Anal. Calcd. for $C_7H_8N_4S$: C, 46.66; H, 4.48; N, 31.10; Found: C, 46.37; H, 4.45; N, 30.60.

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[CONTRIBUTION FROM THE KETTERING-MEYER LABORATORY,[1] SOUTHERN RESEARCH INSTITUTE]

Synthesis of Potential Anticancer Agents. XXI. Nitrosated Sulfonamides Related to Myleran

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A number of *N,N'*-polymethylenebis[*N*-nitrosomethanesulfonamide]'s and *N,N'*-dimethyl-*N,N'*-dinitrosoalkanedisulfonamides, structurally related to the anticancer agent Myleran and isomeric Myleran, respectively, have been prepared by the nitrosation of the corresponding bissulfonamides. In contrast, the nitrosation of simple *N*-substituted methanesulfonamides gave unstable products.

Current interest in the anticancer activity exhibited by 1-methyl-3-nitro-1-nitrosoguanidine[2,3] and particularly by 1-methyl-1-nitrosourea[3] against Leukemia L1210 in mice has focused attention on other *N*-nitroso compounds, such as *N*-nitrososulfonamides,[4] that have the common property of undergoing basic decomposition to give diazomethane. In the search for possible new anticancer agents containing a methyl-*N*-nitrosoamino group, a logical approach would appear to be the replacement of the functional group of known anticancer agents by a nitrosated function of the type described above. On the basis of structural similarity to the tetramethylene ester of methanesulfonic acid (Myleran), the synthesis and screening of certain bifunctional aliphatic nitrososulfonamides (Table I) were undertaken. Myleran belongs to a class of alkylating agents first reported as effective agents in the chemotherapy of neoplastic diseases by Haddow and Timmis[5] in 1953.

The following types of isomeric bisnitrososulfonamides have been prepared by the nitrosation of the corresponding bis-sulfonamides (see Table I): (1) *N,N'*-dimethyl-*N,N'*-dinitrosoalkanedisulfonamides (IIIa, b, c) and (2) *N,N'*-polymethylenebis-[*N*-nitrosomethanesulfonamide]'s (IVa,b,c). These nitrosations were performed by treating formic acid solutions of the bis-sulfonamides Ia, b, c and IIa, b, c with aqueous sodium nitrite solution. Pure samples of the bisnitrososulfonamides of each class are relatively stable solids when kept cool and dry; some have been stored for several months without appreciable decomposition. One mode of decomposition was observed when a sample of *N,N'*-tetramethylenebis[*N*-nitrosomethanesulfonamide] (VIb) was stored for six months at room temperature with no special precaution to keep it anhydrous: denitrosation to the corresponding bis-sulfonamide IIb occurred (*cf.* the thermal denitrosations of *N*-nitrosomethanesulfonanilide and *N*-nitroso-*p*-toluenesulfonanilide described by de Boer[6]). The liquid nitrosates derived from *N*-methyl[7]-, *N*-benzyl- and *N*-(*p*-chlorobenzyl)methanesulfonamides (VIa, b) are too unstable to permit isolation of pure products. The bisnitrososulfonamides IIIb and IVb were subjected to thermal decomposition in chlorobenzene by a procedure similar to that employed by de Boer in his study of the decomposition of *N*-methyl-[6] and other *N*-alkyl-*p*-toluenesulfonamides.[8] Compound IIIb evolved nitrogen smoothly at 90°, and relatively pure dimethyl 1,4-butanedisulfonate crystallized from the cooled reaction mixture, whereas IVb evolved nitrogen slowly at 85°, but the reaction product separated as an acidic brown oil, indicating that the tetramethylene ester of methanesulfonic acid apparently formed underwent excessive decomposition (m.p.[9] of pure Myleran, 116°).

The intermediate alkanedisulfonyl chlorides used to prepare the *N,N'*-dimethylalkanedisulfonamides Ia, b, c were also converted by treatment with sodium methoxide into the corresponding dimethyl

(1) Affiliated with Sloan-Kettering Institute. This work was supported by funds from the National Institutes of Health, Contract No. SA-43-ph-1740, and from the C. F. Kettering Foundation. Part XX, J. A. Montgomery and K. Hewson, *J. Am. Chem. Soc.*, **82**, 463 (1960).

(2) J. Leiter and M. A. Schneiderman, *Cancer Research*, 19, No. 3, Pt. 2, 31 (1959).

(3) Frank M. Schabel, Jr., *et al.*, Southern Research Institute, unpublished results.

(4) T. J. de Boer and H. J. Backer, *Rec. trav. chim.*, **73**, 229 (1954); *Org. Syntheses*, **34**, 96 (1954).

(5) A. Haddow and G. M. Timmis, *Lancet*, **264**, 207 (1953).

(6) T. J. de Boer, *Rec. trav. chim.*, **73**, 677 (1954).

(7) Method of preparation similar to that described by J. N. Baxter, J. Cymerman-Craig, and J. B. Willis, *J. Chem. Soc.*, 669 (1955) except that benzene was the solvent; yield, 80%; b.p., 132–134°/1 mm.

(8) D. H. Hey and T. J. de Boer, *Rec. trav. chim.*, **73**, 686 (1954).

(9) G. A. Haggis and L. N. Owen, *J. Chem. Soc.*, 389 (1953).

TABLE I

BISSULFONAMIDES, BISNITROSOSULFONAMIDES, BISSULFONATES AND METHANESULFONAMIDES

Compound (No.)	Yield, %	Recrystn. Solvent[a]	M.P.°, [b]	Formula	Carbon, % Calcd.	Carbon, % Found	Hydrogen, % Calcd.	Hydrogen, % Found
Bissulfonamides: A. $CH_3NHO_2S(CH_2)_nSO_2NHCH_3$								
n = 3(Ia)	67[c]	A	120	$C_5H_{14}N_2O_4S_2$	26.07	25.83	6.13	6.21
n = 4(Ib)	70[d]	A	177	$C_6H_{16}N_2O_4S_2$	29.49	29.54	6.60	6.22
n = 5(Ic)	77[d]	A	148	$C_7H_{18}N_2O_4S_2$	32.54	32.44	7.02	6.81
B. $CH_3SO_2NH(CH_2)_nNHO_2SCH_3$								
n = 3(IIa)	32[c]	B	115	$C_5H_{14}N_2O_4S_2$	26.07	26.35	6.13	6.00[e]
n = 4(IIb)	40[d]	B	134	$C_6H_{16}N_2O_4S_2$	29.49	29.49	6.60	6.60
n = 5(IIc)	44[c]	A	110	$C_7H_{18}N_2O_4S_2$	32.54	32.86	7.02	7.14[f]
Bisnitrososulfonamides: A. $CH_3N(NO)O_2S(CH_2)_nSO_2N(NO)CH_3$								
n = 3(IIIa)	52[d]	C	108[g]	$C_5H_{12}N_4O_6S_2$	20.83	21.09	4.20	4.28
n = 4(IIIb)	76[d]	D	142[g]	$C_6H_{14}N_4O_6S_2$	23.83	23.84	4.67	4.71[h]
n = 5(IIIc)	69[d]	C	87[g]	$C_7H_{16}N_4O_6S_2$	26.58	26.81	5.10	5.10
B. $CH_3SO_2N(NO)(CH_2)_nN(NO)O_2SCH_3$								
n = 3(IVa)	52[d]	B[i]	77[g]	$C_5H_{12}N_4O_6S_2$	20.83	20.99	4.20	4.50
n = 4(IVb)	65[d]	B	114[g]	$C_6H_{14}N_4O_6S_2$	23.83	24.13	4.67	4.71[j]
n = 5(IVc)	49[d]	C	94[g]	$C_7H_{16}N_4O_6S_2$	26.58	26.59	5.10	5.36
Bissulfonates: $CH_3OO_2S(CH)_nSO_2OCH_3$								
n = 3(Va)	46[d]	E, F	46–47[k]	$C_5H_{12}O_6S_2$	25.85	25.92	5.21	5.20
n = 4(Vb)	54[d]	B	90	$C_6H_{14}O_6S_2$	29.26	29.44	5.73	5.72
n = 5(Vc)	52[d]	B	51–52	$C_7H_{16}O_6S_2$	32.29	32.26	6.20	6.15
Methanesulfonamides: CH_3SO_2NRR'								
R = H, R′ = $C_6H_5CH_2$ (VIa)	84[d]	G	65	$C_8H_{11}NO_2S$	51.86	52.01	5.99	6.00[l]
R = H, R′ = p-$ClC_6H_4CH_2$ (VIb)	70[d]	A	134	$C_8H_{10}ClNO_2S$	43.73	43.39	4.59	4.50
R = R′ = p-$ClC_6H_4CH_2$ (VIc)	61[c]	H	124	$C_{15}H_{15}Cl_2NO_2S$	52.33	52.45	4.39	4.56
NRR′=-N⟨⟩S (VId)	25[c]	H	136	$C_5H_{11}NO_2S_2$	33.13	32.98	6.12	6.20

[a] A, water; B, methyl alcohol; C, tetrahydofuran–petroleum ether pair; D, tetrahydrofuran; E, propyl alcohol; F, ethyl ether; G, benzene–petroleum ether pair; H, isopropyl alcohol. [b] M.p.'s >60° determined on a Kofler Heizbank; <60°, in a capillary. [c] Based on a recrystallized product. [d] Based on crude product of m.p. within 4° of that of the pure product. [e] Calcd.: N, 12.17; found: N, 12.17. [f] Calcd.: N, 10.85; found: N, 10.68. [g] Melts with decomposition (gas evolution). [h] Calcd.: S, 21.21; found: S, 21.38. [i] Solvent C equally effective. [j] Calcd.: S, 21.21; found: S, 21.60. [k] Lit.[10] m.p. 45°. [l] Calcd.: N, 7.39; found: N, 7.69.

alkanedisulfonates Va, b, c, which are isomeric with Myleran or homologs of Myleran. Geiseler and Kuschmiers[10] recently reported the preparation of one of these esters, dimethyl 1,3-propanedisulfonate (Va), by the methylation of the disulfonic acid with diazomethane. These compounds are bifunctional alkylating agents of a type not previously screened for anticancer activity. Dimethyl 1,3-propanedisulfonate is somewhat water-soluble and hydrolyzes rather rapidly in aqueous solution.

The preparation of *N*-(*p*-chlorobenzyl)methanesulfonamide (VIc) was initially attempted by the *p*-chlorobenzylation of methanesulfonamide in dimethylformamide in the presence of potassium carbonate; the product isolated was the dialkylated product, *N*,*N*-di(*p*-chlorobenzyl)methanesulfonamide (VIc), which could be obtained in good yield from such a procedure designed to give dialkylation. When bis(2-chloroethyl) sulfide was the alkylating agent, cycloalkylation resulted to give 4-(methylsulfonyl)thiamorpholine (VIc), which can be recrystallized from dilute sodium hydroxide solution—a fact that substantiates the assigned structure.

Further substantiation of the structure of the cycloalkylated product VIc is found in a comparison of the characteristic infrared absorption bands of a selected group of the sulfonamides described in this paper (Table II): the absence of NH stretching absorption bands around 3200 cm.$^{-1}$ distinguishes an *N*,*N*-disubstituted sulfonamide from unsubstituted and *N*-monosubstituted sulfonamides. The broadness of the NH stretching band shown by methanesulfonamide is indicative of a much greater degree of hydrogen bonding than is the case with *N*-monosubstituted sulfonamides which show relatively sharp NH absorption bands around 3275 cm.$^{-1}$ The intense bands associated with the asymmetrical and symmetrical stretching vibrations of the sulfonyl group in sulfonamides are the strongest bands in the spectrum of each compound of Table II. These observations are in substantial agreement with

(10) G. Geiseler and R. Kuschmiers, *Chem. Ber.*, 91, 1881 (1958).

those previously reported concerning the spectra of methanesulfonamide and related compounds.[11]

TABLE II
CHARACTERISTIC INFRARED ABSORPTION BANDS OF SULFONAMIDES IN THE SOLID STATE[a]

Compound	νNH (cm.$^{-1}$)	νSO$_2$N (cm.$^{-1}$) Asymmetric S—O Stretching	νSO$_2$N (cm.$^{-1}$) Symmetric S—O Stretching
$CH_3SO_2NH_2$	3500–3000(m)[b]	1320(s)	1150(s)
Ic	3280, 3245 (m-s)	1320(s)	1120(s)
IIc	3280(m-s)	1300(s)	1140, 1125 (s)
VIc	...	1325(s)	1150(s)
VId	...	1325(s)	1150(s)

[a] Perkin-Elmer Model 21 spectrophotometer, sodium chloride prism, potassium bromide disk technique used. [b] (m), Medium; (s), strong; }, doublet.

Preparations of the compounds described in this paper are summarized in Table I; typical procedures are given in the Experimental section.

EXPERIMENTAL

1,5-Pentanedisulfonyl chloride.[12] This procedure is an adaptation of that described by Autenrieth and Bölli[13] for the preparation of 1,3-propanedisulfonyl chloride. A mixture of 20 g. (0.087 mole) of 1,5-dibromopentane, 24 g. (0.19 mole) of sodium sulfite and 45 ml. of water was heated under reflux for 7 hr. The resulting solution was filtered hot and evaporated to dryness under reduced pressure. The residue (41 g.), further dried at 115°, was ground fine and mixed with 45 g. (0.22 mole) of powdered phosphorus pentachloride. The mixture was heated cautiously at first until the initial vigorous reaction had subsided and then at about 110° for 30 min. (the liberated bromine was swept away from time to time in a stream of nitrogen). After being cooled, the semisolid reaction mixture was triturated well with a mixture of ice and water. The solid was collected, washed with water and air-dried: yield, 20 g. (85%); m.p., 63°.[15] The crude disulfonyl chloride was stored in a freezer until used. Treating an ethyl ether solution of a sample of crude disulfonyl chloride with calcium chloride and Norit and then adding petroleum ether gave a 67% recovery of tiny white needles, m.p. 66°[15] (lit.[14] m.p. 66°).

N,N'-Dimethyl-1,5-pentanedisulfonamide (Ic). Anhydrous methylamine was intermittently bubbled through a filtered solution of 6.9 g. (0.026 mole) of crude 1,5-pentanedisulfonyl chloride in 140 ml. of benzene, cooled initially to 6° in an ice-water bath, until the exothermic reaction was complete (the flow of amine was stopped each time the temperature of the mixture reached 15°). The benzene and excess amine were then removed under reduced pressure. The solid residue was triturated with cold water, and the insoluble bissulfonamide[16] was collected and dried *in vacuo;* yield, 5.1 g. (77%); m.p., 145°. Recrystallization from water gave an 80% recovery of fine colorless needles, m.p. 148° (analysis given in Table I).

N,N'-Tetramethylenebis[methanesulfonamide] (IIb). A solution of 6.50 g. (56.8 mmoles) of methanesulfonyl chloride in 15 ml. of benzene was added dropwise to a well stirred suspension of 7.85 g. (56.8 mmoles) of anhydrous potassium carbonate in a solution of 2.50 g. (28.4 mmoles) of 1,4-butanediamine[17] at such a rate that the temperature of the mixture did not rise above 45°. The mixture was heated under reflux for an hour and then allowed to cool. The solid that had separated was collected, washed with benzene, air-dried and then triturated with 50 ml. of water.[18] The undissolved bisulfonamide was collected, washed sparingly with water and air-dried: weight, 2.31 g.; m.p., 132°. Additional product of m.p. 130° was obtained by concentrating the combined filtrate and washings; total yield, 2.75 g. (40%). Recrystallization of the major crop from methyl alcohol gave the analytically pure product of Table I as small colorless needles, m.p. 134°.

N,N'-Dimethyl-N,N'-dinitroso-1,5-pentanedisulfonamide (IIIc). Crude *N,N'*-dimethyl-1,5-pentanedisulfonamide (1.6 g., 6.2 mmoles) was dissolved in 18 ml. of warm formic acid,[19] the solution clarified by filtration and the filtrate cooled to 4° with stirring. To the resulting suspension was added dropwise a solution of 1.1 g. (16 mmoles) of sodium nitrite in 3 ml. of water. Stirring was continued at 4° for an hour after the addition was complete, and the solid that had formed was collected and washed with water. Dilution of the formic acid filtrate with the aqueous washings precipitated more solid. The combined precipitates were then washed well with ice-cold 2% aqueous sodium hydroxide. The residual solid was collected, washed with water and dried *in vacuo* over phosphorus pentoxide: yield, 1.35 g. (69%); m.p., 89° dec. Recrystallization from tetrahydrofuran–petroleum ether gave 1.1 g. of shiny yellow crystals, m.p. 87° dec. Analyses are given in Table I.

N,N'-Trimethylenebis[N-nitrosomethanesulfonamide] (IVa). *N,N'*-Trimethylenebis[methanesulfonamide] (3.99 g., 17.3 mmoles) was dissolved in 15 ml. of warm formic acid, and the solution was cooled to 3°. A solution of 2.98 g. (43.1 mmoles) of sodium nitrite in 5 ml. of water was added dropwise to the well stirred sulfonamide solution at 4–7° over a period of 40 min. After three quarters of the nitrite solution had been added, a yellow solid precipitated; additional formic acid (5 ml.) was added to thin the suspension. Stirring of the cold mixture was continued for 1 hr. after the addition was complete. Water (28 ml.) was added to the suspension to complete the precipitation, and the yellow solid was col-

(11) J. N. Baxter, J. Cymerman-Craigs, and J. B. Willis, *J. Chem. Soc.*, 669 (1955).

(12) 1,3-Propanedisulfonyl chloride was prepared similarly: crude yield, 82%; fine white needles from an ethyl ether–petroleum ether pair (ethyl ether solution treated with calcium chloride and Norit), m.p. 46.5–47°;[15] (lit.[10,13,14] m.p. 48°, 45°). 1,4-Butanedisulfonyl chloride, m.p. 86°;[15] was prepared according to B. Helferich and H. Grünert, *Ber.*, **74B**, 1531 (1941).

(13) W. Autenrieth and E. Bölli, *Ber.*, **58B**, 2144 (1925).

(14) P. W. Clutterbuck and J. B. Cohen, *J. Chem. Soc.*, 121, 120 (1922).

(15) Kofler Heizbank.

(16) In preparations of Ia and Ib concentration of the aqueous filtrate gave additional crops of products.

(17) Aldrich Chemical Co., Inc., Milwaukee, Wis.

(18) Compound IIa was isolated from the benzene-insoluble solid by dissolving the solid in hot water, treating with Norit, adjusting *p*H to 6, evaporating to dryness *in vacuo*, extracting the residue with hot acetonitrile, evaporating the acetonitrile solution to dryness and recrystallizing the residue from methyl alcohol; yield 32% in 2 crops of colorless crystals, m.p. 115°. Compound IIc was isolated by stirring the benzene-insoluble solid in water, acidifying to *p*H 3 with hydrochloric acid and collecting the crude product that precipitated. The dried crude product, after being washed with boiling petroleum ether, was recrystallized from water; yield 44% of colorless plates, m.p. 110°.

(19) The ratio of formic acid to sulfonamide used in these nitrosations varied with solubility; a 25% excess of nitrite (usually in *ca.* 30% aqueous solution) per sulfonamide function was usually found expedient. The following formic acid ratios (ml. formic acid/g. bissulfonamide) were used in the nitrosations not described in detail: IIIa, 2.5; IIIb, 44; IVb, 4.1; IVc, 11.

lected, triturated with cold 2% aqueous sodium hydroxide, washed well with cold water and dried *in vacuo* over phosphorus pentoxide: yield, 2.60 g. (52%); m.p., 77° dec. Analytically pure pale yellow needles, m.p. 77° dec., were obtained by recrystallization of a small sample from methyl alcohol (see Table I). The major portion of the product was recrystallized from tetrahydrofuran–petroleum ether to give dense yellow crystals, m.p. 76–77° dec., in 80% recovery.

Dimethyl 1,4-butanedisulfonate (Vb). A methanolic solution of sodium methoxide (0.92 g., 40 mmoles, of sodium in 50 ml. of methyl alcohol) was added to a stirred solution of 5.1 g. (20 mmoles) of crude 1,4-butanedisulfonyl chloride in 50 ml. of methyl alcohol, cooled to 5° in an ice water bath, at such a rate that the temperature of the mixture did not rise above 15°. After the addition, the reaction mixture was stirred at room temperature for 1 hr. The white powder that had precipitated was collected by filtration, triturated with 25 ml. of cold water, and dried *in vacuo* over phosphorus pentoxide: weight, 1.37 g.; m.p., 88°. The methyl alcohol filtrate yielded a second crop, 0.85 g. of colorless plates, m.p. 86°. An additional 0.44 g. of colorless plates, m.p. 90°, was obtained by evaporating the above filtrate to dryness *in vacuo*, triturating the residue with cold water and recrystallizing the insoluble material from methyl alcohol: total yield, 2.66 g. (54%).[20] Recrystallization of the first crop from 25 ml. of methyl alcohol gave the analytically pure sample of Table I as shiny colorless plates, m.p. 90°, in 80% recovery.

N-Benzylmethanesulfonamide (VIa).[21] A solution of 10.7 g. (0.093 mole) of methanesulfonyl chloride in 50 ml. of benzene was added dropwise to a well stirred solution of 30 g. (0.28 mole) of benzylamine at such a rate that the temperature did not rise above 37°, addition time *ca.* 2.5 hr. The mixture was stirred for an additional half hour, allowed to stand overnight, then heated under reflux for *ca.* 1 hr. and cooled. The precipitated benzylamine hydrochloride was removed by filtration, and the solvent evaporated from the filtrate under reduced pressure. The oily residue was treated with 175 ml. of water, and the resulting mixture acidified to *p*H 1 with hydrochloric acid. The solid that formed was collected, washed with water and dried: yield, 13.5 g.; m.p., 64°. Additional crops (2.0 g.) melting in the range 64 to 66° were obtained when the filtrates were refrigerated; total yield, 84%. Recrystallization of the combined crops from benzene–petroleum ether gave 11.7 g. of colorless platelets, m.p. 65° (analysis given in Table I.)

N,N-Di(p-chlorobenzyl)methanesulfonamide (VIc). α,*p*-Dichlorotoluene (7.00 g., 43.5 mmoles) was added to a well stirred mixture of 2.00 g. (21.0 mmoles) of methanesulfonamide,[22] 6.00 g. (43.5 mmoles) of anhydrous potassium carbonate and 20 ml. of dimethylformamide. The mixture was heated at 100° for 1 hr., then cooled and poured into 100 ml. of water. The suspension (*p*H 9) was chilled and the white solid that had formed was collected, washed with water, and dried *in vacuo* over phosphorus pentoxide: yield, 4.42 g. (61%); m.p., 122°. Recrystallization from 35 ml. of isopropyl alcohol gave 3.55 g. of colorless needles, m.p. 124°, analysis of which is recorded in Table I.

4-(Methylsulfonyl)thiamorpholine (VId). To a well stirred mixture of 1.80 g. (19.0 mmoles) of methanesulfonamide,[22] 5.25 g. (38.0 mmoles) of anhydrous potassium carbonate and 15 ml. of dimethylformamide was added all at once 2.5 ml. (19 mmoles) of bis(2-chloroethyl) sulfide.[23] The mixture was heated at 100–110° for 2 hr., then cooled and poured into 25 ml. of water. The viscous semisolid that separated hardened when chilled, and was collected and washed with ethyl ether. The tan residue, after trituration with 2% aqueous sodium hydroxide solution, weighed 0.44 g., m.p. 131°. Recrystallization from isopropyl alcohol (after treatment with Norit) gave 0.24 g. of white platelets, m.p. 136° (analysis given in Table I).

The aqueous dimethylformamide filtrate was extracted with ethyl ether and the ethereal layer was combined with the above ether washings. Evaporations of the solvent left an orange oil in which long needles formed. These were collected, triturated with 2% sodium hydroxide solution, and recrystallized from isopropyl alcohol (to which the filtrate from the first recrystallization had been added) with Norit treatment: 0.40 g. of white platelets, m.p. 134°. Additional product (0.24 g., m.p. 134°) was obtained from the original alkaline extract by adjusting the *p*H to 7, evaporating to dryness, redissolving the residue in 10 ml. of water, acidifying to *p*H 3, and extracting the precipitate that formed with hot isopropyl alcohol. Total yield was 0.86 g. (25%).

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(20) Compound Va was recovered from the methyl alcohol filtrate by evaporating under reduced pressure to a small volume, then adding small volumes of water and ethyl ether with cooling. The crude crystals thus obtained were triturated sparingly with cold water and recrystallized. Compound Vc was similarly isolated by adding ethyl ether to the concentrated methyl alcohol suspension, triturating the crystals thus obtained with water and recrystallizing from methyl alcohol to give colorless platelets. In subsequent preparations of these sulfonates, the use of an excess of sodium up to 10% appeared to stabilize the esters during the work-up.

(21) *N*-(*p*-Chlorobenzyl)methanesulfonamide (VIc) was prepared similarly, except that appreciable product was recovered from the benzene filtrate by evaporation, treatment of the residue with water and acidification, extraction of the dried precipitate with hot acetonitrile, and finally extraction with warm sodium hydroxide solution, acidification, and recrystallization of the precipitate from isopropyl alcohol.

(22) Preparation was based on that of G. M. McGowan, *J. prakt. Chem.* [2], **30**, 281 (1884), except that the crude product was extracted with hot acetonitrile. Evaporation of the solvent gave methanesulfonamide, m.p. 92°, in 90% yield. Duguet, *Rec. trav. chim.*, **21**, 75 (1902), reported m.p. 90°.

(23) A. M. Reeves and S. Love, *Science*, **107**, 204 (1948).