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SYNTHESIS OF ISOMERIC PAIRS OF IMIDAZOLE N-OXIDES

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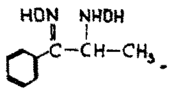
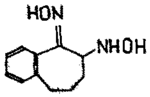
Several α-halogenketones have been found to react with hydroxylamine to yield α-hydroxylaminooximes along with α-dioximes (1). The configuration of the formers has been established by comparing their ultraviolet absorption spectra with those of related oximes of the known configuration. The configuration of anti-isomers was confirmed by their ability to form Fe and Cu complexes.

Condensation of anti-alkyl forms of N-(1-hydroxyimino-1-phenylpropyl-2)hydroxylamine (I,m.p.164.0-166.0°) and N-(1-hydroxyimino-2,3-benzocycloheptyl-7)hydroxylamine (II,m.p. 187.0-188.0°) with acetaldehyde resulted in 1-hydroxy-2,5-dimethyl-4-phenyl-3-imidazoline-3-oxide (III,m.p.93.5-94.5°, 80%) and in 1-hydroxy-2-methyl-[2',3'-benzocycloheptyl-(7',1':5,4)-3-imidazoline-3-oxide] (IV,m.p.141.0-142.0°), respectively. III and IV refluxed with acetic or benzoic anhydrides in chloroform gave acyl derivatives of III and IV (V,m.p.85.5-86.0°; VI,m.p.100.0-100.5°; VII,m.p.81.5-82.0°).



I



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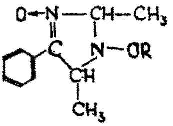
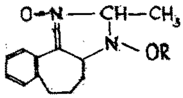


III R=H

V R=CH_3CO

VI R=C_6H_5CO



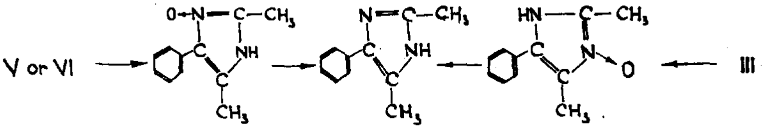
IV R=H

VII R=CH_3CO

Heating of V or VI in vacuo afforded a product (VIII, m.p.149.0-150.0°) empirical formula of which ($C_{11}H_{12}N_2O$) was in accordance with the elimination of a molecule of carboxylic acid from V or VI. The ultraviolet spectra of VIII(λ_{max}^{EtOH} 252 mμ (log ε 4.01)) shows no broad band at 290-296 mμ (log ε 4.2-4.3) characteristic of $C_6H_5-\underset{|}{C}=\underset{|}{N}\rightarrow O$ chromophore in spectra III,IV and V. The n.m.r. spectrum of VIII taken on JNM-3 spectrometer (40 Mc) using a 30% $CDCl_3$ solution consists of the three sharp singlets (cf.(2)), an area ratio being about 6:5:1. The peak at 8.00 τ corresponds to six hydrogen atoms of two methyl groups, the peak at 2.75 τ to five hydrogen atoms of benzene ring and the peak at -5.17 τ indicates that we were dealing with a strong hydrogen bond. The treatment of VIII with phosphorus trichloride in chloroform yielded 2,4(5)-dimethyl-5(4)-phenylmidazole (IX) identified by infrared spectrum and by a melting point of a mixture with authentic sample (3). On the basis of these facts we concluded that VIII had the structure of 2.5-dimethyl-4-phenylimidazole-3-oxide or its tautomeric form carrying hydroxygen function in 3-position.

The determination of the molecular weight of VIII by the isothermic distillation method in chloroform solution indicated that VIII has been appreciably associated. At a concentration of 10% it exhibited an apparent molecular weight of 7-9 times of the formula weight. These findings were confirmed by noting one of the n.m.r. signals in a very low field.

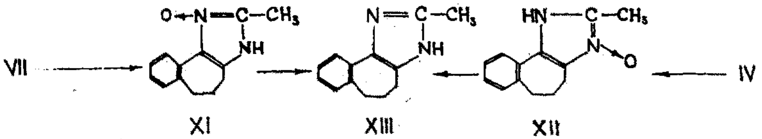
When ethanol solution of V or VI was treated with dry hydrogen chloride hydrochloride VIII (m.p.205.0-206.0°) was formed. However, the action of hydrogen chloride upon ethanol solution of III gave also rise to hydrochloride X (m.p.213.0-215.0°), mixed melting point of which with hydrochloride VIII showed depression. The elemental analysis of free base (X,m.p.162.0-163.0°) indicated the composition of VIII ($C_{11}H_{12}N_2O$) while these compounds differed in infrared and ultraviolet spectra. The ultraviolet spectrum of X (λ_{max}^{EtOH} 270 mμ (log ε 4.07)) does not posses a broad band at 290-296 mμ indicating the absence of $C_6H_5-\overset{|}{C}=\overset{|}{N}\rightarrow O$ group. The n.m.r. spectra of X is consistent with that of VIII both in position of bands (7.88, 2.85 and -5.78 τ.) and the area ratio. X reacted with phosphorus trichloride to yield IX. The above evidence suggested that X and VIII differed only in the position of the oxygen which might be attached to one of the two of nitrogen atoms.



VIII IX X

The n.m.r. spectrum and the molecular weight determination of XI point to the same degree of association as VIII.

VII and IV when treated under similar conditions resulted in 2-methyl- [2',3'-benzocycloheptyl-(7',1':5,4)-imidazole-3-oxide] (XI,m.p.232.0-233.0°) and 2-methyl- [2',3'-benzocycloheptyl-(7',1':4,5)-imidazole-3-oxide] (XII,m.p.212.0-213.0°), respectively.



XI and XII reacted with phosphorus trichloride to form 2-methyl-[2',3'-benzocycloheptyl-(7',1':4,5)-imidazole] (XIII hydrochloride,m.p.265.0-267.0°).

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