AZIDES OF N-SUBSTITUTED AZIRIDINE-2-CARBOXYLIC ACIDS. REACTION WITH METHYL ESTERS OF AMINO ACIDS

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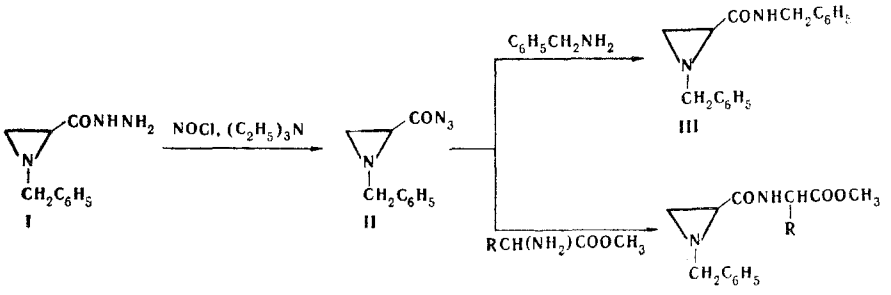
The corresponding azide was obtained by nitrosation of 1-benzylaziridine-2-carboxylic acid hydrazide. Reaction of the azide with methyl esters of amino acids gave N-(1-benzyl-2-aziridinylcarbonyl)-substituted methyl esters of amino acids.

Acyl azides are extremely reactive compounds, on the basis of which organic substances of various classes can be obtained [1]. For the first time in the aziridinecarboxylic acid series we have obtained an azide, viz., 1-benzylaziridine-2-carboxylic acid azide (II).

Because of the instability of the aziridine ring in acidic media [2] the selection of known [1] methods for the preparation of acyl azides is extremely limited. We used a method involving the synthesis of acyl azides through the corresponding hydrazides [3]; for this, we selected nitrosyl chloride as the nitrating agent.



IV a R=H; b R=Me; c R=*i*-Pr; d R=CH_2Ph; e R=$CH_2C_6H_4OH$-*p*; f R=$CH_2CH_2SCH_3$; g R=CH_2COOMe; h R=CH_2CH_2COOMe

As expected, azide II proved to be unstable, and it was therefore used in the subsequent reactions without isolation from the reaction mixture. The IR spectrum of azide II contains the characteristic absorption band of an azido group at 2160 cm^{-1}. To identify azide II we carried out the reaction with benzylamine [4]. The structure of amide III is confirmed by a comparison of the physicochemical characteristics with those of a sample with a genuinely known structure* and the PMR and IR spectroscopic data.

To study the reactivity of azide II we carried out the reaction with a series of methyl esters of amino acids. Since the chlorides of aziridinecarboxylic acids (like the acids themselves) are unknown, substituted amides of the IVa-h type cannot be obtained by direct acylation of amino acids, and their preparation by other methods is difficult because of the multistep nature of the synthesis. The structures of amides IVa-h are confirmed by the PMR and IR spectroscopic data (Tables 1 and 2). The signals of the protons of the aziridine ring show up in the PMR spectra of the compounds obtained as an H_A quartet and H_B and H_C doublets; this is characteristic for 1,2-substituted aziridines. The ratio of the constants of spin–spin coupling of the H_B and H_C protons makes it possible to assign the signal at stronger field to the H_B proton and the signal at weaker field to the H_C proton ($J_{cis} > J_{trans}$).

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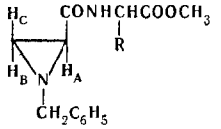
TABLE 1. Parameters of the PMR Spectra of IVa-h (CCl_4)



Compound	R	δ, ppm						
		Ph (s)	NCH_2 (s)	H_A, H_B, H_C (m)	NH (br s)	CH (m)	OMe (s)	R
IVa	H	7,27	3,47	1,73—2,28	6.91	3,89 (CH_2)	3,64	
IVb	CH_3	7,13	3,42	1,47—2,16	6,64	4,09—4,47	3,60	1,29 (3H, d)
IVc	$CH(CH_3)_2$	7,27	3,49	1,67—2,31	6,96	4,24—4,51	3,67	1,96—2,31 (1H, m), 0,69—1,01 (6H, m)
IVd	CH_2Ph	7,07	3,33	1,37—2,12	6,53	4,27—4,73	3,49	7,07—6,99 (5H, m), 2,89 (2H, d)
IVe	$CH_2C_6H_4OH$-*p*	7,22	3,39	1,58—2,19	7,00	4,84—4,50	3,61	6,47—7,00 (4H, m), 2,90 (2H, d)
IVf	$CH_2CH_2SCH_3$	7,25	3,46	1,60—2,22	6,99	4,40—4,71	3,66	2,22—2,50 (4H, m), 1,89 (3H, s)
IVg	CH_2COOMe	7,26	3,49	1,61 –2,20	7,26	4,56—4,83	3,65	2,79 (2H, q), 3,59 (3H, s)
IVh	CH_2CH_2COOMe	7,26	3,44	1,62 –2,40	6,93	4,32—4,63	3,66	1,84 (4H, m), 3,58 (3H, s)

TABLE 2. Characteristic Frequencies (cm^{-1}) in the IR Spectra of IVa-h

Compound	ν_{CH} (aziridine ring)	δ (aziridine ring)	ν CONH	ν COOMe
IVa	3040, 3075	1210	1695	1760
IVb	3040, 3085	1210	1690	1745
IVc	3040, 3075	1210	1690	1740
IVd	3035, 3075	1210	1690	1750
IVe	3045, 3080	1210	1680	1750
IVf	3030, 3070	1230	1680	1740
IVg	3030, 3065	1210	1685	1740
IVh	3035, 3070	1210	1690	1750

EXPERIMENTAL

The PMR spectra of 10% solutions of the compounds in CCl_4 were obtained with a Perkin-Elmer R-12A spectrometer (60 MHz) with tetramethylsilane as the internal standard. The IR spectra of solutions of the compounds in CCl_4 (0.01 mole/liter) were obtained with a UR-20 spectrometer.

1-Benzylaziridine-2-carboxylic Acid Azide (II). A solution of 0.66 g (0.01 mole) of nitrosyl chloride [6] in 10 ml of absolute dioxane was added with stirring at −20°C in the course of 10 min to a mixture of 1.97 g (0.01 mole) of 1-benzylaziridine-2-carboxylic acid hydrazide [5] and 1.4 ml (0.01 mole) of triethylamine in 50 ml of absolute ether, and the resulting mixture was stirred at the same temperature for 15 min. The precipitated triethylamine hydrochloride was removed by filtration. Because of its instability in the pure form, the resulting solution of azide II was used directly for the subsequent reaction with the methyl esters of amino acids. For the investigation of azide II, the solution was evaporated, and the residue (light-yellow oil) was dissolved in CCl_4. IR spectrum: 2160 (N_3) and 1750 cm^{-1} (C=O).

1-Benzylaziridine-2-carboxylic Acid Benzylamide (III). A 1.0-ml (0.01 mole) of benzylamine was added to a solution of azide II, and the reaction mixture was allowed to stand at 0°C for 12 h. It was then evaporated, and the residue was poured into water. The resulting oil subsequently crystallized and was recrystallized from aqueous ethanol (1:1) to give 0.5 g (20%) of amide III with mp 99°C. PMR spectrum: 1.58-2.29 (3H, m, 2-H, 3-H), 3.51 (2H, s, 1-CH_2), 4.18 [2H, d, CH_2 (amide)], 6.87-7.38 (10H, m, 2Ph), and 8.00 ppm (1H, broad s, NH). IR spectrum: 1220 (aziridine ring), 1670 (C=O), 3250 cm^{-1} (NH). Found: C 77.1; H 7.0; N 10.9%. $C_{17}H_{18}N_2O$. Calculated: C 76.7; H 6.8; N 10.5%.

N-(1-Benzyl-2-aziridinyl-carbonyl)amino Acid Methyl Esters (IVa-h, Table 3). A solution of 0.01 mole of the methyl ester of the corresponding amino acid in 5 ml of absolute ether

TABLE 3. N-(1-Benzyl-2-aziridinyl-carbonyl)amino Acid Methyl Esters (IVa-h)

Compound	R_f	Found, %			Empirical formula	Calculated, %			Yield, %
		C	H	N		C	H	N	
IVa	0,48	62,5	6,7	10,9	$C_{13}H_{16}N_2O_3$	62,9	6,5	11,3	10
IVb	0,75	63,7	6,8	10,4	$C_{14}H_{18}N_2O_3$	64,1	6,9	10,7	15
IVc	0,72	65,8	7,5	10,1	$C_{16}H_{22}N_2O_3$	66,2	7,6	9,7	12
IVd	0,60	70,8	6,3	8,1	$C_{20}H_{22}N_2O_3$	71,0	6,5	8,3	20
IVe	0,57	67,5	6,1	7,5	$C_{20}H_{22}N_2O_4$	67,8	6,2	7,9	18
IVf	0,55	59,1	7,2	8,8	$C_{16}H_{22}N_2O_3S$	59,6	6,8	8,7	14
IVg	0,43	59,6	6,5	8,8	$C_{16}H_{20}N_2O_5$	60,0	6,3	8,8	15
IVh	0,37	60,7	6,7	8,0	$C_{17}H_{22}N_2O_5$	61,1	6,6	8,4	10

was added to the solution of azide II obtained by the method described above, and the mixture was allowed to stand at 0°C for 12 h. The solvent was removed by distillation, and the residue was transferred to a preprepared plate with silica gel (Merck) and chromatographed in an ether—ethyl acetate system (1:1).

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SYNTHESIS OF cis-1-METHYL-2-ARYL-3-AROYLAZIRIDINES

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trans-1-Methyl-2-aryl-3-aroylaziridines readily undergo epimerization to give the corresponding cis isomers in high yields in the presence of catalytic amounts of quaternary ammonium bases (trimethylbenzylammonium or triethylmethylammonium hydroxide). The structures of the compounds obtained were established on the basis of the IR and PMR spectra and the results of elementary analysis.

3-Aroylaziridines are promising substances for the preparation of various nitrogen-containing polyfunctional organic compounds. The preparative methods for the synthesis of trans-3-aroylaziridines have undergone a great deal of development [1, 2], while very little study has been devoted to the development of methods for the preparation of the cis derivatives of aroylaziridines. The isomerization of trans-3-aroylaziridines in the presence of bases [3] evidently may serve as the most practicable method for the synthesis of cis-3-aroylaziridines. However, in the known examples of isomerization [3, 4] the cis isomers are obtained in 40-50% yields, and the reaction time reaches 7-8 days. Sodium methoxide and potassium tert-butoxide have been used as the bases. The solvents were methanol and tert-butyl alcohol, as well as alcohol—tetrahydrofuran (THF) and benzene—ether solvent mixtures.

According to [4], the isomerization of trans-3-aroylaziridines in the presence of bases to the thermodynamically more stable [4] cis isomers proceeds through a step involving the

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