[Contribution from the Procter & Gamble Co., Miami Valley Laboratories]

Syntheses and Facile Cleavage of Five-Membered Ring Sultams[1]

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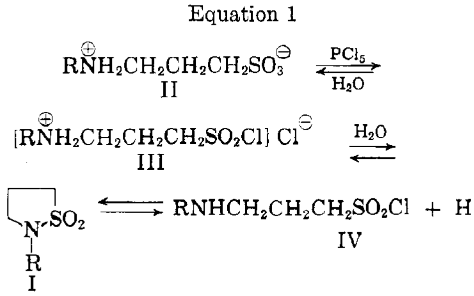
Five-membered *N*-alkylsultams (I), prepared from the corresponding *N*-alkylpropane sultaines, $R\overset{\oplus}{N}H_2CH_2CH_2CH_2SO_3^{\ominus}$ (II) or 3-bromopropanesulfonamides, $BrCH_2CH_2CH_2SO_2NHR$ (VII), were cleaved rapidly, at room temperature and below, by methanolic or ethereal hydrogen bromide or hydrogen chloride solution, and at 118° by acetic acid. In methanol or acetic acid the products of sultam cleavage were the corresponding sultaines (II, 60–80% yields), while in ether the amine hydrohalide salts $[R\overset{\oplus}{N}H_2CH_2CH_2CH_2SO_2A]A^{\ominus}$ (A = Br or Cl) were obtained in 81–98% yields. In contrast, a series of acyclic sulfonamides was unaffected under the same acid conditions. The mechanism of the cleavage and the facility of the reaction are discussed.

Cyclic sulfonamides, commonly termed sultams by analogy to the name lactam for cyclic carboxyamides, have seen widespread application as therapeutical agents.[2a] Most of the attention has centered on aromatic sultams,[2b] although recently the synthesis of a number of aliphatic sultams[2b] has appeared.[3-9] Virtually no information has been published on the chemical reactivity of the latter class of compounds. This paper describes the syntheses of some *N*-acyl, *N*-aryl, and *N*-alkyl-substituted five-membered sultams (I) and the surprisingly facile cleavage of these compounds with acid.

Preparation of sultams. Common procedures for preparing sultams include (1) thermal or base-catalyzed cyclization of γ- or δ-halogen, hydroxy, alkoxy or acetoxy substituted alkane sulfonamides,[3-9] (2) light-catalyzed sulfochlorination of primary aliphatic amine hydrochlorides followed by cyclization with base and subsequent *N*-alkylation with an alkyl halide,[3-10] (3) dehydration of *N*-arylammonium alkane sulfonates,[6,7] and (4) in the specific instance of unsaturated sultams, the direct condensation at elevated temperatures of the corresponding sultones with ammonia or primary amines.[8]

We have found that best yields of five-membered sultams were obtained by trituration of the respective *N*-alkyl sultaines[11] (II) with phosphorus pentachloride at room temperature or below followed by work-up in water at 0–5°. Although the intermediate sulfonyl chloride was not isolated in this reaction, the mechanism undoubtedly involves

Equation 1



I, II, III, IV c, R = C_4H_9; d, R = $C_{10}H_{21}$; e, R = $C_{12}H_{25}$; f, R = $C_{18}H_{37}$; h, R = p-CH_3—C_6H_5; i, R = C_6H_5; j, R = p-NH_2—C_6H_5.

formation of the amine hydrochloride (III) which is rapidly deprotonated by water and cyclized to the corresponding sultam (Equation 1).

Although direct treatment of the sultaine with phosphorus pentachloride appears to be the simplest synthesis of sultams, preparation of the *N*-alkyl derivatives *via* the respective 3-bromopropane-1-sulfonamides (VII)[3] was investigated and found to be a preferred procedure for certain sultams. The 3-bromopropane sulfonamides (VII) were prepared from propane sultone as outlined in Equation 2. The 3-bromopropane sulfonyl chloride (VI) was prepared by triturating the corresponding potassium sulfonate (V) with phosphorus pentachloride at room temperature. Surprisingly, at temperatures above 110° the product decomposed rapidly with the elimination of

(1) Presented at the 139th Meeting of the American Chemical Society, St. Louis, Mo., March 1961.

(2)(a) Ahmed Mustafa, *Chem. Revs.*, **54**, 206 (1954). (b) Mustafa uses the term aromatic sultam to imply cyclic sulfonamides fused to an aromatic ring, such as benzylsultam or 1,8-naphthosultam. The term aliphatic sultam implies cyclic sulfonamides which are not fused to an aromatic ring, such as propane sultam (Ia).

(3) J. H. Helberger, G. Manecke, and H. H. Fischer, *Ann.*, **562**, 23 (1949).

(4) H. Feichtinger and H. Tummes, German Pat. **930,210** (July 11, 1955) [*Chem. Abstr.*, **50**, 8748 (1956)]; U. S. Pat. **2,783,198** (February 26, 1957); Brit. Pat. **786,059** (November 13, 1957); Ger. Pat. **930,209** (July 11, 1955).

(5) I. G. Farbenind. A.-G., Belg. Pat. **450,737** (June, 1943) [*Chem. Abstr.*, **42**, 209 (1948)].

(6) B. Helferich and R. Behnisch, U. S. Pat. **2,916,486** (December 8, 1959).

(7) W. Dirscherl, F. W. Weingarten, and K. Otto, *Ann.*, **588**, 200 (1954).

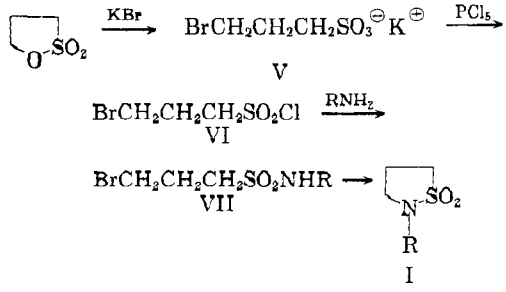
(8) B. Helferich and B. Talweg, U. S. Pat. **2,917,512** (December 15, 1959).

(9) B. Helferich and K. G. Kleh, *Ann.*, **635**, 91 (1960).

(10) H. Feichtinger, U. S. Pat. **2,806,056** (September 10, 1957).

(11) The term sultaine is used here to denote ammonium alkane sulfonates, $R\overset{\oplus}{N}H_2(CH_2)_nSO_3^{\ominus}$, analogous to the term betaine applied to the ammonium alkane carboxylates, $R\overset{\oplus}{N}H_2(CH_2)_nCO_2^{\ominus}$.

Equation 2



I, VII a, R = H; b, R = CH_3; e, R = $C_{12}H_{25}$; g, R = $C_{11}H_{23}CO$

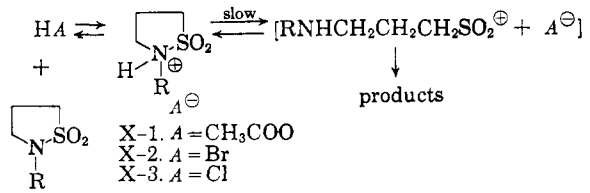
sulfur dioxide and formation of 1,3-dibromopropane (XV, 5%) 1-bromo-3-chloropropane (XIV, 11%), and 1,3-dichloropropane (XVI, 1%). The sulfonate itself was stable to heat but the sulfonyl chloride, which was formed rapidly at low temperatures, underwent decomposition catalyzed by potassium chloride and heat.[12] Although cyclization of the amide could be effected by pyrolysis at 200°, by catalysis with a tertiary amine, or by aqueous or methanolic alkali, best yields of *N*-alkyl substituted sultams invariably were obtained by refluxing a 1:1:1 molar mixture of sodium hydroxide-triethylamine-sulfonamide in methanol. Use of triethylamine alone for cyclization of the *N*-alkyl sulfonamides afforded a mixture of the quaternary salt $[(C_2H_5)_3\overset{\oplus}{N}CH_2CH_2CH_2SO_2NHR]Br^{\ominus}$ (XII) and sultam, while tributylphosphine, a stronger base and better nucleophile, afforded only the quaternary $[(n\text{-}C_4H_9)_3\overset{\oplus}{P}CH_2CH_2CH_2SO_2NHC_{12}H_{25}]\,Br^{\ominus}$ (XIII) in 83% yield. On the other hand, *N*-lauroyl propane sultam (Ig) was prepared with remarkable ease by cyclization of the sulfonamide (VIIg) with triethylamine without formation of the corresponding quaternary salt. Alkali could not be used for cyclization since the sultam Ig was readily cleaved by dilute base with subsequent formation of sodium laurate and propane sultam.

The *N*-arylsultams mentioned in this paper were prepared from the corresponding sultaines as outlined in Equation 1. However, *N*-*p*-nitrophenylsultam (Ik) could not be synthesized by either of the methods outlined in equation 1 or 2, but was obtained in good yield by oxidation of *N*-*p*-aminophenylsultam (Ij) with trifluoroperacetic acid.

Acid cleavage of sultams. The cleavage of sulfonamides, particularly aromatic sulfonamides, has been a major problem for the organic chemist since development of the Hinsberg method for separation of primary, secondary and tertiary amines. The cleavage of sulfonamides by acid normally occurs only under rather vigorous conditions, *e.g.* concentrated hydrochloric acid at 150–200°.[13] Feichtinger, however, reported that propane sultam and *N*-methyl propane sultam were cleaved by hydrogen chloride in benzene at 25°.[14] We have found that *N*-dodecylsultam (Ie) was cleaved rapidly at room temperature and below in methanolic hydrogen bromide or hydrogen chloride solution with the formation of the sultaine IIe in 80% and 61% yields, respectively. In ether, the products were the amine hydrohalides $[C_{12}H_{25}\overset{\oplus}{N}H_2CH_2CH_2CH_2SO_2Br]\,Br^{\ominus}$ (XI-2-e) (81%) or $[C_{12}H_{25}\overset{\oplus}{N}H_2CH_2CH_2CH_2SO_2Cl]\,Cl^{\ominus}$ (XI-3-e) (96%). Similarly, cleavage in glacial acetic acid at 118° afforded the sultaine IIe in 72% yield along with acetic anhydride. Attempts to cleave Ie with a weaker acid such as phenol gave no cleavage products. Propane sultam (Ia), *N*-butyl (Ic), *N*-decyl (Id), and *N*-octadecyl (If) propane sultams similarly were cleaved by hydrogen chloride, hydrogen bromide or acetic acid, but not by phenol. Results of the acid cleavage studies are listed in Table Ia. Since there are no reported instances in which relatively weak acids such as carboxylic acids cleave sulfonamides without catalysis by inorganic or Lewis acids, the facile cleavage of sultams seems quite surprising.

The mechanism of the acid cleavage can be depicted as proceeding through the conjugate acid of the sultam followed by dissociation into an intermediate amino alkane sulfonylonium ion, a mechanism proposed by Klamann and Hofbauer[15] for cleavage of aromatic sulfonamides (Equation 3). Although no direct proof exists for an intermediate conjugate acid of the type X, Klamann's work on aromatic sulfonamides suggested that protonation was required as an initial step in the rate-determining process.[15] If an intermediate

Equation 3



I. R = alkyl

(12) The thermal decomposition of alkyl sulfonyl chlorides is known and several rather contrasting mechanisms have been proposed for their mode of decomposition. (a) V. A. Rieche and E. Nanmann, *J. prakt. Chem.*, 9, 108 (1959). (b) H. F. Herbandson, W. S. Kelley and J. Versnel, *J. Am. Chem. Soc.*, 80, 3301 (1958). (c) A. P. Terent'ev and A. I. Gershenovich, *Zhur. Obshchei Khim.*, 23, 204 (1953). [*Chem. Abstr.*, 48, 2568 (1954)]. (d) F. S. Kipping and W. J. Pope, *J. Chem. Soc.*, 63, 550 (1893); 67, 357 (1895). (e) H. Limpricht and von Pechmann, *Chem. Ber.*, 6, 534 (1873). (f) H. Kolbe, *Ann.*, 122, 38 (1862).

(13) For an excellent review article on methods for cleavage of sulfonamides see S. Searles and S. Nukina, *Chem. Revs.*, 59, 1077 (1959).

(14) H. Feichtinger and Siegfried Puschof, German Patent 1,038,054 (September 4, 1958) [*Chem. Abstr.*, 54, 22367 (1960)].

(15) D. Klamann and G. Hofbauer, *Ann.*, 581, 182 (1953).

TABLE Ia

ACID CLEAVAGE OF SULTAMS

		Reagent				
		Ethereal HCl	Ethereal HBr	Methanolic HBr	Methanolic HCl	CH_3COOH
		% Yield of		% Yield of		
Sultam	R	$[RNH_2^{\oplus}CH_2CH_2CH_2SO_2A]A^{\ominus}$		$R\overset{\oplus}{N}H_2CH_2CH_2CH_2SO_4^{\ominus}$		
Ia	H	55	—			26
Ic	C_4H_9	89	—			96
Id	$C_{10}H_{21}$	95	—			79
Ie	$C_{12}H_{25}$	96	81	74	61	72
If	$C_{18}H_{37}$	98	—			86
Ih	p-CH_3—C_6H_5	78	93			
Ii	C_6H_5	77	91			
Ik	p-NO_2—C_6H_5	0	—			

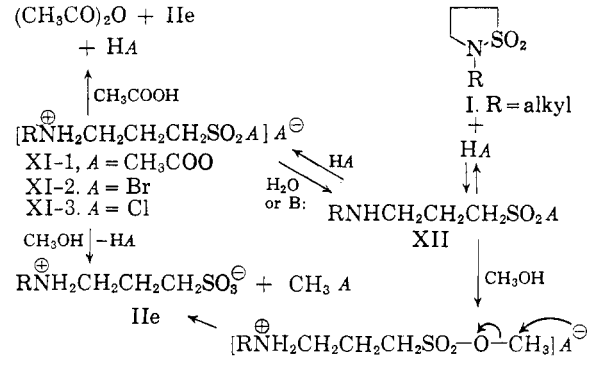
conjugate acid were involved prior to or during the rate determining process, then increasing the basicity of the sulfonamide would be expected to increase the rate of cleavage, while decreasing the basicity should hinder cleavage. The observed facts were that electron-withdrawing groups substituted either on the nitrogen or sulfur atom of the above sulfonamides did hinder cleavage while electron-donating groups facilitated cleavage. Thus, *p*-nitrophenylsulfonamides required much more drastic conditions for cleavage than the corresponding phenyl or *p*-methylphenylsulfonamides. The effect of the nitro-group decreased in the order *ortho*, *para*, *meta*.

Scission of the five-membered sultam would also require initial protonation of the sulfonamide nitrogen since the ease of cleavage was governed by the strength of the acid employed. Thus, the reaction proceeded rapidly at room temperature with etheral hydrogen bromide or hydrogen chloride, while temperatures of above 100° were required for cleavage of the sultam in acetic acid. No cleavage reaction took place in phenol even after three hours of treatment at 182°. Further evidence for initial protonation of the sultam nitrogen was given by a study of the relative ease of cleavage of the three sultams: *N*-*p*-nitrophenyl (Ik), *N*-*p*-tolyl (Ih), and *N*-phenylpropane sultam (Ii). The sultam Ik was not cleaved by anhydrous etheral hydrogen bromide while the latter two compounds were cleaved as readily as the *N*-alkyl substituted sultams.

The conversion of I to XI is an equilibrium process which appears to require two moles of acid, the first mole to cleave the sultam to an acyclic intermeidate XII, and the second mole to protonate the intermediate XII, thereby shifting the equilibrium to the products (Equation 4). Evidence for this statement is found in the fact that the amine hydrobromide $[C_{12}H_{25}\overset{\oplus}{N}H_2CH_2CH_2CH_2SO_2Br]\ Br^{\ominus}$ (XI-2-e), a stable compound when stored in the absence of water, was rapidly deprotonated by water with formation of the sultam Ie in 34% yield. This reaction is the same process observed in the preparation of I from alkyl sultaines with phosphorus pentachloride (Equation 1). A striking example of the ease with which XI-2-e is converted back to sultam is shown by the reaction of XI-2-e with butylamine. In this reaction the sultam Ie was obtained in 78% yield, while no product resulting from attack of butylamine on the sulfur atom was isolated. Use of only one mole of acid instead of an excess resulted in formation of approximately one-half the yield of product, indicating further that two moles of acid are required to drive the reaction to completion.

Whether the amine hydrohalide or the sultaine (II) is isolated in these reactions depends, of course, upon the reactivity of the solvent with the

Equation 4



intermediate amine hydrohalide XI or the sulfonyl intermediate XII.

The cleavage of sulfonamides by concentrated hydrogen bromide at elevated temperatures normally leads to oxidation-reduction products and not the sulfonyl bromide.[16] Cleavage of *N*-phenyl-*p*-tolylsulfonamide with hydrogen bromide in acetic acid, for example, afforded di(*p*-tolylsulfide), *p*-bromoaniline hydrobromide, and *N*-(2,4-dibromophenyl)-*p*-tolylsulfonamide.[16c] It was proposed that the disulfide in these reactions resulted *via* the sulfenyl bromide which in turn was generated from the sulfonyl bromide.[16a,b] In our work, however, the sultaines or sulfonyl bromides were obtained in 80–100% yields and were not accompanied by

TABLE Ib

ACID TREATMENT OF ACYCLIC SULFONAMIDES

Sulfonamide	R	R′	R″	% Recovery of Starting Material: Ethereal HCl	Methanolic HCl	Ethereal HBr	Methanolic HBr	CH_3COOH
XIIIa	CH_3	$C_{12}H_{25}$	CH_3	100	90	100	—	95
XIIIb	CH_3	C_2H_5	C_2H_5	100	—	60	—	90
XIIIc	CH_3	C_3H_7	C_3H_7	100	—	100	—	93
XIIId	CH_3	C_4H_9	C_4H_9	100	—	96	80	98
XIIIe	C_4H_9	$C_{12}H_{25}$	CH_3	100	—	94	95	80
XIIIf	C_4H_9	C_2H_5	C_2H_5	100	90	95	—	100

reduction products or bromine. Further reduction of sulfonyl bromide may have been prevented by the fact that the products invariably crystallized rapidly from solution.

In the only reported instances of acetolysis of sulfonamides, cleavage occurred only in the presence of added Lewis or inorganic acids.[13,17] When a catalyst was not employed, reaction occurred only at temperatures above 200°[18] but the products were the result of amide interchange and not acid cleavage.

$$RSO_2NR'_2 + R''COOH \rightleftharpoons RSO_3H + R''CONR'_2$$

However, no amide interchange products were isolated when the alkyl sultams were treated with acetic acid. Apparently the acetolysis of sultams proceeds by a normal acid-catalyzed mechanism with formation of a highly reactive mixed anhydride (XI-1). It is possible that cleavage occurs via an amide interchange reaction followed by immediate conversion of the amide $R''CONR'_2$ to sultaine II and acetic anhydride. Such a mechanism is unlikely, however, since disubstituted amides of the type $RCONR_2$ are known and, though readily hydrolyzed by aqueous acid or alkali, are quite stable to carboxylic acids at the temperatures involved in this reaction.[19]

Since no systematic study of the cleavage of acyclic sulfonamides has been reported, particularly under the extremely mild conditions employed here, we prepared a number of such compounds and subjected them to the same acid conditions which were so effective in cleaving the *N*-alkyl sultams. In no instance was an acyclic sulfonamide of the type $RSO_2NR'R''$ (XIII) cleaved. Starting material was recovered quantitatively except where operational processes rendered this difficult (see Table Ib).

Helferich and Kleh[9] reported recently that boiling 18% sulfuric acid does not cleave the six-membered-ring compound, *N*-4-acetamidophenylbutane sultam, but does cleave the corresponding five-membered *N*-4-acetamidophenyl propane sultam. This observation suggests that six-membered sultams behave like acyclic sulfonamides toward acid. This striking difference in behavior of the five-membered sultam and other sulfonamides is difficult to rationalize on the basis of current information. Apparently the five-membered sultam exhibits strain which is relieved as the sulfur-nitrogen bond is partially broken. Brown[20] has pointed out that reactions which proceed from a fully tetrahedral five-membered ring through a trigonal intermediate show enhanced rates due to decrease in bond oppositions.[21] The conjugate acid of the sultam probably exists as a fully tetrahedral structure. If we were to assume that the sulfonyl group changes its geometry either by rotation or hybridization as the sulfur-nitrogen bond begins to break, then relief of bond opposition could be extended to explain the sultam cleavages. This and other explanations for the relative ease of five-membered sultam cleavage remain entirely speculative at this stage.

EXPERIMENTAL

Melting points were taken in an Ace Glass Hershberg melting point bath using calibrated Anschuetz thermometers. Boiling points were taken on standard thermometers and are uncorrected. Infrared spectra were recorded on a Perkin-Elmer model 21 spectrophotometer or a Perkin-Elmer Infracord spectrophotometer. We are indebted to Mr. W. D. MacMillan and his associates for the microanalyses, to Dr. W. L. Courchene and Mr. Z. T. Pace for infrared interpretations and to Dr. T. J. Flautt and associates for NMR data and interpretations. The NMR spectra were obtained with a Varian high resolution instrument, model V4200B, at a frequency of 60 mc. The samples were

(16)(a) H. R. Snyder and H. C. Geller, *J. Am. Chem. Soc.*, **74**, 4864–6 (1952). (b) H. R. Snyder and R. E. Heckert, *J. Am. Chem. Soc.*, **74**, 2006 (1952). (c) D. I. Weisblat, B. J. Magerlein, and D. R. Myers, *J. Am. Chem. Soc.*, **75**, 3630 (1953). (d) H. Stetter and H. Hansmann, *Ber.*, **90**, 2728 (1957). (e) D. Klamann and G. Hofbauer, *Montasch Chem.*, **84**, 62 (1953). (f) H. Ohle, H. Friedeberg, and G. Haeseler, *Ber.*, **69**, 2311 (1936).

(17)(a) F. Ullmann, *Ann.*, **327**, 110 (1903). (b) G. Schroeter, *Angew. Chem.*, **39**, 1460 (1926).

(18)(a) W. F. Short and P. Oxley, Brit. Pat. **587,810** (May 6, 1947); [*Chem. Abstr.*, **43**, 689 (1949)]. (b) W. M. Schubert, *J. Am. Chem. Soc.*, **71**, 2639 (1949).

(19) C. D. Hurd and M. F. Dull, *J. Am. Chem. Soc.*, **54**, 2436 (1932).

(20) For pertinent references see H. C. Brown, J. H. Brewster, and H. Shechter, *J. Am. Chem. Soc.*, **76**, 467 (1954).

(21) K. S. Pitzer, *Science*, **101**, 672 (1945); J. E. Kilpatrick, K. S. Pitzer, and R. Spitzer, *J. Am. Chem. Soc.*, **69**, 2483 (1947).

run in carbon tetrachloride solution using tetramethylsilane as an internal reference. Calibration of the spectrogram abscissa was accomplished by the usual sideband technique. The chemical shift of tetramethylsilane was taken to be 10.00 p.p.m.[22]

Preparation of sultaines IIa. The sultaines were prepared from propane sultone[23] and the corresponding amines or ammonia in acetone or acetonitrile solution according to the method of Furukawa.[24] The sultaines, % yield from propane sultone, physical constants, elemental analyses and solvent used for recrystallization are listed in Table II. Characteristic infrared absorption for sultaines: 3.2–3.3 μ (NH stretch); 6.5 μ (NH bend); 8.0–8.6 and 9.5–9.7 μ ($-SO_3^{\ominus}$).

Preparation of 3-bromopropane-1-sulfonyl chloride (VI). A mixture of 201.5 g. (0.84 mole) of potassium 3-bromopropane-1-sulfonate (V), prepared from propane sultone and potassium bromide according to the method of Helberger,[3] was triturated with 200 g. (0.96 mole) of phosphorus pentachloride in a period of 3–4 min. After dilution with chloroform, trituration was continued for 15 min. when the mixture was diluted with ether to precipitate excess phosphorus pentachloride. The phosphorus pentachloride was removed by filtration through filter cell and the phosphorus oxychloride removed under reduced pressure. The product was distilled through a Nester and Faust 36-in. spinning band column to afford 125.5 g. (69%) of 3-bromopropane-1-sulonyl chloride (VI), b.p.$_{1.8}$ 85° (lit. b.p.$_{1.5}$ 96–100°[25]); infrared: 7.3 and 8.6 μ (SO_2).

Anal. Calcd. for $C_3H_6BrClSO_2$: C, 16.29; H, 2.71; S, 14.47; Cl, 16.00. Found: C, 16.38; H, 2.76; S, 14.48; Cl, 15.95.

In a separate run the reaction mixture was heated to 110° before removal of excess phosphorus pentachloride and potassium chloride. After removal of phosphorus oxychloride and distillation from a 250 × 25 mm. Vigreux column there was obtained from 659 g. (2.75 moles) of sulfonate, 11.2 g. (2%) of VI, b.p.$_{1.5}$ 80–90°, and 81.8 g. of material, b.p.$_{1.5}$ 25–40° indicated by gas chromatography to consist of 1-bromo-3-chloropropane (XIV) (76%; 11% yield), 1,3-dibromopropane (XV) (7%; 1% yield) and 1,3-dichloropropane (XVI) (17%; 5% yield). Identification of peaks was made by comparison with authentic samples of XIV, XV, and XVI, respectively, on a 10-ft., 1/4-in. diameter stainless steel column containing 30% succinic acid-triethylene glycol polymer on 60/80 mesh Chromosorb at 118° and 50 ml./min. helium flow rate. The products were isolated by fractional distillation through an 18-in. Nester and Faust semimicro spinning band column. Compound XVI had a b.p. of 120°$_{751}$, n_D^{25} 1.4531 (lit. b.p. 119.5°$_{756}$, n_D^{20} 1.4487).[26] The infrared spectrum of XVI and an authentic sample of 1,3-dichloropropane were identical in every respect. The NMR spectrum was consistent with the assigned structure: two bands, one consisting of two superimposed triplets centering at 6.49 p.p.m. (C_1 and C_3 protons) and a quintet at 7.86 p.p.m. (C_2 protons).

Compound XIV had a b.p. of 40°/11 mm., n_D^{25} 1.4828 (lit. b.p.$_{62}$ 68–70°,[27] n_D^{26} 1.4875.)[28] The infrared spectrum

TABLE II

SULTAINES $R\overset{\oplus}{N}H_2CH_2CH_2CH_2SO_3^{\ominus}$ (II)

R	Radical	Recrystallization Solvent	Yield, %	M.P.	C, %		H, %		S, %		N, %		O, %	
					Calcd.	Found	Calcd.	Found	Calcd.	Found	Calcd.	Found	Calcd.	Found
IIa	H	Ethanol	96	200 dec.	25.91	25.83	6.48	6.50	—	—	10.07	10.04	—	—
IIb	C_4H_9	Methanol-ether	59	155.2–156.8	43.05	41.86	8.58	8.54	16.41	16.61	7.19	6.98	24.74	24.64
IId	$C_{10}H_{21}$	Methanol	37	200 dec.	55.89	56.02	10.46	10.38	11.46	11.63	5.01	5.04	—	—
IIe	$C_{12}H_{25}$	Methanol	50	245–250 dec.	58.60	58.34	10.82	10.45	—	—	4.56	4.66	—	—
IIf	$C_{18}H_{37}$	Methanol	—	200 dec.	64.42	64.52	11.58	11.31	8.19	8.15	3.58	3.58	—	—
IIh	p-CH_3—C_6H_5	Methanol	42	270–272 dec.	52.39	52.45	6.60	6.72	—	—	6.11	5.88	—	—
IIi	C_6H_5	Methanol	39	275–277 dec.	50.10	50.32	6.08	5.99	—	—	6.50	6.45	—	—
IIj	p-NH_2—C_6H_5	Methanol	70	295 dec.	46.95	47.00	6.13	5.87	12.17	12.14	13.90	13.82	—	—

(22) Following the convention proposed by G. V. D. Tiers, *J. Phys. Chem.*, **62**, 1151 (1958).

(23) J. H. Helberger, *Ann.*, **588**, 76 (1954).

(24) K. Furukawa, T. Okada, I. Tamai, and R. Oda, *Kogyo Kagaku Zasshi*, **59**, 221 (1956) [*Chem. Abstr.*, **51**, 10362 (1957)]; Brit. Pat. **764,340**.

(25) R. Adams and J. B. Campbell, *J. Am. Chem. Soc.*, **72**, 128 (1950).

(26) A. I. Vogel, *J. Chem. Soc.*, 644 (1948).

(27) M. S. Kharasch and H. C. Brown, *J. Am. Chem. Soc.*, **61**, 2145 (1939).

(28) K. W. F. Kohlrausch and G. P. Ypsilanti, *Z. physik. Chem.* (B), **32**, 414 (1936).

TABLE III

SULFONAMIDES $BrCH_2CH_2CH_2SO_2NHR$ (VII)

R	Radical	Recrystallization Solvent	Yield, %	Phys. Const.	C, % Calcd.	C, % Found	H, % Calcd.	H, % Found	N, % Calcd.	N, % Found	S, % Calcd.	S, % Found	Br, % Calcd.	Br, % Found	O, % Calcd.	O, % Found
VIIa	H	Chloroform-ethanol	32	M.p. 59.0–60.2	17.82	18.22	3.99	3.78	6.93	6.95	15.87	15.82	39.51	38.98		
VIIc	CH_3		74	B.p. 130°/0.1 mm.[a]												
VIIe	$C_{12}H_{25}$	Ether-methanol	80	M.p. 79.4–80.6°	48.65	49.15	8.65	8.62	3.79	3.87	8.56	8.58	21.58	21.57	8.67	9.07

[a] Sulfonamide partially cyclized during distillation and was therefore not analyzed.

of XIV and an authentic sample of 1-chloro-3-bromopropane were identical in every respect. The NMR spectrum of XIV was consistent with the assigned structure: Two bands, one consisting of two overlapping triplets centering at 6.48 and 6.62 p.p.m. (C_1 and C_3 protons) and a quintet centered at 7.72 p.p.m. (C_2 protons).

Anal. Calcd. for C_3H_6BrCl: C, 22.90; H, 3.83; Br, 50.40. Found: C, 22.55; H, 4.18; Br, 50.60.

Compound XV had b.p. 52°/10 mm., $n_D^{25} = 1.5205$ (lit. b.p. 167.8–167.9°/760[29] $n_D^{25} = 1.5209$).[30] The infrared spectrum of XV and an authentic spectrum of 1,3-dibromopropane were identical in every respect. The NMR spectrum of XII was consistent with the assigned structure: Two bands, one consisting of two overlapping triplets centering at 6.63 p.p.m. and a quintet at 7.80 p.p.m.

Anal. Calcd. for $C_3H_6Br_2$: C, 17.84; H, 3.07; Br, 79.15. Found: C, 17.86; H, 3.01; Br, 78.70.

Preparation of N-alkyl-3-bromopropanesulfonamides (VII). In a typical run, to 30.0 g. (0.136 mole) of the sulfonyl chloride (VI) dissolved in 150 ml. of ether was added 50.4 g. (0.272 mole) of dodecylamine dissolved in ether. After 1 hr. of vigorous stirring, the dodecylamine hydrochloride which precipitated from solution was removed by filtration through filter-cell and the ether evaporated under reduced pressure. The residue was crystallized from ether-methanol to afford 40.0 g. (80%) of VIIe as lustrous plates, m.p. 79.4–80.6°. Further recrystallization from ether or ether-methanol gave no change in melting point. The yield, physical constants, elemental analyses, and solvent used for recrystallization of the *N*-alkylsulfonamides are listed in Table III. The infrared spectrum which was typical for the alkyl sulfonamides showed characteristic peaks: 3.0 μ (NH stretch); 7.65 μ and 8.75 μ (SO_2), absence of NH bending in 6.0–6.5μ region.

Because of the ease of displacement of the 3-bromo group with amines it was necessary to keep the reaction temperature low and to employ an exact 2:1 molar ratio of amine to sulfonyl chloride. In the case of the amide VIIa a clean product could be obtained only if tetrahydrofuran was used as solvent and the reaction temperature was maintained at 5° or below. In a typical run 26 g. (0.117 mole) of VI was added dropwise to a solution of 4.0 g. (0.234 mole) of ammonia in 450 ml. of tetrahydrofuran (freshly distilled over lithium aluminum hydride) maintained at 0–5° by means of an ice bath. All operations were performed under a nitrogen atmosphere with vigorous stirring. After addition of VI was complete, the ammonium chloride was removed by filtration, the tetrahydrofuran removed under reduced pressure and the residue (7.5 g.; 32%) recrystallized in colorless needles from ethanol-chloroform, m.p. 55–57.2°. The product was recrystallized from ethanol-chloroform until a constant m.p. of 59.0–60.2° was obtained.

Preparation of sultams I. The sultams, method of preparation, % yield from sultaine or 3-bromopropane sulfonamide, physical constants, solvent used for recrystallization and elemental analyses are listed in Table IV.

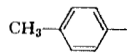
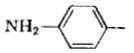
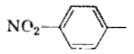
Method 1. Treatment of sultaine with phosphorus pentachloride. In a typical run, 3.3 g. (0.01 mole) of sultaine IIe and 4.0 g. (0.02 mole) of phosphorus pentachloride were triturated in a mortar for 5 min. at room temperature until a viscous oil replaced the solid mass. The mixture was diluted with ice water, extracted with chloroform, the chloroform layer washed with cold water and dried over magnesium sulfate. Evaporation of solvent under reduced pressure and recrystallization from petroleum ether (b.p. 30–60°) afforded 1.5 g. (50%) of the sultam Ie as colorless plates, m.p. 41–42°. Typical infrared spectrum: 7.7 μ and 8.8 μ (SO_2); absence of NH stretch at 3.0 μ.

(29) A. A. Ashdown, L. Harris, and R. T. Armstrong, *J. Am. Chem. Soc.*, 58, 850 (1936).

(30) C. P. Smyth and W. S. Walls, *J. Am. Chem. Soc.*, 54, 2266 (1932).

TABLE IV

Sultams  (I)

R	Radical	Method[c]	Recryst. Solvent	Yield, %	M.P.	B.P./1 mm.	n_D^{25}	C, % Calcd.	C, % Found	H, % Calcd.	H, % Found	N, % Calcd.	N, % Found	S, % Calcd.	S, % Found
Ia	H	4	—	25–50	—	180	1.4815	29.72	29.74	5.81	6.11	11.56	10.51	—	—
Ib	CH_3	4	Acetone	10											
Ib	CH_3	3	"	32	45–47			35.53	35.38	6.57	6.54	10.37	10.27	—	—
Ic	C_4H_9	1	—	35		135	1.4714	47.44	47.30	8.53	8.76	7.91	7.76	18.06	17.88
Id	$C_{10}H_{21}$	1	Petroleum-ether	50	26.5–27.5			59.74	59.93	10.41	10.91	5.36	5.37	12.25	12.39
Ie	$C_{12}H_{25}$	4[a]	Methanol	25[a]											
		4[b]	Acetone or	13	43.8–45										
		3	Petroleum-ether	89	43–44			62.25	62.37	10.80	10.84	4.84	4.88	11.06	10.57
		1	"	50	41–42										
		2	"	58	41–42.5										
If	$C_{18}H_{37}$	1	Ether	55	63.5–64.5			67.52	67.83	11.60	11.44	3.75	3.46	8.57	8.32
Ig	$C_{11}H_{23}CO$	5	Ether-ethanol	63	63–64			59.38	59.05	9.64	9.50	4.62	4.44	10.55	10.50
Ih		1	Acetone	55	91.4–92			56.86	56.53	6.20	6.14	6.63	6.61	15.15	15.47
I		1	"	60	120–121			54.82	55.02	5.62	5.73	7.10	7.01	16.23	16.51
Ij		1	Ethanol	23	153–155			50.94	50.92	5.70	5.79	13.20	12.87	15.08	15.05
Ik		6	Acetone	50	152–154			44.63	44.48	4.16	4.14	11.57	11.60	—	—

[a] Pyrolysis at atmospheric pressure; yield based on sultaine formed from resultant cleavage of sultam by acid. [b] Pyrolysis at 0.1 mm. vacuum. [c] Method 1: Treatment of sultaine II with phosphorus pentachloride. Method 2: Treatment of *N*-alkyl 3-bromopropanesulfonamides VII with 1 molar quantity of sodium hydroxide in methanol. Method 3: Treatment of VII with equimolar quantities of triethylamine-sodium hydroxide in methanol. Method 4: Pyrolysis of VII. Method 5: Treatment of VII with triethylamine. Method 6: Trifluoroperacetic acid oxidation of Ij.

TABLE V

AMMONIUM PROPANE SULFONYL CHLORIDE HYDROCHLORIDES (XI-3)

$[\overset{\oplus}{R}NH_2CH_2CH_2CH_2SO_2Cl]Cl^{\ominus}$

	R	M.P.	C, %		H, %		N, %		S, %	
			Calcd.	Found	Calcd.	Found	Calcd.	Found	Calcd.	Found
XI-3-a	H	143–144 dec.	18.56	18.92	4.64	4.61	7.22	7.22	16.55	17.02
XI-3-b	C_4H_9	129–130.2	33.57	33.85	6.58	7.07	5.55	5.59	12.80	13.30
XI-3-d	$C_{10}H_{21}$	116.6–119.2 dec.	46.70	46.71	8.57	8.57	4.20	4.22	9.59	9.99
XI-3-e	$C_{12}H_{25}$	123–127 dec.	49.72	49.96	9.18	8.96	3.86	3.83	8.83	8.90
XI-3-f	$C_{18}H_{37}$	125–135 dec.	56.28	56.88	10.15	10.39	3.14	3.17	7.18	7.04
XI-3-h	p-$CH_3C_6H_5$	93.6–94.8	42.25	42.76	5.31	5.37	4.93	4.82	11.27	11.14
XI-3-i	C_6H_5	111.8–113	40.00	40.12	4.85	4.50	5.19	5.07	11.85	12.14

Method 2. Treatment of 3-bromopropanesulfonamides with equimolar quantity of sodium hydroxide in methanol. To 2.0 g. (0.0054 mole) of VIIe dissolved in 20 ml. of methanol was added 0.215 g. (0.0054 mole) of powdered sodium hydroxide and the mixture refluxed for 2 hr. After removal of methanol under reduced pressure, the residue was extracted with ether, the ethereal mixture filtered to remove sodium bromide and the solvent removed under reduced pressure. Recrystallization from petroleum ether (b.p. 30–60°) afforded 1.6 g. (58%) of Ie, m.p. 41.0–42.5°.

Method 3. Treatment of 3-bromopropanesulfonamides with equimolar quantity of sodium hydroxide, and triethylamine in methanol. A mixture of 44.0 g. (0.108 mole) of VIIe in 400 ml. of ethanol containing 4.8 g. (0.108 mole) of sodium hydroxide and 12.5 g. (0.108 mole) of triethylamine was refluxed for 2 hr., then cooled, the solvent removed under reduced pressure and the residue recrystallized from petroleum ether to afford 30.5 g. (89%) of Ie, m.p. 42–43°. The product was recrystallized from petroleum ether for analysis, m.p. 43–44°.

Method 4. Pyrolysis of 3-bromopropanesulfonamides. (a) *Pyrolysis under reduced pressure.* Into a 10-ml. modified Hickman still was placed 5.0 g. (0.0135 mole) of VIIe and a pressure of 0.1 mm. maintained as the temperature of the pot was slowly raised and held at 200°. Decomposition, as noted by evolution of hydrogen bromide, ceased after about 2 hr., the hydrogen bromide which evolved being collected by means of Dry Ice and sodium hydroxide traps. The dark residue was decolorized with charcoal and recrystallized from acetone to yield 0.50 g. (13%) of sultam Ie, m.p. 43.8–45.0°.

(b) *Pyrolysis at atmospheric pressure.* The sulfonamide (VIIe) (2.0 g.) was stored for 16 hr. at 160°. The oily residue which resulted was dissolved in methanol and the colorless needles which precipitated were collected and recrystallized from petroleum ether-alcohol to afford 0.45 g. (25%) of sultaine IIe. The infrared spectrum was identical with IIe from reaction of propane sultone and dodecylamine.

Method 5. Reaction of N-dodecyl-3-bromopropane-1-sulfonamide with triethylamine. A solution of sulfonamide VIIe (1.0 g.; 0.0027 mole) in 20 ml. (14.58 g.) of triethylamine was heated at reflux for 2 hr. during which time a precipitate settled from solution. The waxy solid was collected by filtration and recrystallized from alcohol-ether to afford 0.114 g. (9%) of crystals, m.p. 91–95°. The infrared spectrum was consistent with the structure $[(C_2H_5)_3\overset{\oplus}{N}CH_2CH_2CH_2SO_2NHC_{12}H_{25}]Br^{\ominus}$ (XII): 3.0 μ (NH stretching); 7.6 and 8.8 μ (SO_2). When the reaction was carried out in an autoclave at 130–180° small yields of sultam resulted along with elimination products of XII.

Reaction of N-dodecyl-3-bromopropanesulfonamide with tributylphosphine. Formation of quaternary (XIII). To 7.7 g. (0.021 mole) of VIIe in a 100 ml. three-neck, round-bottom flask fitted with mechanical stirrer, condenser, dropping funnel and nitrogen system, was added 50 ml. of tri-*n*-butylphosphine and the mixture heated for 24 hr. at 150° with vigorous stirring. The mixture was cooled to room temperature, diluted with petroleum ether and the bottom layer, which consisted of the quaternary XIII with traces of tri-*n*-butylphosphine, was partitioned, then washed many times with petroleum ether. The petroleum ether was removed from the product under reduced pressure and the pure quaternary XIII was isolated as a colorless viscous liquid (6.5 g., 55%). Yields of 83% and 99% were obtained on two other runs starting with 2 g. and 30.3 g. of VIIe, respectively. The quaternary was insoluble in organic solvents but very soluble in water. Infrared spectrum: 3.2 μ (NH stretch); 7.7 and 8.7 μ (SO_2); 8.2 and 9.1 μ (P–C).

Anal. Calcd. for $C_{27}H_{58}SO_2NBr$: C, 56.70; H, 10.35; N, 2.44; S, 5.54; P, 5.39. Found: C, 56.88; H, 10.50; N, 2.31; S, 5.70; P, 5.72.

Preparation of N-lauroylpropane sultam Ig. To a solution of 1.61 g. (0.07 mole) of sodium dissolved in 100 ml. of absolute ethanol was added 14.10 g. (0.07 mole) of 3-bromopropane-1-sulfonamide and the mixture stirred vigorously at room temperature for 2 hr. (heating results in some cyclization to sultam). The ethanol was removed under reduced pressure and the resulting solid crushed to a fine powder and dried under reduced pressure. The infrared spectrum indicated the presence of the sodium salt of the sulfonamide and not sultam: SO_2 stretching at 8.0–8.5 (b) and 9.4 μ (s) (sultam infrared: SO_2 stretching at 7.6 and 8.8 μ).

To a suspension of 8.3 g. (0.058 mole) of the sodium salt of VIIe in 150 ml. of freshly distilled bis-2-ethoxyethyl ether (distilled over lithium aluminum hydride) contained in a Morton flask, fitted with reflux condenser, mechanical stirrer, dropping funnel and nitrogen system, was added dropwise a solution of 13.0 g. (0.060 mole) of lauroyl chloride (b.p. 132.4°/10 mm.) in 100 ml. of bis-2-ethoxyethyl ether. The mixture was refluxed for 4.5 hr. with vigorous stirring, then the bulk of the bis-2-ethoxyethyl ether (approximately 200 ml.) was removed under reduced pressure (b.p. 45°/1.8 mm.). The mixture was cooled to room temperature, diluted with water and extracted with ether. The ethereal solution was washed with water, dried and solvent evaporated under reduced pressure. The residue was recrystallized from ether to afford 5.0 g. (36%) of *N*-lauroyl-3-bromosulfonamide VIIg, m.p. 45–49. This compound was not analyzed but the infrared spectrum was consistent with the structure *N*-lauroyl-3-bromopropane-1-sulfonamide (VIIg). λ 3.0 μ (NH stretching); 5.95 μ (C=O stretching); 7.5–8.6 and 8.8 μ (SO_2 stretching). Attempted recrystallization of the product from ethanol afforded increasing quantities of sultam Ig, m.p. 63.8–64.6°, identical with Ig prepared below.

To 0.5 g. (0.0013 mole) of VIIg was added 10 ml. of triethylamine and this mixture refluxed for 16 hr. After removal of the amine under reduced pressure the residue was diluted with water, extracted with petroleum ether, the ethereal layer washed with cold dilute hydrochloric acid, cold 5% sodium bicarbonate solution, and water, dried over magnesium sulfate and evaporated to dryness. Recrystallization from ether afforded 0.25 g. (63%) of *N*-lauroylpropanesultam (Ig) as colorless plates, m.p. 55.0–59.5°. The product

was recrystallized from ether-alcohol for analysis, m.p. 63.8–64.6° (see Table III for analytical data); infrared spectrum: 5.92 (C=O); 7.4–7.6 and 8.7 μ (SO_2). When 0.100 g. of Ig was refluxed in 20 ml. of 10% sodium hydroxide for 2 hr., then acidified, the sultam Ig was converted quantitatively into lauric acid (structure confirmed by comparison of the infrared spectrum with authentic lauric acid) and propane sultam.

Preparation of N-p-nitrophenylpropanesultam (Ik). To 17.70 g. (0.164 mole) of *p*-phenylenediamine dissolved in 300 ml. of acetonitrile and placed in a 1-l. round-bottom, three-neck flask fitted with mechanical stirrer, reflux condenser and dropping funnel was added dropwise with stirring 20.0 g. (0.164 mole) of propane sultone dissolved in 200 ml. of acetonitrile over a period of 30 min. After 1 hr. of reflux the mixture was cooled to room temperature and the light purple solid was collected, washed with ether and recrystallized from ethanol to afford 26.0 g. (70%) of *N-p*-aminophenylammonium-3-propane-1-sulfonate (IIj) m.p. 295° dec. (see Table II for analyses). The sultaine was treated with phosphorus pentachloride as described in method 1 for preparation of sultams. From 24.0 g. (0.104 moles) of sultaine there was obtained 5.0 g. (23%) of *N-p*-aminophenylpropanesultam (Ij) as yellow prisms, m.p. 153–155° (see Table IV for analyses).

A solution of 2.35 g. (0.011 mole) of Ij dissolved in 100 ml. of warm methylene chloride was added dropwise over a period of 20 min. to a cold solution of trifluoroperacetic acid, prepared from 17.0 ml. of acetic anhydride and 2.7 ml. of 90% hydrogen peroxide according to the method of Emmons.[31] The reaction mixture, which turned dark red upon addition of the sultam Ij, was heated at reflux for 1 hr., then cooled to room temperature, diluted with water and extracted with methylene chloride. The combined methylene chloride layers were washed with 10% sodium carbonate and water, dried, and evaporated under reduced pressure to afford 1.28 g. (50%) of *N-p*-nitrophenylpropane sultam (Ik) as brownish yellow crystals from acetone, m.p. 153–154°; infrared spectrum: absence of NH stretch in 2.8–4.0 μ region; 6.25, 7.4 μ (strong bands, NO_2); 6.25, 6.6 μ (aromatic); 7.65, 8.7 μ (SO_2); 11.9 μ (*p*-disubstitution). (See Table IV for analyses.)

Cleavage of sultams with acids. The same general procedure was employed for cleavage of each of the sultams and is described in detail for *N*-dodecylsultam. Although propane sultam was insoluble in ether, this sultam was readily cleaved in heterogeneous suspension although stirring and a longer reaction period (1 hr.) were required. A 1:1 mixture of methylene chloride-ether served as an equally suitable solvent for the cleavage reactions. *p*-Nitrophenylsultam was insoluble in ether but soluble in the mixed solvents.

(a) *Methanolic hydrogen chloride.* Anhydrous hydrogen chloride was bubbled into a solution of 2.0 g. (0.069 mole) of Ie in 75 ml. of absolute methanol with stirring until the solution was saturated. Stirring was continued for 45 min. at room temperature and the methanol evaporated under reduced pressure to one-half volume then stored overnight. The colorless needles of sultaine IIe which precipitated were recrystallized in long needles from ethanol, m.p. 245–250° dec., 1.3 g. (61%). The infrared spectrum of the product and IIe prepared from propane sultone and dodecylamine were identical.

(b) *Methanolic hydrogen bromide.* The procedure was exactly the same as described above for the cleavage in methanolic hydrogen chloride. From 5.0 g. (0.017 mole) of Ie there was obtained 3.9 g. (74%) of sultaine IIe.

(c) *Ethereal hydrogen bromide. Formation of amine hydrobromide* XI-2-e. A solution of 2.0 g. (0.069 mole) of sultam Ie, dissolved in 100 ml. of anhydrous absolute ether and placed in a round-bottom flask fitted with mechanical stirrer and maintained under a nitrogen atmosphere, was saturated with dry hydrogen bromide. A precipitate began

(31) W. D. Emmons, *J. Am. Chem. Soc.*, **76**, 3470 (1954).

TABLE VI

SULFONAMIDES $RSO_2NR'R''$ (XIII)

Compound	R	R′	R″	Recryst. Solvent	M.P.	B.P./Mm.	n_D^{25}	Yield, %	C, %		H, %		N, %	
									Calcd.	Found	Calcd.	Found	Calcd.	Found
XIIIa	CH_3	$C_{12}H_{25}$	CH_3	Methanol	36–37	—	—	78	60.61	60.99	11.26	11.14	5.05	5.02
XIIIb	CH_3	C_2H_5	C_2H_5	—	—	56/0.1	1.4465	91	39.73	39.73	8.67	8.69	9.27	9.20
XIIIc	CH_3	C_3H_7	C_3H_7	—	—	75/0.5	1.4482	77	46.91	46.54	9.56	9.47	7.82	7.74
XIIId	CH_3	C_4H_9	C_4H_9	—	—	89/0.2	1.4503	96	52.15	51.90	10.21	10.25	6.76	6.76
XIIIe	C_4H_9	$C_{12}H_{25}$	CH_3	Methanol	27.8–28.4	—	—	81	63.92	63.94	11.65	11.58	4.38	4.23
XIIIf	C_4H_9	C_2H_5	C_2H_5	—	—	80/0.2	1.4502	86	49.72	49.63	9.91	9.81	7.25	7.24

to form almost immediately upon addition of hydrogen bromide and was collected, after 30 min. of rapid stirring, by filtration under a nitrogen atmosphere. The colorless flakes were washed well with ether and dried under vacuum for analysis to afford 2.5 g. (81%) of XI-2-e, m.p. 210–215°; infrared: 3.6–4.0 μ (NH stretch); 6.3 μ (NH bend); 7.48 and 8.7 μ (SO_2).

Anal. Calcd. for $C_{15}H_{33}NSO_2Br_2$: C, 40.00; H, 7.39; N, 3.10; S, 7.10; Br, 35.40. Found: C, 40.43; H, 7.64; N, 3.36; S, 7.29; Br, 35.38.

(d) *Ethereal hydrogen chloride. Formation of amine hydrochloride* XI-3-e. The procedure was the same as employed for cleavage of the sultam with ethereal hydrogen bromide. From 1.0 g. (0.0035 mole) of Ie there was obtained 1.2 g. (96%) of XI-3-e as colorless plates, m.p. 205° dec.; infrared: 3.6–4.0 μ (NH stretch); 6.3 μ (NH bend); 7.48 and 8.7 μ (SO_2). The analyses and physical constants of the sulfonyl chloride amine hydrochlorides formed are listed in Table V.

(e) *Excess acetic acid.* A solution of 2.0 g. (0.069 mole) of sultam Ie in 20 ml. of glacial acetic acid was heated at reflux for 1 hr., then was cooled to room temperature. The colorless needles which precipitated were collected to afford 1.2 g. (72%) of sultaine IIe, m.p. 245–250° dec. The infrared spectrum of the product was identical with sultaine IIe.

(f) *1:1 Molar quantity of acetic acid to sultam.* Treatment of 2.0 g. (0.0069 mole) of sultam Ie with 0.415 g. (0.0069 mole) of glacial acetic acid afforded 0.6 g. (29%) of sultaine IIe upon cooling of the reaction mixture. The crystals were washed well with ether and solvent removed from the mother liquors. An infrared spectrum of the residue indicated the presence of acetic anhydride: 5.5 and 5.7 μ.[32]

(g) *Phenol.* A solution of 6.5 g. (0.022 mole) of sultam Ie in 15.4 g. of freshly distilled phenol was heated at reflux for 3 hr. under a nitrogen atmosphere. Dilution of the reaction mixture with ether and removal of phenol under reduced pressure, b.p.$_{18}$ 88,° gave a recovery of 5.0 g. (77%) of unchanged sultam, m.p. 42.4–43.8° after recrystallization from petroleum ether.

Reaction of sulfonyl bromide amine hydrobromide XI-2-e *with water.* A mixture of 0.5 g. (0.001 mole) of XI-2-e and 20 ml. of water was stirred rapidly for 15 min. followed by extraction with ether. The ethereal layer was washed with water, dried, and evaporated to afford 0.29 g. (91%) of crude sultam. The infrared spectrum was identical with Ie. Recrystallization from petroleum ether afforded 0.11 g. (35%) of pure sultam, m.p. 42–43°.

Reaction of XI-2-e *with butylamine.* To 1.0 g. (0.002 mole) of XI-2-e was added dropwise 5 ml. (7.0 g., 0.7 mole) of *n*-butylamine. Reaction occurred immediately and the excess butylamine was removed by evaporation on the steam bath. The mixture was diluted with cold water and the precipitated solid recrystallized from petroleum ether to afford 0.5 g. (78%) of sultam Ie, m.p. 43–45°.

Preparation of the straight-chain aliphatic sulfonamides (XIII). The same general procedure was employed for preparation of the sulfonamides XIIIa-f; the preparation of *N*-methyl-*N*-dodecylsulfonamide is described below. To 17.4 g. (0.087 mole) of methyldodecylamine dissolved in 400 ml. of ether was added dropwise 5.0 g. (0.04 mole) of methane sulfonyl chloride dissolved in 75 ml. of ether and the mixture stirred for 1 hr. after addition of the sulfonyl chloride was complete. The precipitated amine hydrochloride was removed by filtration, the ether evaporated under reduced pressure and the residue recrystallized from methanol in long needles, m.p. 36–37°, 9.5 g. (78%). The sulfonamides prepared, solvent used for recrystallization, physical constants, yield from the corresponding alkane sulfonyl chloride, and elemental analyses are listed in Table VI. Yields are based upon recrystallized products or, in the instance of liquid products, upon material isolated after distillation through a Nester and Faust 24-in. spinning band column.

Attempted cleavage of aliphatic sulfonamides. Ethereal hydrogen bromide or hydrogen chloride. A solution of 2.0 g. of the sulfonamide in 40 ml. of anhydrous ether was saturated with dry hydrogen bromide or hydrogen chloride by bubbling the gas through the solution for a period of 1 hr. The solvent was removed under a stream of nitrogen and the recovered residue identified by comparison of physical constants and infrared spectrum with starting sulfonamide.

Methanolic hydrogen bromide or hydrogen chloride. The procedure was the same as the one employed for cleavage of the sultams in methanolic acid except that solvent was completely removed under reduced pressure and the residue identified in both instances as starting sulfonamide.

Acetic acid. A solution of 2.0 g. of the sulfonamide in 25 ml. of glacial acetic acid was heated at reflux for 16–24 hr. and the acetic acid removed by lyophilization. The residue was identified by infrared and physical constants. The sulfonamides treated, reaction conditions, and per cent recovery of starting material are listed in Table Ib. In no instance was any product other than starting sulfonamide isolated when simple straight-chain aliphatic sulfonamides were treated under the conditions described above.

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(32) L. J. Bellamy, *The Infra-red Spectra of Complex Molecules*, Wiley, New York, 1958, p. 127.