CH_α bond weakening that arises when π spin (and charges) density is introduced at oxygen and sulfur.

We compare the proton ESR methyl-group isotropic splittings for formally $\rho^{\pi}_X = 1$ radicals in Table V. We shall discuss these data in terms of the simple McConnell equation $a(MeX) = Q_{MeX}{}^{H}\rho^{\pi}_X$ because rapid methyl-group rotation averages out HC−X lone-pair angle effects. The effective $Q_{MeX}{}^{H}$ values must vary substantially among these examples, which have over a 30-G range in a(Me), because ρ^{π}_X only differs from 1.0 by the amount of spin removal to the methyl hydrogens by hyperconjugation. Data are not available to calculate ρ^{π}_X for the heteroatom-centered examples in the way Fessende and Schuler[25] did for alkyl radicals, finding that a methyl group removes 8.1% of the available spin, so that ρ^{π}_c for $Me_2CH\cdot$ is $(1 - 0.081)^2 = 0.84_5$. We suggest that nevertheless a valuable qualitative conclusion may be safely drawn from these data.

It is generally accepted that hyperconjugation is of major importance in determining the size of methyl ESR splittings. Despite the possibly variable effect of spin polarization, which makes assignment of all of the observed a(Me) differences only to differences in hyperconjugation uncertain, the very large differences in a(Me) observed for the cations $Me_2S^{+}\cdot < Me_2NH^{+}\cdot < Me_2O^{+}\cdot$ must reflect the relative importance of hyperconjugation in these species.

Nishikida and Williams[31] estimated $Q_{MeS}{}^{H}$ to be 12.7 G for the methyl sulfinyl radical. It must be greater than 20.4 for $Me_2S^{+}\cdot$, and an increase in $Q_{Me}{}^{H}$ with increasing positive charge at the central atom seems reasonable, as hyperconjugation is clearly more favorable in cations than in neutral species. The $Q_{MeS^{+}\cdot}{}^{H}$ value of about 18 estimated above for sulfenamides from the nitrogen splitting thus seems reasonable.

The 110% increase in a(Me) seen in comparing the cations of dimethyl ether and dimethyl sulfide is only consistent with a significantly smaller lowering in CH_α bond strength for a given amount of spin (and charge) at sulfur than at oxygen. We propose that this less effective hyperconjugative CH_α bond weakening for sulfur-centered spin than for oxygen-centered spin is the reason for much longer lifetimes for sulfenamide than for hydroxylamine radical cations. The longer CS bond length and mismatch in orbital size when comparing $H{-}CO^{+}\cdot$ and $H{-}CS^{+}\cdot$ hyperconjugative interaction seem to be a reasonable rationalization for the decrease in hyperconjugative spin delocalization and hence in CH_α reactivity. The same considerations also rationalize the experimental fact that it is CH bonds α to N, and not those α to S in sulfenamide radical cations, that must be protected from cleavage to achieve long radical lifetimes; the a value for dimethylamine radical cation is 68% larger than that for dimethyl sulfide radical cation.

Conclusions

Acyclic trialkylsulfenamides were shown by PE spectroscopy to exist in the expected perpendicular N and S π lone-pair geometry, to have IP_1 values in the range $0.2_6 \pm 0.2$ eV higher than their hydrazine analogues (S replaced by NMe), and to have even smaller $IP_2 - IP_1$ differences than their hydrazine analogues. Replacement of CH_2 next to N by S raises the barrier for nitrogen inversion. ESR spectroscopy shows that sulfenamide radical cations resemble hydrazine radical cations in having slow NS rotation and nearly equal nitrogen and sulfur spin densities (estimated at $\rho^{\pi}_N = 0.54$). In contrast to hydroxylamines, sulfenamides give radical cations that are long-lived enough for $E^{\circ\prime}$ measurement. Because pyridine and neutral sulfenamide decompose the radical cation, and Bredt's rule protection at N increases lifetime, the cation radicals are argued to decompose by NCH_α cleavage. Five trialkylsulfenamides were 10–13 kcal/mol thermodynamically more difficult to oxidize than their hydrazine analogues, which was attributed to a combination of less favorable σ inductive effect and three-electron π-bond resonance energy.

The rate of trialkylsulfenamide decomposition happens to be convenient for the measurement of proton transfer rates by electrochemical methods, which is not true for other $(R_2NX)^{+}\cdot$ examples of which we are aware. The HC−N lone-pair angle dependence on deprotonation rate is of considerable interest to us, and experiments to study this are planned.

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Experimental Section

1-(Methylthio)pyrrolidine (1). A 31.9-mL (47.9 mmol) sample of 1.5 M *n*-BuLi was added dropwise, via cannula, to 4 mL (3.41 g, 47.9 mmol) of pyrrolidine and 75 mL of pentane chilled to 0 °C. After 5 min at 0 °C and 30 min at room temperature, 4.5 g (47.9 mmol) of dimethyl disulfide in 35 mL of pentane was added, and the mixture was stirred at room temperature for 24 h. After filtration through a pad of Celite, removal of solvent at reduced pressure, and distillation twice (bp 76–78 °C (62 mm), **1** was obtained as a colorless oil: 2.03 g (36% yield); ^{1}H NMR ($CDCl_3$) δ 2.92 (m, 4 H), 2.14 (s, 3 H), 1.78 (m, 4 H); ^{13}C NMR ($CDCl_3$) δ 53.88 (t), 25.28 (t), 12.81 (q); mass spectral peak match for $C_5H_{11}NS$.

1-(Methylthio)piperidine (2). Previously made by groups of Davis[32] and Minato,[33] we prepared **2** from 3.0 g (35.2 mmol) of piperidine by the same method as for **1**, giving 3.31 g (21.9%) of **2** as a colorless oil: bp 96–102 °C (70 mm); ^{1}H NMR δ 2.90 (m, 4 H), 2.19 (s, 3 H), 1.47–1.80 (m, 4 H), 1.20–1.47 (m, 2 H); ^{13}C NMR ($CDCl_3$) δ 56.59 (t), 27.27 (t), 23.24 (t), 12.42 (q); mass spectral peak match for $C_6H_{13}NS$.

(Methylthio)diisopropylamine (3) was prepared from 5 mL (35.4 mmol) of diisopropylamine by the same method as **1**, giving 3.52 g (67.5%) of **3** as a colorless oil: bp 76–80 °C (59 mm); ^{1}H NMR ($CDCl_3$) δ 3.25 (septet, J = 7 Hz, 2 H), 2.19 (s, 3 H), 1.12 (d, J = 7 Hz, 12 H); ^{13}C NMR ($CDCl_3$) δ 57.87 (d), 26.61 (q), 22.63 (q); mass spectral peak match for $C_7H_{17}NS$.

9-(Methylthio)-9-azabicyclo[3.3.1]nonane (4). A solution of 2.25 g of 9-ABN·HCl (vacuum dried at 88 °C, 20 h) in 15 mL of THF was treated with 17.8 mL (1.56 M, 27.8 mmol) of *n*-butyllithium at −78 °C, and after warming the solution to 0 °C for 15 min and recooling to −78 °C, 1.25 mL (13.9 mmol) of dimethyl disulfide in 3 mL of THF was added. After 19 h at room temperature, the mixture was treated with 5 g of Na_2CO_3 dissolved in 25 mL of water and the aqueous layer separated and extracted with 3 × 25 mL of ether. After drying the solution over K_2CO_3, concentration gave 2.37 g of crude product. Two Kugelrohr distillations gave **4** as a colorless liquid: 1.71 g (71.9%); 82–88 °C bp (1.8 mm); ^{1}H NMR ($CDCl_3$) δ 3.08 (br s, 2 H), 2.26 (s, 3 He, 2.1–1.2 (m, 12 H); ^{13}C NMR ($CDCl_3$) δ 57.63 (d), 29.92 (t), 24.18 (q), 20.21 (t); mass spectral peak match for $C_9H_{17}NS$.

(*tert*-Butylthio)dimethylamine (5) was prepared by the method of Himel[34] and purified by distillation (bp 75–80 °C (25 mm)) followed by preparative GC on 15% XF-1150 on Chromosorb W 60/80, 147 °C: ^{1}H NMR ($CDCl_3$) δ 2.71 (s, 6 H), 1.19 (s, 9 H); ^{13}C NMR ($CDCl_3$) δ 51.23 (q), 47.98 (s), 28.60 (q); mass spectral peak match for $C_6H_{15}NS$.

1-(*tert*-Butylthio)pyrrolidine (6) was prepared by the general method of Himel[34] and purified by distillation (bp 76–79 °C (69 mm)), chromatography on alumina (hexane eluent), and preparative GC (XF- 1150, 150 °C): ^{1}H NMR ($CDCl_3$) δ 3.04 (m, 2 H), 1.72 (m, 2 H), 1.18 (s, 9 H); ^{13}C NMR ($CDCl_3$) δ 58.96 (t), 47.70 (s), 28.87 (q), 25.84 (t); mass spectral peak match for $C_8H_{17}NS$.

(*tert*-Butylthio)diisopropylamine (7) was prepared by the method of Himel[34] employing *tert*-butylsulfenyl bromide (bp 120 °C (85 mm)) and purified by column chromatography on alumina (hexene eluent): ^{1}H NMR ($CDCl_3$) δ 3.17 (septet, J = 6.5 Hz, 2 H), 1.16 (s, 9 H), 1.08 (d, J = 6.5 Hz, 12 H); ^{13}C NMR ($CDCl_3$) δ 55.10 (d), 45.55 (s), 29.48 (q), 22.63 (q); mass spectral peak match for $C_{10}H_{23}NS$.

The electrochemical,[12] photoelectron spectroscopic,[20] ^{13}C NMR,[13] and ESR[23] equipment and techniques employed have been described earlier.

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Registry No. 1, 83312-64-5; **1**$^+$·, 83312-70-3; **2**, 7257-48-9; **3**, 83312-65-6; **4**, 83312-66-7; **4**$^+$·, 83312-69-0; **5**, 64037-64-5; **6**, 83312-67-8; **7**, 83312-68-9; **8**, 64776-29-0; 9-ABN·HCl, 6760-43-6; 9-ABN·Li, 73309-01-0; pyridine, 110-86-1; tris(*p*-bromophenyl)aminium hexachloroantiminate, 40927-19-3; pyrrolidine, 123-75-1; pyrrolidine lithium salt, 4439-90-1; dimethyl disulfide, 624-92-0; piperidine, 110-89-4; diisopropylamine, 108-18-9; *tert*-butylsulfenyl bromide, 83312-71-4.

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(35) **Note Added in Proof**: Our splittings agree with those reported (Izvoka, A.; Kobayoshi, M. *Chem. Lett.* **1981**, 1603) for trimethyl- and *N,N*-diethyl-*S*-methylsulfenamide radical cations. We only became aware of this paper after ours was submitted.

An Effective Approach to Stereocontrolled Lactone Annulation. Application to the Total Synthesis of Pentalenolactone E Methyl Ester and a Partial Elaboration of Quadrone

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Abstract: α,β-Unsaturated esters having a diquinane framework are produced through regiocontrolled alkylation of cyclopentanone enolates with methyl 4-bromo-3-methoxycrotonate, base-promoted cyclization, and ketalization. Controlled reduction of the carbalkoxy group, application of the Claisen rearrangement, and implementation of an intramolecular Michael addition–oxidation sequence lead efficiently to tricyclic lactones. Of two such molecules, one has been transformed into pentalenolactone E methyl ester (**2**) and the other investigated as a possible precursor to quadrone. The ketone acetal **16** was transformed into the homologous α,β-unsaturated ester **20b** by iodine oxidation of the corresponding hydrazone and reaction of the vinyl iodide so produced (**20a**) with the nickel carbonyl–sodium methoxide reagent system to arrive at **2**. Unmasking of the lactone functionality was achieved conventionally, and the α-methylene carbon was introduced by heating with methoxymagnesium carbonate at 175 °C followed by suitable condensation with formaldehyde.

Not unexpectedly, the last decade has witnessed revolutionary advances in the field of microbiological fermentation. Of particular note here is the attention that has been paid to *Aspergillus terreus* and certain strains of *Streptomyces*,[2] studies that have been rewarded by the isolation of a rich array of unusually structured products, some of which exhibit intriguing biological activity. Thus, the toxigenic fungus *A. terreus* is known to produce not only metabolites such as terreic acid,[3] quadrone (**1**),[4] aspterric

(1) Merck Fellow, 1981–1982.

(2) Included in this group are *S. chromofuscus*, *S. griseochromogenes*, and *S. baarnensis*.

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