7. B. Ya. Eryshev and N. N. Suvorov, Khim. Geterotsikl. Soedin., No. 2, 216 (1980).
8. V. N. Belov and S. G. Polyakova, Proceedings of the All-Union Scientific-Research Institute of Synthetic and Natural Fragrant Substances. The Chemistry and Technology of Fragrant Substances and Essential Oils [in Russian], Pishchepromizdat, Moscow (1965), p. 3.
9. H. E. Fritz, J. Org. Chem., 28, 1324 (1963).
10. L. B. Shagalov, N. N. Suvorov, V. G. Avramenko, B. Ya. Eryshev, and P. I. Mushulov, USSR Inventor's Certificate No. 181,119; Byull. Izobret., No. 9 (1966).
11. E. J. Jonson and D. G. Crosbi, J. Org. Chem., 28, 1246 (1963).

STERIC EFFECTS IN THE SYNTHESIS OF INDOLES FROM PYRIDINIUM SALTS

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In the synthesis of indoles from pyridinium salts the degree of transamination depends on the character of the alkyl group attached to the nitrogen atom of the amine and its nucleophilicity. The yields of indoles decrease as the steric hindrance becomes greater.

We have previously proposed a fundamentally new approach to the synthesis of the indole two-ring system based on the transformation of the pyridine ring under the influence of substituted ketones in the presence of bases [1].

It is known that pyridinium salts tend to undergo transamination in the step involving an acyclic intermediate, which leads to other pyridinium salts or products of their recyclization to give anilines [2, 3]. 1,2,4,6-Tetramethyl-3-nitropyridinium iodide (I) is a convenient model for a detailed study of transamination in the synthesis of indoles. In this case, under the influence of methylamine and acetone, we observed the maximum yield (60%) of 1,2,5,7-tetramethylindole (II); this evidently indicates the small amount of steric hindrance created by the methylamino group in the formation of the indole two-ring system.

N-Alkylindoles are formed in 23-26% yields by the action of solutions of n-butylamine, n-nonylamine, and n-cetylamine in acetone on nitropyridinium iodide I; this indicates the low degree of sensitivity of the reaction to a change in the length of the hydrocarbon chain in the starting aliphatic amine. However, the presence of indole II (4-7%) in the last two cases is evidently explained only by an incomplete exchange reaction because of the greater preferability of the smaller methylamine residue in the type A intermediate.

The yields of the corresponding indoles IIId and IIIe increase to 35-41% when the reaction is carried out in an acetone solution of isopropylamine or sec-butylamine (branching at the α-carbon atom). In this case, despite the greater degree of branching of the hydrocarbon chains attached to the nitrogen atom of the amine, the greater nucleophilicity of these amines in the reaction is probably the decisive factor.

Finally, indole derivatives IIIf and IIIg are formed in 3 and 10% yields, respectively, by the action of tert-butylamine and α-phenylethylamine in acetone on nitropyridinium iodide I; one should have expected this, considering the steric volumes of the substituents in these amines.

Thus, in the synthesis of indoles from pyridinium salts, the degree of transamination depends on the character of the alkyl group attached to the nitrogen atom of the amine and its nucleophilicity. The yields of indoles decrease as the steric hindrance becomes greater.

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TABLE 1. Reaction of Nitropyridinium Iodide I with Acetone and Amines and Properties of the Resulting Indoles

Amine, R	Indole, N—R	mp, °C	M^+	PMR spectrum, δ, ppm				Yield, %
				2-, 4- and 6-Me	3-H	5-H and 7-H	protons of the N-alkyl substituent	
n-C_4H_9	IIIa*, n-C_4H_9	Oil	215	2,17—2,33; 2s	6,00, s	6,56—6,69; 2s	0,76—1,76 (m, C_3H_7), 3,69 (t, CH_2N, $J=7$ Hz)	23
n-C_9H_{19}	IIIb, n-C_9H_{19}	Oil	285	2,13—2,36; 2s	6,03, s	6,56—6,69; 2s	0,83—1,83 (m, C_8H_{17}), 3,63 (t, CH_2N, $J=7$ Hz)	26
	II CH_3	82—83	173	2,27—2,47; 3s	6,27, s	6,83—6,97; 2s	3,43 (s, CH_3N)	7
n-$C_{16}H_{33}$	IIIc, n-$C_{16}H_{33}$	44—46	383	2,33—2,41; 2s	6,12, s	6,63—6,82; 2s	0,87—1,20 (m, $C_{15}H_{31}$), 3,90 (t, CH_2N, $J=7$ Hz)	26
	II, CH_3	82—83	173	2,27—2,47; 3s	6,27, s	6,83—6,97; 2s	3,43 (s, CH_3N)	4
iso-C_3H_7	IIId, iso-C_3H_7	55—57	201	2,31—2,33; 2s	6,07, s	6,61—7,00; 2s	1.48 (d, $(CH_3)_2$, $J=7$ Hz), 4,30—4,74 (m, CH)	41
sec-C_4H_7	IIIe†, sec-C_4H_9	Oil	215	2,13—2,36; 3s	6,03, s	6,56—6,93; 2s	0,53 (t, CH_3, $J_{CH_3CH_2}=7$ Hz), 1,31 (d, CH_3, $J_{CH_3CH}=7$ Hz), 1,43—2,10 (m, CH_2)	35
tert-C_4H_9	IIIf, tert-C_4H_9		215	2,40—2,53; 2s	6,12, s	6,67—7,23; 2s	1,73 [s, $(CH_3)_3$]	3
	II, CH_3		173	2,27—2,47; 3s	6,27, s	6,83—6,97; 2s	3,43 (s, CH_3N)	6
$C_6H_5CHCH_3$	IIIg., $C_6H_5CHCH_3$	Oil	263	2,17—2,40; 3s	6,13, s	6,59—7,03; 2s	1,79 (d, CH_3, $J=7$ Hz), 5,59 (q, CH, $J=7$ Hz), 7,03 (m, C_6H_5)	10
	II, CH_3		173	2,27—2,47; 3s	6,27, s	6,83—6,97; 2s	3,43 (s, CH_3N)	1

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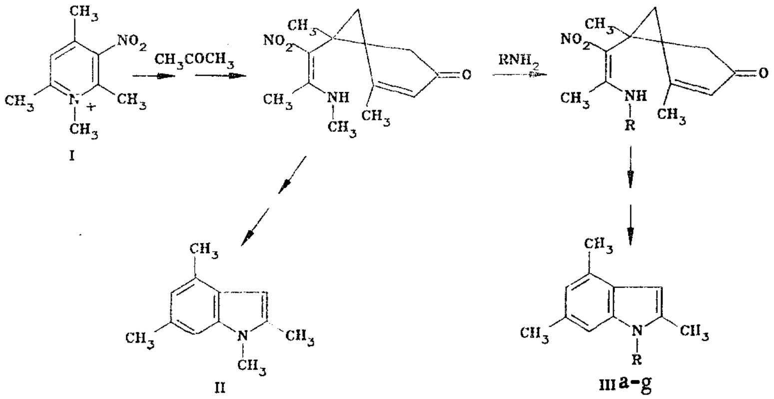
*Found, %: C 84.6, H 10.1. $C_{15}H_{21}N$. Calculated, %: C 83.7, H 9.8.

†Found, %: C 83.9, H 9.8. $C_{15}H_{21}N$. Calculated, %: C 83.7, H 9.8.



The compositions and structures of the compounds obtained were proved by UV, PMR, and mass spectrometry and the results of elementary analysis. The positions of the two methyl groups in the benzene ring of indoles IIIa-g correspond to their positions in tetramethylindole II, for which the character of substitution was established by means of the ^{13}C NMR spectra, including those with partial decoupling of the protons* by the method described for 4-ethyl- and 4-propyl-1,2,6,7-tetramethylindole [4].

The data obtained constitute an argument in favor of the proposed scheme of the formation of indoles from pyridinium salts [1].

EXPERIMENTAL

The PMR spectra of solutions of the compounds in $CDCl_3$ were recorded with a Varian T-60 spectrometer with hexamethyldisiloxane (HMDS) as the standard. The molecular masses were determined mass spectrally with a Finnigan-402 spectrometer. The course of the reactions was monitored by means of thin-layer chromatography (Silufol UV-254).

General Method for the Synthesis of the Alkylindoles. A mixture of 10 mmole of nitropyridinium iodide I and 20 ml of a 10% solution of the alkylamine in the ketone was allowed to stand at room temperature for 5-7 days, after which the mixture was evaporated, and the residue was extracted with hexane. The indoles were separated with a column packed with silica gel L (100/160 μ) in a benzene–hexane system (1:4) (see Table 1).

LITERATURE CITED

1. S. P. Gromov and Yu. G. Bundel', Dokl. Akad. Nauk SSSR, 281, 585 (1985).
2. A. N. Kost, S. P. Gromov, and R. S. Sagitullin, Tetrahedron, 37, 3423 (1981).
3. N. E. Grigor'eva and M. D. Yavlinskii, Ukr. Khim. Zh., 18, 82 (1952).
4. M. A. Yurovskaya, V. A. Chertkov, A. Z. Afanas'ev, and F. V. Ienkina, Khim. Geterotsikl. Soedin., No. 4, 509 (1985).

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