REACTION OF 2-AMINOMETHYLAZIRIDINE WITH α-UNSATURATED CARBONYL COMPOUNDS

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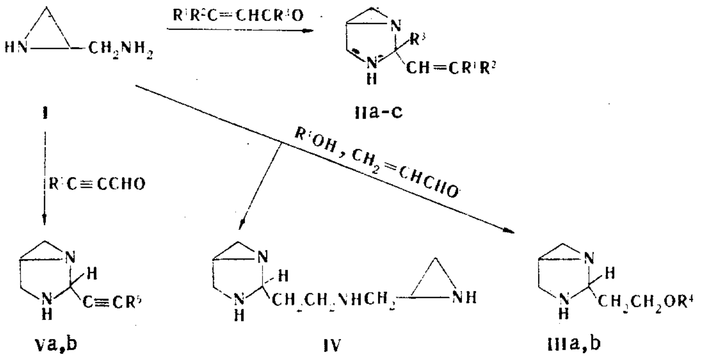
2-(Substituted vinyl)-1,3-diazabicyclo[3.1.0]hexanes are formed in the reaction of 2-aminomethylaziridine with some α-unsaturated carbonyl compounds containing a C=C bond in the α position, whereas 2-(substituted ethynyl)-1,3-diazabicyclo[3.1.0]hexanes are formed with α-acetylenic aldehydes. It was established by PMR spectroscopy that the 2-substituted 1,3-diazabicyclo[3.1.0]hexanes are mixtures of endo and exo isomers.

In a continuation of our research on the reactivity of 2-aminomethylaziridine (I) [1, 2] with carbonyl compounds, we studied its reaction with some α-unsaturated oxo compounds. Proceeding from the structure of I, which has primary and secondary amino groups, one might assume the formation of both 3,4-addition products and products of condensation at the carbonyl group.

The formation of 2-(substituted vinyl)-1,3-diazabicyclo[3.1.0]hexanes (IIa-c) is observed in the reaction of I with α-unsaturated carbonyl compounds, specifically with benzalacetone, mesitylene oxide, and cinnamaldehyde. This makes it possible to conclude that the reaction takes place primarily at the carbonyl group. No products of 3,4 addition of aziridine I to the activated C=C bond are formed.

2-Vinyl-1,3-diazabicyclo[3.1.0]hexane is not formed in the reaction of 2-aminomethylaziridine with acrolein. Polymeric products are formed in aprotic solvents [benzene, ether, or dimethyl sulfoxide (DMS)]; however, we isolated IIIa or IIIb in the case of a solution in methanol or ethanol when aziridine I was added to the acrolein, whereas the chief product in the case of reverse mixing of the reagents is IV.



II a $R^1=C_6H_5$, $R^2=R^3=H$; b $R^1=C_6H_5$, $R^2=H$, $R^3=CH_3$; c $R^1=R^2=R^3=CH_3$; III a $R^4=CH_3$; b $R^4=C_2H_5$; V a $R^5=H$; b $R^5=C_6H_5$

The formation of 2-(β-alkoxyethyl)-1,3-diazabicyclo[3.1.0]hexanes IIIa and IIIb can be represented by two alternative schemes. According to the first scheme, acrolein adds the corresponding alcohol under the conditions of the synthesis, and the base that catalyzes this reaction is starting acridine I. The intermediately formed β-alkoxypropionaldehyde reacts with aziridine I to give final products IIIa and IIIb. The other possible scheme includes a step involving the formation of intermediate 2-vinyl-1,3-diazaabicyclo[3.1.0]hexane, which may then subsequently add the corresponding alcohol to give IIIa or IIIb.

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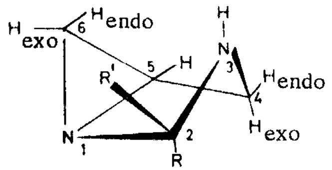
TABLE 1. Parameters of the PMR Spectra of IIa-c and Va, b



Compound	R	R'	Isomer	Chemical shift, δ, ppm								J, Hz*				
				exo-6-H	endo-6H	5-H	endo-4-H	exo-4H	NH	R	R'	6, exo-5	6, endo-5	4,4	4, exo-5	exo-4 exo-6
IIa	$C_6H_5CH=CH$	H	exo	1,42	1,15	2,19	2,92	2,72	1,9	6,08 (α−H), 6,64 (β−H), 7,1−7,4 (C_6H_5)	4.28	4,6	3,0	−11,5	3,0	1,0
	H	$C_6H_5CH=CH$	endo	1,28	1,02	2,21	3,04	2,86	1,9	4,35	6,08 (α−H), 6,64 (β−H), 7,1−7,4 (C_6H_5)	4,6	3,0	−11,5	3,0	1,1
IIb	$C_6H_5CH=CH$	CH_3	exo	1,38	1,05	2,17	3,00	2,80	1,4	6,08 (α−H), 6,78 (β−H), 7,3 (C_6H_5)	1,25	4,6	2,7	−12,0	3,0	—
	CH_3	$C_6H_5CH=CH$	endo	1,38	1,00	2,22	3,00	2,80	1,4	1,25	6,25 (α−H), 6,55 (β−H), 7,3 (C_6H_5)	4,6	2,7	−12,0	3,0	—
IIc	$(CH_3)_2C=CH$	CH_3	exo	1,24	0,98	2,22	2,97	2,82	2,5	4,67 (CH), 1,80 and 1,70 (CH_3)	1,06	4,6	3,0	−12,0	3,0	1,0
	CH_3	$(CH_3)_2C=CH$	endo	1,23	0,98	2,18	2,97	2,82	2,5	1,10	5,22 (CH), 1,80 and 1,70 (CH_3)	4,6	3,0	−12,0	3,0	1,0
Va	$HC\equiv C$	H	exo	1,48	1,25	2,37	3,25	2,88	2,2	2,40†	4,49	4,5	3,0	−12,0	2,3	0,5
	H	$HC\equiv C$	endo	1,46	1,39	2,37	3,25	2,88	2,2	4,36	2,50	4,5	3,0	−12,0	2,3	0,5
Vb	$C_6H_5C\equiv C$	H	exo	1,55	1,25	2,40	3,25	2,96	2,4	7,1—7,6	4,72	4,5	3,0	−12,0	2,8	0,5
	H	$C_6H_5C\equiv C$	endo	1,55	1,44	2,40	3,25	2,96	2,4	4,65	7,1−7,6	4,5	3,0	−12,0	2,8	0,5

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*$^2J_{6,6}$ and $^3J_{4,\text{endo-}5}$ < 0.5 Hz.

†^4J = 2.1 Hz.

The data from the PMR spectrum of a mixture of acrolein in methanol provide evidence in favor of the first assumption. When catalytic amounts of aziridine I are present, the triplet (J = 3 Hz) of an aldehyde proton at δ 9.6 ppm is observed in the PMR spectrum of the reaction mixture, and the multiplet at δ 6.6 and 6.2 ppm of the vinyl group of acrolein is absent.

When the reagents are mixed in the reverse order, the reaction is probably realized through an intermediate step involving the nucleophilic addition of 2-aminomethylaziridine I to the C=C bond of acrolein to give β-aminomethylaziridinylpropionaldehyde, which in turn reacts with aziridine I to give IV. However, a scheme including a step involving the formation of intermediate 2-vinyl-1,3-diazabicyclo[3.1.0]hexane is fundamentally possible in this case also. The structures of IIIa, IIIb, and IV were proved on the basis of the IR and PMR spectra.

The reactivity of aziridine I was also investigated in reactions with α-acetylenic aldehydes. The presence in the molecules of such aldehydes of two reaction centers — the activated C=C bond and the carbonyl group — permits the formation of both 3,4-addition products and products of condensation at the carbonyl group. Nevertheless, primarily bicyclic products were obtained in this case also. The reaction of aziridine I with propargyl and phenylpropargyl aldehydes leads to the formation of 2-substituted 1,3-diazabicyclo[3.1.0]hexanes Va and Vb. This result is in agreement with the previously published data [3] on primary attack of aziridines at the aldehyde group to give acetylenic derivatives of α-aziridinylcarbinols, which are the kinetic products and, in the case of aziridine I, are converted to compounds of the V type.

An analysis of the PMR spectra makes it possible to conclude that 2-substituted 1,3-diazabicyclo[3.1.0]hexanes IIa-c and Va, b are mixtures of endo and exo isomers (Table 1). The physical constants of IIa-c and Va, b are presented in Table 2.

EXPERIMENTAL

The PMR spectra of CCl_4 solutions of the compounds were recorded with a Perkin–Elmer R12 A spectrometer (60 MHz) with tetramethylsilane as the internal standard. The IR spectra of liquid films or suspensions of the compounds in mineral oil and hexachlorobutadiene were obtained with a UR-20 spectrometer.

2-Styryl-1,3-diazabicyclo[3.1.0]hexane (IIa). A solution of 13 ml (0.1 mole) of cinnamaldehyde in 50 ml of absolute ethanol was added with stirring and cooling (with cold water) to a solution of 7.2 g (0.1 mole) of aziridine I in absolute ethanol, and the mixture was allowed to stand at 18° for 2 h. It was then dried with anhydrous sodium sulfate and filtered, and the solvent was evaporated from the filtrate. The residue distilled at 164-166° (2 mm) to give 15 g (80%) of a light-yellow viscous oil. IR spectrum: 3270 (NH) and 1590 cm^{-1}(C=C).

2-Methyl-2-styryl-1,3-diazabicyclo[3.1.0]hexane (IIb). A solution of 14.8 g (0.1 mole) of I in 50 ml of absolute ethanol was added to a solution of 7.2 g (0.1 mole) of I in 50 ml of absolute ethanol, and the mixture was refluxed until the peaks of the starting components vanished on the chromatogram of the reaction mixture. The clear solution was then dried with anhydrous sodium sulfate and evaporated, and the residue was vacuum distilled at 150-152° (2 mm) to give 15 g (75%) of IIb. IR spectrum: 3280 (NH) and 1605 cm^{-1} (C=C).

2-Isopropenyl-2-methyl-1,3-diazabicyclo[3.1.0]hexane (IIc). A solution of 11.3 ml (9.1 moles) of mesitylene oxide in 50 ml of absolute ethanol was added at 18-20° to a solution of 7.2 g (0.1 mole) of I in 50 ml of absolute ethanol, and the mixture was allowed to stand at

TABLE 2. Physical Constants of IIa-c and Va, b

Compound	bp, °C (mm, Hg)	n_D^{20}	Found, %			Empirical formula	Calc., %			Yield, %
			C	H	N		C	H	N	
IIa	164—166 (2)	1,5675	77,3	7,3	15,2	$C_{12}H_{14}N_2$	77,4	7,5	15,1	80
IIb	150—152 (2)	1,5736	77,9	7,8	14,1	$C_{13}H_{16}N_2$	78,0	8,0	14,0	75
IIc	120—122 (0,05)	1,4790	68,4	11,6	19,9	$C_{10}H_{17}N_2$	68,6	11,4	20,0	78
Va	66—68*	—	66,9	7,5	26,2	$C_6H_8N_2$	66,6	7,4	25,9	55
Vb	95—98 (0,005)	—	77,4	6,9	14,9	$C_{12}H_{12}N_2$	77,8	6,6	15,2	63

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*This compound has mp 66-68°.

room temperature for 2 h. It was then dried with anhydrous sulfate and evaporated. The residue was vacuum distilled at 120-122° (0.05 mm) to give 10 g (78%) of IIc. Ir spectrum: 3289 (NH) and 1580 cm^{-1} (C=C).

2-(β-Alkoxyethyl)-1,3-diazabicyclo[3.1.0]hexanes (IIIa,b). A solution of 7.2 g (0.1 mole) of I in 50 ml of the appropriate absolute alcohol was added with vigorous stirring and cooling (with ice water) to a solution of 6.7 ml (0.1 mole) of acrolein in 50 ml of the same alcohol, and the mixture was stirred at 18-20° for 2 h. It was then dried with anhydrous sodium sulfate, and the solvent was evaporated at 40° (150 mm). The residue was vacuum distilled.

2-(β-Methoxyethyl)-1,3-diazabicyclo[3.1.0]hexane (IIIa). This compound [10 g (71%)] had bp 40-42° (0.04 mm) and n_D^{20} 1.4625. Found:C 60.0; H 9.6; N 19.2%. $C_7H_{14}N_2O$. Calculated: C 59.5; H 9.7; N 19.6%. IR spectrum: 3280 cm^{-1} (NH). PMR spectrum: 1.16 and 1.24 (two d, J = 4.7 Hz, exo-6-H); 1.13 and 1.01 (two d, J - 2.9 Hz, endo-6-H); 2.2 (m, 5-H); 2.8-3.1 (m, exo-4-H and endo-4-H); 2.8 (broad s, NH); 3.78 and 3.74 (two t, J = 7 Hz, 2-H); 1.5-1.8 (m, CH_2); 3.3-3.6 (m, OCH_2); 3.28 and 3.26 ppm (two s, OCH_3).

2-(β-Ethoxyethyl)-1,3-diazabicyclo[3.1.0]hexane (IIIb). This compound [17 g (84%)] had bp 47-50° (0.03 mm) and n_D^{20} 1.4672. Found: C 61.8; H 10.0; N 18.2%. $C_8H_{16}N_2O$. Calculated: C 61.5; H 10.3; N 17.9%. IR spectrum: 3260 cm^{-1} (NH).

2-(2-Aziridinylmethylaminoethyl)-1,3-diazabicyclo[3.1.0]hexane (IV). A solution of 6.7 ml (0.1 mole) of freshly distilled acrolein in 50 ml of absolute ethanol was added with stirring and cooling (ice water) to a solution of 7.2 g (0.1 mole) of I in 50 ml of absolute ethanol, and the mixture was stirred at room temperature for 2 h. It was then dried with anhydrous sodium sulfate and evaporated, and the residue was distilled at 80-82° (0.02 mm) to give 13 g (72%) of a colorless liquid with n_D^{20} 1.5260. Found: C59.6; H 9.5; N 30.6%. $C_9H_{18}H_4$. Calculated: C 59.3; H 9.9; N 30.8%. IR spectrum: 3340 cm^{-1} (NH).

2-Ethynyl-1,3-diazabicyclo[3.1.0]hexane (Va). A solution of 7.2 g (0.1 mole) of I in 20 ml of absolute methanol was added with stirring at 0° to a solution of 5.4 g (0.1 mole) of propargyl aldehyde in 20 ml of absolute methanol, after which the temperature was raised to room temperature, and the mixture was stirred at this temperature for 4 h. The solvent was evaporated, and the residue was vacuum distilled at 56° (0.005 mm). The distilled product crystallized to give 5.9 g (55%) of a product with mp 66-68°. IR spectrum: 3200-3230 (NH) and 2125 cm^{-1} (C≡C).

2-(β-Phenylethynyl)-1,3-diazabicyclo[3.1.0]hexane (Vb). A solution of 7.2 g (0.1 mole) of I in 30 ml of absolute methanol was added with stirring at 0° to a solution of 13 g (0.1 mole) of phenylpropargyl aldehyde in 30 ml of absolute methanol, after which the temperature was raised to room temperature, and the mixture was stirred at this temperature for 4 h. The methanol was then evaporated, and the residue was vacuum distilled at 89-91° (0.005 mm) to give 11.9 g (63%) of Vb. IR spectrum: 3275 (NH) and 2250 cm^{-1} (C≡C).

Reaction of Acrolein with Methanol in the Presence of Catalytic Amounts of 2-Aminomethylaziridine. A solution of acrolein in methanol and catalytic amounts of I were placed in an ampul for recording PMR spectra, and the spectrum was recorded. A triplet (J = 3 Hz) of an aldehyde proton at δ 9.6 ppm was observed in the PMR spectrum, but the multiplet of the vinyl group of acrolein at δ 6.6 and 6.2 ppm was absent.

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