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CYCLIZATION OF N-ALKYLAZINIUM CATIONS WITH BIFUNCTIONAL NUCLEOPHILES.

23.* ELECTROCHEMICAL CRITERIA FOR ELECTROPHILICITY IN 1,4-DIAZINIUM CATIONS AND THEIR PARTICIPATION IN CYCLIZATIONS WITH ACETOACETAMIDE

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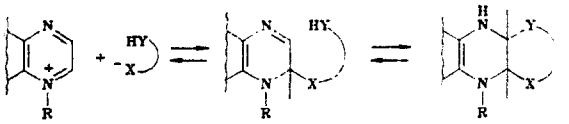
The polarographic reduction potentials $E_{\frac{1}{2}}$ of the pyrazinium, quinoxalinium, benzoquinoxalinium, pyrido[2,3-b]pyrazinium, and pteridinium cations were determined. Annellation of a benzene ring increases the electrophilicity of the diazinium cations to a greater degree than the introduction of such electron acceptors as aza, aminocarbonyl, or methoxycarbonyl groups. The boundary between the active and inactive 1,4-diazinium salts was determined; cations with $E_{\frac{1}{2}}$ values more negative than −0.50 V do not form either stable covalent adducts or cyclic diadducts through annellation of the dinucleophiles to the pyrazine ring.

The reactions of N-alkyl-substituted pyrazinium, quinoxalinium, pyrido[2,3-b]pyrazinium, and pteridinium cations with bifunctional nucleophiles can lead to the formation of cyclic adducts [2-4]. Cyclizations of this type include two consecutive reversible nucleophilic addition reactions, i.e., addition of the carbon and heteroatomic anionic centers of the dinucleophile X and Y to the $C_{(2)}$ and $C_{(3)}$ carbon atoms of the pyrazine ring. In the first stage the positively charged 1,4-diazinium cation takes part in the reaction, while the second can be regarded as intramolecular addition to the C=N bond of the pyrazine ring.



X, Y=CH, N, O, S

The outcome of the reactions is determined by a whole series of factors such as the basicity and nucleophilicity of the anionic centers X and Y, the electrophilicity of the 1,4-diazinium ions, the stability of the monoaddition products, the size of the HX–YH linking unit, the geometry of the obtained ring, the electrophilicity of the C=N bond in the 1,2-dihydropyrazines, and others. The structure of the diazines affects the nucleophilic addition

*For Communication 22, see [1].

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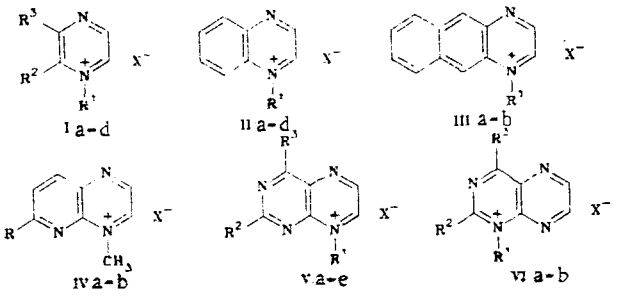
processes both to the diazinium cations (the first stage) and to the dihydropyrazines (second stage) [2].

In the present communication we wish to dwell on only one factor, i.e., to investigate the variation in the electrophilicity of the initial 1,4-diazinium cations as a function of their structure, i.e., the presence of substituents in the pyrazine ring including the annellation of one and two benzene rings and pyridine and pyrimidine rings. In order to obtain quantitative characteristics reflecting the susceptibility of the diazinium cations to reaction with nucleophiles we studied their electrochemical reduction at a rotating platinum disc with ring. The investigated 1,4-diazinium salts are represented by the following series of compounds:



I a-d II a-d III a-b IV a-b V a-e VI a-b

I a,d $R^1=C_2H_5$, b,c $R^1=CH_3$; a-c $R^2=H$, d $R^2=COOCH_3$; a $R^3=H$, b $R^3=CONH_2$, c,d $R^3=COOCH_3$; a,d $X=BF_4$, b,c X=I; II a,b $R^1=CH_3$, c,d $R^1=C_2H_5$; a,c X=I, b $X=ClO_4$, d $X=BF_4$; III a $R=CH_3$, b $R=C_2H_5$; a X=I, b $X=BF_4$; IV a $R=N(CH_3)_2$, b R=morpholino V, VI a-d $R^1=C_2H_5$, e $R^1=CH_3$; a $R^2=H$, b $R^2=SCH_3$, c $R^2=$ morpholino d $R^2=$ piperidino, e $R^2=N(CH_3)_2$; a,b $R^3=$ morpholino, c-e $R^3=CH_3$; a,d $X=BF_4$, e $X=SO_3F$

In order to convince ourselves that substitution of the counterion and transition from the N-methyl cations to the N-ethyl salts does not have a significant effect on the electron-accepting characteristics we represented the quinoxalinium cations by the series of salts (IIa-d) and (IIIa, b). The substituents at position 6 of the pyridopyrazines (IVa, b) and also at position 2 of the pteridines (Vb-e) were introduced so as to direct the quaternization to the $N_{(4)}$ and $N_{(8)}$ nitrogen atoms, respectively, and to position 4 of the pteridinium salts (Va-e) and prevent hydration of the cations at the $C_{(4)}$ carbon atom. The isomeric pteridinium salts (VIa, b) were studied for comparison.

The electrochemical reduction of the cations (I-V) in DMFA at the platinum disk takes place with the addition of one electron leading to the corresponding radicals. The latter are recorded at the ring, which has a constant potential corresponding to the beginning of the reduction wave on the disk. The stability of the radicals differs, as can be judged from the values of the current yield Q (Table 1). The anomalously high values of the current yield for compounds (IIIa, b, Vc) are evidently due to the occurrence of side reactions. Differences are observed in the reduction wave currents of the cations (I-VI) (Table 1), and low values of i are recorded during the reduction of the pteridinium cations (Va-d, VIa) and also the salts (Ic) and (IIIb). We explained this by partial hydration of these salts by trace quantities of water contained in the solvent, since the pK_{R^+} values of these cations demonstrate the ease of their hydration (Table 1).

The half-wave reduction potentials of the cations (I-V), given in Table 1, lie in the range between −0.16 and −0.67 V. The dependence of $E_{1/2}$ on the structure of the diazinium salt obeys the common relationships previously observed [5] in the series of azinium cations; annellation of a benzene ring and the introduction of the aza group or other electron-withdrawing groups shift the $E_{1/2}$ potential of the reduction wave into the region of more positive values.

The unsubstituted N-ethylpyrazinium cation is the least active ($E_{1/2}$ = −0.67 V). The introduction of one or two accepting groups into the pyrazine ring increases the electrophilicity but to a lesser degree than the annellation of one or two benzene rings. The quinoxalinium cations (IIa-d) are reduced in the range between −0.34 and −0.37 V, irrespective of the counterion and substitution of the N-methyl by the N-ethyl group. The pteridinium cations (Va-e) have similar $E_{1/2}$ values between −0.26 and −0.35 V, while the most electrophilic are the benzo[g]quinoxalinium cations (IIIa, b), which have $E_{1/2}$ values of −0.16 and −0.18 V.

The electrochemical reduction of the cations (I-V) models the first stage of the reaction with the nucleophilic reagents, since electron transfer from the nucleophile may be the first

TABLE 1. Polarographic Behavior of 1,4-Diazinium Salts (I-VI) at a Rotating Platinum Disk Electrode with Ring in DMFA with 0.1 N $(C_4H_9)_4NClO_4$ Supporting Electrolyte with Reference to a Saturated Calomel Electrode. Concentration of Salts (I-VI) $5 \cdot 10^{-4}$ M

Compound	Disk		Ring*			pK_{R^+} [12]
	$E_{1/2}$, V	i, μA	$E_{1/2}$, V	i, μA	Q, %	
Ia	−0.67	16.0	−0.68	0.61	31.8	
Ib	−0.50	9.0	−0.50	0.03	2.8	8.04
Ic	−0.44	7.1	—	0.02	2	6.37
Id	−0.20	9.2	—	0.02	2	3.22
IIa	−0.34	12.8	−0.34	0.04	2.6	8.62
IIb	−0.37	11.1	−0.37	0.15	11.3	8.62
IIc	−0.36	13.0	−0.35	0.23	14.7	9.26
IId	−0.37	10.6	−0.38	0.16	12.6	9.26
IIIa	−0.16	9.3	−0.19	1.27	113.0	5.73
IIIb	−0.18	6.7	−0.20	1.1	137.5	6.32
IVa	−0.56	11.8	−0.58	0.04	2.8	12.5
IVb	−0.51	10.3	−0.55	0.03	2.4	—
Va	−0.26	7.0	—	0.02	2	5.00
Vb	−0.30	8.0	−0.34	0.03	3.1	7.01
Vc	−0.29	7.1	−0.27	1.54	181	6.74
Vd	−0.35	7.5	—	0.02	2	7.63
Ve	−0.32	5.4	—	0.02	2	7.24
VIa	−0.69	7.6	−0.69	0.03	3.3	—
VIb	−0.74	11.4	−0.78	0.13	9.5	—

*A constant ring potential equal to the potential at the foot of the reduction wave at the disk.

elementary event of the reaction. The subsequent fate of the radicals formed during one-electron reduction of the 1,4-diazinium ions was not investigated in the work. It is known [5] that they can dimerize, undergo protonation, or undergo further reduction. Thus, the electrochemical reduction of 2,3-diphenyl-1-methylquinoxalinium in a proton-donating medium includes two one-electron stages; the first leads to the formation of the radical and the second to 1,2-dihydroquinoxaline [6].

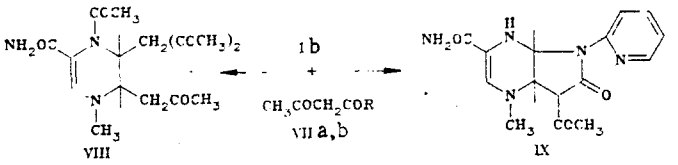
As known, the electrochemical reduction potentials characterize the electron-accepting capacity of the whole molecule, and the energy of its lowest unoccupied orbital. Published data on the electrochemical reduction of condensed pyrazines (derivatives of pyrido[2,3-b]-pyrazine [7] and the pteridine [8-10]) indicate that the electron-active part in these systems is localized in the pyrazine ring, since the products from reduction in a proton-donating medium are derivatives of dihydro- and tetrahydropteridine or pyrido[2,3-b]pyrazine. This gives reason to suppose that one and the same pyrazinium fragment is electrochemically active during the reduction of the whole series of cations (I-V) having the positive charge in the pyrazine ring and including the condensed pyrido[2,3-b]pyrazinium (IVa, b) and pteridinium (Va-e) systems.

Comparison of the half-wave potentials of the pteridinium cations (Va-e) [11, 12] with the $E_{1/2}$ values of the other 1,4-diazinium salts shows that the substituted pteridinium salts occupy an intermediate position between the quinoxalinium (IIa-d) and benzoquinoxalinium (IIIa, b) salts in their electron-accepting characteristics (Table 1). The electrophilicity of the pteridinium salts decreases significantly in the transition from the cations (Va, b) to the isomeric salts (VIa, b), in which the positive charge is delocalized not in the pyrazine but in the pyrimidine ring. The $E_{1/2}$ potential of the reduction wave of the cations (VIa, b) is shifted into the region between −0.69 and −0.74 V (Table 1). We note that such differences in the reduction potentials of the isomeric pteridinium cations (V) and (VI) can be used in the polarographic analysis of the mixtures formed as a result of the quaternization of pteridines.

The electrophilicity of diazinium cations is one of the factors which determine their participation in reactions with nucleophiles. The other quantitative characteristic is the pK_{R^+} values (Table 1), which reflect the ease of formation of the pseudobases [13]. Strict-

ly speaking, the pK_R+ values reflect not only the affinity of the 1,4-diazinium cations to the nucleophiles but also the stability of the hydroxyl adducts. A direct relationship is not therefore observed during comparison of the $E_{1/2}$ and pK_R+ values for the whole series of cations (I-V). At the same time, the relation between these characteristics is obvious, since the introduction of electron-withdrawing groups into the pyrazine ring not only increases the electrophilicity of the diazinium salts but also has a stabilizing effect on the adducts which they form with nucleophiles. Thus, the least electrophilic pyrazinium cation with $E_{1/2}$ = −0.67 V does not form stable adducts with nucleophiles, and the pK_R+ value could not be determined. It is also natural that a good correlation (r = 0.949) is observed between pK_R+ and $E_{1/2}$ values during examination of the narrower series of bicyclic quinoxalinium (IIa-d) and pteridinium (Va-e) cations (nine compounds).

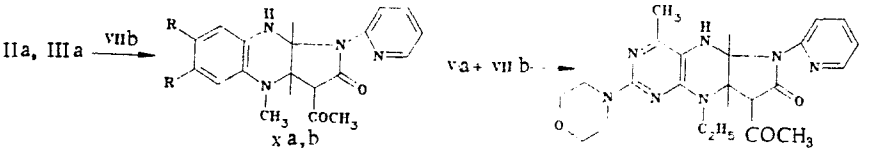
We will now consider whether there is a relation between the $E_{1/2}$ values and the participation of the diazinium cations in cyclizations with dinucleophiles. For a qualitative assessment of the participation of the diazinium salts in cyclizations with dinucleophiles in the present work we investigated the reactions of pyrazinium (Ia, b), quinoxalinium (IIa), benzoquinoxalinium (IIIa), and pteridinium (Vc) salts with N-(2-pyridyl)acetoacetamide (VIIb). The main conclusion which can be reached on the basis of the obtained results and also from examination of data on cyclizations of this type [2-4] is that 1,4-diazinium cations with $E_{1/2}$ values more positive than −0.5 V enter into reactions with dinucleophiles. The unsubstituted pyrazinium cation (Ia), which is reduced at −0.67 V, does not form either stable adducts with simple nucleophiles or the products from cyclization with dinucleophiles. The pyrazinium cation (Ib), which has an accepting substituent ($E_{1/2}$ = −0.50 V), is already capable of giving cyclic adducts but with a limited range of nucleophiles. Thus, in the reaction of the cation (Ib) with acetylacetone (VIIa) the product from diaddition of acetylacetone (VIII) is formed instead of the expected cyclic furo[2,3-b]-annellated pyrazine, but pyrrolo[2,3-b]pyrazine (IX) is formed in the reaction with the amide (VIIb).



VIIa R = CH_3, b R = 2-pyridylamino

The quinoxalinium (IIa) ($E_{1/2}$ = −0.34 V), benzoquinoxalinium (IIIa) ($E_{1/2}$ = −0.16 V), and also the pteridinium (Vc) ($E_{1/2}$ = −0.29 V) cations readily form cyclic adducts with the amide (VIIb).

The structure of the diaddition product (VIII) was established on the basis of the ^1H and ^{13}C NMR spectra by comparison with the spectral data for the product from the diaddition of acetylacetone to the quinoxalinium cation [14]. The composition and structure of the cyclization products (Xa, b) and (XI) were confirmed by the data from elemental analysis and by the PMR spectra, given in Tables 2 and 3, and also by the mass spectra (see Experimental). We will not dwell on the evidence for the structure of the cycloadducts (IX, Xa, b, XI), since the PMR spectra of their close structural analogs were examined in detail in [15, 16].



X a R = H, b R = benzo

Comparison of the $E_{1/2}$ values with data on the reactivity of pyrido[2,3-b]pyrazinium and pteridinium salts, which have the charge not in the pyrazine but in the pyridine and pyrimidine rings, respectively, also show differences in the direction of their reactions with dinucleophiles with significant change in the electrophilicity of the cations. Thus, the 5-methopyrido[2,3-b]pyrazinium cation, which has $E_{1/2}$ = −0.344 V [5], enters into cyclization with β-dicarbonyl compounds with annellation of the furan ring to the pyrazine ring [2, 3], whereas the reactions of the pteridinium salts (VIa, b) ($E_{1/2}$ = −0.69 and −0.74 V) with mono- and dinucleophiles do not affect the pyrazine ring [11]. Thus, these salts have approximately

TABLE 2. Pyrrolo[2,3-b]-Annellated Pyrazines and Quinoxalines (IX, Xa, b) and Pyrrolo[2,3-g]pteridine (XI)

Compound	T_{mp}, °C	Found, %			Molecular formula	Calculated, %			Yield, %
		C	H	N		C	H	N	
IX	154—155	56.7	5.4	22.4	$C_{15}H_{17}N_5O_3$	57.1	5.4	22.2	67
Xa	137	67.3	5.6	17.4	$C_{16}H_{16}N_4O_2$	67.1	5.6	17.4	93
Xb	192—193	70.8	5.5	15.1	$C_{22}H_{20}N_4O_2$	71.0	5.4	15.0	87
XI	149—150	60.4	6.3	22.6	$C_{22}H_{27}N_7O_5$	60.4	6.2	22.4	79

TABLE 3. PMR Spectra of Compounds (IX-XI)

Compound*	Chemical shifts, δ, ppm, and SSCC, Hz								
	α-H	β-H	$^3J_{\alpha\beta}$	N—R	others	NH, bd	3-H, d	$^3J_{3\alpha}$	$^3J(H_\beta H_{NH})$	$^3J(H_\alpha H_{NH})$
IX	4.22 m	5.28 bd	3.5	2.80 (3H, s)	2.45 (3H, s, $COCH_3$), 6, 70 (2H, s, $CONH_2$), 7.0—8.6 (m, 4H pyridine ring)		4.02	9.0		
Xa	4.77 dd	5.98 dd	7.7	2.83 (3H, s)	2.48 (3H, s, $COCH_3$); 6.3—8.5 (8H, m, arom. protons)	5.73	3.85	7.7	1.7	—
Xb	4.83 dd	6.05 dd	8.1	2.90 (3H, s)	2.46 (3H, s, $COCH_3$); 6.7—8.5 (10H, m, (arom. protons)	6.00	3.80	7.7	1.5	—
XI	4.75 m	5.58 dd	5.6	1.18 (3H, t, CH_3); 3.0—4.0 (2H, m, NCH_2)	2.13 (3H, s, CH_3); 2.54 (3H, s, $COCH_3$); 3.3—4.2 (m, 8H (morpholine ring); 7.0—8.6 (4H, m, arom. protons)	5.25	4.00	8.2	2.9	1.0

*Compound (IX) in DMSO-d_6, compounds (Xa, b, XI) in deuterochloroform.

the same region of $E_{1/2}$ values, in the order of −0.5 V, separating the diazinium cations with a reactive pyrazine ring from those not forming stable adducts in the pyrazine ring.

The data considered above show that the electron-withdrawing characteristics of the pyrazine ring are reflected in the stability of the covalent adducts and of the hydroxyl complexes, in particular (the pK_R+ values). The $E_{1/2}$ values can therefore be used as one of the criteria for assessing the reactivity of diazinium cations.

EXPERIMENTAL

The electrochemical reduction of the diazinium cations was realized on a rotating platinum disk electrode with ring in DMFA. The concentration of the substances was $5 \cdot 10^{-4}$ M, and the supporting electrolyte was 0.1 N tetrabutylammonium perchlorate. The experimental procedure and the purification of the solvent were described in [17].

The quaternary pyrazinium (Ia, b, d) [12, 18], quinoxalinium (IIa-d) [19], benzoquinoxalinium (IIIa, b) [12, 19], pyrido[2,3-b]pyrazinium (IVa,b) [20], and pteridinium ((Va, VIa) [11] and (Vb, c, VIb) [12]) salts were obtained by the previously described methods.

3-Methoxycarbonyl-1-methylpyrazinium Iodide (Ic). A mixture of 2.5 g (18 mmole) of methyl pyrazine-3-carboxylate, 20 ml of methyl iodide, and 0.5 ml of DMSO was kept at 20°C for 12 h. The precipitated salt (Ic) was filtered off and recrystallized from ethanol. The yield was 4.7 g (94%); mp 149-150°C. PMR spectrum (DMSO-d_6): 4.08 (3H, s, $COOCH_3$), 4.53 (3H, s, N—CH_3), 9.46 (1H, d, $^3J_{6,5}$ = 4 Hz, 5-H), 9.67 (1H, m, 6-H), 9.80 ppm (1H, bs, 2-H). Found, %: C 29.6, H 3.3, N 9.9. $C_7H_9IN_2O_2$. Calculated, %: C 30.0, H 3.2, N 10.0.

The quaternary pteridinium salts (Vd-e) were obtained by quaternization of the corresponding 2-dialkylamino-4-methylpteridines with triethyloxonium fluoroborate and methyl fluorosulfonate. The starting material for the production of 2-dialkylamino-4-methylpteridines was 6-amino-4-methyl-5-nitro-2-chloropyrimidine [21].

6-Amino-2-dimethylamino-4-methyl-5-nitropyrimidine. The compound was obtained from the corresponding 2-chloropyrimidine by the method in [22]. The yield was 70%, mp 150°C (yellow needles, from ethanol). Found, %: C 43.0, H 5.8. $C_7H_{11}N_5O_2$. Calculated, %: C 42.6, H 5.6. PMR spectrum (deuterochloroform): 2.67 (3H, s, CH_3), 3.18 [6H, s, $N(CH_3)_2$], 6.72 ppm (2H, bs, NH_2).

6-Amino-2-piperidino-4-methyl-5-nitropyrimidine. The compound was obtained by analogy with the 2-morpholino-substituted derivative [12]. The yield was 62%; mp 135-136°C (from ethanol). PMR spectrum (acetone-d_6): 1.58 (6H, m, protons of piperidine ring), 2.52 (3H, s, CH_3), 3.5-4.0 (4H, m, protons of piperidine ring), 7.42 ppm (2H, bs, NH_2). Found, %: C 50.6, H 6.4, N 29.7. $C_{10}H_{15}N_5O_2$. Calculated, %: C 50.6, H 6.4, N 29.5.

The 6-amino-2-dialkylamino-4-methyl-5-nitropyrimidines were converted into the corresponding 5,6-diaminopyrimidines by the method in [12].

5,6-Diamino-2-dimethylamino-4-methylpyrimidine. The compound was obtained with a yield of 30%; mp 153°C (from ethyl acetate). PMR spectrum (deuterochloroform): 2.22 (3H, s, CH_3), 2.35 (2H, bs, NH_2), 3.05 [6H, s, $N(CH_3)_2$], 4.74 ppm (2H, bs, NH_2). Found, %: C 50.4, H 7.7, $C_7H_{13}N_5$. Calculated, %: C 50.3, H 7.8.

5,6-Diamino-4-methyl-2-piperidinopyrimidine. The compound was obtained by a method similar to that described above. The yield was 65%, mp 142°C (from ethyl acetate). PMR spectrum (deuterochloroform): 1.59 (6H, m, protons of piperidine ring), 2.24 (3H, s, CH_3), 2.49 (2H, bs, NH_2), 3.65 (4H, m, protons of piperidine ring), 4.88 ppm (2H, bs, NH_2). Found, %: C 58.1, H 8.4, N 33.4. $C_{10}H_{17}N_5$. Calculated, %: C 57.9, H 8.2, N 33.8.

2-Dimethylamino-4-methylpteridine. The compound was obtained by the cyclization of 5,6-diamino-2-dimethylamino-4-methylpyrimidine with dioxa-2,3-diol in ethanol by the method given in [12] for 2-morpholino-4-methylpteridine. The yield was 74%; mp 154°C (from ethanol). PMR spectrum (deuterochloroform): 2.85 (3H, s, CH_3), 3.36 [6H, s, $N(CH_3)_2$], 8.38 (1H, d, 6-H, $^3J_{6,7}$ = 1.9 Hz), 8.72 ppm (1H, d, 7-H). Found, %: C 57.1, H 6.0. $C_9H_{11}N_5$. Calculated, %: C 57.1, H 5.9.

4-Methyl-2-piperidinopteridine. The compound was obtained by the same method with a 50% yield; mp 97°C (from petroleum ether, 70-100°C). PMR spectrum (deuterochloroform): 1.73 (6H, m, protons of piperidine ring), 2.98 (3H, s, CH_3), 4.05 (4H, m, protons of piperidine ring), 8.44 (1H, d, 6-H, $^3J_{6,7}$ = 2.0 Hz), 8.78 ppm (1H, d, 7-H). Found, %: C 62.5, H 6.5, N 30.3. $C_{12}H_{15}N_5$. Calculated, %: C 62.8, H 6.6, N 30.6.

4-Methyl-2-piperidino-8-ethylpteridinium Fluoroborate (Vd). To a suspension of 1.0 g (4.36 mmole) of 4-methyl-2-piperidinopteridine in 2 ml of dry methylene chloride we added a solution of 1 g (5.23 mmole) of triethyloxonium fluoroborate in 2 ml of methylene chloride, and this led to the dissolution of the initial pteridine. The reaction solution was kept at 20°C for 15 min and poured into 30 ml of absolute ether. The precipitated salt (Vd) was filtered off and washed with ether. The yield was 0.9 g (60%); mp 107-110°C. PMR spectrum (deuterochloroform): 1.67 (3H, t, CH_3), 1.80 (6H, m, protons of piperidine ring), 2.93 (3H, s, CH_3), 4.12 (4H, m, protons of piperidine ring), 4.82 (2H, q, N—CH_2), 8.72 (1H, d, 6-H, $^3J_{6,7}$ = 3.7 Hz), 8.89 ppm (1H, d, 7-H). Found, %: C 48.3, H 5.9, N 20.2. $C_{14}H_{20}BF_4N_5$. Calculated, %: C 48.7, H 5.8, N 20.3.

2-Dimethylamino-4-methyl-8-methylpteridinium Fluorosulfonate (Ve). To a suspension of 0.6 g (3.17 mmole) of 2-dimethylamino-4-methylpteridine in 2 ml of dry methylene chloride we added dropwise with cooling in ice and stirring 0.4 g (3.49 mmole, 0.3 ml) of methyl fluorosulfonate. The reaction mixture was kept at 0°C for 15 min, after which the precipitated salt (Ve) was separated and washed with absolute ether. The yield was 0.82 g (86%); mp 130-135°C (decomp.). PMR spectrum (deuterochloroform): 2.92 (3H, s, CH_3), 3.43 (3H, s, N—CH_3), 3.51 (3H, s, N—CH_3), 4.34 (3H, s, N—CH_3), 8.72 (1H, d, 6-H, $^3J_{6,7}$ = 3.5 Hz), 8.99 ppm (1H, d, 7-H). Found, %: C 39.9, H 5.0, N 22.8. $C_{10}H_{14}FN_5O_3S$. Calculated, %: C 39.6, H 4.7, N 23.1.

2-Acetonyl-4-acetyl-5-carbamoyl-3-(pentane-2,4-dion-3-yl)-1-methyl-1,2,3,4-tetrahydropyrazine (VIII). To a suspension of 1.5 g (5.7 mmole) of 1-methyl-3-carbamoylpyrazinium

iodide (Ib) in 4 ml of ethanol we added 1.2 ml (12 mmole) of acetylacetone. The mixture was heated at 50°C, and 1.5 ml (11 mmole) of triethylamine was added with stirring. The solution was kept at 50°C for 5 min and left at 20°C for 1 h. The precipitated compound (VIII) was filtered off and washed with ethanol and ether. The yield was 0.8 g (42%), and the product formed colorless needles from ethanol; mp 204-205°C. PMR spectrum (DMFA-d_7): 2.05 (3H, s, $COCH_3$), 2.11 (3H, s, $COCH_3$), 2.22 (3H, s, $COCH_3$), 2.30 (3H, s, $COCH_3$), 3.00 (3H, s, $N-CH_3$), 2.2-2.8 (2H, m, CH_2), 3.59 (1H, ddd, 2-H, $^3J_{2,3} = 1.3\ ^3J_2$, CH = 5.8, $^3J_2$, CH = 8.0 Hz), 3.73 (1H, d, CH, ^{3}JCH,3 = 11.1 Hz); 5.48 (1H, dd, 3-H), 6.50 (2H, bs, $CONH_2$), 7.05 ppm (1H, s, 6-H). ^{13}C NMR spectrum (DMSO-d_6): 21.7 ($NCOH_3$); 29.5 (3 $COCH_3$), 41.0 (NCH_3), 44.4 (CH_2—CO); 46.6 (b, $C_{(2)}$), 55.1 ($C_{(3)}$), 66.9 [$CH(COCH_3)_2$], 102.4 ($C_{(5)}$), 132.7 ($C_{(6)}$), 166.1 ($CONH_2$); 200.8, 201.4, and 205.2 ppm (C=O). Found, %: C 57.1, H 6.9, N 12.5. $C_{16}H_{23}N_3O_5$. Calculated, %: C 56.9, H 6.9, N 12.5.

3-Acetyl-4-methyl-1-(2-pyridyl)-2,3,3a,4,11,11a-hexahydro-1H-pyrrolo[2,3-b]benzo[g]-quinoxaline (Xb). To a suspension of 1 g (3.1 mmole) of N-methylbenzo[g]quinoxalinium iodide (IIIa) in 3 ml of ethanol we added 1 g (5.6 mmole) of N-(2-pyridyl)acetoacetamide (VIIb) and 1 ml (6.9 mmole) of triethylamine. The mixture was stirred at 20°C for 5-10 min until the reagent had completely dissolved. The precipitated compound (Xb) was then quickly filtered off and recrystallized from ethanol. The yield was 1 g (87%); mp 192-193°C (Tables 2 and 3). Mass spectrum:* 55 (12), 57 (14), 58 (12), 69 (12), 78 (13), 93 (12), 94 (12), 195 (100), 196 (19), 235 (11), 278 (15), 372 (M^+, 15).

3-Acetyl-4-methyl-1-(2-pyridyl)-2,3,3a,4,9,9a-hexahydro-1H-pyrrolo[2,3-b]quinoxaline (Xa). The compound was obtained by the same method from N-methylquinoxalinium iodide (IIa) and the amide (VIIb). The yield was 93%; mp 137°C (Tables 2 and 3). Mass spectrum: 77 (10), 78 (18), 93 (13), 94 (18), 120 (11), 131 (11), 145 (100), 146 (20), 159 (10), 13 (185), 228 (13), 322 (M^+, 20).

3-Acetyl-6-carbamoyl-4-methyl-1-(2-pyridyl)-2,3,3a,4,7,7a-hexahydro-1H-pyrrolo[2,3-b]-pyrazine (IX). The compound was obtained similarity from 3-carbamoyl-1-methylpyrazinium iodide and the amide (VIIb) by heating the reaction mixture at 70°C for 1 h. The yield was 67%; mp 154-155°C (Tables 2 and 3).

8-Acetyl-4-methyl-2-morpholino-6-(2-pyridyl)-9-ethyl-5,5a,7,8,8a,9-hexahydro-6H-pyrrolo-[2,3-g]pteridin-7-one (XI). To a suspension of 0.5 g (1.44 mmole) of 4-methyl-2-morpholino-8-ethylpteridinium fluoroborate (Vc) and 0.26 g (1.44 mmole) of N-(2-pyridyl)acetoacetamide (VIIb) in 2 ml of ethanol we added dropwise with stirring 0.3 ml (2.16 mmole) of triethylamine. The mixture was stirred at 20°C for 10 min until the initial substances had dissolved and an abundant precipitate of (XI) had formed. The precipitate was separated and recrystallized from ethanol. The yield was 0.5 g (79%); mp 149-150°C (Table 2 and 3). Mass spectrum: 51 (21), 52 (11), 58 (23), 66 (15), 67 (92), 78 (47), 79 (11), 82 (17), 85 (13), 93 (11), 94 (96), 95 (26), 120 (11), 121 (33), 135 (23), 163 (34), 178 (42), 260 (100), 261 (26), 437 (M^+).

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CYCLIZATION OF N-ALKYLAZINIUM CATIONS WITH BIFUNCTIONAL NUCLEOPHILES. 24.* SYNTHESIS OF CONDENSED 1,2,4-TRIAZINO- AND 1,2,4-OXADIAZINO[5,6-b]QUINOXALINE SYSTEMS

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Cyclization of quinoxalinium salts with amidoximes and amidhydrazones yields partially hydrogenated derivatives of new 1,2,4-oxadiazino- and 1,2,4-triazino[5,6-b]quinoxaline heterocyclic systems.

Condensed tricyclic systems containing the quinoxaline bicycle are of considerable interest. A special place is occupied by the alloxazine heterocyclic system, viz., the pyrimido-[4,5-b]annellated quinoxaline. This is the structural basis of flavin adenyl dinucleotide, riboflavin, and other flavins that play an important role in biochemical processes [2].

Between flavins and quinoxalines there is not only a formal structural similarity, but also a definite resemblance in chemical behavior. It is known that flavin thioanalogs [3, 4] and 1,3,10-trimethylalloxazinium salts [5] can add two alcohol or thioalcohol molecules, just as in the reactions of quaternary quinoxalinium salts [6]. The structural and chemical resemblance of flavins to quinoxalines, and the possibility of annelation of six-membered heterocycles to quinoxalines suggests the use of the reactions of quinoxalinium salts to synthesize structural analogs of flavins. The present work was an attempt to annelate six-membered rings containing a 1,3-diazino segment to quinoxalines. For this purpose we studied the reactions of quinoxalinium salts I with amidohydrazones II and amidoximes III; the latter are aminoazomethynes that potentially might play the role of 1,4-bifunctional nucleophile and annelate a 1,2,4-triazine or 1,2,4-oxadiazine segment to a quinoxaline framework.

*For Communication 23, see [1].

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