

# **This student paper was written as an assignment in the graduate course**

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**Methyl Radical: Just like Mother's Little Helper**

by

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Abbreviations:

ALS, Amyotrophic Lateral Sclerosis  
•CH<sub>3</sub>, Methyl radical  
DMSO, Dimethyl Sulfoxide  
ESR, Electron Spin Resonance

H<sub>2</sub>O<sub>2</sub>, Hydrogen Peroxide  
O<sub>2</sub>, Dioxygen  
•OH, Hydroxyl Radical

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Abstract:

Methyl radical is a small but by no means insignificant molecule, it is generally created by the removal of more reactive radicals, which can be more damaging to biological systems. Many interesting things are known about the methyl radical as well as scientific methodology used to detect the radical. The methyl radical is useful in the propagation of radicals by replacing a more reactive radical with a less reactive molecule as the chain reaction occurs. Thus, understanding this function of the methyl radical will further our understanding of the behavior of this specific radical and radicals in general.

### Introduction:

Radicals, or free radicals as these atoms or molecules are often known, are species that have at least one unpaired electron. These unpaired electrons often seek to form new chemical bonds. Free radicals have been shown to be involved in many different diseases and disease processes such as cancer, ALS, aging and many more. The methyl radical is an important member of the radical family. Methyl radical is generally created from the reaction of a different, more reactive and therefore more damaging radical, such as the hydroxyl radical. The methyl radical that is created by these reactions does not last long and is oxidized to yet another radical. The attempt to reduce the more reactive radicals from damaging critical molecules is an important process. These reactive radicals can attack DNA and other critical biomolecules that are not as easily repaired. The many interesting facts about methyl radicals will be discussed in the following sections.

### Methyl Radical Background:

The methyl radical is a carbon-centered radical that is designated  $\bullet\text{CH}_3$ . The structure of a methyl radical has hydrogens bonded to the carbon in sigma bond formation and the free electron resides in the p orbital as demonstrated in Figure 1.

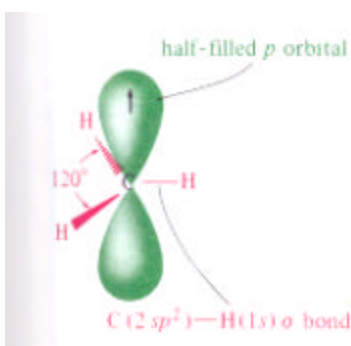


Figure 1: The structure of the methyl radical is that of an  $sp^2$  hybridized carbon with the unpaired electron in a 2p orbital [1].

Radicals are species that contain at least one unpaired electron and the methyl radical is no exception. The unpaired electron for the methyl radical is centered on the carbon [7]. As a radical, the methyl radical is a reasonably simple type of radical, having one carbon and three hydrogens. The molecular weight of  $\bullet\text{CH}_3$  is 15.03 g/mol [10]. Methyl radical is a relatively planar radical with at most a  $15^\circ$  angle out of plane [1]. This planar quality makes the radical unlikely to invert its bonds to a different orientation. Since the methyl radical has one more electron than the methyl cation, the overall structure is neutral. This radical species is quite unstable compared with other carbon based radicals and is also at a higher energy state.

Possessing the extra electron causes the radical to react with other species in what is generally called a chain reaction or radical propagation. Chain processes involve the reaction of one radical with another species thus leading to the formation of a second radical. Only when there is a termination of the radical is this chain reaction stopped. The methyl radical is helpful for reactions because the three hydrogens that are attached to the carbon are made of strong bonds, which makes it easier for the methyl radical to try and obtain another electron to fill its orbitals.

Examples of the effects of the methyl radical are seen in the weathering effects on wood. Weathering is considered the discoloration and aging process of wood. Weathered wood is not the same as rotten wood, which has more to do with decay as compared to aging. Aging (weathering) involves the chemical deterioration of the molecular structures that make up the wood. This deterioration involves free radicals. Increasing the hydration of wood not only helps promote rotting but also enhances the aging process by increasing the production of free radicals [4]. When water or UV light from the sun impinges on the wood there is oxidation of the wood surface. This initial oxidation does not penetrate very deep because of the limitations of the

distance light can travel into wood. In the presence of these phenomena there is an increase of carbon to oxygen bonds and a decrease in the carbon-to-carbon bonds because of the photochemical reactions [4]. Oxidation *via* newly made free radicals along the chain reaction causes the oxidation to move farther into the wood than the light can reach. As an experimental model the wood that is kept inside has a lower free radical concentration as compared to the wood that is present outside and exposed to the sunlight [4].

#### Methyl Radical Detection Methods:

Now that the basic chemical reactions the methyl radical participates in are understood, how can methyl radical be detected. ESR can be used to measure and monitor the amounts of free radical that are generated in a specific reaction. In the previously mentioned wood weathering experiments the researchers studying these phenomena used ESR to measure the carbon free radicals in the different layers of wood [4]. As mentioned before the methyl radical is more likely to dissociate *via* a chain reaction to a more stable radical and this dissociation is measured using ESR. When measured by direct ESR the methyl radical gives four lines with intensity ratios 1:3:3:1 as seen in Figure 2 [7].

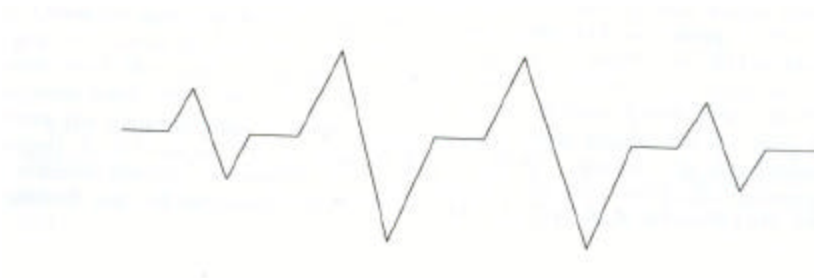


Figure 2: ESR spectrum containing four lines of intensity 1:3:3:1. The spectrum contains four lines of this intensity because the unpaired electron on the carbon is close to the three hydrogens [7].

ESR is not the only method of measuring and detecting radicals. UV absorbance can be used to detect radicals. Methyl radical can be observed by UV spectroscopy at wavelengths less than 240 nm [5].

The methyl radical, since it is reasonably unstable, is generally an intermediate in the radical chain reaction. This is why it is referred to as a helper. Another source of methyl radical is DMSO, which is a radioprotector. DMSO is considered a radioprotector because it is extremely efficient at scavenging  $\bullet\text{OH}$ . One of the products of this reaction is  $\bullet\text{CH}_3$ .

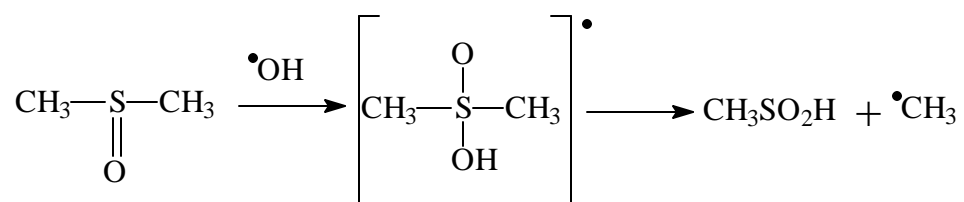


Figure 3: This reaction demonstrates the scavenging abilities of DMSO to the  $\bullet\text{OH}$ . One of the products is a less reactive  $\bullet\text{CH}_3$  [12].

Methyl radical is much less reactive than  $\bullet\text{OH}$  and is the reason the DMSO is effective.

However, as mentioned previously the methyl radical is also not a favored state and therefore will change into something else. The fate of the  $\bullet\text{CH}_3$  needs to be considered. As a helper for the chain reaction, methyl radical reacts in the presence of  $\text{O}_2$  and is rapidly changed to the more stable methylperoxyl radical ( $\text{CH}_3\text{OO}\bullet$ ) [12]. This methylperoxyl radical is more stable than the methyl radical adding to the idea that the methyl radical is involved in radical species propagation. DMSO is used as a probe for hydroxyl radical in biological systems. Using ESR along with the DMSO reaction elucidates how DMSO is also a reductant for  $\bullet\text{OH}$  and reacts with it to give  $\bullet\text{CH}_3$  as shown in Figure 4.

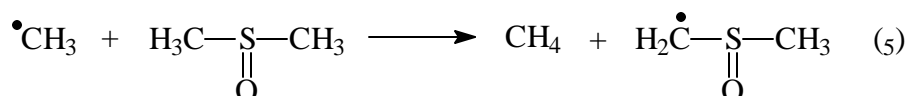
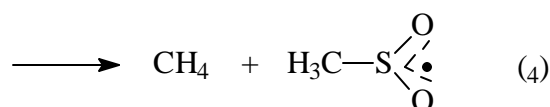
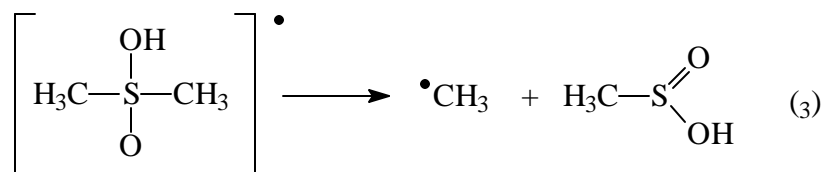
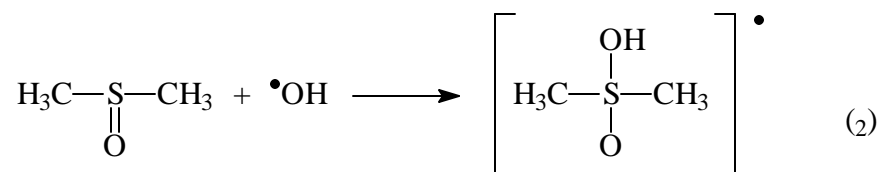
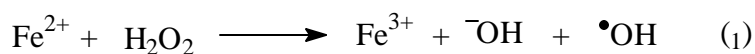


Figure 4: Scheme of DMSO reacting with  $\bullet\text{OH}$  as demonstrated by Asmus' work using pulse radiolysis [2]. In (1) the  $\bullet\text{OH}$  is formed, in (2) DMSO scavenges  $\bullet\text{OH}$  to the intermediate and then to  $\bullet\text{CH}_3$  [2]. (3) and (4) show the reaction of  $\bullet\text{CH}_3$  to methane and the methylperoxyl radical [2].

As mentioned earlier, the way to get rid of the radicals is to have chain termination. The methyl radical is not a strong candidate for chain termination [5]. A radical is more easily terminated when it is in a more stable state. In the presence of acid the exclusive product is methane because the  $\bullet\text{CH}_3$  is rapidly reduced in the acidic solution [3]. This reaction at the more acidic pH competes with the scavenging of  $\text{O}_2$ .

#### Methyl Radical Biochemistry and Kinetics:

Now that detection of radicals *via* ESR and reactions with DMSO and others are understood let's focus attention on the kinds of reactions  $\bullet\text{CH}_3$  will undergo. The methyl radical



is more reactive than other alkyl radicals, and is best at H atom abstraction [5]. The absolute rate constant for  $\bullet\text{CH}_3$  is sixty times larger than the absolute rate constants of other alkyl radicals.

Methyl radical can be formed or dismutated. The rate constant for the formation of  $\bullet\text{CH}_3$  by the reaction of hydroxyl radical with DMSO is  $k = 6.6 \times 10^9 \text{ M}^{-1} \text{ s}^{-1}$  [8]. Another reaction involves the dismutation of methyl radical in the presence of  $\text{O}_2$ . The rate constant for the reaction of methyl radical with  $\text{O}_2$  is  $k = 1 \times 10^9 \text{ M}^{-1} \text{ s}^{-1}$  [5]. As can be seen by both of these rate constants, the reactions are favored because the molecule would like to get to the most stable species. A third reaction of  $\bullet\text{CH}_3$  is with  $\text{H}_2\text{O}_2$ . This reaction forms methane and  $\text{HO}_2\bullet$  [2]. The more you increase the concentration of hydrogen peroxide the higher the steady-state concentration of methyl radical, with a concurrent decrease in the amount of methane produced [2]. These kinetic reactions show that methyl radical is important as a helper in bringing molecules to their steady-state.

### Summary:

In summary it is important to understand the mechanism and the function of the methyl radical. The methyl radical's function seems to be to help suppress more damaging radicals from reacting with critical biomolecules. The decrease in deleterious reactions with biomolecules is beneficial to most every biological system known. Thus, the lack of stability should not detract, but add to the importance of methyl radical and its function.

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