SYNTHESIS AND REDUCTION OF DERIVATIVES OF AZIRIDINEMONO- AND -DICARBOXYLIC ACIDS

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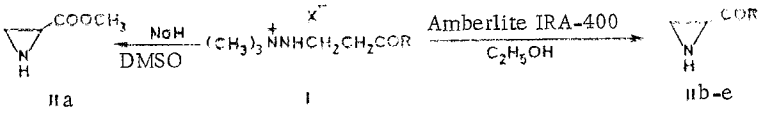
Amides and esters of aziridine-2-carboxylic acid were synthesized by the reaction of 1,1,1-trimethyl-2-(2-carboxyethyl)hydrazinium derivatives with an anion-exchange resin or with sodium hydride. Enamines were obtained from 1,1,1-trimethyl-2-[1,2-bis(alkoxycarbonyl)ethyl]hydrazinium salts and basic agents. Methods for the synthesis of amides of aziridine-2,2- and aziridine-2,3-dicarboxylic acids were developed. The stereochemistry of the esters and amides of aziridine-2,3-dicarboxylic acids was established. Dialkylcarbamoylaziridines were reduced with lithium aluminum hydride to 2-(N,N-dialkylaminomethyl)aziridines. The reduction of esters of aziridine-2-carboxylic acid and their functionally substituted derivatives leads to the formation of 2-hydroxymethylaziridines. An O-silylation product was obtained by silylation of 2-hydroxymethylaziridine.

Derivatives of aziridinecarboxylic acids have found application as anticancer and immunostimulating agents [1, 2]. The aim of the present research was to obtain analogs of the known anticancer agent 1,2-dicarbamoylaziridine [2]. We have previously shown that aziridine-2-carboxylic acid derivatives are formed in the reaction of substituted (in the ethyl group) 1,1,1-trimethyl-2-ethylhydrazinium salts I with sodium methoxide in methanol [3]. Aziridine-2-carboxylic acid derivatives were also obtained from dibromopropionic acid derivatives [4].

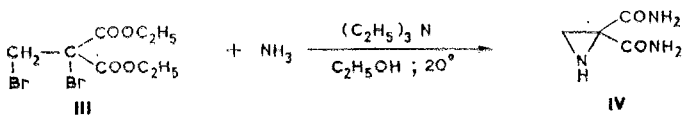
In order to develop a method for the synthesis of derivatives of 1H-aziridinemono- and -dicarboxylic acids we carried out reactions involving cyclization of 1,1,1-trimethyl-2-[2-(alkoxycarbonyl)ethyl]- and -2-(carbamoylethyl)hydrazinium salts under various conditions. The reaction of ester Ia with sodium hydride in DMSO leads to the formation of 2-methoxycarbonylaziridine (IIa), which, however, upon distillation forms an azeotropic mixture with DMSO. Ester IIa cannot be completely freed of DMSO by the freezing-out technique. We therefore used the reaction of alcohol solutions of amides Ib-e with strongly basic anion-exchange resins for the synthesis of aziridine-2-carboxylic acid amides; amides IIb-e are formed in 80-90% yields in this case, whereas the yield of diethylamide IIb is 56% by the method in [3].



IIa I IIb-e

II b $R=N(C_2H_5)_2$; c $R=N(C_4H_9)_2$; d $R=NHC_2H_5$; e $R=NH_2$

The literature contains information indicating that diethyl aziridine-2,2-dicarboxylate was obtained by the reaction of dibromo derivative III with ammonia [5]; experimental data are not presented in [5]. When we carried out the reaction in the presence of triethylamine, we obtained exclusively aziridine-2,2-dicarboxamide (IV) in good yield.



III IV

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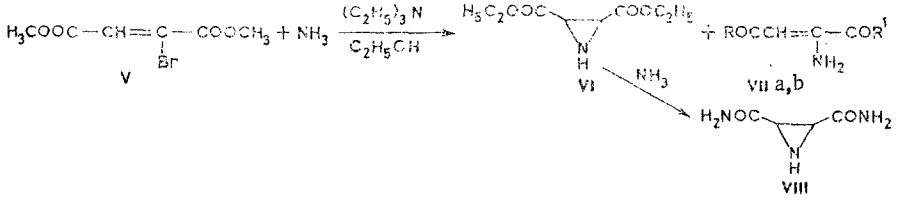
TABLE 1. Parameters of the ^1H and ^{13}C NMR Spectra of the Aziridines

Compound	R	R¹	R²	Solvent	^1H chemical shifts,[a] δ, ppm					^{13}C chemical shifts, δ, ppm		
					3-H	R	R¹	R²	NH	$C_{(2)}$	$C_{(3)}$	remaining C
IIa	H	$COOCH_3$	H	CCl_4	1,89	1,73	3,70	2,47	1,1			
IIb	H	$CON(C_2H_5)_2$	H	CCl_4	1,57	1,62	3,40 and 3,48 (CH_2); 1,22 and 1,06 (CH_3)	2,43	2,2			
IIc	H	$CON(C_4H_9)_2$	H	CCl_4	1,5	1,5	3,4 (α-CH_2); 1,3—2,0 (β,γ-CH_2); 0,98 (CH_3)	2,45	2,2			
IId	H	$CONHC_2H_5$	H	DMSO	1,68	1,68	3,2 (CH_2); 1,11 (CH_3); 3,0 (NH)	2,25	1,1			
IIe	H	$CONH_2$	H	DMSO	1,48	1,58	7,7 and 7,2	2,26	1,0			
IV	H	$CONH_2$	$CONH_2$	DMSO	1,74	2,03	7,4 and 7,1	8,5 and 7,7	2,3	38,1	34,6	172,7 and 169,3 (C=O)
VI	$COOC_2H_5$	H	$COOC_2H_5$	$CDCl_3$	2,90	4,26 (CH_2); 1,33 (CH_3)	2,90	4,26 (CH_2) 1,33 (CH_3)	1,8	36,4	36,4	170,1 (CO); 62,5 (CH_2); 14,6 (CH_3)
VIII	$CONH_2$	H	$CONH_2$	DMSO	2,48	7,5 7,1	2,48	7,5 and 7,1	2,1	35,7	35,7	170,8 (CO)

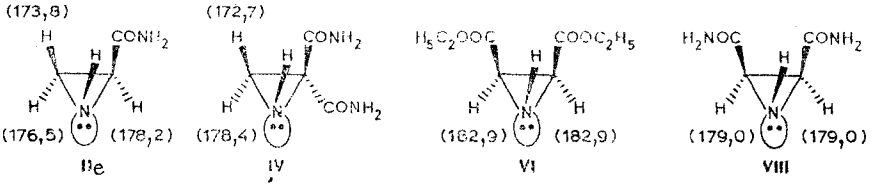
[a]Note: $^2J_{23} \approx 1.7$, $^3J_{23}^{cis} \approx 5.2$, and $^3J_{23}^{trans} \approx 3.1$ Hz.

It has been reported [6] that the reaction of diethyl dibromosuccinate with ammonia leads to diethyl aziridine-2,3-dicarboxylate. Berlin and co-workers [6] indicate the formation of trans-diester VI. Furukawa and co-workers [7] proved the trans configuration by studying the NMR spectra of 1-chloro-2,3-dimethoxycarbonylaziridine [7]. We obtained diester VI from dimethyl ester V in ethanol.



VII a R=OCH_3, R^1=OC_2H_5; b R=NH_2, R^1=OCH_3

Diamide VIII was obtained by ammonolysis of diester VI in ethanol at room temperature.



The structures of the synthesized compounds were proved by NMR spectroscopy (see Table 1). It is of particular interest to establish the stereochemistry of VI and VIII, as well as the orientation of the NH proton of the aziridine ring. These problems were solved by means of the $^1J_{^{13}C-H}$ values for the ring carbon atoms (the J values in hertz are given in parentheses).

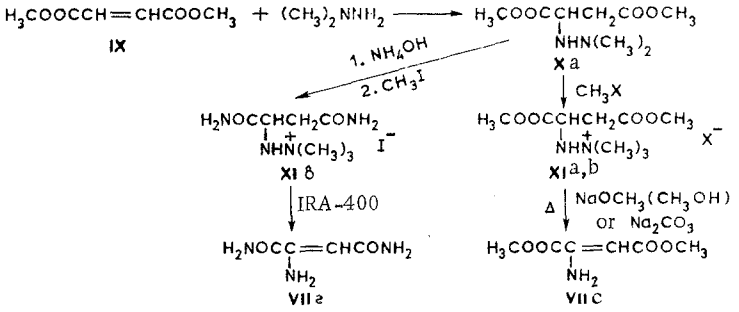
In the spectrum of IV, which may serve as a model for aziridines VI and VIII, both $^1J_{^{13}C-H}$ values are split markedly; in analogy with alkylaziridines [8, 9], the larger value corresponds to coupling with the proton in a trans orientation with respect to the ring NH proton. An analysis of the temperature dependence of the PMR spectrum of amide IV provides evidence for a significant barrier to inversion of the nitrogen atom in this compound ($\Delta G_{340}^{\neq}$ = 18.1 ± 0.3 kcal/mole). In the spectrum of IIe, judging from the ring $^1J_{^{13}C-H}$ values, the NH proton is cis-oriented relative to the $CONH_2$ group. In ester VI and amide VIII molecules $^1J_{^{13}C-H}$ = 179-183 Hz. Aziridines VI and VIII are therefore cis isomers with an NH hydrogen atom that is also oriented to favor both cis substituents. The preferableness of this orientation of the NH proton is due to an intramolecular hydrogen bond of the latter

TABLE 2. Parameters of the PMR Spectra of Aminobutenedioic Acid Derivatives $RCOCH=C(NH_2)COR^1$

Compound	R	R'	Solvent	δ, ppm			
				CH	NH_2	R	R'
VIIa	OCH_3	OC_2H_5	$CDCl_3$	5,49	6,4	3,69	4,27 (CH_2) 1,27 (CH_3)
VIIb	OCH_3	NH_2	DMSO	5,08	7,1	3,56	7,8 and 7,5
VIIc	OCH_3	OCH_3	$CDCl_3$	5,49	6,4	3,69	3,83
VIId	NH_2	NH_2	DMSO	4,97	6,5	7,6 and 7,3	7,6 and 7,3

with the CO group of the substituent. Evidence for this is provided by the small effect of the temperature on the chemical shift of the NH resonance, which is characteristic for an intramolecular hydrogen bond ($\Delta\delta/\Delta t = 0.7 \cdot 10^{-3}$ ppm/deg). It is apparent that the pronounced difference in the chemical shifts for the NH protons of the geminal $CONH_2$ groups in aziridine can also be explained by the existence of a hydrogen bond, inasmuch as the measured barriers to rotation relative to the amide bond differ only slightly ($\Delta G_{353}^{\neq} = 17.4 \pm 0.3$ kcal/mole for cis-$CONH_2$ and $\Delta G_{343}^{\neq} = 17.2 \pm 0.3$ kcal/mole for trans-$CONH_2$). This may also explain the appreciable difference in the ^{13}C chemical shifts of the CO group for aziridine IV (Table 1).

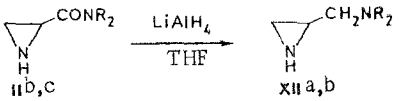
The preparation of aziridine-2,3-dicarboxylic diesters is fraught with experimental difficulties in the separation of the products of ring-chain isomerization, as, for example, in the case of VI and VII, which are formed both by the method in [6] and by the reaction of dimethyl maleate with N-unsubstituted diphenylsulfimine [7]. To solve this problem we studied the cyclization of succinic acid derivatives XIa-c by means of various cyclizing agents. Starting diesters XIa, b were obtained by the reaction of derivatives of maleic or fumaric acid with excess 1,1-dimethylhydrazine with subsequent alkylation of adduct X. Diamide XIc with prepared by ammonolysis of adduct Xa with subsequent alkylation of the resulting diamide Xb. We showed that heating succinic acid derivatives XIa-c with sodium methoxide for 20 h leads to the formation of enamines VIIc, d. The presence of aziridine derivatives was not recorded in the reaction mixture. A similar reaction pathway was also observed in the reaction of salts XIa-c with other basic agents. Thus enamines VIIc, d were also obtained when esters XIa, b were heated in the presence of potassium carbonate or when amide XIc was treated with the strongly basic anion-exchange resin IRA-400.



XI a X=I; b X=Br

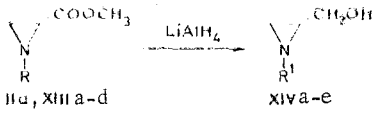
N-Substituted 2-aziridinylcarbinols were obtained by reduction of esters of N-alkyl- and N-arylaziridine-2-carboxylic acids at room temperature or at higher temperatures [10, 11]. It has been reported [12] that a similar reaction at −70°C gave aldehydes, which were isolated in the free form and characterized by conversion to imines and hydrazones. 1H-Aziridin-2-ylcarbinols are formed from α-ketoximes in the Grignard reaction [13]. However, the reactions of esters and amides of aziridine-2-carboxylic acid, as well as its N-functionally substituted derivatives, which could lead to similar derivatives by a simpler pathway, have not been previously studied.

We have shown that 2-dialkylcarbamoylaziridines IIb, c in refluxing tetrahydrofuran (THF) react readily with lithium aluminum hydride to give the previously unknown aziridinylmethylamines XIIa, b.



XII a $R=C_2H_5$; b $R=C_4H_9$

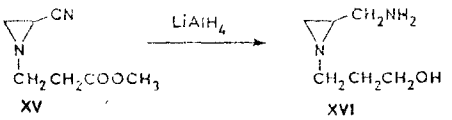
The reduction of 2-methoxycarbonylaziridine (IIa) was carried out with various reducing agents. Only starting ester IIa was isolated from the reaction mixture after heating ester IIa with sodium borohydride in methanol or in polyethylene glycol. The reduction of ester IIa with lithium aluminum hydride at 35-40°C in ether or THF leads to the formation of 2-hydroxymethylaziridine (XIVa) in good yield. Other aziridinylcarbinols and aziridinyldicarbinols were similarly obtained.



IIa $R=H$; XIII a $R=CH_3$; b $R=COOCH_3$; c $R=CH_2CH_2COOCH_3$; d $R=CH_2CH_2CN$;
XIV a $R^1=H$; b $R^1=CH_3$; c $R^1=CH_2OH$; d $R^1=CH_2CH_2CH_2OH$; e $R=CH_2CH_2CH_2NH_2$

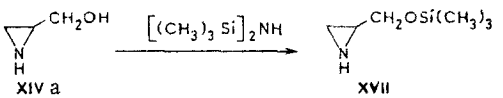
Carbinols XIVa-e are viscous high-boiling liquids that are stable at room temperature. In the reduction of diester XIIIb we isolated dicarbinol XIVc, the structure of which was proved by PMR spectroscopy. This glycol was found to be thermally unstable and was converted to carbinol XIVa during distillation.

The reduction of nitrile XV under the conditions described above led to the formation of amino alcohol XVI.



The structures of carbinols XIVa-d and aminocarbinols XIVe and XVI were established by NMR spectroscopy.

Acyclic amino alcohols are silylated more readily at the oxygen atom than at the nitrogen atom by various silylating agents [14, 15]. In a continuation of our systematic study of the reactivities of amino alcohol [16] we investigated the silylation of the previously unknown aziridinylcarbinols XIV. To exclude the acidic polymerization of the aziridine ring we used hexamethyldisilazane as the silylating agent. The reaction proceeds at room temperature without a solvent in excess hexamethyldisilazane and leads to the formation of O-silylated aziridines such as XVII.



EXPERIMENTAL

The ^1H and ^{13}C NMR spectra were recorded with Perkin-Elmer R12A (60 MHz) and Brucker WH 90/DS (90 MHz) spectrometers with hexamethyldisiloxane and cyclohexane (δ 27.44 ppm) as the internal standards for the ^1H and ^{13}C spectra, respectively. The IR spectra of mineral oil suspensions were recorded with a UR-20 spectrometer. The melting points were determined with a Kofler microscope stage.

2-Methoxycarbonylaziridine (IIa). A 28.6-g (0.1 mole) sample of salt Ia was added dropwise to a suspension of 3.6 g (0.15 mole) of sodium hydride in 20 ml of absolute DMSO, during which the liberation of trimethylamine was observed. The mixture was heated on a water bath for 4 h and treated with 750 ml of ether. The solvent was evaporated at reduced pressure and room temperature, and the residue was distilled at reduced pressure with collection of the fraction with bp 56-62°C (8 mm). Freezing at −10°C led to 2-methoxycarbonylaziridine, which contained DMSO in a ratio of 1:1 (73% yield). The PMR spectra are presented in Table 1.

TABLE 3. Aziridine-2-carboxylic Acid Amides

Compound	bp, °C (mm)	n_D^{20}	Found, %			Empirical formula	Calc., %			Yield, %
			C	H	N		C	H	N	
IIb	74 (2)	1,4725	59,7	9,9	19,1	$C_7H_{14}N_2O$	59,2	9,9	19,8	95[a]
IIc	130 (6)	1,4677	66,2	11,3	14,0	$C_{11}H_{22}N_2O$	66,7	11,1	14,1	98
IId	100 (3)	1,4659	52,4	8,5	24,8	$C_6H_{10}N_2O$	52,6	8,8	24,5	92
IIe	132,5—133[b]	—	41,7	6,6	36,2	$C_3H_6N_2O$	41,8	6,8	36,4	78

[a]According to the data in [3], this compound was obtained in 56% yield. [b]This is the melting point; according to the data in [10], this compound had mp 116-118°C.

TABLE 4. Derivatives of 2-Substituted Succinic Acids

Compound	mp, °C	Found, %			Empirical formula	Calc., %			Yield, %
		C	H	N		C	H	N	
Xa	91—94 (2)[a]	46,7	8,1	13,2	$C_8H_{17}N_2O_4$	46,8	8,3	13,6	83
XIa	113	31,0	5,4	7,9	$C_9H_{19}IN_2O_4$	31,2	5,5	8,1	87
XIb	110—111	35,9	6,4	9,3	$C_9H_{19}BrN_2O_4$	36,1	6,4	9,4	92
XIc	163—164	27,8	5,2	21,7	$C_7H_{17}IN_2O_4$	26,6	5,4	17,7	78

[a]This is the boiling point; n_D^{20} 1.4448.

General Method for the Preparation of N-Substituted 2-Carbamoylaziridines (IIb-e). A solution of 0.2 mole of salt Ib-e in 500 ml of absolute methanol was passed through a column packed with Amberlite IRA-400 anion-exchange resin that had been rendered throughly anhydrous with absolute ethanol by elution with 700 ml of absolute ethanol, and the eluates were combined. The solvent was evaporated at reduced pressure, and the residue was fractionated at reduced pressure (IIb-d) or crystallized from ethanol (IIe). The physicochemical characteristics of the compounds obtained are presented in Tables 1 and 3.

2,2-Dicarbamoylaziridine (IV). A solution of 13.6 g of dibromo derivative III in 80 ml of absolute ethanol was cooled to 0°C and saturated with 10.0 g (0.6 mole) of ammonia, after which 5.6 ml (40 mmole) of triethylamine was added dropwise with stirring to the solution, and the mixture was stirred at 20°C for another 12 h. The precipitate was removed by filtration, the filtrate was evaporated to dryness, and the residue was treated with acetonitrile. The precipitate was removed by filtration, and both precipitates were combined, dissolved in aqueous alcohol, and passed through a column packed with the strongly basic Amberlite IRA-400 anion-exchange resin. The solvents were evaporated to give 3.5 g (66%) of diamide IV with mp 167-168°C (from ethanol or water). The parameters of the ^1H and ^{13}C NMR spectra are presented in Table 1. IR spectrum (in mineral oil): 1675 and 1690 (C=O); 3280, 3350, and 3425 cm^{-1} (NH). Found: C 37.6; H 5.4; N 32.4%. $C_4H_7N_3O_2$. Calculated: C 37.2; H 5.5; N 32.5%.

cis-2,3-Dicarbamoylaziridine (VIII). A solution of 0.8 g (4 mmole) of diester VI [6] in 25 ml of ethanol was saturated with ammonia at room temperature, after which the mixture was allowed to stand at 20°C for 24 h. The solvent was evaporated to dryness to give 0.5 g (96%) of diamide VIII with mp 187-188°C (from ethanol). The parameters of the NMR spectra are presented in Table 1. Found: C 37.2; H 5.7; N 32.3%. $C_4H_7N_3O_2$. Calculated: C 37.2; H 5.5; N 32.5%.

Dimethyl (2,2-Dimethylhydrazino)succinate (Xa). A) A 158-g (2.63 moles) sample of 1,1-dimethylhydrazine was added to 100 g (0.69 mole) of dimethyl maleate, and the mixture was heated on a water bath for 3 h. The excess dimethylhydrazine was removed by distillation at reduced pressure, and the residue was distilled.

B) A 45.3-g (0.75 mole) sample of 1,1-dimethylhydrazine was added with stirring to a suspension of 99 g (0.69 mole) of dimethyl fumarate in 50 ml of methanol, and the mixture was heated on a water bath for 4 h. The unchanged dimethylhydrazine and methanol were removed by distillation at reduced pressure and room temperature, and the residue was distilled *in vacuo* to give 65 g (47%) of a colorless liquid with bp 90-93°C (1.5 mm) and n_D^{20}

TABLE 5. Parameters of the PMR Spectra of 1,2-Disubstituted Aziridines

Compound	X	R	Solvent	δ, ppm								J, Hz				
				H_a	H_b	H_c	CH_2	R			X	$^3J_{12}$	$^3J_{13}$	$^2J_{23}$	$^3J_{1\text{-}CH_2}$	$^2J_{CH_2X}$
								H_α	$H_{\beta,\gamma}$	H_δ						
XIIa	$N(C_2H_5)_2$	H	CCl_4	1,90	1,57	1,18	2,4	0,4	—	—	2,54 (CH_2) 0,99 (CH_3)	5,6	3,1	0	6,1	—
XIIb	$N(C_4H_9)_2$	H	CCl_4	1,90	1,6	1,2	2,4	0,8	—	—	1,1—2,3 (CH_2); 0,9 (CH_3)	5,4	2,9	0	—	—
XIVa	OH	H	$CDCl_3$	2,28	1,84	1,53	3,33 и 3,83	—	—	—	—	5,9	3,3	0	6,1 and 3,3	12,0
XIVb	OH	CH_3	D_2O	1,54	1,18	1,65	3,18 и 3,69	2,30	—	—	—	5,7	2,9	0	5,8 and 2,4	11,6
XIVc	OH	CH_2OH	D_2O	1,90	1,57	1,62	3,40 и 3,57	3,93	—	—	—	6,0	3,0	0	5,4 and 5,4	11,3
XIVd	OH	$(CH_2)_3OH$	$CDCl_3$	1,63	1,32	1,69	3,25 и 3,74	2,4	1,76	3,74	4,2	5,8	2,9	0	6,6 and 2,8	11,8
XIVe	OH	$(CH_2)_3NH_2$	D_2O	1,6	1,82	1,42	3,34 и 3,60	2,3	1,64	2,64	—	5,7	3,0	0	6,2 and 4,6	11,6
XVI	NH_2	$(CH_2)_3OH$	$CDCl_3$	1,45	1,22	1,64	2,83 и 2,46	2,35	1,73	3,77	2,3	5,9	2,8	0	3,6 and 3,6	13,3
XVII	$OSi(CH_3)_3$	H	$CDCl_3$	2,13	1,69	1,49	3,40	—	—	—	—	5,3	2,8	0	4,0	—

TABLE 6. 1,2-Disubstituted Aziridines

Compound	bp, °C (mm)	n_D^{20}	Found, %			Empirical formula	Calc., %			Yield, %
			C	H	N		C	H	N	
XIIa	30 (1)	1,4579	66,0	12,8	21,9	$C_7H_{16}N_2$	65,6	12,6	21,8	75
XIIb	90 (5)	1,4558	71,3	13,2	15,0	$C_{11}H_{24}N_2$	71,8	13,0	15,3	85
XIVa	45 (0,005)[a]	1,4658	49,1	9,2	19,1	C_3H_7NO	49,3	9,7	19,2	52
XIVb	42 (3)[b]	—	54,8	10,2	15,8	C_4H_9NO	55,1	10,4	16,1	75
XIVd	100 (0,003)[a]	1,4760	54,5	9,7	10,3	$C_6H_{13}NO_2$	54,9	10,0	10,7	50
XIVe	125 (0,002)[a]	1,4786	55,1	10,6	21,0	$C_6H_{14}N_2O$	55,4	10,8	21,5	48
XVII	56 (12)	1,4288	49,4	10,0	9,5	$C_6H_{15}NOSi$	49,6	10,4	9,6	65

[a]These are the bath temperatures. [b]According to the data in [11], this compound was obtained in 70% yield and had bp 40°C (2.5 mm).

1.4448. PMR spectrum (in DMSO): δ 2.35 [6H, s, $N(CH_3)_2$], 2.60 (2H, dd, J = 6.0 Hz, CH_2), 2.9 (1H, s, NH), 3.60 and 3.78 (3H, and 3H, s, OCH_3), and 3.80 ppm (1H, d, J = 6.0 Hz, CH).

(2,2-Dimethylhydrazino)succinic Acid Diamide (Xb). A mixture of 51 g of ester Xa and 350 ml of 25% ammonium hydroxide was heated on a water bath for 3 h, after which the solvent was removed by distillation at reduced pressure to give a glassy mass.

1,1,1-Trimethyl-2-[1,2-bis(methoxycarbonyl)ethyl]hydrazinium Iodide (XIa). A 17.0-g (0.12 mole) sample of methyl iodide was added to a solution of 20.5 g (0.1 mole) of diester Xa in 200 ml of absolute ethanol, and the mixture was heated on a water bath for 2 h. It was then cooled, and the precipitate was recrystallized from ethanol or ethanol–ethyl acetate (Table 4).

1,1,1-Trimethyl-2-[1,2-bis(methoxycarbonyl)ethyl]hydrazinium Bromide (XIb, Table 4). An 11.4-g (0.12 mole) sample of cooled methyl bromide was added to a solution of 20.5 g (0.1 mole) of diester Xa in 200 ml of absolute ethanol, and the mixture was heated on a water bath for 2 h. The mixture was cooled, and the precipitate was recrystallized from ethanol. PMR spectrum (in D_2O): δ 2.98 (2H, dd, J = 5.6 Hz, CH_2), 3.43 [9H, s $(CH_3)_3\overset{+}{N}$], 3.75 and 3.86 (3H and 3H, s, OCH_3), and 4.55 ppm (1H, dd, J = 5.6 Hz, CH).

1,1,1-Trimethyl-2-[1,2-bis(carbamoyl)ethyl]hydrazinium Iodide (XIc, Table 4). A 17.0 g (0.12 mole) sample of methyl iodide was added to a solution of 17.5 g (0.1 mole) of diamide Xb in 200 ml of absolute ethanol, and the mixture was heated on a water bath for 2 h. It was then cooled, and the precipitate was recrystallized from ethanol. PMR spectrum (in DMSO): δ 2.33 (2H, dd, J = 6.1 Hz, CH_2), 3.20 [9H, s, $(CH_3)_3\overset{+}{N}$], 4.16 (1H, m, CH), 6.5 (1H, d, J = 6.3 Hz, NH), 7.3 and 7.6 (2H, s, $CONH_2$), and 6.9 and 7.3 ppm (2H, s, $CONH_2$).

2-Aminobutenedioic Acid Diamide (VIId). A solution of 12.0 g (32 mmole) of diamide XIc in 80 ml of water was passed through a column packed with the strongly basic IRA-400 anion-exchange resin. A 1.2-g (27%) sample of a colorless precipitate with mp 225°C (dec., from water) (mp 208-209°C [18]) formed from the aqueous solution. The parameters of the PMR spectra are presented in Table 2. Found: C 37.8; H 5.3; N 32.9%. $C_4H_7N_3O_2$. Calculated: C 37.2; H 5.5; N 32.5%.

Dimethyl 2-Aminofumarate (VIIc). A mixture of 60 g (0.2 mole) of thoroughly ground diester XIc and 41.4 g (0.3 mole) of potassium carbonate was heated in a rotary evaporator flask at 150°C. The distillate was collected, and the aqueous layer was frozen. The organic phase was triturated to accelerate crystallization. Workup gave 12.5 g (39%) of colorless crystals with mp 91-92°C (from ethanol) (mp 90-92°C (for the E isomer) and mp 30-32°C (for the Z isomer) [19]). The parameters of the PMR spectrum are presented in Table 2. Found: C 45.0; H 5.6; N 8.7%. $C_6H_9NO_4$. Calculated: C 45.3; H 5.7; N 8.8%.

General Method for the Preparation of 2-Dialkylaminomethylaziridines (XIIa, b). A solution of 0.2 mole of amide IIb, c in 100 ml of dry THF was added dropwise to a solution of 0.25 mole of lithium aluminum hydride in 250 ml of THF, and the mixture was refluxed with stirring for 20 h. The calcium chloride tube was removed, and the mixture was refluxed for another 10 h. Water (20 ml) was added dropwise, the mixture was filtered, and the precipitate was washed with methanol. The filtrates were combined, dried with anhydrous sodium sulfate, and distilled at reduced pressure. The physicochemical characteristics and parameters of the PMR spectra are presented in Tables 5 and 6.

General Method for the Preparation of 2-Hydroxymethylaziridines (XIVa-e). A solution of 0.1 mole of aziridines IIa and XIIIa in 20 ml of dry ether or a solution of 0.07 mole of aziridines XIIIb-d in 20 ml of dry ether or THF was added dropwise with stirring to a suspension of 7.6 g (0.2 mole) of lithium aluminum hydride in 200 ml of dry ether, the temperature of the reaction mixture was raised to 35-40°C, and the mixture was stirred at the indicated temperature for another 6 h. It was then cooled slowly, and 15 ml of water was added slowly dropwise. The mixture was poured into a chromatographic column and washed with 500 ml of THF, and the combined extracts were dried with anhydrous sodium sulfate and distilled at reduced pressure (Tables 5 and 6).

1-(3-Hydroxypropyl)-2-aminomethylaziridine (XVI). This compound was obtained from nitrile XV by a method similar to the procedure used to prepare carbinols XIVa-e. The parameters of the spectra are presented in Table 5.

2-(Trimethylsiloxymethyl)aziridine (XVII). A 7.26-g (45 mmole) sample of hexamethyldisilazane was added to 1.46 g (20 mmole) of 2-hydroxymethylaziridine (XIVa), and the mixture was stirred at room temperature for 48 h. The unchanged hexamethyldisilazane was removed by distillation, and the residue was distilled at reduced pressure (Tables 5 and 6).

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