

Sulfamic Acid and Its N-Substituted Derivatives

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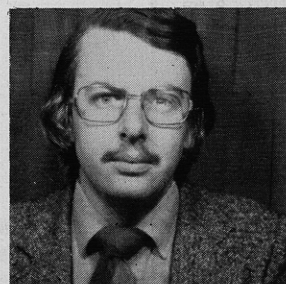
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I. Introduction and Scope

Sulfamic acid chemistry was extensively reviewed by Audrieth, Sveda, Sisler, and Butler in *Chemical Reviews* in 1940.¹ Later, the reviews of Gilbert² (1965) and of Burton and Nickless³ (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 Symposium on Sulfamic Acid in Milan in 1966, Bicelli⁶ presented a short review on sulfamic acid and sulfamates, and Romagnani⁷ gave a bibliography with over 450 references on sulfamic acid and its electrometallurgical applications. Scott and Spillane⁸⁻¹⁰ have reviewed the important mechanistic aspects of sulfamic acid chemistry to about the end of 1972. In the last review¹⁰

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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 Gilbert² and Burton and Nickless³ 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, $-\text{CONHSO}_3^-$, and sulfonylsulfamates, $-\text{SO}_2\text{NHSO}_3^-$; (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., $=\text{NSO}_3\text{H}$, 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 $=\text{NSO}_2\text{N}=\text{}$, $-\text{CONHSO}_2\text{NH}_2$, 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 study¹³ 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 diffraction¹⁵ and X-ray¹⁶ 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 , $\text{K}_2\text{NH}(\text{SO}_3)_2$, and $\text{K}_3\text{N}(\text{SO}_3)_3$, following a detailed X-ray diffraction study of potassium nitrilotrisulfonate.¹⁸ These compounds have similar S–O bond distances and the O–S–O bond angles are similar, but the nitrilo-

trisulfonate 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 $\text{K}_3\text{N}(\text{SO}_3)_3$. A monoclinic–orthorhombic transition has been found for cyclohexylsulfamic acid from X-ray studies.¹⁹

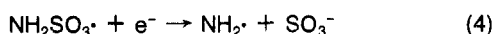
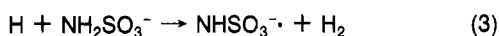
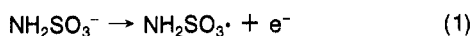
2. Infrared and Raman Spectroscopy

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 $\lambda = 2537\text{-}\text{\AA}$ 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 $\text{NH}_3^+\text{SO}_3^-$ and $\text{ND}_3^+\text{SO}_3^-$ 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's²³ 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 assigned²⁴ 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^- , $\text{CH}_3\text{NHSO}_3^-$, $\text{CH}_3\text{NDSO}_3^-$, and $(\text{CH}_3)_2\text{NSO}_3^-$ 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 $\text{NH}_2\text{SeO}_3^-$, $\text{CH}_3\text{NHSeO}_3^-$, and $(\text{CH}_3)_2\text{NSeO}_3^-$. 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

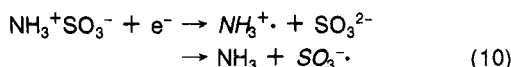
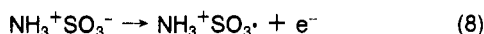
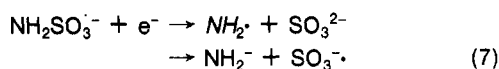
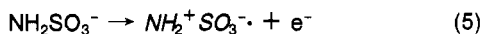
3. Magnetic Resonance Spectroscopy

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 $\text{ND}_2\text{SO}_3^-\text{K}^+$ 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 $\text{NH}_2^+\text{SO}_3^-$ (formed by irradiation of sulfamic acid enriched to 95% in ^{15}N) has been measured at 300, 77, and 4 K.³⁰ The same group³¹ has shown that γ irradiation at 77 K of a crystal of $^{15}\text{NH}_2\text{SO}_3^-\text{K}^+$ gives rise to the radicals NHSO_3^- , NH_2^\cdot , and $\text{NH}_2\text{SO}_3^\cdot$ possibly by the radiolysis mechanism shown in eq 1–4. However, this



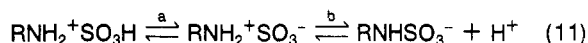
mechanism is now thought to be in error.³² Exposure of sulfamic acid and sulfamate ions to ⁶⁰Co γ rays at 77 K gave rise to the changes (radicals observed are in italics) shown in eq 5–10.



Another group³³ has studied the temperature dependence of the ESR spectrum of the first formed radical ($\text{NH}_2^+\text{SO}_3^\cdot$) 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^\cdot radical.³⁴ A triplet has been observed at 200 K following direct hydrogen addition (after bombardment with gaseous hydrogen atoms) to C₆ 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.



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 potentiometrically³⁶ as 1.19, from sucrose inversion rates³⁷ as 1.06, and from emf measurements³⁸ 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 7.99³⁹) and in Me_2SO (pK_a 6.5⁴⁰) 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 ($R = \text{H}$) 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 ($R = n\text{-Bu}$, $n\text{-Pr}$, *sec*-Bu, and cyclohexyl) have been determined by potentiometric, conductometric, and magnetic resonance (¹³C 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 $R = \text{C}_6\text{H}_5$, 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 $R = p\text{-CH}_3\text{OC}_6\text{H}_4$, $pK_a = 1.62 \pm 0.2$ ⁴⁶ measured in perchloric acid ($m = 0.80$). Recently, pK_a 's have been measured for the series $R = \text{C}_6\text{H}_5$, $p\text{-ClC}_6\text{H}_4$, $p\text{-BrC}_6\text{H}_4$, $p\text{-CH}_3\text{C}_6\text{H}_4$, $p\text{-C}_2\text{H}_5\text{C}_6\text{H}_4$, $p\text{-CH}_3\text{OC}_6\text{H}_4$, and $p\text{-C}_2\text{H}_5\text{OC}_6\text{H}_4$, and for *N*-methyl-*N*-phenyl-sulfamates.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 data⁴⁸ in which the protonation occurring was described by the acidity function, H_s^1 , defined as being equal to $H_0 - 2 \log a_{\text{H}_2\text{O}}$. 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 ($R = m\text{-ClC}_6\text{H}_4$) to -2.04 ($R = p\text{-CH}_3\text{C}_6\text{H}_4$).⁴⁸

Protonation on nitrogen to give the zwitterion, $\text{RNH}_2^+\text{SO}_3^-$, 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, $\text{NH}_3^+\text{SO}_3^-$, 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 acids⁵² support the contention that the acids exist as zwitterions, $\text{NH}_3^+\text{SO}_3^-$, $\text{NH}_3^+\text{C}_6\text{H}_4\text{SO}_3^-$, and $\text{NH}_3^+\text{CH}_2\text{CH}_2\text{SO}_3^-$, 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

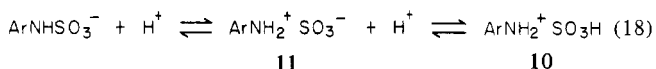
The thermal decomposition of sulfamic acid in a humid atmosphere proceeds via the formation of ammonium pyrosulfate, $(\text{NH}_4)_2\text{S}_2\text{O}_7$, and it decomposes to sulfate at higher temperatures. Differential thermal analysis (DTA) and thermal gravimetric analysis (TGA) have been used to 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 $\text{UO}_2(\text{NH}_2\text{SO}_3)_2 \cdot 2\text{H}_2\text{O}$. Capestan has extended his earlier studies of the pyrolysis of the

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 pre-equilibrium 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.⁸⁴ 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 (ΔH^\ddagger and ΔS^\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*-phenylsulfamates⁸⁵ 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, $\text{ArNH}_2\text{SO}_2\text{Ar}^+$. The hydrolysis rate of these species is much lower than that of the monoprotinated zwitterion **11**.



A series of kinetic equations are set up on the basis of eq 18, involving **10** and **11**. These equations allowed the measurement of $\text{p}K_a$'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 monoproteination 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

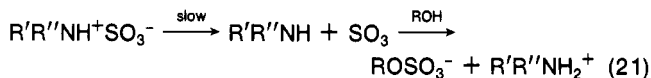
analysis is that the previously measured values of +3.3 in strong acid may not be related directly to the rate-determining step since they include a ρ for the diprotonation step. Since this latter ρ is negative (~ -1), the positive ρ values for the rate-limiting step will be in the region of 4, indicating 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.



In 1964, Nakano and Yamaguchi⁸⁶ measured rates of ethanolysis ($\text{R} = \text{Et}$) for 12 different sulfamic acids, including several disubstituted compounds, and for the *N*-sulfonic acids of morpholine and piperidine. With $\text{R}' = \text{H}$, the order of reactivity for variation in R' decreased for the series normal > iso > secondary; for the three disubstituted compounds studied ($\text{R}' = \text{R}''$) 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.



A Russian group⁸⁷ 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.⁸⁹⁻⁹³ Vulakh and Loktev⁸⁹ 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 $\text{DMF}\cdot\text{SO}_3$ 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, $\text{H}_2\text{NS(OR)(O}^-\text{)O}_2\text{OH}$, 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 $\text{S}_{\text{N}}2$ mechanism, of a $\text{DMF}\cdot\text{SO}_3$ complex. Some

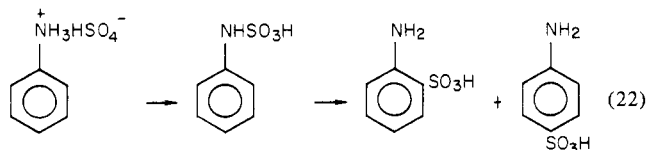
results on the sulfation of other hexadecanols under homogeneous conditions led to similar mechanistic conclusions.⁹³ Because of its relevance to the mechanism of the sulfation reaction, the kinetics of solvolysis of sulfamic acid in DMF have been extensively studied.⁹⁴ The rate-determining formation of a DMF-SO₃ intermediate leads to eventual products such as NH₃·DMF·SO₃ and HO₃SNHSO₃NH₄.

C. Rearrangement

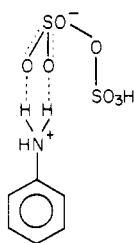
The rearrangement of phenylsulfamic acid to give ring-substituted sulfonic acids is of considerable interest not only because of controversy about its molecularity but also because it has been implicated in the mechanism of the sulfonation of aniline and in the Piria reaction. Both inter- and intramolecular 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 Spillane⁹⁵ have rearranged potassium phenylsulfamate to sulfanilic acid in dioxane at 373 K in the presence of an equimolar amount of 98% sulfuric-³⁵S 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-³⁵S acid or sulfamate-³⁵S 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

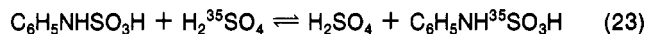
Vrba and Allan^{98,99} studied the mechanisms of the sulfonation of aniline and the rearrangement of phenylsulfamic acid in excess 97% sulfuric acid at 313 and 373 K. In both the sulfonation of aniline and the rearrangement of phenylsulfamic acid, they obtained a mixture of orthanilic and sulfanilic 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.



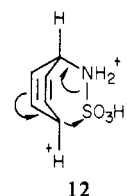
The N-sulfonation step was thought to involve pyrosulfuric acid:



The rate law for the rearrangement step is $v = kh_0 \cdot [\text{PhNH}_2\text{SO}_3\text{H}^+]$ 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



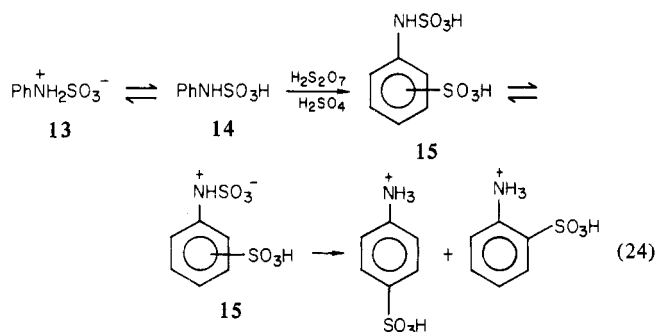
intramolecular mechanism was suggested to occur, after N-protonation of phenylsulfamic acid, by deformation of the aromatic ring (12) so that the migrating SO₃H group was close to the para position. A similar species could be drawn to account for the formation of orthanilic acid.



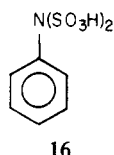
Whatever the molecularity of the rearrangement, the overall scheme (eq 22) for the sulfonation of aniline is supported by other data from the same authors. In an earlier report¹⁰⁰ they showed that the rearrangement of *m*-chlorophenylsulfamic acid and the sulfonation of *m*-chloroaniline with sulfuric acid at 473 K gave the same product sulfonic acids. In a later paper¹⁰¹ 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's¹⁰⁴ 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



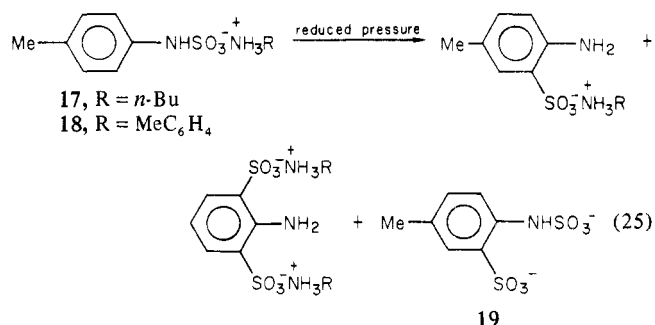
studies indicated that while **13** was the major species present in the strong sulfuric acid used, **14** was the reacting species. The diprotonated form, $\text{PhNH}_2\text{SO}_3\text{H}^+$, was ruled out since it would not be expected to be much more reactive than the anilinium ion (phenylsulfamic 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^{107,108} 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. Yamaguchi¹⁰⁷ has shown that heating ammonium phenylsulfamate with urea at 413 K for 8 h gave 60% orthanilic acid. In the second report¹⁰⁸ 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.

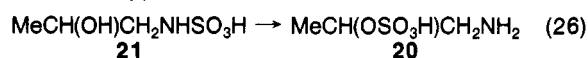
In very recent work, Kanetani and Yamaguchi¹⁰⁹ have shown that thermolysis of the neat sulfamate salts **17** or **18** at temperatures from 393 to 433 K and from 383 to 453 K, respectively, gives rise to substantial amounts of mono- and disulfonated products together with a smaller amount (up to 20%) 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

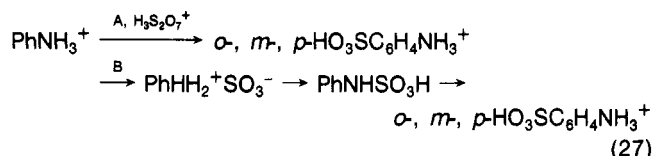


regarding the intermediacy of such compounds in the rearrangement.

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.

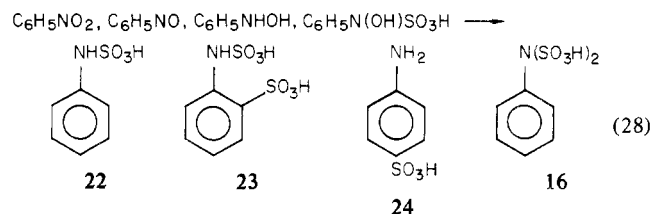


Cerfontain and Maarsen¹¹¹ have produced evidence which suggests that the sulfonation of aniline can occur by two independent and, at times, competing routes (eq 27) in ca. 100% H_2SO_4 . Path A involves direct electrophilic attack by $\text{H}_3^+\text{S}_2\text{O}_7$

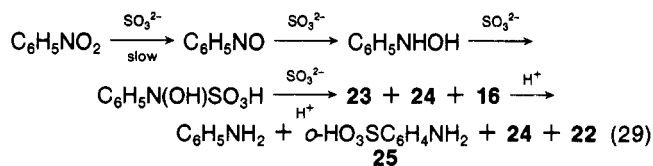


on the anilinium ion and path B involves the intermediacy of phenylsulfamic acid. Increasing temperature and decreasing sulfuric acid concentration favor path B. Path A is followed exclusively at room temperature in a large excess of fuming sulfuric acid, but at higher temperatures with concentrated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

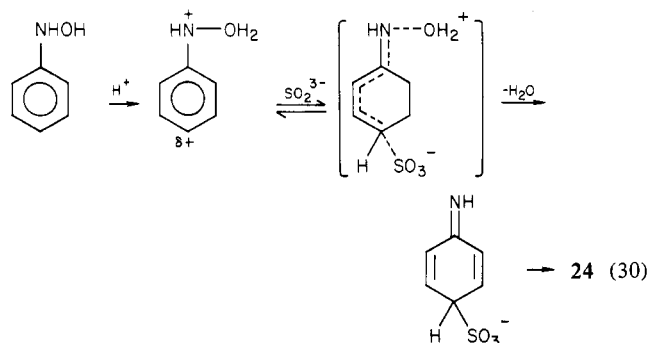
The involvement of sulfamic acid rearrangements in the Pira reaction is uncertain, but the intermediacy of sulfamic acids is well established. Vrba and Allan¹¹² have produced chromatographic evidence to show that starting from nitrobenzene, nitrosobenzene, phenylhydroxylamine, or phenylhydroxylamine-*N*-sulfonic 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).



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



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



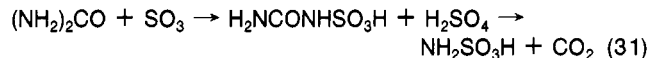
reaction are **25**, **24**, and aniline, and these will arise when the final acid hydrolysis step is allowed to proceed. Thus, **22** will give aniline, **23** will give **25**, **24** will remain unchanged, and **16**, depending on the extent of hydrolysis, may give rise to **22** and/or aniline. The 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



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, $\text{HN}(\text{SO}_3\text{NH}_4)_2$, 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, $\text{N}(\text{SO}_3\text{NH}_4)_3$, 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, $\text{H}_2\text{N}(\text{NH})\text{NH}_2 \cdot \text{NH}_2\text{SO}_3\text{H}$, has been prepared by the reaction of $\text{H}_2\text{NC}(\text{NH})\text{NHCH}$ and ammonium sulfamate¹²³ 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 reviewed¹²⁵ and extended recently.^{126,127} The synthetic aspects as such have not been reviewed.

a. Chlorosulfonic Acid

The basic procedure of Audrieth and Sveda¹²⁸ using chlorosulfonic acid as the sulfamating agent and the appropriate amine is the most commonly employed method. In a series of papers, Unterhalt and Böschmeyer have synthesized cycloalkylsulfamates of varying ring size¹²⁹ 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 compounds¹³² and cyclopentylmethylsulfamate¹³³ using almost exclusively the chlorosulfonic acid method. Benson and Spillane¹²⁵ 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.⁴⁸

b. Amine–Sulfur Trioxide and Sulfur Trioxide

High yields of cyclohexylsulfamate have been reported by Yamaguchi and Nakano¹³⁴ in the aqueous reaction of cyclohexylamine with $\text{Me}_3\text{N}-\text{SO}_3$, $\text{Et}_3\text{N}-\text{SO}_3$, $\text{Me}_2\text{BzN}-\text{SO}_3$, and *N*-methylmorpholine- SO_3 . $\text{Et}_3\text{N}-\text{SO}_3$ 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 $\text{Me}_3\text{N}-\text{SO}_3$ 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^{138,139} 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 $\text{R}^1\text{N}=\text{CR}^2\text{R}^3$ with SO_3 .¹⁴⁰ A 98.5% yield of isopropylsulfamic acid was reported in reaction 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).



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.¹²⁸ It is not clear if this method is applicable to the synthesis of aromatic sulfamates.

c. Sulfur Dioxide and Bisulfites

Yamaguchi¹⁴⁵ 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 isoamyl-sulfamates 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

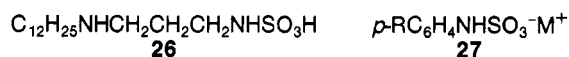
e. Miscellaneous

Yamaguchi has prepared in good yield several alkyl- and cyclohexylsulfamates by reaction of monosubstituted sulfamides, RNHSO₂NH₂, 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 SO₃(BuO)₃PO with cyclohexylamine¹⁵⁵ and by the hydrolysis of cyclohexylsulfamyloxysilane (prepared by reaction of cyclohexylaminosilane and SO₃).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 Et₃N-SO₃, prepared in situ in chloroform, and *n*-dodecylamine.¹⁵⁸ Penta-decylsulfamate 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

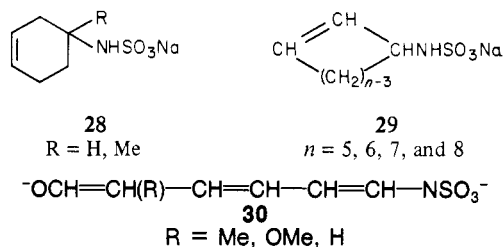
A French patent gives the preparation of 3-(laurylamino)-propylsulfamate (26) by reaction of C₁₂H₂₅NH(CH₂)₃NH₂ with chlorosulfonic and chloroethylsulfonic acids.¹⁶¹ This sulfamate is used as a germicide. Compounds such as 27, where R is



a straight-chain C₁₀₋₁₆ alkyl group and M is an alkali metal or the ammonium ion, have been synthesized by a sequence involving nitration of a *p*-RC₆H₅ 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 C₁₀₋₂₂ chains have been prepared¹⁶³ 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, (CH₂=CHC(H₂)₂)₂NSO₃H, has been reported.¹⁶⁴ An interesting series of cycloalkenylsulfamates, 28 and 29, have been made by sulfamation of the appropriate amines with Me₃N-SO₃.¹⁶⁵ 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



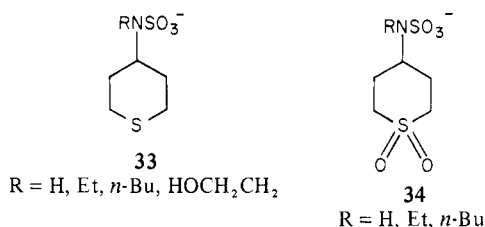
5. Halosulfamates

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 re-

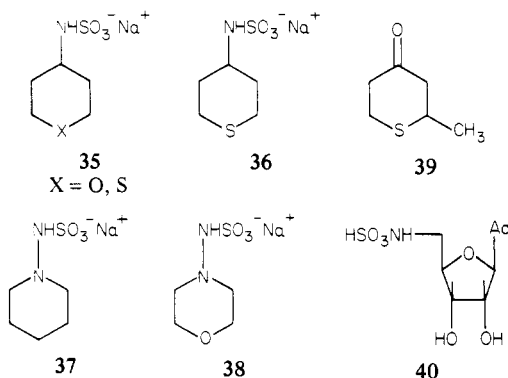
versibly formed. Both compound are unstable and have not been isolated. In earlier work, Traube reported the isolation of 31 in the form of some of its crystalline salts.¹⁶⁸ The dichlorosulfamate is also reported in a French patent.¹⁶⁹ Stabilized aqueous solutions of dichlorosulfamic acid have been prepared 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 HNF₂ and SO₃.¹⁷²

6. Heterocyclic Sulfamates

The interesting tetrahydro-2*H*-thiopyransulfamates 33 and 34 have been reported.¹⁷³ 33 (R = H, 42%) was prepared by



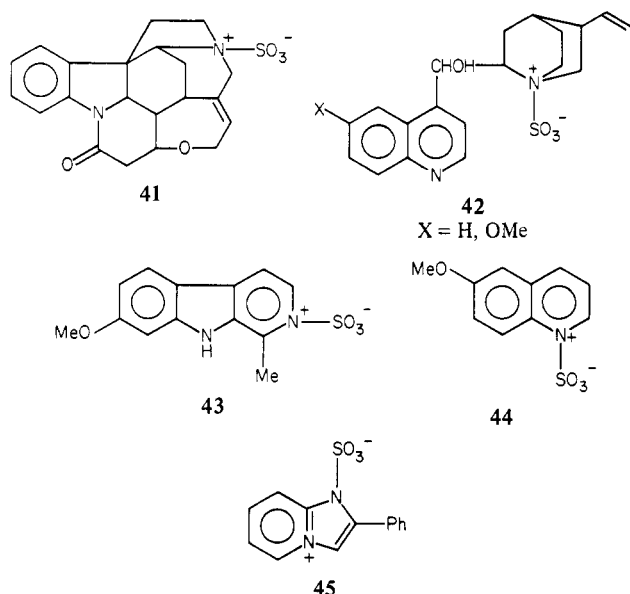
reaction of Me₃N-SO₃ in chloroform with tetrahydro-2*H*-thiopyran-4-amine. 34 (R = H) was formed from 33 (R = H) by using H₂O₂ in glacial acetic acid/acetic anhydride. 33 (R = CH₃(CH₂)₃) was prepared by reduction of tetrahydro-2*H*-thiopyran-4-one with sodium cyanoborohydride and reaction with *n*-butylamine, 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 NHSO₃⁻ was thought to be a necessary condition for sweetness in cyclamate-type compounds.^{125,128} 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 acid¹²⁵ and with ammonium imidodisulfonate in an autoclave.¹⁵⁷ In the preparation of 36, Michael addition involving methyl 3-mercaptopropionate and methyl crotonate and subsequent

Dieckmann condensation were used to prepare the ketone **39**.¹⁷⁵ 5'-Sulfamino-5'-deoxyadenosine (**40**) was prepared by reaction of $\text{Me}_3\text{N}-\text{SO}_3^-$ 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 Whiting¹⁷⁷ 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**, $\text{X} = \text{H}$), quinine- (**42**, $\text{X} = \text{OMe}$), and harmine-sulfamates (**43**) were prepared and also 6-methoxyquinoline- (**44**) and 2-phenylimidazo[1,2-a]pyridine-sulfamates (**45**).



7. Sulfamate Salts

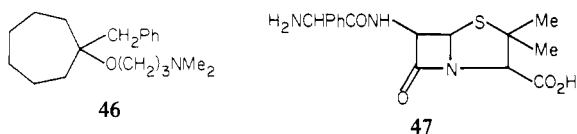
A very large number of sulfamate salts of a variety of basic compounds have been reported. Most of these compounds have been prepared because of their use or potential in medicine.

a. NH_2SO_3^- Salts

Quinine,¹⁷⁸ urotropine,¹⁷⁹ erythromycin,^{180,181} and hycanthone¹⁸² sulfamate salts have been prepared. The surfactants $\text{R}(\text{CH}_2)_3\text{N}[(\text{CH}_2\text{CH}(\text{OH})\text{CH}_2\text{O})_n\text{X}][\text{CH}_2\text{CH}(\text{OH})\text{CH}_2\text{O}]_n\text{SO}_3\text{NH}_4$ with $\text{R} = \text{C}_{8-18}$ alkyl or alkoxy, $\text{X} = \text{H}$ or SO_3NH_4 , $n = 2-4$, were prepared.¹⁸³ A large number of triarylmethanesulfamate dyes have been made.^{184,185}

b. $\text{C}_6\text{H}_{11}\text{NHSO}_3^-$ Salts

Cyclohexylsulfamate salts of erythromycin,¹⁸¹ choline and dicholine,¹⁸⁶ neomycin B hexakis,¹⁸⁷ and acyloxypropoxy-indoles¹⁸⁸ have been made. The cyclohexylsulfamate salt of **46**^{189,190} has antitumor and vasodilatory activity. A number of quaternary ammonium cyclohexylsulfamate salts which are biocidally active have been reported.¹⁹¹



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 lincomycin¹⁹⁸ 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 $\text{RNHSO}_3^-\text{N}^+\text{R}^1\text{R}^2\text{R}^3\text{R}^4$ (typically $\text{R}^1 = \text{R}^2 = \text{Me}$, $\text{R}^3 = \text{benzyl}$, $\text{R}^4 = \text{dodecyl}$), 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. Gilbert¹⁹⁹ has briefly reviewed the use of sulfamic acid as a sulfating agent.

a. General

The use of amine oxides,²⁰⁰ urea,^{201,202} and thiourea²⁰² 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 $\text{Me}_3\text{N}-\text{SO}_3^-$.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

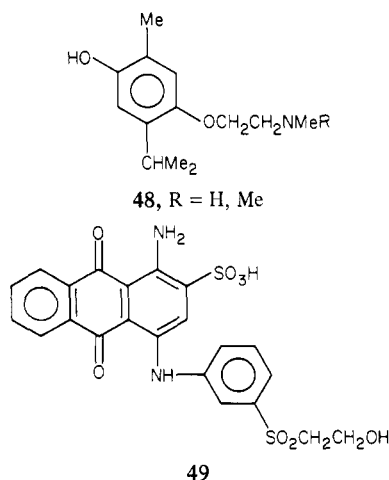
The sulfoesterification of higher aliphatic alcohols has been reviewed some years ago.²⁰⁶ The catalytic effect of a large number of Lewis bases on the reaction of cetyl alcohol with sulfamic acid has been probed.²⁰⁷ The decreasing catalytic activity of the catalysts correlated fairly well with diminishing electron-donating ability. The same Russian group has made detailed studies on the sulfation with sulfamic acid of C_{10-18} alcohols.²⁰⁸⁻²¹⁰ *N*-Methylpyrrolidone²¹¹ and a di- or polyphosphate²¹² 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 imido-disulfonate, with $\text{Me}_3\text{N}-\text{SO}_3^-$, 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 $\text{C}_{19-29}\text{H}_{27-39}\text{CH}_2\text{OH}$. 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.^{218,219} C_{8-25} 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} dehydroisandrosterone,²²¹ estrone,²²¹ 2-methoxyestrone,²²¹ ethy-

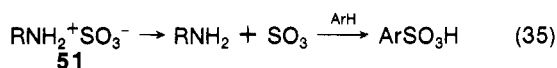
nylestradiol,²²¹ and ethynylestradiol 3-methyl ether.²²¹ The syntheses of vitamin D₂ sulfate,²²³ using sulfamic acid, of adenosine 5'-sulfate (65%) and D-galactose 6-sulfate (55%), using cyclohexylsulfamic acid in anhydrous pyridine, and of riboflavin sulfate (23%), using morpholine-*N*-sulfonic acid in Me₂SO-pyridine, have been achieved.²²⁴ Sulfates of **48**²²⁵ and **49**²²⁶ were prepared with sulfamic acid.



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

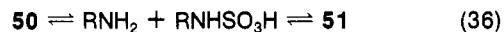
Although sulfamic acid has been widely used as sulfating²²⁸ (preceding section) and sulfamating²²⁹ (see II.D.2.d) agents, its use in sulfonation has been minor.²³⁰ Two papers which have appeared in recent years show that alkylsulfamic acids can be used as efficient sulfonating agents to sulfonate aniline,²³¹ *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., RNHSO₃⁻RNH₃⁺ (**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



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 Yamaguchi¹⁰⁹ 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*-BuNHSO₃H and **51** (R = *n*-Bu) (eq 36). **51** (R = *n*-Bu) is considered to be the sulfonating species



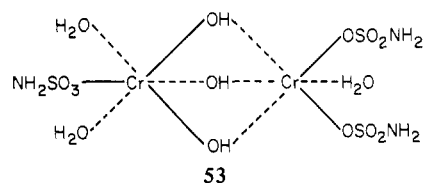
and the sulfonation step is regarded as being a bimolecular nucleophilic attack by the 4-methylaniline on **51** to give 4-methylphenylsulfamate. Similar schemes are presented to account for the formation of **52** and the ring mono- and disulfonates.

The reaction of isobutene, CH₂=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 CH₂=C(Me)-CH₂SO₃⁻, 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, Me₂=CHSO₃⁻.

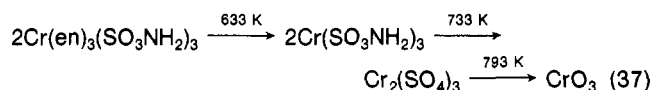
F. Sulfamate-Metal Bonds

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



molecules of water on heating to 423 K, and it undergoes a structural change at this temperature.²³⁶ The same Russian group²³⁷ has prepared tris(ethylenediamine)chromium sulfamate, Cr(en)₃(SO₃NH₂)₃, from chromium sulfate, ethylenediamine, and barium sulfamate. Detailed thermogravimetric analysis suggested that the path shown in eq 37 was followed in its decomposition.



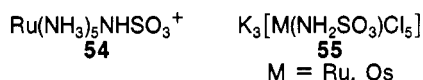
The X-ray diffraction patterns of the tris complex are compared with those of hydroxochromium(III) sulfamate (**53**). The complex [Cr(H₂O)₃(NH₂SO₃)₃]²³⁸ involves nitrogen coordinated sulfamate and thus differs from the related zinc, cobalt, and nickel complexes of general formula M(H₂O)₄(NH₂SO₃)₂, prepared 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 Np²³⁷ and Pu²³⁸ 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.

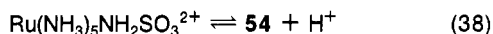
Ferrous sulfamate can be prepared directly and its hydrolysis inhibited by passing oxygen into a suspension of the powdered metal in aqueous sulfamic acid until no unreacted metal remains

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 $[\text{Ru}(\text{NH}_3)_5]^{3+}$ 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) amines, which are known to bond through nitrogen, confirmed that in **54** the sulfamate-metal bond is through nitrogen.



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

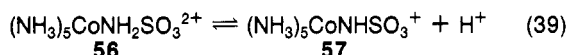


determined as 2.6 at 0.1 M ionic strength at 298 K. The new complexes of ruthenium and osmium (**55**) have been prepared from potassium hexachlororuthenate(III) and sodium hexachloroosmate(IV), respectively, by refluxing or warming with sulfamic acid.²⁴⁴ Infrared spectroscopic data suggest that sulfamate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

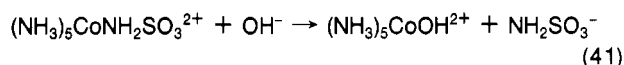
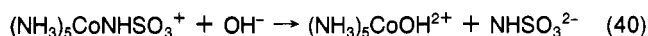
2. Cobalt and Nickel Subgroups

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 Jordan²⁴⁶ 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

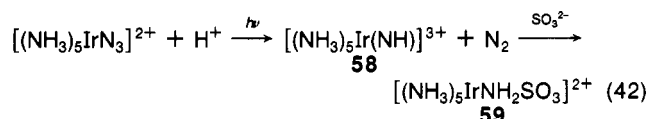


5.83 at 298 K (ionic strength ~ 0.004). In alkaline hydrolysis, **57** will be the form mainly present, and the rate law for the hydrolysis has terms independent of hydroxide ion and first order in hydroxide ion. Two reaction paths, shown in eq 40 and 41,



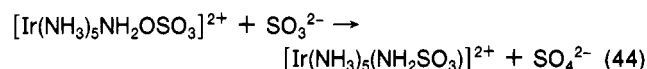
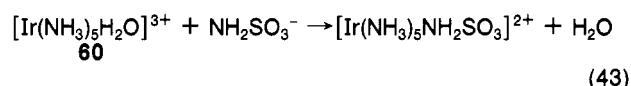
appear to occur. A S_N1cB mechanism would appear to be probable.

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 $[\text{Co}(\text{NH}_3)_5\text{OH}_2]^{3+}$. The cobalt and nickel complexes $[\text{M}(\text{H}_2\text{O})_4(\text{NH}_2\text{SO}_3)_2]$ (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).²³⁸ 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 $[\text{Ir}(\text{NH}_3)_5\text{NH}_2\text{SO}_3]^{2+}$ in three different ways.²⁴⁸ 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 ru-



thenium(III) complex can be prepared by the same route, but

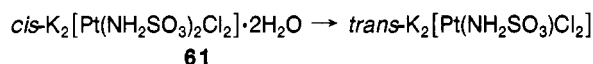
of course it was reported earlier.²⁴³ Second, the aquo complex **60** and sulfamate ion gave a product with the same properties as **59**. Third, the reaction of the hydroxylamine O-sulfate complex with sulfite ion gave an identical product.



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.

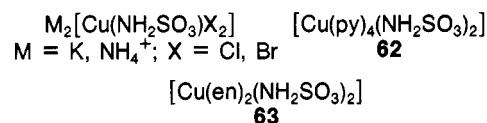
The palladium complex $\text{K}_2[\text{Pd}(\text{NH}_2\text{SO}_3)_2\text{Cl}_2]$ was prepared from the reaction of sulfamic acid and potassium tetrachloropalladate(II).²⁴⁴

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



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**,²³⁸ and the ethylenediamine complex **63**.²³⁸

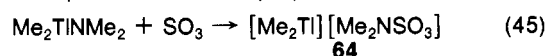


Interestingly, two forms of copper sulfamate, $\text{Cu}(\text{NH}_2\text{SO}_3)_2 \cdot 2\text{H}_2\text{O}$, have been recognized. They appear to be linkage isomers involving N- and O-linked sulfamate groups.²³⁸ The stability constant for copper sulfamate has been determined from a polarographic study.²⁵³

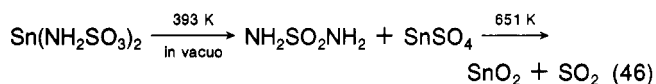
Zinc and cadmium sulfamates have been prepared by passing oxygen into a suspension of the metal in sulfamic acid.²⁴² Emf measurements, activity coefficient determinations, and freezing point depression measurements have been made on these sulfamates.²⁴⁵ Stability constants were calculated for zinc and cadmium sulfamates at 298 K from potentiometric data on measurements in sodium sulfamate solutions.²⁵⁴ The complex $[\text{Zn}(\text{H}_2\text{O})_4(\text{NH}_2\text{SO}_3)_2]$ has sulfamate coordinated to the metal via oxygen.²³⁸ 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

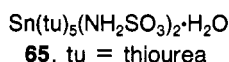
Aluminum sulfamate has been reported²⁴² and the thallium sulfamate complex **64** has been prepared.²⁵⁵



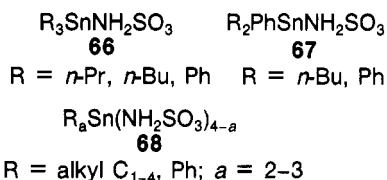
Tin(II) sulfamate has been prepared by addition of the metal to a solution of copper sulfamate and sulfamic acid.²⁵⁶ The sulfamate formed is thought to be the normal tin(II) compound $\text{Sn}(\text{NH}_2\text{SO}_3)_2$, though it cannot be isolated pure (only with admixed sulfamic acid). It undergoes thermal decomposition as shown in eq 46.



$\text{Sn}(\text{MeNHSO}_3)_2$ 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

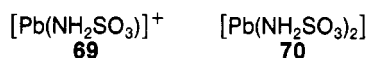


been studied and found to give the same products as tin(II) sulfamate. Infrared data suggest that the Sn-S bonds are weak in **65**.²⁵⁷ A variety of tin sulfamate complexes corresponding to **66**,²⁵⁸⁻²⁶⁰ **67**,²⁶¹ and **68**²⁶² have been prepared, generally by reaction of sulfamic acid with an oxide.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



was heated with bis(tributyl) oxide, $(n\text{-Bu})_2\text{O}$, 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 $\text{Bu}_3\text{SnNHSO}_3\text{SnBu}_3$. Bis(tributyltin) imino-disulfonate 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



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 sulfamate⁵⁶ (prepared by Capestan²⁶⁶) 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

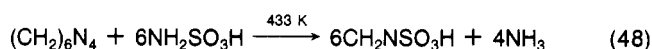
Sulfamic acid has been recommended as a standard in acid-base titrimetry and detailed purification procedures have been given.^{268,269} A very precise method for the assay of standard sulfamic acid using differential electrolytic potentiometry has been described.²⁷⁰ Sulfamic acid has also been used as a standard in nonaqueous titrimetry.²⁷¹

Sulfamic acid is a useful trap for nitroso species in the denitrosation of *N*-methyl-*N*-nitrosoaniline²⁷² 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 air²⁸¹ 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

$$\text{H}_2\text{NSO}_3\text{H} + \text{C}_6\text{H}_5\text{CHOHCOC}_6\text{H}_5 \rightarrow \text{C}_6\text{H}_7\text{COCOC}_6\text{H}_5 + \text{H}_2\text{O} + \text{NH}_3 + \text{SO}_2 \quad (47)$$


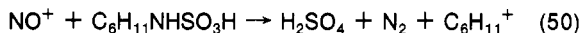
47 illustrates the fusion with benzoin which works for sulfamic acid only. The liberated sulfur dioxide can be detected by using suitable tests. Equation 48 illustrates dry heating with hexammine; detection of the liberated ammonia gas is indicative of the presence of sulfamic acid. Equation 49 involves 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

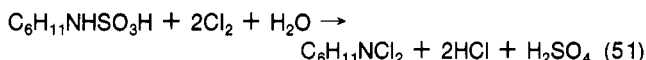
Richardson²⁹⁰ has reviewed the analytical chemistry of cycloamates up to 1966, and only papers appearing after this date

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



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-naphthylamine²⁹² 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-H₂SO₄ 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



region and can be determined.³⁰¹ Percent recoveries for cyclamate determinations in a variety of foods were on average $102 \pm 1.8\%$.

Sodium cyclamate has been determined by isotope dilution analysis. Cyclamate-³⁵S was synthesized from cyclohexyl isocyanate and H₂³⁵SO₄.³⁰² Renwick and Williams have of course used cyclamate-¹⁴C in some of their studies.^{303a,303b}

TLC can be used to detect cyclamate in the presence of saccharin and dulcin³⁰⁴ 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. Romagnani⁷ 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 baths³²⁶ 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 paper³³¹), 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

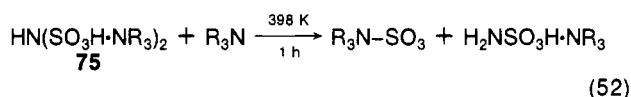
Gilbert³³² has reviewed the syntheses, properties, and uses of the various amine-sulfur trioxide complexes, i.e., pyridine-sulfur trioxide, tri(methyl)ethylamine-sulfur trioxide, dimethylaniline-sulfur trioxide, and 2-methylpyridine-sulfur trioxide. These complexes find their principal applications as reagents for sulfation, sulfonation, and sulfamation.

1. Physical, Theoretical, and Synthetic Aspects

Ab initio calculations have been done on NH₃-SO₃; the net interaction energy is -74.6 kJ mol⁻¹, showing that SO₃ is an unusually strong Lewis acid.³³³ R₃N-SO₃ (R = Et, *n*-Pr, *n*-Bu)

complexes have an experimental magnetooptical rotation 173 μ rad 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., MeNH₂, with SO₃ 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 SO₃ 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 SO₃ with dimethylamine.³³⁷

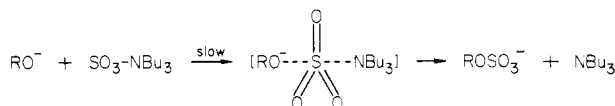
R₃N-SO₃ complexes have been prepared by heating the imidodisulfonate 75.^{338a} Thus,



where R = lower alkyl (e.g., *n*-Bu), NR₃ = pyridine, picoline, 2,4-lutidine, quinoline, *N*-methylmorpholine, PhCH₂NMe₂. If NR₃ = PhNR₂, then the product obtained was the *N,N*-dialkylsulfanilic acid.^{338b} The HNF₂ and MeNF₂ 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 NH₃-SO₃ under an ammonia atmosphere.³³⁹ The addition of about 4% Me₃N-SO₃ 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*-Bu₃N-SO₃ 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 Et₃N-sulfur trioxide complexes.³⁴² Ascorbic acid has been sulfated with Me₃N-SO₃ to give disodium L-ascorbic 2-sulfate.³⁴³ The sulfates of lithocholic, glycolithocholic, and tauroolithocholic acids have been made by reaction with Et₃N-SO₃ 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 Me₃N-, Et₃N-, and DMF-sulfur trioxide adducts have been used in the sulfation of polysaccharides, e.g., agarose,³⁴⁶ amylopectin,³⁴⁷ and starch.³⁴⁸

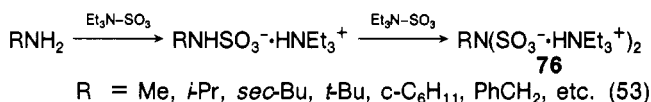
Ethylene-vinyl acetate copolymer has been sulfated with Me₃N-SO₃ in carbon tetrachloride-DMF containing maleic acid,³⁴⁸ and the same reagent has been used to sulfate 5'-amino-5'-deoxythymidine.¹⁷⁶ Pyridine-sulfur trioxide deoxygenates allylic and benzylic alcohols, probably via the sulfated esters, i.e., ROSO₃⁻·HNC₅H₅⁺. Thus, *trans,trans*-farnesol gives

trans,trans-2,6,10-trimethyldodeca-2,6,10-triene.^{349a} Gibberellin A₃ has been oxidized with pyridine-sulfur trioxide in Me₂SO.^{349b}

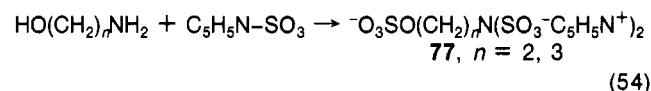
3. Use in Sulfonation and Sulfamation

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

Et₃N-SO₃ has been used to sulfamate cyclohexylamine¹³⁵ in 90% yield, and Me₃N-SO₃ 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 Et₃N-SO₃ (eq 53).³⁵⁵



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



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

4. Hydrolysis

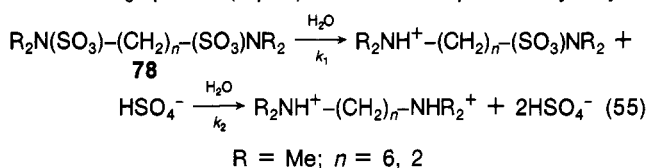
a. Me₃N-, Et₃N-, Me₂EtN-, and Et₂MeN-SO₃

Fleischfresser and Lauder³⁵⁸ 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 (Me₃N-SO₃) and -80.4 J K⁻¹ mol⁻¹ (Et₃N-SO₃). 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 Et₃N-SO₃. Later work by the Russian group on the alkaline hydrolysis of Me₃N-SO₃³⁶¹ and Et₃N-SO₃³⁶² supported the bimolecular mechanism proposed by the Australian workers. Work by Krueger and Johnson³⁶³ on the base hydrolysis of Me₃N-SO₃ has substantiated the earlier findings. Bentley³⁶⁴ 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 Et₃N-SO₃ and Me₃N-SO₃. A change in the mechanism of hydrolysis of Me₃N-SO₃ from S_N2 in the presence of base to a dissociative mechanism in water has been proposed³⁶⁵ 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 $\text{Me}_2\text{EtN-SO}_3^{366}$ and $\text{Et}_2\text{MeN-SO}_3^{367}$ 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 $\text{Me}_3\text{N-}$, $\text{Me}_2\text{EtN-}$, $\text{MeEt}_2\text{N-}$, and $\text{Et}_3\text{N-SO}_3^{367}$.

The same Russian group has also studied the kinetics of hydrolysis of compounds **78**³⁶⁸ which lose first one and then the second SO_3 species (eq 55). The first step of the hydrolysis



is rate limiting and the overall hydrolysis is first order. The entropy of activation of **78** ($n = 6$) was $-40.2 \text{ J K}^{-1} \text{ mol}^{-1}$. **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 $\text{p}K_{\text{B}}$ of **78** ($n = 6$) is very similar to the $\text{p}K_{\text{B}}$ of MeEt_2N , and it is found that the rates of hydrolysis of **78** ($n = 6$) and $\text{MeEt}_2\text{N-SO}_3$ 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 $\text{p}K_{\text{B}}$ values of the parent amines, with a decrease in $\text{p}K_{\text{B}}$ (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 $\text{p}K_{\text{B}}$ values. The activation energies of the two hydrolyses are almost the same, and the difference is seen as being due to entropy. ΔS^\ddagger is about $-95.5 \text{ J K}^{-1} \text{ mol}^{-1}$ for β -picoline- SO_3 , while for pyridine- SO_3 a value of $-44.4 \text{ J K}^{-1} \text{ mol}^{-1}$ has been reported.³⁷⁰

However, later work reports the following thermodynamic parameters for pyridine- SO_3 hydrolysis: energy of activation $74.2 \text{ K J mol}^{-1}$ and $\Delta S^\ddagger = -59.9 \text{ J K}^{-1} \text{ mol}^{-1}$.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 $\text{p}K_{\text{B}}$ 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

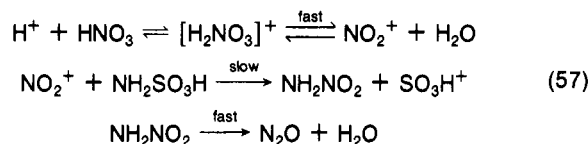
The reaction of sulfamic acid with nitric acid (eq 56) has been studied recently on an industrial scale.³⁷³ The reaction of nitric



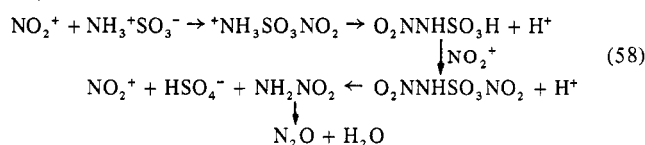
acid with sodium sulfamate to give nitramide (70%, under optimum conditions) has been investigated.³⁷⁴

Three groups³⁷⁵⁻³⁷⁷ have been investigating the mechanism of the reaction of nitric and sulfamic acids. Reaction 56 is first

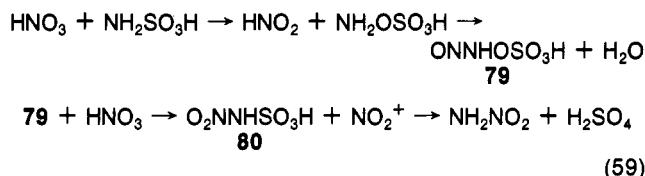
order in sulfamic acid and the variation of rate with acidity approximates to a second-order dependence on H_0 .³⁷⁵ This suggests a mechanism involving the nitronium ion, and a rate-determining electrophilic substitution at the amino group of sulfamic acid (partially present as $\text{NH}_2\text{SO}_3\text{H}$) with SO_3H^+ as the leaving group has been proposed (eq 57).³⁷⁵ The nitramide



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).



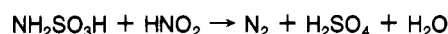
An alternative reaction scheme (eq 59) not involving initial nitration of the sulfamic acid is also suggested.³⁷⁶ This involves the formation of hydroxylamine-*O*-sulfonic acid and reaction with nitrous acid to give the *N*-nitroso compound **79** which reacts with nitric acid to give **80**, which can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



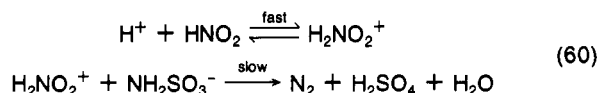
A study of the reaction using H^{15}NO_3 indicates that N_2O arises only partially from nitramide and also from the dimerization of HNO , a species which is thought to arise from the HNO_3 - $\text{N-H}_2\text{SO}_3\text{H}$ reaction.³⁷⁷

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



at acidities less than 0.25 M, was of the type shown in eq 60.³⁷⁸



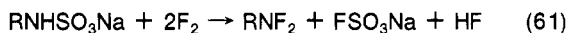
The protonated nitrous acid species reacts with sulfamate ion in a slow step. In the acid range -0.25 – 3 M a second pathway emerges in which H_2NO_2^+ attacks sulfamic acid (now mainly present). The involvement of intermediates such as $\text{ONNH}_3\text{SO}_3^-$ and HON=NSO_3^- in the slow step is 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 $\text{Pt}(\text{NO}_2)_4^{2-}$, $\text{Pd}(\text{NO}_2)_4^{2-}$, $\text{Rh}(\text{NO}_2)_6^{3-}$, and $\text{Co}(\text{NO}_2)_6^{3-}$ were studied by measuring the nitrogen evolved.³⁸¹

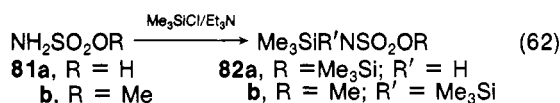
3. Other Reactions

High yields of alkylidifluoramines 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

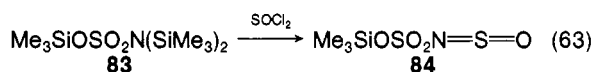


$\text{R} = \text{C}_{1-5}$ straight or branched alkyl

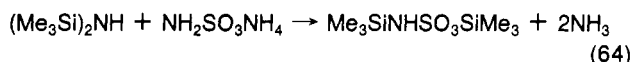
the methyl ester of sulfamic acid and of sulfamic acid with trimethylchlorosilane/triethylamine has been described (eq 62).³⁸³



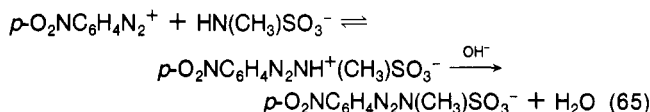
The trisilylated compound **83** can be obtained from **81a** by using an excess of reagents. **83** reacts with thionyl chloride to give *N*-sulfynylamides, **84**. **82a** has been prepared in 78% yield by



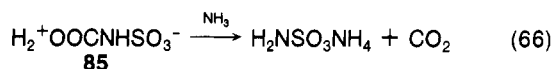
reaction of hexamethyldisilazane with ammonium sulfamate (eq 64).³⁸⁴ **82a** is a highly efficient silylating agent.



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

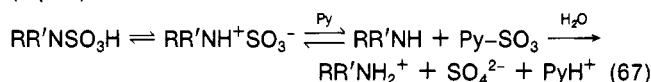


gives ammonium sulfamate and methylamine by nucleophilic attack on sulfur.³⁹² Ureasulfonic acid undergoes nucleophilic attack by water to give sulfocarbamic acid (**85**) which is decarboxylated to give ammonium sulfamate in the presence of ammonia (eq 66).³⁹² A qualitative study of the acid-catalyzed



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 $(\text{ArCH}_2)_2\text{NH}$ 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 hydro-

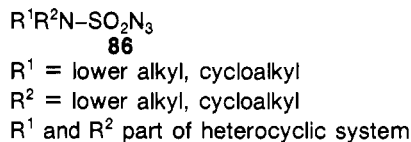
genation of the $-\text{CH}=\text{NSO}_3\text{K}$ compounds formed over Raney nickel (70% average yields).³⁹³ In another study the mechanism of the catalytic cleavage of the N-S bond in sulfamic acid and its derivatives has been examined. Nagasawa and Yoshidome³⁹⁴ have studied the catalytic decomposition 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).



III. Sulfamyl Azides, Esters, and Halides

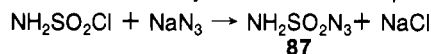
A. Sulfamyl Azides

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

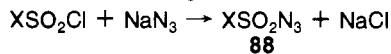


were prepared by reacting the corresponding sulfamyl halide with alkali azide in an aqueous alcoholic solution at room temperature up to about 323 K. The heterocyclic compounds are prepared by reacting the corresponding amine hydrochlorides with sulfuryl chloride to give the *N*-sulfonyl chloride which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

The parent sulfamyl azide, $\text{NH}_2\text{SO}_2\text{N}_3$ (**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



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.³⁹⁸ 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



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.

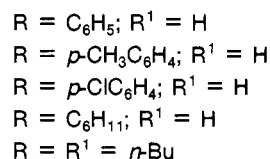
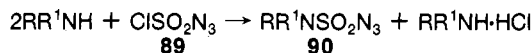
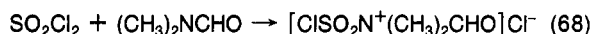


TABLE I. Amines Reacted with ClSO_2N_3

$\text{R}^1\text{C}_6\text{H}_4\text{NHR}^2$	% yield $\text{R}^1\text{C}_6\text{H}_4\text{NR}^2\text{SO}_2\text{N}_3$
$\text{R}^1 = \text{R}^2 = \text{H}$	50
$\text{R}^1 = \text{Me}, \text{R}^2 = \text{H}$	47
$\text{R}^1 = \text{OMe}, \text{R}^2 = \text{H}$	47
$\text{R}^1 = \text{H}, \text{R}^2 = \text{Me}$	64
$\text{R}^1 = \text{NHAc}, \text{R}^2 = \text{H}$	25

Griffiths³⁹⁹ 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 Vernon³⁹⁶ 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



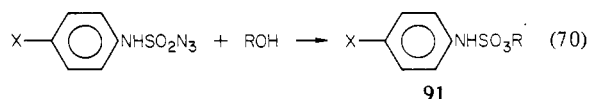
was found to be contaminated with sulfuryl chloride which had a deleterious effect on the reaction of chlorosulfonyl azides with amines. Changing the solvent to acetonitrile enabled **89** to be prepared free of sulfuryl chloride. In addition sodium azide had a high solubility in acetonitrile.

Shozda³⁹⁶ 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. Griffiths³⁹⁹ studied the reaction of

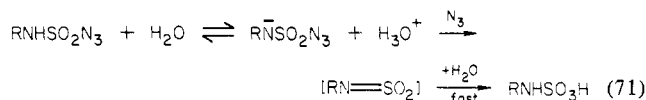


aniline with the now safe acetonitrile or methylene chloride solution of chlorosulfonyl azide. A 1 M portion of aniline and triethylamine (the latter prevents formation of anilinium hydrochloride) gave several byproducts and a low yield of phenylsulfamyl azide. The effect of inorganic bases such as sodium acetate, carbonate, and hydrogen carbonate was then studied. Thus, when an equimolar solution of aniline and ClSO_2N_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.

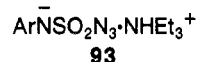
Griffiths³⁹⁹ found that these phenylsulfamyl azides were very reactive toward substitution by alcohols to give the corresponding alkylsulfamates, **91**.



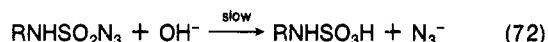
Matier and Comer^{400,401} prepared a wide range of azides including aromatic sulfamyl and *N*-benzyl-*N*-methyl-, piperazine-, and a number of mono- and dialkylsulfamyl azides. The hypotensive and hydrolytic stabilities of the azides have been examined. The authors consider the following mechanism (eq 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).



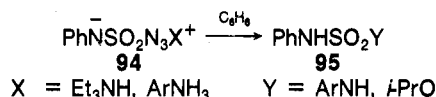
The above initial equilibrium ionization is supported in that (i) monosubstituted sulfamyl azides are extremely reactive in aqueous base while disubstituted sulfamyl azides (which cannot react by the mechanism in eq 71) are little affected by aqueous base; (ii) mono- and disubstituted azides are quite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



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 $\text{S}_{\text{N}}2$ 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.

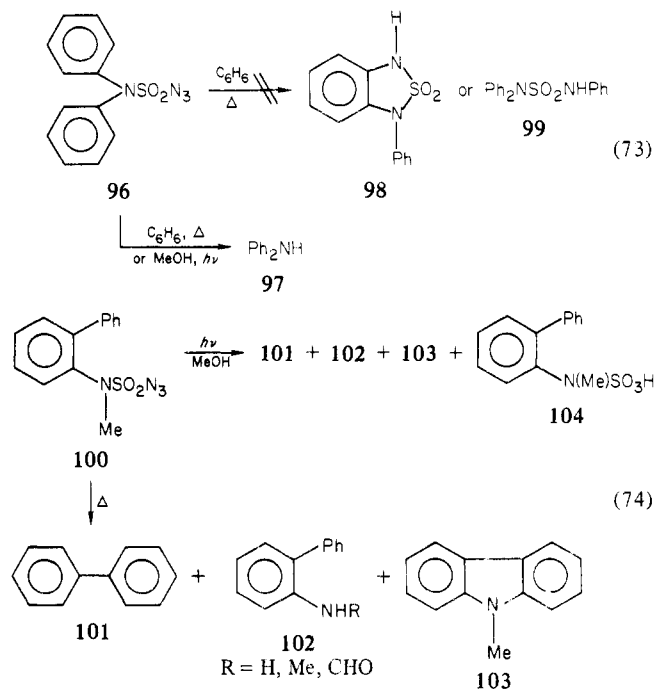


As mentioned above, phenylsulfamyl azide reacts to form salts of the type $\text{PhNSO}_2\text{N}_3\text{X}^+$ (**94**). These salts are quite reactive toward nucleophiles to give compounds of the type **95**. These



reactions are considered to occur via the sulfonylamine, $\text{RN}=\text{SO}_2$ (**92**), which is similar to the intermediate proposed above in the hydrolysis of azides. This type of species was generated by Burgess⁴⁰² 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 sulfamyl nitrenes, $\text{RR}'\text{NSO}_2\text{N}$, have not been reported. Abramovitch has recently attempted to generate this species.⁴⁰⁶ Thermolysis of *N,N*-dimethylsulfamyl azide⁴⁰⁸ 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 easily⁴⁰⁷ and since formation of five- and seven-membered rings by intramolecular substitution by a sulfonyl nitrene occurs,^{407,408} an attempt was made to detect the formation of sulfamyl nitrenes 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 sulfamyl nitrene were detected. Photolysis of **96** in methanol did not produce the desired products indicative of sulfamyl nitrene 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

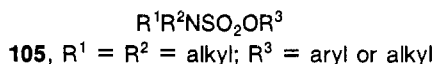


intramolecular or from intermolecular reaction in benzene were observed. Among the products identified were biphenyl (**101**), 2-(methylamino)biphenyl (**102**, R = Me), 2-formamidobiphenyl (**102**, R = CHO), and *N*-methylcarbazole (**103**). Photolysis of the azide **100** in methanol and acetonitrile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

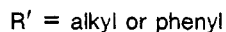
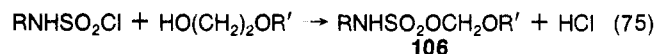
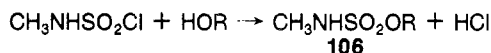
B. Sulfamyl Esters

1. Synthesis

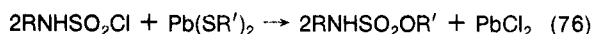
The esters of *N,N*-dialkylsulfamic acids (**105**) have been prepared by a variety of procedures: (1) metathesis of di-



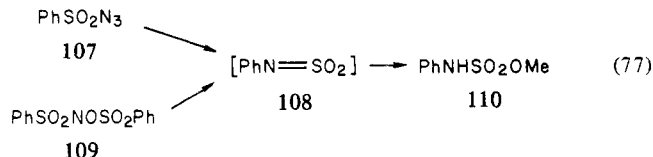
alkylsulfamyl chlorides with sodium alkoxide,⁴⁰⁹ (2) action of the appropriate ester of chlorosulfonic acid on dialkylamines,⁴⁰⁹ (3) action of dialkylsulfamyl chlorides on the sodium salts of substituted phenols.⁴¹⁰ Esters of monoalkylsulfamic acids (**106**) have been reported by Appel and Senkpiel,⁴¹¹ and Sowada⁴¹² has reported their synthesis by the reaction of symmetrically substituted sulfamides with nitrous acid in the presence of alcohols. Weiss and Schulze⁴¹³ have prepared a similar series by the solvolysis of various monoalkylsulfamyl chlorides (eq 75). The



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

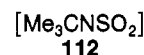


The methyl ester of phenylsulfamic acid has been prepared by the photolysis of benzenesulfonyl azide in methanol. Lwowski and Scheiffele⁴¹⁴ consider the reaction to proceed via a Curtius-type rearrangement of benzenesulfonyl azide (**107**) followed by addition of methanol to an intermediate *N*-phenylsulfonylamine (**108**). When the potassium salt of *N*-(*p*-nitrobenzenesulfon-



oxy)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 acid⁴¹⁵ by treating iminosulfuroxydifluoride with sodium ethoxide; Griffiths³⁹⁹ has prepared similar esters by refluxing arylsulfamyl azides in benzene and methanol.

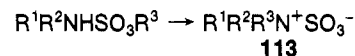
A rather interesting preparation of a sulfamate ester was carried out by Weinstein and Chang⁴¹⁶ who prepared methyl *tert*-butylsulfamate (**111**) by treating *N,N'*-di-*tert*-butylsulfamide with 3 equiv of *tert*-butyl hypochlorite. A mechanism is proposed which involves an intermediate *N*-sulfonyl-*tert*-butylamine (**112**). The scope of this reaction as a route to sulfamate esters has not been explored.



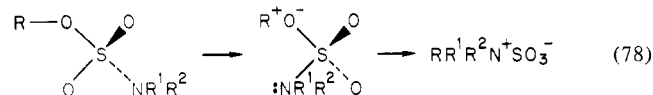
Aryl esters of sulfamic acids have been prepared by the reaction of phenols with sulfamyl chloride,^{417,418} chlorosulfonyl isocyanate,^{419,420} and isocyanates (ArOSO₂NCO) with water.⁴²¹ Hedayatullah has prepared a similar series by reduction of aryloxysulfonyl azides with a variety of reducing agents including copper in methanol⁴²² and also with sodium borohydride in tetrahydrofuran.⁴²³

2. Rearrangement

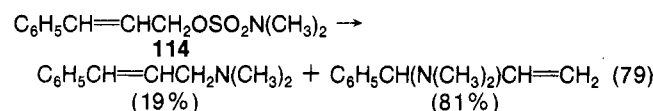
The rearrangement of sulfamate esters to betaines (**113**) has been reported.⁴²⁴ White⁴²⁵ has examined the behavior of optically active groups R³ in the reaction using dimethylsulfamate esters, (CH₃)₂NSO₂R³, as substrates. The resulting betaines



were hydrolyzed to sulfates and amines (R¹R²NR³); the latter were evaluated optically. When the R³ group was C₆H₅C*HCH₃ (optically active), the yields of amine [(CH₃)₂NCH(CH₃)C₆H₅], the extent of retention of optical activity, and the solvent were respectively as follows: 60%, 0%, CH₃OCH₂CH₂CH₃; 20%, 7%, CCl₄; 11%, 24%, CHCl₃; 11%, 67%, CH₃COOH. White concluded that the rearrangement involved ionic intermediates (eq 78). Other mechanisms, however, such as elimination and

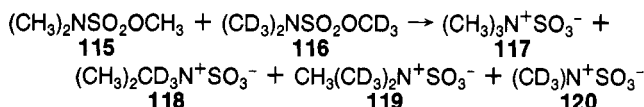


substitution processes, are implicated when compounds with allylic groups such as *trans*-cinnamyl (**114**) are involved; the product contained some *trans* S_N1 product but contained mostly material derived from an S_N1' process. If a true intramolecular



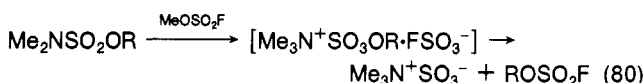
process was occurring, Ziegler and Orchin⁴²⁶ considered that on heating two different esters together the product betaines should show no alkyl group exchange provided that both rearrange at the same rate. Experiments showed that (CH₃)₂NSO₂OC₂H₅ and (CH₃)(C₂H₅)NSO₂OCH₃ rearrange at approximately the 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, (CH₃)₂SO₂-OCH₃, 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.



The same ratio was obtained when the reaction was carried out at different concentration levels, i.e., $[\textbf{115}] = [\textbf{116}] = 1.0$ 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.

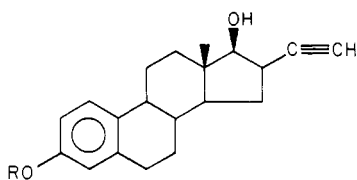
Betaines have also been observed in the reaction of alkyl *N,N*-dimethylsulfamates with methyl fluorosulfonate (eq 80).⁴²⁸



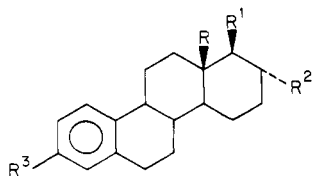
When the alkyl group of the ester is a simple straight chain this provides a convenient procedure for the preparation of primary alkyl fluorosulfates.

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 $\text{PhCH}_2\text{Et}_3\text{N}^+\text{Cl}^-$.

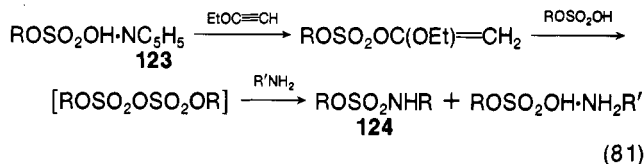
**121**

R = Et₂NSO₂, 1-pyrrolidinosulfonyl, 1-piperidinosulfonyl

**122**

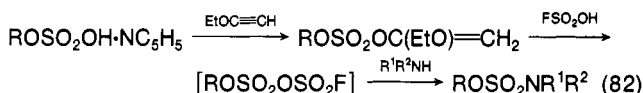
R = Me, Et; R¹ = OH, O; R² = C≡CH; R³ = R⁴R⁵NSO₂O;
R⁴R⁵ = Me, Et; R⁴R⁵N = pyrrolidino, morpholino, piperidino

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



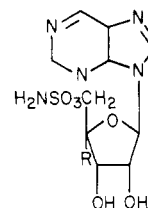
from the fact that in a very dry medium the compounds do not react with amines, but on addition of water hydrolysis occurs to give pyrosulfate which then reacts with amines. If the ethoxy vinyl ether is used in the reaction with a stronger acid, then the mixed anhydride should react with formation of 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 studies⁴⁴⁰ 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



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.

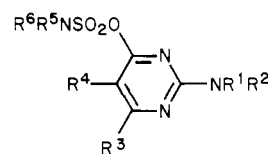
Nucleocidin is one of the few known antibiotics containing the sulfamate ester group. Shuman, Robins, and Robins⁴⁴¹ have now reported the synthesis of nucleoside sulfamates. The general procedure involves the reaction of sulfamyl chloride with a suitably blocked nucleoside.^{442,443} The adenosine ester **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

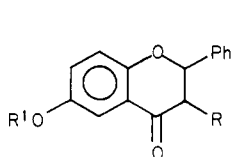
**126**

R¹ = H, lower alkyl; R² = lower alkyl, allyl; R³ = alkyl C₁₋₃;
R⁴ = butyl or allyl; R⁵ = R⁶ = lower alkyl; NR⁵R⁶ = 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.⁴⁴⁸⁻⁴⁵⁶ The main synthetic route involved was the nucleophilic displacement of chlorine from mono- and dialkylsulfamyl chlorides by various nucleophilic groups, both alkyl and aromatic.

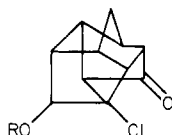
The sulfamate function as the ester is incorporated into a wide range of dyes of various types, including azo dyes⁴⁵⁷⁻⁴⁶⁰ and anthraquinone polyester dyes.⁴⁶¹⁻⁴⁶⁴

Esterification of glycols⁴⁶⁵ by reaction with alkyl- and dialkylsulfamyl halides leads to sulfamate esters which have been found useful as contraceptives. Alkyl flavanone compounds⁴⁶⁶ (127) which are esters of sulfamic acid were found to lower cholesterol in blood serum. Esters of the type 128⁴⁶⁷ 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; R¹ = NH₂SO₂

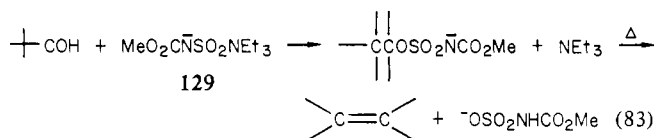


128

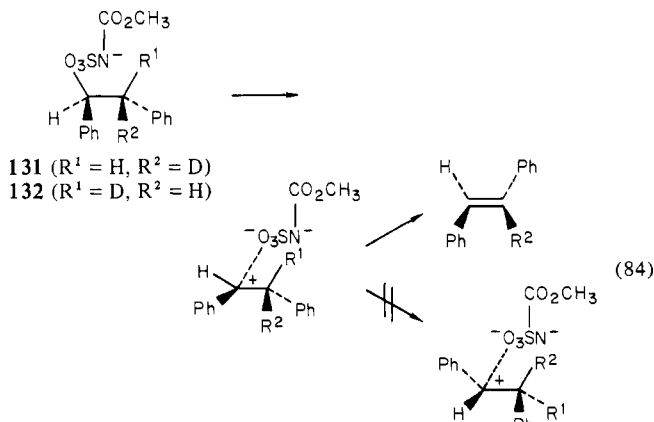
R = NHCH₂Ph, NH₂, morpholino

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^{468,469} and involves the use of the *N*-(carbomethoxy)sulfamate ester 129 (see eq 83).

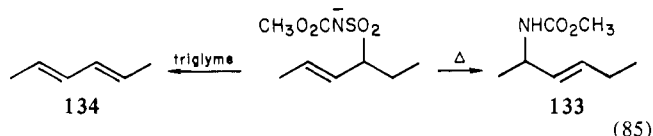


The kinetics of the solvolytic elimination reaction of 1,2-diphenylethyl *N*-(carbomethoxy)sulfamate triethylammonium salt (130) in ethanol gave only *trans*-stilbene with a first-order rate constant of $2.66 \times 10^{-6} \text{ s}^{-1}$ with $\Delta H^\ddagger = 90.9 \text{ K J mol}^{-1}$ and $\Delta S^\ddagger = 13.8 \text{ J mol}^{-1} \text{ K}^{-1}$. 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.

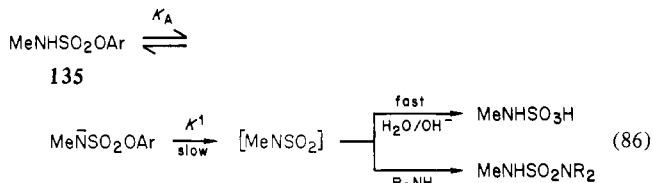


Reaction conditions determined the type of product when the reaction was applied to allylic alcohols. The thermal decom-

position of sodium 4-hex-2-enyl *N*-(carbomethoxy)sulfamate gives 90% rearranged urethane 133 while reaction in triglyme gives the diene 134.

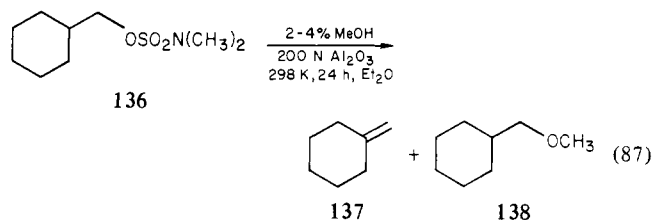


Evidence consistent with an E1cB mechanism for the hydrolysis of the aryl esters of methylsulfamic acid (135) is presented by Williams.^{470,471} The rate constants for the hy-

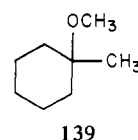


drolysis of the esters were found to be independent of pH in the alkaline region. The Brønsted β_{19} value for the hydrolysis reaction is -2.9 and differs from the value -1.1 obtained for the corresponding *N,N*-dimethyl series. Thus the dialkyl series is considered to react via an addition-elimination 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.

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.



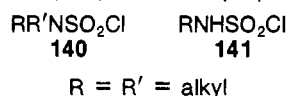
C. Sulfamyl Halides

1. Synthesis

a. Sulfamyl Chlorides

Dialkylsulfamyl chlorides (140) have been reported by Ziegler and Orchin⁴²⁶ and by Binkley and Degering.⁴⁰⁹ The corresponding

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



Schulze.⁴⁷⁴ The procedure involves the reaction of alkylamines⁴⁷⁵ or alkylamine hydrochlorides⁴⁷⁶⁻⁴⁷⁸ with sulfuryl chloride (eq 88). Sulfuryl chloride reacts also with dialkylsulfamides to



yield sulfamyl halides⁴⁷⁹ (eq 89).

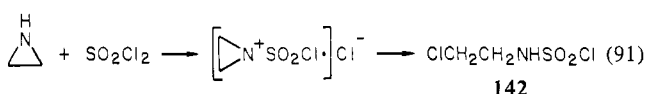


Alkylsulfamic acids have been used as starting materials for the synthesis of sulfamyl halides. Hamprecht et al. have reported the reaction of alkylsulfamic acids with thionyl chloride⁴⁸⁰ and carbonyl chloride^{481,482} to give high yields of the corresponding sulfamyl halides. Phosphorus pentachloride has also been used with sulfamic acids to yield the sulfamyl halides.⁴⁸³ Kloek and Leschinsky⁴⁸⁴ 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).

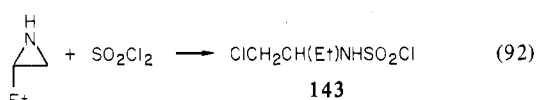


R = alkyl for a or b; R = alkyl or aryl for c

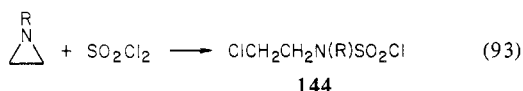
Various reagents and methods have been used in the synthesis of alkylsulfamyl halides.⁴⁸⁵ Hamprecht has reported on the novel use of aziridines and sulfuryl chloride to prepare β -chlorosulfamyl chlorides (eq 91). Substituted aziridines un-



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-



tended to include *N*-alkylaziridines which react in a similar manner to yield β -chloroethyl-*N*-alkylsulfamyl chlorides, **144** (eq 93).⁴⁸⁶



Alkyl chlorinated dialkylsulfamyl halides have been formed by reaction of the corresponding sulfamic acids or halides with paraformaldehyde and SOCl_2 or PCl_5 .^{487,488} In addition, chlorosulfonyl isocyanate has been found to react with tertiary alcohols⁴⁸⁹ to yield the corresponding sulfamyl chlorides.

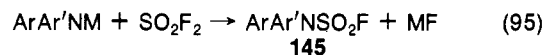
b. Sulfamyl Fluorides and Fluoro-Substituted Sulfamyl Chlorides

Monoalkylsulfamyl fluorides have been prepared by the reaction of sulfamyl chlorides with hydrogen fluoride⁴⁹⁰ (eq 94).



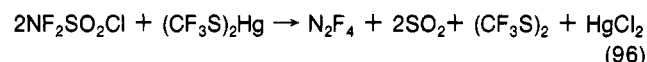
In addition, substituted sulfamyl fluorides, $\text{Cl}_2\text{FCCSNHSO}_2\text{F}$, have been prepared and their insecticidal properties reported.⁴⁹¹ Roesky^{492a} reacted secondary amines with sulfuryl chlorofluoride, SO_2FCl , to obtain dialkylsulfamyl halides. Some disubstitution occurred, however, leading to the formation of sulfamide. He

has chlorinated dimethylsulfamyl fluoride, $\text{Me}_2\text{NSO}_2\text{F}$, to obtain the interesting disubstituted sulfamyl fluoride $(\text{Cl}_2\text{CH})_2\text{NSO}_2\text{F}$.^{492b} Novel diarylsulfamyl fluorides^{493,494} ($\text{ArAr}'\text{NSO}_2\text{F}$, **145**) have been prepared by the reaction of sulfuryl fluoride with lithium and sodium salts of secondary diarylamines (eq 95).



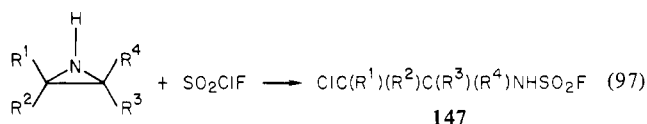
M = Li, Na

The unsubstituted parent sulfamyl fluoride⁴⁹⁵ 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, $\text{NF}_2\text{SO}_2\text{F}$,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 ($\text{NF}_2\text{SO}_2\text{Cl}$) has now been prepared⁴⁹⁹ 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).



N,N-Dichlorosulfamyl fluoride ($\text{NCl}_2\text{SO}_2\text{F}$, **146**) was prepared by Roesky⁵⁰⁰ by reaction of $\text{FSO}_2\text{N}=\text{S}=\text{O}$ 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 $[(\text{C}_6\text{H}_5)_4\text{Y}]^+ [\text{FSO}_2\text{NCl}]^-$ (Y = P, As). Likewise *N*-(trifluoromethyl)sulfamyl fluoride ($\text{CF}_3\text{NHSO}_2\text{F}$) is characterized as its tetraphenylarsonium salt.⁵⁰¹

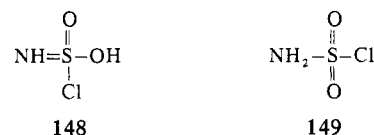
β -Chloro-substituted sulfamyl fluorides (**147**) have been formed by Hamprecht by reaction of substituted aziridines with chlorosulfonyl fluoride^{486,502} (eq 97). In no case was the sulfamyl



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

2. Physical Studies

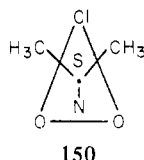
The imido form of sulfamyl chloride (**148**) is not in equilibrium with the normal form (**149**). This conclusion was reached from



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 $(\text{CH}_3)_2\text{NSO}_2\text{X}$, where X = F, Cl, Br. Calculation of the force constants S-X gave good agreement with the observed spectra with $f_{\text{S-F}}$ 4.15, $f_{\text{S-Cl}}$ 2.65, and $f_{\text{S-Br}}$ 2.38 mdyn/Å. Two further groups have re-

corded the infrared spectrum of dimethylsulfamyl chloride. Paetzold and Rönsch⁵⁰⁵ 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 $[(CH_3)_2N]_2SO$, $[(CH_3)_2N]_2SO_2$, 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 Hargittai⁵⁰⁷ established that $(CH_3)_2NHSO_2Cl$ is present in the internal rotational form **150**. Hargittai and Brunvoll⁵⁰⁸ reinvestigated the structure



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 study⁵⁰⁹ 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 Deich⁵¹⁰ measured the nuclear quadrupole frequencies (³⁵Cl) 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 ³⁵Cl NOR frequency of sulfamyl chloride⁵¹¹ 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

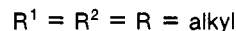
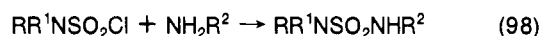
3. Reactions

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 (sulfamylloxy)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).

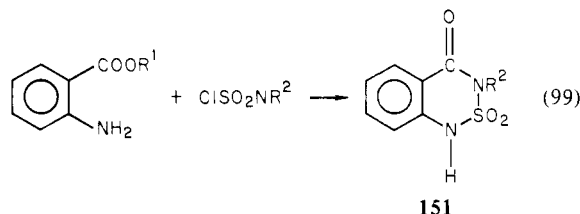
b. Sulfamide and Cyclic Compound Syntheses

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

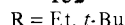
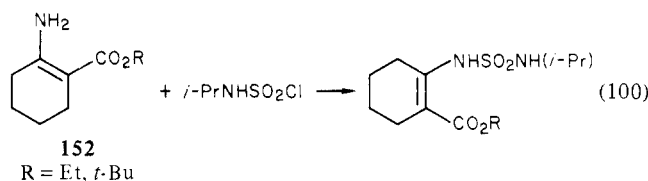


Mono- or dialkylsulfamyl chlorides are generally used with alkyl groups in the range C_{1-3} . A wide range of sulfamides have been prepared, including α -(aminoalkyl)-4-hydroxy-3-(sulfamylamino)benzyl alcohols⁵¹⁷⁻⁵¹⁹ (adrenergic stimulants), sulfamido-phenethanolamines⁵²⁰ (antiarrhythmic agents), 2-(aminobenzimidazole)sulfonamides⁵²¹ (fungicides), and *N,N'*-substituted sulfamides⁵²² (herbicides).

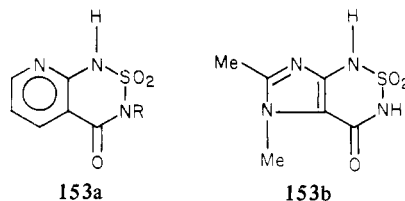
Cohen and Klarberg,⁵²³ Hamprecht,^{524-527a} and Bancroft et al.^{527b} demonstrated the synthetic usefulness of sulfamyl chlorides in the preparation of heterocyclic compounds such as 2,1,3-benzothiadiazin-4-one 2,2-dioxides (**151**). Kloeck and Leschin-



sky⁵²⁸ 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



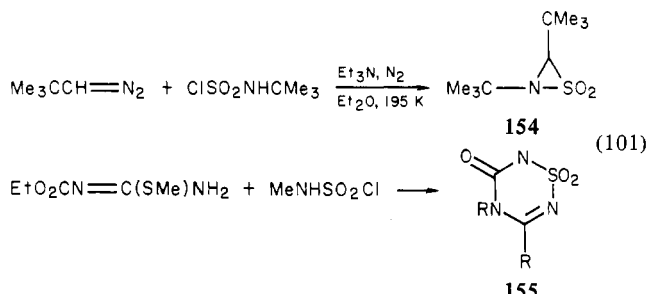
of Cohen and Klarberg (aqueous base) (if a simple straight-chain sulfamyl chloride was used) or by using trifluoroacetic acid/anhydride (when *i*-PrNHSO₂Cl was used). In the presence of a carboxylic amide or a tertiary amine, 1*H*-pyrido[3,2-*e*]-[2,1,3]thiadiazin-4-one 2,2-dioxides (**153a**) were similarly prepared by reaction of alkylsulfamyl halides with methyl 2-aminonicotinate.^{527a} Likewise the imidazothiadiazine dioxide



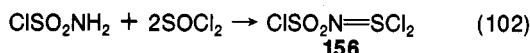
and a pyrimidothiadiazine dioxide are obtained by cyclization reactions with sulfamyl chloride.⁵²⁹ The cyclic systems thiaziridine 1,1-dioxide (**154**)^{530a} and thiatiazine 1,1-dioxide (**155**)^{530b} are prepared by the cycloaddition reactions with sulfamyl chlorides shown in eq 101. In the reaction of *o*-aminodialkylanilines with sulfamyl 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. Roesky⁵⁰¹ has shown that sulfamyl

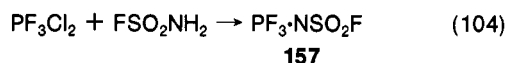


chloride when reacted with thionyl chloride yields the imide **156** which in the presence of excess anhydrous hydrogen fluoride is converted to sulfamyl fluoride which provides an alternative synthesis for this compound.



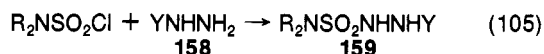
Sulfamyl fluoride has been reacted with diketene in the presence of base to give cyclic products which are useful as artificial sweeteners.⁵³² The low-temperature reaction of sulfamyl chloride has led to a route for the synthesis of the hitherto unknown asymmetrically substituted imidobissulfamides,⁵³³ $\text{H}_2\text{NSO}_2\text{NHSO}_2\text{NR}_2$.

Sulfamyl fluoride undergoes substitution reactions leading to the formation of *N*-fluorosulfamyl fluoride and *N,N*-difluoro-sulfamyl fluoride,⁵³⁴ sulfur oxide difluoride ((fluorosulfonyl)uride),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



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

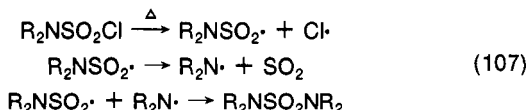
Nucleophilic displacement at sulfamyl sulfur by the hydrazines YNHNH_2 (**158**, Y = benzoyl, 2-pyridyl) yielded the sulfamyl hydrazines, **159**.⁵⁴³ Two other types of reaction involving ho-



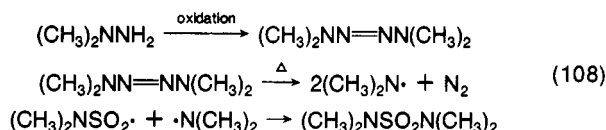
molytic cleavage of the S-Cl bond were observed.⁵⁴³ First, where the hydrazine used was methylhydrazine or 1,1-dimethylhydrazine, the reaction produced tetrasubstituted sulfamides (eq 106). The proposed reaction mechanism is shown



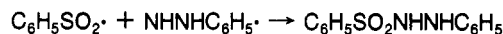
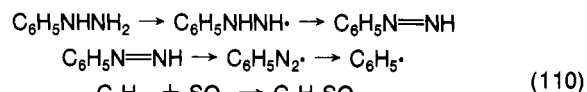
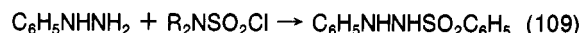
in eq 107. An alternative mechanism in the case of 1,1-di-



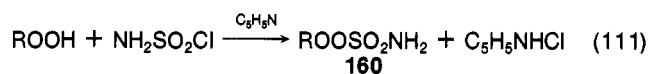
methylhydrazine was considered also to be operative: the oxidation of the hydrazine took place together with homolysis of the halide with the incorporation of the hydrazine radicals into the product (eq 108). Second, the reaction with phenylhydrazine



yielded phenyl-2-benzenesulfonylhydrazide⁵⁴⁴ (eq 109), and the most likely mechanism is shown in eq 110.

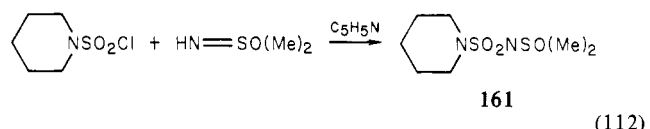


Sulfamyl halides have been used for the synthesis of alkyl-sulfamyl peroxides⁵⁴⁵ **160** by allowing the reaction to occur at 233 K in diethyl ether (eq 111). Hydrolysis of the O-O bond



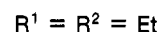
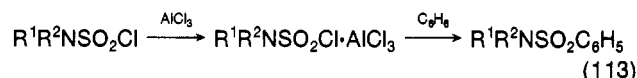
occurs above 263 K to give the following decomposition products: (a) R = *n*-propyl: sulfamic acid, propanol, propyl, propionate, and isopropyl propionate; (b) R = *n*-butyl: sulfamic acid, butanal, 2-methylpropanal, and butyl butyrate.

The synthesis of *N*-sulfamyl dimethylsulfoximines (**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



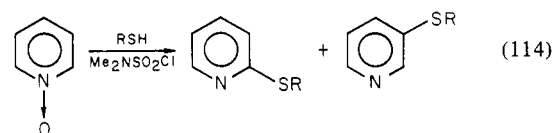
to amines^{546b} involves reaction of the alcohol with chlorosulfonyl isocyanate to give *N*-chlorosulfonylurethanes which decompose to give the sulfamyl chloride of the alcohol. These are best reduced to amines by formation of the *tert*-butoxycarbonylhydrazides and reduction with $\text{Pb}(\text{OAc})_4$.

N,N-Disubstituted sulfonamides have traditionally been obtained by the reaction of a sulfonyl halide with an amine. Gupta⁵⁴⁷ 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-



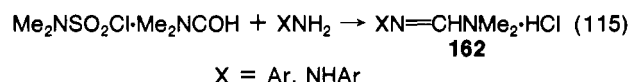
action of sulfamyl halides with Grignard reagents was carried out by Maslil and Petrov⁵⁴⁹ in an attempt to develop a synthetic route to *N,N*-disubstituted sulfonamides. However, the products isolated were diethylamine and *n*-butyl chloride.

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



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

Scott and Barry⁵⁵³ 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**).



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

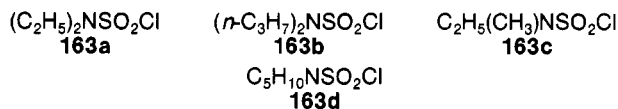
Hall⁵⁵⁴ has reported on the hydrolysis of dimethylsulfamyl chloride, $(\text{CH}_3)_2\text{NSO}_2\text{Cl}$, and concluded that the reaction occurred through an ionization mechanism ($\text{S}_{\text{N}}1$). The possibility of an ionization process can be considered because of the possible stabilization by the amino function. Hall and Lueck⁵⁵⁵ examined



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 dialkylsulfamylum ions produced. They found that the halide reacts very rapidly with the mercuric salt, a reaction which they concluded involved sulfamylum 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 sulfamylum 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 $\text{S}_{\text{N}}2$ 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 ($\text{S}_{\text{N}}1$ or $\text{S}_{\text{N}}2$) of *N,N*-dimethylsulfamyl chloride is a controversial one. Hall has suggested that this compound reacts by an $\text{S}_{\text{N}}1$ mechanism, but more recently, Rogne has proposed an $\text{S}_{\text{N}}2$ -type mechanism. By careful use of a sophisticated mechanistic probe, namely, the temperature coefficient of the enthalpy of activation (ΔC_p^\ddagger), Ko and Robertson⁵⁵⁷ favor an $\text{S}_{\text{N}}1$ -type mechanism. They believe that the more negative value of ΔC_p^\ddagger ($-318.4 \text{ K J mol}^{-1}$) which they observed for the sulfamyl chloride compared with the value of $-230 \text{ K J mol}^{-1}$ 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 $\text{S}_{\text{N}}1$ 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 ($k_{\text{H}}/k_{\text{D}}$) for the hexadeuterio compound is 0.95.

Ko and Robertson⁵⁵⁸ have also studied the mechanism of hydrolysis of the sulfamyl chlorides **163** in water. These



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 ($k_{\text{H}}/k_{\text{D}} = 2$) measured with **163a** and $(\text{CH}_3\text{CD}_2)_2\text{NSO}_2\text{Cl}$. The ΔC_p^\ddagger values for **163a** and **163d** were -153.4 and $-184.4 \text{ K J mol}^{-1}$, respectively, and for **163c** a value of $-255.5 \text{ K J mol}^{-1}$ 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 $\text{S}_{\text{N}}1$ 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 $\text{S}_{\text{N}}1$ 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. ΔC_p^\ddagger would appear to be potentially a very useful diagnostic tool for the detection of subtle distinctions in mechanism.

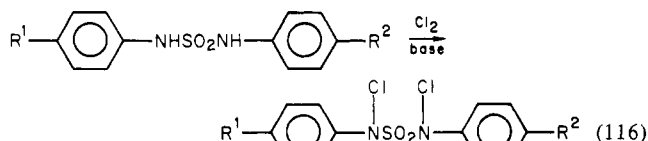
Lee and Kim⁵⁵⁹ have found that the ΔH^\ddagger and ΔS^\ddagger parameters for the exchange of ^{36}Cl , ^{82}Br , and ^{131}I with $\text{Me}_2\text{NSO}_2\text{Cl}$ in dry acetone decreased in the order $\text{Cl}^- > \text{Br}^- > \text{I}^-$. This is the reverse of the order observed for the faster 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 $\text{Me}_2\text{NSO}_2\text{Cl}$ (and some sulfonyl chlorides and MeOSO_2Cl) have been carried out by the same group.⁵⁶⁰ The exchange reaction of $^{36}\text{Cl}^-$ with $\text{Me}_2\text{NSO}_2\text{Cl}$ has also been studied by Cha.⁵⁶¹

IV. Sulfamide

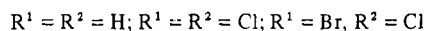
A. Synthesis

Sulfamide ($\text{NH}_2\text{SO}_2\text{NH}_2$) has been prepared by a variety of procedures and the earlier reactions and methods have been reviewed by Audrieth and Sveda.⁵⁶² Ito⁵⁶³ 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 condensates⁵⁶⁴ $(\text{NH}_4\text{NSO}_2)_2$ or $\text{NH}_4\text{N}(\text{SO}_2\text{NH}_2)_2$ depending on the temperature. The condensate, however, can be hydrolyzed and additional sulfamide recovered, thus improving the yield.⁵⁶⁵

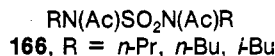
In the early sixties Sowada⁵⁶⁶ presented a short review of the synthesis of sulfamides (see references therein) in which he summarized the three main synthetic routes to sulfamides: (a) reaction of primary amines (alkyl or aryl) with sulfonyl chloride; (b) reaction of primary amines with chlorosulfonic acid; (c) reaction of primary amines ($\text{R} = \text{alkyl, cycloalkyl, aryl}$) with sulfamide. He further extended the range of symmetrical, *N,N'*-disubstituted alkyl- and cycloalkylsulfamides available by reaction a.⁵⁶⁷ The sulfamides RNHSO_2NHR ($\text{R} = \text{alkyl and cycloalkyl}$) were reacted further to form *N,N'*-alkyl-*N,N'*-chlorosulfamides (**164**, $\text{R}(\text{Cl})\text{NSO}_2\text{N}(\text{Cl})\text{R}$, $\text{R} = n\text{-Pr, } i\text{-Pr, } n\text{-Bu, cyclohexyl}$).⁵⁶⁸ The corresponding arylchlorosulfamides (**165**) were prepared by Forster, Gilchrist, and Rees⁵⁶⁹ by the action of excess chlorine in aqueous sodium hydroxide on the corresponding diarylsulfamides (eq 116). Tetrasubstituted alkylsulfamides were prepared by Sowada⁵⁷⁰ 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



165

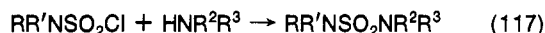


with acetic anhydride.⁵⁷¹ Sowada has also extended the re-



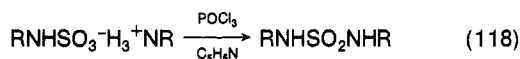
actions of *N,N'*-disubstituted sulfamides to yield tetrasubstituted sulfamides.^{572,573} The reaction procedures mentioned above have been used to synthesize 2-phenylcyclopropylsulfamides,⁵⁷⁴ *N,N*-disubstituted sulfamides,⁵⁷⁵ and *N*-substituted sulfamides.⁵⁷⁶

The reaction of sulfamyl halides with alkyl- and arylamines has been used extensively as a route to sulfamides.⁵⁷⁷⁻⁵⁸² This

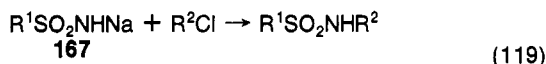


reaction has also been used in the synthesis of *N*-substituted arylsulfamides⁵⁸³⁻⁵⁸⁵ and also (1,2,4-triazol-5-yl)sulfamides.⁵⁸⁶

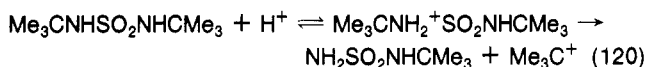
Yamaguchi and Fukuno⁵⁸⁷ have obtained *N,N'*-disubstituted sulfamides by reaction of amine salts of sulfamates with phosphorus oxytrichloride in pyridine (eq 118). The reactions



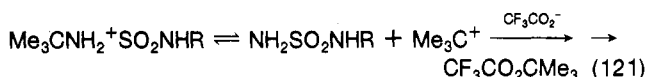
of sodium sulfamides **167** with halides yield *N,N'*-disubstituted sulfamides (eq 119).⁵⁸⁸



The preparation of primary sulfamides, $\text{NH}_2\text{SO}_2\text{NHR}$, from *N,N'*-disubstituted sulfamides has been investigated. Sowada⁵⁸⁹ 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).



Catt and Matier⁵⁹⁰ report a similar reaction of *N-tert*-butyl-*N'*-substituted sulfamides with trifluoroacetic acid (eq 121), which extended Sowada's reaction considerably.



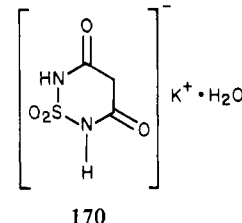
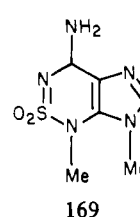
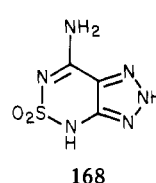
B. Physical Studies

1. Structural

A normal coordinate analysis has been carried out on sulfamide.⁵⁹¹ Disilver sulfamide, $\text{AgNHSO}_2\text{NHAg}$, 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, $\text{Me}_2\text{NSO}_2\text{NMe}_2$, 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

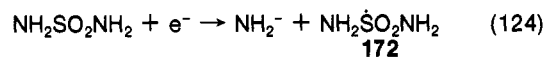
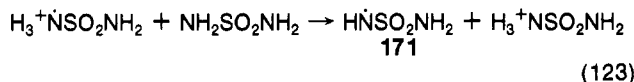
García-Blanco and co-workers have carried out X-ray diffraction studies on a series of 1,2,6-thiadiazine 1,1-dioxides.⁵⁹⁵⁻⁶⁰¹ Single crystals were examined on an automatic Philips PW 1100 four-circle diffractometer with graphite-monochromated Mo $K\alpha$ radiation. Among the compounds studied were 7-amino-2*H*,4*H*-*vic*-triazolo[4,5-*c*]-1,2,6-thiadiazine 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 $\text{NH}_2\text{SO}_2\text{NH}_2$ 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, $\text{NH}_3^+(\text{NH})\text{SO}_2^-$, or isoamidic, $\text{NH}_2(\text{NH})\text{S}(\text{O})\text{OH}$, forms were observed. Sowada⁶⁰³ has reported infrared spectra for a series of di- and tetrasubstituted sulfamides of the general formula $\text{RR}'\text{NSO}_2\text{NRR}'$, 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.⁵⁰⁸

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



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

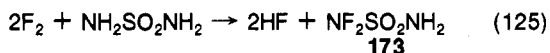
The dissociation energy of $\text{Et}_2\text{NSO}_2\text{NEt}_2$ for the gas-phase reaction giving $(\text{Et}_2\text{N})_2\text{SO} + \text{O}$ has been calculated from measured heats of reaction.⁶⁰⁶ The specific heat of sulfamide has been measured over the range 90–298 K, and its entropy was estimated 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 study⁶⁰⁸ 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

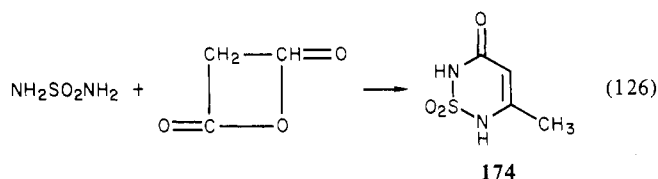
1. Reactions of Sulfamide, $\text{NH}_2\text{SO}_2\text{NH}_2$

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



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 esters⁶¹³ 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-dioxide⁶¹⁵ (**174**). Knollmüller and Reich have prepared 3,7-bis-



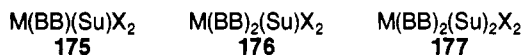
(trichloromethyl)perhydro-1,5,2,4,6,8-dithiatetrazocine 1,1,5,5-tetroxide.⁶¹⁶ Sulfamide has also been used in the preparation of *N,N'*-bis(benzylidene)sulfamides⁶¹⁷ and 2-hydrohexafluoroisobutyric acid derivatives.⁶¹⁸

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 Matsui⁶²³ 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 group⁶²⁴ 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.

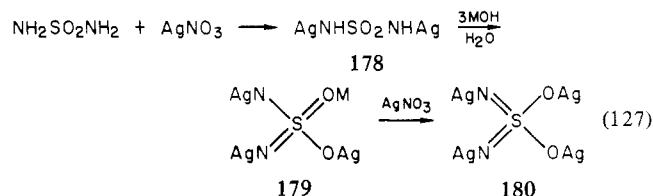
The use of sulfamide and its substituted derivatives as ligands has not been studied extensively. Rhodium chelates⁶²⁵ and mercury(II) complexes⁶²⁶ with sulfamide have been reported; however, the composition was found to vary and has been attributed to hydrolytic decomposition and differences in reaction conditions.^{626,627} Paquin⁶²⁸ has reported on the complexes $\text{M}''\text{A}_2(\text{NHSO}_2\text{NH}_2)_2$, where A is a monoamine or half a diamine molecule. Ouchi and Moeller⁶²⁹ 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



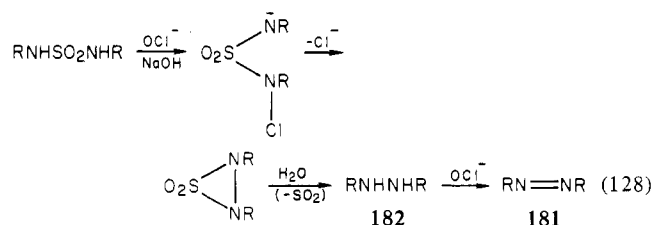
mainly copper, BB is two molecules of ammonia or one molecule of a diamine, Su is sulfamide, and X is a uninegative or dinegative ion. The adducts were found to be stable in the solid state but decompose to the corresponding metal-amine complex and sulfamide when in contact with water. Infrared studies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

The reaction of sulfamide with silver nitrate has been studied. Traube⁶³⁰ has previously shown that *N,N'*-diargentosulfamide (**178**) is formed from the reaction of sulfamide with silver nitrate. Popitsch and Nachbaur⁶³¹ 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.



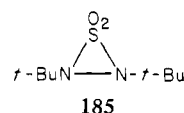
2. Heterocyclic Synthesis Using Sulfamides

Ohme and Schmitz⁶³² 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

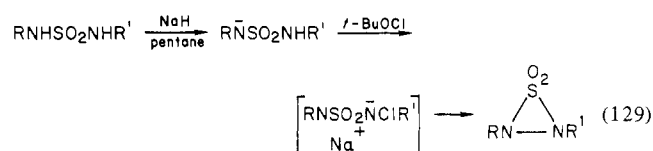


by the fact that when *N,N'*-dipropylsulfamide and *N,N'*-diethylsulfamide were submitted to the reaction no mixed azoalkane ($n\text{-PrN} = n\text{-BuN}$) was obtained. The isolation of di-*N*-propylhydrazine in 50% yield when insufficient hypochlorite was used supports the involvement of *N,N'*-dialkylhydrazines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

Timberlake⁶³⁴ 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

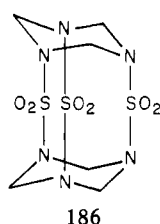


be summarized as in eq 129. Timberlake has studied the

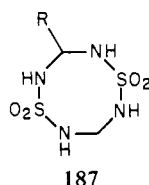


chemistry of the thiadiaziridine 1,1-dioxides and has summarized the reactivity toward a wide variety of chemical reagents.⁶³⁶ Of particular interest is the chemical reactivity toward lithium and Grignard reagents which lead to sulfamides and azo compounds, respectively. Weinstein and Chang have also studied the reactions of *N,N'*-*tert*-butylthiadiaziridine, including hydrolysis, methanolysis, and reactions with various nucleophiles.⁶³⁷ Forster, Gilchrist, and Rees⁶³⁸ considered the oxidation of *N,N'*-diaryl-sulfamides 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'*-dichlorodiarlylsulfamides 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. Gilbert⁶³⁸ et al. formed the novel system **186** by the reaction of sulfamide with paraformaldehyde.

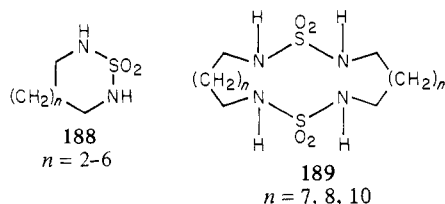


Dusemund⁶³⁹⁻⁶⁴⁴ has studied the reactions of sulfamide and *N*-substituted sulfamides with various aldehydes, including formaldehyde, acetaldehyde, chromone-3-carbaldehyde, succindialdehyde, and phthalaldehyde. The major heterocyclic nucleus formed was a dithiatetraazocene, **187**. The substituents

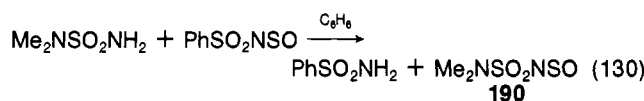


on the nucleus depend on the type of sulfamide and aldehyde used.

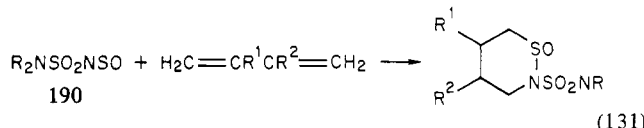
The reaction of sulfamide with diamino compounds has led to the synthesis of heterocyclic systems. Ciaperoni reported that the reaction of sulfamide with ethylenediamine led to the formation of 1,2,5-thiadiazolidine.⁶⁴⁵ Arya and Shenoy⁶⁴⁶ have pointed out that in the reaction of sulfamides with diamines 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 sulfamides⁶⁴⁶⁻⁶⁴⁸ have also been prepared by reaction of sulfamide with the appropriate starting amines.



The literature reveals that sulfamide has been used in the synthesis of a wide range of other heterocyclic compounds, including 3-amino-4*H*-1,2,4,6-thiadiazine 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

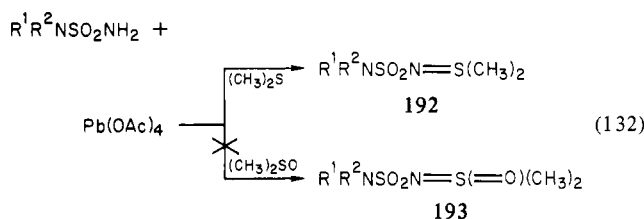


to the formation of the heterocyclic system **191**.

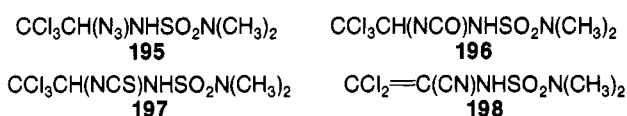


3. Reactions of Sulfamides with Inorganic Reagents

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).



Reaction of *N,N'*-disubstituted sulfamides bearing active hydrogens at α carbons in the presence of base and thionyl chloride led to sulfenimines⁶⁵⁸ (**193**). Reaction of sulfamide with antimony pentachloride⁶⁵⁹ yielded antimony tetrachloroethoxide, $\text{SbCl}_4(\text{OEt})$. *N*-(1,2,2,2-Tetrachloroethyl)-*N',N'*-dimethylsulfamide,⁶⁶⁰ $\text{CCl}_3\text{CHClNHSO}_2\text{N}(\text{CH}_3)_2$ (**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**.



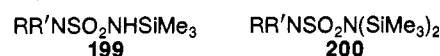
N,N-Difluorosulfamide, prepared by aqueous fluorination of sulfamide, was found to decompose at temperatures above 278 K. Attempts to stabilize the fluorination product by substitution of alkyl groups revealed that cleavage of the N-S bond occurred on fluorination and the corresponding *N,N*-difluoroalkylamine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



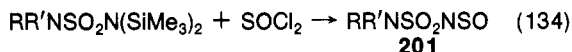
monosubstituted derivatives, since *N,N*-dimethylsulfamide had been shown earlier to produce dimethylfluoramine.⁶⁶¹ It appears that the low volatility and instability of secondary fluoramines limit the application of the reaction to *N,N*-dialkyl substrates.

4. Reactions of Sulfamides with Silyl Reagents

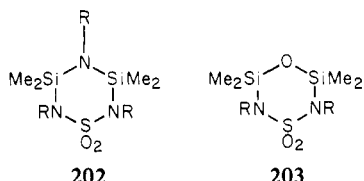
Appel and Montenarh⁶⁶² have reported on the reaction of sulfamides with various silylation reagents and the subsequent reaction of these compounds. The silylation of *N,N*-dialkylsulfamides with hexamethyldisilazane⁶⁶³ or trimethylchlorosilane/triethylamine under various conditions leads to the formation of *N,N*-dimethyl-*N',N'*-mono(trimethylsilyl)sulfamide (**199**) and bis compound **200**. Subsequent reaction of the bis com-



pound **200** with thionyl chloride leads to the synthesis of *N*-sulfinylamides (**201**). Appel⁶⁶⁴ also presents various routes for

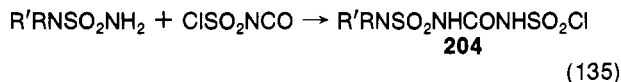


the synthesis of *N,N*-bis(trimethylsilyl)- and *N,N,N',N'*-tetra-kis(trimethylsilyl)sulfamides. The reactions of monosilylated sulfamides have also been reported.⁶⁶⁵ The tris(trimethylsilyl)-sulfonic acids can be readily obtained from the silylamines and trimethyl esters of chlorosulfonic acid.⁶⁶⁶ Wannagat and Labuhn⁶⁶⁷ 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.



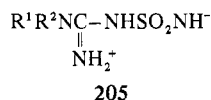
5. Other Reactions

N,N-Dialkyl- and *N,N*-diarylsulfamides react with chlorosulfonyl isocyanate to yield the previously unreported *N*-(chlorosulfonyl)-*N'*-(dialkyl- or diarylsulfamyl)ureas (**204**).⁶⁶⁸ Hydrolysis

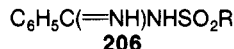


of these compounds led to the formation of *N*-(dialkyl- or diarylsulfamyl)ureas, while pyrolysis led to the formation of sulfamyl chlorides. The fluoro compounds corresponding to **204** have also been reported.⁶⁶⁹

Lombardino⁶⁷⁰ 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.



A Russian group has prepared⁶⁷¹ a number of *N*-sulfonylbenzamidines (**206**) by reaction of benzamidine with sulfamide and *N*-substituted sulfamides. Unlike the corresponding un-



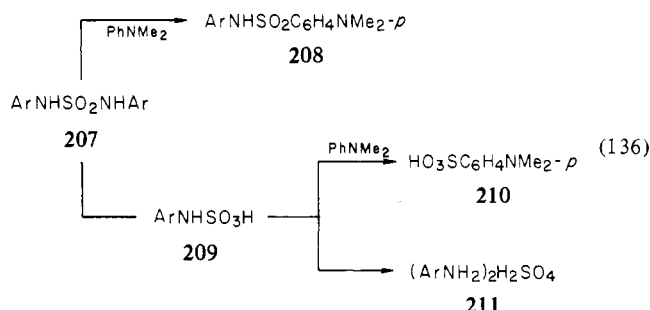
substituted amidines, these materials are not hydrolyzed when heated in aqueous or alcoholic solution.

Yas'kovyakh⁶⁷² et al. have reported on the interaction of tetraethylsulfamide ($Et_4NSO_2NEt_2$) 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.

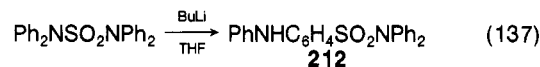
6. Hydrolysis and Rearrangement of Sulfamides

The protonation, rearrangement, and hydrolysis reactions of sulfamides have been reported. Jolly⁶⁷³ studied the exchange rates for sulfamide in both acidic and basic media. The magnitude of k_1 for the protonation of sulfamide itself was $3 \times 10^7 \text{ M}^{-1} \text{ s}^{-1}$, a value similar to that for the protonation of other weak bases (e.g., the rate constant for methanol is $10^8 \text{ M}^{-1} \text{ s}^{-1}$). The rate constant for the reaction of sulfamide with OH^- ($2 \times 10^{11} \text{ M}^{-1} \text{ s}^{-1}$) was consistent with rate constants for the reactions of OH^- with acids stronger than water, $K \sim 10^{10}$ to $10^{11} \text{ M}^{-1} \text{ s}^{-1}$.

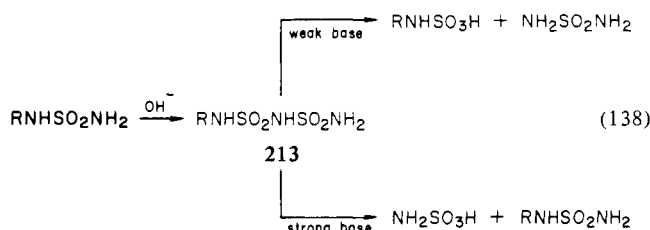
Thermolysis of *N*-substituted sulfamides^{154,674} has led to the formation of the ammonium salts of the corresponding sulfamic acids. A similar reaction has been observed for *N,N'*-disubstituted (alkyl) sulfamides. Scott^{675,676} has shown that *N,N*-diphenylsulfamide rearranged to yield sulfanilamide 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 Spillane⁶⁷⁷ 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. A key process is the transsulfamylation reaction, **207** \rightarrow **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 sulfamides⁶⁷⁸ 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'*-Tetraphenylsulfamide⁶⁷⁹ has been reported to rearrange to the sulfonamide **212** by reaction with butyllithium in tetrahydrofuran.



N-Substituted sulfamides⁶⁸⁰ 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. Yamaguchi⁶⁸¹ 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 Scott⁶⁸² have studied the

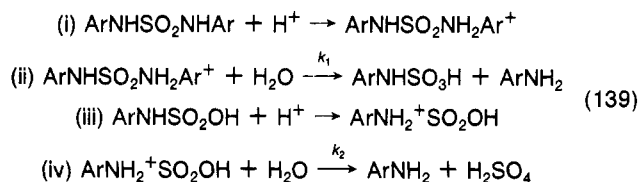


kinetics of hydrolysis of a series of *N,N'*-diarylsulfamides (214)



214, X = H, Me, MeO, Cl and NO₂

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 $\Delta H^\ddagger = 77.2 \text{ K J mol}^{-1}$ and $\Delta S^\ddagger = -121.8 \text{ J mol}^{-1} \text{ K}^{-1}$ was calculated. The above results were considered to be consistent with the mechanism shown in eq 139. Under the



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

- (1) L. F. Audrieth, M. Sveda, H. H. Sisler, and M. J. Butler, *Chem. Rev.*, **26**, 49 (1940).
- (2) E. E. Gilbert, "Sulfonation and Related Reactions", Wiley-Interscience, New York, 1965.
- (3) K. W. C. Burton and G. Nickless in "Inorganic Sulphur Chemistry", G. Nickless, Ed., Elsevier, Amsterdam, 1969, Chapter 18.
- (4) (a) du Pont de Nemours & Co. Product Information Bulletin, "Sulfamic Acid"; no date, but contains references to 1954 and U.S. patents to 1956. (b) D. Santymers and R. Aarons, "Sulfamic Acid and Sulfamates", in "Encyclopedia of Chemical Technology", Vol. 19, 2nd ed., Wiley, 1969, p 242.
- (5) A. Dorlars, *Methoden Org. Chem. (Houben-Weyl)*, 4th ed., **11/2**, 643 (1958); K. W. Wheeler in "An Outline of Organic Nitrogen Compounds", University Lithoprinters, Ypsilanti, MI, 1950.
- (6) L. P. Bicelli, *Proc. Symp. Sulfamic Acid (Milan)*, **19** (1966).
- (7) C. Romagnani, *Proc. Symp. Sulfamic Acid (Milan)*, 495 (1966).
- (8) F. L. Scott and W. J. Spillane, *Mech. React. Sulfur Compd.*, **2**, 133 (1968).
- (9) W. J. Spillane and F. L. Scott, *Mech. React. Sulfur Compd.*, **5**, 59 (1970).
- (10) W. J. Spillane, *Int. J. Sulfur Chem.*, **8**, 469 (1973).
- (11) (a) J. K. Rasmussen and A. Hassner, *Chem. Rev.*, **76**, 389 (1976); (b) R. Graf, *Angew. Chem., Int. Ed. Engl.*, **7**, 172 (1968); (c) "Heparin—Structure, Functions and Clinical Implications", R. A. Bradshaw and S. Wessler, Eds., Plenum, New York, 1975.
- (12) J. W. Bats, P. Coppens, and T. F. Koetzle, *Acta Crystallogr., Sect. B*, **33**, 37 (1977).
- (13) A. F. Cameron and F. D. Duncanson, *Acta Crystallogr., Sect. B*, **32**, 1563 (1976).
- (14) T. Sato, Y. Takahashi, and K. Yabe, *Bull. Chem. Soc. Jpn.*, **40**, 298 (1967); Y. Takahashi, K. Yabe, and T. Sato, *ibid.*, **42**, 2707 (1969); Y. Takahashi and K. Yabe, *ibid.*, **42**, 3064 (1969); Y. Takahashi, *ibid.*, **46**, 2039 (1973).
- (15) V. K. Wadhawan and V. M. Padmanabhan, *Acta Crystallogr., Sect. B*, **28**, 1903 (1972).
- (16) E. B. Cain and F. A. Kanda, *Z. Kristallogr., Kristallgeom., Kristallphys., Kristallchem.*, **135**, 253 (1972); *Chem. Abstr.*, **77**, 14504 (1972).
- (17) G. W. Cox, T. M. Sabine, V. M. Padmanabhan, N. Tu Ban, M. K. Chung, and A. J. Surjadi, *Acta Crystallogr.*, **23**, 578 (1967).
- (18) J. V. Tillack and C. H. L. Kennard, *J. Chem. Soc. A*, 1637 (1970).
- (19) S. D. Bruck and N. R. Stemple, *J. Phys. Chem.*, **71**, 3336 (1967).
- (20) R. S. Katiyar and R. S. Krishnan, *Indian J. Pure Appl. Phys.*, **6**, 686 (1968).
- (21) R. S. Katiyar, *Indian J. Pure Appl. Phys.*, **7**, 10 (1969).
- (22) G. Lucazeau, A. Lautié, and A. Novak, *J. Raman Spectrosc.*, **3**, 161 (1975); A. Lautié, F. Froment, and A. Novak, *Spectrosc. Lett.*, **9**, 289 (1976).
- (23) A. M. Vuagnat and E. L. Wagner, *J. Chem. Phys.*, **26**, 77 (1957).
- (24) M. A. Boisvert, *Diss. Abstr. B*, **29**, 4123 (1969).
- (25) J. Toužin, *Collect. Czech. Chem. Commun.*, **38**, 2384 (1973).
- (26) R. Paetzold, K. Dostal, and A. Ruzicka, *Z. Anorg. Allg. Chem.*, **348**, 1 (1966).
- (27) K. R. K. Easwaran, *Indian J. Pure Appl. Phys.*, **4**, 324 (1966).
- (28) J. Royston and J. A. S. Smith, *J. Chem. Soc., Faraday Trans. 2*, **71**, 1497 (1975).
- (29) B. Pedersen, *Acta Chem. Scand.*, **22**, 1813 (1968).
- (30) N. M. Atherton and J. R. Morton, *Nature (London)*, **209**, 294 (1966).
- (31) J. R. Morton and D. R. Smith, *Can. J. Chem.*, **44**, 1951 (1966).
- (32) S. P. Mishra and M. C. R. Symons, *J. Chem. Res. (S)*, 48 (1977).
- (33) J. P. Michaut, J. Roncin, and K. Leibler, *Chem. Phys. Lett.*, **40**, 28 (1976).
- (34) L. Bonazzola, J. P. Michaut, and J. Roncin, *Can. J. Chem.*, **55**, 2570 (1977).
- (35) J. N. Herak and W. Gordy, *J. Am. Chem. Soc.*, **89**, 3818 (1967); J. N. Herak, *Croat. Chem. Acta*, **40**, 37 (1968).
- (36) M. K. Hargreaves, E. A. Stevinson, and J. Evans, *J. Chem. Soc.*, 4582 (1965).
- (37) A. D. Pethybridge, *J. Chem. Soc. A*, 1345 (1969).
- (38) C. B. Monk and M. F. Amira, *J. Chem. Soc., Faraday Trans. 1*, 1170 (1978).
- (39) A. J. Libbey, Jr., and J. T. Stock, *Anal. Chem.*, **42**, 526 (1970).
- (40) J. Courtot-Coupez and M. Le Démézet, *Bull. Soc. Chim. Fr.*, 1033 (1969).
- (41) B. Jakuszewski and J. Badecka-Jedrzejewska, *Rocz. Chem.*, **42**, 1095 (1968); *Chem. Abstr.*, **69**, 97119 (1968).
- (42) S. Kojima, H. Ichibagase, and S. Iguchi, *Chem. Pharm. Bull.*, **14**, 965 (1966).
- (43) J. M. Talmage, L. Chafetz, and M. Elefant, *J. Pharm. Sci.*, **57**, 1073 (1968).
- (44) W. J. Spillane and J. B. Thomson, *J. Chem. Soc., Perkin Trans. 2*, 580 (1977).
- (45) P. K. Maarsen, R. Bregman, and H. Cerfontain, *Tetrahedron*, **30**, 1211 (1974).
- (46) E. Yu. Belyaev, L. I. Kotlyar, and L. M. Timokhina, *Reakts. Spisobn. Org. Soedin.*, **7**, 294 (1970); *Chem. Abstr.*, **73**, 130383 (1970).
- (47) W. J. Spillane and N. Regan, *J. Chem. Soc., Perkin Trans. 2*, 1180 (1977).
- (48) E. Yu. Belyaev and L. I. Kotlyar, *Zh. Org. Khim.*, **11**, 2089 (1975); *Chem. Abstr.*, **84**, 16622 (1976).
- (49) W. J. Spillane, N. Regan, and F. L. Scott, *J. Chem. Soc., Perkin Trans. 2*, 445 (1974).
- (50) R. McLaughlin, *J. Am. Chem. Soc.*, **89**, 4268 (1967); F. M. Menger and L. Mandell, *ibid.*, **89**, 4424 (1967); P. Olavi, I. Virtanen, and K. Heinämäki, *Suom. Kemistil. B*, **42**, 142 (1969); J. F. Whidby, D. E. Leyden, C. M. Himel, and R. T. Mayer, *J. Phys. Chem.*, **75**, 4058 (1971).
- (51) H. Cerfontain and B. W. Schnitzer, *Recl. Trav. Chim. Pays-Bas*, **91**, 199 (1972).
- (52) H. P. Hopkins, Jr., C.-H. Wu, and L. P. Hepler, *J. Phys. Chem.*, **69**, 2244 (1965).
- (53) J. L. Kurz and J. M. Farrar, *J. Am. Chem. Soc.*, **91**, 6057 (1969).
- (54) G. A. Nash, H. A. Skinner, T. A. Zordan, and L. G. Helper, *J. Chem. Eng. Data*, **13**, 271 (1968).
- (55) K. Sasaki and T. Yokotake, *Tokyo Kogyo Shikensho Hokoku*, **61**, 309 (1966); *Chem. Abstr.*, **66**, 14578 (1967).
- (56) S. Sampath and G. Aravamudan, *Indian J. Chem.*, **9**, 1282 (1971).
- (57) M. Bolte and M. Capestan, *Bull. Soc. Chim. Fr.*, 3981 (1966).
- (58) M. Bolte and M. Capestan, *Bull. Soc. Chim. Fr.*, 865 (1970).
- (59) M. Bolte and M. Capestan, *Bull. Soc. Chim. Fr.*, 868 (1970).
- (60) G. A. Neville, J. C. Ethier, N. F. H. Bright, and R. H. Lake, *J. Assoc. Off. Anal. Chem.*, **54**, 1200 (1971).
- (61) E. M. Turner and P. G. Sears, *J. Inorg. Nucl. Chem.*, **35**, 2087 (1973).
- (62) P. G. Sears, W. H. Fortune, and R. L. Blumenshine, *J. Chem. Eng. Data*, **11**, 406 (1966).
- (63) T. W. Holt and P. G. Sears, *Trans. Ky. Acad. Sci.*, **28**, 1 (1967); *Chem. Abstr.*, **71**, 38183 (1969).
- (64) D. N. Hendrickson, J. M. Hollander, and W. L. Jolly, *Inorg. Chem.*, **8**, 2642 (1969).
- (65) Yu. N. Moskvich, N. A. Sergeev, and G. I. Dotsenko, *Fiz. Tverd. Tela (Leningrad)*, **15**, 2854 (1972); *Chem. Abstr.*, **80**, 8762 (1974).
- (66) W. D. Halstead, *J. Appl. Chem. Biotechnol.*, **21**, 22 (1971).
- (67) Y. Ito, *Kogyo Kagaku Zasshi*, **72**, 1866 (1969); *Chem. Abstr.*, **72**, 16121 (1970).
- (68) Y. Ito, E. Masuda, and T. Kawakami, *Nippon Kagaku Kaishi*, 2100 (1973).
- (69) E. Kimmel and R. Gropsian, *Bul. Stiint. Teh. Inst. Politeh. Timisoara, Ser. Chim.*, **17**, 33 (1972); *Chem. Abstr.*, **79**, 140177 (1973).
- (70) H. H. Emmons and F. D. Froede, *Wiss. Z. Tech. Hochsch. Chem. "Carl Schorlemmer" Leuna-Merseburg*, **14**, 295, 313 (1972); *Chem. Abstr.*, **78**, 164885 (1973); **79**, 97575 (1973).
- (71) N. F. Fedotova and A. S. Fedotov, *Neftepromysl. Delo*, 40 (1977); *Chem. Abstr.*, **87**, 120112 (1977).
- (72) L. D'Souza and R. A. Day, *Science*, **160**, 882 (1968).
- (73) J. P. Candlin and R. G. Wilkins, *J. Chem. Soc.*, 4236 (1960).
- (74) M. N. Hughes and J. R. Lusty, *J. Chem. Soc., Dalton Trans.*, 509 (1977).
- (75) J. M. Notley, *J. Appl. Chem. Biotechnol.*, **23**, 717 (1973).
- (76) A. N. Tsybin and E. N. Fomenko, *Tr. Gos. Nauchno-Issled. Produktov Inst. Azotn. Prom-Stl. Prod. Organ. Sintez*, **27**, 21 (1974); *Chem. Abstr.*, **85**, 149577 (1976).
- (77) V. N. Plakhotnik and A. Kh. Drabkina, *Katal. Katal.*, **13**, 60 (1975).
- (78) V. N. Plakhotnik and A. Kh. Drabkina, *Kinet. Katal.*, **17**, 1177 (1976).
- (79) W. J. Spillane, F. L. Scott, and C. B. Goggin, *Int. J. Sulfur Chem. A*, **1**, 223 (1971).
- (80) J. D. Capps and M. D. Bentley, *J. Org. Chem.*, **33**, 1295 (1968).
- (81) W. J. Spillane, C. B. Goggin, N. Regan, and F. L. Scott, *Int. J. Sulfur Chem.*, **8**, 281 (1973).
- (82) F. L. Scott and W. J. Spillane, *Chem. Ind. (London)*, 1999 (1967).
- (83) E. Yu. Belyaev, L. I. Kotlyar, B. A. Porai-Koshits, and K. A. Serkova, *Reakts. Spisobn. Org. Soedin.*, **5**, 1033 (1968); *Chem. Abstr.*, **71**, 21361 (1969).
- (84) W. J. Spillane, C. B. Goggin, N. Regan, and F. L. Scott, *Int. J. Sulfur Chem.*, **8**, 565 (1976).
- (85) W. J. Spillane, N. Regan, and F. L. Scott, *J. Chem. Soc., Perkin Trans. 2*, 1424 (1976).
- (86) K. Nakano and H. Yamaguchi, *Kogyo Kagaku Zasshi*, **67**, 2055 (1964); *Chem. Abstr.*, **65**, 583b (1966).

- (87) V. P. Savel'yanov and A. S. Titarenko, *Izv. Vyssh. Uchebn. Zaved. Khim. Khim. Tekhnol.*, **19**, 1840 (1976); *Chem. Abstr.*, **86**, 139001 (1977).
- (88) A. S. Titarenko and V. P. Savel'yanov, *Zh. Prikl. Khim.*, **49**, 2693 (1976).
- (89) E. L. Vulakh, G. M. Pakhomova, and S. M. Loktev, *Kinet. Katal.*, **9**, 751 (1968).
- (90) A. S. Titarenko, V. P. Savel'yanov, and L. K. Fiseiskaya, *Tr. Mosk. Khim.-Tekhnol. Inst.*, **74**, 7 (1973); *Chem. Abstr.*, **82**, 30583 (1975).
- (91) B. Yamaguchi, *Yukagaku*, **18**, 188 (1969); *Chem. Abstr.*, **71**, 12237 (1969).
- (92) Yu. B. Kagan, L. I. Zvezdina, A. Ya. Rozovskii, G. M. Pakhomova, and A. N. Bashkurov, *Kinet. Katal.*, **15**, 368 (1974).
- (93) Yu. B. Kagan, A. N. Bashkurov, E. B. Kozlovskaya, L. I. Zvezdina, and A. Ya. Rozovskii, *Neftekhimiya*, **15**, 433 (1975).
- (94) Yu. B. Kagan, G. M. Pakhomova, N. A. Shimanko, A. Yu. Koshevnik, M. V. Shishkina, and R. G. Lokteva, *Kinet. Katal.*, **15**, 23 (1974).
- (95) W. J. Spillane and F. L. Scott, *J. Chem. Soc. B*, 779 (1968).
- (96) W. J. Spillane, F. L. Scott, and C. B. Coggin, *J. Chem. Soc. B*, 2409 (1971).
- (97) V. V. Kozlov, *Zh. Obshch. Khim.*, **27**, 1146 (1957).
- (98) Z. Vrba and Z. J. Allan, *Collect. Czech. Chem. Commun.*, **33**, 2502 (1968).
- (99) Z. Vrba and Z. J. Allan, *Tetrahedron Lett.*, 4507 (1968).
- (100) Z. Vrba and Z. J. Allan, Czechoslovak Patent 113 249 (1963); *Chem. Abstr.*, **63**, 13159a (1965).
- (101) Z. J. Allan and Z. Vrba, *Collect. Czech. Chem. Commun.*, **34**, 272 (1969).
- (102) H. J. Shine in "Aromatic Compounds", MTP Organic Chemistry Series, Vol. 3, H. Zollinger, Ed., Butterworths, London, 1973, Chapter 3.
- (103) Reference 2, p 78.
- (104) P. K. Maarsen and H. Cerfontain, *J. Chem. Soc., Perkin Trans. 2*, 929 (1977).
- (105) P. K. Maarsen and H. Cerfontain, *J. Chem. Soc., Perkin Trans. 2*, 921 (1977).
- (106) P. K. Maarsen and H. Cerfontain, *J. Chem. Soc., Perkin Trans. 2*, 1003 (1977).
- (107) H. Yamaguchi, Japanese Patent 32145 (1975); *Chem. Abstr.*, **83**, 96737 (1975).
- (108) M. Saito, M. Dehara, and O. Manabe, *Nippon Kagaku Kaishi*, 380 (1972).
- (109) F. Kanetani and H. Yamaguchi, *Bull. Chem. Soc. Jpn.*, **51**, 3039 (1978).
- (110) A. S. Bender, F. C. Loew, and P. Resnick, U.S. Patent 3 390 167 (1968); *Chem. Abstr.*, **69**, 86369 (1968).
- (111) P. K. Maarsen and H. Cerfontain, *J. Chem. Soc., Perkin Trans. 2*, 1008 (1977).
- (112) Z. Vrba and Z. J. Allan, *Collect. Czech. Chem. Commun.*, **33**, 431 (1968).
- (113) Z. Vrba and Z. J. Allan, *Collect. Czech. Chem. Commun.*, **33**, 4426 (1968).
- (114) I. Kojima, T. Watanabe, and T. Eguchi, Japanese Patent 10045 (1971); *Chem. Abstr.*, **75**, 23320 (1971).
- (115) E. Kimmel, R. Gropsian, and A. Cotosman, *Bul. Stiint. Teh. Inst. Politeh. Timisoara*, **11**, 447 (1966); *Chem. Abstr.*, **68**, 56012 (1968).
- (116) (a) S. Takahashi, S. Kusakabe, K. Shimawaki, and S. Sasaki, Japanese Patent 07648 (1970); *Chem. Abstr.*, **73**, 5508 (1970); (b) Y. Ito, *Kogyo Kagaku Zasshi*, **71**, 357 (1968); *Chem. Abstr.*, **69**, 80892 (1968).
- (117) A. Madej and A. Rokosz, *Chem. Anal. (Warsaw)*, **21**, 271 (1976).
- (118) H. Z. Hofmeister, German Patent 1 915 723; *Chem. Abstr.*, **74**, 5147 (1971).
- (119) M. Miki, K. Katsu, K. Ihara, T. Matsumoto, M. Matsuda, and H. Arimoto, Japanese Patent 05 439 (1973); *Chem. Abstr.*, **80**, 5381 (1974).
- (120) Y. Ito, Japanese Patent 05 440 (1973); *Chem. Abstr.*, **80**, 17026 (1974).
- (121) K. Naito, M. Yoshida, M. Shieh, and T. Okabe, *Bull. Chem. Soc. Jpn.*, **43**, 1365 (1970).
- (122) L. F. Nikitina and V. N. Stepanova, *Khim. Prom.*, **44**, 353 (1968); *Chem. Abstr.*, **69**, 28919 (1968).
- (123) I. Hirotsu, M. Nishiuchi, K. Ohuchi, and R. Kodama, Japanese Patent 129 523 (1975); *Chem. Abstr.*, **84**, 43377 (1976); I. Hirotsu, M. Nishiuchi, and K. Ohuchi, Japanese Patent 129 522 (1975); *Chem. Abstr.*, **84**, 43379 (1976).
- (124) K. Tanihara and M. Nakagawa, Japanese Patent 99 121 (1973); *Chem. Abstr.*, **80**, 95310 (1974).
- (125) G. A. Benson and W. J. Spillane, *J. Med. Chem.*, **19**, 869 (1976).
- (126) F. Pautet and C. Nofre, *Pharm. Acta Helv.*, **53**, 231 (1978).
- (127) F. Pautet and C. Nofre, *Z. Lebensm.-Unters.-Forsch.*, **166**, 167 (1978).
- (128) L. F. Audrieth and M. Sveda, *J. Org. Chem.*, **9**, 89 (1944).
- (129) B. Unterhalt and L. Böschmeyer, *Z. Lebensm.-Unters.-Forsch.*, **145**, 93 (1971).
- (130) B. Unterhalt and L. Böschmeyer, *Z. Lebensm.-Unters.-Forsch.*, **149**, 227 (1972).
- (131) B. Unterhalt and L. Böschmeyer, *Z. Lebensm.-Unters.-Forsch.*, **158**, 35 (1975).
- (132) C. Nofre and F. Pautet, *Bull. Soc. Chim. Fr.*, 686 (1975).
- (133) C. Nofre and F. Pautet, *Naturwissenschaften*, **62**, 97 (1975).
- (134) H. Yamaguchi and K. Nakano, Japanese Patent 14 972 (1972); *Chem. Abstr.*, **77**, 61364 (1972).
- (135) A. Calder and J. Whetstone, British Patent 1 395 497 (1975); *Chem. Abstr.*, **83**, 96567 (1975).
- (136) H. Yamaguchi and K. Nakano, Japanese Patent 3452 (1966); *Chem. Abstr.*, **64**, 19413e (1966).
- (137) H. Yamaguchi and K. Nakano, Japanese Patent 18 295 (1965); *Chem. Abstr.*, **63**, 17976c (1965).
- (138) C. F. Cardy, C. A. Crampton, and D. G. Bowen, British Patent 1 109 503 (1968); *Chem. Abstr.*, **69**, 26861 (1968).
- (139) C. F. Cardy, C. A. Crampton, D. G. Bowen, and A. Poole, British Patent 1 109 664 (1968); *Chem. Abstr.*, **69**, 86371 (1968).
- (140) H. Merkle and A. Mueller, German Patent 2 628 195 (1977); *Chem. Abstr.*, **88**, 50283 (1978).
- (141) J. Zimer and K. G. Kleb, British Patent 1 185 439 (1970); *Chem. Abstr.*, **73**, 25012 (1970).
- (142) R. Fischer, German Patent 2 424 371 (1975); *Chem. Abstr.*, **84**, 73649 (1976).
- (143) H. Yamaguchi, Japanese Patent 17 319 (1963); *Chem. Abstr.*, **60**, 4010g (1964).
- (144) G. Hamprecht, D. Mangold, and K. H. König, German Patent 2 164 197 (1973); *Chem. Abstr.*, **79**, 78098 (1973).
- (145) H. Yamaguchi, Japanese Patent 17 318 (1963); *Chem. Abstr.*, **60**, 4010g (1964).
- (146) H. Yamaguchi, Japanese Patent 8815 (1964); *Chem. Abstr.*, **61**, 11892 (1964).
- (147) Commercial Solvents Corp., British Patent 1 144 968 (1969); *Chem. Abstr.*, **70**, 114706 (1969).
- (148) D. G. Bowen, C. F. Cardy, D. A. Hutton, and P. J. Webster, British Patent 1 030 376 (1966); *Chem. Abstr.*, **65**, 5366g (1966).
- (149) E. Dönges, R. Kohlhaas, and D. Wick, German Patent 1 249 262 (1968); *Chem. Abstr.*, **68**, 12549 (1968).
- (150) D. Wick, E. Heubach, and R. Kohlhaas, German Patent 1 268 141 (1968); *Chem. Abstr.*, **69**, 51694 (1968).
- (151) H. Yamaguchi, Japanese Patent 17 317 (1963); *Chem. Abstr.*, **60**, 4010g (1964).
- (152) H. Yamaguchi and K. Nakano, Japanese Patent 19 963 (1960); *Chem. Abstr.*, **60**, 2801b (1964).
- (153) H. Yamaguchi, Japanese Patent 17 316 (1963); *Chem. Abstr.*, **60**, 4010g (1964).
- (154) H. Yamaguchi, Japanese Patent 17 912 (1964); *Chem. Abstr.*, **62**, 5230 (1965).
- (155) A. E. Sowerby and M. Hewitt, British Patent 1 290 850 (1972); *Chem. Abstr.*, **78**, 15644 (1973).
- (156) R. C. Anderson, F. F. Guicciardi, and J. Jack, British Patent 1 110 846 (1968); *Chem. Abstr.*, **69**, 66980 (1968).
- (157) H. Yamaguchi, Japanese Patent 13 056 (1963); *Chem. Abstr.*, **60**, 2771a (1964).
- (158) J. M. Caldero, C. Ciuro, J. M. Pulmarti-Codina, L. Feliu, and A. Jurado, *Afinidad*, **26**, 99 (1969).
- (159) H. Yamaguchi and K. Nakano, Japanese Patent 2455 (1964); *Chem. Abstr.*, **60**, 14406a (1964).
- (160) T. Lesiak, E. Heleski, and E. Dziemianko, *Rocz. Chem.*, **48**, 1837 (1974).
- (161) B. Gluck, French Patent 1 536 593 (1968); *Chem. Abstr.*, **71**, 126324 (1969).
- (162) D. M. Marquis, U.S. Patent 3 342 856 (1967); *Chem. Abstr.*, **68**, 21675 (1968).
- (163) R. W. Hill, U.S. Patent 3 580 944 (1972); *Chem. Abstr.*, **75**, 64878 (1971).
- (164) T. Harada and K. Arai, Japanese Patent 35 792 (1970); *Chem. Abstr.*, **74**, 64688 (1971).
- (165) M. Avramoff and W. Taub, *Eur. J. Med. Chem.-Chim. Ther.*, **13**, 81 (1978).
- (166) J. Becher, N. Hauns, and T. Pedersen, *Acta Chem. Scand., Ser. B*, **29**, 124 (1975).
- (167) R. W. Self, J. C. Watkins, Jr., and J. K. Sullins, U.S. Patent 3 328 294 (1966); *Chem. Abstr.*, **67**, 76192 (1967).
- (168) W. Traube and E. Von Drathen, *Chem. Ber.*, **51**, 111 (1918).
- (169) E. I. du Pont de Nemours, French Patent 2 087 248 (1972); *Chem. Abstr.*, **77**, 103666 (1972).
- (170) W. C. Golton and A. F. Rutkiewicz, U.S. Patent 3 749 672 (1973); *Chem. Abstr.*, **79**, 93755 (1973).
- (171) A. F. Rutkiewicz, U.S. Patent 3 767 586 (1973); *Chem. Abstr.*, **80**, 49917 (1974).
- (172) J. N. Keith, R. J. Douthart, W. K. Sumida, and I. J. Solomon, *Adv. Chem. Ser.*, **No. 54**, 141 (1965).
- (173) G. R. Wendt and M. W. Winkley, U.S. Patent 3 787 442 (1974); *Chem. Abstr.*, **80**, 82669 (1974).
- (174) B. Unterhalt and L. Böschmeyer, *Naturwissenschaften*, **59**, 271 (1972).
- (175) B. Unterhalt and L. Böschmeyer, *Z. Lebensm.-Unters.-Forsch.*, **161**, 275 (1976).
- (176) W. S. Mungall, L. J. Lemmen, K. L. Lemmen, J. K. Dethmers, and L. L. Norling, *J. Med. Chem.*, **21**, 704 (1978).
- (177) J. T. Edward and J. Whiting, *Can. J. Chem.*, **49**, 3502 (1971).
- (178) S. Kageyama and H. Inoue, Japanese Patent 02 595 (1970); *Chem. Abstr.*, **72**, 90697 (1972).
- (179) Z. Wirpsza, *Polimery*, **14**, 152 (1969).
- (180) V. Falzoni, Canadian Patent 988 514 (1976); *Chem. Abstr.*, **85**, 44918 (1976).
- (181) P. H. Jones, E. K. Rowley, A. L. Weiss, D. L. Bishop, and A. H. C. Chun, *J. Pharm. Sci.*, **58**, 337 (1969).
- (182) A. Yarinsky and H. Freele, *J. Trop. Med. Hyg.*, **73**, 23 (1970).
- (183) K. G. Mizuch, N. N. Vlasova, E. N. Anishchuk, L. V. Vasil'eva, and E. L. Shcherbukhina, U.S.S.R. Patent 469 685 (1975); *Chem. Abstr.*, **83**, 62425 (1975).
- (184) W. Yamaya and S. Fujino, U.S. Patent 3 538 105 (1970); *Chem. Abstr.*, **77**, 36407 (1972).
- (185) W. Yamatani and S. Fujino, French Patent 1 470 451 (1967); *Chem. Abstr.*, **67**, 91684 (1967).
- (186) L. R. Overby, French Patent M1585 (1962); *Chem. Abstr.*, **64**, 15767f (1966).

- (187) S. A. Andreu, Spanish Patent 423600 (1976); *Chem. Abstr.*, **86**, 161291 (1977).
- (188) Sandoz Ltd., Swiss Patent 570 375 (1975); *Chem. Abstr.*, **84**, 105388 (1976).
- (189) S. A. Andreu Laboratories, German Patent 2 455 051 (1975); *Chem. Abstr.*, **83**, 96697 (1975).
- (190) A. H. Pujol and S. B. Rabassa, German Patent 2 457 571 (1975); *Chem. Abstr.*, **84**, 16929 (1976).
- (191) W. J. Shibe, Jr., and M. Sittenfield, U.S. Patent 3 344 018 (1967); *Chem. Abstr.*, **68**, 68669 (1968).
- (192) (a) J. M. Puigmarti, J. M. Sala, L. Feliu, M. Izquierdo, and A. Jurado, *Chim. Ther.*, **2**, 268 (1967); (b) Laboratories Hosbon, Spanish Patent 395 559 (1974); *Chem. Abstr.*, **83**, 78964 (1975).
- (193) A. Jurado and J. M. Puigmarti, U.S. Patent 3 536 759 (1970); *Chem. Abstr.*, **77**, 39216 (1972).
- (194) A. Jurado and J. M. Puigmarti, U.S. Patent 3 658 989 (1972); *Chem. Abstr.*, **77**, 130628 (1972).
- (195) Laboratories Hosbon, French Patent 2 138 498 (1973); *Chem. Abstr.*, **79**, 83485 (1973).
- (196) Laboratories Hosbon, Spanish Patent 395 566 (1973); *Chem. Abstr.*, **80**, 133423 (1974).
- (197) G. D. Searle & Co., British Patent 1 253 317 (1971); *Chem. Abstr.*, **76**, 25307 (1972).
- (198) B. J. Magerlein, U.S. Patent 3 304 229 (1967); *Chem. Abstr.*, **66**, 108253 (1967).
- (199) Reference 2, Chapter 6, p. 33.
- (200) E. L. Vulakh and S. M. Loktev, U.S.S.R. Patent 227 473 (1968); *Chem. Abstr.*, **71**, 12538 (1969).
- (201) I. S. Sukhoterlin, I. Kondrat'eva, I. K. Getmanskil, and D. M. Bolyanovskii, U.S.S.R. Patent 243 127 (1969); *Chem. Abstr.*, **71**, 90805 (1969).
- (202) V. P. Savel'yanov, L. G. Ezhova, and A. S. Titarenko, *Maslo-Zhir. Prom.*, **20** (1973); *Chem. Abstr.*, **78**, 149193 (1973).
- (203) A. S. Titarenko and V. P. Savel'yanov, *Zh. Prikl. Khim. (Leningrad)*, **49**, 2693 (1976).
- (204) H. Yamaguchi and K. Yamane, *Hiroshima Daigaku Kogakubu Kenkyu Hokoku*, **16**, 277 (1968).
- (205) A. S. Titarenko and V. P. Savel'yanov, *Zh. Anal. Khim.*, **32**, 137 (1977).
- (206) S. M. Loktev and E. L. Vulakh, *Abh. Deut. Akad. Wiss. Berlin, Kl. Chem., Geol. Biol.*, **107** (1966).
- (207) E. L. Bulakh, S. M. Loktev, and T. F. Chestnova, *Zh. Vses. Khim. Ova.*, **14**, 591 (1969).
- (208) S. M. Loktev, G. M. Pakhomova, T. F. Chestnova, E. L. Vulakh, and A. M. Loktev, *Neftepererab. Neftekhim. (Moscow)*, **32** (1970).
- (209) S. M. Loktev, E. L. Vulakh, G. G. Repetskii, I. Ya. Azbel, and A. M. Loktev, *Khim. Prom. (Moscow)*, **45**, 730 (1969).
- (210) E. L. Vulakh, S. M. Loktev, and T. F. Chestnova, *Zh. Vses. Khim. Ova.*, **14**, 469 (1969).
- (211) T. P. Burmistrova, A. A. Khitrik, N. N. Terpilovskii, A. G. Petrov, G. A. Tolstikov, U. M. Dzhemilev, A. Kh. Sharipov, and R. M. Masagutov, U.S.S.R. Patent 524 799 (1976); *Chem. Abstr.*, **85**, 159457 (1976).
- (212) R. Grimmer and G. Moser, German (East) Patent 51 853 (1966); *Chem. Abstr.*, **66**, 65097 (1967).
- (213) H. Yamaguchi, *Asahi Garasu Kogyo Gijutsu Shorei-kai Kenkyu Hokoku*, **14**, 207 (1968).
- (214) H. Pasternak and E. Szmidtgal, *Iluszcze, Srodki Piorace, Kosmet.*, **11**, 158 (1967).
- (215) H. Yamaguchi and T. Oomori, *Hiroshima Daigaku Kogakubu Kenkyu Hokoku*, **16**, 283 (1968).
- (216) T. M. Makhmudov and N. A. Khodzhaev, *Zh. Prikl. Khim. (Leningrad)*, **44**, 2756 (1971).
- (217) G. M. Pakhomova, S. M. Loktev, E. A. Rezvova, and Yu. B. Kagan, *Zh. Vses. Khim. Ova.*, **17**, 477 (1972).
- (218) I. S. Sukhoterlin, I. B. Kondrat'eva, and G. A. Pankrat'eva, U.S.S.R. Patent 405 875 (1973); *Chem. Abstr.*, **80**, 70355 (1974).
- (219) S. M. Loktev, G. M. Pakhomova, T. F. Chestnova, E. A. Rezvova, A. M. Loktev, and Yu. B. Kagan, *Neftepererab. Neftekhim. (Moscow)*, **42** (1972).
- (220) (a) J. M. Walts and L. M. Schenk, U.S. Patent 3 395 170 (1968); *Chem. Abstr.*, **69**, 86351 (1968); (b) R. Steckler, U.S. Patent 3 839 393 (1974); *Chem. Abstr.*, **82**, 44003 (1975).
- (221) J. P. Joseph, J. P. Dusza, and S. Bernstein, *Steroids*, **7**, 577 (1966).
- (222) M. Tozawa, *Tokyo Joshi Ika Daigaku Zasshi*, **83**, 104 (1968).
- (223) M. Higaki, M. Takahashi, T. Suzuki, and Y. Sahashi, *J. Vitaminol.*, **11**, 261 (1965).
- (224) K. Nagasawa and H. Yoshidome, *Chem. Pharm. Bull.*, **18**, 2023 (1970).
- (225) K. O. Vollmer and M. Herrmann, German Patent 2 238 260 (1974); *Chem. Abstr.*, **80**, 133006 (1974).
- (226) H. Remy, U.S. Patent 3 372 170 (1968); *Chem. Abstr.*, **69**, 44568 (1968).
- (227) E. L. Morehouse, U.S. Patent 3 997 580 (1976); *Chem. Abstr.*, **86**, 74894 (1977).
- (228) Reference 2, Chapter 6.
- (229) Reference 2, Chapter 7.
- (230) Reference 2, p. 20.
- (231) F. L. Scott, J. A. Barry, and W. J. Spillane, *J. Chem. Soc., Perkin Trans. 1*, 2663 (1972).
- (232) V. A. Koptuyg, "Isomerization of Aromatic Compounds", N. N. Vorozhtsov, Jr., Ed., Oldbourne Press, London, 1965.
- (233) K. Nakagami, K. Matsuura, and T. Jyotaki, Japanese Patent 32 828 (1973); *Chem. Abstr.*, **79**, 136805 (1973).
- (234) K. Nakagami, K. Matsuura, and T. Uetaki, Japanese Patent 05 690 (1975); *Chem. Abstr.*, **83**, 58113 (1975).
- (235) O. Tubertini, M. G. Bettoli, and G. Bertocchi, *Ann. Chim. (Rome)*, **57**, 555 (1967).
- (236) I. I. Kalinichenko and K. A. Kotyaeva, *Tr. Ural. Politekh. Inst.*, **84** (1970).
- (237) K. A. Kotyaeva and I. I. Kalinichenko, *Zh. Neorg. Khim.*, **19**, 2112 (1974).
- (238) M. N. Hughes, J. R. Lusty, and T. J. Barton, *J. Chem. Soc., Dalton Trans.*, 1478 (1975).
- (239) R. S. Iyer, J. C. Laul, M. V. Ramaniah, C. L. Rao, and N. Srinivasan, *Proc. 3rd Nucl. Radiat. Chem. Symp.*, 359 (1967).
- (240) N. E. Bibler, *Nucl. Technol.*, **34**, 412 (1977).
- (241) M. N. Nadkarni, V. V. S. Mani, A. Ramanujam, G. Lal, and R. T. Kulkarni, *Proc. 3rd Nucl. Radiat. Chem. Symp.*, 351 (1967).
- (242) A. Fischer, U.S. Patent 3 321 273 (1967); *Chem. Abstr.*, **67**, 45673 (1967).
- (243) J. N. Armor and H. Taube, *Inorg. Chem.*, **10**, 1570 (1971).
- (244) W. P. Griffith and D. Pawson, *J. Chem. Soc., Dalton Trans.*, 524 (1973).
- (245) G. L. Coccia, *Proc. Symp. Sulfamic Acid (Milan)*, 29 (1966).
- (246) L. L. Po and R. B. Jordan, *Inorg. Chem.*, **7**, 526 (1968).
- (247) E. Sushynski, A. Van Roodseelaar, and R. B. Jordan, *Inorg. Chem.*, **11**, 1887 (1972).
- (248) T. R. Weaver and F. Basolo, *Inorg. Chem.*, **13**, 1535 (1974).
- (249) V. E. Apostolov and V. N. Veremil, U.S.S.R. Patent 452 543 (1974); *Chem. Abstr.*, **82**, 158311 (1975).
- (250) S. I. Berezina, R. M. Sageeva, L. A. Abdakhmanova, and I. Kh. Muzeev, *Elektrokhimiya*, **13**, 1900 (1977).
- (251) Yu. N. Kukushkin and O. V. Stefanova, *Zh. Neorg. Khim.*, **22**, 851 (1977).
- (252) A. Lautie and L. Lecuir, *Spectrochim. Acta, Part A*, **32**, 1323 (1976).
- (253) D. Anselmi, G. Farnia and E. Vianello, *Electrochim. Met.*, **3**, 391 (1968).
- (254) G. G. Nifant'eva, A. V. Fedorova, A. M. Robov, and V. A. Fedorov, *Koord. Khim.*, **4**, 372 (1978).
- (255) B. Walther, R. Mahrwald, C. Jahn, and W. Klar, *Z. Anorg. Allg. Chem.*, **423**, 144 (1976).
- (256) J. D. Cassidy and M. Moser, *Proc. Symp. Sulfamic Acid (Milan)*, 47 (1966).
- (257) J. D. Cassidy, W. Moser, J. D. Donaldson, A. Jelen, and D. G. Nicholson, *J. Chem. Soc. A*, 173 (1970).
- (258) K. Nishimoto, G. Fuse, and M. Nakanishi, German Patent 1 214 684 (1966); *Chem. Abstr.*, **65**, 3908g (1966).
- (259) M. Nakanishi and A. Tsuda, Japanese Patent 24 100 (1969); *Chem. Abstr.*, **71**, 128715 (1969).
- (260) S. J. Blunden, A. H. Chapman, A. J. Crowe, and P. J. Smith, *Int. Pest Control*, **20**, 5 (1978).
- (261) M. Nakanishi and A. Tsuda, Japanese Patent 17 141 (1966); *Chem. Abstr.*, **66**, 11049 (1967).
- (262) M. Nakanishi and A. Tsuda, Japanese Patent 30 180 (1971); *Chem. Abstr.*, **75**, 151908 (1971).
- (263) M. Nakanishi and A. Tsuda, Japanese Patent 1977 (1967); *Chem. Abstr.*, **66**, 115803 (1967).
- (264) M. I. Zimmerman and E. Giesbrecht, *An. Acad. Bras. Cienc.*, **45**, 99 (1973).
- (265) W. O. Baker, French Patent 1 539 787 (1968); *Chem. Abstr.*, **71**, 84469 (1969).
- (266) M. Capestan, *Ann. Chim.*, **5**, 222 (1960).
- (267) J. M. Cleveland, *Inorg. Chem.*, **7**, 874 (1968).
- (268) E. Bishop, *Analyst*, **92**, 587 (1967).
- (269) E. Bishop, *Pure Appl. Chem.*, **18**, 443 (1969).
- (270) E. Bishop and M. Riley, *Analyst*, **98**, 426 (1973).
- (271) L. Przyborowski, *Ann. Univ. Mariae Curie-Sklodowska, Sect. D*, **30**, 1 (1975).
- (272) (a) D. Biggs and D. L. H. Williams, *J. Chem. Soc., Perkin Trans. 2*, 107 (1975); (b) D. Biggs and D. L. H. Williams, *ibid.*, 601 (1976).
- (273) D. L. H. Williams, *J. Chem. Soc., Perkin Trans. 2*, 128 (1977).
- (274) M. H. Hashmi, S. P. Hamdani, and M. Sarwar, *Pak. J. Sci. Ind. Res.*, **17**, 206 (1975).
- (275) S. Oka, Japanese Patent 88 442 (1976); *Chem. Abstr.*, **85**, 171281 (1976).
- (276) G. Knittel, D. Ertel, and P. Dressler, *Chem. Abstr.*, **86**, 23234 (1977).
- (277) T. V. Slyusarskaya, E. V. Chumak, and A. D. Gol'tman, *Ukr. Khim. Zh. (Ukr. Ed.)*, **42**, 1084 (1976).
- (278) K. Takahashi, S. Fuse, and J. Mogi, *Ishikawajima-Harima Gihō*, **16**, 246 (1976).
- (279) S. S. M. Hassan, *Anal. Chim. Acta*, **53**, 449 (1971).
- (280) A. Nobuharu, *Bunseki Kagaku*, **15**, 976 (1966).
- (281) B. Dimitriades, *Health Lab. Sci.*, **12**, 271 (1975).
- (282) J. I. Peterson and D. S. Young, *Clin. Chem.*, **17**, 954 (1971).
- (283) F. Feigl, D. Goldstein, and E. Libergott, *Isr. J. Chem.*, **6**, 813 (1968).
- (284) Y. Ito, *Nippon Kagaku Kaishi*, 329 (1972).
- (285) K. A. Kotyaeva, I. I. Kalinichenko, and V. I. Ovcharenko, *Tr. Ural. Politekh. Inst.*, 102 (1967).
- (286) A. K. Zhdanov and S. Jatrudakis, *Tr. Tashk. Gos. Univ.*, 167 (1968).
- (287) Y. Takayoshi and H. Ikuko, *Bunseki Kagaku*, **16**, 927 (1967).
- (288) T. A. Lazareva, *Nov. Obl. Prom.-Sanit. Khim.*, 85 (1969).
- (289) W. C. Butts, *Anal. Lett.*, **3**, 29 (1970).
- (290) M. L. Richardson, *Talanta*, **14**, 385 (1967).
- (291) A. J. Shenton and R. M. Johnson, *Tetrahedron*, **27**, 1461 (1971).
- (292) A. J. Shenton and R. M. Johnson, *Analyst*, **98**, 745 (1973).
- (293) A. J. Shenton and R. M. Johnson, *Analyst*, **98**, 749 (1973).
- (294) W. Groebel and A. Wessels, *Dtsch. Lebensm.-Rundsch.*, **68**, 393 (1972).
- (295) M. Takeuchi, H. Kashiwagi, K. Washizuka, and T. Matsui, *Eisei Kagaku*, **18**, 324 (1972).
- (296) D. E. Johnson, H. B. Nunn, and S. Bruckenstein, *Anal. Chem.*, **40**, 368 (1968).

- (297) G. A. Benson and W. J. Spillane, *J. Pharm. Sci.*, **65**, 1841 (1976).
(298) G. A. Benson and W. J. Spillane, *Anal. Chem.*, **48**, 2149 (1976).
(299) W. J. Spillane and G. A. Benson, *J. Pharm. Sci.*, **67**, 226 (1978).
(300) (a) C. T. Berry and R. J. Crossland, *Analyst*, **95**, 291 (1970); (b) K. Maruyama, K. Kawanabe, A. Fujioka, and S. Iijima, *Yakugaku Zasshi*, **91**, 579 (1971).
(301) D. Hoo and C. Hu, *Anal. Chem.*, **44**, 2111 (1972).
(302) K. Shimada, U. Matsumoto, T. Hiraga, Y. Shibusawa, and Y. Nagase, *Yakugaku Zasshi*, **97**, 849 (1977).
(303) (a) A. G. Renwick and R. T. Williams, *Biochem. J.*, **129**, 869 (1972); (b) B. S. Drasar, A. G. Renwick, and R. T. Williams, *Biochem. J.*, **129**, 881 (1972).
(304) B. Mueller and J. Ludwig, *Mitteilungsbl. GDCh-Fachgruppe Lebensmittelchem. Gerichth. Chem.*, **26**, 3 (1972).
(305) H. Thielemann, *Sci. Pharm.*, **42**, 93 (1974).
(306) M. I. La Rotonda and L. Ferrara, *Boll. Soc. Ital. Biol. Sper.*, **51**, 690 (1975).
(307) K. Lemieszek-Chodorowska, *Rocz. Pantstw. Zakl. Hig.*, **29**, 271 (1978).
(308) V. A. Belyaev and V. L. Rudkovskii, German Patent 2 602 327 (1977); *Chem. Abstr.*, **87**, 185829 (1977).
(309) J. Mayer, J. Lenz, and M. Henkel, German Patent 1 908 094 (1970); *Chem. Abstr.*, **73**, 99596 (1970).
(310) H. A. Wright, French Patent 1 525 761 (1968); *Chem. Abstr.*, **71**, 13979 (1969).
(311) K. Kawai, K. Shigematsu, and S. Maeda, Japanese Patent 16 216 (1969); *Chem. Abstr.*, **72**, 22305 (1970).
(312) K. Iwasaki, K. Yamaguchi, J. Inomata, Y. Otsuka, and K. Kasahara, Japanese Patent 13 584 (1970); *Chem. Abstr.*, **73**, 77829 (1970).
(313) R. Sh. Derevyanko, L. V. Sorokina, B. Ya. Eryshev, and V. M. Brusentseva, *Khim. Tekhnol. (Kiev)*, **24** (1975).
(314) K. Yasuhiko, *Kogyo Kagaku Zasshi*, **69**, 561 (1966); *Chem. Abstr.*, **65**, 15519c (1966).
(315) O. Yagyu and H. Fukuzaki, Japanese Patent 39 388 (1978); *Chem. Abstr.*, **89**, 130175 (1978).
(316) N. I. Grishko, V. V. Mashkova, T. B. Muraviyanskaya, R. P. Komarova, G. V. Fedotova, Yu. B. Kagan, S. M. Loktev, A. I. Kutepova, T. A. Abakumova, and N. M. Suvorova, U.S.S.R. Patent 215 933 (1968); *Chem. Abstr.*, **69**, 66917 (1968).
(317) B. O. Lindgren and H. T. Nilsson, Swedish Patent 353 899 (1973); *Chem. Abstr.*, **80**, 47659 (1974).
(318) H. J. Quadbeck-Seeger and P. Tonne, German Patent 2 328 757 (1975); *Chem. Abstr.*, **82**, 125055 (1975).
(319) S. Komoto and R. Hasegawa, Japanese Patent 113534 (1975); *Chem. Abstr.*, **83**, 206020 (1975).
(320) S. Nakatani, Japanese Patent 09369 (1970); *Chem. Abstr.*, **73**, 14203 (1970).
(321) K. Tan, K. Takahashi, Y. Ishibashi, T. Matsuda, and Y. Takada, *Hokkaido Daigaku Kogakubu Kenkyu Hokoku*, **97** (1973).
(322) I. Yoshiharu, H. Akira, F. Kiyohisa, K. Yasuhiko, and S. Tetsuo, *Nippon Kagaku Zasshi*, **87**, 752 (1966).
(323) A. Takahashi and S. Takahashi, *Kobunshi Kagaku*, **26**, 485 (1969).
(324) J. T. Galambos and J. R. McCain, *Anal. Biochim.*, **19**, 119 (1967).
(325) S. Samukawa and T. Nakagawa, Japanese Patent 46140 (1974); *Chem. Abstr.*, **83**, 61276 (1975).
(326) C. Romagnani, *Proc. Symp. Sulfamic Acid (Milan)*, **43** (1966).
(327) R. Piontelli, *Proc. Symp. Sulfamic Acid (Milan)*, **429** (1966).
(328) (a) R. Piontelli, B. Mazza, and P. Pedferri, *Electrochim. Met.*, **2**, 141 (1967); (b) R. Piontelli, B. Mazza, and P. Pedferri, *Electrochim. Met.*, **3**, 42 (1968); (c) R. Piontelli, B. Mazza, and P. Pedferri, *Atti Accad. Naz. Lincei, Rend., Cl. Sci. Fis., Mat. Nat.*, **42**, 591 (1967).
(329) P. M. Strocchi, R. Peruzzi, A. Rozzoli, A. Sinigaglia, and B. Vincentini, *Corsi Semin. Chim.*, **123** (1968).
(330) (a) R. A. F. Hammond, *Metalloberflaechen-Angew. Electrochem.*, **26**, 130 (1972); (b) R. A. F. Hammond, *Metalloberflaechen-Angew. Electrochem.*, **26**, 291 (1972); (c) H. Grossmann, *Galvanotechnik*, **68**, 48 (1977).
(331) K. Sommer, German Patent 2 346 751 (1975); *Chem. Abstr.*, **83**, 30242 (1975).
(332) Reference 2, Chapter 1.
(333) J. E. Douglas, G. L. Kenyon, and P. A. Kollman, *Chem. Phys. Lett.*, **57**, 553 (1978).
(334) D. Voigt, P. Dagnac, and L. Fournes, *Ann. Genie Chim.*, **3**, 62 (1967).
(335) A. P. Mel'nik, B. V. Passet, A. A. Alovainikov, and G. M. Gaevoi, *Reakts. Sposobn. Org. Soedin.*, **10**, 665 (1973).
(336) F. Kanetani and H. Yamaguchi, *Yuki Gosei Kagaku Kyokai Shi*, **30**, 539 (1972).
(337) H. Yamaguchi and F. Kanetani, *Yuki Gosei Kagaku Kyokai Shi*, **31**, 79 (1973).
(338) (a) H. Yamaguchi, Japanese Patent 10 024 (1973); *Chem. Abstr.*, **79**, 4991 (1973); (b) H. Yamaguchi and T. Fujii, *Nippon Kagaku Kaishi*, **2157** (1973).
(339) K. Tanihara, *Chem. Lett.*, **147** (1974).
(340) V. Parshikov, B. V. Passet, and N. Kopeina, *Org. React. (USSR)*, **13**, 310 (1976).
(341) B. V. Passet and V. Parshikov, *Org. React. (USSR)*, **13**, 555 (1976).
(342) (a) D. Saiga, T. Yanagigawa, K. Kobayashi, M. Nagayama, M. Miyoshi, and T. Maeyama, Japanese Patent 89 786 (1974); *Chem. Abstr.*, **82**, 74704 (1975); (b) D. Saiga, T. Yanagawa, M. Mizuta, and I. Kadoya, Japanese Patent 16 393 (1976); *Chem. Abstr.*, **85**, 65099 (1976); (c) D. Saiga, T. Yanagawa, and Y. Kawada, Japanese Patent 148 782 (1976); *Chem. Abstr.*, **86**, 141924 (1977); (d) D. Saiga, T. Yanagawa, Y. Kawada, and K. Nakayama, Japanese Patent 13 586 (1977); *Chem. Abstr.*, **86**, 173353 (1977).
(343) M. Nezu, E. Hayashi, H. Sato, and M. Harakawa, Japanese Patent 25 010 (1977); *Chem. Abstr.*, **87**, 73386 (1977).
(344) K. Tserng and P. D. Klein, *J. Lipid Res.*, **18**, 491 (1977).
(345) M. Wang, K. Imai, and Z. Tamura, *Chem. Pharm. Bull.*, **20**, 187 (1972).
(346) K. B. Guiseley, *Am. Chem. Soc. Symp. Ser.*, **77**, 148 (1978).
(347) L. H. Kruger and O. B. Wurzburg, U.S. Patent 3 441 558 (1969); *Chem. Abstr.*, **71**, 14 394 (1969).
(348) M. Miwa, Japanese Patent 85 188 (1974); *Chem. Abstr.*, **82**, 73700 (1975).
(349) (a) E. J. Corey and K. Achiwa, *J. Org. Chem.*, **34**, 3667 (1969); (b) E. P. Serebryakov, N. S. Kobrina, and B. Foigt, *Izv. Akad. Nauk SSSR, Ser. Khim.*, **2644** (1974).
(350) T. Shimura, Japanese Patent 106 819 (1977); *Chem. Abstr.*, **88**, 75313 (1978).
(351) T. Shimura, T. Sekiguchi, and E. Manda, *Nippon Kagaku Kaishi*, **847** (1977).
(352) J. O. Morley, *J. Chem. Soc., Perkin Trans. 2*, **1554** (1976).
(353) (a) T. Shimura and E. Manda, *Nippon Kagaku Kaishi*, **1588** (1978); (b) T. Shimura and E. Manda, *ibid.*, **1532** (1978).
(354) V. M. Reznikov and V. S. Lisova, *Khim. Drev.*, **70** (1975).
(355) F. Kanetani and H. Yamaguchi, *Bull. Chem. Soc. Jpn.*, **47**, 2713 (1974).
(356) F. Kanetani and H. Yamaguchi, *Yuki Gosei Kagaku Kyokai Shi.*, **32**, 460 (1974).
(357) Y. Inoue and K. Nagasawa, *J. Org. Chem.*, **38**, 1810 (1973).
(358) B. E. Fleischfresser and I. Lauder, *Aust. J. Chem.*, **15**, 251 (1962).
(359) I. G. Ryss and L. P. Bogdanova, *Zh. Neorg. Khim.*, **7**, 1316 (1962).
(360) I. G. Ryss and L. P. Bogdanova, *Zh. Neorg. Khim.*, **8**, 24 (1963).
(361) I. G. Ryss and L. P. Bogdanova, *Kinet. Katal.*, **7**, 169 (1966).
(362) I. G. Ryss and L. P. Bogdanova, *Zh. Neorg. Khim.*, **10**, 172 (1965).
(363) J. Krueger and W. A. Johnson, *Inorg. Chem.*, **7**, 679 (1968).
(364) M. D. Bentley, S. E. Bowie, and R. D. Limoges, *J. Phys. Chem.*, **75**, 1763 (1971).
(365) M. J. Blandamer, J. Burgess, and S. H. Morris, *J. Chem. Soc., Dalton Trans.*, **2118** (1975).
(366) I. G. Ryss, L. P. Bogdanova, S. L. Idel's, and T. N. Kotlyar, *Zh. Neorg. Khim.*, **14**, 2991 (1969).
(367) I. G. Ryss, L. P. Bogdanova, S. L. Idel's, and T. N. Kotlyar, *Kinet. Katal.*, **11**, 1057 (1970).
(368) L. P. Bogdanova and T. N. Kotlyar, *Kinet. Katal.*, **14**, 245 (1973).
(369) I. G. Ryss and L. P. Bogdanova, *Zh. Neorg. Khim.*, **12**, 2091 (1967).
(370) I. G. Ryss and D. B. Donskaya, *Dokl. Akad. Nauk SSSR*, **133**, 882 (1960).
(371) I. G. Ryss and T. N. Kotlyar, *Kinet. Katal.*, **11**, 244 (1970).
(372) L. P. Bogdanova and T. N. Kotlyar, *Kinet. Katal.*, **16**, 812 (1975).
(373) T. Matsumoto, Y. Akuzu, Y. Ozaki, and Y. Ikejiri, Japanese Patent 140 496 (1977); *Chem. Abstr.*, **88**, 107503 (1978).
(374) S. Teller-Pollon and J. Heubel, *Rev. Chim. Miner.*, **4**, 413 (1967).
(375) D. Attwood and G. Stedman, *J. Chem. Soc., Dalton Trans.*, **508** (1976).
(376) (a) M. N. Hughes and J. R. Lusty, *Inorg. Nucl. Chem. Lett.*, **13**, 37 (1977); (b) M. N. Hughes, J. R. Lusty, and H. L. Wallis, *J. Chem. Soc., Dalton Trans.*, **530** (1978).
(377) L. S. Dzelzkalns and F. T. Bonner, *Inorg. Chem.*, **17**, 3710 (1978).
(378) M. N. Hughes, *J. Chem. Soc. A*, **902** (1967).
(379) P. Biddle and J. H. Miles, *J. Inorg. Nucl. Chem.*, **30**, 1291 (1968).
(380) A. Kinawi and H. Kia, *J. Clin. Chem. Clin. Biochem.*, **16**, 365 (1978).
(381) Yu. N. Kukushkin and O. V. Stefanova, *Zh. Neorg. Khim.*, **22**, 3375 (1977).
(382) R. A. Wiesboeck and J. K. Ruff, *Tetrahedron*, **26**, 837 (1970).
(383) R. Appel and M. Montenarh, *Chem. Ber.*, **108**, 2340 (1975).
(384) B. E. Cooper and S. Westall, *J. Organomet. Chem.*, **118**, 135 (1976).
(385) V. L. Plakidin, S. Pokhila, L. N. Sidorenko, V. I. Zaitons, K. I. Shchedrovich, and V. B. Pisov, U.S.S.R. Patent 449 040 (1974); *Chem. Abstr.*, **82**, 155874 (1975).
(386) V. T. Lazareva and R. D. Erlikh, *Zh. Vses. Khim. Ova.*, **12**, 356 (1967).
(387) V. B. Piskov, V. P. Kasperovich, and M. I. Chernyakhovskaya, *Zh. Prikl. Khim. (Leningrad)*, **46**, 220 (1973).
(388) N. S. Kozlov, V. V. Andreyanov, and A. G. Klein, *Uch. Zap.-Yarosl. Gos. Pedagog. Inst.*, **161**, 61 (1976).
(389) A. D. Argoudelis, S. A. Mizsak, and P. A. Meulman, *J. Antibiot.*, **27**, 564 (1974).
(390) A. H. Berrie and N. Hughes, German Patent 1 932 810 (1970); *Chem. Abstr.*, **73**, 4931 (1970).
(391) Ch. N. Barnakov, L. L. Chipulis, L. A. Bukareva, I. L. Bagal, and B. A. Porai-Koshits, *Zh. Org. Khim.*, **8**, 110 (1972).
(392) A. R. Butler and C. Glidewell, *J. Chem. Res. (S)*, **239** (1978).
(393) S. Yamaguchi, *Nippon Kagaku Zasshi*, **89**, 1099 (1968).
(394) K. Nagasawa and H. Yoshidome, *Chem. Pharm. Bull.*, **17**, 1316 (1969).
(395) W. B. Hardy and F. H. Adams, U.S. Patent 2 863 866 (1958); *Chem. Abstr.*, **53**, 7988e (1959).
(396) R. J. Shozda and J. A. Vernon, *J. Org. Chem.*, **32**, 2876 (1967).
(397) R. J. Shozda, U.S. Patent 3 418 088 (1966); *Chem. Abstr.*, **70**, 49132d (1969).
(398) W. Traube, *Chem. Ber.*, **24**, 360 (1891).
(399) J. Griffiths, *J. Chem. Soc. C*, **3191** (1971).
(400) W. L. Matier, W. T. Comer, and D. Deitchman, *J. Med. Chem.*, **15**, 539 (1972).
(401) W. L. Matier and W. T. Comer, German Patent 2 110 535 (1971); *Chem. Abstr.*, **75**, 150893 (1971).
(402) G. M. Atkins, Jr. and E. M. Burgess, *Am. Chem. Soc.*, **94**, 6135 (1972).
(403) W. Lwowski and E. Scheiffele, *J. Am. Chem. Soc.*, **87**, 4359 (1965).
(404) R. A. Abramovitch and R. G. Sutherland, *Fortschr. Chem. Forsch.*, **60**, 1 (1970).
(405) R. A. Abramovitch and W. D. Holcomb, *J. Am. Chem. Soc.*, **97**, 676 (1975).

- (406) R. A. Abramovitch and K. Miyashita, *J. Chem. Soc., Perkin Trans. 1*, 2413 (1975).
- (407) R. A. Abramovitch in "Organic Reactive Intermediates", S. P. McManus, Ed., Academic Press, New York, 1973, p. 127.
- (408) R. A. Abramovitch, C. I. Azogu, and I. T. McMaster, *J. Am. Chem. Soc.*, **91**, 1219 (1969).
- (409) W. W. Binkley and E. F. Degering, *J. Am. Chem. Soc.*, **61**, 3250 (1939).
- (410) C. Corral and A. M. Municio, *An. Ri. Soc. Esp. Fis. Quim., Ser. B*, **60**, 341 (1964).
- (411) R. Appel and N. Senkpiel, *Z. Anorg. Allgem. Chem.*, **310**, 94 (1961).
- (412) R. Sowada, *J. Prakt. Chem.*, **29**, 328 (1965).
- (413) G. Weiss and G. Schulze, *Justus Liebigs Ann. Chem.*, **729**, 40 (1969).
- (414) W. Lwowski, R. De. Mauriac, T. W. Mattingly, Jr., and E. Scheffele, *Tetrahedron Lett.*, 3285 (1964).
- (415) R. Cramer and D. D. Coffman, *J. Org. Chem.*, **26**, 4010 (1961).
- (416) B. Weinstein and H. H. Chang, *Tetrahedron Lett.*, 901 (1974).
- (417) E. Merian, *Helv. Chim. Acta*, **43**, 1122 (1960).
- (418) E. Otto and R. Muschaweck, German Patent 2 418 217 (1975); *Chem. Abstr.*, **84**, 16980 (1976).
- (419) G. Lohaus, *Chem. Ber.*, **105**, 2791 (1972).
- (420) M. Hedayatullah and J. F. Brault, *C. R. Hebd. Seances Acad. Sci., Ser. C*, **285**, 153 (1977).
- (421) Hoechst Farbwerke A-G., French Patent 1 554 976; *Chem. Abstr.*, **72**, 55051 (1970).
- (422) M. Hedayatullah and A. Guy, *Tetrahedron Lett.*, 2455 (1975).
- (423) M. Hedayatullah and A. Guy, *Synthesis*, 357 (1978).
- (424) W. Traube, H. Zander, and H. Gaffron, *Chem. Ber.*, **57**, 1045 (1924).
- (425) E. H. White and C. A. Elliger, *J. Am. Chem. Soc.*, **87**, 5261 (1965).
- (426) P. F. Ziegler and M. Orchin, *J. Org. Chem.*, **33**, 443 (1968).
- (427) P. Marquarding, A. Schutz, and I. Ugi, *Chem. Ber.*, **110**, 2656 (1977).
- (428) J. F. King and T. M. Lee, *J. Chem. Soc., Chem. Commun.*, 48 (1978).
- (429) K. Prezewowski, H. Laurent, H. Hofmeister, R. Wlechet, F. Neumann, and Y. Nishino, German Patent 2 426 778 (1975); *Chem. Abstr.*, **84**, 150838 (1976).
- (430) K. Prezewowsky, H. Laurent, H. Hofmeister, R. Wlechet, F. Neumann, and Y. Nishino, German Patent 2 426 779 (1975); *Chem. Abstr.*, **86**, 106891 (1977).
- (431) S. Schwarz and G. Weber, *Z. Chem.*, **15**, 270 (1975).
- (432) S. Schwarz, G. Weber, and F. Kuehner, *Z. Chem.*, **10**, 299 (1970).
- (433) E. J. Sasmor, British Patent 1 124 720 (1968); *Chem. Abstr.*, **70**, 4415g (1969).
- (434) S. Schwarz and G. Weber, *Z. Chem.*, **14**, 15 (1974).
- (435) S. Schwarz, G. Weber, and M. Schreiber, *Pharmazie*, **30**, 17 (1975).
- (436) S. Schwarz and G. Weber, German Patent (East) 114 806 (1975); *Chem. Abstr.*, **85**, 63238 (1976).
- (437) T. Tsuchiya, I. Watanabe, M. Yoshida, F. Nakamura, T. Usui, M. Kitamura, and S. Umezawa, *Tetrahedron Lett.*, 3365 (1978).
- (438) N. K. Kochetkov, A. I. Usov, and V. V. Deryabin, *Zh. Obshch. Khim.*, **42**, 2763 (1972).
- (439) N. K. Kochetkov, A. I. Usov, and V. V. Deryabin, *Zh. Obshch. Khim.*, **44**, 904 (1974).
- (440) N. K. Kochetkov, A. I. Usov, and V. V. Deryabin, *Dokl. Akad. Nauk SSSR*, **216**, 97 (1974).
- (441) M. J. Robins, R. K. Robins, and D. A. Shuman, U.S. Patent 3 622 561 (1971); *Chem. Abstr.*, **76**, 34532 (1972).
- (442) D. A. Shuman, R. K. Robins, and M. J. Robins, *J. Am. Chem. Soc.*, **91**, 3391 (1969).
- (443) D. A. Shuman, M. J. Robins, and R. K. Robins, *J. Am. Chem. Soc.*, **92**, 3434 (1970).
- (444) J. J. Jaffe, J. J. McCormack, and E. Meymerian, *Exp. Parasitol.*, **28**, 535 (1970).
- (445) A. M. Cole, J. A. Turner, and B. K. Snell, German Patent 2 265 029 (1976); *Chem. Abstr.*, **84**, 146123 (1976).
- (446) Imperial Chemicals Industries, German Patent 2 265 028 (1975); *Chem. Abstr.*, **84**, 164825 (1976).
- (447) A. M. Cole, J. Turner and B. K. Snell, German Patent 2 246 645 (1973); *Chem. Abstr.*, **78**, 159654 59654 (1973).
- (448) V. Konecny, Czech Patent 147 244 (1973); *Chem. Abstr.*, **78**, 159215 (1973).
- (449) A. Fischer, H. Hansen, W. Rohr, and G. Hamprecht, German Patent 2 417 764 (1975); *Chem. Abstr.*, **84**, 30709 (1976).
- (450) A. Fischer, W. Rohr, and R. Schmidt, German Patent 2 364 876 (1975); *Chem. Abstr.*, **83**, 131341 (1975).
- (451) D. Mangold, A. Fischer, W. Rohr, and G. Hamprecht, German Patent 2 310 757 (1974); *Chem. Abstr.*, **82**, 4032 (1975).
- (452) G. Steinbrunn and A. Fischer, German Patent 1 204 879 (1965); *Chem. Abstr.*, **64**, 13321e (1966).
- (453) A. Fischer, German Patent 2352537 (1975); *Chem. Abstr.*, **83**, 109806 (1975).
- (454) L. D. Markley, U.S. Patent 3 900 509 (1975); *Chem. Abstr.*, **83**, 178311 (1975).
- (455) E. Kuehle, E. Klauke, and L. Eue, German Patent 2 334 607 (1975); *Chem. Abstr.*, **82**, 139805 (1975).
- (456) Badische Anilin- und Soda Fabrik, French Patent 2 008 319 (1970); *Chem. Abstr.*, **73**, 130902 (1970).
- (457) A. Brulard and A. Gerbaux, German Patent 2 531 445 (1976); *Chem. Abstr.*, **84**, 137214 (1976).
- (458) U. Zirnigbl, German Patent 2 142 334 (1972); *Chem. Abstr.*, **77**, 36383 (1972).
- (459) Cassella Farbwerke Mainkur, Netherlands Patent 6 610 943 (1967); *Chem. Abstr.*, **67**, 65393 (1967).
- (460) H. von Brachel, E. Heinrich, O. Graewinger, K. Hintermeier, and H. Kindler, German Patent 1 813 385 (1970); *Chem. Abstr.*, **73**, 99995 (1970).
- (461) G. Lamm, German Patent 2 309 637 (1974); *Chem. Abstr.*, **82**, 45017 (1975).
- (462) Cassella Farbwerke Mainkur, Belgian Patent 668 889 (1965); *Chem. Abstr.*, **65**, 9066e (1966).
- (463) Cassella Farbwerke Mainkur, Netherlands Patent 6 510 813 (1966); *Chem. Abstr.*, **65**, 2392c (1966).
- (464) A. Brulard and A. Gerbaux, Belgian Patent 834 836 (1976); *Chem. Abstr.*, **86**, 157041 (1977).
- (465) A. F. Hirsch, German Patent 2 559 210 (1976); *Chem. Abstr.*, **85**, 142662 (1976).
- (466) J. Kraemer, K. Freisberg, and H. Halpaap, German Patent 1 543 744 (1974); *Chem. Abstr.*, **82**, 43176 (1975).
- (467) G. A. Tolstikov, B. M. Lerman, and F. Z. Galin, *Zh. Org. Khim.*, **13**, 1634 (1977).
- (468) E. M. Burgess, H. R. Penton, Jr., and E. A. Taylor, *J. Am. Chem. Soc.*, **92**, 5224 (1970).
- (469) E. M. Burgess, H. R. Penton, Jr., and E. A. Taylor, *J. Org. Chem.*, **38**, 26 (1973).
- (470) K. T. Douglas and A. Williams, *J. Chem. Soc., Chem. Commun.*, 356 (1973).
- (471) A. Williams and K. T. Douglas, *J. Chem. Soc., Perkin Trans. 2*, 1727 (1974).
- (472) G. H. Posner, D. Z. Rogers, C. M. Kinzig, and G. M. Gurria, *Tetrahedron Lett.*, 3597 (1975).
- (473) G. H. Posner, G. M. Gurria, and K. A. Babiak, *J. Org. Chem.*, **42**, 3173 (1977).
- (474) G. Weiss and G. Schulze, German Patent 1 121 060 (1962); *Chem. Abstr.*, **57**, 667c (1962).
- (475) G. Weiss and G. Schulze, German Patent 1 493 486 (1973); *Chem. Abstr.*, **78**, 124029 (1973).
- (476) N. C. Hansen, *Acta Chem. Scand.*, **17**, 2141 (1963).
- (477) G. Weiss and G. Schulze, *Justus Liebigs Ann. Chem.*, **729**, 40 (1969).
- (478) G. Schulze and G. Weiss, Belgian Patent 667 311 (1966); *Chem. Abstr.*, **65**, 5368c (1966).
- (479) G. Schulze and G. Weiss, German Patent 1 237 582 (1967); *Chem. Abstr.*, **67**, 53 679 (1967).
- (480) G. Hamprecht, D. Mangold, and K. H. Koenig, German Patent 2 164 176 (1973); *Chem. Abstr.*, **78**, 65789 (1973).
- (481) K. H. Koenig and G. Hamprecht, German Patent 2 513 997 (1976); *Chem. Abstr.*, **86**, 43182 (1977).
- (482) K. H. Koenig and G. Hamprecht, German Patent 2 514 646 (1976); *Chem. Abstr.*, **86**, 43183 (1977).
- (483) K. H. Koenig and G. Hamprecht, German Patent 2 514 937 (1976); *Chem. Abstr.*, **86**, 54973 (1977).
- (484) J. A. Kloek and K. L. Leschinsky, *J. Org. Chem.*, **41**, 4028 (1976).
- (485) G. Hamprecht, A. Zeldler, K. H. Konig, and D. Mangold, *Kem.-Kemi*, **1**, 590 (1974).
- (486) G. Hamprecht, private communication.
- (487) G. Hamprecht, German Patent 2 553 460 (1977); *Chem. Abstr.*, **87**, 101939 (1977).
- (488) S. Kersten and G. Hamprecht, German Patent 2 553 461 (1977); *Chem. Abstr.*, **87**, 84522 (1977).
- (489) W. Rohr and G. Hamprecht, German Patent 2 401 819 (1975); *Chem. Abstr.*, **83**, 178310 (1975).
- (490) K. Grohe, German Patent 1 943 233 (1971); *Chem. Abstr.*, **74**, 111546 (1971).
- (491) E. Kuehle, E. Klauke, and K. Grohe, German Patent 1 943 234 (1971); *Chem. Abstr.*, **74**, 111547 (1971).
- (492) (a) H. W. Roesky and A. Hoff, *Chem. Ber.*, **98**, 2429 (1965); (b) H. W. Roesky, *Inorg. Nucl. Chem. Lett.*, **6**, 795 (1970).
- (493) J. H. Pearson and C. C. Chappelow, U.S. Patent 3 336 382 (1967); *Chem. Abstr.*, **68**, 77950 (1968).
- (494) J. H. Pearson and C. C. Chappelow, U.S. Patent 3 534 096 (1970); *Chem. Abstr.*, **74**, 22556 (1971).
- (495) L. K. Huber and H. C. Mandell, Jr., U.S. Patent 3 431 088 (1969); *Chem. Abstr.*, **70**, 89299 (1969).
- (496) C. L. Bumgardner and M. Lustig, *Inorg. Chem.*, **2**, 662 (1963).
- (497) M. Lustig, C. L. Bumgardner, F. A. Johnson, and J. K. Ruff, *Inorg. Chem.*, **3**, 1165 (1964).
- (498) G. W. Fraser, J. M. Shreeve, M. Lustig, and C. L. Bumgardner, *Inorg. Synth.*, **12**, 299 (1970).
- (499) L. M. Zaborowski and J. M. Shreeve, *Inorg. Chem.*, **10**, 407 (1971).
- (500) H. W. Roesky, *Angew. Chem., Int. Ed. Engl.*, **10**, 265 (1971).
- (501) H. W. Roesky, *Angew. Chem., Int. Ed. Engl.*, **7**, 63 (1968).
- (502) G. Hamprecht, German Patent 2 301 207 (1974); *Chem. Abstr.*, **81**, 120038 (1974).
- (503) W. Schneider, G. Kessler, and H. A. Lehmann, *Z. Anorg. Allg. Chem.*, **356**, 239 (1968).
- (504) H. Bürger, K. Burczyk, A. Blaschette, and H. Safari, *Spectrochim. Acta, Part A*, **27**, 1073 (1971).
- (505) R. Paetzold and E. Rönsch, *Spectrochim. Acta, Part A*, **26**, 569 (1970).
- (506) F. Török, E. Páldi, S. Dobos, and G. Fogarasi, *Acta Chim. Acad. Sci. Hung.*, **83**, 417 (1970).
- (507) L. V. Vilkov and I. Hargittai, *Acta Chim. Acad. Sci. Hung.*, **52**, 423 (1967).
- (508) I. Hargittai and J. Brunvoll, *Acta Chem. Scand., Ser. A*, **30**, 634 (1976).
- (509) W. B. Jennings and R. Spratt, *J. Chem. Soc. D*, 1418 (1970).
- (510) I. P. Biryukov and A. Ya. Deich, *Russ. J. Phys. Chem.*, **47**, 1039 (1973).
- (511) R. M. Hart and M. A. Whithead, *Trans. Faraday Soc.*, **67**, 3451 (1971).
- (512) A. Fischer and W. Rohr, German Patent 2 324 592 (1974); *Chem. Abstr.*, **82**, 86268 (1975).
- (513) J. E. Dunbar, U.S. Patent 3 082 238 (1963); *Chem. Abstr.*, **59**, 3852g (1963).
- (514) A. Fischer and W. Rohr, German Patent 2 219 923 (1973); *Chem. Abstr.*, **80**, 27127 (1974).
- (515) A. Fischer, G. Hamprecht, D. Mangold, and W. Rohr, U.S. Patent 3 954 827 (1976); *Chem. Abstr.*, **85**, 77682 (1976).
- (516) W. Rohr, H. Hansen, and A. Fischer, German Patent 2 351 608 (1975);

- Chem. Abstr.*, **83**, 114018 (1975).
- (517) C. Kaiser and S. Ross, U.S. Patent 3 793 460 (1974); *Chem. Abstr.*, **80**, 108214 (1974).
- (518) C. Kaiser and S. Ross, U.S. Patent 3 711 545 (1973); *Chem. Abstr.*, **78**, 110869 (1973).
- (519) W. T. Comer and J. D. Catt, German Patent 2 444 193 (1975); *Chem. Abstr.*, **83**, 58481 (1975).
- (520) W. T. Comer and J. D. Catt, U.S. Patent 4 044 151 (1977); *Chem. Abstr.*, **87**, 151833 (1977).
- (521) A. Widdig, E. Kuehle, F. Grewe, and H. Kaspers, German Patent 2 206 010 (1973); *Chem. Abstr.*, **79**, 115589 (1973).
- (522) F. J. Blechler, P. Tritsch, and P. Luttenbacher, French Patent 2 076 734 (1971); *Chem. Abstr.*, **77**, 34172 (1972).
- (523) E. Cohen and B. Klarberg, *J. Am. Chem. Soc.*, **84**, 1994 (1962).
- (524) D. Mangold, K. H. Koenig, and G. Hamprecht, German Patent 2 357 063 (1975); *Chem. Abstr.*, **83**, 131644 (1975).
- (525) A. Fischer, K. H. Koenig, and G. Hamprecht, German Patent 2 349 114 (1975); *Chem. Abstr.*, **83**, 43390 (1975).
- (526) G. Hamprecht and K. H. Koenig, U.S. Patent 3 822 257 (1974); *Chem. Abstr.*, **82**, 171098 (1975).
- (527) (a) A. Fischer, W. Rohr, and G. Hamprecht, German Patent 2 430 353 (1976); *Chem. Abstr.*, **84**, 135728 (1976); (b) K. C. C. Bancroft, L. H. Morcos Guindi, and A. F. Temple, *J. Heterocycl. Chem.*, **15**, 1521 (1978).
- (528) J. A. Kloek and K. L. Leschinsky, *J. Org. Chem.*, **43**, 3824 (1978).
- (529) A. Edenhofer and W. Meister, *Helv. Chim. Acta*, **60**, 521 (1977).
- (530) (a) H. Quast and F. Kees, *Angew. Chem., Int. Ed. Engl.*, **13**, 742 (1974); (b) I. T. Kay, German Patent 2 508 832 (1975); *Chem. Abstr.*, **84**, 59585 (1976).
- (531) J. Martin, O. Meth-Cohn, and H. Suschitzky, *Tetrahedron Lett.*, 4495 (1973).
- (532) H. Pietsch, K. Claus, H. Jensen, and E. Schmidt, German Patent 2 453 063 (1976); *Chem. Abstr.*, **86**, 105973 (1977).
- (533) R. Appel and R. Helwerth, *Angew. Chem., Int. Ed. Engl.*, **6**, 952 (1967).
- (534) H. W. Roesky, *Angew. Chem., Int. Ed. Engl.*, **7**, 630 (1968).
- (535) O. Glemser, H. W. Roesky, and P. R. Heinze, *Angew. Chem., Int. Ed. Engl.*, **6**, 710 (1967).
- (536) E. Schmidt, K. Claus, H. Jensen, and H. Pietsch, German Patent 2 457 032 (1976); *Chem. Abstr.*, **85**, 162792 (1976).
- (537) H. W. Roesky, *Angew. Chem., Int. Ed. Engl.*, **7**, 218 (1968).
- (538) H. W. Roesky, *Inorg. Nucl. Chem. Lett.*, **4**, 147 (1968).
- (539) M. Lustig, *Inorg. Chem.*, **8**, 443 (1969).
- (540) H. W. Roesky and W. C. Boewing, *Z. Naturforsch. B*, **24**, 1250 (1969).
- (541) G. N. Sausen, U.S. Patent 3 376 117 (1968); *Chem. Abstr.*, **68**, 105638 (1968).
- (542) G. N. Sausen, U.S. Patent 3 214 465 (1965); *Chem. Abstr.*, **64**, 3350e (1966).
- (543) F. L. Scott and J. A. Barry, *Tetrahedron Lett.*, 513 (1968).
- (544) F. L. Scott and J. A. Barry, *Tetrahedron Lett.*, 2461 (1968).
- (545) A. Blaschette, *Angew. Chem., Int. Ed. Engl.*, **10**, 522 (1971).
- (546) (a) M. Okahara, K. Matsunaga, and S. Komori, *Synthesis*, 203 (1972); (b) J. B. Hendrickson and I. Joffe, *J. Am. Chem. Soc.*, **95**, 4083 (1973).
- (547) S. K. Gupta, *Synthesis*, 39 (1977).
- (548) G. A. Olah, S. Kobayashi, and J. Nishimura, *J. Am. Chem. Soc.*, **95**, 564 (1973).
- (549) L. K. Masili and A. A. Petrov, *Zh. Org. Khim.*, **6**, 396 (1970).
- (550) L. Bauer, T. E. Dickerhofe, and K. Y. Tserng, *J. Heterocycl. Chem.*, **12**, 797 (1975).
- (551) A. Blaschette, D. Rinne, and H. Safari, *Chem.-Ztg.*, **99**, 88 (1975).
- (552) A. Blaschette and H. Safari, *Z. Naturforsch. B*, **25**, 319 (1970).
- (553) F. L. Scott and J. A. Barry, *Tetrahedron Lett.*, 2457 (1968).
- (554) H. K. Hall, Jr., *J. Am. Chem. Soc.*, **78**, 1450 (1956).
- (555) H. K. Hall and C. H. Lueck, *J. Org. Chem.*, **28**, 2818 (1963).
- (556) O. Rogne, *J. Chem. Soc. B*, 663 (1969).
- (557) E. C. F. Ko and R. E. Robertson, *J. Am. Chem. Soc.*, **94**, 573 (1972).
- (558) E. C. F. Ko and R. E. Robertson, *Can. J. Chem.*, **50**, 946 (1972).
- (559) I. Lee and S. C. Kim, *Dachan Hwahak Hwojee*, **17**, 406 (1973).
- (560) I. Lee, U. R. Kim, and S. H. Bai, *Dachan Hwahak Hwojee*, **18**, 171 (1974).
- (561) O. J. Cha, *Hwahak Kyoyuk*, **4**, 75 (1977).
- (562) Reference 1, p 76.
- (563) Y. Ito, E. Masuda, and S. Uchida, *Kogyo Kagaku Zasshi*, **62**, 501 (1959); *Chem. Abstr.*, **57**, 8188c (1962).
- (564) Y. Ito, *Tokyo Kogyo Shikensho Hokoku*, **56**, 356 (1961); *Chem. Abstr.*, **62**, 8650f (1965).
- (565) Y. Ito and E. Masuda, *Kogyo Kagaku Zasshi*, **67**, 777 (1964); *Chem. Abstr.*, **61**, 6654 (1964).
- (566) R. Sowada, *J. Prakt. Chem.*, **20**, 310 (1963).
- (567) R. Sowada, *Z. Chem.*, **2**, 341 (1962).
- (568) R. Sowada, *J. Prakt. Chem.*, **23**, 128 (1964).
- (569) D. L. Forster, T. L. Gilchrist, and C. W. Rees, *J. Chem. Soc. C*, 993 (1971).
- (570) R. Sowada, *J. Prakt. Chem.*, **25**, 88 (1964).
- (571) R. Sowada, *J. Prakt. Chem.*, **26**, 184 (1964).
- (572) R. Sowada, *J. Prakt. Chem.*, **33**, 240 (1966).
- (573) R. Sowada, *J. Prakt. Chem.*, **33**, 247 (1966).
- (574) J. J. Lafferty and B. Loev, U.S. Patent 3 147 305 (1964); *Chem. Abstr.*, **61**, 13243f (1964).
- (575) J. M. McManus, J. W. McFarland, C. F. Gerber, W. M. McLamore, and G. D. Laubach, *J. Med. Chem.*, **8**, 766 (1965).
- (576) Ciba Ltd., Belgian Patent 640 160 (1964); *Chem. Abstr.*, **62**, 16134f (1965).
- (577) A. Vandi, T. Moeller, and L. F. Audrieth, *J. Org. Chem.*, **26**, 1136 (1961).
- (578) C. J. Paget, J. W. Chamberlain, and J. H. Wikel, German Patent 2 638 551 (1977); *Chem. Abstr.*, **87**, 53298f (1977).
- (579) V. P. Arya, F. Fernandes, S. P. Ghate, F. X. R. Costa-Pereira, and Y. H. Wasaiwalla, *Indian J. Chem.*, **10**, 686 (1972).
- (580) T. Kamiya, K. Tanaka, and Y. Saito, Japanese Patent 52 151 (1976); *Chem. Abstr.*, **85**, 177072 (1976).
- (581) G. M. Atkins, Jr., and E. M. Burgess, *J. Am. Chem. Soc.*, **89**, 2502 (1967).
- (582) A. Vandi, T. Moeller, and L. F. Audrieth, *J. Org. Chem.*, **26**, 3478 (1961).
- (583) J. D. Catt and W. L. Matier, German Patent 2 444 192 (1975); *Chem. Abstr.*, **83**, 113968 (1975).
- (584) C. Metzger and W. Merz, German Patent 2 646 884, (1978); *Chem. Abstr.*, **89**, 42795 (1978).
- (585) C. E. Day, P. E. Schurr, D. E. Emmert, R. E. TenBrink, and D. Lednicher, *J. Med. Chem.*, **18**, 1065 (1975).
- (586) G. H. Alt and J. A. Kloek, U.S. Patent 4 013 448 (1977); *Chem. Abstr.*, **87**, 53395 (1977).
- (587) H. Yamaguchi and H. Fukuno, *Nippon Kagaku Kaishi*, 1349 (1977).
- (588) E. S. Levchenko and L. V. Budnik, *Zh. Org. Khim.*, **11**, 2044 (1974).
- (589) R. Sowada, *Z. Chem.*, **8**, 25 (1968).
- (590) J. D. Catt and W. L. Matier, *J. Org. Chem.*, **39**, 566 (1974).
- (591) C. R. Gopinath and K. S. R. Rao, *Curr. Sci.*, **44**, 107 (1975).
- (592) H. Greschonig, E. Nachbaur, and H. Krischner, *Acta Crystallogr., Sect. B*, **33**, 3595 (1977).
- (593) T. Jordan, H. W. Smith, L. L. Lohr, Jr., and W. N. Lipscomb, *J. Am. Chem. Soc.*, **85**, 846 (1963).
- (594) I. Hargittai, E. Vajda, and A. Szöke, *J. Mol. Struct.*, **18**, 381 (1973).
- (595) C. Foces-Foces, P. Smith-Verdier, F. Florencio-Sabate, and S. García-Blanco, *Acta Crystallogr., Sect. B*, **31**, 140 (1975).
- (596) C. Foces-Foces, F. H. Cano, and S. García-Blanco, *Acta Crystallogr., Sect. B*, **31**, 1427 (1975).
- (597) C. Foces-Foces, F. H. Cano, and S. García-Blanco, *Acta Crystallogr., Sect. B*, **31**, 2310 (1975).
- (598) C. Foces-Foces, F. H. Cano, and S. García-Blanco, *Acta Crystallogr., Sect. B*, **31**, 2245 (1975).
- (599) P. Smith-Verdier, F. Florencio, S. García-Blanco, and J. G. Rodríguez, *Acta Crystallogr., Sect. B*, **33**, 2812 (1977).
- (600) M. D. Cabezuolo, F. H. Cano, C. Foces-Foces, and S. García-Blanco, *Acta Crystallogr., Sect. B*, **33**, 3598 (1977).
- (601) M. D. Cabezuolo, C. Foces-Foces, F. H. Cano, and S. García-Blanco, *Acta Crystallogr., Sect. B*, **34**, 3069 (1978).
- (602) I. W. Herrick and E. L. Wagner, *Spectrochim. Acta*, **21**, 1569 (1965).
- (603) R. Sowada, *J. Prakt. Chem.*, **311**, 228 (1969).
- (604) R. Sowada, *J. Prakt. Chem.*, **311**, 350 (1969).
- (605) H. Negita, T. Kubo, and K. Shibata, *Bull. Chem. Soc. Jpn.*, **48**, 675 (1975).
- (606) A. P. Claydon and C. T. Mortimer, *J. Chem. Soc.*, 3212 (1962).
- (607) J. Cuéllar and Y. Montell, *Bull. Soc. Chim. Fr.*, 892 (1966).
- (608) M. Dabkowska and S. Zytomirski, *Ann. Univ. Mariae Curie-Skłodowska Sect. AA*, **9** (1971); *Chem. Abstr.*, **78**, 164713 (1973).
- (609) Y. Montell, *Bull. Soc. Chim. Fr.*, 2479 (1971).
- (610) Y. Montell, *Bull. Soc. Chim. Fr.*, 2474 (1971).
- (611) (a) R. Wiesboeck and J. K. Ruff, *Inorg. Chem.*, **4**, 123 (1965); (b) A. Engelbrecht, E. Mayer, and C. Pupp, *Monatsh. Chem.*, **95**, 633 (1964).
- (612) D. J. Jaszka and D. Curtis, U.S. Patent 3 879 528 (1975); *Chem. Abstr.*, **83**, 45437 (1975).
- (613) R. W. Hill, U.S. Patent 3 661 830 (1972); *Chem. Abstr.*, **75**, 64878 (1971).
- (614) P. H. Derible, D. Humbert, and C. Dumont, German Patent 2 433 681 (1975); *Chem. Abstr.*, **82**, 139681 (1975).
- (615) R. Die, J. Diez, G. García-Muñoz, R. Madronero, and M. Stud, *J. Heterocycl. Chem.*, **9**, 973 (1972).
- (616) M. Knollmüller and K. R. Reich, *Monatsh. Chem.*, **106**, 1095 (1975).
- (617) E. Ziegler and W. Rüf, *Z. Naturforsch. B*, **30**, 951 (1975).
- (618) N. Aktaev, V. D. Li, G. A. Sokol'skii, and I. L. Knunyants, *Zh. Org. Khim.*, **9**, 462 (1973).
- (619) F. L. Scott and H. Q. Smith, U.S. Patent 3 039 997 (1962); *Chem. Abstr.*, **57**, 8740f (1962).
- (620) F. L. Scott and H. Q. Smith, U.S. Department of Commerce, Office of Technical Services, 148 135 (1959); *Chem. Abstr.*, **56**, 15662i (1962).
- (621) R. A. Florentine, G. Barth-Wehrnald, I. Mockrin, I. Popoff, and R. Riordan, U.S. Department of Commerce, Office of Technical Services, AD 256811 (1961); *Chem. Abstr.*, **58**, 1591b (1963).
- (622) (a) K. Nara, O. Manabe, and H. Hiyama, *Yuki Gosei Kagaku Kyokai Shi*, **27**, 980 (1969); *Chem. Abstr.*, **72**, 33131 (1970); (b) A. Ciaperoni, L. Mariani, and G. B. Gechele, *Chim. Ind. (Milan)*, **49**, 385 (1967).
- (623) Y. Yoshihiro and Y. Matsui, *Nippon Kagaku Zasshi*, **85**, 122 (1964).
- (624) L. Villanua and P. Calvo, *An. R. Acad. Farm.*, **41**, 159 (1975).
- (625) L. N. Balyatinskaya and U. F. Milyaev, *Koord. Khim.*, **2**, 1594 (1976); *Chem. Abstr.*, **86**, 79586 (1977).
- (626) F. G. Mann, *J. Chem. Soc.*, 412 (1933).
- (627) K. Brodersen, L. Stumpp, and G. Krauss, *Chem. Ber.*, **93**, 375 (1960).
- (628) A. M. Paquin, *Kunststoffe*, **37**, 25 (1947).
- (629) A. Ouchi and T. Moeller, *J. Inorg. Nucl. Chem.*, **27**, 1635 (1965).
- (630) W. Traube, *Chem. Ber.*, **26**, 607 (1893).
- (631) E. Nachbaur and A. Popitsch, *Angew. Chem., Int. Ed. Engl.*, **12**, 339 (1973).
- (632) R. Ohme and E. Schmitz, *Angew. Chem., Int. Ed. Engl.*, **4**, 433 (1965).
- (633) R. Ohme and H. Preuschhof, *Justus Liebigs Ann. Chem.*, **713**, 74 (1968).
- (634) J. W. Timberlake, M. L. Hodges, and K. Betterton, *Synthesis*, 632 (1977).
- (635) (a) J. W. Timberlake and M. L. Hodges, *J. Am. Chem. Soc.*, **95**, 634 (1973); (b) H. Quast and F. Kees, *Tetrahedron Lett.*, **19**, 1655 (1973).
- (636) J. W. Timberlake, M. L. Hodges, and A. W. Garner, *Tetrahedron Lett.*, 3843 (1973).
- (637) H. H. Chang and B. Weinstein, *J. Chem. Soc., Perkin Trans. 1*, 1601 (1977).
- (638) J. B. Kang, B. S. Thyagarajan, E. E. Gilbert, and V. Siele, *Int. J. Sulfur Chem., Part A*, **1**, 261 (1971).

- (639) J. Dusemund, *Arch. Pharm. (Weinheim, Ger.)*, **307**, 881 (1974).
(640) J. Dusemund, *Arch. Pharm. (Weinheim, Ger.)*, **310**, 404 (1977).
(641) J. Dusemund, *Arch. Pharm. (Weinheim, Ger.)*, **310**, 417 (1977).
(642) J. Dusemund, *Arch. Pharm. (Weinheim, Ger.)*, **310**, 449 (1977).
(643) J. Dusemund, *Arch. Pharm. (Weinheim, Ger.)*, **310**, 435 (1977).
(644) J. Dusemund, *Arch. Pharm. (Weinheim, Ger.)*, **310**, 600 (1977).
(645) A. Claperoni, A. Vandi, G. Stea, G. B. Gechele, and B. Minasso, *Chim. Ind. (Milan)*, **47**, 1200 (1965).
(646) V. P. Arya and S. J. Shenoy, *Indian J. Chem.*, **14B**, 766 (1976).
(647) M. Knollmüller, *Monatsh. Chem.*, **102**, 1055 (1971).
(648) M. Knollmüller, *Monatsh. Chem.*, **105**, 114 (1974).
(649) E. Grigat, German Patent 2 026 625 (1971); *Chem. Abstr.*, **76**, 72564 (1972).
(650) A. Ouchi and T. Moeller, *J. Org. Chem.*, **29**, 1865 (1964).
(651) J. B. Wright, *J. Org. Chem.*, **29**, 1905 (1964).
(652) C. Ochoa and M. Stud, Spanish Patent 459 524 (1978); *Chem. Abstr.*, **90**, 72243 (1979).
(653) C. Ochoa and M. Stud, *J. Heterocycl. Chem.*, **15**, 221 (1978).
(654) P. Goya and M. Stud, *J. Heterocycl. Chem.*, **15**, 253 (1978).
(655) M. Preiss, *Chem. Ber.*, **111**, 1915 (1978).
(656) (a) S. K. Chiu, M. Dube, L. Keifer, S. Szilagyi, and J. W. Timberlake, *J. Org. Chem.*, **43**, 61 (1978); (b) H. L. McKendry, U.S. Patent 3 920 641 (1975); *Chem. Abstr.*, **84**, 44176 (1976); (c) J. Diez, G. García-Muñoz, R. Madronero, and M. Stud, *J. Heterocycl. Chem.*, **10**, 469 (1973); (d) H. L. McKendry, U.S. Patent 4 014 888 (1977); *Chem. Abstr.*, **87**, 53400 (1977).
(657) Y. G. Balan, E. S. Levehenko, and A. V. Kirsanov, *Zh. Org. Khim.*, **3**, 2063 (1967).
(658) T. Saito and T. Hiraoka, *Chem. Pharm. Bull.*, **25**, 792 (1977).
(659) F. Beger, and H. P. Latscha, *Chem.-Ztg.*, **97**, 272 (1973).
(660) B. S. Drach, A. P. Martynyuk, G. N. Mis'kevich, and O. P. Lobanov, *Zh. Org. Khim.*, **13**, 1404 (1977).
(661) R. A. Wiesboeck and J. K. Ruff, *Inorg. Chem.*, **5**, 1629 (1966).
(662) R. Appel and M. Montenarh, *Z. Naturforsch. B*, **31**, 993 (1976).
(663) R. Appel and M. Montenarh, *Chem. Ber.*, **108**, 2340 (1975).
(664) R. Appel and M. Montenarh, *Chem. Ber.*, **108**, 1442 (1975).
(665) R. Appel and M. Montenarh, *Chem. Ber.*, **111**, 759 (1978).
(666) W. Buss, H. J. Krannich, and W. Sundermeyer, *Z. Naturforsch. B*, **30**, 842 (1975).
(667) U. Wannagat and D. Labuhn, *Z. Anorg. Allg. Chem.*, **402**, 147 (1973).
(668) R. Appel and M. Montenarh, *Chem. Ber.*, **108**, 618 (1975).
(669) R. Appel and M. Montenarh, *Chem. Ber.*, **110**, 2368 (1977).
(670) J. G. Lombardino, *J. Org. Chem.*, **28**, 861 (1963).
(671) V. M. Cherkasov, T. A. Dashevskaya, and L. I. Baranova, *Zh. Org. Khim.*, **4**, 1636 (1968).
(672) A. Yas'kovyuk, M. M. Belei, Ya. M. Tsikanchuk, and R. G. Makitra, *Zh. Obshch. Khim.*, **47**, 184 (1977).
(673) M. Garrett, T. Tao, and W. L. Jolly, *J. Phys. Chem.*, **68**, 824 (1964).
(674) H. Yamaguchi, Japanese Patent 970 (1962); *Chem. Abstr.*, **58**, 2382f (1963).
(675) F. L. Scott, C. W. Schaumann, and J. P. King, *J. Org. Chem.*, **26**, 985 (1961).
(676) F. L. Scott and O. J. J. Broderick, *Chem. Ind. (London)*, 1058 (1962).
(677) F. L. Scott, J. A. Barry, and W. J. Spillane, *J. Chem. Soc., Perkin Trans. 1*, 2666 (1972).
(678) W. J. Spillane, J. A. Barry, W. A. Heaphy, and F. L. Scott, *Z. Naturforsch. B*, **29**, 702 (1974).
(679) D. Hellwinkel and M. Supp, *Tetrahedron Lett.*, 1499 (1975).
(680) H. Yamaguchi and K. Nakano, *Hiroshima Daigaku Kogakubu Kenkyu Hokoku*, **21**, 23 (1972); *Chem. Abstr.*, **79**, 65420 (1973).
(681) H. Yamaguchi and K. Tsujihara, *Hiroshima Daigaku Kogakubu Kenkyu Hokoku*, **23**, 7 (1974); *Chem. Abstr.*, **83**, 113269 (1975).
(682) W. J. Spillane, J. A. Barry, and F. L. Scott, *J. Chem. Soc., Perkin Trans. 2*, 481 (1973).