

SYNTHESES IN THE PYRIDINE SERIES. VII.* QUATERNARY SALTS OF SOME β -AMINOALKYL(2-PYRIDYL)SULFIDES

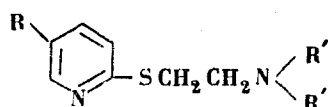
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The conditions for preparing certain β -dialkylaminoethyl(2-pyridyl)sulfides and their quaternary salts are investigated.

Alkyl halides add to β -dialkylaminoethyl(2-pyridyl)sulfides in a 1:1 molar ratio, and the point of addition depends on the structure of the 2-pyridylsulfides, viz., the nature of the groups at the tertiary aliphatic amino group and the basicity of the cyclic nitrogen atom.

Quaternary ammonium salts of certain heterocyclic compounds, inter alia pyridine, that contain the $-\text{NHCH}_2\text{CH}_2\text{NR}_2$ and $\text{O}-\text{CH}_2\text{CH}_2\text{NR}_2$ groups, are biologically active [2-9]. The present paper deals with the preparation of a series of salts of certain β -dialkylaminoethyl(2-pyridyl)sulfides having the general formula:



I R=H, R'=CH₃; II R=H, R'=C₂H₅; III R=NO₂, R'=CH₃; IV R=NO₂, R'=C₂H₅.

The sulfides are synthesized by known methods (Table 1). 2-Mercaptopyridines and β -dialkylaminoethylchlorides are brought to react in equimolecular amounts, by heating at various pH values in water or alcohol. Sulfides III and IV are also obtained from 5-nitro-2-chloropyridine and the appropriate β -dialkylaminoethylmercaptans. The structure of the sulfides is confirmed by their ir absorption spectra, containing well-marked absorptions in the regions 1580 and 1100-1135 cm^{-1} . Unlike 4-pyridylsulfides of the same composition [10], the resultant 2-pyridylsulfides give monoquaternary compounds with methyl and ethyl iodides. It can be assumed that in 2-pyridylsulfides, unlike 4-pyridylsulfides, the alkyl group is not coplanar, and that this prevents two alkyl halide molecules from being added. A non-coplanar structure has previously been observed for phenyl(2-pyridyl)sulfide.

TABLE 1
Dialkylaminoethyl(2-pyridyl)sulfides

Compound	Mp, °C	Bp, °C (Pressure, mm)	Formula	Found, %		Calc., %	
				N	S	N	S
Dimethylaminoethyl(2-pyridyl)sulfide (I)	—	91—93 (3)	C ₉ H ₁₄ N ₂ S*	15.24 15.03	17.72 17.91	15.37	17.59
Diethylaminoethyl(2-pyridyl)sulfide (II)	—	130—132 (4)	C ₁₁ H ₁₈ N ₂ S**	13.33 13.48	15.46 15.68	13.32	15.24
Dimethylaminoethyl(5-nitro-2-pyridyl)sulfide (III)	40—42	—	C ₉ H ₁₃ N ₃ O ₂ S	18.11 18.43	14.13 14.43	18.50	14.11
Diethylaminoethyl(5-nitro-2-pyridyl)sulfide (IV)	50—52	—	C ₁₁ H ₁₇ N ₃ O ₂ S	16.21 16.48	12.63 12.90	16.46	12.56

* d_4^{20} 0.951, n_D^{20} 1.560; MR_D 56.3, calc. MR_D 55.63.

** d_4^{20} 1.018, n_D^{20} 1.5400; MR_D 64.56, calc. MR_D 64.84.

*For part VI see [1].

The quaternary salts prepared (Table 2) have various structures, depending on whether it is the nitrogen of the heterocyclic ring or that of the aliphatic chain that participates in salt formation. The intensities of the above-mentioned absorption bands in the ir spectra of the sulfides are practically identical. This makes it possible to draw conclusions regarding the nitrogen atoms taking part in salt formation from the change in intensity of the appropriate absorption band in the spectra of the quaternary salts. Thus, a significant change in intensity (lowering of the maximum) of the absorption bands is found in the regions 1580 and 1100 cm^{-1} for the spectrum of the methiodide of sulfide I, at 1580 cm^{-1} for the methiodide of sulfide II, and in the region 1100 cm^{-1} for the methiodides of sulfides III and IV. This shows that when $R=H$ and $R'=CH_3$, both nitrogen atoms participate in salt formation. Then the reaction product is a mixture of two quaternary salts of the same composition. When $R=H$, $R'=C_2H_5$, this kind of salt is formed because of the nitrogen atom of the heterocyclic ring. Obviously, in this case the steric effect of the ethyl groups prevents addition of the alkyl halides to the nitrogen of the aliphatic chain. When $R=NO_2$, $R'=CH_3$ and C_2H_5 , salt formation involves the nitrogen atom of the aliphatic chain. The decrease in basicity of the nitrogen atom of the heterocyclic ring, due to the electron-acceptor effect of the nitro group, evidently conditions its passivity in salt formation. The absorption spectra of the ethiodides were not observed, but it is to be assumed that they are similar in structure to those of the methiodides.

EXPERIMENTAL*

Synthesis of the sulfides. I and II are obtained by refluxing a solution of 2-mercaptopyridine [11] with an equimolecular amount of dialkylaminoethylchloride hydrochloride and sodium hydroxide for 2 hr. At the end of reaction the sodium chloride is filtered out, the alcohol taken off, and the residue vacuum-distilled. Sulfide yield 70-75%. To prepare III and IV, equimolecular amounts of 5-nitro-2-chloropyridine [12] and the appropriate β -dialkylaminomercaptan are used in the reaction mixture. Reaction takes place in alcohol either at the boiling point of the mixture or at 15-20°. The reaction mixture is cooled to 0-3°, the precipitate filtered off, washed a few times with hot acetone, and recrystallized from alcohol. Hydrochloride yield 65-80%. III and IV are precipitated quantitatively when aqueous solutions of the hydrochlorides are neutralized with sodium bicarbonate.

Preparing the quaternary salts. Sulfides I, III, and IV are reacted with three times the theoretical amount of alkyl halide in alcohol at room temperature or under reflux. At room temperature reaction takes 3-5 days, at boiling temperature 1-2 hr. The precipitate of quaternary salt is filtered off, and recrystallized from alcohol. The yield is almost quantitative.

Heating II with alkyl halides gives resinous, brown substances, from which it is impossible to separate the desired individual product. Hence reaction is effected at 15°.

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TABLE 2

Quaternary salts of dialkylaminoethyl(2-pyridyl)sulfides

Starting material	Mp picrate, °C	Mp hydrochloride, °C	Mp methiodide, °C	Formula	Found, %		Calc., %		Mp ethiodide, °C	Formula	Found, %		Calc., %	
					N	I	N	I			N	I	N	I
I	130—132	194—196	183—184 (decomp.)	$C_{10}H_{17}N_2SI$	8.94	39.1	8.64	39.14	150—152	$C_{11}H_{19}N_2SI$	8.01	35.98	8.28	37.52
II	103—105	—	130—132	$C_{12}H_{21}N_2SI$	8.60	40.4	7.95	36.03	182—184	$C_{13}H_{23}N_2SI$	8.17	36.80	7.64	34.64
III	167—170	182—183	190—192 (decomp.)	$C_{10}H_{16}N_3O_2SI$	7.89	35.44	11.37	34.37	218—220 (decomp.)	$C_{11}H_{18}N_3O_2SI$	7.65	34.69	10.96	33.12
IV	—	173—174	172—174 (decomp.)	$C_{12}H_{20}N_3O_2SI$	8.11	35.67	10.58	31.96	206—208 (decomp.)	$C_{13}H_{22}N_3O_2SI$	7.32	35.1	10.22	30.85
					10.32	32.22					10.47	32.18		
					10.54	32.35					10.63	31.93		
											9.88	29.72		
											10.07	29.67		

*Found: S 9.13; 9.29%. Calculated: S 9.46%.

**Found: S 8.31; 8.43%. Calculated: S 8.36%

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