ASYMMETRIC NONBRIDGEHEAD NITROGEN.

11.* DERIVATIVES OF 1-ALKOXYAZIRIDINE-2,2-DICARBOXYLIC ACIDS

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1-Alkoxyaziridine-2-carboxylic and -?,2-dicarboxylic esters [2, 3] are typified by a high nitrogen inversion barrier N($\Delta G^{\neq}$ = 30-32 kcal/mole); the electronegative substituents on the ring N and C atoms determine their thermal and chemical stability while the functional groups control the possibility of reactions with chiral reagents. Derivatives of 1-alkoxyaziridine-2,2-dicarboxylic acids are therefore of interest for possible resolution into optical antipodes with the N atom as the only asymmetric center.

The esters of these acids can be synthesized by the reaction scheme (Table 1, Fig. 1)

$$CH_2{=}C(COOEt)_2 \xrightarrow[CCl_4]{Br_2} BrCH_2CBr(COOEt)_2 \xrightarrow[Et_3N,\ MeCN]{RONH_2} RONCH_2C(COOEt)_2 \quad (1)$$

(Et₃N, MeCN)

R = Me (I), Et (II), *i*-Pr (III)

Methylamine and aniline in this scheme yield 1-methyl- and 1-phenylaziridine-2,2-dicarboxylic esters (IV) and (IVa). Attempted synthesis of an aziridine by reaction (2) gave only debromination

$$Me_2CBrCBr(COOMe)_2 \xrightarrow[Et_3N,\ MeCN]{MeONH_2} Me_2C{=}C(COOMe)_2 \quad (2)$$

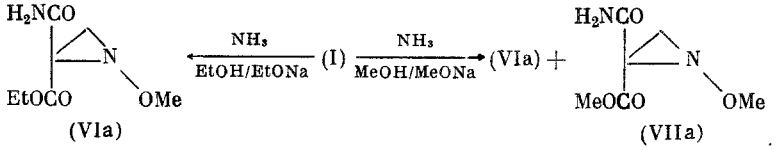
The formation of alkoxyaziridines seems to depend on the ratio of the rate of nucleophilic substitution and subsequent cyclization to that of the competing debromination. The isolation under equivalent conditions but in the absence of the alkoxyamine of diethyl methylenemalonate only [scheme (1)] excludes the possibility of intermediate dehydrobromination.

Compound (I) is transesterified by prolonged refluxing in absolute methanol

$$(I) \xrightarrow{MeOH/MeONa} MeONCH_2C(COOMe)_2\ (V) \quad (3)$$

though it remains unchanged by the action of ?-methanol (in the absence of solvent, MeONa, 100°C, 20 h).

Nucleophilic substitution reactions (amination and saponification) involving the ester group trans to the N-substituent of the 1-alkoxyaziridine-2,2-dicarboxylic esters [2] are stereospecific. Thus ammonolysis of (I) with a slight excess of NH_3 containing traces of alcoholate at 20°C in EtOH gives monoamide (VIIa) while in MeOH partial transesterification forms a 1:4 mixture of (VIa) and (VIIa)



(VIa) (VIIa) (4)

The PMR spectra indicate that the amides are formed as a single isomer (Fig. 2); the second isomer cannot be detected in the reaction mixture after removal of the solvent and

*For Part 10, see [1].

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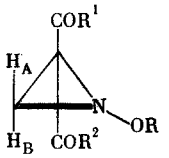
TABLE 1. Derivatives of 1-Alkoxy-2,2-Dicarboxylic Acids,



Compound	R	R¹	R²	Yield, %	bp, °C (p, mm Hg) and mp, °C	n_D^{20}	$\nu_{C=O}$ Molecular	Found / Calculated, % C	H	N
(I)	Me	EtO	EtO	53	65–68(0,5)	1,4412	1739	49,70 / 49,76	7,16 / 6,96	6,44 / 6,45
(II)	Et	EtO	EtO	42,5	80(0,5)	1,4411	1730	52,05 / 51,94	7,62 / 7,41	6,04 / 6,06
(III)	*i*-Pr	EtO	EtO	39	81–82(0,5)	1,4419	1735	53,94 / 53,86	7,96 / 7,81	5,63 / 5,71
(IV)	(MeN)	EtO	EtO	64,5	69–70(0,6)	1,4410	–	53,76 / 53,74	7,51 / 7,51	6,99 / 6,96
(V)	Me	MeO	MeO	74	66–67(0,5)	1,4453	1740	44,53 / 44,45	6,00 / 5,86	7,34 / 7,40
(VIa)	Me	H_2N	EtO	49,7	73	–	1730 * 1685	44,56 / 44,68	6,43 / 6,43	14,74 / 14,89
(VIb)	Me	EtO	H_2N	26	123	–	1710 * 1665	44,59 / 44,68	6,47 / 6,43	14,78 / 14,89
(VIIa)	Me	H_2N	MeO	34,4	98	–	1738 * 1690	41,20 / 41,38	5,67 / 5,79	16,00 / 16,08
(VIII)	Me	H_2N	H_2N	73,7	158	–	1720 * 1590	37,94 / 37,74	5,72 / 5,70	26,40 / 26,40
(IX)	Me	KO	EtO	82,5	188 (dec.)	–	–	36,99 / 37,11	4,47 / 4,43	6,25 / 6,16
(Xa)	Me	HO	EtO	95	67–68	–	1730 * 1705	44,44 / 44,45	5,86 / 5,86	7,45 / 7,40
(XIb)	Me	MeO	EtO	100	72(0,6–0,7)	–	1738	47,40 / 47,29	6,65 / 6,45	6,67 / 6,89

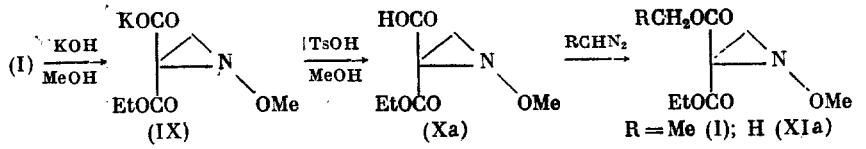
*In KBr tablet.

unreacted (I). That the amides have the same configuration follows from the conversion of (VIa) to (VIIa) by exhaustive transesterification of the reaction mixture (for assignment of the configuration, see below). Unlike (I) [scheme (3)] transesterification of monoamide (VIIa) can be carried out under mild conditions. Exhaustive ammonlysis of (I) with a large excess of NH_3 goes easily at 20°C

$$(I) \xrightarrow[MeOH/MeONa]{\text{excess } NH_3} \underset{(VIII)}{MeONCH_2C(CONH_2)_2} \qquad (5)$$

which we may attribute to activation of the ester carbonyl as a result of the intramolecular hydrogen bond with the amide group (a six-membered ring).

Saponification of (I) by 1 mole of KOH in MeOH at 20°C gives the monopotassium salt (IX), whence monoacid (Xa) can be isolated (Table 1)



(6)

The PMR spectrum indicates that acid (Xa) is formed as a single isomer. It is exceptionally stable both when heated (120°C, 15 min) and also in acidic media and is easily esterified by diazoalkanes (Fig. 1).

Monoamide (VIa) [scheme (4)] has a different PMR spectrum to that of isomer (VIb), prepared by the following scheme (7).

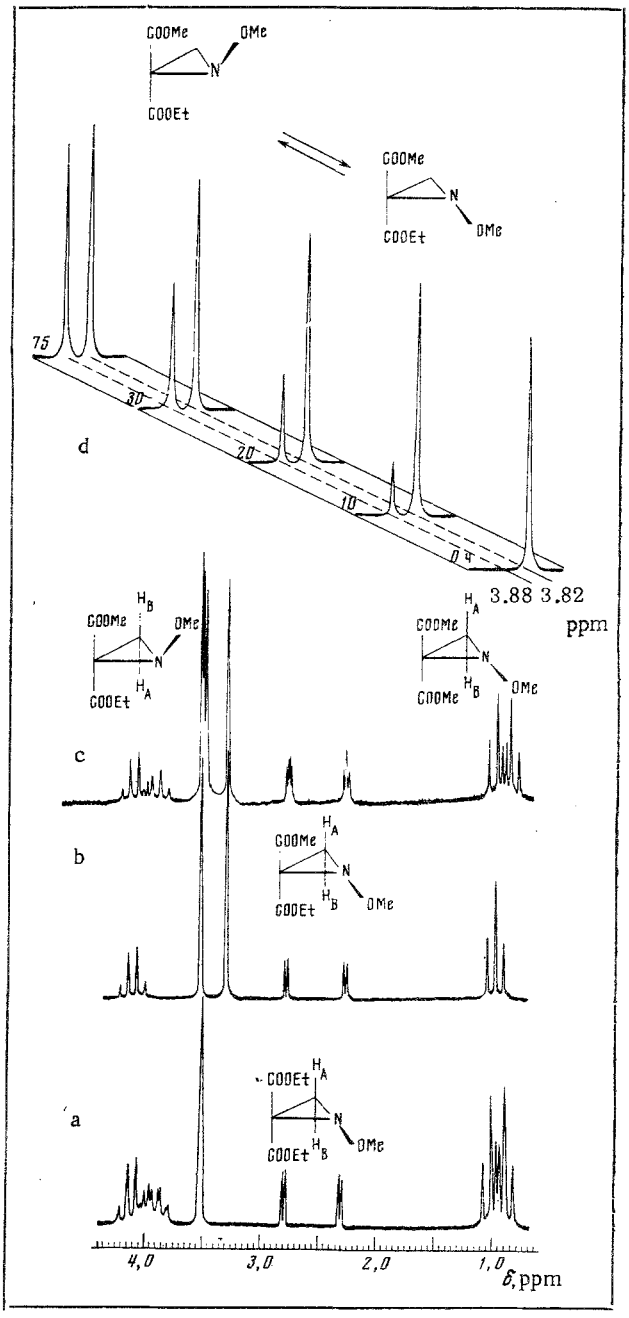
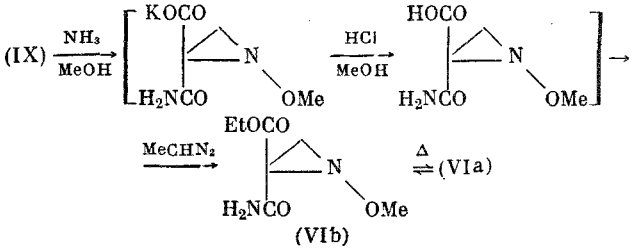


Fig. 1. PMR spectra (100 MHz, 5% molar solutions in C_6H_6) of: a) (I); b) (XIa); c) equilibrium mixture of (XIa) and (XIb) after heating (72 h, 100°C); d) MeOCO signals in (XIa) and (XIb) (60 MHz) during thermal isomerization of (XIa) in $CdCl_3$ at 100°C; the ratio of integrated intensities is 52.5:47.5.



(7)

but it is identical to the latter's thermal isomerization product (Fig. 2). Consequently (VIa) and (IX) have the same configuration and ammonolysis and saponification are thus equally stereospecific. The trans-stereospecificity of these reactions is confirmed by the thermal isomerization of the products (Table 2)

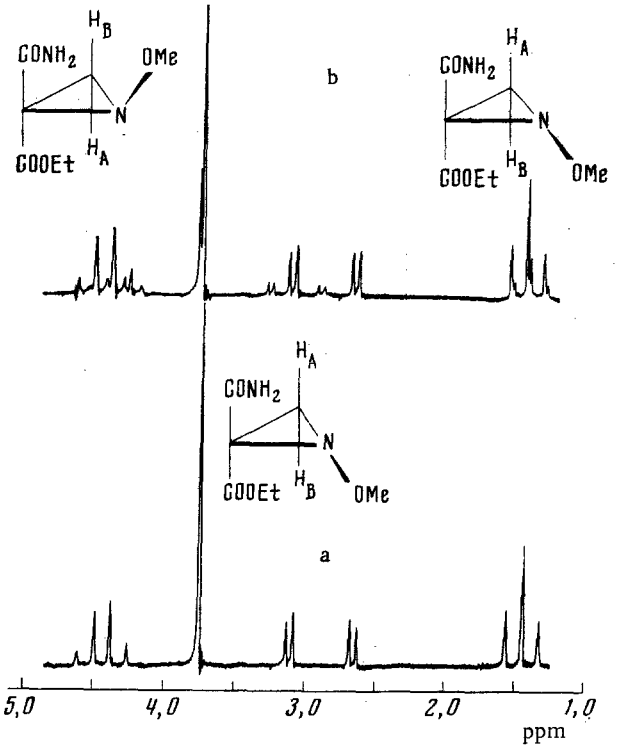
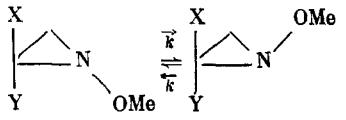
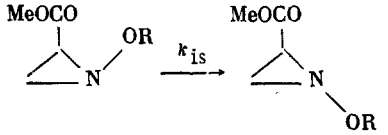


Fig. 2. PMR spectra (100 MHz, 5% molar solutions in $CDCl_3$) of: a) monoamide (VIa); b) equilibrium mixture of (VIa) and (VIb) after heating (50 h, 100°C).



(8)

since the order of equilibrium isomer ratios (Table 3) accords with the known order of conformational energies of the substituents: EtOCO < MeOCO < HOCO < CO_2^- [6]. We have previously established the configurations of 1-alkoxyaziridine-2-carboxylic esters on the basis of their irreversible cis–trans isomerization [2]



R = Me (XII), Et (XIII), *i*-Pr (XIV)

We assign the ring proton signals in the PMR spectra (Table 4) as we did those of the 1-alkoxyaziridine-2-carboxylic esters [2], in terms of the relative broadening of the signals $C_{A/B}$ (Table 5), which is known to be greater for the protons cis to the nitrogen lone pair [7, 8]. The reduction in $C_{A/B}$ in the order (I) > (II) > (III) seems to arise from the increasing repulsion between the RON and EtOCO groups, which causes a reduction in the inversion barrier [see Table 2, (XII)-(XIV)] and accordingly an increase in the p-character of the nitrogen lone pair (for a pure lone pair $C_{A/B}$ = 1). The low value of $C_{A/B}$ for (Xa), (VIa), and (VIIa) may be due to the existence of hydrogen bonding of the COOH and $CONH_2$ groups with the cis-oriented nitrogen lone pair, since for example the protonation of aldoximes considerably reduces the broadening of the signals [7]. This assignment is confirmed by the change in the chemical shifts induced by an aromatic solvent (ASIS effect [9, 10]). The conceptual basis of this effect is that the protons of groups solvated by the aromatic solvent are shielded more strongly. Preferential solvation takes place on the side of least electron density. The preferential solvation of imines and aziridines by benzene takes place on the side of the N-substituent [10], but oximes and oxime ethers are solvated on the side of the nitrogen lone pair [9]. On this basis we assign the higher ASIS effect in alkoxyaziridines to the protons and groups thans to RON (Table 6). We assign the signals

TABLE 2. Activation Parameters for Nitrogen Inversion in Alkoxyaziridines[a]

Compound	Group	Solvent	T., °C	$\vec{k}\cdot10^5$, sec^{-1}	$\overleftarrow{k}\cdot10^5$, sec^{-1}	$\Delta\vec{G}^{\neq}$, kcal/mole	$\Delta\overleftarrow{G}^{\neq}$, kcal/mole	$\tau_{1/2}$, h
(I)[b]	–	C_2Cl_4	100	0,65	–	30,8	–	14,6
(XIa)[c]	MeOCO	$CDCl_3$	100	0,79	0,86	30,7	30,6	11,7
(Xa)[b]	CH_2(Et)	CD_3OD	100	0,75	1,60	30,7	30,1	8,19
(VIII)[b]	–	CD_3OD	100	0,85	–	30,6	–	11,3
(VIIa)	Ring CH_2	$CDCl_3$	100	0,84	3,26	30,6	29,6	4,7
(VIa)	Ring CH_2	$CDCl_3$	100	0,75	2,99	30,7	29,7	5,2
(VI6)	CH_2(Et)	CD_3OD	100	1,42	0,33	30,2	31,3	11,0
(XII)	MeOCO	C_6H_6	142	13,7	–	31.9	–	1,4
	MeOCO(MeON)	$PhNO_2$	142	13,4(11,9)	–	31.9(32,0)	–	1,4(1.6)
	MeOCO(MeON)	$PhNO_2$	121	5,8(5,7)	–	30,9	–	3,3
	MeOCO(MeON)	$PhNO_2$	100	0,38	–	31,2	–	50,7
(XIII)	MeOCO	C_6H_6	100	1,10	–	30,4	–	17,5
(XIV)	MeOCO	C_6H_6	100	1,80	–	30,1	–	10,7
(IV)	Ring CH_2	$CDCl_3$	47[d]	k=29,97	–	16,61	–	0,012c
	Me(Et)	$CDCl_3$	19[d]	k=4,66	–	16,17	–	0,074c
(IVa)	Ring CH_2	$CHFCl_2$	–45[d]	k=55,5	–	11,4	–	$0{,}54\cdot10^{-2}$sec

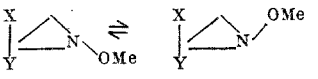
[a]The kinetics of isomerization on heating (accuracy ±0.1°C) in sealed evacuated tubes were followed by measuring the integrated intensity of the PMR signals of the particular groups. The rate constants for isomerization (k_{is}) were calculated by least squares [4]. The rate constants for nitrogen inversion in the direct ($\vec{k}$) and reverse ($\overleftarrow{k}$) reactions were determined from k_{is} for the reversible equilibrium process. For the irreversible isomerization of (XII)-(XIV) k_{is} is numerically equal to k_{inv}. The change in the free energy of activation for inversion ($\Delta G^{\neq}$) was found from the Eyring equation [5]. The half-life ($\tau_{1/2}$) was calculated from the equation for first-order reactions.

[b]From the kinetics of racemization of an optically active sample [3].

[c]Decomposition of the sample (~10%) occurred during isomerization.

[d]Coalescence temperature.

TABLE 3. Equilibrium Isomer Ratios of Alkoxyaziridines at 100°C (%)*

Compound	X	Y	Solvent		
(XIa)	MeOCO	EtOCO	$CDCl_3$	52,5	47,5
(Xa)	HOCO	EtOCO	CD_3OD	~68	~32
(VIIa)	H_2NCO	MeOCO	$CDCl_3$	79,5	20,5
(VIa)	H_2NCO	EtOCO	$CDCl_3$	79,9	20,1
			CD_3OD	81,1	18,9
(IX)†	KOCO	EtOCO	CD_3OD	100	0

*From the PMR spectra at 60 MHz.

†Isomerization was not observed on heating for 50 h.

of the ROCO group in the symmetrical derivatives on the basis of the identical chemical shifts of the cis- or trans-ROCO group in the unsymmetrical derivatives; compare compounds (I), (V), and (XIa), (XIb) (Table 4, Fig. 1). Identically oriented ROCO groups and ring protons (cis or trans) show synchronicity of the ASIS effect (Table 6). Thus the nitrogen lone pairs in alkoxyaziridines has a shielding effect on the ring protons and substituents in comparison with the RON substituent.

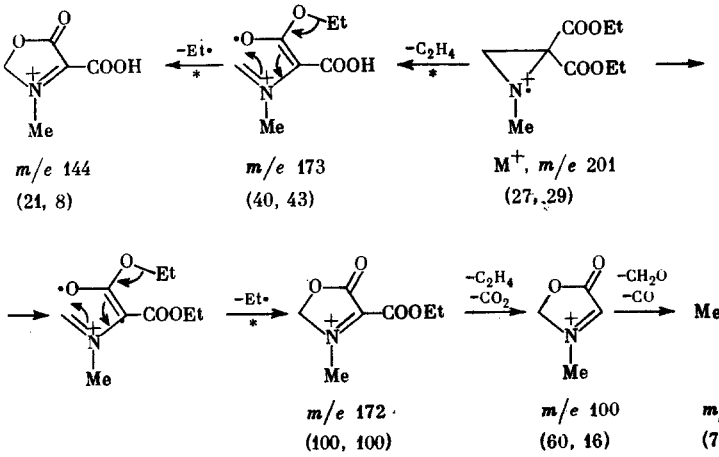
We follow [2, 8] in assigning a negative sign to the J_{AB} constant (Table 4), which is also in accord with the increase in the absolute value of J_{AB} in solvents of higher dielectric constant [11]. Increased steric interactions of the cis-oriented substituents in position 1 and 2 is accompanied by increase in J_{AB}.

TABLE 4. PMR Parameters of Derivatives of 1-Alkoxyaziridine-2,2-dicarboxylic Acids (5% molar solutions in C_6H_6, 100 MHz, δ, ppm, from TMS, J, Hz)

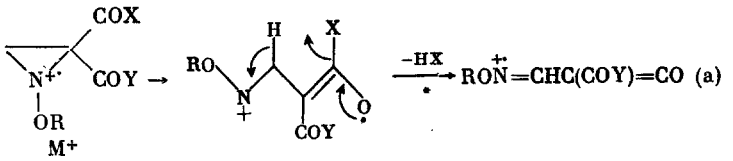
Compound	H ring		R=Me	R¹		R²		J_{AB}		
	A	B		Me	CH_2	Me	CH_2	C_6H_6	CCl_4	$CDCl_3$
(I)	2,269	2,762	3,525	0,885	3,905 3,920	1,000	4,110	−2,8	−2,6	−2,9
(II)	2,266	2,782	0,960 [b]	0,835	3,880 3,920	0,960	4,095 4,110	−2,6	−2,4	—
(III)	2,242	2,787	1,020 [c] 1,150	0,840	3,935 3,950	0,980	4,050 4,065	−2,4	−2,2	—
(V)	2,210	2,700	3,440	3,230	—	3,410	—	−2,9	−2,7	—
(VIa)	2,185	2,849	3,415	—	—	0,985	4,085	−2,8	—	−2,9
(VIb)	2,582	3,155	3,510	0,875	3,875	—	—	−2,5	—	−2,7
(VIIa)	2,148	2,842	3,455	—	—	3,370	—	−2,9	—	−3,0
(VIIb)	2,542	3,118	3,490	3,270	—	—	—	−2,5	—	−2,7
(VIII) [a]	2,400	2,750	3,560	—	—	—	—	−3,2 [a]	—	—
(IX) [a]	2,220	2,420	3,437	—	—	1,210	4,080	−2,2 [a]	—	—
(Xa) [a,c]	2,531	2,781	3,593	—	—	1,294	4,294	−3,0 [a]	—	—
(Xb) [a]	2,418	2,830	3,593	—	—	1,268	4,231	−2,8 [a]	—	—
(XIa)	2,275	2,775	3,525	3,310	—	0,995	4,105	−2,8	−2,7	−2,9
(XIb)	2,313	2,775	3,515	0,890	3,925	3,495	—	−2,8	—	−3,0

[a] In CD_3OD (60 MHz).
[b] 3.9 (CH_2).
[c] 4.18 (CH).
[d] In C_6H_6 the signals in the PMR spectrum (100 MHz) are broadened as a result of the formation of diasteromeric associates, since the signals are sharp in the spectrum of optically pure (Xa) [3].

We have studied the mass spectra of the synthetic compounds. Electron impact induces similar rearrangement fragmentation of (IV) and of the corresponding monoester [12]



and also of derivatives of 1-alkoxyaziridine-2,2-dicarboxylic and -2-monocarboxylic acids [2]



Here (a): (I) m/e 171 (58, 100); (II) m/e 185 (34, 100); (V) m/e 157 (100, 100); (VIa) m/e 171 (100, 100) and m/e 142 (28, 24); (VIIa) m/e 157 (57, 100), m/e 142 (14, 29); (VIII) m/e 142 (53); (Xa) m/e 171 (33); m/e 143 (43); (XIa) m/e 171 (73, 82), and m/e 157 (100, 100) with preferential loss of NH_3 in monoamides (VIa) and (VIIa) and also of EtOH in monoester (XIa) (the relative intensities at 30 and 12 eV appear in brackets).

TABLE 5. Relative Broadening of the Ring Proton Signals $C_{A/B}$* in the PMR Spectra of Some derivatives of 1-alkoxyaziridine-2,2-dicarboxylic Acids (100 MHz, 5% molar solutions)

Compound	C_6H_6	CCl_4	$CDCl_3$
(V)	1,45	1,40	–
(I)	1,40	1,35	1,20
(II)	1,35	1,30	—
(III)	1,25	–	–
(Xa)	1,20	–	1,25
(VIa)	1,10	–	1,10
(VIIa)	–	–	1,10

*$C_{A/B} = D_A/D_B$, where D_A and D_B are the broadening of the signals of protons A and B. For example $D_A = 100\ (d_A/h_A)/[(d_A/h_A) + (d_B/h_B)]$, where d_A and d_B are the total widths at half-height; h_A and h_B are the total peak heights, whence $C_{A/B} = d_A h_B/d_B h_A$. The expression for the peak areas $S_A = S_B = k_A d_A h_A = k_B d_B h_B$, where the coefficients are assumed equal, $k_A = k_B$, gives $C_{A/B} = h_B^2/h_A^2$.

EXPERIMENTAL

Spectra were recorded with Varian HA-100 (100 MHz) and Jeol JNM-C60-HL spectrometers, UR-10 and UR-20 spectrophotometers, and an MX-1303 mass spectrometer.

Diethyl methylenemalonate was prepared by the method of [13], yield 65%, bp 125-130°C (25 mm); PMR spectrum (CCl_4, 60 MHz, δ, ppm): 1.28 (Me); 4.10 (CH_2), J = 7 Hz 6.18 (CH_2=). Diethyl α,β-dibromomethylmalonate was prepared following [14], yeild 52%, bp 105-113°C (1.5 mm).

Debromination of Diethyl α,β-Dibromomethylmalonate. A solution of diethyl α,β-dibromomethylmalonate (19.6g, 0.06 mole) and Et_3N (5.96g, 0.06 mole) in CH_3CN (150 ml) was left for seven days at 20°C; the solvent was removed and the product was extracted with ether. We obtained diethyl methylenemalonate (3.15g, 35%), bp 125-130°C (25 mm), which was identified with an authentic sample from the PMR spectrum.

Diethyl 1-Methoxyaziridine-2,2-dicarboxylate (I). A solution of diethyl α,β-dibromomethylmalonate (16.6g, 0.05 mole), methoxyamine (2.4g, 0.05 mole), and NEt_3 (10.1g, 0.1 mole) in CH_3CN (150 ml) was left for four days at 20°C, whereupon it was refluxed for 12 h. After removal of the solvent the product was extracted with ether and distilled. We obtained (I) (5.8g) (Table 1). We synthesized (II) and (III) by the same procedure (Table 1).

Dimethyl Isopropylidenemalonate was prepared by the method of [15], yield 42%, bp 63-66°C (1 mm). PMR spectrum (C_6H_6, δ, ppm): 1.45 (MeC); 3.36 (MeO).

Dimethyl α,β-Dibromoisopropylmalonate was prepared from dimethyl isopropylidenemalonate (72.3g, 0.42 mole) and bromine (67.2g, 0.42 mole) in $CHCl_3$ (500 ml), yield 112 g (80%), bp 108-110°C (1 mm).

Attempted Synthesis of Dimethyl 1-Methoxy-2,2-Dimethylaziridine-3,3-Dicarboxylate. Under the conditions of the synthesis of (I), dimethyl α,β-dibromoisopropylidenemalonate (16.6g, 0.05 mole), CH_3ONH_2 (2.4g, 0.05 mole), and NEt_3 (10.1g, 0.1 mole) yielded dimethyl isopropylidenemalonate (5.2g, 60%), which was identified with an authentic sample from the PMR spectrum.

TABLE 6. Change in Chemical Shifts Induced by Aromatic Solvent (ASIS effect): $\Delta\nu^{C_6H_6}_{CDCl_3} = \nu_{CDCl_3} - \nu_{C_6H_6}$ and for (I)-(V) $\Delta\nu^{C_6H_6}_{CCl_4} = \nu_{CCl_4} - \nu_{C_6H_6}$ (5% molar solutions, 100 MHz)

Compound	H ring		R=Me	R¹		R²	
	A	B		Me	CH_2	Me	CH_2
(I)	26,2	9,1	11,7	39,3	34,0 34,5	31,5	20,5
(I)*	15,0	−6,2	11,0	46,0	40,5 43,5	36,0	27,0 28,5
(II)*	11,6	−8,0	15,0 †	44,5	32,0 31,0	34,0	17,5 18,0
(III)*	14,7	−7,1	6,0 −2,0	44,5	25,0 24,5	33,0	15,0 16,5
(V)*	21,6	1,4	14,0	51,0	–	37,0	–
(VIa)	33,3	11,1	24,5	–	–	32,5	23,5
(VIb)	19,9	0	16,5	42,5	37,7	–	–
(VIIa)	26,8	4,4	15,0	–	–	45,5	–
(VIIb)	22,6	1,3	14,1	–	–	49,1	–
(Xa)	33,7	17,4	17,0	–	–	31,3	26,0
(XIa)	30,0	12,5	16,2	51,0	–	33,5	24,5
(XIb)	25,8	10,3	17,2	39,7	35,5	38,5	–

*$\Delta\nu^{C_6H_6}_{CCl_4}$.

†For the CH_2 protons 0.5 and −2.0 Hz.

Diethyl 1-Methylaziridine-2,2-dicarboxylate (IV). A solution of α,β-dibromomethylmalonate (3.6g), methylamine (0.5g), and NEt_3 (2.18g) in CH_3CN (150 ml) was left at 20°C for six days, whereupon it was refluxed for 12 h. After removal of the solvent the product was extracted with ether and distilled. We obtained (IV) (1.4g) (Table 1). PMR spectrum (60 MHz, $CDCl_3$ at −20°C, δ, ppm): 1.32 and 1.35 (Me), J = 7.4 Hz; 2.20 and 2.37 (ring CH_2), J_{AB} = 1.35 Hz; 2.54 (MeNO; 4.28, 4.32 (AB) and 4.34 (CH_2O).

Diethyl 1-Phenylaziridine-2,2-dicarboxylate (IVa). A solution of diethyl α,β-dibromomethylmalonate (10g), aniline (2.8g), and NEt_3 (6g) in CH_3CN (100 ml) was left at 20°C for four days, whereupon it was refluxed for 10 h. After removal of the solvent the product was extracted with ether and purified by chromatography on silica gel (elution by 1:3 hexane-$CHCl_3$). We obtained (IVa) (6.5g, 82.6%). PMR spectrum (80 MHz, $CHFCl_2$, 20°C, δ, ppm): 1.23 (Me); J = 7 Hz; 2.78 (ring CH_2; at −90°C Δν = 25 Hz). The product was characterized as the diamide. A solution of (IVa) (5.2g) in absolute methanol (50 ml), saturated with NH_3 and containing traces of MeONa, was left at 20°C for seven days. After removal of the solvent the residue was washed with ether and recrystallized from MeOH. We obtained the diamide (3.8g, 93%), mp 156-157°C. Found: C 58.53; H 5.56; N 20.51%. $C_{10}H_{11}N_3O_2$. Calculated: C 58.53; H 5.40; N 20.40%.

Dimethyl 1-Methoxyaziridine-2,2-dicarboxylate (V). A solution of (I) (5.4g) in absolute CH_3OH (200 ml) containing traces of MeONa was refluxed for 8 h. The solvent was then removed; absolute methanol (200 ml) was added and the mixture was refluxed for a further 8 h. Distillation gave (V) (3.5g) (Table 1).

Ethyl trans-2-Carbamoyl-1-methoxyaziridine-2-carboxylate (VIa). A solution of (I) (3.25g) and liquid NH_3 (3 ml) in absolute EtOH (100 ml) containing traces of EtONa was left at 20°C for four days. After removal of the solvent the residue was washed with ether and recrystallized from CCl_4. We obtained (VIa) (1.4g) (Table 1). The ethereal extract yielded unreacted (I) (1.45g, 40%).

Methyl trans-2-Carbamoyl-1-methoxyaziridine-2-carboxylate (VIIa). Under the conditions of the preceding synthesis, (I) (5.24g) and liquid NH_3 (5 ml) in absolute MeOH (100 ml) containing traces of MeONa yielded after crystallization from EtOH a mixture of (VIIa) and (VIa) (4:1 from the PMR spectrum), which was dissolved in absolute MeOH (20 ml) containing traces of MeONa and left at 20°C for seven days. After removal of the solvent the residue was crystallized from CCl_4. We obtained (VIIa) (1.5g) (Table 1).

1-Methoxyaziridine-2,2-dicarboxamide (VIII). A solution of (I) (6g) in absolute MeOH (75 ml), saturated with NH_3 and containing traces of MeONa, was left at 20°C for seven days. After removal of the solvent the residue was washed with CH_3CN and crystallized from EtOH. We obtained (VIII) (3.14g) (Table 1).

Potassium cis-Ethyl 1-Methoxyaziridine-2,2-dicarboxylate (IX). A solution of (I) (8.68g) and KOH (2.24g) in EtOH (20 ml) was left at 20°C for 5 h and then at 0°C for 12 h. The precipitate was removed, washed with absolute ether, and crystallized from EtOH. We obtained (IX) (7.5g) (Table 1).

Ethyl cis-2-Carbamoyl-1-methoxyaziridine-2-carboxylate (VIb). A solution of (IX) (1.36 g) and liquid NH_3 (5 ml) in absolute methanol (50 ml) containing traces of MeONa was left at 20°C for seven days. The mixture was concentrated; the residue was dissolved in absolute MeOH (50 ml) and the solution, stirred and maintained at 0°C, was treated with methanolic HCl to pH 2-3. The precipitate was removed and a benzene solution of diazoethane was added to the filtrate at 0°C until the yellow color persisted. After removal of the solvent the product was extracted with $CHCl_3$ and recrystallized from C_6H_6. We obtained (VIb) (0.28g) (Table 1).

cis-2-(Ethoxycarbonyl)-1-methoxyaziridine-2-dicarboxylic Acid (Xa). A solution of p-toluenesulfonic acid hydrate in absolute CH_3OH (10 ml) was gradually added at 20°C to a solution of (IX) (2.4g) in absolute MeOH (20 ml). After 1 h the solvent was removed; the residue was extracted with absolute ether (40 ml) and after concentration the product was crystallized from CCl_4—heptane. We obtained (Xa) (1.92g) (Table 1).

cis-Ethyl Methyl 1-Methoxyaziridine-2,2-dicarboxylate (XIa). A solution of (Xa) (0.95 g) in ether (10 ml) at 0°C was treated with an ethereal solution of diazomethane until the yellow color persisted. Removal of the solvent and distillation gave (XIa) in quantitative yield (Table 1). We prepared (I) in ~100% yield similarly from (Xa) and diazoethane.

CONCLUSIONS

1. We have synthesized 1-alkoxyaziridine-2,2-dicarboxylic esters by reaction of alkoxyamines with diethyl α,β-dibromomethylmalonate and studied their PMR and mass spectra.

2. We have established the trans-stereospecificity of the amination and saponification of 1-alkoxyaziridine-2,2-dicarboxylic esters.

3. We have studied the kinetics of the equilibrium cis—trans isomerization of unsymmetrically substituted derivatives of 1-alkoxyaziridine-2,2-dicarboxylic acids.

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INTERACTION OF 1-METHYLENE-3,5,7-TRIMETHYL-2,4,6,8-TETRATHIA-PROTOADAMANTANE WITH THIOACETIC ACID

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Continuing the investigation of the structural conversions of 2,4,6,8-tetrathiaadamantanes and 2,4,6,8-tetrathiaprotoadamantanes, we studied the inberaction of 1-methylene-3,5,7-trimethyl-2,4,6,8-tetrathiaprotoadamantane (I) [1] with thioacetic acid (TAA). It was established that I reacted with TAA under mild conditions in the absence of catalysts and initiators to give three isomeric thiolacetates. Thus, by reacting equimolar amounts of TAA and olefin I in ether, thiolacetate II is formed as the only reaction product. The structure of the latter compound is deduced from its PMR spectrum showing a singlet for the three CH_3 groups (δ 1.56 ppm) and a singlet for the two protons of the CCH_2S group (δ 3.41 ppm). Thiolacetate II is a product of the anti-Markovnikov-rule addition of TAA and a rearrangement of 2,4,6,8-tetrathiaprotoadamantane into 2,4,6,8-tetrathiaadamantane. This new arrangment allowed for the first time the preparation of the 1,3,5,7-tetramethyl-2,4,6,8-tetrathiaadamantane derivatives substituted at the CH_3 group. Contrary to the rearrangments involving Cl^- or OH^- anions [1, 2], the rearrangement leading to thiolacetate II proceeds with a proton displacement.

By reacting olefin I with a threefold molar excess of TAA in ether, a mixture of thiolacetates II and III is obtained in a 1:1 ratio. The structure of thiolacetate III, an unrearranged product of the anti-Markovnikov-rule TAA addition, is confirmed by the PMR spectrum.

By the interaction of olefin I with a fourfold molar excess of TAA in the absence of the solvent at about 20°C thiolacetate IV is formed as the Markovnikov-rule addition product of TAA. Its characteristics, obtained by GLC, IR spectra and PMR spectra are completely identical with those obtained for the reaction product of TAA with 1-chloro-1,3,5,7-tetramethyl-2,4,6,8-tetrathiaprotoadamantane [3]. In a series of experiments* thiolacetate IV was obtained as the only product, whereas in other experiments a mixture of thiolacetates II and III was obtained in ratios of 1:1.3 up to 1:2 and contained $\leq$6% of IV. The reaction of I with an excess of TAA at the boiling point yields a mixture of II (35-70%), III (5-15%), and IV (15-60%).†

It is apparent that, in the reaction of TAA with olefins in the absence of catalysts and initiators, an ionic TAA addition following the Markovnikov rule can take place along with a free-radical addition leading to the anti-rule addition products. Traces of contaminants (peroxides, sulfur) as well as light and oxygen can exert a substantial influence on

*Experiments were simultaneously carried out under identical conditions in dull winter days. In another series of experiments, performed in sunny summer days, only II and III were obtained.

†In a series of simultaneous experiments.

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