CC/NUMBER 44
NOVEMBER 3, 1986

This Week's Citation Classic®

Janzen E G. Spin trapping. *Account. Chem. Res.* 4:31-40, 1971.
[Department of Chemistry, University of Georgia, Athens, GA]

This article described an approach to the detection and identification of short-lived free radicals that is based on a chemical trapping process where the addition product reaches concentration levels sufficient for detection by electron spin resonance spectroscopy. The terms spin trap, spin trapping, and spin adduct were defined. Advantages and disadvantages of two different types of spin traps, nitrones and nitroso compounds, were discussed. Examples of spin trapping reactions were also included. [The *SCI*® indicates that this paper has been cited in over 515 publications.]

Edward G. Janzen
Department of Chemistry
and Biochemistry
Guelph-Waterloo Centre for
Graduate Work in Chemistry
University of Guelph
Guelph, Ontario N1G 2W1
Canada

September 19, 1986

It is probably fair to say that for the first 20 years after its invention, electron spin resonance (ESR) had fallen short of its expected potential as a powerful tool for the mechanistically inclined chemist interested in the *in situ* detection and identification of free radical intermediates under ambient reaction conditions. The major obstacle to more effective utilization of the technique is the fact that the steady-state concentrations of free radicals in most reactions do not exceed the detection limits of ESR spectroscopy.

The notion that perhaps the magnitude of the β-hydrogen hyperfine splitting constants could be used to assign structure was on my mind when Barry Blackburn, a postdoctoral fellow in our group at the University of Georgia, brought a paper by Iwamura and Inamoto[1] to my attention: it showed that 2-cyanopropyl and 2-carbomethoxypropyl radicals could be added to the carbon atoms of nitrones to produce relatively stable nitroxide radicals. I felt compelled to investigate the possibility that this was a general reaction and that this type of addition could be used as an analytical tool for the detection and identification of free radicals.

Since the magnitude of β-hydrogen hyperfine splittings depends on the equilibrium conformation of the alkyl group bonded to the nitroxyl function, a different ESR spectrum should in principle be produced for each different radical trapped. This proposal was first presented with examples at a Free Radical Symposium organized by W.A. Pryor at the 156th American Chemical Society Meeting in Atlantic City on September 8-13 in 1968. In the first communication,[2] the method was called a trapping technique, but later the name "spin trapping" was coined for this method.[3] We called the compounds used for detecting radicals "spin traps" and the addition products "spin adducts." It should be noted that others had similar ideas with respect to the detection of radicals except that nitroso compounds were used. References to papers from four other groups around the world (Sweden, England, Japan, and Australia) are included in the *Accounts* publication.

The usefulness of the spin trapping approach in the search for free radicals has become particularly attractive to the biological scientist. Fortunately, common nitrones are nontoxic and appear to survive within many biological systems long enough to allow the detection of radicals. Indeed, the novelist Arthur Hailey comes very close when he proposes that certain compounds might be coadministered with drugs "to quench free radicals produced in...."[4]

The high frequency of citation is probably linked to the growing popularity of this approach in the detection of free radicals in biological systems. Also important is the fact that the paper was published in a readily available journal of general interest. Other reviews can be recommended for further reading.[5,6]

Finally, it is a pleasure to add that my name was selected by the Canadian Society for Chemistry of the Chemical Institute of Canada to receive the 1986 Syntex Award in Physical Organic Chemistry for work in the area of spin trapping.

1. **Iwamura M & Inamoto N.** Novel radical 1,3-addition to nitrones. *Bull. Chem. Soc. Jpn.* 40:702-3, 1967. (Cited 60 times.)
2. **Janzen E G & Blackburn B J.** Detection and identification of short-lived free radicals by an electron spin resonance trapping technique. *J. Amer. Chem. Soc.* 90:5909-10, 1968. (Cited 100 times.)
3. ————. Detection and identification of short-lived free radicals by electron spin resonance trapping techniques (spin trapping). Photolysis of organolead, tin and mercury compounds. *J. Amer. Chem. Soc.* 91:4481-90, 1969. (Cited 210 times.)
4. **Hailey A.** *Strong medicine.* New York: Doubleday, 1984. 456 p.
5. **Janzen E G.** A critical review of spin trapping in biological systems. (Pryor W A, ed.) *Free radicals in biology.* New York: Academic Press, 1980. Vol. IV. p. 115-54.
6. **Janzen E G, Stronks H J, DuBose C M, Poyer J L & McCay P B.** Chemistry and biology of spin-trapping radical associated with halocarbon metabolism *in vitro* and *in vivo*. *Environ. Health Perspect.* 64:151-70, 1985.

2A-14