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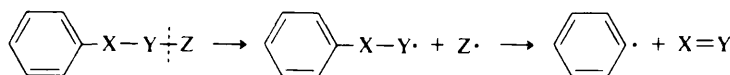
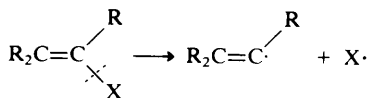
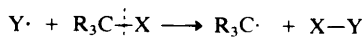
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Free-Radical Reactions

12.1. Generation and Characterization of Free Radicals

12.1.1. Background

A free-radical reaction is a chemical process in which molecules having unpaired electrons are involved. The radical species could be a starting compound or a product, but in organic chemistry the most common cases are reactions that involve radicals as intermediates. Most of the reactions discussed to this point have been heterolytic processes involving polar intermediates and/or transition states in which all electrons remained paired throughout the course of the reaction. In radical reactions, *homolytic* bond cleavages occur. The generalized reactions shown below illustrate the formation of alkyl, vinyl, and aryl free radicals by hypothetical homolytic processes.

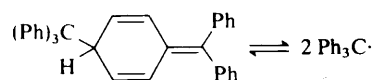


The idea that substituted carbon atoms with seven valence electrons could be involved in organic reactions took firm hold in the 1930s. Two experimental studies have special historical significance in the development of the concept of free-radical reactions. The work of Gomberg around 1900 provided evidence that when triphenyl-

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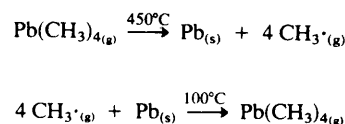
CHAPTER 12
FREE-RADICAL
REACTIONS

methyl chloride was treated with silver metal, the resulting solution contained $\text{Ph}_3\text{C}\cdot$ in equilibrium with a less reactive molecule. It was originally thought that the more stable molecule was hexaphenylethane, but eventually this was shown not to be so. The dimeric product is actually a cyclohexadiene derivative.¹



The dissociation constant is small, only about $2 \times 10^{-4} M$ at room temperature. The presence of the small amount of the radical at equilibrium was deduced from observation of reactions that could not be reasonably attributed to a normal hydrocarbon.

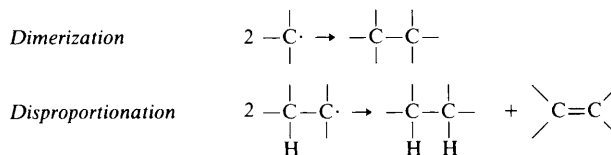
The second set of experiments was carried out in 1929 by Paneth. The decomposition of tetramethyllead was carried out in such a way that the decomposition products were carried by a flow of inert gas over a film of lead metal. The lead was observed to disappear, with re-formation of tetramethyllead. The conclusion was reached that methyl radicals must exist long enough in the gas phase to be transported from the point of decomposition to the lead film.



Since these early experiments, a great deal of additional information about the existence and properties of free-radical intermediates has been developed. In this chapter, we will discuss the structure of free radicals and some of the special properties associated with free radicals. We will also discuss some of the key chemical reactions in which free-radical intermediates are involved.

12.1.2. Stable and Persistent Free Radicals

Most organic free radicals have very short lifetimes, but various structural features enhance stability. Radicals without special stabilization rapidly dimerize or disproportionate. The usual disproportionation process involves transfer of a hydrogen from the carbon β to the radical site, leading to formation of an alkane and an alkene.

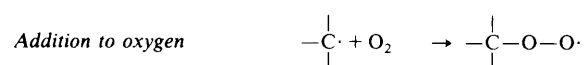
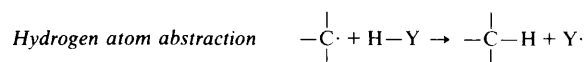


1. H. Lankamp, W. Th. Nauta, and C. MacLean, *Tetrahedron Lett.*, 249 (1968); J. M. McBride, *Tetrahedron* **30**, 2009 (1974); K. J. Skinner, H. S. Hochester, and J. M. McBride, *J. Am. Chem. Soc.* **96**, 4301 (1974).

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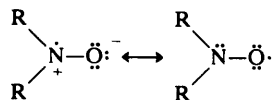
Radicals also rapidly abstract hydrogen or other atoms from many types of solvents, and most radicals are highly reactive toward oxygen.



A few free radicals are indefinitely stable. Entries 1, 4, and 6 in Scheme 12.1 are examples. These molecules are just as stable under ordinary conditions of temperature and atmosphere as typical closed-shell molecules. Entry 2 is somewhat less stable to oxygen, although it can exist indefinitely in the absence of oxygen. The structures shown in entries 1, 2, and 4 all permit extensive delocalization of the unpaired electron into aromatic rings. These highly delocalized radicals show no tendency toward dimerization or disproportionation. Radicals that have long lifetimes and are resistant to dimerization or other routes for bimolecular self-annihilation are called *stable free radicals*. The term *inert free radical* has been suggested for species such as entry 4, which is unreactive under ordinary conditions and is thermally stable even at 300°C.²

Entry 3 in Scheme 12.1 has only alkyl substituents and yet has a significant lifetime in the absence of oxygen. The tris(*t*-butyl)methyl radical has an even longer lifetime, with a half-life of about 20 min at 25°C.³ The steric hindrance provided by the *t*-butyl substituents greatly retards the rates of dimerization and disproportionation of these radicals. They remain highly reactive toward oxygen, however. The term *persistent radicals* is used to describe these species, since their extended lifetimes have more to do with kinetic factors than with inherent stability.⁴ Entry 5 is a sterically hindered perfluorinated radical, which is even more stable than similar alkyl radicals.

There are only a few functional groups that contain an unpaired electron and yet are stable in a wide variety of structural environments. The best example is the nitroxide group, and there are numerous specific nitroxide radicals which have been prepared and characterized.



Many of these compounds are very stable under normal conditions, and heterolytic reactions can be carried out on other functional groups in the molecule without destroying the nitroxide group.⁵

2. M. Ballester, *Acc. Chem. Res.* **18**, 380 (1985).

3. G. D. Mendenhall, D. Griller, D. Lindsay, T. T. Tidwell, and K. U. Ingold, *J. Am. Chem. Soc.* **96**, 2441 (1974).

4. For a review of various types of persistent radicals, see D. Griller and K. U. Ingold, *Acc. Chem. Res.* **9**, 13 (1976).

5. For reviews of the preparation, reactions, and uses of nitroxide radicals, see J. F. W. Keana, *Chem. Rev.* **78**, 37 (1978); L. J. Berliner (ed.), *Spin-Labeling*, Vol. 2, Academic Press, New York, 1979.

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