(lit.[25] mp 253–257°); the acid was identified by comparison with an authentic sample.[26]

2-Biphenylylbenzylphosphinic Acid.—Thus compound was prepared[22] from 2-biphenyldiazonium tetrafluoroborate and benzylphosphonous dichloride by the method of Freedman and Doak:[27] yield 21%; mp 168–170°.

Anal. Calcd for $C_{19}H_{17}O_2P$: C, 74.02; H, 5.56; P, 10.05. Found: C, 74.20; H, 5.73; P, 9.62.

Cleavage of 5-Phenyldibenzophosphole 5-Oxide (II).—This compound (2.0 g) was cleaved by the procedure described for 5-benzyldibenzophosphole 5-oxide. 2-Biphenylylphenylphosphinic acid, 1.6 g (75%), mp 173–176° (lit.[28] mp 180–181°), was isolated and shown to be identical (mixture melting point and ir) with an authentic sample (see below). About 0.3 g (15%) of the phosphine oxide II was recovered from the reaction mixture.

2-Biphenylylphenylphosphinic Acid.—This compound was prepared from 2-biphenyldiazonium tetrafluoroborate and phenylphosphonous dichloride by the usual method:[27] yield 18%; mp 177–179° (lit.[28] mp 180–181°).

Cleavage of 5-Benzyl-5-phenyldibenzophospholium Chloride (III).—The phospholium salt III (1.4 g) was dissolved in 40 ml of a 1:1 acetone–water mixture. Sodium hydroxide (9 ml of a 20% solution) was added, and the mixture was allowed to sit for 24 hr. The acetone was evaporated and the aqueous mixture was extracted with two 15-ml portions of chloroform. The extracts were combined and stripped leaving 5-phenyldibenzophosphole 5-oxide (II): yield 1.0 g (100%); mp 162–165°. The compound was identical with the sample prepared above.

(25) L. D. Freedman and G. O. Doak, *J. Org. Chem.*, **21**, 238 (1956).
(26) G. O. Doak, L. D. Freedman, and J. B. Levy, *ibid.*, **29**, 2382 (1964).
(27) L. D. Freedman and G. O. Doak, *J. Amer. Chem. Soc.*, **74**, 2884 (1952).
(28) I. G. M. Campbell and J. K. Way, *J. Chem. Soc.*, 2133 (1961).

Cleavage of 5-Benzyl-5-methyldibenzophospholium Iodide (VI).—The phospholium salt VI (2.8 g) was cleaved by the procedure described for 5-benzyl-5-phenyldibenzophospholium chloride (III). 5-Methyldibenzophosphole 5-oxide was obtained as a hemihydrate after recrystallization from benzene–petroleum ether: yield 1.3 g (90%); mp 89–91°; nmr τ 8.21 (d, J_{P-H} = 13.6 cps, 3, CH_3P), 7.42 (s, 1, H_2O), 2.0–2.8 (m, 8, aromatic H). The ir spectrum showed the O–H stretching at 3470 and 3520 cm^{-1}. The water could be removed by heating the hemihydrate for 2 hr *in vacuo* over phosphorus pentoxide; the loss of water was demonstrated by an appropriate weight loss, the disappearance of the O–H stretching in the ir, and of the τ 7.42 peak in the nmr spectrum.

Anal. Calcd for $C_{13}H_{11}OP \cdot 0.5H_2O$: C, 70.00; H, 5.42; P, 13.88. Found: C, 70.45; H, 5.57; P, 14.01.

The compound was identical (melting point, mixture melting point, and ir) with an authentic sample prepared by the procedure given below.

5-Methyldibenzophosphole 5-Oxide.—5-Methyldibenzophosphole was prepared from 5-phenyldibenzophosphole (0.029 mol) and methyl iodide (0.029 mol) by the procedure described for 5-benzyldibenzophosphole (IV): yield 44%; bp 110° (10 μ) [lit.[4] bp 103° (0.2 mm)]; nmr τ 8.69 (s, 3, CH_3P), 2.3–2.8 (m, 8, aromatic H).

Anal. Calcd for $C_{13}H_{11}P$: C, 78.77; H, 5.60. Found: C, 78.60; H, 5.73.

The phosphine was oxidized with hydrogen peroxide to the phosphine oxide hemihydrate (70%), mp 88–90°.

Registry No.—III, 19190-36-4; IV, 19190-37-5; V, 19190-38-6; VI, 19190-39-7; 5-methyldibenzophosphole 5-oxide, 19190-40-0.

Some Novel Sulfonamides. The Chlorosulfonation of Aryl Alkyl Sulfides

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The chlorosulfonation of three methylthio-substituted benzenes has been investigated. With two of the compounds, the reaction proved satisfactory for preparation of sulfonamide derivatives. In the more favorable case, 2,4-dimethylthioacetanilide readily gave a crystalline sulfonyl chloride. Subsequent oxidation gave the corresponding disulfones. Various tetrasubstituted compounds were readily characterized by bands for isolated aromatic hydrogens in their proton magnetic resonance (pmr) spectra. Lack of splitting in these bands along with the facile substitution in the presence of the two methylthio-directing groups favors assignment of a 1,2,4,5-substitution pattern for these compounds. Analysis of the pmr spectra provides a rough correlation of chemical-shift parameters for the sulfonyl and methylthio substituents.

A study of some sulfonation reactions with simple alkyl aryl sulfides has shown participation by the sulfur as a sulfonium group in attack on the aromatic ring to give diarylalkylsulfonium salts. This reaction occurs with methyl *p*-tolyl sulfide at 20°. When the ring is somewhat deactivated, as with methyl *p*-chlorophenyl sulfide, some sulfonation is observed and this occurs *ortho* to the methylthio group.[1] An earlier study of the substitution of methyl phenyl sulfide reports that both bromination and sulfonation occur primarily in the *para* position.[2]

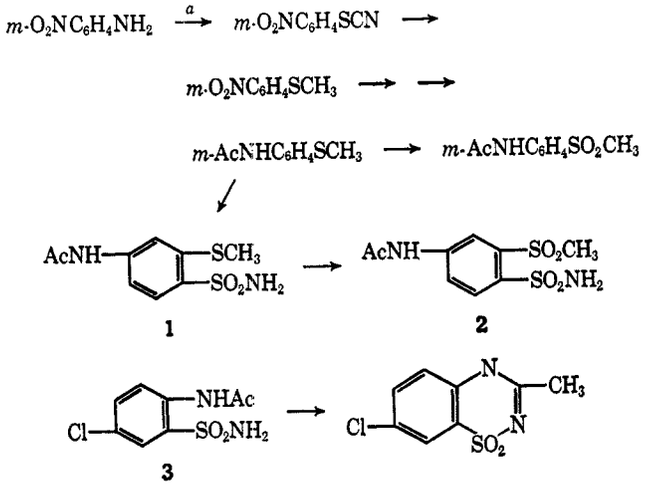
In work directed toward the preparation of new sulfonamides, chlorosulfonation of highly reactive methylthio-substituted benzenes was utilized. In addition to using cold chlorosulfonic acid, use of chloroform as a cosolvent in the two-phase procedure of Huntress and Carten[3] for characterization of aryl alkyl ethers was also used. This procedure was found to give better results than without the use of a cosolvent in the one case in which it was tried.

m-Methylthioacetanilide[4] was prepared and further characterized by oxidation with perbenzoic acid to the sulfone[4] (Scheme I). It was also chlorosulfonated followed by treatment with ammonia to give a new

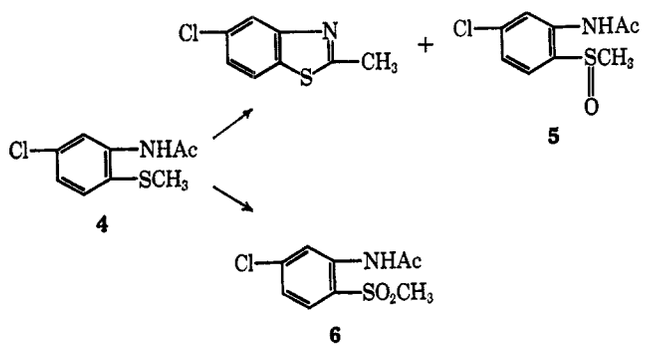
(1) F. Krollpfeiffer and W. Hahn, *Chem. Ber.*, **86**, 1049 (1953).
(2) T. Van Hove, *Bull. Sci. Acad. Roy. Belg.*, **12**, (5), 929 (1926); *Chem. Abstr.*, **21**, 2256 (1927).
(3) E. H. Huntress and F. H. Carten, *J. Amer. Chem. Soc.*, **62**, 511, 603 (1940).
(4) (a) Th. Zinke and J. Müller, *Ber.*, **46**, 775 (1913); (b) H. Gilman and G. A. Martin, *J. Amer. Chem. Soc.*, **74**, 5317 (1952).

methylthiosulfamylacetanilide (**1**).[5] This compound was further transformed to the sulfone **2.** The position

SCHEME I



SCHEME II



[a] K. Brand and H. W. Leyerzapf, *Ber.* **70B**, 284 (1937).

2-Methylthio-5-chloroacetanilide (**4**, Scheme II) was prepared from 2-methylthio-5-chloronitrobenzene[8] by stannous chloride reduction followed by acetylation with acetic anhydride–acetic acid. A single attempt at chlorosulfonation under relatively mild conditions gave no sulfonation, but did result in S demethylation and ring closure to 5-chloro-2-methylbenzothiazole.[9] Under slightly more vigorous conditions, **4** gave the benzothiazole and a small amount of a product which appeared, from its analysis and infrared[10] (ir) and pmr spectra, to be the sulfoxide **5.**

The sulfone **6** was also prepared from **4** by perbenzoic acid oxidation.

Treatment of 2,4-dimethylthioacetanilide[11] with cold chlorosulfonic acid (Scheme III) and reaction of the product (**7**) with concentrated ammonium hydroxide or dimethylamine gave the corresponding sulfamylacetanilide (**8**) and dimethylsulfamyl acetanilide (**9**).

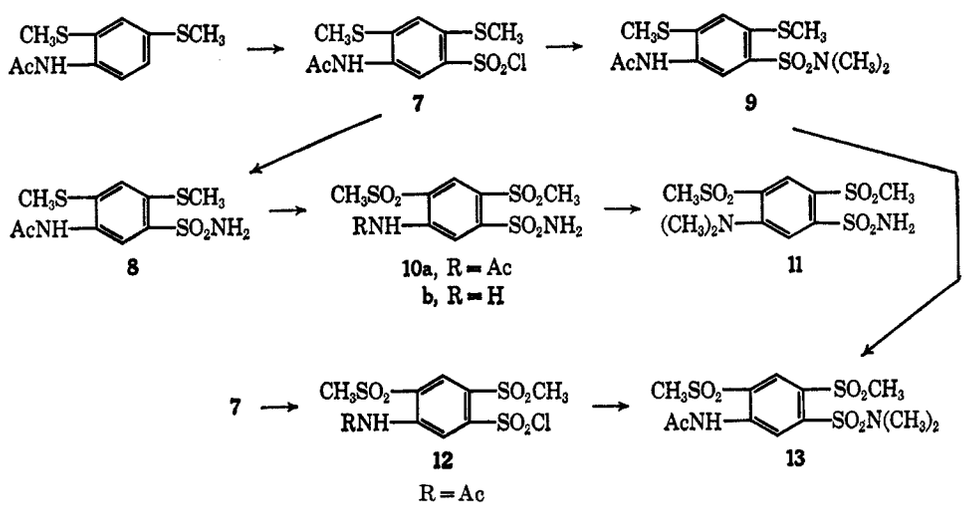
In the preparation of **7,** pure, crystalline sulfonyl halide was readily isolated when chloroform was used as a cosolvent for the chlorosulfonation.[3]

Oxidation of **8** with perbenzoic acid gave the disulfone **10a** which was hydrolyzed to the free amine **10b.**

An attempt was made to prepare the dimethylsulfonyl compound corresponding to **9** by stepwise methylation of the potassium salt of **10a** in the presence of a large excess of methyl iodide. When most of the initial equivalent of base had been used up, the process was repeated. This brought the pH to 8 from which it appeared that the methyl iodide had reacted preferentially either with hydroxide ion or with the sulfamyl anions of **10a** and further with its monomethylsulfamyl derivative.

However, two additional treatments with base and excess methyl iodide produced a 57% yield of a substance with no N-acetyl and only two N-methyl substituents, though the total iodide and base used

SCHEME III



of the sulfamyl group in **1** was inferred from its failure to undergo pyrolytic ring closure at a temperature in excess of that required for ring closure[6] of 2-sulfamyl-4-chloroacetanilide (**3**).[7]

(5) A sulfamyl derivative of *o*-methylthioacetanilide has been reported [R. Specklin and J. Meybeck, *Bull. Soc. Chim. Fr.*, 621 (1951)].

(6) (a) F. C. Novello, S. C. Bell, E. L. A. Abrams, C. Ziegler, and J. M. Sprague, *J. Org. Chem.*, **25**, 965 (1960); (b) J. G. Topliss, M. H. Sherlock, H. Reimann, L. M. Konzelman, E. P. Shapiro, B. W. Pettersen, H. Schneider, and N. Sperber, *J. Med. Chem.*, **6**, 122 (1963).

(7) S. Suzue and S. Hayashi, *Yakugaku Zasshi*, **82**, 1192 (1962); *Chem. Abstr.*, **58**, 5689 (1963).

(8) (a) H. H. Hodgson and F. W. Handley, *J. Soc. Chem. Ind.*, **46**, 435-6T (1927); *Chem. Abstr.*, **22**, 950 (1928). (b) D. A. Skinner and E. L. Wampler U. S. Patent 2,557,520 (1951). (c) The ethylthio homolog has been described.[5]

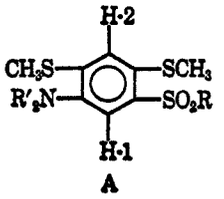
(9) H. P. Lankelma and A. E. Knauf, *J. Amer. Chem. Soc.*, **53**, 309 (1931).

(10) F. G. Bordwell and P. J. Boutan, *ibid.*, **79**, 717 (1957).

(11) H. H. Hodgson and F. W. Handley, *J. Chem. Soc.*, 162 (1928).

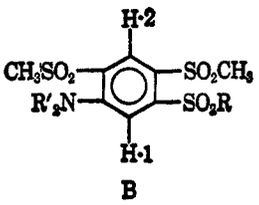
TABLE I

PROTON MAGNETIC RESONANCE PEAKS IN DMSO FOR STRUCTURES A–C



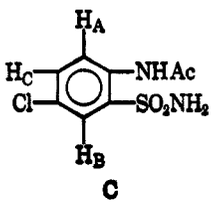
A

Compound	R′	R	δ (H-1)	δ (H-2)	δ $(NCH_3)_2$	δ (SCH_3)	δ (Ac)
8	Ac, H	NH_2	7.79	7.20		2.56, 2.59	2.07
9	Ac, H	$N(CH_3)_2$	7.70	7.15	2.74	2.57, 2.57	2.06
7	Ac, H	Cl	7.70	7.00		2.41, 2.44	2.00



B

Compound	R′	R	δ (H-1)	δ (H-2)	δ $(NCH_3)_2$	δ (SO_2CH_3)	δ (Ac)
10b	H	NH_2	7.72	8.28		3.20, 3.37	
11	CH_3	NH_2	7.46	8.38	2.95	3.32, 3.32	
13	Ac, H	$N(CH_3)_2$	8.63	8.95	2.98	3.38, 3.45	2.28
10a	Ac, H	NH_2	8.58	9.18		3.48, 3.50	2.28
12	Ac, H	Cl	8.55	8.90		3.32, 3.35	2.19



C

δ (H_A)	δ (H_B)	δ (H_C)	
8.21 (J_{AC} = 11Hz)	7.86 (J_{BC} = 3 Hz)	7.65 (J_{CA} = 8.4 Hz; J_{CB} = 2.5 Hz)	7.42

would have allowed formation of the N,N,N′,N′-tetramethyl derivative (plus 1 equiv of acetic acid on introduction of the last methyl group). Consequently, it was concluded that hydrolysis of the acetyl group occurred readily with subsequent methylation of the amino nitrogen but not of the sulfonamide anion to give **11**. It is of interest that the amino group exhibits a much greater nucleophilic reactivity than the $-SO_2NH$ anion in spite of the former's vinylogous relationship to the methylsulfonyl groups.

Since direct methylation of the sulfamyl nitrogen of **10a** could not be achieved, preliminary studies of two other routes to the dimethylsulfamyl compound **13** were made. Oxidation of **7** with 4 equiv of *m*-chloroperbenzoic acid gave a compound with the expected pmr peaks for **12** (Table I), but which also contained incompletely oxidized material to the extent of *ca.* 20% (δ 2.82, CH_3SO-). An earlier attempt to convert **7** into **12** under milder conditions gave a higher proportion (*ca.* 50% based on total acetyl methyl) of this sulfoxide methyl with, in addition, another sulfoxide methyl at δ 2.72 to the extent of *ca.* 20%.

Permanganate oxidation[12] of **9** in aqueous acetic acid gave a product which was probably **13** based on comparison of its ir spectrum with that of a crude product obtained from **12** and dimethylamine.

Proton Magnetic Resonance Spectra.—The pmr spectra for compounds of Scheme III are summarized in Table I. As no attempt was made to standardize conditions for observation of the NH_2 protons, these are not included, though their positions generally provided reliable confirmation for the sulfonamide group and for electronegatively substituted aromatic amines (see Experimental Section). The proton between the two methylthio groups of A (Table I, H-2) is clearly different from the one *ortho* to the sulfamyl and acetamido groups. The latter (H-1) is deshielded by the acetamido and sulfonamido group as predicted from structure C (Table I) in which the individual protons can be identified through their coupling constants.[13] These assignments for H-1 and H-2 in structure A (Table I) parallel also the expected *ortho* effects for electronegative and electropositive substituents in both chloroform[14] and dimethyl sulfoxide[15] (DMSO). Com-

(12) R. W. Bost, J. O. Turner, and R. D. Norton, *J. Amer. Chem. Soc.*, **54**, 1985 (1932).

(13) J. W. Emsley, J. Feeney, and L. H. Sutcliffe, "High Resolution Nuclear Magnetic Resonance Spectroscopy," Vol. II, Pergamon Press, Inc., New York, N. Y., 1966, p 770.

(14) (a) P. L. Corio and B. P. Dailey, *J. Amer. Chem. Soc.*, **78**, 3043 (1956); (b) J. S. Martin and B. P. Dailey, *J. Chem. Phys.*, **39**, 1722 (1963).

(15) J. B. Leane and R. E. Richards, *Trans. Faraday Soc.*, **55**, 707 (1959); also ref 13, p 767.

parison of halosulfonyl and nitrosubstituted benzenes shows that the sulfonyl group effects somewhat greater deshielding of the *ortho* position (0.1–0.2 ppm) and somewhat less deshielding at the *meta* position (*ca.* 0.2 ppm) than the nitro group.[16,14a] Thus, hydrogens *ortho* to a sulfonyl group should be deshielded by *ca.* 1.1 ppm and there should be essentially no *meta* effect (*o*-NO_2, −0.955 ppm;[14a] *m*-NO_2, −0.155 ppm[14a]). The pmr of *p*-acetamidoanisole[17] suggest that the acetamido group is somewhat deshielding to an *ortho* hydrogen (*ca.* 0.1 ppm) and has essentially no *meta* effect when reported values[14a] for methoxy are considered.

On this basis, the shielding of H-2 in structure A (especially 7) is essentially due only to the two methylthio groups. This gives an *ortho* shielding effect of approximately 0.2 ppm per methylthio group which is somewhat less than that reported for methoxy.[14a] One would also expect, for structure A, a deshielding of H-1 by approximately 1.2 ppm due to the combined effects of the *o*-sulfonyl and *o*-acetamido groups. The lesser observed shift from benzene of 0.3–0.4 ppm is attributable to a combination of *ortho* steric effects (lowering −M for AcNH and SO_2), *meta* shielding by the CH_3S groups, and electrical interaction of the *para* substituents.

Turning to structure B, assignment of the relative positions of H-1 and H-2 is less clear. If the *meta* effect of methylsulfonyl is comparable with what is reported in the literature[16,14a] for halosulfonyl, then H-1 in **10a, 12,** and **13** should differ from that in structure A essentially by the elimination of shielding due to two *m* methylthio groups. This still requires an unusually large shielding from *m* methylthio of 0.4–0.45 ppm compared with that of methoxy[14a] of 0.1 ppm. However, accommodation of H-2 of **10a, 12,** and **13** by elimination of a shielding per methylthio group of 0.1–0.2 ppm and estimation of an *o* methylsulfonyl shielding of 0.8–0.9 is in good agreement with what one would expect from consideration of methoxy,[14a] chlorosulfonyl,[16] and nitro[16] substituents.

The *m* amino shielding parameters for H-2 of **10b** and **11** (compared with that of acetamido, **10a**) appears to be larger than reported[14a] and is undoubtedly complicated by steric effects and probably also by some hydrogen bonding in **10b** to the adjacent methylsulfonyl oxygens. Similarly, some *m* methylsulfonyl deshielding in **10b** and **11** would appear necessary to overcome the effect on H-1 of changing from acetamido (**7, 8,** and **9**) to amino (**10b** and **11**). This undoubtedly also involves some interaction of *ortho* substituents. However, it should be noted that the anomalies regarding these two parameters (*m* methylsulfonyl deshielding and *m* amino shielding) would be even more pronounced if H-1 and H-2 of **10b** and **11** were reversed. The position of H-1 in **10b** and **11** also may reflect the acidic nature of R'_2N as a vinylogous sulfonamide with the internal effect of the *o*- and *p* sulfone groups resembling closely that of acetylation of an amino function. The amino group of **10b,** when compared with **8,** using derived[13–16,18] and observed values from Table II, gives an *ortho* amino effect of 0.47 ppm which is lower than the 0.77 value previously reported[14a] for compounds without similar vinylogous interaction with, or hydrogen bonding to, electronegative substituents.

(16) T. Schaefer and W. G. Schneider, *J. Chem. Phys.*, **32**, 1218 (1960).
(17) C. Heathcock, *Can. J. Chem.*, **40**, 1865 (1962).
(18) See footnote *a*, Scheme I.

TABLE II

ESTIMATES OF SHIELDING CONSTANTS[a] FOR METHYLTHIO, METHYLSULFONYL, AND ACETAMIDO GROUPS IN DMSO

	ortho	*meta*
CH_3S	−0.2	−0.1 to −0.2
CH_3SO_2	0.8–0.9	<0.2[b]
CH_3CONH	0.1	0.0

[a] Expressed as δ (parts per million) less than tetramethylsilane (TMS) as an internal standard. [b] Probably nearer to 0.0 from literature values[16,14a] for chlorosulfonyl discussed in the text.

An interesting example of resonance effects and/or *ortho* hydrogen bonding is that of 2,4-dinitroaniline. Its ring protons have been measured in DMSO[19] and give a value for the proton *ortho* to the amino group of 7.13 ppm. Allowing for the effect of *m* nitro groups,[14a] this requires an *o* amino shielding of 0.6 ppm compared with a reported value of 0.77.[14a] Thus, similar interaction of methylsulfonyl and amino groups in **10b** and **11** is not unexpected.

Experimental Section[20]

***m*-Methylthionitrobenzene.**—*m*-Nitrophenyl thiocyanate[18] (40 g) in 250 ml of methanol was treated with a solution of 40 g of potassium hydroxide in 40 ml of water and the reaction mixture was heated under reflux for 35 min in an atmosphere of nitrogen. Water (200 ml) was added followed by 42 g of dimethyl sulfate over 30 min at 25–30°. Another 10 g of dimethyl sulfate was added at this temperature, 10 g more at 55–60° which produced a neutral reaction mixture, and a final 2–3 g along with equivalent 8.5 *N* potassium hydroxide portionwise. The reaction mixture was cooled and extracted with methylene chloride. Drying and removal of solvent gave 37.5 g of *m*-methylthionitrobenzene,[18] bp 119–124° (1.5 mm).

***m*-Methylthioacetanilide.**—*m*-Methylthionitrobenzene (37.5 g) was added to a solution of 160 g of stannous chloride in 200 ml of concentrated hydrochloric acid at 10° with stirring. The reaction mixture was exothermic to 35° and was warmed to 45°. The temperature continued to rise spontaneously to 85–90°. When the exothermic reaction abated, heating was continued for 20 min at 90–95°. Cooling and addition of ice gave a solid (10–15 g) which was treated with excess 8.5 *N* potassium hydroxide and extracted with methylene chloride to give 6.0 g of the amine after removal of solvent.

The filtrate was treated with 470 ml of 8.5 *N* potassium hydroxide and extracted with methylene chloride to give an additional 25.5 g of *m*-methylthioaniline;[4b] the ir and ultraviolet (uv) spectra were identical with those of the material described above.

To a solution of 12 g of the amine in 200 ml of water and 7.2 ml of concentrated hydrochloric acid was added 10 ml of acetic anhydride and a solution of 8.5 g of sodium acetate in 48 ml of water. Ice and water were added to give 13.86 g of *m*-methylthioacetanilide, mp 80–81.5° (lit. mp 75°[4a] and 78–78.5°[4b]).

Anal. Calcd for $C_9H_{11}NOS$: N, 7.73. Found: N, 7.91.

***m*-Methylsulfonylacetanilide.**—*m*-Methylthioacetanilide (1 g) was oxidized with perbenzoic acid in benzene to give, after re-

(19) Pmr data were determined in hexadeuteriodimethyl sulfoxide at 60 Mcps and are expressed as parts per million less than the field required for resonance of tetramethylsilane. Where the functional group is given, the intensity corresponds to the proper number of hydrogens.

(20) The author wishes to thank Dr. R. T. Dillon and the staff of the analytical department of G. D. Searle & Co. for the data reported. He is also grateful to Messrs. C. H. Yen and A. R. Zigman for preparation of additional quantities of certain of the compounds described herein and to Dr. Roy Bible for consultation regarding the pmr spectra.

crystallization from ethanol–ether, 680 mg of *m*-methylsulfonylacetanilide, mp 139–140° (lit. mp 137°[4a] and 136.8–137.5°[4b]).

Anal. Calcd for $C_9H_{11}NO_3S$: N, 6.57. Found: N, 6.37.

3-Methylthio-4-sulfamylacetanilide (1).—*m*-Methylthioacetanalide (1.0 g) was added portionwise to 5 ml of chlorosulfonic acid at room temperature. The reaction mixture was warmed to 45° over 10 min and then poured onto ice to give a paste from which the supernatant liquid was decanted. The residue was taken up in ethanol and the solution was saturated with ammonia and warmed for 15 min. The ethanol solution was adjusted to pH 6 by addition of dilute acid and was boiled down and filtered hot to give plates of mp 230–233°. This material was taken up in dilute potassium hydroxide and was reprecipitated by addition of hydrochloric acid. The solid was collected, washed, and dried to give 250 mg of very fine needles: mp 228–231°; $\lambda_{max}^{CHCl_3}$ 2.96, 3.22, 5.92, 7.51, 7.58, 8.62, 8.74 μ; δ[19] 2.16 (Ac), 2.57 (CH_3S), 7.36 (SO_2NH_2), 7.61, 7.66, 7.78, 7.81, 7.92, 7.95, 7.98, 8.12 (ArH multiplet), 10.23 (NH).

Anal. Calcd for $C_9H_{12}N_2O_3S_2$: C, 41.52; H, 4.65; N, 10.76. Found: C, 42.04; H, 4.70; N, 10.75.

The original ethanol filtrate gave a second crop of 80 mg, mp 222–227°, reduced to 50–60 mg by recrystallization from ethanol, mp 228–232°; the ir spectrum was identical with that of the material described above.

3-Methylsulfonyl-4-sulfamylacetanilide (2).—3-Methylthio-4-sulfamylacetanilide (270 mg) was dissolved in 2 ml of dimethylformamide and 5.5 ml of 0.7 *N* perbenzoic acid in benzene was added over 15 min. The reaction mixture was blown down on the steam bath and was triturated with 10 ml of benzene and 10 ml of water to give a solid product. Recrystallization from water and then from methanol gave 82.3 mg: mp 223.5–225.5°; λ_{max}^{KBr} 2.94, 2.98, 3.14, 3.24, 5.93, 7.25, 7.5, 7.63, 8.6, 8.75, 8.95 μ.

Anal. Calcd for $C_9H_{12}N_2O_5S_2$: N, 9.59. Found: N, 9.52.

2-Sulfamyl-4-chloroacetanilide and Its Pyrolysis.—This substance was prepared by acetylation of the amine[6b] with acetyl chloride in dioxane.[6a] From 300 mg there was obtained 218 mg of the desired product after recrystallization from methanol: mp 207–213.5° (lit.[7] mp 217–219°) [bubbling and resolidification of the melt (ring closure) began at 215–220°]; λ_{max}^{KBr} 2.96, 3.01, 3.12, 3.26, 5.91 μ; $\lambda_{max}^{CH_3OH}$ 251.5 mμ (ϵ 12,600), 295 (2410).

Anal. Calcd for $C_8H_9ClN_2SO_3$: C, 38.63; H, 3.65; N, 11.27. Found: C, 38.55; H, 3.66; N, 11.04.

Gradual heating of 43 mg of the material from 215 to 225° over 10 min in a nitrogen atmosphere gave, after trituration with hot methanol, 20 mg of 7-chloro-3-methyl-1,2,4-benzothiadiazine 1,1-dioxide, mp 324–327° (lit.[6b] mp 330–331°) which was identified by comparison (ir and uv) with an authentic sample.[6b]

Attempted Ring Closure of 3-Methylthio-4-sulfamylacetanilide (1).—3-Methylthio-4-sulfamylacetanilide (**1**, 74 mg) was heated gradually over 30 min from 235 to 250° under nitrogen. Trituration with methanol gave 28 mg of starting material, mp 228–230°, identified spectrally and by mixture melting point. The methanol filtrate was taken to dryness. The solid residue had mp 211–220° and ir and uv spectra identical with those of starting material.

2-Methylthio-5-chloronitrobenzene.[8a,b]—2,5-Dichloronitrobenzene (40 g) was added to a solution of 300 ml of methanol and 26 ml of 8.5 *N* potassium hydroxide which had been saturated with methyl mercaptan. An additional 23 ml of 8.5 *N* potassium hydroxide was added over 20 min while continuing the methyl mercaptan addition. Methanol (300 ml) was added and the reaction mixture was heated under reflux for 30 min. It was then poured onto ice and diluted to 3 l. to give 40.5 g of 2-methylthio-5-chloronitrobenzene, mp 135.5–136°.

Anal. Calcd for $C_6H_3Cl_2NO_2$: S, 15.75; N, 6.88. Found: S, 16.19; N, 6.94.

2-Methylthio-5-chloroacetanilide (4).—2-Methylthio-5-chloronitrobenzene (20 g) was added to a freshly prepared solution of 80 g of stannous chloride in 100 ml of concentrated hydrochloric acid. After slight warming, the reaction was quite exothermic and required external cooling. After this initial period, heating was continued at 95–100° for 10–15 min. The reaction mixture was cooled and ice and 160 g of potassium hydroxide were added alternately until the reaction mixture was basic. Extraction with methylene chloride gave 20 g of the crude amine.

The amine (17 g) in 50 ml of acetic acid and 5 ml of acetic anhydride was heated under reflux for 5 hr. The reaction mixture was diluted with water and the crude product was recrystallized from benzene–petroleum ether (bp 62–70°) to give 10.17 g of **4**, mp 96–97.5°.[21]

Anal. Calcd for $C_9H_{10}ClNOS$: S, 14.86; N, 6.50. Found: S, 14.90; N, 6.50.

Attempted Chlorosulfonation of 4. A.—Compound **4** (1 g) was added to 5 ml of chlorosulfonic acid at 5–10° and the reaction mixture was stirred for an additional 60 min at 40–45°. The reaction mixture was added gradually to ice and extracted with methylene chloride to give 0.52 g of a solid. The solid was triturated with 10 ml of concentrated aqueous ammonia solution and warmed to 50–60°. Cooling gave 370 mg of crude 5-chloro-2-methylbenzothiazole, mp 62–67°. Sublimation gave pure material of mp 68–70° (lit.[9] mp 68–69°) which was identified by mixture melting point with an authentic sample and comparison of ir spectra.

When the experiment was repeated without treatment with ammonia, the same product (46.5 mg from 340 mg) was isolated.

B.—Treatment of 2 g of **4** with chlorosulfonic acid for 10 min followed by warming at 50–55° for 1 hr gave 1.06 g, mp 143–157°. Recrystallization from methylene chloride–ether gave 200 mg of 2-methylsulfinyl-5-chloroacetanilide (**5**): mp 164–165°; $\lambda_{max}^{CHCl_3,CS_2}$ 3.1, 5.8, 7.1, 7.9, 9.5,[10] 9.7 μ;[10] $\delta_{max}^{CDCl_3}$ 2.18 (Ac), 2.89 (CH_3SO), 7.15 (multiplet, 2-ArH), 8.5 (doublet, ArH, J = 3–4 hz), 10.6 (NH).

Anal. Calcd for $C_9H_{10}ClNO_2S$: C, 46.7; H, 4.36; S, 13.87. Found: C, 46.51; H, 4.50; S, 14.12.

The residue obtained from the filtrate was essentially pure 5-chloro-2-methylbenzothiazole,[9] 530 mg, mp 66–70°.

2-Methylsulfonyl-5-chloroacetanilide (6).—Compound **4** (1 g) was dissolved in 10 ml of benzene and 28 ml of 0.94 *N* perbenzoic acid in benzene was added over 5 min. After stirring for another 15–20 min, the reaction mixture was diluted with benzene and was extracted with 5% sodium carbonate solution and water. The benzene was removed and the residue was recrystallized from acetone–ether to give 0.62 g of **6**, mp 161.5–162.5°.[22]

Anal. Calcd for $C_9H_{10}ClNO_3S$: N, 5.66; S, 12.94. Found: N, 5.52; S, 12.68.

2,4-Dimethylthio-5-sulfamylacetanilide (8).—2,4-Dimethylthioacetanilide [15 g, mp 111–113° (lit.[11] mp 114°)] was added over 15 min to 125 ml of ice-cold chlorosulfonic acid with stirring. The reaction mixture was stirred for an additional 10 min and was then quenched by dropwise addition to ice over 25 min. The aqueous mixture was extracted with methylene chloride, the solution was dried, and the solvent was evaporated to 100 ml in an evaporating dish. Concentrated ammonium hydroxide (300 ml) was added and the mixture was warmed with occasional stirring until the methylene chloride and most of the water had evaporated. After standing overnight, the residue was triturated with hot water and was cooled by addition of ice and filtered to give 14.2 g of 2,4-dimethylthio-5-sulfamylacetanilide: mp 193–195° (recrystallization from ethanol raised the melting point to 194–196.5° without change in the ir spectrum); λ_{max}^{KBr} 2.98, 5.98, 7.37, 7.53, 8.62 μ; $\lambda_{max}^{CH_3OH}$ 261.5 mμ (ϵ 27,600); δ 7.27 (SO_2NH_2), 9.40 (NH) (see also Table I).

Anal. Calcd for $C_{10}H_{14}N_2O_3S_3$: N, 9.15; S, 31.39. Found: N, 9.28; S, 31.14.

2,4-Dimethylthio-5-(N,N-dimethyl)sulfamylacetanilide (9).—2,4-Dimethylthioacetanilide[11] (510 mg) in 20 ml of dry, alcohol-free chloroform[3] was cooled in an ice bath and treated dropwise over 5 min with stirring with 3 ml of chlorosulfonic acid. After 20 min, the reaction mixture was poured onto ice and the solid which separated was collected and treated with 20 ml of cold dimethylamine in an evaporating dish. Trituration and evaporation of excess dimethylamine at room temperature gave a solid. The solid was taken up in methylene chloride–benzene and the solution was dried and clarified. On evaporation of the methylene chloride, crystallization gave 436 mg of 2,4-dimethylthio-5-(N,N-dimethyl)sulfamylacetanilide: mp 127–128.5°; $\lambda_{max}^{CHCl_3}$ 2.98, 3.32, 3.42, 5.88, and 6.42 μ; $\lambda_{max}^{CH_3OH}$ 264 mμ (ϵ 28,100) with shoulders at 277–285 and 310–322; δ 9.42 (NH) (see also Table I).

Anal. Calcd for $C_{12}H_{18}N_2O_3S_3$: C, 43.09; H, 5.42; N, 8.38. Found: C, 43.23; H, 5.42; N, 8.39.

2,4-Dimethylthio-5-chlorosulfonylacetanilide (7).—For isolation of **7**, the solid (or semisolid paste) which separated after quenching the reaction from the two-phase chlorosulfonation (above) was separated from the water and chloroform and was taken up in methylene chloride (difficultly soluble). The remaining aqueous layer was further extracted with methylene

(21) The 4-chloro isomer has been reported.[9]

(22) An isomer of **6** has been reported.[8a]

chloride and benzene and the combined organic extracts were dried (Na_2SO_4) and boiled down with benzene to induce crystallization. From 1.5 g of dimethylthioacetanilide, this gave 1.47 g, mp 183.5–184° dec. The original chloroform layer was extracted with cold water, dried, and blown down with nitrogen; crystallization from methylene chloride–benzene gave 150 mg, mp 184–186° dec, and dilution of the combined filtrates with *n*-pentane gave another 110 mg of sulfonyl halide, mp 183.5–184° dec. The first two crops were recrystallized from methylene chloride–cyclohexane to give 1.33 g, of fine, light yellow needles: mp 183.5–184° dec;[23] $\lambda_{max}^{CHCl_3}$ 2.9–2.95, 5.84 (5.88 sh), 6.92, 7.54, and 7.76 μ; $\lambda_{max}^{CH_3OH}$ 265.5 mμ (ϵ 23,500).

Anal. Calcd for $C_{10}H_{12}ClNO_3S_3$: C, 36.92; H, 3.72; Cl, 10.88. Found: C, 37.24; H, 3.90; Cl, 10.94.

2,4-Dimethylsulfonyl-5-sulfamylacetanilide (10a).—2,4-Dimethylthio-5-sulfamylacetanilide (2 g) was dissolved in hot acetic acid. The solution was stirred and cooled to approximately 60° and 150 ml of 0.28 *M* perbenzoic acid in benzene was added over 10 min with stirring. The reaction mixture was then heated for 40 min on the steam bath and cooled to give 1.9 g: mp 298–300° dec; λ_{max}^{KBr} 2.96, 2.99, 3.08, 5.84, 7.6, 8.5, 8.7 μ; δ 3.31 (NH), 7.0–8.5 (SO_2NH_2) (see also Table I).

Anal. Calcd for $C_{10}H_{14}N_2O_7S_3$: C, 32.92; H, 3.81; N, 7.56; S, 25.97. Found: C, 32.92; H, 4.07; N, 7.75; S, 25.79.

2,4-Dimethylsulfonyl-5-sulfamylaniline (10b).—2,4-Dimethylsulfonyl-5-sulfamylacetanilide (1.17 g) was suspended in 20 ml of ethanol and 3.0 ml of 8.5 *N* aqueous potassium hydroxide was added. The solution was stirred for 1.5 hr and then heated under reflux for 20 min. The reaction mixture was poured onto ice and neutralized with concentrated hydrochloric acid. The precipitate was collected and was recrystallized from pyridine–water to give 820 mg: mp 288–292° with slight decomposition; λ_{max}^{KBr} 2.86, 2.94, 3.05, 7.7, 8.55, 8.8 μ; $\lambda_{max}^{CH_3OH}$ 226 mμ (ϵ 27,600), 271 (17,650), 325 (5060); δ 7.2 (NH_2), 7.4 (SO_2NH_2) (see also Table I).

Anal. Calcd for $C_8H_{12}N_2O_6S_3$: N, 8.53; S, 29.29. Found: N, 8.31; S, 29.01.

N,N-Dimethyl(2,4-dimethylsulfonyl-5-sulfamyl)aniline (11).—2,4-Dimethylthio-5-sulfamylacetanilide (2 g), 20 ml of methanol, 5.0 ml of methyl iodide, and 0.64 ml (5% in excess of 1 equiv) of 8.5 *N* potassium hydroxide were heated under reflux with stirring for 20 min. At this point some of the starting material had not dissolved and the pH was 8–10. An additional 0.64 ml of base was added and the reaction mixture was heated under reflux for 40 min (pH 8). The reaction mixture was cooled, an additional 5.0 ml of methyl iodide was added, and two additional base treatments (0.64 ml each) with 40-min (to pH 6) and 25-min reflux periods, respectively, were made.

After cooling, dilution with water gave a product of mp 228–231°. Recrystallization from ethanol gave 300 mg: mp 231–233°; λ_{max}^{KBr} 2.85, 2.94, 7.66, 8.65 μ; $\lambda_{max}^{CH_3OH}$ 220 mμ (ϵ 20,850), 268 (18,500), 327 (5100); δ 7.36 (SO_2NH_2) (see also Table I). Resonance bands at δ 2.74 and 2.80 are in the correct position for the corresponding dimethylsulfamyl compounds. These bands and the amino band at δ 6.88 indicate approximately 15% of materials methylated on the sulfamyl nitrogen and lacking methylation on the amino nitrogen.

Anal. Calcd for $C_{10}H_{16}N_2O_6S_3$: N, 7.86; S, 26.97. Found: N, 7.51; S, 27.19.

The ethanol filtrate gave a second crop of 800 mg, mp 229–232°. The ir spectrum was identical with that of the first crop.

Oxidation of 7.—*m*-Chloroperbenzoic acid (550 mg, 10% excess) and 200 mg of **7** were dissolved in 3 ml of acetic acid. An initial vigorous reaction was followed by heating for 20 min at 65–70°. The reaction mixture was cooled and diluted with ice and water to give a solid, mp 157.5–168.5° dec. It was taken up in methylene chloride, dried, and crystallized by addition of ether to give 71 mg of **12**: mp 179.5–185° dec; $\lambda_{max}^{CH_3OH}$ 225 mμ (ϵ 27,400), 263 (14,300), 303 (6550); for δ values see Table I.

Anal. Calcd for $C_{10}H_{12}ClNO_7S_3$: C, 30.81; H, 3.10. Found: C, 31.12; H, 3.13.

2,4-Dimethylsulfonyl-5-(N,N-dimethyl)sulfamylacetanilide (13). A. From 9.—A solution of 150 mg of potassium permanganate (one oxygen equivalent in excess) in 3 ml of water was added dropwise to 150 mg of **9** in 2 ml of acetic acid with slight warming for the first half of the addition and then at room temperature. Ice and water were added to give a dark solid which was suspended in dilute aqueous sulfuric acid and treated with 500 mg of sodium bisulfite. This gave 50 mg of a tan precipitate, mp 128.5–129.5°, which was not further investigated.

The original filtrate was clarified by treatment with 100–200 mg of sodium bisulfite to give a clear solution which was combined with the filtrate from the tan precipitate. The solution was basified and extracted with chloroform to give a solid. The material was washed with methanol to give 46 mg, mp 233–236°. Recrystallization from dimethylformamide–water raised the melting point to 250–258° and, finally, recrystallization from pyridine–water gave 28 mg, mp 253–258° with softening from 243°.

On further standing a third crop of 68 mg, mp 228–228.5°, was obtained from the filtrate. Recrystallization from methylene chloride–methanol gave 42.5 mg of **13**: mp 226–227°; λ_{max}^{KBr} 2.99, 5.87, 6.3 (sh), 6.4, 6.7, 7.6 μ; $\lambda_{max}^{CH_3OH}$ 223.5 mμ (ϵ 27,700), 262 (ϵ 17,400), 304 (7450); for δ values, see Table I.

Anal. Calcd for $C_{12}H_{18}N_2O_7S_3$: C, 36.18; H, 4.55. Found: C, 36.41; H, 4.51.

B. From 12.—Trituration of 40 mg of **12** with 5–10 ml of cold dimethylamine gave a light yellow solid after evaporation of excess amine. This was dissolved in a mixture of methylene chloride, methanol, and water and the organic solvents were blown off with nitrogen. Standing overnight gave 26 mg of crystals, mp 200–233°. Attempts at further purification were unsuccessful. A crop of 4 mg, mp 184–216°, had an ir spectrum similar to that of **13** obtained in A (above), but with considerably diminished bands at 2.99 and 5.87 and additional absorption at 2.90 μ (NH_2), suggesting that hydrolysis to the free amine of **13** had occurred in part.

Registry No.—**1**, 19185-64-9; **2**, 19185-65-0; **4**, 19185-66-1; **5**, 19185-67-2; **6**, 19185-68-3; **7**, 19185-69-4; **8**, 19185-70-7; **9**, 19185-71-8; **10a**, 19185-72-9; **10b**, 19185-73-0; **11**, 19185-74-1; **12**, 19185-75-2; **13**, 19185-76-3; 2-sulfamyl-4-chloroacetanilide, 19185-77-4.

(23) This and the earlier samples resolidified immediately after very rapid decomposition (bubbling) to a light reddish brown amorphous solid. This material partially liquified further to *ca.* 220° showing further resolidification and darkening above 250°.