aqueous solution was made alkaline to pH 8 with concentrated K_2CO_3 solution, and the acicular precipitate was removed by filtration, dried, and recrystallized from methanol. The yield was 0.96 g (85%).

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NEW DATA ON DERIVATIVES OF 1-ALKOXYAZIRIDINE-2-CARBOXYLIC ACIDS*

A. V. Prosyanik, S. V. Bondarenko,
V. I. Markov, I. I. Chervin,
M. D. Isobaev, S. D. Kushch,
and R. G. Kostyanovskii

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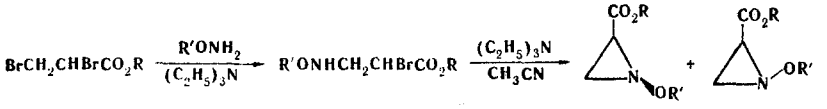
Esters of β-alkoxyamino-α-bromopropionic acids were obtained by reaction of α,β-dibromopropionic acid esters with alkoxyamines in the presence of triethylamine at 20°C for 1 month. When the products are refluxed in acetonitrile in the presence of triethylamine, they are converted to aziridines. Selective amidation of the alkoxyaziridines with excess dimethylamine in absolute methanol in the presence of sodium methoxide leads to enrichment with the cis isomer. The parameters of inversion of the nitrogen atom in the alkoxyaziridines were determined.

An increase in the fraction of the cis isomer as the volume of R is increased was observed in the preparation of methyl 1-alkoxyaziridine-2-carboxylates from methyl α,β-dibromopropionate and alkoxyamines ($RONH_2$) (in acetonitrile in the presence of triethylamine, at 20°C for 4 days, followed by refluxing for 5 h) [2]. The irreversible cis—trans isomerization that is possible under these conditions evidently does not affect the ratio of the isomers formed (see [2] and the information presented below).

To exclude postisomerization of the 1-alkoxyaziridines, the reaction was carried out at 20°C for 1 month (according to the data in [2], $\tau_{1/2} > 100$ yr at 20°C). However, only the corresponding β-alkoxyamino-α-bromopropionic acid esters I-VI (Table 1), which are stable at



I-VI VIII-XIII

I, VIII R=R'=CH_3; II, IX R=CH_3, R'=C_2H_5; III, X R=CH_3, R'=i-C_3H_7; IV, XI R=C_2H_5; R'=CH_3; V, XII R=i-C_3H_7, R'=CH_3; VI, XIII R=t-C_4H_9, R'=CH_3

20°C and when they are heated briefly to 100°C, are obtained in high yields in this case; refluxing in acetonitrile in the presence of triethylamine leads to the corresponding aziridines VIII-XIII (Table 2).

The yields of the alkoxyaziridines increase as the refluxing time is increased, while the trans/cis isomer ratio decreases as the volume of the alkyl substituent in the NOR and

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F. É. Dzerzhinskii Dnepropetrovsk Institute of Chemical Technology, Dnepropetrovsk 320005. Institute of Chemical Physics, Academy of Sciences of the USSR, Moscow 117334.

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TABLE 1. Derivatives of β-Alkoxyamino-α-bromopropionic Acids $RONHCH_2CHBrCOR'$

Compound	R	R'	bp, °C (mm)	n_D^{18}	IR spectrum, ν, cm⁻¹ C=O	IR spectrum, ν, cm⁻¹ NH	PMR spectrum, δ, ppm[a] Me (R)	Me (R')	CH₂[b]	CH[c]	NH	N found, %	Empirical formula	N calc., %	Yield, %
I	Me	OMe	70—71 (3)	1,4679	1731	3270	3,44	3,83	3,27 3,43	4,56	5,71	6,6	$C_5H_{10}BrNO_3$	6,6	63
II	Et	OMe	83 (4)	1,4657	1732	3271	1,15[d]	3,81	3,12 3,28	4,55	5,45	6,2	$C_6H_{12}BrNO_3$	6,2	49
III	*i*-Pr	OMe	82—84 (4)	1,4635	1735	3271	1,02[e]	3,80	3,23 3,39	4,56	5,34	5,9	$C_7H_{14}BrNO_3$	5,8	50
IV	Me	OEt	79—80 (3)	1,4625	1729	3266	3,51	1,33[f]	3,27 3,43	4,55	5,67	6,0	$C_6H_{12}BrNO_3$	6,2	63
V	Me	OPr-*i*	79—80 (3)	1,4561	1723	3270	3,51	1,33[g]	3,26 3,42	4,50	5,70	5,8	$C_7H_{14}BrNO_3$	5,8	55
VI	Me	OBu-*t*	81—82 (4)	1,4560	1724	3272	3,50	1,48	3,22 3,38	4,44	5,61	5,5	$C_8H_{16}BrNO_3$	5,5	27
VII	Me	SMe	47—48 (2)	1,4694	1733	3275	3,46	3,75	3,22 3,38	4,46	5,64	6,1	$C_5H_{10}BrNO_2S$	6,1	65

[a]At 80 MHz, 10% solutions in CCl_4. [b]$^2J_{H-H}$ = 7.5 Hz. [c]J = 7.00 Hz. [d]δ_{CH_2} 3.82 ppm, J = 7.0 Hz. [e]δ_{CH} 3.82 ppm, J = 6.0 Hz. [f]δ_{CH_2} 4.28 ppm, J = 7.3 Hz. [g]δ_{CH} 5.12 ppm, J = 6.5 Hz.

TABLE 2. Derivatives of 1-Alkoxyaziridine-2-carboxylic Acids

Compound	bp, °C (mm)	n_D^{16}	IR spectrum, $\nu_{C=O}$, cm⁻¹	trans/cis ratio	N found, %	Empirical formula	N calc., %	Yield, %
VIII	57 (12)	1,4362	1732	7,0	—	—	—	49
IX	56—57 (5)	1,4361	1732	4,3	—	—	—	50
X	50—51 (4)	1,4360	1732	2,6	—	—	—	40
XI	63—64 (7)	1,4379	1730	3,0	9,6	$C_6H_{11}NO_3$	9,6	51
XII	67—68 (6)	1,4335	1726	2,6	8,8	$C_7H_{13}NO_3$	8,8	53
cis-XII	38—40 (2)	—	1724	cis	—	—	—	20
XIII	75—76 (7)	1,4392	1723	2,1	8,1	$C_8H_{15}NO_3$	8,1	44
XIV	31—32 (3)	1,4388[a]	1730	2,6	9,4	$C_5H_9NO_2S$	9,5	12
XV	44—45 (3)	1,4485[a]	1728	trans	8,7	$C_6H_{11}NO_2S$	8,7	35
XVI	50,5—51 (3)	1,4450[b]	1730	trans	7,8	$C_7H_{13}NO_2S$	8,0	38
XVII	81—82 (2)	—	1745	3,0	19,5	$C_6H_{12}N_2O_2$	19,4	67

[a]This is the n_D^{18} value. [b]This is the n_D^{20} value.

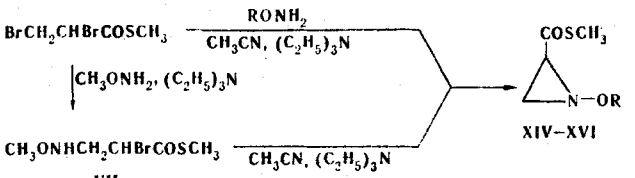
TABLE 3. Change in the Yields and trans/cis Isomer Ratios of the Alkoxyaziridines with Time

Reaction time, h	Yield, % (trans/cis ratio)[a] VIII	IX	X	XI	XII	XIII
4	33 (10,0)	50 (4,3)	40 (2,6)	22 (5,0)	31 (5,0)	15 (4,0)
5	—	55 (2,0)	78 (1,3)	—	—	—
7	49 (7,0)	—	—	51 (3,0)	53 (2,6)	44 (2,1)

[a]Determined by PMR spectroscopy; the values were the same when the products were investigated before and after distillation.

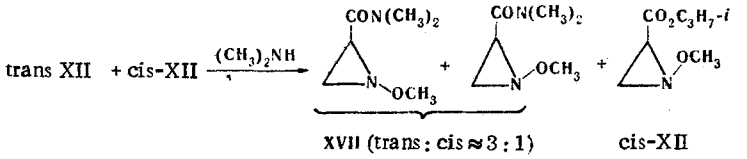
CO_2R groups is increased (Table 3).

In the case of thiomethyl esters a mixture of cis and trans isomers was obtained only for the methoxyamino derivative; the pure trans isomers were isolated in the remaining cases:



XIV R = CH_3; XV R = C_2H_5; XVI R = i-C_3H_7

We have previously observed trans stereospecificity of nucleophilic substitution at the ester group in esters of 1-alkoxyaziridine-2-carboxylic [2] and -2,2-dicarboxylic [3] acids; this trans stereospecificity was confirmed by the results of x-ray diffraction analysis [1]. We used this phenomenon to enrich the aziridines with the cis isomer. Considerable enrichment of the unchanged residue with the cis isomer was achieved by one treatment of alkoxyaziridines VIII and XI-XIII with excess dimethylamine in absolute methanol in the presence of sodium methoxide for 2 weeks. The pure cis isomer (cis-XII) was isolated in the case of ispropyl 1-methoxyaziridine-2-carboxylate:



XVII (trans : cis ≈ 3 : 1) cis-XII

The structures of all of the synthesized alkoxyaziridines were confirmed by their PMR spectra; typical data are presented for XVII (see the experimental section and [2]).

The kinetics of the cis-trans isomerization of the alkoxyaziridines were studied by PMR spectroscopy, and the activation parameters of inversion (Table 4), which attest to only a slight change in the barrier to inversion of nitrogen as a function of substituents in the ROM and RO_2C groups, were determined. The increase in the barrier in the case of alkoxyaziridine XVII can evidently be explained by a decrease in the effective volume of the planar amide group.

TABLE 4. Activation Parameters for the Inversion of Nitrogen in Alkoxyaziridines[a]

Compound	Starting percentage of the cis isomer, %	Observed group	$k \cdot 10^5$[b] sec^{-1}	$\Delta G^{\neq}_{120}$ kJ/mole	$\tau_{1/2}$ (120°), h
VIII	18,3	MeO_2C	1,09	134,3	17,7
IX	22,4	MeO_2C	2,32	131,8	8,3
X	34,2	MeO_2C	2,73	131,4	7,05
XI	35,0	MeON	3,44	130,5	5,6
XII	33,1	MeON	1,18	133,9	16,3
XIII	38,3	MeON	1,88	132,6	10,2
XIV	27,8	MeON	1,73	133,0	11,1
XVII	29,3	MeON	0,40	137,6	48,1
XVIII	46,0	MeON	0,95	134,7	20,3

[a]The rates of isomerization [at 120 ± 0.1°C in C_2Cl_4, and for XVII in CCl_4 and XVIII (1-methoxyaziridine-2-carboxamide [2]) in CD_3OD] in sealed evacuated ampuls were monitored by measurement of the integral intensities of the PMR signals of the indicated groups. The isomerization rate constants (k) were calculated by the method of least squares [4]) with a MIR-2 computer. The change in the free energy of activation of inversion ($\Delta G^{\neq}$) was found from the Eyring equation [5]. The half-conversion time ($\tau_{1/2}$) was calculated from a first-order equation. [b]The accuracy was $\pm 0.002 \cdot 10^{-5}$.

One should note the closeness of the barriers to cis–trans isomerization of aziridine XI and to racemization of the corresponding symmetrically substituted (–)-1-methoxyaziridine-2, 2-dicarboxylic acid ester [6]. This indicates that the configurational stabilities of symetrically substituted analogs, the study of which is beyond the limits of the possibility of the NMR method ($\Delta G^{\neq} > 100$ kJ/mole), can be estimated from the energy parameters of the cis–trans isomerization of monosubstituted aziridines.

EXPERIMENTAL

The PMR spectra were recorded with a Jeol JNM-C60-HL spectrometer (60 MHz). The IR spectra were recorded with a UR-20 spectrometer.

Ethyl α,β-Dibromopropionate. A solution of 158 g (0.7 mole) of α,β-dibromopropionic acid, 138 g (2.1 mole) of ethanol, and 7 ml of concentrated sulfuric acid in 250 ml of chloroform was refluxed in a Soxhlet apparatus (the extractor thimble was filled with $MgSO_4$) for 48 h, after which the solvent was removed, and the residue was extracted with ether, washed successfully with 1% $KHCO_3$ solution and water, and dried with magnesium sulfate. The ether was removed, and the product was vacuum distilled to give a product with bp 40-41°C (1 mm) and n_D^{20} 1.5003 (see [7]) in 51% yield.

Isopropyl α,β-Dibromopropionate. This compound, with bp 80-81°C (5 mm) and n_D^{20} 1.4911, was similarly obtained in 69% yield.

Thiomethyl α,β-Dibromopropionate. A suspension of 10.2 g (0.15 mole) of MeSNa and 36.7 g (0.15 mole) of α,β-dibromopropionyl chloride in 150 ml of absolute ether was refluxed for 1 h, after which it was allowed to stand overnight. The precipitate was removed by filtration, the filtrate was evaporated, and the residue was distilled to give the product, with bp 55°C (3 mm) and n_D^{20} 1.5110, in 72% yield.

Methyl β-Methoxyamino-α-bromopropionate (I). A solution of 12.3 g (0.05 mole) of methyl α,β-dibromopropionate [7] in 50 ml of acetonitrile was added gradually with cooling to a solution of 2.35 g (0.05 mole) of methoxyamine and 10.1 g (0.1 mole) of triethylamine in 150 ml of acetonitrile; the mixture was maintained at 20°C for 5 days. The solvent was removed in the cold, and the residue was extracted with ether. The ether was removed, and the reaction product was distilled in vacuo to give 6.7 g (63%) of ester I (Table 1).

Compounds II-VII (Table 1) were similarly obtained.

Methyl cis- and trans-1-Methoxyaziridine-2-carboxylates (VIII). A solution of 8.9 g (42 mmole) of ester I and 4.2 g (42 mmole) of triethylamine in 150 ml of acetonitrile was refluxed for 7 h, after which the solvent was removed at 20°C, and the residue was extracted with ether. The ether was removed, and the reaction product was distilled in vacuo to give 2.7 g (49%) of aziridine VIII (Table 2).

Compounds IX-XIII (Table 2) were similarly obtained.

Thiomethyl cis- and trans-1-Methoxyaziridine-2-carboxylic Acids (XIV). A total of 0.44 g (12%) of aziridine XIV (Table 2) was obtained from 1.2 g (25 mmole) of methoxyamine, 5.1 g (50 mmole) of triethylamine, and 6.6 g (25 mmole) of thiomethyl α,β-dibromopropionate in 150 ml of acetonitrile under modified conditions for the synthesis of ester I (by reaction at 20°C for 4 days and subsequent refluxing for 12 h).

Compounds XV and XVI (Table 2) were similarly obtained.

Isopropyl cis-1-Methoxyaziridine-2-carboxylate (cis-XII) and cis- and trans-1-Methoxyaziridine-2-carboxylic Acid Dimethylamides (XVII). A solution of 14.8 g (0.102 mole) of a mixture of aziridines XII in 100 ml of absolute methanol saturated with dimethylamine was maintained at 20°C in the presence of MeONa for 2 weeks, after which the solvent and excess dimethylamine were removed, and the residue was distilled in vacuo to give 2.9 g (20%) of cis-aziridine XII [bp 38-40°C (2 mm)] and 9.0 g (67%) of a mixture of amides XVII with bp 81-82°C (2 mm) (Table 2). PMR spectrum (80 MHz, CCl_4), δ: cis isomer, 3.39 (MeO), 3.14 and 2.84 (Me_2N), 2.55 (H_A), 2.26 (H_C), and 1.90 ppm (H_B), J_{AB} = 6.9, J_{AC} = 6.2, and J_{BC} = –2.1 Hz; trans isomer, 3.45 (MeO), 3.17 and 2.85 (Me_2N), 2.57 (H_A), 2.15 (H_C), and 1.92 ppm (H_B), J_{AB} = 8.5, J_{AC} = 6.0, and J_{BC} = –1.7 Hz.

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INDOLE DERIVATIVES. 120.* SYNTHESIS OF HIGHER ω-(3-INDOLYL)ALKANOIC ACIDS BY ALKYLATION OF INDOLE LACTONES

B. Ya. Eryshev and N. N. Suvorov

UDC 547.757.07:542.953

The alkylation of indole with the tridecanolide, pentadecanolide, and oxo lactones of ω-hydroxyethoxyundecanoic and ω-hydroxybutoxyundecanoic acids was investigated. Higher indolylalkanoic acids, viz., ω-(3-indolyl)undecanoic, ω-(3-indolyl)tridecanoic, and ω-(3-indolyl)pentadecanoic acids, were obtained. The scheme of the alkylation of indole with oxo lactones, and the difference in the rates of the reactions of the ester and lactone bonds, were established from the reaction products.

Methods for the preparation of γ-(3-indolyl)butyric acid by the reaction of indole with γ-butyrolactone in the presence of alkali in an autoclave at 250°C and in a solvent at normal pressure are known [2].

It seemed of interest to ascertain the possibility of the preparation of higher 3-indolylalkanoic acids by this method, and the use of other less aggressive catalysts. For this, we used lactones, such as the tridecanolide, pentadecanolide, and oxo lactones of ω-hydroxyethoxyundecanoic acid and ω-hydroxybutoxyundecanoic acid, and various weak bases as the catalysts.

The studies showed that the tridecanolide and pentadecanolide react with indole to give the corresponding acids in 62-95% yields. Under the given conditions, oxo lactones IIa and IIb form ω-(3-indolyl)undecanoic acid in 10-15% yield. In addition to the acid, a substance that, according to the results of elementary analysis and IR spectroscopy, has the 3-indolylethyl decyl ether structure, was isolated from the neutral reaction products by thin-layer chromatography (TLC). On the basis of the results, it may be stated that both the lactone and ether bond participate in the alkylation of indole with oxo lactones under the conditions presented above via the scheme:

*See [1] for communication 119.

D. I. Mendeleev Moscow Institute of Chemical Technology, Moscow 125047. Translated from Khimiya Getetotsiklicheskikh Soedinenii, No. 2, pp. 216-217, February, 1980. Original article submitted March 28, 1978; revision submitted June 11, 1979.

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