12. K. Lehmstedt and H. Haudertmark, Ber., 63, 1229 (1930).
13. N. A. Korchevin, V. A. Usov, and M. G. Voronkov, Khim. Geterotsikl. Soedin., No. 5, 713 (1974).
14. B. J. Whitlock and H. W. Whitlock, J. Org. Chem., 37, 3559 (1972).
15. C. A. Buehler and D. E. Pearson, Survey of Organic Syntheses, Wiley, New York (1970).
16. L. Fieser and M. Fieser, Reagents for Organic Synthesis, Vol. 1, Wiley.

REACTION OF AZIRIDINES WITH ACETYLENIC γ-HYDROXY ALDEHYDES

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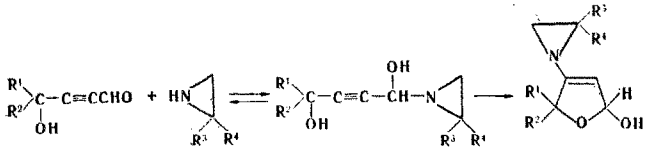
The corresponding acetylenic aziridino hydroxy carbinols were obtained by the reaction of aziridine, 2,2-dimethylaziridine, and methyl aziridine-2-carboxylate with 4-hydroxy-4-methylpent-2-yn-1-al and 3-(1-hydroxycyclohexyl)prop-2-yn-1-al. It is shown that the latter at room temperature undergo isomerization with time to 2-hydroxy-4-aziridino-5,5-dialkyldihydrofurans. The isomerization of acetylenic aziridinocarbinols, which includes an intermediate step involving retrodecomposition of the aziridino(hydroxy)carbinols to the starting aldehydes and aziridines, was investigated by dynamic NMR spectroscopy.

We have previously shown [1] that the reaction of 1-H-aziridines with propargyl and phenylpropargyl aldehydes gives acetylenic α-aziridinocarbinols, which are isomerized to β-aziridinoacroleins at room temperature. The mechanism of the isomerization, which includes an intermediate step involving the retrodecomposition of the acetylenic aziridinocarbinols to the starting aldehydes and aziridines with subsequent formation of β-aziridinoacroleins, was established.

To confirm the general character of the reactivities of 1-H-aziridines with α-acetylenic aldehydes and to ascertain the limits of the applicability of this reaction in the synthesis of acetylenic α-aziridinocarbinols and β-aziridinoacroleins we investigated the reaction of aziridines with acetylenic γ-hydroxy aldehydes. It is known [2] that 2-methoxy-4-dialkylaminodihydrofurans are formed in the reaction of secondary amines with acetylenic γ-hydroxy aldehydes in anhydrous methanol. However, the reaction is accompanied by resinification when it is carried out in absolute benzene or ether.

As a result of the study it was shown that the reaction of aziridine (IIIa), and 2,2-dimethyl- (IIIb) and 2-carbomethoxyaziridine (IIIc) with acetylenic γ-hydroxy aldehydes (I, II) in absolute ether at −30 deg C gives acetylenic aziridino(hydroxy)carbinols IVa-c and Va-c. The latter are colorless crystalline compounds, the physicochemical characteristics of which are presented in Table 1.



I, II III a-c IV-V a-c VI-VII a-c

I, IV, VI $R^1=R^2=CH_3$; II, V, VII $R^1-R^2=-(CH_2)_5-$; III-VII a $R^3=R^4=H$; b $R^3=R^4=CH_3$; c $R^3=H$, $R^4=COOCH_3$

The IR spectra of acetylenic aziridino(hydroxy)carbinols IVa-c and Va-c are characterized by absorption bands of the stretching vibrations of a hydroxy group at 3300-3400 cm^{-1}, absorption maxima of a triple bond at 2240-2260 cm^{-1}, and C−H stretching vibrations of the aziridine ring at 3070-3080 cm^{-1}. No bands are present in the region characteristic for the absorption of conjugated C=O and C=C bonds.

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TABLE 1. Characteristics of IVa-c and Va-c

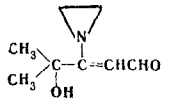
Compound	mp, °C	IR spectrum, cm^{-1}			Found, %			Empirical formula	Calc., %			Yield, %
		OH	C≡C	C=O	C	H	N		C	H	N	
IVa	60—62	3360	2250	—	61,9	8,3	9,2	$C_8H_{13}NO_2$	61,9	8,4	9,0	90
IVb	64—65	3320	2220	—	65,6	9,2	7,7	$C_{10}H_{17}NO_2$	65,6	9,3	7,6	84
IVc	70—71	3340	2210	1735	56,4	7,0	6,4	$C_{10}H_{15}NO_4$	56,3	7,0	6,6	88
Va	68—69	3330	2240	—	67,3	8,8	7,2	$C_{11}H_{17}NO_2$	67,7	8,7	7,2	94
Vb	71—72	3300	2235	—	70,1	9,2	6,2	$C_{13}H_{21}NO_2$	70,0	9,4	6,3	92
Vc	76—78	3315	2210	1740	61,4	7,4	5,6	$C_{13}H_{19}NO_4$	61,7	7,5	5,5	87

TABLE 2. 2-Hydroxy-4-aziridino-5,5-dialkyldihydrofurans VIa-c and VIIa-c

Compound	mp, °C	IR spectrum, cm^{-1}			Found, %			Empirical formula	Calc., %		
		OH	C=O	C=C	C	H	N		C	H	N
VIa	82—83	3230	—	1655	61,8	8,3	9,1	$C_8H_{13}NO_2$	61,9	8,4	9,0
VIb	101—102	3400	—	1650	65,3	9,4	7,7	$C_{10}H_{17}NO_2$	65,6	9,3	7,6
VIc	116—117	3480	1745	1665	56,2	7,1	6,5	$C_{10}H_{15}NO_4$	56,3	7,0	6,6
VIa	93—95	3405	—	1650	67,5	8,3	7,2	$C_{11}H_{17}NO_2$	67,7	8,7	7,2
VIIb	123—124	3385	—	1645	69,9	9,5	6,3	$C_{13}H_{21}NO_2$	70,0	9,4	6,3
VIIc	131—132	3460	—	1660	61,6	7,4	5,6	$C_{13}H_{19}NO_4$	61,7	7,5	5,5

Aziridino(hydroxy)carbinols IVa-c and Va-c undergo isomerization at room temperature with time to give 2-hydroxy-4-aziridinodihydrofurans VIa-c and VIIa-c in quantitative yields; the products are crystalline substances (Table 2). This conclusion was reached on the basis of an analysis of the IR spectra of isomerization products VIa-c and VIIa-c, which contain an intense absorption band of the C=C bond of the dihydrofuran ring at 1650-1665 cm^{-1} but do not contain the stretching vibrations of an acetylenic bond at 2240-2260 cm^{-1}. The structures of VIa-c and VIIa-c are also confirmed by the data from PMR spectroscopy (Table 3).

The high rate of isomerization in solutions makes it impossible to record the PMR spectra of individual aziridino(hydroxy)carbinols IVa-c and Va-c. However, it is possible to follow the isomerization by means of dynamic NMR spectroscopy. Thus, in addition to signals at δ1.67 and 4.32 ppm, which evidently correspond to the absorption of the protons of the aziridine ring and the $-\overset{|}{\underset{|}{C}}-H$ group of IVa, doublets with J = 7.5 Hz, which are characteristic for the vinyl and formyl protons [1] of aldehyde VIIIa, and signals at δ 4.78 and 5.84 ppm from the protons of the dihydrofuran ring of VIa appear when the PMR spectrum of aziridino(hydroxy)carbinol IVa in deuterochloroform solution is recorded. The protons of the aziridine ring of VIIIa and VIa



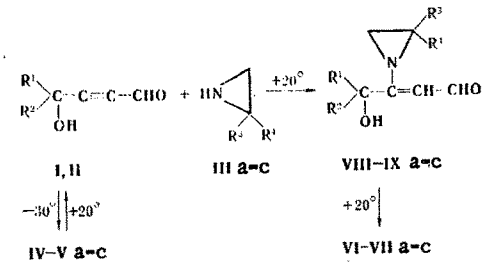
VIII a

absorb at δ 2.39 and 1.90 ppm, respectively. An appreciable increase in the intensity of the signals of VIa and VIIIa together with a simultaneous decrease in the resonance absorption for aziridino(hydroxy)carbinol IVa are observed when the PMR spectrum of this mixture is rerecorded, and the isomerization terminates with complete conversion to dihydrofuran VIa after 50 min.

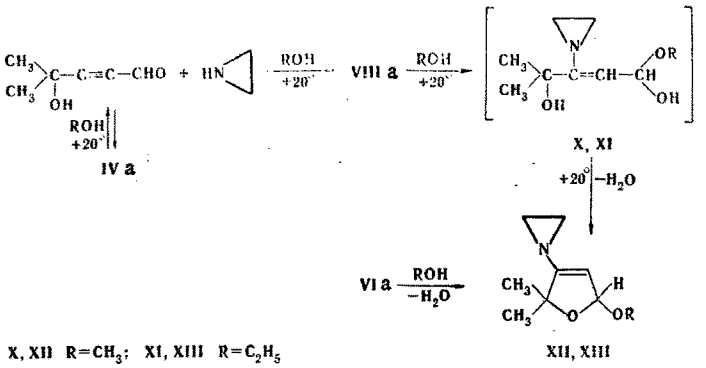
These data make it possible to conclude that acetylenic aziridino(hydroxy)carbinol IVa is converted during the isomerization process to aziridino aldehyde VIIIa, which in turn undergoes cyclization to dihydrofuran VIa. Since, according to the data in [1], the rearrangement of aziridino(hydroxy)carbinols IVa-c and Va-c to aziridino aldehydes VIIIa-c and IXa-c should include an intermediate step involving the retrodecomposition of IVa-c and Va-c to the starting aziridines and aldehydes, the entire isomerization process can be represented by the following scheme:

TABLE 3. PMR Spectra of 2-Hydroxy-4-aziridino-5,5-dialkyldihydrofurans (VIa-c and VIIa-c)

Compound	R^1	R^2	R^3	R^4	Chemical shifts, δ, ppm							
					2-H	OH	3-H	R^1	R^2	CH_2	R^3	R^4
VIa	CH_3	CH_3	H	H	5,84 br.s	3,04 br.s	4,79 s	1,38 s	1,49 s	1,90 s	1,90 s	1,90 s
VIb	CH_3	CH_3	CH_3	CH_3	5,75 br.s	3,67 br.s	4,63 s	1,21 s	1,21 s	1,76 s	1,35 s	1,35 s
VIc	CH_3	CH_3	$COOCH_3$	H	5,79 br.s	3,55 br.s	4,76 s	1,40 s	1,32 s	2,00 m	3,75 s	2,41 m
VIIa	$-(CH_2)_5-$		H	H	5,81 br.s	3,24 br.s	4,76 s	1,66 m	1,66 m	1,89 s.	1,89 s	1,89 s
VIIb	$-(CH_2)_5-$		CH_3	CH_3	5,12 br.s	2,48 br.s	4,39 s	1,57 m	1,57 m	1,75 s	1,17 s	1,17 s
VIIc	$-(CH_2)_5-$		$COOCH_3$	H	5,60 br.s	2,59 br.s	4,89 s	1,59 m	1,59 m	2,07 m	3,78 s	2,48 m



When we carried out the isomerization of aziridino(hydroxy)carbinol IVa in methanol or ethanol solution, we obtained the corresponding 2-alkoxy-4-aziridinodihydrofurans XII and XIII. In this case the initially



formed aziridino aldehyde VIIIa evidently reacts with alcohols to give the corresponding intermediate hemiacetals X and XI, which subsequently undergo cyclization to alkoxyaziridinodihydrofurans XII and XIII. The same compounds were isolated when 2-hydroxy-4-aziridinodihydrofuran VIa was refluxed in alcohol solutions.

Thus acetylenic aziridino(hydroxy)carbinols are obtained in the reaction of acetylenic γ-hydroxy aldehydes with aziridines at −30 deg C. However, the isomerization of the latter, in contrast to the isomerization of aziridines with propargyl and phenylpropargyl aldehydes [1], does not stop with the formation of eneaziridino aldehydes, and the final products are 2-hydroxy-4-aziridino-5,5-dialkyldihydrofurans.

EXPERIMENTAL

The PMR spectra of 5% solutions of the compounds in $CDCl_3$ were recorded with a WH-90 Bruker spectometer with tetramethylsilane as the internal standard. The IR spectra of mineral oil suspensions, hexachlorobutadiene solutions, or liquid films of the compounds were obtained with a UR-20 spectrometer.

Acetylenic Aziridino(hydroxy)carbinols IVa-c and Va-c. A solution of a 0.03-mole sample of the corresponding aziridine IIIa-c in 10 ml of absolute ether was added with stirring at −30 deg C to a solution of a 0.03-mole sample of acetylenic γ-hydroxy aldehyde I [3] or II in 20 ml of absolute diethyl ether, and the resulting crystals were removed by filtration, washed with absolute ether, and dried in vacuo to give colorless crystalline aziridino(hydroxy)carbinols IVa-c and Va-c (Table 1).

2-Hydroxy-4-aziridino-5,5-dialkyldihydrofurans VIa-c and VIIa-c. Crystalline IVa was allowed to stand in a sealed flask at room temperature. The isomerization was monitored by means of thin-layer chromatography [Silufol UV-254, ether−pentane (3:1)]. After 12 h, IVa underwent quantitative isomerization to dihydrofuran VIa. Compounds VIb,c and VIIa-c, the physicochemical characteristics of which are presented

in Table 2, were similarly obtained in quantitative yield.

2-Alkoxy-4-aziridino-5,5-dimethyldihydrofurans XII and XIII. A 1.13-g (7 mmole) sample of IVa was dissolved in 10 ml of absolute methanol or ethanol, and the solution was allowed to stand at room temperature for 12 h. The alcohol was removed by evaporation, and the residue was distilled in vacuo to give the products. A total of 1.16 g (98%) of 2-methoxy-4-aziridino-5,5-dimethyldihydrofuran (XII), with bp 28-30 deg C (0.01 mm), was obtained. Found: C 63.9; H 8.7; N 8.4%. $C_9H_{15}NO_2$. Calculated: C 63.9; H 8.9; N 8.3%. IR spectrum: 1655 cm^{-1} (C=C). PMR spectrum, δ: 5.45 (s, 1H, 2-H), 4.69 (s, 1H, 3-H), 3.31 (s, 3H, OCH_3), 1.81 [s, 4H, $N(CH_2)_2$], 1.38 (s, 3H, CH_3), and 1.30 ppm (s, 3H, CH_3). A total of 1.22 g (95%) of 2-ethoxy-4-aziridino-5,5-dimethyldihydrofuran (XIII), with bp 34-35 deg C (0.01 mm), was obtained. Found: C 65.3; H 9.3; N 7.3%. $C_{10}H_{17}NO_2$. Calculated: C 65.67; H 9.3; N 7.6%. IR spectrum: 1665 cm^{-1} (C=C). PMR spectrum, δ: 5.46 (s, 1H, 2-H), 4.64 (s, 1H, 3-H), 3.51 (m, 2H, OCH_2), 1.81 [s, 4H, $N(CH_2)_2$], 1.39 (s, 3H, 5-CH_3), 1.29 (s, 3H, 5-CH_3), and 1.14 ppm (t, 3H, CH_3).

Reaction of 2-Hydroxy-4-aziridino-5,5-dimethyldihydrofuran (VIa) with Alcohols. A 1.6-g (0.01 mole) sample of VIa was refluxed for 8 h in a solution (30 ml) of methanol or ethanol, after which the solvent was removed by evaporation, and the residue was identified by PMR spectroscopy as the corresponding 2-methoxy-4-aziridino-5,5-dimethyldihydrofuran (XII) [1.6 g (94%)] or, respectively, 2-ethoxy derivative XIII [1.7 g (91%)].

LITERATURE CITED

1. A. V. Eremeev, D. A. Tikhomirov, and É. É. Liepin'sh, Khim. Geterotsikl. Soedin., No. 2, 207 (1977).
2. A. S. Medvedeva, L. P. Safronova, I. D. Kalikhman, and M. G. Voronkov, Izv. Akad. Nauk SSSR, Ser. Khim., No. 8, 1799 (1976).
3. A. S. Medvedeva, L. P. Safronova, G. G. Chichkareva, and M. G. Voronkov, Izv. Akad. Nauk SSSR, Ser Khim., No. 1, 121 (1976).

SYNTHESIS AND REACTIONS OF BENZOFORMYLINDOLES

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A method was developed for the synthesis of 5- or 6-formylindoles by reaction of 5- or 6-aminomethylindoles with hexamethylenetetramine in acidic media. 1-Methyl-7-formylindole was obtained by recyclization of nicotyrine methiodide under the influence of alkaline agents. The corresponding vinylindoles were obtained by condensation of formylindoles with nitromethane, nitroethane, and malonic acid. The structures of the products were proved by alternative synthesis, the results of elementary analysis, and the UV, IR, PMR, and mass spectra.

In [1] it is shown that aldehydes of the indole series with a formyl group attached to the benzene ring may be convenient starting substances, for example, for the synthesis of aminoethylindoles. This is also true of aldehydes of the tetrahydrocarbazole series, although it has been reported that the carbonyl group in these compounds has extremely low reactivity [2]. Troxler synthesized such aldehydes by reduction of the corresponding nitriles with sodium hyposulfite in the presence of Raney nickel in acetic acid containing pyridine [1]. However, it is often necessary to use circuitous pathways to obtain the nitriles themselves, since the corresponding acids are difficult to convert to even the chlorides [2, 3]. The direct introduction of a formyl group in the benzene ring of the indole molecule is difficult. Only 5-methoxy-6-formylindoles have been obtained by this method [4].

Having samples of 5- and 6-aminomethylindoles [5, 6] at our disposal, we investigated the possibility of

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