SYNTHESIS OF PYRIDO[2,3-b]QUINOXALINE DERIVATIVES

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Studies on the series of 4-oxo-1,4-dihydroquinoline-3-carboxylic acid derivatives led to the preparation of highly active antibacterial preparations with a wide spectrum of activity, e.g. oxolinic acid, norfloxacin, cyprofloxacin, etc. [1]. In recent years, in the search for new analogs of oxolinic acid, studies in the field of the synthesis of bi- and tricyclic systems, in which the key fragment of the oxolinic acid, 1-alkyl-4-oxo-1,4-dihydro-3-carboxypyridine, is condensed with other heterocycles, have been greatly developed. Among the compounds synthesized, compounds were discovered with a high antibacterial activity, and some of these have been introduced in the medical practice [1].

We contemplated a synthesis of tri- and tetracyclic analogs of oxolinic acid, which are derivatives of pyrido[2,4-b]quinoxaline. To carry out these syntheses, we chose a scheme, which has already been successfully used for the preparation of analogs of oxolinic acid in the series of quinoline derivatives [2, 6]. The key compound in the scheme selected was the ethyl ester of (3-chloro-2-quinoxaloyl)acetic acid (I). This compound was obtained by the reaction of 3-chloroquinozaline-2-carboxylic acid (II) with $SOCl_2$, condensation of the acid chloride (III) formed with Na-malonic ester, and monodecarbethoxylation of the diethyl ester of (3-chloro-2-quinaxoloyl)malonic acid (IV) obtained.

In the synthesis of cyprofloxacin the monodecarbethoxylation reaction was carried out by heating the diethyl ester of 2,4-dichloro-5-fluorobenzoylmalonic acid in a toluenesulfonic acid–water mixture. When a similar reaction was carried out with compound IV under the conditions of patent [2], and also with different variations in temperature and the ratio between the reagents, the yield of I was negligible, and there was intense resinification of the reaction mixture. Compound I was obtained by heating IV in a saturated aqueous solution of NaCl. To obtain a tetracyclic analog of oxolinic acid, 4-oxo-1,4-dihydro-3-carboxy-1,2-trimethylenepyrido[2,3-b]quinoxaline (V), compound I was reacted with O-methylbutyrolactim (VI) in a dimethyl sulfoxide medium. Thus the expected enamino ester (VII) was obtained, and its structure was confirmed by elemental and spectral analyses. The reaction of VII with NaH was accompanied by a closure of the pyridine ring with the formation of ester VIII. After hydrolysis of its carbethoxy group, ester VIII gave an analog of oxolinic acid V.

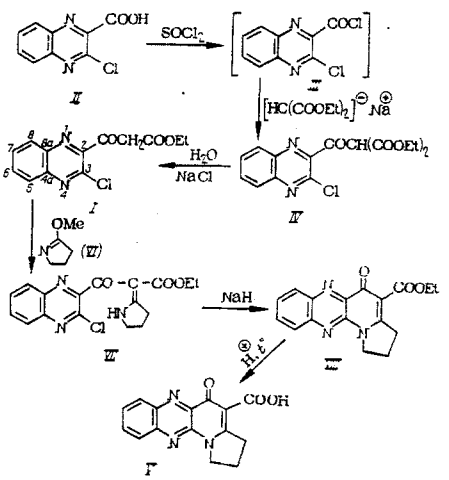

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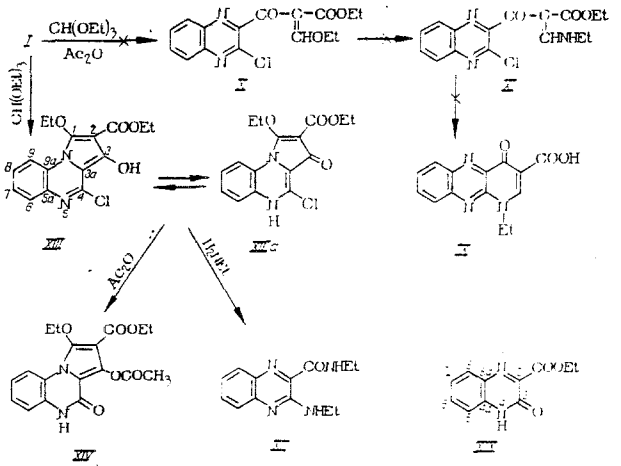
TABLE 1. Data of ^1H NMR Spectra of Compounds I, XIII, XIV

Compound	δ, ppm			
	$\overset{O}{\overset{\|}{C}}-OC_2H_5$	OC_2H_5	aromatic protons	NH or OH
I	1,22 (CH_3)	—	7,97 (m,2 p.u.)	—
	4,18 (CH_2)	—	8,14 (m,2 p.u.)	
in $CDCl_3$				
XIII	1,46* (CH_3)	1,54* (CH_3)	7,35 (m,2 p.u.)	
	4,40 (CH_2)	4,48 (CH_2)	7,40 (d 1 p.u.)	9,20
in $CDCl_3$			8,38 (d, 1 p.u.)	
	1,36 (CH_3)	1,46 (CH_3)	7,40—7,60 (m,3 p.u.)	9,44
in D-$DMSO_4$	4,37 (CH_2)	4,41 (CH_2)	8,44 (d, 1 p.u.)	
XIV	1,29* (CH_3)	1,46* (CH_3)	7,28 (m, 3 p.u.)	11,20
	4,24 (CH_2)	4,42 (CH_2)	8,42 (d, 1 p.u.)	
in D-DMSO				

*For the $COOCH_2CH_3$ and OCH_2CH_3 groups in compounds XIII and XIV, the signals can be assigned in the reverse way.

Note. Compound I: δ 4.28 ppm: $\left(\begin{matrix}O & O\\ \| & \|\\ CCH_2C\end{matrix}\right)$. Compound XIX: δ 2.29 ppm $\left(\begin{matrix}O\\ \|\\ OCCH_3\end{matrix}\right)$.

To synthesize a tricyclic analog of oxolinic acid, in particular, 1-ethyl-4-oxo-1,4-dihydro-3-carboxypyrido[2,3-b]quinoxaline (IX) by this scheme, we had to obtain from I the α-ethoxymethylene derivative (X) and from it the ethylaminomethylene derivative (XI), and to convert XI by the above reactions into acid IX. In an attempt to synthesize compound X by the condensation of I with orthoformic ester in the presence of Ac_2O (at 65-70°C), two compounds were formed: the main reaction product (XIII) containing chlorine, and, as an inappreciable admixture, compound XIV, which does not contain chlorine. The amount of compound XIV increased with increase in temperature, and at 100-105°C it became the main reaction product. Further investigations showed that compound XIII can be obtained without the participation of Ac_2O by heating I with orthoformic ester at a higher temperature (100-105°C), when compound XIV is not formed under these conditions. In turn, compound XIV was obtained by heating XIII with Ac_2O. Thus, the sequence of reaction I→XIII→XIV has been confirmed.



The data of elemental analysis and the mass of the molecular ion of compound XIII conformed with structure X, but the chemical properties of compound XIII did not correspond to structure X, and also differed from the properties of α-ethoxymethylene derivative 2,4-dichloro-5-fluorobenzoylacetic ester already described [2]. Compound XIII dissolved in a dilute aqueous solution of NaOH, and after prolonged standing of the alkaline solution, it could be isolated on acidification in an unchanged state. It did not react with ethylamine under the conditions described in [2], but in methylene chloride or acetonitrile, it slowly reacted with ethylamine to form not the expected aminomethylene derivative XI, but a compound, which, ac-

TABLE 2. Data of ^{13}C NMR Spectra of Compounds XIII and XIV

Compound	δ, ppm																
	$C_{(1)}$	$C_{(2)}$	$C_{(3)}$	$C_{(3a)}$	$C_{(4)}$	$C^{*}_{(5a)}$	$C^{*}_{(6)}$	$C_{(7)}$	$C_{(8)}$	$C^{*}_{(9)}$	$C^{*}_{(9a)}$	$\overset{O}{\overset{\|\|}{C}}OC_2H_5$	$\overset{O}{\overset{\|\|}{C}}OC_2H_5$	OC_2H_5	$\overset{O}{\overset{\|\|}{C}}OCH_3$	$\overset{O}{\overset{\|\|}{C}}OCH_3$	solvent
XIII	143,0**	93,4	143,8	102,0	144,4*	136,3	128,5	127,1	126,4	116,7	126,1	14,1 (CH_3) 61,1 (CH_2)	165,7	15,1 (CH_3) 72,8 (CH_2)	—	—	$CDCl_3$
XIV***	145,0	98,5	135,7	106,7*4*	153,4*4*	129,2	116,4	122,5	126,4	117,2	121,5	13,6 (CH_3) 59,7 (CH_2)	160,7	14,6 (CH_3) 72,5 (CH_2)	20,1	167,9	D-DMCO

*In the spectra of XIII and XIV, the SSC constant for $C_{(5a)}$, $C_{(6)}$, $C_{(9)}$ and $C_{(9a)}$ with the ortho protons of the benzene ring is $J_{C,H} \sim 4.5$ Hz, and with the meta protons it is ~7-8 Hz.

**Under the conditions of running the spectrum of XIII without the suppression of protons, the signal at 144.4 ppm remains narrow, while at 143.0 ppm it is slightly broadened; the assignment of these signals to $C_{(4)}$ and $C_{(1)}$, respectively, is based on this fact.

***Temperature of running the spectrum of compound XIV 65°C.

4*Under the conditions of running the spectrum of XIV, without the suppression of protons, the $C_{(9a)}$, is evident in the form of a low-intensity broadened multiplet signal due to the SSC with $N_{(5)}H$, and $C_{(4)}$ in the form of an intense narrow signal (no reaction with $N_{(5)}$).

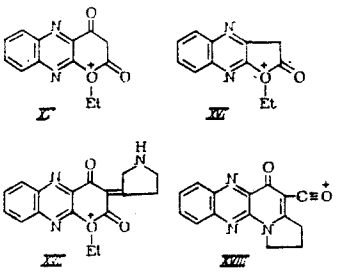
cording to the elemental analysis, IR and mass spectral data, had a structure that corresponded to 2-ethylamino-3-(ethylcarboxamido)quinoxaline (XII).

Because of the characteristic features of the chemical behavior of compound XIII, we examined its ^1H, ^{13}C NMR and mass spectra in detail. The spectral investigation showed that compound XIII is not a derivative of quinoxaline X, but, most probably, has a tricyclic structure, and is 1-ethoxy-2-carbethoxy-3-hydroxy-4-chloropyrrolo[1,2-a]quinoxaline XIII or its tautomer (XIIIa). In the ^1H NMR spectrum of compound XIII (Table 1) there was no signal of the vinyl group -CH=C- proton, characteristic of structure X, but a broadened signal of an OH or NH group proton was observed at 9.2-9.4 ppm. An appreciable difference was also observed in the positions of the signals of the benzene ring protons in the spectra of the quinoxaline derivative I and compound XIII. In the spectrum of I, the signals of the aromatic protons appeared in the form of two multiplets with centers at 7.91 and 8.14 ppm (2 p. u. each), while in the spectrum of XIII, there was a weakfield shift of one of the ring protons into the 8.38-8.44 ppm region that appeared in the form of a doublet with split components. The signals of the remaining aromatic protons were present in the 7.4-7.6 ppm region (3 p.u.) in the form of a multiplet. The weak field shift of a signal of one of the aromatic protons may indicate a change in the structure of the heterocyclic fragment of the molecule. In accordance with the proposed structure (XIII or XIIIa) the weak-field signal was assigned to the $H_{(9)}$ proton. Its descreening was probably determined by the influence of the ethoxy group, present at $C_{(1)}$. A similar weak-field shift of the $H_{(9)}$ signal had already been observed in the ^1H NMR spectrum of pyrrolo[1,2-a]quinoxaline derivatives when chlorine or bromine were introduced into the 1-position of the ring [4]. The data of the ^{13}C NMR spectrum (Table 2) also corresponded to structure XIII. In this spectrum, the signal of the vinyl carbon, directly bound to the hydrogen atom, was missing, while signals of 8 quaternary carbon atoms appeared (instead of 7 characteristic of structure X). Four signals of the carbon atoms of the benzene fragment of the molecule directly bound to the hydrogen atoms appeared at 128.5, 127.1, 126.4 and 116.7 ppm, and the signal of one of the carbon atoms (δ 116.7 ppm) underwent an appreciable strong-field shift ($\Delta\delta\sim$10-12 ppm) in comparison with the case of signals of the remaining three carbon atoms. It should be noted that in the spectrum of the quinoxaline derivative I, all the four signals of the benzene ring carbon atoms are present in the 128-133.2 ppm region (see experimental part). The signal at 116.7 ppm in the spectrum of XIII could be related to the $C_{(9)}$ carbon atom, subjected to both the so-called "steric compression effect" due to the approach of the $C_{(9)}$ H to the ethoxy group at $C_{(1)}$ (which conformed with the descreening of the $H_{(9)}$ proton in the ^1H NMR spectrum). The same effect explains a strong field shift of the signal of the bridging $C_{(9)}$ carbon (by 10 ppm, compared with the $C_{(5a)}$ signal in the same compound and by $\sim$13 ppm with respect to the bridging $C_{(8a)}$ carbon atom of compound I).* The quaternary signals were assigned to the $C_{(9a)}$ and $C_{(5a)}$ carbon atoms according to their multiplicity in a spectrum run without suppression of protons. The two signals appear in the form of quartets due to the spin-spin coupling (SSC) with benzene ring protons (see Table 2). Under the same conditions of running the spectrum, the signals of the quaternary $C_{(3a)}$, $C_{(3)}$ and $C_{(2)}$ atoms appeared in the form of a doublet, which can be related to the SSC with the OH group protons [^3J ($C_{(3a)}$, OH) 7.5 Hz, ^2J (C_3, OH) 5.0 Hz and ^3J (C_2, OH) 3.6 Hz]. This was confirmed when the spectrum of compound XIII was run in a mixture of $CDCl_3$+CD_3OD. Under these conditions the hydrogen of the OH group was substituted by deuterium and the splitting of the $C_{(3a)}$, $C_{(3)}$ and $C_{(2)}$ signals disappeared, while the multiplicity of signals of other carbon atoms was retained. The above data confirmed the presence of a hydroxyl group at $C_{(3)}$, which indicated the existence of this compound preferentially in the hydroxy form XIII.

The data on the comparison of the mass spectra of XIII and the quinoxaline derivatives (I and VII) agreed with the information obtained from the NMR spectra. The molecule of I is slightly stable to electron impact, M^+ 278 (8).† According to the DADI spectra, one of the paths of fragmentation of I was the elimination of a chlorine atom with the formation of a stable ion, probably the cyclic structure XV, 243 (90). The structure of ion XV was confirmed by further elimination of the CO fragment with the formation of ion XVI, 215 (24), which is not very probable for a linear structure.

*For compound I, the difference in the values of the chemical shifts of the bridging $C_{(4a)}$ and $C_{(8a)}$ carbon atoms did not exceed 3 ppm.

†Here and below, the m/z values are given for ions, and the intensity of ions is given in brackets (in % with respect to the maximal); for the chlorine-containing ions the mass of Cl is taken as 35.



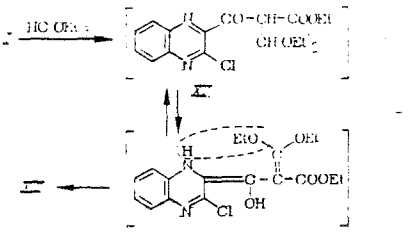
Another path of fragmentation of I was a successive rupture of bonds in the side chain: $(M - OC_2H_5)^+$ 233 (20), $(233 - CH_2CO)^+$ 191 (33) and $(191 - CO)^+$ 163 (100). The character of the fragmentation of VII was close to that in the case of compound I. Thus M^+ of compound VII has a peak with m/z 345 (15); the maximally intense peak $(M - Cl)^+$ 310 belonged to an ion with a cyclic structure XVII, from which ion $(M - Cl - CO)^+$ 282 (11), similar to ion XVI, was formed by elimination of CO. There was also a rupture in the side-chain bonds $(M - OC_2H_5)^+$ 300 (8) followed by the elimination of HCl and the formation of another stable ion (XVIII) 264 (37).

In contrast to the spectra of I and VII, in the mass spectrum of XIII there appears a fairly intense peak on a molecular ion M^+ 334 (32), and there was no elimination of chlorine during the primary decomposition events. One positive hydrogen ion was detected in the molecule, since when a CD_3OD sample was treated in a direct introduction system, there was an 1 amu shift of M^+ in the mass spectrum; the tracer disappeared during the first decomposition event, namely, the elimination of C_2H_5OH. This confirmed the decomposition of the hydroxy form of compound XIII. According to the DADI spectra, the fragmentation of compound XIII also corresponded to its structure. The fragmentation proceeded as follows: $(M - OC_2H_5)^+$, 289 (5), $(M - HOC_2H_5)^*$ 288 (8), $(M - C_2H_5)^+$ 305 (10), $(305 - HOC_2H_5)^+$ 259 (100), $(259 - OC - C - CO)^+$ 191 (86), $(191 - CO)^+$ 163 (97). According to the value of the molecular ion and the data of elemental analysis, compound XIV, which was obtained in the reaction of XIII with Ac_2O, corresponded to the derivative of compound XIII, in which chlorine was replaced by an acetoxy group. The ^1H NMR spectrum of compound XIV was close to the spectrum of XIII (see Table 1). The same was also true of its mass spectrum. The fragmentation of compound XIV differed from that of compound XIII, mainly in the low stability of the molecular ion, due to the presence of an acetal group. After it split, a fragment formed that, as in XIII, was fairly stable to electron impact (see experimental part). Compound XIV can have several isomeric structures, the most probable being structure XIV, that is 1-ethoxy-2-carbethoxy-3-acetoxy-4-oxo-4,5-dihydro- pyrrolo[1,2-a]quinoxaline. This conclusion was drawn from the spectral data. The possible existence of a tautomeric form with a keto group at the 3-position, as in XIIIa, was excluded, since in the ^{13}C NMR spectrum there was no signal of the ketonic C=O carbon (in the 190-200 ppm region, see Table 2). The presence of an amide fragment -NH-C=O was proved by comparing the ^{13}C NMR spectra of compounds XIII, XIV, and the model quinoxaline derivative, 3-oxo-3,4-dihydro-2-carbethoxy-quinoxaline (XIX). In the spectrum of XIV, as in that of XIII, in the weak field region there are signals of four aromatic carbon atoms directly bound to the hydrogen atoms. This part of the spectrum of compound XIV, however, differed from that of the spectrum of XIII. In the former shifts of two carbon atoms (116.4 and 117.2 ppm., see Table 2) into a stronger field were observed. One of these, in analogy with the spectrum of XIII, was assigned to $C_{(9)}$ and the other to $C_{(6)}$. The shift of the signal of this carbon atom into the stronger field is explained by the influence of the NH-C=O fragment, as observed in the spectrum of compound XIX for $C_{(5)}$ ($\delta C_{(5)}$, $C_{(6)}$, $C_{(7)}$ and $C_{(8)}$ 115.7, 123.8, 129.0, and 132.0, respectively). It should also be noted that the chemical shifts of amide carbon signals in compounds XIV and XIX are also similar (153.4 and 152.2 ppm). The structure of XIV was confirmed by mass spectral and ^1H NMR data. In the ^1H NMR spectrum a broadened signal at 11.2 ppm was observed, which indicated the presence of a labile hydrogen atom in the molecule, which, according to mass spectrum data, is retained even during extensive decomposition.

A pyrrolo[1,2-a]quinoxaline and some of its derivatives are described in the literature. They are synthesized by closing the quinoxaline ring, starting from pyrrole derivatives [5], or from quinoxaline derivatives [4]. In the preparation of pyrrolo[1,2-a]quinoxalines from the quinoixaline derivatives by known methods, the main condition is the presence of a methyl or an active methylene group at the α-position to the cyclic nitrogen atom. Therefore, the formation of pyrrolo[1,2-a]quinoxaline from quinoxaline substituted by a $COCH_2COOC_2H_5$ group at the α-position was somewhat unexpected, and the mechanism of this reaction requires special investigation. It is, however, known that when orthoformic ester reacts with compounds con-

taining an active methylene group, an intermediate diethylacetal can be formed, from which the corresponding ethoxymethylene derivative is usually formed by splitting ethanol [3]. If we take these data into account, we can assume that one of the possible variants of the transformation of I into XIII is the formation of an intermediate diethylacrtal XX in this reaction. The acetal undergoes tautomeric prototropic transformations of the triad and pentade types, with a proton transfer to the cyclic nitrogen atom, followed by splitting of an alcohol molecule.

This supposition agrees with the fact that in the absence of possible protropic transformations, as in the case of the reaction of I with O-methylbutyrolactim VI, the reaction proceeds "normally" with the formation of compound VII.



In experiments in vitro, compound V had a low activity (62.5 μg/ml) toward to Staphylococcus. The derivatives of pyrrolo[1,2-a]quinoxaline did not exhibit any noticeable antibacterial activity.

EXPERIMENTAL

The ^1H and ^{13}C NMR spectra were recorded on XL-200 and XL-200 spectrometers (Varian, Switzerland). The mass spectra were obtained on MAT-112 chromato-mass spectrometer ("Varian", GFR) with direct introduction of the sample into the ionic source. Energy of ionizing electron, 70 eV. Temperature of the ionization chamber, 180°C. The IR spectra were run on a Perkin-Elmer 457 spectrophotometer (Switzerland) in mineral oil. The chromatography was carried out on Silufol-254 plates (CSSR) in a benzene-ethanol (99:1) system of solvents. The melting points were determined on a PTP-1 apparatus at a rate of heating near the melting point of 1-3°C per min.

Diethyl Ester of (3-Chloro-2-quinoxaloyl)malonic Acid (IV). A 145 ml portion of $SOCl_2$ is added to 12.6 g (60.4 mmoles) of II. The mixture is boiled for 4 h, and $SOCl_2$ is distilled off. The solution of acid chloride (III) obtained in 150 ml of dry toluene is added gradually and with stirring at 10°C to a Namalonic ester [prepared from 19.44 g (151.7 mmoles) of malonic ester and 2.76 g (120 mmoles) of sodium] in 90 ml of toluene, and the mixture is stirred for 1 h at 15-20°C and 15-20 h at 5°C. The precipitate is filtered, washed with toluene and ether, and dissolved in water. The solution is treated with CH_2Cl_2 and the aqueous layer is acidified with HCl. The mixture obtained is extracted by CH_2Cl_2. The solvent is evaporated, and 13 ml of a 4:1 alcohol–water mixture are added to the residue. The mixture is held at 5°C for 1 h and is separated to yield 11.88 g (56.1%) of IV, mp 63-64°C (from a 4:1 alcohol–water mixture). Found, %: C 54.79; H 4.76; Cl 10.28; N 8.50. $C_{16}H_{15}ClN_2O_5$. Calculated %: C 54.78; H 4.31; Cl 10.11; N 7.99.

Ethyl Ester of (3-Chloro-2-quinoxaloyl)acetic Acid (I). A 5 g portion of IV in 50 ml of a saturated aqueous solution of NaCl is stirred at 90-95°C for 1 h 45 min. The mixture is then cooled and, after adding 20 ml of water, is extracted by CH_2Cl_2. After the evaporation of solvent, 3 ml of a 9:1 methanol–water mixture are added to the residue, and the precipitate obtained is filtered to yield 2.62 g (66.2%) of I, mp 53-55°C (from methanol). R_f 0.41. Found, %: C 56.62; H 3.97; N 10.04. $C_{13}H_{11}ClN_2OC$. Calculated, %: 56.02; H 3.98; N 10.05. IR spectrum, ν, cm^{-1}: 1708 and 1738 (the CO group in $COCH_2$ and $COOC_2H_5$). ^{13}C NMR spectrum (in $CDCl_3$), δ, ppm: 167.1 ($COOC_2H_5$), 61.3 and 13.9 ($COOCH_2CH_3$), 191.8 ($COCH_2$), 46.2 ($COCH_2$), 144.9 ($C_{(2)}$), 144.1 ($C_{(3)}$), 130.9-133.2 ($C_{(5)}$, $C_{(6)}$, 128.0-129.5 ($C_{(7)}$, $C_{(8)}$), 142.4 ($C_{(4a)}$) ($C_{(4a)}$), 138.9 ($C_{(8a)}$). The $C_{(4a)}$ and $C_{(8a)}$ signals can be assigned in a reverse way. Under the conditions of running the spectrum without suppression of protons, the signals of these atoms appear in the form of quartets due to SSC with meta-protons of the benzene ring.

Ethyl Ester of (3-Chloro-2-quinoxaloyl)-α-(2-pyrrolididene)-acetic Acid (VII). A mixture of 0.42 g (1.5 mmole) of VI and 0.7 ml of dimethyl sulfoxide is left to stand for two and a half days at 20°C. A 2 ml portion of water is added, and the mixture is held at 5°C for 15 h, and then is filtered to yield 0.39 g (75%) of VII, mp 134-136°C (from methanol). Found, %:

C 58.98; H 4.40; Cl 10.08; N 11.93. $C_{17}H_{16}ClN_3O_3$. Calculated, %: C 59.05; H 4.66; Cl 10.25; N 12.15.

1,2-Trimethylene-4-oxo-1,4-dihydro-3-carbethoxypyrido[2,3-b]-quinoxaline (VIII). Sodium hydride NaH (0.17 g, 7.1 mmoles) is added in small portions at 15-20°C, with stirring, to a solution of 0.96 g (2.8 mmoles) of VII in 8.5 ml of dry toluene, while the temperature is maintained at 20°C; the mixture is stirred at this temperature for another 2 h, and then is poured into 35 ml of 1 N HCl. The mixture is neutralized with an aqueous ammonia solution and filtered to yield 0.6 g (70%) of VIII, mp 295-297°C (dec., from n-butanol). Found, %: 66.35; H 5.01; N 13.83. $C_{17}H_{15}N_3O_3$. Calculated, %: C 66.01; H 4.89; N 13.58. IR spectrum, ν_{max}, cm^{-1}: 1640, 1690 (amide and carbethoxy CO). Mass spectrum: M^+ 309.

1,2-Trimethylene-4-oxo-1,4-dihydro-3-carboxypyrido[2,3-b]-quinoxaline (V). A solution of 0.2 g (0.65 mmole) of VIII in 15 ml of 2.5 N HCl is boiled for 8 h, and then cooled and filtered. The precipitate is dissolved at the boiling point in $CHCl_3$, the solution is treated with activated charcoal, filtered, and $CHCl_3$ is distilled off to yield 0.17 g (93.5%) of V, mp 290-292°C (dec., from glacial AcOH). Found, %: C 63.94; H 4.14; N 15.40, $C_{15}H_{11}N_3O_3$. Calculated, %: C 64.05; H 3.94; N 14.94.

1-Ethoxy-2-carbethoxy-3-hydroxy-4-chloropyrrolo[1,2-a]quinoxaline (XIII). A mixture of 1.12 g (4 mmoles) of I, 1.21 g (12 mmoles) of Ac_2O and 1.14 g (8 mmoles) of orthoformic ester is stirred for 5 h at 65-67°C, then is cooled and filtered. The precipitate is treated with 25 ml of CH_2Cl_2 and filtered to yield 0.05 g (2.5%) of XIV. After the removal of solvent from the filtrate, 1.01 g (75.4%) of XIII is obtained, mp 169-170°C (dec., from ethyl acetate). Found, %: C 57.47; H 4.58; Cl 10.58; N 8.29. $C_{16}H_{15}ClN_2O_4$. Calculated, %: C 57.51; H 4.51; Cl 10.59; N 8.36. IR spectrum, ν_{max}, cm^{-1}: 1655 (CO) and 3100-3200 (OH assoc.).

B. A mixture of 0.3 g of I in 0.7 ml of orthoformic ester is heated for 3.5 at 100-105°C, then is cooled, the precipitate is filtered and washed with methanol. Yield, 0.3 g (83.3%) of a compound that was identical in all its parameters with compound XIII.

1-Ethoxy-2-carbethoxy-3-acetoxy-4-oxo-4,5-dihydropyrrolo[1,2-b] quinoxaline (XIV). A. A mixture of 0.28 g (1 mmole) of I, 0.28 g (2 mmoles) of orthoformic ester, and 0.3 g (3 mmoles) of Ac_2O is heated for 1 h at 100-105°C. It is then cooled, after adding 1 ml of methanol, left to stand for 24 h, at 5°C, and then filtered. The precipitate is stirred with 10 ml of CH_2Cl_2. and filtered again. Yield 0.22 g (61.39%) of XIV, R_f 0.09, mp 244-245°C (from n-butanol). Found, %: C 60.54; H 5.18; N 7.68. $C_{18}H_{18}N_2O_6$. Calculated, %: C 60.33; H 5.06; N 7.82. IR spectrum, ν_{max} cm^{-1}: 1768 and 1680 ($COCH_3$ and $COOC_2H_5$). Mass spectrum: M^+ 358 (5) (M^+ deuterated 359), $(M - COCH_2)^+$ 316 (90). Then, one path of fragmentation: $(316 - C_2H_5)^+$ 287 (7), $(287 - HOC_2H_5)^+$ 241 (43), $(287 - OC_2H_5)^+$ 242 (100), $(241 - OC = C = CO)^+$ 173 (52) $(173 - CO)^+$ 145 (33). The other path of fragmentation: $(316 - OC_2H_5)^+$ 271 (7), $(316 - HOC_2H_5)^+$ 270 (7).

B. A 0.2 g portion (0.6 mmole) of XII is heated in 0.65 ml of Ac_2O at 100-105°C, and then the mixture is cooled and of Ac_2O at 100-105°C, and then the mixture is cooled and filtered. Yield, 0.14 g of a compound, which with respect to melting point, IR spectrum and the R_f value, is identical with compound XIX described under A.

^1H NMR (D-DMFA) and ^{13}C (D-DMSO) NMR spectra of compound XIX were obtained by the method in [7]. ^1H NMR: 1.37 (t, CH_3CH_2) 4.43 (q, CH_3CH_2), 7.45, 7.85 (d, $H_{(5)}$, $H_{(8)}$), 7.4, 7.68 (t, $H_{(6)}H_{(7)}$), 12.72 (br. s., NH). ^{13}C NMR: 14.0 (CH_3CH_2O), 61.7 (CH_3CH_2O), 132.0, 129.0, 123.8 ($C_{(6)}$, $C_{(7)}$, $C_{(8)}$), 115.7 ($C_{(5)}$), (O-C=O, ^3J O-$COCH_2$ = 3.2 Hz), 130.6, 132.6 ($C_{(4a)}$, C(8a), 152.2 (C(3)), 150.4 (C(2)).

2-Ethylamino-3-(ethylcarboxamido)quinoxaline (XII). A 0.36 ml portion of a 35% solution of ethylamine (0.126 g, 2.8 mmoles) is added to a solution of 0.17 g (0.5 mmole) of XIII in 5 ml of CH_2Cl_2. The reaction mixture is held at 20°C to a complete disappearance of the spot of XIII on the chromatogram (R_f 0.27). After the completion of the reaction (5 days), only one spot with R_f 0.32 appears on the chromatogram. The solution is evaporated in vacuo to dryness, 0.5 ml of methanol is added, the mixture is cooled and filtered to yield 0.07 g of XII (57.3%), mp 131-133°C (from methanol). Found, %: C 63.99; H 6.43; N 23.24. $C_{13}H_{16}N_4O$. Calculated, %: C 63.91; H 6.60; N 22.94. Mass spectrum: M^+ 244. IR spectrum, ν_{max} cm^{-1}: 1650 (amide CO), 3300 and 3370 (amide NH and NHC_2H_5).

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