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INFLUENCE OF THE RADICAL CENTER ON THE BASIC HYDROLYSIS REACTION OF 4-DIHALOMETHYL-3-IMIDAZOLINE-3-OXIDE

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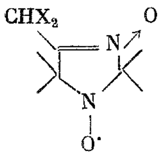
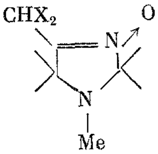
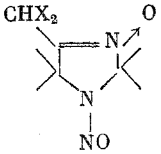
We previously discovered the influence of the radical center (RC) on the reactivities of functional groups not directly connected to it in the instance of deoxygenation of the nitrone group in derivatives of 3-imidazoline-3-oxide [1]. Study of the chemical properties of the paramagnetic (Ia, b) and diamagnetic (IIa, b), (IIIa, b) derivatives of 3-imidazoline-3-oxide containing a dihalomethyl group showed that the nitroxyl RC has a substantial influence on its reactivity in the basic hydrolysis reaction. This influence is manifested either in a significant change in the reaction rate or in a change in its direction.



(Ia, b)



(IIa, b)



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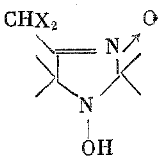
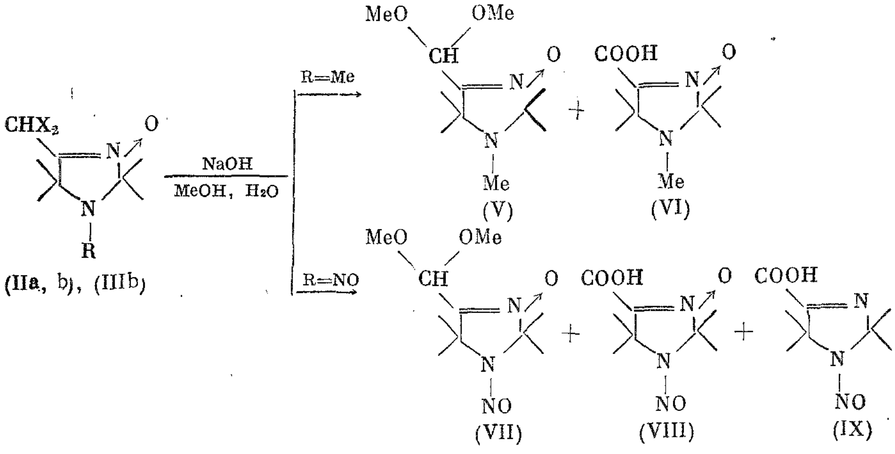


(IVa, b)

X=Cl (a), Br (b).

The choice of diamagnetic derivatives containing 1-methyl-(IIa) [2], (IIb) and 1-nitroso groups (IIIa, b) is dictated, first by the various electronic influences on the reaction center*, and second by their stabilities to oxidation to radicals (Ia) and (Ib) under the reaction conditions. On the strength of the second reason hydroxylamines (IVa) and (IVb) were excluded from consideration as diamagnetic analogs of radicals (Ia) and (Ib).

By the reaction of NaOH in aqueous methanolic solution the diamagnetic derivatives (IIa) (240 h) and (IIb) (120 h) (monitoring during the course of the reaction and at the end was carried out by TLC) were converted into acetal (V) (yield 60-90%) and to the carboxylic acid (VI) (1-2%), the 1-nitroso derivative (IIIb) (70 h) to the acetal (VII) (40%) and the acids (VIII) (20%) and (IX) (15%)



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*Results of the study of the electronic influence of substitution in position 1 on the reaction center by the method of ^{13}C NMR spectra, and also by measurement of the pK_a of 4-carboxylic acids will be published separately.

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TABLE 1. Reaction of Radical (Ia) with Aqueous-Alcoholic NaOH in the Presence of Nitroxyl Radicals (R-O•)

R—O·	Mole ratio (Ia)/RO·	Reaction conditions used	Reaction products and yields, %			
			(XII)	(XIII)	RH	others
–	–	1a	30	27		
–	–	2a	37	10		(XVIa), 6
–	–	3a	38	13		(XVIa), 6
(XVIII)	0,5	1a	76	5	(XIX), 17	
(XVIII)	1	1a	50	12	(XIX), 27	
(XVIII)	2	2a	51	6	(XIX), 28	(XVIa), 4
(XXIV)*	2	2a	42	10	(XXIX)† 5	
(XXVII)	2	2a	58	4	(XXX) ‡, 70	
(XVIII)	0,5	2a	63	3	(XIX), 12	(XX), 2, (XXI), 4
(XXIV)	0,5	2a	44	4	(XXIX), 10	(XXI), 4

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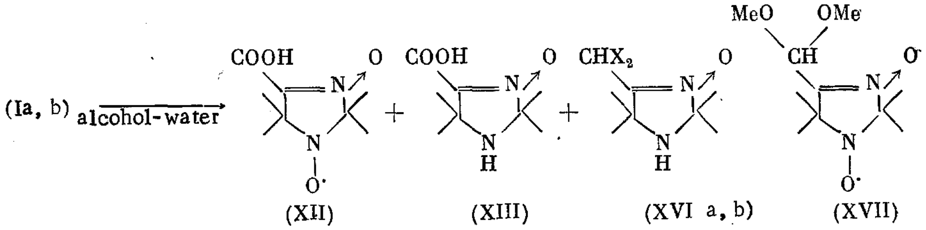
*2,2,5,5-Tetramethyl-4-phenyl-3-imidazoline-1-oxyl (XXIV).
†2,2,5,5-Tetramethyl-4-phenyl-3-imidazoline (XXIX).
‡4,4,5,5-Tetramethyl-2-phenyl-2-imidazoline (XXX).

We noted that the same results were obtained on carrying out the reaction in an argon atmosphere. We determined the ratios of acids (VIII) and (IX) from the intensities of the signals of the gem-dimethyl group of (VIII) at 2.06 ppm and of (IX) at 1.67 and 1.76 ppm in the PMR spectrum of mixtures of (VIII) and (IX), and also in the form of esters (X) and (XI) after separating them by column chromatography after treating the acid mixture with diazomethane.

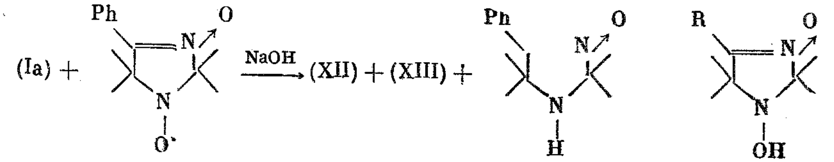
The paramagnetic derivatives (Ia, b) under the same conditions independent of the atmosphere (air or argon) are converted in from 30-60 sec to 100 min (monitoring by TLC) respectively to the radical acid (XII) and the amino acid (XIII), separated in the form of their methyl esters (XIV) and (XV). It should be noted that the ratio of (XII) to (XIII) depends on the method of adding reagents. The dichloro (XVIa) and dibromo (XVIb) derivatives formed in this way are unstable under basic conditions and on longer contact with the base are completely broken down. The dichloro derivative (XVIa) may be separated by rapid processing of the reaction mixture or by using a limited amount of base



The acetal radical (XVII) is not formed in this reaction, but is obtained independently by oxidizing the acetal (V) with H_2O_2, and under basic conditions similar to those described does not undergo any change in the course of several days.

However, the reactions of radicals (Ia) and (Ib) in a base proceed significantly faster than the analogous reactions of diamagnetic derivatives. (II) and (III), in which the dichloro derivative (Ia) reacts faster than the dibromo derivative (Ib) is in contrast to the diamagnetic dichloro (IIa) and dibromo derivatives (IIb). The process of nucleophilic substitution is accompanied by oxidation of the reaction center by the nitroxyl group, which is reduced to an amino group, in this way forming the secondary amines (XIII) and (XVI). The reason for such different chemical behavior of diamagnetic and paramagnetic derivatives of 3-imidazoline-3-oxides is probably the presence in the latter of RC's, which on the one hand modify the reactivities of the nitrone group of the dihalomethyl compound in a distinct manner, and on the other hand cause it to emerge as an oxidizing agent.

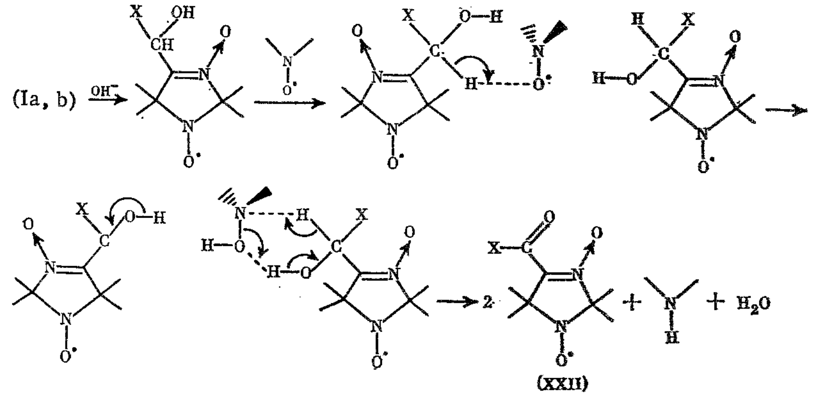
The following data verify the dual role of RCs. For the reaction of radical (Ia) with NaOH under the conditions described above, but in the presence of equimolar quantities of radical (XVIII) an increased yield of radical acid (XII) results and a decreased yield of amino acid (XIII), but radical (XVIII) is partially reduced to amino derivatives (XIX). On increasing the amount of radical (XVIII) in the reaction mixture the yield of the radical acid (XII) increases still more, the yield of amino acid (XIII) decreases, but the combined yield increases to 80% (see Experimental and Table 1). It should be noted that in this reaction 1-hydroxyl derivatives of (XX) and (XXI) are formed in many instances along with (XII), (XIII), and (XIX)



(XVIII) (XIX) (XX), (XXI)

R=Ph (XX); COOH (XXI).

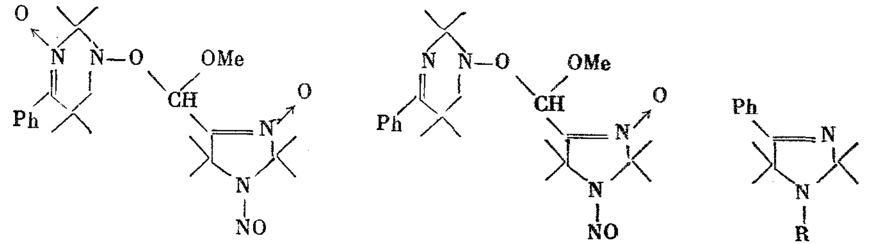
Moreover, on increasing the concentration of nitroxyl radicals in the reaction mixture, which can emerge as oxidizing agents in the reaction in question, the proportion of transformation of radicals (Ia) or (Ib) increases to 80% and the ratio of the overall yield of products of oxidation by the nitroxyl groups (XII) and (XIII) to the total yield of reduction products (XIII) and (XIX) is equal to 2:1. In other words for every two carboxyl groups, one amino group is formed, i.e., the RC comes forward and immediately oxidizes two reaction centers of the substrate. The hypothetical mechanism of this reaction could be the mechanism including the intermediate formation of the acid halide (XXII)



(XXII)

Favoring such a mechanism is the formation of the 1-hydroxyl derivatives (XX) and (XXI) in a number of instances, and also the necessity for minimal steric hindrance for radical oxidants having more accessible RC's (see below), i.e., having a planar ring including the nitroxyl fragment [3, 4].

The nitroxyl radical of (XVIII) plays a quite different role on introducing it into the reaction mixture with the derivative (IIIb). In this instance also as in the absence of radical (XVIII), acetal (VII) and imino acid (IX) are formed, the nitroso carboxylic acid (VIII) is absent, and a product of the type of acetal (XXIII) is formed



(XXIII) (XXV) (XXIV), (XXVI)

R=O· (XXIV); OH (XXVI).

The structure of compound (XXIII) was established on the basis of spectral data (Tables 2 and 3) and the elemental analysis data (Table 4). All spectral characteristics of compound (XXIII): IR, UV, PMR (see Table 2) are superimposable or close to it corresponding to the spectra of the acetal (VII) or the 1-hydroxy-4-phenylnitrone (XX).

Thus on interaction of the diamagnetic derivative (IIIb) with base, the introduction into the reaction mixture of the nitroxyl radical of (XVIII) does not lead to an increase of the yield of product (VIII) containing carboxyl and nitrone groups, as occurred in the instances of the reactions with radicals (Ia, b) with base, but to complete suppression of

TABLE 2. Spectral Characteristics of Derivatives of 1-Nitroso-3-imidazoline-3-oxide

Compound	UV spectrum λ, (log ε) nm	IR spectra, ν, cm^{-1}	PMR spectra, form A/form B*			Ratio A/B
			$2-CH_3$	$5-CH_3$	R	
(VII)	240(4,22)	1595(C=N) 2850(OCH_3)	$\frac{1,71}{1,94}$	$\frac{1,92}{1,71}$	$\frac{3,58}{3,56}$ (6H, OCH_3), 5,60 (1H, CH)	70/30
(VIII)	245(4,08)	1580(C=N), 1750(C=O)	$\frac{1,83}{2,04}$	$\frac{2,04^{\dagger}}{1,83}$		†
(IX)	235(3,96)	1640(C=N), 1720(C=O)	$\frac{1,67}{1,85}$	$\frac{1,88}{1,76}$		45/55
(X)	233(3,89) 274(4,05)	1560(C=N), 1745(C=O) 1710(C=O)	$\frac{1,75}{1,95}$	$\frac{1,97}{1,77}$	$\frac{3,93}{3,90}$ (3H, OCH_3)	70/30
(XI)	204(3,55) 235(3,87)	1640(C=N), 1735(C=O)	$\frac{1,69}{1,89}$	$\frac{1,89}{1,75}$	$\frac{3,97}{3,95}$ (3H, OCH_3)	50/50
(XXIII)	206(4,20) 240(4,33)	1595(C=N)	$\frac{1,71}{1,94}$	$\frac{1,92}{1,71}$	$\frac{3,70}{3,65}$ (3H, OCH_3), 5,88(1H, CH)	70/30
	234(4,32) 284(3,86)	1560(C=N)	1,71	1,62	7,27–7,44m (3H), 7,99–8,20 m (2H)–C_6H_5	
(XXV)	204(4,31) 239(4,36)	1590(C=N) 1610(C=N)	$\frac{1,76}{2,00}$	$\frac{2,00}{1,76}$	$\frac{3,78}{3,74}$ (3H, OCH_3), 6,01(1H, CH)	70/30
			1,57	1,57	7,40–7,60m (3H), 7,84–8,07 m (2H)–C_6H_5	

---

*1-Nitroso compounds in solution exist in the form of a mixture of two stereoisomers [2].

†Exists in one form A or B, but the signals of the two forms coincide.

its formation. In this instance radical (XVIII) appearing in any amount is an inhibitor of oxidation. Analogously in the presence of radical (XXIV) inhibition of the formation of the nitronecarboxylic acid (VIII) was observed, and product (XXV) was formed, the spectral characteristics of which are practically superimposable on the spectra of the acetal (VII) and phenylimine (see Tables 2 and 3).

From the data shown above it follows that the nitroxyl group essentially modifies the reactivity of the dihalomethyl compound's nitrone group in the same molecule as the nitroxyl radical (Ia) or (Ib) making it significantly high in comparison with the reactivity of the diamagnetic analog, with a great tendency toward oxidation by the nitroxyl RC. It should be noted that in the case of the paramagnetic derivatives (Ia) and (Ib) a transformation of the reactivities of the nitrone group dihalomethyl compound takes place: The dichloromethyl derivative (Ia) under identical conditions reacts about 100 times as fast as the dibromomethyl derivative (Ib), whereas the diamagnetic dichloromethyl derivative (IIa) reacts only about half as fast as the dibromomethyl derivative (IIb). We note also that in the reactions of radicals (Ia, b) the RC is reduced to an amino group, but at the same time it is known that the reduction of a nitroxyl group to an amino group goes only under drastic conditions only by the action of strong deoxygenating agents [5].

With the aim of explaining the factors influencing the ability of the nitroxyl radicals to act as oxidizing agents in the reaction under consideration, we carried out the reaction of radical (Ia) with base in the presence of nitroxyl radicals of various types, differing in steric requirements [6] as well as oxidizing properties [7]. The question of participating or nonparticipating radicals as oxidants was resolved with respect to the amount of paramagnetic (XII) and diamagnetic (XIII) acid and by the presence of the reduction product of the radical $R-O^{\bullet}$ introduced, the corresponding secondary amine (RH). We carried out the experiments using various mole ratios of substrate and oxidant as well as various methods of mixing.

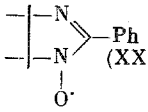
It was found that in the reaction of radicals (Ia, b) with a base, radicals of the series 3-imidazoline-3-oxide, 3-imidazoline, 2-imidazoline and imidazolidinone might serve as oxidants. The oxidizing activity of these radicals in the reactions under consideration

TABLE 3. ^{13}C NMR Spectral Data for Compounds (VII), (XX), (XXIII), (XXV), (XXVI)

Compound	2,2-CH_3	5,5-CH_3	C^2	C^5	C^4-N	CH_3OC-H	C_6H_5	OCH_3	Solvent
(VII)	21,6	28,6	90,7	67,8	140,8	99,2	–	56,8	$CHCl_3$, $CDCl_3$
	22,4	27,7	89,7	69,3		99,3			
(XX)	23,7	24,4	90,1	66,6	140,1	–	C^1 129,5	–	DMSO-d_6
							o 128,0		
							m 127,5		
							p 129,2		
(XXIII)	21,4	23,2	91,7	67,1	141,2		C^1 128,2	59,6	$CHCl_3$, $CDCl_3$
	22,7	27,3	90,7	68,5	139,0	102,6	*o* 128,0		
	22,3	28,8	89,7	69,2	138,6	101,8	*m* 127,4		
							p 129,6		
(XXV)	22,5	27,4	90,8	65,6	172,5		C^1 133,3	59,4	$CHCl_3$, $CDCl_3$
	20,7	28,5	90,1	67,4	140,3	102,6	*o* 128,1		
			89,8	68,2	139,3	102,2	*m* 127,5		
							p 129,9		
(XXVI)	23,9	25,9	88,3	69,6	171,9	–	C^1 133,2	–	DMSO-d_6
							o 128,0		
							m 127,2		
							p 129,6		

increases with an increase in their oxidizing properties [7]. The data obtained on carrying out the reaction of radical (Ia) with a base in the presence of 0.5 moles of nitroxyl radical (R–O•) might serve as an illustration of this. The oxidative properties of the radicals increase within the series [7]

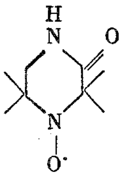
(XXIV) < (XVIII) <



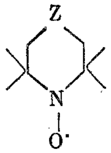
(XXVIII)

As is evident from the data of Table 1, with increase in oxidizing properties of the nitroxyl radicals, the ratios of the yields of paramagnetic (XII) and diamagnetic (XIII) acids and the yields of reduction products of the radicals (RH) are increased.

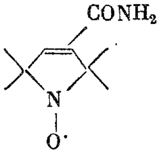
However, the oxidizing capabilities of the radicals are not determining factors in their participation as oxidants in this reaction. Thus nitroxyl radicals (XXXI)-(XXXVI) [5] having similar and under numerous circumstances stronger oxidizing properties [7], were separated from the reaction mixture in unchanged form with practically quantitative yields. The corresponding radical acids (XII) and amino acids (XIII) even in the presence of a twofold excess of these radicals are likewise preserved unchanged just as in the absence of radicals (R–O•)



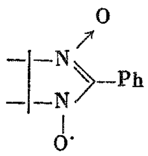
(XXXI)



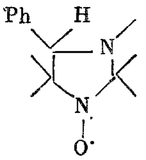
(XXXII)



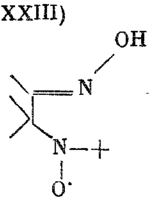
(XXXIII)



(XXXIV)



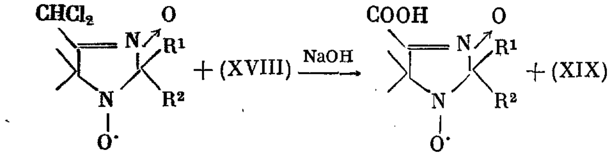
(XXXV)



(XXXVI)

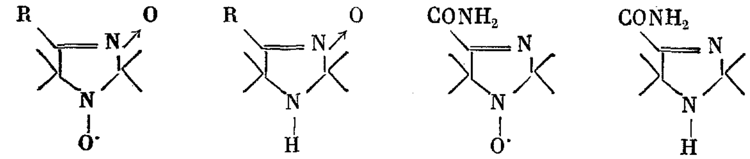
Z = CHOH, C=O, C=NON

The reaction of basic hydrolysis of paramagnetic 4-dichloromethyl-3-imidazoline-3-oxides can be used for syntheses of particular radical acids as well as for reduction products of the nitroxyl group, i.e., secondary amines in the series of 2- and 3-imidazolines and imidazolidinones. An example of the use of this reaction for synthesis of new acid radicals might be the hydrolysis reaction of radicals (XXXVII) and (XXXVIII) in the presence of an excess of radical (XVIII)

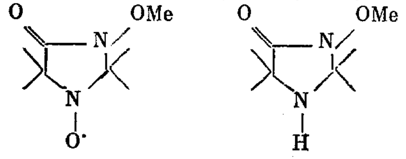


(XXXVII), (XXXVIII) (XXXIX), (XL)

R^1=Me, R^2=C_6H_{13} (XXXVII), (XXXIX), R^1+R^2=$(CH_2)_4$ (XXXVIII), (XL)



(XLI)—(XLIII) (XLVI)—(XLVIII) (XLIV) (XLIX)



(XLV) (L)

R = CH=CHPh (XLI), (XLVI), p-FC_6H_4 (XLII), (XLVII), p-MeC_6H_4 (XLIII), (XLVIII)

Using 3-imidazoline-3-oxide (XLI)-(XLIII), 3-imidazoline (XLIV), and imidazolidinone (XLV) radical as oxidants in the reaction of (Ia) with a base makes it possible to obtain amines (XLVI)-(L) very easily.

EXPERIMENTAL

The IR spectra were recorded on a UR-20 spectrophotometer in KBr (C 0.25%). UV spectra were taken on an SF-16 in C_2H_5OH. PMR spectra were recorded on a Varian A56-60A apparatus in a 5-7% solution in $CDCl_3$ with HMDS as an internal standard (δ scale). ^{13}C NMR spectra were recorded on Varian XL 200 for 10-15% solutions in DMSO-d_6 and on a Bruker HX-90 for 10-15% solutions in $CDCl_3$. The spectral characteristics of the compounds synthesized are shown in Tables 2 and 3, the elemental analysis data, melting points, and yields in Table 4.

4-Dibromomethyl-1-nitroso-2,2,5,5-tetramethyl-3-imidazolin-3-oxide (IIIb) was obtained from 1-nitroso-2,2,4,5,5-pentamethyl-3-imidazoline-3-oxide [8] according to [9].

Preparation of 4-Dichloromethyl Derivatives (IIa), (XXXVII) and (XXXVIII). 4-Dichloromethyl-1,2,2,5,5-pentamethyl-3-imidazoline-3-oxide (IIa) was obtained from 1,2,2,4,5,5-hexamethyl-3-imidazoline-3-oxide [8], 2-hexyl-4-dichloromethyl-2,5,5-trimethyl-3-imidazoline-3-oxide-1-oxyl (XXXVII) from 2-hexyl-2,4,5,5-tetramethyl-3-imidazoline-3-oxide-1-oxyl, 5,5-dimethyl-4-dichloromethyl-2-spirocyclopentan-3-imidazoline-3-oxide-1-oxyl (XXXVIII) from 2-spirocyclopentan-4,5,5-trimethyl-3-imidazoline-3-oxide-1-oxyl by chlorinating with NClS according to [9].

Reaction of 4-Dihalodimethyl Derivatives (IIa, b) with Aqueous Methanolic NaOH. To a solution of 0.0125 moles NaOH in 3.5 ml H_2O and 40 ml MeOH was added with stirring 0.0033 moles of (IIa) or (IIb) which was stirred until completely dissolved and let stand at 20°C until disappearance of the starting (II) (determined by TLC). The solvent was distilled off, 5 ml H_2O added, the solution extracted with $CHCl_3$. From the extract after chromatographing on a silica gel column (eluant, $CHCl_3$) there was obtained 4-dimethoxymethyl-1,2,2,5,5-pentamethyl-3-imidazoline-3-oxide (V). The aqueous solution was acidified with 7% HCl to pH 1-2, extracted with $CHCl_3$, the extract dried over $MgSO_4$, and filtered. After distilling off the $CHCl_3$, 4-carboxy-1,2,2,5,5-pentamethyl-3-imidazoline-3-oxide was obtained.

Reaction of the 4-Dibromo Derivative (IIIb) with Aqueous Methanolic NaOH. a) In the absence of nitroxyl radicals. The reaction is carried out according to the method given above. From the basic solution by extraction with $CHCl_3$ with subsequent chromatography on SiO_2 (eluant $CHCl_3$), 4-dimethoxy-1-nitroso-2,2,5,5-tetramethyl-3-imidazoline-3-oxide (VII) was obtained. From the acid solution by extraction with $CHCl_3$ there was obtained a mixture of (VIII) and (IX). The mixture of (VIII) and (IX) was treated with an ether solution of

TABLE 4. Yields, Melting Points and Elemental Analysis Data of the Compounds Synthesized

Compound	Yield, %	mp, °C	Found, %			Molecular formula	Calculated, %		
			C	H	N		C	H	N
(IIa)	73	130–132 (hexane)	44,7	6,5	11,6	$C_9H_{16}Cl_2N_2O$ [a]	45,2	6,7	11,7
(IIIб)	61	155–157 (ethanol)	28,3	4,0	12,0	$C_8H_{13}Br_2N_3O_2$	28,0	3,8	12,2
(V)	90	Oil	57,8	9,4	12,0	$C_{11}H_{22}N_2O_3$	57,4	9,6	12,2
(VI)	3	83–84 (heptane)	53,5	8,0	13,9	$C_9H_{16}N_2O_3$	54,0	8,0	14,0
(VII)	45	54–56 (heptane)	48,7	7,9	17,1	$C_{10}H_{19}N_3O_4$	49,0	7,8	17,1
(VIII)	80	144–146 (alcohol)	45,1	6,5	19,7	$C_8H_{13}N_3O_4$	44,7	6,0	19,5
(IX)	15	107–109	48,3	6,7	20,7	$C_8H_{13}N_3O_3$	48,2	6,5	21,1
(X)	15	68–70 (heptane)	47,0	6,7	18,2	$C_9H_{15}N_3O_4$	47,2	6,6	18,3
(XI)	12	Oil	51,1	7,0	19,5	$C_9H_{15}N_3O_3$	50,7	7,0	19,7
(XIII)	80	85–88 (hexane)	51,6	8,0	15,1	$C_8H_{14}N_2O_3$	51,6	7,5	15,1
(XV)	28	Oil	53,6	7,8	13,8	$C_9H_{16}N_2O_3$	54,0	8,0	14,0
(XVIa)	18	117–119 (heptane)	42,3	6,1	12,1	$C_8H_{14}Cl_2N_2O$ [b]	42,7	6,2	12,4
(XVII)	50	65–66 (hexane)	52,0	8,5	12,2	$C_{10}H_{19}N_2O_4$	52,0	8,2	12,1
(XXIII)	20	162–165 (heptane)	59,2	7,5	15,4	$C_{22}H_{33}N_5O_5$ [c]	59,1	7,4	15,7
(XXV)	20	Oil	59,9	7,5	15,7	$C_{22}H_{33}N_5O_4$	61,3	7,7	16,2
(XXIX)	10	54–57 (subl.)	70,8	9,4	12,7	$C_{13}H_{18}N_2 \cdot H_2O$	70,9	9,1	12,7
(XXX)	70	145–147 (heptane)	77,0	8,8	13,7	$C_{13}H_{18}N_2$	77,2	8,9	13,9
(XXXVII)	50	Oil	50,6	6,3	8,7	$C_{13}H_{20}Cl_2N_2O_2$ [d]	50,8	6,5	9,1
(XXXVIII)	60	72–74 (subl.)	45,2	5,6	10,5	$C_{10}H_{15}Cl_2N_2O_2$ [e]	45,2	5,6	10,5
(XXXIX)	68	Oil	59,2	7,5	10,0	$C_{14}H_{22}N_2O_4$	59,6	7,8	9,9
(XL)	70	78–81	52,8	6,7	12,0	$C_{10}H_{15}N_2O_4$	52,9	6,6	12 3
(XLVI)	28	165–167 (alcohol)	74,2	8,5	11,5	$C_{15}H_{20}N_2O$	73,8	8,2	11,5
(XLVII)	27	72–74 (subl.)	66,2	7,2	11,8	$C_{13}H_{17}FN_2O$ [f]	66,1	7,2	11,9
(XLVIII)	28	75–77 (heptane)	72,8	8,8	12,1	$C_{14}H_{20}N_2O$	72,4	8,6	12,1
(XLIX)	9	165–167 (heptane)	56,7	9,0	24,7	$C_8H_{15}N_3O$	56,8	8,9	12,1
(L)	30	97–99 (heptane)	55,5	9,3	16,2	$C_8H_{16}N_2O_2$	55,8	9,3	16,3

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[a] Found: Cl 29.6%. Calculated: Cl 29.7%.
[b] Found: Cl 31.2%. Calculated: Cl 31.6%.
[c] Molecular weight was determined by vapor phase osmometry. Found: 420, calculated: 447.
[d] Found: Cl 22.6%. Calculated: Cl 23.1%.
[e] Found: Cl 26.7%. Calculated: Cl 26.7%.
[f] Found: F 7.9%. Calculated: F 8.1%.

diazomethane (from 0.5 g N-nitroso-N-methylurea), the mixture of esters of (X) and (XI) obtained was separated on a SiO_2 column (eluant $CHCl_3$). 4-Carbomethoxy-1-nitroso-2,2,5,5-tetramethyl-3-imidazoline (XI) and 4-carbomethoxy-1-nitroso-2,2,5,5-tetramethyl-3-imidazoline-3-oxide (X) were obtained in a ratio of 45:55.

b) In the presence of radical (XVIII). The reaction was by the method described above, but in an aqueous methanolic solution in which 0.0033 moles of radical (XVIII) [10] had been previously dissolved. The chloroform extract from the basic solution, after distilling off the $CHCl_3$ was chromatographed on a SiO_2 column (eluant, ether), separating sequentially: 79% of the starting (XVIII), 31% acetal (VII) and 20% 4-[methoxy(2',2',5',5'-tetramethyl-4'-phenyl-3'-imidazoline-1'-oxy]methyl-1-nitroso-2,2,5,5-tetramethyl-3-imidazoline-3-oxide (XXIII). After acidifying the aqueous solution with 7% HCl to a pH of 1-2, by extraction with $CHCl_3$ 4-carboxy-1-nitroso-2,2,5,5-tetramethyl-3-imidazoline (IX) was separated out in 12% yield.

c) In the presence of radical (XXIV) [10]. The reaction and the separation of products was carried out according to method b). Separated subsequently: 75% of starting radical (XXIV), 20% 4-[methoxy(2',2',5',5'-tetramethyl-4'-phenyl-3'-imidazoline-1'-oxy)]methyl-1-nitroso-2,2,5,5-tetramethyl-3-imidazoline-3-oxide (XXV), 17% acetal (VII) and 15% acid (IX).

4-Dimethoxymethyl-2,2,5,5-tetramethyl-3-imidazoline-3-oxide-1-oxyl (XVII). Compound (XVII) obtained by oxidizing (V) by the method of [8], was purified by chromatography on a SiO_2 column (eluant, $CHCl_3$) and recrystallized from hexane.

Reaction of 4-Dihalo Derivatives (Ia, b), (XXXVII), (XXXVIII) with Aqueous Alcoholic NaOH. a) Reactions of (Ia, b) in the absence of nitroxyl radicals. 1a) To a solution of 0.015 moles NaOH in 4 ml H_2O and 60 ml EtOH or MeOH was added with stirring 0.005 moles (Ia) or (Ib) in small portions. After removal of the starting material (by TLC) the alcohol was distilled off, the residue dissolved in 10 ml H_2O, washed several times with small portions of $CHCl_3$, dried over $MgSO_4$, the aqueous layer acidified with 7% HCl to a pH 1-2, extracted with $CHCl_3$ which was dried over $MgSO_4$, filtered, and the $CHCl_3$ distilled off. The acid mixture of (XII) and (XIII) was treated with an ether solution of diazomethane (from 1 g N-nitroso-N-methylurea). After chromatographing on a SiO_2 solumn (eluant, $CHCl_3$) ester (XIV) [10] and 4-carbomethoxy-2,2,5,5-tetramethyl-3-imidazoline-3-oxide (XI) were obtained in 30 and 27% yields respectively.

2a) To a solution of 0.015 moles NaOH in 4 ml H_2O and 30 ml EtOH with stirring was added at once the entire solution of 0.005 moles (Ia) or (Ib) in 30 ml EtOH. It was processed as in 1a). From the basic extract after chromatography on a SiO_2 column (eluant, $CHCl_3$) 4-dichloromethyl-2,2,5,5-tetramethyl-3-imidazoline-3-oxide (XVIa) was separated in 6% yield. From the acid extract after treatment with diazomethane, esters (XIV) and (XV) were separated in 37 and 10% yields respectively.

3a) To a solution of 0.015 moles NaOH in 4 ml water and 60 ml EtOH was added at once with stirring 0.005 moles (Ia) or (Ib). It was processed as in 2a). Esters (XIV) and (XV) were separated in yields of 38 and 13% respectively and (XVIa) was separated in a yield of 6%.

4a) By the method of 3a) using 0.01 moles of NaOH, the dihalocompound (XVIa) was separated in 18% yield.

b) Reactions of (Ia) in the presence of nitroxyl radicals. Reactions were carried out under the conditions of 1a)-3a) first dissolving from 0.5 to 2 moles nitroxyl radicals for 1 mole of (Ia) in aqueous alcoholic NaOH solution. By chromatography of the basic extract on a SiO_2 column (eluant, $CHCl_3$), unreacted nitroxyl radicals, compound (XVIa), and the corresponding nitroxyl radical of the secondary amine were separated. On carrying out the reaction by the method of 2a) using 2 moles of nitroxyl radical there was found 2-3% of the corresponding 1-hydroxyl derivatives and 12-14% of the secondary amine. The quantity of the 1-hydroxyl derivative is determined by the quantity of the nitroxyl radical, obtained by chromatographic separation on a SiO_2 column (eluant, $CHCl_3$) by oxidizing the mixture of 1-hydroxyl derivative and amine with PbO_2 (amines under these conditions are not oxidized).

By method b) 2,2,5,5-tetramethyl-4-phenyl-3-imidazoline (XXIX), compounds (XIX) [8], 4-styryl-(XLVI), 4-p-fluorophenyl-(XLVII), 4-p-tolyl-(XLVIII), 2,2,5,5-tetramethyl-3-imidazoline-3-oxides, 4,4,5,5-tetramethyl-2-phenyl-2-imidazoline (XXX), 4-carbamidoyl-2,2,5,5-tetramethyl-3-imidazoline (XLIX), and 3-methoxy-4-keto-2,2,5,5-tetramethylimidazolidine (L) were obtained. All these compounds have IR and UV spectra close to the spectra of the corresponding nitroxyl radicals, but the band for the NH group appears at 3280-2250 cm^{-1} in the IR spectrum.

The ratios of the esters (XIV), (XV) and (XXI) obtained from the acid extract after treatment with diazomethane were determined chromatographically as in 1a). On using 2 moles (XVIII) (method 2a)) their yields were 60, 3, and 4% respectively, and for 2 moles of (XXIV): 44, 4 and 4%.

c) Acids (XXXIX) and (XL). Under the conditions of method 3a) in the presence of 2 moles of (XVIII), 2-hexyl-4-carboxy-2,5,5-trimethyl-3-imidazoline-3-oxide-1-oxyl (XXXIX) and 5,5-dimethyl-4-carboxy-2-spirocyclopentan-3-imidazoline-3-oxide-1-oxyl (XL) were obtained from (XXXVII) and (XXXVIII) respectively.

4-Carboxy-2,2,5,5-tetramethyl-3-imidazoline-3-oxide. To a solution of 0.24 g of ester (XV) in 5 ml MeOH was added a 2 N solution of KOH to a pH of around 10. After 15 min the alcohol was distilled off, 5 ml of water added to the residue, which was acidified to pH 1, extracted with $CHCl_3$, the extract dried over $MgSO_4$, and filtered. After boiling off the solvent and the residue (XIII) was recrystallized from hexane. 4-Carboxyl-1-nitroso-2,2,5,5-tetramethyl-3-imidazoline-3-oxide (VIII) was obtained from ester (X) in an analogous manner.

CONCLUSIONS

1. The nitroxyl group in 4-dihalomethyl-3-imidazoline-3-oxide-1-oxyls substantially modifies the reactivity of the dihalomethyl group, giving it greater activity in comparison with the diamagnetic analog in the basic hydrolysis reaction and greater inclination to oxidation by the radical center.

2. The main products of hydrolysis in aqueous alcohol of diamagnetic 4-dihalomethyl-3-imidazoline-3-oxide are 4-dialkoxymethyl derivatives, and of nitroxyl radicals with the 4-dihalodimethyl group, a mixture of paramagnetic and diamagnetic 4-carboxy-3-imidazoline-3-oxides.

3. In contrast to the diamagnetic, in the paramagnetic derivatives of 4-dihalodimethyl-3-imidazoline-3-oxides the reactivity changes in going from the dibromomethyl to the dichloromethyl derivative, i.e., the rate of basic hydrolysis increases.

4. Under the reaction conditions of basic hydrolysis the paramagnetic 4-dihalomethyl-3-imidazoline-3-oxides are oxidized by radicals of the 3-imidazoline-3-oxide, 2- and 3-imidazoline and imidazolidinone series; the radical centers of these are easily reduced to amino groups.

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