Stereospecific Spin Trapping 5,5-Dimethyl-Δ^1-pyrroline *N*-Oxide (DMPO) Derivatives, 5-Alkyl-5-methyl-Δ^1-pyrroline *N*-Oxides

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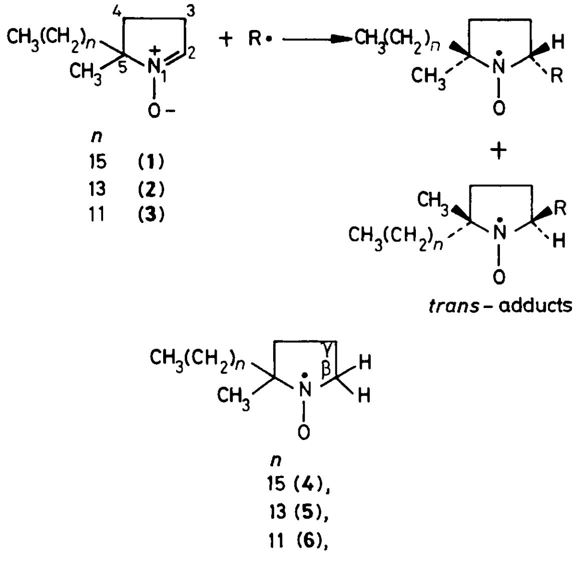
Ten 5,5-disubstituted-Δ^1-pyrroline *N*-oxides containing a chiral carbon at C-5 have been prepared and the stereospecificity of spin trapping has been demonstrated.

Although three derivatives of 5,5-dimethyl-Δ^1-pyrroline *N*-oxide (DMPO) have been synthesized to trap the t-butoxyl radical, the synthetic route is complicated.[1] Furthermore, these nitrones containing a chiral carbon at C-5 were not able stereospecifically or stereoselectively to trap the t-butoxyl radical. In order to study stereochemistry in spin trapping and effectively to detect free radicals in biphasic media such as biological membranes, we systematically prepared ten 5-alkyl-5-methyl-Δ^1-pyrroline (1,2-didehydropyrrolidine) *N*-oxides, in which the alkyl groups were n-hexadecyl (**1**), n-tetradecyl (**2**), n-dodecyl (**3**), n-decyl, n-nonyl, n-octyl, n-hexyl, n-pentyl, n-butyl, and n-propyl, by the literature method,[2] and characterized the structures by i.r., ^{1}H n.m.r., and mass spectroscopy. Five nitrones, (**1**), (**2**), and (**3**), and the n-octyl and n-pentyl derivatives have not been reported previously.

In each of these nitrones, C-5 is a chiral centre. So, four possible isomeric spin adducts of the trapping reaction should be afforded, and *trans*- and *cis*-adducts should show different



Scheme 1

hyperfine splitting constants (h.f.s.c.s) of the protons linked to the β-carbon atom because the C^{β}–H bonds of *trans*- and *cis*-adducts have different orientations with respect to the semi-occupied p-orbital of the nitrogen atom.[3] In order to demonstrate this hypothesis, the nitrones (**1**), (**2**), and (**3**) were reduced with $LiAlH_4$ in diethyl ether for 1 h, then a small amount of water was added; extraction with benzene, followed by air-oxidation[4,5] gave the corresponding nitroxides (**4**), (**5**), and (**6**). The following h.f.s.c. values were obtained (**4**), a_N 13.8, $a^{\beta}_{H_1}$ 17.4, $a^{\beta}_{H_2}$ 19.3; (**5**), $a_N = 13.9$, $a^{\beta}_{H_1}$ 17.5, $a^{\beta}_{H_2}$ 19.2; (**6**), a_N 13.8, $a^{\beta}_{H_1}$ 17.5, $a^{\beta}_{H_2}$ 19.1 G ($G = 10^{-4}$ T) in benzene solution. These results indicate that the two β-hydrogens in (**4**), (**5**), and (**6**) are substantially magnetically inequivalent. We thus conclude that the β-hydrogen in the *trans*-adduct is magnetically different from that in the *cis*-adduct, and different h.f.s.c. values should be shown in the e.s.r. spectrum if *trans*- and *cis*-adducts were afforded within the same spin trapping reaction. In comparison, DMPO was also treated by the procedure used for (**1**), (**2**), and (**3**) to give dimethyltetrahydropyrrolyl-1-oxy for which the h.f.s.c. values of the two β-hydrogens were the same, 19.0 G.

When nitrone (**3**), which is a racemic mixture, traps $\cdot CH_2OH$, $CH_3\dot{C}HOH$, $(CH_3)_2\dot{C}OH$, $C_2H_5\dot{C}HOH$, $C_2H_5O\dot{C}HCH_3$, tetrahydrofuranyl, dioxanyl, and t-butoxyl radicals, only a pair of *trans*-adducts are produced according to the e.s.r. spectra. The e.s.r. spectra of these spin adducts are the same as those obtained from DMPO.[6] So these spin trapping reactions are stereospecific, or the stereoselectivity is so high that a pair of *cis*-adducts cannot be detected by the e.s.r. method as illustrated in Scheme 1.

The steric hindrance of n-dodecyl is greater than that of the methyl group, so free radicals should add to the nitrone (**3**) from the *trans* direction more easily to afford *trans*-isomers in the stereospecific case. These spin trapping reactions are probably kinetically controlled. The n-nonyl derivative reacts with Grignard and alkyl-lithium reagents to give the *trans*-isomer.[2,7,8] This is consistent with our results.

However, when nitrones (**1**), (**2**), and (**3**) react with the $(CH_3CH_2)_2N\dot{C}HCH_3$ radical, which is generated by photolysis of triethylamine and benzophenone in benzene, at least two spin adducts are afforded according to the e.s.r. spectra. For example, h.f.s.c. values of spin adducts of nitrone (**1**) with this radical are a_N 13.5, a_H 16.8, and a_N 13.4, a_H 22.9 G, respectively, and the ratio of the e.s.r. peak heights of the corresponding adducts is about 3.3 : 1. It is surprising that the other seven nitrones and DMPO trap this radical to give similar spectra. Are these spin trapping reactions stereoselective or stereospecific? Further studies are in progress to resolve this dichotomy.

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