# Radical (chemistry)

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*For other uses, see radical and free radical (disambiguation).*

In chemistry, **radicals** (often referred to as **free radicals**) are atoms, molecules or ions with unpaired electrons on an otherwise open shell configuration. These unpaired electrons are usually highly reactive, so radicals are likely to take part in chemical reactions. Radicals play an important role in combustion, atmospheric chemistry, polymerization, plasma chemistry, biochemistry, and many other chemical processes, including human physiology. For example, superoxide and nitric oxide regulate many biological processes, such as controlling vascular tone. "Radical" and "free radical" are frequently used interchangeably, although a radical may be trapped within a *solvent cage* or be otherwise bound. The first organic free radical identified was triphenylmethyl radical, by Moses Gomberg in 1900 at the University of Michigan.

Historically, the term *radical* has also been used for bound parts of the molecule, especially when they remain unchanged in reactions. These are now called functional groups. For example, methyl alcohol was described as consisting of a methyl "radical" and a hydroxyl "radical". Neither are radicals in the modern chemical sense, as they are permanently bound to each other, and have no unpaired, reactive electrons. They can, however, be observed as radicals in mass spectrometry after breaking down the substance with a hail of energetic electrons.

Moses Gomberg, the founder of radical chemistry (*1866-1947*)

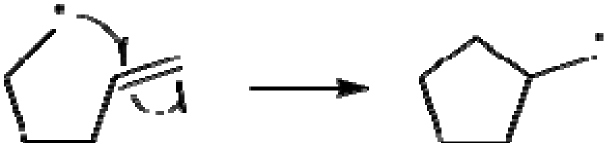
# Depicting radicals in chemical reactions

In written chemical equations, free radicals are frequently denoted by a dot placed immediately to the right of the atomic symbol or molecular formula as follows:

$$Cl_2 \xrightarrow{u.v.} Cl\cdot + Cl\cdot$$

*Chlorine gas can be broken down by ultraviolet light to form atomic chlorine radicals.*

Radical reaction mechanisms use single-headed arrows to depict the movement of single electrons:



The homolytic cleavage of the breaking bond is drawn with a 'fish-hook' arrow to distinguish from the usual movement of two electrons depicted by a standard curly arrow. It should be noted that the second electron of the breaking bond also moves to pair up with the attacking radical electron; this is not explicitly indicated in this case.

In chemistry, free radicals take part in radical addition and radical substitution as reactive intermediates. Chain reactions involving free radicals can usually be divided into three distinct processes: *initiation*, *propagation*, and *termination*.

- **Initiation** reactions are those which result in a net increase in the number of free radicals. They may involve the formation of free radicals from stable species as in Reaction 1 above or they may involve reactions of free radicals with stable species to form more free radicals.
- **Propagation** reactions are those reactions involving free radicals in which the total number of free radicals remains the same.
- **Termination** reactions are those reactions resulting in a net decrease in the number of free radicals. Typically two free radicals combine to form a more stable species, for example: $2Cl\cdot \rightarrow Cl_2$

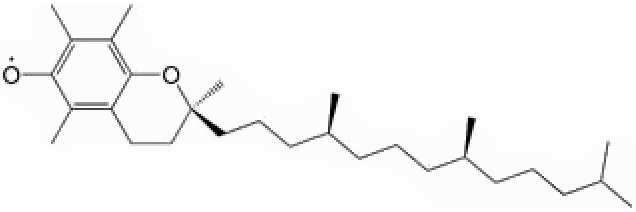
# Formation

The formation of radicals may involve breaking of covalent bonds homolytically, a process that requires significant amounts of energy. For example, splitting $H_2$ into $2H\cdot$ has a $\Delta H^\circ$ of +435 kJ/mol, and $Cl_2$ into $2Cl\cdot$ has a $\Delta H^\circ$ of +243 kJ/mol. This is known as the homolytic bond dissociation energy, and is usually abbreviated as the symbol $DH^\circ$. The bond energy between two covalently bonded atoms is affected by the structure of the molecule as a whole, not just the identity of the two atoms, and radicals requiring more energy to form are less stable than those requiring less energy. Homolytic bond cleavage most often happens between two atoms of similar electronegativity. In organic chemistry this is often the O-O bond in peroxide species or O-N bonds.

However, propagation is a very exothermic reaction. Note that most species are electrically neutral although radical ions do exist.

Radicals may also be formed by single electron oxidation or reduction of an atom or molecule. An example is the production of superoxide by the electron transport chain. Early studies of organometallic chemistry, especially tetra-alkyl lead species by F.A. Paneth and K. Hahnfeld in the 1930's supported heterolytic fission of bonds and a radical based mechanism.

# Persistence and stability



The radical derived from *α-tocopherol*

Long lived radicals can be placed into two categories

- **Stable Radicals**

  The prime example of a stable radical is molecular dioxygen $O_2$. Organic radicals can be long lived if they occur in a conjugated π system, such as the radical derived from α-tocopherol (vitamin E). Albeit there exist hundreds of known examples of thiazyl radicals which show remarkable kinetic and thermodynamic stability, with only a very limited extent of π resonance stabilization [1][2].

- **Persistent Radicals**[3]

  Persistent radical compounds are those whose longevity is due to steric crowding around the radical center and makes it physically difficult for the radical to react with another molecule. Examples of these include Gomberg's triphenylmethyl radical, Fremy's salt (Potassium nitrosodisulfonate, $(KSO_3)_2NO\cdot$), nitroxides, (general formula $R_2NO\cdot$) such as TEMPO, verdazyls, nitronyl nitroxides, and azephenylenyls and radicals derived from PTM (perchlorophenylmethyl radical) and TTM (tris(2,4,6-trichlorophenylmethyl radical). The longest-lived free radical is melanin, which may persist for millions of years. Persistent radical are generated in great quantity during combustion, and "may be responsible for the oxidative stress resulting in cardiopulmonary disease and probably cancer that has been attributed to exposure to airborne fine particles." PMID 18678037[4]

- Diradicals are molecules containing two radical centers. Multiple radical centers can exist in a molecule. In fact, much to the surprise of many, molecular oxygen naturally (i.e. atmospheric dioxygen) exists as a diradical (in its ground state as triplet oxygen). The high reactivity of atmospheric oxygen is owed somewhat to its diradical state (albeit non-radical states of dioxygen are actually less stable). The existence of atmospheric molecular oxygen as a triplet-state genuine radical results in its paramagnetic character, which can be easily demonstrated, i.e. by attraction of oxygen to an external magnet. (Note however that paramagnetism does not necessarily imply radical character.)

# Reactivity

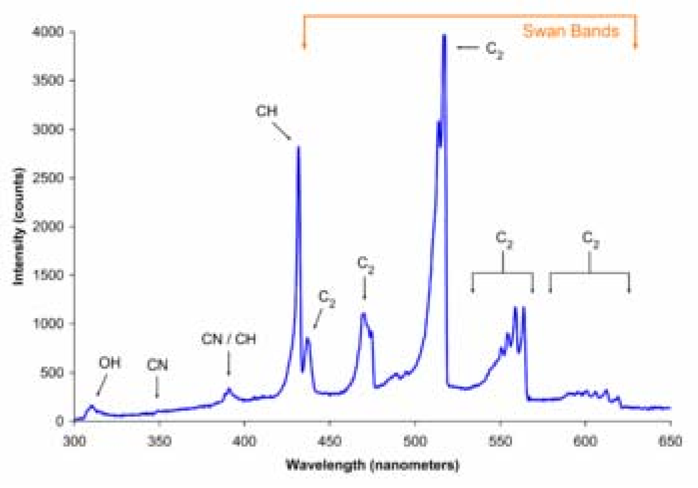
*Main article: Free radical reaction*

Radical alkyl intermediates are stabilized by similar criteria as carbocations: the more substituted the radical center is, the more stable it is. This will direct their reactions: formation of a tertiary radical ($R_3C\cdot$) is favored over secondary ($R_2HC\cdot$) or primary ($RH_2C\cdot$). However, radicals next to functional groups, such as carbonyl, nitrile, and ether are even more stable than tertiary alkyl radicals.

Radicals attack double bonds, but unlike similar ions, they are not as much directed by electrostatic interactions. For example, the reactivity of nucleophilic ions with α,β-unsaturated compounds (C=C-C=O) is directed by the electron-withdrawing effect of the oxygen, resulting in a partial positive charge on the carbonyl carbon. There are two reactions that are observed in the ionic case: the carbonyl is attacked in a direct addition to carbonyl, or the vinyl is attacked in conjugate addition, and in either case, the charge on the nucleophile is taken by the oxygen. Radicals add rapidly to the double bond, and the resulting α-radical carbonyl is relatively stable; it can couple with another molecule or be oxidized. Nonetheless, the electrophilic/neutrophilic character of radicals has been shown in a variety of instances (e.g., in the alternating tendency of the copolymerization of maleic anhydride (electrophilic) and styrene (slightly nucleophilic).

In intramolecular reactions, precise control can be achieved despite the extreme reactivity of radicals. Radicals will attack the closest reactive site the most readily. Therefore, when there is a choice, a preference for five-membered rings is observed: four-membered rings are too strained, and collisions with carbons five or more atoms away in the chain are infrequent.

# Combustion



Spectrum of the blue flame from a butane torch showing excited molecular radical band emission and Swan bands.

*Main article: Combustion#Reaction mechanism*

Probably the most familiar free-radical reaction for most people is combustion. The oxygen molecule is a stable diradical, best represented by ·O-O·, which is stable because the spins of the electrons are parallel. The ground state of oxygen is an unreactive spin-unpaired (triplet) diradical, but an extremely reactive spin-paired (singlet) state is available. In order for combustion to occur, the energy barrier between these must be overcome. This barrier can be overcome by heat, requiring high temperatures, or can be lowered by enzymes to initiate reactions at the temperatures inside living things.

Combustion is comprised of various radical chain reactions that the singlet radical can initiate. The flammability of a given material is strongly dependent on the concentration of free radicals that must be obtained before initiation and propagation reactions dominate leading to combustion of the material. Once the combustible material has been consumed, termination reactions again dominate and the flame dies out. Propagation or termination reactions can be promoted to alter flammability. Tetraethyl lead was once commonly added to gasoline, because lead itself deactivates free radicals in the gasoline-air mixture. This prevents the combustion from initiating in an uncontrolled manner or in unburnt residues (engine knocking) or premature ignition (preignition).

When a hydrocarbon is burned, a large number of different oxygen radicals are involved. The first thing to form is a hydroperoxide radical (HOO·), which reacts further into hydroperoxides that break up into hydroxide radicals.

## Polymerization

In addition to combustion, many polymerization reactions involve free radicals. As a result many plastics, enamels, and other polymers are formed through radical polymerization.

Recent advances in radical polymerization methods, known as Living Radical Polymerization, include:

- Reversible Addition-Fragmentation chain Transfer (RAFT)
- Atom Transfer Radical Polymerization (ATRP)
- Nitroxide Mediated Polymerization (NMP)

These methods produce polymers with a much narrower distribution of molecular weights.

# Atmospheric radicals

The most common radical in the lower atmosphere is molecular dioxygen. Other free radicals are produced through photodissociation of source molecules. In the lower atmosphere the most important examples are the photodissociation of nitrogen dioxide to give an oxygen atom and nitric oxide which plays a key role in smog formation and the photodissociation of ozone to give the exited oxygen atom O(1D). In the upper atmosphere a particularly important source of radicals is the photodissociation of normally unreactive chlorofluorocarbons by solar ultraviolet radiation or by reactions with other stratospheric constituents. These free radicals then react with ozone in a catalytic chain reaction which destroys the ozone, but regenerates the free radical, allowing it to participate in additional reactions. Such reactions are believed to be the primary cause of depletion of the ozone layer and this is why the use of chlorofluorocarbons as refrigerants has been restricted.

# Free radicals in biology

Free radicals play an important role in a number of biological processes, some of which are necessary for life, such as the intracellular killing of bacteria by neutrophil granulocytes. Free radicals have also been implicated in certain cell signalling processes [5]. This is dubbed redox signaling.

The two most important oxygen-centered free radicals are superoxide and hydroxyl radical. They are derived from molecular oxygen under reducing conditions. However, because of their reactivity, these same free radicals can participate in unwanted side reactions resulting in cell damage. Many forms of cancer are thought to be the result of reactions between free radicals and DNA, resulting in mutations that can adversely affect the cell cycle and potentially lead to malignancy. Some of the symptoms of aging such as atherosclerosis are also attributed to free-radical induced oxidation of many of the chemicals making up the body. In addition free radicals contribute to alcohol-induced liver damage, perhaps more than alcohol itself. Radicals in cigarette smoke have been implicated in inactivation of alpha 1-antitrypsin in the lung. This process promotes the development of emphysema.

Free radicals may also be involved in Parkinson's disease, senile and drug-induced deafness, schizophrenia, and Alzheimer's. The classic free-radical syndrome, the iron-storage disease hemochromatosis, is typically associated with a constellation of free-radical-related symptoms including movement disorder, psychosis, skin pigmentary melanin abnormalities, deafness, arthritis, and diabetes mellitus. The free radical theory of aging proposes that free radicals underlie the aging process itself, whereas the process of mitohomesis suggests that repeated exposure to free radicals may extend life span.

Because free radicals are necessary for life, the body has a number of mechanisms to minimize free radical induced damage and to repair damage which does occur, such as the enzymes superoxide dismutase, catalase, glutathione peroxidase and glutathione reductase. In addition, antioxidants play a key role in these defense mechanisms. These are often the three vitamins, vitamin A, vitamin C and vitamin E and polyphenol antioxidants. Further, there is good evidence bilirubin and uric acid can act as antioxidants to help neutralize certain free radicals. Bilirubin comes from the breakdown of red blood cells' contents, while uric acid is a breakdown product of purines. Too much bilirubin, though, can lead to jaundice, which could eventually damage the central nervous system, while too much uric acid causes gout [6].