OXIDATIVE ALKOXYLATION OF 4H-IMIDAZOLE N-OXIDES AS A NEW METHOD OF SYNTHESIS OF STABLE NITROXYL RADICALS OF THE 2- AND 3-IMIDAZOLINE SERIES WITH ALKOXY GROUPS AT THE α-CARBON ATOM OF THE RADICAL CENTER

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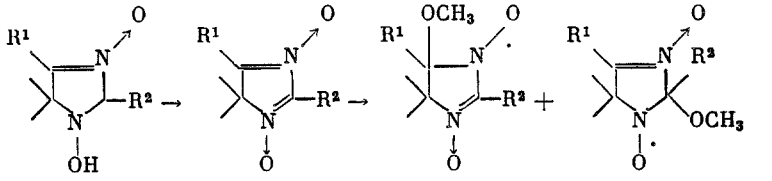
Oxidation of 1-hydroxy-5,5-dimethyl-3-imidazoline 3-oxides in methanol with PbO_2 leads to the formation of stable nitroxyl radicals (NR) of the 2- and 3-imidazoline series [1]. The synthesis of a wide range of 3-imidazoline 3-oxides and 3-imidazolines [2], and 4H-imidazole di- and mono-N-oxides [3] made possible a detailed study of this reaction.

During the oxidation of 1-hydroxy-4-R^1-2-R^2-5,5-dimethyl-3-imidazoline 3-oxides (Ia-q) in methanol with PbO_2, nitronylnitroxyl radicals (NNR) (IIIa-k, m, o) and NR (IVa-e, i, k-q) are formed. The reaction proceeds via the formation of 4H-imidazole-1,3-dioxides (IIa-q). When the latter are used as the starting compounds the ratio between the products does not change. In ethanol and in other alcohols, the oxidation of 2,4-disubstituted 3-imidazoline 3-oxides (Ia-q) stops at the stage of the 4H-imidazole 1,3-dioxides (IIa-q) formation.



(Ia-q) (IIa-q) (IIIa-k,m,o) (IVa-e,i,k-q)

R' = Ph (a-j), 2-furyl (k), 5-CH_3-2-furyl (ℓ,m), 2-thienyl (n,o), 5-CH_3-2-thienyl (p,q). R^2 = CH_3 (a,ℓ,n), Ph (b,k,o,p), o-FC_6H_4 (c), m-$O_2NC_6H_4$ (d,m), 3-Py (e,q), p-$H_2NC_6H_4$ (f), p-$(CH_3)_2NC_6H_4$ (g), o-HOC_6H_4 (h), 2-furyl (i), 2-thienyl (j).

Increase in the electron-donor character of substituent R^1 and electron-acceptor character of substituent R^2 results in an increase in the yield of NR (IV), while contrary to this, increase in the acceptor properties of R^1 and donor properties of R^2 favors the preferential formation of NNR (III) (Table 1).

The NNR (IIIb-k, m, o) obtained are intensely blue stable compounds, while the violet-colored NNR (IIIa) decomposes slowly even at −5°C. The UV spectra of the NNR (IIIa-k, m, o) show absorption maxima at 595-750 nm ($\log \varepsilon$ = 2.5-3.2), the positions of which are strongly dependent on the substituents R^2 [4]. The IR spectra of these radicals have vibration bands of methoxy groups at 2850 and 1100 cm^{-1}. The EPR spectra of (III) are in the form of a quintet with $a_N^1 = a_N^3 = 7.5$ Oe.

The NR (IVa-e, i, k-q) are stable orange or brown-colored crystalline compounds, the character of whose UV spectra is determined by the absorption of α-phenyl- or α-heteroaryl-nitronic groups [4]. The IR spectra of these compounds show vibration bands of methoxy groups at 2850 cm^{-1} and conjugated nitronic groups at 1540-1550 cm^{-1}. Reduction of (IVa, b) with zinc in the presence of NH_4Cl gave colorless compounds (Va, b), the structure of which was confirmed by the ^1H and ^{13}C NMR spectral data [5]. Compounds (Va, b) can be oxidized by PbO_2 or MnO_2 into the initial NR, while the reduction product of (IIIb) is oxidized by atmospheric oxygen already during its separation (cf. [6]).

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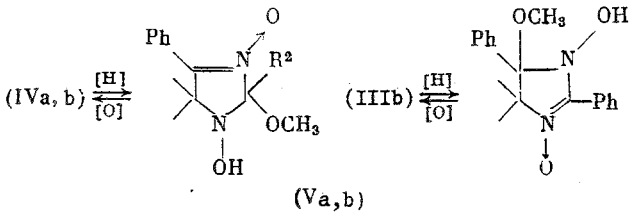
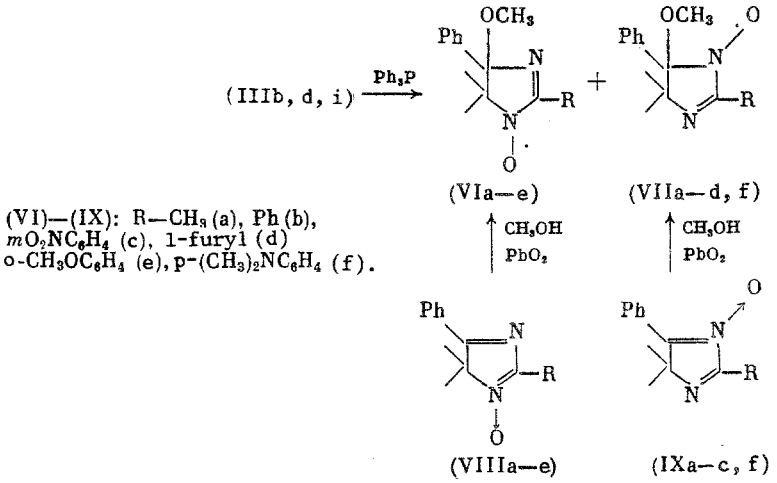


(Va,b)

The characteristics of the compounds obtained are given in Table 2.

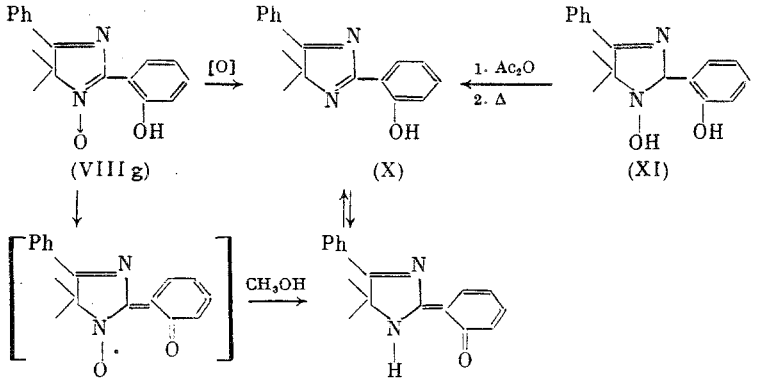
During the oxidation of compounds (Ia-q), in addition to (III) and (IV), small amounts of two further compounds are formed, having an EPR spectrum characteristic of iminonitroxyl radicals (INR) [7]. The INR (VIb, c, d) and (VIIb, c, d) were isolated from the reaction mixture, and their yield increased with increase in the reaction time. The same INR were obtained by treating (IIIb, d, i) with Ph_3P [8].



(VI)—(IX): R—CH_3 (a), Ph (b), $mO_2NC_6H_4$ (c), 1-furyl (d) o-$CH_3OC_6H_4$ (e), p-$(CH_3)_2NC_6H_4$ (f).

The NNR (III) lose the O atom much more readily than 4,4,5,5-tetramethyl-2-phenyl-2-imidazoline 3-oxide-1-oxyl [7]. Thus, reduction under similar conditions of this NNR and (IIIb) takes 48 and 2 h, respectively. The INR (VIa-e) and (VIIa-c, f) were obtained by the oxidation of 4H-imidazole N-oxides (VIIIa-e) and (IXa-c, f) in methanol with PbO_2.

Oxidation of compound (VIIIg) in methanol with PbO_2 gives 4H-imidazole (X) instead of the expected INR, the structure of which was confirmed by an alternative synthesis from 3-imidazoline (XI). The corresponding INR were also not obtained by the reduction of NNR (IIIh) with Ph_3P, possibly because of their instability. The formation of compound (X), which is stable to the action of Ph_3P also was not observed. It can be assumed that the formation of 4H-imidazole (X) is the result of the oxidation of the phenoxyl fragment, followed by deoxygenation of the nitroxyl radical formed



The INR (VIa-e) and (VIIa-c, f) are stable bright-red, violet or brown compounds, the HFS of the EPR spectra of which are determined by splitting on two nitrogen atoms with HFI constants differing by a factor of approximately 2, (VIa-e): a_N^1 = 8.5-9.3 Oe, a_N^3 = 4.0-4.3 Oe, g = 2.0062; (VIIa-c, f): a_N' = 8.1-8.7 Oe, a_N^3 = 3.9-4.1 Oe, g = 2.0062.

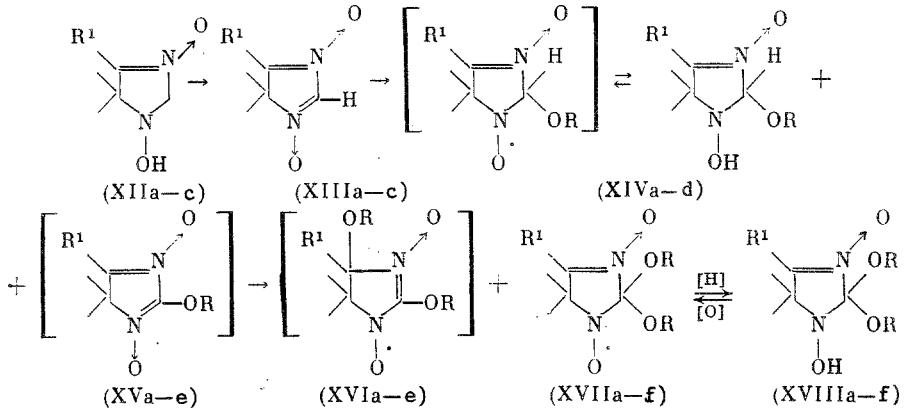
TABLE 1. Yields of NR and NNR during Oxidation of Compounds (Ia-q) and (XIIa-c)

Starting compound	NNR	Yield of NNR, %	NR	Yield of NR, %	Starting compound	NNR	Yield of NNR, %	NR	Yield of NR, %
(Ia)	(IIIa)	15	(IVa)	25	(Iℓ)	(IIIℓ)	0	(IVℓ)	62
(Ib)	(IIIb)	65	(IVb)	30	(Im)	(IIIm)	5	(IVm)	92
(Ic)	(IIIc)	55	(IVc)	30	(In)	(IIIn)	0	(IVn)	75
(Id)	(IIId	60	(IVd)	35	(Io)	(IIIo)	6	(IVo)	70
(Ie)	(IIIe)	50	(IVe)	20	(Ip)	(IIIp)	0	(IVp)	76
(If)	(IIIf)	90	(IVf)	0	(Iq)	(IIIq)	0	(IVq)	80
(Ig)	(IIIg)	90	(IVg)	0	(XIIa)	–	–	(XVIId)	80
(Ih)	(IIIh)	40	(IVh)	0	(XIIa)	–	–	(XVIIe)	10
(Ii)	(IIIi)	65	(IVi)	15	(XIIb)	–	–	(XVIIb)	60
(Ij)	(IIIj)	65	(IVj)	0	(XIIc)	–	–	(XVIIc)	62
(Ik)	(IIIk)	25	(IVk)	50					

TABLE 2. Characteristics of Synthesized Compounds

Compound	Mp, °C	Found, %			Empirical formula	Calculated, %			Element (found/calculated)
		C	H	N		C	H	N	
(IIIc)	131–134	65,5	5,6	8,7	$C_{18}H_{18}N_2O_3F$	65,6	5,5	8,3	F(6,2/5,8)
(IIId)	173–175	61,1	5,2	11,9	$C_{18}H_{18}N_3O_5$	60,7	5,1	11,8	
(IIIe)	125–127	65,3	5,2	13,2	$C_{17}H_{18}N_3O_3$	65,4	5,8	13,5	
(IIIf)	143–149	66,1	6,3	12,7	$C_{18}H_{20}N_3O_3$	66,2	6,1	12,9	
(IIIg)	163–164	67,4	6,9	11,5	$C_{20}H_{24}N_3O_3$	67,8	6,8	11,9	
(IIIh)	131–133	66,0	5,8	8,6	$C_{18}H_{19}N_2O_4$	66,0	5,8	8,6	
(IIIi)	144–146	63,9	5,7	9,3	$C_{16}H_{17}N_2O_4$	63,8	5,7	9,3	
(IIIj)	165–168	60,5	5,4	8,5	$C_{16}H_{17}N_2O_3S$	60,6	5,4	8,8	S(10,5/10,1)
(IIIk)	94–96	63,8	5,7	9,2	$C_{16}H_{17}N_2O_4$	63,8	5,7	9,3	
(IIIm)	142–143	56,8	5,1	11,7	$C_{17}H_{18}N_3O_6$	56,7	5,0	11,7	
(IIIo)	117–118	61,0	5,4	8,8	$C_{16}H_{17}N_2O_3S$	60,6	5,4	8,8	
(IVc)	131–133	65,3	5,3	8,4	$C_{18}H_{18}N_2O_3F$	65,6	5,5	8,5	F(6,2/5,8)
(IVd)	113–115	60,4	5,1	11,9	$C_{18}H_{18}N_3O_5$	60,7	5,1	11,8	
(IVe)	179–181	65,3	5,9	13,4	$C_{17}H_{18}N_3O_3$	65,4	5,8	13,5	
(IVi)	145–146	63,4	6,0	9,0	$C_{16}H_{17}N_2O_4$	63,8	5,7	9,3	
(IVk)	117–118	63,6	5,7	8,9	$C_{16}H_{17}N_2O_4$	63,8	5,7	9,3	
(IVℓ)	145–146	57,0	6,8	10,9	$C_{12}H_{17}N_2O_4$	56,9	6,7	11,1	
(IVm)	149–150	56,7	5,1	11,9	$C_{17}H_{18}N_3O_6$	56,7	5,0	11,7	
(IVn)	163–164	51,9	6,0	11,2	$C_{11}H_{15}N_2O_3S$	51,8	5,9	11,0	S(13,1/12,6)
(IVo)	180–182	60,5	5,3	8,6	$C_{16}H_{17}N_2O_3S$	60,6	5,4	8,8	S(11,6/11,1)
(IVp)	153–154	61,3	5,9	8,3	$C_{17}H_{19}N_2O_3S$	61,6	5,7	8,4	S(9,4/9,7)
(IVq)	167–168	57,6	5,4	12,6	$C_{16}H_{18}N_3O_3S$	57,8	5,4	12,6	S(9,5/9,6)
(Va)	124–126	62,7	7,0	11,4	$C_{13}H_{18}N_2O_3$	62,4	7,2	11,2	
(Vb)	150–152	69,1	6,6	8,8	$C_{18}H_{20}N_2O_3$	69,2	6,4	9,0	
(VIa)	40–42	67,4	7,2	12,2	$C_{13}H_{17}N_2O_2$	67,0	7,3	12,0	
(VIc)	167–169	63,1	5,3	12,4	$C_{18}H_{18}N_3O_4$	63,5	5,3	12,4	
(VId)	100–102	67,8	6,0	9,4	$C_{16}H_{17}N_2O_3$	67,4	6,0	9,8	
(VIe)	63–65	70,8	6,7	8,5	$C_{19}H_{21}N_3O_3$	70,1	6,5	8,6	
(VIIa)	Oil	66,7	7,0	12,3	$C_{13}H_{17}N_2O_2$	67,0	7,3	12,0	
(VIIc)	134–135	63,5	5,3	12,7	$C_{18}H_{18}N_3O_4$	63,5	5,3	12,4	
(VIId)	125–127	67,9	6,2	10,0	$C_{16}H_{17}N_2O_3$	67,4	6,0	9,8	
(VIIf)	140–141	70,2	7,4	12,7	$C_{20}H_{24}N_3O_2$	69,9	7,4	12,8	
(X)	103–104	77,7	6,2	10,6	$C_{17}H_{16}N_2O$	77,3	6,1	10,6	
(XVIIb)	159–161	52,5	6,1	11,2	$C_{11}H_{15}N_2O_5$	51,8	5,9	11,0	
(XVIIc)	181–183	48,7	5,5	10,1	$C_{11}H_{15}N_2O_4S$	48,7	5,5	10,3	S(11,6/11,8)
(XVIId)	77–79	61,7	7,1	9,3	$C_{15}H_{21}N_2O_4$	61,4	7,2	9,6	
(XVIIe)	87–90	63,5	7,9	8,6	$C_{17}H_{25}N_2O_4$	63,6	7,8	8,7	
(XVIIf)	132–135	59,2	5,9	10,4	$C_{13}H_{15}N_2O_4$	59,3	5,7	10,6	
(XVIIIa)	160–162	58,4	6,9	10,1	$C_{13}H_{18}N_2O_4$	58,6	6,8	10,5	
(XVIIId)	155–159	60,5	7,5	9,4	$C_{15}H_{22}N_2O_4$	61,2	7,5	9,5	
(XVIIIe)	167–170	63,2	8,2	8,7	$C_{17}H_{26}N_2O_4$	63,3	8,1	8,7	
(XVIIIf)	200–203	59,2	6,1	10,5	$C_{13}H_{16}N_2O_4$	59,0	6,1	10,6	
(XIX)	85–87	62,2	6,8	11,1	$C_{13}H_{17}N_2O_3$	62,6	6,9	11,2	
(XXIIa)	83–85	62,5	6,8	10,8	$C_{13}H_{17}N_2O_3$	62,6	6,9	11,2	
(XXIIb)	93–95	63,2	6,1	10,9	$C_{13}H_{15}N_2O_3$	63,2	6,1	11,3	

In contrast to 3-imidazoline 3-oxides (Ia-q), the oxidation of the corresponding derivatives unsubstituted in the 2-position leads to NR which are stable not only in methanol, but also in other alcohols (ROH).



(XIIa–c) (XIIIa–c) (XIVa–d)

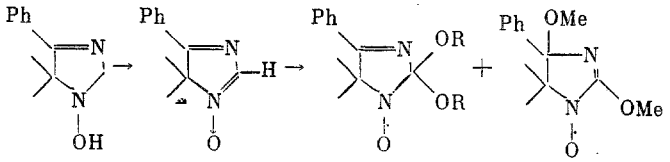
(XVa–e) (XVIa–e) (XVIIa–f) (XVIIIa–f)

R^1=Ph (a, d-f), 2-furyl (b); 2-thienyl (c); R = Me (a-c), Et (d), *i*-Pr (e); R + R=—CH_2CH_2—(f).

The formation of the intermediate compound (XIIIa) was detected by means of TLC, compounds (XIVd) and (XVIIId) were separated from the reaction mixture. Compound (XVd) could not be isolated or prepared by the oxidation of compound (XIVd). The main products of oxidation of compounds (XIIa-c) are NR (XVIIa-e), which are stable red or brown colored compounds. Reduction of these NR with zinc in the presence of NH_4Cl gave compounds (XVIIIa, d, e), the structure of which was confirmed by PMR spectral data. The formation of the NNR in this reaction is indicated by the appearance of a characteristic blue color at the beginning of the reaction and a quintet in the EPR spectrum of the reaction mixture. The NNR (XVIa-e) are unstable and INR (XIX) was separated from the reaction mixture in low yield (see above).

Increase in the volume of the R group in the alcohol results in a sharp retardation of the reaction, and the oxidation in isopropanol already proceeds very slowly (60 h), while oxidation in n-butanol in general does not lead to radicals. Oxidation of compound (XIIa) in ethylene glycol with PbO_2 does not lead to satisfactory results, since ethylene glycol is rapidly oxidized by PbO_2. Compound (XVIIIf) could be obtained in a high yield by using MnO_2 as the oxidizing agent; its oxidation gave NR (XVIIf) in a high yield.

During the oxidation of 3-imidazoline (XX) or 4H-imidazole 3-oxide (XXI) under similar conditions, NR (XXIIb) was obtained. Oxidation of (XX) or (XXI) in methanol with PbO_2 gave both the INR (XIX) and NR (XXIIa)



(XX) (XXI) (XXIIa, b) (XIX)

R=Me (XXIIa), R + R=—CH_2CH_2—(XXIIb).

Thus, with the proposed approach to the synthesis of the NR it is possible, firstly, to obtain stable NR containing alkoxy groups in the immediate environment of the radical center, which have several new spectral properties [8], and secondly to obtain NR of several types: derivatives of 3-imidazoline 3-oxide, 3-imidazoline, 2-imidazoline, and 4H-imidazole N-oxides. The third advantage of this method consists in possibilities of wide variation of substituents R^1 and R^2 because of the availability of the starting compounds with various substituents [2, 3].

EXPERIMENTAL

The IR spectra were recorded on a UR-20 spectrometer in KBr tablets (concentration 0.25%, ℓ = 1 mm). The UV spectra were run in alcohol on a Specord UV-VIS spectrophotometer. The IR and UV spectra of most of the synthesized compounds are to be published in [4]. The PMR spectra were recorded on a Varian A56/60A spectrometer (60 MHz) for 10-15% solutions, using HMDS

as internal standard (0.04 ppm, relative to TMS). The EPR spectra were obtained on an RE-1306 apparatus. A Fremy's salt was used for measuring the g-factors (a_N = 13.09 Oe, g = 2.0057). The course of the reaction was monitored by TLC on Silufol UV-254 plates, using chloroform as eluent.

General Method for the Preparation of 5,5-Dimethyl-4-methoxy-2-imidazoline 3-Oxide-1-oxyls (IIIa-k, m, o) and 5,5-Dimethyl-2-methoxy-3-imidazoline 3-Oxide-1-oxyls (IVa-e, i, k-q). A mixture of 0.01 mole of a 3-imidazoline 3-oxide (Ia-q) or 4H-imidazole 1,3-dioxide (IIa-q), 10-15 g of PbO_2 and 100 ml of methanol was stirred using a magnetic stirrer to the disappearance of 4H-imidazole 1,3-dioxide according to TLC (usually 20-25 h). The oxidizing agent was filtered, washed with 50 ml of methanol and 300 ml of ether. The combined solution was evaporated to dryness, the mass formed was separated by chromatography on a column with silica gel, using chloroform as eluent. Compounds (IIIb-k, m, o) were recrystallized from hexane, (IVa-e, i, k-q) from a 1:1 hexane–ethyl acetate mixture. The formation of INR (VI) and (VII) was observed by means of TLC. Compounds (VIb, c, d) and (VIId) were isolated in yields of 5, 3, 7 and 10%, respectively.

General Method for the Preparation of 4,4-Dimethyl-5-methoxy-5-phenyl-2-imidazoline 1-Oxyls (VIIa-c, f). A mixture of 0.0025 mole of 4H-imidazole 1-oxide (IXa-c, f), 5 g of PbO_2 and 20 ml of methanol was stirred by a magnetic stirrer to the disappearance of the starting compound according to TLC, which usually took 5-7 h. The reaction mixture was treated as in the preceding experiment. In the preparation of the INR (VIIf), the chromatographic separation was carried out on aluminum oxide. The INR obtained were recrystallized from hexane. Given are: compound (yield, %): (VIIa) (70), (VIIb) (90), (VIIc) (90), (VIIf) (30).

5,5-Dimethyl-4-methoxy-4-phenyl-2-imidazoline 1-oxyls (VIa-e) were obtained in a similar way by oxidation of 4H-imidazole 3-oxides (VIIIa-e). The reaction takes 7-14 days. Given are: compound (yield, %): (VIa) (60), (VIb) (70), (VIc) (70), (VId) (50), (VIe) (60). 2-(2-Hydroxyphenyl)-4,4-dimethyl-5-phenyl-4H-imidazole (X) was obtained in a 30% yield by oxidizing 4H-imidazole 3-oxide (VIIIg) under the same conditions.

4H-Imidazole (X) was obtained by an alternate synthesis by acylation of 3-imidazoline (XI) with acetic anhydride in chloroform, followed by thermolysis of 1-acetoxy-2-(2-hydroxyphenyl)-5,5-dimethyl-4-phenyl-3-imidazoline, obtained without its isolation (cf. [3]). Compound (X) was separated by chromatography on a column with silica gel, using ether as eluent, and recrystallized from hexane, yield 80%. PMR spectrum (CCl_4, δ, ppm): 1.63 s (6H, gem-CH_3), 7.57 m and 8.30 m (3H and 2H, Ph), 7.00 m, 8.13 m, and 7.30 m (2H, 1H, and 1H, o-C_6H_4·OH), 11.90 s (1H, OH). ^{13}C NMR spectrum (δ, ppm): 24.7 (CH_3), 195.5 (C_2), 171.0 (C_4), 80.8 (C_5), Ph: 130.3 (C_i), 128.6 (C_o), 129.0 (C_m), 130.4 (C_p), o-C_6H_4OH: 115.0 (C_i), 160.7 and 132.0 (C_o), 116.6 and 118.3 (C_m), 132.6 (C_p).

General Method for the Preparation of 2,2-Dialkoxy-5,5-dimethyl-3-imidazoline 3-Oxide-1-oxyls (XVIIa-e). A mixture of 0.01 mole of 3-imidazoline 3-oxide (XIIa-c), 10-15 g of PbO_2, and 100 ml of the corresponding alcohol was stirred by a magnetic stirrer. The time required for completing the reaction was: in methanol – 3 h, in ethanol – 20 h, in isopropanol – 80 h. The oxidizing agent was filtered off, washed with 300 ml of ether, and the combined solutions were evaporated. The NR (XVIIa-e) were separated by chromatography on a column with silica gel, using chloroform as eluent, and recrystallized from hexane. During the oxidation of compound (XIIa), in addition to NR (XVIIa), INR (XIX) was also obtained in a 2% yield. Following the oxidation of compound (XIIa) in ethanol for 10 h, compounds (XIVd) and (XVIIId) were isolated in a similar way in yields of 30 and 10%, respectively. The spectral data of compound (XIVd) coincide with those given in [9].

General Method of Reduction of NR (IVa, b) and (XVIIa, d, e). A solution of 0.5 g of NH_4Cl in 5 ml of water was added to a solution of 0.0025 mole of NR in 20 ml of ethanol, after which 1 g of a PTs-12 zinc powder was added. The suspension was stirred by a magnetic stirrer to the disappearance of the color of the NR (15-20 min). The precipitate was filtered, the solution was evaporated, and the residue was recrystallized from alcohol [compounds (Va, b) and (XVIIIa) or from an 1:1 ethyl acetate–hexane mixture [compounds (XVIIId, e)]. Given are: compound, yield, %, PMR spectrum (solvent, δ, ppm): (Va), 75, $CDCl_3$, 1.53 s (6H, gem-CH_3), 1.41 s (3H, CH_3), 3.15 s (3H, OCH_3), 7.56 m and 8.20 m (3H and 2H, 2-Ph), 8.43 s (1H, OH); (Vb), 80, $CDCl_3$, 1.26 s and 1.43 s (3H and 3H, gem-CH_3), 3.37 s (3H, OCH_3), 7.60 m and 8.20 m (3H and 2H, 4-Ph), 7.30 m (5H, 2-Ph), 8.56 s (1H, OH); (XVIIId), 80, $(CD_3)_2CO$, 1.55 s (6H, gem-CH_3), 1.19 t and 3.92 q (6H and 4H, Et, J = 7 Hz), 7.65 m and 8.31 m (3H and 2H, Ph); (XVIIIe), 70, $(CD_3)_2CO$, 1.53 s (6H, gem-CH_3), 1.16 d, 1.23 d, and

4.38 m (6H, 6H and 2H, $CH(CH_3)_2$, J = 6 Hz), 7.43 m and 8.28 m (3H and 2H, Ph), 6.90 s (1H, OH). PMR spectrum of (XVIIIa), see in [1], yield 80%).

Dioxolane-2-spiro-2'-(1'-hydroxy-5',5'-dimethyl-4'-phenyl-3'-imidazoline 3'-Oxide) (XVIIIf). A 5-g portion of compound (XIIa) was dissolved in 100 ml of ethylene glycol at 60-80°C and 15 g of MnO_2 was added. The suspension was shaken vigorously for 1 h, and allowed to stand for 5 days with periodic shaking. The reaction mixture was diluted with 300 ml of a saturated solution of NaCl in water and extracted with $CHCl_3$ (10 × 50 ml). The extract was dried over $MgSO_4$ and evaporated to dryness. A 15-ml portion of a NaCl solution was added to the residue, and the precipitate that separated (XVIIIf) was filtered off and recrystallized from ethyl acetate, yield 80%. PMR spectrum [$(CD_3)_2CO$, δ, ppm]: 1.57 s (6H, gem-CH_3), 4.41 m (4H, CH_2CH_2), 7.50 m and 8.37 m (3H and 2H, Ph), 7.60 s (1H, OH).

Dioxolane-2-spiro-2'-(5',5'-dimethyl-4'-phenyl-3'-imidazoline 1'-oxyl) (XXIIb was obtained by oxidation of compound (XX) in a similar way as described in the preceding experiment. The extract was dried over $MgSO_4$, evaporated to dryness and chromatographed on a column with silica gel, deactivated by addition of 20% of water, and using methylene chloride as eluent. The NR (XXIIb) was recrystallized from hexane, yield 60%.

5,5-Dimethyl-2,2-dimethoxy-4-phenyl-3-imidazoline 1-Oxyl (XXIIa) and 5,5-Dimethyl-2,4-dimethoxy-4-phenyl-2-imidazoline 1-Oxyl (XIX). A mixture of 0.01 mole compound (XX) or (XXI), 10-15 g of PbO_2, and 100 ml of methanol was stirred by a magnetic stirrer for 5 h, the oxidizing agent was filtered off, and washed with 300 ml of ether. The combined solution was evaporated to dryness and chromatographed as in the preceding experiment. Radicals (XIX) and (XXIIa) were recrystallized from hexane, yields, 65 and 20%, respectively.

Dioxolane-2-spiro-2'-(5',5'-dimethyl-4'-phenyl-3'-imidazoline 3'-Oxide-1'-oxyl (XVIIf). A 1-g portion of compound (XVIIIf) was dissolved in 20 ml of $CHCl_3$ and 1.5 g of MnO_2 was added. The suspension was stirred by a magnetic stirrer up to the disappearance of compound (XVIIIf) according to TLC. The residue was filtered off and the solution was evaporated. Radical (XVIIf) was isolated by chromatography on a column with silica gel, using chloroform as eluent, and recrystallized from hexane, yield 50%.

Deoxygenation of NNR (IIId, i) with Ph_3P was carried out in a similar way as described in [8]. The INR (VIc, d) and (VIIc, d) obtained were recrystallized from hexane, yields 20, 20, 75, and 65%, respectively. The melting points, yields and elemental analysis data of compounds (IIIa, b), (IVa, b), (VIb), (VIIb), and (XVIIa) are given in [8].

CONCLUSIONS

1. Oxidation of 5-R^1-2R^2-4H-imidazole 1,3-dioxides in methanol with lead dioxide leads to the formation of stable nitroxyl and nitronylnitroxyl radicals with methoxy groups at the α-carbon atom of the radical center. The ratio between these radicals is determined by the electronic character of the substituents at the 2- and 5-positions of the heterocyclic ring.

2. Oxidation of 4H-imidazole 1-oxides and 4H-imidazole 3-oxides in methanol with lead dioxide leads to the formation of iminonitroxyl radicals.

3. Oxidation of 2-unsubstituted 4H-imidazole 1,3-dioxides and 4H-imidazole 3-oxides in alcohols by lead or manganese dioxides leads to 2,2-dialkoxy-substituted stable nitroxyl radicals, which are derivatives of 3-imidazoline 3-oxide and 3-imidazoline.

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STUDY OF HALOGENATION OF 5(6)-HYDROXYBENZIMIDAZOLE AND ITS DERIVATIVES

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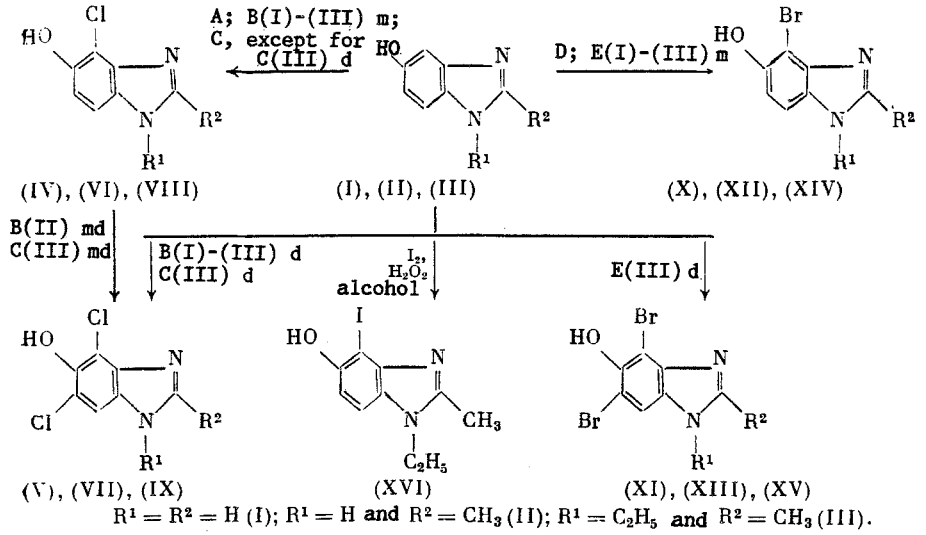
Derivatives of 5(6)-hydroxybenzimidazole have antioxidant properties and the ability to stimulate plant growth [1, 2]. It therefore appeared to be expedient to continue the search for biologically active compounds in this series. For this purpose, we studied the halogenation of 5(6)-hydroxybenzimidazole (I) and some of its derivatives, which also made it possible to investigate the characteristic features of the behavior of the benzimidazole ring in electrophilic substitution reactions.

Comparison of the reactivity of 5-hydroxybenzimidazolone, or its N,N'-dimethyl derivative shows that the 6-position of the benzene ring displays higher activity than the 4-position [3]. We found earlier [4], using the aminomethylation of (I) and its 2-methyl derivative (II) as an example that the benzene ring of benzimidazole is to some extent deactivated with respect to electrophilic substitution by the imidazole ring annelated with it. Thus, in contrast to phenol, the aminomethylation of (I) was successful only when it was carried out with an excess of secondary amine and after prolonged heating, while in an acid medium. Mannich bases were formed in low yield. In view of the results obtained, which indicate nonunequivocality of the occurrence of the electrophilic substitution of (I) and (II), depending on the conditions under which it is being carried out, we carried out the halogenation of (I) and its derivatives using various agents in weakly basic and acidic media. As starting compounds we selected (I), (II), and 1-ethyl-2-methyl-(I) (III).

The first stage in the investigation was the study of the chlorination of (I)-(III) using SO_2Cl_2 or a mixture of H_2O_2 with an aqueous or alcoholic solution of HCl. Chlorination by means of SO_2Cl_2 (method A) proceeds smoothly even at 20°C in a practically quantitative yield. Increase in the amount of SO_2Cl_2 and the reaction time, and also heating to 90°C [method A(I)-(III)d] do not lead to the formation of a dichlorosubstituted product, i.e., SO_2Cl_2 acts selectively only at the 4-position.



$R^1 = R^2 = H$ (I); $R^1 = H$ and $R^2 = CH_3$ (II); $R^1 = C_2H_5$ and $R^2 = CH_3$ (III).

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