

Free Radicals

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Free radicals are complexes of abnormal valency, which possess additive properties, but do not carry an electrical charge and are not free ions.¹ Since Lavoisier introduced his theory of radicals in 1785 there has been the conviction among chemists that the radicals of organic chemistry could be isolated in the free state. Gay-Lussac in 1815 thought that he had done this when he obtained a gas of composition CN when he heated mercuric cyanide. Bunsen, Frankland, and Kolbe obtained by various methods cacodyl $(\text{CH}_3)_2\text{As}$, methyl, and amyl radicals. However, with the revival of the Avogadro hypothesis in 1864, it became evident that the so-called free radicals which these chemists had prepared were in reality compounds of exactly twice the molecular weight of the free radicals. Kekule then brought forth his structural theory in which he stated that the carbon atom was always quadrivalent, and therefore free radicals were incapable of existence. This view was held until the beginning of the twentieth century, when Gomberg of the University of Michigan prepared triphenyl-methyl.

In 1897 Gomberg was investigating a reliable test for a hydrogen atom on a methyl carbon atom. He succeeded in his efforts, and went further to try his test on a two carbon atom compound. To do this, he had to prepare hexaphenylethane. The usual method was used in the synthesis; i.e., the interaction of triphenylchloromethane and an active metal.²



However, on analysis this compound seemed to contain oxygen; this was verified after the synthesis of the compound in an atmosphere of carbon dioxide. This compound on analysis was found to have the same composition as hexaphenylethane, and yet in its reactions it differed widely

¹Wieland, *Ber.*, 33, 3150 (1900).

²Gomberg, *J. Am.Chem. Soc.*, 20, 773 (1898).

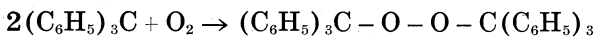
from what one would expect of a substituted ethane. It reacted readily with oxygen, the halogens, nitric oxide, and sodium. From this evidence, Gomberg concluded that he had prepared the free radical triphenylmethyl. In his preparation of free radicals of the triarylmethyl type, the syntheses were carried out under carefully regulated conditions: (1) exclusion of water; (2) absence of oxygen; (3) absence of sunlight; (4) exclusion of acids.³

After Gomberg's unexpected discovery there followed numerous investigations which produced radicals containing bivalent and quadrivalent nitrogen, univalent oxygen, univalent sulphur, and other elements of abnormal valence.

The triarylmethyls are generally colorless solids; the solid form is assumed to be the bimolecular form of the radicals. When the solid form is dissolved in benzene, the resulting solution is highly colored. This coloration of the solution is thought to be the result of the formation of free radicals from the dissociation of the hexaarylethane. Early investigators believed that the intensity of coloration of the solution was proportional to the degree of dissociation; however, colorimetric analyses paralleled with dissociation determinations have shown that this effect is qualitatively but not quantitatively indicative of the presence of free radicals in solution. Gomberg⁴ showed that the color of these solutions was the result of the formation of a quinoid tautomer of the free radical; i.e., there is an equilibrium between the benzenoid and quinoid forms of triphenylmethyl.

However, the equilibrium between hexaphenylethane and triphenylmethyl is not proportionally effected by changes in the equilibrium of the benzenoid and quinoid tautomers.⁵

The triarylmethyls are extremely reactive; they combine readily with oxygen, halogens, sodium, and with other free radicals. With oxygen, triphenylmethyl forms triphenylmethyl peroxide.

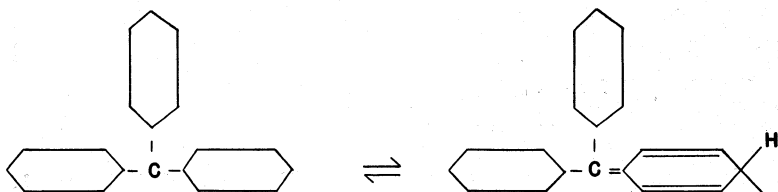


This reaction is sometimes used to determine the percentage

³Gomberg, *Chem. Rev.*, 1, 91 (1924).

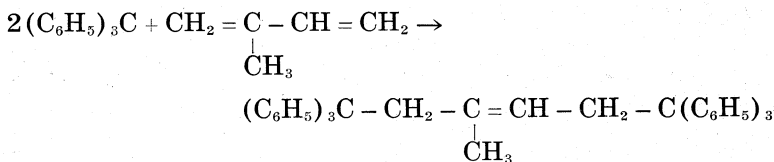
⁴Gomberg and Blicke, *J. Am. Chem. Soc.*, 45, 1765 (1923).

⁵Gomberg, *Chem. Rev.*, 1, 91 (1924).



of dissociated hexaarylethanes, since the peroxide formation proceeds with much greater speed than the dynamic equilibrium of the dissociation of the ethane into radicals. Hydrogen, in the presence of a catalyst, reduces triphenylmethyl to triphenylmethane, and this radical is also capable of abstracting hydrogen from phenylhydrazine, phenol, and hydrazobenzene.

$2(\text{C}_6\text{H}_5)_3\text{C} + \text{C}_6\text{H}_5\text{NHNHC}_6\text{H}_5 \rightarrow 2(\text{C}_6\text{H}_5)_3\text{CH} + \text{C}_6\text{H}_5\text{NNC}_6\text{H}_5$
 Triphenylmethyl reacts with unsaturated compounds in the same way that all addition reactions take place with them, e.g., 1,1,1,6,6,6, hexaphenyl-3-methylhexene-3 is formed when triphenylmethyl adds to isoprene.⁶



One of the characteristic reactions undergone by all free radicals is disproportionation, which takes place in sunlight or in the presence of traces of mineral acids. The products of this reaction are triphenylmethane and phenylbiphenylenemethane in the case of triphenylmethyl. Nitric oxide reacts readily with triphenylmethyl to form nitrosotriphenylmethyl, $(\text{C}_6\text{H}_5)_3\text{CN}=\text{O}$, which undergoes further reaction to undetermined products.

In a discussion of free radicals other than triphenylmethyl, we will encounter compounds which lie on the borderline between free radicals and stable undissociated compounds. These erratic compounds do not show dissociation in solution, but the scission of the ethane bond takes place

⁶Conant and Scherp, *J. Am. Chem. Soc.*, 53, 1941(1931).

with active reagents to give products identical with derivatives of free radicals.

The sym.-tetraaryldialkylethanes show a tendency to dissociate into diarylalkylmethyl which usually disproportionates quickly; e.g., sym.-tetraphenyldimethylethane dissociates slightly into 1,1 diphenylethyl which then decomposes spontaneously into 1,1 diphenylethane and 1,1 diphenylethylene. The introduction of more complicated alkyl (secondary or tertiary) and aryl groups on the ethane seems to increase its dissociation greatly, since sym.-tetra-p-biphenyl-di-tert.-butylethane dissociates 74 per cent in dilute solutions to give di-p-biphenyl-tert.-butylmethyl radicals.⁷

Substitution of different alkyl groups for the hydrogen atoms of bixanthyl gives widely varying values for the percentage of dissociation into free radicals. Conant⁸ has divided these groups into three classes, according to their effectiveness in producing dissociation.

Class I: cyclohexyl, isopropyl, sec.-butyl.

Class II: benzyl, p-chlorobenzyl, isobutyl, *alpha*-naphthylmethyl.

Class III: methyl, ethyl, n-butyl, n-hexyl, isoamyl, phenylethyl.

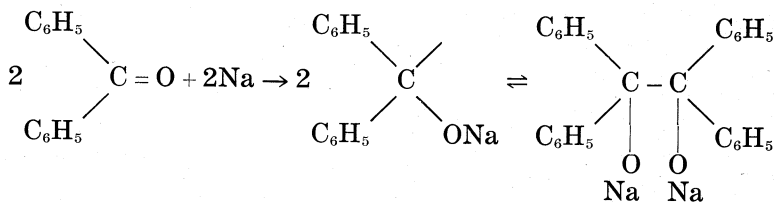
The substituted bixanthyls which contain groups from Class I are dissociated at 25° C., those of Class II at 60°-70° C., and the members of Class III are only slightly dissociated even above 140° C.

The diarylhydroxyl radicals (R₂COH) have been postulated to exist as an intermediate product of the reduction of aromatic ketones to pinacols R₂C(OH)C(OH)R₂, but the isolation of these radicals has never been accomplished. However, if we replace the hydrogen atoms of the hydroxyl groups by alkali metals, we obtain a salt which seems to dissociate into free radicals. Since 1891 it has been known that aromatic ketones react with sodium to give sodium

⁷Conant and Schultz, *ibid.*, 55, 2098 (1933).

⁸Conant, Small, and Sloan, *ibid.*, 48, 1743 (1926).

ketyls, but it was 1913 before it was shown that these ketyls were free radicals formed by the addition of an atom of sodium to a molecule of ketone.⁹



The matter of the dissociation of alkali pinacolates into ketyls is still a matter of contention, since in the past five years two investigators have obtained results differing as much as one per cent¹⁰ to eighty-five per cent¹¹ for the dissociation of the pinacols.

Although Frankland in 1850 succeeded in producing free ethyl radicals by electrolysis, his results were considered unreliable because of the revival of the Avogadro hypothesis. His "ethyl" was proved to be butane; and yet if he had used some of the more recent techniques, his results would not have been repudiated. In 1929 Paneth¹² was able to produce free methyl and ethyl radicals by the thermal decomposition of the tetraalkyl lead compounds, but since the half-life period of free methyl is .006 second he was forced to devise a method of isolation of the free radical before it could combine to form ethane. The free radical under reduced pressure was passed through a tube which was lined with a thin mirror of lead, with which the radicals readily reacted. He observed that if the lead mirrors were placed at a distance greater than 32 centimeters the radicals did not react with the lead, but instead combined to form ethane. From this observation, he was able to calculate the half-life period of the radical involved. Paneth's investigation also led to

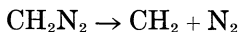
⁹Schlenk and Hofeditz, *Ber.*, 62, 1334 (1929).

¹⁰Doescher and Wheland, *J. Am. Chem. Soc.*, 56, 2011 (1934).

¹¹Sugden, *J. Chem. Soc.*, 440 (1936).

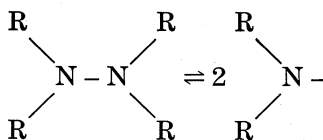
¹²Paneth and Hofeditz, *Ber.*, 62, 1335 (1929).

the discovery of free methylene radicals,¹³ which are obtained by the pyrolysis of diazomethane.

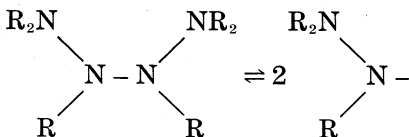


Azomethane when heated to 500°C. decomposes to give methylene radicals, which are detected by the formation of polymerized telluro-formaldehyde $(\text{HCHTe})_n$ on tellurium mirrors. This same compound when heated to 600°C. gives methyl radicals, which form dimethylditelluride $(\text{CH}_3\text{-Te-Te-CH}_3)$.¹⁴

Free radicals containing bivalent or quadrivalent nitrogen have been synthesized, although these compounds are not so numerous as those of trivalent carbon. Tetraarylhydrazines show slight dissociation into diarylamino radicals;



while hexaaryltetrazanes dissociate into triarylhazryl radicals.



These radicals are dissociated to a much greater extent by the substitution of an acyl group for one of the aryl groups. Tetravalent nitrogen radicals can be obtained by mild oxidation of N-diarylhydroxamines to diarylnitrogen oxides or by the electrolysis of tetramethyl ammonium chloride.¹⁵

Radicals containing monovalent oxygen are formed by the dissociation of the diarylperoxides, which are obtained by the mild oxidation of phenols. Many other radicals have been investigated which contain elements of abnormal valence; among these are univalent sulphur, trivalent tin, trivalent lead, divalent arsenic, and trivalent boron radicals.

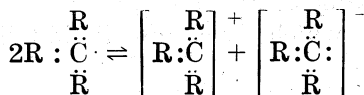
The physical properties of free radicals differ widely from those of organic compounds of normal valence. In

¹³Rice and Glasebrook, *J. Am. Chem. Soc.*, 55, 4329(1933).

¹⁴Rice and Glasebrook, *ibid.*, 56, 2381(1934).

¹⁵McCoy and Moore, *ibid.*, 33, 273(1911).

non-ionizing solvents such as benzene, toluene, or naphthalene triphenylmethyl and other free radicals do not show ionization, but in polar solvents such as liquid sulphur dioxide the triphenylmethyl radicals are ionized into triphenylmethyl cations and anions by an exchange of electrons.



The stability of free radicals varies widely, depending upon the nature of the substituent groups of the radical. Some of these compounds show their characteristic activity for months, while others decompose in a few minutes. Often the radicals undergo oxidation, reduction, or polymerization spontaneously.

One of the first abnormal physical properties of free radicals to show itself was the inconsistent molecular weights. Since the free radicals and the dimolecular form are in equilibrium, the molecular weight will lie between the molecular weights of the two forms. This observation is used to calculate the percentage dissociation of certain compounds into free radicals.¹⁶

The dissociation of compounds into free radicals is dependent upon pressure, temperature, concentration, and the nature of the solvent. With an increase in temperature there is a corresponding increase in dissociation; e.g., hexaphenylethane is dissociated only slightly in a 2% benzene solution at room temperature, while at 80° C. it is dissociated 27%. The dissociation is inversely proportional to the concentration of the free radical. Thus a 2% solution of diphenylbixanthyl in naphthalene is 65% dissociated, while a 5.5% solution is only 50% dissociated; i.e., solutions of free radicals do not obey Beer's law.¹⁷ The nature of the solvent also has a decided effect on dissociation; thus nitrobenzene, benzene, and cyclohexane are very similar solvents, but they show a variable influence on dissociation

¹⁶Gomberg, *Chem. Rev.*, 1, 91 (1924).

¹⁷Piccard, *Ann.*, 381, 347 (1911).

(nitrobenzene > benzene > cyclohexane). The effect of pressure on the scission of the ethane bond is not detectable in the case of liquid or solid substituted ethanes, but the gaseous free radicals are found to be more prevalent at low pressures. Another factor which seems to favor dissociation is the vibrational wave energy which strikes the undissociated molecules. It has been shown that free methyl radicals can be produced by the photolysis of methyl iodide with light waves ($\lambda=4100\text{\AA}$).¹⁸ The most influential factor in the extent of dissociation is the nature of the aryl groups attached to the ethane carbon atoms; thus for a given solvent at a fixed temperature and concentration, the dissociation of a substituted ethane may vary from practically zero to 100%. The aryl groups in the order of their effect on dissociation are: *alpha*-naphthyl > p-benzyl-oxyphenyl > b-naphthyl > xanthyl > p-biphenyl > phenyl > p-tolyl > p-chlorophenyl.¹⁹ From this empirical arrangement of aryl groups, one can roughly predict the extent of dissociation of hexaarylethanes.

By far the most distinguishing characteristic of free radicals is the paramagnetism which they show. Since all free radicals contain an odd number of electrons, the magnetically non-compensated electron causes the molecule to be very reactive and these odd molecules²⁰ are attracted by magnetic fields. The measurement of this paramagnetic susceptibility gives a reliable indication of the extent of dissociation of the molecules into free radicals.

Several theories of dissociation of compounds into radicals have been offered. One hypothesis accounts for dissociation by consideration of the size and weight of the substituent groups. The steric hindrance of these large groups tends to weaken the ethane bond. The fact that many free radicals have large groups would seem to support this theory, yet the cyclohexyl group, which is about the same size as the phenyl group has much less effect on the dissociation of the ethane bond than does the phenyl group. There are numerous other examples which conflict with this

¹⁸Bates and Spence, *J. Am. Chem. Soc.*, 53, 1689(1931).

¹⁹Walden, "Chemie der freien Radikale," Hirzel, Leipzig (1924).

²⁰Lewis, *Chem. Rev.*, I, 231(1934).

theory. Other investigators have considered unsaturation to be a necessary condition for dissociation, but this theory fails to account for the positive effects of alkyl groups upon dissociation. According to Pauling the dissociation is not due to the weakening of the ethane bond, but to the stabilization of the free radicals because of resonance. The fact that the ethane bond or hexaphenylethane is weaker than the ordinary carbon to carbon bond by about 30 kg-cal., and that this theory considers alkyl groups to have no more effect than hydrogen atoms on dissociation is sufficient to show that this theory does not completely explain dissociation. Thus we find that none of the theories of dissociation are satisfactory; when a more inclusive theory is established it will probably explain many of the peculiar properties of free radicals.

The concept of free radicals has done a great deal to explain the numerous side reactions of organic chemistry. The Wurtz-Fittig reaction, for example, of chlorobenzene and sodium produce biphenyl, benzene, diphenyl benzene, and triphenylene. One can readily explain the formation of these various end products by assuming the intermediate formation of free phenyl radicals which can disproportionate as well as associate. The Grignard reactions may also be more clearly understood by consideration of free radicals, as may the thermal decomposition of many organic compounds. It has been suggested recently by Freundlich that enzymes are free radicals which induce chain reactions to take place.

Much work has been done in the past few years to find new reactions of free radicals as well as to develop better techniques for the study of their physical and chemical properties. Free radicals have been produced by light waves, ultra-sonic waves, and by electrical discharges. Specific reagents have been perfected for their individual detection. But by far the greatest obstruction to the adaptability of the free radical concept to a broader scope is the lack of understanding of the dissociation of molecules. When this matter has been sufficiently explained much of the uncertainty of organic reactions will be eliminated.