B) A 2-mmole sample of indolylaminovinyl ketone was dissolved in 5 ml of Dowtherm, and the solution was refluxed for 30 min, after which it was cooled and diluted with hexane, and the precipitate was removed by filtration and washed with hexane.

The products were purified and separated (in the case of the formation of isomers) by the following methods: a) sublimation; b) recrystallization from alcohol, and c) preparative separation on a loose layer of Al_2O_3 (Brockmann activity II). The preparative conditions, the purification method, and the physical constants of the products are presented in Table 2, and the PMR spectra are presented in Table 3. Incorrect numbering of the atoms of pyrroloquinolines was presented in [13].

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RESEARCH ON PYRROLO[3,2-f]INDOLIZINES.

V.* SYNTHESIS AND PROPERTIES OF 4-(ω-ALKOXYCARBONYLALKYL)- AND 4-PHENYL-6H-PYRROLOINDOLIZINES

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UDC 547.759.4'745.07

3-(α-Oxo-ω-alkoxycarbonylalkyl)- and 3-benzoyl-substituted pyrroles undergo condensation with α-unsubstituted pyrroles to give 6H-pyrrolo[3,2-f]indolizines that contain higher acid residues or a phenyl group in the 4 position of the heteroring.

We have previously observed the intramolecular condensation of 3-acetyldipyrrolemethanes to 6H-pyrrolo[3,2-f]indolizines [2]. In the present research we extended this reaction to other alkyl-substituted pyrroles during a study of the reaction of 3-(α-oxo-ω-alkoxycarbonylalkyl)- and 3-benzoyl-substituted pyrroles (II) with alkylpyrroles (III). The starting 1-

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*See [1] for communication IV.

M. V. Lomonosov Moscow Institute of Fine Chemical Technology, Moscow 119435. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 6, pp. 777-780, June, 1977. Original article submitted February 23, 1976; revision submitted May 27, 1976.

TABLE 1. 3-(α-Oxo-ω-alkoxycarbonylalkyl)pyrroles (I)

Compound	R^1	mp, °C	Found, %			Empirical formula	Calc., %			IR spectrum, ν, cm⁻¹			Yield, %
			C	H	N		C	H	N	$COOCH_3$ (C_2H_5) (R^1)	$COOC_2H_5$ attached to $C_{(5)}$	COR^1	
Ia	$(CH_2)_2COOCH_3$	124—125[a]	59,8	6,8	5,0	$C_{14}H_{19}NO_5$	59,8	6,8	5,0	1740	1652		71
Ib	$(CH_2)_4COOCH_3$	100—101[a]	62,2	7,5	4,9	$C_{16}H_{23}NO_5$	62,1	7,5	4,5	1746	1670	1660	97
Ic	$(CH_2)_5COOC_2H_5$	70—71[b]	63,9	8,5	4,4	$C_{18}H_{27}NO_5$	64,1	8,1	4,2	1740	1695	1645	93
Id	$(CH_2)_7COOC_2H_5$	64—65[b]	65,8	8,5	4,0	$C_{20}H_{31}NO_5$	65,7	8,6	3,8	1748	1669		80
Ie	$(CH_2)_8COOC_2H_5$	88—89[b]	66,6	8,8	3,9	$C_{21}H_{33}NO_5$	66,5	8,8	3,7	1740	1675	1660	70

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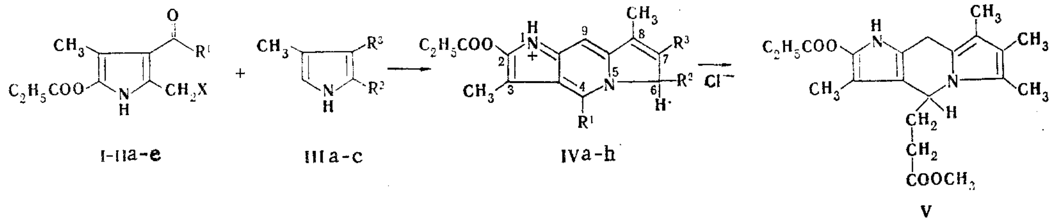
[a] From isopropyl alcohol. [b] From benzene with hexane.

(3-pyrrolyl)-1-oxo carboxylic acid esters (I, Table 1) were obtained by Friedel-Crafts acylation of 2,4-dimethyl-5-ethoxycarbonylpyrrole with dicarboxylic acid monoester chlorides.



I X = H; II X = Cl; III a $R^2 = R^3 = CH_3$; b $R^2 = H$, $R^3 = CH_3$; c $R^2 = CH_3$, $R^3 = C_2H_5$

The IR spectra of acyl-substituted pyrroles Ia-e contain the absorption band of an ester group at 1740-1748 cm^{-1} and a less distinctly expressed band of a keto group at 1645-1660 cm^{-1}. In the spectra of Ia and Id the latter is superimposed on the absorption band of the ester group attached to $C_{(5)}$.

Treatment of pyrroles Ia-e with sulfuryl chloride in chlorobenzene at 50° leads to IIa-e, which, after precipitation with hexane, were subjected without further purification to reaction with α-unsubstituted pyrroles III. As a result, we obtained 6H-pyrrolo[2,3-f]indolizines IVa-e containing alkoxycarbonylalkyl substituents in the 4 position. Under the same conditions 3-benzoylpyrrole (II, $R^1 = C_6H_5$) [3] is converted to 4-phenyl-6H-pyrrolo[3,2-f]-indolizines (IVf-h, Table 2).

The UV spectra of the pyrroloindolizines are characterized by the presence of intense absorption at 257-263 nm and less pronounced transitions at 311-314 and 320-326 nm.

The IR spectra of pyrroloindolizines IVa-e (Table 2) contain absorption bands at 1722-1725 cm^{-1} corresponding to the groups in the 2 and 4 positions of the heteroring; these bands are resolved at 1722 and 1748 cm^{-1} only in the spectrum of IVb. In the spectra of pyrroloindolizines IVf-h the bands at 1718-1720 cm^{-1} correspond to the ester group. The presence of an intense band at 1625-1635 cm^{-1} is also characteristic for all of the compounds obtained in this research, and the band at 1660-1669 cm^{-1} evidently corresponds to an isolated double bond.

The general regularities previously observed for 6H-pyrrolo[3,2-f]indolizines [4] are retained in the PMR spectra of IVa-h. At the same time, the presence of a phenyl group leads to a shift of the signal of the methyl group in the 3 position to strong field by ~1 ppm as compared with 4-methyl-substituted pyrroloindolizines [4]. This sort of shift may constitute evidence for redistribution, under the influence of the phenyl substituent, of the charges between the two nitrogen atoms.

In the spectra of pyrroloindolizines IVa,c one's attention is drawn to the absence of signals of ester groups of aliphatic acids.

For additional confirmation of the structure of pyrroloindolizine IVa we reduced it to the corresponding trihydro derivative (V) with sodium borohydride.

TABLE 2. 6H-Pyrrolo[3,2-f]indolizines

Compound	R¹	R²	R³	mp, °C	Found, %				Empirical formula	Calc., %				UV spectrum, λmax, nm (ε · 10⁻³)	IR spectrum, ν, cm⁻¹		Yield, %
					C	H	Cl	N		C	H	Cl	N		COOC₂H₅	C=C	
IVa	$(CH_2)_2COOCH_3$	CH_3	CH_3	210[a]	59,6	6,2	8,4	6,2	$C_{21}H_{26}N_2O_4 \cdot HCl \cdot H_2O$	59,4	6,6	8,3	6,6	258 (41,7), 262 (39,8), 311 (12,0), 321 (12,2)	1722	1665, 1635	38
IVb	$(CH_2)_4COOCH_3$	CH_3	CH_3	185[a]	61,1	7,4	8,0	6,1	$C_{23}H_{30}N_2O_4 \cdot HCl \cdot H_2O$	61,0	7,3	7,8	6,2	258 (42,2), 263 (42,7), 311 (13,8), 323 (15,6)	1722 1748	1669, 1634	18
IVc	$(CH_2)_5COOC_2H_5$	CH_3	CH_3	180—181[a]	62,6	7,7	7,7	5,9	$C_{25}H_{34}N_2O_4 \cdot HCl \cdot H_2O$	62,4	7,8	7,4	5,8	258 (57,8), 262 (57,4), 311 (17,2), 321 (17,6)	1722	1663, 1634	28
IVd	$(CH_2)_7COOC_2H_5$	CH_3	CH_3	131—133[b]	66,4	8,3	7,5	5,9	$C_{27}H_{38}N_2O_4 \cdot HCl$	66,1	8,0	7,2	5,7	258 (42,5), 262 (42,7), 312 (13,3), 322 (13,8)	1725	1665, 1634	30
IVe	$(CH_2)_8COOC_2H_5$	CH_3	CH_3	156—157[b]	64,1	8,4	7,1	5,4	$C_{28}H_{40}N_2O_4 \cdot HCl \cdot H_2O$	64,3	8,3	6,8	5,4	258 (48,4), 263 (48,4), 310 (11,25), 321 (9,88)	1725	1667, 1635	39
IVf	C_6H_5	CH_3	CH_3	278—279[a]	66,5	6,6	8,5	6,7	$C_{23}H_{24}N_2O_2 \cdot HCl \cdot H_2O$	66,6	6,6	8,5	6,8	262 (47,0), 314 (10,1), 325 (14,2)	1718	1660[d], 1625	32
IVg	C_6H_5	H	CH_3	264[c]	65,9	6,1	8,7	6,6	$C_{22}H_{22}N_2O_2 \cdot HCl \cdot H_2O$	65,9	6,3	8,8	7,0	256 (50,8), 262 (50,4), 310 (15,8), 322 (17,6)	1720	1667, 1632	47
IVh	C_6H_5	CH_3	C_2H_5	246—247[a]	70,2	6,7	8,8	6,8	$C_{24}H_{26}N_2O_2 \cdot HCl$	70,2	6,6	8,6	8,8	261 (46,7), 314 (10,9), 326 (13,3)	1718	1650[d], 1625	36

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[a] From acetic acid with ether. [b] From chloroform with ether. [c] From nitromethane. [d] Weak.

TABLE 3. PMR Spectra of 6H-Pyrrolo[3,2-f]indolizines (δ, ppm)

Compound	Solvent[a]	Chemical shifts of the substituents in positions[b]												
		NH	9	2		3	7	8	6-CH_3	6-H	4-			
		s		q	t	s					CH_2	$(CH_2)_n$	CH_2	COOR'
IVa	B	—	7,1	4,18	1,1	2,5	1,74	1,74	1,32d	5,1m	3,6m	2,64m		—
IVb	A	—	7,92	4,43	1,45	2,78	2,08	1,95	1,65d	5,6m	3,5m	—[c]	2,42m	3,62s
IVc	B	—	7,1	4,67	1,57	2,97	2,22	2,22	1,75d	5,37m	3,7m	1,82m	2,63m	—
IVe	A	—	7,88	4,33	1,43	2,7	2,18	2,06	1,76d	5,56m	3,45m		—[d]	3,98q 1,15t
IVf	B	—	7,7	4,64	1,54	2,3	2,12	2,12	1,28d	5,3q		7,7—7,88m[e]		
IVg	A	10,9	7,78	4,26	1,37	1,87	2,04	2,04	—	4,8s		7,63m[e]		
IVh	B	—	7,6	4,60	1,5	2,24	2,6q 1,22t	2,1	—d	5,38q		7,6—7,88m[e]		

[a] Deuterochloroform (A) and trifluoroacetic acid (B). [b] Abbreviations: s is singlet, d is doublet, t is triplet, q is quartet, and m is multiplet. [c] The precise values cannot be determined because of superimposition of the signals at 1.9-2.8 ppm. [d] The precise values cannot be determined because of superimposition of the signals at 1.3-1.5 ppm. [e] Protons of the benzene ring.

EXPERIMENTAL

The IR spectra of KBr pellets of the compounds were recorded with a Perkin–Elmer 257 spectrometer. The UV spectra of methanol solutions were recorded with a Hitachi EPS-3T spectrophotometer. The PMR spectra were measured with a JNM-4H-100 spectrometer with tetramethylsilane as the internal standard. The chlorides of the dicarboxylic acid monoesters were obtained by known methods [5].

Acylation of 2,4-Dimethyl-5-ethoxycarbonylpyrrole. A solution of 1.1 mole of stannous chloride in dichloroethane was added dropwise with vigorous stirring to a cooled (to 0°) suspension of 1 mole of 2,4-dimethyl-5-ethoxycarbonylpyrrole and 1.2 moles of dicarboxylic acid monoester chloride in dichloroethane, after which the mixture was stirred at 20° for 2 h. The solvent was then removed in vacuo, and finely crushed ice was added to the residue. The aqueous mixture was acidified with concentrated HCl, and the precipitate was removed by filtration, washed with water, and recrystallized. The characteristics of the acylpyrroles obtained (I) are presented in Table 1.

6H-Pyrrolo[3,2-f]indolizines (IV, Table 2). A solution of equimolar amounts of pyrrole II, obtained by chlorination of I by the method in [4], and pyrrole III in DMF was heated at 120° in a nitrogen atmosphere for 20 min, after which it was cooled and treated with a mixture of ether and acetone (9:1). The resulting precipitate was removed by filtration, washed with ether, and recrystallized.

3,6,7,8-Tetramethyl-4-(β-methoxycarbonylethyl)-2-ethoxycarbonyl-1,4,9-trihydropyrrolo[3,2-f]indolizine (V). A 0.12-g (3 mmole) sample of sodium borohydride was added in portions with stirring to a solution of 0.4 g (1 mmole) of hydrochloride IVa in 10 ml of ethanol, during which the initial yellow coloration vanished as the last portions of borohydride were added. The mixture was stirred for 1 h, after which it was poured into 100 ml of water, and the white precipitate was removed by filtration and dried to give 0.27 g (72%) of a product with mp 142-143° (from benzene with hexane). IR spectrum: 3320 (NH), 1745 ($COOCH_3$), and 1673 cm^{-1} ($COOC_2H_5$). Found: C 67.8; H 7.7; N 7.2%. $C_{21}H_{28}N_1O_4$. Calculated: C 67.7; H 7.6; N 7.5%.

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