RECYCLIZATION OF 2-(2-ACYLETHYL)PYRIDINIUM SALTS

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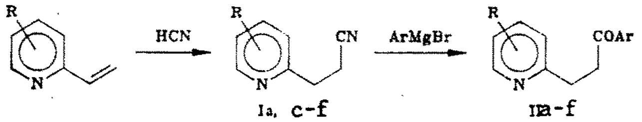
UDC 547.823'821.3'754.07:
543.422

Recyclization of 2-(2-acylethyl)pyridinium salts on treatment with nucleophiles may occur in different ways, to give heterocyclic compounds of various classes, namely indoles (the Kost–Sagitullin reaction products), 4-aminoindoles, and 3-hydroxy-1,2,3,4-tetrahydroquinolines, the formation of which constitute novel reactions in the recyclization of pyridinium salts.

Pyridinium salts bearing in the 2-position an alkyl chain which has a carbonyl group in the δ-position are known to recyclize to give quinolines [1]. On the assumption that the Kost–Sagitullin reaction with pyridinium compounds with a carbonyl group in the γ-position leads to the formation of the corresponding indoles, we have examined the recyclization of 2-(2-acylethyl)pyridinium salts by treatment with nucleophiles. The acyl groups used were benzoyl and 2-thenoyl, and in addition methyl groups were introduced into the pyridine ring in various positions.

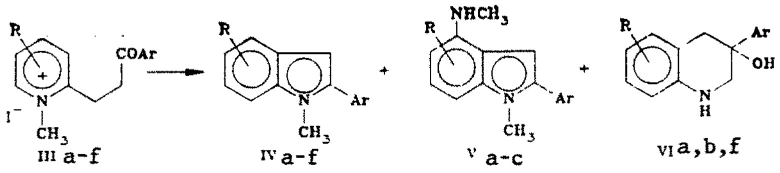
The required 2-(2-acylethyl)pyridines (IIa-f) were obtained by reacting the appropriate 2-vinylpyridines with hydrogen cyanide, followed by condensation of the resulting 2-pyridylpropionitriles with arylmagnesium bromides.



I, II a R=H, c R=3-CH$_3$, d R=4-CH$_3$, e R=5-CH$_3$, f R=6-CH$_3$, II$^{a,c-f}$ Ar=Ph;
b R=H, Ar= 2-thienyl

Since there have been no reports of the preparation of 2-(2-acylethyl)pyridines in this way, we varied the proportions of the reactants (nitrile and arylmagnesium bromide) and some other reaction conditions (duration of boiling, mode of decomposition of the complex, and method of hydrolysis of the Schiff's base). The best results were obtained using a fivefold excess of the arylmagnesium bromide. The 2-(2-acylethyl)pyridines (IIa-f) were obtained in this way in yields of 45-65%. The pyridinium salts (IIIa-f) were obtained by reacting the ketones (IIa-f) with methyl iodide.

The recyclization of 2-alkylpyridinium salts which do not contain acceptor substituents in the ring is preferably carried out using sulfite reactants [2]. The reaction of 1-methyl-2-(2-benzoylethyl)pyridinium iodide (IIa) with a mixture of aqueous solutions of methylammonium bisulfite and methylamine at 150°C was examined. According to TLC, the reaction mixture contained more than ten products, although most of these were present in amounts too small to be isolable preparatively. Three products were isolated preparatively.



Compound	R	Compound	R	Compound	R	Compound	R	Compound	R	Compound	R
IIIa	H	IIId	4-Me	IVa	H	IVd	6-Me	Va	H	VIa	H
IIIb	H	IIIe	5-Me	IVb	H	IVe	5-Me	Vb	H	VIb	H
IIIc	3-Me	IIIf	6-Me	IVc	7-Me	IVf	4-Me	Vc	7-Me	VIf	5-Me

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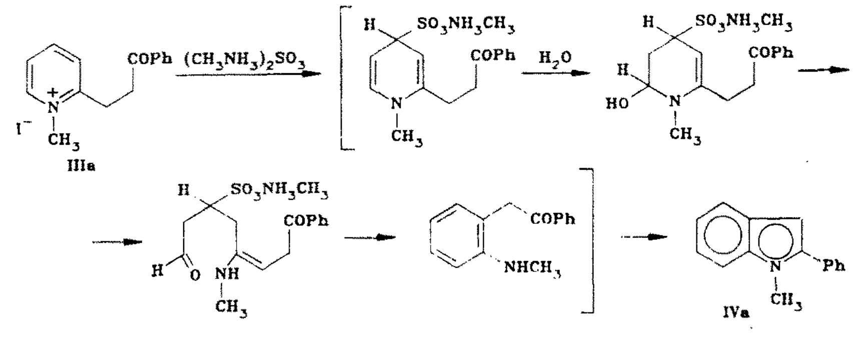
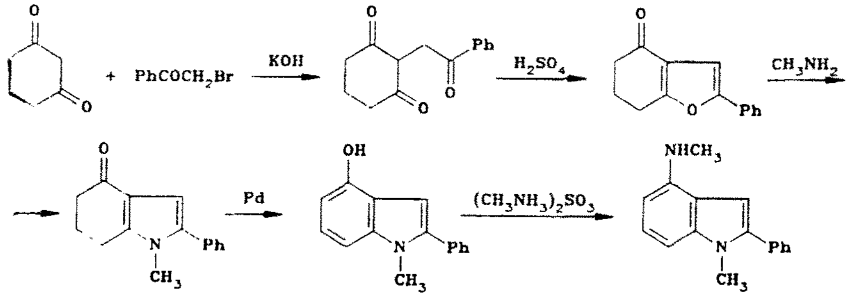
The first of these, obtained in 4% yield, was from its spectral data 1-methyl-2-phenylindole (IVa). The structure of this compound was more firmly established by its preparation from 2-phenylindole and methyl iodide in the presence of sodium hydroxide and tetramethylammonium iodide in a two-phase water–benzene system. The indole (IVa) may arise by the reaction sequence proposed for the Kost–Sagitullin rearrangement [2].

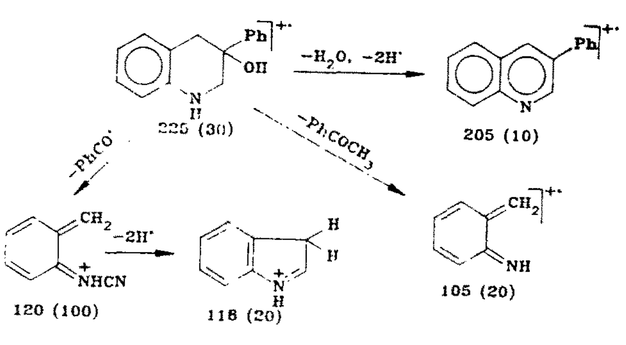


The second product, isolated from the reaction mixture in a yield of 3%, was, from its IR (3400 cm^{-1}, NH), PMR, and mass spectra assigned the structure 1-methyl-2-phenyl-4-methylaminoindole (Va). In order to confirm its structure, the aminoindole (Va) was obtained by direct synthesis, as follows:



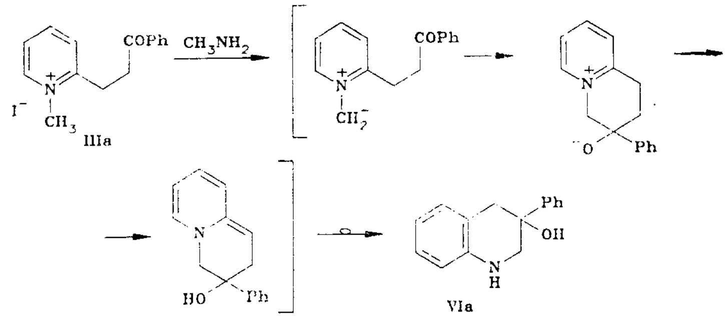
Apparently, treatment with the nucleophile results in opening of the pyridine ring in the salt (IIIa), followed by closure of either the six-membered carbocycle, or the five-membered pyrrole ring, this being a novel reaction in the recyclization of pyridinium salts which differs from the enamine rearrangement in that incorporation of the reagent into the Kost–Sagitullin reaction product does not occur.

The third product, obtained in 1.5% yield, was from its spectral properties 3-hydroxy-3-phenyl-1,2,3,4-tetrahydroquinoline (VIa), the IR spectrum of which showed absorption at 3500 and 3400 cm^{-1} (OH, NH). Mass spectral fragmentation of this compound occurs as follows:



The breakdown of the molecular ion follows three main routes: 1) Successive (or synchronous) loss of a molecule of H_2O and H_2 gives the pseudomolecular 3-phenylquinoline ion (10%); 2) retrodiene breakdown with the formation of ions with m/z 105 (I 20%); and 3) the principal mode, involving fission of the heterocycle with successive elimination of a benzoyl radical and a molecule of H_2. The PMR spectrum shows signals for the hydroxyl (3.86) and amine (5.25 ppm) protons. The protons in the methylene groups in positions 2 and 4 of the tetrahydroquinoline give rise to two pairs of doublets, that for 4-H at 2.71 and 3.14 ppm, spin-spin coupling constant 16 Hz, and that for 2-H at 3.09 and 3.40 ppm, J 11.5 Hz.

The formation of the tetrahydroquinoline (VIa) may be shown as follows:



The first step appears to involve deprotonation of the N-methyl group to give a betaine, which then cyclizes to form the tetrahydroquinoline nucleus, which finds an analogy in the literature [3]. Removal of a proton from an N-benzyl substituent by treatment with caustic alkali is described, followed by condensation of the resulting zwitterion with carbonyl compounds. This reaction, however, occurs only with acceptor N-substituents such as p-nitrobenzyl. In our case, deprotonation of the N-methyl group occurs on treatment with a weaker base, together with intramolecular condensation of the resulting anionic center at the carbonyl group present in the molecule. The subsequent stage consists in the isomerizational recyclization of the quinolizine nucleus to the quinoline ring, as in the known recyclization of indolizines [4].

In order to improve the yields of products of recyclization of pyridinium salts, and to modify the rearrangement routes, novel reagents were used which had not previously been employed in the Kost–Sagitullin recyclization (Table 1). Replacement of the aqueous methylamine in the sulfite reagent by alcoholic methylamine gave a 17% yield of the aminoindole (Va), and a 5% yield of the tetrahydroquinoline (VIa). The indole (IVa) was, however, present in the reaction mixture in trace amounts only. The best overall yield of reaction products (55%) was obtained using as the nucleophilic reagent a mixture of sodium sulfite and alcoholic methylamine. In this case, the aminoindole (Va) was formed in 5% yield. It is likely that the reactions leading to the formation of the aminoindole (Va) are to some extent connected with the presence of water in the reactant. When water is present in the reaction mixture in only trace amounts, formation of the aminoindole (Va) is reduced, so that the yields of the recyclization products (IVa) and (VIa) are increased.

In order to assess the influence of the aryl substituent on the course of recyclization, 1-methyl-2-[2-(2-thenoyl)ethyl]pyridinium iodide (IIIb) was employed as a model compound. The reaction was found to follow a course similar to that of the analogous recyclization of the salt (IIIa), giving three main products, namely 1-methyl-2-(2-thienyl)indole (IVb), 1-methyl-2-(2-thienyl)-4-methylaminoindole (Vb), and 3-hydroxy-3-(2-thienyl)-1,2,3,4-tetrahydroquinoline (VIb) (Table 2).

It would be expected that the introduction of a methyl substituent into the 6-position of the pyridine ring would make possible a new mode of rearrangement, namely recyclization involving the 6-methyl group. On the other hand, the presence of this substituent should prevent the formation of the aminoindole, since aromatization of the rearrangement product is more likely to result in loss of a molecule of methylamine than of a methyl group.

TABLE 1. Yields of Rearrangement Products on Reacting the Pyridinium Salts (III) with Various Reagents

Salt	Reagents*	Reaction conditions		Yields of products, %			Salt	Reagents*	Reaction conditions		Yield of products, %		
		T, °C	time, h	IV	V	VI			T, °C	time, h	IV	V	VI
IIIa	A	150	30	4	3	2	IIIc	C	150	30	10	9	—
	B	150	30	8	—	2		D	175	10	14	5	—
	C	100	20	—	8	—	IIId	C	150	30	6	—	—
	C	150	30	—	17	5		D	175	10	5	—	—
	C	175	30	5	12	6	IIIe	C	150	30	6	—	—
	D	150	30	5	3	5		D	175	10	10	—	—
IIIb	D	175	10	35	6	14	IIIf	C	150	30	23	—	9
	C	150	30	3	10	8		D	175	10	5	—	4
	D	175	10	2	1	4							

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*See Experimental.

TABLE 2. Spectral Data for Indoles (IV), Aminoindoles (V), and Tetrahydroquinolines (VI)

Compound	Empirical formula	mp, °C	PMR spectrum, δ, ppm (in CD_3COCD_3)	Mass spectrum, m/z (I_{rel}, %)
IVa	$C_{15}H_{13}N$	100...101 [8]	3,71 (3H, s, 1-CH_3); 6,48 (1H, s, 3-H); 7,01 (1H, d.d.d, $J_{54}=7,5$ Hz, $J_{56}=81$, $J_{57}=1$ Hz, 5-H); 7,12 (1H, d.d.d $J_{65}=8$, $J_{67}=8$, $J_{64}=1$ Hz, 6-H); 7,37 (2H, m, p-H, 4-H); 7,47 (2H, m, m-H); 7,51 (3H, m, o-H, 7-H)	—
IVb	$C_{13}H_{11}NS$	87...89	3,83 (3H, s, 1-CH_3); 6,58 (1H, s, 3-H); 7,00 (1H, d.d.d., $J_{54}=8$, $J_{56}=8$, $J_{57}=$ =1 Hz 5-H); 7,15 (2H, m, 6-H, 4-H thiophene); 7,29 (1H, d.d $J_{34}=4$, $J_{35}=1,5$ Hz 3-H thiophene); 7,38 (1H, d.d $J_{45}=8$ Hz 4-H); 7,50 (1H, br.s., $J_{76}=8$ Hz 7-H); 7,51 (1H, d.d, $J_{54}=5,5$, $J_{53}=1,5$ Hz 5-H thiophene)	213 (100), 198 (15), 196 (10), 106,5 (10), 81 (30), 77 (6)
IVc	$C_{16}H_{15}N$	98...99	2,78 (3H, s, 7-CH_3); 3,94 (3H, s, 1-CH_3); 6,48 (1H, s, 3-H); 6,88 (1H, br.d $J_{65}=8$ Hz, 6-H); 6,91 (1H, d.d $J_{54}=7,5$, $J_{56}=8$ Hz, 5-H); 7,34 (1H, br.d $J_{45}=8$ Hz., 4-H); 7,41 (1H, m, p-H); 7,49 (2H, m, m-H); 7,53 (2H, m, o-H)	221 (100), 206 (10), 205 (10), 204 (11), 179 (7), 178 (7), 110,5 (18), 91 (15), 77 (17)
IVd	$C_{16}H_{15}N$	82...84	2,46 (3H, s, 6-CH_3); 3,75 (3H, s, 1-CH_3); 6,48 (1H, s, 3-H); 6,91 (1H, br.d $J_{54}=8$ Hz, 5-H); 7,23 (1H, br.s, 7-H); 7,41 (1H, m, p-H); 7,43 (1H, d, $J_{45}=8$ Hz, 4-H); 7,49 (2H, m, m-H); 7,57 (2H, m, p-H)	221 (100), 205 (15), 206 (11), 204 (11), 179 (7), 178 (7), 110,5 (20), 91 (11), 77 (15)
IVe	$C_{16}H_{15}N$	123...124 [9]	2,40 (3H, s, 5-CH_3); 3,76 (3H, s, 1-CH_3); 6,45 (1H, s 3-H); 7,04 (1H, d.d., $J_{67}=8$, $J_{64}=1,5$ Hz, 6-H); 7,32 (1H, m $J_{76}=8$ Hz, 7-H); 7,36 (1H, br.s 4-H); 7,42 (1H, m p-H); 7,51 (2H, m, m-H); 7,58 (2H, m o-H)	
IVf	$C_{16}H_{15}N$	85...87	2,47 (3H, m, 4-CH_3); 3,71 (3H, s, 1-CH_3); 6,53 (1H, s 3-H); 6,85 (1H, br.d $J_{56}=8$ Hz, 5-H); 7,07 (1H, d.d, $J_{65}=8$, $J_{67}=8$ Hz., 6-H); 7,47 (1H, br.d $J_{75}=8$ Hz, 7-H)	221 (100), 206 (13), 205 (16), 204 (18), 179 (8), 178 (9), 110,5 (13), 91 (15), 77 (10)
Vb	$C_{16}H_{16}N_2$	108...109	2,73 (1H, br.s N—H); 2,86 (3H, s, N—CH_3); 3,64 (3H, s 1-CH_3); 6,13 (1H, d $J_{56}=8$ Hz., 5-H); 6,55 (1H, s 3-H); 6,67 (1H, c $J_{76}=8$ Hz 7-H); 6,98 (1H, d.d 6-H); 7,31 (1H, s, p-H); 7,40 (2H, m, m-H); 7,47 (2H, m, o-H)	236 (100), 235 (15), 221 (37), 207 (19), 194 (17), 165 (10), 118 (12), 110 (7), 77 (7)
V[illegible]	$C_{14}H_{14}N_2S$	99...101	2,85 (3H, s N—CH_3); 3,72 (3H, s 1-CH_3); 5,10 (1H, br.s, N—H); 6,11 (1H, d $J_{56}=8$ Hz, 5-H); 6,65 (1H, d $J_{76}=8$ Hz, 7-H); 6,66 (1H, s, 3-H); 6,98 (1H, d.d $J_{65}=8$, $J_{67}=8$ Hz, 6-H); 7,00 (1H, d.d $J_{43}=4$, $J_{45}=5$ Hz, 4-H thiophene); 7,10 (1H, d.d, $J_{34}=4$, $J_{35}=1,5$ Hz 3-H thiophene); 7,32 (1H, d.d, $J_{54}=5$, $J_{43}=1,5$ Hz 5-H thiophene);	242 (100), 241 (16), 227 (40), 213 (25), 200 (20), 127 (12), 111 (16), 106 (16), 104 (16), 97 (25), 95 (30), 91 (16), 85 (25), 83 (35), 81 (30), 77 (16)
Vc	$C_{17}H_{18}N_2$	70...72	2,61 (3H, s, 7-CH_3); 2,84 (3H, s N—CH_3); 2,87 (1H, br.s, N—H); 3,86 (3H, s 1-CH_3); 6,01 (1H, d $J_{56}=7,5$ Hz 5-H); 6,51 (1H, s 3-H); 6,68 (1H, br.d, $J_{65}=7,5$ Hz 6-H); 7,33 (1H, m, p-H); 7,42 (2H, m m-H); 7,46 (2H, m, o-H)	250 (100), 242 (25), 235 (33), 221 (17), 207 (13), 194 (9), 125 (13), 117,5 (9), 117 (13), 110,5 (13), 89 (9), 77 (13)
VIa	$C_{15}H_{15}NO$	115...116	2,71 (1H, d.d, $J=16$, $J=3$ Hz., 4-H); 3,09 (1H, br.d., $J=11,5$ Hz, 2-H); 3,14 (1H, br.d $J=16$ Hz 4-H); 3,40 (1H, br.d $J=11,5$ Hz, 2-H); 3,86 (1H, s OH); 5,25 (1H, br.d, N—H); 6,49 (1H, d.d.d $J_{65}=8$, $J_{67}=8$, $J_{68}=1$ Hz, 6-H); 6,55 (1H, br.d., $J_{87}=8$ Hz 8-H); 6,88 (2H, m, 5-H, 7-H); 7,18 (1H, m, p-H); 7,20 (2H, m m-H); 7,52 (2H, m, o-H)	225 (30), 205 (10), 120 (100), 118 (17), 106 (13), 105 (20), 91 (15), 77 (20)
VIb	$C_{13}H_{13}NOS$	97...98	2,92 (1H, d.d, $J=16$, $J=2,5$ Hz, 4-H); 3,52 (1H, br.d, $J=16$ Hz, 4-H); 3,59 (1H, d.d $J=12$, $J=2,5$ Hz, 2-H); 3,71 (1H, br.d $J=12$ Hz, 2-H); 4,44 (1H, s, OH); 5,42 (1H, br.s N—H); 6,48 (1H, d.d.d, $J_{65}=8$, $J_{67}=8$, $J_{68}=1$ Hz, 6-H); 6,52 (1H, br.d $J_{87}=8$ Hz, 8-H); 6,86 (1H, br.d $J_{57}=8$ Hz, 5-H); 6,88 (2H, m, 7-H, 4-H thiophene) 6,92 (1H, br.d $J_{34}=4$, $J_{35}=1,5$ Hz, 3-H thiophene); 7,22 (1H, thiophene) $J_{54}=5$, $J_{53}=15$ Hz, 5-H thiophene)	231 (30), 211 (12), 121 (12), 120 (100), 116 (17), 111 (12), 106 (10), 91 (15), 77 (8)
VIf	$C_{16}H_{17}NO$	131...133	2,07 (3H, s, 5-CH_3); 2,70 (1H, d.d, $J=17$, $J=2,5$ Hz, 4-H); 3,01 (1H, br.d $J=17$ Hz 4-H); 3,05 (1H, d.d, $J=11,5$, $J=2,5$ Hz, 2-H); 3,35 (1H, br.d $J=11,5$ Hz., 2-H); 3,58 (1H, s, OH); 5,22 (1H, br.s N—H); 6,43 (1H, br.d $J_{87}=8$ Hz, 8-H); 6,47 (1H, br.s $J_{67}=8$ Hz, 6-H); 6,81 (1H. d.d, $J_{76}=8$, $J_{78}=$ =8 Hz, 7-H); 7,21 (1H, m p-H); 7,31 (2H, m, m-H); 7,55 (2H, m, o-H)	239 (55), 220 (5), 219 (10), 135 (10), 134 (100), 132 (10), 120 (11), 105 (10), 91 (9), 77 (11)

TABLE 3. Properties of Nitriles (I)

Compound	Empirical formula	mp, °C	mp of picrate, °C	n_D^{20}	PMR spectrum, δ, ppm (in CCl_4)	Yield, %
Ia	$C_8H_8N_2$	98...99	—	1,5170 [6]	2,6...3,25 (4H, m, CH_2CH_2); 7,05...8,0 (3H, m, Ar); 8,55 (1H, d.d, $J_{65}=6$, $J_{64}=1,5$ Hz, 6-H)	38
Ic	$C_9H_{10}N_2$	96...98	127...128	1,5235	2,3 (3H, s, 3-CH_3); 2,6...3,2 (4H, m, CH_2CH_2); 7,05 (1H, m, 5-H); 7,45 (1H, d.d $J_{45}=6$, $J_{46}=1,5$ Hz, 4-H); 8,35 (1H, d.d, $J_{65}=6$, $J_{64}=1,5$ Hz, 6-H)	50
Id	$C_9H_{10}N_2$	103...106	128...129	1,5080	2,55 (3H, s, 4-CH_3); 2,90...3,35 (4H, m, CH_2CH_2); 7,15 (1H, d, $J_{56}=5$ Hz, 5-H); 7,2 (1H, s 3-H); 8,6 (1H, d $J_{65}=5$ Hz, 6-H)	53
Ie	$C_9H_{10}N_2$	97...99	145...146	1,5130	2,25 (3H, s 5-CH_3); 2,6...3,1 (4H, m, CH_2CH_2); 7,0 (1H, d $J_{34}=8$ Hz, 3-H); 7,3 (1H, d.d, $J_{43}=8$, $J_{46}=2$ Hz, 4-H); 8,25 (1H, d $J_{64}=2$ Hz, 6-H)	33
If	$C_9H_{10}N_2$	82...84	98...100	1,5265	2,45 (3H, s, 6-CH_3); 2,6...3,1 (4H, m CH_2CH_2); 6,8...7,6 (3H, m, Ar)	53

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*For compounds (Ia, c, d) the pressure was 2 mm, and for (Ie, f), 1 mm.

TABLE 4. Properties of Ketones (II) and Their Salts (III)

Compound	Empirical formula	bp of ketone (II), °C*	mp, °C**	mp of salt (III), °C	PMR spectrum of ketone (II), δ, ppm (in CCl_4)	IR spectrum of ketone (II), cm^{-1} (C=O)	Yield of ketone (II) salt(III), %
IIa	$C_{14}H_{13}NO$	168...170	60...61 [7]	168...170	2,9...3,6 (4H, m, CH_2CH_2); 6,8...8,05 (8H, m, Ar); 8,4 (1H, d.d $J_{65}=6$, $J_{64}=1,5$ Hz, 6-H)	—	64 (89)
IIb	$C_{13}H_{11}NOS$	160...162	119...121	152...154	2,9...3,5 (4H, m, CH_2CH_2); 6,8...7,8 (6H, m, Ar); 8,5 (1H, d.d $J_{65}=6$, $J_{64}=1$ Hz, 6-H)	—	58 (82)
IIc	$C_{15}H_{15}NO$	156...158	147...148	155...156	2,35 (3H, c, 3-CH_3); 2,95...3,65 (4H, m, CH_2CH_2); 6,95 (1H, d.d. $J_{56}=5$, $J_{54}=6$ Hz, 5-H); 7,2...7,5 (5H, m Ar); 8,0 (1H, d.d, $J_{45}=6$, $J_{46}=2$ Hz 4-H); 8,3 (1H, d.d, $J_{65}=5$ Hz, $J_{64}=2$ Hz 6-H)	1683	47 (95)
IId	$C_{15}H_{15}NO$	160...161	118...120	176...178	2,3 (3H, s 4-CH_3); 3,0...3,45 (4H, m, CH_2CH_2); 6,65...8,05 (7H, m, Ar); 8,25 (1H, m, $J_{64}=5$ Hz, 6-H)	1685	43 (94)
IIe	$C_{15}H_{15}NO$	168...170	123...124	187...188	2,25 (3H, s, 5-CH_3); 2,9...3,55 (4H, m, CH_2CH_2); 6,9...8,0 (7H, m, Ar); 8,25 (1H, d $J_{64}=2$ Hz 6-H)	1690	48 (94)
IIf	$C_{15}H_{15}NO$	138...140	125...126	162...163	2,45 (3H, s, 6-CH_3); 2,9...3,55 (4H, m, CH_2CH_2); 6,80...8,15 (8H, m, Ar)	1688	48 (95)

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*Pressure 1 mm.

**(IIa) as the ketone and (IIb-f) as the picrate.

The recyclization of the 1,6-dimethyl-2-(2-benzoylethyl)pyridinium salt (IIIf) was effected by treatment with a mixture of aqueous methylammonium sulfite and alcoholic methylamine. Two products were isolated from the reaction mixture, viz., 1,4-dimethyl-2-phenylindole (IVf) in 23% yield, and 3-hydroxy-3-phenyl-5-methyl-1,2,3,4-tetrahydroquinoline (VIf) in 9% yield. The corresponding aminoindole (Vf) was not detected, as would be expected from the above considerations, nor products of the rearrangement of the salt (IIIf) involving the 6-methyl substituent.

When the recyclization of 1,4-dimethyl-2-(2-benzoylethyl)pyridinium iodide (IIId) was carried out, from the reaction mixture there was isolated 6% of 1,6-dimethyl-2-phenylindole (IVd). It would seem that the methyl substituent in the 4-position of the pyridine ring prevents attack of the sulfite anion, so that the yield of the indole (IVd) is low, and is independent of the reagent used. In this instance, it was not possible to isolate any other rearrangement products.

The introduction of a methyl substituent into the 3- or 5-position of 2-methylpyridinium salts is known to weaken the N–C_2 bond, resulting in a decrease in the selectivity of the reaction as a result of the possibility of the rearrangement occurring in two ways, with rupture of either the N–C_6 or the N–C_2 bond [2].

Recyclization of the 1,5-dimethyl-2-(2-benzoylethyl)pyridinium salt (IIIe) affords 1,5-dimethyl-2-phenylindole (IVe) in 10% yield. On recyclization of 1,3-dimethyl-2-(2-benzoylethyl)pyridinium iodide (IIIc), there were isolated 1,7-dimethyl-2-phenylindole (IVc) (10%) and 1,7-dimethyl-2-phenyl-4-methylaminoindole (Vc) (9%). The formation of (IVc) and (Vc) is in accordance with the proposed reaction sequences, in which the methyl group in the 3-position in the starting pyridinium salt should appear in the 7-position of the indole ring.

The structures of the indoles (IV) were proved by high-resolution PMR spectroscopy (Table 3). Examination of the spectral data confirms the structures assigned to them on the basis of the reaction mechanism, by assigning unambiguously the positions of the methyl groups in the indole ring. For example, in the case of the indole (IVc), the spectrum shows characteristic changes in the chemical shifts of the protons of the methyl groups present in the 1- and 7-positions (mutual descreening of the alkyl groups [5]), and the signal for the protons of the N–CH_3 methyl groups is seen at 3.94 ppm, whereas in the case of (IVa, d-f), in which the 7-position is occupied by hydrogen, the signal for the protons of the N-methyl group is seen at 3.71-3.76 ppm. The protons of the methyl group in the 7-position are also seen at lower field (2.78 ppm) as compared with the protons of the methyl groups in the 4-, 5-, and 6-positions (2.40-2.47 ppm).

EXPERIMENTAL

Infra-red spectra were obtained on UR-20 and Specord-75 instruments in Vaseline grease, films, and CCl_4. Proton magnetic resonance spectra were obtained on Tesla BS-467 (60 MHz) and Bruker (500 MHz) instruments, internal standard TMS. Mass spectra were obtained on a Varian MAT-111 with direct sample introduction into the ionization zone, ionizing electron energy 70 eV.

The progress of the reactions was monitored by TLC on Silufol UV-254 plates.

The elemental analyses of the products for C, H, and N were in agreement with the calculated values.

β-(2-Pyridyl)propionitriles (Ia, c-f) (Table 3). To a solution of 0.5 mole of the appropriate 2-vinylpyridine in 120 ml of acetic anhydride was added with cooling 1 mole of potassium cyanide in 120 ml of water. The mixture was heated for 20 h at 75°C, neutralized with sodium carbonate solution, and extracted with chloroform. The solvent was removed, and the residue fractionated in vacuo.

2-(2-Acylethyl)pyridines (IIa-f) (Table 4). To the Grignard reagent obtained from 0.25 mole of magnesium and 0.25 mole of the aryl bromide in 75 ml of dry ether there was added 0.05 mole of the β-(2-pyridyl)propionitrile (Ib-f) in 25 ml of ether. The mixture was brought to the boil, cooled, and 5 ml of water and 100 ml of 5 N sulfuric acid added. The aqueous layer was boiled for 1.5 h, neutralized with sodium carbonate, and extracted with chloroform. The extract was dried, the chloroform removed, and the residue fractionated in vacuo.

1-Methyl-2-(2-acylethyl)pyridinium Iodides (IIIa-f) (Table 3). A mixture of 0.01 mole of the 2-(2-acylethyl)pyridine (IIa-f) and 15 ml (0.25 mole) of methyl iodide was kept for 24 h. The crystals which separated were filtered off, washed with acetone, and dried.

Recyclization of 1-Methyl-2-(2-benzoylethyl)pyridinium Iodides (IIIa-f). A. A mixture of 2 mmoles of the pyridinium iodide (Ia-f), 5 ml of 40% aqueous methylammonium bisulfite, and 5 ml of 25% aqueous methylamine was heated in a sealed ampul for 25-35 h at 150°C. The mixture was then extracted with benzene, and the benzene extract separated on a column of silica gel (100/160 μ) in the system benzene–ethyl acetate–hexane (1:1:3).

B. A mixture of 2 mmoles of the pyridinium iodide (Ia-d) and 10 ml of 34% alcoholic methylamine was heated in a sealed ampul at 150°C for 25-30 h. The alcohol was distilled off, and the residue worked up as described in method A.

C. A mixture of 2 mmoles of the pyridium iodide (Ia-d), 3 ml of 40% aqueous methylammonium bisulfite, and 6 ml of 34% alcoholic methylamine was heated in a sealed ampul at 150°C for 25-35 h. The mixture was extracted with benzene, and worked up as in method A.

D. A mixture of 2 mmoles of the pyridium iodide (Ia-d), 1.26 g (0.01 mole) of sodium bisulfite, and 10 ml of 34% alcoholic methylamine was heated in a sealed ampul at 175°C for 10-12 h. The mixture was worked up as in method A.

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REACTIONS OF N-(4-METHOXYBENZYLIDENE)-N,N-DIALKYLIMINIUM AND 2-(4-METHOXYPHENYL)PYRIDINIUM SALTS WITH ALIPHATIC AMINES

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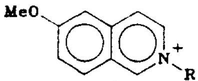
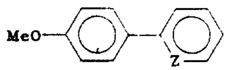
UDC 547.821.3'823'554.07

The reaction of 4-methoxybenzylideneiminium salts with methylamine and dimethylamine on heating results in replacement of the MeO group by an alkylamino-group, whereas the reaction with piperidine affords 3,5-bis-(4-methoxybenzyl)pyridine. N-Methyl-2-(4-methoxyphenyl)pyridinium iodide on treatment with methylamine undergoes dealkylation to the arylpyridine.

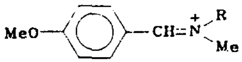
It is well known that the $> C=\overset{+}{N} <$ group in isoquinolinium salts activates the 6-position of the heterocyclic system, facilitating replacement of the alkoxy-group on treatment with primary aliphatic amines [1]. We have now examined the possibility of carrying out this reaction with compounds in which the $> C=\overset{+}{N} <$ group is not incorporated into the aromatic system, by treatment with nucleophiles. The compounds of this type chosen for study were the 2-(4-methoxyphenyl)pyridinium salts (IIa, b) and the N-(4-methoxybenzylidene)-N,N-dialkyliminium salts (IIIa, b), which in respect of the position of the C=N bond relative to the methoxy-group and the benzene ring is formally analogous to the isoquinoline salt (I).



I



II a-c



III a,b

II a Z=NMe$^+$, b Z=NH$^+$, c Z=N; III a R=Me, b R=*tert*-Bu

M. V. Lomonosov Moscow State University, Moscow 117234. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 9, pp. 1226-1229, September, 1990. Original article submitted September 12, 1989.

0009-3122/90/2609-1022$12.50 ©1991 Plenum Publishing Corporation