1-Phenyl-2,4-dimethyl-4-(α-alkoxybenzyl)-3,5-dioxopyrazolidine (V). A. The combined ether extracts, obtained during the synthesis of compounds IIIa and b were dried with sodium sulfate, filtered, and evaporated to dryness, to afford a pale-yellow oil (IIIa) or precipitate (IIIb), from which after thin-layer chromatographic purification of alumin was obtained a colorless oil (IIIa) or crystals (IIIb), containing (TLC) two spots with very similar R_f values. Further recrystallization from ethanol gave chromatographically homogeneous Va and b. Pure Vb was also isolated during the synthesis of IIIb (see above).

B. Methyl iodide (0.24 mole) was added to a solution of 40 mmoles of compound IIIa or b in a freshly prepared solution of 80 mmoles of sodium in 80 ml of absolute methanol (for Ve, 170 ml of absolute ethanol). The mixture was left at 20° for 96-120 h and worked up as in the preparation of IIIa-d; compound V was isolated from the ether extract as described in A. During the preparation of Vb, after extraction, an additional 22% of chromatographically homogeneous Vb was isolated.

On acidifying the aqueous solutions, the starting materials IIIa and b were recovered.

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REACTION OF 4-AMINOIMADAZO[4.5-c]PYRIDIN-2-ONES WITH α-BROMOMETHYLKETONES

Yu. M. Yutilov and K. M. Khabarov

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The reactions of 4-amino derivatives of imidazo[4.5-c]pyridin-2-ones with α-bromomethylketones have been studied. Depending on the nature of the reagents and the reaction conditions, either 5-acylmethyl salts of the starting amine or 2-substituted imidazo[4.5-c]imidazo[1.2-a]pyridin-8-ones can be obtained. The latter compounds are also easily obtained by treatment of the 5-acylmethyl salts with alkali.

The facile nitration of imidazo[4.5-c]pyridin-2-one in the 4-position has opened up many new possibilities for the preparation of a wide variety of substituted derivatives of this compound [1-3]. Two of these new compounds which are of widespread interest are 4-amino-1-methylimidazo[4.5-c]pyridin-2-one (Ib) and its 3-methyl congener (Ia). Previous work has established that the base Ia can be readily alkylated at the nitrogen atom of the pyridine ring upon treatment with alkyl halides [4]. In the present paper we report our results of the study of the reactions of Ia and b with α-bromomethylketones (IIb-h) and α-bromoacetaldehyde (IIa).

The addition of the aliphatic α-bromomethylketones IIa-d to amine Ia occurs upon reflux in alcoholic solution over 1-2 h and gives salts IIIa-d in high yield (Table 1). Clemmenson reduction of the acetonyl bromide IIIb gives, after acidification of the reaction mixture with hydrogen iodide, the iodide salt of 4-amino-5-n-propyl-1,3-dimethylimidazo[4.5-c]pyridinium-2-one (V), which has been previously prepared form amine Ia with n-propyl iodide [4]. This observation, coupled with the similarities in the UV spectra of the quaternary salts IIIa-d (Table 1), leads us to believe that reaction of amine Ia with the α-bromomethylketones IIa-d generates the 5-acylmethyl salts IIIa-d.

Institute of Physical Organic Chemistry and Petroleum Chemistry, Academy of Sciences of the Ukrainian SSR, Donetsk, 340114.

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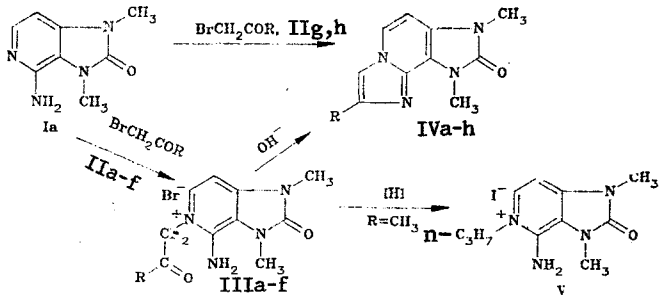
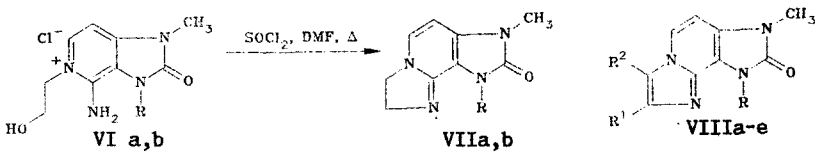


II, III, IV a R = H; b R = CH_3; c R = $C(CH_3)_3$; d R = 2'-Ad; e R = 3'4'-$(CH_3O)_2C_6H_3$; f R = β-naphthyl; g R = C_6H_5; h R = p-$NO_2C_6H_4$

Treatment of the acylmethyl salts IIIa-d with basic solutions releases the free bases IVa-d. Compound IVa was shown to be identical to the dehydrogenation product of 8-oxo-7,9-dimethyl-2,3-dihydroimidazo[4.5-c]imidazo[1.2-a]pyridine (VIIa), which was obtained via reaction of chloride VIa with thionyl chloride in refluxing DMF. In an analogous manner salt IVb could be converted to the hydrochloride of VIIb. The IR spectra of compounds VIIa and b do not contain absorption bands due to OH and NH_2 groups, which are characteristic of the precursor salts VIa and b (3260-3275 and 3370-3400 cm^{-1}). The latter compounds are easily obtained in high yields via reaction of amines Ia and b with ethylene chlorohydrin. Their IR spectra are similar to that of iodide V.



VI, VII a R = CH_3; b R = H; VII a-d R = R^2 = H; e R = R^2 = CH_3; a R^1 = CH_3, b R^1 = Ph; c R^1 = p-$CH_3OC_6H_4$; d R^1 = 3,4-$(CH_3O)_2C_6H_3$; e R^1 = H

Aromatic α-bromomethylketones IIe and f also react with amine Ia to generate salts IIIe and f, which can be converted to the tricyclic structural derivatives IVe and f upon treatment with base. It was not possible, however, to isolate acylmethyl salts from the reaction of amine Ia with the bromoketones IIIg and h. In these cases the 2-arylimidazo[4.5-c]imidazo-[1.2-a]pyridines IVg and h were isolated directly, whereas half of the starting amine was converted to the hydrobromide salt. If the reactions are carried out in refluxing DMF, the hydrobromide salts of imidazo[4.5-c]imidazo[1.2-a]pyridines, namely, VIIIa-e, can be isolated directly, without any intermediates, from the reactions of the amines Ia and b with equivalent amounts of the α-bromomethylketones IIb, e, and g, p-methoxyphenacyl bromide, or α-bromopropionaldehyde.

The structures of the imidazo[4.5-c]imidazo[1.2-a]pyridines IVa-h and VIIIa-e were confirmed on the basis of their spectral data. The IR spectra of the acylmethyl salts IIIa-f (Table 1) contain two carbonyl group stretching bands (1700-1715 and 1715-1730 cm^{-1}), as well as N–H stretching bands (3270-3400 cm^{-1}), whereas the spectra of the free bases IVa-h (Table 2) contain only one carbonyl group stretching frequency due to the C=O of the imidazole ring at 1690-1720 cm^{-1}. The PMR spectra of compounds IVb-h and VIIIa-d (Table 3) contain signals due to the 3-H aromatic proton at 7.66-7.83 ppm in the case of an alkyl substituent in position 2, and at 8.08-8.17 ppm in the case of an aryl substituent in the 2-position. The spectrum of compound IVa contains two doublets due to the vicinal protons of the imidazole ring (2,3-H) at 7.83 and 8.00 ppm; the spin–spin coupling constant is 2.2 Hz, which is characteristic of 2,3-unsubstituted imidazo[1.2-a]pyridines [5]. These data imply that both the bases IVa-h as well as the hydrobromide salts VIIIa-e contain tricyclic aromatic structures. Methylation of compound VIIIa with dimethyl sulfate in basic solution gave compound IVb.

In order to verify the structures of the cyclization products arising from amines Ia and b with α-bromomethylketones, an independent synthesis of a model compound, namely imidazo-

TABLE 1. Acylmethyl Salts of 4-Amino-1,3-dimethylimidazo[4.5-c]pyridin-2-one

Compound	mp, °C (from alcohol)	IR spectrum, $\nu_{C=O}$ cm^{-1}	UV spectrum, λ_{max}, nm (lg ε)	Found, %				Molecular formula	Calculated, %				Yield, %
				C	H	Br	N		C	H	Br	N	
IIIa	263—264	1730, 1715	229 (4,38), 254 (3,74), 293 (3,95)	39,4	4,7	26,8	18,3	$C_{10}H_{13}BrN_4O_2$	39,9	4,4	26,5	18,6	53
IIIb	281—283	1720, 1700	229 (4,36), 253 (3,74), 290 (3,86)	42,4	5,0	25,3	18,3	$C_{11}H_{15}BrN_4O_2$	41,9	4,8	25,4	17,8	91
IIIc	280—281	1720, 1700	225 (4,71), 252 (3,73), 292 (3,95)	47,1	5,7	21,9	15,4	$C_{14}H_{21}BrN_4O_2$	47,1	5,9	22,4	15,7	66
IIId	267—270	1725, 1700	229 (4,72), 272 (3,90), 291 (4,09)	54,9	6,4	17,9	13,1	$C_{20}H_{27}BrN_4O_2$	55,2	6,3	18,4	12,9	55
IIIe	243—244	1715, 1700	—	49,8	5,3	18,0	13,0	$C_{18}H_{21}BrN_4O_4$	49,4	4,8	18,3	12,8	46
IIIf	285—287	1725, 1705	—	54,4	5,0	17,4	12,7	$C_{20}H_{19}BrN_4O_2 \cdot H_2O$	53,9	4,8	17,9	12,6	59

TABLE 2. Imidazo[4.5-c]imidazo[1.2-a]pyridines

Compound	mp, °C (from ethanol)*	IR spectrum, $\nu_{C=O}$, cm^{-1}	Found, %			Molecular formula	Calc. %			Yield, %
			C	H	N		C	H	N	
IVa	222—224	1670, 1700	59,2	4,9	27,3	$C_{16}H_{10}N_4O$	59,4	5,0	27,7	66
IVb	229—230	1660, 1700	61,3	5,7	25,6	$C_{17}H_{12}N_4O$	61,1	5,6	25,9	73
IVc	224—225	1660, 1700	65,3	7,2	21,5	$C_{14}H_{18}N_4O$	65,1	7,0	21,7	68
IVd	285—287	1660, 1690	71,7	7,5	16,9	$C_{20}H_{24}N_4O$	71,4	7,2	16,7	74
IVe	238—240	1660, 1690	64,1	5,5	16,4	$C_{18}H_{18}N_4O_3$	63,9	5,4	16,6	78
IVf	238—240	1670, 1700	68,8	5,3	16,4	$C_{20}H_{16}N_4O \cdot H_2O$	69,3	5,2	16,2	71
IVg	258—260	1670, 1690	69,3	5,1	20,0	$C_{16}H_{14}N_4O$	69,1	5,1	20,1	58
IVh	350	1670, 1720	59,8	4,2	21,9	$C_{16}H_{13}N_5O_3$	59,4	4,1	21,7	83
VIIIa	258—260	1660, 1700	42,4	4,2	19,6	$C_{16}H_{10}N_4O \cdot HBr$	42,4	3,9	19,8	28
VIIIb	350	1660, 1690, 1730	52,1	4,0	16,4	$C_{15}H_{12}N_4O \cdot HBr$	52,2	3,8	16,2	42
VIIIc	302—304	1670, 1705, 1730	48,4	4,7	14,8	$C_{16}H_{14}N_4O_2 \cdot HBr \cdot H_2O$	48,9	4,4	14,3	53
VIIId	342—343	1660, 1700, 1730	50,4	4,4	14,0	$C_{17}H_{16}N_4O_3 \cdot HBr$	50,4	4,2	13,8	46
VIIIe	218—219	—	44,0	4,3	18,4	$C_{17}H_{12}N_4O \cdot HBr$	44,5	4,4	18,9	32
X	271—273	—	59,7	4,3	21,9	$C_{16}H_{13}N_5O_3$	59,4	4,1	21,7	35

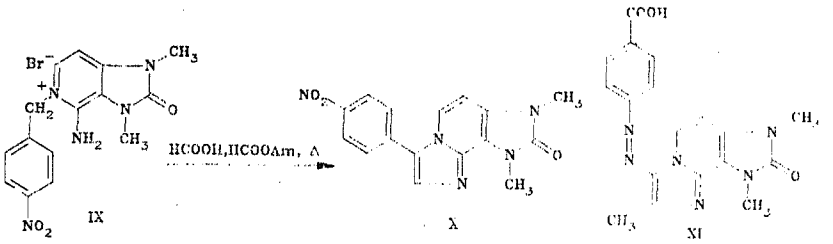
*Compound IVa was crystallized out of water, and compounds IVh and VIII out of DMF.

TABLE 3. PMR specra of Imidazo[4.5-c]iidazo[1.2-a]pyridines

Compound	Chemical shift, δ, ppm			
	5,6-H*	2-R	3-R	N—CH_3
IVa	7,48; 8,50	7,83; 8,00 (2H, 2 d, J=2,2 Hz)		3,70; 3,97
IVb	7,46; 8,41	2,64 (3H)	7,73	3,75; 4,05
IVc	7,42; 8,40	1,50 (9H)	7,70	3,70; 3,97
IVd	7,45; 8,40	1,91 (3H, CH); 2,13 (12H, CH_2)	7,66	3,70; 3,95
IVe	8,55; 7,23—7,60 [4H, m, 5(6)-H and C_6H_3]		8,10	3,75; 4,00—4,05 [9H, m., $(CH_3O)_2$, N—CH_3]
IVf	8,37; 7,27—7,90 [8H, m, 5(6)-H and $C_{10}H_7$]		8,08	3,60; 3,82
IVg	8,55; 7,50—7,80 [6H, m, 5(6)-H and C_6H_5]		8,15	3,78; 4,05
IVh	7,63; 8,02—8,73 [6H, m, 5(6)-H, 3-H and C_6H_4]			3,78; 4,07
VIIIa	7,42; 8,43	2,55	7,70	3,67
VIIIb	8,57; 7,40—7,87 [6H, m, 5(6)-H, C_6H_5]		8,17	3,67
VIIIc	7,42; 8,48	3,92 (CH_3O); 7,10; 7,68 (2 d, J=8,5 Hz, C_6H_4)	8,07	3,63
VIIId	8,50; 7,10—7,55 [4H, m, 5(6)-H and C_6H_3]; 4,05 (6H, two OCH_3)		8,10	3,73
VIIIe	7,62; 8,33	7,67	2,68 (3H, s, CH_3)	3,73; 4,03
X	7,02†; 8,07—8,60 [5H, m, 5(6)-H and C_6H_4]	7,80	—	3,58; 3,85

*J = 7.0 Hz.
†J = 7.5 Hz.

[4.5-c]imidazo[1.2-a]pyridine X, with a p-nitrophenyl substituent in the 3-position, was carried out; a mixture of the amine salt of Ia and p-nitrophenylbenzyl bromide was refluxed with an excess of a formic acid—amyl formate mixture. The PMR spectrum of the resulting material, 3-(p-nitrophenyl)imidazo[4.5-c]imidazo[1.2-a]pyridine X, does not contain a methylene group signal at 5.85 ppm, which is present in the spectrum of salt IX, but does contain a signal for the 2-H proton at 8.47 ppm. A mixture of base X and its 2-isomer IVh exhibits a temperature depression for a mixed melting point sample, which serves as further evidence of the structures of the imidazo[4.5-c]imidazo[1.2-a]pyridines IVe-h and VIIIb-d, i.e., it confirms the 2-position of the substituent groups.



In analogy with the behavior described previously for imidazo[1.2-a]pyridine [6], the 3-substituted imidazo [4.5-c]imidazo[1.2-a]pyridine derivatives VIIIe and X also do not undergo nitrogen coupling reactions, although the 2-methyl derivative IVb reacts with the diazonium salt derived from p-aminobenzoic acid to give 8-oxo-2,7,9-trimethylimidazo[4.5-c]imidazo[1.2-a]pyridine-3-azo-4'-benzoic acid (XI). The PMR spectrum of the azo compound XI does not contain a signal due to the proton in the 3-position.

EXPERIMENTAL

IR spectra were recorded on a UR-20 spectrophotometer using vaseline mulls, and PMR spectra were obtained on a Tesla BS-467C (60 MHz) spectrometer using solutions in trifluoroacetic acid versus TMS as internal standard. UV spectra were taken on a Spectromom-204 spectrophotometer for water solutions.

The properties of compounds III, IV, VIII, and X are summarized in Tables 1 and 2.

Acylmethyl Salts of 4-Amino-1,3-dimethylimidazo[4.5-c]pyridin-2-ones (IIIa-f). A solution of 1.00 mmole of amine Ia and 1.10-1.15 mmole of α-bromomethylketone IIa-f in 6 ml of ethanol was refluxed 2 h and then cooled. The precipitate was removed by filtration, washed with acetone, and dried.

2-Substituted 8-Oxo-7,9-dimethylimidazo[4.5-c]imidazo[1.2-a]pyridines (IVg, h). A mixture (or suspension) of 10 mmole of acylmethyl salt IIIa-f in 5 ml of water was treated with 3 ml of a 45% aqueous NaOH solution and heated on a boiling water bath for 0.5 h. After cooling to room temperature the precipitate was removed by filtration, washed with ice water, and dried.

2-Arylsubstituted 8-Oxo-7,9-dimethylimidazo[4.5-c]imidazo[1.2-a]pyridines (IVg, h). A mixture of 1.12 mmole of amine Ia and 0.57 mmole of α-bromomethylketone IIg and h in 4 ml of ethanol was refluxed 1 h. The precipitate was filtered, washed with water, and dried. Evaporation of the alcohol solvent and basification of the residue yielded 0.09 g (0.51 mmole) of recovered amine Ia.

4-Amino-5-n-propyl-1,3-dimethylimidazo[4.5-c]pyridinium-2-one Iodide (V). A. A mixture of 0.18 g (1.01 mmole) of amine Ia, 0.35 g (0.20 ml, 2.03 mmole) of n-propyl iodide, and 3 ml of DMF was refluxed for 1 h; the solvent was removed under aspirator vacuum, and the residue was crystallized out of ethanol. Yield 0.18 g (51%), mp 262-264°C (from ethanol). UV spectrum, λ_{max} (log ε): 232 (4.70), 259 (3.62), 302 nm (3.76). Found: C 37.5; H 5.3; I 36.6; N 16.0%. $C_{11}H_{17}IN_4O$. Calculated: C 37.9; H 4.9; I 36.5; N 16.1%.

B. A mixture of 1.0 g of zinc powder, 0.1 g of $HgCl_2$, and 0.05 ml of 36% HCl and 1.5 ml of water was shaken, the aqueous layer was decanted, and 2.0 ml of 36% HCl, 1.0 ml of water, and 0.50 g (1.59 mmole) of salt IIIb was added; the mixture was refluxed 12 h, and then every 4 h 0.5 ml of 36% HCl was added. The mixture was evaporated to dryness and washed with ether (3 × 8 ml); to the residue was added 2 ml of a 40% aqueous NaOH solution, and the precipitate was filtered, dissolved in 1.5 ml of concentrated HI, evaporated to dryness again, and finally crystallized from ethanol. Yield 0.22 g (40%), mp 262-263°C. This material does not exhibit a temperature depression in a mixed melting point determination with a sample from A.

4-Amino-5-(β-hydroxyethyl)-1,3-dimethylimidazo[4.5-c]pyridinium-2-one Chloride (VIa). A solution of 0.99 g (5.56 mmole) of amine Ia in 1.80 g (1.50 ml, 22.3 mmole) ethylene chlorohydrin was heated at 160-170°C for 1 h. Excess ethylene chlorohydrin was evaporated under aspirator vacuum, and the residue was washed with hot isopropyl alcohol, followed by acetone, and then dried. Yield 1.38 g (96%), mp 228-229°C (from ethanol). UV spectrum, λ_{max} (log ε): 235 (4.74), 260 (3.61), 304 nm (3.92). Found: C 46.6; H 6.1; Cl 13.9; N 21.7% $C_{10}H_{15}ClN_4O_2$. Calculated: C 46.4; H 5.8; Cl 13.7; N 21.7%.

4-Amino-5-(β-hydroxyethyl)-1-methylimidazo[4.5-c]pyridinium-2-one Chloride (VIb). A solution of 1.20 g (7.32 mmoles) of amine Ib and 2.40 (35.70 mmoles) of ethylene chlorohydrin in

7 ml of DMF was refluxed for 1.5 h. After cooling the precipitate was removed by filtration, washed with acetone, and dried. Yield 1.07 g (60%), mp 283-284°C (from DMF). UV spectrum, λ_{max} (log ε): 234 (4.82), 304 nm (4.12). Found: C 44.2; H 5.4; Cl 14.1; N 22.9%. $C_9H_{13}ClN_4O_2$. Calculated: C 44.2; H 5.4; Cl 14.5; N 22.9%.

8-Oxo-7,9-dimethyl-2,3-dihydroimidazo[4.5-c]imidazo[1.2-a]pyridine (VIIa). A mixture of 1.29 g (5.0 mmole) of chloride VIa and 0.50 ml (7.0 mmole) of thionyl chloride in 8 ml of DMF was refluxed for 0.5 h. The solution was concentrated under vacuum to one-fourth of the original volume, cooled, and filtered to remove the hydrochloride VIIa. Yield 1.10 g (91%), mp 296-298°C (from ethanol). PMR spectrum: 3.60, 3.73 (2s, two N–CH_3); 4.23, 4.83 (2 × 2H, 2t, J_{23} = 8.5 Hz, CH_2CH_2); 7.03, 7.90 ppm (2 × 1H, 2d, J_{56} = 7.0 Hz, 5,6-H). Found: C 49.9; H 5.5; Cl 15.1; N 23.1%. $C_{10}H_{12}N_4O \cdot HCl$. Calculated: C 49.9; H 5.4; Cl 14.7; N 23.3%.

A solution of 0.28 g (1.16 mmole) of hydrochloride VIIa in 0.8 ml of water was treated with 2 ml of a 45% aqueous NaOH solution; the resulting precipitate of base was removed by filtration, washed with cold water, and dried. Yield 0.20 g (67%), mp 215-217°C (from ethanol). IR spectrum ($CHCl_3$): 1700 cm^{-1} (C=O). UV spectrum, λ_{max} (log ε): 238 (4.35), 264 (3.36), 315 nm (3.57). Found: N 21.5%. $C_{10}H_{12}N_4O \cdot 3H_2O$. Calculated: N 21.7%.

8-Oxo-7-methyl-2,3-dihydroimidazo[4.5-c]imidazo[1.2-a]pyridine Hydrochloride (VIIb·HCl). This compound was prepared from chloride VIb in a manner analogous to that for hydrochloride VIIa. Yield 93%, mp 262-264°C (from DMF). PMR spectrum: 3.60 (3H, s, N–CH_3); 4.25, 4.87 (2 × 2H, 2t, J_{23} = 8.5 Hz, CH_2CH_2); 7.02, 7.92 ppm (2 × Hz, CH_2CH_2); = 7.0 Hz, 5,6-H). Found: C 41.3; H 5.7; Cl 14.0; N 21.1%. $C_9H_{10}N_4O \cdot HCl \cdot 2H_2O$. Calculated: C 44.2; H 5.4; Cl 14.5; N 22.9%.

Dehydrogenation of 8-Oxo-7,9-dimethyl-2,3-dihydroimidazo[4.5-c]imidazo[1.2-a]pyridine (VIIa). A mixture of 0.51 g (1.97 mmole) of base VIIa and 0.21 g (1.32 mmole) of potassium permanganate in 50 ml of acetone was refluxed for 1 h. The residue was removed by filtration and washed with acetone, and the combined acetone solutions were evaporated and the residue crystallized from water. Yield 0.42 g (83%), mp 222-224°C (from water). The sample did not exhibit a melting point depression upon mixing with a sample of IVa.

Hydrobromides of 2-Substituted 8-Oxo-7-methylimidazo[4.5-c]imidazo[1.2-a]pyridines (VIIIa-d). A mixture of 0.18 g (1.00 mmole) of amine Ib and 1.10-1.15 mmole of one of the α-bromomethylketones IIb, e, or g or p-methoxyphenacyl bromide in 10 ml of DMF was refluxed for 1.5 h. The mixture was cooled and the precipitate was filtered, washed with alcohol and ether, and dried.

Hydrobromide of 8-Oxo-3.7,9-trimethylimidazo[4.5-c]imidazo[1.2-a]pyridine (VIIe). This was prepared from amine Ia and α-bromopropionaldehyde in a manner analogous to the procedure used above for compounds VIIIa-d.

Methylation of 8-Oxo-2,7-dimethylimidazo[4.5-c]imidazo[1.2-a]pyridine. A suspension of 0.20 g (0.71 mmole) of hydrobromide VIIIa in a solution of 0.30 g (5.36 mmoles) of KOH in 4.5 ml of water was treated with 0.33 ml (3.50 mmoles) of dimethyl sulfate and the mixture was maintained for 0.5 h, and then an additional 0.08 ml (0.85 mmole) of dimethyl sulfate in 2 ml of 8.3% KOH solution was added; the mixture was then allowed to stand overnight. The precipitate was removed by filtration, washed with water, and dried. Yield 0.10 g (65%), mp 229-231°C (from alcohol). The substance is identical in all respects to a smple of IVb.

4-Amino-5-(p-nitrobenzyl)-1,3-dimethylimidazo[4.5-c]pyridinium-2-one Bromide (IX). A mixture of 0.60 g (3.4 mmole) of amine Ia and 0.73 g (3.4 mmole) of p-nitrobenzyl bromide in 10 ml of methanol was refluxed for 2 h. The solution was concentrated to $^1/_4$ volume, cooled, and the precipitate was filtered, washed with ether, and dried. Yield 1.02 g (77%), mp 296-297°C (from methanol). PMR spectrum: 3.68, 3.97 (2s, two N–CH_3); 5.85 (2H, s, N–CH_2); 7.25, 8.07 (2 × 1H, 2d, J_{56} = 7.0 Hz, 5,6-H); 7.50, 8.38 (2 × 2H, 2d, $J_{2'3'} = J_{5'6'}$ = 8.5 Hz, 2', 3', 5', 6'-H). Found: C 45.2; H 4.5; Br 20.3; N 17.8%. $C_{15}H_{16}BrN_5O_3$. Calculated: C 45.7; H 4.1; Br 20.3; N 17.8%.

8-Oxo-3(p-nitrophenyl)-7,9-dimethylimidazo[4.5-c]imidazo[1.2-a]pyridine (X). A mixture of 0.35 g (0.89 mmole) of bromide IX, 2.5 ml of 99% formic acid, and 2.5 ml of amyl formate was heated at 170-175°C for 2 h; the solvent was removed under vacuum and the residue was neutralized with aqueous ammonia, washed with water, and crystallized from DMF. Yield 0.10 g (35%).

8-Oxo-2,7,9-trimethylimidazo[4.5-c]imidazo[1.2-a]pyridine-3-azo-4'-benzoic Acid (XI). A solution of 0.12 g Na_2CO_3 in 5 ml of water was treated with 0.28 g (2.04 mmoles) of p-aminobenzoic acid, 0.15 g (2.17 mmoles) $NaNO_2$, and 2 ml of water. The solution was then poured onto a mixture of 2.5 g ice and 0.5 ml 36% HCl and an alcoholic solution of 0.43 g (2.00 mmoles) of compound IVb was added. After 15 min the resulting bright red precipitate was filtered, washed with water and acetone, and dried. Yield 0.50 g (69%), mp 348-350°C (from DMF). Found: C 58.8; H 4.8; N 23.0%. $C_{18}H_{16}N_6O_3$. Calculated: C 59.3; H 4.4; N 23.1%.

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EFFECTS OF ACIDS ON ORIENTATION IN THE REACTION OF 5-FORMYL-4-(1-PYRIDINO)AZOLE 2-OXIDES WITH AROMATIC AMINES

R. O. Kochkanyan, A. N. Zaritovskii, A. B. Kruglova, and N. A. Klyuev

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Azole betaines containing vicinal formyl and pyridinium groups react with aromatic amines to give, when protonated by weak or strong acids, azolidine-2,4-dione-5-aldehyde azomethines (I) or 4-aryliminoazolidin-2-ones (II), respectively. Compound (I) is formed by the intramolecular migration of the oxygen in the 4-position of the azole, and (II) by decarbonylation of the original betaine. The orientation in the reaction of dicentric nucleophiles (hydrazines and o-phenylenediamine) is independent of the extent of protonation, giving betaine hydrazones and azolo[4,5-b]benzodiazepines, respectively. The PMR mass spectra of the products are discussed.

The orientation of nucleophilic substitution in betaines, including nucleotides, displays special features as a result of the presence of charged centers, and it has received little attention. Studies in this area could lead to an understanding of the processes occurring in point mutations resulting from replacement of a pair of heterocyclic bases in nucleotides.

Azole betainealdehydes (I) may be regarded as systems with a masked electrophilic function resulting from the participation of the formyl group in delocalization of the negative charge. This feature of betaines can, depending on the reaction medium, have a marked effect on the orientation of nucleo philic substitution reactions, as a result of the selective solvation of the solvent at the cationoid or anionoid moieties. We have previously reported that mineral acid salts of betaines react with tertiary nitrogeneous bases [1] and triarylphosphines [2] with replacement of one cation by another to give new betaine salts, and when the betaines themselves react with ammonia or hydrogen sulfide tricyclic systems are obtained. We have not examined the reaction of betaines with nitrogeneous bases containing a primary

Institute of Physical Chemistry and Carbon Chemistry, Academy of Sciences of the Ukrainian SSR, Donetsk, 340114.

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