

A STABLE NITROXIDE - 2,2,5,5-TETRAMETHYL-3-IMIDAZOLINE-3-OXIDE-1-OXYL - A REAGENT FOR SPIN LABELLING VIA 1,3-DIPOLAR CYCLOADDITION

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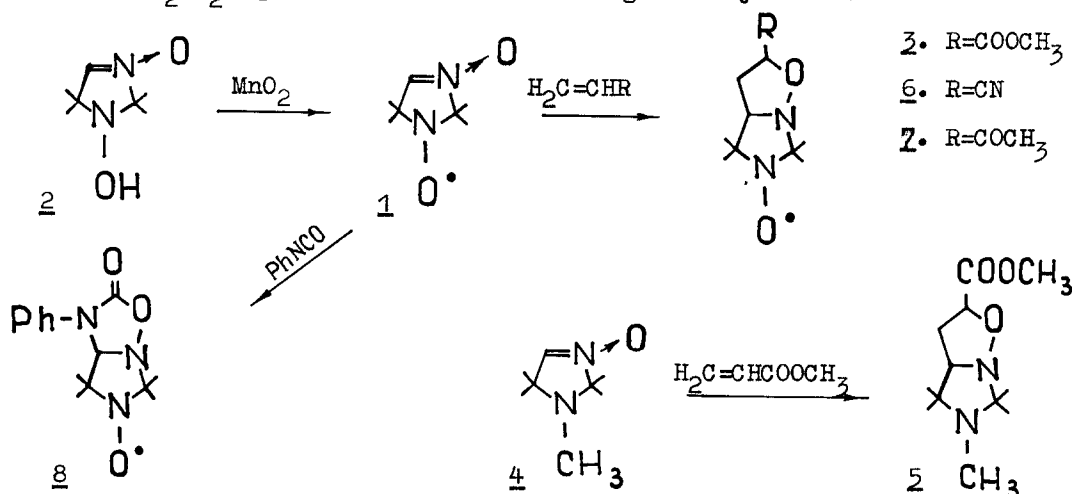
Summary: The paramagnetic heterocyclic aldonitrone, 2,2,5,5-tetramethyl-3-imidazoline-3-oxide-1-oxyl, reacts with C=C and C=N containing dipolarophiles to yield cycloadducts with radical centres.

Nitrones react as 1,3-dipoles in 1,3-dipolar cycloaddition reactions to give a number of heterocyclic systems which may be converted to compounds of various classes including natural products¹. As a part of our studies of the chemistry of 3-imidazoline-3-oxides containing the nitrone group and nitroxide centre in the same heterocycle², we examined some 1,3-dipolar cycloaddition reactions of the aldonitrone-radical **1**, which may be considered as models of spin labeling of molecules with multiple bonds. It should be noted that introduction of the nitroxide fragment through both atoms of a multiple bond has obvious advantages over the usual methods of spin label introduction via acylation, alkylation, etc., since it allows the exclusion of the independent rotation of radical moiety³.

3-Imidazoline-3-oxide-1-oxyl **1** was found to be a convenient synthon for the syntheses of nitroxides using 1,3-dipolar cycloaddition reactions. The nitrone-radical **1** is available by oxidation of 1-hydroxy-3-imidazoline-3-oxide² **2** with MnO₂ in CHCl₃ for 3 h at 20° and may be stored at room temperature for several days.

Upon standing in an excess of methyl acrylate for 10 h at 20°, **1** nearly quantitatively forms adduct **3** [m.p. 101-103°(from hexane); IR: 1740, 1210 cm⁻¹; UV: 235 nm (lg ε = 3,69)]. Treatment of the diamagnetic analogue

of 1, 1,2,2,5,5-pentamethyl-3-imidazoline-3-oxide 4, with methyl acrylate in the same conditions leads to the isoxazolidine 5 [oil, IR: 1740, 1210 cm^{-1}], whose PMR spectrum (the multiplicity of the signal of the H in α -position to the carbomethoxy group)⁴ indicates a 5-substituted isoxazolidine structure. The similarity between the IR spectra of 3 and 5 suggests the same type of structure for 3. The reaction of 1 with acrylonitrile proceeds in a similar way and gives the 5-cyanoisoxazolidine 6 [m.p. 125-127°(from hexane); IR: 2250 cm^{-1} ; UV: 235 nm ($\lg \epsilon = 3,53$); yield 91%]. Likewise, methyl vinyl ketone reacts with 1 to form the cycloadduct 7 [m.p. 59-60°(from hexane); IR: 1710 cm^{-1} ; UV: 230 nm ($\lg \epsilon = 3,45$); yield 50%]. When the reactions are conducted in CH_2Cl_2 equimolar ratio of the reagents may be used.



The reaction of 1 with phenyl isocyanate also leads to the stable cycloadduct 8 [m.p. 185-186°(from ethyl acetate); IR: 1760 cm^{-1} ; UV: 239 nm ($\lg \epsilon = 4,19$); yield 65%] along with 2 (20%).

These results display 1 as the first representative of a new class of spin labels - cycloaddictive, which may be used like acylating, alkylating and chelating nitroxides in biochemical and analytical research.

REFERENCES AND NOTES

1. Tufariello J.J., *Acc. Chem. Res.*, 1979, 12, 396
2. Volodarsky L.B., Grigor'ev I.A., Sagdeev R.Z. In: *Biological Magnetic Resonance*. Vol. 2/ Ed. L.J.Berliner. N.Y.-L., Plenum Press, 1980, 169
3. *Spin Labeling. Theory and applications.*/ Ed. L.J.Berliner. N.Y.-San Fr.-L., Academic Press, 1976
4. A detailed discussion of the spectra will be presented elsewhere.

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