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Chemically Accurate Calculations of Rate Constants of Spin Trap-Hydroxyl Radical Addition Reactions

Submitted in partial fulfillment of undergraduate honors requirements

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ABSTRACT

Composite Quantum Chemistry Calculations of Spin Traps and Reaction Products

By

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The DMPO type spin trap 5,5-Dimethyl-1-pyrroline N-oxide (DMPO) and the exceptionally similar spin trap 2-ethoxycarbonyl-2-methyl-3,4-dihydro-2H-pyrrole-l-oxide (EMPO) are widely studied in computational and theoretical works. This particular study examines the addition reactions that both these molecules undergo with the carcinogenic hydroxyl radical. This work used a relatively new approximation method, called the correlation consistent composite approach or ccCA, for carrying out quantum mechanical calculations to give the free energies of the products and reactants of the reactions. The free energies are to be used to extrapolate the rate constants of the reactions from the Arrhenius equation. Though both the spin traps studied have been widely examined and assessed in both theoretical and experimental work, accurately calculated rate constants have not been previously obtained using computational methods. The results obtained here will help to assess the efficiency and the accuracy of the ccCA method, as well as lead to the design of better, more novel spin traps.

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INTRODUCTION

A radical is a chemical species containing one or more unpaired electrons.[1] “Free radicals” are generally defined in the same way, but to be more precise free radicals are radical species that can exist independently. There are copious amounts of different types of radicals that exist, and they may be generally classified by the atom on which the unpaired spin, or electron, is localized. Radicals may be formed from many different types of chemical compounds containing different types of elements. Compounds made from a central metal atom, like tin and lead, have been found to form free radicals when surrounded by ligands.[2] Cellular activity in biological systems causes free radicals to be formed in humans very regularly.[3] Different radicals are formed in the body of humans by normal processes and external influences, and reactive radical species are created regularly in small amounts in the body by way of aerobic cellular processes.[4] Free radicals in the body are not generally beneficial to humans, however.

Reactive oxygen species are oxygen-based radicals that are reactive enough to modify protein or DNA molecules permanently or temporarily changing cellular activity.[5] Reactive oxygen species include superoxide, peroxide, and hydroxyl radicals.[5] Due to these radicals being present in the body they have been linked to a number of biological phenomena that have negative effects. Carcinogenesis, mutation, degenerative diseases, inflammation, aging, and other diseases have been found to have reactive oxygen species involved in the development process.[6] Reactive oxygen species have also been found to be involved in the development of melanoma.[5] The oxidation of nucleic acids is caused by reactive oxygen species and has been linked to neurological diseases, atherosclerosis, and caner.[7] One can see that reactive oxygen species cause a significant number of problems in the human body. This has driven research to find the cause of production of reactive oxygen species in the human body.

Generation of Hydroxyl Radicals

Cellular and biological processes produce radicals and reactive oxygen species regularly in the body.[3, 4] However, problems occur in cells and biological systems when the number of radicals produced is too copious due to the radicals oxidizing biomolecules.[4] The Fenton Reaction has been determined to be the main cause of overproduction of radicals in cells.[4] The Fenton Reaction produces the hydroxyl radical (•OH); this radical is very reactive and leads to the formation of other radicals. The hydroxyl radical has great potential to oxidize biomolecules and is a very problematic radical in the body. The explanation for why the hydroxyl radical is overproduced in cells is in the chemistry of the Fenton Reaction.

The Fenton Reaction is a reaction between iron (II) and H_2O_2 in which iron is oxidized and H_2O_2 is split. The general reaction is [8]:

$$H_2O_2 + Fe^{2+} \rightarrow \bullet OH + OH^- + Fe^{3+} \tag{1-1}$$

Nevertheless, other redox active metal ions, such as Cu^+, can reduce hydrogen peroxide in this way.[9] Fenton first discovered the oxidative properties of iron and ferric ions in 1876 [10], and Fenton’s first publication regarding mechanisms of iron-mediated oxidation was in 1894.[11] Fenton was not the one who purposed the reaction’s significance in biological systems, however. From 1932-1934 Haber, Weiss, and Willstäter proposed the involvement of the free hydroxyl radicals resulting from the iron (II)/H_2O_2 system of reactions.[8] It is now known and widely accepted that the Fenton Reaction and Fenton Chemistry are of great significance in biological systems in the formation of cancer and cancerous cells.

The Fenton Reaction occurs in the human body when there is an over concentration of iron in the body. However, the hemoglobin complex in blood cells is formed by iron and iron has been deemed bio-essential in aerobic life.[4] Radical-induced DNA damage in cells occurs at the phosphate backbone and nucleotide bases.[9] Positively charged metal ions may localize near the phosphate backbone of DNA, and when H_2O_2 is near localized ions that are redox active, like iron, the Fenton Reaction takes place.[9] The production of reactive species in close proximity to the DNA causes DNA damage due to reactions with these species.[9]

Radicals may also be formed by multiple different methods in solution so that researchers may study them. Of course, the Fenton Reaction that takes place in the body can be replicated in the lab to produce radicals. There are other methods of producing hydroxyl radicals for study, however. One of those methods is the photolysis of hydrogen peroxide. The photolysis of H_2O_2 was first studied by Baxendale and Wilson.[12] They reported that it took one Einstein of incident 254 nm UV radiation to decompose 1 mol of H_2O_2.[12] The photolysis yields 2 mol of hydroxyl radical with the general reaction being [13]:

$$H_2O_2 + hv \rightarrow 2 \bullet OH \tag{1-2}$$

Other hydroperoxides can generate the hydroxyl radical, but the mechanism is generally the same.[13]

Another method in which hydroxyl radicals may be formed in solution involves potassium nitrate. First, the peroxynitrite ion is formed from the UV irradiation of alkaline nitrate crystals.[14] Plumb and Edwards found that the peroxynitrite ion is the primary product when solid nitrates are exposed 254 nm UV light.[15] The peroxynitrite is then added to an aqueous solution of a neutral pH where the hemolytic cleavage of the peroxy bond produces the hydroxyl radical and nitrogen dioxide.[16] The general reaction in aqueous solution is [16]:

$$O{=}N{-}OO\cdot \rightarrow NO_2 + \bullet OH \qquad (1\text{-}3)$$

The hydroxyl radical has a very high rate constant that is approximately 10^9 $dm^3mol^{-1}s^{-1}$ for reactions with many species found in biological systems.[17] One can see from the extremely high rate constant that the hydroxyl radical is very reactive. The reactions of hydroxyl radicals may be classified into three categories: electron transfer, hydrogen abstraction, and addition reactions. Organic species can react with hydroxyl radicals in each of these reactions and inorganic species can even react with hydroxyl radicals by some of them.

Reactions of Hydroxyl Radicals

Electron transfer reactions with hydroxyl radicals are relatively simple. The name of the reaction explains how the reaction wonderfully. As with every reaction involving hydroxyl reactions, electron transfer reactions happen between organic species and hydroxyl radicals.[18] An example of this is the reaction of the azide ion and hydroxyl radicals [18]:

$$N_3{}^- + \bullet OH \rightarrow \bullet N_3 + OH^- \qquad (1\text{-}4)$$

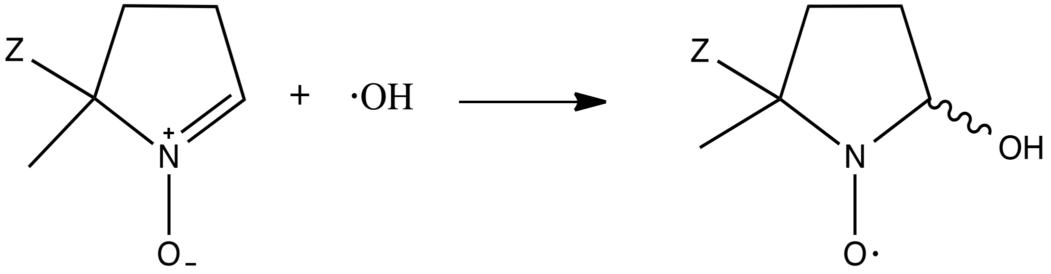
However, the electron transfer reaction can take place between hydroxyl radicals and inorganic species as well.[19] Species such as Fe(II), As(III), and Cu(I) can undergo single electron oxidations to react with hydroxyl radicals.[19]

Hydroxyl radicals can also undergo hydrogen abstraction reactions with most organic compounds, but the hydrogen abstraction reaction does not occur with inorganic species. Some of the most common types of hydrogen abstraction reactions are those between alcohols and hydroxyl radicals as alcohols are often used to scavenge radicals.[18] An example of the reaction between hydroxyl radicals and alcohols is that between tert-butanol and the hydroxyl radical [18]:

$$\bullet OH + (CH_3)_3COH \rightarrow \bullet CH_2(CH_3)_2COH + H_2O \qquad (1\text{-}5)$$

However, alcohols are not the only hydrocarbons and organic species that react with the hydroxyl radicals. Halocarbons with at least one hydrogen are able to undergo hydrogen abstraction reactions with hydroxyl radicals.[20] These types of halocarbons are of interest as possible replacements for refrigerants, lubricants, solvents, fire suppressants, and other applications.[20]

The last type of reaction that hydroxyl radicals participate in is the addition reaction. This type of reaction takes place mainly between hydroxyl radicals and aromatic or unsaturated aliphatic species. Addition reactions generally produce hydroxycyclohexadienyl-type radicals.[21] The general reaction scheme for the addition reaction is as follows [41]:



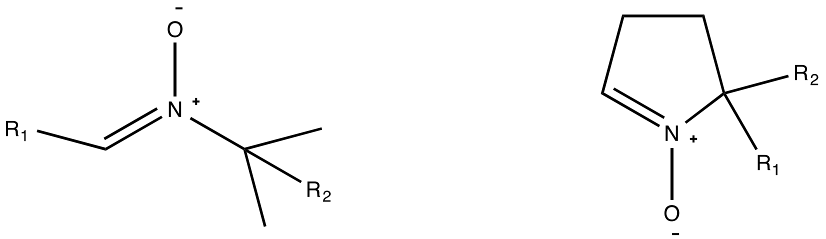
(1-6)

The addition reactions involving hydroxyl radicals have become very important in recent research in many different fields. These reactions are involved in environmental pollutants arising from the burning of fossil fuels.[21] The addition reaction is the reaction that takes place with the various bases found in DNA.[22] It has been experimentally observed that hydroxyl radicals can react with all the various bases found in DNA and form stable products.[23, 24] Once the radicals react with the DNA bases the DNA is damaged and, if the DNA repair enzymes can not repair the DNA, the cell either dies or becomes cancerous.[9] The addition reaction is probably most important radical reaction in the research fields of detecting and studying radicals. This is because it is addition reactions that are involved in spin trapping to stabilize radicals so that they may be studied.[25]

Spin Traps

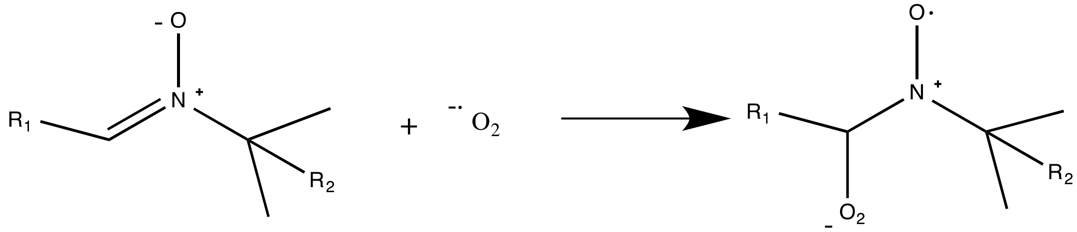
Researchers must study radicals to understand how they participate in biological processes and cause damage to biomolecules. However, the high reactivity of hydroxyl and other types of radicals causes them to have extremely short lifetimes. The short lifetimes of radicals cause problems for research and have led to scientists using indirect means to study radicals. There are various means of studying radicals, but the most commonly used technique for studying radicals is Electron Spin Resonance (ESR)/Electron Paramagnetic Resonance (EPR) Spectroscopy.[26] With any method used to study radicals there must be some way to extend the life of radicals or produce radicals that are more stable. The most direct way of detecting and stabilizing radicals for ESR/EPR is spin trapping.[27] Spin trapping involves the addition of a primary free radical across the double bond of a diamagnetic compound to form a radical adduct more stable than the original radical.[27] The compounds that form the radical adduct with the original radical are referred to as spin traps [28], hence the name “spin trapping.”

Spin traps were first developed because of innovations that were needed in detection and characterization of free radicals.[29] The idea of spin traps originated in the published works of Iwamura and Inamoto that displayed the reaction of cyano radicals and spin traps that formed a stable adduct.[30, 31] The first propositions for the uses of the addition reactions contained in the papers of Iwamura and Inamoto were made by Janzen and Blackburn.[28, 32] Since the discovery of spin traps, research has improved methods of detecting and characterizing radicals while also making more sophisticated and effective spin traps. Spin traps have continued to improve and be used by researchers since their discovery. Biochemists have been using spin traps for their intended purposes in experimentation for a number of years.[33-35] Spin traps have been found to trap an array of different radicals over years of experimental research. Some spin traps that have been used primarily for biological radicals have even been found to possess the ability to trap inorganic radicals.[36] Research in spin traps has come a long way since their discovery. Publications now show that spin traps may be divided into two main classes: PBN-type and DMPO-type.[37] PBN-type spin traps are linear where as the DMPO-type of radicals are cyclic.[37] PBN-type spin traps have rings in the structure, but the base of the structure and site at which radicals react is part of a linear structure.[44] In DMPO-type spin traps the radicals add directly to the ring and the ring is the base of the structure.[37] The following figure shows the basic structure and addition reactions of both types of spin traps [41, 44]:



PBN-based nitrones DMPO-based nitrones

Addtion reaction of PBN-based nitrones



Addition reaction of DMPO-based nitrones

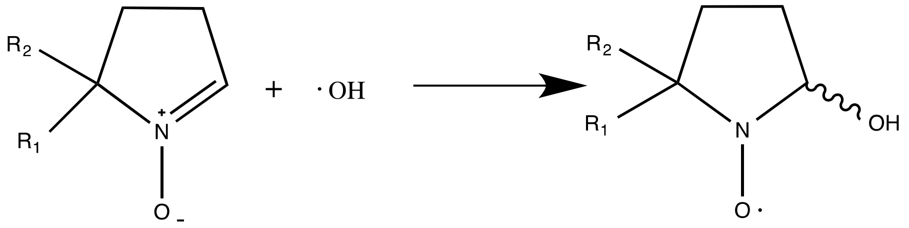


Figure 1. PBN-type and DMPO-type spin traps and their reactions.[41, 44]

Both classes are nitrones, but the PBN-type of nitrones are not as researched and are not as well characterized as the DMPO-type of spin traps.

Though PBN-type spin traps are not as well studied and researched as DMPO-type spin traps, there has been several PBN-type spin traps that have been successfully synthesized. Some of the PBN-types to be synthesized are α-substituted methoxy, amino, mercapto, and cyano nitrones.[38, 39] There have also been some β-phosphorylated PBN-type nitrones to be successfully synthesized.[40] There are more DMPO-type nitrones than PBN-type. Some of the DMPO-type of spin traps known to be susceptible to reaction with the hydroxyl radical includes: 5, 5-Dimethyl-1-pyrroline *N*-oxide (DMPO) [41], 2-ethoxycarbonyl-2-methyl-3, 4-dihydro-2*H*-pyrrole-l-oxide (EMPO) [42], 5-*tert*-butoxycarbonyl 5-methyl-1-pyrroline *N*-oxide (BMPO or BocMPO) [41, 43], 5-(diethoxyphosphoryl)-5-methyl-1-pyrroline-*N*-oxide (DEPMPO) [41], among other derivatives similar to these spin traps.[41] Both types of spin traps have spin trapping qualities that scientist desire, but both types of spin traps do have their flaws. PBN-type spin traps are limited in their ability to distinguish among radicals.[37] DMPO-type spin traps are limited in their ability to produce stable adducts and their overall spin trapping efficiency.[37]

Chapter 2

QUANTUM MECHANICS

The Schrödinger Equation

At the end of the nineteenth century, many scientists believed that all essential discoveries had been made and all that remained was the clearing up of a few minor details.[45] Classical mechanics was sufficient at describing macroscopic particles and problems.[26] However, due to the deterministic nature of classical mechanics, problems arise when microscopic problems and systems are evaluated. It was not until the advent of quantum mechanics that molecular and atomic systems could be evaluated.[45] Prior to quantum mechanics, chemistry was principally an empirical science.[46] It was not until some key experiments showed conflict in the results compared to the classical mechanic predictions that scientists began to believe that there was much that had yet to discovered in the physical world.[46]

There were two different kinds of experiments that were in conflict with classical mechanic predictions. The two classes of experiments were ones that found light could not be described singularly using wave theory and ones that found particles exhibited wave like behavior.[46] The two phenomena that showed the particle nature in light were black body radiation and the photoelectric effect.[45-47] Black body radiation could not be described using classical mechanics as the predictions became less and less accurate as observation progressed through the UV region of light.[45] Max Planck used what is now referred to as his "quantum postulate" to describe black body radiation.[45] In this postulate, Planck showed that energy exists in discrete states or "bundles," and the exchange of energy was quantized.[45, 47] Albert

Einstein then used Planck's quantum postulate to describe the photoelectric effect.[45] By viewing energy as existing in quantized states, Einstein related the kinetic energy of electrons ejected from metals being struck by light to the frequency of the incident light waves.[45]

Moreover, some of the phenomena observed showing the wave like behavior of particles were atomic spectra and electron diffraction.[45, 46] Niels Bohr first attempted to explain the atomic emission spectra. He did so by applying Planck's quantum postulate and developing a classical model of the hydrogen atom in which electrons were seen as orbiting the nucleus.[46] Bohr's theory of the atom was excellent at describing the emission spectra of the hydrogen atom and other one-electron atoms, but it failed to sufficiently describe the spectra of atoms with any more electrons.[46] This showed that while Bohr's theory was good and made use of the proper principles, it was ultimately incomplete.[46] Electron diffraction is an example of particles behaving like a wave and Louis de Broglie was the first to postulate why particles can behave in this way.[45] Though no experimentation had shown wave-particle duality in matter, de Broglie postulated that just as light can behave as a particle and wave in certain instances so could matter.[45, 46, 48] Werner Heisenberg realized de Broigle's postulate had a consequence that he named the uncertainty principle.[45,46] The uncertainty principle originally only observed the momentum and position of a particle and had the following forms [45, 46]:

$$\Delta x \Delta p_x \geq \frac{\hbar}{2} \tag{2-1}$$

The uncertainty principle is a consequence of wave-particle duality and shows that the momentum and positions of a particle cannot be simultaneously measured to exactness. Contradicting phenomena and postulates like the uncertainty principle show that classical mechanics cannot explain the microscopic and a better form of mechanics was needed; thus, quantum mechanics was born.

The general quantum hypothesis was first formulated, independently, by Werner Heisenberg and Erwin Schrödinger in 1925.[45] At first glance the two look different, but Schrödinger showed the two to be mathematically equivalent.[50] Chemical study generally tends to use the Schrödinger version that uses differential equations rather than matrix algebra. Quantum mechanics suggests that a function exists called a wave or state function that explains a quantum mechanical system.[45-47, 49] Any information about a quantum mechanical system may be derived from the wave function for the system and the function is represented by the symbol Ψ.[45-47 49] A quantum mechanical system evolves through time according to the time-dependent Schrödinger equation [50-53]:

$$\frac{-\hbar}{i}\frac{\partial\Psi(\mathrm{x},\mathrm{t})}{\partial t}=\frac{-\hbar^2}{2m}\nabla^2\Psi(x,t)+V(x,t)\Psi(x,t) \tag{2-2}$$

where *m* represemts the mass of the particle, $\hbar$ is the reduced Planck's constant equal to *h/2π,* and ∇^2 is the Laplacian operator. The Laplacian operator is given as [50-53]:

$$\nabla^2=\frac{\partial^2}{\partial x^2}+\frac{\partial^2}{\partial y^2}+\frac{\partial^2}{\partial z^2} \tag{2-3}$$

All possible information about a quantum mechanical system can be derived from the wave function of the quantum mechanical system.[45, 46] The probability for locating a particle at a certain point is given by the equation [54]:

$$|\Psi(x,t)|^2 \tag{2-4}$$

This equation gives the probability of finding a particle at a given time *t* between the coordinates *x* to *x+dx.*[54] This was first proposed by Max Born and is known as Born's postulate.[54] Most quantum mechanical applications do not have a need to account for time as a variable. When the potential energy of a quantum mechanical system is independent of time and only dependent on position the time-dependent Schrödinger equation can be separated into two functions and solved using the separation of variables method [45]:

$$\Psi(x,t) = \psi(x)f(t) \tag{2-5}$$

By substituting Equation 2-2 and differentiating with respect to time the following expression is obtained [26]:

$$\frac{-\hbar^2}{2m} f(t) \frac{d^2\psi(x)}{dx^2} + V\psi(x)f(t) = \frac{-\hbar}{i}\frac{df(t)}{dt}\psi(x) \tag{2-6}$$

The equation can then be divided by $\Psi(\mathrm{x},\mathrm{t}) = \psi(\mathrm{x})\mathrm{f(t)}$ to give the following [26]:

$$\frac{-\hbar^2}{2m}\frac{1}{\psi(x)}\frac{d^2\psi(x)}{dx^2} + V(x)\psi(x) = \frac{-\hbar}{i}\frac{1}{f(t)}\frac{df(t)}{dt} \tag{2-7}$$

The left hand side of the equation is independent of time and the right hand side of the equation is independent of position. The two sides of the equations are equal to the energy of the system.[45] By relating the left hand side to energy, *E,* the time-independent Schrödinger equation for a particle of mass *m* can be obtained [45]:

$$\frac{-\hbar^2}{2m}\frac{d^2\psi(x)}{dx^2} + V(x)\psi(x) = E\psi(x) \tag{2-8}$$

The time-independent Schrödinger equation is much more widely used in quantum mechanics than the time-dependent Schrödinger equation.[45] Solutions to the time-independent Schrödinger equation are called stationary states, and this is because the probability densities for these states are independent of time.[55] For every physical observable there exists a quantum mechanical operator, and these operators may yield an eigenvalue for the Schrödinger equation.[45-47] A quantum mechanical operator is a symbol that corresponds to an action that is to be performed on whatever follows it.[45, 46] The Hamiltonian operator gives the total energy of a system, which is the sum of the kinetic and potential energies [45]:

$$\hat{H} = \frac{\hat{p}_x}{2m} + V(x) \tag{2-9}$$

or

$$\hat{H} = \frac{-\hbar^2}{2m}\frac{d^2}{dx^2} + V(x) \tag{2-10}$$

The Schrödinger equation is an eigenvalue problem with the wave equation being the eigenfunction and the total energy being the eigenvalue.[51] The Hamiltonian operator is the operator that corresponds to these particular eigenvalues and eigenfunctions [45]:

$$\hat{H}\psi = E\psi \tag{2-11}$$

The equations covered above can account for and describe both the angular momentum and orbital angular momentum; however, an electron, also, posses an intrinsic angular momentum.[45] The intrinsic angular momentum is generally called the spin angular momentum, or spin.[45] The concept of spin is a purely quantum mechanical phenomenon.[45] This is due to the fact that there are no analogues that can describe spin in classical mechanics.[45] Spin is included in a wave function as an additional hypothesis [26], but the spin does not affect the energy of a one electron system.[45] The Schrödinger equation accounting for spin is of the following form [45]:

$$\Psi(x,y,z,\sigma) = \psi(x,y,z)\alpha(\sigma) \text{ or } \psi(x,y,z)\beta(\sigma) \tag{2-12}$$

In this equation the α and β functions correspond to m_S values of 1/2 or -1/2.[45] Though the spin does not affect the energy of a system it does double the number of possible energy states of a quantum mechanical system.[26] The energy states are given by $\psi\alpha$ and $\psi\beta$. The introduction of spin leads to a postulate of quantum mechanics. No experiments can distinguish one electron from another.[45] Therefore, the Schrödinger equation for a two electron atom can take either of the following forms [45, 46]:

$$\psi(1,2) = 1s\alpha(1)1s\beta(2) \tag{2-13}$$

or

$$\psi(2,1) = 1s\alpha(2)1s\beta(1) \tag{2-14}$$

Mathematically speaking, antisymmetry requires that linear combinations involving all possible labeling of electrons must be taken.[45] For example, the linear combinations of a two-electron atom, such as helium, would be [45]:

$$\Psi_1 = \psi(1,2) + \psi(2,1) = 1s\alpha(1)1s\beta(2) + 1s\alpha(2)1s\beta(1) \tag{2-15}$$

and

$$\Psi_2 = \psi(1,2) - \psi(2,1) = 1s\alpha(1)1s\beta(2) - 1s\alpha(2)1s\beta(1) \tag{2-16}$$

Both equations seem to be reasonable for the helium atom, but experiment has shown that the second equation describes the ground state of helium.[45] This second equation is antisymmetric, which means that the sign of the equation will change if the terms are interchanged:

$$\Psi(2,1) = \psi(2,1) - \psi(1,2) = -\Psi(1,2) \tag{2-17}$$

This is part of what lead to the postulate of quantum mechanics that states: all electronic wave functions must be antisymmetric under the interchange of any two electrons.[45] This postulate is also known as the Pauli Exclusion Principle.[45] The Pauli Exclusion Principle is generally applied to the wave functions of multi electron atoms.

The Schrödinger equation for multi-electron systems are much more complicated than those of single electron atoms. The added electron introduces a considerable amount of complication to the Schrödinger equation. The Hamiltonian operator of helium atom, for example, takes the following form [45]:

$$\hat{H} = \left(-\frac{\hbar^2}{2M}\nabla^2 - \frac{\hbar^2}{2m_e}{\nabla_1}^2 - \frac{\hbar^2}{2m_e}{\nabla_2}^2\right) + \left(-\frac{2e^2}{4\pi\varepsilon_0|R-r_1|} - \frac{2e^2}{4\pi\varepsilon_0|R-r_2|} - \frac{e^2}{4\pi\varepsilon_0|r_1-r_2|}\right) \tag{2-18}$$

Where ∇^2 is the Laplacian operator with respect to the nucleus, ${\nabla_1}^2$ and ${\nabla_2}^2$ are the Laplacian operators for the two electrons, M is the mass of the nucleus, $m_e$is the mass of an electron, R is the position of the helium nucleus, and r_1 and $r_2$are the positions of the electrons.[45] Through some approximations the Hamiltonian for the helium atom can be simplified. The simplified Hamiltonian for the helium atom takes the following form [45]:

$$\hat{H} = -\frac{\hbar^2}{2m_e}\left({\nabla_1}^2 + {\nabla_2}^2\right) - \frac{2e^2}{4\pi\varepsilon_0}\left(\frac{1}{r_1} + \frac{1}{r_2}\right) + \frac{e^2}{4\pi\varepsilon_0|r_1-r_2|} \tag{2-19}$$

However, even the simplified version of the Hamiltonian does not allow the Schrödinger equation of helium to be solved exactly. The $\frac{e^2}{4\pi\varepsilon_0|r_1-r_2|}$ term is responsible for the complication in solving the Schrödinger equation of a helium atom.[45] This term accounts for the electron-electron repulsion that takes place between the electrons, and if it were not for this term the Schrödinger equation of a helium atom would simply be the sum of the Hamiltonian operators of two hydrogen-like Schrödinger equations.[45] The electron-electron repulsion term makes the Hamiltonian for helium a three-body problem; moreover, the mathematics for solving three body problems are not yet known.[45] Because there are no mathematics to solve exactly for a three body problem approximation methods must be used to solve for multi body Schrödinger equations.

Approximations

The Hamiltonian for the simplest molecule, H_2^+, may be written as follows [46]:

$$\hat{H} = -\frac{1}{2M_a}\nabla^2{}_a - \frac{1}{2M_b}\nabla^2{}_b - \frac{1}{2}\nabla^2{}_e - \frac{1}{r_a} - \frac{1}{r_b} + \frac{1}{R_{ab}} \tag{2-20}$$

In the Hamiltonian, the first two terms, $-\frac{1}{2M_a}\nabla^2{}_a - \frac{1}{2M_b}\nabla^2{}_b$, are the kinetic energy terms for the two nuclei, the $-\frac{1}{2}\nabla^2{}_e$ term is the kinetic energy of the electron, the $-\frac{1}{r_a} - \frac{1}{r_b}$ terms are the coulomb attraction between the electron and the nuclei, and the $+\frac{1}{R_{ab}}$ term is the nuclear repulsion between the nuclei.[46] To simplify the Hamiltonian from the original an approximation may be made to eliminate certain terms from the operator. The approximation used in the treatment of the Hamiltonian of the helium atom is the Born-Oppenheimer Approximation.[45, 46] Many works have been done describing the mathematics and applicability of the Born-Oppenheimer Approximation [56-58], and some have even been done to further study and describe the H_2^+ ion.[59] This term is synonymous with the infinitely heavy nucleus approximation when looking at individual atoms and reduces the Hamiltonian for molecules just as the infinitely heavy nucleus approximation did for the Hamiltonian of the helium atom.[45] In the Born-Oppenheimer Approximation the nuclei are seen as fixed in space and allow for the omission of any terms involving the movement or masses of the nuclei.[45] This approximation is made based on the fact that the nuclei are much larger than the electrons and are moving much more slowly than the electrons, and because of this huge velocity difference the electrons can compensate for nuclei movement instantaneously.[45, 46] The reduced Hamiltonian for the H_2^+ ion takes the following form upon application of the approximation:

$$\hat{H} = -\frac{1}{2}\nabla^2 - \frac{1}{r_a} - \frac{1}{r_b} + \frac{1}{R} \tag{2-21}$$

In the reduced Hamiltonian, the $-\frac{1}{2}\nabla^2$ term is the kinetic energy of the electron, the r_a and r_b terms are the distances of the electron from nucleus a and b, and R is the distance between the nuclei, which is treated as an adjustable parameter.[45] The Hamiltonian for the H_2^+ molecule is completely solvable; however, when a quantum mechanical system has more then one electron present, like the case of helium, the Hamiltonian will contain a term for the electron-electron repulsion that cannot be omitted by approximation.[45] The electron-electron repulsion again makes the Schrödinger equation a three-body problem, which cannot be solved with our current mathematics.[45] Approximation methods are used to solve Schrödinger equations with more electron-electron repulsion terms to give very accurate results.

One of the simplest approximation methods used is the variational method. The variational method is generally used in calculations and considerations of the ground state of systems.[45] In the ground state, the wave function can be represented in the following form [45]:

$$\hat{H}\psi_0 = E_0\psi_0 \tag{2-22}$$

The equation may then be multiplied by the complex conjugate of the ground state wave function, solved for the energy, and integrated over all space to give [45]:

$$E_0 = \frac{\int \psi_0{}^* \hat{H}\psi_0 d\tau}{\int \psi_0{}^* \psi_0 d\tau} \tag{2-23}$$

The $d\tau$ in the equation represents the appropriate volume element for the wave equation.[45] In the variational theorem, the ψ_0 is substituted for another function ϕ and the corresponding energy is calculated by the following [45]:

$$E_\phi = \frac{\int \phi^* \hat{H}\phi d\tau}{\int \phi^* \phi d\tau} \tag{2-24}$$

The variational principle states that E_{ϕ} will be greater than the actual ground state energy and can be represented by the following [45]:

$$E_{\phi} \geq E_0 \tag{2-25}$$

The variational principle states that an upper bound for the ground state energy can be calculated by using any trial function (ϕ) that is well behaved and satisfies the boundary conditions associated with the problem of interest.[45, 46] It also states that the closer the trial function is to the actual ground state wave function the closer the trial function energy will be to the actual ground state energy.[45] The trial function will depend on some arbitrary parameters, $\alpha, \beta, \gamma, \ldots,$ called variational parameters.[45] The energy must then also depend upon the parameters and can be represented as follows [45]:

$$E_{\phi}(\alpha, \beta, \gamma, \ldots) \geq E_0 \tag{2-26}$$

The E_{ϕ} is then minimized with respect to the variational parameters allowing the determination for the best possible ground state energy that can be obtained from the trial function.[45]

Another simpler approximation, commonly used for less complex problems, is perturbation theory. The governing idea behind perturbation theory is that if one has an unsolvable wave function that is very close, but not quite the same as, a wave function that can be solved then the Hamiltonian operator can be written as [45, 46, 60]:

$$\hat{H} = \hat{H}^{(0)} + \hat{H}^{(1)} \tag{2-27}$$

The Schrödinger equation that can be solved exactly is [45]:

$$\hat{H}^{(0)}\psi^{(0)} = E^{(0)}\psi^{(0)} \tag{2-28}$$

In the Hamiltonian, the second term is a perturbation that is small compared to the original Hamiltonian operator ($\hat{H}^{(0)}$).[46] To apply perturbation theory to finding the solution of the of the unsolvable Schrödinger equation the wave equation and the energy are written in the following fashion [45]:

$$\psi = \psi^{(0)} + \psi^{(1)} + \psi^{(2)} + \cdots \tag{2-29}$$

and

$$E = E^{(0)} + E^{(1)} + E^{(2)} + \cdots \tag{2-30}$$

The first terms in both equations are given by the solution to the unperturbed problem and the following terms are successive corrections.[45] The basic assumption in perturbation theory is that the successive corrections will become increasingly less significant until they converge and give the best possible solution to the quantum mechanical problem that can not be solved exactly.[45, 46] Perturbation theory and slight variations of perturbation theory are used in various kinds of quantum mechanical and computational studies.[61, 62] One can see that perturbation theory is a useful approximation method still used in research today.

The wave function of hydrogen is one of the simplest wave equations and can be solved exactly. However, the wave equations of more complex multi electron atoms and molecules cannot be solved exactly. The variable hindering the solvation of multi electron systems is electron-electron repulsion.[45] The electron-electron repulsion depends upon the position of the electrons in the system; therefore, the repulsion term must be a variable that changes with position to correspond with reality.[45, 46] With the addition of electron-electron repulsion that Schrödinger equation for multi electron systems becomes a three-body problem even upon application of the Born-Oppenheimer approximation.[45]

Hartree-Fock Theory is an approximation theory that takes the repulsion term in the multi-electron Schrödinger equations by making the term a fixed term corresponding to the average repulsion.[45, 46] Hartree-Fock theory uses the concept of having electrons in orbitals.[45] The helium is the simplest example to demonstrate Hartree-Fock theory and the Hartree method. The two-electron wave function can first be written as a product of orbitals [45, 46]:

$$\psi(\boldsymbol{r_1}, \boldsymbol{r}_2) = \phi(\boldsymbol{r}_1)\phi(\boldsymbol{r_2}) \tag{2-31}$$

It is written as a product of the functions representing the orbitals the electrons are in and can be considered equal in this case as the two electrons in a helium atom are in the same 1s atomic orbital. The probability distribution of electron two is $\phi^*(\mathbf{r}_2)\ \phi(\mathbf{r}_2)d\mathbf{r}_2$ and can be interpreted as a charge density.[45] Therefore, the potential energy experienced by electron 1 experiences due to electron 2 is [45, 46]:

$$V_1{}^{eff}(r_1) = \int \phi^*(\boldsymbol{r}_2)\frac{1}{r_{12}}\phi(\boldsymbol{r_2})d\boldsymbol{r_2} \tag{2-32}$$

The superscript “eff” emphasizes that the potential is an effective, or average, potential energy.[45] The equation for the potential energy, as well as the other equations in the Hartree-Fock method, is in atomic units for easier notation and understanding.[45] The Hamiltonian for this method is defined as an effective one electron Hamiltonian of the following form [45, 46]:

$$\widehat{H}_1{}^{eff}(\boldsymbol{r_1}) = -\frac{1}{2}\nabla_{\boldsymbol{1}}{}^{\boldsymbol{2}} - \frac{2}{r_1} + V_1{}^{eff}(r_1) \tag{2-33}$$

The Schrödinger equation corresponding to the Hamiltonian above is [45]:

$$\widehat{H}_1{}^{eff}(\boldsymbol{r_1})\phi(\boldsymbol{r_1}) = \boldsymbol{\epsilon_1}\phi(\boldsymbol{r_1}) \tag{2-34}$$

The method of solving the Hartree-Fock equations of quantum mechanical systems like the one for the Helium atom is called the self-consistent field method.[45, 46] It is because of this that the Hartree-Fock method is more formally called Hartree-Fock Self Consistent Field (HF-SCF) method.[45] The procedure for solving the Hartree-Fock equation is as follows [45, 46]:

1. A form for the wave equation of the electron orbitals is guessed and used to evaluate the effective potential energy.
2. The effective potential energy equation is then solved using the guessed form of the wave equation.
3. The effective potential energy that was obtained is then used to evaluate the Schrödinger equation.
4. The new form of the Schrödinger equation is then used to evaluate a new, presumably better, effective potential energy.
5. The process is repeated until the convergence of the solutions is sufficient.

If one was to apply the HF-SCF method to systems other than the helium atom, the potential energy equation and the Hamiltonian are simply adjusted to contain more nuclei or electrons. An example of another system HF-SCF method works well for is the H_2^+ molecule. The adjusted Hamiltonian for this molecule is of the following notation [45]:

$$\widehat{H} = -\frac{1}{2}\left(\nabla_1{}^2 + \nabla_2{}^2\right) - \frac{1}{r_1} - \frac{1}{r_2} + \frac{1}{r_{12}} \tag{2-35}$$

The Schrödinger equation solved in the same self-consistent field method used for helium. The HF-SCF method is widely used in computational research.[63-66] HF-SCF is a very useful approximation method because it can give accurate results in calculation.[45] The accuracy of this method and the self-consistent nature are what undoubtedly makes it one of the most widely used computational methods in research today.

Perturbation theory is an approximation theory that can be used in simple quantum mechanical calculations that are carried out by hand as well as in more complex calculations requiring computational software. When perturbation theory is used in methods using computational software the Møller-Plesset (MP) perturbation theory is generally used.[46]

Møller and Plesset originally developed the theory to use the Hartree-Fock equation as the zero order perturbation theory term.[67, 68] However, Møller-Pleset differs from perturbation in that the first order perturbation and the charge density in the first order correction go to zero.[68] The second order corrections in Møller-Plesset calculations are greatly simplified by the special property of the first-order correction. In computational works the two most commonly used orders of theory are second (MP2) and fourth order (MP4).[46] The second order theory involves the excitation of two electrons relative to the ground state energy, while fourth order theory involves up to four electrons that are in excited states relative to the ground state energy.[46] MP2 calculations require a relatively modest amount of additional effort compared to Hartree-Fock calculations and can provide slight improvements in the solutions to certain problems like stable organic molecules.[45] There are multiple applications and types of studies in which Møller-Plesset has been applied in research.[69-71]

Many post Hartree-Fock methods have been developed since the advent of the Hartree-Fock Method to account for and advance upon the shortcomings of Hartree-Fock.[72] One inadequacy experienced in Hartree-Fock methods is that electron motion and repulsion are not represented in an instantaneous manner but rather an average.[72] One type of method that attempts to go beyond Hartee-Fock is Coupled-Cluster (CC) Theory. CC methods derive a wavefunction using the Hartree-Fock equation and adding a term for electron excitation.[46, 72] The equation used in CC methods may be represented in the following way [46]:

$$\psi_{CC} = e^{T}\Phi_0 \tag{2-36}$$

where

$$T = T_1 + T_2 + T_3 \; .... \tag{2-37}$$

The *"T"* term in the equation describes the excitations where T_1 represents the single excitation, T_2 represents double excitation, and so forth.[46] An advantage of the exponential term in CC methods describing the electron excitation is that excitations to all orders can be included, describing more of the correlation energy.[46] At each excitation beyond the first an increasing number of terms describes each excitation, inevitably complicating the term.[72] However, there is sufficient theoretical and numerical evidence that shows that contributions to the excitation term drastically decrease after the double excitation term.[72] This has led to the most commonly used CC method called Coupled-Cluster Singles-and-Doubles (CCSD) method which only includes the single and double excitations, as the name implies.[46, 72] There is also a CC method including the triple excited state that was termed the Coupled-Cluster Singles-Doubles-and-Triples (CCSDT).[72] The CCSD(T) method is another type of coupled cluster method that includes triple excitation states, but the CCSD(T) method uses a CCSD calculation followed by a perturbational approximation for the triple excited state.[72] The CCSD(T) method also differs from the CCSDT method in that it calculates systems as closed shelled and scales to one less order of magnitude with respect to the number of atoms [72]. The CC method does, unfortunately, have the disadvantage of being much more time consuming than the calculations carried out in Hartree-Fock methods.[46] Nevertheless, the great amount of time needed to carry out CC methods has not hindered the use of them as CC methods have been applied to a plethora of different aspects of computational research.[73-75]

Another method that is widely used in computational chemistry is Density Functional Theory. Density Functional Theory methods of computation are generally always based on the fundamental mathematical theorems of Hohenberg and Kohn.[46, 76] The first Hohenberg-Kohn theorem states that the ground-state electronic energy of an atom or molecule is a functional of the electron density.[46, 76] The term “functional” used in the theorem refers to a function of a function, and in the case of Density Functional Theory means that the ground state energy has a functional dependence on the electron density, which is a function of the electron coordinates.[46] The second theorem that Density Functional Theory relies on is rather apparent when thought of in classical terms. The second Hohenberg-Kohn theorem states that the electron density that minimizes the energy of the overall functional is the true electron density for the Schrödinger equation.[76] The function for the total electronic energy can be written in the following way [46]:

$$E = T + V_{nucl} + V_{rep} + E_{xc} \tag{2-38}$$

In the equation, T is the electronic kinetic energy, V_{nucl} is the attraction of the electrons to the nuclei, V_{rep} is the interelectronic coulomb repulsion, and E_{xc} is the exchange correlation energy.[46] As stated previously the energy is reliant on the electron density; therefore, the terms in the energy function have the electron density in the expressions. The general expression for the kinetic energy term is quite complicated and not fully known, but the expression is traditionally written in the following form [46]:

$$T = \frac{3}{10}(3\pi^2)^{2/3}\int \rho^{5/3} d\tau \tag{2-39}$$

The term for the electron density is ρ and it is the term that makes this expression and the others functionals of the electron density.[46] However, the kinetic energy term and others like it are rarely used in applications to molecules.[46] The more traditional expression containing the wave equation is [46]:

$$T = -\frac{1}{2}\sum_i \int \psi_i \nabla^2 \psi_i d\tau \tag{2-40}$$

The next term in the energy expression is the attraction of the electrons to the nuclei. The expression for this term can be written in the following form [46]:

$$V_{nucl} = -\sum_{a} \int \frac{Z_a \rho(1)}{r_{1a}} d\tau_1 \tag{2-41}$$

The interelectronic coulomb repulsion term is written as an expression that is dependent upon the electron density just as the electron attraction [46]:

$$V_{rep} = \frac{1}{2} \iint \frac{\rho(1)\rho(2)}{r_{12}} d\tau_1 d\tau_2 \tag{2-42}$$

The last term in the energy expression is the exchange term, which represents the effects of electron exchange and correlation on the total energy.[46] There is not an exact known expression for this term, but many approximate expressions have been developed that lead to a number of methods.[46] The simplest expression for this exchange term is called the local density approximation (LDA) and is given by the following expression [46]:

$$E_{xc} = -\frac{9}{8}\left(\frac{3}{\pi}\right)^{1/5} \alpha \int \rho(1)^{4/3} d\tau_1 \tag{2-43}$$

where α is equal to unity for a free-electron gas and values of about 0.7 are commonly used for molecules.[46] The LDA for the exchange term is generally not of high enough accuracy.[46] Nevertheless, the quality of the results can be improved by adding correction terms to the exchange expression that depend on the gradient of the electron energy.[46] The expressions for the total energy can be expressed in terms of electron density in Density Functional Theory, thus, eliminating the need to determine the wavefunction.[46] It is, however, difficult to obtain high accuracy from the approach excluding the wavefunction; therefore, a more common practice is to determining the electron density from wavefunctions obtained from self-consistent field calculations.[46] This approach involves solving the following equation [46]:

$$F\psi = \varepsilon\psi \tag{2-44}$$

where

$$F(1) = -\frac{1}{2}\nabla_1{}^2 - \sum_a \frac{Z_a}{r_{1a}} + \sum_j J_j(1) + V_{xc} \tag{2-45}$$

and

$$V_{xc} = \frac{\partial E_{xc}}{\partial \rho} \tag{2-46}$$

The theory gives the Kohn-Sham orbitals, ψ_i, and the electron density is obtained from the sum over occupied orbitals by the following [46]:

$$\rho = \sum_i |\psi_i|^2 \tag{2-47}$$

The advantage to Density Functional Theory is that the effort required to determine the electron equation is similar to or less than the effort required for Hartree-Fock calculations with the accuracy obtained in MP2 calculations.[46] Density Functional Theory has been used in a wide variety of research subjects and disciplines.[77-79] Density Functional Theory is still used in computational and theoretical works in chemistry today.[46]

Not all computational methods and approximation theories used are singularly focused on obtaining calculations through one specific method. Some computational methods can give the energy of a system, among other things, through the combination of other computational methods of varying accuracy and efficiency. One of the most recently developed methods using the combination of different computations is the correlation consistent composite approach (ccCA).[80, 81] The ccCA method is able to use successive calculation from varying methods to give the energy of a system on a final corrected function.[80, 81] The commanding principle of a “composite method” is to mimic the accuracy of more expensive and often computationally tasking methods using additive approximations obtained from the different calculations.[80] The expectation for the successive approximations used is that the error in each approximation will cancel, at least partially, when combined in the corrected term.[80] The energy function for the ccCA method is [82]:

$$E_{ccCA} = \Delta E_{MP2/CBS} + \Delta E_{CC} + \Delta E_{CV} + \Delta E_{SR} + \Delta E_{ZPE} \tag{2-48}$$

All of the terms in the function for the energy are determined from approximations in the ccCA computation. The first term in the overall energy function is the energy calculated from the second order Møller-Plesset (MP2) complete basis set calculation.[80, 81] However, a complete basis set cannot actually be used, so this calculation is extrapolated from successive MP2 calculations of increasingly larger basis sets.[80, 81] The next term in the function is the correlation correction, which is the difference between the CCSD(T) calculation and an MP2 calculation that uses a moderately sized basis set [82]:

$$\Delta E_{CC} = E_{\mathrm{CCSD(T)/cc-pVTZ}} - E_{MP2/cc-pVTZ} \tag{2-49}$$

The next term in the overall energy function is the core valence correction.[82] This correction is given by the difference between an MP2 calculation over all the electrons in the molecule and an MP2 using only the valence electrons.[80, 81] This correction is given by the following equation [82]:

$$\Delta E_{CV} = E_{MP2(FCI)/aug-cc-pCVTZ} - E_{MP2/aug-cc-pVTZ} \tag{2-50}$$

The basis sets used in calculations for the core valence correction are augmented basis sets and include diffuse functions.[82] The next term in the overall energy function is the scalar-relativistic correction.[82] It is calculated using the Douglas-Kroll method and is given by the following equation [82]:

$$\Delta E_{SR} = E_{MP2/cc-pVTZ-DK} - E_{MP2/cc-pVTZ} \tag{2-51}$$

The final term in the overall energy function is the zero point energy correction.[82] This term is obtained from a vibrational frequency calculation using a DFT approximation.[81] The ccCA method has been used in a few different types of computational and theoretical research [83-85], but the method remains relatively new and unexplored.

CHAPTER 3

METHODOLOGY AND RESULTS

Overview

In this research, two spin traps were evaluated computationally to determine the rate constants of the spin trap-hydroxyl radical addition reactions that each undergoes. The two spin traps chosen for this work were 5, 5-Dimethyl-1-pyrroline N-oxide (DMPO) and 2-ethoxycarbonyl-2-methyl-3, 4-dihydro-2H-pyrrole-l-oxide (EMPO). These two spin traps were chosen because of the common occurrence of both spin traps in both computational and experimental research literature. Both spin traps undergo an addition reaction with the hydroxyl radical as discussed in the introduction. The structure of the two spin traps can be seen in better detail in the following figures.

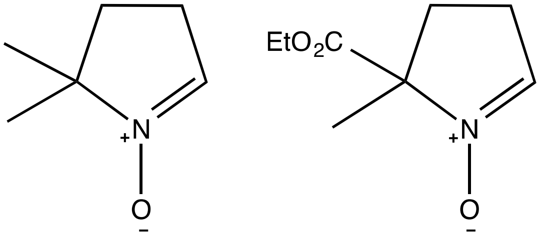


Figure 2. Skeletal structures of DMPO (left) and EMPO (right).

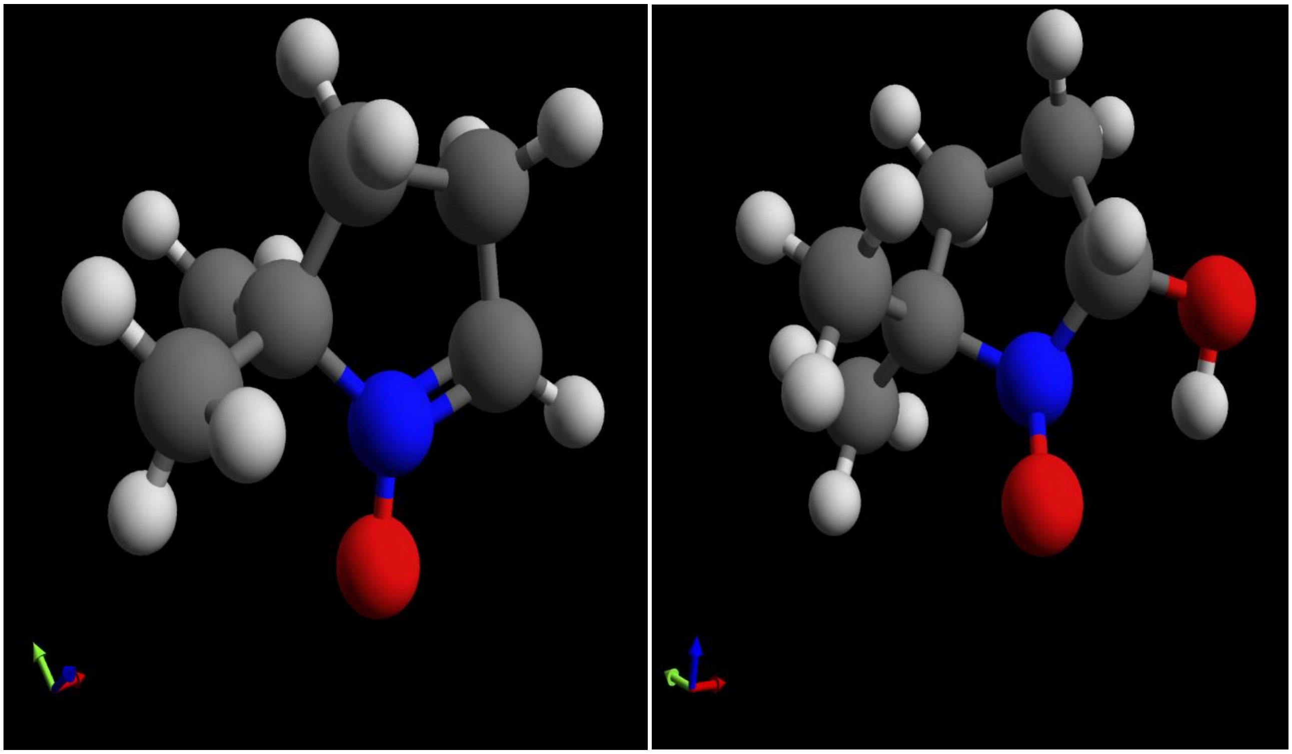


Figure 3. Ball and stick model of DMPO (left) and the DMPO-OH adduct (right).

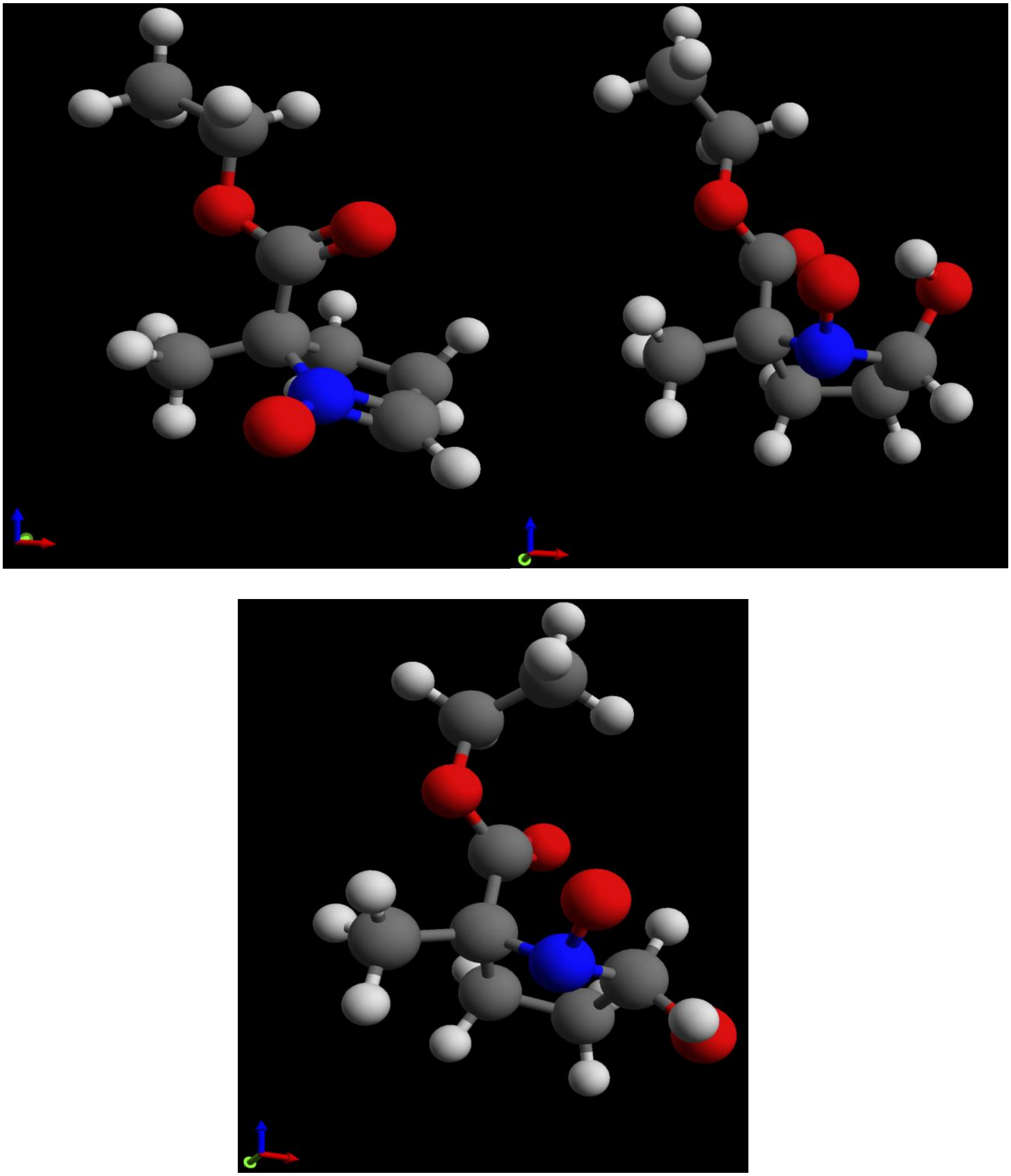


Figure 4. Ball and stick model of EMPO (top left), the EMPO-OH adduct where the hydroxyl group adds on the same side as the ester (top right), and the EMPO-OH adduct where the hydroxyl group adds on the side opposite the ester (bottom).

Computational Details

The approximation method used to evaluate the free energies of the hydroxyl radical, the two spin traps, and the three spin trap-radical adducts was the ccCA method.[80-82] As stated earlier this method uses successive calculations using different approximation methods to give energies that are used in a corrected energy term to give the corrected energy for the approximation. NWChem computational software was used to carry out the calculations and the particular variation of the ccCA method native to this software was used [82]. The first step in this particular ccCA method is a geometry optimization carried out using Hartree-Fock Self-Consistent Field using the cc-pVTZ basis set [80] and DFT/B3LYP (DFT using the B3LYP functional [86]). The geometry optimization is followed by successive energy calculations using second order Møller-Plesset (MP2) approximations using the following basis sets, respectively: cc-pVTZ, aug-cc-pVDZ, aug-cc-pVTZ, aug-cc-pVQZ, FC1/cc-pCVTZ,, ccpVTZ-DK. The MP2 calculations were followed by a CCSD(T) calculation that used the cc-pVTZ basis set. Once the calculations are finished the correction terms for the energy are extrapolated from the various approximations. The input files used for the ccCA calculation are given in the following figures.

Table I. NWChem input file for hydroxyl radical ccCA calculation.

```
scratch_dir /home/shorthb/nwchem_scratch
Title "OH_ccCA_Edit"

Start  OH_ccCA_Edit

echo

charge 0

geometry autosym units angstrom
 O     0.00000     0.00000     -0.109917
 H     0.00000     0.00000     0.864702
end
```

Table I. (Continued)

```
ecce_print /home/shorthb/nwchem_run/Summer/OH_ccCA_Edit/ecce.out

ccca
  dft
  uhf
  tce
  nopen 1
end

task ccca
```

Table II. NWChem input file for DMPO ccCA calculation.

```
scratch_dir /scratch/shorthb
Title "DMPO-ccCA_Edit-3-1"

Start  DMPO-ccCA_Edit-3-1

echo

memory 200 mw

charge 0

geometry autosym units angstrom
 C     0.337359     1.97947     -0.00186963
 H     0.426525     2.79208     0.721196
 C     1.28281     0.801965     0.329254
 H     1.53573     0.823478     1.38899
 H     2.21420     0.845030     -0.232651
 C     0.485642     -0.475560     0.0127460
 C     0.619267     -1.56823     1.06337
 H     0.401201     -1.18227     2.05953
 H     -0.0723824     -2.38106     0.851983
 H     1.63774     -1.95829     1.06092
 C     0.743325     -1.02032     -1.39286
 H     6.90963e-05     -1.77657     -1.64047
 H     0.692955     -0.228147     -2.14117
 H     1.73391     -1.47330     -1.44049
 N     -0.954276     0.0388375     0.0287678
 H     0.553191     2.41594     -0.983381
 C     -1.00721     1.33932     0.0209321
 H     -1.96978     1.82352     -0.0193157
```

Table II. (Continued)

```
 O     -1.90522     -0.788972     -0.00174647
end

ecce_print /home/shorthb/nwchem_run/Summer/DMPO-ccCA_Edit-3-
1/ecce.out

basis "ao basis" spherical print
H    S
    33.870000000000     0.006068000000
     5.095000000000     0.045308000000
     1.159000000000     0.202822000000
H    S
     0.325800000000     1.000000000000
H    S
     0.102700000000     1.000000000000
H    P
     1.407000000000     1.000000000000
H    P
     0.388000000000     1.000000000000
H    D
     1.057000000000     1.000000000000
O    S
 15330.000000000000     0.000508000000    -0.000115000000
  2299.000000000000     0.003929000000    -0.000895000000
   522.400000000000     0.020243000000    -0.004636000000
   147.300000000000     0.079181000000    -0.018724000000
    47.550000000000     0.230687000000    -0.058463000000
    16.760000000000     0.433118000000    -0.136463000000
     6.207000000000     0.350260000000    -0.175740000000
     0.688200000000    -0.008154000000     0.603418000000
O    S
     1.752000000000     1.000000000000
O    S
     0.238400000000     1.000000000000
O    P
    34.460000000000     0.015928000000
     7.749000000000     0.099740000000
     2.280000000000     0.310492000000
O    P
     0.715600000000     1.000000000000
O    P
     0.214000000000     1.000000000000
O    D
     2.314000000000     1.000000000000
```

Table II. (Continued)

```
O    D
     0.645000000000     1.000000000000
O    F
     1.428000000000     1.000000000000
C    S
  8236.000000000000     0.000531000000    -0.000113000000
  1235.000000000000     0.004108000000    -0.000878000000
   280.800000000000     0.021087000000    -0.004540000000
    79.270000000000     0.081853000000    -0.018133000000
    25.590000000000     0.234817000000    -0.055760000000
     8.997000000000     0.434401000000    -0.126895000000
     3.319000000000     0.346129000000    -0.170352000000
     0.364300000000    -0.008983000000     0.598684000000
C    S
     0.905900000000     1.000000000000
C    S
     0.128500000000     1.000000000000
C    P
    18.710000000000     0.014031000000
     4.133000000000     0.086866000000
     1.200000000000     0.290216000000
C    P
     0.382700000000     1.000000000000
C    P
     0.120900000000     1.000000000000
C    D
     1.097000000000     1.000000000000
C    D
     0.318000000000     1.000000000000
C    F
     0.761000000000     1.000000000000
N    S
 11420.000000000000     0.000523000000    -0.000115000000
  1712.000000000000     0.004045000000    -0.000895000000
   389.300000000000     0.020775000000    -0.004624000000
   110.000000000000     0.080727000000    -0.018528000000
    35.570000000000     0.233074000000    -0.057339000000
    12.540000000000     0.433501000000    -0.132076000000
     4.644000000000     0.347472000000    -0.172510000000
     0.511800000000    -0.008508000000     0.599944000000
N    S
     1.293000000000     1.000000000000
N    S
     0.178700000000     1.000000000000
```

Table II. (Continued)

```
N    P
    26.630000000000     0.014670000000
     5.948000000000     0.091764000000
     1.742000000000     0.298683000000
N    P
     0.555000000000     1.000000000000
N    P
     0.172500000000     1.000000000000
N    D
     1.654000000000     1.000000000000
N    D
     0.469000000000     1.000000000000
N    F
     1.093000000000     1.000000000000
END

scf
  direct
end


dft
  direct
  mult 1
  XC b3lyp
  iterations 200
  mulliken
end

mp2
  scratchdisk 2048
end

ccsd
  nodisk
end

driver
  default
  maxiter 100
end

task ccca
```

Table III. NWChem input file for EMPO ccCA calculation.

```
scratch_dir /scratch/shorthb
Title "EMPO_ccCA_Edit"

Start  EMPO_ccCA_Edit

echo

charge 0

geometry autosym units angstrom
 C     1.22758     2.64109     0.178266
 H     2.16428     2.42414     -0.341462
 H     1.31254     3.64904     0.588612
 C     0.932977     1.59272     1.27531
 H     0.503731     2.07751     2.15079
 H     1.83078     1.06527     1.58578
 C     -0.113778     0.635879     0.675696
 C     -1.26534     0.281922     1.60011
 H     -1.69753     1.19331     2.01307
 H     -2.03603     -0.256657     1.05709
 H     -0.911236     -0.339184     2.42188
 C     0.0668116     2.49921     -0.740292
 N     -0.657518     1.44500     -0.506036
 H     -0.192478     3.12805     -1.57687
 C     0.574878     -0.579275     0.0270123
 O     1.61651     -0.491964     -0.575576
 O     -0.0986627     -1.71741     0.202416
 C     0.455874     -2.89745     -0.432629
 H     1.45885     -3.06244     -0.0393157
 H     0.543802     -2.69980     -1.50033
 C     -0.472103     -4.05327     -0.139757
 H     -1.46920     -3.86195     -0.534952
 H     -0.0858459     -4.95968     -0.607373
 H     -0.553038     -4.23024     0.932620
 O     -1.66867     1.01766     -1.12533
end

ecce_print
/home/shorthb/nwchem_run/Summer/EMPO_ccCA_Edit/ecce.out

basis "ao basis" spherical print
H    S
    33.870000000000     0.006068000000
     5.095000000000     0.045308000000
```

Table III. (Continued)

```
     1.159000000000     0.202822000000
H    S
     0.325800000000     1.000000000000
H    S
     0.102700000000     1.000000000000
H    P
     1.407000000000     1.000000000000
H    P
     0.388000000000     1.000000000000
H    D
     1.057000000000     1.000000000000
O    S
 15330.000000000000     0.000508000000    -0.000115000000
  2299.000000000000     0.003929000000    -0.000895000000
   522.400000000000     0.020243000000    -0.004636000000
   147.300000000000     0.079181000000    -0.018724000000
    47.550000000000     0.230687000000    -0.058463000000
    16.760000000000     0.433118000000    -0.136463000000
     6.207000000000     0.350260000000    -0.175740000000
     0.688200000000    -0.008154000000     0.603418000000
O    S
     1.752000000000     1.000000000000
O    S
     0.238400000000     1.000000000000
O    P
    34.460000000000     0.015928000000
     7.749000000000     0.099740000000
     2.280000000000     0.310492000000
O    P
     0.715600000000     1.000000000000
O    P
     0.214000000000     1.000000000000
O    D
     2.314000000000     1.000000000000
O    D
     0.645000000000     1.000000000000
O    F
     1.428000000000     1.000000000000
C    S
  8236.000000000000     0.000531000000    -0.000113000000
  1235.000000000000     0.004108000000    -0.000878000000
   280.800000000000     0.021087000000    -0.004540000000
    79.270000000000     0.081853000000    -0.018133000000
```

Table III. (Continued)

```
     25.590000000000     0.234817000000    -0.055760000000
      8.997000000000     0.434401000000    -0.126895000000
      3.319000000000     0.346129000000    -0.170352000000
      0.364300000000    -0.008983000000     0.598684000000
C     S
      0.905900000000     1.000000000000
C     S
      0.128500000000     1.000000000000
C     P
     18.710000000000     0.014031000000
      4.133000000000     0.086866000000
      1.200000000000     0.290216000000
C     P
      0.382700000000     1.000000000000
C     P
      0.120900000000     1.000000000000
C     D
      1.097000000000     1.000000000000
C     D
      0.318000000000     1.000000000000
C     F
      0.761000000000     1.000000000000
N     S
  11420.000000000000     0.000523000000    -0.000115000000
   1712.000000000000     0.004045000000    -0.000895000000
    389.300000000000     0.020775000000    -0.004624000000
    110.000000000000     0.080727000000    -0.018528000000
     35.570000000000     0.233074000000    -0.057339000000
     12.540000000000     0.433501000000    -0.132076000000
      4.644000000000     0.347472000000    -0.172510000000
      0.511800000000    -0.008508000000     0.599944000000
N     S
      1.293000000000     1.000000000000
N     S
      0.178700000000     1.000000000000
N     P
     26.630000000000     0.014670000000
      5.948000000000     0.091764000000
      1.742000000000     0.298683000000
N     P
      0.555000000000     1.000000000000
N     P
      0.172500000000     1.000000000000
N     D
```

Table III. (Continued)

```
     1.654000000000     1.000000000000
N    D
     0.469000000000     1.000000000000
N    F
     1.093000000000     1.000000000000
END

dft
  mult 1
  XC b3lyp
  iterations 200
  mulliken
end

driver
  default
  maxiter 100
end

task ccca
```

Table IV. NWChem input file for DMPO-OH ccCA calculation.

```
scratch_dir /scratch/shorthb
Title "DMPO-OH_CCCA_Edit-1"

Start  DMPO-OH_CCCA_Edit-1

echo

memory 200 mw

charge 0

geometry autosym units angstrom
 C     1.44201     1.07257     -0.631279
 H     1.61836     0.915646     -1.69584
 H     2.12555     1.84449     -0.284749
 C     1.57825     -0.247004     0.153766
 H     1.78454     -0.0291230     1.20114
 H     2.38811     -0.868950     -0.224975
 C     0.212333     -0.952171     0.0258281
 C     -0.236783     -1.64271     1.31255
```

Table IV. (Continued)

```
 H     -0.217039     -0.947699     2.15191
 H     -1.25222     -2.02117     1.20451
 H     0.426288     -2.47886     1.53817
 C     0.152930     -1.92424     -1.15956
 H     -0.878593     -2.22528     -1.34096
 H     0.539044     -1.46460     -2.07033
 H     0.743298     -2.81697     -0.949011
 N     -0.688384     0.202252     -0.267218
 O     -1.95575     0.135315     -0.204474
 C     -0.00217926     1.48763     -0.412872
 H     -0.455539     2.01846     -1.25279
 O     -0.102091     2.26056     0.770331
 H     -1.04056     2.38223     0.957389
end

ecce_print /home/shorthb/nwchem_run/Summer/DMPO-OH_CCCA_Edit-
2/ecce.out

basis “ao basis” 46artesian print
  H library “6-31G”
  O library “6-31G”
  C library “6-31G”
  N library “6-31G”
END

scf
  direct
  ROHF
  nopen 1
  maxiter 200
end

dft
  direct
end

mp2
  scratchdisk 2048
end

ccsd
  nodisk
end
```

Table IV. (Continued)

```
driver
  default
  maxiter 100
end

ccca
  dft
  uhf
  tce
  nopen 1
end

task ccca
```

Table V. NWChem input file for EMPO-OH ccCA calculation.

```
scratch_dir /scratch/shorthb
Title "EMPO-OH_CCCA_Edit-1"

Start  EMPO-OH_CCCA_Edit-1

echo

charge 0

geometry autosym units angstrom
 C     -0.155741     0.172467     -0.0727843
 H     0.210643     -0.432633     -0.931561
 H     -0.917985     0.898964     -0.418484
 C     1.04096     0.863080     0.573428
 H     0.655721     1.72637     1.16593
 H     1.78081     1.23402     -0.163131
 C     1.61334     -0.197255     1.51020
 C     2.25849     0.469223     2.72358
 H     1.50654     1.07531     3.27140
 H     2.67999     -0.290007     3.41095
 H     3.06890     1.14797     2.38269
 C     2.59410     -1.08846     0.765296
 O     2.15144     -2.08013     0.180555
 O     3.94106     -0.717554     0.674503
 C     4.65213     -1.60559     -0.165425
 H     4.22360     -1.58864     -1.19107
 H     4.61007     -2.63891     0.243228
 C     6.11152     -1.19896     -0.259897
 H     6.58683     -1.22663     0.739338
```

Table V. (Continued)

```
 H     6.64935     -1.90473     -0.926280
 H     6.20231     -0.179087     -0.679982
 C     -0.694101     -0.741911     1.02216
 N     0.440207     -0.950662     1.88223
 O     0.510375     -1.91342     2.59525
 O     -1.13334     -1.95909     0.473612
 H     -2.07771     -2.07950     0.753975
 H     -1.49782     -0.207723     1.57977
end

ecce_print /home/shorthb/nwchem_run/Summer/EMPO-OH_CCCA_Edit-
1/ecce.out

basis "ao basis" cartesian print
  H library "6-31G"
  O library "6-31G"
  C library "6-31G"
  N library "6-31G"
END

scf
  ROHF
  nopen 1
  maxiter 200
end

driver
  default
  maxiter 100
end

ccca
  dft
  uhf
  tce
  nopen 1
end

task ccca
```

As the title implies, the property of focus that this research set out to find is the rate constants of the various addition reactions of the spin traps and the hydroxyl radical. However, finding the rate constants is a trivial part of the process of this research as the rate constant is just extrapolated from the free energies. There is no approximation method or calculation included in the ccCA method that accounts for the rate constants. The free energies obtained from the ccCA calculations are used to obtain the rate constants upon finding the free energies of both the products and reactants. The following equation is the Arrhenius Equation and is the equation from which the rate constants are extrapolated:

$$k = Aexp(\frac{-E_a}{RT}) \tag{3-1}$$

Results and Discussion

The spin traps that were evaluated in this study were chosen because of the frequent occurrence of both in computational and experimental literature pertaining to spin traps and spin trapping. The results obtained thus far from the ccCA method are not very explanatory of the work that has been done towards the progress of this research. There were multiple problems that occurred along the course of this research that were both predicted and unforeseen. The original research equipment had 4-terabytes of hard drive space to run the calculations, but this equipment was insufficient as the calculation crashed the 4-terabyte drive array rendering it unusable. The research came down to a waiting game, as it was necessary to acquire funds and then to purchase new and better equipment with double the terabytes of the original equipment. After finally receiving the equipment, the ccCA method ran well, but took weeks to complete the entre calculation for just the hydroxyl radical. While the time being taken to complete the calculation was a problem that was predicted, the time still hindered the production of more results. The new equipment was excellent and got the research farther than the original equipment, but the 8-terabyts of hard drive space was still insufficient once the calculation got to the CCSD(T) calculation. Once the calculation failed on the new equipment the calculations were moved to the university cluster and is currently still running using 9-terabytes of the university’s 13-terabytes. There are some intermediate results in the following tables, but no rate constants have been given yet as there have not been enough results obtained from the energy calculations.

Table VI . Free Energies of reactants and products of the reactions.

•OH	DMPO	EMPO	DMPO-OH	EMPO-OHa	EMPO-OHb
-75.706059	Pending	Pending	Pending	Pending	Pending

Table VII. Intermediate results for the ccCA calculations in Hartrees.

Energy Step	•OH	DMPO	EMPO	DMPO-OH	EMPO-OHa	EMPO-OHb
Geometry (B3LYP/cc-pVTZ)	-75.7269664807	-365.3125198058	-593.2684816829	-441.1642975980	-669.1216274864	-669.1217436298
MP2/cc-pVTZ	-75.2635160463	-364.4438152262	-591.9418567600	-440.1537846895	-667.6519272416	-667.6529770718
MP2/aug-cc-pVDZ	-75.2553200242	-364.1493071639	-591.4752250098	-439.8038135147	-667.1296587330	-667.1309298976
MP2/aug-cc-pVTZ	-75.2721004602	-364.4740587438	-591.9900526021	-440.1905549779	-667.7064489052	-667.7074640326
MP2/aug-cc-pVQZ	-75.2769812228	-364.5768829976	Pending	Pending	Pending	Pending
MP2(FC1)/cc-pCVTZ	-75.2722744406	-364.4853921046	-592.3384436472	-440.6466444626	Pending	-668.3727279819
MP2/ccpVTZ-DK	-75.3154449765	-364.8743750302	-591.9199357664	-440.3745246980	Pending	-668.0069385321
CCSD(T)/cc-pVTZ	-75.6377121160	Pending	Pending	Pending	Pending	Pending

CHAPTER 4

CONCLUSIONS

The ccCA method is a relatively new and untested method that has been scarcely explored in computational literature. Due to the fact that this method has little research to reference there were some problems with the method that hindered the production of more results. There can be no realistic conclusions made from the little results obtained thus far. The calculations in the ccCA method took much more hard drive space than was ever imagined at the start of this project, and the time taken to complete all of the approximations in the ccCA method was much more than predicted at the beginning of the research. However, the calculations are still running and will hopefully provide accurate results in the not to distant future.

REFERENCES

1. Brown WH, Foote CS, Iverson BL, Anslyn E. *Organic chemistry*. 6th ed.Cengage Learning: Mason, Ohio, 2012; 301.
2. Becker M, Foster C, Franzen C, Hartrath J, Kirsten E, Knuth J, Klinkhammer KW, Sharma A, Hinderberger D. Persistent Radicals of Trivalent Tin and Lead. *Inorg Chem.* **2008**, 47, 9965-78.
3. Roberfroid MB, Calderon PB. Definitions, Properties, and Reactions of Radicals. *Free Radicals and Oxidation Phenomena in Biological Systems*; Marcel Dekker: New York; 1995; 15.
4. Prousek J. Fenton chemistry in biology and medicine. *Pure Appl Chem* **2007**, 79. 2325-38.
5. Liu-Smith F, Dellinger R, Meyskens Jr. FL. Updates of Reactive Oxygen Species in Melanoma Etiology and Progression. *Arch Biochem Biophys* **2014,** (0).
6. Kohen R, Nyska A. Oxidation of Biological Systems: Oxidative Stress Phenomena, Antioxidants, Redox Reactions, and Methods for their Quantification. *Toxicological Pathology* **2002,** *30*, 620-650.
7. Cadet J, Wagner J R. Oxidatively Generated Base Damage to Cellular DNA by Hydroxyl Radical and One-Electron Oxidants: Similarities and Differences. *Archives of Biochemistry and Biophysics* **2014.**
8. Simic M. Free radical mechanisms in autoxidation processes. *J Chem Educ* **1981**, 58. 125-31.
9. Perron NR, Brumaghim. A Review of the Antioxidant Mechanisms of Polyphenol Compounds Related to Iron Binding. *Cell Biochem Biophys* **2009** 53. 75-100.
10. Wardman P, Candeia LP. Fenton chemistry: An introduction. *Radiation Research*

1996, 145. 523-31.

11. Fenton HJH. Oxidation of tartaric acid in presence of iron. *J Chem Soc* **1894**, 65. 899-910.

12. Tarr, M. A. *Chemical Degradation Methods for Wastes and Pollutants: Environmental and Industrial Applications.* Marcel Dekker Inc.: New York, NY, 2003; 25.

13. Jones, C. W. *Applications of Hydrogen Peroxide and Derivatives.* The Royal Society of Chemistry: Cambridge, UK, 1999; 45.

14. Anan'ev V, Kriger L, Poroshina M. Peroxynitrite formation by ^{60}Co gamma-ray irradiation of alkali nitrate crystals. *Chemical Physics Letters* **2002,** 364. 554-558.

15. Plumb RC, Edwards JO. Color centers in UV-irradiated nitrates. *J. Phys. Chem.* **1992,** 3245–3247.

16. Trujillo M, Naviliat M, Alvarez MN, Peluffo G, Radi R. Peroynitrite biochemistry: formation, reactions, and detection. *Analusis.* **2000,** 518-527.

17. Halliwell B, Gutteridge J. *Free radicals in biology and medicine.* 4th ed. Oxford University Press: Oxford, UK, 1999.

18. Nalawade P, Naumov S, Kapoor S. Comparative study of p-amino benzhydrazide and m amino benzhydrazideby free radicals and free electron transfer. *J. of Phys. Org. Chem.* **2013,** 26. 870-878.

19. Benjamin M, Lawler DF. *Water Quality Engineering; Physical/Chemical Treatment Process.* John Wiley and Sons Inc.: Hoboken, New Jersey, 2013; 470.

20. Demore WB**.** Experimental and estimated rate constants for the reactions of hydroxyl radicals with several halocarbons. *J. Phys. Chem.* **1996,** 100. 5813-5820.

21. Shiroudi A, Deleuze MS, Canneaux S. Theoretical study of the oxidation mechanisms of

naphthalene initiated by hydroxyl radicals: the OH-addition pathway. *J. Phys. Chem. A.* **2014,** 118. 4593-4610.

22. Yadav A, Mishra PC. Reactivities of hydroxyl and perhydroxyl radicals toward cytosine and thymine: A comparative study. *International Journal of Quantum Chemistry.* **2013,** 113. 56-62.
23. Simandan T, Sun J, Dix TA. Oxidation of DNA bases, deoxyribonucleosides and homopolymers by peroxyl radicals. *Biochem. J.* **1998,** 335. 233-240.
24. Fujita S, Steenken S. Pattern of hydroxyl radical addition to uracil and methyl- and carboxyl-substituted uracils. Electron transfer of hydroxyl adducts with N,N,N',N'-tetramethyl-p-phenylenediamine and tetranitromethane. *J. Am. Chem. Soc.* **1981,** 103. 2540-2545.
25. Kim SU, Villamena, F. Relativities of superoxide and hydroperoxyl radicals with disubstituted cyclic nitrones: a DFT study. *J. Phys. Chem. A.* **2012,** 116. 886-898.
26. Konda SSM. Computational Investigation of Spin Traps Using Hybrid Solvation Models. Masters Thesis, East Tennessee State University, Johnson City, TN, 2009.
27. Mason RP, Knecht KT. In Vivio Detection of Radical Adducts by Electron Spin Resonance. *Methods in Enzymology: Oxygen Radicals in Biological Systems Part C,* Packer, L; Academic Press Inc.: San Diego, California, 1994; 233, 112.
28. Janzen EG, Blackburn BJ. Detection and identification of short-lived free radicals by an electron spin resonance-trapping technique. *J. Am. Chem. Soc.***1968,** 90. 5909–5910.
29. Tande JF. A Computational Chemistry Study of Spin Traps. Masters Thesis, East Tennessee State University, Johnson City, TN, 2007.
30. Iwamura M, Inamoto N. Novel formation of nitroxide radicals by radical addition to nitrones. *Bull. Chem. Soc. Japan.* **1967,** 40: 702-703.

31. Iwamura M, Inamoto N. Reactions of nitrones with free radicals I. radical 1,3-addition to nitrones. *Bull. Chem. Soc. Japan.* **1970,** 43: 856-860.

32. Janzen EG, Blackburn BJ. Detection and identification of short-lived free radicals by electron spin resonance trapping techniques (spin trapping). Photolysis of organolead, -tin, and -mercury compounds. *J. Am. Chem. Soc.* **1969,** 90: 4481-4490.

33. Swartz HM. Interactions between cells and nitroxides and their implications for their uses as bio physical probes and as metabolically responsive contrast agents for *in vivo* NMR. *Bull. Mag. Reson.* **1986,** 8: 172-175.

34. Pou S, Pou WS, Bredt DS, Snyder SH, Rosen GM. Generation of superoxide by purified brain nitric oxide synthase. *J. Biol. Chem.* **1992,** 267: 24173-24176

35. Harbour JR, Bolton JR. Superoxide formation in spinach chloroplasts: Electron spin resonance detection by spin trapping. *Biochem. And Biophys. Res. Comm.* **1975,** 64: 803-807.

36. Villamena F, Locigno EJ, Rockenbauer A, Hadad CM, Zweier JL. Theoretical and experimental studies of the spin trapping of inorganic radicals by 5,5-dimethyl-1-pyrroline N-oxide (DMPO). 2. carbonate radical anion. *J Phys Chem A.* **2007,** 111: 384-391.

37. Villamena F, Rockenbauer A, Galluci J, Velayuthaum M, Hadad CM, Zweier JM. Spin trapping by 5-carbamoyl-5-methyl-1-pyrroline *N*-oxide (AMPO): theoretical and experimental studies. *J. Org. Chem.* **2004,** 69: 7994-8003.

38. Acken BJ, Gallis DE, Warshaw JA, Crist DR. Electrochemical behavior of *C*-methoxy, amino, cyano, and mercapto nitrones. *Can. J. Chem.* **1992,** 70: 2076-2080.

39. Gallis DE, Warshaw JA, Acken BJ, Crist DR. Electronic nature of *C*-methoxy, amino, cyano,

and mercapto nitrones. *Coll. Czech. Chem. Comm.* **1993,** 58: 125-141.

40. Zeghdaoui A, Tuccio B, Finet JP, Cerri V, Tordo P. β-Phosphorylated α-phenyl-*N*-*tert*-butylnitrone (PBN) analogues: a new series of spin traps for oxyl radicals. *J. Chem. Soc., Perkin Trans. 2.* **1995,** 12: 2087-2089.

41. Villamena FA, Hadad CM, Zweier JL. Theoretical study of the spin trapping of hydroxyl radical by cyclic nitrones: a density functional theory approach. *J. Am. Chem. Soc.* **2004,** 126: 1816-1829.

42. Olive G, Mercier A, Moigne FL, Rockenbauer A, Tordo P. 2-ethoxycarbonyl-2-methyl-3,4-dihydro-2*H*-pyrrole-1-oxide: evaluation of the spin trapping properties**.** *Free Rad. Biol. & Med.* **2000,** 28: 403-408.

43. Zhao H, Joseph J, Zhang H, Karoui H, Kalyanaraman B. Synthesis and biochemical applications of a solid cyclic nitrone spin trap: a relatively superior trap for detecting superoxide anions and glutathiyl radicals. *Free Rad. Biol. & Med.* **2001,** 31: 599-606.

44. Liu Y, Wang L, Nie Z, Ji Y, Liu Y, Liu K, Tian Q. Effect of the phosphoryl substituent in the linear nitrone on the spin trapping of superoxide radical and the stability of the superoxide adduct: combined experimental and theoretical studies. *J. Org. Chem.* **2006,** 71: 7753-7762.

45. McQuarrie D, Simon J. *Physical Chemistry: A Molecular Approach.* University Science Books: United States, 1997.

46. Ratner M A, Schatz G C. *Introduction to Quantum Mechanics in Chemistry.* Prentice Hall: Upper Saddle River, New Jersey, 2001.

47. McMahon D. *Quantum Mechanics Demystified.* McGraw-Hill: New York, 2006.

48. Cullen, K. *Physics: The People Behind The Science.* Chelsea House Books, United States,

2006.

49. Bowman G E. *Essential Quantum Mechanics.* Oxford University Press, New York, 2008.

50. Schrödinger E. On the relationship of the Heisenberg-Born-Jordan quantum mechanics to mine. *Ann der Phy.* **1926,** 79: 734-757.

51. Schrödinger E. Quantization as an eigenvalue problem. *Ann. der Phy.* **1926,** 79: 361-376.

52. Schrödinger E. Quantization as an eigenvalue problem. *Ann. der Phy.* **1926,** 79: 489-527.

53. Schrödinger E. Quantization as an eigenvalue problem. *Ann. der Phy.* **1926,** 79: 94-106.

54. Born M. On the quantum mechanics of collisions. *Zur. Quant. der Natur.* **1926,** 37: 863-867.

55. Levi A F L. *Applied Quantum Mechanics.* Cambridge University Press, New York, 2003.

56. Jecko T. On the mathematical treatment of the born-oppenheimer approximation. *J. of Math. Phys.* **2014,** 55: 53504.

57. Braaten E, Langmack E, Smith D H. Born-oppenheimer approximation of the XYZ mesos. *High Ener. Phys Phenom.* **2014,** 1-40.

58. Diestler DJ. Beyond the born-oppenheimer approximation: a treatment of electronic flux density in electronically adiabatic molecular processes. *J. Phys Chem. A.* **2013,** 117: 4698-4708.

59. Yu C, Fu N, Dai C, Wang H, Zhang G, Yao J, Time-dependent born-oppenheimer approximation approach for schrödinger equation: application to H_2^+. *Optics Communications.* **2013,** 300: 199-203.

60. Schumacher B, Westmoreland M. *Quantum Processes, Systems, & Information.* Cambridge University Press, New York, 2010.

61. Gil-Marin H, Wagner C, Noreña J, Verde L, Percival W. Dark matter and halo bispectrum in

redshift space: theory and applications. *J. of Cosmology and Astroparticle Phys.* **2014,** 2014: 29.

62. Perlin E Y, Levitskii R S, Ivanov A V, Eliseev K A. Nonlinear optical absorption in crystals with deep impurities: I. Probablilities of two-center phototransitions between band and impurity states. *Optics and Spectroscopy.* **2015,** 118: 229-234.
63. Zhu W, Ding G, Dong B. Gate modulation and angle-resolved photoabsorption spectra of zigzag-edge grapheme nanoribbons. *J. Appl. Phys.* **2013,** 113: 103510-1-103510-5.
64. Han Y, Liu Y, Rockenbauer A, Zweier J, Durand G, Villamena F, Lipophilic ß-cyclodextrin cyclic-nitrone conjugate: synthesis and spin trapping studies. *J. Org. Chem.* **2009,** 74: 5369-5380.
65. Chiesa M, Paganini M C, Spoto G, Giamello E, Valentin C, Del Vitto A, Pacchioni G. Single electron traps at the surface of polycrystalline MgO: assignment of the main trapping sites. *J. Phy. Chem. B.* **2005,** 109: 7314-7322.
66. Wang H. Iterative calculation of energy eigenstates employing the multilayer multiconfiguration time-dependent hartree theory. *J. Phys. Chem. A* **2014,** 118: 9253-9261.
67. Schafer H. *Quantum Chemistry: The Development of Ab Initio Methods in Molecular Electronic Structure Theory*. Clarendon Press: Oxford, Uk, 1984.
68. Møller C, Plesset M. Note on an approximation treatment for many-electron systems. *Phys. Rev.* **1934,** 46: 618-622.
69. Badawi H, Förner W, Al-Saadi A. DFT-B3LYP versus MP2, MP3, and MP4 calculations of the structural stability of azidoketene O=C=CH-NNN. *J. Mol. Struc.: THEOCHEM.* **2004,** 712: 131-138.

70. Fletcher G, Fedorov D, Pruitt S, Windus T, Gordon M. Large-Scale MP2 calculations on the blue gene architecture using the fragment molecular orbital method. *J. Chem. Theory Comput.* **2012,** 8: 75-79.

71. An W, Bulusu S, Gao Y, Zeng X. Relative stability of planar versus double-ring tubular isomers of neutral and anionic boron cluster B_{20} and B_{20}^-. **2006,** 124: 154310-1-154310-6.

72. Jerzy C. *Quantum-Mechanical Prediction of Thermochemical Data.* Kluwer Academic Publishers: New York, NY, 2001.

73. Mahapatra U S, Chattopadhyay S. Diagnosis of the performance of the state-specific multireference coupled-cluster method with different truncation schemes. *J. Comp. Chem.* **2012,** 33: 1285-1303.

74. Napolion B, Huang M, Watts J D. Coupled-cluster study of isomers of H_2SO_2. *J. Phys. Chem. A.* **2008,** 112: 4158-4164.

75. Schröder B, Weser O, Sebaid P, Botschwina P. Theoretical rovibrational spectroscopy beyond fc-CCSD(T): the cation CNC^+. *Molecular Physics: An International Journal at the Interface Between Chemistry and Physics.* **2015,** 1.

76. Sholl D, Steckel J. *Density Functional Theory: A Practical Introduction.* John Wiley & Sons Inc.: Hoboken, NJ, 2009.

77. Bachrach S. Microsolvation of glycine: A DFT study. *J. Phys. Chem. A.* **2008,** 112: 3722-3730.

78. Spulber M, Schlick S, Villemena F. Guest inclusion in cucurbiturils studied by ESR and DFT: The case of nitroxide radicals and spin adducts of DMPO and MNP. *J. Phys. Chem. A.* **2012,** 116: 8475-8483.

79. Cataldo P, Castillo M, Brandán S. Quantum mechanical modeling of flouromethylated-pyrrol

derivatives a study on their reactivities, structures, and vibrational properties. *J. Phys. Chem. & Biophys.* **2014,** 4: 1-9.

80. DeYonker N, Cudari T, Wilson A. The correlation consistent composite approach (ccCA): An alternative to the Gaussian-n methods. *J. Chem. Phys.* **2006,** 124:114104-1-114104-13.
81. Deyonker N, Cundari T, Wilson A. The correlation consistent composite approach (ccCA): Efficient and pan-periodic kinetics and thermodynamics. *Mol. Phys.* **2009,** 107: 1107.
82. Valiev M, Bylaska E J, Govind N, Kowalski K, Straatsma T. P., van Dam H. J. J., Wang D., Nieplocha J., Apra E., Windus T. L., de Jong W. A. “NWChem: A comprehensive and scalable open-source solution for a large scale molecular simulations” Compt. Phys. Commun. 2010, 181, 1477.
83. Ho D S, DeYonker N, Wilson A, Cundari T. Accurate enthalpies of formation of alkali and alkaline earth metal oxides and hydroxides: assessment of the correlation consistent composite approach (ccCA). *J. Phys. Chem. A.* **2006,** 110: 9767-9770.
84. Mintz B, Parks J. Benchmark interaction energies for biologically relevant noncovalent complexes containing divalent sulfur. *J. Phys. Chem. A.* **2012,** 116: 1086-1092.
85. South C, Schoendorff G, Wilson A. MR-ccCA: A route for accurate ground and excited state potential energy curves and spectroscopic properties for third-row diatomic molecules. *Comp. Theor. Chem.* **2014,** 1040: 72-83.
86. Becke, A. D. Densityfunctional thermochemistry. III. The role of exact exchange. *J. Chem. Phys.* **1993,** 98: 1372-1377.