UDC 547.782

CHEMISTRY OF α-HYDROXYLAMINOOXIMES

VII. Condensation of Anti-α-hydroxylaminooximes with Ketones and Preparation of N-oxides of 2-Isoimidazole*

L. B. Volodarskii, A. N. Lysak, and V. A. Koptyug

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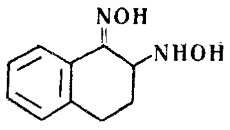
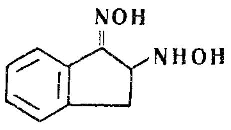
The direction taken by the reaction of α-hydroxylaminooximes (prepared by the action of hydroxylamine on α-halogenoketones) with aldehydes depends on the geometric configuration of the oxime group, cis isomers reacting with benzaldehyde to give N-substituted α-phenylnitrones and with acetaldehyde to give derivatives of 4H-1,2,5-oxadiazine. Anti-α-hydroxylaminooxime and acetaldehyde give substituted 1-hydroxy-3-imidazolin-3-oxide. The structures of the compounds synthesized check by analyses of their UV and IR spectra.

In a previous paper [1] it was shown that reaction of α-halogenoketones with hydroxylamine gives, in addition to dioximes, α-hydroxylaminooximes. In this connection, in the case of α-bromopropiophenone, we isolated two isomeric α-hydroxylaminooximes. By means of IR and PMR spectra it was shown that the isomerism of these compounds is due to difference in the geometric configuration of the oxime group, and steric assignments were made, both for those isomers, and for other α-hydroxylaminooximes. Thus N-(1-oximino-1,2,3,4-tetrahydronaphth-2-yl)-(I), N-(1-oximinoindan-2-yl)-(II), and N-(1-oximino-1-phenylpropyl-2)-(III, mp 156°–158°) hydroxylamines are assigned syn structures, while N-(1-oximino-1-phenylpropyl-2)-(IV, mp 164°–166°), N-1-oximino-2,3-benzycycloheptyl-7-)-(V), and N-(1-oximino-1-phenyl-2-methylpropyl-2)-(VI) hydroxylamines are assigned anti structures.



I



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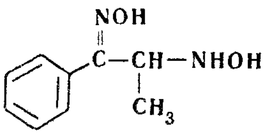

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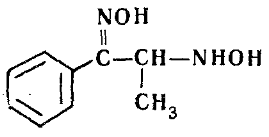
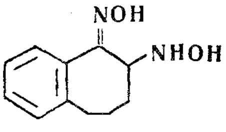
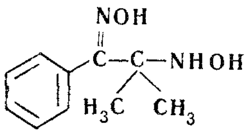


IV



V



VI

It was natural to assume that compounds of one kind of configuration would have closely similar chemical properties. Thus, by analogy with the reactions of I [2, 3], II and III were expected to react with aromatic aldehydes to give the corresponding nitrones, and with aliphatic aldehydes to give oxadiazines.

Actually, reaction of II and III with benzaldehyde give colorless crystalline compounds whose analyses correspond to, respectively $C_{16}H_{14}N_2O_2$ (VII) and $C_{16}H_{16}N_2O_2$ (VIII), and corresponding to compounds formed by condensation of the compounds with benzaldehyde accompanied by splitting out of a molecule of water. The IR spectrum of VII has an intense absorption band at 1140 cm^{-1}, and that of VIII one at 1145 cm^{-1} (Fig. 1), due to valence vibrations of the semipolar bond N $\rightarrow$O [2]. The UV spectra of VII and VIII (Fig. 2) are close to the curves obtained by summation of the UV spectra of II and III (or of the oximes of the appropriate ketones) with the UV spectrum of N-methyl-α-phenylnitrone (IX). On the basis of these results (cf., [2]), VII is ascribed a structure of N-(1-oximinoindan-2-yl)-α-phenylnitrone, and VIII of N-(1-oximino-1-phenylpropyl-2)-α-phenylnitrone.

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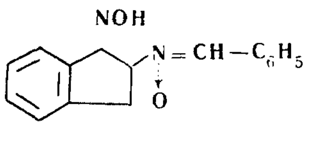
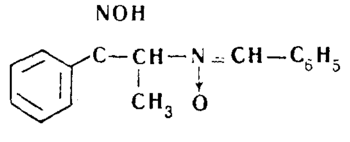
* For Part VI see [1].



VII



VIII

Treatment of II and III with acetaldehyde gave colorless crystalline compounds with formulas $C_{11}H_{12}N_2O_2$ (X) and $C_{11}H_{14}N_2O_2$ (XI), corresponding to condensation of II and III with acetaldehyde and splitting out of a molecule of water. As was to be expected with oxadiazines [3], the IR spectra of X and XI lacked absorption bands in the region of N → O bond valence vibrations (1100–1250 cm^{-1}). Unlike the benzaldehyde condensation products (VII and VIII), X and XI have UV spectra (Fig. 2) close to those of the starting α-hydroxylaminoiximes II and III.

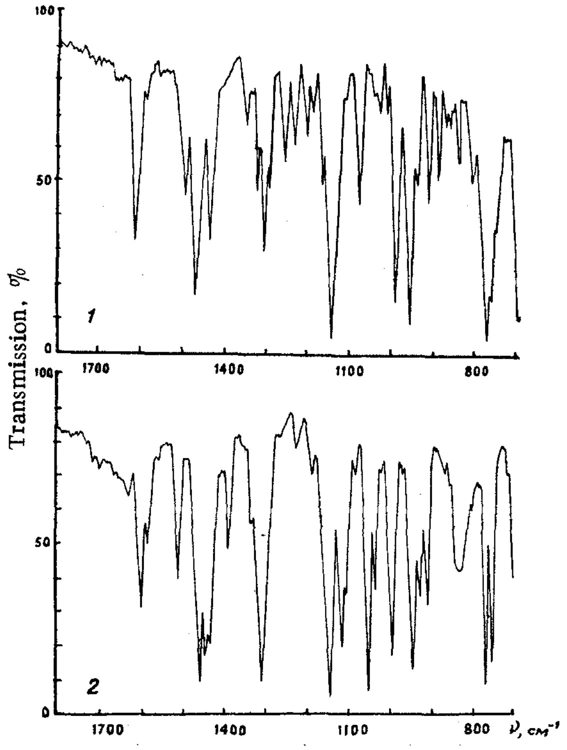


Fig. 1. IR spectra in KBr: 1) VII, 2) VIII.

The action of benzoyl chloride on a pyridine solution of X gave a monobenzoyl derivative X (XII). Heating XI with benzoic anhydride in chloroform gave the monobenzoyl derivative XI (XIII). The IR spectra of XII and XIII show intense absorption bands at 1250 at 1752 cm^{-1} $(C_6H_5-\overset{\overset{\displaystyle O}{\|}}{C}-O-)$. The UV spectra of XII and XIII (Fig. 2) were close to the curve obtained by summation of the UV spectra of, respectively, the oxime of indanone and the oxime of propiophenone with that of the benzoyl derivative of N-hydroxypiperidine (XIV). Hence the hydroxyl which acylates does not form part of the oximino group [3]. The results obtained made it possible to ascribe to XII the structure 5-benzoyloxy-6-methyl-5, 6-dihydro [indanyl-(1', 2': 3, 4) -1, 2, 5-oxadiazine], and to XIII the structure 5-benzoyloxy-4, 6-dimethyl-3-phenyl-5, 6-dihydro-4H-1, 2, 5-oxadiazine.

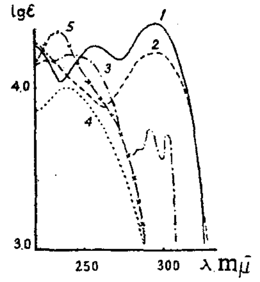
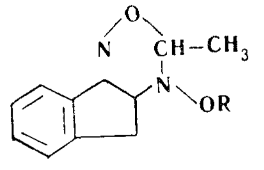
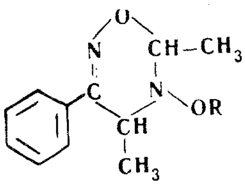


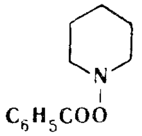
Fig. 2. UV spectra in EtOH: 1) VII, 2) VIII, 3) X, 4) XI, 5) XIII.



X R=H, XII R=C_6H_5CO



XI R=H, XIII R=C_6H_5CO



XIV

Thus the structures of the products obtained by condensing II and III with aldehydes shows, that formation of nitrones and oxadiazines is actually a general reaction for α-hydroxylaminooximes having a cis oxime group.

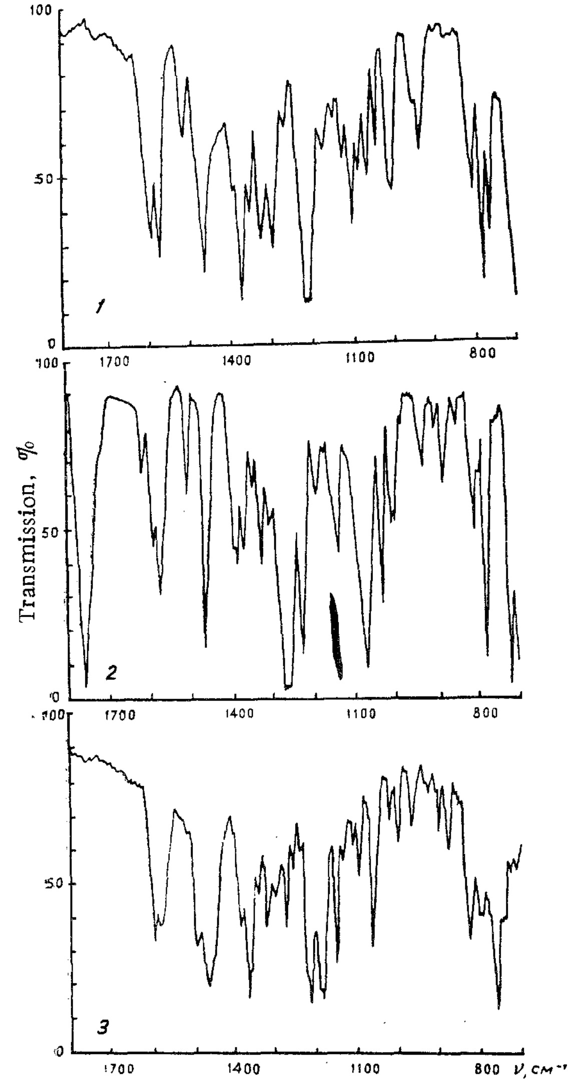
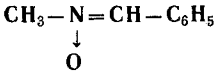


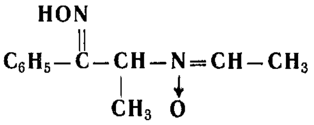
Fig. 3. IR spectra in KBr: 1) XV; 2) XVI; 3) XXII.

Different results are obtained by reacting aliphatic aldehydes with α-hydroxylaminooximes, with an anti oxime group. Thus reaction of IV with acetaldehyde gives compound XV, whose formula $C_{11}H_{14}N_2O_2$ also corresponds to that of a product formed by condensation with splitting out of a molecule of water. However, the IR spectrum of XV, unlike that of isomeric XI, has an intense band at 1210 cm^{-1} (Fig. 3), which can be put down to vibrations of the N →O semipolar double bond. The UV spectrum of XV (Fig. 4), differs markedly from that of the starting α-hydroxylaminooxime IV, while the UV spectrum of the isomeric XI closely resembled that of the starting α -hydroxylaminooximine III. Thus if with compound XI the chromophoric system of propiophenone oxime was retained (see above), formation of XV is evidently bound up with complete rearrangement of the chromophoric system. The UV spectrum of XV closely resembled that of IX (Fig. 4), indicating that XV contains the phenylnitrone group $O\leftarrow\underset{|}{N}=\underset{|}{C}-C_6H_5$. Hence, XV cannot be a nitrone of structure A, as then its UV spectrum would coincide with that of the starting α-hydroxylamine IV (The contribution of an isolated nitrone group to the absorption is not great [3]).



$CH_3-\underset{\underset{O}{\downarrow}}{N}=CH-C_6H_5$

IX



$C_6H_5-\overset{\overset{HON}{\|}}{C}-\underset{CH_3}{\underset{|}{CH}}-\underset{\underset{O}{\downarrow}}{N}=CH-CH_3$

A

The IR spectrum of XV has a wide absorption band with a maximum at 3280 cm^{-1}, corresponding to an OH group linked by a hydrogen bond. On acylation that band vanishes. The IR spectrum of the benzoyl derivative of XV (XVI) shows bands at 1265 and 1760 cm^{-1} ($C_6H_5\overset{\overset{O}{\|}}{C}-O-$). These results, in conjunction with elementary analysis data, show that the molecule of XV contains a hydroxyl group. The UV spectrum of XVI was identical with the curve obtained by summation of the UV spectra of XV and XIV (Fig. 4).

The UV spectrum of the acetyl derivative of XV (XVII) is practically identical with that of XV itself. The cryoscopic molecular weight in benzene found for XVII (244.0) was close to that calculated (248.3), so that the possibility of dimerization of nitrone A by a 1, 3 dipolar type of addition [4] could be rejected.

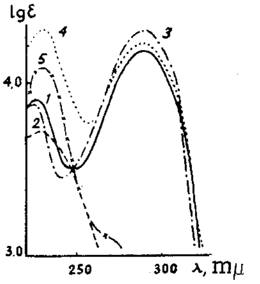
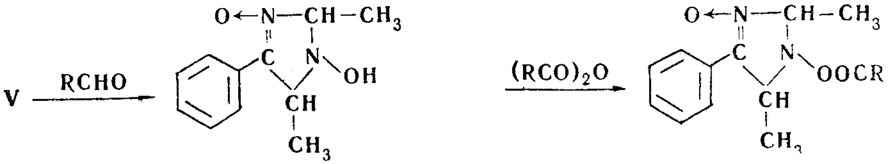


Fig. 4. UV spectra EtOH: 1) XV; 2) IV; 3) IX; 4) XVI; 5) XIV.

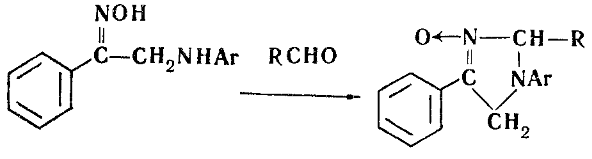
The elementary analysis of XV, and its containing a phenylnitrone and hydroxyl group, led us to conclude that it is 1-hydroxy-2, 5-dimethyl-4-phenyl-3-imidazolin-3-oxide, and that XVI and XVII are the corresponding O-acyl derivatives.



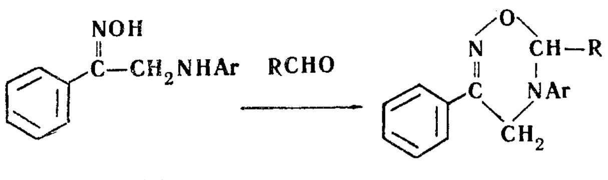
XV

XVI R=C_6H_5, XVII R=CH_3

In this connection it is of interest to note that according to the literature [5], the course taken by the reaction between aldehydes and oximes of phenacylanilines, which are structural analogs of the α-hydroxylaminoximes III and IV, depends on the configuration of the oxime group. Syn oximes are converted into derivatives of 4H-1, 2, 5-oxadiazine (XIX), and anti oximes (XX) to 3-imidazolin-3-oxides (XXI). The first of these reactions is like the conversion of III to 4H-1, 2, 5-oxadiazine (XI) which we have observed, and the second to the conversion of IV to 1-hydroxy-3-imidazolin-3-oxide (XV).

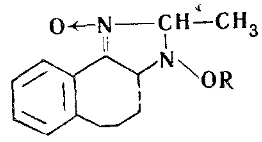


XVIII R=H, C_6H_5 XIX



XX R=H, C_6H_5 XXI

It might be expected that other anti-α-hydroxylaminoximes would condense with aliphatic aldehydes to give products of similar structure. Reaction of V with acetaldehyde gave a condensation product of formula $C_{13}H_{16}N_2O_2$ (XXII). Its UV spectrum (Fig. 5), unlike that of the starting compound V, exhibits a band with a maximum at 290–294 mμ (lg ε 4.02) which is characteristic of compounds containing the $O\leftarrow \underset{|}{N}=\underset{|}{C}-C_6H_5$. In the N → O valence vibrations region, the IR



XXII R=H
XXIII R=CH₃CO

spectrum of XXII (Fig. 3) has 2 intense bands, at 1180 and 1207 cm^{-1}. Treatment of XXII with acetic anhydride in chloroform gave a monoacetyl derivative of XXII, (XXIII). In harmony with these results, XXII is ascribed a structure 1-hydroxy-2-methyl [2', 3'-benzcycloheptyl-(7', 1' : 5, 4)-3-imidazolin-3-oxide], and XXIII is considered to be its O-acyl derivative.

Table 1

Condensation Products from α-Hydroxylaminooximes and Aldehydes

Compound no.	Mp, °C	Formula	Found, %						Calculated, %		
			C		H		N		C	H	N
VII	190—190.5	$C_{16}H_{14}N_2O_2$	72.8	72.4	5.2	5.4	10.5	10.5	72.3	5.3	10.5
VIII	173—174	$C_{16}H_{16}N_2O_2$	71.3	71.7	6.2	6.0	10.6	10.7	71.7	6.0	10.4
X	180—180.5	$C_{11}H_{12}N_2O_2$	65.1	64.9	5.8	5.6	13.3	13.3	64.7	5.9	13.7
XI	145—146.5	$C_{11}H_{14}N_2O_2$	64.5	64.4	7.0	7.0	14.0	13.8	64.1	6.8	13.6
XV	93.5—94.5	$C_{11}H_{14}N_2O_2$	63.9	64.0	6.7	6.8	14.1	13.8	64.1	6.8	13.6
XXII	141—142	$C_{13}H_{16}N_2O_2$	67.3	67.5	7.0	6.9	12.2	12.0	67.2	6.9	12.1

The structures of the 1-hydroxy-3-imidazolin-3-oxides obtained are confirmed by their acyl derivatives readily splitting off a molecule of carbon dioxide, to give the imidazole N-oxide. This reaction will be considered in a subsequent paper.

Experimental

The IR spectra were recorded by a UR-10 spectrophotometer, the solids being tabletted with KBr (concentration 0.5%, tablet thickness 1 mm). UV spectra were measured with a SF-4 spectrophotometer, the solvent being EtOH. N-Methyl-α-phenylnitrone (IX) was prepared as described in [6].

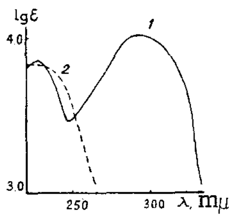


Fig. 5. UV spectrum in EtOH: 1) XXII; 2) V.

Condensation of α-hydroxylaminooximes with aldehydes. 1.2 mole benzaldehyde or 2–3 moles acetaldehyde was added to a mixture of α-hydroxylaminooxime (1 mole) in 4 times its weight of MeOH, and the mixture brought to the boil, when the precipitate dissolved. About half the MeOH was distilled off, the remaining liquid was cooled, the precipitate filtered off, and recrystallized from a small amount of EtOH.

To obtain XV from the reaction products, the solvent was distilled off completely, the remaining oily material dissolved in $CHCl_3$, the solution dried over $MgSO_4$, and excess diisopropyl ether added. The precipitate which formed on standing was recrystallized from the latter.

XXII was recrystallized from absolute EtOH.

The yields of condensation products were 80–100%. Table 1 gives their mps and elementary analytical data.

Benzoylation of 1,2,5-oxadiazines (X and XI). 0.1 ml pyridine and a solution of 0.16 g (1.2 mmole) benzoylchloride in 1 ml benzene were added to a suspension of 0.2 g (1 mmole) X in 1 ml benzene. The mixture was shaken for 20 min, washed with water, then with 5% Na_2CO_3 solution, dried over $MgSO_4$, and diluted with petrol ether. The colorless precipitate of 5-benzoyloxy-6-methyl-5,6-dihydro[indanyl-(1', 2': 3, 4)-1, 2, 5-oxadiazine](XII) was filtered off, yield 0.16 g (56%).

Table 2

Acyl Derivatives of Condensation Products from α-Hydroxylaminooximes and Aldehydes

Compound no.	Mp, °C	Empirical formula	Found, %			Calculated, %		
			C	H	N	C	H	N
XII	125—126	$C_{18}H_{16}N_2O_3$	70.3 70.2	5.2 5.4	9.1 9.1	70.2	5.2	9.1
XIII	121—121,5	$C_{18}H_{18}N_2O_3$	69.9 69.8	6.0 6.1	9.3 9.3	69.8	5.8	9.0
XVI	100—100.5	$C_{18}H_{18}N_2O_3$	69.8 69.6	6.0 5.9	9.4 9.4	69.8	5.8	9.0
XVII	85.5—86	$C_{13}H_{16}N_2O_3$	62.9 62.9	6.3 6.5	11.1 11.0	62.9	6.4	11.3
XXIII	81.5—82	$C_{15}H_{18}N_2O_3$	65.9 65.7	7.0 7.0	10.5 10.4	65.7	6.6	10.2

A solution of 2.7 g (12 mmole) benzoic anhydride in 10 ml $CHCl_3$ was added to 2.0 g (9.7 mmole) XI, and the mixture brought to the boil, boiled for 10 min, cooled, washed with 5% Na_2CO_3, then with water, dried over $MgSO_4$, and the solvent vacuum-distilled off. The residual oil was dissolved in EtOH, and kept in a refrigerator. The precipitatate of 5-benzoyloxy-4, 6-dimethyl-3-phenyl-5, 6-dihydro-4H-1, 2, 5-oxadiazine (XIII) was recrystallized from EtOH (40% yield). Mps and elementary analytical data for XII and XIII are given in Table 2.

Acylation of 1-hydroxy-3-imidazolin-3-oxides. The reaction was carried out, using benzoic or acetic anhydride, in a way similar to that described above. The oil which remained after taking off the $CHCl_3$ was dissolved in Et_2O, the solution cooled, the precipitate of 1-acyloxy-3-imidazolin-3-oxide derivative (XVI, XVII, and XXIII) filtered off, and washed with ether. The yields of products were 30-50%. The compounds were unstable; 24-30 hr after having been prepared, their mps were found to have fallen markedly, they smelled of acid, and oozed. Consequently determinations of mps, elementary compositions, molecular weights, and UV and IR spectra were carried out immediately after preparation.

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Novosibirsk Institute of Organic Chemistry, Siberian
Division, AS USSR