# CYCLIZATION OF N-ALKYLAZINIUM CATIONS WITH BIFUNCTIONAL NUCLEOPHILES.

## 16.* σ-ADDUCTS OF QUINOXALINIUM SALTS WITH AMINES, ALCOHOLS, AND ENOLATES AND THEIR ROLE IN CYCLIZATIONS WITH β-DICARBONYL COMPOUNDS

V. N. Charushin, M. G. Ponizovskii,
O. N. Chupakhin, E. O. Sidorov, and
I. M. Sosonkin

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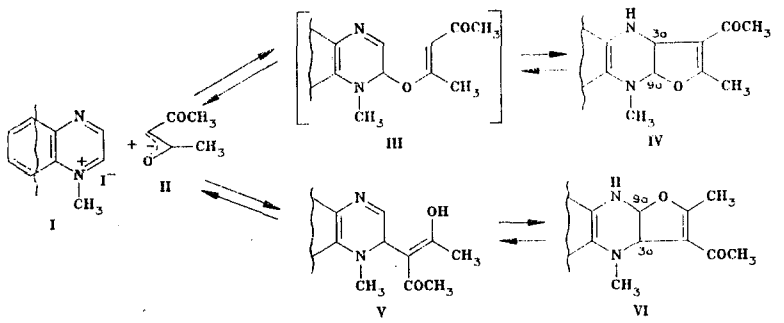
In the reaction of N-methylquinoxalinium iodide with acetylacetone at −30°C, the formation of 3-acetyl-2,4-dimethyl-3a,4,9,9a-tetrahydrofuro[2,3-b]quinoxaline has been recorded by $^1$H NMR spectroscopy, this being a regioisomer of the 3-acetyl-2,9-dimethyl-3a,4,9,9a-tetrahydro[2,3-b]quinoxaline formed in this reaction at temperatures above −10°C. σ-Adducts of the N-methylquinoxalinium cation with alcohols, amines, and β-diketones have also been identified, and their role in cyclizations leading to the annelation of a furan ring is discussed.

We have previously [2, 3] described the synthesis of tetrahydrofuro[2,3-b]quinoxalines by the cyclization of N-alkylquinozalinium salts with β-dicarbonyl compounds in the presence of di- or triethylamine.



The ambident nature of enolates [4] permits the possibility of the formation in the first stage of the reaction of the products of O- and C-addition in position 2 of the quinoxalinium cation, and, therefore, as the result of the cyclization of N-methylquinoxalinium iodide (I) with acetylacetone (II), one could expect the formation of the regioisomeric furo[2,3-b]quinoxalines (IV) and (VI). However, in preceding investigations no cycloadducts of the type (VI) were recorded. The hypothesis has been put forward of a stagewise occurrence of cyclizations through the intermediate formation of the product of O-addition (III) [2, 3]. The participation in them of σ-adducts with a different structure, such as (V), was not considered, and no attempts to detect any intermediates have hitherto been made. In view of the fact that the formation of furo[2,3,-b]quinoxalines (IV) takes place in an alcoholic medium in the presence of di- or triethylamine the appearance during the reaction of lyate complexes and also their participation in cyclization appeared likely.

The aim of the present work was to establish general laws of the formation of adducts in the reactions of the cation (I) with N-, O-, and C-nucleophiles, and to study their properties and role in cyclizations with β-dicarbonyl compounds.

*For Communication 15, see [1].

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TABLE 1. Conditions for the Formation of Mono- and Diadducts of N-Methylquinoxalinium Iodide (I) with Amines, Alcohols, and CH-Active Compounds and Their Chemical Transformations (from their $^1$H NMR spectra)

| Reagents | Solvent | Temperature, °C | Reaction products* |
|---|---|---|---|
| I+HN(C$_2$H$_5$)$_2$ (1 : 2) | CD$_3$OD | −40 | VIIa |
| | CD$_3$OD | 35 | VIIa+VIIIa (1 : 1) |
| | CDCl$_3$ | 35 | VIIc |
| | (CD$_3$)$_2$SO | 35 | VIIc |
| | O(C$_2$H$_5$)$_2$† | 20 | VIIc |
| I+N(C$_2$H$_5$)$_3$ (1 : 2) | CD$_3$OD | −40 | VIIa |
| | CD$_3$OD | 35 | VIIa+VIIIa (1 : 1) |
| I+H$_2$NC$_2$H$_5$ (2 : 5) | (CD$_3$)$_2$SO | 35 | VIIb+VIIIb (2 : 3) |
| I+H$_2$NC$_2$H$_5$ (1 : 3) | (CD$_3$)$_2$SO | 35 | VIIIb |
| | CDCl$_3$ | 35 | VIIIb |
| | CD$_3$OD | 35 | VIIIb |
| I+(CH$_3$)$_2$CHOH+N(C$_2$H$_5$)$_3$ (1 : 1 : 1) and (1 : 2 : 2) | CDCl$_3$ | 35 | VIIg |
| I+CH$_2$(COCH$_3$)$_2$+N(C$_2$H$_5$)$_3$ (1 : 1 : 1) and (1 : 2 : 1) | CDCl$_3$ | −40 | VIId |
| I+CH$_2$(COOC$_2$H$_5$)$_2$+N(C$_2$H$_5$)$_3$ (1 : 1 : 1) | CDCl$_3$ | 35 | VIIe |
| VIIc+CD$_3$OD (1 : 1) | CDCl$_3$ | 35 | VIIa |
| | (CD$_3$)$_2$SO | 35 | VIIa |
| | CCl$_4$ | 35 | VIIa |
| VIIc+D$_2$O (1 : 1) | (CD$_3$)$_2$SO | 35 | VIIf |
| VIIc+(CH$_3$)$_2$CHOH (1 : 10) | CDCl$_3$ | 35 | VIIg |
| VIIc+H$_2$NC$_2$H$_5$ (1 : 2) | CDCl$_3$ | 35 | VIIIb |
| | (CD$_3$)$_2$SO | 35 | VIIIb |
| VIIc+CH$_2$(COOC$_2$H$_5$)$_2$ (1 : 1) | CDCl$_3$ | 35 | VIIe |
| VIIc+CH$_2$(COCH$_3$)$_2$ (1 : 1) | CDCl$_3$ | 35 | IV |
| | CCl$_4$ | 35 | IV |
| | (CD$_3$)$_2$SO | 35 | IV |
| | O(C$_2$H$_5$)$_2$† | 20 | IV |
| VIId+CH$_2$(COCH$_3$)$_2$ (1 : 1) | CDCl$_3$ | −20÷+35 | IV |
| VIIa+CH$_2$(COCH$_3$)$_2$ (1 : 1) | CDCl$_3$ | 35 | IV |
| | (CD$_3$)$_2$SO | 35 | IV |
| VIIe+CD$_3$OD (1 : 1) | CDCl$_3$ | 35 | VIIa |

*Complete conversion of the initial reactants into the covalent adducts. No by-products of the reaction whatever nor signals of the initial salt (I) were observed in the $^1$H NMR spectra.

†Obtained preparatively (see the Experimental part).

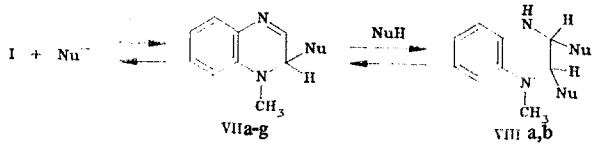
The products of the addition of nucleophiles to an azine nucleus are usually unstable, but can be recorded in NMR spectra [5, 6]. It has been shown by $^1$H NMR spectroscopy that in the first stage of the reactions of the N-methylquinoxalinium cation with N-, O-, and C-nucleophiles such as aliphatic agents, alcohols, and β-dicarbonyl compounds the formation of the covalent adducts (VIIa-g) takes place. When these reactants were added to the salt (I), the signal of the initial cation disappeared completely and the recorded spectra of the reaction mixtures showed the quantitative formation of the σ-adducts (VIIa, c-e, g) (Tables 1 and 2). In a number of cases, the dihydroquinoxalines formed retained their capacity for the secondary addition of a nucleophilic reagent and, in the absence of steric hindrance gave the diadducts (VIIIa, b) (Tables 1 and 2). The ratio of compounds (VII) and (VIII) in the equilibrium mixture, and also the temperature intervals within which the mono- or the diadduct existed depended predominantly on the nature of the reactants (Table 1). Such behavior of the cation (I) with respect to nucleophiles agrees well with results of investigations [7, 8] in which the capacity of 1,4-diazinium cations for adding nucleophiles was likewise observed.

The methoxide anion formed at −40°C in methanol-d$_4$ in the presence of a base (di- or triethylamine or lithium methanolate) gave a single product with the salt (I) — the methoxyl adduct (VIIa), readily identified from its two characteristic doublets of the 2-H and 3-H protons at 5.30 and 7.56 ppm with the vicinal constants $^3J_{2,3}$ = 3.4 Hz (Tables 1 and 2). At 0°C, the signals of the tetrahydroquinoxaline (VIIIa) appeared in the $^1$H NMR spectrum. The chemical shifts of the signals of the methoxyl complexes (VIIa) and (VIIIa), and also their ratio agree well with information [7] on the interaction of the salt (I) with lithium methanolate in methanol-d$_4$ (Table 2).

TABLE 2. $^1$H NMR Spectra of Mono- and Diadducts of N-Methylquinoxalinium Iodide (I) with Amines, Alcohols, and CH-Active Compounds

| Adduct | Reaction conditions | | Chemical shifts, δ, ppm | | | | $^3J_{2,3}$, Hz |
|---|---|---|---|---|---|---|---|
| | solvent (lit.) | temperature, °C | 2-H* | 3-H* | $NCH_3$, s | arom. protons | |
| VII a | $CD_3OD$ | −40 | 5,30 | 7,56 | 3,20 | 6,7—7,6 | 3,4 |
| | $CD_3OD$ | 35 | 5,23 | 7,52 | 3,19 | 6,7—7,5 | 3,4 |
| | $CD_3OD$ [7] | 20 | 5,37 | 7,66 | 3,23 | 6,9—7,5 | 3 |
| | $CDCl_3$ | 35 | 5,22 | 7,53 | 3,14 | 6,6—7,6 | 3,5 |
| | $CCl_4$ | 35 | 5,21 | 7,45 | 3,10 | 6,6—7,5 | 3,5 |
| | $(CD_3)_2SO$ | 35 | 5,24 | 7,58 | 3,17 | 6,6—7,7 | 3,4 |
| VII b | $(CD_3)_2SO$ | 35 | 4,71 | 7,41 | 3,00 | 6,6—7,5 | 3,8 |
| VII c | $CDCl_3$ | 35 | 4,70 | 7,41 | 2,92 | 6,4—7,5 | 3,5 |
| | $CCl_4$ | 35 | 4,63 | 7,28 | 2,89 | 6,3—7,4 | 3,5 |
| | $(CD_3)_2SO$ | 35 | 4,82 | 7,39 | 2,91 | 6,3—7,5 | 3,3 |
| VII d | $CDCl_3$ | −40 | 4,88 d.d | 7,59 | 2,85 | 6,5—7,7 | 4,0 |
| VII e | $CDCl_3$ | 35 | 4,67 d.d | 7,66 | 2,97 | 6,4—7,9 | 4,5 |
| VII f | $(CD_3)_2SO$ | 35 | 5,20 | 7,61 | 3,07 | 6,7—7,6 | 3,1 |
| VII g | $CDCl_3$ | 35 | 5,25 | 7,57 | 3,10 | 6,5—7,6 | 3,5 |
| VIIIa | $CD_3OD$ | 35 | 4,56 s | 4,56 s | 3,14 | 6,63 s | — |
| | $CD_3OD$ [7] | 20 | 4,62 s | 4,62 s | 3,20 | 6,67 s | — |
| VIIIb † | $(CD_3)_2SO$ | 35 | 3,90 | 3,96 | 3,04 | 6,3—7,0 | 2,3 |
| | $CDCl_3$ | 35 | 4,07 | 4,14 | 3,00 | 6,2—6,9 | 2,5 |
| | $CD_3OD$ | 35 | 4,02 | 4,07 | 3,10 | 6,55 s | 2,5 |

*Doublet if not otherwise specified.
†The assignment of the signals of the 2-H and 3-H protons may be the opposite.




VII, VIIIa Nu=$OCH_3$; b Nu=$NHC_2H_5$; VIIc Nu=$N(C_2H_5)_2$; d Nu=$CH(COCH_3)_2$; e Nu=$CH(COOC_2H_5)_2$; f Nu=OH; g Nu=$OCH(CH_3)_2$

The concentration of the product (VIIIa) increased with a rise in the temperature, and at 25°C the ratio of (VIIa) and (VIIIa) was 1:1. The ratio of the mono- and diadducts in the mixture was determined by measuring the intensities of the signals of the 2-H proton of compound (VIIa) (doublet at 5.23 ppm) and of the 2-H and 3-H protons of the tetrahydroquinoxaline (VIIIa) (common peak at 4.56 ppm). It was impossible to shift the equilibrium appreciably in the direction of the tetrahydroquinoxaline (VIIIa) by increasing the concentration of base in the reaction mixture. In addition to the temperature dependence, the equilibrium contents of the mono- and diadducts were affected by steric factors. Thus, in the reaction with isopropanol, the cation (I) formed only the monoadduct (VIIg), while tert-butanol did not add to the quinoxaline (I) at all.

The reaction of cation (I) with ethylamine took place somewhat differently. At a ratio of ethylamine to the salt (I) of 5:2 in dry DMSO-$d_6$ at 35°C, a mixture of the mono- and diadducts (VIIb) and (VIIIb) was formed (Tables 1 and 2). An increase in the ratio of ethylamine to the salt (I) in the reaction mixture to 3:1 and more led to the complete shifting of the equilibrium in the direction of the diadduct (VIIIb) (disappearance of the doublets of the dihydroquinoxaline (VIIb) at 4.71 and 7.41 ppm with $^3J_{2,3}$ = 3.8 Hz and to a corresponding increase in the intensity of the signals of the diadduct (VIIIb) at 3.90 and 3.96 ppm) (Tables 1 and 2). Attempts to find conditions under which only the monoadduct (VIIb) could be detected in the reaction mixtures were unsuccessful. Lowering the reaction temperature (−40 to −20°C) demanded the use of other solvents, such as DMFA-$d_7$ and $CDCl_3$, in which the reaction of the salt (I) with ethylamine took place in a manner different from that in DMSO, with the formation of a complex mixture of unidentified products not containing the covalent adducts (VIIb) and (VIIIb).

In the reaction mixture of salt (I) with diethylamine in DMSO-$d_6$, only the monoadduct (VIIc) was recorded (Fig. 1 and Tables 1 and 2), and this because of steric hindrance, was

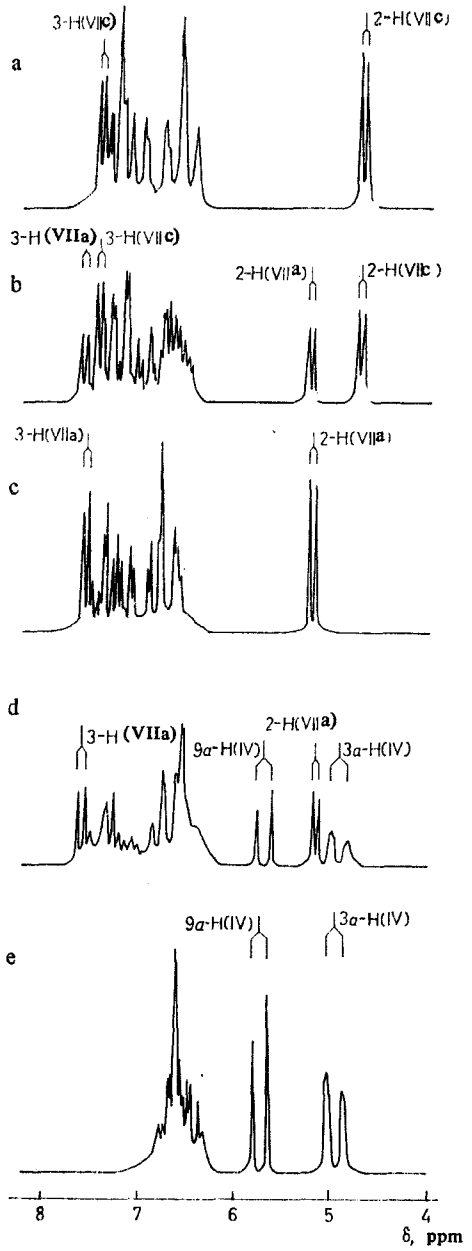
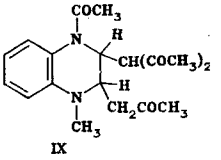



Fig. 1. $^1$H NMR spectra of reaction mixtures (in $CDCl_3$ at 35°C); a) adduct of N-methylquinoxalinium with diethylamine (VIIc); b, c) its transformation into the methoxyl adduct (VIIa) on the addition of 0.5 and 1 equiv. of $CD_3OD$, respectively; d, e) the formation of the furo[2,3-b]quinoxaline (IV) on the addition of 0.5 and 1 equiv., respectively, of acetylacetone to the O-adduct (VIIa).

incapable of the secondary addition of diethylamine even in the presence of a tenfold excess of it at 35°C. However, the formation of the dihydroquinoxaline (VIIc) in aprotic solvents such as DMSO, chloroform, and ethyl ether took place in quantitative yield. Solutions of the adduct (VIIc) in aprotic solvents were stable at 35°C for several hours, making it possible to work preparatively with them (see the Experimental part).

C-nucleophiles derived from β-dicarbonyl compounds gave only the dihydroquinoxalines (VIId, e) in the reactions under consideration. For example, on reaction with the salt (I) at 35°C in $CDCl_3$ in the presence of triethylamine, malonic ester formed the dihydroquinoxaline (VIIe), the equilibrium being shifted completely in the direction of the addition product (VIIe) according to $^1$H NMR spectroscopy (Tables 1 and 2). In the reaction of the cation (I)

with acetylacetone in the presence of triethylamine it was again possible to record the C-adduct (VIId), but only at temperatures from −40 to −35°C (Tables 1 and 2). A proof of the C-addition of malonate and acetylacetonate in the σ-adducts (VIId, e) was provided by the multiplicity of the signal of the 2-H proton appearing in the $^1$H NMR spectra as a doublet of doublets through spin-spin coupling both with the 3-proton and with the proton of the CH group of the substituent, while on deuterium exchange of the active CH group of the dicarbonyl residue the signal of the 2-H proton assumed the form of a doublet. It is important to emphasize that even at low temperatures the C,O-ambient acetylacetonate exhibits the properties only of a C-nucleophile with respect to the cation (I). The formation of diadducts in the reactions of salt (I) with β-dicarbonyl compounds was not recorded, although the formation of the tetrahydroquinoxaline (IX) has been described previously [9].



IX

Below we consider the transformation of the N-, O-, and C-adducts (VIIa-g) under the action of nucleophilic reagents.

(VIIc ⇄ VIIa, f, g, e)

On the addition of methanol to a solution of the dihydroquinoxaline (VIIc) in one of the following solvents — chloroform, carbon tetrachloride, or dry DMSO — the diethylamine residue was displaced completely by a residue of the alcohol, leading to the methoxyl adduct (VIIa) (Fig. 1, Tables 1 and 2).

The O-adduct (VIIa) formed had lower-field chemical shifts of the 2-H and 3-H protons, and it can readily be identified from this characteristic (Fig. 1, Tables 1 and 2). The diethylamino group of compound (VIIc) was also readily replaced by a hydroxy group, and it was therefore possible to record the presence of the N-adduct (VIIc) in the $^1$H NMR spectra only in absolute solvents. When even minute amounts of water were present in DMSO the product of covalent hydration (VIIf) was recorded in the spectra (Tables 1 and 2). The reaction of compound (VIIc) with isopropanol in chloroform also took place smoothly, giving the adduct (VIIg) (Tables 1 and 2).

The diethylamino group in adduct (VIIc) was likewise replaced by C-nucleophiles. Such exchange took place on the addition of malonic ester to a solution of compound (VIIc) in chloroform (Tables 1 and 2). The C-adduct (VIIe) formed was, in its turn, readily converted under the action of methanol into the methoxyl complex (VIIa).

In the tetrahydroquinoxaline (VIIIb), the amino group was not replaced by methoxy residues. Conversely, the reaction of ethylamine both with the dihydroquinoxazoline (VIIa, c) and with a mixture of the methoxy complexes (VIIa, VIIIa) led to their complete conversion into the diadduct (VIIIb). Even in methanolic solution, i.e., in the presence of a manyfold excess of the alcohol, the mixing of the salt (I) with three equivalents of ethylamine led exclusively to the addition product (VIIIb).

One equivalent of ethylamine was consumed in binding the hydriodic acid.

Thus, the capacity of some nucleophilic reagents for displacing others at the sp$^3$ carbon atom in each of the dihydroquinoxalines (VIIa-g) can be represented by the following series:

$$C_2H_5NH_2 > CH_3OH \simeq H_2O \simeq (CH_3)_2CHOH > CH_2(COCH_3)_2 \simeq CH_2(COOC_2H_5)_2 > (C_2H_5)_2NH \gg (CH_3)_3COH$$

It follows from a consideration of this series that not only nucleophilicity but also, and to a very large degree, steric factors affect the course of the transformations in the series of σ-adducts (VIIa-g). The series given also indicates the possibility of obtaining some 1,2-dihydroquinoxalines from others by exchanging nucleophiles.

The question of the route by which these transformations take place — synchronous ($S_N2$) or dissociative ($S_N1$) — has not been investigated in the present work and remains a matter for discussion. For the analogous transformations in a series of anionic σ-complexes a

dissociative mechanism including the pre-equilibrium protonation of the σ-complex is assumed [5, 10-12].

The results obtained permit the assumption that in a reaction mixture including the cation (I), a proton-donating solvent (an alcohol, water) and also a base (amine) and a CH-active compound (β-diketone), the N-, O-, and C-adducts may be present simultaneously. The ease of formation of the covalent adducts and also the transformations of some adducts into others create the possibility for their participation as intermediates on the pathway to the furo-[2,3-b]quinoxalines. The possibility of the participation of the dihydroquinoxalines (VIIa) and (VIIc) in cyclization with β-diketones has not been refuted by an experimental check, either. Thus, the addition of acetylacetone to a solution of the N-adduct (VIIc) or the O-adduct (VIIa) in such solvents as chloroform, $CCl_4$, methanol, and diethyl ether at 20-30°C led instantaneously to the furo[2,3-b]quinoxaline (IV) (Fig. 1, Table 1, Experimental part). With acetylacetone the mixture of methoxy complexes (VIIa) and (VIIIa) gives the same furo-[2,3-b]quinoxaline (IV), and an analysis of the fall in the intensities of the signals in the $^1$H NMR spectra on the addition of various amounts of acetylacetone showed that only the mono-adduct (VIIa) was involved in the cyclization. The tetrahydroquinoxaline (VIIIa) took part in the reaction only after the splitting out of one molecule of methanol, i.e., it began with the dissociation of the dihydro compound (VIIa).

The product of the C-addition of acetylacetone to the cation (I) — compound (VIId), recorded at −40°C — underwent transformation in two directions. According to the $^1$H NMR spectra, at −30°C it cyclized intramolecularly to the furo[2,3-b]quinoxaline (VI). This was shown by the signals of the 3a-H and 9a-H protons of compound (VI) at 4.63 and 5.99 ppm, respectively, with $^3J_{3a,9a}$ = 7 Hz, since the region of values of vicinal constants $^3J$ = 7-9 Hz is characteristic for compounds in which a tetrahydropyrazine ring is linked to a five-membered heterocycle, and corresponds to the cis orientation of the protons at the nodal carbon atoms [13]. In the case of the diaddition of nucleophiles at positions 2 and 3 of the cation (I), the protons of the tetrahydropyrazine ring have the trans orientation with $^3J_{2,3}$ = 2-4 Hz, as follows from the literature [9], and also from Table 2 (see $^3J_{2,3}$ for compound (VIIIb)). The furo[2,3-b]quinoxaline (VI) existed in $CDCl_3$ solution at −30°C in equilibrium with the dihydroquinoxaline (VIId). When the temperature was raised to −20°C the intensity of the signals of the furo[2,3-b]quinoxaline (VI) in the $^1$H NMR spectra fell and the concentration of the C-adduct (VIId) became so small that its residual signals could hardly be detected in the spectrum even with high amplification. At the same time, in the $^1$H NMR spectrum at −20°C a group of signals appeared which indicated the formation of the regioisomeric furo-[2, 3-b]quinoxaline (IV): a doublet of the 9a-H proton at 5.78 ppm and a broadened doublet of the 3a-H proton at 5.04 ppm (Fig. 2), the signals of the protons of methyl, N-methyl, and acetyl groups, and also of those of a benzene ring (the complete $^1$H NMR spectrum of compound (IV) is given in [2]). A comparison of the chemical shifts of the protons at the nodal carbon atoms in the regioisomeric furo[2,3-b]quinoxalines (IV) and (VI) showed that, as was to be expected, on passing from compound (IV) to the regioisomer (VI) the signal of the 3a-H proton shifted upfield because of the greater donor effect of the N-methyl group as compared with that of the NH group. For the same reason, the 9a-H proton of compound (VI) resonated in a weaker field as compared with compound (IV) (Fig. 2). A further rise in the temperature of a solution of the C-adduct (VIId) in $CDCl_3$ to −5°C caused the conversion of the furo[2, 3-b]-quinoxaline (VI) into the regioisomer (IV), obviously through its previous dissociation to the C-adduct (VIId). At temperatures ranging from −5 to +35°C only the signals of compound (IV) were recorded in the $^1$H NMR spectra, and it was possible to obtain this compound preparatively (see the Experimental part), unlike its regioisomer (VI), whose low stability in the cyclic form did not permit its isolation from solution and its characterization as an individual compound.

Obviously, the cause of the regioselectivity of the cyclization of the cation (I) with β-dicarbonyl compounds is the higher thermodynamic stability of one of the regioisomers, namely the furo[2,3-b]quinoxaline (IV). Considering the formation of the furo[2,3-b]quinoxalines (IV) and (VI) as a manifestation of ring-chain isomerism [14] for the O- and C-adducts of the ambident enolate (II) with the cation (I), the greater stability of the cyclic form (VI) can be explained by the fact that the $C_3$—$C_{3a}$ bond arising in the process of intramolecular cyclization of the O-adduct (III) is stronger than the $C_{9a}$—O bond in the furo[2,3-b]quinoxaline (VI), which readily dissociates even at low temperatures ranging from −20 to −30°C. Another probable mechanism explaining the orientation of the furan ring in the cyclization product (VI) includes the C-addition of the β-diketone in position 3 of one of the σ-adducts (VIIa, c, d) initially formed, with the subsequent intramolecular displacement of the nucleophile from position 2.

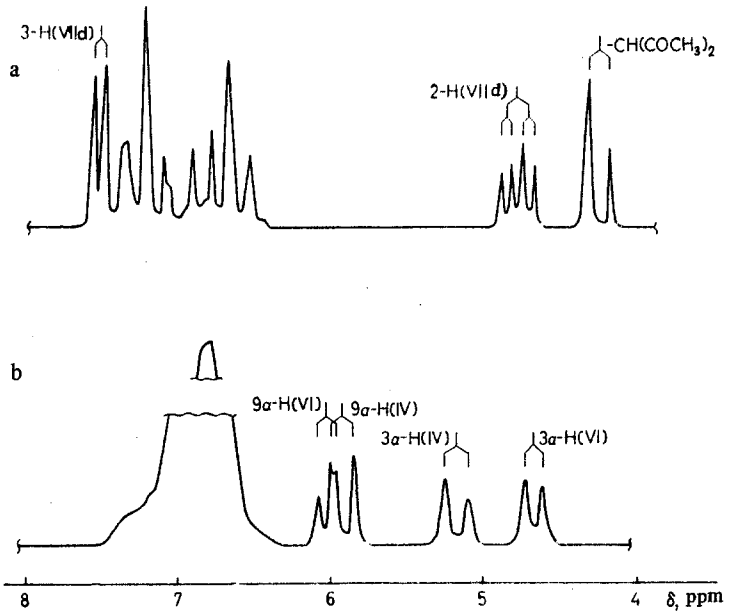
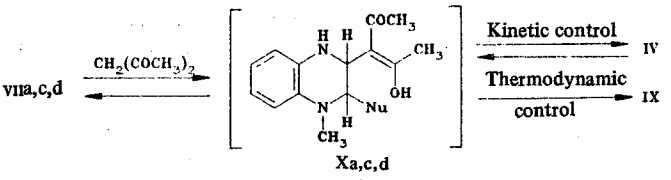



Fig. 2. $^1$H NMR spectra (in $CDCl_3$): a) the C-adduct (VIId) at −40°C; c) the mixture of the regioisomeric furo[2,3-b]-quinoxalines (IV) and (VI) formed on raising the temperature to −20°C.




VII, X [a] Nu=$OCH_3$; c Nu=$N(C_2H_5)_2$; d Nu=$CH(COCH_3)_2$

The suggested mechanism permits an explanation of the regioorientation of the furan ring relative to the pyrazine ring based on the formation of the Michael adducts (X) that are usual for β-diketones and does not have recourse to a consideration of the unusual product of O-addition (III). A similar mechanism for the formation of furo[2,3-b]quinoxalines, including the C-addition of an enolate to the $C_{(3)}$ carbon atom of 2-chloroquinoxaline with the subsequent replacement of the halogen, has recently been suggested by Carver and Wolfe [15].

In conclusion, we may mention that the results obtained in work on the formation of lyate complexes and adducts with amines in the reactions of quinoxalinium salts with bifunctional nucleophiles must be taken into account for predicting the regioorientation and spatial structures of cycloadducts. We have already made use of these ideas in [16] in which, by means of conditions excluding the formation of adducts with the solvent, the complete reversal of the regioorientation of a thiazole ring annelated to a quinoxaline ring was achieved.

## EXPERIMENTAL

$^1$H NMR spectra were recorded on a Perkin–Elmer R-12B (60 MHz) instrument with HMDS as internal standard.

N-Methylquinoxalinium iodide (I) was obtained as described previously [2]. The covalent adducts of the cation (I) with water (VIIf), with methanol (VIIa, VIIIa), with isopropanol (VIIg), with ethylamine (VIIb, VIIIb), with diethylamine (VIIc), with acetylacetone (VIId), and with diethyl malonate (VIIe) were detected in $^1$H NMR spectra.

General Procedure for Performing the Experiments. A weighed sample of N-methylquinoxalinium iodide (I) taken in amounts of 38-44 mg (0.14-0.16 mmole) was treated with 0.3 ml of a solvent (see Table 1), and the mixture was kept at the temperature shown in Table 1 for 10 min. The given amount of the salt (I) dissolved completely in DMSO but only partially in methanol, $CDCl_3$, and $CCl_4$ and in these cases, therefore, the reaction was performed in a heterogeneous system. A solution of the base (ethyl-, diethyl-, or triethylamine) or CH-active compound in admixture with triethylamine in 0.2 ml of the same solvent was prepared separately where the required amounts of substances were checked by weighing (the ratios of the reactants are shown in Table 1). The solution obtained was thermostated for 10 min and was mixed with the solution or suspension of the salt (I), with vigorous shaking in a thermostat several times. A light-yellow solution was formed which was rapidly transferred to the previously thermostated ampul of the NMR spectrometer, and the spectrum was recorded. The preparation of the sample and recording of the first general spectrum took 10-15 min after the mixing of the reactants. The $^1H$ NMR spectra recorded in this period showed the complete conversion of the initial salt (I) into the covalent adducts (VIIa-g) and (VIIIa, b) (Table 1). Adduct (VIIa) was formed quantitatively at −40°C but at temperatures above 0°C only as a mixture with the diadduct (VIIIa); adduct (VIIb) was obtained only in admixture with the diadduct (VIIIb). The total yield of the pairs of compounds (VIIa) + (VIIIa) and (VIIb) + (VIIIb) was 100%, calculated on the initial salt (I). The adducts (VIIc-e) and (VIIIb) were obtained quantitatively from the salt (I), and the adducts (VIIf, g) also in 100% yield but by the replacement of the diethylamino group in (VIIc) on reaction with water and isopropanol (Table 1). The characteristics of the $^1H$ NMR spectra of compounds (VIIa-g, VIIIa, b) are given in Table 2.

2-Diethylamino-1-methyl-1,2-dihydroquinoxaline (VIIc). With stirring, 2.3 ml (22 mmole) of dry diethylamine was added to a suspension of 3 g (11 mmole) of N-methylquinoxalinium iodide (I) in 10 ml of absolute diethyl ether. The reaction mixture was stirred for 5 min, after which the diethylamine hydriodide was filtered off, and the solvent was distilled off in vacuum at room temperature, giving compound (VIIc) in the form of a light-yellow oil. Yield 2.1 g (91%). The $^1H$ NMR spectrum of compound (VIIc) is given in Fig. 1, and also in Table 2. The results of elementary analysis and chromatography are not given, since the adduct (VIIc) was stable for 1-2 h only in solution; in the air the substance decomposed in a few minutes, as it also did on alumina and silica gel during chromatography.

3-Acetyl-2,9-dimethyl-3a,4,9,9a-tetrahydrofuro[2,3-b]quinoxaline (IV). At room temperature, 1 ml (10 mmole) of acetylacetone was added to 2.1 g (10 mmole) of compound (VIIc) in 5 ml of diethyl ether. After 1-2 min, the colorless precipitate of compound (IV) that had formed was filtered off and washed with ethanol and ether. Yield 1.9 g (77%), mp 118-120°C (decomp.). The characteristics of the $^1H$ NMR and IR spectra of substances (IV) obtained by this method, and also from N-methylquinoxalinium iodide by the procedure of [2], agreed completely with those given in the literature [2, 3].

The interaction of the dihydroquinoxaline (VIIc) with acetylacetone, leading to the furo[2,3-b]quinoxaline (IV) took place similarly in other solvents — $CDCl_3$, $CCl_4$, and methanol. In the last case, the methoxyl adduct (VIIa), formed instantaneously when the dihydroquinoxaline (VIIc) was dissolved in the methanol, took part in the reaction.

3-Acetyl-2,4-dimethyl-3a,4,9,9a-tetrahydrofuro[2,3-b]quinoxaline (VI) was recorded in the $^1H$ NMR spectra in $CDCl_3$ at −20°C in admixture with the regioisomer (IV) (see text and Fig. 2).

The synthesis of 2-acetonyl-4-acetyl-1-methyl-3-(2,4-dioxopent-3-yl)-1,2,3,4-tetrahydroquinoxaline (IX) and its characteristics have been given in a previous paper [9].

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PYRIMIDINE DERIVATIVES.

# 58.* A NEW METHOD FOR SYNTHESIZING 7-AMINOPYRROLO[2,3-d]-PYRIMIDINE DERIVATIVES

R. G. Melik-Ogandzhanyan, A. S. Gapoyan,
V. É. Khachatryan, and V. S. Mirzoyan

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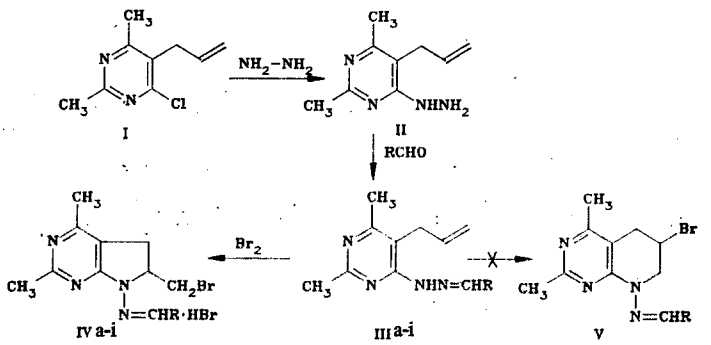
A number of aldimines of 7-aminopyrrolo[2,3-d]pyrimidine have been synthesized by the action of bromine on hydrazones of 5-allyl-4-hydrazinopyridine. The structures of the compounds obtained were confirmed by IR spectroscopy and mass spectrometry.

Continuing the development of new methods for synthesizing condensed pyrimidine systems [1-3] presenting interest as physiological compounds [4-6], in the present work we have shown the possibility of obtaining 7-aminopyrrolo[2,3-d]pyrimidine derivatives (IVa-i) by the following scheme:




III, IV a R=$C_6H_5$; b R=4-$FC_6H_4$; c R=4-$CH_3OC_6H_4$; d R=4-$O_2NC_6H_4$; e R=4-$(CH_3)_2NC_6H_4$; f R=4-$(ClCH_2CH_2)_2NC_6H_4$; g R=2-$HOC_6H_4$; h R=3-$CH_3O$, 4-$HOC_6H_3$; i R=CH=$CHC_6H_5$

*For Communication 57, see [1].

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