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Stable Nitroxides With Hydrogen At α-Carbon of the Nitroxyl Group

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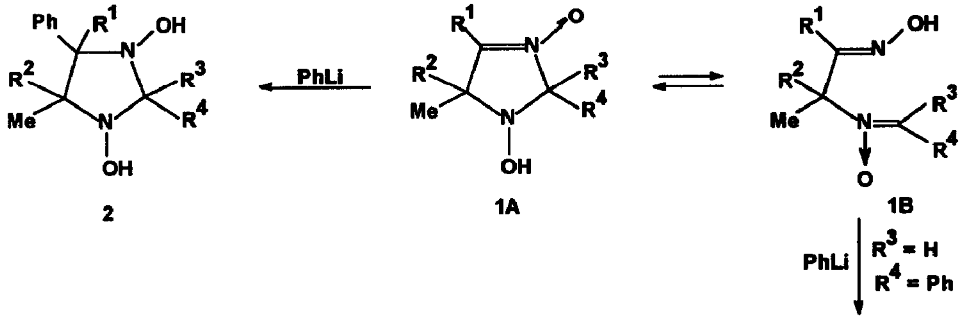
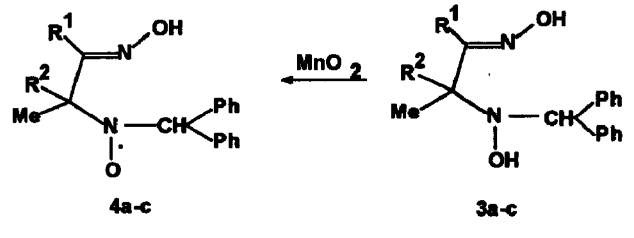
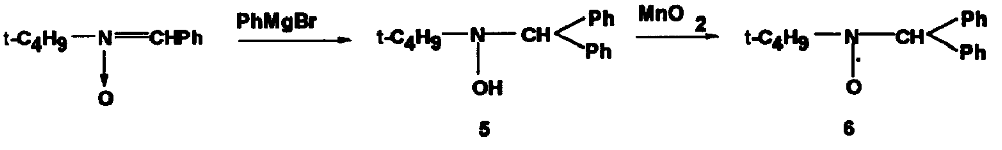
Abstract: The reactions of 1-hydroxy-3-imidazoline-3-oxides containing hydrogen in the 2-position with PhLi or PhMgBr lead to acyclic α-hydroxylaminooximes. The oxidation of the latter gives stable acyclic nitroxides with hydrogen at the α-carbon atom.

Recently, we have shown that the reaction route of 3-imidazoline-3-oxides **1** containing hydrogen in the 2-position (R^3 = H) with organolithium compounds depends on the tautomeric form of the substrate.[1] When compound **1** exists in the form **1A** the reaction leads to dihydroxyimidazolidines **2**, and when it exists in form **1B** (R^4 = Ph), the reactions both with phenyllithium and phenylmagnesium bromide lead to hydroxylaminooximes **3a-c**.[2]





3,4	R^1	R^2
a	Ph	CH_3
b	CH_3	CH_3
c	$(CH_2)_4$	



We have unexpectedly found that the compounds formed in the oxidation of hydroxylaminooximes **3** with MnO_2 or PbO_2 in ether were not 3-imidazoline-3-oxides of type **1** (ref.[3]) but stable acyclic nitroxides **4a-c** containing hydrogen at the α-carbon atom of the of the nitroxyl group.[4] These compounds were isolated individually and proved to be stable in the crystalline state at 0° C for an unlimited period of time. A sufficient condition for stability of such compounds seems to be the presence of two phenyl groups at the α-carbon atom bonded with hydrogen. Indeed, the reaction of the widely used phenyl-N-tert-butyl-nitrone (PBN) with phenyllithium and subsequent oxidation of the intermediate hydroxylamine **5** led to the stable radical **6** (note.[4]) which was reported to be a spin adduct,[5] and was even synthesized for use as a spin probe,[6] but was not isolated and characteterized individually. The nitroxides with hydrogen at the α-carbon atom are usually unstable because of their easy disproportionation to hydroxylamine and nitrone.[7] As oposed to this, the radicals **4** and **6** do not undergo disproportionation to form the corresponding hydroxylamine and nitrone, and are not transformed into nitrones when oxidized by MnO_2.

References and Notes

1 . Reznikov V.A. Volodarsky L.B. *Izv. Akad. Nauk Russ. Ser. Khim.* **1993** (in press).

2. All the compounds synthesized have correct elemental analysis data. Compound, yield, %, and m.p. °C (hexane-ethyl acetate mixture) are given: **3a**, 90, 139-141; **3b**, 75, 136-137; **3c**, 75, 120-122. Hydroxylamine **5** is purified chromatographically on a silica gel, eluent $CHCl_3$, yield 90% (oil).

3. Martin V.V., Kobrin V.S., Volodarsky L.B. *Izv. Sib. Otd. Akad. Nauk SSSR. Ser. Khim. Nauk*, **1977**, *3*, 153-157.

4. Compound, yield, %, m.p. °C (hexane) and ESR-spectra are given: **4a**, 90, 130-132, a_N = 14.5, a_H = 1.8 G ($CHCl_3$, without O_2); **4b**, 95, 133-135, a_N = 15.7, a_H = 3.2 G (water); **4c**, 95, 103-104, a_N = 16.0, a_H = 2.7 G (water); **6**, 90, 111-113, a_N = 16.0, a_H = 2.7 G (water). There is one more constant (≈ 0.8 G, doblet) in the ESR spectrum of nitroxide **4a**, the nature of which is unknown.

5. Janzen E.G., Haire D.R. Two Decades of Spin Trapping in: *Advances in Free Radical Chemistry*, JAI Press Inc, **1990**, 253-295.

6. Kotage Y., Janzen E.G. *J. Am. Chem. Soc.* **1989**, *111*, 2066-2070.

7. Keana J.F.W. Synthesis and Chemistry of Nitroxide Spin Labels, in: *Spin Labeling in Pharmacology*, Holtzman J.L. (Ed.), Academic Press, Orlando Fla., **1984**, 1-85.

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