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CYCLIZATIONS OF N-ALKYLAZINIUM CATIONS WITH BIFUNCTIONAL NUCLEOPHILES.

19.* CRYSTAL STRUCTURE OF THE KINETIC PRODUCT OF THE REACTION OF N-METHYLQUINOXALINIUM IODIDE WITH THIOACETAMIDE

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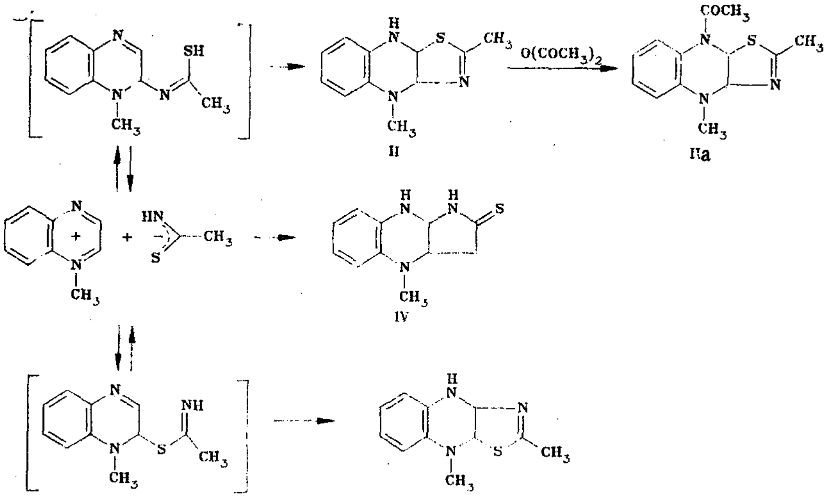
The mutual orientation of the heterorings and the three-dimensional structure of the kinetic product of the reaction of N-methylquinoxalinium iodide with thioacetamide were established by x-ray diffraction analysis of 2,4-dimethyl-9-acetyl-3*a*,4,9,9*a*-tetrahydrothiazolo[4,5-b]quinoxaline.

The ambident properties of thioamides in reactions with electrophilic reagents are well known [2]. The ratio of the N- and S-isomeric products depends on the nature of the electrophilic agent and on whether the reaction is carried out under conditions of kinetic or thermodynamic control. As a rule, the rate of S addition is higher, and reactions such as protonation and alkylation proceed primarily at the sulfur atom [2]. It is also known that N-acylated products are formed in the reactions of thioamides with acylating agents, although one cannot exclude the possibility that this takes place through kinetically controlled S acylation [2].

It has been previously shown [3, 4] that the reactions of the N-methylquinoxalinium cation (I) with thioamides proceed with the participation of both reaction centers (N and S) and lead to cyclic adducts, viz., thiazolo[4,5-b]quinoxalines; however, the regioorientation of the thiazole ring in the cyclization products may differ and depends on the reaction conditions. Structure II was assigned to the kinetic product of the reaction of cation I with thioacetamide on the basis of the ^1H and ^{13}C NMR spectra [3], whereas regioisomeric thiazolo[4,5-b]quinoxaline III and pyrrolo[2,3-b]quinoxaline-2-thione IV are formed under conditions of thermodynamic control [4].



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*See [1] for communication 18.

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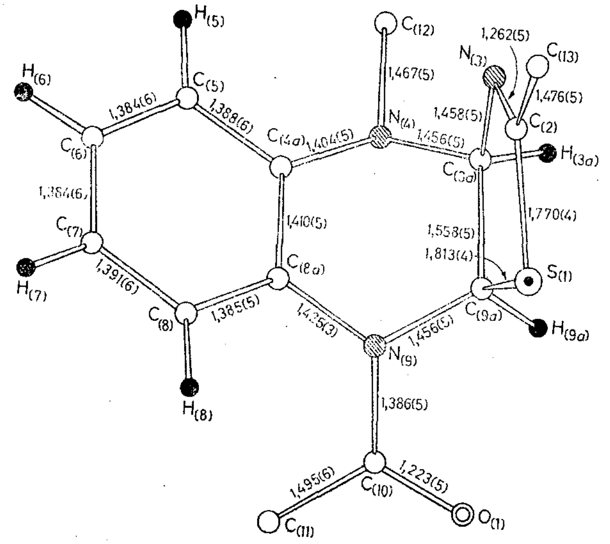

Fig. 1. Structure of the 2,4-dimethyl-9-acetyl-3*a*,4,9,9*a*-tetrahydrothiazolo[4,5-b]quinoxaline molecule.

TABLE 1. Bond Angles (ω, deg) of IIa

Angle	ω	Angle	ω	Angle	ω
$C_{(2)}S_{(1)}C_{(9a)}$	91,1 (2)	$N_{(3)}C_{(2)}C_{(13)}$	125,4 (4)	$C_{(7)}C_{(8)}C_{(8a)}$	119,5 (4)
$C_{(2)}N_{(3)}C_{(3a)}$	114,1 (3)	$N_{(3)}C_{(3a)}N_{(4)}$	111,8 (3)	$C_{(4a)}C_{(8a)}N_{(9)}$	116,0 (3)
$C_{(3a)}N_{(4)}C_{(4a)}$	114,1 (3)	$N_{(3)}C_{(3a)}C_{(9a)}$	111,1 (3)	$N_{(9)}C_{(8a)}C_{(8)}$	123,1 (3)
$C_{(3a)}N_{(4)}C_{(12)}$	113,0 (3)	$N_{(4)}C_{(3a)}C_{(9a)}$	110,5 (3)	$C_{(4a)}C_{(8a)}C_{(8)}$	120,9 (3)
$C_{(4a)}N_{(4)}C_{(12)}$	117,5 (3)	$N_{(4)}C_{(4a)}C_{(5)}$	125,4 (3)	$S_{(1)}C_{(9a)}N_{(9)}$	112,6 (3)
$C_{(8a)}N_{(9)}C_{(9a)}$	116,9 (3)	$N_{(4)}C_{(4a)}C_{(8a)}$	116,4 (3)	$S_{(1)}C_{(9a)}C_{(3a)}$	105,1 (3)
$C_{(8a)}N_{(9)}C_{(10)}$	126,0 (3)	$C_{(5)}C_{(4a)}C_{(8a)}$	118,2 (3)	$N_{(9)}C_{(9a)}C_{(3a)}$	113,1 (3)
$C_{(9a)}N_{(9)}C_{(10)}$	117,1 (3)	$C_{(4a)}C_{(5)}C_{(6)}$	120,8 (4)	$O_{(1)}C_{(10)}N_{(9)}$	119,9 (3)
$S_{(1)}C_{(2)}N_{(3)}$	117,3 (3)	$C_{(5)}C_{(6)}C_{(7)}$	120,5 (4)	$O_{(1)}C_{(10)}C_{(11)}$	120,9 (4)
$S_{(1)}C_{(2)}C_{(13)}$	117,3 (3)	$C_{(6)}C_{(7)}C_{(8)}$	119,9 (4)	$N_{(9)}C_{(10)}C_{(11)}$	119,3 (3)

Considering the unusual orientation of the thiazole ring in kinetic product II, which suggests N addition of thioacetamide in the first step of the reaction, as well as the necessity for the identification of the structure of one of the regioisomers for the unambiguous assignment of the signals in the ^{13}C NMR spectra of II and III, we carried out an x-ray diffraction study of thiazolo[4,5-b]quinoxaline II, which was obtained in the form of N-acetyl derivative IIa.

The geometry of the IIa molecule (without the hydrogen atoms of the methyl groups), the numbering of the atoms, and the principal bond lengths are shown in Fig. 1, and the bond angles are presented in Table 1.

The tetrahydropyrazine ring in thiazolo[4,5-b]quinoxaline IIa has a twisted boat conformation: the $C_{(3a)}$ and $C_{(9a)}$ atoms deviate 1.001(4) Å and 0.857(4) Å, respectively, from the plane of the remaining four atoms of the ring, which is realized with an accuracy of 0.007(4) Å. The existence of the tetrahydropyrazine ring in a boat conformation was previously found for furo[2,3-b]quinoxalines [5] and is evidently a characteristic feature of the three-dimensional structure of tetrahydroquinoxalines condensed with five-membered heterorings. The Cramer–Pople parameters for this ring, modified in conformity with the results in [6], have the following values: Q = 0.758 Å, θ = 99.23°, ψ = 98.24°, and σ = 0.87°. The $N_{(4)}$ atom has a pyramidal configuration of the bonds (the sum of the bond angles is 334.6°) and actually lies in the plane of the benzene ring, deviating 0.023(3) Å from it, whereas the $N_{(9)}$ atom has a planar configuration and deviates 0.101(3) Å from the plane of the benzene ring. The different deviations of the nitrogen atoms from the plane of the benzene ring and the unequal lengths of the $N_{(4)}$–$C_{(4a)}$ and $N_{(9)}$–$C_{(8a)}$ bonds [1.405(5) and 1.425(5) Å] constitute evidence for the participation of the unshared electron pair of the $N_{(4)}$ atom in conjugation with the π system of the

TABLE 2. Coordinates ($\cdot 10^4$) of the Nonhydrogen Atoms and Their Equivalent Isotropic Temperature Factors (Å^2) $B^{eq}_{iso} = \frac{1}{3}\sum_{ij} B_{ij} a^*_i a^*_j (\bar{a}_i \bar{a}_j)$ for IIa

Atom	x	y	z	B^{eq}_{iso}	Atom	x	y	z	B^{eq}_{iso}
$S_{(1)}$	1112(1)	1428(1)	7433(1)	4,52(3)	$C_{(6)}$	−4848(4)	3165(4)	6819(3)	4,1(1)
$O_{(1)}$	−696(3)	−1119(3)	5762(2)	4,08(9)	$C_{(7)}$	−4580(4)	1921(4)	7247(3)	3,8(1)
$N_{(3)}$	255(3)	3791(3)	6770(2)	3,32(9)	$C_{(8)}$	−3479(4)	1122(4)	7076(3)	3,2(1)
$N_{(4)}$	−1964(3)	3244(3)	5495(2)	3,30(9)	$C_{(8a)}$	−2677(4)	1571(3	6462(3)	2,7(1)
$N_{(9)}$	−1588(3)	788(3)	6205(2)	2,93(9)	$C_{(9a)}$	−207(4)	1445(4)	6225(3)	3,4(1)
$C_{(2)}$	1007(4)	3177(4)	7518(3)	3,1(1)	$C_{(10)}$	−1749(4)	−521(4)	5894(3)	3,2(1)
$C_{(3a)}$	−410(4)	2938(4)	5933(3)	3,3(1)	$C_{(11)}$	−3214(5)	−1186(4)	5730(3)	4,3(1)
$C_{(4a)}$	−2881(4)	2866(4)	6071(3)	3,0(1)	$C_{(12)}$	−2203(5)	4561(5)	5038(3)	4,8(1)
$C_{(5)}$	−3984(4)	3644(4)	6256(3)	3,8(1)	$C_{(13)}$	1826(5)	3797(4)	8455(3)	4,3(1)

TABLE 3. Coordinates ($\cdot 10^3$) of the Hydrogen Atoms of IIa

Atom	x	y	z	Atom	x	y	z
$H_{(3a)}$	10(5)	307(4)	538(3)	$H_{(11,3)}$	−314(4)	−177(4)	641(3)
$H_{(5)}$	−420(4)	453(4)	598(3)	$H_{(12,1)}$	−319(4)	464(4)	462(3)
$H_{(6)}$	−565(4)	369(4)	691(3)	$H_{(12,2)}$	−192(4)	526(4)	556(3)
$H_{(7)}$	−513(5)	161(4)	769(3)	$H_{(12,3)}$	−146(4)	463(4)	461(3)
$H_{(8)}$	−318(4)	23(4)	750(3)	$H_{(13,1)}$	275(4)	364(4)	860(3)
$H_{(9a)}$	23(4)	103(4)	573(3)	$H_{(13,2)}$	165(4)	474(4)	846(3)
$H_{(11,1)}$	−407(4)	−59(4)	555(3)	$H_{(13,3)}$	162(4)	340(4)	903(3)
$H_{(11,2)}$	−340(4)	−180(4)	517(3)				

benzene ring and for the absence of such conjugation for the acetylated $N_{(9)}$ atom. Interaction of the unshared pair of electrons of the $N_{(9)}$ atom with the $C_{(10)}=O_{(4)}$ group leads to a square-trigonal configuration of the bonds of this atom. The absence of conjugation along the $N_{(9)}-C_{(8a)}$ bond is also confirmed by the substantial deviation of the acetyl group $[O_{(1)}C_{(10)}-C_{(11)}]$, which includes the $N_{(9)}$ atom, from the plane of the benzene ring. The dihedral angle between these planes is 49.4°. This rotation of the acetyl group also promotes a decrease in the steric strain in the molecule due to the short intramolecular $C_{(8)} \ldots C_{(11)}$ contact of 3.068(6) Å. This sort of nonequivalence of the nitrogen atoms is characteristic for tetrahydroquinoxalines in which one of the nitrogen atoms participates in conjugation with the double bond of the substituent [5, 7, 8]. If both nitrogen atoms have alkyl substituents, the $N-C(sp^2)$ bonds become equal [9]. The differences between the $N_{(4)}$ and $N_{(9)}$ atoms in the IIa molecule do not, however, affect the lengths of the $N-C(sp^3)$ bonds, which are equal to one another [1.456(5) Å].

The thiazoline ring in the IIa molecule has an envelope conformation with a deviation of the $C_{(9a)}$ atom of 0.198(4) Å from the plane of the remaining four atoms of the ring, which is realized with an accuracy of 0.003(3) Å. The rms planes of the thiazoline ring and the quinoxaline system form a dihedral angle of 90.8° with one another. The geometrical parameters of 4,5-dihydrothiazoles were examined in [10, 11] but primarily in the case of 2-aminothiazoline derivatives. The presence of a methyl group in the 2 position in thiazolo[4,5-b]quinoxaline IIa leads to certain changes in the geometry of the thiazoline ring as compared with the geometry presented in [10, 11]. Since conjugation of the π system of the $C_{(2)}=N_{(3)}$ bond with the substituent in the 2 position of the thiazoline ring is not possible in the IIa molecule, this double bond is localized in the ring, and its length [1.262(5) Å] is the shortest of the $C_{(2)}=N_{(3)}$ bond lengths presented in [10, 11]. The increase in the $C_{(3a)}-C_{(9a)}$ bond length to 1.558(5) Å (the maximum value of the length of this bond presented in [10] is 1.549 Å) is evidently due to its simultaneous incorporation in two heterorings. The remaining bond lengths and bond angles in the IIa molecule have the normal values. Short intermolecular contacts are not observed in the structure.

The x-ray diffraction study made it possible to unambiguously establish the structure of the kinetic product of the reaction of the I cation with thioacetamide and confirmed the conclusions drawn on the basis of the ^1H and ^{13}C NMR spectra.* In particular, the conclusion re-

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*We analyzed the ^1H and ^{13}C NMR spectra of regioisomeric thiazolo[4,5-b]quinoxalines in [12].

garding the cis orientation of the nodal 3*a*-H and 9*a*-H atoms in the case of fusion of five-membered heterorings with the tetrahydroquinoxaline framework (Fig. 1), which was drawn on the basis of the vicinal $^3J_{3a,9a}$ spin-spin coupling constants (SSCC) [12], was confirmed.

EXPERIMENTAL

2,4-Dimethyl-9-acetyl-3*a*,4,9,9*a*-tetrahydrothiazolo[4,5-b]quinoxaline (IIa) was synthesized by the method in [3]. Crystals of IIa, obtained by recrystallization from acetone in the form of clear colorless plates, were monoclinic and had the following parameters at 20°C: a = 9.448(1), b = 10.074(1), c = 14.233(2) Å, β = 106.562(8)°, d_{calc} = 1.33 g/cm³, z = 4, and space group $P2_1/n$. The cell parameters and intensities of 1741 independent reflections, 1498 of which with $I \geqslant 2\sigma$, were used in the decoding and refining of the structure; the measurements were made with a Hilger-Watts automatic four-circle diffractometer ($\lambda_{Cu\ K_\alpha}$, graphite monochromator, θ/2θ scanning, $\theta \leqslant 66°$). The structure was decoded by the direct method by means of the MULTAN program and was refined by the total-matrix method of least squares within the anisotropic approximation for all of the nonhydrogen atoms. All of the hydrogen atoms, which were included in the refinement with fixed B_{iso} = 6 Å², were revealed from a differential series. The final divergence factors were as follows: R = 0.053 and R_W = 0.056. All of the calculations were made with an Eklips S/200 computer by means of the INEXTL program [13].

The coordinates of the nonhydrogen atoms are presented in Table 2, and the coordinates of the hydrogen atoms are presented in Table 3.

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