

reactive solvents, *e.g.*, solid Ne, is obvious. (2) If only magnetic results are needed, the optical methods would be more convenient if they could be carried out at 77°K. The percentage change in the phosphorescence intensity would be extremely small upon microwave saturation. Thus, very sensitive techniques should be developed. At these temperatures, the population of the three levels equilibrates before emission and thus the excited system loses memory of how it is formed. Information concerning the mechanisms of the intersystem-crossing process cannot be obtained at these temperatures. (3) The value of spin-lattice relaxation rate constants should be extracted at different temperatures and in different hosts. These constants should be sensitive to the structure of molecular solids at low temperatures. (4) These techniques should be applied to many molecules in order to understand fully the magnetic, the nonradiative, and the radiative properties of the triplet state.

**B. Theoretical Research Studies.** (1) What are the mechanisms of the spin-lattice relaxation process between the *z*f levels in zero field in molecular solids at low temperatures? The proposed mechanisms in ionic crystals involve the modulation of the crystal field by lattice vibrations. This modulation is transmitted to the orbital motion of the excited electron which, due to the large spin-orbit interaction in these systems, is strongly coupled to the spin motion. This coupling

offers a mechanism by which the spin system exchanges energy with the lattice. Due to the small nuclear charge, spin-orbit interactions are smaller in aromatic organic than in ionic compounds. The modulation of the spin-spin interaction by modulating the crystal field of the lattice by lattice vibrations might thus turn out to be also important in these systems. In any case, theoretical examination of this problem (at any level of sophistication) seems necessary. (2) The best available molecular wavefunctions can be tested by attempting to calculate the endor spectrum in the triplet state. While theoretical calculations are successful in calculating triplet-triplet energies, their intensity predictions can sometimes be off by at least an order of magnitude. Endor frequencies might be useful in correcting the triplet state wavefunctions. (3) The question of whether or not the formation of the lowest triplet state induces nuclear polarization requires theoretical clarification (*i.e.*, is the steady-state population of the  $\tau_{11}$  level equal that of the  $\tau_{12}$  level in Figure 6?). Experimental work should also be carried out once the theoretical considerations are found to be fruitful.

*I wish to thank Professors A. Maki and C. Harris, Drs. O. Kalman, T. Kuan, W. Moomaw, and D. Tinti, and Messrs. L. Hall and D. Owens for their very fruitful collaboration. The generous continuing support of the U. S. Atomic Energy Commission is greatly acknowledged.*

## Spin Trapping

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The direct detection and identification of short-lived free radicals by electron spin resonance (esr) is possible only if the radicals are produced in relatively high concentrations in the esr cavity by intense *in situ* irradiation or by rapid-mixing flow systems. Sometimes esr equipment has been substantially modified to increase sensitivity and resolution.

Recently two indirect techniques for the detection and identification of low concentrations of free radicals in reacting systems have been developed: CIDNP<sup>1</sup> and spin trapping. The former depends on the strong polarization of certain nuclear spins by the unpaired electron during the molecule's existence as a free radi-

cal. The latter involves trapping of a reactive free radical by an addition reaction to produce a more stable radical, detectable by esr, whose hyperfine coupling parameters permit identification of the initial radical trapped. In both techniques commonly available magnetic resonance equipment can be used.

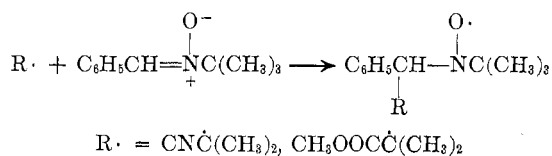
### Development of the Spin-Trapping Technique

The possibility that a radical addition reaction might provide a means of detecting short-lived radicals had initially been considered during mechanistic studies of the dehydrogenation of hydroaromatics with hot nitrobenzene<sup>2</sup> and thermal decomposition of nitro aromatics.<sup>3</sup> In connection with an attempt to detect hydrogen atom transfer to nitrobenzene or azoxybenzene from diphenylhydroxymethyl radicals produced by thermal

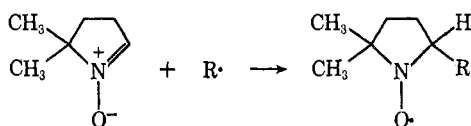
(1) H. Fischer and J. Bargon, *Accounts Chem. Res.*, **2**, 110 (1969); M. Cocivera and A. M. Trozzolo, *J. Amer. Chem. Soc.*, **92**, 1772 (1970); G. L. Closs and A. D. Trifunac, *ibid.*, **92**, 2183, 2186 (1970); G. L. Closs, C. E. Doubleday, and D. R. Paulson, *ibid.*, **92**, 2185 (1970); A. R. Lepley, P. M. Cook, and G. F. Willard, *ibid.*, **92**, 1101 (1970); H. R. Ward, R. C. Lawler, H. Y. Loken, and R. A. Cooper, *ibid.*, **91**, 4928 (1969).

(2) E. G. Janzen, *Chem. Eng. News*, **43**, 50 (Sept 27, 1965).  
(3) E. G. Janzen, *J. Amer. Chem. Soc.*, **87**, 3531 (1965).

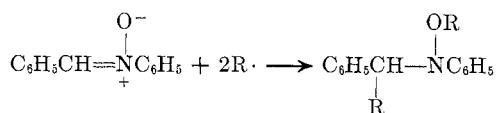
decomposition of benzopinacol,<sup>2</sup> two papers by Iwamura and Inamoto<sup>4</sup> drew the attention of Dr. Barry Blackburn in our group. These authors showed that 2-cyano- and 2-carbomethoxypropyl radicals add to the carbon atom of phenyl *tert*-butyl nitron to produce a stable nitroxide. A cyclic nitron derived from



pyrrolidine exhibited the same radical addition reaction to give a less stable cyclic nitroxide. Further-

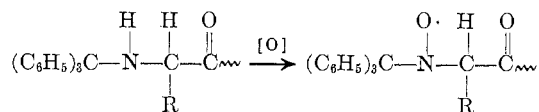


more, hydroxylamine derivatives resulting from the addition of two radicals could be isolated from reactions with diphenyl and phenyl benzyl nitron. Also a



bis(diphenyl) nitron,  $[C_6H_5N^+(O^-)=CH-]_2$ , gave the product of addition of two 2-cyanopropyl radicals. This paper prompted us to try phenyl *tert*-butyl nitron as a hydrogen atom acceptor in the thermal decomposition of benzopinacol. However, it proved to be unsuitable because of substantial spontaneous nitroxide radical production when heated by itself at the temperature needed. Some substituted diphenyl nitrons gave esr spectra rich in hyperfine splitting under similar conditions but were unsuitable for unambiguous analysis because of the complex spectra obtained.

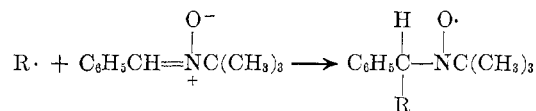
In the meantime in our group Dr. Otto Maender was investigating the possibility that the magnitude of the  $\beta$ -hydrogen coupling in trityl nitroxides of certain amino acids and peptides could be used to provide structural information about the amino acid or peptide. Since



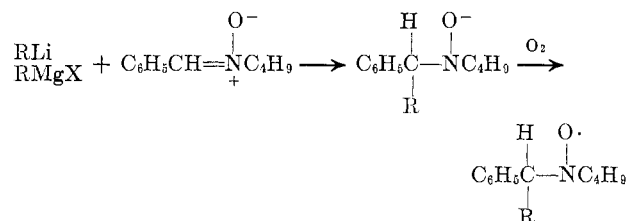
the  $\beta$ -hydrogen ( $\beta$ -H) coupling depends on the dihedral angle between the C-H bond and the p orbital on nitrogen which in turn depends on the bulkiness of the groups attached to the  $\beta$  carbon, the  $\beta$ -H hyperfine coupling should be unique for each amino acid and peptide. This work, which proved successful,<sup>5</sup> and Iwamura and Inamoto's prompted the notion that the nitron function could be used as a radical detector

which at the same time might identify the radical trapped through the magnitude of the  $\beta$ -H hyperfine coupling.

Initial experiments with phenyl *tert*-butyl nitron (PBN) and methyl, ethyl, *n*-butyl, benzyl, and phenyl radical precursors in benzene readily provided esr spectra at room temperature consistent with nitrogen and  $\beta$ -hydrogen hyperfine coupling of  $\alpha$ -substituted benzyl *tert*-butyl nitroxides. However, the difference in the

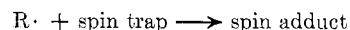


$\beta$ -H coupling as a function of structure of radical trapped was found to be very small: *e.g.*,  $A_{\beta}^H = 3.4, 3.2, 3.1, 2.4,$  and  $2.1$  G for methyl, ethyl, *n*-butyl, benzyl, and phenyl radicals trapped, respectively, with little change in nitroxide nitrogen coupling. In order to dispel our fears that the nitroxides might not have the structures proposed, but rather, due to some artifact of the system, might all be the same nitroxide, we synthesized these nitroxides by independent routes. We found that the addition of organolithium and Grignard compounds to the nitron followed by air oxidation produced the same nitroxide, in high yield, as produced by the radical addition reactions.



The feasibility of the method was thus demonstrated. This work was first presented at a free radicals symposium<sup>6</sup> and preliminarily published<sup>7</sup> late in 1968. A more detailed paper on the technique is also available.<sup>8</sup> This work describes the trapping of methyl, ethyl, *n*-butyl, phenyl, and benzyl radicals from the photolysis of a variety of organolead, -tin, and -mercury compounds. It was shown that the order of photolytic cleavage based on the intensity of the nitroxide spectrum obtained was phenyl > alkyl  $\gg$  acetate or halide.

Since some similarities exist between the process of spin labeling<sup>9</sup> and radical trapping, we named the technique of detecting and identifying short-lived free radicals by addition to an unsaturated function to produce an esr detectable radical "spin trapping."<sup>8</sup> The addition product of the short-lived radical and the spin trap was called a "spin adduct."<sup>8</sup>



(6) E. G. Janzen and B. J. Blackburn, 156th National Meeting of the American Chemical Society, Atlantic City, N. J., Sept 8-13, 1968, Abstract No. ORGN 86.

(7) E. G. Janzen and B. J. Blackburn, *J. Amer. Chem. Soc.*, **90**, 5909 (1968).

(8) E. G. Janzen and B. J. Blackburn, *ibid.*, **91**, 4481 (1969).

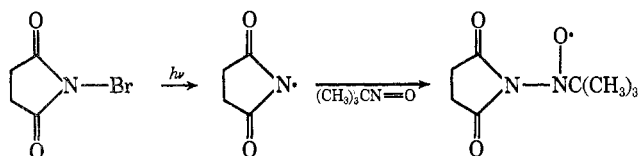
(9) C. L. Hamilton and H. M. McConnell in "Structural Chemistry and Molecular Biology," A. Rich and N. Davidson, Ed., W. H. Freeman and Co., San Francisco, Calif., 1968, p 115; O. H. Griffith and A. S. Waggoner, *Accounts Chem. Res.*, **2**, 17 (1969).

(4) M. Iwamura and N. Inamoto, *Bull. Chem. Soc. Jap.*, **40**, 702, 703 (1967); see also (added in proof) M. Iwamura and N. Inamoto, *ibid.*, **43**, 856, 860 (1970).

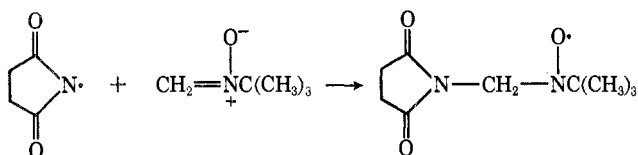
(5) O. W. Maender and E. G. Janzen, *J. Org. Chem.*, **34**, 4072 (1969).



The carbazyl radical produced by the same reagent from succinimide has also been trapped by NtB.<sup>20</sup> Moreover, Lagercrantz and Forshult<sup>21</sup> have trapped the succinimidyl and phthalimidyl radicals with NtB during photolysis of the parent *N*-bromo derivatives in carbon tetrachloride, chloroform, or methylene chloride.

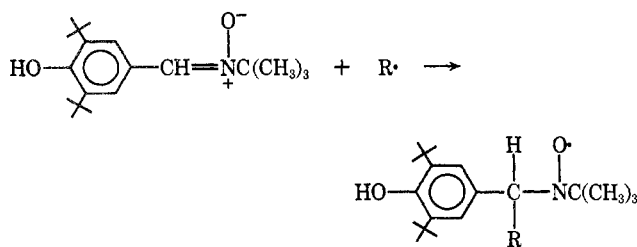


These workers also investigated the photolysis of *N*-halogen imides in the presence of excess amounts of olefin and obtained spectra which were preliminarily assigned to the spin adducts produced by radicals formed by the loss of  $\alpha$  hydrogens. Chalfont, *et al.*,<sup>22</sup> showed that the succinimidyl radical could also be trapped by *tert*-butyl nitron, although phenyl *tert*-



butyl nitron appeared too unreactive to trap this radical. The latter observation is in agreement with our own experience with *N*-bromosuccinimide and phenyl *tert*-butyl nitron. From preliminary experiments *tert*-butyl nitron appears to promise high reactivity toward radical addition reactions, particularly for nitrogen- or oxygen-centered radicals.<sup>15,22</sup>

The usefulness of a novel "bifunctional" trap has recently been described. Pacifici and Browning<sup>23</sup> found that methyl, 2-cyanopropyl, 2-hydroxypropyl, and phenyl radicals add to 3,5-di-*tert*-butyl-4-hydroxyphenyl *tert*-butyl nitron to give normal nitroxide spin adducts. However the oxy radicals derived from



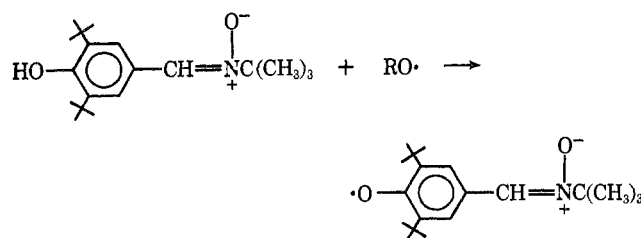
acetyl, benzoyl, and cumyl peroxides as well as triplet benzophenone produced the stable phenoxy radical by phenol hydrogen abstraction. Since the spectra of these two stable radicals (a nitroxide and a phenoxy) are very different, this trap readily distinguishes between carbon- and oxygen-centered radicals.

(20) S. Terabe and R. Konaka, *J. Amer. Chem. Soc.*, **91**, 5655 (1969).

(21) C. Lagercrantz and S. Forshult, *Acta Chem. Scand.*, **23**, 708 (1969).

(22) G. R. Chalfont, M. J. Perkins, and A. Horsfield, *J. Chem. Soc.*, 401 (1970).

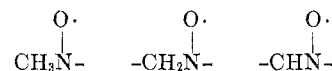
(23) J. G. Pacifici and H. L. Browning, Jr., *J. Amer. Chem. Soc.*, **92**, 5231 (1970).



### Comparisons of Nitroso and Nitron Spin Traps

Although it is too early in the development of spin trapping to make a detailed comparison of the effectiveness of different spin traps, it is clear that certain advantages exist for each of the spin traps used (nitroso-*tert*-butane (NtB), 2-methyl-2-nitroso-3-butanone, nitrosobenzene, phenyl *tert*-butyl nitron (PBN), and the unsubstituted *tert*-butyl nitron). The main advantage of using nitroso compounds is that the information concerning the structure of the radical trapped is more easily extracted from the spectrum.

(1) The multiplicity of the splitting pattern immediately gives the number of hydrogens attached to the carbon of the alkyl radical trapped



In this regard nitrosoalkanes with a tertiary carbon group ( $>\text{CN}=\text{O}$ ) are preferred over nitrosobenzene because a spectrum of fewer lines is obtained.

(2) Trapping of aryl radicals can be readily distinguished by the additional proton hyperfine splitting due to delocalization of the unpaired electron to the aromatic carbon atoms. The magnitude of the pro-

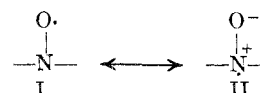


ton coupling is found to be in the order: para  $\gtrsim$  ortho  $>$  meta. (Vinyl radicals should also give spin adducts with predictable splitting patterns but no work has been reported on these nitroxides.)

(3) Radicals with the electron localized on atoms with a nuclear spin give adducts with characteristic hyperfine coupling, *e.g.*, nitrogen radicals give an additional triplet splitting ( $>\text{N}-\text{N}(\text{O}\cdot)-$ ).

(4) The magnitude of the nitrogen hyperfine coupling ( $A_N$ ) varies substantially according to the atoms attached. Although  $A_N$  varies in the range of 13–16 G for dialkyl nitroxides depending on the inductive electron-withdrawing nature of the groups attached,<sup>24,25</sup>  $A_N = 27$ –28 G for alkoxy alkyl nitroxides,<sup>11,12</sup> 17–18.5 G for thiyl alkyl nitroxides,<sup>16,17</sup> and 7–8.5 G for acyl

(24) Electronegative groups decrease  $A_N$  because I is favored over II



For a discussion of this effect see ref 25.

(25) E. G. Janzen, *Accounts Chem. Res.*, **2**, 279 (1969).

alkyl nitroxides.<sup>12</sup> Aryl groups attached to the nitroxide function decrease  $A_N$  due to delocalization of the unpaired electron.

(5) The  $g$  values of the spin adducts also vary detectably with the kind of atom attached to the nitroxide function. The  $g$  value goes up with increase in atomic number for the same amount of spin in contact with the atom. This effect is most marked when first row elements are compared with second row elements: *e.g.*,<sup>16</sup>  $\text{HOCH}_2\text{N}(\text{O}\cdot)\text{C}(\text{CH}_3)_3$ ,  $g = 2.0060$ ;  $\text{CH}_3(\text{CH}_2)_3\text{SN}(\text{O}\cdot)\text{C}(\text{CH}_3)_3$ ,  $g = 2.0070$ .

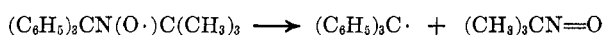
Another advantage is that many spin adducts of nitroso compounds (but not all; see subsequent sections) are unusually stable radicals. Apparently all alkyl, aryl, aralkyl, and acyl nitroxides have transient stability if generated *in situ* in the esr cavity. Azyl nitroxides ( $>\text{N}-\text{N}(\text{O}\cdot)-$ ) also appear to be stable. Vinyl, allyl, or olefinic nitroxides have not been studied enough to warrant generalization. Alkoxy nitroxides are less stable. Thiyl nitroxides are quite unstable and are only detectable during *in situ* generation of radicals.

The main disadvantages of the use of nitroso spin traps are the following.

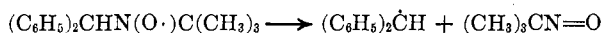
(1) The strong tendency of nitroso compounds to dimerize; for example, uv irradiation of 2-methyl-2-nitroso-3-butanone is required to dissociate the dimer to the active monomer form,<sup>14</sup> and both nitroso-*tert*-butane and nitrosobenzene exist significantly in the dimer form at room temperature; solutions of primary and secondary nitrosoalkanes contain only trace amounts of monomer at room temperatures.<sup>26</sup>

(2) Certain spin adducts of nitroso compounds are unstable. Since the adding radical is bonded directly to the nitroxide function, the possibility that a reverse reaction or some other cleavage reaction of the nitroxide is favorable always exists.

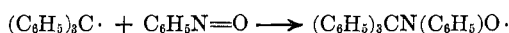
Thus, certain trityl alkyl nitroxides (*e.g.*, isopropyl, 2- and 3-pentyl, *tert*-butyl) dissociate to trityl radical and nitrosoalkane,<sup>5</sup> and preliminary results in our lab-



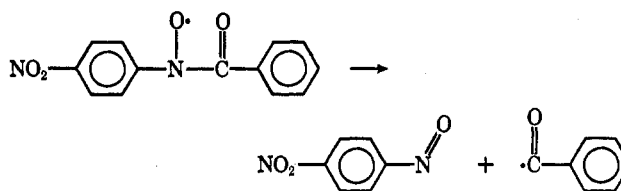
oratory indicate that benzhydryl *tert*-butyl nitroxide may decompose in the same way above room temperatures. Phenyl trityl nitroxide, on the other hand,



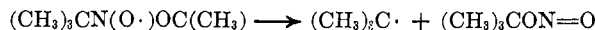
is stable at room temperature,<sup>5</sup> and trityl radical has been trapped by nitrosobenzene.<sup>27</sup>



Although acyl *tert*-butyl nitroxides appear to have considerable stability,<sup>12</sup> the stability of the aromatic derivatives has a marked substituent effect. Thus *p*-nitrophenyl benzoyl nitroxide decomposes at room temperatures within minutes.<sup>28</sup>



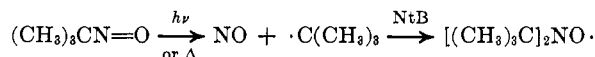
Alkoxy alkyl nitroxides are also unstable. Thus *tert*-butoxy *tert*-butyl nitroxide decomposes to *tert*-



butyl nitrite and *tert*-butyl radicals,<sup>10,12</sup> or reversibly to *tert*-butoxy radicals and nitroso-*tert*-butane.<sup>29</sup>

Other apparently unstable spin adducts of nitroso-butane are halogen and acyloxy nitroxides, *e.g.*,  $\text{XN}(\text{O}\cdot)\text{C}(\text{CH}_3)_3$ ,  $\text{X} = \text{F}, \text{Cl}, \text{Br}, \text{I}$ , and  $\text{RCOON}(\text{O}\cdot)\text{C}(\text{CH}_3)_3$ ,  $\text{R} = \text{CH}_3, \text{C}_6\text{H}_5$ , etc.

(3) The photolysis or thermal decomposition of nitroso compounds leads to nitroxides. These are produced by homolytic cleavage followed by trapping of the radical formed. The spectra of such rad-



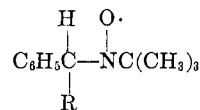
icals may seriously overlap the region of most interest. This problem can sometimes be avoided by light filtering. Although di-*n*-butyl nitroxide is produced from NtB by both uv (320–360  $\mu\text{m}$ ) and red (660–680  $\mu\text{m}$ ) light the spectral region between these absorption ranges is inactive.<sup>10</sup> With nitrosobenzene only uv irradiation gives diphenyl nitroxide.<sup>10</sup>

The main advantages of the use of phenyl *tert*-butyl nitroxide are the following.

(1) Phenyl *tert*-butyl nitroxide (PBN) is a stable compound and as a solid not overly sensitive to light, oxygen, or water vapor. It is soluble in a large number of solvents to fairly high concentrations ( $\sim 0.1 M$ ).

(2) In inert solvents such as benzene photolysis of PBN does not produce significant concentration of nitroxide radicals; *i.e.*, control photolyses are generally good. In hydrogen atom donating solvents, however, this is not true (see section on disadvantages).

(3) Spin adducts of PBN should all be inherently stable since a carbon atom separates the nitroxide function from the group which was the trapped radical.



Exceptions to this generalization may be those spin adducts, as in the case of NtB, wherein R is a bulky and/or a resonance stabilized radical. Thus trityl radical is not trapped by PBN and the spin adduct, if synthesized independently, is not stable.<sup>8</sup>

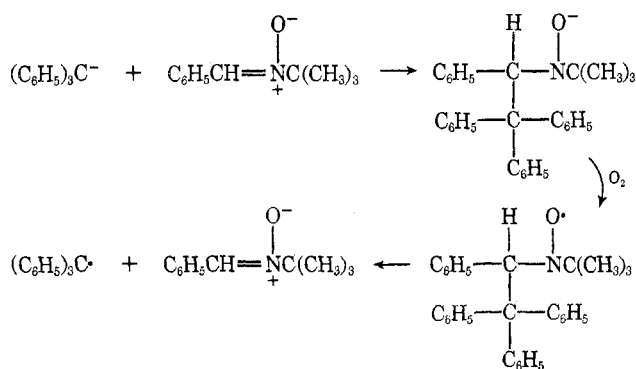
(28) O. W. Maender, Ph.D. Thesis, "An Electron Spin Resonance Study of Substituted  $\alpha$ -Ketonitroxides and Related Systems," University of Georgia, Athens, Ga., 1968; for discussion see ref 25.

(29) See P. J. Cowley and L. H. Sutcliffe, Abstracts of Chemical Society Meeting, Nottingham, England, April 1969, as cited in ref 30.

(30) M. J. Perkins, P. Ward, and A. Horsfield, *J. Chem. Soc.*, 395 (1970).

(26) A. Mackor, Th. A. J. W. Wajer, and Th. J. deBoer, *Tetrahedron Lett.*, 2757 (1967).

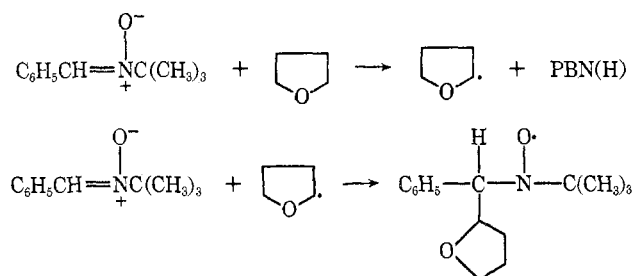
(27) G. A. Abakumov and G. A. Razuvaev, *Dokl. Chem.*, **182**, 95 (1968).



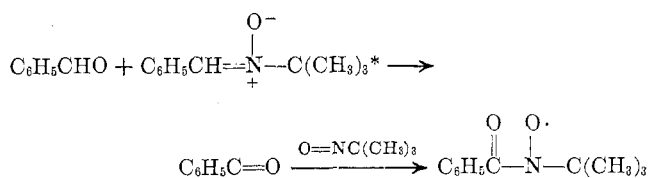
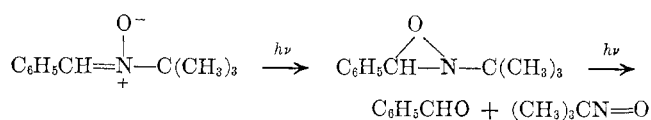
The use of PBN as a spin trap also has some disadvantages, which follow.

(1) The information regarding the nature and structure of the radical trapped is difficult to obtain from the spectrum of the spin adduct. In general the spectrum always consists of a triplet of doublets due to the nitrogen and  $\beta$ -H coupling of the spin adduct. Although the magnitudes of both coupling constants depend significantly on the bulk and electronegativity of the R group,  $\text{C}_6\text{H}_5\text{CHRN}[\text{C}(\text{CH}_3)_3]\text{O}^\cdot$ , the differences in N and  $\beta$ -H couplings between various spin adducts are small, and serious overlap can occur when more than one spin adduct is present in solution. Another variable which depends on the bulk of R is the line width of the lines in the spectrum. Thus the phenyl spin adduct, benzhydryl *tert*-butyl nitroxide, exhibits sharper lines than the *n*-butyl spin adduct. This result must be due to incomplete averaging of the various conformations at room temperature in the *n*-butyl case. This effect can be useful in a qualitative way.

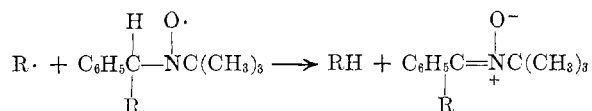
(2) Photolysis of PBN in certain solvents rapidly produces spin adducts derived from solvent radicals. Thus in tetrahydrofuran the tetrahydrofuranyl radical is trapped when solutions of PBN are photolyzed. Since this result is not observed when a filter of PBN solution is used (although other photolytic reactions do occur), PBN excitation must be involved. By analogy to benzophenone and nitrobenzene photochemistry a hydrogen abstraction reaction is visual-



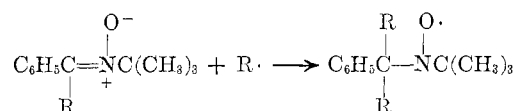
ized. Even in benzene, intense radiation has been shown to produce benzoyl *tert*-butyl nitroxide, presumably *via* photolysis of the oxazirane.<sup>31</sup>



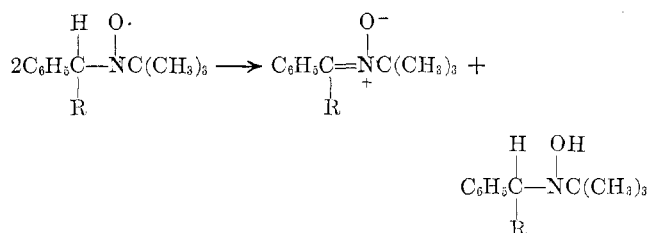
(3) A third disadvantage of PBN we know very little about is the possible instability of the spin adduct because of the tertiary nature of the  $\beta$  hydrogen. It would appear that this hydrogen would be very vulnerable to abstraction by radicals. Surprisingly this



appears not to be a serious problem in our experience since (with two exceptions where free atoms are involved) evidence has not been obtained for "double" spin trapping which would happen if a major portion of the starting amount of phenyl *tert*-butyl nitroxide were converted through the spin adduct into the trisubsti-



tuted nitroxide. The exceptions arise in the case of spin trapping of fluorine and chlorine atoms. This will be discussed in a later section. These observations may mean that a considerable steric barrier exists to  $\beta$ -hydrogen abstraction. This barrier undoubtedly also increases the stability of the spin adducts with respect to disproportionation. For example,



we have been able to isolate benzhydryl *tert*-butyl nitroxide as a stable (although impure) solid from the spin trapping of phenyl radicals from the decomposition of phenylazotriphenylmethane in solution. Our observations are in accord with the conclusion reached by Adamic, *et al.*,<sup>32</sup> that the disproportionation of a dialkyl nitroxide, diethyl nitroxide, proceeds through the dimer of the radical.

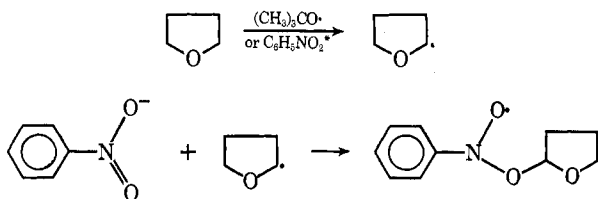
(4) The addition reaction of certain organometallic reagents such as organolithium and Grignard compounds to the nitroxide function, although a route to specific nitroxides, also presents a disadvantage in that the application of spin trapping to the study of neutral radical intermediates in reactions of these systems cannot be made.

(31) A. L. Bluhm and J. Weinstein, *J. Amer. Chem. Soc.*, **92**, 1444 (1970).

(32) K. Adamic, D. F. Bowman, and K. U. Ingold, *ibid.*, **92**, 1093 (1970).

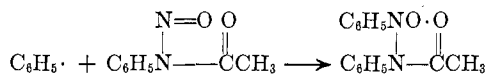
### Other Spin Traps

It is of interest that nitrobenzene is quite an effective spin trap for certain radicals. The additions of  $\alpha$ -alkoxy radicals derived from ethers have been studied in most detail; *e.g.*<sup>33</sup>



Unfortunately the spin adducts are quite unstable and are only observable under conditions of *in situ* generation of the  $\alpha$ -alkoxy radicals.

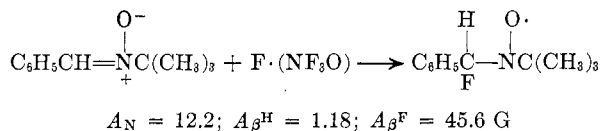
*N*-Nitroso compounds also appear to trap radicals.<sup>19</sup>



From a comparison of nitroso and nitrene spin traps it can be concluded that more than one spin trap might be used in a given mechanistic study. However, not enough is known about the trapping chemistry of nitroso and nitrene compounds to really predict the structure of the best trap. Further synthesis of new spin traps designed to do certain jobs better than those available to date are in progress. Eventually it is hoped a variety of spin traps will be available to the researcher each especially suited for a particular application.

### Applications of Spin Trapping

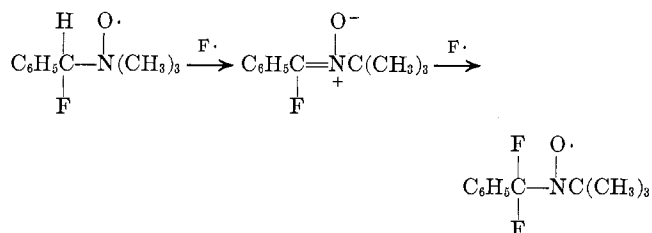
**Atom Trapping.** It is clear that numerous different types of radicals can be trapped by NtB and PBN. But can atoms be trapped? After repeated attempts to obtain the monofluoro spin adduct of PBN by the reaction with silver difluoride (a mild fluorinating agent) in which all trials gave only  $\alpha,\alpha$ -difluorobenzyl *tert*-butyl nitroxide, we were successful in obtaining the spectrum of  $\alpha$ -fluorobenzyl *tert*-butyl nitroxide from the room temperature thermal decomposition of trifluoramine oxide in benzene.<sup>34</sup>



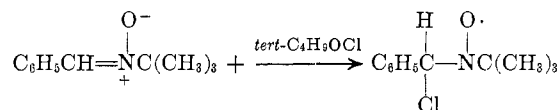
After extended periods of time or with higher concentrations of  $\text{NF}_3\text{O}$ , the monofluoro spin adduct is replaced by the difluoro nitroxide derivative. Since  $\text{NF}_3\text{O}$  is considered to be a mild fluorinating agent<sup>35</sup> and can be photolyzed in a matrix to give detectable

amounts of  $\text{NF}_2\text{O}\cdot$ , the mechanism of decomposition appears to involve fluorine atoms.

Detection of the monofluoro spin adduct in the presence of  $\text{NF}_3\text{O}$  is promising evidence that fluorine atoms can be detected by PBN. It is of interest to note that the appearance of  $\alpha,\alpha$ -difluorobenzyl *tert*-butyl nitroxide in place of the fluorine atom spin adduct indicates that the initial spin adduct reacts with fluorine atom by hydrogen atom abstraction to produce a phenyl-fluoromethyl *tert*-butyl nitrene which in turn traps more fluorine atoms.

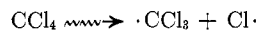


Chlorine atoms have also been successfully trapped by PBN. In the room temperature thermal decomposition of *tert*-butyl hypochlorite in benzene a very unusual spectrum is obtained<sup>36</sup> which shows a very large double quartet splitting due to  $I = 3/2$  of the two naturally abundant isotopes of chlorine: <sup>35</sup>Cl (75.4%) and <sup>37</sup>Cl (24.6%).



$$A_N = 12.1; A_{\beta^{\text{H}}} = 0.75; A_{\beta^{\text{Cl}}} = 4.88, 6.05 \text{ G}$$

An interesting application of this discovery has been made by Dr. Irene Lopp.<sup>37</sup> The  $\gamma$  radiolysis (<sup>60</sup>Co) of  $\text{CCl}_4$  containing PBN in an evacuated cell at source temperatures or lower produces readily detectable amounts of both the chlorine atom spin adduct and the trichloromethyl radical spin adduct after removal of the cell from the source. This result is in good agreement with work in the literature which shows that molecular chlorine and hexachloroethane are the only isolated products of  $\gamma$  radiolysis of carbon tetrachloride. Thus spin trapping may have important utility



in mechanistic studies of high energy degradation. Further investigations are under way.

If fluorine and chlorine atoms can be trapped under conditions where the spin adducts are stable, it should be possible to trap other atoms with PBN: obviously hydrogen atom. Benzyl *tert*-butyl nitroxide, the hydrogen atom spin adduct of PBN, is produced with tri-*n*-butyltin hydride<sup>8</sup> although the possibility of hydrogen atom or hydride ion transfer has not been ruled out. More work is needed. Leaver and Ram-

$$\text{C}_6\text{H}_5\text{CH}=\overset{\text{O}^-}{\underset{+}{\text{N}}}(\text{CH}_3)_3 + (n\text{-C}_4\text{H}_9)_3\text{SnH} \longrightarrow \text{C}_6\text{H}_5\text{CH}_2-\overset{\text{O}\cdot}{\underset{+}{\text{N}}}(\text{CH}_3)_3$$

(33) E. G. Janzen and J. L. Gerlock, *J. Amer. Chem. Soc.*, **91**, 3108 (1969).

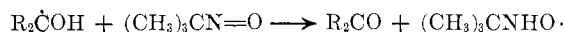
(34) Unpublished work of Dr. B. R. Knauer.

(35) W. B. Fox, J. S. MacKenzie, E. R. McCarthy, J. R. Holmes, R. F. Stahl, and R. Juurick, *Inorg. Chem.*, **7**, 2064 (1968); W. B. Fox, J. S. MacKenzie, N. Vanderkooi, B. Sukornick, C. A. Wamser, J. R. Holmes, R. E. Eibeck, and B. B. Stewart, *J. Amer. Chem. Soc.*, **88**, 2604 (1966); we are grateful to Allied Chemical Corp. and Dr. W. B. Fox for providing us with a sample of  $\text{NF}_3\text{O}$ .

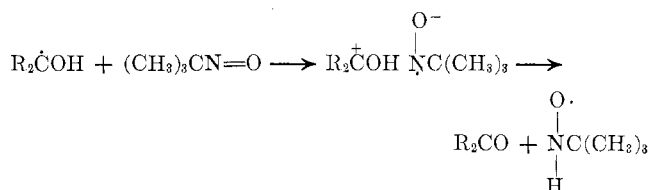
(36) E. G. Janzen, B. R. Knauer, L. T. Williams, and W. B. Harrison, *J. Phys. Chem.*, **74**, 3025 (1970).

(37) Unpublished work of Dr. I. Lopp in our laboratories.

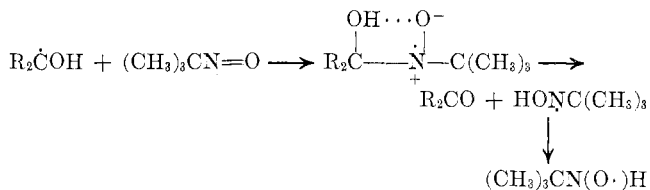
say<sup>16</sup> detected *tert*-butyl hydronitroxide from NtB in the presence of diphenylhydroxymethyl radical. The same radical was also observed by Perkins, *et al.*,<sup>30</sup> with NtB and 2-hydroxypropyl radicals. These results would appear to indicate hydrogen atom transfer to the spin trap. However we have found that *tert*-



butyl hydronitroxide formation appears to be favored by the addition of water to the system (an alcohol).<sup>38</sup> This observation supports an electron transfer mechanism followed by protonation.



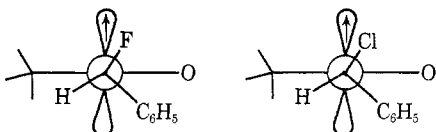
Finally the possible cleavage of an initially produced spin adduct cannot be ruled out.



This mechanism seems most likely for the diphenylhydroxymethyl spin adduct considering the ready cleavage found for trityl *tert*-butyl nitroxides.<sup>5</sup>

The two examples involving atom trapping, fluorine and chlorine, serve to illustrate one of the advantages of PBN over NtB as a spin trap. No example of a stable fluoro or chloro nitroxide where the halogen atom is directly attached to the nitroxide is known. We have failed in numerous attempts to make the fluoro *tert*-butyl nitroxide from NtB. The halogen atom spin adducts of NtB thus appear to be too unstable to detect. The spin adducts of PBN on the other hand appear to be relatively stable under certain reaction conditions.

At this point it is also pertinent to point out that the technique of spin trapping provides a versatile route to a variety of nitroxides which might be very difficult to synthesize by conventional synthetic routes. Thus the monofluoro and monochloro spin adducts of PBN provided us with two very unusual nitroxides in that in both cases the halogen hyperfine coupling was the largest ever reported for  $\beta$ -halo-substituted nitroxides. From the value of the  $\beta$ -hydrogen coupling in each case, the dihedral angle of the C-F and C-Cl bonds could be calculated<sup>34,36</sup> (14 and 18°, respectively). The conformation deduced for the nitroxide is

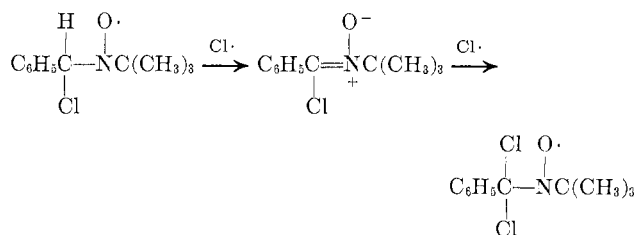


(38) Unpublished work of L. T. Williams in our laboratories.

The unusually large fluorine and chlorine coupling is due to the small dihedral angle for the C-F and C-Cl bonds.

**Gas-Phase Free-Radical Trapping.** Direct detection of gas-phase free radicals by esr, although possible for certain atoms and diatomic radicals, is difficult or impossible for larger radicals. The detection of gas-phase free radicals by spin trapping would seem to be a very important application of this technique. Our plan was to pass the free radicals in a carrier gas over a solid support containing the spin trap. In fact, solid powdered PBN can be used by itself. Thus if powdered PBN is placed in the esr cavity a rather broad set of three doublets is obtained when nitrogen containing alkyl radicals is passed over the material.<sup>39</sup> The spectrum can be sharpened by dissolving the powder in degassed benzene and verified by comparison with an authentic spectrum of the alkyl spin adduct. By this method ethyl (from photolysis of tetraethyllead), perfluoroethyl (from photolysis of perfluoroazoethane), benzyl (from photolysis of benzyl bromide), and methyl (from photolysis of acetone) radicals have been detected.<sup>39,40</sup>

The gas-phase photolysis of *tert*-butyl hypochlorite gives a spectrum consistent with  $\alpha,\alpha$ -dichlorobenzyl *tert*-butyl spin adduct.<sup>36,40</sup> This observation appears to be another example (as found for fluorine atoms) of a reaction between the initially formed spin adduct and a free atom to produce a new nitrone which traps more chlorine atoms.



**Spin Trapping of Radicals in Solids.** Lagercrantz and Forshult<sup>41</sup> first showed that spin trapping could be applied to the detection of radicals present in solids. In their study various aliphatic and amino acid salts were  $\gamma$  irradiated and subsequently dissolved in aqueous (in some cases, basic, 0.25 M NaOH) NtB. The spin adducts detected were consistent with loss of  $\alpha$ -hydrogen atom in the case of sodium acetate,  $\beta$ -alanine, potassium malonate, and succinic acid. Glycine and  $\alpha$ -alanine gave radicals by loss of the amino group. The spectrum of the spin adduct did not permit distinguishing between the above two possibilities for glutamic acid hydrochloride. These results are in good agreement with conclusions previously reached by other workers from esr spectra of the radicals as present in the solid powder, indicating that the addition to NtB

(39) E. G. Janzen and J. L. Gerlock, *Nature*, **222**, 867 (1969).

(40) B. Knauer, J. L. Gerlock, and E. G. Janzen, Southeast Regional Meeting of the American Chemical Society, Richmond, Va., Nov 5-8, 1969.

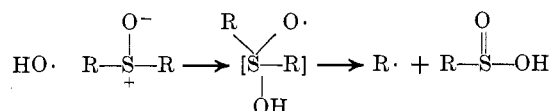
(41) C. Lagercrantz and S. Forshult, *Nature*, **218**, 1247 (1968).



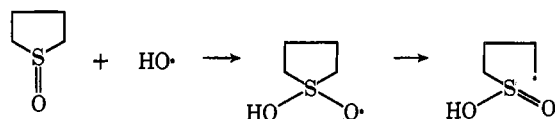
competes well with other reactions of the radicals as they dissolve. Since structural assignments are difficult to make for powder esr spectra the spin trapping technique appears to provide a valuable means of identifying radicals trapped in solid matrixes.

A similar technique has been applied to the detection of organometallic radicals produced in the  $\gamma$  radiolysis of triphenyl group IV halides.<sup>42</sup> Thus irradiation of triphenyltin chloride powder gives a broad structureless signal. Dissolution of this powder in benzene containing PBN under vacuum gives a spin adduct whose structure was verified by the synthetic route outlined earlier involving triphenyltinlithium. On this basis it was concluded that triphenyltin radical is produced in the  $\gamma$  radiolysis of triphenyltin chloride.

**Radical Displacement Reactions.** An elegant application of spin trapping has been made in a study of the reactions of hydroxy radicals. Using NtB or 2-methyl-2-nitroso-3-butanone as a spin trap it was shown that hydroxy radicals, produced by photolysis of hydrogen peroxide, react with aliphatic sulfoxides to produce alkyl radicals derived from the parent sulfoxides.<sup>43</sup>

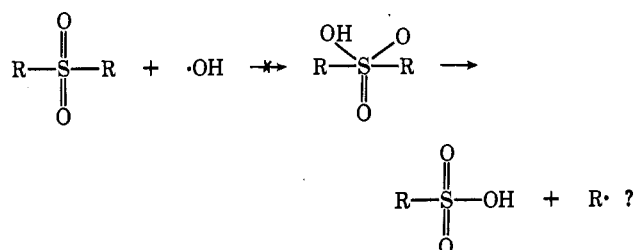


Thus methyl, ethyl, *n*- and isopropyl, *n*-, iso-, and *sec*-butyl, *n*-pentyl, *n*-hexyl, and benzyl radicals were trapped in the reaction of hydroxy radicals with the corresponding symmetrical parent sulfoxide. Methyl ethyl and methyl *n*-propyl sulfoxides gave both possible radicals. Tetrahydrothiophene sulfoxide gave a spectrum consistent with a spin adduct derived from cleavage of the alicyclic ring. No radicals could be detected



from diallyl or diphenyl sulfoxides.

Of interest is the observation that no analogous reaction occurred with sulfones. Some hydrogen atom abstraction on long-chain alkyl groups was indicated, but no radicals by direct displacement were observed.



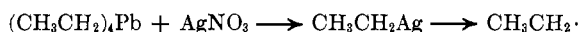
One can conclude from this result that the sulfone valence is saturated with respect to radical addition reactions.

This work<sup>43</sup> serves to further illustrate the advantages of spin trapping as a research tool in mechanism studies. Although Norman and coworkers<sup>44</sup> had previously demonstrated that hydroxy radicals react with dimethyl sulfoxide to produce methyl radicals, their technique involved the use of a large amount of material, a fast-flow apparatus, and highly acidic aqueous solutions for the reaction. The experiments of Lagercrantz and Forschult required approximately a milliliter or less of material.

### Comparison of Spin Trapping with CIDNP<sup>38</sup>

The number of systems wherein nuclear magnetic resonance emission or enhanced adsorption (CIDNP) has been detected is growing rapidly.<sup>9</sup> Since this phenomenon is due to the existence of short-lived free radicals or diradicals (or triplets) the observation of CIDNP is itself diagnostic of short-lived free radicals in the system. However, the converse (as in esr) is very difficult to maintain: free radicals are not necessarily absent if no CIDNP is detected, since the detection of CIDNP depends on numerous experimental variables not easily selected for a given experiment.

It occurred to us that it would be interesting to see if CIDNP could be detected in a system wherein radicals are detectable by spin trapping. The known formation of ethyl radicals in the reaction of silver nitrate with tetraethyllead, presumably through the intermediacy of ethylsilver,<sup>45</sup> had already been verified in our laboratory.<sup>46</sup>



Nmr experiments in dimethoxyethane containing small amounts of water readily gave strong enhanced absorption in the methylene region and strong emission in the methyl region. Since the final spectrum was identical with that of butane these peaks have been assigned to butane, produced presumably from the dimerization of ethyl radicals. The possibility of ethane emission could not be ruled out. No ethylene emission or absorption could be detected, however. Spin-trapping experiments either with PBN or NtB gave strong signals due to the ethyl spin adducts.

Nmr experiments with tetra-*n*-butyllead under similar conditions again gave enhanced methylene absorption and methyl emission, although these results were much more difficult to obtain.<sup>47</sup> In addition, emission was detected in the vinyl region. These CIDNP results are attributed to *n*-butyl radical disproportionation and dimerization reactions. Spin trapping with PBN or NtB gave strong signals due to the *n*-butyl spin adducts.

Nmr experiments with tetramethyllead, tetraphenyl-

(44) W. T. Dixon, R. O. C. Norman, and A. L. Buley, *J. Chem. Soc.*, 3625 (1964).

(45) F. Glockling and D. Kingston, *ibid.*, 3001 (1959).

(46) L. T. Williams and E. G. Janzen, 159th National Meeting of the American Chemical Society, Houston, Texas, Feb 22-27, 1970, Abstract No. ORGN 20.

(47) Initial trials in fact were negative, and only through persistence were the correct conditions found for detection of CIDNP.

(42) Unpublished work of W. B. Harrison in our laboratories.

(43) C. Lagercrantz and S. Forschult, *Acta Chem. Scand.*, **23**, 811 (1969).

lead, hexaphenyldilead, tetramethyltin, and tetra-*n*-butyltin were all negative, although by spin trapping methyl, phenyl, or *n*-butyl radicals could be readily detected in the reaction of silver nitrate with the above compounds. From these preliminary comparisons it is clear that the two techniques may be complementary in nature. Radicals can probably be detected at lower concentrations and more readily by spin trapping. However, information about the history of the radical ion can sometimes be deduced from CIDNP experiments which is not of course accessible by spin trapping.

### Comparisons of Relative Radical Reactivities

A comparison of the intensities of the esr signals obtained from different spin adducts produced by the addition of different radicals both present in the same solution might provide information about the relative reactivities of radicals. The esr spectra of the spin adducts obtained in the photolyses of perfluoroalkyl iodides in the presence of NtB have been described.<sup>48</sup> The spin adduct yield from photolysis of 2-iodoperfluoropropane was 6.3 times greater than the spin adduct yield from iodoperfluoroethane when photolyzed in the same solution. Similarly the spin adduct yield from the photolysis of the iodoperfluoroethane was 7.1 times that produced from trifluoromethyl iodide in the same solution. It was thus concluded that the photolytic stabilities of the perfluoroalkyl iodides were in the order  $\text{CF}_3\text{I} > \text{CF}_3\text{CF}_2\text{I} > (\text{CF}_3)_2\text{CFI}$ . Presumably the stability of the perfluoroalkyl radicals determined the order of this sequence.

A preliminary comparison of the reactivity of toluene and ethylbenzene toward *tert*-butoxy radicals has also been made by spin trapping.<sup>30</sup> Thus *tert*-butoxy radical was used to produce the benzyl and 1-phenethyl radicals in toluene-ethylbenzene mixtures to be trapped by NtB. From the ratio of the integrated peaks due to the respective spin adducts it was concluded that ethylbenzene is 8.6 times more reactive toward *tert*-butoxy radicals than toluene. This compares with a literature value of 2.3 times obtained from competitive chlorination using *tert*-butyl hypochlorite.<sup>49</sup>

The use of spin trapping for quantitative work such as measuring relative radical reactivities appears to be somewhat premature. A better understanding of the factors influencing the rates of spin trapping and the pathways of decomposition of the spin adducts is required before more than qualitative results can be expected. In the work described it was assumed that the rates of addition to the spin trap would not differ significantly for the radicals being compared and that the decay mechanisms of the spin adducts would remain the same in the presence of different radicals. Nothing is known about either of these factors at this time. With the presently used spin traps these assumptions could be seriously contested.

Competitive experiments of a different nature have been initiated in our laboratories<sup>34,38</sup> in an attempt to gain some knowledge about these factors. In these experiments radicals are trapped by PBN in the presence of galvinoxyl. The decay of the galvinoxyl signal is monitored simultaneously with the appearance of the PBN spin adduct signal in a solution containing initially only galvinoxyl, PBN, and a radical source (*e.g.*, phenylazotriphenylmethane). Preliminary experiments indicate that galvinoxyl traps phenyl radicals  $10^4$  times faster than does PBN.

This number is significant in connection with our earlier results<sup>8</sup> which indicated that acetoxy radicals could be trapped by PBN. Unless the rate of trapping of acetoxy radical is much greater than the rate of phenyl radical trapping ( $\sim 10^4$  times), an unlikely possibility, it appears that the formation of the acetoxy spin adduct of PBN from, for example, lead acetates and acetaldehyde oxidations (we have not studied acetyl peroxide) is an artifact of the system. Since literature data for the rapid rate of decarboxylation of acetoxy radicals produced from acetyl peroxide ( $\sim 10^9 \text{ sec}^{-1}$ ) are extremely compelling, the lifetime of the acetoxy radical must be increased in the presence of PBN, possibly by complexing.

*I acknowledge the financial support of this work by AFOSR-OAR, U. S. Air Force, through Grant No. 1069-66, and NAPCA, HEW-PHS, through Grant No. AP01096-01.*

(48) K. J. Klabunde, *J. Amer. Chem. Soc.*, **92**, 2427 (1970).

(49) C. Walling and B. B. Jacknow, *ibid.*, **82**, 6108 (1960).