methanol and concentrated on a steam-bath under an air jet in an unsuccessful attempt to induce crystallization.

Chromatographic separation of a sample of the oily residue on alumina permitted the isolation of 1.02 g. of crystalline material (m.p. 158–160°). Recrystallization from benzene and ethanol afforded a solid of m.p. 160–161.5°. The yield, extrapolated from a plot of the weight of the eluted material *versus* fraction number, was 90% of the theoretical amount, while the material balance for the chromatograph was 91.5%.

Anal. Calcd. for $C_{30}H_{20}O$: C, 90.88; H, 5.09. Found: C, 91.21, 90.82; H, 5.28, 4.78.

The infrared spectrum of this substance, determined in Nujol mull, has bands assignable to *para*-substitution (848 cm.$^{-1}$), a mono-substituted benzene ring (698 cm.$^{-1}$) and a conjugated five-membered cyclic ketone (1717 cm.$^{-1}$). It is noteworthy that only one major peak was detected in a plot of the weight of the eluted material *versus* fraction number. Similarly the infrared spectrum of a sample of the oil which was subsequently chromatographed indicated the presence of only the conjugated carbonyl group (1726 cm.$^{-1}$, CS_2).

Acknowledgment.—The authors are indebted to the Office of Ordnance Research, U. S. Army (Contract No. DA-11-022-ORD-874), for partial support of this investigation.

URBANA, ILLINOIS

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, FACULTY OF SCIENCE, CAIRO UNIVERSITY]

The Chemistry of Sultams. II.[1] Chloromethylation and Bromination of Substituted 1,8-Naphthosultam. Reaction of 1,8-Naphthosultam with Organic Halides

BY AHMED MUSTAFA AND MOHAMED IBRAHIM ALI

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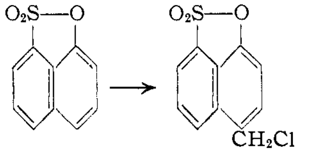
N-Arylsulfonyl derivatives of 1,8-naphthosultam (IIIa,b) undergo chloromethylation to yield the corresponding 4-chloromethyl derivatives (IVa,b), together with V in the case of IIIa. IVa is readily reduced to 4-methyl-N-phenylsulfonyl-1,8-naphthosultam, and both IVa,b condense with *p*-cresol and with 2,4-dimethylphenol to give the products VIIa-d (Table I), respectively. Whereas the bromination of N-methyl-1,8-naphthosultam leads to the formation of the monobromo derivative IXb and to the dibromo derivative (Xb), N-acetyl-1,8-naphthosultam leads mainly to the formation of the monobromo derivative IXc. Similarly, the bromination of the N-aroyl- and N-arylsulfonyl derivatives yields monobromo derivatives, presumably the 4-bromo compounds. The 2,4-dibromo derivatives (Xc,d) now have been prepared by acetylation and by benzoylation of 2,4-dibromo-1,8-naphthosultam. A number of new N-substituted 1,8-naphthosultams (XIa-h, XIIa-f) (Tables II and III) have been synthesized for pharmacological testing. Water-soluble salts of 1,8-naphthosultam with piperidine, benzylamine and cyclohexylamine now have been prepared.

(a) **Chloromethylation.**—Recently, it has been shown[2] that 1,8-naphthosultone (I) condenses with paraformaldehyde and hydrogen chloride in the presence of anhydrous zinc chloride to form 4-chloromethyl-1-naphthol-8-sulfonic acid sultone (II) (*cf.* A).

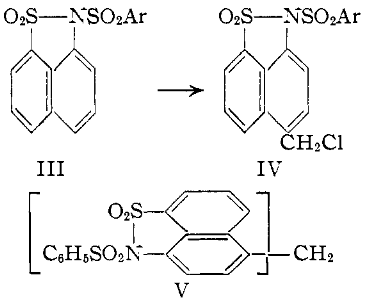


(A)

I II

We now have investigated the behavior of the N-arylsulfonyl derivatives of 1,8-naphthosultam, the nitrogen analog of I, toward chloromethylating agents.[3] Thus, when an acetic acid solution of N-phenylsulfonyl-1,8-naphthosultam (IIIa) is treated with paraformaldehyde, hydrogen chloride and zinc chloride under the same experimental conditions for the chloromethylation of I, 4-chloromethyl-N-phenylsulfonyl-1,8-naphthosultam (IVa), is obtained together with a high melting substance which analyzes correctly for a compound like V.[4] Similarly, 4-chloromethyl-N-(*p*-tolylsulfonyl)-1,8-naphthosultam (IVb) is obtained from N-(*p*-tolylsulfonyl)-1,8-naphthosultam (IIIb).

Although substitution may occur in more than one way, only one product was isolated. Fractional crystallization of the crude reaction product failed to reveal the presence of any other isomer. It seemed probable, by analogy with the behavior of I and with α-naphthyl ethers,[3,5] that the chloromethyl group in IV occupied the 4-position of the nucleus in preference to the 2-position.[1]



a, Ar = C_6H_5; b, Ar = $C_6H_4CH_3$-*p*

IVa,b are valuable intermediates for the production of 4-substituted derivatives of 1,8-naphthosultam. Thus, when IVa is treated with zinc dust and acetic acid, it is reduced readily to 4-methyl-N-phenylsulfonyl-1,8-naphthosultam (VI). Condensation of IVa and IVb with *p*-cresol and with 2,4-dimethylphenol leads to the formation of VIIa-d, respectively.

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(1) Part I, A. Mustafa and M. I. Ali, THIS JOURNAL, **77**, 4593 (1955).

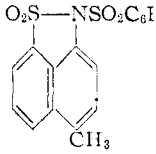
(2) G. Schetty, *Helv. Chim. Acta*, **32**, 24 (1949).

(3) *Cf.* A. Mustafa, *Chem. Revs.*, **54**, 195 (1954).

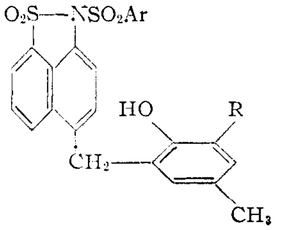
(4) R. Adams, "Organic Reactions," Vol. I, John Wiley and Sons, Inc., New York, N. Y., 1942, p. 65.

(5) There have been several reports of the reactions of 1,8-naphthosultam and its N-substituted derivatives, which show similarity to α-naphthol and α-naphthyl ethers, *e.g.*, the behavior of 1,8-naphthosultam toward chlorine (T. Zincke and G. Schürmann, *Ann.*, **412**, 718 (1916)), in condensation with isatin, isatin chloride and isatinanilide (P. Friedländer and L. Sander, *Ber.*, **57**, 637 (1924), W. König and E. Wagner, *ibid.*, **57**, 1056 (1924)), and in coupling with diazotized solutions (W. König and J. Keil, *ibid.*, **55**, 2149 (1922), W. König and K. Köhler, *ibid.*, **55**, 2139 (1922)).

(b) **Bromination.**—Whereas the action of bromine on an acetic acid solution of 1,8-naphthosultam (VIIIa) gives 2,4-dibromo-1,8-naphthosultam (Xa),[6,7] the action of the same reagent on a chloroform solution of N-acetyl-1,8-naphthosultam (VIIIc) leads to the formation of a monobromo derivative,[8] which is believed to be more likely N-acetyl-4-bromo-1,8-naphthosultam (IXc).



VI



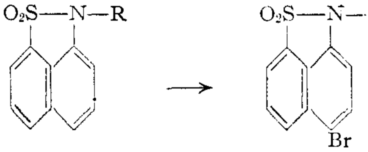
VIIa, Ar = C_6H_5; R = H
b, Ar = C_6H_5; R = CH_3
c, Ar = $C_6H_4CH_3$-*p*; R = H
d, Ar = $C_6H_4CH_3$-*p*; R = CH_3

We now have carried out the bromination of VIIIc after the procedure described by Dannerth,[6] and obtained a product of a melting point ranging between 164–167°. When VIIIc is allowed to react with an excess of bromine (up to 2 moles) in acetic acid at room temperature, an 80% yield of a product that melts at 180°, presumably IXc, is obtained. Fractional crystallization of the crude product failed to reveal the presence of any other isomer. It is not identical with N-acetyl-2,4-dibromo-1,8-naphthosultam (Xc), obtained by the action of acetic anhydride on Xa. When IXc is treated with hot aqueous sodium hydroxide, 4-bromo-1,8-naphthosultam (IXa) is obtained.

Similarly, the action of bromine on an acetic acid or a chloroform solution of N-aroyl and N-arylsulfonyl derivatives of 1,8-naphthosultam (VIIId-f) leads to the formation of N-benzoyl-4-bromo- (IXd), 4-bromo-N-phenylsulfonyl- (IXe) and 4-bromo-N-*p*-tolylsulfonyl-1,8- naphthosultam (IXf), respectively. IXd and IXe also have been obtained when a pyridine solution of IXa is treated with benzoyl chloride and with benzenesulfonyl chloride, respectively. The dibromo derivative of VIIId now has been obtained by the action of benzoyl chloride on Xa.

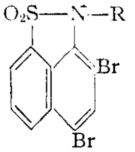
When an acetic acid solution of N-methyl-1,8-naphthosultam (VIIIb) is treated with bromine (one mole), a monobromo derivative presumably 4-bromo-N-methyl-1,8-naphthosultam (IXb), is obtained exclusively, whereas the treatment of VIIIb with an excess of bromine (two moles) leads to the formation of 2,4-dibromo-N-methyl-1,8-naphthosultam (Xb) in an almost quantitative yield. The latter compound, Xb, also is produced by the methylation of Xa with methyl sulfate in alkaline medium.

The behavior of VIIIb and VIIIc toward excess of bromine may simulate, in some respects, the behavior of N-alkylaniline and acetanilide toward the electrophilic attacking reagent, giving both *ortho* and *para* substitution in the first case and almost exclusively *para* substitution in the case of acetanilide. This, perhaps, may be attributed to steric hindrance[9]; meanwhile other factors,[10] *e.g.*, the permanent inductive effect of substituents[11] on the nitrogen atom are undoubtedly involved.



VIII
a, R = H
b, R = CH_3
c, R = $COCH_3$

IX
d, R = COC_6H_5
e, R = $SO_2C_6H_5$
f, R = $SO_2C_6H_4CH_3$-*p*



Xa, R = H
b, R = CH_3
c, R = $COCH_3$
d, R = COC_6H_5

(c) **Reaction with Organic Halides.**—In connection with a study of the pharmacological action of sulfur-containing compounds against bilharziasis,[12] a number of N-substituted derivatives of 1,8-naphthosultam now have been prepared. The imino group in VIIIa has assumed an acid nature, owing to the influence of the negative SO_2 group.[3] Thus, when a suspension of the sodium salt of VIIIa in ethyl alcohol is allowed to react with α-halo-esters (*e.g.*, ethyl chloroformate, ethyl chloroacetate and ethyl bromomalonate) with α-haloketones (*e.g.*, chloroacetone, phenacyl bromide and *p*-bromophenacyl bromide), with alkyl halides (*e.g.*, allyl bromide) and with aralkyl halides (*e.g.*, *p*-nitrobenzyl chloride), the corresponding N-substituted, 1,8-naphthosultam derivatives (XIa-h) are obtained, respectively. Similarly, the action of methylene iodide and ethylene bromide yields XIIa and XIIb, respectively.[13]

The reaction product with ethylene bromohydrin and VIIIa was isolated as its benzoyl derivative XI (R = $CH_2CH_2OCOC_6H_5$). XId forms an oxime readily when treated with hydroxylamine hydrochloride in the presence of sodium acetate.

Acid chlorides condense readily with 1,8-naphthosultam in presence of pyridine to give crystalline compounds, believed to have a structure like, for

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[6] F. Dannerth, THIS JOURNAL, **29**, 2322 (1907).

[7] T. Zincke and C. Julicher, *Ann.*, **411**, 195 (1916).

[8] Compare the action of bromine on N-acetyl-1-naphthylamine in carbon disulfide (P. Rother, *Ber.*, **4**, 850 (1871); A. Prager, *ibid.*, **18**, 2158 (1885); G. B. Crippa and G. Perroncito, *Gazz. chim. ital.*, **65**, 1250 (1935); *C. A.*, **30**, 5577 (1936)), and on N-benzenesulfonyl-1-naphthylamine in acetic acid (G. T. Morgan and W. Godden, *J. Chem. Soc.*, **97**, 1711 (1910)), leading to the formation of the corresponding 4-bromo derivatives.

[9] E. E. Royals, "Advanced Organic Chemistry," Prentice–Hall, Inc., New York, N. Y., 1954, p. 436.

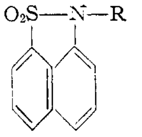
[10] See R. J. W. Le Fèvre, *J. Chem. Soc.*, 977, 980 (1933); 1501 (1934); S. N. Ganguly and R. J. W. Le Fèvre, *ibid.*, 848, 852 (1934).

[11] A. Lapworth and R. Robinson, *Mem. Proc. Manchester Lit. Phil. Soc.*, **72**, 43 (1927); *C. A.*, **23**, 2947 (1929).

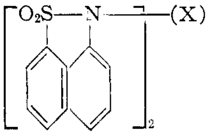
[12] A. Mustafa, A. H. E. Harhash and M. Kamel, THIS JOURNAL, **77**, 3860 (1955); A. Mustafa, W. Asker and M. E. E. Sobhy, *ibid.*, **77**, 5121 (1955).

[13] (a) 1,8-Naphthosultam shows similarity to α-naphthol toward the action of active halogen-containing compounds; *e.g.*, *cf.* the reactivity of α-naphthol toward ethylidene bromide (M. R. Fosse, *Bull. soc. chim.*, [3] **23**, 512 (1900)), ethylene bromide (G. Koelle, *Ber.*, **13**, 1953 (1880)) and chloroacetone (R. Stoermer, *Ann.*, **312**, 237 (1900); (b) *cf.* H. Stetter and E.-E. Roos, *Ber.*, **87**, 566 (1954); **88**, 1390 (1955)), for the interaction of arylsulfonyl derivatives of amines with dihalogen organic compounds.

example, XIIc. The reaction has been successively investigated with phosgene, oxalyl chloride, succinyl chloride and phthaloyl chloride, yielding XIIc-f, respectively. The reaction products are insoluble in aqueous sodium hydroxide and do not give any color with ferric chloride.

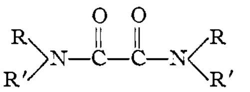


XIa, R = $COOC_2H_5$
b, R = $CH_2COOC_2H_5$
c, R = $CH(OOC_2H_5)_2$
d, R = CH_2COCH_3
e, R = $CH_2COC_6H_5$
f, R = $CH_2COC_6H_4Br$-*p*
g, R = $CH_2CH{:}CH_2$
h, R = $CH_2C_6H_4NO_2$-*p*



XIIa, X = CH_3
b, X = CH_2CH_2
c, X = CO
d, X = COCO
e, X = $COCH_2CH_2CO$
f, X = $C_6H_4(CO)_2$-*o*

Similarly, the action of oxalyl chloride on the monoarylsulfonyl derivatives of aromatic amines, *viz.*, benzenesulfonanilide, N-*p*-toluenesulfonyl-4-bromoaniline and N-*p*-toluenesulfonyl-1-naphthylamine, now has been investigated. The reaction products (XIIIa-c) form colorless crystals which are insoluble in aqueous sodium hydroxide.



$$(R)(R')N-C(=O)-C(=O)-N(R)(R')$$

XIIIa, R = C_6H_5; R' = $SO_2C_6H_5$
b, R = C_6H_4Br-*p*; R' = $SO_2C_6H_4CH_3$-*p*
c, R = 1-$C_{10}H_7$; R' = $SO_2C_6H_4CH_3$-*p*

To effect the solubility of the parent compound 1,8-naphthosultam (VIIIa) in water, we now have found that treatment of a benzene solution of VIIIa with piperidine, benzylamine and with cyclohexylamine leads to the formation of yellow water-soluble salts. VIIIa is recovered readily when these salts are treated with acids or with sodium hydroxide.[14] No such salt formation has been observed with aniline, methylaniline or with pyrrole.

Experimental

Chloromethylation of: (a) **N-Phenylsulfonyl-1,8-naphthosultam** (IIIa).—To a solution of 5 g. of IIIa[1] in 150 ml. of acetic acid saturated with hydrogen chloride (warming on a steam-bath may be necessary to bring IIIa into solution) was added 1.1 g. of paraformaldehyde and 1.1 g. of freshly fused zinc chloride. A stream of dry hydrogen chloride was allowed to pass into the reaction mixture at 80° for two hours, after which time the stream of the gas was stopped and the reaction mixture was kept at 80° for 18 hours. It was then poured into ice-cold water and the solid so obtained was collected, dried and treated with an excess of hot chloroform. The chloroform solution was filtered from the insoluble material (A), concentrated and a few ml. of petroleum ether (b.p. 60–80°) added, whereat colorless crystals (*ca.* 3.2 g.) separated. 4-Chloromethyl-N-phenylsulfonyl-1,8-naphthosultam (IVa) is soluble in acetic acid and chloroform, but difficultly soluble in benzene and petroleum ether. It was crystallized from chloroform, m.p. 200°.

Anal. Calcd. for $C_{17}H_{12}ClNO_4S_2$: C, 51.94; H, 3.05; Cl, 9.02; N, 3.56; S, 16.27. Found: C, 51.44; H, 3.16; Cl, 8.91; N, 3.56; S, 15.97.

The insoluble material (A) (*ca.* 0.9 g.) was crystallized from nitrobenzene, m.p. above 300°. V is difficultly soluble in acetic acid, benzene and chloroform. It does not give any color with sulfuric acid.

Anal. Calcd. for $C_{33}H_{22}N_2O_8S_4$: C, 56.41; H, 3.13; N, 3.98; S, 18.25. Found: C, 56.23; H, 2.94; N, 3.76; S, 18.08.

(b) **N-*p*-Tolylsulfonyl-1,8-naphthosultam** (IIIb).—In a similar manner, the chloromethylation of 5 g. of IIIb,[1] as described above, leads to the formation of colorless crystals (*ca.* 3.4 g.) of 4-chloromethyl-N-*p*-tolylsulfonyl-1,8-naphthosultam (IVb) from chloroform, m.p. 212–213°. It is soluble in chloroform and acetic acid, but difficultly soluble in ethyl alcohol, benzene and light petroleum.

Anal. Calcd. for $C_{18}H_{14}ClNO_4S_2$: C, 53.02; H, 3.44; Cl, 8.11; N, 3.44; S, 15.70. Found: C, 52.67; H, 3.22; Cl, 7.97; N, 3.34; S, 15.25.

Reaction of the Chloromethyl Derivatives with: (a) **Zinc Dust.**—To a solution of 1.2 g. of IVa in 50 ml. of glacial acetic acid was added 2 g. of zinc dust and the reaction mixture was refluxed for 18 hours. It was filtered while hot, and the filtrate was poured into ice-cold water. The solid, so obtained, was collected, washed with water, crystallized from chloroform and finally from xylene as colorless crystals (*ca.* 0.48 g.), m.p. 252°. 4-Methyl-N-phenylsulfonyl-1,8-naphthosultam (VI) is soluble in chloroform and acetic acid, difficultly soluble in petroleum ether.

Anal. Calcd. for $C_{17}H_{13}NO_4S_2$: C, 56.82; H, 3.62; N, 3.90; S, 17.82. Found: C, 56.82; H, 3.56; N, 4.30; S, 17.56.

(b) **Phenols.**—A mixture of 0.5 g. of each of N-phenylsulfonyl- (IVa) and of N-*p*-tolylsulfonyl-1,8-naphthosultam (IVb) and 2 g. of *p*-cresol was heated at 140–150° (bath temperature) for one hour. The viscous reaction product was cooled, triturated with cold dilute ethyl alcohol and the solid, so obtained, was thoroughly washed with water (*cf.* Table I).

When the condensation reaction was carried out with 2,4-dimethylphenol, the reaction mixture was heated for two hours at 140–150°.

The reaction products listed in Table I, are colorless; they are difficultly soluble in cold aqueous sodium hydroxide and do not develop any color when treated with sulfuric acid.

Action of Bromine on: (a) **N-Acetyl-1,8-naphthosultam** (VIIIc).—The bromination was carried out after the procedure described by Dannerth,[6] using 1 g. of VIIIc, 0.2 ml. (one mole) of bromine and 40 ml. of chloroform. The reaction mixture was left aside at room temperature for 24 hours. The solid residue that was obtained after the slow evaporation of the chloroform was crystallized from glacial acetic acid as colorless crystals, m.p. 164–167°.[15]

The above experiment was repeated using 2 g. of VIIIc, 0.6 ml. (2 moles) of bromine and 35 ml. of glacial acetic acid, and the reaction mixture was kept overnight at room temperature. The crystals that separated were collected and recrystallized from acetic acid, m.p. 180–181°, yield *ca.* 85%. N-Acetyl-4-bromo-1,8-naphthosultam (IXc) gives m.p. of about 170° when admixed with the product prepared after Dannerth; it (the former) depresses the m.p. of N-acetyl-2,4-dibromo-1,8-naphthosultam (Xc) (see below).

Anal. Calcd. for $C_{12}H_8BrNO_3S$: C, 44.16; H, 2.45; Br, 24.54; N, 4.29; S, 9.82. Found: C, 44.65; H, 2.47; Br, 24.40; N, 4.15; S, 9.80.

When the previous reaction mixture is heated, 2,4-dibromo-1,8-naphthosultam is formed as the main product (m.p. and mixed m.p.[6]).

4-Bromo-1,8-naphthosultam (IXa).—A suspension of 2 g. of IXc in 150 ml. of aqueous sodium hydroxide (5%) was heated until all the solid went into solution. The yellow solution thus obtained was filtered from any insoluble material and acidified with cold dilute hydrochloric acid. The solid that separated was collected, washed with cold water, dried and crystallized from xylene as colorless crystals (1.5 g.), m.p. 207–209°. 4-Bromo-1,8-naphthosultam (IXa) is soluble in chloroform, hot xylene, but sparingly soluble in petroleum ether (b.p. 80–100°).

Anal. Calcd. for $C_{10}H_6BrNO_2S$: C, 42.26; H, 2.11; Br, 28.17; N, 4.93; S, 11.27. Found: C, 42.57; H, 2.31; Br, 27.90; N, 4.91; S, 11.10.

Treatment of 1 g. of 2,4-dibromo-1,8-naphthosultam (Xa)[6] with 3 ml. of acetic anhydride, followed by bringing

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[14] 1,8-Naphthosultam forms yellow, difficultly soluble salts with barium hydroxide (*cf.* ref. 6).

[15] F. Dannerth gave m.p. 162° (*cf.* ref. 6, p. 1326).

TABLE I

4-SUBSTITUTED N-ARYLSULFONYL-1,8-NAPHTHOSULTAM DERIVATIVES (VII)

4-Substituted derivative	M.p.,[a] °C.	Yield, %	Solvent for crystn.[b]	Formula	Carbon, %		Hydrogen, %		Nitrogen, %		Sulfur, %	
					Calcd.	Found	Calcd.	Found	Calcd.	Found	Calcd.	Found
VIIa	194–195	76	A	$C_{24}H_{19}NO_5S_2$	61.93	61.44	4.09	4.01	3.01	2.96	13.76	13.35
VIIb	220–221	81	B	$C_{25}H_{21}NO_5S_2$	62.63	62.23	4.48	4.38	2.92	2.95	13.37	12.95
VIIc	188–189	74	C	$C_{25}H_{21}NO_5S_2$	62.63	62.18	4.48	4.40	2.92	2.74	13.37	13.04
VIId	167–169	68	C	$C_{26}H_{23}NO_5S_2$	63.30	62.87	4.67	4.87	2.84	3.08	12.98	12.56

[a] Melting points are uncorrected. [b] A, dilute ethyl alcohol; B, acetic acid; C, ethyl alcohol (95%).

TABLE II

N-SUBSTITUTED 1,8-NAPHTHOSULTAM DERIVATIVES (XI)

Deriv.	M.p.,[a] °C.	Yield, %	Solvent for crystn.[b]	Color with H_2SO_4	Formula	Carbon, %		Hydrogen, %		Nitrogen, %		Sulfur, %	
						Calcd.	Found	Calcd.	Found	Calcd.	Found	Calcd.	Found
XIa	164–165	84	A	No color	$C_{13}H_{11}NO_4S$	56.31	56.24	3.97	3.88	5.05	5.15	11.55	11.45
XIb	147–148	78	A	No color	$C_{14}H_{13}NO_4S$	57.73	57.48	4.47	4.40	4.81	4.77	10.99	11.12
XIc	121–122	81	A	Blue-green	$C_{17}H_{17}NO_6S$	56.17	56.19	4.68	4.45	3.86	3.81	8.81	8.85
XId	149–150	74	A	No color	$C_{13}H_{11}NO_3S$	59.99	59.57	4.23	4.30	5.38	5.45	12.30	11.65
XIe	180–181	68	B	Blue-green	$C_{18}H_{13}NO_3S$	66.88	67.16	4.02	4.17	4.33	4.20	9.91	9.58
XIf	230	72	B	Blue-green	$C_{18}H_{12}NO_3SBr$[c]	53.74	53.81	2.99	2.92	3.48	3.06	7.96	7.88
XIg	70–71	75	C	Pale brown	$C_{13}H_{11}NO_2S$	63.66	63.52	4.49	4.37	5.71	5.39	13.06	12.70
XIh	163–164	84	B	Blue-green	$C_{17}H_{12}N_2O_4S$	60.00	60.44	3.53	3.70	8.24	7.89	9.41	8.80

[a] Melting points are uncorrected. [b] A, ethyl alcohol (95%); B, acetic acid; C, ethyl alcohol (dilute). [c] Bromine: calcd. 19.90; found 19.53.

TABLE III

N-SUBSTITUTED 1,8-NAPHTHOSULTAM DERIVATIVES (XII)

Deriv.	M.p.,[a] °C.	Yield, %	Solvent for crystn.[b]	Color with H_2SO_4	Formula	Carbon, %		Hydrogen, %		Nitrogen, %		Sulfur, %	
						Calcd.	Found	Calcd.	Found	Calcd.	Found	Calcd.	Found
XIIa	276–278	81	A	Blue	$C_{21}H_{14}N_2O_4S_2$	59.71	59.82	3.32	3.10	6.63	6.55	15.17	14.76
XIIb	262–263	78	B	No color	$C_{22}H_{16}N_2O_4S_2$	60.54	59.90	3.67	3.81	6.42	6.25	14.68	14.90
XIIc	305 dec.	72	A	No color	$C_{21}H_{12}N_2O_5S_2$	57.80	57.88	2.75	2.83	6.42	6.80	14.68	15.20
XIId	Above 350	68	A	No color	$C_{22}H_{12}N_2O_6S_2$	56.89	56.64	2.59	2.56	6.03	5.70	13.79	13.45
XIIe	325 dec.	77	A	No color	$C_{24}H_{16}N_2O_6S_2$	58.53	58.52	3.25	3.47	5.69	5.45	13.01	12.72
XIIf	270 dec.	82	A	Yellow	$C_{28}H_{16}N_2O_6S_2$	62.23	62.58	2.96	2.81	5.19	5.04	11.85	11.80

[a] Melting points are uncorrected. [b] A, nitrobenzene; B, acetic acid.

the reaction mixture to boiling under reflux for 2 hours, then pouring into ice-cold water and crystallization of the solid, so obtained, from ethyl alcohol, gave colorless crystals (*ca.* 0.75 g.) of N-acetyl-2,4-dibromo-1,8-naphthosultam (Xc), m.p. 155–157°. It is soluble in hot benzene and chloroform. It gives a pale yellow color with concentrated sulfuric acid.

Anal. Calcd. for $C_{12}H_7Br_2NO_3S$: C, 35.56; H, 1.73; Br, 39.50; N, 3.46; S, 7.90. Found: C, 35.35; H, 1.53; Br, 39.40; N, 2.86; S, 7.85.

(b) **N-Benzoyl- (VIIId), N-Phenylsulfonyl- (VIIIe) and N-*p*-Tolylsulfonyl-1,8-naphthosultam (VIIIf).**—A solution of 0.05 mole of each of VIIId, VIIIe, and of VIIIf in warm glacial acetic acid (a large volume of the acid was needed to bring VIIIe and VIIIf into solution) was treated with 0.075 mole of bromine and the reaction mixture was kept overnight at room temperature. The crystals that separated were collected and worked out as follows.

N-Benzoyl-4-bromo-1,8-naphthosultam (IXd) forms colorless crystals from acetic acid, m.p. 174–175°, yield *ca.* 80%. It is soluble in chloroform and gives a yellow color with sulfuric acid.

Anal. Calcd. for $C_{17}H_{10}BrNO_3S$: C, 52.58; H, 2.58; Br, 20.62; N, 3.61; S, 8.25. Found: C, 52.25; H, 2.52; Br, 20.45; N, 4.04; S, 8.08.

4-Bromo-N-phenylsulfonyl-1,8-naphthosultam (IXe) crystallizes readily from acetic acid as colorless crystals, m.p. 253–255°, yield *ca.* 77%. It does not give any color with sulfuric acid.

Anal. Calcd. for $C_{16}H_{10}BrNO_4S_2$: C, 45.28; H, 2.36; Br, 18.87; N, 3.30; S, 15.10. Found: C, 45.78; H, 2.49; Br, 19.20; N, 3.20; S, 14.66.

4-Bromo-N-*p*-tolylsulfonyl-1,8-naphthosultam (IXf) forms colorless crystals from a mixture of chloroform and light petroleum (b.p. 50–60°), m.p. 250–251°, *ca.* 82%. It is difficultly soluble in acetic acid.

Anal. Calcd. for $C_{17}H_{12}BrNO_4S_2$: C, 46.57; H, 2.74; Br, 18.27; N, 3.20; S, 14.61. Found: C, 46.22; H, 2.46; Br, 18.06; N, 3.40; S, 14.64.

When chloroform was used as a solvent instead of acetic acid in the bromination of VIIId and VIIIf, similar results were obtained in nearly the same yields.

A solution of 1 g. of 4-bromo-1,8-naphthosultam (IXa) in 20 ml. of dry pyridine was treated with 1 ml. of benzoyl chloride. The reaction mixture was heated (steam-bath) for one hour, then poured into ice-cold water. The solid so obtained was crystallized from acetic acid and was identified as IXd (m.p. and mixed m.p.). Similarly, the treatment of IXa with benzenesulfonyl chloride gave IXe (m.p. and mixed m.p.) in almost quantitative yield.

N-Benzoyl-2,4-dibromo-1,8-naphthosultam (Xd).—To 0.8 g. of Xa in 20 ml. of dry pyridine, was added about 1 ml. of benzoyl chloride, then heated on a steam-bath for one hour, and poured into ice-cold water. The solid so obtained was crystallized from acetic acid, m.p. 190–191°.

Anal. Calcd. for $C_{17}H_9Br_2NO_3S$: C, 43.68; H, 1.93; Br, 34.26; N, 3.00; S, 6.85. Found: C, 43.62; H, 2.10; Br, 34.45; N, 2.98; S, 6.88.

(c) **N-Methyl-1,8-naphthosultam (VIIIb).**—A solution of 1 g. of VIIIb in 15 ml. of acetic acid was treated with a solution of 0.25 ml. of bromine in 5 ml. of acetic acid. The crystals that separated were collected and recrystallized from ethyl alcohol as almost colorless crystals (*ca.* 0.8 g.), m.p. 228–229°. 4-Bromo-N-methyl-1,8-naphthosultam (IXb) is soluble in benzene and xylene, sparingly soluble in petroleum ether and gives a greenish color with sulfuric acid.

Anal. Calcd. for $C_{11}H_8BrNO_2S$: C, 44.29; H, 2.68;

Br, 26.84; N, 4.70; S, 10.74. Found: C, 44.21; H, 2.51; Br, 26.95; N, 4.70; S, 10.73.

When the above experiment was repeated using a solution of 0.6 ml. of bromine in 5 ml. of acetic acid, under the same experimental conditions, pale yellow crystals were obtained which were recrystallized from ethyl alcohol; yield *ca.* 78%. 2,4-Dibromo-N-methyl-1,8-naphthosultam (Xb) melts at 165–166° and gives a pale yellow color with sulfuric acid.

Anal. Calcd. for $C_{11}H_7Br_2NO_2S$: C, 35.01; H, 1.86; Br, 42.44; N, 3.71; S, 8.49. Found: C, 35.24; H, 1.68; Br, 42.25; N, 3.16; S, 8.31.

Xb was proved to be identical (m.p. and mixed m.p.) with the product obtained (70% yield) by treating a solution of 0.8 g. of 2,4-dibromo-1,8-naphthosultam (Xa), in 50 ml. of 3% aqueous sodium hydroxide solution, with 2 ml. of methyl sulfate, in the usual manner, followed by crystallization from ethyl alcohol.

Reaction of 1,8-Naphthosultam with Organic Halides. (a) Formation of XIa–h and XIIa, b.—To a suspension of 1 g. of the sodium salt of 1,8-naphthosultam (VIIIa) (prepared by treating an alcoholic solution of VIIIa with a solution of an equivalent amount of sodium hydroxide in the least amount of alcohol) in 40 ml. of ethyl alcohol, was added an excess of the appropriate halogen compound. The reaction mixture was refluxed for a period ranging between 2–6 hours, till almost all the yellow sodium salt disappeared, and then the solution was filtered while hot. The residue, obtained after evaporation of the alcoholic solution almost to dryness, was triturated with boiling water, filtered off and crystallized from a suitable solvent (*cf.* Tables II and III). In the case of methylene iodide and methylene bromide, the reaction mixture was refluxed for 2–3 days.

The reaction product, obtained in the case of ethylene bromohydrin, was an oily substance, which, upon treatment with benzoyl chloride in the presence of aqueous sodium hydroxide solution (Schotten–Baumann), gave the corresponding benzoyl derivative (XI, R = $CH_2CH_2OCOC_6H_5$). It was crystallized from ethyl alcohol as colorless crystals, m.p. 122–123°.

Anal. Calcd. for $C_{19}H_{15}NO_4S$: C, 64.59; H, 4.26; N, 3.97; S, 9.06. Found: C, 64.50; H, 4.40; N, 3.84; S, 8.93.

The oxime of N-acetonyl-1,8-naphthosultam (XId) was formed when a solution of 0.7 g. of XId in 40 ml. of ethyl alcohol was treated with 0.5 g. of hydroxylamine hydrochloride and 0.7 g. of sodium acetate and the reaction mixture was refluxed for 5 hours. It formed colorless crystals (*ca.* 0.5 g.) from ethyl alcohol, m.p. 172–173°.

Anal. Calcd. for $C_{13}H_{12}N_2O_3S$: C, 56.52; H, 4.35; N, 10.14; S, 11.60. Found: C, 56.68; H, 4.24; N, 9.95; S, 11.55.

(b) Action of Acid Chlorides on 1,8-Naphthosultam. Formation of XIIc–f.—About 0.01 mole of 1,8-naphthosultam (VIIIa) was dissolved in 25 ml. of dry pyridine, cooled and treated with 0.005 mole of the appropriate acid chloride. The reaction mixture was heated on a steam-bath for one hour, then poured into cold water. The precipitate formed was filtered off, triturated with dilute aqueous sodium hydroxide (*ca.* 20 ml. of 5% solution), washed with water, dried and crystallized from a suitable solvent (*cf.* Table III).

Action of Oxalyl Chloride on Mono-arylsulfonyl Derivatives of Aromatic Amines.—Three grams (2 moles) of benzenesulfonanilide was dissolved in 25 ml. of dry pyridine, cooled, treated with 0.8 g. (1 mole) of oxalyl chloride, heated on a steam-bath for 1 hour, then poured into cold water. The precipitate formed was collected, triturated with dilute aqueous sodium hydroxide (30 ml. of 5% solution), filtered off and washed with water. XIIa was crystallized from acetic acid as colorless crystals, m.p. 178°, yield *ca.* 90%.

Anal. Calcd. for $C_{26}H_{20}N_2O_6S_2$: C, 60.00; H, 3.85; N, 5.38; S, 12.31. Found: C, 60.13; H, 3.72; N, 5.69; S, 11.80.

Similarly, oxalyl chloride reacted with N-*p*-toluenesulfonyl-4-bromoaniline to give XIIIb in 88% yield. XIIIb was crystallized as colorless crystals from acetic acid, m.p. 204–205°.

Anal. Calcd. for $C_{28}H_{22}Br_2N_2O_6S_2$: C, 47.95; H, 3.12; Br, 22.66; N, 3.97; S, 9.07. Found: C, 47.98; H, 2.94; Br, 22.80; N, 3.90; S, 8.72.

N-*p*-Tolylsulfonyl-4-bromoaniline was prepared as follows. A suspension of 7 g. of *p*-bromoaniline in about 100 ml. of 10% aqueous sodium hydroxide solution was treated with 8.5 g. of *p*-toluenesulfonyl chloride, heated on a steam-bath for some time, then filtered from any precipitate. The alkaline filtrate was acidified with hydrochloric acid and the precipitate formed was filtered off and washed with water. It was crystallized from dilute alcohol, m.p. 98–99°. It is very soluble in alcohol and benzene.

Anal. Calcd. for $C_{13}H_{12}BrNO_2S$: C, 47.85; H, 3.68; Br, 24.54; N, 4.29; S, 9.82. Found: C, 48.20; H, 3.69; Br, 24.30; N, 4.51; S, 9.60.

XIIIc was prepared in the same manner as XIIIb from oxalyl chloride and N-*p*-toluenesulfonyl-1-naphthylamine in 86% yield. It was crystallized from acetic acid or nitrobenzene, m.p. 214°.

Anal. Calcd. for $C_{36}H_{28}N_2O_6S_2$: C, 66.67; H, 4.32; N, 4.32; S, 9.88. Found: C, 66.36; H, 4.13; N, 4.00; S, 9.56.

Salt Formation with 1,8-Naphthosultam.—A solution of 0.5 g. of VIIIa in 20 ml. of dry benzene was treated with few drops (*ca.* 0.5 ml.) of freshly distilled piperidine. The resulting yellow solution was left aside for one hour at room temperature. The yellow crystals that separated on the addition of a few ml. of petroleum ether (b.p. 80–100°), were collected, washed with dry ether, and no further crystallization was found necessary, m.p. 184°. The salt is readily soluble in water and ethyl alcohol, giving yellow solutions. VIIIa is readily regenerated when the piperidinium salt was treated with hydrochloric acid; yield *ca.* 75%.

Anal. Calcd. for $C_{15}H_{18}N_2O_2S$: C, 62.07; H, 6.21; N, 9.66; S, 11.04. Found: C, 62.51; H, 6.37; N, 9.26; S, 11.00.

Similarly, the action of benzylamine on VIIIa, as described above, leads to the formation of yellow crystals of the benzylammonium salt, m.p. 135–136°, yield *ca.* 82%.

Anal. Calcd. for $C_{17}H_{16}N_2O_2S$: C, 65.37; H, 5.13; N, 8.97; S, 10.26. Found: C, 65.32; H, 5.15; N, 9.23; S, 10.35.

Cyclohexylamine forms, with VIIIa, yellow crystals, m.p. 180°, yield *ca.* 78%.

Anal. Calcd. for $C_{16}H_{21}N_2O_2S$: C, 62.95; H, 6.89; N, 9.18; S, 10.49. Found: C, 62.99; H, 6.54; N, 9.10; S, 10.47.

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