Reduction-Resistant Nitroxides

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Nitroxide spin probes and spin labels have found a broad application in biophysical and biomedical research. Natural antioxidants and enzymatic systems may reduce nitroxides to diamagnetic compounds.[1] These undesired reactions may complicate EPR studies of biological samples using nitroxides. Some modern research areas, such as in-cell EPR/PELDOR measurements and in vivo NMR and EPR imaging require especially high stability of the paramagnetic agent. Introduction of several bulky alkyl substituents larger than methyl group to α-carbons of nitroxyl group is a fruitful approach to increase the resistance of nitroxides to reduction. Some of these so-called "sterically shielded" or "sterically hindered" nitroxides demonstrate more than two orders of magnitude lower decay rates in the presence of ascorbate than similar tetramethyl-substituted nitroxides.[2] Their lifetimes in tissue homogenates may exceed those of triarylmethyl (TAM) radicals.[3]

Impressive progress in molecular design and synthesis of new sterically shielded nitroxides was achieved in the recent few years, and redox properties of the new nitroxides were studied [4-7]. Alternative mechanisms of decay of sterically shielded nitroxides in biological systems are discussed. The peculiarities of the EPR spectra were shown and the nature of additional hyperfine splitting was investigated. Some examples of application of sterically shielded nitroxides are given.

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