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REGIO- AND STEREOSELECTIVE SYNTHESIS OF TETRAHYDROINDOLYSINES, TETRAHYDROPYRIDIN-6-OLATES, AND CYCLOPROPANES FROM PYRIDINIUM YLIDES AND UNSATURATED NITRILES

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The regio- and stereoselectivity of the reactions of pyridinium ylides with unsaturated nitriles are dependent on the electronic nature of the substituent in position 3 of the pyridine ring. The reaction of 1-carbamoylmethylide-3-cyanopyridinium with arylmethylenemalononitriles or arylmethylcyanoacetic esters proceeds regio- and stereoselectively with the formation of substituted 2-aryl-3-carbamoyl-6-cyano-2,3-trans- or 2,3-cis-1,2,3,8a-tetrahydroindolysines. The condensation of pyridinium 1-carbamoylmethylide with arylmethylenecyanoacetic ether leads to 4-aryl-2-oxo-3-(1-pyridinio)-5-cyano-3,4-trans-1,2,3,4-tetrahydropyridin-6-olates. The reaction of pyridinium (3-methylpyridinium) 1-carbamoylmethylide with arylmethylenemalononitriles results in the formation of 2-aryl-1,1-dicyano-3-carbamoyl-3-(1-pyridinio)- or (3-methyl-1-pyridinio)-1-propanides, which undergo stereoselective 1,3-transelimination with the formation of 3-aryl-1,1-dicyano-2-carbamoylcyclopropanes.

Pyridinium ylides are widely used in the synthesis of carbo and heterocylic compounds [1, 2]. The second reagent in these reactions is an unsaturated carbonyl compound of the ethylene and acetylene series. Examples of the use of unsaturated nitriles in reactions with pyridinium ylides are few and are limited to a few reactions of ylides with acrylonitrile [1-3]. In continuation of the studies of the reactions of unsaturated nitriles with various nucleophilic agents [4, 5], we have investigated the reaction of arylmethylenenitriles with pyridinium ylides.

The pyridinium ylides were not isolated, but rather were generated in the reaction mixture by treating pyridinium salts (Ia-c) in ethanol with triethylamine. The reaction of 3-cyanopyridinium ylide (IIa) with compounds (IIIa-h) and (IVa, b) in ethanol at 25°C proceeds via the path of 1,3-dipolar cycloaddition with the formation of tetrahydroindolysines (VA-h) and (VIa, b) (Tables 1, 2; Scheme 1). According to IR and PMR spectroscopic data, the reaction of formation of indolysines proceeds with high regio- and stereoselectivity. Of the two possible directions of formation of substituted 6-cyanoindolysines or 8-cyanoindolysines the first direction is realized in practice. In PMR spectra of compounds (V) and (VI) the signals of the hydrogen atoms atoms C^3H and $C^{8a}H$ appear in the form of a doublet doublet and doublet in the region of 5.21-5.58, 5.28-5.62

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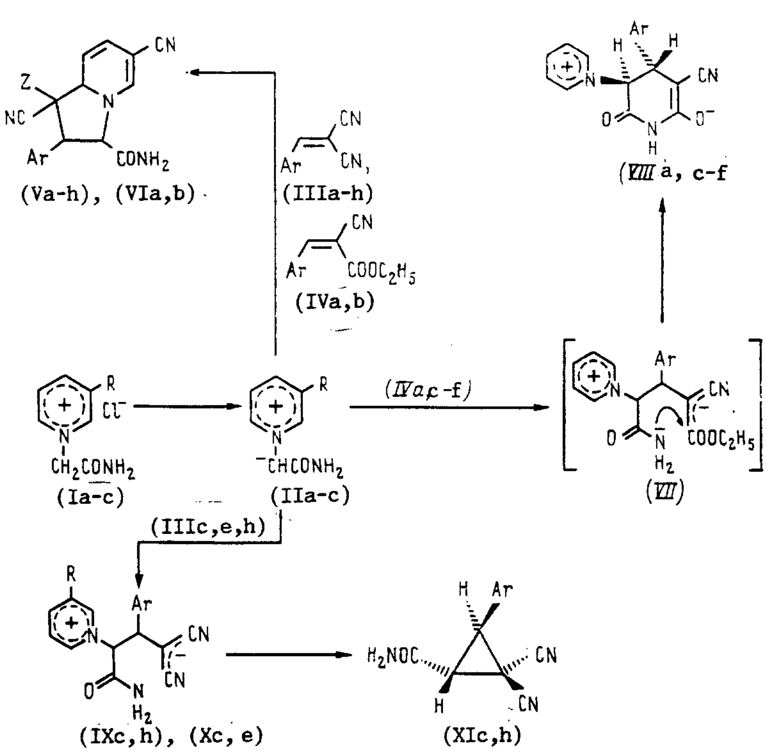
Scheme 1



(I), (II): R = CN (a), H (b), CH_3 (c). (III): Ar = 2-NO_2 (a), 2,6-$Cl_2C_6H_3$ (b), C_6H_5 (c), 4-BrC_6H_5 (d), 4-FC_6H_4 (e), 3-FC_6H_4 (f), 2-ClC_6H_4 (g), 3-pyridyl (h). (IV): Ar = 4-FC_6H_4 (a), 2-$CH_3OC_6H_4$ (b), C_6H_5 (c), 3-FC_6H_4 (d), 4-BrC_6H_4 (e), 4-ClC_6H_4 (f). (V): Z = CN; Ar = 2-$NO_2C_6H_4$ (a), 2,6-$Cl_2C_6H_3$ (b), C_6H_5 (c), 4-BrC_6H_4 (d), 4-FC_6H_4 (e), 3-FC_6H_4 (f), 2-ClC_6H_4 (g), 3pyridyl (h). (VI): Z = $COOC_2H_5$; Ar = 4-FC_6H_4 (a). 2-$CH_3OC_6H_4$ (b). (VIII): Ar = 4-FC_6H_4 (a), C_6H_5 (c), 3-FC_6H_4 (d), 4-BrC_6H_4 (e). 4-ClC_6H_4 (f). (IX): R = H; Ar = C_6H_5 (c), 3pyridyl (h),(X). R = CH_3; Ar = C_6H_5 (c), 4-FC_6H_4 (e). (XI): Ar = = C_6H_5 (c), 3- pyridyl (h).

and 5.23-5.67 ppm respectively with coupling constant $^3J_{H^8,H^{8a}}$ = 1.5-3.3 Hz. From the Karplus–Conroy equation [6] $\varphi_{HC^8C^{8a}H}$ = 68-74° is evidence that the $C^{8a}H$ hydrogen atom is positioned pseudoaxially relative to the C^8H hydrogen atom, which is in the plane of the coplanar diene fragment $C^5C^6C^7C^8$ of the molecules of compounds (V) and (VI). Therefore, the C^1–C^{8a} bond is in pseudoequatorial position relative to the diene fragment and the C^1 atom is out of this plane. In the series of compounds (V) one of the geminal nitrile groups on the C^1 atom is evidently positioned pseudoaxially, while the other is positioned pseudoequatorially. The different spatial orientation of the substituents C≡N and Z appears in the transition from compounds (V) to (VI); the chemical shift of the $C^{8a}H$ hydrogen shifts into the strong field by $\Delta\delta$ = 0.35 ppm. Here the chemical shift of C^2H remains unchanged (Table 2). Therefore, the dominant effect on the strong field shift of the signal of the C^2H hydrogen atom is made not by the electronic factor of the $COOC_2H_5$ group, but by the stereoscreening factor, which can develop only in cis-pseudoaxial position of the group relative to the $C^{8a}H$ hydrogen atom. The planarity of the $C^5C^6C^7C^8$ fragment is indicated by the characteristic chemical shifts of the C^5H and C^7H hydrogen atoms (Table 2). Here the signal of the C^7H hydrogen atom appears in the form of a doublet with the coupling constant that is characteristic for the diene fragment [7] $^3J_{H^7,H^8}$ = 9.1-10.3 Hz.

The multiplicity of the signals of the C^2H and C^3H hydrogens and their coupling constants ^3J are evidence of the high stereoselectivity of the reaction of compounds (IIa) and (III), and (IV). The signals of the C^2H and C^3H hydrogen atoms appear in the form of two doublets in the region 4.38-5.28 and 4.91-5.33 ppm with coupling constant $^3J_{H^2,H^3}$ = 4.4-8.8 Hz. Data calculated from the Karplus–Conroy equation [6] indicate that at such values of the coupling constant $^3J_{H^2,H^3}$ the torsion angle has two values $\varphi_{H-C^2-C^3-H}$ = 55-141° and

TABLE 1. 2-Aryl-3-carbamoyl-1,1,6-tricyano-1,2,3,8a-tetrahydroindolysines (V) and 2-Aryl-1,6-dicyano-3-carbamoyl-1-ethoxycarbonyl-1,2,3,8a-tetrahydroindolysines (VI)

Compound	Yield, %	mp, °C	Empirical formula	Found/Calculated, %			
				C	H	Hal	N
(Va)	73	128–130	$C_{18}H_{12}N_6O_3$	59.78 / 60,00	3,17 / 3,36		23,07 / 23,32
(Vb)	78	135–137	$C_{18}H_{11}Cl_2N_5O$	56,04 / 56,27	2,67 / 2,89	18,32 / 18,45	18,35 / 18,23
(Vc)	82	139–142	$C_{18}H_{13}N_5O$	68,37 / 68,56	3,92 / 3,15		22,04 / 22,21
(Vd)	84	144–145	$C_{18}H_{12}BrN_5O$	58,62 / 58,84	2,92 / 3,07	20,09 / 20,27	17,82 / 17,76
(Ve)	92	153–154	$C_{18}H_{12}FN_5O$	64,58 / 64,86	3,61 / 3,63	5,42 / 5,70	20,73 / 21,01
(Vf)	80	137–138	$C_{18}H_{12}FN_5O$	64,80 / 64,86	3,58 / 3,63	5,39 / 5,70	21,07 / 21,01
(Vg)	87	119–120	$C_{18}H_{12}ClN_5O$	61,53 / 61,81	3,30 / 3,46	10,28 / 10,14	19,68 / 20,02
(Vh)	95	137–139	$C_{17}H_{12}N_6O$	64,32 / 64.55	3,61 / 3,83		26,34 / 26,57
(VIa)	90	162–164	$C_{20}H_{17}FN_4O_3$	62,90 / 63,15	3,28 / 3,46	4,60 / 4,99	14,87 / 14,73
(VIb)	74	225–227	$C_{21}H_{20}N_4O_4$	64,37 / 64.28	5,03 / 5.14		14,38 / 14.28

$\varphi^{2}_{H-C^2-C^3-H} = 22$-116°. Taking into account the characteristic coupling constants for the tetrahydroindolysines that were obtained earlier [8], one can note that the C^2H and C^3H hydrogen atoms in the molecules of compounds (V) and (VI) have torsion angle $\varphi^{1}_{H-C^2-C^3-H} =$ 55-141° (Table 2). In compounds (Vc-h) and (VIa, b) the torsion angle is $\varphi^{1}_{H-C^2-C^3-H} = 131$-141° and the C^2H and C^3H hydrogen atoms are situated transpseudoaxially and therefore the substituents Ar and $CONH_2$ are positioned trans-pseudoequatorially. With this arrangement of functional substituents and hydrogen atoms bonded to the C^2 and C^3 atoms the C^2 atom must stick out on the opposite side from the C^1 atom relative to the planar fragment $C^5C^6C^7C^8$. The C^3 carbon atom emerges in the opposite direction relative to the C^2 atom. Therefore, the C^2H hydrogen is oriented cis-pseudoaxially, while the C^3H hydrogen is situated trans-pseudoaxially relative to the $C^{8a}H$ hydrogen, respectively. In the compounds (Va, b) the coupling constant $^3J_{H^2,\ H^3} = 4.4$-4.7 Hz and the torsion angle has values $\varphi_{H-C^2-C^3-H} = 55$-57° (Table 2). The decrease of the coupling constant and the torsion angle in the molecules of compounds (Va, b) is connected with the insertion, in ortho position of the benzene ring, of bulky substituents, nitro groups or two chlorine atoms. This results in the C^2H and C^3H hydrogen atoms in the molecules of compounds (Va, b) being situated cis-pseudoaxially, while the substituents Ar and $CONH_2$ are situated cis-pseudoequatorially. This arrangement of hydrogen atoms is accompanied by partial deshielding of the C^2H hydrogen by the substituents $2-NO_2C_6H_4$, $2.6-Cl_2C_6H_3$ and $CONH_2$ and a shift of its signal in the PMR spectra into weak fields by $\Delta\delta = 0.5$-0.9 ppm by comparison with compounds (Vc-f). In the molecules of compounds (Vg) and (VIb), which contain substituents Cl or CH_3O in ortho position, the coupling constant decreases negligibly $^3J_{H^2,\ H^3} = 6.9$-7.3 Hz (Table 2). The IR spectroscopic data also confirm the structure of tetrahydroindolysines (V) and (VI) (Table 2).

Taking into consideration what was said above, as well as the construction of models after Stuart–Briegleb, one can see that the five-membered heterocycle has a twist conformation, and the substituted dihydropyridine cycle is in the conformation of a half-chair. The stereoselectivity of reactions of 1,3-dipolar cycloaddition of pyridinium ylide (IIa) to unsaturated nitriles (III) and (IV) is affected by the bulky substituent in ortho position of the arylmethylenemalononitrile. In the case of ortho-substituted compounds (IIIa, b) the reaction takes place with the formation of substituted 2,3-cis-1,2,3,8a-tetrahydroindolysines (Va, b)

TABLE 2. IR and PMR Spectra of 2-Aryl-3-carbamoyl-1,1,6-tricyano-1,2,3,8a-tetrahydroindolysines (V) and 2-Aryl-1,6-dicyano-3-carbamoyl-1-ethoxycarbonyl-1,2,3,8a-tetrahydroindolysines (VI)

Compound	IR spectrum (ν, cm^{-1})				PMR spectrum										φ, deg	
					δ, ppm							^3J, Hz				
	CONH$_2$	6-C≡N	1-C≡N, R	NH$_2$	C^{3}H (d)	C^{2}H (d)	C^{8a}H (d)	C^{8}H (d.d)	C^{7}H (d)	Ar, C^{5}H (m)	NH (s)	$J_{H^2H^3}$	$J_{H^8H^{8a}}$	$J_{H^7H^8}$	$\varphi_{H-C^8-C^{8a}-H}$	$\varphi_{H-C^2-C^3-H}$
(Va)	1646 1687	2223	2258	3308 3434	4,99	4,58	5,67^a	5,57 5,61	6,48	7,76 7,90	7,67 8,06	4,7	2,7	9,3	71	55
(Vb)	1645 1694	2215	2258	3315 3444	5,33	5,28	5,48	5,58 5,62	6,45	7,50 7,67	7,78 7,93	4,4	3,0	9,9	69	57
(Vc)	1678 1648	2215	2252	3210 3380 3395	4,95	4,38	5,53^a	5,49 5,54	6,33	7,50	7,62 7,78	8,4	2,5	9,2	74	139
(Vd)	1648 1678	2218	2250	3330 3460	4,93	4,39	5,51^a	5,44 5,56	6,31	7,39 s 7,45 d 7,70 d	7,62 7,75	8,8	2,8	10,3	71	141
(Ve)	1645 1690	2216	2252	3342 3457	4,94	4,41	5,53^a	5,48 5,56	6,32	7,35 7,60	7,67 7,80	8,3	2,8	10,3	71	139
(Vf)	1644 1692	2198	2250	3338 3455	4,98^b	4,45	5,53^a	5,51 5,55	6,33	7,38 7,50	7,62 7,78	8,2	3,0	9,1	69	138
(Vg)	1645 1695	2203	2250	3340 3455	4,91	4,98	5,62	5,53 5,58	6,38	7,50 7,66	7,71	6,9	3,3	9,9	66	131
(Vh)	1644 1696	2212	2254	3130 3405	5,03	4,71	5,64	5,52 5,58	6,33	7,31 s 7,52 t 8,05 d 8,63 s 8,75 d	7,52 7,81	8,5	3,0	9,8	69	140
(VIa)	1645 1675 1698sh	2210	2248 1737	3330 3415	4,94^c	4,45	5,28^a	5,26 5,35	6,20	7,37 7,58	7,50 7,78	8,3	3,0	9,6	69	139
(VIb)	1645 1688	2214	2247 1735	3332 3418	4,91^d	4,44	5,23^a	5,21 5,28	6,16	7,03 7,35 7,46 7,50	7,48 7,76	7,3	3,0	9,7	69	133

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[a] Overlaps with signals of C^{8}H proton.

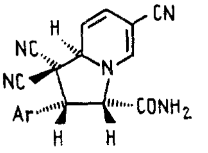
[b] Signals of C^{2}H, C^{3}H, C^{8}H, C^{7}H protons are doubled and appear in the regions (δ, ppm): 4.42 d, 4.93 d; 5.53 and 5.54 d.d; 6.31 d, respectively.

[c] Signals of C$_2$H$_5$ protons (δ, ppm): 1.35 t (3H, CH$_3$); 4.24 q (2H, CH$_2$, ^3J = 7.3 Hz).

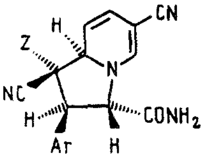
[d] Signals of C$_2$H$_5$ protons (δ, ppm): 1.37 t (3H, CH$_3$); 4.22 q (2H, CH$_2$, ^3J = 7.3 Hz); signals of CH$_3$ protons (δ, ppm): 3.7 s (3H, CH$_3$).

TABLE 3. 4-Aryl-2-oxo-3-(1-pyridinio)-5-cyano-3,4-trans-1,2,3,4-tetrahydropyridin-6-olates (VIII)

Compound	Yield, %	mp, °C	Empirical formula	Found/Calculated, % C	H	Hal	N
(VIIIa)	78	242–245	$C_{17}H_{12}FN_3O_2$	65,72/66,02	3,74/3,91	5.74/6,14	13,53/13,59
(VIIIc)	70	233–235	$C_{17}H_{13}N_3O_2$	69.67/70,09	4,36/4,50		14.18/14,42
(VIIId)	86	240–243	$C_{17}H_{12}FN_3O_2$	65.80/66,02	3,73/3,91	5,83/6,14	13.33/13,59
(VIIIe)	98	243–245	$C_{17}H_{12}BrN_3O_2$	54,92/55,16	3,24/3,27	21,31/21,58	11,31/11,35
(VIIIf)	92	246–248	$C_{17}H_{12}ClN_3O_2$	62,53/62.68	3.54/3.71	10,62/10.88	12,72/12.90



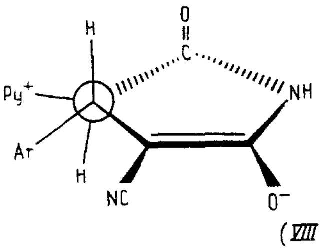
(Va,b)



(Vc-h), (VIa,b)

The absence of an electron-acceptor substituent in position 3 of the pyridinium ylide leads to a change of the regioselectivity of the reactions of the pyridinium ylides with arylmethylenecyanoacetic esters and to the formation of substituted tetrahydropyridin-6-olates. The change of direction of the reaction can be attributed to the increase of the electron density in position 6 of pyridinium ylide (IIb) by comparison with the 3-cyano-pyridinium ylide (IIa), which is in agreement with quantum chemical calculations of the electron density in molecules of quaternized azines [9]. This leads to bromination of the reaction of nucleophilic addition of the pyridinium ylide (IIb) to compounds (IVa, c-f) over the reaction of synchronous 1,3-dipolar cycloaddition and to the formation of a Michael adduct (VII). The subsequent intramolecular condensation of (VII) leads to pyridin-6-olates (VIIIa, c-f) (Tables 3 and 4). The reaction products are stabilized in the form of betaines with separation and delocalization of positive and negative charges in the Py$^+$ and N...C...C^5...C^6-...O$^-$ fragments. Because of this the absorption band of the C≡N group in the IR spectra of compounds (VIII) is intensive and shifted into the low-frequency region to 2174-2180 cm^{-1} (Table 4).

The PMR spectra of compounds (VIII) contain, besides the signals of NH, Py$^+$ and Ar groups, doublet signals of the C^{3}H and C^{4}H protons in the region of 5.96-5.98 and 4.48-4.52 ppm with coupling constant $^3J_{H^3,\ H^4}$ = 12.9-13.2 Hz (Table 4). For these coupling constant values the torsion angle calculated by the Karplus–Conroy equation [6] is in the range of $\varphi_{H-C^3-C^4-H} \geq 173°$. Therefore, the C^{3}H and C^{4}H hydrogen atoms are situated trans-pseudo-axially, while the substituents Ar and Py$^+$ are situated trans-pseudoequatorially. Considering that the N...C...C^5...C^6...O$^-$ fragment with the C^4 and N^1 atoms adjacent to it is planar, one can consider that the pyridin-6-olates are in the conformation of a half-chair (VIIIa), similar to the hydrogenated salts of 3-cyanopyridin-2-thiolates [10]



(VIIIA)

TABLE 4. IR and PMR Spectra of 4-Aryl-2-oxo-3-(1-pyridinio)-5-cyano-3,4-trans-1,2,3,4-tetrahydropyridin-6-olates (VIII)

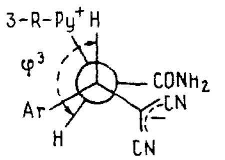
Compound	IR spectrum (ν, cm^{-1})					PMR spectrum							
						δ, ppm; J, Hz							
	NH	CH	C≡N	C=O	NH	NH (s)	Ar (m)	C^3H (d)	C^4H (d)	$^3J_{H^3,H^4}$	protons of Py$^+$ (pyridinium)		
											C^2H, C^6H (d)	C^4H (t)	C^3H, C^5H (t)
(VIIIa)	3428	2840 2968	2180	1694	1638	9,94	7,09	5,96	4,50	13,4	8,85	8,48	8,03
(VIIIc)	3420	2855 2963	2174	1703	1634	9,88	7,14	5,98	4,47	13,1	8,86	8,51	8,03
(VIIId)	3429	2853 2945	2170	1706	1632	9,92	7,15	5,97	4,49	13,1	8,84	8,46	8,02
(VIIIe)	3420	2815 2974	2175	1703	1638	9,78	7,09 d, 7,35 d ^3J=8,1	5,96	4,48	12,9	8,81	8,48	7,99
(VIIIf)	3417	2827 2963	2178	1700	1635	9,79	7,20 d, 7,53 d ^3J=8.2	5,96	4,52	13,2	8,81	8,39	7,98

TABLE 5. 2-Aryl-1,1-dicyano-3-(1-pyridinio)-1-propanides (IX) and 2-Aryl-1,1-dicyano-3-[1-(3-methylpyridinio)]-1-propanides (X)

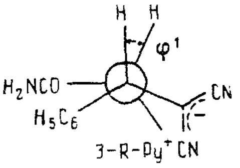
Compound	Yield, %	mp, °C	Empirical formula	$\frac{\text{Found}}{\text{Calculated}}$, %		
				C	H	N
(IXc)	92	174–176	$C_{17}H_{14}N_4O$	$\frac{70,12}{70,33}$	$\frac{4,74}{4,86}$	$\frac{19,42}{19,30}$
(IXh)	58	159–162	$C_{16}H_{13}N_5O$	$\frac{65,82}{65,97}$	$\frac{4,34}{4,50}$	$\frac{23,92}{24,04}$
(Xc)	87	137–139	$C_{18}H_{16}N_4O$	$\frac{70,87}{71,04}$	$\frac{5,12}{5,30}$	$\frac{18,22}{18,41}$
(Xe)	92	139–140	$C_{18}H_{15}FN_4O$	$\frac{67,15}{67,07}$	$\frac{4,48}{4,69}$	$\frac{17,12}{17,38}$

In this conformation the $C^2{=}O$ group emerges from the plane of conjugation with the p-electrons of the nitrogen, which leads to a significant increase of the frequency of the vibrations ($\Delta\nu \approx 40$-$50\ cm^{-1}$) of the C=O group in the IR spectra of compounds (VIII) by comparison with the absorption band of the C=O group in the coplanar molecules of 2-(1H)-pyridones [11].

As one moves from arylmethylenecyanoacetic ethers (IV) to arylmethylenemalononitriles (III) the reaction with pyridinium and picolinium ylides (Ib, c) changes direction. The reaction of ylides (Ib, c) with arylindenemalononitriles (IIIc, e, h) in ethanol at 25°C results in the formation of compounds (IX) and (X) (Tables 5 and 6). Compounds (IX) and (X), upon prolonged standing in ethanol or with heating to 60-70°C in dimethyl sulfoxide, are converted to cyclopropanes (XI). In this case the reaction proceeds stereoselectively with the formation of transcyclopropanes (XI). In studying the structure of the 1,4-ylides (IX) and (X), we established some factors that determine the stereoselectivity of the reactions of formation of cyclopropanes. According to the IR spectroscopic data, compounds (IX) and (X) are stabilized in the form of pyridinium 1,4-ylides with separation and delocalization of positive and negative charges in the Py^+ and $C(CN)_2$ fragments. The redistribution of electron density leads to a sharp decrease of the frequency of vibrations of the C≡N groups to 2100-2108 and 2165-2168 cm^{-1} (Table 6) by comparison with the conjugated nitriles [12]. The delocalization of the positive charge in the pyridine substituent leads to a shift, in the PMR spectra, of the signals of its protons into the weak field, which is characteristic for quaternized azines [6]. According to the PMR spectroscopic data compound (IXc) is a mixture of isomers at the $C^2{-}C^3$ bond. The signals of the C^2H and C^3H protons appear in the form of four doublets in the region 3.63 and 3.81 ppm with coupling constant $^3J_1$ = 8.5 Hz and 3.85 and 5.58 ppm with coupling constant $^3J_2$ = 11.8 Hz. Calculation of the torsion angles by the Karplus–Conroy equation [6] showed that the coupling constant $^3J_1$ corresponds to two angles $\varphi^1_{H\text{-}C^2\text{-}C^3\text{-}H} = 31°$ and $\varphi^2_{H\text{-}C^2\text{-}C^3\text{-}H} = 140°$, while coupling constant $^3J_2$ corresponds to one angle $\varphi^3_{H\text{-}C^2\text{-}C^3\text{-}H} = 161°$. Considering the coupling constants that are characteristic for ethane derivatives [8], as well as the steric stress, the isomer with torsion angle $\varphi^2_{H\text{-}C^2\text{-}C^3\text{-}H} = 140°$ can be eliminated. Therefore, compound (IXc) is a mixture of isomers with antiperiplanar (IX A) and synclinal (IX B) arrangement of hydrogen atoms in a ratio of 4:3, respectively



(IX A, C), (X A, B)



(IX B)

In contrast to this, pyridinium 1,4-ylides (IXh, Xc, e) are a single isomer. In this case the signals of the C^2H and C^3H protons appear in the form of two doublets in the region of 3.83-3.96 and 5.52-5.54 ppm with coupling constant ^3J = 11.5-12.0 Hz (Table 6). The calculated torsion angle for molecules of compounds (IXh) and (Xc, e) is in the range $\varphi_{H-C^2-C^3-H}$ = 158-163°. Therefore, the molecules of these compounds have antiperiplanar

TABLE 6. IR and PMR Spectra of 2-Aryl-1,1-dicyano-3-(1-pyridinio)-1-propanides (IX) and 2-Aryl-1,1-dicyano-3-[1-(3-methylpyridinio)]-1-propanides (X)

Compound	IR spectrum (ν, cm⁻¹)				PMR spectrum									$\varphi_{H-C^2-C^3-H}$, deg
					δ, ppm									
	NH	C≡N	C=O	δ NH	protons Py⁺, 3-CH₃Py⁺			NH₂ (s)	Ar (m)	C³H (d)	C²H (d)	CH₃ (s)	$^3J_{H^2,H^3}$, Hz	
					C²H, C⁶H	C⁴H	C³H, C⁵H							
(IXc)	3186 3277 3328	2103 2166	1705	1633	8,73d 9,12d	8,25 t	7,78 t 7,93 t	7,52	7,30–7,44	5,58 *	3,83		11,8	161
(IXh)	3180 3270 3352	2100 2168	1695	1628	8,72d 9,18	8,28	7,83 m	7,60 8,12	7,38 q (C⁵H), 8,48 (C⁴H), 8,55 (C²H, C⁶H)	5,52	3,96		12,0	163
(Xc)	3184 3265	2108 2165	1686	1620	7,83–8,57			7,54 8,10	7,30–7,44	5,54	3,85	2,48	11,5	158
(Xe)	3279	2104 2168	1695	1637	7,82–8,57			7,53 8,04	7,82–8,57	5,53	3,83	2,47	11,5	158

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*Chemical shifts and coupling constants of isomer (IXc) with synclinal position of hydrogen atoms (δ, ppm): 3.63 d C^2H, $^3J_{H^2,H^3}$ = 8.5 Hz); 3.81 d (C^3H, $^3J_{H^2,H^3}$ = 8.5 Hz).

arrangement of C^2H and C^3H hydrogen atoms, like isomer (IX A). Considering that of the mixture of isomers (IX A, B) and isomers (IX C, X A, B) only trans-cyclopropanes (XI) form, it can be noted: firstly, a necessary condition for this transformation is complete conversion of isomer (IX B) to (IX A) with participation of the Michael retroreaction; secondly, this reaction follows the type of 1,3-transelimination [13], which assumes antiperiplanar arrangement of the nucleophilic $C(CN)_2^-$ and the nucleophilic 3-R-Py^+ groups in isomers (IXA, C) and (XA, B). This high stereoelectronic control eliminates the possibility of the transformation of isomer (IXB) to cis-cyclopropane.

EXPERIMENTAL

The IR spectra were acquired on a Perkin-Elmer 577 spectrometer in KBr wafers. The PMR spectra were recorded on a Bruker WM-250 instrument (250 MHz) in DMSO-d_6 relative to TMS. The individuality of the compounds was checked by TLC on Silufol UV-254 plates in a 3:5 acetone:hexane system.

Substituted 2-Aryl-3-carbamoyl-6-cyano-1,2,3,8a-tetrahydroindolysines (V) and (VI). To a mixture of 10 mmoles salt (Ia) and 10 mmoles compound (III) or (IV) in 20 ml ethanol was added 10 mmoles triethylamine. The reaction mixture was stirred for 12-15 h at 25°C, the precipitate was filtered out, washed with ethanol and hexane. Tetrahydroindolysines (V) and (VI) were obtained after recrystallization from ethanol or nitromethane (Tables 1, 2).

4-Aryl-2-oxo-3-(1-pyridinio)-5-cyano-3,4-trans-1,2,3,4-tetrahydropyridin-6-olates (VIII). A mixture of 10 mmoles salt (Ib), 10 mmoles compound (IVa, c-f), and 10 mmoles triethylamine in 25-35 ml ethanol was mixed for 10-12 h at 25°C. The precipitate was filtered out, washed with ethanol and hexane, and recrystallized from nitromethane (Tables 3, 4).

2-Aryl-1,1-dicyano-3-carbamoyl-3-(1-pyridinio)-1-propanides (IX) and 2-Aryl-1,1-dicyano-3-carbamoyl-3-[1-(3-methylpyridinio)]-1-propanides (X). To a mixture of 10 mmoles salt (Ib, c), 10 mmoles compound (IIIc, e, h) in 20 ml ethanol was added 10 mmoles triethylamine and the reaction mxiture was stirred for 3-4 h at 25°C. The precipitate was filtered out, washed with ethanol and hexane. Data on compounds (IX) and (X) are given in Tables 5 and 6.

trans-1,1-Dicyano-2-carbamoyl-3-phenylcyclopropane (XIc). 10 mmole compound (IXc) or (Xc) was heated in 20 ml DMSO at 60-70°C for 5-10 min. The reaction mixture was cooled to 25°C, diluted with 50 ml water, the precipitate was filtered out, washed with ethanol and hexane. The product was 89% (XIc), mp 158°C (from ethanol). IR spectrum (ν, cm^{-1}): 1600 δNH_2, 1738 CO, 2260 CN, 3288 NH_2. PMR spectrum (δ, ppm): 3.49 d (1H, C^2H, $^3J_{H^2,H^3} = 5.1$ Hz), 4.08 d (1H, C^3H), 7.40 m (5H, C_6H_5), 9.03 and 9.18 s (2H, NH_2). Found: C 68.11; H 4.12; N 19.80%. $C_{12}H_9N_3O$. Calculated C 68.24; H 4.30; N 19.89%.

trans-1,1-Dicyano-2-carbamoyl-3-(3-pyridyl)cyclopropane (XIh). It is obtained by analogy with compound (XIc). The yield is 88%, mp 235°C (dec.) (from ethanol). IR spectrum (ν, cm^{-1}): 1663 δNH_2, 1726 CO, 2248 CN, 3230 NH_2. PMR spectrum (δ, ppm): 3.58 d (1H, C^2H, $^3J_{H^2,H^3} = 5.1$ Hz), 4.18 d (1H, C^3H), 7.46 d. d (1H, C^6H-pyridyl), 7.78 d (1H, C^4H-pyridyl, $^3J_{H^4,H^5} = 8.1$ Hz), 8.57 d (1H, C^6H-pyridyl, $^3J_{H^5,H^6} = 4.9$ Hz), 8.68 s (1H, C^2H-pyridyl), 9.09 and 9.22 c (2H, NH_2). Found: C 62.07; H 3.68; N 26.34%. $C_{11}H_8N_4O$. Calculated: C 62.26; H 3.80; N 26.40%.

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ELECTROCHEMICAL ALKYLATION OF 2,2'-DIPYRIDYLAMINE

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A method was developed for preparation of alkyl-(2,2'-dipyridyl)amines, consisting of the reaction of alkyl halides with the N anion electrochemically generated from 2,2'-dipyridylamine. The alkylation occurs regiospecifically, and CH_2Cl_2 can also be used as the methylating agent. Complexes of alkyl-(2,2'-dipyridyl)-amines with Pd(2+) and Cu(2+) salts were obtained.

2,2'-Dipyridylamine (I) is widely used as a chelating ligand in coordination chemistry. Many complexes of various metals containing (I) in deprotonated or neutral form are known [1-4]. Apparently, products of alkylation of (I) at an exocyclic nitrogen atom, alkyl-(2,2'-dipyridyl)amines (ADPA), can also be used as chelate formers. With respect to their structure, complexes of metals with ADPA should apparently be analogous to chelates of un-deprotonated (I).

However, the literature contains almost no information on ADPA, probably because of certain difficulties in their synthesis. As is known, alkylation of 2-aminopyridine occurs at the nitrogen atom of the pyridine ring, and only in the presence of strong bases, such as $NaNH_2$, is it possible to carry out substitution at the amino group [5]. 2-(Alkylamino)-pyridines behave similarly, and, correspondingly, during heating with alkyl halides, (I) is alkylated exclusively at the ring nitrogen atoms [6, 7]. The reaction of (I) with CH_2I_2 results in formation of a six-membered ring involving both nitrogen atoms of pyridine rings. In a patent [8], Webb et al. attempted to obtain methyl-(2,2'dipyridyl)amine by the reaction of MeI with (I) in the presence of NaH, but the desired product was recovered only as a dihydrobromide and in low yield.

Recently it was shown that the electrochemical generation of N anions from nitrogenous bases containing the NH group open up interesting possibilities in carrying out N-alkylation processes [9, 10]. In the present paper, we consider the formation of ADPA from (I) and alkyl halides under conditions of cathodic electrolysis (see preliminary communication [11]).

According to data of voltammetric measurements, there was one wave (Fig. 1, curve 1) with $E_{\frac{1}{2}} = -2.6$ V (with respect to Ag/0.1 N Ag^+) on the polarization curves of reduction of (I) at a Pt rotating disk electrode in a 0.1 N solution of Bu_4NBF_4 in abs. MeCN. According to coulometric measurements, the height of this wave corresponded to transfer of one electron. On the polarization curves recorded during potentiostatic (E = −2.7 V) electrolysis of (I), an anodic wave with $E_{1/2} = -0.4$ V (curve 2) appeared and grew. It can be assumed that the species undergoing oxidation at $E_{1/2} = -0.4$ V was an anion that was generated as a result of cathodic cleavage of the N–H bond (cf. with [9] and [10]). A confirmation of this is the fact that the addition of MeI to the solution after electrolysis of (I) led to disappearance of the anodic wave with $E_{1/2} = -0.4$ V on the polarization curves. Apparently, anion (II), which was formed under conditions of cathodic electrolysis, was alkylated in the presence of MeI. This was indicated by the appearance (curve 3) of a wave of oxidation

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