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A ROUTE TO STABLE NITROXIDE RADICALS OF IMIDAZOLINE N-OXIDE

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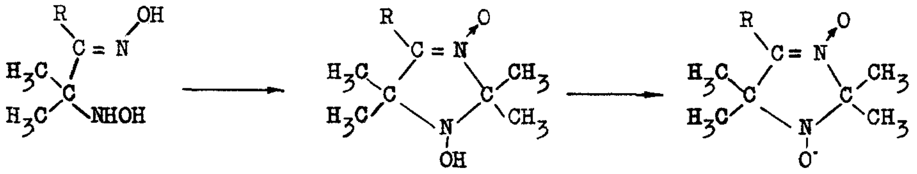
Recently interest has arisen to various classes of stable nitrogen free radicals, particularly to nitroxides (1). We have previously reported the formation of 1-hydroxy-3-imidazoline-3-oxides in the reaction of anti-α-hydroxylaminooximes with aldehydes (2). We have now employed this reaction to prepare 1-hydroxy-2,2,5,5-tetramethyl-3-imidazoline-3-oxides for the purpose of their further oxidation into heterocyclic free radicals with nitrone group screened from the radical center by four methyl substituents of the heminal type.

The reaction of N-(1-hydroxyimino-2-methyl-1-phenylpropyl-2)hydroxylamine (I) (3) with acetone (cf.(2)) in a sealed tube at 140-150° during 8-10 hours afforded 1-hydroxy-2,2,5,5-tetramethyl-4-phenyl-3-imidazoline-3-oxide (II) as colourless needles in a 50% yeild, m.p.194-195°. (Found: C,66.7; H,7.9; N,12.0.$C_{13}H_{18}N_2O_2$ requires C,66.7; H,7.7; N,12.0%). Similar reaction of N-(3-hydroxyimino-2-methylbuthyl-2)hydroxylamine (III) (4) with acetone afforded 1-hydroxy-2,2,4,5.5-pentamethyl-3-imidazoline-3-oxide (IV) as colourless needles in a 20% yield, m.p.196–198°.(Found: C,55.8; H,9.3; N,16.2. $C_8H_{16}N_2O_2$ requires C,55.8; H,9.3; N,16.3%).

The n.m.r. spectrum of II measured with JNM-4H-100 spectrometer in a 3% solution in CD_3OD (internal standard TMS) exhibits two singlets at 8.46 and 8.55τ (gem-dimethyl groups) and aromatic proton absorption in region of 2.0–3.1τ ; areas 6:6:5. The n.m.r. spectrum of IV exhibits two singlets at 8.58 and 8.73τ (gem-dimethyl groups) and a singlet at 8.04τ (CH_3 in the position 4); areas 6:6:3. The shift of the gem-dimethyl peaks in the n.m.r. spectrum of II compared with IV due to the effect of the benzene ring was in the expected direction in accord with their structures.



I R = C_6H_5 II R = C_6H_5 V R = C_6H_5

III R = CH_3 IV R = CH_3 VI R = CH_3

Cyclic hydroxylamine (II) readily reacted with Tollens' reagent to give pale orange plates (V) in a 70% yeild, m.p.104–105° (from petroleum ether). (Found: C;66.5; H,7.3; N,12.3;mol wt, 233 (mass spectrum).$C_{13}H_{17}N_2O_2$requires C,66.9; H,7.3; N,12,0%;mol wt, 233.3).The oxidation of cyclic hydroxylamine (IV) with hydrogen peroxide (5) results in pale yellow plates (VI) in a 70% yeild. Sublimation of the plates gave a product with m.p.72–74°. (Found: C,55.9; H,9.0; N,16.4. $C_8H_{15}N_2O_2$ requires C,56.1; H,8.8; N,16.4%). The infrared spectra of V and VI showed absorption bands similar to the bands in the spectra of II and IV, respectively, but had no bands in the region of stretching and bending modes of the hydroxyl group (3400-3600 and 1000-1100cm^{-1}). The ultraviolet spectra of V and VI were identical to those of II and IV, respectively.

The n.m.r. spectrum of V (in a 50% solution in CCl_4, internal standard dioxane) shows an intense band at 23.6 τ (12 protons of four α-methyl groups) and absorption in the region of 2.0-3.6 τ (5 protons of benzene ring). Recently it has been found that the band of α-methyl protons of 2,2,6,6-tetramethylpiperidine-1-nitroxide is shifted to very high field (6). The n.m.r. spectrum of VI (in a 34% solution in $CDCl_3$, internal standard dioxane) shows the same band at 23.6 τ (12 protons of four α-methyl groups) and a band at -0,5 τ (3 protons of the β-methyl group, cf.(6)).

The e.s.r. spectra of V and VI consist of 1:1:1 triplets (a_N=15.5 Oe) characteristic of similar nitroxides (1). Thus it appears that the products of oxidation of II and IV are true 2,2,5,5-tetramethyl-4-phenyl- and 2,2,4,5,5-pentamethyl-3-imidazoline-3-oxide-1-nitroxide (V and VI).

The nitroxide (V) is quite stable in diffuse light, at temperature below 80° and during chromatography on alumina, and no change are observed on storage for several months in the air. The reduction of V by hydrazine hydrate results in II. The nitroxide (VI) is rather less stable than V, particularly in solutions at elevated temperatures.

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