obtained by the method in [10], at 110-120°C for 4 h until it had dissolved completely. The solution was then cooled and poured into 50 ml of water, and the precipitate was removed by filtration, washed with water until the wash water was neutral, and dried to give 0.39 g of XVb. The filtrate was neutralized with sodium carbonate, and the resulting precipitate was removed by filtration, washed with water, and dried to give 0.48 g of XVa.

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RECYCLIZATION OF PYRIDINIUM SALTS WITH EXCHANGE AS A METHOD FOR THE PREPARATION OF N-SUBSTITUTED AROMATIC AMINES

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The conditions for the formation of N-substituted aromatic amines in the sulfite variant of recyclization of pyridinium salts, as well as the structural factors that affect the yields of the final substances, were investigated.

It has been previously shown that the rearrangements of quaternary pyridinium salts to N-alkylanilines are accompanied by various competitive processes, the chief of which are dealkylation of the quaternary pyridinium salt to give the starting pyridine base, hydrolysis of the open intermediate with the subsequent formation of phenol, and transamination in the step involving the open intermediate to give an aromatic amine with a radical attached to the nitrogen atom that differs from that in the starting pyridinium salt [1-3]. Until recently, all of these processes were considered to be side reactions and undesirable. However, an analysis of the accumulated experimental data made it possible to assume that the last reaction may have independent synthetic value as a fundamentally new method for the introduction of aromatic radicals into nitrogen bases. In this connection, it was necessary to ascertain the optimum reaction conditions and structural factors that affect the course of the transamination.

2-Picolinium (Ia) and 2-methyl-5-ethylpyridinium (Ib) propyliodides were used as the principal model structures for the investigation. We chose these compounds due to the fact

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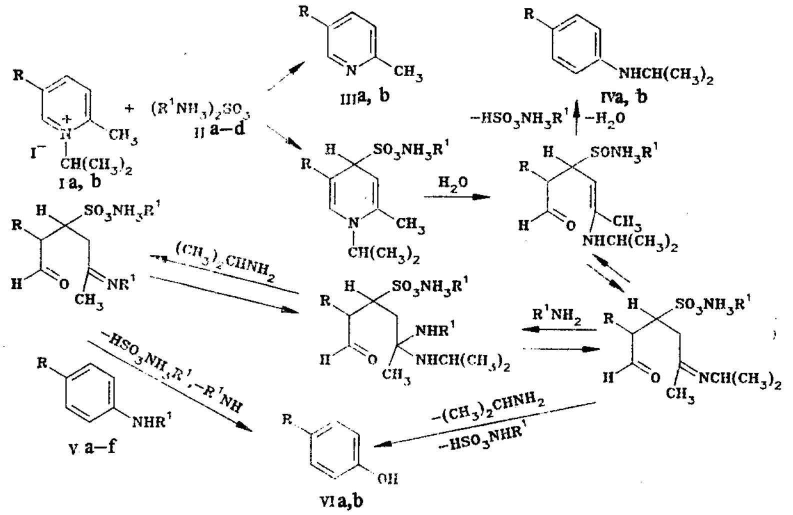
that the presence of a branched radical attached to the nitrogen atom could facilitate exchange of the alkylamine fragment and simultaneously hinder the competitive dealkylation of starting quaternary salts Ia,b due to steric restrictions with respect to nucleophilic attack of the carbon atom directly bonded to the pyridinium nitrogen atom.

On the basis of the previously proposed mechanism of the sulfite variant of the rearrangement of N-alkylpyridinium salts [1] the recyclization of Ia, b with exchange of the alkylamine fragment and the competitive reactions can be represented by a common scheme (see the scheme presented below).

In view of the fact that the transamination of enamines proceeds reversibly [4], the excess free amine in the reaction medium should have a substantial effect on the reaction pathway. The nature of the free amine and the amine that constitutes the alkylamine fragment of the starting pyridinium salt may also play an important role.

Experiments showed that 2-picolinium propuliodide (Ia) undergoes rearrangement to N-methylaniline (Va) in 71% yield under the influence of methylamine sulfite (IIa), whereas the product of direct rearrangement, viz., N-isopropylaniline (IVa), is formed in only trace amounts. The dealkylation product, viz., 2-picoline (IIIa), is also absent.

Thus the recyclization of salt Ia under the influence of methylamine sulfite takes place with complete exchange of the isopropylamine fragment for a methylamine fragment. The reaction is virtually complete in 15 h, and the temperature range from 180°C to 200°C can be considered to be the optimum range. In the case of a threefold excess of free methylamine in the reaction medium the yield of N-methylaniline (Va) was 69%, and a further increase in the excess free base increased the yield of Va only slightly. For example, the yield of N-methylaniline was 71% in the case of a 12-fold excess of methylamine in the reaction medium.



I, III, IV, VI a R=H, b R=C_2H_5; Va–d R=H, e, f R=C_2H_5; II, V R^1=CH_3, b R^1=C_2H_5, c R^1=C_4H_9, d R^1=C_6H_{11}; e R^1=CH_3, f R^1=C_2H_5

To study the effect of the nature of the amine on the course of the exchange recyclization we carried out the rearrangement of salt Ia using the sulfites of various alkylamines. We found that the rearrangement of salt Ia under the influence of sulfites of primary alkylamines proceeds with complete exchange of the alkylamine fragment. The products of hydrolysis (VIa) and dealkylation (IIIa) are formed in trace amounts, which were detected by chromatography.

It has been previously noted that the introduction of alkyl groups into the β position of the pyridine ring decreases the electron-deficient character of the ring and creates steric hindrance to the addition of the sulfite anion, which leads to a sharp decrease in the yields of N-alkylanilines [1]. In fact, 4-ethyl-N-methylaniline (Ve) was obtained in 21% yield in the recyclization of 2-methyl-5-ethylpyridinium isopropyliodide (Ib) under the influence of methylamine sulfite (IIa). Dealkylation of the starting quaternary salt Ib to give 2-methyl-5-ethylpyridine (IIIb) in 51% yield is the principal reaction pathway in this case. The product of direct rearrangement, viz., 4-ethyl-N-isopropylaniline (IVb), is absent.

TABLE 1. Characteristics of Va-f

Compound	R_f*	IR spectrum, cm^{-1} (NH)	PMR spectrum, δ, ppm (J, Hz)				Yield, %
			$N-\underset{\diagdown}{\overset{\diagup}{C}}-H$	NH	aromatic protons	remaining protons	
Va	0,64	3320	3,03	3,87	6,68—7,49		71
Vb	0,81	3320	3,25	3,5	6,5—7,5	1,37 (t, CH_3, $J = 7$)	52
Vc	0,56	3320	3,27	3,58	6,63—7,5	1,17—1,95 (m, C_3H_7)	71
Vd	0,80	3320	—	3,32	6,3—7,2	1,0—2,2 (m, C_6H_{11})	29
Ve	0,62	3320	2,96	3,62	6.5—7,25	1,42 (t, CH_3, $J = 7$)	21
Vf	0,64	3320	3,25	3,45	6,5—7,25	1,38 (t, $2CH_3$, $J = 7$), 2,71 (q, CH_2, $J = 7$)	24

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*The following solvents were used: hexane—ether (1:1) for Va, d-f, benzene—ether (10:1) for Vb, and benzene for Vc.

In comparing this result with the previously obtained data on the rearrangement of 2-methyl-5-ethylpyridine methiodide under the influence of methylamine sulfite [1] one may note a decrease in the contribution of dealkylation on passing from the "compact" methyl radical attached to the nitrogen atom of the quaternary salt to the bulkier isopropyl radical (from 70% to 51%). In the recyclization of salt Ib under the influence of ethylamine sulfite (IIb) the yield of dealkylation product IIIb decreases markedly and amounts to 3.5%. Consequently, the dealkylation of salt Ib is realized only when one uses a nucleophile such as methylamine, the steric volume of which is minimal, and direct nucleophilic attack of the carbon atom directly bonded to the pyridinium nitrogen atom has fewer steric limitations than when ethylamine is used.

Thus the results that we obtained constitute evidence that the recyclization of pyridinium salts with exchange of the alkylamine fragment can be used for synthetic purposes as a new method for the introduction of aromatic radicals into primary amines.

EXPERIMENTAL

The PMR spectra of solutions of the compounds in CCl_4 were recorded with a Tesla BS-467A spectrometer (60 MHz) with hexamethyldisiloxane (HMDS) as the internal standard. The IR spectra of mineral oil suspensions were obtained with a UR-20 spectrometer. Analysis by gas-liquid chromatography (GLC) was carried out with an LKhM-8MD chromatograph (first model) with a catharometer and a 2 m by 3 mm column packed with 15% Carbowax 6000 on Chromaton N-AW-HMDS (0.250-0.315 mm); the carrier gas was helium, and the flow rate was 20 ml/min. Analysis by thin-layer chromatography (TLC) was carried out on Silufol plates in an ether—hexane system (1:1) with detection by iodine vapors.

Isopropyliodides Ia, b. These compounds were obtained by heating the corresponding pyridine bases with a 1.5-fold excess of isopropyl iodide for 12-24 h in a flask equipped with a reflux condenser. The reaction of 9.3 g (0.1 mole) of base IIIa gave 25.3 g (96%) of salt Ia with mp 150-151°C (isopropyl alcohol). Found: C 41.2; H 5.2%. $C_9H_{14}IN$. Calculated: C 41.1; H 5.4%. The reaction of 12.1 g (0.1 mole) of base IIIb gave 24.7 g (85%) of salt Ib with mp 109-110°C [from absolute alcohol—ether (1:3)]. Found: C 45.2; H 6.1%. $C_{11}H_{18}IN$. Calculated C 45.4; H 6.2%.

Reaction of Isopropyliodides Ia, b with Alkylamine Sulfites (General Method). An 85-mmole sample of a 25% aqueous solution of the alkylamine and 25 mmole of the alkylamine bisulfite, obtained by saturation of a 25% aqueous solution of the alkylamine with gaseous SO_2, were added to 5 mmole of Ia, b, and the mixture was heated in a sealed ampul at 200°C for 30 h. The reaction mixture was extracted with ether (four 10-ml portions), and the extract was dried over $MgSO_4$. The ether and excess alkylamine were removed by distillation *in vacuo*, and the residue was chromatographed under pressure [6] with a column (l = 50, d = 1 cm) packed with Chemapol 100/160 silica gel. N-Alkylanilines IVa-g were eluted with hexane—ether (95:5). Hexane with an increasing percentage of ether (from 5% to 100%) served as the eluent for the isolation of the remaining components of the mixture (III and VI). The initial identification of the compounds obtained was made by means of analysis by GLC by comparison of the retention times with those of genuine samples. The characteristics of the N-alkylanilines are presented in Table 1.

Reaction of Salt Ia with Methylamine Sulfite. A 5.3-ml (40 mmole) sample of a 25% aqueous solution of methylamine and 3.8 ml (25 mmole) of methylamine bisulfite, obtained by the general method, were added to 5 mmole of Ia, and the mixture was heated in a sealed ampul at 180°C for 15 h. Aniline IVa was isolated by the general method. A 0.37-g (69%) sample of Va was obtained. The results of analysis by GLC and IR and PMR spectroscopy of Va were in agreement with the data for a genuine sample.

In the case of a 12-fold excess of free methylamine in the reaction medium the yield of Va was 71%.

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ELECTROCHEMICAL TRANSFORMATIONS OF 4-(NITROARYL)-1,2- AND -1,4-DIHYDROPYRIDINES IN ACETONITRILE

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The potentials of the electrolytic oxidation and reduction of 3,5-diethoxycarbonyl-1,2- and -1,4-dihydropyridines with a nitroaryl substituent in the 4 position and their oxidized forms were determined by the method of a rotating disk electrode with a ring. The mechanism of the electrochemical oxidation of the starting dihydropyridines in acetonitrile on a graphite electrode was ascertained. The first step in the electrolytic reduction of the starting dihydropyridines is the addition of an electron to the nitro group to give anion radicals, the fine electronic structures and the hyperfine structure (hfs) constants of which were determined by EPR spectroscopy. The pyridinium fragment in the electrolytic oxidation products is reduced more readily than the nitro group in the aryl substituent.

In a continuation of our systematic study of the mechanism of the electrochemical oxidation (EO) of derivatives of 1,4- and 1,2-dihydropyridine (DHP) we directed our attention to compounds that contain a nitro group in the 4-aryl substituent of the dihydropyridine ring. A number of compounds of this type (for example, nifedipine or fenigidine) have pronounced biological activity and have found application in medical practice [1]. From the point of view of the redox transformations these compounds are characterized by the fact that they contain two electrolytically active centers, one of which is capable of electrolytic reduction (the nitro group), the other of which is capable of electrolytic oxidation (the dihydropyridine fragment). This makes it necessary to ascertain the ranges of the potentials of the corresponding transformations and the character of the interaction both between the individual groupings in the starting molecule and between the intermediates in the electrochemical transformations.

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