IODOCYCLIZATION OF N,N-DIALKYLAMINO-2-METHYL-4-PENTEN-2-OL OXIDES

I. REACTION PRODUCTS

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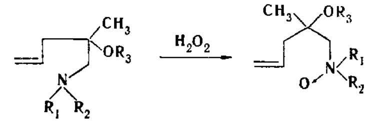
It is shown that in the iodination of N,N-dialkylamino-2-methyl-4-penten-2-ol and N,N-diethylamino-3-butene oxides the N-oxide group participates in the intramolecular cyclization of these compounds. N,N-Dialkyl-4-methyl-4-hydroxy-6-iodomethyltetrahydro-1,2-oxazine iodides were obtained by iodination of the former, whereas the latter under similar conditions gives N,N-diethyl-5-iodomethyltetrahydro-1,2-oxazolinium iodide.

Electrophilic addition to compounds that contain carbon–carbon multiple bonds and bifunctional groups often proceeds with intramolecular participation of the latter, as a result of which various heterocyclic systems are formed [1]. The amino group of ω-pentenylamines participates particularly readily in these reactions. The addition of electrophilic agents to it proceeds with the formation of quaternary pyrrolidinium salts [1-3].

Continuing our study of the participation of various electron-donor groups of unsaturated compounds in intramolecular cyclization reactions that proceed under the influence of electrophilic agents, it seemed of interest to ascertain the possibility of the participation of the N-oxide group in these reactions and to determine the reactivity of the N-oxide group as compared with the amino group of unsaturated amines.

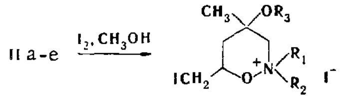
In this connection, we synthesized a number of N-oxides of N,N-dialkylamino-2-methyl-4-penten-2-ols and their esters.



I a-g IIa-e

I, IIa $R_1=R_2=C_2H_5$, $R_3=H$; b $R_1=R_2=-(CH_2)_5-$, $R_3=H$; c $R_1=R_2=-CH_2CH_2OCH_2CH_2-$, $R_3=H$; d $R_1=R_2=-(CH_2)_5-$, $R_3=CH_3CO-$; e $R_1=R_2=-(CH_2)_6-$, $R_3=H$; f $R_1=R_2=-(CH_2)_2-$, $R_3=H$; g $R_1=C_2H_5$, $R_2=C_6H_5$, $R_3=H$

Tetrahydro-1,2-oxazinium salts are formed in almost quantitative yields in the iodination of IIa-e.



III

IIIa $R_1=R_2=C_2H_5$, $R_3=H$; b $R_1=R_2=-(CH_2)_5-$, $R_3=H$; c $R_1=R_2=-CH_2CH_2OCH_2CH_2-$, $R_3=H$; d $R_1=R_2=-(CH_2)_5-$, $R_3=CH_3CO-$; e $R_1=R_2=-(CH_2)_6-$, $R_3=H$

The IR spectra of Id-g and IIa-e (see Tables 1 and 3) contain absorption bands of double bonds at 1645 cm^{-1}, of hydroxyl groups at 3400 cm^{-1}, and of the N→O bond at 925 cm^{-1} in IIa-e.

The IR spectra of quaternary pyrrolidinium and tetrahydro-1,3-oxazinium salts (see Tables 2 and 4) contain absorption bands of a hydroxyl group at 340 cm^{-1} and broad absorption bands at 2400-3000 cm^{-1}, which are characteristic for quaternary ammonium salts. The absorption bands of N→O bonds vanish in the IR spectra of IIIa-e, and new absorption bands of NOC groupings appear at 1023-1032 cm^{-1}. The absorption bands of double bonds at 1645 cm^{-1} are absent in the IR spectra of pyrrolidinium and tetrahydro-1,3-oxazinium derivatives.

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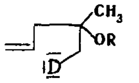
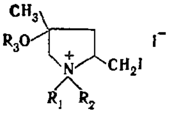
TABLE 1. 1-N,N-Dialkylamino-2-methyl-4-penten-2-ols and Their Esters



Compound	$-\overline{D}\vert$	R	bp, °C (mm)	n_D^{20}	d_4^{20}	Empirical formula	Found		Calc.		IR spectrum, cm⁻¹		Yield, %
							N, %	MR_D	N, %	MR_D	C=C	OH	
Id	$-N(CH_2)_5$	CH_3CO-	61–62 (1)	1,4620	0,9523	$C_{13}H_{23}NO_2$	6,6	65,04	6,2	65,33	1650	—	69
Ie	$-N(CH_2)_6$	H	97–99 (4)	1,4783	0,9382	$C_{12}H_{23}NO$	7,2	60,10	7,1	60,61	1645	3450	72
If	$-N(CH_2)_2$	H	40–42 (2)	1,4670	0,9379	$C_8H_{15}NO$	10,1	41,66	9,9	42,02	1650	3430	62
Ig	$-N(C_2H_5)(C_6H_5)$	H	110–111 (1)	1,5462	1,0006	$C_{14}H_{21}NO$	6,5	69,18	6,4	68,30	1655	3420	53

TABLE 2. 2-Iodomethyl-4-methyl-4-hydroxy(carbomethoxy)pyrrolidinium Iodides



R_1	R_2	R_3	mp, °C	Empirical formula	Found, %		Calc., %		IR spectrum, cm⁻¹		
					N	I	N	I	OH	$>\overset{+}{N}<$	C=O
$-(CH_2)_5-$		CH_3CO-	181–182*	$C_{13}H_{23}I_2NO$	2,9	52,96	2,92	52,97	—	3000–2900	1720
$-(CH_2)_6-$		H	154–155	$C_{12}H_{23}I_2NO$	3,1	56,3	3,1	56,3	3340	3000–2500	—
$-(CH_2)_2-$		H	194–196	$C_8H_{15}I_2NO$	3,7	63,8	3,5	64,2	3350	3000–2400	—
C_6H_5	C_2H_5	H	101–103	$C_{14}H_{21}I_2NO$	3,0	53,2	2,9	53,6	3330	3000–2800	—

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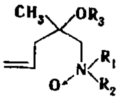
*Recrystallization from acetone–methanol.

TABLE 3. N-Oxides of 1-N,N-Dialkylamino-2-methyl-4-penten-2-ols and Their Esters



Compound	R_1	R_2	R_3	mp, °C	Empirical formula	N, %		IR spectrum, cm⁻¹				Yield, %
						found	calc.	C=C	$N \to O$	OH	C=O	
IIa	C_2H_5	C_2H_5	H	—	$C_{10}H_{21}NO_2$	7,8	7,6	1645	926	3350	—	50
IIb	$-(CH_2)_5-$		H	66–67*	$C_{11}H_{21}NO_2$	7,4	7,1	1645	930	3300	—	52
IIc	$-CH_2CH_2OCH_2CH_2-$		H	74–75	$C_{10}H_{19}NO_3$	7,0	7,0	1650	935	3400	—	50
IId	$-(CH_2)_5-$		CH_3CO-	—	$C_{13}H_{23}NO_3$	6.02	5,8	1520	920	—	1720	47
IIe	$-(CH_2)_6-$		H	—	$C_{12}H_{23}NO_2$	6,5	6.6	1650	930	3400	—	53

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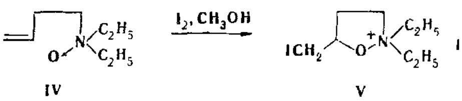
*Crystallization from carbon tetrachloride.

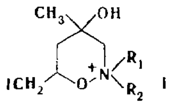
The stereochemistry of the iodination of IIa-e has not yet been studied.

The participation of the oxygen atom of unsaturated N-oxides in their heterocyclization reactions is also confirmed by the fact that N,N-diethylamino-3-butene does not react with iodine under the conditions of iodination of unsaturated N-oxides. This behavior of the latter in the iodination reaction should evidently be explained by the energic disadvantageousness of the formation of a four-membered ring, whereas N-oxide IV obtained from it forms a tetrahydro-1,2-oxazolinium salt (V) in good yield under these conditions.



IV V

TABLE 4. 4-Methyl-4-hydroxy-6-iodomethyltetrahydro-1,2-oxazinium Iodides



Compound	R_1	R_2	mp, °C	Empirical formula	Found, %			Calc., %			IR spectrum, cm^{-1}		
					C	H	I	C	H	I	NOC	CN	OH
IIIa	C_2H_5	C_2H_5	136—137*	$C_{10}H_{21}I_2NO_2$	27,2	4,6	57,5	27,2	4,8	57.5	1032	1050	3400
IIIb	$-(CH_2)_5-$		150—151†	$C_{11}H_{21}I_2NO_2$	29.2	4.6	55.3	29.2	4.7	56.0	1023	1060	3390
IIIc	$-CH_2CH_2OCH_2CH_2-$		144—145	$C_{10}H_{19}I_2NO_3$	26,5	4.1	55.6	26,4	4,2	55,7	1025	1048	3390
IIIe	$-(CH_2)_6-$		155—156	$C_{12}H_{23}I_2NO_2$	30,7	5,0	54,3	30.9	4.9	54,4	1030	1060	3380

*Recrystallized from acetone—methanol.

†Also obtained by iodination of IId.

EXPERIMENTAL

The PMR spectra of D_2O and CF_3COOH solutions of the compounds were recorded with a spectrometer with an operating frequency of 80 MHz and hexamethyldisiloxane as the external standard. The IR spectra of KBr pellets of the compounds were recorded with a UR-10 spectrometer.

N,N-Substituted 1-Amino-2-methyl-4-penten-2-ols (Ia-g). These compounds were synthesized by reaction of 2-methyl-2-allyloxirane with secondary amines in the presence of catalytic amounts of water. An exception to this procedure was Ig, for the formation of which refluxing of the starting reagents in methanol for 20 h was necessary. Amino compounds Ia-c were previously described in [2]; the remaining compounds are presented in Table 1.

The iodination of Ia-g was carried out in methanol solution at room temperature [2]. The cyclic products were obtained in quantitative yields and were recrystallized from acetone-methanol. Iodocyclization products Id-g are presented in Table 2; Ia-c were previously described in [2]. The PMR spectrum of, for example, N,N-diethyl-2-iodomethyl-4-methyl-4-hydroxypyrrolidinium iodide contains the following proton signals (δ): $-CH_2I$ 3.5, CH (ring) 4.2-4.9, and CH_2 (ring) 2.0-3.4 ppm.

1-Piperidino-2-methyl-4-penten-2-ol Acetate (Id). This compound, with bp 61-62° (1 mm), d_4^{20} 0.9523, and n_D^{20} 1.4620, was obtained in 69% yield by refluxing 1-piperidino-2-methyl-4-penten-2-ol and acetyl chloride in benzene for 10 h. IR spectrum, cm^{-1}: 1645 (C=C) and 1720 (C=O). Found: N 6.6%; MR_D 65.04. $C_{13}H_{23}NO_2$. Calculated: N 6.2%; MR_D 65.33.

1-N,N-Diethylamino-2-methyl-4-penten-2-ol N-Oxide (IIa). A) A 25-ml sample of 33% hydrogen peroxide was added dropwise to 2.7 g (0.015 mole) of Ia in 10 ml of water, and the mixture was allowed to stand at room temperature for 24 h. It was then treated with 0.2 g of platinum black to decompose the excess hydrogen peroxide, after which the platinum black was removed by filtration, and the aqueous solution was treated with two 50-ml portions of ether to remove the unchanged Ia. The aqueous solution was vacuum evaporated to obtain a transparent viscous liquid, which was treated with two 20-ml portions of absolute benzene. The benzene was removed by vacuum distillation to give a slightly yellowish viscous liquid.

N-Oxides IIb-e were similarly obtained (see Table 3).

B) A mixture of 2.5 g (0.026 mole) of 2-methyl-2-allyloxirane and 4.5 g (0.05 mole) of N,N-diethylhydroxylamine in 10 ml of methanol was refluxed for 6 h, after which the methanol was removed in vacuo, and the residual liquid was treated with three 10-ml samples of dry benzene. The benzene was removed by distillation, and the residue was evacuated with an oil pump to give 1.3 g (50%) of product. According to the results of elementary analysis and the IR spectra (see Table 3), the product corresponded to the N-oxide obtained by method A.

The iodination of IIa-e was carried out in the same way as the iodination of Ia-g. Data on the quaternary tetrahydro-1,2-oxazinium salts IIIa-e are presented in Table 4. In the PMR spectrum of, for example, IIIb, the following proton signals (δ) are resolved: 1.67 (CH_3) singlet, 3.7-4.2 (CH_2), 1.8-2.3 ($C-CH_2$ and CH_2I), and 4.5 ppm (OH).

1-N,N-Diethylamino-3-butene N-Oxide (IV). This compound was obtained by method A by oxidation of 2.2 g (0.016 mole) of 1-N,N-diethylamino-3-butene. Workup gave 1.5 g (63%) of IV as a viscous liquid. IR spectrum, cm^{-1}: 920 (N→O) and 1645 (C=C). Found: C 67.0; H 12.0; N 9.9%. $C_8H_{17}NO$. Calculated: C 67.2; H 11.9; N 9.8%.

N,N-Diethyl-5-iodomethyltetrahydro-1,2-oxazolinium Iodide (V). This compound, with mp 127-128° (acetone-methanol), was obtained in quantitative yield by iodination of IV by the method used to iodinate IIa-e.

IR spectrum, cm^{-1}: 1010 (NOC), 1050 (CNO), 3000-2500 ($\geq\overset{+}{N}-$). Found: N 3.7; I 63.6%. $C_8H_{17}I_2NO$. Calculated: N 3.7; I 63.9%.

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ATRANES

XLVIII.* KINETICS AND MECHANISM OF THE HYDROLYSIS OF 1-(α-CHLOROALKYL)SILATRANES

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The kinetics of the hydrolysis of 1-(α-chloroalkyl)silatranes $RSi(OCH_2CH_2)_n[OCH(CH_3)CH_2]_{3-n}N$, (where $R = ClCH_2$, Cl_2CH, and CH_3ClCH, and $n = 1-3$) at 25°C in neutral and acidic aqueous and aqueous alcoholic media with H_2O, ^2H_2O, and $H_2{}^{18}O$ were studied. The rate of hydrolysis in acidic media is considerably higher than in neutral media. The introduction of methyl groups in the 3, 7, and 10 position of the atrane ring and an increase in the electronegativity of the substituent attached to the silicon atom lower the rate of hydrolysis. According to the mass spectrometric data, the triethanolamine formed during hydrolysis in $H_2{}^{18}O$ does not contain ^{18}O, which indicates hydrolytic cleavage of the Si–O bond rather than the O–C bond.

In order to ascertain the effect of the nature of the substituent attached to the silicon atom in the atrane ring on the hydrolytic stability of the molecule, we studied the hydrolysis of 1-(α-chloroalkyl)silatranes with the general formula $RSi(OCH_2CH_2)_n[OCH(CH_3)CH_2]_{3-n}N$, (where $R = ClCH_2$, Cl_2CH and CH_3ClCH, and $n = 1-3$) by polarography.

The silatranes were hydrolyzed at 25° in dilute acidic and neutral aqueous and aqueous alcohol solutions.

The reaction rate in neutral media was calculated from a first-order equation [2], since H_2O is the reagent and the change in its concentration with respect to the substrate is insignificant; the rate in acidic media was measured by a second-order equation [3] because of bonding of HCl with the reaction products.

The rate constants for the hydrolysis of 1-(chloromethyl)silatrane in water and in 25 and 50% (by volume) aqueous ethanol increase rapidly as the water concentration increases both in neutral and acidic media (Table 1).

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*See [1] for communication LXVII.

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