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Synthesis of Sulphonic Acids and Sultam Derivatives

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Abstract□Reaction of propane-1,3-sultone with amines gave N-substituted aminosulphonic acids **2a-i.** Dehydration of **2a-c** with $POCl_3$ gave the corresponding sultams **3a-c.** Propane-1,3-sultone **1** reacted with tertury amines to give the betaiene salts **4-11.** 2,4-Dimethyl-1,3-butadiene-1,4-sultone **12** condensed with amines to give N-substituted-2,4-dimethyl -1,3-butadiene-1,4-sultams **13a** and **13b.** The reaction of **3a, 13a** with hydrazine hydrate gave acid hydrazides **3d** or **13c.** Compounds **3d, 13c** reacted with isocyanates to yield urea derivatives **14a-c, 15a-c.**

Keywords□Sultones and sultams.

The reactions of sultones and sultams were the subject of previous investigations[1-3], due to their importance and applications in the biological as well as industrial fields[4-6]. The present investigation deals with synthesis of newer sultams by reaction of propane-1,3-sultone with primary amines to give the corresponding aminosulphonic acids. These sulphonic acids are cyclized through heating with phosphorous oxychloride to give the corresponding sultams.

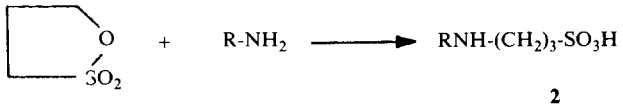
The reaction of propane-1,3-sultone (**1**) with amines such as 4-aminoethylbenzoate, 4-iodoaniline, tetradecylamine, 1,4-diamino-2,6-dichlorobenzene, 1,8-diaminonaphthaline, 2-amino-5-diethylaminopentane, 3-amino-5-methylisoxazole, 2-amino-5-mercapto-1,3,4-thiadiazole and 4-aminoantipyrine gave the corresponding 3N-substituted-aminopropane-1-sulphonic acids **2a-i,** respectively. The structure of the compounds **2a-i** was confirmed by analytical data, infrared and ^{1}H-NMR spectra. The IR spectra of **2a-i** show absorption bands at 3300, 1510 cm^{-1} (NH), 1350, 1210, 1160 and 600 cm^{-1} (SO_3H), ^{1}H-NMR spectrum of **2a** shows δ = 7.7-7.5 (d, NH), 6.7-6.2 (m, 4H, aromatic) 4.2-4.1 (d, CH_2-S), 3.3-3.1 (t, CH_2N), 2.4-2.7 (m, CH_2) and 1.4-1.2 (t, CH_3 ester).

The compounds **2a-c** were cyclized to the corresponding sultams **3a-c** through boiling with $POCl_3$. The infrared spectra of **3a-c** show bands in the region of 1270-1300 cm^{-1} characteristic for SO_2-N in sultam. ^{1}H-NMR spectrum of **3b** shows δ = 7.7-6.8 (m 4H aromatic), 3.7-3.5 (t CH_2-S), 3.4-3.2 (t CH_2-N) and 2.6-2.3 (m CH_2).

On the other hand propane-1,3-sultone (**1**) reacts with tertury amines to give the corresponding betaiene salts. Thus, compound **1** reacts with triethylamine, pyridine, 2-picoline, 3-picoline or quinoline to yield the betaiene salts **4-8,** respectively. Similarly **1** reacts with caffeine, papaverine or ephedrine to give the water soluble derivatives **9-11,** respectively. The structures of the betaiene salts **4-11** now reported rests on analytical data, on the fact that they are water soluble, that their infrared spectra show absorption bands at 1420, 1820, 1200, 1120 cm^{-1} (SO_3^-) and 1420, 820 cm^{-1} (C_4N^+). ^{1}H-NMR spectrum of **4** shows o = 3.5-3.1 (t, 8CH_2-N), 2.6-2.4 (t, CH_2S), 2.1-1.6 (m, CH_2) and 1.4-1 (m, 9H, 3CH_3).

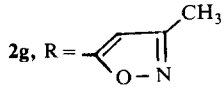
It is reported that unstaturated sultones react with amines to give directly the corresponding sultam[1,3]. Thus, the sultone **12** reacts with 4-aminomethylbenzoate or 2-amino-4-methylpyrimidine to give N-substituted-2, 4-dimethyl-1, 3-butadiene-1, 4-sultams **13a-b,** respectively. The sultams **3a,** or **13c** react with hydrazine hydrate to give the hydrazides **3d,** or **13c.** Treatment of **3d** or **13c** with phenylisocyanate, phenylisothiocynate or allylisothiocynate yields the corresponding urea or thiourea derivatives **14a-c** or **15a-c.** IR spectra of **14b, 14c, 15b** and **15c** show bands at 1500, 1400, 1100, 730 cm^{-1} (N-CS-N), 1270-1300 cm^{-1} (SO_2-N sultam).

^{1}H-NMR spectrum of **14b** shows δ = 8.0-7.9 (d, 3NH), 7.5-7.4 (m, 9H aromatic), 3.8-3.6 (t, CH_2S), 3.5-3.3 (t, CH_2N) and 2.7-2.5 (m, CH_2).



1 2

2a, R = 4-$COOCH_3C_6H_4$
b, R = 4-I C_6H_4
c, R = $CH_2(CH_2)_{12}\ CH_3$
d, R = 3,5-Cl_2-4-$NH_2C_6H_2$
e, R = 1-$C_{10}H_6$-8-NH_2
f, R = $CH(CH_2)_3(C_2H_5)_2$ (CH_3)



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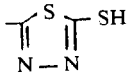

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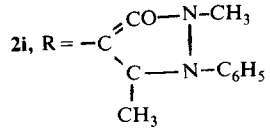
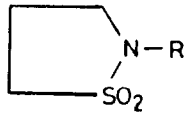


2i, R =



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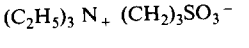

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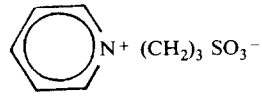
3a, R = 4-$COOCH_3C_6H_4$
b, R = 4-I C_6H_4
c, R = $CH_2(CH_2)_{12}\ CH_3$
d, R = 4-$NH_2NHCOC_6H_4$



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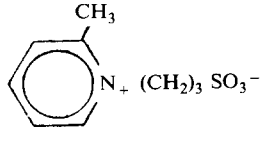

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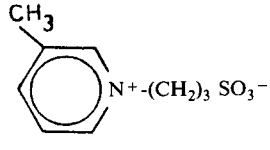

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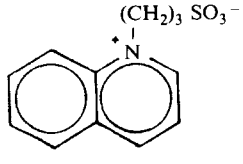

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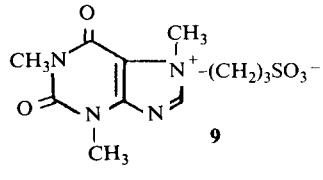

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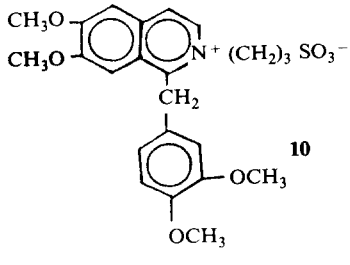

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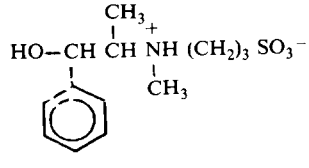

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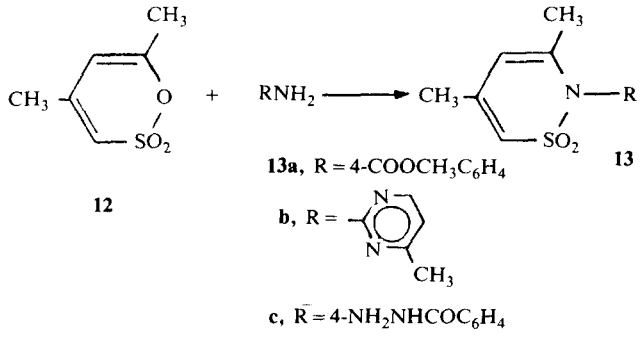

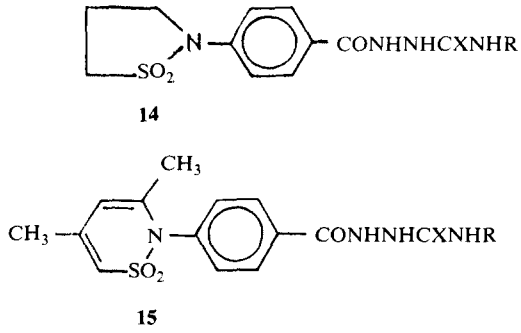

14, 15	R	X
a	C_6H_5	O
b	C_6H_5	S
c	$CH_2CH=CH_2$	S

EXPERIMENTAL METHODS

Reaction of propane-1,3-sultone with amines: Formation of 2a-i

The sultone **1** (0.01 mol) in 50 m*l* l-butanol was refluxed with the appropriate amine (0.01 mol) for 3 hr. After concentration and cooling, the product was filtered off, washed with methanol and crystallized from acetic acid to give **2a-i** (Table I).

Cyclization of 2a-c: Formation of 3a-c

A mixture of **2a-c** (2g) and $POCl_3$ (10 m*l*) was refluxed for 4 hr. The reaction mixture was allowed to cool, then added to cold water. The solid that separated was filtered off, washed with water and crystallized from methanol to give **3a-c** (Table I).

Reaction of propane-1,3-sultone with tertury amines: Formation of betaiene salts 4-11

A solution of propane-1,3-sultone (0.01 mol) in dry acetone (40 m*l*) and the appropriate amine (0.01 mol) was refluxed for 8 hr. After concentration and cooling the solid product which was separated was crystallized from acetic acid to give **4-11** as colourless crystals soluble in water and undergo no acidity towards $NaHCO_3$ solution. (Table I)

Reaction of 2,4-dimethyl-1,3-butadiene-1,4-sultone 12 with amines: Formation of N-substituted-2,4-dimethyl-1,3-butadiene-1,4-sultams 13a and 13b

A mixture of **12** (0.01 mol) and the appropriate amine (0.01 mol) was fused at 130°C for one hour. The fused mass allowed to cool then treated with 2 N HCl to get rid off the unreacted amine. The product was filtered off, washed with water and crystalized from ethanol to give **13a** and **13b** (Table I).

Reaction of 3a and 13a with hydrazine hydrate: Formation of 3d and 13c

A solution of the sultam **3a** or **13a** (0.01 mol) in ethanol (30 m*l*) was treated with hydrazine hydrate (2 m*l*). The solution was refluxed for 3 hr. After cooling the products were filtered off and crystallized from ethanol to give **3d** or **13c** (Table I).

Reaction of 3d and 13c with isocyanates: Formation of 14a-c and 15a-c

To a solution of **3d** or **13c** (0.01 mol) in sodium-dried benzene (50 m*l*), the appropriate isocyanate was added. The solution was refluxed for 6 hr. After cooling, the product was filtered off and crystallized from methanol to give **14a-c** or **15a-c** (Table I).

Table I. Elemental analysis data

No.	Formula	M.p. (°C)	Yield (%)	Analysis (%) Calcd./Found C	H	N	S
2a	$C_{11}H_{15}NO_5S$	230	70	48.35	5.49	5.12	
				48.21	5.16	5.38	
2b	$C_9H_{12}INO_3S$	199	89	31.67	3.52	4.11	
				31.90	3.24	4.00	
2c	$C_{17}H_{37}NO_3S$	275	69	60.90	11.45	4.17	
				60.72	11.53	4.47	
2d	$C_9H_{12}Cl_2N_2O_3S$	248	70	36.13	4.01	9.36	
				36.22	4.11	9.36	
2e	$C_{13}H_{16}N_2O_3S$	330	71	55.71	5.72		11.42
				55.23	5.49		11.49
2f	$C_{12}H_{28}N_2O_3S$	180	57	51.42	10.00		
				51.29	10.05		
2g	$C_7H_{12}N_2O_4S$	252	54	38.18	5.45	12.73	14.55
				38.11	5.62	12.55	14.61
2h	$C_5H_9N_3O_3S_3$	245	94	23.53	3.53	16.47	37.65
				23.43	3.43	16.55	37.21
2i	$C_{14}H_{19}N_3O_4S$	246	40	51.69	5.84	12.92	
				51.01	5.80	12.28	
3a	$C_{11}H_{13}NO_4S$	170	66	51.76	5.20		12.55
				51.41	5.10		12.21
3b	$C_9H_{10}INO_2S$	162	82	33.44	3.09	4.33	
				33.22	3.19	4.43	
3c	$C_{17}H_{35}NO_2S$	56	83	64.35	11.04	4.42	
				64.38	10.91	4.55	
3d	$C_{10}H_{13}N_3O_3S$	218	70	47.05	5.10	16.47	12.55
				47.71	5.04	16.52	12.45
4	$C_9H_{21}NO_3S$	278	89	48.43	9.42	6.28	14.35
				48.60	9.71	6.37	14.52
5	$C_8H_{11}NO_3S$	290	70	47.76	5.47	6.97	
				47.81	5.65	6.77	
6	$C_9H_{13}NO_3S$	270	85	50.23	6.05	6.51	
				50.26	6.07	6.71	
7	$C_9H_{13}NO_3S$	283	84	50.23	6.05	6.51	
				50.37	6.18	6.42	
8	$C_{12}H_{13}NO_3S$	310	60	57.37	5.18	5.58	
				57.27	5.11	5.51	
9	$C_{11}H_{16}N_4O_5S$	235	90	41.77	5.06	17.82	
				41.71	5.21	17.85	
10	$C_{23}H_{27}NO_7S$	270	86	59.87	5.86		6.94
				59.51	5.59		6.81
11	$C_{13}H_{21}NO_4S$	215	54	54.36	7.32	4.88	
				54.79	7.65	4.45	
13a	$C_{14}H_{15}NO_4S$	176	65	57.34	5.12	4.78	10.92
				57.34	5.10	4.79	10.29
13b	$C_{11}H_{13}N_3O_2S$	157	70	52.59	5.18	16.73	
				52.45	5.12	16.51	
13c	$C_{13}H_{15}N_3O_3S$	284	67			14.33	10.29
						14.48	10.01
14a	$C_{17}H_{18}N_4O_4S$	156	60	54.55	4.81	14.97	8.55
				54.62	4.76	14.88	8.67
14b	$C_{17}H_{18}N_4O_3S_2$	191	65	52.31	4.62		16.41
				52.31	4.82		16.59
14c	$C_{14}H_{18}N_4O_3S_2$	190	60	47.46	5.08	15.82	
				47.56	5.11	15.82	
15a	$C_{20}H_{20}N_4O_4S$	215	67	58.25	4.85	13.59	
				58.60	4.62	13.49	
15b	$C_{20}H_{20}N_4O_3S_2$	169	55	56.07	4.67	13.08	14.95
				56.82	4.54	13.11	14.56
15c	$C_{17}H_{20}N_4O_3S_2$	174	50	52.04	5.10	14.29	16.33
				51.82	5.01	14.11	16.23

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