structure shown in Figure 1.[12] Theory was confirmed by the ^{13}C NMR spectrum of **3**, which showed only 11 signals, thereby proving that the dilactone possesses C_2 symmetry. The conformation depicted in Figure 1 places all four substituents on the perimeter of **3** in equatorial orientations, a feature that undoubtedly contributes to the ready formation of this eight-membered ring.[13]

(12) Calculations carried out with the MMX 87 force field found a global minimum for the syn conformer (Figure 1) below that of the anti confomer by ~8.5 kcal/mol. The difference ($E_{anti} - E_{syn}$) was found to reside primarily in torsional strain (~5.7 kcal/mol), with an additional ~1.9 kcal/mol resulting from 1,4-interactions.

(13) A MMX calculation on bourgeanic acid (1) found a global minimum in which the two chains are orthogonal, the carbonyl groups are syn, and the hydroxyl and carboxyl groups are oriented toward each other at a distance of 4.6 Å.

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Supplementary Material Available: Characterization data for **6**, **7**, **9**, **10**, **12**, **13**, **14**, **15**, **2**, **16**, **17**, and **1** (3 pages). Ordering information is given on any current masthead page.

Articles

Hydrolysis Rates of Saturated Acyclic and Cyclic Sulfinamides: X-ray Crystal Structures of an Acyclic Sulfinamide and γ-Ammoniopropanesulfinate

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The rates of the neutral hydrolysis of a saturated acyclic sulfinamide, *N,N*-dimethylmethanesulfinamide ($CH_3S(O)N(CH_3)_2$), the monocyclic compounds (isothiazolidine 1-oxide, 2-(1-phenylethyl)isothiazolidine 1-oxide, tetrahydrothiazine 1-oxide) and the bicyclic compounds (9-thia-1-azabicyclo[4.3.0]nonane 9-oxide and 2-thia-1-azabicyclo[4.3.0]nonane 2-oxide) were determined in D_2O using ^1H NMR at 65 °C. The first-order rate constants are similar to those of β-lactams. Activation parameters were determined for the acyclic, one cyclic, and one bicyclic sulfinamide. The striking feature which arises is that the parameters for the hydrolysis of the acyclic sulfinamide ($\Delta H^{\ddagger} = 11 \pm 4$ kcal mol^{-1}; $\Delta S^{\ddagger} = -47 \bullet 11$ cal mol^{-1} K^{-1}) are much different from both the monocyclic sulfinamide and the bicyclic sulfinamide ($\Delta H^{\ddagger} \sim 23 \pm 2$ kcal/mol^{-1}; $\Delta S^{\ddagger} \sim -15 \pm 4$ cal mol^{-1} K^{-1}, respectively). As a consequence, the acyclic sulfinamide hydrolyzes about 25 times faster than the cyclic sulfinamides. Most other heterocyclic compounds hydrolyze more rapidly than their acyclic analogues. Thus, the factors influencing the relative rates of hydrolysis of sulfinamides appear to be acting in a unique manner. The X-ray crystal structure of the first simple sulfinamide, *N*-(1-phenylethyl)methanesulfinamide, and a zwitterionic ammoniosulfinate, 3-((1-phenylethyl)ammonio)propanesulfinate, are also reported.

Introduction

A few years ago, we prepared the first saturated cyclic sulfinamides which represented a missing class of heterocyclic compounds.[1,2] Since these compounds are prepared by the oxidative cyclization of appropriately substituted amine disulfides with iodine in aqueous solution, they must be hydrolytically stable. As a first step to an understanding of the chemistry of saturated mono- and bicyclic sulfinamides, we embarked on a study of their rates of hydrolysis in aqueous solution in order to compare their relative reactivity with related heterocyclic compounds such as sultines and lactams. As a frame of reference for the hydrolysis of sulfinamides in general, we studied the rates of hydrolysis of an acyclic model compound, *N,N*-dimethylmethanesulfinamide ($CH_3S(O)N(CH_3)_2$), and compared these rates to those of the monocyclic compounds, isothiazolidine 1-oxide, 2-(1-phenylethyl)isothiazolidine 1-oxide, tetrahydrothiazine 1-oxide, and of the bicyclic compounds, 9-thia-1-azabicyclo[4.3.0]nonane 9-oxide and 2-thia-1-azabicyclo[4.3.0]nonane 2-oxide. Activation parameters were determined for the acyclic, one cyclic, and one bicyclic sulfinamide.

The X-ray crystal structures of the first simple sulfinamide, *N*-(1-phenylethyl)methanesulfinamide, and a zwitterionic ammoniosulfinate, 3-((1-phenylethyl)ammonio)propanesulfinate, are also reported.

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Results

The hydrolysis of the sulfinamides in deuterium oxide were determined by use of ^1H NMR. As the reaction proceeds, the sulfinamide peaks decrease in area and peaks corresponding to the sulfinate and the ammonium ion increase in area. All reactions were followed through at least 80% completion, and at least 10 data points were taken. The neutral hydrolysis of the sulfinamides, *N,N*-dimethylmethanesulfinamide, isothiazolidine 1-oxide, 2-

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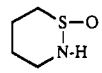
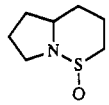
R = H, isothiazolidine 1-oxide

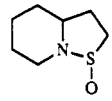


tetrahydrothiazine 1-oxide

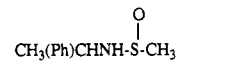
R = $CH(CH_3)Ph$, 2-(1-phenylethyl)isothiazolidine 1-oxide



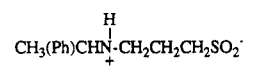
2-thia-1-azabicyclo[4.3.0]nonane 2-oxide



9-thia-1-azabicyclo[4.3.0]nonane 9-oxide



N-(1-phenylethyl)methanesulfinamide



3-(1-phenylethylammonio)propanesulfinate

(1-phenylethyl)isothiazolidine 1-oxide, tetrahydrothiazine 1-oxide, 9-thia-1-azabicyclo[4.3.0]nonane 9-oxide, and 2-thia-1-azabicyclo[4.3.0]nonane 2-oxide, were found to be first-order processes. Pseudo-first-order rate constants for these acyclic and cyclic sulfinamides at various temperatures and pD or pH are given in Table I. The rate data are available for all the sulfinamides at the common temperature of 65 °C and a pD or pH of 7.4–7.7.

The hydrolysis data in deuterium oxide for two monocyclic sulfinamides in acidic, neutral and basic solutions are given in Table I. At pD ~ 7, the rates of hydrolysis are relatively slow and insensitive to changes in pH and can therefore be measured accurately by ^1H NMR. The rates are enhanced 10-fold in acid (pD = 3) over the rates in neutral solution, just as seen in other cyclic esters and amides. In basic solutions (pD = 10) the rate of hydrolysis of isothiazolidine 1-oxide increased by a factor of 3, while that of the N-substituted analogue was unchanged.

To assess the deuterium oxide isotope effect on the reaction, the rates of hydrolysis of isothiazolidine 1-oxide and its N-substituted analogue were followed in H_2O as well as in D_2O at 65 °C (Table I). For both compounds, the kinetic isotope effect, k_{H_2O}/k_{D_2O}, shows a 1.7-fold rate enhancement in water relative to deuterium oxide.

Activation parameters were obtained for three different sulfinamides in order to account for their different reactivities (Table II). A sample plot of $\ln k/T$ vs $1/T$ for the acyclic sulfinamide is shown in the supplementary material.

A crystal of *N*-(1-phenylethyl)methanesulfinamide, suitable for X-ray structure determination, was obtained by dissolving the yellow solid in warm diethyl ether and placing the solution in a capped NMR tube under argon. The tube was placed in a dry-box for 5 days, and, upon very slow evaporation of the ether, colorless crystals formed. The relative experimental parameters for the X-ray structure determination are given as supplementary material. A computer projection of the structure is reproduced in Figure 1. Calculations from the atomic coordinates indicate that nitrogen lies 0.325 Å out of the hydrogen–sulfur–carbon plane and sulfur lies 0.673 Å out of the carbon–oxygen–nitrogen plane. The dihedral angle between the lone pair of electrons on nitrogen and the lone pair on sulfur is calculated to be 63°.

A crystal of the zwitterionic 3-((1-phenylethyl)ammonio)propanesulfinate, the hydrolysis product of 2-(1-phenylethyl)isothiazolidine 1-oxide, suitable for X-ray structure determination was obtained by dissolving the cyclic sulfinamide in chloroform and allowing the solution to hydrolyze under ordinary atmospheric conditions for several months. The relative experimental parameters for the X-ray structure determination of 3-((1-phenylethyl)ammonio)propanesulfinate are given as supplementary material. A computer projection of the structure is reproduced in Figure 2.

Table I. Hydrolysis of Sulfinamides

D_2O	compound	T, °C	pD	$k \times 10^6$, s^{-1}	r
	$CH_3S(O)N(CH_3)_2$	55.0	7.4	28 ± 3	0.997
		60.0	7.6	35 ± 3	0.997
		65.0	7.4	50 ± 9	0.995
		74.9	7.4	90 ± 12	0.995
	isothiazolidine 1-oxide	65.0	7.7	4.7 ± 0.4	0.996
		70.0	7.7	7.6 ± 0.4	0.998
		75.0	7.7	13 ± 1	0.997
		65.0	3.0	41 ± 7	0.982
		65.0	10.0	14 ± 1	1.00
	2-(1-phenylethyl)isothiazolidine 1-oxide	65.0	7.5	2.5 ± 0.1	0.997
		65.0	3.0	21 ± 1	0.997
		65.0	10.0	2.2 ± 0.4	0.991
	tetrahydrothiazine 1-oxide	65.0	7.4	1.8 ± 0.1	0.999
	9-thia-1-azabicyclo[4.3.0]nonane 9-oxide	60.0	7.4	1.5 ± 0.1	1.00
		65.0	7.4	2.7 ± 0.2	0.999
		73.0	7.4	5.9 ± 0.5	0.997
	2-thia-1-azabicyclo[4.3.0]nonane 2-oxide	65.0	7.7	1.9 ± 0.1	0.995

H_2O	compound	T, °C	pH	$k \times 10^6$, s^{-1}	k_{H_2O}/k_{D_2O}
	isothiazolidine 1-oxide	65.0	7.7	7.8 ± 0.2	1.7 ± 0.2
	2-(1-phenylethyl)isothiazolidine 1-oxide	65.0	7.7	4.4 ± 0.2	1.8 ± 0.1

Table II. Activation Parameters for Neutral Sulfinamide Hydrolysis in D_2O

	$CH_3S(O)N(CH_3)_2$	isothiazolidine 1-oxide	9-thia-1-azabicyclo[4.3.0]nonane 9-oxide
$\Delta H^{\ddagger}$, kcal mol^{-1}	13 ± 4	23 ± 2	24 ± 2
$\Delta S^{\ddagger}$, cal mol^{-1} K^{-1} (r)	−41 ± 11 (1.00)	−16 ± 4 (1.00)	−15 ± 7 (0.999)
E_a, kcal mol^{-1} (r)	14 ± 4 (0.997)	23 ± 3 (1.00)	24 ± 2 (0.999)
$\Delta G^{\ddagger}_{65}$, kcal mol^{-1}	27 ± 8	28 ± 3	29 ± 4

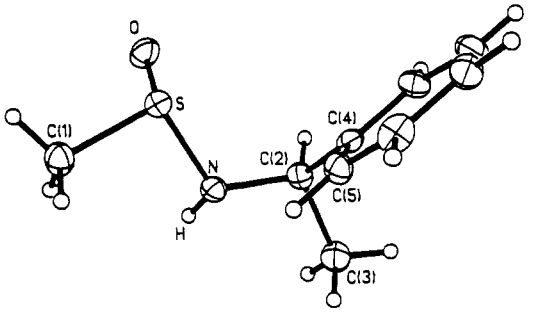


Figure 1. X-ray crystal structure of *N*-(1-phenylethyl)-methanesulfinamide, $C_9H_{13}NOS$.

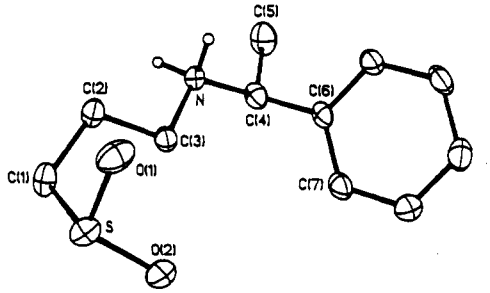


Figure 2. X-ray crystal structure of *N*-((1-phenylethyl)ammonio)propanesulfinate, $C_{11}H_{14}NO_2S$.

Discussion

Although the hydrolysis of arenesulfinamides has been reported in acid and base, the hydrolysis of aliphatic sulfinamides has not been studied. Some important background on the mechanism of nucleophilic substitution at sulfinyl sulfur is gained by reviewing the work on arenesulfinamides.

Biasotti and Andersen[3] studied the influence of aromatic substitution on the rates of alkaline hydrolysis of a series of arenesulfinamides where the aromatic ring is attached to the sulfinyl sulfur. A Hammett plot gives a positive ρ value, indicating that the transition state is stabilized by electron-withdrawing substituents, thus the electron density at sulfur is greater in the transition state than in the ground state and bond formation between hydroxide ion and sulfur has proceeded further than bond breaking between sulfur and nitrogen in the transition state. No excess oxygen-18 was incorporated into the unhydrolyzed sulfinamide which was recovered from partial hydrolysis of *N*-mesityl-*p*-toluenesulfinamide in an alkaline solution of $H_2{}^{18}O$. Therefore, if an intermediate sulfurane forms, an appreciable amount of it does not revert back to labeled starting material. However, this does not rule out the existence of an intermediate because the rate of oxygen equilibration of the intermediate might be much slower than its rate of decomposition and therefore no oxygen exchange would be observed. In fact, negative charge development would be maximized if an intermediate is formed, but when a strong electron-withdrawing substituent (p-NO_2) was placed in the aromatic ring, no significant resonance effect was observed. These results argue against the existence of a sulfurane intermediate in the alkaline hydrolysis of arenesulfinamides.

Asefi and Tillett[4] studied the acid-catalyzed hydrolysis of substituted arenesulfinamides. They found that the entropy of activation ($\Delta S^{\ddagger} = -29.5$ cal mol^{-1} K^{-1}) falls in the range usually associated with a bimolecular mechanism, but no firm conclusions regarding the formation of a sulfurane intermediate were made. It is generally accepted that diaxial or diequatorial displacement of entering and leaving groups on a trigonal-bipyramidal intermediate should lead to inversion of configuration, whereas axial–equatorial displacement should lead to retention of configuration at sulfur. The majority of reported cases of displacement reactions at sulfinyl sulfur occur with high stereoselectivity and take place with inversion of configuration at sulfur.[5] The best example of this process can be seen by the full or predominant inversion of configuration during the acid-catalyzed alcoholysis of chiral *N*,*N*-diethyltoluenesulfinamide with primary alcohols.[6] However, this is not always the case since the acid-catalyzed alcoholysis of a closely related chiral arenesulfinamide, *N*,*N*-diisopropyltoluenesulfinamide, gives predominant retention of configuration when secondary alcohols are used as the solvent. Although the isopropyl derivative must solvolyze by a different mechanism, the reaction can still proceed via axial attack and axial departure as long as three pseudorotations can occur between the time the solvent attacks and the leaving group departs.[5]

The kinetic solvent isotope effect contains primary contributions from any hydrogen atom undergoing transfer and secondary contributions from hydrogen atoms not undergoing transfer.[7] The observed kinetic isotope effect, k_{H_2O}/k_{D_2O}, is 1.7 for both isothiazolidine 1-oxide and its N-substituted analogue. This result is consistent with water (deuterium oxide) acting as the nucleophile (not hydroxide ion (deuteroxide ion)) and partial transfer of a proton from water to the sulfinamide nitrogen. If hydroxide ion (deuteroxide ion) was the nucleophile, the isotope effect would be less than one since deuteroxide ion is a stronger base than hydroxide ion. Additionally, the sensitivity of $k_{hydrolysis}$ to increasing [OH^-] would have been greater. The value of 1.7 is consistent with only secondary effects. For example, in a study of the hydrolysis of benzoylimidazoles,[8] the maximum value for a secondary isotope effect for a product-like transition state would be ~2.3. For a reactant-like transition state in which a proton is directly attached to nitrogen the value would be 2.0 and for a reactant-like transition state in which a proton is directly attached to oxygen the value would be 3.0.[7]

Our initial studies were carried out under the conditions reported for the acid-catalyzed lactam hydrolysis,[9] but we found that the sulfinamides were completely hydrolyzed within minutes. Thus, we examined the hydrolysis of aliphatic sulfinamides in neutral deuterium oxide and determined that the reactions have pseudo-first-order rate constants in the range of (2–50) $\times 10^{-6}$ s^{-1} at 65 °C. Hine[10] studied the rates of formamide hydrolysis in neutral water and reports a first-order rate constant of 8.4×10^{-8} s^{-1} in the pH range 5–7 at 80 °C. From our data we can calculate that *N*,*N*-dimethylmethanesulfinamide would hydrolyze with a rate constant of 1.2×10^{-4} s^{-1} at pD = 7.5–7.8 at 80 °C. Thus, the acyclic sulfinamide hydrolyzes ~10^3 times faster than an acyclic amide. However, β-lactams react faster than acyclic amides and undergo spontaneous neutral hydrolysis at about the same rate as the sulfinamides. For example, penicillin G hydrolyzes with a rate constant of 4.4×10^{-7} s^{-1} in deuterium oxide at 60 °C and 2.0×10^{-6} s^{-1} in water at 60 °C.[11] The kinetic isotope effect ($k_{H_2O}/k_{D_2O} = 4.5$) on the rate of hydrolysis of penicillin G and the large negative entropy of activation ($\Delta S^{\ddagger} = -30$ cal mol^{-1} K^{-1}) are consistent with spontaneous hydrolysis involving nucleophilic attack on the β-lactam by a water molecule which is facilitated by neighboring water molecules.

The relative reactivities of saturated sulfinamides towards neutral hydrolysis at 65 °C reveal that (1) an acyclic sulfinamide hydrolyzes as much as 25 times faster than the cyclic sulfinamides, (2) the five-membered ring sulfinamides hydrolyze faster than the six-membered ring sulfinamides, and (3) the five-membered ring sulfinamide with a proton on the nitrogen hydrolyzes twice as fast as the five-membered ring sulfinamides with an alkyl group on the nitrogen. The second two generalizations regarding the relative rates of hydrolysis of the sulfinamides may not be particularly meaningful because the differences in rates are rather small and the relative order may change at another temperature. A more informative approach is to examine the activation parameters for the hydrolysis reactions (Table II). The striking feature which arises is that the activation parameters for the hydrolysis of the acyclic sulfinamide in deuterium oxide ($\Delta H^{\ddagger} = 13 \pm 4$ kcal mol^{-1}; $\Delta S^{\ddagger} = -47 \pm 11$ cal mol^{-1} K^{-1}) are much different from

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both the monocyclic sulfinamide and the bicyclic sulfinamide ($\Delta H^{\ddagger}$ = 23 ± 2 and 24 ± 2 kcal mol^{-1}; $\Delta S^{\ddagger}$ = −16 ± 4 and −15 ± 2 cal mol^{-1} K^{-1}, respectively). Even though there are differences in $\Delta H^{\ddagger}$ and $\Delta S^{\ddagger}$, the value of $\Delta G^{\ddagger}$ is essentially constant. However, the range in $\Delta S^{\ddagger}$ for the neutral hydrolysis of the sulfinamides (−15 to −47 cal mol^{-1} K^{-1}) is similar to that obtained for the neutral hydrolysis of a series of penicillins, where $\Delta S^{\ddagger}$ varies from −7 to −49 cal mol^{-1} K^{-1}, depending upon the structure of the penicillin derivative and whether the acid portion is undissociated or ionized on C-3.[12] Unfortunately, no attempts at interpreting the large variations of $\Delta S^{\ddagger}$ in penicillins has been made.

A change in mechanism between two similar reactants is sometimes indicated by widely differing entropies of activation.[13] One example is the acid-catalyzed hydrolysis of esters.[13] The loss of translational and rotational freedom of a water molecule associated with a bimolecular process should lead to lower entropies of activation relative to the unimolecular case. This is indeed the situation where entropy of activation values for acid-catalyzed unimolecular ester hydrolysis are typically 0 to +10 cal mol^{-1} K^{-1}, while the entropy of activation values for acid-catalyzed bimolecular ester hydrolysis are in the range of −15 to −30 cal mol^{-1} K^{-1}. One explanation for the large entropy differential (about 30 cal mol^{-1} K^{-1}) is the loss of freedom of a water molecule. However, the entropy of freezing liquid water is only −5.26 cal mol^{-1} K^{-1}.

A study by Bell and McDougall[14] on the hydration of ketones and aldehydes shows considerable variation of entropies with structure. Entropy of activation values ranging from −8 cal mol^{-1} K^{-1} for monochloroacetone to −31 cal mol^{-1} K^{-1} for formaldehyde are given; the average value being approximately −18 cal mol^{-1} K^{-1}. Therefore it may be more reasonable to attribute 18 cal mol^{-1} K^{-1} to the loss of entropy from incorporation of a water molecule. Kreevoy[15] suggests that an additional 10–15 cal mol^{-1} K^{-1} can be accounted for by the fact that the two hydrogen atoms of the attacking water molecule take on substantial positive changes in the transition state and can be effective in immobilizing additional solvent molecules. Thus up to 25–30 cal mol^{-1} K^{-1} may be attributed to the entropy of the incorporation of a water molecule into the transition state in a hydrolysis reaction.

Both organic sulfites and carbonates hydrolyze in base. The cyclic derivatives hydrolyze more rapidly than do the acyclic, mainly due to the more negative entropy of activation of the acyclic analogue.[16] This "entropy-strain principle" is attributed to the greater supression of molecular motion between the ground state and the transition state in the acyclic compound than in the more rigid five-membered ring.[16]

A possible mechanism for the neutral hydrolysis of the sulfinamides can be considered based on the values of the activation parameters and the kinetic isotope effect. In both acyclic and cyclic sulfinamides we believe that a water molecule attacks the sulfinyl sulfur along an extension of the S–N bond axis (i.e. the σ^* orbital), resulting in a charge separation in the transition state leading to cleavage. The high positive value of $\Delta H^{\ddagger}$ for the cyclic sulfinamides suggests that the S–N bond in more difficult to cleave in cyclic sulfinamides than in the acyclic sulfinamides. The high negative value of $\Delta S^{\ddagger}$ for the acyclic sulfinamides suggests that there may be little aquation of S(O)–N group in the ground state due to the rapid rotation around the S(O)–N bond.[17] Therefore, many water molecules may have to be ordered in the transition state to facilitate the cleavage into two separate ions, the sulfinate anion and the ammonium cation. In the cyclic sulfinamides rotation is restricted and water molecules can readily solvate both the ground state and the transition state. Thus much less reorganization of solvent is necessary to attain the transition state for the hydrolytic cleavage of the S(O)–N bond into the zwitterion.

There are some similarities and some differences between the observed pattern of relative reactivities of the sulfinamides and those of amides, lactams, sulfinate esters, sultines, and sulfonamides. The hydrolysis of amides and monocyclic lactams is generally studied in either acid or base because there is no significant uncatalyzed reaction. In the hydrolysis of amides and lactams in aqueous sulfuric acid at 25 °C, the six-membered ring (2-piperidone) hydrolyzes approximately 10 times faster than the five-membered ring (2-pyrrolidone) and approximately 30 times that of an acyclic amide, *N*-ethylacetamide.[9] These results are opposite to those observed for the neutral hydrolysis of the sulfinamides where the acyclic sulfinamide hydrolyzes faster than both cyclic compounds.

Sulfinate esters and sultines are hydrolyzed in base to give hydroxy acids. The five-membered ring sultine is hydrolyzed faster than the six-membered ring sultine.[18] For these sultines the difference in reactivity is believed to lie in the entropy of activation ($\Delta S^{\ddagger}$ = −35 cal mol^{-1} K^{-1} for the five-membered ring to −43 cal mol^{-1} K^{-1} for the six-membered ring) because the enthalpy effects are small ($\Delta H^{\ddagger}$ = 4–5 kcal mol^{-1}). The relatively rigid five-membered ring is already constrained more than the six-membered ring in the ground state and therefore less energy is required to reach the transition state. However in this series, the acyclic sulfinate ester reacts at 60% of the rate of the five-membered ring. The enhanced reactivity of the acyclic molecule partially comes from the more positive value of $\Delta S^{\ddagger}$ ($\Delta H^{\ddagger}$ = 6 kcal mol^{-1}; $\Delta S^{\ddagger}$ = −31 cal mol^{-1} K^{-1}) but the cause was not discussed.[18]

Sulfonamides, in contrast to sulfinamides, are resistent to hydrolysis.[19] A typical method of hydrolysis involves heating with concentrated hydrochloric acid in a sealed tube at 150–170 °C.[20] Sulfonamides are extremely stable toward basic hydrolysis and can sometimes survive fusion in an 80% sodium hydroxide solution.[19]

The unusually rapid cleavage of aliphatic sulfinamides relative to their cyclic analogs is unique among a large series of heterocyclic compounds. In addition to lactams and sultines discussed earlier, five-membered ring cyclic phosphates, phosphonates, aromatic sulfates, and sulfonates all hydrolyze 10^5–10^7 times faster than their acyclic analogues due to ring strain.[18] Thus the factors which influence the hydrolysis of cyclic sulfinamides appear to be exactly opposite those of other heterocyclic compounds.

Crystal Structures

N-(1-Phenylethyl)methanesulfinamide is the first noncomplexed sulfinamide which has been analyzed by X-ray

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crystallography (Figure 1). In contrast to the prediction by Moriarity,[17] the nitrogen is not planar. The sum of the bond angles is 340.2°, suggesting a geometry about nitrogen which is about halfway between planar and pyramidal and a hybridization intermediate between sp^3 (328.5°) and sp^2 (360°). The nitrogen lies 0.3250 Å out of the sulfur–carbon(2)–hydrogen plane. The sulfur–nitrogen bond distance of 1.667 Å is smaller than the theoretically calculated value of 1.74 Å from Pauling's atomic radii for a sulfur–nitrogen single bond. The sulfur atom lies 0.673 Å out of the carbon(1)–oxygen–nitrogen plane and the sum of the bond angles about sulfur is 311.9°. The average bond angle about sulfur in the sulfinamide is 104.0°, a value which is 5.5° smaller than the tetrahedral angle of 109.5°.

Calculations indicate that the lone pair on sulfur and the lone pair on nitrogen of the sulfinamide form a dihedral angle of 63°. It appears that the "gauche effect" dictates the geometry of molecules with one or more lone pairs or polar bonds on adjacent atoms. This theory developed by Wolfe[21] proposes that the most stable conformation of these molecules has the maximum number of gauche interactions between adjacent lone pairs and/or polar bonds. Collin and Lipscomb[22] concluded by an X-ray structure determination that hydrazine, H_2NNH_2, has either the eclipsed (C_{2v} symmetry) or a semieclipsed (C_2) conformation. Later, the energy of hydrazine was calculated (CNDO) as a function of dihedral angle (ω).[23] Like the sulfinamide the most stable configuration for hydrazine is predicted to be skewed with $\omega = 65.0°$. In another cyclic molecule with lone pairs on adjacent sulfur and nitrogen atoms (dehydromethionine) the angle between the lone pair on the sulfur and the lone pair on the nitrogen is approximately 90°.[24] Although this angle is somewhat larger than the gauche angle of 60°, the dihedral angle between the lone pairs is still closer to 60° than to 180°.

In the zwitterionic 3-((1-phenylethyl)ammonio)-propanesulfinate shown in Figure 2, the two S–O bonds are of approximately equal length (1.509 (2) and 1.514 (2) Å), and both hydrogen atoms on nitrogen are involved in hydrogen bonding to the oxygens of the neighboring molecules (NH···O(1′) = 2.728 Å; NH···O(2″) = 2.712 Å). Another zwitterionic ammoniosulfinate, ((quinuclidinodifluorometyl)thio)difluoromethanesulfinate exists as two crystallographically independent molecules,[24] both of which have slightly shortened, but essentially equal, sulfur–oxygen bond lengths of 1.47 Å due to the inductive effect of the neighboring difluoromethylene group.

Experimental Section

Equipment. A Radiometer Copenhagen PHM 82 standard pH meter was used in combination with a Model ABU 80 autoburette and TTT 60 titrator for acidity measurements and product runs. When the hydrolysis reactions were run in deuterium oxide a correction to the pH meter reading was applied to obtain the pD value.[26] ^1H NMR spectra were obtained on either a Varian EM 390 or a General Electric QE-300FT spectrometer. ^{13}C NMR were recorded on a General Electric QE-300 FT spectrometer.

Hydrolysis. All hydrolysis reactions except the reaction of *N,N*-dimethylmethanesulfinamide at 75 °C were kept in a Lauda K2/R circulating constant temperature bath. All ^1H NMR spectra of the hydrolysis of isothiazolidine 1-oxide and 2-(1-phenylethyl)isothiazolidine 1-oxide were run on Varian EM-390 spectrometer operating at 90 MHz. ^1H NMR spectra of the hydrolysis of tetrahydro-1,2-thiazine 1-oxide, *N*-(1-phenylethyl)methanesulfinamide, 9-thia-1-azabicyclo[4.3.0]nonane 9-oxide and 2-thia-1-azabicyclo[4.3.0]nonane 2-oxide at 55, 60, 65, 73, and 80 °C and of *N,N*-dimethylmethanesulfinamide at 55, 60, and 65 °C were run on a General Electric QE-300 FT spectrometer operating at 300 MHz. ^1H NMR spectra of the hydrolysis of *N,N*-dimethylmethanesulfinamide at 75 °C were run on a Nicolet NT-500 FT spectrometer operating at 500 MHz with a variable temperature probe set at 75 °C and on the QE-300 at other temperatures. Doubly deionized H_2O or 99.8 atom % D (Aldrich Chemical Co.) were used as solvents. The pD (pH) was adjusted by use of potassium carbonate or D_2SO_4 (H_2SO_4) and varied <0.3 units during a run.

As the reactions proceeded, the sulfinamide peaks decreased in area and peaks corresponding to the sulphinic acid salts increased in area. All reactions were followed through at least 80% completion with at least 10 data points taken. For each spectrum taken at time t, the percentage of reactant remaining was calculated by determining the ratio of a sulfinamide peak to the sum of that peak plus a sulphinic acid peak, depending upon which peaks were best resolved for a particular reaction. For example, for *N,N*-dimethylmethanesulfinamide the singlet at δ 2.72 due to the two methyl groups on the nitrogen of the sulfinamide decreased in area, and a singlet at δ 2.67 due to the two methyl groups of dimethylammonium ion, the cationic product of hydrolysis, increased in area as the reaction proceeded. The pseudo-first-order rate constants (k) were obtained by plots of ln (% reactant) versus time, with correlation coefficients of greater than 0.990 through 70% completion.

The preparation of the following cyclic sulfinamides by iodine oxidation of the corresponding amine disulfides or amine thiols has been described:[2,27] isothiazolidine 1-oxide, 2-(1-phenylethyl)isothiazolidine 1-oxide, tetrahydro-1,2-thiazine 1-oxide, 9-thia-1-azabicyclo[4.3.0]nonane 9-oxide, and 2-thia-1-azabicyclo[4.3.0]nonane 2-oxide.

***N*-(1-Phenylethyl)methanesulfinamide** was prepared by modification of the method of Moriarty.[17] Methanesulfinyl chloride[28] (3.00 g, 30.4 mmol) was dissolved in 15 mL ether in a 50-mL flask and cooled in an ice bath. 1-Phenylethylamine (7.37 g, 60.8 mmol) in 15 mL of ether was added dropwise through an addition funnel, and a rubber septum with a disposable glass pipette through the top was used to stopper the flask in order to vent the solution and prevent loss of ether. The solution was allowed to warm to room temperature and stirred for 4 h. The white solid amine salt was filtered off, and the solvent was removed from the remaining solution under reduced pressure to give a thick yellow liquid. Flash chromatography with 10% ethanol–chloroform (R_f = 0.43) gave a light yellow solid. Recrystallization from ether gave white crystals (0.55 g, 10%) and an X-ray crystal structure was obtained. ^1H NMR ($CDCl_3$, 90 MHz): δ 7.25 (s, 5 H, aromatic H), 4.50 (m, 1 H, CH), 4.05 (br, 1 H, NH), 2.55 (s, 3 H, SCH_3), 1.45 (d, 3 H, CH_3). ^1H NMR (D_2O, 300 MHz): δ 7.39 (s, 5 H, arom H), 4.50 (q, 1 H, CH), 2.69 (s, 3 H, SCH_3), 1.48 (d, 3 H, CH_3).

***N,N*-Dimethylmethanesulfinamide** was prepared as described for *N*-(1-phenylethyl)methanesulfinamide. The clear liquid (62.1%) was obtained with bp 34–35 °C (0.20 Torr) [lit.[17] bp 31–32 °C (0.20 Torr)]. ^1H NMR ($CDCl_3$, 90 MHz): δ 2.73 (s, 6 H, $N(CH_3)_2$), 2.55 (s, 3 H, SCH_3). ^1H NMR (D_2O, 300 MHz): δ 2.73 (s, 6 H, $N(CH_3)_2$), 2.66 (s, 3 H, SCH_3).

3-((1-Phenylethyl)ammonio)propanesulfinate was obtained as long, colorless crystals suitable for X-ray analysis by dissolving 2-(1-phenylethyl)isothiazolidine 1-oxide in chloroform and allowing the sulfinamide to hydrolyze under ordinary atmospheric conditions for five months. ^1H NMR (D_2O, 300 MHz): δ 1.62 (d, 3 H, CH_3), 1.90 (q, 2 H), 2.35 (m, 2 H), 2.85 (m, 1 H), 3.02 (M, 1 h), 4.36 (q, 1 H, NCH), 7.44 (m, 5 H, aromatic H).

Crystallography. All crystal structure determinations were performed by Dr. Marilyn M. Olmstead. Single-crystal X-ray diffraction data were obtained on a Syntex $P2_1$ diffractometer equipped with a graphite monochromator using Mo Kα radiation

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(λ = 0.71069). Only random fluctuations of less than 2% in the intensities of two standard reflections were observed during the course of data collection. The structure of *N*-(1-phenylethyl)-methanesulfinamide was solved by direct methods and an absorption correction was applied. Final refinement was carried out with anisotropic thermal parameters for all non-hydrogen atoms. The largest feature on a final difference map was 0.31 e Å^{-3} in height. The largest shift in the final cycle of refinement was 0.030 for overall scale. A summary of the relative experimental parameters for the X-ray structure determination of the sulfinamide, atomic coordinates, isotropic thermal parameters, a listing of the bond distances and bond angles as well as hydrogen-atom coordinates are given as supplementary materials. A computer projection of the structure is reproduced in Figure 1.

The relative experimental parameters for the X-ray structure determination of 3-((1-phenylethyl)ammonio)propanesulfinate are summarized in the supplementary material. No decay in the intensities of two standard reflections was observed during the course of data collection. The structure was solved by direct methods, and an absorption correction was applied. The handedness was determined to be correct as found by use of the SHELXTL routine for this purpose. Final refinement was carried out with anisotropic thermal parameters for all non-hydrogen atoms. Hydrogen atoms bonded to carbon were included at calculated positions using a riding model, with C–H of 0.96 Å and $U_H = 1.2U_C$. The largest feature on a final difference map was 0.65 e Å^{-3} in height in the approximate position of the sulfur lone pair. The largest shift in the final cycle of refinement was 0.013. Atomic coordinates, isotropic thermal parameters, a listing of the bond distances and bond angles as well as hydrogen-atom coordinates are given as supplementary material. A computer projection of the structure is reproduced in Figure 2.

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Supplementary Material Available: The relative experimental parameters for the X-ray structure determination of the sulfinamide along with atomic coordinates, isotropic thermal parameters, a listing of the bond distances and bond angles as well as hydrogen atom coordinates for *N*-(1-phenylethyl)-methanesulfinamide and 3-((1-phenylethyl)ammonio)propanesulfinate (7 pages). Ordering information is given on any current masthead page.

Mechanism of Dicyanoanthracene-Photosensitized Oxygenation of 1,1,2,2-Tetraarylcyclopropanes and 1,1,3,3-Tetraarylpropenes

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1,1,2,2-Tetraphenylcyclopropane (**2a**) and electron-donor-substituted 1,1-diaryl-2,2-diphenylcyclopropanes **2b–f** as well as correspondingly substituted 1,1-diaryl-3,3-diphenylpropenes **5a–e** and 3,3-diaryl-1,1-diphenylpropenes **6a–e** were irradiated in CCl_4 and acetonitrile in the presence of oxygen and various sensitizers. The cyclopropanes as well as the propenes are inert toward singlet oxygen in both solvents. In electron-transfer-induced oxygenation reactions, photosensitized by 9,10-dicyanoanthracene in acetonitrile, cyclopropanes **2d–f**, carrying efficient electron-donating 4-methoxyphenyl and 4-phenoxyphenyl groups, yield 1,2-dioxolanes **3d–f** exclusively. Cyclopropanes **2b** and **2c**, which carry less efficient electron-donating 4-methylphenyl groups, give rise to dioxolanes **3b** and **3c**, respectively, as major products. In addition, allylic hydroperoxides **4b** and **4c** are formed, which are further oxygenated to benzophenone (**10**) and the corresponding diaryl ketones **7b** and **7c**. 1,1,2,2-Tetraphenylcyclopropane (**2a**) yields dioxolane **3a** and allylic hydroperoxide **4a** in a ratio of 3:2 as major products; in addition, 1,1,3,3-tetraphenylpropene (**5a** = **6a**) is formed as a minor product that is oxygenated under the reaction conditions to benzophenone (**10**) and diphenylacetaldehyde (**8**). By use of biphenyl (co-sensitizer), lithium perchlorate (special salt effect), and *p*-benzoquinone (quencher of $O_2^{\bullet-}$), it is shown that cyclopropanes **2a–f** are oxygenated in chain reactions involving (1) 1,3-radical cations $\mathbf{2}^{\bullet+}$ rather than 1,3-triplet biradicals and (2) triplet ground-state oxygen rather than the superoxide radical anion. Use of 1,8-dihydroxyanthraquinone as a sensitizer supports these results. Propenes **5a–e** and **6a–e** yield ketones and aldehydes as major products by reactions of 1,2-radical cations $\mathbf{5}^{\bullet+}$ and $\mathbf{6}^{\bullet+}$ with $O_2^{\bullet-}$ as the oxygenating species. Dioxolanes and allylic hydroperoxides are not produced from these propenes. A mechanism is developed for the electron-transfer-induced photooxygenation of 1,1,2,2-tetraarylcyclopropanes **2** that shows that the increase of the resonance stabilization of the 1,3-radical cation $\mathbf{2}^{\bullet+}$, caused by substitution of phenyl groups by electron-releasing aryl groups and demonstrated by the concomitantly decreasing oxidation potential of **2**, plays the essential role in determining oxygenation rates and product formation.

Introduction

In oxygen- or air-saturated polar solvents, aryl-substituted cyclopropanes (CP) may be converted into 1,2-dioxolanes by photosensitization with 9,10-dicyanoanthracene (DCA)[1,2] or quinones.[3] These conversions proceed by electron-transfer-induced photooxygenation reactions, for which three different mechanisms have been discussed: the first, involving the superoxide radical anion

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