NEW DERIVATIVES OF IMIDAZOLINE 3-OXIDE AND THIAZOLINE WITH 2,6-DIALKYLPHENOL FRAGMENTS

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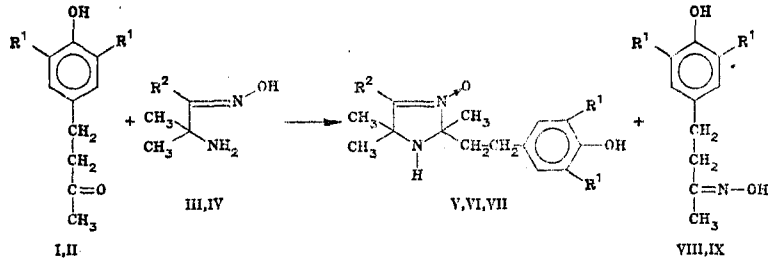
(2,6-Dialkyl-4-hydroxyphenyl)-2-butanones and aminooxides were used to obtain the corresponding 3-imidazoline 3-oxides. Nitrosylation of 3-imidazoline 3-oxide containing a phenol substituent proceeds either at the imidazoline ring amino group or at the phenol fragment. Intermolecular cyclization of (2,6-di-tert-butyl-4-hydroxyphenyl)-2-butanone with sulfur and ammonia gave a 3-thiazoline as two diastereomers.

A promising area of research in the chemistry of polymer stabilizers lies in the creation of additives with a broad action range which protect the polymer from the action of light, heat and atmospheric oxygen. The structure of such compounds consists, as a rule, of two functional fragments, specifically, a sterically-hindered phenol and heterocycle such as piperidine [1, 2] and hydantoin [3].

In the present work, we synthesized new imidazoline and thiazoline derivatives containing a phenol moiety. Interest in such heterocyclic compounds is related to the use of several 4-thiazolines as light stabilizers for polyolefins [4]. Compositions of 3-thiazolines and thiurams act as thermal stabilizers [5], while benzimidazoline-2-thiones have been proposed for use as oil and rubber antioxidants [6].

Imidazoline derivatives have been synthesized by the acid-catalyzed condensation of ketones with aminooximes [7], while thiazoline derivatives have been prepared by the reaction of ketones with sulfur and gaseous ammonia [8]. Readily available 4-(3,5-dialkyl-4-hydroxyphenyl)-2-butanones I and II prepared by the alkylation of 2,6-dialkylphenols by methyl vinyl ketone in the presence of bases [9] were used as the starting materials.

Heating butanones I and II with 3-amino-3-methyl-2-oximinobutane (III) and I with aminooxime IV in the presence of p-toluenesulfonic acid leads to the corresponding 3-imidazoline 3-oxides V-VII.



I, V, VII, IX $R^1 = t\text{-}C_4H_9$; II, VI, VIII $R^1 = CH_3$; III, V, VI $R^2 = CH_3$; IV, VII $R^2 = C_6H_5$

The condensation of ketones I and II with aminooxime III proceeds rather smoothly to give high yields of 3-imidazoline 3-oxides (~80%). The use of a 2.5-fold excess of aminooxime III in the reaction with ketone II leads to a side reaction involving the formation of butanone oxime VIII in 62% yield. A similar conversion was observed in the condensation of ketone I with aminooxime IV; the yield of the product, oxime IX, was 5% in this case.

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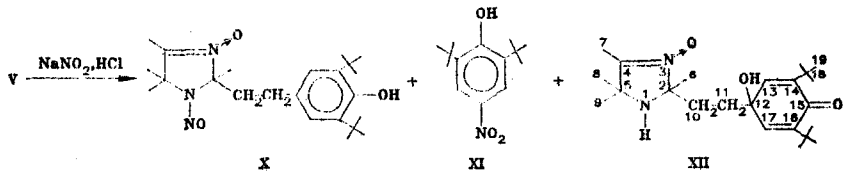
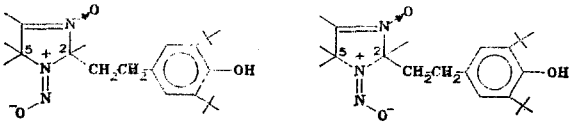
3-Imidazoline 3-oxides readily undergo nitrosylation [7] to give sterically-hindered nitrosoamines, which have not been extensively studied. The reaction of V with $NaNO_2$ was carried out in order to study the effect of the phenol substituent on the nucleophilic properties of 3-imidazolines.



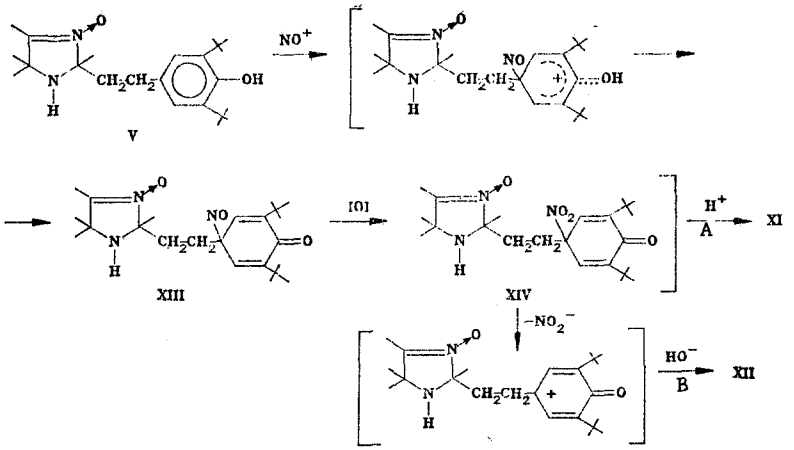
The PMR and elemental analysis data (Tables 1 and 2) permit the unequivocal assignment of structure X to one of the reaction products. N-Nitroso compounds are known to exist in solution as two stereomeric forms [7]. The signal for such forms XA and XB in the PMR spectrum were assigned taking account of the anisotropic effect of the N-nitroso group on the β-methyl group protons [10] of the imidazoline fragment and the aromatic ring protons.



In addition to substitution in the imidazoline ring, the phenol fragment in nitrosylated leading to the formation of 4-nitro-2,6-di-tert-butylphenol (XI) and XII. The IR spectrum of XII shows bands at 1680 and 1655 (C=O and C=C),, 1625 (heterocyclic nitrone C=N) and 3610 cm^{-1} (OH). The PMR spectrum indicates cyclohexadiene and imidazoline 3-oxide fragments in XII (Table 1). Further proof for the structure was obtained in the ^{13}C NMR spectrum in $CDCl_3$ which shows signals at 186.9 and 89.8 ppm related to the carbonyl carbon atom and carbon atom attached to the OH group. Hence, XII was assigned the structure of 2,4,5,5-tetramethyl-2-[2-(1-hydroxy-3,5-di-tert-butylcyclohexadien-2,5-onyl)-1-ethyl]-3-imidazoline-3-oxide.

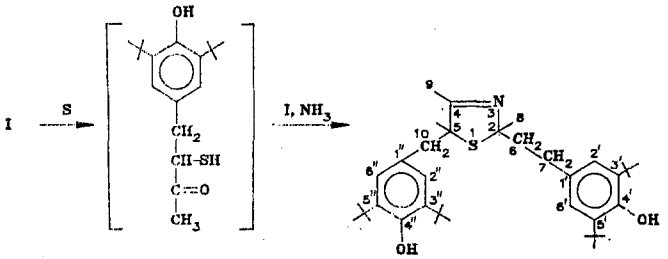
The formation of XI and XII may be represented by a scheme beginning with the attack of the para positive relative to the benzene ring hydroxyl group by a nitrosium cation [11] and oxidation of intermediate XIII and quinonitrile XIV [12]. Due to its instability [13], XIV is rapidly converted by two independent pathways. Pathway A involves the loss of an alkylene heterocyclic substituent from the geminal unit [14]. Pathway B involves substitution of the nitro group by a hydroxy group and the formation of quinol XII [14, 15].

Thus, the presence of the 2-(3,5-di-tert-butyl-4-hydroxyphenyl)ethyl fragment in the structure of 3-imidazoline-3-oxide V sharply reduces the selectivity of the nitrosylation at the amino group due to the appearance of an additional reaction site in the phenol substituent.



The intermolecular cyclization of ketones by the action of sulfur and ammonia with the formation of 3-thiazolines has been studied by Asinger [8]. Various aliphatic, alicyclic and heterocyclic ketones with at least one hydrogen atom in the α-position relative to the carbonyl group undergo this reaction. Such conversions for carbonyl derivatives of 2,6-dialkylphenols have not been reported. We have prepared 3-thiazoline XVI by heating ketone I with sulfur and gaseous ammonia for 7 h at 120°C.

Thiazoline XVI is a 1:1 mixture of diastereomers XVIA and XVIB which may be separated by crystallization. The IR spectra of these compounds show a band at 1660 cm^{-1} (C=N) characteristic for thiazolines [16]. Further proof of the product structure was obtained from the PMR and ^{13}C NMR spectral data (Tables 2 and 3).



XV XVI

Preliminary experiments of the compounds synthesized showed that some of them have both thermal and light stabilizing action. The results of these tests will be published separately.

EXPERIMENTAL

The IR spectra were taken on a UR-20 spectrometer in CCl_4 and KBr pellets. The UV spectra were taken on a Specord UV-VIS spectrometer in ethanol. The PMR spectra were taken on a Varian A-56/60A spectrometer for V, VII, and IX in CCl_4, for VI, X, and XII in $CDCl_3$ and for VII in CD_3OD. The ^{13}C NMR spectra were taken in $CDCl_3$ on Bruker HX-90 and WP-200SY at 22.63 MHz.

The yields, melting points and elemental analysis data for V-XII and XVI in Table 4.

2,4,5,5-Tetramethyl-2-[2-(3,5-di-tert-butyl-4-hydroxyphenyl)-1-ethyl]-3-imidazoline 3-oxide (V). A mixture of 29 g (105 mmoles) ketone I, 12 g (103 mmoles) aminooxime III and 0.05 g p-toluenesulfonic acid was heated in an argon stream for 2 h at 80°C and 8 h at 130°C. The cooled glassy mass was treated with hexane. The precipitate was filtered off, washed with hexane and dried to yield 31 g V.

2,4,5,5-Tetramethyl-2-[2-(3,5-dimethyl-4-hydroxyphenyl)-1-ethyl]-3-imidazoline 3-oxide (VI). A. A mixture of 0.3 g (1.56 mmole) ketone II, 0.177 g (1.53 mmoles) aminooxime III and 1.5 mg p-toluenesulfonic acid was maintained in an argon stream for 2 h at 80°C and for 8 h at 130°C. After cooling, the glassy mass was separated by column chromatography of silica gel with gradient elution using chloroform–ethanol to yield 0.076 g starting ketone II and 0.346 g VI.

B. Heating and subsequent treatment of a mixture of 5.5 g (29 mmoles) ketone II, 8.4 g (72 mmoles) aminooxime III and 20 mg p-toluenesulfonic acid under the conditions described in A gave 3.7 g 2-oximino-4-(3,5-dimethyl-4-hydroxyphenyl)butane (VIII) and 2.2 g imidazoline 3-oxide VI.

2,5,5-Trimethyl-4-phenyl-2-[2-di-tert-butyl-4-hydroxyphenyl-1-ethyl]-3-imidazoline 3-oxide (VII) was obtained analogously under conditions described in procedure A from 5.52 g (20 mmoles) ketone I, 3.5 g (19.7 mmoles) aminooxime IV and 15 mg p-toluenesulfonic acid. Column chromatography gave 2.3 g starting ketone I, 0.3 g 2-oximino-4-(3,5-di-tert-butyl-4-hydroxyphenyl)butane (IX), and 4 g 3-imidazoline 3-oxide VII.

Nitrosylation of 3-imidazoline 3-oxide (V). A sample of 62 ml 5% hydrochloric acid (pH 2-3) and 50 ml 10% aqueous $NaNO_2$ was added to a solution of 11.5 g (30 mmoles) V in 200 ml 50% aqueous ethanol and maintained for 3 h at room temperature. The oil separated was extracted with chloroform, dried over $MgSO_4$ and evaporated to give 12 g product, which was subjected to column chromatography on silica gel with gradient elution using chloroform–ethanol to give five fractions containing 0.5 g (7%) 4-nitro-2,6-di-tert-butylphenol XI

TABLE 1. Spectral Indices for V-X and XII

Compound	IR spectrum, cm^{-1} [solvent]	UV spectrum, λ_{max} nm (log ε)	PMR spectrum[a], δ, ppm						
			R^2	$2CH_3$	CH_3	CH_2—CH_2	H_{arom}	R^1	OH
V	1610 [CCl_4] (C=N); 3650 (OH)	228 (4,20) 278 (3,30)	1,84	1,20 1,26	1,34	2,12c	6,77	1,34	4,99
VI	1655 [KBr] (C=N)	224,2 (4,23); 277,8 (3,27)	1,97	1,27; 1,30	1,51	2,28c	6,72	1,16	6,27
VII	1540 [CCl_4] (C=N); 3650 (OH)	284 (3,96)	8,59c 7,29c	1,57 1,54	1,44 —	2,28[c]	6,86	1,39	4,96
VIII	1610 [KBr] (C=N)	281 (3,76)	—	—	—	2,52c	6,67	2,14	—
IX	1635 [KBr] (C=N); 3635 (OH)	278 (3,29)	—	—		2,55c	6,84	1,34	4,84
X[b]	1625 [KBr] (C=N)	229 (4,32); 278 (3,41); 304 (3,00)	2,11 (a) 2,19 (b)	1,64 1,66 (a) 1,89 1,84 (b)	2,02 (b) 1,76 (a)	2,54	7,00 (a) 6,94 (b)	1,39	5,14
XII	1625 [CCl_4] (C=N); 1655 (C=C); 1680 (C=O); 3610 (OH)	233 (4,38)	2,01	1,32	1,51	1,77	6,56	1,17	—

[a]1.81 ppm for VIII and IX (CH_3—C=N—OH). [b]Slight predominance of the B form. [c]Multiplet center.

TABLE 2. Spectral Indices for XVIA and SVIB

Compound	IR spectrum, cm^{-1} [solvent]	UV spectrum, λ_{max} nm (log ε)	PMR spectrum (in $CDCl_3$), δ, ppm								
			t-C_4H_9	H arom	6-CH_2	7-CH_2	10-CH_2[a]	CH	8-CH_3	9-CH_3	OH
XVIA	1660 [$CHCl_3$] (C=N); 3640 (OH)	278 (3,60)	1,42	7,00; 7,04	2,47b 2,75c	2,04c	3,05	4,58c	1,65	2,15	5,08; 5,12
XVIB	1660 [CCl_4] (C=N); 3640 (OH)	278 (3,57)	1,42	6,94; 7,00	2,39 b 2,66 c	2,04[c]	3,05	4,53c	1,42	2,17	5,01; 5,08

[a]Multiplet center (ABX system) for XVIA, J_{AB} = 14, J_{AX} = 4, J_{BX} = 12 Hz; for XVIB, J_{AB} = 14, J_{AX} = 4, J_{BX} = 8 Hz. [b]Center of triplet of doublets, J = 12, J = 4 Hz. [c]Multiplet center.

TABLE 3. Chemical Shifts (ppm) in the ^{13}C NMR Spectra of XVIA and XVIB

Carbon atom	XVIA	XVIB	Carbon atom	XVIA	XVIB
$C_{(2)}$	s, 89,1	s, 89,4	$C_{(12)}$	q, 30,2	q, 30,3
$C_{(4)}$	s, 168,2	s, 167,6	C (1′)	s, 129,3	s, 129,6
$C_{(5)}$	d, 65,0	q, 65,2	C (1″)	s, 132,4	s, 131,1
$C_{(6)}$	t, 46,4	t, 46,8	$C_{(2',6')}$	d, 124,7	d, 124,6
$C_{(7)}$	t, 31,9	t, 31,4	C (2″,6″)	d, 125,2	d, 125,8
$C_{(8)}$	q, 32,3	q, 32,0	C (3′,3″,5′,5″)	s, 135,7	s, 135,4
$C_{(9)}$	q, 18,3	q, 18,3	C (4′)	s, 151,6	s, 151,6
$C_{(10)}$	t, 41,2	t, 41,1	C (4″)	s, 152,4	s, 152,4
$C_{(11)}$	s, 34,1	s, 34,2			

(identified by comparison with the PMR and IR spectra of an authentic sample), 3.7 g 1-nitroso-2-[2-(3,5-di-tert-butyl-4-hydroxyphenyl)-1-ethyl]-3-imidazoline 3-oxide (X), 3.8 g 3-imidazoline 3-oxide V, and 2.2 g 2,4,5,5-tetramethyl-2-[2-(1-hydroxy-3,5-di-tert-butylcylohexadien-2,5-onyl)-1-ethyl]-3-imidazoline 3-oxide (XII). ^{13}C NMR spectrum: 186.2 ($C_{(15)}$), 176.3 ($C_{(4)}$), 145.9 ($C_{(14,16)}$), 142.4 ($C_{(13,17)}$), 89.8 ($C_{(12)}$), 68.5 ($C_{(2)}$), 61.6 ($C_{(5)}$), 35.7 ($C_{(11)}$), 34.5 ($C_{(18)}$), 32.9 ($C_{(10)}$), 29.3 ($C_{(19)}$), 28.0, 27.7 ($C_{(8,9)}$), 26.3 ($C_{(6)}$), 9.2 ppm ($C_{(7)}$).

TABLE 4. Indices for the Compounds Synthesized

Compound	Mp, °C	Found, %			Chemical formula	Calculated, %			Yield, %
		C	H	N(S)		C	H	N(S)	
V	175—177	73,80	10,31	7,48	$C_{23}H_{38}N_2O_2$	73,75	10,23	7,48	78
VI	129—130	70,39	9,07	9,62	$C_{17}H_{26}N_2O_2$	70,31	9,02	9,64	76
VII	133—135	77,13	9,11	6,39	$C_{28}H_{40}N_2O_2$	77,02	9,23	6,41	47
VIII	200—201	69,49	8,30	6,75	$C_{12}H_{17}NO_2$	69,54	8,27	6,75	62
IX	126—128	74,23	10,00	4,80	$C_{18}H_{29}NO_2$	74,19	10,03	4,80	5
X	159—161	68,57	9,53	10,41	$C_{23}H_{37}N_3O_2$	68,55	9,57	10,41	30
XII	162—164	70,69	9,85	7,16	$C_{23}H_{38}N_2O_3$	70,73	9,81	7,17	18
XVI a	134—135	76,35	9,71	2,47 (5,64)	$C_{36}H_{55}NO_2S$	76,42	9,80	2,47 (5,67)	25
XVI b	85—87	76,37	9,77	2,47 (5,63)	$C_{36}H_{55}NO_2S$	76,42	9,80	2,47 (5,67)	25

[a]V, VII, IX, XVIA and XVIB were crystallized from hexane, VI, VIII, X, and XII were crystallized from 1:2 ethyl acetate—hexane. [b]Relative to the starting ketone.

2-4-Dimethyl-2-[2-(3,5-ditert-butyl-4-hydroxyphenyl)-1-ethyl]-5-(3,5-di-tertbutyl-4-hydroxybenzyl)-3-thiazoline (XVI). A mixture of 10 g (36 mmoles) ketone I and 0.864 g (27 mmoles) sulfur was heated for 7 h at 120°C in a stream of ammonia. After cooling, the glassy, dark red mass crystallized upon the addition of hexane to yield 5 g 3-thiazoline XVI as diastereomers XVIA and XVIB. Three-fold washing with hot hexane gave 2.5 g of insoluble diastereomer XVIA as a colorless precipitate. Evaporation of the filtrate gave 2.5 g colorless diastereomer XVIB which turns pink upon exposure to light.

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