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NITRATION OF IMIDAZOLINE-N-OXIDE NITROXIDES CONTAINING THE ARYL NITRONE GROUP

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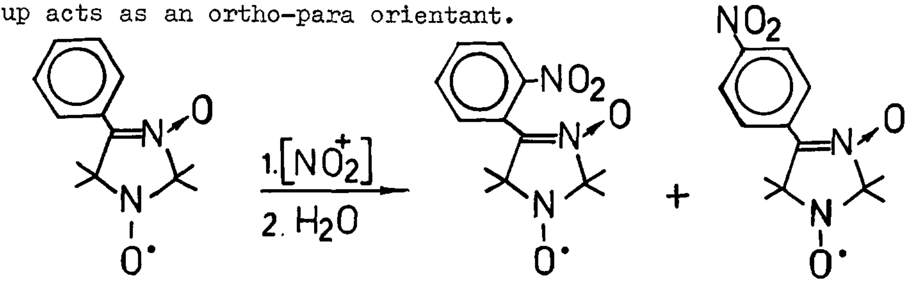
Summary: Nitration of 4-aryl-3-imidazoline-3-oxide nitroxyl radicals leads to 4-nitroaryl-3-imidazoline-3-oxide nitroxides via oxammonium salts formation, the nitrone group being an ortho-para orientant.

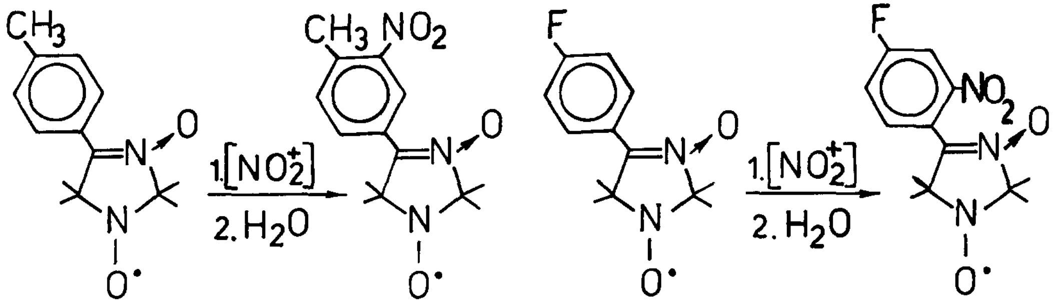
3-Imidazoline nitroxyl radicals exceed all known radicals in stability to protic and Lewis acids [1]. This expands the pH range of media used for chemical transformations of these radicals, provided that the final product retains the radical centre. In this connection we studied the ability of 4-aryl-2,2,5,5-tetramethyl-3-imidazoline-3-oxide nitroxides (1a-c) containing the aryl nitrone group to undergo nitration in concentrated H_2SO_4. Literature contains no data on nitration of nitroxyl radicals and α-aryl nitrones, nor on the orienting ability of the nitrone group in the aromatic electrophilic substitution reactions (see ref. [2]).

Treatment of H_2SO_4 solution of radical 1a with potassium, sodium, silver, mercury nitrates or HNO_3 at $-5 \div 10^{\circ}C$ during 0.5 hour followed by dilution with ice water and extraction with $CHCl_3$ gives 4-o-nitrophenyl- 2 (m.p.165-167°) and 4-p-nitrophenyl- 3 (m.p.205-206°) nitroxyl radicals in 60 and 30%, respectively [3]. The IR spectra of both radicals show intensive bands corresponding to NO_2 vibrations at 1530 and 1360 cm^{-1}. The UV spectra of ortho- 2 and para- 3 isomers reveal substantial differences indicating an out-of-plane deviation of the nitrone group of ortho-nitrophenyl group in radical 2: λ max=250 nm ($\lg\varepsilon$=4.20) 2; λ max=245 nm ($\lg\varepsilon$=4.16) and 345 nm ($\lg\varepsilon$=3.96) **3**. Radicals **2** and **3** were reduced with hydroxylamine in ethanol to the corresponding 1-hydroxyderivatives **4** and **5**, whose PMR spectra show the presence of ortho- and para-nitrogroup in the products **2** and **4**, **3** and **5**, respectively [4]. Under nitration conditions the nitrone group acts as an ortho-para orientant.



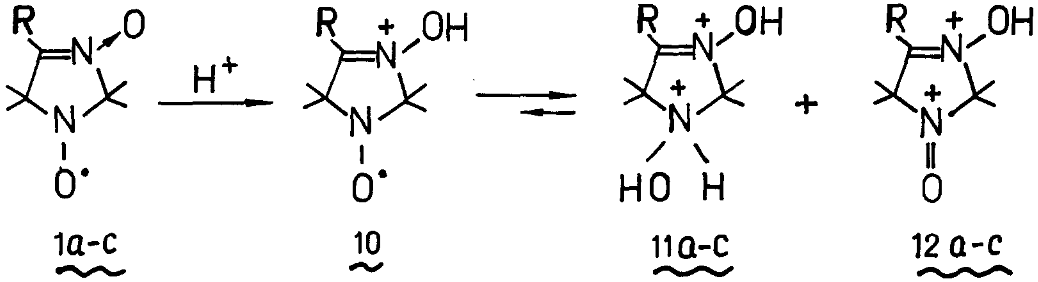
1a **2** **3**

If there are other orienting groups at the benzene ring, such as para-CH_3 **1b** or para-F **1c**, nitration gives respectively meta-isomer **6** (85%; m.p.187-189°C) (relative to the nitrone group) and ortho-isomer **7** (30%; 166-168°C). The UV spectrum of radical **7** is similar to that of radical **2**: λ max = 245 nm ($\lg\varepsilon$= 4.20) and the two λ max values in the UV spectrum of meta-isomer **6** are intermediate between λ max in ortho- and para-isomers: λ max = 270 nm ($\lg\varepsilon$= 4.11) and 296 nm ($\lg\varepsilon$= 4.10). The PMR spectra of the corresponding diamagnetic 1-hydroxyderivatives **8** and **9** confirm the assigned structures [5].



1b **6** **1c** **7**

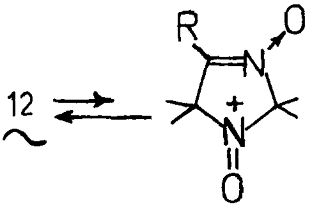
As shown by the PMR spectra, under nitration conditions the radical centre is completely converted to oxammonium group via disproportionation and oxidation. The PMR spectra of deeply-coloured solutions of radicals **1a** - **1c** in D_2SO_4 represent the superposition of the spectra of two diamagnetic products: diprotonated hydroxylamine **11a** - **c** and protonated oxammonium salt **12a** - **c**. This indicates a reversible disproportionation of radicals **1a** - **c** in concentrated H_2SO_4 (D_2SO_4), which is almost completely shifted towards formation of products **11** and **12**.



R = C_6H_5 (a), para-$CH_3C_6H_4$ (b), para-FC_6H_4 (c).

The PMR spectra of pure 1-hydroxy-4-aryl-2,2,5,5-tetramethyl-3-imidazoline-3-oxides (**11a** - **c**) in D_2SO_4 allowed to unambiguously assign the signals in the PMR spectra of the mixture of the products **11a** - **c** + **12a** - **c**; e.g.: **11a** - 2.38 and 2.22 ppm (3H and 3H, 2-CH_3 and 2-CH_3), 2.28 and 2.22 ppm (3H and 3H, 5-CH_3 and 5-CH_3), 8.16 m (2H, ortho), 7.89 m (2H, meta), 8.06 m (1H, para); **12a** - 2.56 broad (12H, 2,5-$(CH_3)_4$), 8.52 m (2H, ortho), 8.03 m (2H, meta), 8.18 m (1H, para). The signals of gem-CH_3 groups were assigned on the basis of the analysis of the PMR spectrum of compound **11a** containing gem-CD_3 groups at position 2. Protonation of the nitrone group results in a 31 ppm downfield shift of the C_4 signal in the ^{13}C NMR spectrum of compound **11a**: unprotonated hydroxylamine **11a** in DMSO-d_6- δC_4-140.1 ppm, protonated form of **11a** - δC_4-171.4 ppm. The signals of C_2 and C_5 atoms in the ^{13}C NMR spectrum of **11a** are shifted downfield by 8 and 16 ppm respectively, relative to C_2 and C_5 signals in the spectrum of unprotonated hydroxylamine **11a**. In the presence of a strong oxidant (nitrating mixture) compounds **10** and **11** are completely converted to oxammonium salt **12**. Dilution of the product with water leads to practically quantitative conversion of oxammonium group to the nitroxyl one [6].

In conditions of the nitration reaction, the oxammonium salt **12**, which is a dication, is presumably in equilibrium with a small amount of the deprotonated oxammonium salt **13**, a monocation, and it is the monocation which undergoes attack by the nitronium cation.



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1. L.B.Volodarsky, I.A.Grigor'ev, R.Z.Sagdeev. In: Biological Magnetic Resonance. Vol. 2 / Ed. L.J.Berliner, J.Reuben. N.Y. - L., Plenum-Press, 1980, p. 169.
2. E.Breuer. In: The Chemistry of Functional Groups. Supplement F. Part 1/ Ed. S.Patai. Chichester - New York - Brisbane - Toronto - Singapore: Intersci 1982, p. 459.
3. The elemental analysis data for all the compounds involved are corrected.
4. **4**: UV λ max ($\lg \varepsilon$): 250 (4.10); PMR (in CD$_3$OD, δ , ppm): 7.75 m (3H); 8.21 m (1H), 1.40 s (6H, (CH$_3$)$_2$, 1.52 s (6H, (CH$_3$)$_2$).
   5: UV λ max ($\lg \varepsilon$): 247 (4.14), 340 (3.94). PMR (in CD$_3$OD, δ , ppm): 8.30 s (4H), 1.50 (6H, (CH$_3$)$_2$), 1.53 (6H, (CH$_3$)$_2$).
5. **8**: UV λ max ($\lg \varepsilon$): 273 (4.10), 295 (4.08). PMR (in CD$_3$OD, δ , ppm): 8.90 d (1H, J = 2 Hz), 8.16 and 7.64 (2H, AB-system, J = 7.5 Hz), 2.64 s (3H, p-CH$_3$), 1.57 and 1.55 s (6H and 6H, (CH$_3$)$_2$ and (CH$_3$)$_2$).
   9: UV λ max ($\lg \varepsilon$): 244 (4.10). PMR (in CD$_3$OD, δ , ppm): 8.12 and 7.96 (1H), 7.75 and 7.64 (2H), 1.50 and 1.40 (6H and 6H, (CH$_3$)$_2$ and (CH$_3$)$_2$).
6. E.G.Rozantsev, "Free Nitroxyl Radicals", Plenum Press, New York, 1970.

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