Sulfamic Acid and Its N-Substituted Derivatives

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I. Introduction and Scope

Sulfamic acid chemistry was extensively reviewed by Audrieth, Sveda, Sisler, and Butler in *Chemical Reviews* in 1940.[1] Later, the reviews of Gilbert[2] (1965) and of Burton and Nickless[3] (1969) updated the Audrieth review. These two reviews cover the literature comprehensively up to the early sixties. Some broad industrial aspects of sulfamic acid chemistry have been reviewed about 1956[4a] and in 1969.[4b] Some other early, limited or perhaps not readily available reviews have appeared.[5] At the Sympsoium on Sulfamic Acid in Milan in 1966, Bicelli[6] presented a short review on sulfamic acid and sulfamates, and Romagnani[7] gave a bibliography with over 450 references on sulfamic acid and its electrometallurgical applications. Scott and Spillane[8–10] have reviewed the important mechanistic aspects of sulfamic acid chemistry to about the end of 1972. In the last review[10]

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of the series, synthetic developments for most of 1970 through 1971 and part of 1972 were also noted.

Our intention was to commence where the reviews of Gilbert[2] and Burton and Nickless[3] have left off and to continue up to the end of 1978. Thus, in general, references cited in these reviews have been excluded unless their inclusion was necessary for a proper discussion of later results. The major journals have been covered to the end of 1978 and *Chemical Abstracts* almost to mid-1979. Thus, the period covered by the review runs from the mid-sixties to approximately the end of 1978.

The literature coverage of the review is reflected in the Contents listing. The arrangement of this review follows broadly that of Audrieth's review, with a number of major exclusions (to be referred to). In the 14–15-year span which the review embraces, several thousand publications have appeared, and it was felt that in order to avoid a review of inordinate size, a number of definite and arguably peripheral areas of sulfamic acid chemistry should be excluded. The choice of what to exclude and what not to exclude was sometimes made easier in the knowledge of the existence of recent reviews in these areas. The principal exclusions were the following: (i) carbonylsulfamates, $-CONHSO_3^-$, and sulfonylsulfamates, $-SO_2NHSO_3^-$; (ii) chlorosulfonyl isocyanate, $ClSO_2NCO$[11a,b] (unless used to synthesize sulfamate functions); (iii) sulfamates joined to double bond nitrogen or to phosphorus, e.g., $=NSO_3H$, etc.; (iv) (aryl- and alkyl-) hydroxylsulfamic acids, e.g., $HONHSO_3H$ (these are seen as derivatives of hydroxylamine, rather than as sulfamic acids); (v) heparin;[11c] (vi) sulfamides of the type $=NSO_2N=$, $-CONHSO_2NH_2$, etc.; and (vii) imidodisulfonates (unless used in the synthesis of compounds covered in the review) and nitrilosulfonates.

II. Sulfamic Acid

A. Physical Studies

1. X-ray and Neutron Diffraction

The use of combined X-ray and neutron diffraction studies on single crystals has shown that it is possible to observe the bonding electrons in molecular crystals with sufficient precision to analyze the nature of the bonding and to calculate the charges on the various atoms involved. This method has recently been used to determine the deformation electron density in sulfamic acid.[12] A population analysis indicated that the net charge on the S atom is +0.7 to +1.0 e, −0.3 to −0.5 e on the O atom, and +0.12 e on the H atoms, while that on the N atom is close to unity. The bond lengths and angles calculated from the X-ray and neutron parameters are in good agreement. An independent X-ray study[13] gives similar bond lengths, but some of the bond angles, particularly the S–N–H and H–N–H angles, are notably different. An X-ray emission spectroscopic study of a large number of sulfur compounds, including sulfamic acid, has been carried out.[14] The mean number of valence electrons on the sulfur atom of sulfamic acid is calculated as 4.24 ± 0.06 by using the equation given by Coulson and Zauli.[14]

The crystal structure of ammonium sulfamate has been determined by using neutron diffraction[15] and X-ray[16] methods. The dimensions of the sulfamate tetrahedron are similar to those previously reported for potassium sulfamate.[17] Both groups give almost identical bond lengths for the S–O and N–S bonds in the sulfamate ion. The N–S bond length (1.63 Å) lies in between that for a single (1.74 Å) and double (1.54 Å) bond. This "average" bond length is attributed to d_π–p_π overlap of d orbitals of sulfur with p orbitals of nitrogen. Full structural data are now available for the series KNH_2SO_3, $K_2NH(SO_3)_2$, and $K_3N(SO_3)_3$, following a detailed X-ray diffraction study of potassium nitrilotrisulfonate.[16] These compounds have similar S–O bond distances and the O–S–O bond angles are similar, but the nitrilotrisulfonate has a longer N–S bond (1.72 Å) than the sulfamate or imidodisulfonate ions—a fact attributed to weaker d_π–p_π overlap in $K_3N(SO_3)_3$. A monoclinic–orthorhombic transition has been found for cyclohexylsulfamic acid from X-ray studies.[19]

2. Infrared and Raman Spectroscopy

The Raman and infrared spectra of sodium sulfamate monohydrate and calcium sulfamate tetrahydrate have been measured.[20] Raman spectra were recorded in the single-crystal form by using λ = 2537-Å excitation. Infrared spectra were measured over the range 400–4000 cm^{-1}. Detailed assignments of the observed spectra have been made with the aid of normal coordinate analysis of the sulfamate ion. The internal vibrations of the sulfamate ion have been computed and show good agreement with the experimental values.[21] A normal coordinate analysis was carried out by using a potential function of the Urey–Bradley type to calculate force constants. A laser Raman study of single crystals of $NH_3^+SO_3^-$ and $ND_3^+SO_3^-$ at 300 and 30 K has been reported for the 5–4000-cm^{-1} range, and an infrared study of polycrystalline samples has been made in the 60–4000-cm^{-1} region.[22] Assignments in terms of factor group symmetry species rotational and vibrational vibrations are given. Vuagnat and Wagner's[23] assignment of the 3140-cm^{-1} infrared band to a ν_s NH_3 vibration is seen as being incorrect. This band is assigned instead to a NH_3 stretching fundamental. The NH stretching frequencies are correlated with the N···O distances, and the ν NH bandwidth and structure are discussed. A polarized infrared study of single-crystal sulfamic acid has shown that Vuagnat and Wagner's assignment of the 1274-cm^{-1} absorption to a SO_3 symmetric stretching vibration is also incorrect, and this vibration is now assigned[24] to the band at 1069 cm^{-1}. A new assignment for the degenerate NH_3 deformation at 1795 cm^{-1} (rather than 1534 cm^{-1}, as given by earlier workers) has also been made.[24] The infrared and Raman spectra of the anions $NH_2SO_3^-$, $NHDSO_3^-$, $ND_2SO_3^-$, $CH_3NHSO_3^-$, $CH_3NDSO_3^-$, and $(CH_3)_2NSO_3^-$ have been reported and assigned.[25] The vibrational spectra of the dimethylsulfamate anion have been interpreted on the basis of a comparison with those of the sulfamate and methylsulfamate anions. Infrared spectra are also reported and assigned for the selenium series $NH_2SeO_3^-$, $CH_3NHSeO_3^-$, and $(CH_3)_2NSeO_3^-$. The infrared spectra of a variety of silver salts of a number of sulfur and selenium compounds containing the function NXO_3 (X = S, Se) have been reported.[26]

3. Magnetic Resonance Spectroscopy

A NMR study on potassium sulfamate has shown that the proton–proton distance is 1.635 ± 0.005 Å and that these hydrogen atoms do not lie in the mirror plane but in a plane perpendicular to it containing the N–S bond,[27] a conclusion corroborated by a more recent deuteron magnetic resonance study on single crystals of $ND_2SO_3^-K^+$ at 195 K.[28] The DND angle is 109.2° and the N–D distance is 1.004 Å, in excellent agreement with the values for the HNH angle (110.1°) and the N–H distance (1.007 Å) obtained in a previous neutron diffraction study of potassium sulfamate.[17] Analysis of the NMR spectra of nine metallic sulfamates and sulfamides shows that the proton–proton distance lies between 1.74 and 1.64 Å, the N–H distance between 1.004 and 1.065 Å, and the HNH angle between 105.6 (cadmium sulfamate) and 115.2° (lithium sulfamate).[29] The HNH angle (112.1°) and the N–H distance (1.047 Å) are larger than the values cited above.

The ESR spectrum of the radical $NH_2^+SO_3^-\cdot$ (formed by irradiation of sulfamic acid enriched to 95% in ^{15}N) has been measured at 300, 77, and 4 K.[30] The same group[31] has shown that γ irradiation at 77 K of a crystal of $^{15}NH_2SO_3^-K^+$ gives rise to the radicals $NHSO_3^-\cdot$, $NH_2\cdot$, and $NH_2SO_3\cdot$ possibly by the radiolysis mechanism shown in eq 1–4. However, this

$$NH_2SO_3^- \rightarrow NH_2SO_3\cdot + e^- \quad (1)$$

$$NH_2SO_3\cdot + e^- \rightarrow NHSO_3^{-}\cdot + H \quad (2)$$

$$H + NH_2SO_3^- \rightarrow NHSO_3^{-}\cdot + H_2 \quad (3)$$

$$NH_2SO_3\cdot + e^- \rightarrow NH_2\cdot + SO_3^- \quad (4)$$

mechanism is now thought to be in error.[32] Exposure of sulfamic acid and sulfamate ions to ^{60}Co γ rays at 77 K gave rise to the changes (radicals observed are in italics) shown in eq 5–10.

$$NH_2SO_3^- \rightarrow \mathit{NH_2^+SO_3^-}\cdot + e^- \quad (5)$$

$$NH_2^+SO_3^- + NH_2SO_3^- \rightarrow \mathit{NHSO_3^-}\cdot + NH_3^+SO_3^- \quad (6)$$

$$NH_2SO_3^- + e^- \rightarrow \mathit{NH_2}\cdot + SO_3^{2-} \rightarrow NH_2^- + SO_3^-\cdot \quad (7)$$

$$NH_3^+SO_3^- \rightarrow NH_3^+SO_3\cdot + e^- \quad (8)$$

$$NH_3^+SO_3\cdot + NH_3^+SO_3^- \rightarrow \mathit{NH_2^+SO_3^-}\cdot + NH_3^+SO_3H \quad (9)$$

$$NH_3^+SO_3^- + e^- \rightarrow \mathit{NH_3^+}\cdot + SO_3^{2-} \rightarrow NH_3 + \mathit{SO_3^-}\cdot \quad (10)$$

Another group[33] has studied the temperature dependence of the ESR spectrum of the first formed radical ($NH_2^+SO_3^-\cdot$) in the above reactions. The radical was trapped in γ-irradiated sulfamic acid single crystals. The temperature dependence of the protons' and nitrogen coupling tensors allows a complete description of the potential well hindering the reorientation of the NH_2^+ group. The nitrogen and proton dipolar coupling tensors for the motionless radical are also calculated. More recently, the same group has performed a similar study with the $NHSO_3^-$· radical.[34] A triplet has been observed at 200 K following direct hydrogen addition (after bombardment with gaseous hydrogen atoms) to C_6 of uracil-5-sulfamic acid.[35]

4. Protonation Equilibria

In principle, the equilibria shown in eq 11 may occur with sulfamic acids (which are generally regarded as being zwitterionic in the solid state and in solution.

$$RNH_2^+SO_3H \overset{a}{\rightleftharpoons} RNH_2^+SO_3^- \overset{b}{\rightleftharpoons} RNHSO_3^- + H^+ \quad (11)$$

With amino acids both types of equilibria are generally observable, but because of the strength of aliphatic sulfonic acids, the equilibrium corresponding to step a would be observable only in strong acids, and in such acids solubility problems and competing hydrolysis will arise. Practically all the available ionization data on sulfonic acids therefore relate to step b type equilibria. The pK_a in water of sulfamic acid has been determined potentiometrically[36] as 1.19, from sucrose inversion rates[37] as 1.06, and from emf measurements[38] as 1.04. Values are also available in some other solvents.[36,39,40] Sulfamic acid is a much weaker acid in DMF (dimethylformamide) (pK_a 7.99[39]) and in Me_2SO (pK_a 6.5[40]) than in water. The lower acid strength in DMF has been attributed partially to weak solvation of the small sulfamate ion in that solvent. Some limited data for step a (R = H) are available.[41]

Two somewhat divergent literature values have been reported for the pK_a of *N*-cyclohexylsulfamic acid.[42,43] In a recent study the pK_a's of several aliphatic/alicyclic sulfamates (R = *n*-Bu, *n*-Pr, *sec*-Bu, and cyclohexyl) have been determined by potentiometric, conductometric, and magnetic resonance (^{13}C and ^1H) methods.[44] As would be expected, the aliphatic/alicyclic compounds are weaker acids than sulfamic acid itself, and the pK_a's are in the range 1–1.9. The agreement between the pK_a values determined by the different methods was good. The pK_a for cyclohexylsulfamic acid was found to be 1.71 ± 0.29, in reasonable agreement with the earlier value (1.9) reported by a Japanese group.[42]

Protonation of aromatic sulfamates occurs in strong acid due to their lower (compared to the aliphatic sulfamates) basicity. The protonation is not fully described by H_0 or H_A.[45] For R = C_6H_5, a pK_a of −2.03 ± 0.05[45] measured in sulfuric acid has been found, based on H_0 (*m*, the slope of a plot of the log of the ionization ratios vs. $-H_0$, was 0.87), and for R = *p*-$CH_3OC_6H_4$, pK_a = 1.62 ± 0.2[46] measured in perchloric acid (*m* = 0.80). Recently, pK_a's have been measured for the series R = C_6H_5, *p*-ClC_6H_4, *p*-BrC_6H_4, *p*-$CH_3C_6H_4$, *p*-$C_2H_5C_6H_4$, *p*-$CH_3OC_6H_4$, and *p*-$C_2H_5OC_6H_4$, and for *N*-methyl-*N*-phenylsulfamates.[47] A UV method was used, but where possible ^1H NMR was also employed to determine the ionization ratios. The agreement between the pK_a values obtained by the two methods was good. pK_a values were also calculated by using the Bunnett and Olsen equation, and these values are in good agreement with some recent Russian data[48] in which the protonation occurring was described by the acidity function, H_s^1, defined as being equal to $H_0 - 2 \log a_{H_2O}$. The pK_a of N^1-naphthylsulfamate is −1.45 (based on H_0).[49]

Some data are available for the other equilibrium in eq 11, i.e., step a. Protonation occurs on oxygen, and not surprisingly the amide acidity function, H_A, is followed. The pK_a values obtained range from −2.67 (R = *m*-ClC_6H_4) to −2.04 (R = *p*-$CH_3C_6H_4$).[46]

Protonation on nitrogen to give the zwitterion, $RNH_2^+SO_3^-$, rather than on oxygen to give the neutral species, $RNHSO_3H$, has been favored in eq 11. N-Protonation is preferred for several reasons, namely, (i) there is considerable evidence that the zwitterionic form of sulfamic acid, $NH_3^+SO_3^-$, is important in solution (see elsewhere in this section, i.e., II.A); (ii) studies on the basicity and sites of protonation of sulfonamides have been interpreted in favor of nitrogen protonation at the sulfonamide group;[50] (iii) the fact that H_0 is the most appropriate acidity function suggests that protonation is on nitrogen;[45] and (iv) the Hammett ρ value obtained from the data on the arylsulfamates is about −1.65, and while this value is not close to the ρ for the protonation of anilines (−2.7), nevertheless it points to N-protonation since values much closer to the value (0.7) for the ionization of benzenesulfonic acids[45,51] would be expected if O-protonation was occurring.

5. Thermochemical and Pyrolytic

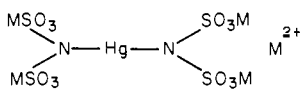
The heats of solution and of ionization of sulfamic acid, sulfanilic acid, and taurine have been measured by calorimetry. The small negative calculated entropies of ionization for sulfamic acid (−15.8[52] and −13.3[53] J mol^{-1} K^{-1}) and the other acids[52] support the contention that the acids exist as zwitterions, $NH_3^+SO_3^-$, $NH_3^+C_6H_4SO_3^-$, and $NH_3^+CH_2CH_2SO_3^-$, respectively, in aqueous solution. The heat of formation for crystalline sulfamic acid has been calculated by two groups[52,54] from measurements of the heat of reaction of sulfamic acid and sodium nitrite in acid solution. The values reported for ΔH_f° are −683.9 and −683.0 K J mol^{-1}.[54] The specific heat of ammonium sulfamate has been measured over the range 90 to 298 K.[55]

The thermal decomposition of sulfamic acid in a humid atmosphere proceeds via the formation of ammonium pyrosulfate, $(NH_4)_2S_2O_7$, and it decomposes to sulfate at higher temperatures. Differential thermal analysis (DTA) and thermal gravimetric analysis (TGA) have been used to examine the various intermediates in the pyrolysis of sulfamic acid and uranyl sulfamate (**1**).[56] The decomposition of **1** involves the sequence shown in eq 12.

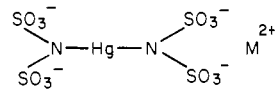
In the isomerization of **2** to give the double salt **3**, $x \leq 1.5$. This is not consistent with an earlier claim by Capestan (cited in ref 56) that the intermediate was $UO_2(NH_2SO_3)\cdot 2H_2O$. Capestan has extended his earlier studies of the pyrolysis of the

$$UO_2(NH_2SO_3)_2\cdot 4.5H_2O \xrightarrow{323\text{–}423\ K} \underset{\mathbf{1}}{} \quad UO_2(NH_2SO_3)_2\cdot xH_2O\ (x \leq 1.5) \xrightarrow[453\text{–}573\ K]{+H_2O} \underset{\mathbf{2}}{} \quad (NH_4)_2UO_2(SO_4)_2 \xrightarrow{573\text{–}673\ K} \underset{\mathbf{3}}{} (NH_4)_2SO_4\cdot 2UO_2SO_4 \xrightarrow{773\ K} UO_2SO_4 \xrightarrow{1073\ K} U_3O_8 \quad (12)$$

mercury imidodisulfates of potassium and sodium (**4**)[57] to examine the barium, strontium, and calcium compounds (**5**).[56] The



4, M = Na, K



5, M = Ba, Sr, Ca

pyrolysis of compounds **5** was largely analogous to that of compounds **4**, giving rise to the materials $Hg(HgNSO_3)_2$, MSO_4, and NH_4HSO_4, but the strontium compound behaved differently and gave $HgNH_3SO_4$, $SrSO_4$, and NH_4HSO_4. Breaking of the N–S and Hg–N bonds is considered.[59] Thermolysis of the compound $[Hg(NH_3)]_2Hg[N(SO_3)_2]_2$ at 443–463 K gave rise to $Hg(NH_3)_2(NH_2SO_3)_2$, $Hg(NH_3)_2SO_4$, HgO, and H_2SO_4.[59] The relative thermal stabilities of sodium, calcium, and lincomycin cyclamates have been studied by DTA and TGA.[60]

6. Miscellaneous

The existence of the zwitterionic form of sulfamic acid in various solvents is supported by measurements of dielectric constants, dielectric increments, electrostriction values,[61] dipole moments, and conductivities.[62] The dipole moment and apparent molal volume of *N*-cyclohexylsulfamic acid have been reported.[63] The nitrogen 1s electron binding energy in sulfamic acid has been determined as 401.8 eV by X-ray photoelectron spectroscopy.[64] A quadrupole echo has been demonstrated for sulfamic acid under pulse conditions at 90 MHz by using phase detection.[65] The vaporization of sulfamic acid at 600–740 K gives rise to ammonium sulfamate and hexasulfimide, $(NHSO_2)_6$, which is subsequently hydrolyzed.[66]

The equilibrium between ammonium imidodisulfate (**6**) and ammonium sulfamate (**7**) under ammonia gas has been studied over the temperature range 523–563 K[67,68] and is shown in eq 13.

$$\underset{\mathbf{6}}{(NH_4SO_3)_2NH} + NH_3 \rightleftharpoons \underset{\mathbf{7}}{2NH_4SO_3NH_2} \quad (13)$$

Phase equilibria, solubility, and binodal curves were determined for the ternary systems **6**–EtOH–H_2O (at 298 K) and **7**–EtOH–H_2O (at 298 and 313 K).[69] Solubilities and paragenesis of sediments in the systems ammonium sulfate–ammonium sulfamate–water and ammonium nitrate–ammonium sulfamate–water have been examined.[70] No evidence for the existence of double salts in these systems was obtained. The quaternary system ammonium sulfate–ammonium nitrate–ammonium sulfamate–water had the pure salts as solid phases together with the salts $(NH_4)_2SO_4\cdot 2NH_4NO_3$ and $(NH_4)_2SO_4\cdot 3NH_4NO_3$.[70] The solubility of sulfamic acid in water can be doubled at 353 K by the addition of formamide.[71]

Irradiation of sulfamic acid in water with a lamp emitting a continuum from 1800 Å through the visible region or with a lamp emitting a sharp line at 2537 Å gave 75–100% yields of ammonia.[72]

B. Kinetics of Solvolysis and Sulfation

1. Sulfamic Acid

The earlier work of Candlin and Wilkins[73] on the kinetics and mechanism of hydrolysis of sulfamic acid in perchloric acid (10^{-3}–6 M) has been extended recently by Hughes and Lusty.[74] They have generally confirmed Candlin and Wilkins' results, but in addition to the A1 acid-catalyzed decomposition of sulfamate ion, proposed by the latter group, they present evidence that an additional A2 path involving sulfamic acid also occurs. This mechanism represented in eq 14 would predominate or occur

$$\underset{\mathbf{8}}{NH_3{}^+SO_3{}^-} + H^+ \rightleftharpoons \underset{\mathbf{9}}{NH_3{}^+SO_3H} \xrightarrow{H_2O} [NH_4]^+ + H_2SO_4 \quad (14)$$

exclusively above 2 M perchloric acid, the region where a plot of k_{obsd} vs. $[H^+]$ goes through a maximum. The appearance of **9** may also be expected above ~3 M perchloric acid (sulfamate ion should be fully protonated to give **8** at 2.5 M perchloric acid, assuming a pK_a of 1.00 (see II.A.4). The kinetics of hydrolysis of sulfamic acid have been measured over pH (1–3) and temperature (323–343 K) ranges of interest in electroplating processes.[75] The hydrolysis of sulfamic acid at pH from 0.5 to 1.3 and temperatures from 353 to 373 K has been followed kinetically.[76] A paper with the strange and apparently contradictory title "Possibility of acid catalysis in the hydrolysis of the sulfaminate anion in an alkaline medium" has appeared.[77] In alkaline media, hydrolysis, which proceeds according to eq 15,

$$NH_2SO_3{}^- + OH^- \rightarrow NH_3 + SO_4{}^{2-} \quad (15)$$

is slow and a temperature of 503 K (pH 8.98–10.43) was employed. Not surprisingly the hydrolysis rate decreases with increasing alkalinity. A direct S_N2 type attack by OH^- on the sulfamate sulfur is suggested as the likely mechanism.[76]

2. Aliphatic, Alicyclic, and Aromatic Sulfamates

The kinetics of hydrolysis of several *N*-alkyl-, *N*,*N*-diethyl-, and *N*-cyclohexylsulfamates have been studied in aqueous perchloric acid (0.1–6 M) and in dioxane–water containing added perchloric acid at 368 and 383 K.[79] A plot of k_{obsd} vs. $[H^+]$ goes through a maximum at about 1.5 M perchloric acid for cyclohexylsulfamate. A number of mechanistic criteria have been used to examine the hydrolysis. The mechanism of hydrolysis of these compounds is seen as involving a preequilibrium protonation followed by a rate-determining A2 hydrolytic decomposition of the sulfamates as shown in eq 16. The pree-

$$RR'NSO_3{}^- + H^+ \rightleftharpoons RR'NH^+SO_3{}^- \xrightarrow[slow]{H_2O} RR'NH + H_2SO_4 \quad (16)$$

quilibrium complicates the interpretation of rate data since much of the data has been measured in regions of acidity where this initial step is important. On the basis of entropy data, *N*-isopropyl- and *N*-cyclohexylsulfamates may involve a borderline A1/A2 mechanism of hydrolysis. Limited rate data for the hydrolysis of sodium sulfamate and of *N*-cyclohexyl-*N*-benzyl- and *N*-phenylsulfamates in 1.41 M perchloric acid at various temperatures have been reported. Under similar conditions (1.41 M acid, 373 K) phenylsulfamate hydrolyzes 3100 times faster than cyclohexylsulfamate.[60] The hydrolysis rates of 15 aliphatic (including disubstituted), alicyclic, and aromatic sulfamates have been correlated as a Taft polar plus steric equation of the type

$$\log K = \log K_0 + \rho^*\Sigma\sigma^* + \sigma\Sigma E_s{}^c \quad (17)$$

where ρ^* is +2.4 and δ is −0.9. This ρ^* is a composite value since it will include a (negative) ρ^* for the protonation step, as this is not complete in the 0.54 M perchloric acid used in the study.[61]

Two preliminary and simultaneous studies of the rates of hydrolysis of a series of para-substituted phenylsulfamates were made in 90:10 (v/v) water–acetone containing 0.09 M hydrochloric acid at 323 and 348 K[62] and in 52.27% perchloric acid at 298 K.[63] Various mechanistic tests carried out in the first study indicated that an A2-type mechanism was being followed.

A Hammett ρ value of +0.95 was obtained. The ρ value obtainable from the data in the second study was approximately +3. The explanation for this discrepancy in ρ values was put forward simultaneously by both groups.[9,46] It was suggested that the hydrolysis involved two steps (see eq 16): a preequilibrium protonation (which will have a negative ρ) and a second step which may be either a unimolecular fission (A1) or an associative mechanism involving solvent attack at sulfamyl sulfur (both processes should have positive ρ values). Thus the ρ values obtained in dilute acid (as in the first study) will be composites reflecting both the effects of substituents on the protonation and nitrogen–sulfur heterolysis steps. The ρ value obtained in the second (Russian) study was measured in strong acid under conditions where these arylsulfamates will be fully protonated, and thus this value can be related to the nitrogen–sulfur cleavage. In fact, Belyaev and Kotlyar have shown that ρ may vary from +1 (in 19.4% perchloric acid) to about +3.3 (in >57% perchloric acid).

Support for an A2 path in the acid-catalyzed hydrolysis of phenylsulfamate salts has come from salt effects, from solvent isotope effects, and from Bunnett and Bunnett and Olsen analyses of rate data.[64] Large differences in solvation between the intermediate zwitterion and the transition state leading to products are thought to be responsible for anomalous values of the Arrhenius parameters ($\Delta H^{\ddagger}$ and $\Delta S^{\ddagger}$) which are generally positive rather than negative as expected for bimolecular hydrolysis. The kinetics and mechanism of the acid-catalyzed hydrolysis of 1-naphthyl-[49] and *N*-methyl-*N*-phenylsulfamates[65] in a number of acids have been examined. The employment of similar mechanistic criteria has led to the conclusion that an A2 mechanism also operates in the decomposition of these compounds.

Using the acidity function H_s' to describe the protonation of arylsulfamates (see II.A.4), Belyaev and Kotlyar have found that Bunnett plots are not linear but involve an initial plateau and then a straight line of decreasing rate as the activity of water is decreased. They argue that the nondependence of the logarithmic rate constants on the log of the water activity over the plateau region indicates that an A2 mechanism cannot be operative, and that, therefore, an A1 mechanism must be operative instead. The decrease in rate in stronger acids is considered to be due to the formation of the relatively unreactive diprotonated sulfamate **10**, which is compared to a protonated sulfanilide, $ArNH_2SO_2Ar^+$. The hydrolysis rate of these species is much lower than that of the monoprotonated zwitterion **11**.

$$\underset{\textbf{11}}{ArNHSO_3^-} + H^+ \rightleftharpoons \underset{\textbf{10}}{ArNH_2^+SO_3^-} + H^+ \rightleftharpoons ArNH_2^+SO_3H \quad (18)$$

$$\textbf{11} \xrightarrow{\text{slow}} ArNH_2 + SO_3 \quad (19)$$

A series of kinetic equations are set up on the basis of eq 18, involving **10** and **11**. These equations allowed the measurement of pK_a's for the equilibrium involving **10** and **11** (using H_A) and led to several experimentally confirmable predictions. When the A1 mechanism (eq 19) is considered in conjunction with **10** and **11**, a rate equation is derived which leads to certain predictions for the limiting cases of dilute and concentrated acid media. In dilute acid, the observed ρ value is equal to the difference in ρ for the rate-determining step and the ρ for the monoprotonation step. In concentrated acid, the observed ρ is equal to the sum of the ρ values for the rate-determining step and the second (diprotonation) step.

This analysis shows that formation of the less reactive species, **10**, is a likely explanation for the decrease in rate in strong acids. It does not, however, offer clear support for the involvement of an A1 mechanism in the acid-catalyzed hydrolysis of arylsulfamates. An important implication of the Russian analysis is that the previously measured values of +3.3 in strong acid may not be related directly to the rate-determining step since they include a ρ for the diprotonation step. Since this latter ρ is negative (~−1), the positive ρ values for the rate-limiting step will be in the region of 4, indicating the considerable effect of substituents on the arylsulfamate hydrolysis.

3. Sulfation

This process involves O-sulfonation (sulfation) of alcohols, giving the alkylammonium salts of alkyl sulfates as shown in eq 20.

$$ROH + R'R''NSO_3H \rightarrow ROSO_3H{\cdot}NHR'R'' \quad (20)$$

In 1964, Nakano and Yamaguchi[66] measured rates of ethanolysis (R = Et) for 12 different sulfamic acids, including several disubstituted compounds, and for the *N*-sulfonic acids of morpholine and piperidine. With R'' = H, the order of reactivity for variation in R' decreased for the series normal > iso > secondary; for the three disubstituted compounds studied (R' = R'') the order decreased for *n*-Bu > Et > Me. The effect of variation in alcohol structure was examined by using cyclohexylsulfamic acid. For 14 alcohols the rates of sulfation followed the order primary > secondary > tertiary > phenols. The reaction was first order in sulfamic acid, and the rate was much greater with disubstituted sulfamic acids than with monosubstituted acids. These workers view the mechanism of these sulfations as involving a rate-determining unimolecular cleavage of the sulfamic acid followed by a fast alcoholysis reaction, as shown in eq 21.

$$R'R''NH^+SO_3^- \xrightarrow{\text{slow}} R'R''NH + SO_3 \xrightarrow{ROH} ROSO_3^- + R'R''NH_2^+ \quad (21)$$

A Russian group[67] has found that the rate constants for sulfation with sulfamic acid decrease in the order primary unbranched alcohols > secondary and primary branched alcohols > ethylene glycol monoethers > ethylene glycol. Within the primary alcohol series the rate increased (with one or two exceptions) with the length of the unbranched alkyl chain. The same group,[88] in a detailed kinetic study of the reaction between sulfamic acid and methanol, showed that generally acids or bases have no catalytic effect. However, weak bases increase the solubility of sulfamic acid due to complex formation and increase the rate of reaction.

The sulfation of higher aliphatic alcohols gives rise to alkyl sulfates which are important industrially as surfactants. A number of papers have examined the kinetics and mechanism of the reaction of hexadecanols, notably cetyl alcohol, with sulfamic acid.[69-93] Vulakh and Loktev[69] have shown that a common rate-determining step is involved in the sulfation of cetyl alcohol by sulfamic acid in the presence of dimethylformamide (DMF) and in the solvolysis of sulfamic acid in DMF. The sulfation reaction is zero order in alcohol and first order in sulfamic acid, a finding corroborated by another Russian group.[90] Both reactions are seen as involving slow formation of a DMF–SO_3 complex, which with an enhanced sulfating ability compared to sulfamic acid reacts quantitatively and very rapidly with cetyl alcohol in the sulfation reaction. In a Japanese study,[91] the mechanism of the same reaction is viewed as involving protonation of cetyl alcohol by sulfamic acid, reversible formation of an addition intermediate, $H_2NS(OR)(O^-)O_2OH$, protonation on nitrogen (by the protonated alcohol), and migration of the ammonium ion.

The kinetics of the catalytic sulfation of cetyl alcohol with sulfamic acid in the presence of DMF under heterogeneous conditions has also been studied,[92] since the industrial preparation of cetyl sulfate is performed in the presence of undissolved sulfamic acid. Again, the rate-determining stage is the formation, possibly by an S_N2 mechanism, of a DMF–SO_3 complex. Some

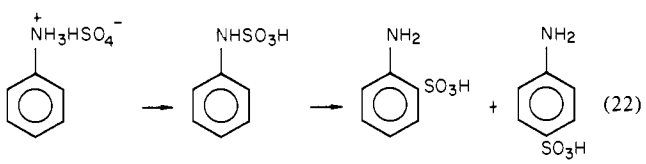
results on the sulfation of other hexadecanols under homogeneous conditions led to similar mechanistic conclusions.[93] Because of its relevance to the mechanism of the sulfation reaction, the kinetics of solvolysis of sulfamic acid in DMF have been extensively studied.[94] The rate-determining formation of a $DMF-SO_3$ intermediate leads to eventual products such as $NH_3 \cdot DMF \cdot SO_3$ and $HO_3SNHSO_3NH_4$.

C. Rearrangement

The rearrangement of phenylsulfamic acid to give ring-substituted sulfonic acids is of considerable interest not only because of controversy about its molecularity but also because it has been implicated in the mechanism of the sulfonation of aniline and in the Piria reaction. Both inter- and intramolecular mechanisms have been supported in the rearrangement, and in the case of the rearrangement of 1-naphthylsulfamic acid the mechanism appears to be partially intramolecular.

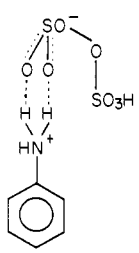
Scott and Spillane[95] have rearranged potassium phenylsulfamate to sulfanilic acid in dioxane at 373 K in the presence of an equimolar amount of 98% sulfuric-^{35}S acid. That the rearrangement is intermolecular was shown by the facts that the recovered sulfanilic acid had 50% of the activity of the original sulfuric acid, and if a 1:2 molar ratio of sulfamate to sulfuric acid was employed the product sulfanilic acid had 65% of the original label. Moreover, in runs using equimolar quantities, after a short time, rapid N-desulfonation of sulfamates occurred, as evidenced by the doubling of the amount of sulfate in the medium, and then a slow C-resulfonation took place. Migration of the sulfonic acid group of 1-naphthylsulfamic acid takes place partially (~45%) by an intramolecular path in dioxane at 373 K in the presence of equimolar 98% sulfuric acid.[96] This result was established from radiochemical experiments employing either sulfamate and sulfuric-^{35}S acid or sulfamate-^{35}S and sulfuric acid. It was suggested that the species which produces the product 1,4-naphthylaminesulfonic acid may be a multiply sulfonated 1-naphthylamine which both desulfonates to give the 1,4-acid and resulfonates the available 1-naphthylamine to give more product. Sodium 2-naphthylsulfamate did not rearrange in dioxane at 373 K in the presence of an equimolar quantity of 98% sulfuric acid, nor could it be rearranged under conditions previously reported.[97]

Vrba and Allan[96,99] studied the mechanisms of the sulfonation of aniline and the rearrangement of phenylsulfamic acid in excess 97% sulfuric acid at 313 and 373 K. In both the sulfonation of aniline and the rearrangement of phenylsulfamic acid, they obtained a mixture of orthanilic and sulfanilic acids in the proportion of 15:85, respectively. They suggested that the sulfonation of aniline involves a rate-determining N-sulfonation followed by a rapid rearrangement of the phenylsulfamic acid formed ($t_{1/2}$ ~ 6.9 h). The overall sulfonation rate, under identical conditions (313 K), was ~100 days.



(22)

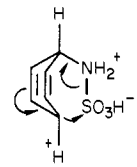
The N-sulfonation step was thought to involve pyrosulfuric acid:



The rate law for the rearrangement step is $v = kh_0 \cdot [PhNH_2SO_3H^+]$ which is analogous to the rate equation established for the intramolecular nitramine rearrangement. On this evidence these authors suggested that the phenylsulfamic acid rearrangement was also intramolecular. This ignored the fact that in the nitramine rearrangement the proportion of ortho to para products is approximately reversed. A radiochemical technique could not be used to probe the mechanism of the rearrangement since the equilibrium shown in eq 23 occurs very rapidly ($t_{1/2}$ ~ 1.08 h at 313 K) in 97% sulfuric acid. The

$$C_6H_5NHSO_3H + H_2{}^{35}SO_4 \rightleftharpoons H_2SO_4 + C_6H_5NH^{35}SO_3H \quad (23)$$

intramolecular mechanism was suggested to occur, after N-protonation of phenylsulfamic acid, by deformation of the aromatic ring (**12**) so that the migrating SO_3H group was close to the para position. A similar species could be drawn to account for the formation of orthanilic acid.



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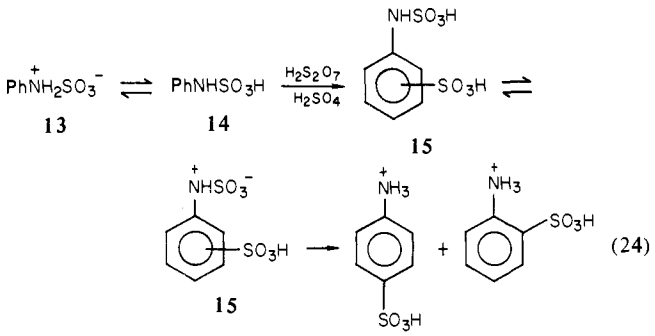
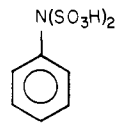
Whatever the molecularity of the rearrangement, the overall scheme (eq 22) for the sulfonation of aniline is supported by other data from the same authors. In an earlier report[100] they showed that the rearrangement of *m*-chlorophenylsulfamic acid and the sulfonation of *m*-chloroaniline with sulfuric acid at 473 K gave the same product sulfonic acids. In a later paper[101] they found that either the sulfonation of aniline (at 453 K) with excess 97% sulfuric acid or the rearrangement of orthanilic or phenylsulfamic acids (under the same conditions) leads to equal proportions of the same products, namely, sulfanilic acid (principally) and aniline-2,4-disulfonic acid.

The contradiction between the intermolecular mechanism proposed by Scott and Spillane and the intramolecular mechanism of Vrba and Allan has been pointed out.[102] The conditions used by Scott and Spillane may be compared to "baking conditions"[103] inasmuch as the solid sulfamate did not dissolve in the dioxane–sulfuric acid medium at 373 K. These conditions were essentially pyrolytic and heterogeneous. Vrba and Allan, on the other hand, used 97% sulfuric acid as medium and were able to obtain homogeneous conditions even at 313 K. Such conditions are comparable to those used in the liquid-phase sulfonation of aniline.[103] This difference in conditions may result in a change in mechanism—a view supported by Cerfontain and Maarsen's[104] recent experiments carried out under heterogeneous and homogeneous conditions by using potassium phenylsulfamate in 99.9% sulfuric acid. Unlike the former conditions, after 20 min at 373 K the reaction mixture consisted of ~10% orthanilic acid, ~50% sulfanilic acid, and ~40% anilinium ion, while under homogeneous conditions the products, after 20 min, were orthanilic acid (~15%), sulfanilic acid (~80%), and aniline-2,4-disulfonic acid (~4%).

Maarsen and Cerfontain,[105] in some elegant work, have produced good evidence that the "rearrangement" of phenylsulfamic acid in 96–100% sulfuric acid at 298 K involves an initial C-sulfonation followed by N-desulfonation to yield orthanilic and sulfanilic acids. Their full scheme is shown in eq 24. The intermediacy of the elusive *o*- and *p*-sulfophenylsulfamic acids (**15**) was supported by UV and NMR observations, though attempts to synthesize a sulfophenylsulfamate either by the reaction of sulfur trioxide with sulfanilic acid or sodium sulfanilate or by the reaction of pyridine–sulfur trioxide with the sulfanilate were unsuccessful. Quenching experiments on rearrangement mixtures also supported the intermediacy of sulfophenylsulfamate



rather than aniline-*N*,*N*-disulfonic acid (**16**). Kinetic and product



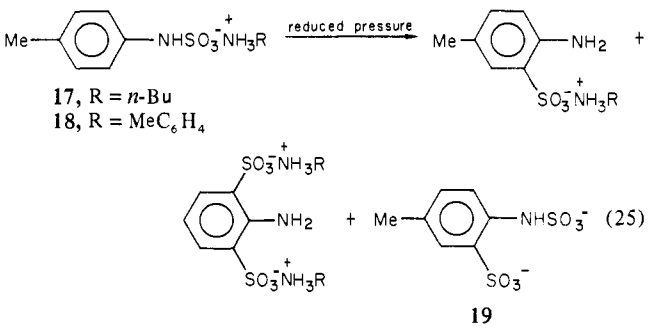
studies indicated that while **13** was the major species present in the strong sulfuric acid used, **14** was the reacting species. The diprotonated form, $PhNH_2SO_3H^+$, was ruled out since it would not be expected to be much more reactive than the anilinium ion (phenylsulfamic acid in 96–100% sulfuric acid is sulfonated at least 10^3 times faster than the anilinium ion), and it should, like the anilinium ion, give rise to predominant meta and para substitution rather than the ortho and para substitution observed. A suitable model for study of the sulfonation of phenylsulfamic acid in the form of the O-protonated species **14** was provided by methanesulfonanilide, $PhNHSO_2Me$, and these workers have reported such a study.[106]

Competition between solvolysis and sulfonation occurs when phenylsulfamic acid is present in 70–96% sulfuric acid.[104] In <70% acid solvolysis occurs exclusively and in >96% acid only sulfonation takes place. In the latter percent of acid the *o*- and *p*-sulfophenylsulfamates formed are subsequently solvolyzed (see eq 24). In 99.9–100.2% sulfuric acid some aniline-2,4-di- and a little aniline-2,4,6-trisulfonic acids are formed by further sulfonation of the sulfophenylsulfamic acids (followed by solvolysis). The active species in solvolysis is the zwitterionic form, **13** (see II.B), and in sulfonation the undissociated form, **14**.

There are two independent Japanese reports[107,106] involving the preparation of orthanilic acid in high yield by reaction of aniline with sulfamic acid. In both reports ammonium phenylsulfamate could be isolated from the reaction medium, and on further heating at higher temperatures in situ the phenylsulfamate rearranged. Yamaguchi[107] has shown that heating ammonium phenylsulfamate with urea at 413 K for 8 h gave 60% orthanilic acid. In the second report[106] ammonium phenylsulfamate precipitated at 403 K from the reaction of aniline and sulfamic acid. At 413 K, the phenylsulfamate redissolved and was converted to orthanilic acid (42%) in a reaction conducted at 433 K for 12 h. The conditions used by Yamaguchi appear to be heterogeneous, while those of the second report are homogeneous at higher temperatures. There seems to be no explicit mechanistic information available on these two interesting examples of the phenylsulfamic acid rearrangement.

In very recent work, Kanetani and Yamaguchi[109] have shown that thermolysis of the neat sulfamate salts **17** or **18** at temperatures from 393 to 433 K and from 383 to 453 K, respectively, gives rise to substantial amounts of mono- and disulfonated products together with a smaller amount (up to 20%) of a 2-sulfo-4-methylphenylsulfamate, **19** (see eq 25).

Reaction of *n*-butylsulfamate (butylammonium salt) and 4-methylaniline gave **19**, as did the thermolysis of the 4-methylanilinium salt of *n*-butylsulfamic acid. The isolation of **19** from the phenylsulfamic acid rearrangement and its independent preparation confirm the findings of Cerfontain and Maarsen



regarding the intermediacy of such compounds in the rearrangement.

An interesting sulfamic acid rearrangement shown in eq 26 has been reported.[110] 2-Hydroxypropylamine is sulfated to give **20** and sulfamated to give **21** with sulfur trioxide. The latter compound rearranged in 100% yield in refluxing dry mesitylene. **21** could be synthesized unambiguously from 2-hydroxypropylamine and pyridine–sulfur trioxide.

$$\underset{\mathbf{21}}{MeCH(OH)CH_2NHSO_3H} \rightarrow \underset{\mathbf{20}}{MeCH(OSO_3H)CH_2NH_2} \quad (26)$$

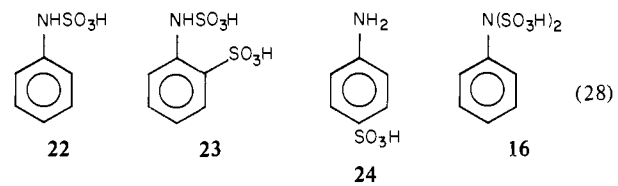
Cerfontain and Maarsen[111] have produced evidence which suggests that the sulfonation of aniline can occur by two independent and, at times, competing routes (eq 27) in ca. 100% H_2SO_4. Path A involves direct electrophilic attack by $H_3{}^+S_2O_7$

$$PhNH_3{}^+ \xrightarrow{A,\ H_3S_2O_7{}^+} o\text{-, } m\text{-, } p\text{-}HO_3SC_6H_4NH_3{}^+$$
$$\xrightarrow{B} PhHH_2{}^+SO_3{}^- \rightarrow PhNHSO_3H \rightarrow o\text{-, } m\text{-, } p\text{-}HO_3SC_6H_4NH_3{}^+ \quad (27)$$

on the anilinium ion and path B involves the intermediacy of phenylsulfamic acid. Increasing temperature and decreasing sulfuric acid concentration favor path B. Path A is followed exclusively at room temperature in a large excess of fuming sulfuric acid, but at higher temperatures with concentrated aqueous sulfuric acid and high substrate concentrations path B is followed.

The involvement of sulfamic acid rearrangements in the Piria reaction is uncertain, but the intermediacy of sulfamic acids is well established. Vrba and Allan[112] have produced chromatographic evidence to show that starting from nitrobenzene, nitrosobenzene, phenylhydroxylamine, or phenylhydroxylamine-*N*-sulfonic acid in weak acid with sodium sulfite at 298 K the same reduction products (in approximately the same proportions), **22**, **23**, **24**, and **16**, are obtained (eq 28).

$$C_6H_5NO_2,\ C_6H_5NO,\ C_6H_5NHOH,\ C_6H_5N(OH)SO_3H \rightarrow$$

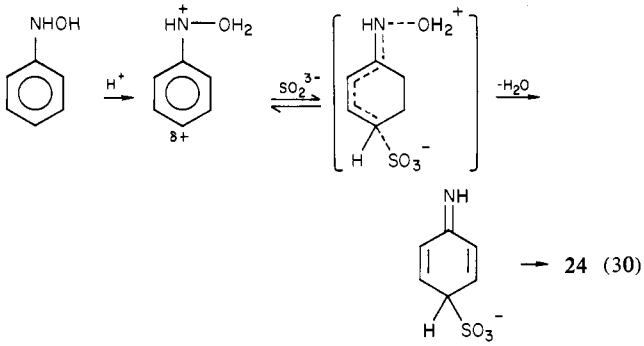


(28)

For the mechanism of the Piria reaction the sequence shown in eq 29 is supported by the work of Vrba and Allan.

$$C_6H_5NO_2 \xrightarrow[\text{slow}]{SO_3{}^{2-}} C_6H_5NO \xrightarrow{SO_3{}^{2-}} C_6H_5NHOH \xrightarrow{SO_3{}^{2-}}$$
$$C_6H_5N(OH)SO_3H \xrightarrow[H^+]{SO_3{}^{2-}} \mathbf{23} + \mathbf{24} + \mathbf{16} \xrightarrow{H^+}$$
$$\underset{\mathbf{25}}{C_6H_5NH_2} + o\text{-}HO_3SC_6H_4NH_2 + \mathbf{24} + \mathbf{22} \quad (29)$$

The anilinesulfonic acids produced in the Piria reaction are seen as arising by a mechanism such as that shown in eq 30. A similar mechanism is suggested to account for the formation of other products/intermediates. The final products of the Piria



→ 24 (30)

reaction are **25**, **24**, and aniline, and these will arise when the final acid hydrolysis step is allowed to proceed. Thus, **22** will give aniline, **23** will give **25**, **24** will remain unchanged, and **16**, depending on the extent of hydrolysis, may give rise to **22** and/or aniline. The key intermediates (reactants) in the Piria reaction appear to be phenylhydroxylamine and phenylhydroxylamine-*N*-sulfonic acid.

The Piria reduction of 1- and 2-nitronaphthalenes has also been studied by Vrba and Allan,[113] and a variety of products, whose formation can be accounted for in terms of the above ideas, were obtained.

D. Synthesis

1. Sulfamic Acid, Ammonium Sulfamate, etc.

The widely used manufacturing process (eq 31) involving the reaction of urea with fuming sulfuric acid has been modified to give yields >98%.[114] A purer product has been obtained from

$$(NH_2)_2CO + SO_3 \rightarrow H_2NCONHSO_3H + H_2SO_4 \rightarrow NH_2SO_3H + CO_2 \quad (31)$$

the same reaction by the use of an ion-exchange resin.[115] 90% of very pure sulfamic acid has been obtained from the hydrolysis of ammonium imidodisulfonate, $HN(SO_3NH_4)_2$, and the formation of side products has been inhibited.[116a] Optimum reaction conditions have been found for this process.[116b]

A method for preparing large single crystals of sulfamic acid has been described.[117] Industrial preparation of sulfamic acid and ammonium sulfamate by the reaction of ammonia and sulfur trioxide has been patented.[118] Japanese patents have appeared on the production of ammonium sulfamate by the same reaction[119,120] and by the reaction of ammonium imidodisulfonate or ammonium nitridotrisulfonate, $N(SO_3NH_4)_3$, with ammonia.[120] The oxidation of ammonium thiosulfate with compressed oxygen in aqueous ammonia solution gave mainly ammonium sulfamate (~60%) and sulfate (~35%) as products. The optimum conditions for the industrial manufacture were established.[121] A new industrial method for the manufacture of ammonium sulfamate from the hydrolysis of imidodisulfonates, obtained in the reaction of ammonia with sulfur trioxide at 523–543 K, has been proposed.[122]

Guanidine sulfamate, $H_2N(:NH)NH_2 \cdot NH_2SO_3H$, has been prepared by the reaction of $H_2NC(:NH)NHCH$ and ammonium sulfamate[123] and by the reaction under pressure of urea with ammonium sulfamate in the presence of ammonia gas.[124]

2. Aliphatic, Alicyclic, and Aromatic Sulfamates

Much of the work in this area has been pursued with a view toward elucidating the structure–activity relationships related to sweeteners of the cyclamate (*N*-cyclohexylsulfamate) type or to the development of new artificial sweeteners. The structure–taste aspects have been reviewed[125] and extended recently.[126,127] The synthetic aspects as such have not been reviewed.

a. Chlorosulfonic Acid

The basic procedure of Audrieth and Sveda[126] using chlorosulfonic acid as the sulfamating agent and the appropriate amine is the most commonly employed method. In a series of papers, Unterhalt and Böschemeyer have synthesized cycloalkylsulfamates of varying ring size[129] up to cyclononyl,[130] various mono- and disubstituted cyclopentyl- and cyclohexylsulfamates,[129,130] *cis*- and *trans*-2-methylcyclohexylsulfamates,[131] and some branched aliphatic sulfamates.[130] Nofre and Pautet have synthesized 25 different straight and branched aliphatic compounds[132] and cyclopentylmethylsulfamate[133] using almost exclusively the chlorosulfonic acid method. Benson and Spillane[125] synthesized a number of straight and branched aliphatic sulfamates, several secondary sulfamates, and 1-adamantyl- and cyclododecylsulfamates. A few new ring-substituted phenylsulfamates have been reported.[46]

b. Amine–Sulfur Trioxide and Sulfur Trioxide

High yields of cyclohexylsulfamate have been reported by Yamaguchi and Nakano[134] in the aqueous reaction of cyclohexylamine with $Me_3N–SO_3$, $Et_3N–SO_3$, $Me_2BzN–SO_3$, and *N*-methylmorpholine–SO_3. $Et_3N–SO_3$ on successive refluxing with cyclohexylamine in anhydrous dichloromethane gave a 90% yield of cyclohexylsulfamate.[135] Ethylsulfamate and several *N*-sulfonates, e.g., morpholine *N*-sulfonate, have been prepared by using $Me_3N–SO_3$ and the appropriate amines.[136] Pyridine–SO_3 has been used to prepare methylsulfamic acid.[132] Pyridine–$2SO_3$ has been used to prepare phenyl- (70%) and *N*-ethyl-*N*-phenylsulfamates (35%), several ring substituted phenylsulfamates (good yields), and 1-naphthylsulfamate.[137] Cyclohexyl-,[138] cyclopentyl-,[139] isobutyl-,[139] and isoamylsulfamates[136,139] have been prepared in good yields in a gas-phase reaction between sulfur trioxide and the vaporized amines. Both cyclohexyl- and isopropylsulfamic acids have been prepared by a novel route involving reaction of Schiff bases of the type $R^1N{=}CR^2R^3$ with SO_3.[140] A 98.5% yield of isopropylsulfamic acid was reported in reaction 32.

$$Me_2CHN{=}CHCHMe_2 + SO_3 \rightarrow Me_2CHNHSO_3H \quad (32)$$

Cyclohexyl-, propyl-, isopropyl-, and methylsulfamic acids have been prepared in good yield by the addition of ureas to SO_3 in an organic solvent.[141,142] Symmetrical ureas, RNHCONHR, were usually used, but in the case of methylsulfamic acid synthesis was achieved by using either MeNHCONHMe or $MeNHCONH_2$.[141]

Yamaguchi has given details of the reaction of isobutyl isocyanate with oleum to give isobutylsulfamate.[143] This reaction has been extended considerably by Hamprecht, Mangold, and König,[144] who have synthesized in more than 90% yield 19 sulfamic acids by the reaction of the appropriate isocyanates with oleum in an inert solvent (carbon tetrachloride, cyclohexane, chlorobenzene) (eq 33).

$$RNCO + H_2SO_4 \rightarrow RNHSO_3H + CO_2 \quad (33)$$

R included 2-norbornyl, cyclobutyl, cyclohexylethyl, 1,2-dimethylpropyl, dimethylhexyl, 1,3-dimethylbutyl, 1,2,2-trimethylpropyl, and 1-ethyl-2-methoxypropyl. This route appears to be highly suitable for the synthesis of a wide variety of sulfamates, provided the isocyanates are available. The yields obtained are far superior to those of the Audrieth and Sveda method.[126] It is not clear if this method is applicable to the synthesis of aromatic sulfamates.

c. Sulfur Dioxide and Bisulfites

Yamaguchi[145] has reacted isobutylhydroxylamine in benzene with sulfur dioxide to give isobutylsulfamic acid. Similarly, isoamylhydroxylamine in sodium bisulfite solution was reacted with sodium bisulfite to give isoamylsulfamic acid (56%).[146] The bisulfite method could also be used for preparing isobutylsulfamic acid.[145] These bisulfite reactions are examples of the Piria

reaction, where a nitro compound or one of its reduction products is reacted with bisulfites to yield sulfamic acids.[2] Cyclohexylsulfamic acid (74%) has been synthesized with zinc, tin, and iron catalysts.[147]

d. Sulfamic Acid and Sulfamates

About 90% yields of cyclohexyl-, isobutyl-, and isoamylsulfamates were obtained in the reaction of the appropriate amine in an inert solvent at high temperatures with sodium sulfamate, in the presence of small amounts of either sulfamic acid or acetic acid.[148] Two German patents describe the preparation of cyclohexyl- (90%)[149] and cyclopentylsulfamates (70%)[150] by the reaction of the amines with sulfamic acid in water. Yamaguchi prepared isoamylsulfamate by reaction at 443 K of sulfamic acid and isoamylamine.[151]

e. Miscellaneous

Yamaguchi has prepared in good yield several alkyl- and cyclohexylsulfamates by reaction of monosubstituted sulfamides, $RNHSO_2NH_2$, in water in an autoclave at elevated temperatures.[152,153] N,N'-Disubstituted sulfamides, including diphenylsulfamide, also cleave to give sulfamates under these conditions.[154] Cyclohexylsulfamate has also been prepared by the reaction of $SO_3(BuO)_3PO$ with cyclohexylamine[155] and by the hydrolysis of cyclohexylsulfamyloxysilane (prepared by reaction of cyclohexylaminosilane and SO_3).[156] Using ammonium imidodisulfonate, the preparation of isopropyl-, *n*-butyl-, isobutyl-, benzyl-, and 3-methylcyclopentylsulfamates has been described by Yamaguchi,[157] who reacted the appropriate amine in an autoclave at 443 K. A 20% yield of isopropylsulfamate was reported.

3. Long-Chain Sulfamates

These sulfamates are useful as surface-active agents. Dodecylsulfamic acid was prepared in 80% yield from $Et_3N–SO_3$, prepared in situ in chloroform, and *n*-dodecylamine.[156] Pentadecylsulfamate was prepared as described above (II.D.2.e),[157] and heptadecylsulfamate has been prepared by the same group.[159] A Polish group has prepared octadecylsulfamate by the Audrieth and Sveda method, and they report that it has a high foaming ability and can be used as an emulsifier for water–oil systems.[160]

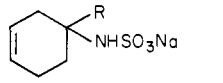
A French patent gives the preparation of 3-(laurylamino)-propylsulfamate (**26**) by reaction of $C_{12}H_{25}NH(CH_2)_3NH_2$ with chlorosulfonic and chloroethylsulfonic acids.[161] This sulfamate is used as a germicide. Compounds such as **27**, where R is

$C_{12}H_{25}NHCH_2CH_2CH_2NHSO_3H$ (**26**) $\quad$ p-$RC_6H_4NHSO_3^-M^+$ (**27**)

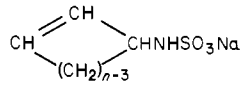
a straight-chain C_{10-16} alkyl group and M is an alkali metal or the ammonium ion, have been synthesized by a sequence involving nitration of a p-RC_6H_5 alkylbenzene, catalytic reduction to the amine, and sulfamation with chlorobenzenesulfonic acid. These compounds are useful as solubilizing agents for slow-dissolving organic acids and as detergents.[162]

4. Sulfamates with a Carbon–Carbon Double Bond

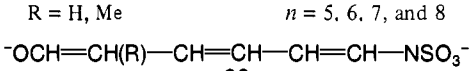
Unsaturated alkyl sulfamates with C_{10-22} chains have been prepared[163] by reaction of the appropriate alkenol with sulfamide in dioxane. Erucyl- and oleylsulfamates have been prepared in this way. Allylsulfamate has been prepared by a method cited above (see II.D.2.e),[157] and diallylsulfamic acid, $(CH_2{=}CHCH_2)_2NSO_3H$, has been reported.[164] An interesting series of cycloalkenylsulfamates, **28** and **29**, have been made by sulfamation of the appropriate amines with $Me_3N–SO_3$.[165] Base attack on 3-substituted pyridinium sulfonates results in ring opening and gives rise to the unstable sulfamate **30**, isolated in about 70% yield as the disodium salt.[166]



28
R = H, Me



29
n = 5, 6, 7, and 8



30
R = Me, OMe, H

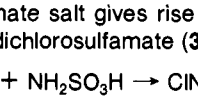
5. Halosulfamates

The reaction of excess hypochlorite with sulfamic acid or a sulfamate salt gives rise to both *N*-chlorosulfamate (**31**) and *N,N*-dichlorosulfamate (**32**).[167] **31** and **32** are apparently reversibly formed. Both compound are unstable and have not been isolated. In earlier work, Traube reported the isolation of **31** in the form of some of its crystalline salts.[168] The dichlorosulfamate is also reported in a French patent.[169] Stabilized aqueous solutions of dichlorosulfamic acid have been prepared by use of buffers which maintain the pH between 4 and 11.[170] Greater than 90% retention of active chlorine could be achieved after 12 days.[171] The formation of *N,N*-difluorosulfamic acid has been postulated in the reaction of HNF_2 and SO_3.[172]

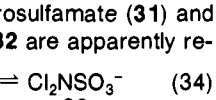
$$HClO + NH_2SO_3H \rightarrow \underset{\textbf{31}}{ClNHSO_3^-} + H_2O \rightleftharpoons \underset{\textbf{32}}{Cl_2NSO_3^-} \qquad (34)$$

6. Heterocyclic Sulfamates

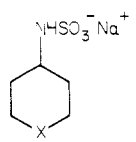
The interesting tetrahydro-2*H*-thiopyransulfamates **33** and **34** have been reported.[173] **33** (R = H, 42%) was prepared by reaction of $Me_3N–SO_3$ in chloroform with tetrahydro-2*H*-thiopyran-4-amine. **34** (R = H) was formed from **33** (R = H) by using H_2O_2 in glacial acetic acid/acetic anhydride. **33** (R = $CH_3(CH_2)_3$) was prepared by reduction of tetrahydro-2*H*-thiopyran-4-one with sodium cyanoborohydride and reaction with *n*-butylamine, followed by sulfamation as before. **33** and **34** are sweet despite the fact that the amino hydrogen has been replaced in most of them. The presence of the grouping $NHSO_3^-$ was thought to be a necessary condition for sweetness in cyclamate-type compounds.[125,126] Other cyclamate analogues prepared include **35**,[174] **36**,[175], **37**,[125,157] and **38**.[125,157] **37** and **38** were prepared both by sulfamation with chlorosulfonic acid[125] and with ammonium imidodisulfonate in an autoclave.[157] In the preparation of **36**, Michael addition involving methyl 3-mercaptopropionate and methyl crotonate and subsequent



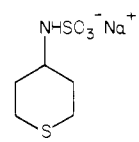
33
R = H, Et, *n*-Bu, $HOCH_2CH_2$



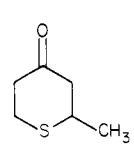
34
R = H, Et, *n*-Bu



35
X = O, S



36



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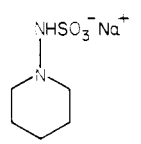

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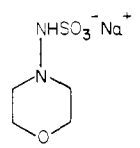
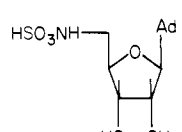


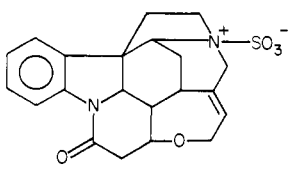
38



40

Dieckmann condensation were used to prepare the ketone **39**.[175] 5′-Sulfamino-5′-deoxyadenosine (**40**) was prepared by reaction of $Me_3N–SO_3$ with 5′-amino-5′-deoxyadenosine in anhydrous methanol.[176]

In connection with a mechanistic study of the reaction of amine oxides with SO_2, Edwards and Whiting[177] have prepared a number of sulfamates of several alkaloids and heterocycles. Methods used were rearrangement of sulfitoamines to sulfamic acids, pyridine–sulfur trioxide, chlorosulfonic acid in chloroform, sulfur trioxide in 1,2-dichloroethane, and sodium dithionate in water. Strychnine- (**41**), cinchonine- (**42**, X = H), quinine- (**42**, X = OMe), and harminesulfamates (**43**) were prepared and also 6-methoxyquinoline- (**44**) and 2-phenylimidazo[1,2-*a*]pyridine-sulfamates (**45**).



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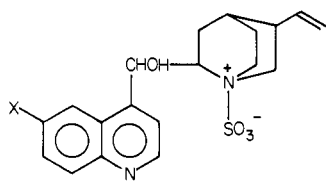
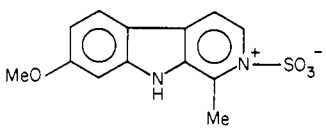


42
X = H, OMe



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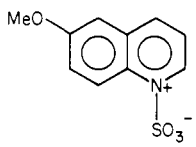

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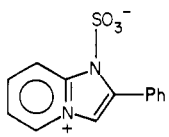

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7. *Sulfamate Salts*

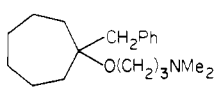
A very large number of sulfamate salts of a variety of basic compounds have been reported. Most of these compounds have been prepared because of their use or potential in medicine.

a. $NH_2SO_3^-$ Salts

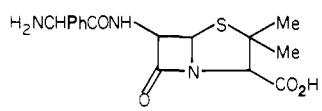
Quinine,[176] urotropine,[179] erythromycin,[160,161] and hycanthone[162] sulfamate salts have been prepared. The surfactants $R(CH_2)_3N[(CH_2CH(OH)CH_2O)_nX][CH_2CH(OH)CH_2O]_nSO_3NH_4$ with R = C_{6-16} alkyl or alkoxy, X = H or SO_3NH_4, n = 2–4, were prepared.[163] A large number of triarylmethanesulfamate dyes have been made.[164,165]

b. $c\text{-}C_6H_{11}NHSO_3^-$ Salts

Cyclohexylsulfamate salts of erythromycin,[161] choline and dicholine,[166] neomycin B hexakis,[167] and acyloxypropoxyindoles[168] have been made. The cyclohexylsulfamate salt of **46**[169,190] has antitumor and vasodilatory activity. A number of quaternary ammonium cyclohexylsulfamate salts which are biocidally active have been reported.[191]



46



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c. Alkyl- and Arylsulfamate Salts

Attempts to obtain antibiotics with prolonged activity and the absence of side effects have lead to the synthesis of a number of *N*-(*n*-alkyl)sulfamate salts of tetracyclines. *n*-Butyl-, *n*-hexyl-, *n*-dodecyl-, and *n*-hexadecylsulfamates have been prepared in a warm alcohol medium.[191–194] *n*-Butyl-, *n*-pentyl-, *n*-hexyl-, and *n*-dodecylsulfamates of D-α-aminobenzylpenicillin (**47**) have been made in the same laboratory.[195,196] Eight alkylsulfamate salts of phenothiazine compounds are reported.[197] The phenyl- and *N*-methyl-*N*-phenylsulfamate salts of lincomycin[196] are less bitter than lincomycin, and they increase the stability of the antibiotic preparations. Quaternary ammonium salts of phenyl-, *n*-hexyl-, and piperidinesulfamates have been reported.[191] These compounds, of the general formula $RNHSO_3^-N^+R^1R^2R^3R^4$ (typically $R^1 = R^2$ = Me, R^3 = benzyl, R^4 = dodecyl), are biocidally active.

E. Sulfation and Sulfonation

1. *Sulfation*

This process involves O-sulfonation of alcohols, as outlined in eq 20 (II.B.3). Long-chain alcohols give rise to alkyl sulfates which are useful as surface-active compounds and detergents, and much interest has centered on the sulfation of such compounds. Gilbert[199] has briefly reviewed the use of sulfamic acid as a sulfating agent.

a. General

The use of amine oxides,[200] urea,[201,202] and thiourea[202] as catalysts for the formation of alkyl sulfates in the reaction of sulfamic acid with alcohols has been supported. The inhibiting effect of acids and bases on the sulfation of methanol with sulfamic acid has been noted.[203] The formation of a cake in the reaction mixture during the sulfation of various aliphatic alcohols with sulfamic acid has interfered with the process, but this disadvantage can be overcome by using small amounts of $Me_3N–SO_3$.[204] An analytical method claimed to be superior to previously reported methods for the determination of ammonium alkyl sulfates has been described. It involves potentiometric titration with strong base.[205]

b. Long-Chain Alcohols

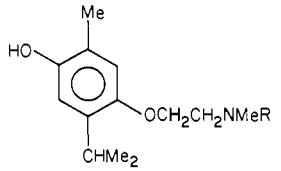
The sulfoesterification of higher aliphatic alcohols has been reviewed some years ago.[206] The catalytic effect of a large number of Lewis bases on the reaction of cetyl alcohol with sulfamic acid has been probed.[207] The decreasing catalytic activity of the catalysts correlated fairly well with diminishing electron-donating ability. The same Russian group has made detailed studies on the sulfation with sulfamic acid of C_{10-16} alcohols.[208–210] *N*-Methylpyrrolidone[211] and a di- or polyphosphate[212] have also been used as catalysts for the sulfation of higher alcohols. Two groups have independently sulfated the unsaturated compound oleyl alcohol.[213,214] Ammonium imidodisulfonate, with $Me_3N–SO_3$, DMF, or urea, has been used to sulfate higher alcohols.[215]

Secondary alcohols have been successfully sulfated in 90% yields with sulfamic acid and urea or DMF.[216] These alcohols were of the type $C_{19-29}H_{27-39}CH_2OH$. With C_{12-20} secondary alcohols similar and other catalysts gave a maximum yield of 50%.[217] Mixtures of primary and secondary higher alcohols have been sulfated with sulfamic acid and urea.[216,219] C_{6-25} secondary alcohols, notably 2-octanol, 2-pentacosanol, or 2-, 3-, and 4-dodecanols (mixed), have been quantitatively sulfated with sulfamic acid and ethylene (propylene) oxides.[220a] 2-Hydroxyethyl methacrylate gave the ammonium salt of (sulfatoethyl)methacrylate on treatment with sulfamic acid.[220b]

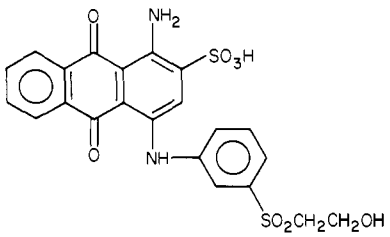
c. Other Compounds

The sulfates of a number of steroids have been prepared by using sulfamic acid and pyridine as catalysts. Yields ranging from 30 to 66% have been achieved with the following steroids: cholesterol,[221,222] testosterone,[221] pregnenolone,[221,222] dehydroisoandrosterone,[221] estrone,[221] 2-methoxyestrone,[221] ethy-

nylestradiol,[221] and ethynylestradiol 3-methyl ether.[221] The syntheses of vitamin D_2 sulfate,[223] using sulfamic acid, of adenosine 5′-sulfate (65%) and D-galactose 6-sulfate (55%), using cyclohexylsulfamic acid in anhydrous pyridine, and of riboflavin sulfate (23%), using morpholine-*N*-sulfonic acid in Me_2SO–pyridine, have been achieved.[224] Sulfates of **48**[225] and **49**[226] were prepared with sulfamic acid.



48, R = H, Me



49

Silicone sulfates, which are useful as surfactants, foaming agents, and emulsifiers, have been prepared by reaction of silicone alcohols with sulfamic acid in the presence of urea.[227]

2. Sulfonation

Although sulfamic acid has been widely used as sulfating[226] (preceding section) and sulfamating[229] (see II.D.2.d) agents, its use in sulfonation has been minor.[230] Two papers which have appeared in recent years show that alkylsulfamic acids can be used as efficient sulfonating agents to sulfonate aniline,[231] *N,N*-dimethylaniline,[231] anisole,[231] and 4-methylaniline.[109] *n*-Butyl- and cyclohexylsulfamic acids are excellent sulfonating agents at 423–468 K for the first three compounds. The yields of the corresponding para-substituted benzenesulfonic acids are ≥90%. When the sulfamic acids are used as their alkylammonium salts, i.e., $RNHSO_3^-RNH_3^+$ (**50**), or when morpholinium morpholine-*N*-sulfonate is used, they are substantially less effective as sulfonating agents and fail, for example, to sulfonate anisole. The mechanism of these transsulfonation reactions is seen as involving the zwitterionic form of the sulfamic acids, which may dissociate to give sulfur trioxide, with the aromatic nuclei present then acting as traps for the liberated sulfur trioxide (eq 35). The lower reactivity of the alkylammonium salts which

$$\underset{\mathbf{51}}{RNH_2^+SO_3^-} \rightarrow RNH_2 + SO_3 \xrightarrow{ArH} ArSO_3H \qquad (35)$$

exist not as internal zwitterions (**51**) but as the true salts (**50**) may then be accounted for by the greater difficulty of generating sulfur trioxide from such species. A second possible mechanism may involve direct sulfonation of the amine by the sulfamic acid (or sulfamic acid zwitterion). There are a number of precedents for such a sulfonation mechanism.[232]

In the second, very recent, study Kanetani and Yamaguchi[109] have shown that in the reaction of **50** (R = *n*-Bu) with 4-methylaniline a variety of sulfonated products can form depending on the reaction temperature. At lower temperatures 4-methylphenylsulfamate was the major product, and the hitherto unisolated compound, 2-sulfo-4-methylphenylsulfamate (**52**), was also formed. However, at higher temperatures the main products were 4-methylaniline-2-sulfonate and 4-methylaniline-2,6-disulfonate. The isolation and characterization of **52** are of importance in connection with the rearrangement of arylsulfamic acids (see II.C). These authors favor an initial dissociation of **50** (R = *n*-Bu) into *n*-butylamine and the free acid, followed by an equilibrium between *n*-$BuNHSO_3H$ and **51** (R = *n*-Bu) (eq 36). **51** (R = *n*-Bu) is considered to be the sulfonating species

$$\mathbf{50} \rightleftharpoons RNH_2 + RNHSO_3H \rightleftharpoons \mathbf{51} \qquad (36)$$

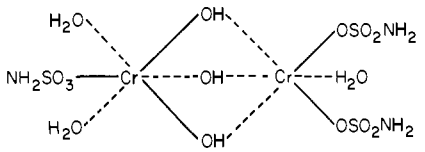
and the sulfonation step is regarded as being a bimolecular nucleophilic attack by the 4-methylaniline on **51** to give 4-methylphenylsulfamate. Similar schemes are presented to account for the formation of **52** and the ring mono- and disulfonates.

The reaction of isobutene, CH_2=C(Me)Me, with sulfamic acid can apparently lead to different sulfonates under analogous reaction conditions.[233,234] Thus, a mixture of isobutene, acetic acid, and sulfamic acid on heating at 353 K (300 mm pressure) for 4 h gives 2-methyl-2-propenesulfonate,[233] CH_2=C(Me)-$CH_2SO_3^-$, but isobutene (at 300 mm) when passed at 353 K into a mixture of 400 g of acetic acid and 48.6 g of sulfamic acid which was stirred for 4 h gave, after distillation to remove the acetic acid, 78 g of 2,2-dimethyl-1-propenesulfonate, Me_2=$CHSO_3^-$.

F. Sulfamate–Metal Bonds

1. Vanadium, Chromium, Manganese, and Iron Subgroups

A polarographic and spectrophotometric study of V^V (presumably vanadyl ion) in sulfamic acid solution suggested that complex formation between the metal cation and the sulfamate anion did not occur.[235] The chromium sulfamate **53** loses three



53

molecules of water on heating to 423 K, and it undergoes a structural change at this temperature.[236] The same Russian group[237] has prepared tris(ethylenediamine)chromium sulfamate, $Cr(en)_3(SO_3NH_2)_3$, from chromium sulfate, ethylenediamine, and barium sulfamate. Detailed thermogravimetric analysis suggested that the path shown in eq 37 was followed in its decomposition.

$$2Cr(en)_3(SO_3NH_2)_3 \xrightarrow{633\ K} 2Cr(SO_3NH_2)_3 \xrightarrow{733\ K} Cr_2(SO_4)_3 \xrightarrow{793\ K} CrO_3 \qquad (37)$$

The X-ray diffraction patterns of the tris complex are compared with those of hydroxochromium(III) sulfamate (**53**). The complex $[Cr(H_2O)_3(NH_2SO_3)_3]$[236] involves nitrogen coordinated sulfamate and thus differs from the related zinc, cobalt, and nickel complexes of general formula $M(H_2O)_4(NH_2SO_3)_2$, prepared by the same group, which involve oxygen coordination. No evidence was obtained for complex formation of sulfamate ions with either Mo^{VI} or W^{VI} when they were studied in sulfamic acid solution.[235]

The rate of oxidation of ferrous sulfamate in 1–7 M nitric acid is first order in ferrous ion and has an activation energy of 99 K J mol^{-1}.[239] The sulfamate was moderately stable at room temperature and low acid concentrations, but the rate of oxidation to ferric ion rose quickly at higher temperatures of acid concentrations. The radiolytic oxidation of ferrous sulfamate in feed solutions for solvent purification of Np^{237} and Pu^{236} from spent nuclear fuels has been investigated.[240] The process of extracting plutonium from uranium by reducing Pu^{IV} was studied by using ferrous sulfamate and hydrazine as reductants.[241] A mixture of the two reductants gave the best results.

Ferrous sulfamate can be prepared directly and its hydrolysis inhibited by passing oxygen into a suspension of the powdered metal in aqueous sulfamic acid until no unreacted metal remains

or until the pH reaches 4–6.5. The best reaction temperature is 308–323 K.[242]

Sulfamate complexes are frequently prepared by direct reaction of sulfamate ion with a metal. The new complex, sulfamatopentaammineruthenium(III), **54**, has been prepared by a novel route in which $[Ru(NH_3)_6]^{3+}$ reacts with thiosulfate or thiophosphate in the presence of oxygen.[243] An infrared study of **54** and comparison with the infrared spectra of the related sulfamate complexes of cobalt(III) ammines, which are known to bond through nitrogen, confirmed that in **54** the sulfamate–metal bond is through nitrogen.

$Ru(NH_3)_5NHSO_3^+$ (**54**) $\qquad$ $K_3[M(NH_2SO_3)Cl_5]$ (**55**), M = Ru, Os

The pK_a for the acid equilibrium shown in eq 38 has been

$$Ru(NH_3)_5NH_2SO_3^{2+} \rightleftharpoons \mathbf{54} + H^+ \qquad (38)$$

determined as 2.6 at 0.1 M ionic strength at 298 K. The new complexes of ruthenium and osmium (**55**) have been prepared from potassium hexachlororuthenate(III) and sodium hexachloroosmate(IV), respectively, by refluxing or warming with sulfamic acid.[244] Infrared spectroscopic data suggest that sulfamate is bonded to the metal through nitrogen.

2. Cobalt and Nickel Subgroups

The preparation of cobalt and nickel sulfamates has been described as above for ferrous sulfamate.[242] A number of physical measurements, e.g., freezing point depression, emf of cells for sulfamic acid and sulfamates, and activity coefficients, have been carried out with cobalt and nickel sulfamates.[245]

Po and Jordan[246] have prepared the sulfamate complex of pentaamminecobalt(III), **56**, and have studied its rate of alkaline hydrolysis. The pK_a for the acid ionization shown in eq 39 is

$$(NH_3)_5CoNH_2SO_3^{2+} \rightleftharpoons (NH_3)_5CoNHSO_3^+ + H^+ \qquad (39)$$

(**56**) (**57**)

5.83 at 298 K (ionic strength ~0.004). In alkaline hydrolysis, **57** will be the form mainly present, and the rate law for the hydrolysis has terms independent of hydroxide ion and first order in hydroxide ion. Two reaction paths, shown in eq 40 and 41,

$$(NH_3)_5CoNHSO_3^+ + OH^- \rightarrow (NH_3)_5CoOH^{2+} + NHSO_3^{2-} \qquad (40)$$

$$(NH_3)_5CoNH_2SO_3^{2+} + OH^- \rightarrow (NH_3)_5CoOH^{2+} + NH_2SO_3^- \qquad (41)$$

appear to occur. A S_N1cB mechanism would appear to be probable.

In a subsequent paper,[247] the hydrolysis of **56** in aqueous acid has been studied. The first step of the reaction produces a mixture of the N- and O-bonded sulfamate complexes. Subsequent hydrolysis of this equilibrium mixture gives $[Co(NH_3)_5OH_2]^{3+}$. The cobalt and nickel complexes $[M(H_2O)_4(NH_2SO_3)_2]$ (M = Co or Ni) have oxygen coordination between the metal and the sulfamate function in contrast to the analogous chromium complex (see II.F.1).[236] Compounds **55** (M = Rh, Ir) have also been prepared in the same manner as the ruthenium and osmium complexes.[244] In an elegant study, Basolo prepared the new complex $[Ir(NH_3)_5NH_2SO_3]^{2+}$ in three different ways.[246] First, working on the idea that the coordinated nitrene **58**, which behaves as a soft Lewis acid, might be trapped by sulfite ion, they generated the species by photochemical means and then trapped it (eq 42). Incidentally, the analogous ruthenium(III) complex can be prepared by the same route, but

$$[(NH_3)_5IrN_3]^{2+} + H^+ \xrightarrow{h\nu} [(NH_3)_5Ir(NH)]^{3+} + N_2 \xrightarrow{SO_3^{2-}} [(NH_3)_5IrNH_2SO_3]^{2+} \qquad (42)$$

(**58**) (**59**)

of course it was reported earlier.[243] Second, the aquo complex **60** and sulfamate ion gave a product with the same properties as **59**. Third, the reaction of the hydroxylamine *O*-sulfate complex with sulfite ion gave an identical product.

$$[Ir(NH_3)_5H_2O]^{3+} + NH_2SO_3^- \rightarrow [Ir(NH_3)_5NH_2SO_3]^{2+} + H_2O \qquad (43)$$

(**60**)

$$[Ir(NH_3)_5NH_2OSO_3]^{2+} + SO_3^{2-} \rightarrow [Ir(NH_3)_5(NH_2SO_3)]^{2+} + SO_4^{2-} \qquad (44)$$

Nickel sulfamate can be formed from a sulfamic acid and nickel carbonate in the pH range 2.5–4.8.[249] The effects of acidity on the mechanism of the electrochemical reduction of aquo complexes of nickel from sulfamate electrolytes have been described.[250] The ionization constant for the second step of sulfamate ion dissociation was determined.

The palladium complex $K_2[Pd(NH_2SO_3)_2Cl_2]$ was prepared from the reaction of sulfamic acid and potassium tetrachloropalladate(II).[244]

Thermal isomerization of the platinum(II) sulfamate complex **61** to the trans isomer was studied recently.[251]

cis-$K_2[Pt(NH_2SO_3)_2Cl_2]\cdot 2H_2O \rightarrow$ *trans*-$K_2[Pt(NH_2SO_3)Cl_2]$

(**61**)

3. Copper and Zinc Subgroups

Copper sulfamate has been prepared by passing oxygen into a suspension of the metal in sulfamic acid.[242] Copper sulfamate complexes recently reported include the bishalogenocuprates,[252] the pyridine complex **62**,[236] and the ethylenediamine complex **63**.[236]

$M_2[Cu(NH_2SO_3)X_2]$, M = K, NH_4^+; X = Cl, Br $\qquad$ $[Cu(py)_4(NH_2SO_3)_2]$ (**62**)

$[Cu(en)_2(NH_2SO_3)_2]$ (**63**)

Interestingly, two forms of copper sulfamate, $Cu(NH_2SO_3)_2\cdot 2H_2O$, have been recognized. They appear to be linkage isomers involving N- and O-linked sulfamate groups.[236] The stability constant for copper sulfamate has been determined from a polarographic study.[253]

Zinc and cadmium sulfamates have been prepared by passing oxygen into a suspension of the metal in sulfamic acid.[242] Emf measurements, activity coefficient determinations, and freezing point depression measurements have been made on these sulfamates.[245] Stability constants were calculated for zinc and cadmium sulfamates at 298 K from potentiometric data on measurements in sodium sulfamate solutions.[254] The complex $[Zn(H_2O)_4(NH_2SO_3)_2]$ has sulfamate coordinated to the metal via oxygen.[236] A polarographic study of the neutral sulfamate solutions of Zn^{II} and Cd^{II} has shown that complexes involving one, two, and (in the case of zinc) three sulfamate anions, as ligands, are formed.[253] The stability constants of these complexes have been determined. The thermolysis of some mercury imidodisulfates[57-59] has been discussed (II.A.5).

4. Groups 3 and 4

Aluminum sulfamate has been reported[242] and the thallium sulfamate complex **64** has been prepared.[255]

$$Me_2TlNMe_2 + SO_3 \rightarrow [Me_2Tl][Me_2NSO_3] \qquad (45)$$

(**64**)

Tin(II) sulfamate has been prepared by addition of the metal to a solution of copper sulfamate and sulfamic acid.[256] The sulfamate formed is thought to be the normal tin(II) compound $Sn(NH_2SO_3)_2$, though it cannot be isolated pure (only with admixed sulfamic acid). It undergoes thermal decomposition as shown in eq 46.

$$Sn(NH_2SO_3)_2 \xrightarrow[\text{In vacuo}]{393\ K} NH_2SO_2NH_2 + SnSO_4 \xrightarrow{651\ K} SnO_2 + SO_2 \quad (46)$$

$Sn(MeNHSO_3)_2$ has also been prepared and *N*-methylsulfamide has been formed in its thermal decomposition. Pentakis(thiourea)tin(II) sulfamate (**65**) has been made by the same group, and in later studies they report ^{119}Sn Mössbauer parameters for it and for tin(II) sulfamate.[257] Thermal decomposition of **65** has

$$Sn(tu)_5(NH_2SO_3)_2 \cdot H_2O$$
65, tu = thiourea

been studied and found to give the same products as tin(II) sulfamate. Infrared data suggest that the Sn–S bonds are weak in **65**.[257] A variety of tin sulfamate complexes corresponding to **66**,[258-260] **67**,[261] and **68**[262] have been prepared, generally by reaction of sulfamic acid with an oxide. Typically, sulfamic acid

$R_3SnNH_2SO_3$ **66** R = *n*-Pr, *n*-Bu, Ph

$R_2PhSnNH_2SO_3$ **67** R = *n*-Bu, Ph

$R_aSn(NH_2SO_3)_{4-a}$ **68** R = alkyl C_{1-4}, Ph; a = 2–3

was heated with bis(tributyl) oxide, $(n\text{-}Bu_3)_2O$, in a suitable solvent.[260] At lower temperatures tributylstannylation of the sulfamic acid hydroxyl group occurs, while at higher temperatures both the hydroxyl and the amine groups undergo tributylstannylation to give $Bu_3SnNHSO_3SnBu_3$. Bis(tributyltin) iminodisulfonate and ureidosulfonate have been prepared by similar methods.[263]

A polarographic study of neutral sulfamate solutions of Pb^{II} has shown that metal cation complexes involving one and two sulfamate ligands, **69** and **70**,[253] are formed. The stability

$[Pb(NH_2SO_3)]^+$ **69** $[Pb(NH_2SO_3)_2]$ **70**

constants of these complexes have been determined. Activity coefficients, freezing point depression data, and some emf measurements have been made on lead sulfamate solutions.[245]

5. Lanthanide and Actinide Series

In a single paper, the preparation of all the lanthanide(III) sulfamates (except those of europium, thulium, and lutetium) from the reaction of sulfamic acid and the corresponding carbonates is described.[264] Solubility, analytical (% lanthanide and % sulfamate), infrared, and X-ray (powder diffraction method) data were determined. The X-ray data show the existence of two isomorphous series. A preparation containing didymium sulfamate, prepared from the carbonate and sulfamic acid, has been patented as an antiperspirant.[265] Didymium is a special type of Corning glass used as a filter in spectrophotometry. Holmium, one of the lanthanides, is also used as a filter, and this reference to didymium was thus included here.

The thermal decomposition of uranyl sulfamate[56] (prepared by Capestan[266]) has been dealt with (see II.A.5). No evidence for the formation of a complex between U^{VI} and sulfamate was found from a polarographic and spectrophotometric study of U^{VI} in sulfamic acid solution.[235]

Sulfamic acid has been used as a solvent for plutonium metal, and a spectrophotometric study of plutonium complexes in aqueous sulfamate media has shown that Pu^{IV} is complexed by sulfamate ion, but no evidence of sulfamate complexes of Pu^{III} or Pu^{VI} was found.[267]

G. Analytical and Industrial Aspects

1. Analytical

a. Use of Sulfamic Acid in Analysis

Sulfamic acid has been recommended as a standard in acid–base titrimetry and detailed purification procedures have been given.[266,269] A very precise method for the assay of standard sulfamic acid using differential electrolytic potentiometry has been described.[270] Sulfamic acid has also been used as a standard in nonaqueous titrimetry.[271]

Sulfamic acid is a useful trap for nitroso species in the denitrosation of *N*-methyl-*N*-nitrosoaniline[272] and in the reaction of thiourea and *N*-nitroso-*N*-methylaniline.[273] Examples of the determination of nitrite ion with sulfamic acid continue to appear in the literature. Nitrite (in the presence of nitrate, sulfite, sulfate, or phosphate) was determined by potentiometric titration with sulfamic acid. A relative error of 0.2–1.3% is reported.[274] Nitrite in phosphate treatment solutions has been determined from the amount of nitrogen generated when sulfamic acid was added to the treatment solution in a fermentation tube. The method seems to be both rapid and accurate.[275] The photometric determination of nitrite with 1-naphthylamine and sulfamic acid in uranium and plutonium process solutions has been described.[276] A method for the simultaneous determination of nitrite and sulfamate in palladium-plating baths has been reported.[277] The determination of sulfamates in scrubbing solutions used for flue gas treatments has been carried out by hydrolyzing them to ammonia in acid solutions.[278]

Microgasometric determination of both inorganic and organic nitrates has been carried out by reducing them to N_2O with sulfamic acid.[279] Trace amounts of sulfate ion in industrial sulfamic acid have been determined nephelometrically.[280] Sulfamic acid has been used in the determination of ozone in air[281] and for the preservation of urine, and it did not then interfere with the determination of urea, uric acid, creatinine, glucose, phosphorus, and a number of metals.[282]

b. Detection and Determination of Sulfamic Acid

A number of spot tests for the detection of sulfamic acid and some N-substituted sulfamates have been developed.[283] These are based on the three reactions shown in eq 47–49. Equation

$$H_2NSO_3H + C_6H_5CHOHCOC_6H_5 \rightarrow C_6H_7COCOC_6H_5 + H_2O + NH_3 + SO_2 \quad (47)$$

$$(CH_2)_6N_4 + 6NH_2SO_3H \xrightarrow{433\ K} 6CH_2NSO_3H + 4NH_3 \quad (48)$$

$$2NH_2SO_3^- + 3[O] \rightarrow 2SO_4^{2-} + 2H^+ + H_2O \quad (49)$$

47 illustrates the fusion with benzoin which works for sulfamic acid only. The liberated sulfur dioxide can be detected by using suitable tests. Equation 48 illustrates dry heating with hexaammine; detection of the liberated ammonia gas is indicative of the presence of sulfamic acid. Equation 49 involves oxidation with permanganate and this test works well for a variety of N-substituted sulfamates, e.g., cyclohexyl-, substituted cyclohexyl-, and 3-methylcyclopentylsulfamates. Quantitative separation of ammonium sulfamate, ammonium imidodisulfonate, ammonium sulfate, sulfamide, and other N–S compounds has been reported by using ascending paper chromatography.[284]

The potentiometric determination of sulfamate ion (from nickel and chromium sulfamates) and of sulfamic acid by titration with sodium nitrite has been reported.[285] Similarly, sodium nitrite has been used for the amperometric titration of sulfamic acid.[286] Coulometric titration of sulfamic acid has also been used.[287] Two different colorimetric methods capable of determining sulfamic acid with an accuracy of 98–102% have been developed.[288] Gas chromatography of the trimethylsilyl derivative of ammonium sulfamate has been described.[289]

c. Detection and Determination of Cyclohexylsulfamate and Related Sulfamates

Richardson[290] has reviewed the analytical chemistry of cyclamates up to 1966, and only papers appearing after this date

are dealt with in this section. The determination of cyclamate, the artificial sweetener, by reaction with nitrous acid has been examined in detail. Under strong nitrosating conditions, cyclohexanol forms and is converted to cyclohexyl nitrite (76%) together with cyclohexene (23%).[291]

$$NO^+ + C_6H_{11}NHSO_3H \rightarrow H_2SO_4 + N_2 + C_6H_{11}^+ \quad (50)$$

In later papers the same group has shown that cyclamate can be determined either by diazotization of cyclohexyl nitrite with sulfanilamide and then coupling with 2-aminoethyl-1-naphthylamine[292] or by colorimetric determination of unconsumed nitrous acid.[293] For these methods the cyclamate should be present at a concentration of approximately 1 mg/mL. Another group has determined the cyclohexene liberated by GC.[294] Cyclohexyl nitrite can also be converted to cyclohexanol with sulfamic acid, and the absorption produced by the reaction of cyclohexanol with a vanillin–H_2SO_4 reagent can then be determined at 655 nm.[295]

The other major type of method reported since Richardson's review involves hydrolysis of cyclamate and determination of the cyclohexylamine produced. The quantitative hydrolysis of cyclamate can be achieved in aqueous 1.3 M hydrochloric acid at 398 K under 15-psi pressure with a half-life of 1.17 h.[296] Subsequent coupling of the cyclohexylamine produced with alcoholic 1,4-benzoquinone gives a product which can be determined by its absorption at 493 nm. A less forcing but quantitative hydrolysis procedure and the same coupling method have been used to determine cyclopentyl-,[297] cycloheptyl-,[298] cyclooctyl-,[298] and cyclopentylmethylsulfamates,[299] all of which are sweet. An automated method for the determination of cyclohexylamine in cyclamates based on reaction with 4-nitroaniline has been reported.[300a] Fluorimetric determination of cyclamate by hydrolysis in a sodium bicarbonate–acetone media, reaction of the liberated cyclohexylamine with 5-dimethylaminonaphthalene-1-sulfonyl chloride, and subsequent fluorescence measurement at 497 nm have been reported.[300b] An interesting method for determining cyclamate quantitatively involves the addition of excess hypochlorite or chlorine water to an aqueous acid solution of cyclamate, whereupon reaction 51 occurs. The *N,N*-dichlorocyclohexylamine absorbs in the UV

$$C_6H_{11}NHSO_3H + 2Cl_2 + H_2O \rightarrow C_6H_{11}NCl_2 + 2HCl + H_2SO_4 \quad (51)$$

region and can be determined.[301] Percent recoveries for cyclamate determinations in a variety of foods were on average 102 ± 1.8%.

Sodium cyclamate has been determined by isotope dilution analysis. Cyclamate-^{35}S was synthesized from cyclohexyl isocyanate and $H_2{}^{35}SO_4$.[302] Renwick and Williams have of course used cyclamate-^{14}C in some of their studies.[303a,303b]

TLC can be used to detect cyclamate in the presence of saccharin and dulcin[304] and in the presence of saccharin and sorbitol.[305] Cyclamate and saccharin can be detected together, with a detection limit of 1–5 μg, using TLC.[306] Cyclamate, saccharin, and dulcin have been determined together by column chromatography followed by TLC. 2,7-Dichlorofluorescein pinacryptol yellow was used as a spray.[307]

2. Industrial

a. Sulfamic Acid as a Catalyst

Sulfamic acid has found wide application as a catalyst, especially in polymerization processes. Thus, sulfamic acid has been used in the manufacture of isoprene,[308] aminoplast prepolymers (from melamine, urea, formaldehyde,[309] styrene (alkali salt of an organic sulfamate was used),[310] poly(vinyl alcohol) plasticizers (antimony sulfamate was used),[311] propylene (sodium cyclohexylsulfamate),[312] poly(vinylbutyral) (by the acetalization of poly(vinyl acetate)),[313] poly[*p,p'*-bis(hydroxymethyl)diphenyl ether],[314] and methylacrylate ester polymers.[315]

Sulfamic acid has also been extensively used as a catalyst for many organic reactions, most of which are of use in industry. Sulfamic acid catalyzes the esterification of carboxylic acids,[316] the oxidation of aromatic aldehydes (containing phenolic hydroxy groups) to carboxylic acids,[317] the preparation of amines by decarbonylation of carboxamides with sodium hypochlorite,[318] the synthesis of anthraquinonecarboxamides from anthraquinonecarboxylic acids,[319] the isomerization of maleic to fumaric acid,[320] the synthesis of ε-caprolactam from ε-caprolactone and aqueous ammonia,[321] the condensation of sugars with purines,[322] and the acetylation of cellulose.[323] A combination of sulfamate and borate catalysts increases the sensitivity and specificity of the reaction of carbazole with hexuronic acids.[324] *tert*-Butylammonium sulfamate has been used in the vulcanization of rubber.[325]

b. Electrometallurgical Applications

Sulfamic acid is very extensively used in the electroplating and electrodeposition of metals. At the Symposium on Sulfamic Acid in Milan in 1966, these aspects were well covered. Romagnani[7] brought together many of the main references at that time. His list of references also includes many from other areas of sulfamic acid chemistry. Some papers from that Symposium have already been cited (see II.F). Some other important papers dealt with analysis of sulfamate baths[326] and special and possible applications of sulfamate baths.[327] Other papers which appeared after the Symposium include those on the electrochemical behavior of copper(I) and copper(II) sulfamate baths,[328] potentiometric study of metals and alloys in sulfamate baths,[329] and reviews of nickel electroplating in sulfamate baths.[330] Hundreds of other papers have appeared in the last 10 years on electroplating and electrodeposition of many different metals in sulfamate solutions. It is beyond the scope of this review to include these. References to these papers will be found in *Chemical Abstracts*.

c. Uses of Sulfamic Acid

Apart from its catalytic and electrometallurgical uses, sulfamic acid has found wide application in many other areas. Some of the major areas are as a fire retardant or fireproofing agent (here it is interesting to note that there is a report involving the use of the interesting compound ethylenediammonium disulfamate to treat paper[331]), as an anticorrosive agent, as a cross-linking agent for polymers, in the dyeing of fabrics, as a cleaning agent for air, as a herbicide, in pulp bleaching, for scale removal and cleaning metal, in pigment printing, and in producing cigarettes of reduced toxicity. In certain applications specific compounds are used: e.g., for fire-retarding ability guanidine and ammonium sulfamates are best.

There have been very many references in *Chemical Abstracts* to the uses of sulfamic acid: a comprehensive listing of these uses would be outside the range of this review.

H. Amine–Sulfur Trioxide Complexes

Gilbert[332] has reviewed the syntheses, properties, and uses of the various amine–sulfur trioxide complexes, i.e., pyridine–sulfur trioxide, tri(methyl)ethylamine–sulfur trioxide, dimethylaniline–sulfur trioxide, and 2-methylpyridine–sulfur trioxide. These complexes find their principal applications as reagents for sulfation, sulfonation, and sulfamation.

1. Physical, Theoretical, and Synthetic Aspects

Ab initio calculations have been done on NH_3–SO_3; the net interaction energy is −74.6 kJ mol^{-1}, showing that SO_3 is an unusually strong Lewis acid.[333] R_3N–SO_3 (R = Et, *n*-Pr, *n*-Bu)

complexes have an experimental magnetooptical rotation 173 μrad smaller than the calculated sum of the rotations of the component molecules.[334] The heats of formation of pyridine- and DMF-sulfur trioxide adducts have been measured.[335] The reaction products of lower aliphatic amines, e.g., $MeNH_2$, with SO_3 have been studied by using a combination of anion-exchange chromatographic separation and complexometric titrations. The products included *N,N'*-dimethylsulfamide (**71**), methylammonium methylsulfamate (**72**), methylammonium sulfate (**73**), and bis(methylammonium) methylimidodisulfonate (**74**).[336] The gas-phase reaction of methylamine and dimethylamine with sulfur trioxide was also examined. Methylamine and SO_3 gave **72** (66%), **74** (27%), **71** (3.3%), and **73** (8.7%). The yields of **72** and **74** decreased gradually as the percent of **71** and **73** increased. Similar results were obtained in the reaction of SO_3 with dimethylamine.[337]

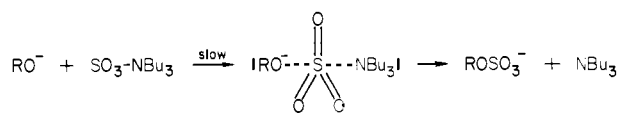
R_3N-SO_3 complexes have been prepared by heating the imidodisulfonate **75**.[336a] Thus,

$$\underset{\mathbf{75}}{HN(SO_3H\cdot NR_3)_2} + R_3N \xrightarrow[1\ h]{396\ K} R_3N-SO_3 + H_2NSO_3H\cdot NR_3 \quad (52)$$

where R = lower alkyl (e.g., *n*-Bu), NR_3 = pyridine, picoline, 2,4-lutidine, quinoline, *N*-methylmorpholine, $PhCH_2NMe_2$. If NR_3 = $PhNR_2$, then the product obtained was the *N,N*-dialkylsulfanilic acid.[336b] The HNF_2 and $MeNF_2$ adducts of sulfur trioxide may be true sulfamic acids.[172]

2. Use in Sulfation

Guanidine sulfate has been prepared in 70% yield by the reaction of urea with NH_3-SO_3 under an ammonia atmosphere.[339] The addition of about 4% Me_3N-SO_3 to sulfamic acid allowed the sulfation of alcohols to proceed without the formation of a cake in the reaction mix.[204] The rates of sulfation with *n*-Bu_3N-SO_3 of 11 alcohols (in excess) have been measured.[340] The rates are first order in sulfur trioxide adduct and a ρ^* value of −4.2 has been obtained for variation in alcohol structure. The mechanism is seen as being of the S_N2 type.



Large negative entropies consistent with this bimolecular mechanism have been observed. Though rates of sulfation (sulfoesterification) with sulfamic acid have been extensively measured (II.B.3), this is the first report on the study of such rates with amine-sulfur trioxide adducts. In a subsequent study the same group used inert solvents, e.g., dichloroethane, as the medium.[341]

Many compounds other than alcohols have been sulfated with amine-sulfur trioxide adducts. Thus, cellulose sulfate has been formed by sulfation of cellulose with pyridine-, γ-picoline- and Et_3N-sulfur trioxide complexes.[342] Ascorbic acid has been sulfated with Me_3N-SO_3 to give disodium L-ascorbic 2-sulfate.[343] The sulfates of lithocholic, glycolithocholic, and taurolithocholic acids have been made by reaction with Et_3N-SO_3 in DMF.[344] The synthesis of two norepinephrine *O*-sulfates involved the use of *N,N*-dimethylaniline- and pyridine-sulfur trioxide complexes to sulfate phenolic groups.[345] Me_3N-, Et_3N-, and DMF-sulfur trioxide adducts have been used in the sulfation of polysaccharides, e.g., agarose,[346] amylopectin,[347] and starch.[346]

Ethylene-vinyl acetate copolymer has been sulfated with Me_3N-SO_3 in carbon tetrachloride-DMF containing maleic acid,[346] and the same reagent has been used to sulfate 5'-amino-5'-deoxythymidine.[176] Pyridine-sulfur trioxide deoxygenates allylic and benzylic alcohols, probably via the sulfated esters, i.e., $ROSO_3^-\cdot HNC_5H_5^+$. Thus, *trans,trans*-farnesol gives *trans,trans*-2,6,10-trimethyldodeca-2,6,10-triene.[349a] Gibberellin A_3 has been oxidized with pyridine-sulfur trioxide in Me_2SO.[349b]

3. Use in Sulfonation and Sulfamation

Phthalocyanines,[350,351] anthracene,[350,352,353a] anthraquinone,[350] and naphthalene[353b] have been sulfonated by using pyridine-sulfur trioxide. Phthalocyanine-copper complex was not sulfonated by other amine-sulfur trioxide adducts.[351] Six sulfonic acids were obtained in the pyridine-sulfur trioxide sulfonation of anthracene. 1- (14%) and 2- (4%) anthracenesulfonic acids and 1,5- (10%), 1,8- (60%), and 2,6- + 2,7- (12%) disulfonic acids were identified.[353a] Pyridine-sulfur trioxide has found use as a mild sulfonating agent for lignin model compounds, e.g., ethylguaiacylcarbinol, guaiacol, and ethylveratrylcarbinol.[354]

Et_3N-SO_3 has been used to sulfamate cyclohexylamine[135] in 90% yield, and Me_3N-SO_3 has found application in the sulfamation of ethylamine, the formation of the N-sulfonates of morpholine and 2-amino-2-methylpropanol,[136] and the sulfamation of 5'-amino-5'-deoxyadenosine to give 5'-sulfamino-5'-deoxyadenosine.[176] A one-step synthesis of N-substituted imidodisulfonates (**76**) has been achieved by using Et_3N-SO_3 (eq 53).[355]

$$RNH_2 \xrightarrow{Et_3N-SO_3} RNHSO_3^-\cdot HNEt_3^+ \xrightarrow{Et_3N-SO_3} \underset{\mathbf{76}}{RN(SO_3^-\cdot HNEt_3^+)_2}$$

R = Me, *i*-Pr, *sec*-Bu, *t*-Bu, c-C_6H_{11}, $PhCH_2$, etc. (53)

The reaction proceeds via the intermediate sulfamates, and in fact with R = *t*-Bu, the sulfamate only was obtained, quantitatively. Most other compounds gave 55–90% yields of **76**. In an earlier paper, the same authors used (principally) 2-picoline-sulfur trioxide as a sulfamating agent for sulfamates.[356] The preparation of sulfatoethyl- (and -propyl-) imidodisulfonates **77** from the hydroxylamines and pyridine-sulfur trioxide involves simultaneous sulfamation and sulfation (eq 54).[357]

$$HO(CH_2)_nNH_2 + C_5H_5N-SO_3 \rightarrow \underset{\mathbf{77},\ n = 2, 3}{^-O_3SO(CH_2)_nN(SO_3^-C_5H_5N^+)_2} \quad (54)$$

Pyridine imidodisulfonate has been used successfully to sulfamate aniline, 1-naphthylamine, and several ring-substituted anilines.[137]

4. Hydrolysis

a. Me_3N-, Et_3N-, Me_2EtN-, and $Et_2MeN-SO_3$

Fleischfresser and Lauder[356] have shown that the hydrolysis of trimethyl- and triethylamine-sulfur trioxide adducts is not acid catalyzed, but the base-catalyzed cleavage of those compounds is second order as expected and may involve bimolecular attack at sulfur, a contention supported by the following entropies obtained by the Australians: −44.8 J K^{-1} mol^{-1} (Me_3N-SO_3) and −80.4 J K^{-1} mol^{-1} (Et_3N-SO_3). About the same time, Ryss and Bogdanova[359,360] obtained an entropy of −58.7 J K^{-1} mol^{-1} for the aqueous hydrolysis of Et_3N-SO_3. Later work by the Russian group on the alkaline hydrolysis of Me_3N-SO_3[361] and Et_3N-SO_3[362] supported the bimolecular mechanism proposed by the Australian workers. Work by Krueger and Johnson[363] on the base hydrolysis of Me_3N-SO_3 has substantiated the earlier findings. Bentley[364] has reasoned that since trialkylamine-sulfur trioxide compounds carry both negative and positive charges their rates of hydrolysis might be accelerated by both cationic and anionic surfactants since the possibility of binding with either type of charged micelle exists. Using the cationic surfactants ETAB and DTAB and the anionic surfactant SHS, they found that each material produces a rate acceleration in the hydrolysis of Et_3N-SO_3 and Me_3N-SO_3. A change in the mechanism of hydrolysis of Me_3N-SO_3 from S_N2 in the presence of base to a dissociative mechanism in water has been proposed[365] on the

basis of a study of salt effects on the rate of hydrolysis of this compound at 336 K in water.

In two papers, Ryss, Bogdanova, and Kotlyar[366,367] have completed a program involving a kinetic study of the aqueous and alkaline hydrolyses of trialkylamine–sulfur trioxide adducts. These papers deal with the hydrolysis of $Me_2EtN–SO_3$[366] and $Et_2MeN–SO_3$[367] adducts. The alkaline hydrolysis of both adducts is seen as involving bimolecular base attack at sulfur (supported again by large negative entropies of activation) with utilization of vacant d orbitals on sulfur. The mechanism of the aqueous hydrolysis is not discussed except to point out that it should not be treated as a second-order process. Some interesting comparisons are made for the aqueous and alkaline hydrolyses of the series $Me_3N–$, $Me_2EtN–$, $MeEt_2N–$, and $Et_3N–SO_3$.[367]

The same Russian group has also studied the kinetics of hydrolysis of compounds **78**[366] which lose first one and then the second SO_3 species (eq 55). The first step of the hydrolysis

$$\underset{\mathbf{78}}{R_2N(SO_3)–(CH_2)_n–(SO_3)NR_2} \xrightarrow[k_1]{H_2O} R_2NH^+–(CH_2)_n–(SO_3)NR_2 + HSO_4^- \xrightarrow[k_2]{H_2O} R_2NH^+–(CH_2)_n–NHR_2^+ + 2HSO_4^- \quad (55)$$

R = Me; n = 6, 2

is rate limiting and the overall hydrolysis is first order. The entropy of activation of **78** (n = 6) was −40.2 J K^{-1} mol^{-1}. **78** (n = 2) was not studied in detail as it is poorly soluble in water and hydrolyzes much more rapidly than **78** (n = 6). The first pK_B of **78** (n = 6) is very similar to the pK_B of $MeEt_2N$, and it is found that the rates of hydrolysis of **78** (n = 6) and $MeEt_2N–SO_3$ are similar; the activation energies and entropies are almost identical. Cleavage of the second N–S bond in **78** (n = 6) is rapid, and the second stage of the reaction does not affect the observed kinetics. Generally, the relative rates of reactions of the trialkylamine–sulfur trioxide complexes and compounds **78** can be rationalized in terms of the pK_B values of the parent amines, with a decrease in pK_B (increase in strength of the amines) corresponding to greater electron-pair donation in the N–S bond and a consequent strengthening of this bond.[367,368]

b. Pyridine– and Picoline–Sulfur Trioxide Adducts

The hydrolysis of β-picoline–SO_3[369] is about 4 times slower than that of pyridine–SO_3 under analogous conditions, despite the fact that the parent amines have fairly similar pK_B values. The activation energies of the two hydrolyses are almost the same, and the difference is seen as being due to entropy. $\Delta S^\ddagger$ is about −95.5 J K^{-1} mol^{-1} for β-picoline–SO_3, while for pyridine–SO_3 a value of −44.4 J K^{-1} mol^{-1} has been reported.[370]

However, later work reports the following thermodynamic parameters for pyridine–SO_3 hydrolysis: energy of activation 74.2 K J mol^{-1} and $\Delta S^\ddagger$ = −59.9 J K^{-1} mol^{-1}.[371] The kinetics of the hydrolysis of α- and γ-picoline–sulfur trioxides have been reported.[372] In the series pyridine–, β-picoline– and γ-picoline–sulfur trioxide the activation energy of hydrolysis increased with decreasing pK_B of the parent amine, corresponding to a strengthening of the N–S bond.[372]

I. Reaction of Sulfamic Acid with Nitric and Nitrous Acids and Other Reactions

1. HNO_3

The reaction of sulfamic acid with nitric acid (eq 56) has been studied recently on an industrial scale.[373] The reaction of nitric

$$NH_2SO_3H + HNO_3 \rightarrow H_2SO_4 + H_2O + N_2O \quad (56)$$

acid with sodium sulfamate to give nitramide (70%, under optimum conditions) has been investigated.[374]

Three groups[375–377] have been investigating the mechanism of the reaction of nitric and sulfamic acids. Reaction 56 is first order in sulfamic acid and the variation of rate with acidity approximates to a second-order dependence on H_0.[375] This suggests a mechanism involving the nitronium ion, and a rate-determining electrophilic substitution at the amino group of sulfamic acid (partially present as NH_2SO_3H) with SO_3H^+ as the leaving group has been proposed (eq 57).[375] The nitramide

$$\begin{aligned} H^+ + HNO_3 &\rightleftharpoons [H_2NO_3]^+ \xrightleftharpoons{\text{fast}} NO_2^+ + H_2O \\ NO_2^+ + NH_2SO_3H &\xrightarrow{\text{slow}} NH_2NO_2 + SO_3H^+ \\ NH_2NO_2 &\xrightarrow{\text{fast}} N_2O + H_2O \end{aligned} \quad (57)$$

undergoes rapid decomposition to dinitrogen oxide and water. Strong evidence for this mechanism is provided by the isolation of nitramide in the reaction of nitric acid and sodium sulfamate.[374] Hughes et al.[376] have shown that the second step in eq 57, i.e., direct displacement by nitronium ion, does not occur. Hughes considers a reaction sequence (eq 58) in which the first step is the generation of the nitronium ion (as in the first step of eq 57).

$$\begin{array}{l} NO_2^+ + NH_3^+SO_3^- \rightarrow {}^+NH_3SO_3NO_2 \rightarrow O_2NNHSO_3H + H^+ \\ \qquad\qquad\qquad\qquad\qquad\qquad\qquad\qquad \downarrow NO_2^+ \\ NO_2^+ + HSO_4^- + NH_2NO_2 \leftarrow O_2NNHSO_3NO_2 + H^+ \\ \qquad\qquad \downarrow \\ \qquad\qquad N_2O + H_2O \end{array} \quad (58)$$

An alternative reaction scheme (eq 59) not involving initial nitration of the sulfamic acid is also suggested.[376] This involves the formation of hydroxylamine-*O*-sulfonic acid and reaction with nitrous acid to give the *N*-nitroso compound **79** which reacts with nitric acid to give **80**, which can then decompose to nitramide and sulfuric acid.

$$\begin{aligned} HNO_3 + NH_2SO_3H &\rightarrow HNO_2 + NH_2OSO_3H \rightarrow \underset{\mathbf{79}}{ONNHOSO_3H} + H_2O \\ \mathbf{79} + HNO_3 &\rightarrow \underset{\mathbf{80}}{O_2NNHSO_3H} + NO_2^+ \rightarrow NH_2NO_2 + H_2SO_4 \end{aligned} \quad (59)$$

A study of the reaction using $H^{15}NO_3$ indicates that N_2O arises only partially from nitramide and also from the dimerization of HNO, a species which is thought to arise from the HNO_3–N-H_2SO_3H reaction.[377]

2. HNO_2

There are many relevant references to the use of nitrous acid in sulfamic acid analytical chemistry in II.G.1. A mechanistic study of the reaction of nitrous acid with sulfamic acid revealed that the mechanism

$$NH_2SO_3H + HNO_2 \rightarrow N_2 + H_2SO_4 + H_2O$$

at acidities less than 0.25 M, was of the type shown in eq 60.[376]

$$\begin{aligned} H^+ + HNO_2 &\xrightleftharpoons{\text{fast}} H_2NO_2^+ \\ H_2NO_2^+ + NH_2SO_3^- &\xrightarrow{\text{slow}} N_2 + H_2SO_4 + H_2O \end{aligned} \quad (60)$$

The protonated nitrous acid species reacts with sulfamate ion in a slow step. In the acid range −0.25–3 M a second pathway emerges in which $H_2NO_2^+$ attacks sulfamic acid (now mainly present). The involvement of intermediates such as $ONNHSO_3^-$ and $HON{=}NSO_3^-$ in the slow step is also suggested. A study of the kinetics of the reaction of nitrous acid and sulfamic acid confirmed the earlier rate law for the reaction.[379]

The pH dependency of the formation and decomposition of the *N*-nitroso derivative found in the reaction of sodium nitrite and cyclohexylsulfamic acid was investigated by photometric measurement of absorbance changes. An optimum yield of the nitroso derivative was obtained at pH 2.45.[380] The kinetics of

the reaction of sulfamic acid with $Pt(NO_2)_4^{2-}$, $Pd(NO_2)_4^{2-}$, $Rh(NO_2)_6^{3-}$, and $Co(NO_2)_6^{3-}$ were studied by measuring the nitrogen evolved.[361]

3. Other Reactions

High yields of alkyldifluoramines have been produced by the reaction of sodium alkylsulfamates with fluorine in an inert gas.[382] The reaction proceeds according to eq 61. The silylation of

$$RNHSO_3Na + 2F_2 \rightarrow RNF_2 + FSO_3Na + HF \quad (61)$$

$R = C_{1-5}$ straight or branched alkyl

the methyl ester of sulfamic acid and of sulfamic acid with trimethylchlorosilane/triethylamine has been described (eq 62).[383]

$$\underset{\textbf{81a, R = H}\quad \textbf{b, R = Me}}{NH_2SO_2OR} \xrightarrow{Me_3SiCl/Et_3N} \underset{\textbf{82a. R = Me}_3\textbf{Si; R' = H}\quad \textbf{b. R = Me; R' = Me}_3\textbf{Si}}{Me_3SiR'NSO_2OR} \quad (62)$$

The trisilylated compound **83** can be obtained from **81a** by using an excess of reagents. **83** reacts with thionyl chloride to give *N*-sulfinylamides, **84**. **82a** has been prepared in 78% yield by

$$\underset{\textbf{83}}{Me_3SiOSO_2N(SiMe_3)_2} \xrightarrow{SOCl_2} \underset{\textbf{84}}{Me_3SiOSO_2N{=}S{=}O} \quad (63)$$

reaction of hexamethyldisilazane with ammonium sulfamate (eq 64).[364] **82a** is a highly efficient silylating agent.

$$(Me_3Si)_2NH + NH_2SO_3NH_4 \rightarrow Me_3SiNHSO_3SiMe_3 + 2NH_3 \quad (64)$$

There are several reports of the use of sulfamic acid (in the presence of sulfuric acid, oleum, or polyphosphoric acid) to effect amidation of carboxylic acids in high yield.[385-387] *p*-Xylene gives 2,2′,5,5′-tetramethyldiphenyl sulfone in 97% yield on treatment with sulfamic acid in polyphosphoric acid.[388] The reaction of the antibiotic streptozotocin with sulfamic acid has been examined, and the structure of the hydantoin formed has been determined.[389] 3-Aminobenzene-*N*,*N*-dimethylsulfamate has been diazotized and coupled with 2,6-dihydroxy-3-carbamoyl-4-methylpyridine to give a new dye used for polyester fibers.[390] Kinetic studies of the formation of diazoamino compounds (triazenes) from the reaction of *p*-nitrophenyldiazonium ion with methylsulfamic acid reveal that the process is two stage (as in the case for other triazenes).[391] The first step is a rate-controlling formation of diazoammonium ion followed by proton abstraction (eq 65). Reaction of methylsulfamic acid with excess ammonia

$$p\text{-}O_2NC_6H_4N_2^+ + HN(CH_3)SO_3^- \rightleftharpoons p\text{-}O_2NC_6H_4N_2NH^+(CH_3)SO_3^- \xrightarrow{OH^-} p\text{-}O_2NC_6H_4N_2N(CH_3)SO_3^- + H_2O \quad (65)$$

gives ammonium sulfamate and methylamine by nucleophilic attack on sulfur.[392] Ureasulfonic acid undergoes nucleophilic attack by water to give sulfocarbamic acid (**85**) which is decarboxylated to give ammonium sulfamate in the presence of ammonia (eq 66).[392] A qualitative study of the acid-catalyzed

$$\underset{\textbf{85}}{H_2{}^+OOCNHSO_3^-} \xrightarrow{NH_3} H_2NSO_3NH_4 + CO_2 \quad (66)$$

hydrolysis of various ring-substituted benzylsulfamates has produced the interesting result that if Ar contains electron-withdrawing substituents, the amine formed was $ArCH_2NH_2$, but if Ar contained electron-donating substituents in the ring, then $(ArCH_2)_2NH$ formed. These results have been explained in terms of a carbonium ion intermediate.[393] The compounds studied were synthesized by a novel route involving condensation of ammonium sulfamate with aromatic aldehydes in methanol with potassium acetate (60% average yields), followed by hydrogenation of the $—CH{=}NSO_3K$ compounds formed over Raney nickel (70% average yields).[393] In another study the mechanism of the catalytic cleavage of the N–S bond in sulfamic acid and its derivatives has been examined. Nagasawa and Yoshidome[394] have studied the catalytic decomposition of sulfamic, cyclohexylsulfamic, benzylsulfamic, piperidine-*N*-sulfonic, and morpholine-*N*-sulfonic acids by pyridine. In anhydrous pyridine not more than 37% formation of cyclohexylamine and cyclohexylamine sulfate occurred in the catalytic decomposition of cyclohexylsulfamic acid at 373 K. At this temperature the addition of 1% water produced 94% hydrolysis within a few minutes. Too much water can inhibit the decomposition. The Japanese workers suggest that the zwitterionic form of cyclohexylsulfamic acid participates in an initial equilibrium prior to N–S bond cleavage. This view is supported by the fact that those sulfamic acids which cannot form zwitterions cleave more slowly (and never completely) than cyclohexylsulfamic acid. A pyridine–SO_3 adduct is seen as intermediate in these reactions (eq 67).

$$RR'NSO_3H \rightleftharpoons RR'NH^+SO_3^- \overset{Py}{\rightleftharpoons} RR'NH + Py{-}SO_3 \xrightarrow{H_2O} RR'NH_2^+ + SO_4^{2-} + PyH^+ \quad (67)$$

III. Sulfamyl Azides, Esters, and Halides

A. Sulfamyl Azides

Organic sulfamyl azides of the type **86** were first prepared by Hardy and Adams.[395] The alkyl and cycloalkyl derivatives

$$\underset{\textbf{86}}{R^1R^2N{-}SO_2N_3}$$

R^1 = lower alkyl, cycloalkyl
R^2 = lower alkyl, cycloalkyl
R^1 and R^2 part of heterocyclic system

were prepared by reacting the corresponding sulfamyl halide with alkali azide in an aqueous alcoholic solution at from room temperature up to about 323 K. The heterocyclic compounds are prepared by reacting the corresponding amine hydrochlorides with sulfuryl chloride to give the *N*-sulfonyl chloride which is then reacted with an alkali azide.

The parent sulfamyl azide, $NH_2SO_2N_3$ (**87**), was isolated by Shozda and Vernon[396,397] as an explosive solid by the reaction of sodium azide with sulfamyl chloride. Attempts to prepare

$$NH_2SO_2Cl + NaN_3 \rightarrow \underset{\textbf{87}}{NH_2SO_2N_3} + NaCl$$

aromatic sulfamyl azides by using the above reaction were limited because of the difficulty of preparing aromatic sulfamyl chlorides. Shozda and Vernon were unable to prepare phenylsulfamyl chloride previously reported by Traube.[396] Two such aromatic sulfonyl azides **88** were prepared by reacting sodium azide with *N*-chlorosulfonylformanilide and *N*-chlorosulfonyl-*p*-toluenesulfonanilide. A more general and convenient synthesis

$$XSO_2Cl + NaN_3 \rightarrow \underset{\textbf{88}}{XSO_2N_3} + NaCl$$

$X = C_6H_5N{-}Tos$, $C_6H_5N{-}CHO$

of sulfamyl azides involves the reaction of aromatic amines with chlorosulfonyl azide (**89**). This explosive reagent is produced in high yield by reacting sulfuryl chloride fluoride with sodium azide in the presence of a catalytic amount of dimethylformamide.

$$2RR^1NH + ClSO_2N_3 \rightarrow \underset{\textbf{89}}{RR^1NSO_2N_3} + \underset{\textbf{90}}{RR^1NH{\cdot}HCl}$$

$R = C_6H_5$; $R^1 = H$
$R = p\text{-}CH_3C_6H_4$; $R^1 = H$
$R = p\text{-}ClC_6H_4$; $R^1 = H$
$R = C_6H_{11}$; $R^1 = H$
$R = R^1 = n\text{-}Bu$

TABLE I. Amines Reacted with $ClSO_2N_3$

$R^1C_6H_4NHR^2$	% yield $R^1C_6H_4NR^2SO_2N_3$
$R^1 = R^2 = H$	50
R^1 = Me, R^2 = H	47
R^1 = OMe, R^2 = H	47
R^1 = H, R^2 = Me	64
R^1 = NHAc, R^2 = H	25

Griffiths[399] studied the preparation of chlorosulfonyl azide (**89**) in various solvents in order to avoid isolating the explosive material. The major problem is that the starting sulfuryl chloride is too reactive toward such solvents as acetone, tetrahydrofuran, and dimethyl sulfoxide. The reaction of equimolar quantities of sodium azide and sulfuryl chloride in benzene and methylene chloride showed that the reaction at room temperature was very slow, with very little conversion to the azide after 60 h. Griffiths considered that the reason for the low conversion was due to the low solubility of sodium azide. When the reaction was carried out in ethyl acetate, in which the azide is more soluble, the conversion was more rapid but still inconveniently long. Shozda and Vernon[396] had previously shown the catalytic effect of dimethylformamide in the reaction of sodium azide with chlorosulfonyl fluoride. Griffiths showed the same catalytic effects of dimethylformamide and also of water when the reaction was carried out in benzene or methylene chloride; completion to the azide was achieved in less than 12 h. The effects of the catalysts were considered to be twofold: (i) increased solubility of the sodium azide and (ii) the formation of a highly reactive intermediate complex which undergoes rapid reaction (see eq 68). This procedure had one disadvantage in that the product

$$SO_2Cl_2 + (CH_3)_2NCHO \rightarrow [ClSO_2N^+(CH_3)_2CHO]Cl^- \quad (68)$$

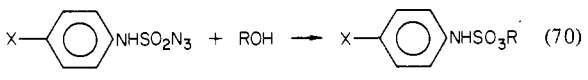
was found to be contaminated with sulfuryl chloride which had a deleterious effect on the reaction of chlorosulfonyl azides with amines. Changing the solvent to acetonitrile enabled **89** to be prepared free of sulfuryl chloride. In addition sodium azide had a high solubility in acetonitrile.

Shozda[396] had previously reacted the explosive compound **89** with alkyl- and arylamines. Yields were low, particularly as half the amine was converted into its hydrochloride during the reaction shown in eq 69. Griffiths[399] studied the reaction of

$$2ArNH_2 + ClSO_2N_3 \rightarrow ArNHSO_2N_3 + ArNH_3^+Cl \quad (69)$$

aniline with the now safe acetonitrile or methylene chloride solution of chlorosulfonyl azide. A 1 M portion of aniline and triethylamine (the latter prevents formation of anilinium hydrochloride) gave several byproducts and a low yield of phenylsulfamyl azide. The effect of inorganic bases such as sodium acetate, carbonate, and hydrogen carbonate was then studied. Thus, when an equimolar solution of aniline and $ClSO_3N_3$ was treated with an excess of sodium hydrogen carbonate (added slowly during the reaction) the reaction was complete after 14 h with yields between 40 and 60%. The added base, in addition to accelerating the reaction, also enables a molar portion of amine to be used. A series of arylsulfamyl azides were prepared by this procedure and the results are summarized in Table I. The results showed that the reaction worked well for the more nucleophilic amines. But if the arylamine contains a strong electron-attracting group in the benzene ring, e.g., *p*-nitro group, the reaction does not proceed.

Griffiths[399] found that these phenylsulfamyl azides were very reactive toward substitution by alcohols to give the corresponding alkylsulfamates, **91**.



(70)

91

Matier and Comer[400,401] prepared a wide range of azides including aromatic sulfamyl and *N*-benzyl-*N*-methyl-, piperazine-, and a number of mono- and dialkylsulfamyl azides. The hypotensive and hydrolytic stabilities of the azides have been examined. The authors consider the following mechanism (eq 71) involving an *N*-sulfonylamine, **92**, to be operative in the hydrolysis of sulfamyl azides (studied in aqueous dioxane at pH 6.0 to 7.0).

$$RNHSO_2N_3 + H_2O \rightleftharpoons R\bar{N}SO_2N_3 + H_3O^+ \xrightarrow{N_3} [RN{=}{=}SO_2) \xrightarrow[fast]{+H_2O} RNHSO_3H \quad (71)$$

The above initial equilibrium ionization is supported in that (i) monosubstituted sulfamyl azides are extremely reactive in aqueous base while disubstituted sulfamyl azides (which cannot react by the mechanism in eq 71) are little affected by aqueous base; (ii) mono- and disubstituted azides are quite stable in aqueous acid; and (iii) monosubstituted sulfamyl azides react with amines in aprotic solvents to form stable salts (**93**).

$$Ar\bar{N}SO_2N_3{\cdot}NHEt_3^+$$
93

The logarithm of the first-order observed rate constants gave a linear plot (slope close to unity) vs. pH (over the pH range 6.0 to 7.0) for the hydrolysis of *n*-propylsulfamyl azide. The reaction then could be base catalyzed with an S_N2 mechanism (eq 72), which may be an important mode of reaction at pH >7, and, as pointed out by the authors, it provides the only mode of reaction for disubstituted sulfamyl azides.

$$RNHSO_2N_3 + OH^- \xrightarrow{slow} RNHSO_3H + N_3^- \quad (72)$$

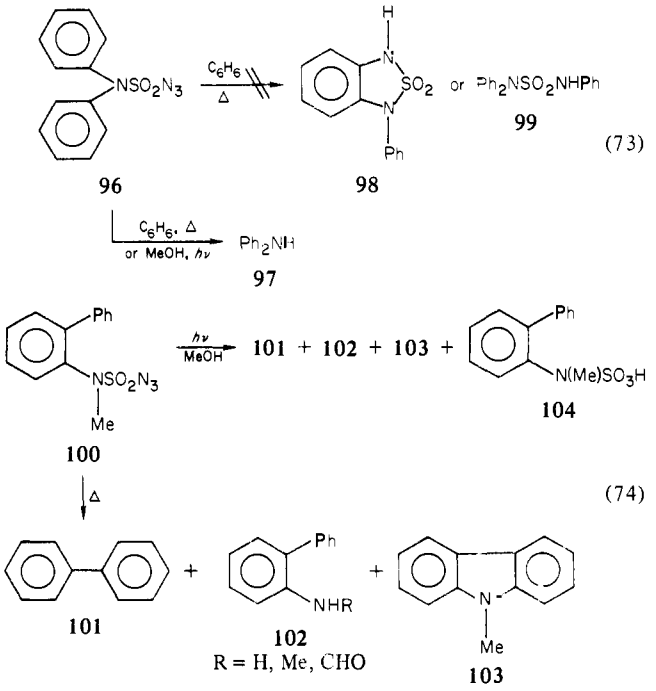
As mentioned above, phenylsulfamyl azide reacts to form salts of the type $Ph\bar{N}SO_2N_3X^+$ (**94**). These salts are quite reactive toward nucleophiles to give compounds of the type **95**. These

$$Ph\bar{N}SO_2N_3X^+ \xrightarrow{C_6H_6} PhNHSO_2Y$$
94 **95**

X = Et_3NH, $ArNH_3$ Y = ArNH, *i*-PrO

reactions are considered to occur via the sulfonylamine, RN$=$$SO_2$ (**92**), which is similar to the intermediate proposed above in the hydrolysis of azides. This type of species was generated by Burgess[402] by treating ethylsulfamyl chloride with triethylamine at low temperature in toluene. The same intermediate has been invoked in the photolysis of benzenesulfonyl azides.[403] Thus the formation of *N,N'*-diarylsulfamides and sulfamic esters from aryl azides constitutes a useful synthetic route to these types of compounds.

Thermolysis of sulfonyl azides gives a series of interesting reactions via the sulfonylnitrenes.[404,405] The corresponding sulfamylnitrenes, $RR'NSO_2N$, have not been reported. Abramovitch has recently attempted to generate this species.[406] Thermolysis of *N,N*-dimethylsulfamyl azide[406] gave as many as 11 products, but no evidence of nitrene formation was obtained. Since intramolecular substitution rather than intermolecular substitution by aryl nitrenes takes place more easily[407] and since formation of five- and seven-membered rings by intramolecular substitution by a sulfonyl nitrene occurs,[407,406] an attempt was made to detect the formation of sulfamylnitrenes by intramolecular substitution with sulfamyl azides. Thermolysis of *N,N*-diphenylsulfamyl azide (**96**) gave diphenylamine (**97**, 54%). No intra- (**98**) or intermolecular (**99**) substitution products from a hoped for sulfamylnitrene were detected. Photolysis of **96** in methanol did not produce the desired products indicative of sulfamylnitrene generation. An alternative approach was the attempted cyclization of (biphenyl-2-yl)-*N*-methylsulfamyl azide (**100**), which was carried out in benzene or dry degassed cyclohexane in the presence of hydroquinone. No products from



intramolecular or from intermolecular reaction in benzene were observed. Among the products identified were biphenyl (**101**), 2-(methylamino)biphenyl (**102**, R = Me), 2-formamidobiphenyl (**102**, R = CHO), and *N*-methylcarbazole (**103**). Photolysis of the azide **100** in methanol and acetonitrile yielded similar products together with *N*-(biphenyl-2-yl)-*N*-methylsulfamate (**104**) but no products which would indicate the generation of sulfamylnitrene. No further reports or attempts to generate the elusive sulfamylnitrene have appeared to date.

B. Sulfamyl Esters

1. Synthesis

The esters of *N*,*N*-dialkylsulfamic acids (**105**) have been prepared by a variety of procedures: (1) metathesis of di-

$$R^1R^2NSO_2OR^3$$

105, $R^1 = R^2$ = alkyl; R^3 = aryl or alkyl

alkylsulfamyl chlorides with sodium alkoxide.[409] (2) action of the appropriate ester of chlorosulfonic acid on dialkylamines,[409] (3) action of dialkylsulfamyl chlorides on the sodium salts of substituted phenols.[410] Esters of monoalkylsulfamic acids (**106**) have been reported by Appel and Senkpiel,[411] and Sowada[412] has reported their synthesis by the reaction of symmetrically substituted sulfamides with nitrous acid in the presence of alcohols. Weiss and Schulze[413] have prepared a similar series by the solvolysis of various monoalkylsulfamyl chlorides (eq 75). The

$$CH_3NHSO_2Cl + HOR \rightarrow \underset{\mathbf{106}}{CH_3NHSO_2OR} + HCl$$

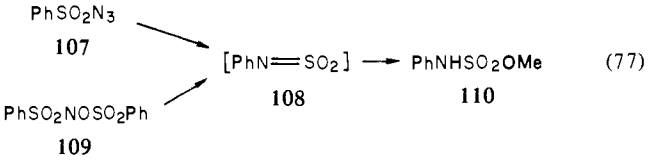
$$RNHSO_2Cl + HO(CH_2)_2OR' \rightarrow \underset{\mathbf{106}}{RNHSO_2OCH_2OR'} + HCl \quad (75)$$

R' = alkyl or phenyl

corresponding thioesters are prepared by reaction of alkylsulfamyl halides with substituted lead sulfides (eq 76).

$$2RNHSO_2Cl + Pb(SR')_2 \rightarrow 2RNHSO_2OR' + PbCl_2 \quad (76)$$

The methyl ester of phenylsulfamic acid has been prepared by the photolysis of benzenesulfonyl azide in methanol. Lwowski and Scheiffele[414] consider the reaction to proceed via a Curtius-type rearrangement of benzenesulfonyl azide (**107**) followed by addition of methanol to an intermediate *N*-phenylsulfonylamine (**108**). When the potassium salt of *N*-(*p*-nitrobenzenesulfonoxy)benzenesulfonamide (**109**) was added to methanol and stirred for 2 days, methyl phenylsulfamate (**110**) was obtained in 67% yield. Other preparations of esters of arylsulfamic acids include the preparation of ethyl-*N*-phenylsulfamic acid[415] by treating iminosulfuroxydifluoride with sodium ethoxide: Griffiths[399] has prepared similar esters by refluxing arylsulfamyl azides in benzene and methanol.



A rather interesting preparation of a sulfamate ester was carried out by Weinstein and Chang[416] who prepared methyl *tert*-butylsulfamate (**111**) by treating *N*,*N*′-di-*tert*-butylsulfamide with 3 equiv of *tert*-butyl hypochlorite. A mechanism is proposed which involves an intermediate *N*-sulfonyl-*tert*-butylamine (**112**). The scope of this reaction as a route to sulfamate esters has not been explored.

$$\underset{\mathbf{112}}{[Me_3CNSO_2]}$$

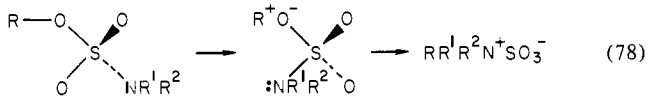
Aryl esters of sulfamic acids have been prepared by the reaction of phenols with sulfamyl chloride,[417,416] chlorosulfonyl isocyanate,[419,420] and isocyanates ($ArOSO_2NCO$) with water.[421] Hedayatullah has prepared a similar series by reduction of aryloxysulfonyl azides with a variety of reducing agents including copper in methanol[422] and also with sodium borohydride in tetrahydrofuran.[423]

2. Rearrangement

The rearrangement of sulfamate esters to betaines (**113**) has been reported.[424] White[425] has examined the behavior of optically active groups R^3 in the reaction using dimethylsulfamate esters, $(CH_3)_2NSO_3R^3$, as substrates. The resulting betaines

$$R^1R^2NHSO_3R^3 \rightarrow \underset{\mathbf{113}}{R^1R^2R^3N^+SO_3^-}$$

were hydrolyzed to sulfates and amines ($R^1R^2NR^3$); the latter were evaluated optically. When the R^3 group was $C_6H_5C^*HCH_3$ (optically active), the yields of amine $[(CH_3)_2NCH(CH_3)C_6H_5]$, the extent of retention of optical activity, and the solvent were respectively as follows: 60%, 0%, $CH_3OCH_2CH_2CH_3$; 20%, 7%, CCl_4; 11%, 24%, $CHCl_3$; 11%, 67%, CH_3COOH. White concluded that the rearrangement involved ionic intermediates (eq 78). Other mechanisms, however, such as elimination and



substitution processes, are implicated when compounds with allylic groups such as *trans*-cinnamyl (**114**) are involved; the product contained some trans S_N1 product but contained mostly material derived from an S_N1' process. If a true intramolecular

$$C_6H_5CH{=}CHCH_2OSO_2N(CH_3)_2 \rightarrow \underset{\mathbf{114}}{}$$

$$\underset{(19\%)}{C_6H_5CH{=}CHCH_2N(CH_3)_2} + \underset{(81\%)}{C_6H_5CH(N(CH_3)_2)CH{=}CH_2} \quad (79)$$

process was occurring, Ziegler and Orchin[426] considered that on heating two different esters together the product betaines should show no alkyl group exchange provided that both rearrange at the same rate. Experiments showed that $(CH_3)_2NSO_2OC_2H_5$ and $(CH_3)(C_2H_5)NSO_2OCH_3$ rearrange at approximately the same rate (2×10^{-5} s^{-1}) when heated in sealed tubes under nitrogen at 303 K. When both esters were heated under the above conditions, the crossed betaine, $(CH_3)_2SO_2{-}OCH_3$, in

addition to the other betaines, was isolated. Also it was shown that heating mixtures of the separate betaines produced no disproportionation between the alkyl groups, and thus the partial intermolecular character of the reaction was demonstrated. The mechanism proposed is ion-pair formation which can accommodate intermolecular exchange as well as internal rearrangement. A later paper by Marquarding,[427] who studied the rearrangement of the esters **115** and **116** to give the possible products **117**, **118**, **119**, and **120**, found that the ratio of the products **117**, **118**, **119**, and **120** was 1:1:1:1 when equimolar amounts of **115** and **116** were heated in acetonitrile at 353 K.

$$\underset{\mathbf{115}}{(CH_3)_2NSO_2OCH_3} + \underset{\mathbf{116}}{(CD_3)_2NSO_2OCD_3} \rightarrow \underset{\mathbf{117}}{(CH_3)_3N^+SO_3^-} + \underset{\mathbf{118}}{(CH_3)_2CD_3N^+SO_3^-} + \underset{\mathbf{119}}{CH_3(CD_3)_2N^+SO_3^-} + \underset{\mathbf{120}}{(CD_3)N^+SO_3^-}$$

The same ratio was obtained when the reaction was carried out at different concentration levels, i.e., [**115**] = [**116**] = 1.0 or 0.04 M. Thus even in dilute solution one cannot prove that the rearrangement occurs partly by an intramolecular mechanism and not exclusively by an intermolecular mechanism.

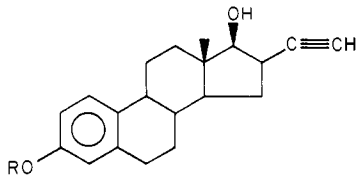
Betaines have also been observed in the reaction of alkyl *N,N*-dimethylsulfamates with methyl fluorosulfonate (eq 80).[426]

$$Me_2NSO_2OR \xrightarrow{MeOSO_2F} [Me_3N^+SO_3OR{\cdot}FSO_3^-] \rightarrow Me_3N^+SO_3^- + ROSO_2F \quad (80)$$

When the alkyl group of the ester is a simple straight chain this provides a convenient procedure for the preparation of primary alkyl fluorosulfates.

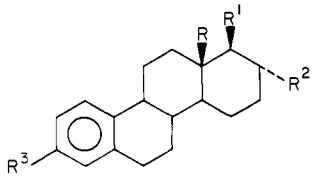
3. Steroidal, Monosaccharide, and Nucleoside Sulfamates

Steroidal sulfamates have been reported.[429-433] Schwarz[434,435] describes two methods for their preparation. In the first, the phenolic hydroxyl group was reacted with alkyl chlorides in sodium methoxide–dimethyl sulfoxide. Thus the steroidal sulfamates **121** were prepared and characterized. In the second, trienylsulfamates[431,436] **122** were prepared in 80–90% yield by sulfamylation of the phenolic hydroxyl group using sulfamyl halides in the presence of phase-transfer reagents such as $PhCH_2Et_3N^+Cl^-$.



121

R = Et_2NSO_2, 1-pyrrolidinosulfonyl, 1-piperidinosulfonyl



122

R = Me, Et; R^1 = OH, O; R^2 = C ≡ CH; R^3 = $R^4R^5NSO_2O$; R^4R^5 = Me, Et; R^4R^5N = pyrrolidino, morpholino, piperidino

The preparation of monosaccharide sulfamates has been reported.[437-440] Kochetkov has reported the reaction of pyridinium monosaccharide hydrogen sulfates (**123**) with amines and the use of ethyl ethynyl ether as a condensing agent.[438,439] The yields were never greater than 30%, however. The results from a detailed study indicated that the reaction proceeds by the scheme shown in eq 81. Evidence for the intermediate comes

$$\underset{\mathbf{123}}{ROSO_2OH{\cdot}NC_5H_5} \xrightarrow{EtOC\equiv CH} ROSO_2OC(OEt)=CH_2 \xrightarrow{ROSO_2OH} [ROSO_2OSO_2OR] \xrightarrow{R'NH_2} \underset{\mathbf{124}}{ROSO_2NHR} + ROSO_2OH{\cdot}NH_2R' \quad (81)$$

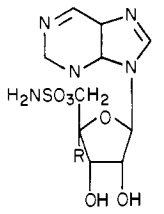
from the fact that in a very dry medium the compounds do not react with amines, but on addition of water hydrolysis occurs to give pyrosulfate which then reacts with amines. If the ethoxy vinyl ether is used in the reaction with a stronger acid, then the mixed anhydride should react with formation of the amide of the weaker acid, thus allowing an increased yield. Evidence for the mixed anhydride is demonstrated when pyridinium *p*-toluenesulfonate and ethyl ethynyl ether are mixed followed by addition of ethyl hydrogen sulfate and benzylamine; *N*-benzyl-*p*-toluenesulfonamide is formed, showing that the active intermediate during the course of the reaction contains residues of both acids, with the weaker acid giving rise to the amide.

Further studies[440] of the preparation of saccharide sulfamates show that if the strong acid in the above sequence was fluorosulfonic acid high yields were obtained (eq 82). The reaction

$$ROSO_2OH{\cdot}NC_5H_5 \xrightarrow{EtOC\equiv CH} ROSO_2OC(EtO)=CH_2 \xrightarrow{FSO_2OH} [ROSO_2OSO_2F] \xrightarrow{R^1R^2NH} ROSO_2NR^1R^2 \quad (82)$$

was found to be independent of the position of the sulfate group or the nature of the amine, and desulfurization was not observed. However, certain limitations in protecting groups for monosaccharides were observed; thus elimination of trityl and 5,6-*O*-isopropylidene groups in D-glucofurans occurred while the same groups in D-galactopyranose were stable. The reaction is also feasible with completely acetylated monosaccharide sulfates.

Nucleocidin is one of the few known antibiotics containing the sulfamate ester group. Shuman, Robins, and Robins[441] have now reported the synthesis of nucleoside sulfamates. The general procedure involves the reaction of sulfamyl chloride with a suitably blocked nucleoside.[442,443] The adenosine ester **125**,[176,444] a structural analogue to nucleocidin, was found to have similar properties to the fluoro compound **125** (R = F), which is the naturally occurring ester.

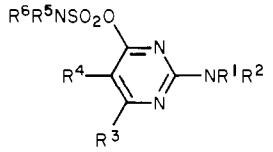


125

R = H, F

4. Miscellaneous

Since 1970 a wide range of different types of sulfamate esters have been reported with many applications, and a short synopsis is now given. The antifungal properties in plants of pyrimidinesulfamate esters **126** have been reported by Cole, Turner, and Snell.[445-447] There exists a large range of other active



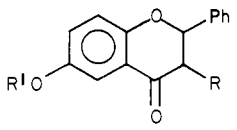
126

R^1 = H, lower alkyl; R^2 = lower alkyl, allyl; R^3 = alkyl C_{1-3}; R^4 = butyl or allyl; R^5 = R^6 = lower alkyl; NR^5R^6 = pyrrolidone

compounds with a wide variety of structural groups in addition to the sulfamate group. The fungicidal and herbicidal properties of these compounds have been reported.[446-458] The main synthetic route involved was the nucleophilic displacement of chlorine from mono- and dialkylsulfamyl chlorides by various nucleophilic groups, both alkyl and aromatic.

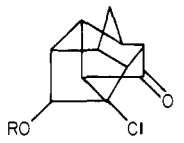
The sulfamate function as the ester is incorporated into a wide range of dyes of various types, including azo dyes[457-460] and anthraquinone polyester dyes.[461-464]

Esterification of glycols[465] by reaction with alkyl- and dialkylsulfamyl halides leads to sulfamate esters which have been found useful as contraceptives. Alkyl flavanone compounds[466] (**127**) which are esters of sulfamic acid were found to lower cholesterol in blood serum. Esters of the type **128**[467] were prepared by reaction of the corresponding diketones with chlorosulfonic acid: the sulfonyl chlorides are then reacted with various amino compounds.



127

R = Me, Et, *n*-Pr; $R^1 = NH_2SO_2$

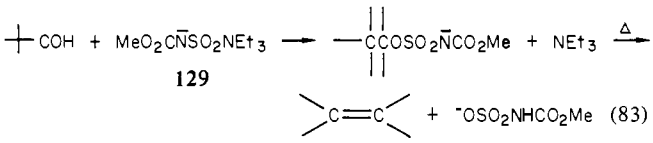


128

R = $NHCH_2Ph$, NH_2, morpholino

5. Elimination Reactions

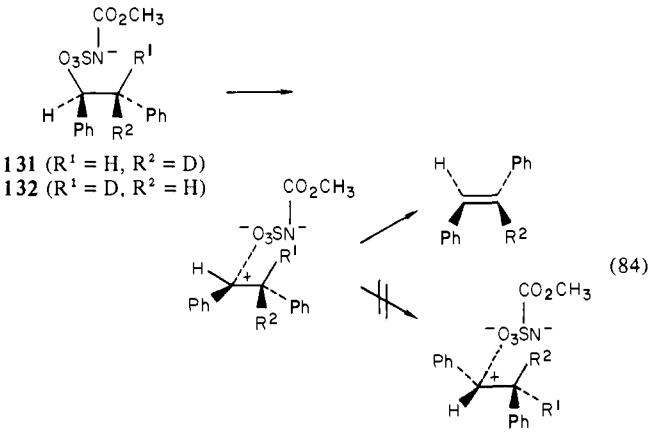
A synthetically useful and facile method for the mild dehydration of secondary and tertiary alcohols to the corresponding olefins was studied by Burgess[466,469] and involves the use of the *N*-(carbomethoxy)sulfamate ester **129** (see eq 83).



129

(83)

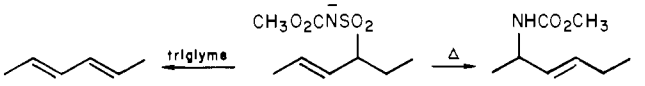
The kinetics of the solvolytic elimination reaction of 1,2-diphenylethyl *N*-(carbomethoxy)sulfamate triethylammonium salt (**130**) in ethanol gave only *trans*-stilbene with a first-order rate constant of 2.66×10^{-6} s^{-1} with $\Delta H^{\ddagger} = 90.9$ K J mol^{-1} and $\Delta S^{\ddagger} = 13.8$ J mol^{-1} K^{-1}. The stereochemical specificity was examined by using *erythro*- and *threo*-2-deuterio-1,2-diphenylethyl *N*-(carbomethoxy)sulfamates, **131** and **132**, respectively. The erythro form (**131**) gave only *trans*-stilbene containing 97.0% deuterium, while the threo form (**132**) gave only protio *trans*-stilbene. The data were considered to be consistent with initial rate-limiting ion-pair formation and fast β-proton transfer to the departing anion. The transfer occurs at a rate which is faster than the interconversion of the erythro and threo forms.



131 (R^1 = H, R^2 = D)
132 (R^1 = D, R^2 = H)

(84)

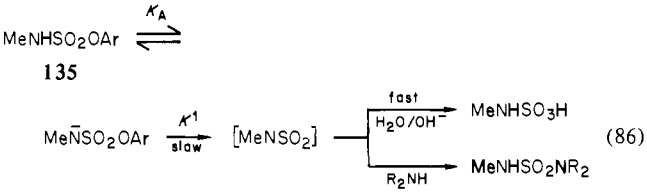
Reaction conditions determined the type of product when the reaction was applied to allylic alcohols. The thermal decomposition of sodium 4-hex-2-enyl *N*-(carbomethoxy)sulfamate gives 90% rearranged urethane **133** while reaction in triglyme gives the diene **134**.



134 **133**

(85)

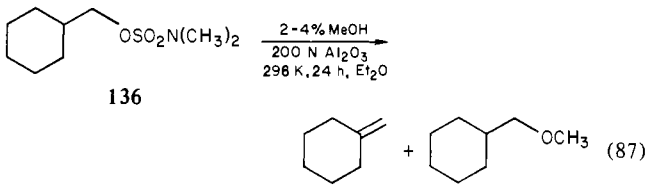
Evidence consistent with an E1cB mechanism for the hydrolysis of the aryl esters of methylsulfamic acid (**135**) is presented by Williams.[470,471] The rate constants for the hydrolysis of the esters were found to be independent of pH in the alkaline region. The Brønsted β_{lg} value for the hydrolysis reaction is −2.9 and differs from the value −1.1 obtained for the corresponding *N*,*N*-dimethyl series. Thus the dialkyl series is considered to react via an addition–elimination pathway, while the monomethyl esters react via an elimination–addition pathway. In addition the 4-nitrophenol *N*-methylamino ester shows a 10^6-fold greater reactivity to hydroxide ion compared to the 4-nitrophenyl ester of the *N*,*N*-dimethylamino series. The elimination–addition pathway for the hydrolysis is shown in eq 86. Consistent with this mechanism is the high ρ value (+2.4). The use of σ^- values indicates considerable phenolate character in the transition state. Further evidence consistent with this mechanism is the nonacceleratory effect of increasing buffer concentrations on the release of the phenol. No acid product is obtained in the presence of the amino buffers; all the observable product is sulfamide, pointing to a rate-limiting release of 4-nitrophenol followed by fast reaction of the amine.



135

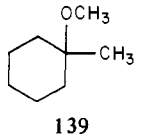
(86)

Posner[472,473] has studied the elimination reactions on alumina surfaces and has found that these reactions take place under very mild conditions. Cyclohexylmethyl *N*,*N*-dimethylsulfamate (**136**) was converted by methanol doped on W-200 neutral dehydrated alumina to a 1:6 ratio of methylenecyclohexane (**137**) and cyclohexylmethyl methyl ether (**138**). Because of the high stereoselectivity, i.e., since no rearrangement to the tertiary ether **139** occurred, it is considered that the reaction proceeds mainly via an S_N2 rather than an S_N1 mechanism.



136 **137** **138**

(87)



139

C. Sulfamyl Halides

1. Synthesis

a. Sulfamyl Chlorides

Dialkylsulfamyl chlorides (**140**) have been reported by Ziegler and Orchin[426] and by Binkley and Degering.[409] The corresponding

alkylsulfamyl halides (**141**) were first prepared by Weiss and

$$\underset{\textbf{140}}{RR'NSO_2Cl} \qquad \underset{\textbf{141}}{RNHSO_2Cl}$$

R = R′ = alkyl

Schulze.[474] The procedure involves the reaction of alkylamines[475] or alkylamine hydrochlorides[476-476] with sulfuryl chloride (eq 88). Sulfuryl chloride reacts also with dialkylsulfamides to

$$RNH_2{\cdot}HCl \xrightarrow{SO_2Cl_2} RNHSO_2Cl \qquad (88)$$

yield sulfamyl halides[479] (eq 89).

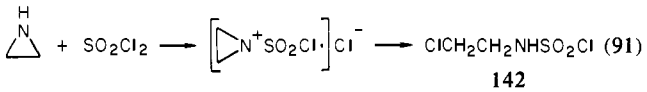
$$RNHSO_2NHR \xrightarrow{SO_2Cl_2} 2RNHSO_2Cl \qquad (89)$$

Alkylsulfamic acids have been used as starting materials for the synthesis of sulfamyl halides. Hamprecht et al. have reported the reaction of alkylsulfamic acids with thionyl chloride[460] and carbonyl chloride[461,462] to give high yields of the corresponding sulfamyl halides. Phosphorus pentachloride has also been used with sulfamic acids to yield the sulfamyl halides.[463] Kloek and Leschinsky[484] have adapted the PCl_5 reagent for use in aromatic solvents and have reported for the first time the synthesis of monoarylsulfamyl chlorides (eq 90).

$$RNHSO_3H \xrightarrow[\text{b. } COCl_2\\ \text{c. } PCl_5]{\text{a. } SOCl_2} RNHSO_2Cl \qquad (90)$$

R = alkyl for a or b; R = alkyl or aryl for c

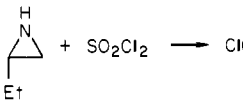
Various reagents and methods have been used in the synthesis of alkylsulfamyl halides.[465] Hamprecht has reported on the novel use of aziridines and sulfuryl chloride to prepare β-chlorosulfamyl chlorides (eq 91). Substituted aziridines un-



$$+ SO_2Cl_2 \longrightarrow \left[\text{N}^+SO_2Cl\cdot\right]Cl^- \longrightarrow ClCH_2CH_2NHSO_2Cl \qquad (91)$$

142

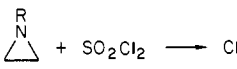
derwent only one type of ring opening, i.e., the butylenimine derivative yielded only the α-branched, (α-chloromethyl)-propylsulfamic acid **143** (eq 92). This reaction has been ex-



$$+ SO_2Cl_2 \longrightarrow ClCH_2CH(Et)NHSO_2Cl \qquad (92)$$

143

tended to include *N*-alkylaziridines which react in a similar manner to yield β-chloroethyl-*N*-alkylsulfamyl chlorides, **144** (eq 93).[466]



$$+ SO_2Cl_2 \longrightarrow ClCH_2CH_2N(R)SO_2Cl \qquad (93)$$

144

Alkyl chlorinated dialkylsulfamyl halides have been formed by reaction of the corresponding sulfamic acids or halides with paraformaldehyde and $SOCl_2$ or PCl_5.[467,466] In addition, chlorosulfonyl isocyanate has been found to react with tertiary alcohols[469] to yield the corresponding sulfamyl chlorides.

b. Sulfamyl Fluorides and Fluoro-Substituted Sulfamyl Chlorides

Monoalkylsulfamyl fluorides have been prepared by the reaction of sulfamyl chlorides with hydrogen fluoride[490] (eq 94).

$$RNHSO_2Cl + HF \rightarrow RNHSO_2F \qquad (94)$$

In addition, substituted sulfamyl fluorides, $Cl_2FCCSNHSO_2F$, have been prepared and their insecticidal properties reported.[491] Roesky[492a] reacted secondary amines with sulfuryl chlorofluoride, SO_2FCl, to obtain dialkylsulfamyl halides. Some disubstitution occurred, however, leading to the formation of sulfamide. He has chlorinated dimethylsulfamyl fluoride, Me_2NSO_2F, to obtain the interesting disubstituted sulfamyl fluoride $(Cl_2CH)_2NSO_2F$.[492b] Novel diarylsulfamyl fluorides[493,494] ($ArAr'NSO_2F$, **145**) have been prepared by the reaction of sulfuryl fluoride with lithium and sodium salts of secondary diarylamines (eq 95).

$$ArAr'NM + SO_2F_2 \rightarrow \underset{\textbf{145}}{ArAr'NSO_2F} + MF \qquad (95)$$

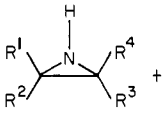
M = Li, Na

The unsubstituted parent sulfamyl fluoride[495] was prepared by Mandell and Huber by reaction of sulfamic acid with PCl_5 in the presence of liquid HF and the Lewis catalyst BF_3. *N,N*-Difluorosulfamyl fluoride, NF_2SO_2F,[496-499] has been synthesized by both thermolysis and photolysis of tetrafluorohydrazine (N_2F_4) and sulfur dioxide. Replacement of the fluorine bonded to the sulfur by chlorine failed; however, *N,N*-difluorosulfamyl chloride (NF_2SO_2Cl) has now been prepared[499] by photolysis of a mixture of tetrafluorohydrazine and sulfuryl chloride at 2537 Å. The new compound is less stable than its sulfamyl fluoride analogue, and it has not proved useful as a synthetic reagent, since the N–S bond and also the S–Cl bond cleave when typical substitution reactions are attempted. Thus, reaction with mercury or bis-[(trifluoromethyl)thio]mercury gave N_2F_4 and SO_2 (eq 96).

$$2NF_2SO_2Cl + (CF_3S)_2Hg \rightarrow N_2F_4 + 2SO_2 + (CF_3S)_2 + HgCl_2 \qquad (96)$$

N,N-Dichlorosulfamyl fluoride (NCl_2SO_2F, **146**) was prepared by Roesky[500] by reaction of $FSO_2N{=}S{=}O$ with chlorine monofluoride (ClF) at room temperature. On the basis of infrared, NMR, and mass spectrometric analysis, it had the structure **146**, rather than $ClFNSO_2Cl$. The compound decomposes on standing to N_2, Cl_2, and FSO_2Cl. It liberates iodine from aqueous potassium iodide solution; the first step involves the formation of $ClNHSO_2F$, which could be isolated in the form of its amide by treatment with tetraphenylphosphonium or -arsonium chloride to give $[(C_6H_5)_4Y]^+[FSO_2NCl]^-$ (Y = P, As). Likewise *N*-(trifluoromethyl)sulfamyl fluoride (CF_3NHSO_2F) is characterized as its tetraphenylarsonium salt.[501]

β-Chloro-substituted sulfamyl fluorides (**147**) have been formed by Hamprecht by reaction of substituted aziridines with chlorosulfonyl fluoride[466,502] (eq 97). In no case was the sulfamyl



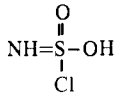
$$+ SO_2ClF \longrightarrow ClC(R^1)(R^2)C(R^3)(R^4)NHSO_2F \qquad (97)$$

147

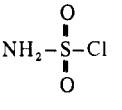
chloride obtained, and, accordingly, it is considered that the heavier halide reacts and migrates to the β position.

2. Physical Studies

The imido form of sulfamyl chloride (**148**) is not in equilibrium with the normal form (**149**). This conclusion was reached from



148

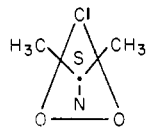


149

measurements of the infrared spectrum of sulfamyl chloride. Infrared and Raman spectra of *N,N*-dimethylsulfamyl chloride indicate that it has a plane of symmetry in the liquid state. Tentative assignments have been made for the spectra recorded.[503] Bürger et al.[504] have measured the infrared and (in part) the Raman spectra of the series $(CH_3)_2NSO_2X$, where X = F, Cl, Br. Calculation of the force constants S–X gave good agreement with the observed spectra with *f* S–F 4.15, *f* S–Cl 2.65, and *f* S–Br 2.38 mdyn/Å. Two further groups have re-

corded the infrared spectrum of dimethylsulfamyl chloride. Paetzold and Rönsch[505] measured the infrared and Raman spectra for the series $[(CH_3)_2N]_2Z$, $[(CH_3)_2N]_2ZO$, and $(CH_3)_2NZOCl$, where Z = Se or S. Z–O force constants are presented and the spectra are considered to be consistent with the existence of two rotational isomeric conformations in the liquid state. Török et al.[506] measured the S–N bond strength in the series $[(CH_2)_2N]_2SO$, $[(CH_3)_2N]_2SO_2$, and $(CH_3)_2NSO_2Cl$. Dimethylsulfamyl chloride was found to have the greatest S–N bond order. This is consistent with the electron-withdrawing effect of the chlorine atom facilitating greater $p\pi$–$d\pi$ interaction between the lone pair of electrons on nitrogen and the empty d orbitals of the sulfur atom.

Electron diffraction studies on *N,N*-dimethylsulfamyl chloride have been carried out by two groups. Vilkov and Hargittai[507] established that $(CH_3)_2NHSO_2Cl$ is present in the internal rotational form **150**. Hargittai and Brunvoll[508] reinvestigated the structure



150

and confirmed the previously established form of rotation around the S–N bond in the molecule. However, they found in their study that the bond lengths were shorter. In addition to experimental-scale error, the differences were attributed to the possibility of tetramethylsulfamide $[(CH_3)_2NSO_2N(CH_3)_2]$ being present as an impurity.

A low-temperature NMR study[509] of diethylsulfamyl chloride (Et_2NSO_2Cl) indicated a considerable barrier to rotation ($\Delta G \sim 48.2$ K J mol^{-1}). The measured barrier is considered to arise from torsion around the N–S bond rather than inversion of the nitrogen atom, and the results are interpreted in terms of directional $p\pi$–$d\pi$ bonding between the nitrogen and the sulfur which is enhanced by the electronegativity of the chlorine atom.

Biryukov and Deich[510] measured the nuclear quadrupole frequencies (^{35}Cl) of compounds containing chlorine and compounds containing chlorine and sulfur in an effort to explain similarities in their properties. Diethylsulfamyl chloride and diethylcarbamoyl chloride showed nonequivalent frequencies, however, and this was attributed to the nonequivalent influence of the competition between the inductive and conjugative effects in the sulfamyl and carbamoyl groups. The ^{35}Cl NOR frequency of sulfamyl chloride[511] has been measured.

The resonance frequency of 32.294 mHz for $MeNHSO_2Cl$ is 2.44 mHz below the value for the parent sulfamyl chloride. The electronegativity differences between the methylamine and the amino groups were insufficient to account for the abnormal frequency lowering, and hydrogen bonding and polarization were considered to be responsible for the observed reduction.

Exposure of sulfamyl chloride to Co γ rays at 77 K by Symons and Mishra led to the detection of $NH_2SO_2\cdot$ radical by ESR.[32]

3. Reactions

a. Ester Synthesis

Sulfamyl halides, in particular alkylsulfamyl chlorides, have been used extensively in the synthesis of esters of sulfamic acid. Interest in such compounds stems from the fact that a wide range of these sulfamate esters possess herbicidal activity. Dialkyl- or monoalkylsulfamyl chlorides are generally used with alkyl groups in the range C_{1-6}; both straight chains and branched chains are used. The range of ester-type compounds prepared from sulfamyl halides include benzofuranyl esters,[512] (sulfamyloxy)acetamides,[513] aryl dialkylsulfamate esters,[514] and substituted *O*-(aminosulfonyl)glycolic anilides[515,516] (see also references in III.B.3 and III.B.1).

b. Sulfamide and Cyclic Compound Syntheses

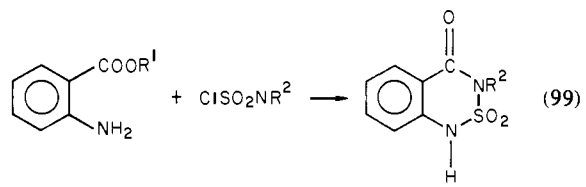
The reaction of amines, both alkyl and aryl, with sulfamyl chlorides is a general route to the synthesis of sulfamides.

$$RR^1NSO_2Cl + NH_2R^2 \rightarrow RR^1NSO_2NHR^2 \qquad (98)$$

$$R^1 = R^2 = R = \text{alkyl}$$

Mono- or dialkylsulfamyl chlorides are generally used with alkyl groups in the range C_{1-3}. A wide range of sulfamides have been prepared, including α-(aminoalkyl)-4-hydroxy-3-(sulfamylamino)benzyl alcohols[517-519] (adrenergic stimulants), sulfamidophenethanolamines[520] (antiarrhythmic agents), 2-(aminobenzimidazole)sulfonamides[521] (fungicides), and N,N′-substituted sulfamides[522] (herbicides).

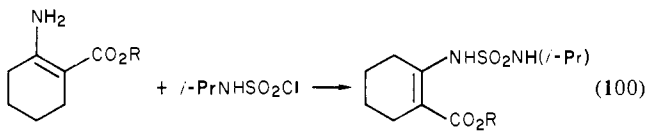
Cohen and Klarberg,[523] Hamprecht,[524-527a] and Bancroft et al.[527b] demonstrated the synthetic usefulness of sulfamyl chlorides in the preparation of heterocyclic compounds such as 2,1,3-benzothiadiazin-4-one 2,2-dioxides (**151**). Kloek and Leschin-



(99)

151

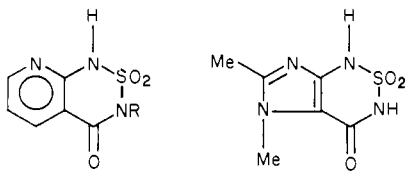
sky[526] have developed a methodology for the extension of the work of Cohen and Klarberg to achieve the synthesis of a variety of reduced and heterosubstituted reduced forms of **151**. The key reaction is that between, for example, isopropylsulfamyl chloride and the enamino esters **152** to give the sulfamide (eq 100). These sulfamides can be prepared by using the conditions



(100)

152
R = Et, *t*-Bu

of Cohen and Klarberg (aqueous base) (if a simple straight-chain sulfamyl chloride was used) or by using trifluoroacetic acid/anhydride (when *i*-$PrNHSO_2Cl$ was used). In the presence of a carboxylic amide or a tertiary amine, 1*H*-pyrido[3.2-e]-[2,1,3]thiadiazin-4-one 2,2-dioxides (**153a**) were similarly prepared by reaction of alkylsulfamyl halides with methyl 2-aminonicotinate.[527a] Likewise the imidazothiadiazine dioxide

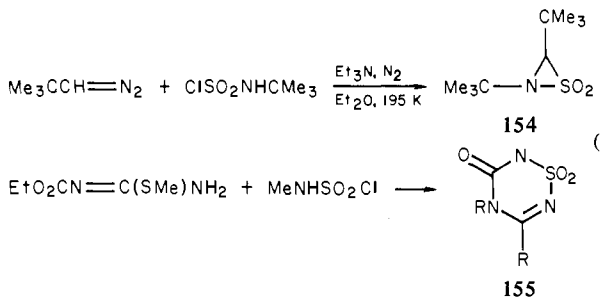


153a **153b**

and a pyrimidothiadiazine dioxide are obtained by cyclization reactions with sulfamyl chloride.[529] The cyclic systems thiaziridine 1,1-dioxide (**154**)[530a] and thiatriazine 1,1-dioxide (**155**)[530b] are prepared by the cycloaddition reactions with sulfamyl chlorides shown in eq 101. In the reaction of *o*-aminodialkylanilines with sulfuryl chloride to give benzamidazoles, *o*-aminodialkylbenzenesulfamyl chlorides (possible precursors of *N*-sulfonylarylimines, $ArN{=}SO_2$) have been suggested as intermediates.[531]

c. Other Reactions

The reactions of $RNHSO_2X$ (X = Cl, F) have been studied widely by different groups. Roesky[501] has shown that sulfamyl



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(101)

155

chloride when reacted with thionyl chloride yields the imide **156** which in the presence of excess anhydrous hydrogen fluoride is converted to sulfamyl fluoride which provides an alternative synthesis for this compound.

$$ClSO_2NH_2 + 2SOCl_2 \rightarrow \underset{\mathbf{156}}{ClSO_2N{=}SCl_2} \quad (102)$$

$$ClSO_2N{=}SCl_2 + 5HF \rightarrow FSO_2NH_2 + SF_4 + 3HCl \quad (103)$$

Sulfamyl fluoride has been reacted with diketene in the presence of base to give cyclic products which are useful as artificial sweeteners.[532] The low-temperature reaction of sulfamyl chloride has led to a route for the synthesis of the hitherto unknown asymmetrically substituted imidobissulfamides,[533] $H_2NSO_2NHSO_2NR_2$.

Sulfamyl fluoride undergoes substitution reactions leading to the formation of *N*-fluorosulfamyl fluoride and *N,N*-difluorosulfamyl fluoride,[534] sulfur oxide difluoride ((fluorosulfonyl)urìde),[535] 3,4-dihydro-2,1,3-oxathiazin-4-one 2,2-dioxides,[536] *N*-chloro-*N*-(trifluoromethyl)fluorosulfonamides,[537] and (trimethylsilyl)-sulfamyl fluorides.[538] (Trifluorophosphazo)sulfuryl fluorides[539,540] (**157**) are prepared by reaction of sulfamyl fluoride with PF_3Cl_2 (eq 104). The use of *N,N*-difluorosulfamyl fluoride as a catalyst

$$PF_3Cl_2 + FSO_2NH_2 \rightarrow \underset{\mathbf{157}}{PF_3{\cdot}NSO_2F} \quad (104)$$

for polymerization has been demonstrated,[541,542] poly(tetrafluoroethylene) being produced by heating tetrafluoroethylene in the presence of *N,N*-difluorosulfamyl fluoride.

Nucleophilic displacement at sulfamyl sulfur by the hydrazines $YNHNH_2$ (**158**, Y = benzoyl, 2-pyridyl) yielded the sulfamyl hydrazines, **159**.[543] Two other types of reaction involving ho-

$$R_2NSO_2Cl + \underset{\mathbf{158}}{YNHNH_2} \rightarrow \underset{\mathbf{159}}{R_2NSO_2NHNHY} \quad (105)$$

molytic cleavage of the S–Cl bond were observed.[543] First, where the hydrazine used was methylhydrazine or 1,1-dimethylhydrazine, the reaction produced tetrasubstituted sulfamides (eq 106). The proposed reaction mechanism is shown

$$2R_2NSO_2Cl \rightarrow R_2NSO_2NR_2 \quad (106)$$

in eq 107. An alternative mechanism in the case of 1,1-di-

$$\begin{aligned} R_2NSO_2Cl &\xrightarrow{\Delta} R_2NSO_2{\cdot} + Cl{\cdot} \\ R_2NSO_2{\cdot} &\rightarrow R_2N{\cdot} + SO_2 \\ R_2NSO_2{\cdot} + R_2N{\cdot} &\rightarrow R_2NSO_2NR_2 \end{aligned} \quad (107)$$

methylhydrazine was considered also to be operative: the oxidation of the hydrazine took place together with homolysis of the halide with the incorporation of the hydrazine radicals into the product (eq 108). Second, the reaction with phenylhydrazine

$$\begin{aligned} (CH_3)_2NNH_2 &\xrightarrow{\text{oxidation}} (CH_3)_2NN{=}NN(CH_3)_2 \\ (CH_3)_2NN{=}NN(CH_3)_2 &\xrightarrow{\Delta} 2(CH_3)_2N{\cdot} + N_2 \\ (CH_3)_2NSO_2{\cdot} + {\cdot}N(CH_3)_2 &\rightarrow (CH_3)_2NSO_2N(CH_3)_2 \end{aligned} \quad (108)$$

yielded phenyl-2-benzenesulfonylhydrazide[544] (eq 109), and the most likely mechanism is shown in eq 110.

$$C_6H_5NHNH_2 + R_2NSO_2Cl \rightarrow C_6H_5NHNHSO_2C_6H_5 \quad (109)$$

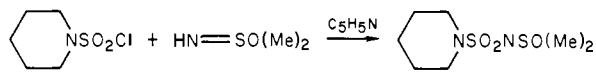
$$\begin{aligned} C_6H_5NHNH_2 &\rightarrow C_6H_5NHNH{\cdot} \rightarrow C_6H_5N{=}NH \\ C_6H_5N{=}NH &\rightarrow C_6H_5N_2{\cdot} \rightarrow C_6H_5{\cdot} \\ C_6H_5{\cdot} + SO_2 &\rightarrow C_6H_5SO_2{\cdot} \\ C_6H_5SO_2{\cdot} + NHNHC_6H_5{\cdot} &\rightarrow C_6H_5SO_2NHNHC_6H_5 \end{aligned} \quad (110)$$

Sulfamyl halides have been used for the synthesis of alkylsulfamyl peroxides[545] **160** by allowing the reaction to occur at 233 K in diethyl ether (eq 111). Hydrolysis of the O–O bond

$$ROOH + NH_2SO_2Cl \xrightarrow{C_5H_5N} \underset{\mathbf{160}}{ROOSO_2NH_2} + C_5H_5NHCl \quad (111)$$

occurs above 263 K to give the following decomposition products: (a) R = *n*-propyl: sulfamic acid, propanol, propyl, propionate, and isopropyl propionate; (b) R = *n*-butyl: sulfamic acid, butanal, 2-methylpropanal, and butyl butyrate.

The synthesis of *N*-sulfamyldimethylsulfoximines (**161**)[546a] has been achieved by reaction of N,N-disubstituted sulfamyl halides in the presence of a tertiary amine with dimethylsulfoximine (eq 112). An efficient method for the conversion of tertiary alcohols



161

(112)

to amines[546b] involves reaction of the alcohol with chlorosulfonyl isocyanate to give *N*-chlorosulfonylurethanes which decompose to give the sulfamyl chloride of the alcohol. These are best reduced to amines by formation of the *tert*-butoxycarbonylhydrazides and reduction with $Pb(OAc)_4$.

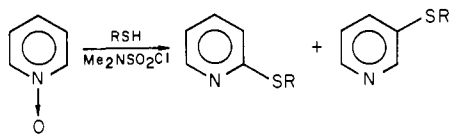
N,N-Disubstituted sulfonamides have traditionally been obtained by the reaction of a sulfonyl halide with an amine. Gupta[547] has shown that N,N-disubstituted sulfonamides can now be prepared by reacting dialkylsulfamyl chloride–aluminum chloride complexes with aromatic hydrocarbons. Sulfamylation of benzene has also been reported by using antimony pentafluoride (SbF_5).[548] Re-

$$R^1R^2NSO_2Cl \xrightarrow{AlCl_3} R^1R^2NSO_2Cl{\cdot}AlCl_3 \xrightarrow{C_6H_6} R^1R^2NSO_2C_6H_5 \quad (113)$$

$$R^1 = R^2 = Et$$

action of sulfamyl halides with Grignard reagents was carried out by Maslii and Petrov[549] in an attempt to develop a synthetic route to N,N-disubstituted sulfonamides. However, the products isolated were diethylamine and *n*-butyl chloride.

Deoxidative substitution of pyridine *N*-oxide by mercaptans in the presence of dimethylsulfamyl chloride yielded the sulfides shown in eq 114.[550] Reaction of a sulfamyl halide with sodium



(114)

bis(trimethylsilyl)amide yielded (trimethylsilyl)sulfamides,[551] while reaction of dialkylsulfamyl halides with the same compound at 243 K yielded dialkylamidosulfinates.[552]

Scott and Barry[553] reported that sulfamyl halides in dimethylformamide solution yield Vilsmeier–Haack reagents, which undergo substitution by reaction with primary aromatic amines to yield formamide hydrochlorides (**162**).

$$Me_2NSO_2Cl{\cdot}Me_2NCOH + XNH_2 \rightarrow \underset{\mathbf{162}}{XN{=}CHNMe_2{\cdot}HCl} \quad (115)$$

X = Ar, NHAr

Reaction of dimethylaniline with those Vilsmeier–Haack reagents gave tetramethylsulfamides (70% yield). At higher

temperatures, (*p*-dimethylamino)benzenesulfonic acid (80%) could be obtained from the same substrate and reagent.

d. Hydrolysis

Hall[554] has reported on the hydrolysis of dimethylsulfamyl chloride, $(CH_3)_2NSO_2Cl$, and concluded that the reaction occurred through an ionization mechanism (S_N1). The possibility of an ionization process can be considered because of the possible stabilization by the amino function. Hall and Lueck[555] examined

$$R_2NSO_2Cl \rightarrow R_2NSO_2^+ + Cl^-$$

this reaction in two ways: first, by promoting the ionization mechanism by using mercuric perchlorate as a powerful electrophilic reagent, and second, by attempting to trap the unstable intermediate dialkylsulfamylium ions produced. They found that the halide reacts very rapidly with the mercuric salt, a reaction which they concluded involved sulfamylium ions ($R_2NSO_2^+$) though these could not be trapped by a variety of nucleophiles. There appears to be no compelling evidence for the formation of the sulfamylium ions solvolytically in the absence of mercuric ions. Rogne,[556] however, studied the hydrolysis of dimethylsulfamyl chloride in water–acetone mixtures and compared the results to that of sulfonyl chlorides in the same solvent system (known to react via S_N2 mechanisms). He reasoned that if solvolysis occurred by two different mechanisms, this would be reflected in differences in activation parameters and sensitivity to added salts and solvent ionizing power. The similarity in activation parameters makes it unlikely that there is any substantial difference between the two activation processes involved.

The question of the mechanism of hydrolysis (S_N1 or S_N2) of *N,N*-dimethylsulfamyl chloride is a controversial one. Hall has suggested that this compound reacts by an S_N1 mechanism, but more recently, Rogne has proposed an S_N2-type mechanism. By careful use of a sophisticated mechanistic probe, namely, the temperature coefficient of the enthalpy of activation ($\Delta C_p^{\pm}$), Ko and Robertson[557] favor an S_N1-type mechanism. They believe that the more negative value of $\Delta C_p^{\pm}$ (−318.4 K J mol^{-1}) which they observed for the sulfamyl chloride compared with the value of −230 K J mol^{-1} found for the hydrolysis of typical sulfonyl chlorides, where there is evidence of considerable nucleophilic interaction, is due to solvent reorganization arising from the displacement of the chloride ion from an intimate ion pair (A) to give a solvent-separated ion pair (B) or even solvent-separated ions (C). For benzenesulfonyl chloride nucleophilic interaction presumably occurs at A, while for the sulfamyl chloride it is not possible to say whether it occurs at B or C or at B and C simultaneously. Steric hindrance plays a major role in impeding the approach of nucleophiles, and the facts that Rogne found a linear acceleration with azide ion and Hall an acceleration with the strong nucleophile *m*-cresoxide ion, but no acceleration of rate with the weaker and bulkier pyrrolidine and piperidine molecules or the solvated hydroxide ion, are consistent with an S_N1 mechanism being favored in the presence of the still weaker base, water—the medium used in the present study. Hall's suggestion that there is resonance electron release from the dimethylamino groups to sulfur (thereby hindering nucleophilic attack) is shown to be unlikely, since the inverse secondary γ-deuterium isotope effect (k_H/k_D) for the hexadeuterio compound is 0.95.

Ko and Robertson[556] have also studied the mechanism of hydrolysis of the sulfamyl chlorides **163** in water. These

$(C_2H_5)_2NSO_2Cl$ **163a** $(n\text{-}C_3H_7)_2NSO_2Cl$ **163b** $C_2H_5(CH_3)NSO_2Cl$ **163c** $C_5H_{10}NSO_2Cl$ **163d**

compounds hydrolyze faster (in water, 288 K) than dimethylsulfamyl chloride by factors of 8.3, 4.0, 3.0, and 2.3, for **163a**, **163b**, **163c**, and **163d**, respectively. The authors have identified the source of these rate differences as being due to steric hindrance to the approach of nucleophile. Also, the α hydrogens of the ethyl groups are favorably placed for hydrogen participation, and that such participation is important is shown by the secondary deuterium isotope effect ($k_H/k_D = 2$) measured with **163a** and $(CH_3CD_2)_2NSO_2Cl$. The $\Delta C_p^{\ddagger}$ values for **163a** and **163d** were −153.4 and −184.4 K J mol^{-1}, respectively, and for **163c** a value of −255.5 K J mol^{-1} was observed. These values are very much lower than the value observed for the dimethylsulfamyl chloride and the values normally observed for halides undergoing hydrolysis by the S_N1 mechanism (−293 to 335 K J mol^{-1}). However, the authors consider that these changing values do not point to a change in hydrolysis mechanism, but instead reflect a real difference in the degree of solvent reorganization in the activation process for the hydrolysis of the various sulfamyl chlorides studied. Thus, the hydrolysis of a halide in water by the S_N1 mechanism need not necessarily be accompanied by a substantial amount of solvent reorganization, which, contrary to classical ideas, implies reduced solvation of the transition state. $\Delta C_p^{\ddagger}$ would appear to be potentially a very useful diagnostic tool for the detection of subtle distinctions in mechanism.

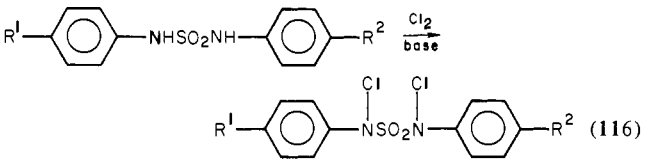
Lee and Kim[559] have found that the $\Delta H^{\ddagger}$ and $\Delta S^{\ddagger}$ parameters for the exchange of ^{36}Cl, ^{82}Br, and ^{131}I with Me_2NSO_2Cl in dry acetone decreased in the order $Cl^- > Br^- > I^-$. This is the reverse of the order observed for the faster reaction with $PhSO_2Cl$. These authors consider their results in terms of the hard–soft acid–base theory and apply this to the two sulfur centers. They conclude that in the transition state for benzenesulfonyl chloride exchange bond forming and breaking have progressed more than in the analogous transition state for nucleophilic exchange of halide in dimethylsulfamyl chloride. Extended Hückel MO calculations on Me_2NSO_2Cl (and some sulfonyl chlorides and $MeOSO_2Cl$) have been carried out by the same group.[560] The exchange reaction of $^{36}Cl^-$ with Me_2NSO_2Cl has also been studied by Cha.[561]

IV. Sulfamide

A. Synthesis

Sulfamide ($NH_2SO_2NH_2$) has been prepared by a variety of procedures and the earlier reactions and methods have been reviewed by Audrieth and Sveda.[562] Ito[563] has studied the gas-phase synthesis of sulfamide. The actual yields of sulfamide were found to decrease if the temperature exceeded 403 K. This has been attributed to the thermal rearrangements in sulfamide leading to the formation of sulfamide condensates[564] $(NH_4NSO_2)_2$ or $NH_4N(SO_2NH_2)_2$ depending on the temperature. The condensate, however, can be hydrolyzed and additional sulfamide recovered, thus improving the yield.[565]

In the early sixties Sowada[566] presented a short review of the synthesis of sulfamides (see references therein) in which he summarized the three main synthetic routes to sulfamides: (a) reaction of primary amines (alkyl or aryl) with sulfuryl chloride; (b) reaction of primary amines with chlorosulfonic acid; (c) reaction of primary amines (R = alkyl, cycloalkyl, aryl) with sulfamide. He further extended the range of symmetrical, N,N′-disubstituted alkyl- and cycloalkylsulfamides available by reaction a.[567] The sulfamides $RNHSO_2NHR$ (R = alkyl and cycloalkyl) were reacted further to form *N,N′*-alkyl-*N,N′*-chlorosulfamides (**164**, R(Cl)NSO_2N(Cl)R, R = *n*-Pr, *i*-Pr, *n*-Bu, cyclohexyl).[588] The corresponding arylchlorosulfamides (**165**) were prepared by Forster, Gilchrist, and Rees[569] by the action of excess chlorine in aqueous sodium hydroxide on the corresponding diarylsulfamides (eq 116). Tetrasubstituted alkylsulfamides were prepared by Sowada[570] by reaction of the dichlorosulfamides **165** with aryl sulfates. Likewise the *N*-alkyl-*N*-acetylsulfamides **166** were prepared by the reaction of N,N′-disubstituted sulfamides



$R^1 = R^2 = H$; $R^1 = R^2 = Cl$; $R^1 = Br$, $R^2 = Cl$

with acetic anhydride.[571] Sowada has also extended the re-

$$RN(Ac)SO_2N(Ac)R$$
166, R = *n*-Pr, *n*-Bu, *i*-Bu

actions of N,N′-disubstituted sulfamides to yield tetrasubstituted sulfamides.[572,573] The reaction procedures mentioned above have been used to synthesize 2-phenylcyclopropylsulfamides.[574] N,N-disubstituted sulfamides,[575] and N-substituted sulfamides.[576]

The reaction of sulfamyl halides with alkyl- and arylamines has been used extensively as a route to sulfamides.[577-562] This

$$RR'NSO_2Cl + HNR^2R^3 \rightarrow RR'NSO_2NR^2R^3 \quad (117)$$

reaction has also been used in the synthesis of N-substituted arylsulfamides[563-565] and also (1,2,4-triazol-5-yl)sulfamides.[566]

Yamaguchi and Fukuno[567] have obtained N,N′-disubstituted sulfamides by reaction of amine salts of sulfamates with phosphorus oxytrichloride in pyridine (eq 118). The reactions

$$RNHSO_3^-H_3^+NR \xrightarrow[C_6H_5N]{POCl_3} RNHSO_2NHR \quad (118)$$

of sodium sulfamides **167** with halides yield N,N′-disubstituted sulfamides (eq 119).[566]

$$R^1SO_2NHNa + R^2Cl \rightarrow R^1SO_2NHR^2 \quad (119)$$
167

R^1 = Me_2N, Me, morpholino; R^2 = 2,4-$(O_2N)_2C_6H_3$

The preparation of primary sulfamides, NH_2SO_2NHR, from N,N′-disubstituted sulfamides has been investigated. Sowada[569] considers that the acid hydrolysis of *N,N′*-di-*tert*-butylsulfamide occurs by protonation of the nitrogen atom, followed by loss of the tertiary butyl group, resulting in the formation of primary sulfamides (eq 120).

$$Me_3CNHSO_2NHCMe_3 + H^+ \rightleftharpoons Me_3CNH_2^+SO_2NHCMe_3 \rightarrow NH_2SO_2NHCMe_3 + Me_3C^+ \quad (120)$$

Catt and Matier[590] report a similar reaction of *N-tert*-butyl-*N′*-substituted sulfamides with trifluoroacetic acid (eq 121), which extended Sowada's reaction considerably.

$$Me_3CNH_2^+SO_2NHR \rightleftharpoons NH_2SO_2NHR + Me_3C^+ \xrightarrow{CF_3CO_2^-} CF_3CO_2CMe_3 \quad (121)$$

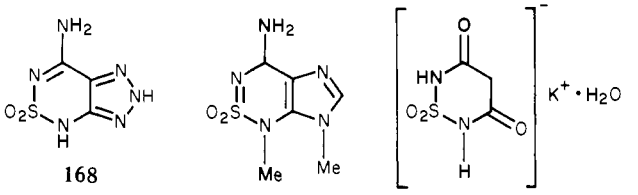
R = substituted C_6H_4, $CH_2CH_2C_6H_5$, H

B. Physical Studies

1. Structural

A normal coordinate analysis has been carried out on sulfamide.[591] Disilver sulfamide, $AgNHSO_2NHAg$, has been the subject of a structural study.[592] The compound belongs to a monoclinic space group. It contains discrete SO_2N_2 tetrahedra; each silver atom is bound to a N tetrahedron. Some years ago an X-ray diffraction study of *N,N,N′,N′*-tetramethylsulfamide, $Me_2NSO_2NMe_2$, gave detailed information on the molecular structure, and all bond angles and distances were determined.[593] These earlier data have more recently been confirmed, in general, from a gas electron diffraction study on the same molecule.[594] Some differences in estimates of the S–N distance and the S–N–C bond angle were thought to be due to a combination of factors, namely, differences in the definition of bond lengths obtained by the two techniques, differences in crystal packing considerations, and the influence of thermal motion.[594]

García-Blanco and co-workers have carried out X-ray diffraction studies on a series of 1,2,6-thiadiazine 1,1-dioxides.[595-601] Single crystals were examined on an automatic Philips PW 1100 four-circle diffractometer with graphite-monochromated Mo Kα radiation. Among the compounds studied were 7-amino-2*H*,4*H*-*vic*-triazolo[4,5-*c*]-1,2,6-thiadiazine 1,1-dioxide (**168**),[596] the purine analogue 4-amino-N^1,N^7-dimethylimidazo[4,5-*c*]-1,2,6-thiadiazine 1,1-dioxide (**169**).[599] and potassium 3,5-dioxo-2*H*,4*H*,6*H*-1,2,6-thiadiazine 1,1-dioxide monohydrate (**170**).[601]



2. Spectroscopic

The infrared spectra of thin sublimed films of sulfamide and deuteriosulfamide have been recorded over the range 300–5000 cm^{-1} at room temperature and 197 and 83 K.[602] The observed spectra have been interpreted satisfactorily on the basis of the structure $NH_2SO_2NH_2$ with site symmetry C_2, almost C_{2v}. The assignments given are consistent with the results of a normal coordinate analysis. Partial double bonding of the S–N bonds was indicated, but no indications of the ionic, $NH_3^+(NH:)SO_2^-$, or isoamidic, $NH_2(NH:)S(O)OH$, forms were observed. Sowada[603] has reported infrared spectra for a series of di- and tetrasubstituted sulfamides of the general formula $RR'NSO_2NRR'$, where typical R's were *n*-Pr, *i*-Pr, *sec*-Bu, cyclohexyl, *i*-Bu, etc., and R′ was H, Et, Me, or Ac. The observed bands are assigned, and the method of Gillespie and Robinson (loc. cit.) was used to calculate data (bond angle, force constant, etc.) for the SO_2 group. Bond and group refractivities have been reported for a number of tetrasubstituted sulfamides.[604] Infrared and NMR spectra have been recorded for tetramethylsulfamide.[506]

Exposure of sulfamide to ^{60}Co γ rays at 77 K gave rise to the reactions shown in eq 122–124.[32] **171** and **172** were

$$NH_2SO_2NH_2 \rightarrow H_3^+\dot{N}SO_2NH_2 + e^- \quad (122)$$

$$H_3^+\dot{N}SO_2NH_2 + NH_2SO_2NH_2 \rightarrow H\dot{N}SO_2NH_2 + H_3^+NSO_2NH_2 \quad (123)$$
171

$$NH_2SO_2NH_2 + e^- \rightarrow NH_2^- + NH_2\dot{S}O_2NH_2 \quad (124)$$
172

identified by ESR spectroscopy. ^{14}N nuclear quadrupole resonance parameters have been reported for sulfamide, *N,N*-dimethylsulfamide, and *N,N,N′,N′*-tetramethylsulfamide. The charge distributions on the nitrogen atoms of these compounds have been compared with those on urea and tetramethylurea.[605]

3. Thermochemical and Pyrolytic

The dissociation energy of $Et_2NSO_2NEt_2$ for the gas-phase reaction giving $(Et_2N)_2SO$ + O has been calculated from measured heats of reaction.[606] The specific heat of sulfamide has been measured over the range 90–298 K, and its entropy was estimated from the observed data.[55] The thermal decomposition of sulfamide gives rise to condensation products, and above 413 K polymerization also occurs.[607] A second study[608] suggests the formation of an unstable cyclic dimer to account for an

exothermic phase transition at 433–493 K. The heat of fusion of sulfamide has been determined.[609] The thermolysis of sulfamide was studied by TDA and conductometry. Mass spectrometric evidence for the ion $NH_2SO_2^+$, which may be responsible for polymerization, was obtained.[609] TDA and TGA have been used in a study of the pyrolysis of imidodisulfamide.[610]

C. Reactions

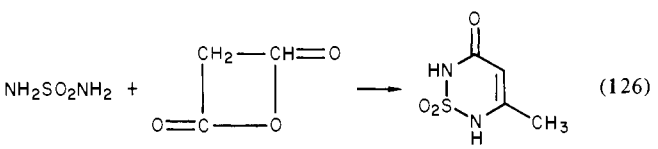
1. Reactions of Sulfamide, $NH_2SO_2NH_2$

Fluorination of aqueous solutions of sulfamide results in the synthesis of *N,N*-difluorosulfamide (eq 125). Derivatives of **173**

$$2F_2 + NH_2SO_2NH_2 \rightarrow 2HF + \underset{\mathbf{173}}{NF_2SO_2NH_2} \qquad (125)$$

as adducts with Lewis bases have been isolated.[611a] The electrochemical fluorination of sulfamide in HF yielded a wide range of inorganic compounds, including SO_2F_2 and NF_3.[611b] The corresponding *N,N*-dichloro compound has been prepared by reaction of sulfamide with Cl_2O.[612] The amino group of sulfamide has been replaced by nucleophiles leading to the formation of alkenylsulfamate esters[613] and (benzyloxy)sulfamides.[614]

The usefulness of sulfamide as a reagent for the synthesis of a wide variety of compounds has been demonstrated. Reaction of sulfamide with diketene has led to the synthesis of the isosteric analogue of 6-methyluracil, namely, the heterocyclic system, 3-methyl-5,6-dihydro-2*H*-1,2,6-thiadiazin-5-one 1,1-dioxide[615] (**174**). Knollmüller and Reich have prepared 3,7-bis-



(126)

174

(trichloromethyl)perhydro-1,5,2,4,6,8-dithiatetrazocine 1,1,5,5-tetroxide.[616] Sulfamide has also been used in the preparation of *N,N'*-bis(benzylidene)sulfamides[617] and 2-hydrohexafluoroisobutyric acid derivatives.[616]

The use of sulfamide in polymer synthesis has been demonstrated.[619-621] Copolymers of sulfamide, formaldehyde, and melamine have been prepared. The products were found to be extremely resistant to chemical attack, but their lack of thermal stability (decomposition in the range 490–540 K) limits their usefulness for high-temperature applications. Sulfamide has also been condensed with ethylenediamine and the resulting product was found to be effective as a cross-linking agent for cellulose fabrics.[622a] Ciaperoni has found that the reaction of disodium sulfamide with aliphatic acid dichlorides has led to formation of linear polymers.[622b]

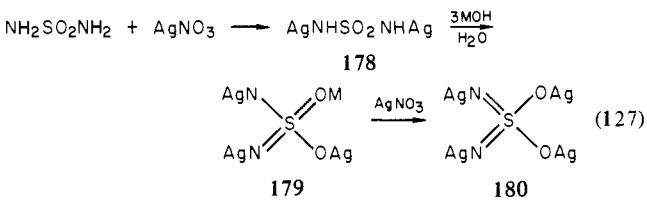
Analytical procedures have been developed for the determination of sulfamide. Yoshiro and Matsui[623] have reported a gas volumetric determination of sulfamide in the presence of ammonium chloride and ammonium sulfamate. The relative error in the determination of sulfamide in samples of known amounts, 0.05–0.5 mg, was less than 1.5%. A Spanish group[624] has determined sulfamide by nonaqueous titration; their procedure involves titration with 0.1 N perchloric acid with acetic acid as solvent and 1-naphtholbenzene as indicator.

The use of sulfamide and its substituted derivatives as ligands has not been studied extensively. Rhodium chelates[625] and mercury(II) complexes[626] with sulfamide have been reported; however, the composition was found to vary and has been attributed to hydrolytic decomposition and differences in reaction conditions.[626,627] Paquin[626] has reported on the complexes $M''A_2(NHSO_2NH_2)_2$, where A is a monoamine or half a diamine molecule. Ouchi and Moeller[629] have prepared a range of copper(II), nickel(II), and zinc compounds in which ammonia or an amine and sulfamide are present. Three types of complexes were reported, namely, **175**, **176**, and **177**, where M is

$M(BB)(Su)X_2$	$M(BB)_2(Su)X_2$	$M(BB)_2(Su)_2X_2$
175	**176**	**177**

mainly copper, BB is two molecules of ammonia or one molecule of a diamine, Su is sulfamide, and X is a uninegative or dinegative ion. The adducts were found to be stable in the solid state but decompose to the corresponding metal–amine complex and sulfamide when in contact with water. Infrared studies indicate weak sulfamide and N-substituted sulfamide interactions with the metal ions in question.

The reaction of sulfamide with silver nitrate has been studied. Traube[630] has previously shown that *N,N'*-diargentosulfamide (**178**) is formed from the reaction of sulfamide with silver nitrate. Popitsch and Nachbaur[631] have reacted **178** with sodium hydroxide to yield trisilver dinitridodioxosulfate (**179**). Further reaction of this compound with silver nitrate yielded the tetrasilver compound **180**. The overall scheme is shown in eq 127.



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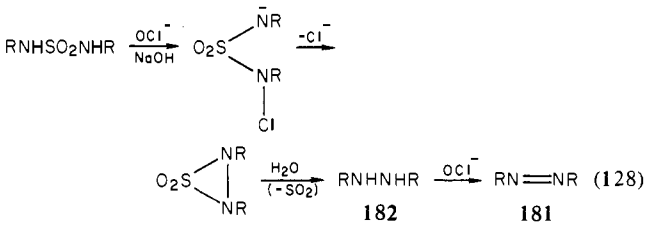
178 **179** **180**

2. Heterocyclic Synthesis Using Sulfamides

Ohme and Schmitz[632] have reported that reaction of *N,N'*-dialkylsulfamides with hypochlorite and base leads to the formation of azoalkanes (**181**) in accordance with the mechanism shown in eq 128. The reaction was intramolecular as shown

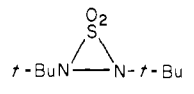


(128)

182 **181**

by the fact that when *N,N'*-dipropylsulfamide and *N,N'*-dibutylsulfamide were submitted to the reaction no mixed azoalkane (*n*-PrN = *n*-BuN) was obtained. The isolation of di-*N*-propylhydrazine in 50% yield when insufficient hypochlorite was used supports the involvement of *N,N'*-dialkylhydrazines as intermediates. The reaction of N,N-disubstituted alkylsulfamides and *N*-monoalkylsulfamides yielded the corresponding hydrazines ($RRNNH_2$, **183**, and $RNHNH_2$, **184**).[633]

Timberlake[634] studied the reaction shown in eq 128 and found a similar conversion of *N,N'*-dialkylsulfamides to azoalkanes by using potassium *tert*-butoxide as the base and *tert*-butyl hypochlorite as the chlorinating agent. He isolated the intermediate 2,3-di-*tert*-butylthiadiaziridine 1,1-dioxides (**185**).[635a] Quast and Kess synthesized 2,3-bis(1-adamantyl)thiadiaziridine 1,1-dioxide.[635b] The overall synthetic route to the thiadiaziridine can



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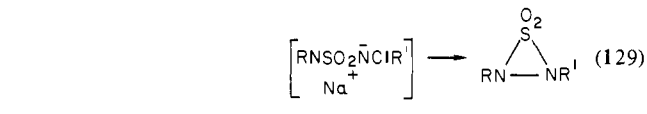
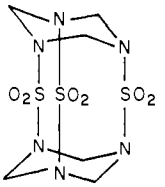
be summarized as in eq 129 Timberlake has studied the



(129)

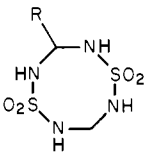
chemistry of the thiadiaziridine 1,1-dioxides and has summarized the reactivity toward a wide variety of chemical reagents.[636] Of particular interest is the chemical reactivity toward lithium and Grignard reagents which lead to sulfamides and azo compounds, respectively. Weinstein and Chang have also studied the reactions of *N,N'-tert*-butylthiadiaziridine, including hydrolysis, methanolysis, and reactions with various nucleophiles.[637] Forster, Gilchrist, and Rees[569] considered the oxidation of *N,N'*-diarylsulfamides with hypochlorite as a possible route to the corresponding arylazo compounds. The desired products were not obtained; however, the end products were quinone anils. The *N,N'*-dichlorodiarylsulfamides yielded small amounts of the corresponding azoalkanes.

Sulfamide, N-substituted sulfamides, and N,N'-disubstituted sulfamides have been condensed with a wide variety of reagents to form heterocyclic systems. Gilbert[636] et al. formed the novel system **186** by the reaction of sulfamide with paraformaldehyde.



186

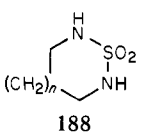
Dusemund[639-644] has studied the reactions of sulfamide and N-substituted sulfamides with various aldehydes, including formaldehyde, acetaldehyde, chromone-3-carbaldehyde, succindialdehyde, and phthalaldehyde. The major heterocyclic nucleus formed was a dithiatetraazocene, **187**. The substituents



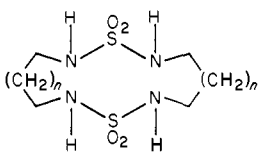
187

on the nucleus depend on the type of sulfamide and aldehyde used.

The reaction of sulfamide with diamino compounds has led to the synthesis of heterocyclic systems. Ciaperoni reported that the reaction of sulfamide with ethylenediamine led to the formation of 1,2,5-thiadiazolidine.[645] Arya and Shenoy[646] have pointed out that in the reaction of sulfamides with diamines where the methylene chain does not exceed eight carbon atoms the product formed will be monomeric in nature (**188**). Macrocycles **189**, however, are formed when the methylene chain exceeds eight carbon atoms. Bicyclic and tricyclic sulfamides[646-648] have also been prepared by reaction of sulfamide with the appropriate starting amines.



188
n = 2-6

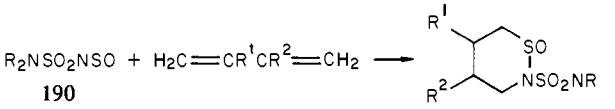


189
n = 7, 8, 10

The literature reveals that sulfamide has been used in the synthesis of a wide range of other heterocyclics compounds, including 3-amino-4*H*-1,2,4,6-thiatriazine 1,1-dioxides,[649] cyclic thiadiazines and thiadiazoles,[650-654] 1,2,5-thiadiazolidine 1,1-dioxides and homologues,[655] pyrazole,[656a] 1,2,6-thiadiazine-4-(3*H*)-one 2,2-dioxides,[656b] 1,2,6-thiadiazine-3(6*H*)-one 1,2-dioxides,[656c] and pyridinecarboxylic acids.[656d] Kirsanov et al.[657] have carried out an exchange reaction on *N,N*-dimethylsulfamide which leads to **190**. The condensation of **190** with dienes leads

$$Me_2NSO_2NH_2 + PhSO_2NSO \xrightarrow{C_6H_6} PhSO_2NH_2 + Me_2NSO_2NSO \quad (130)$$
190

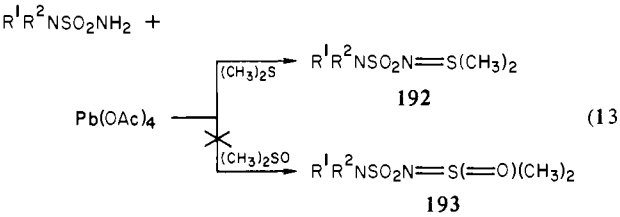
to the formation of the heterocyclic system **191**.



(131)

3. Reactions of Sulfamides with Inorganic Reagents

Reactions of substituted sulfamides with inorganic reagents have been reported. Oxidation of N,N-disubstituted sulfamides[546a] with lead(IV) acetate in dimethyl sulfide yielded the corresponding *N*-sulfamylsulfenimines (**192**). This reaction was unsuccessful in dimethyl sulfoxide, even though the lead(IV) acetate was completely converted to lead(II) acetate in the reaction; the N,N-disubstituted sulfamide was recovered unchanged. It would seem that the competitive oxidation of sulfoxide with lead(IV) acetate takes precedence (eq 132).



(132)

Reaction of N,N'-disubstituted sulfamides bearing active hydrogens at α carbons in the presence of base and thionyl chloride led to sulfenimines[656] (**193**). Reaction of sulfamide with antimony pentachloride[659] yielded antimony tetrachloroethoxide, $SbCl_4(OEt)$. *N*-(1,2,2,2-Tetrachloroethyl)-*N',N'*-dimethylsulfamide,[660] $CCl_3CHClNHSO_2N(CH_3)_2$ (**194**), has been prepared by reaction of *N*-hydroxysulfamide with phosphorus pentachloride. This compound is found to have a very labile chlorine atom which rapidly exchanges with azide, isocyanate, isothiocyanate, and hydrocyanic acid to give **195**–**198**.

$CCl_3CH(N_3)NHSO_2N(CH_3)_2$ **195**
$CCl_3CH(NCO)NHSO_2N(CH_3)_2$ **196**
$CCl_3CH(NCS)NHSO_2N(CH_3)_2$ **197**
$CCl_2{=}C(CN)NHSO_2N(CH_3)_2$ **198**

N,N-Difluorosulfamide, prepared by aqueous fluorination of sulfamide, was found to decompose at temperatures above 278 K. Attempts to stabilize the fluorination product by substitution of alkyl groups revealed that cleavage of the N–S bond occurred on fluorination and the corresponding *N,N*-difluoroalkylamine was formed instead. The reaction (eq 133) is not restricted to

$$RNHSO_2NH_2 + 2F_2 \rightarrow RNF_2 + FSO_2NH_2 + HF \quad (133)$$

monosubstituted derivatives, since *N,N*-dimethylsulfamide had been shown earlier to produce dimethylfluoramine.[661] It appears that the low volatility and instability of secondary fluoramines limit the application of the reaction to N,N-dialkyl substrates.

4. Reactions of Sulfamides with Silyl Reagents

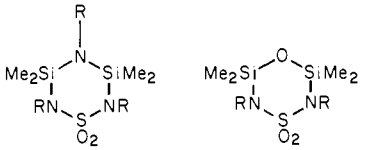
Appel and Montenarh[662] have reported on the reaction of sulfamides with various silylation reagents and the subsequent reaction of these compounds. The silylation of *N,N*-dialkylsulfamides with hexamethyldisilazane[663] or trimethylchlorosilane/triethylamine under various conditions leads to the formation of *N,N*-dimethyl-*N',N'*-mono(trimethylsilyl)sulfamide (**199**) and bis compound **200**. Subsequent reaction of the bis com-

$RR'NSO_2NHSiMe_3$ **199**
$RR'NSO_2N(SiMe_3)_2$ **200**

pound **200** with thionyl chloride leads to the synthesis of *N*-sulfinylamides (**201**). Appel[664] also presents various routes for

$$RR'NSO_2N(SiMe_3)_2 + SOCl_2 \rightarrow \underset{\mathbf{201}}{RR'NSO_2NSO} \quad (134)$$

the synthesis of *N*,*N*-bis(trimethylsilyl)- and *N*,*N*,*N*′,*N*′-tetrakis(trimethylsilyl)sulfamides. The reactions of monosilylated sulfamides have also been reported.[665] The tris(trimethylsilyl)-sulfonic acids can be readily obtained from the silylamines and trimethyl esters of chlorosulfonic acid.[666] Wannagat and Labuhn[667] have reported on the cyclic compounds **202** and **203**, which were prepared by condensation of *N*,*N*′-dialkylsulfamides with $R^1N(SiMe_2Cl)_2$ and $O(SiMe_2Cl)_2$, respectively.



202 **203**

5. Other Reactions

N,*N*-Dialkyl- and *N*,*N*-diarylsulfamides react with chlorosulfonyl isocyanate to yield the previously unreported *N*-(chlorosulfonyl)-*N*′-(dialkyl- or diarylsulfamyl)ureas (**204**).[666] Hydrolysis

$$R'RNSO_2NH_2 + ClSO_2NCO \rightarrow \underset{\mathbf{204}}{R'RNSO_2NHCONHSO_2Cl} \quad (135)$$

of these compounds led to the formation of *N*-(dialkyl- or diarylsulfamyl)ureas, while pyrolysis led to the formation of sulfamyl chlorides. The fluoro compounds corresponding to **204** have also been reported.[669]

Lombardino[670] has reported that the reaction of guanidines with N,N-disubstituted sulfamides did not result in the displacement of ammonia; instead sulfamylguanides (**205**) were produced.

$$R^1R^2NC(=NH_2^+)-NHSO_2NH^- \quad \mathbf{205}$$

A Russian group has prepared[671] a number of *N*-sulfonylbenzamidines (**206**) by reaction of benzamidine with sulfamide and N-substituted sulfamides. Unlike the corresponding un-

$$\underset{\mathbf{206}}{C_6H_5C(=NH)NHSO_2R}$$

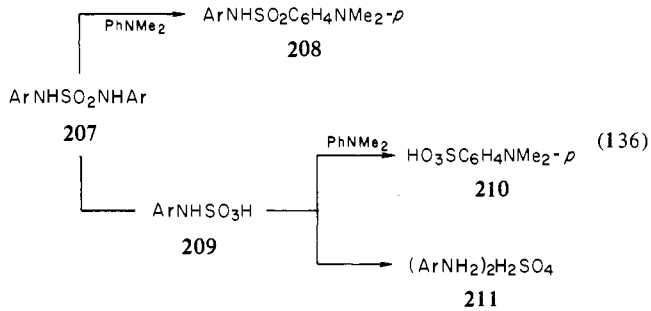
substituted amidines, these materials are not hydrolyzed when heated in aqueous or alcoholic solution.

Yas'kovyak[672] et al. have reported on the interaction of tetraethylsulfamide ($Et_2NSO_2NEt_2$) with the weak electron acceptors CCl_4, $CHCl_3$, and C_2HCl_5. The haloalkanes are considered to form complexes with the sulfamide. Evidence is presented to support the idea that the linkage is effected through the lone pair of the amide nitrogen atom.

6. Hydrolysis and Rearrangement of Sulfamides

The protonation, rearrangement, and hydrolysis reactions of sulfamides have been reported. Jolly[673] studied the exchange rates for sulfamide in both acidic and basic media. The magnitude of k_1 for the protonation of sulfamide itself was 3×10^7 M^{-1} s^{-1}, a value similar to that for the protonation of other weak bases (e.g., the rate constant for methanol is 10^6 M^{-1} s^{-1}). The rate constant for the reaction of sulfamide with OH^- (2×10^{11} M^{-1} s^{-1}) was consistent with rate constants for the reactions of OH^- with acids stronger than water. $K \sim 10^{10}$ to 10^{11} M^{-1} s^{-1}.

Thermolysis of N-substituted sulfamides[154,674] has led to the formation of the ammonium salts of the corresponding sulfamic acids. A similar reaction has been observed for N,N′-disubstituted (alkyl) sulfamides. Scott[675,676] has shown that *N*,*N*-diphenylsulfamide rearranged to yield sulfanilanilide and that the transfer of the sulfonic acid occurred by an intermolecular mechanism. The presence of increasing amounts of water led to the production of increasing amounts of aniline sulfate in the reaction. Scott, Barry, and Spilane[677] have examined the reactions of *N*,*N*′-diarylsulfamides (**207**) under conditions where the nucleophiles water (O center) and dimethylaniline (either C or N centers) can compete in attack at the sulfur hexavalent site of **207**. The various pathways observed are outlined in eq

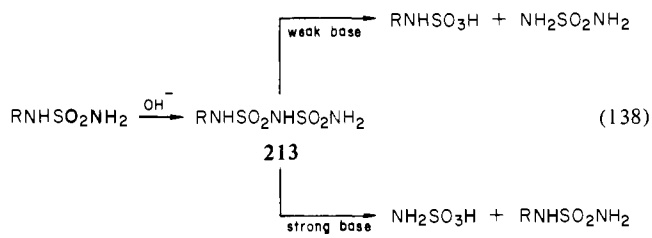


(136)

136. A key process is the transsulfamylation reaction, **207** → **208**, which is considered to involve direct aromatic attack of dimethylaniline on protonated **207**. In the presence of added quantities of water, nucleophilic attack by oxygen to give sulfamic acids **209** opens up the route to sulfonic acids **210** and arylamine sulfates **211**. *N*,*N*′-Dialkylsulfamides were also studied, and *N*,*N*′-dicyclohexylsulfamide reacted in aniline to give in addition to sulfonated products substantial amounts of the cyclohexylammonium salt of cyclohexylsulfamic acid. In the light of Yamaguchi's result[154,674] (see above), these findings substantiate the hypothesis that sulfamic acids are intermediates in the amine-induced cleavages of sulfamides (water being available). N,N,N′,N′-Tetrasubstituted sulfamides[676] were found to be extremely unreactive and do not undergo hydrolysis, amide exchange, or transsulfamylation reactions. This stability contrasts with the case of disubstituted sulfamides which have been found to participate in transsulfamylation and amine-exchange processes. *N*,*N*,*N*′,*N*′-Tetraphenylsulfamide[679] has been reported to rearrange to the sulfonamide **212** by reaction with butyllithium in tetrahydrofuran.

$$Ph_2NSO_2NPh_2 \xrightarrow[THF]{BuLi} \underset{\mathbf{212}}{PhNHC_6H_4SO_2NPh_2} \quad (137)$$

N-Substituted sulfamides[660] have been hydrolyzed in aqueous and basic solutions. *N*-Alkyl- or -benzylsulfamides were hydrolyzed to the corresponding ammonium sulfamates in 40–80% yield in water and to the sodium salt of sulfamates in 65–90% yield with aqueous sodium hydroxide. N,N′-Disubstituted sulfamides yielded the respective sulfamates. Yamaguchi[661] et al. have isolated the intermediate $RNHSO_2NHSO_2NH_2$ (**213**) in the hydrolysis of N-substituted sulfamides. This intermediate was considered to arise from the bimolecular condensation product of $RNHSO_2NH^-$. The resulting product ratio depended on base concentration. Spillane, Barry, and Scott[662] have studied the



(138)

kinetics of hydrolysis of a series of *N,N'*-diarylsulfamides (**214**)

$$p\text{-}XC_6H_4NHSO_2NHC_6H_4X\text{-}p$$
214, X = H, Me, MeO, Cl and NO_2

in 90% 0.1 hydrochloric acid–10% acetone at both 323 and 348 K. From the kinetic data a ρ value of +1.03 with average values of $\Delta H^{\ddagger} = 77.2$ K J mol^{-1} and $\Delta S^{\ddagger} = -121.8$ J mol^{-1} K^{-1} was calculated. The above results were considered to be consistent with the mechanism shown in eq 139. Under the

$$\begin{aligned}
&\text{(i)}\ ArNHSO_2NHAr + H^+ \rightarrow ArNHSO_2NH_2Ar^+ \\
&\text{(ii)}\ ArNHSO_2NH_2Ar^+ + H_2O \xrightarrow{k_1} ArNHSO_3H + ArNH_2 \\
&\text{(iii)}\ ArNHSO_2OH + H^+ \rightarrow ArNH_2{}^+SO_2OH \\
&\text{(iv)}\ ArNH_2{}^+SO_2OH + H_2O \xrightarrow{k_2} ArNH_2 + H_2SO_4
\end{aligned} \qquad (139)$$

conditions of the reaction $k_2 > k_1$ and step ii was considered to be rate determining and to operate via an A2 process. The acid-catalyzed hydrolyses of *N,N'*-diarylsulfamides are much less sensitive to acid concentration than are the corresponding hydrolyses of arylsulfamic acids.

V. References

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