REACTION OF HYDROXYL RADICAL WITH AROMATIC HYDROCARBONS

A THESIS
SUBMITTED TO THE GRADUATE SCHOOL
IN PARTIAL FULFILLMENT OF THE REQUIREMENTS
FOR THE DEGREE
MASTER OF SCIENCE

BY

STEPHEN B. BENZINGER

ADVISOR: DR. JAMES S. POOLE
BALL STATE UNIVERSITY
MUNCIE INDIANA
JULY, 2010
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Committee Approval:

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1.1 Hydroxyl Radical and Reactive Oxygen Species

The hydroxyl radical is a highly reactive free radical that belongs to the general class of compounds known as reactive oxygen species (ROS). These are any oxygen containing species that are short lived, relatively unstable, and have an oxygen atom at their reactive site. It is generally accepted that ROS include the following species:¹

- Hydroxyl (HO\(^{\bullet}\)) and alkoxy (RO\(^{\bullet}\)) radicals,
- Alkylperoxyl (ROO\(^{\bullet}\)) and peroxyl (HOO\(^{\bullet}\)) radicals,
- Superoxide (O\(_2^{\bullet}\)) radicals,
- Singlet oxygen (\(^1\)O\(_2\), which is a photoexcited state), and
- closed shell species including peroxides and ozone (O\(_3\)).

The relative importance of different ROS depends on the discipline in which they are being considered. For example, in environmental studies, ozone is considered an important reactive oxygen species; whereas, in biological studies it is less so.

ROS are important for a number of different chemical processes, such as:

- Combustion and autoxidation processes,
- Ozone generation and depletion in the upper atmosphere and at ground level.²
• Remediation of ground water, either naturally by photochemical generation of
ROS from dissolved organic matter,\(^3\) or artificially by TiO\(_2\)/H\(_2\)O UV photolysis,\(^4\)
• Synthetic organic chemistry, including ozonolysis and other chemical oxidations,
singlet oxygen photochemistry, etc.,\(^5\) and
• Superoxide chemistry; which plays a key role in medicine and biology.\(^6\)
Superoxide can also be a source for hydroxyl radical, which is then a key
intermediate in the damage following ischemia/reperfusion. For example, it has
been reported that the addition of hydrogen peroxide and superoxide ion reported
a depression in the protein synthesis ability of rat brain astrocytes.\(^7\)

Of all of these reactive oxygen species, hydroxyl radical is the one of interest to our
research.

1.2 Detection and Kinetic Investigation of Hydroxyl Radical Reactions

Hydroxyl radical is a highly reactive species that has a lifetime on the order of
nanoseconds; the detection and characterization of hydroxyl radical chemistry can be
difficult. The detection of hydroxyl radical may be achieved in multiple ways through
different methods loosely categorized as direct and indirect methods. The former include
laser flash photolysis, pulse radiolysis, and laser induced fluorescence. The latter
includes techniques such as smog chambers, spin trapping, and product distribution
analysis.
1.2.1 Laser Flash Photolysis

Created in 1967, flash photolysis is a method which won Eigen, Norrish, and Porter a Nobel Prize. With this technique, reactive intermediates are generated by excitation of a precursor using a light pulse produced by a flash lamp. Sub-millisecond timescale studies are possible with this technique, limited by the duration of the light pulse. However, a laser is capable of generating pulses that are high intensity, and temporally well defined (pulses on the ns timescale). This led to the use of nanosecond laser flash photolysis, which allowed the studies of short-lived species such as radicals. Lindqvist is credited with the first report of laser flash photolysis using a nitrogen lamp at 337 nm. A simplified schematic of an LFP instrument is shown below (Figure 1).

![Figure 1. Simplified Schematic of a Typical LFP Instrument.](image-url)
Although there have been many improvements in instrumentation, the basic design is still in practice today. Many different laser sources are available allowing selection over a wide range of wavelengths. Nitrogen and ruby lasers produce wavelengths of 337 nm and 694 nm respectively. Eximer and solid state lasers yield wavelengths ranging from 157 nm to 1064 nm. Nd-YAG lasers are often used; harmonics of 532, 335, and 266 nm wavelengths are available.\textsuperscript{9}

The monitoring beam is usually a xenon arc lamp, which is frequently pulsed to achieve a high intensity beam over short (ms) time scales.\textsuperscript{9} Transmitted light is typically dispersed by a diffraction grating. Detection at a single wavelength can be achieved using a fast photomultiplier tube. Transient spectra may be obtained either by point by point construction of the spectrum at appropriate wavelengths or by capture of the image obtained over a window of wavelengths by a diode array detector or CCD camera. Both approaches allow capture of data in a 3 dimensional matrix in which the vertical axis is signal intensity, and the other two are time and wavelength.

An electronic triggering system is used to synchronize the light pulse from the laser, the light pulse from the arc lamp, and data acquisition by the oscilloscope. The timescales involved require that the triggering system is controlled by the computer.

To generate radicals with LFP, a precursor molecule that will readily break apart (photolyse) at the selected laser wavelength must be used. The choice of wavelength and precursor is dictated by the absorbance properties of the sample. Spectroscopic interference due to absorption of light by the solvent, or of any substrate molecules present in solution is clearly undesirable. Photochemical sources of hydroxyl radical will be discussed in a later section.
Hydroxyl radical does not have a useful UV-visible absorbance in solution; to achieve detection, there must be detectable products of the reaction of hydroxyl radical with a molecule in solution, such as thiocyanate anion. Hydroxyl radical generated by LFP can react with a range of compounds, including thiocyanate anion to generate hydroxide and thiocyanatyl radical (Scheme 1). This thiocyanatyl radical can then react with another equivalent of thiocyanate to form a dithiocyanatyl radical anion, which has a strong absorbance at 475 nm in water.

**Scheme 1.** The Reaction of Hydroxyl Radical with Thiocyanate.

\[
\begin{align*}
\text{HO}^* + \text{SCN}^- & \longrightarrow \text{OH}^- + \text{SCN}^* \\
\text{SCN}^* + \text{SCN}^- & \longrightarrow (\text{SCN})_2^{--}
\end{align*}
\]

475 nm is in the visible range, which is subject to limited spectroscopic interference by most simple organic compounds. The dimeric radical anion in Scheme 1 is the signal carrier for the detection, and is an example of a reporter molecule. A reporter molecule is any molecule that reacts with the species of interest to allow detection. The species of interest was not what was measured, but detection of the reporter directly correlates to the species of interest. Many radicals are invisible to LFP detection, but reporter molecules can be used to be able to measure the kinetics.

An alternative method for hydroxyl radical detection uses *trans*-stilbene as a reporter molecule in non-aqueous solutions. Hydroxyl radical reacts with stilbene to generate a transient species with a strong absorbance at 392 nm that may be used in competitive experiments. The structure of the transient has yet to be unambiguously established.
LFP instruments may be used in two modes, direct detection and competitive experimentation. In a direct detection, the species of interest absorbs at a wavelength that is readily detected and has little or no spectral interference, allowing the determination of absolute rate coefficients. Given the difficulty in detecting HO• directly, competitive experiments must be utilized for this radical. The generalized layout of a competitive experiment is shown in Scheme 2. Hydroxyl radical may react with one of two competitive substrates: reaction with substrate A leads to the formation of a transient that may act as a reporter molecule; whereas, reaction with substrate B yields an intermediate that does not absorb in the same region of the spectrum as the reporter.

**Scheme 2. Generalized Competitive Hydroxyl Radical Reactions.**

\[
\begin{align*}
\text{HO}^• + A & \xrightarrow{k_A} \text{HOA}^• \\
\text{HO}^• + B & \xrightarrow{k_B} \text{HOB}^•
\end{align*}
\]

The peak absorbance of HOA• is determined in the presence \(A^B\) and absence \(A^0\) of B. The concentrations of A and B are ideally much greater than the concentration of the hydroxyl radical and thus the competitive reactions exhibit pseudo-first order behavior. The concentration of B is systematically altered, and a Stern-Volmer analysis of the peak absorbance of HOA• as a function of the concentration of the two competitive substrates yields:

\[
\frac{A_{HOA}^0}{A_{HOA}^B} = 1 + \frac{k_B[B]}{k_A[A]} 
\]  
(Eq. 1)
Thus relative rate coefficients may be determined, and if the absolute rate coefficient for the reporter molecule is known, the absolute rate coefficient for the competitive substrate can be determined.$^{11}$

1.2.2 Pulse Radiolysis

Pulse radiolysis is a technique that uses highly energized gamma radiation to excite and ionize any molecule in the beam path. This technique is often used for the generation of hydroxyl radical, due to the ability of gamma radiation to excite and break apart water molecules (Scheme 3).$^{12}$

\[ \text{H}_2\text{O}^* \xrightleftharpoons{\gamma} \text{H}_2\text{O} \xrightarrow{\gamma} \text{H}_2\text{O}^\cdot + e^- \]
\[ \cdot \text{OH} + \text{H}^\cdot \xrightarrow{} \text{H}_2\text{O}^* \]
\[ \text{H}_2\text{O}^\cdot + n\text{H}_2\text{O} \xrightarrow{} \cdot \text{OH} + \text{H}^+ \]
\[ e^- (+n\text{H}_2\text{O}) \xrightarrow{} e^-_{\text{aq}} \]
\[ \text{H}_2\text{O} + e^-_{\text{aq}} + \text{N}_2\text{O} \xrightarrow{} \cdot \text{OH} + \cdot \text{OH} + \text{N}_2 \]

In the above scheme, H$_2$O* represents an excited state water molecule, and +nH$_2$O denotes the presence of excess water.

Most of the energy absorbed in pulse radiolysis is absorbed by the solvent. Due to the poor selectivity of gamma radiation, it is necessary to use dilute aqueous solutions of the substrate of interest. Clearly the method is limited to compounds that have measurable solubility in water.$^{12}$ Scheme 3 shows the formation of a range of reactive intermediates, but it is possible to sacrifice one radical for the creation of another. This is accomplished if an additive is used, that may successfully compete with the solute. An example of such a system is the addition of N$_2$O to enhance hydroxyl radical formation.
As the gamma radiation is absorbed by the solution, regions of highly ionized species form, called spurs.\textsuperscript{12} Radicals form, as well as $\text{H}_2\text{O}_2$ and $\text{H}_2$. After about $10^{-8}$ seconds (which was determined based on the ability of hydroxyl radicals to dissipate at or close to the diffusion limit), the distribution of radical species becomes homogeneous.\textsuperscript{12} This method is very effective in measuring the kinetics of reactive species in very dilute aqueous solutions. Because it is unselective and destructive, it will not work as effectively in other solvents, as well as in more concentrated solutions.

The hydroxyl radical is still undetectable in this method, so reporter molecules must be used. Thiocyanate anion is a common example. Most of the kinetics are determined competitively.

\textit{1.2.3 Laser Induced Fluorescence}

Laser Induced Fluorescence is an extremely sensitive, non-destructive gas phase method for monitoring free radicals.\textsuperscript{13} It is mainly used to monitor atmospheric free radicals such as hydroxyl, nitrate, methoxy, ethoxy, sulfanyl, and methylsulfanyl radicals. Hydroxyl radicals can either be generated directly to initiate radical reactions (for example by flash photolysis of water vapor), or may be detected as transient products in reaction sequences initiated by other radical species.\textsuperscript{13}

Hydroxyl radical in the gas phase absorbs at 282 nm (this wavelength is accessed with a frequency-doubled dye laser) and fluoresces at 310 nm. The emission is typically collected at 90 degrees from the excitation beam, and is detected by fast PMT (photomultiplier tube) and collected on a digital oscilloscope or alternative method.
LIF is a very specific and soft method of detection, which is desirable and is consequently highly used in atmospheric chemistry. A limitation of LIF is that gas phase samples must be used in, which makes this method undesirable for condensed phase studies such as the one described here.

1.2.4 Electron Spin Resonance (ESR) Based Techniques

In 1968, spin trapping was discovered by Professor Edward Janzen’s group, along with a few others. Spin Trapping is a technique used to detect short lived radicals through stabilization of the transient species, where Electron Spin Resonance (ESR) is used for detection.\(^\text{14}\)

ESR is a technique that detects magnetic resonances of unpaired electrons, often split via hyperfine coupling. This is loosely analogous to NMR spectroscopy, but instead of viewing the spins of excited atomic nuclei, excited electron spins are detected. ESR alone can directly detect more stable radicals, but not very reactive ones due to their short lifetimes. Spin trapping provides means of detecting reactive radicals.

Most of the time, these traps are either nitroso or nitrone compounds, both giving rise to aminoxyl species.\(^\text{14}\) These are shown below in Scheme 4:

**Scheme 4: Spin-trapping Reactions for a Free Radical \(R'\)**

\[
\begin{align*}
(Free \ Radical) & \quad R' + \text{Trap} & \quad & \quad \rightarrow & \quad k_T & \quad \text{SA} \cdot & \quad (\text{Spin Adduct}) \\
R' & \quad \rightarrow & \quad R'N=O & \quad \rightarrow & \quad R \quad \text{N-O} \\
R' & \quad + & \quad R_1\leftrightarrow N\quad O \quad \rightarrow & \quad R_1 \quad R_3 \quad \text{N} \quad O \\
\end{align*}
\]
The successful reaction of these traps with the radicals of interest depends on four factors: the production method of the radical, the reactivity of the solvent and the reagents to the trap, how much if any deoxygenation is required, and the lifetime of the spin adduct (the aminoxyl).\textsuperscript{14} If no deoxygenation is performed, alkyl radicals will react with oxygen.

When looking at nitroso traps versus nitrone traps, nitroso traps have an advantage in the identification of radicals, due to the location of the radical center. Because the added group is directly adjacent to the nitroxide group, more hyperfine splitting occurs.\textsuperscript{14} Evans \textit{et al.} provide an example of ethyl radical with NtB (nitroso-\textit{tert}-butane), the most commonly used spin trap.\textsuperscript{14} The ESR spectrum of the compound NtB-Et, which is the ethyl radical trapped in the NtB, consist of 3 primary bands (interaction with $^{14}\text{N}$), which in turn are split into secondary triplets with 1:2:1 intensity ratio by the interaction of the spin with the 2 methylene hydrogen atoms. Long-ranged coupling with –CH$_3$ is also observed by splitting of the nine major lines into quartets with 1:3:3:1 peak intensities. This helps identify the trapped radical because long range coupling can be observed and used in the identification.\textsuperscript{14}

The nitrone most commonly used is phenyl \textit{N-}tert-butyl nitrone, due to its long shelf life: it was the first nitrone used for spin trapping, and has been used widely since. This particular nitrone is not used for hydroxyl radical; but other nitrones, some of which are water soluble, have been successfully used to probe hydroxyl radical reactions.\textsuperscript{14}
1.2.5 Smog Chambers

Smog chambers are environments where gas phase reactions between different radicals and aromatic compounds are investigated. The conditions used in a smog chamber for the generation of hydroxyl radical are shown below (Scheme 5):\(^{15}\)

**Scheme 5.** Hydroxyl Radical Generation in a Photolytic Smog Chamber.

\[
\begin{align*}
\text{O}_3 \text{N}_2\text{O} & \xrightarrow{h\nu} \text{O} + \text{NO} \\
\text{O} + \text{O}_2 & \rightarrow \text{O}_3 + \text{HO}_2 \\
\text{HO}_2 + \text{NO} & \rightarrow \text{H}_2\text{O} + \text{NO}_2
\end{align*}
\]

Light photodissociates the indirect hydroxyl radical precursors, creating a multi-step means of hydroxyl radical production. The hydroxyl radical can then go on to react with aromatic compounds in the chamber. To prevent the formation of ozone, which is another reactive oxygen species, excess NO is added (Scheme 6).

**Scheme 6.** Addition of NO to Eliminate O\(_3\) Contamination.

\[
\begin{align*}
\text{NO}_2 & \xrightarrow{h\nu} \text{NO} + \text{O} \\
\text{O} + \text{O}_2 & \rightarrow \text{O}_3 \\
\text{NO} + \text{O}_3 & \rightarrow \text{NO}_2 + \text{O}_2
\end{align*}
\]

The products of the reaction of hydroxyl radical with naphthalene in a smog chamber are shown in Scheme 7, overleaf.\(^{15}\)
**Scheme 7.** Reaction Products of Hydroxyl Radical with Naphthalene in a Smog Chamber.

\[
\text{HO}^\bullet + \begin{tikzpicture}
  \draw (-0.5,0) ellipse (0.5 and 0.5);
  \draw (0.5,0) ellipse (0.5 and 0.5);
\end{tikzpicture} \quad \rightarrow \quad \begin{tikzpicture}
  \draw (-0.5,0) ellipse (0.5 and 0.5);
  \draw (-0.5,-1) ellipse (0.5 and 0.5);
  \draw (0,0) ellipse (0.5 and 0.5);
  \draw (0,-1) ellipse (0.5 and 0.5);
\end{tikzpicture} + \begin{tikzpicture}
  \draw (0.5,0) ellipse (0.5 and 0.5);
  \draw (0.5,-1) ellipse (0.5 and 0.5);
  \draw (1,0) ellipse (0.5 and 0.5);
  \draw (1,-1) ellipse (0.5 and 0.5);
\end{tikzpicture}
\]

Smog chambers are a very effective means of producing and reacting hydroxyl radical, but are limited to investigating these reactions in the gas phase. The advantage of these methods is that they rely on product distribution analyses (largely performed using chromatographic methods), which in turn are used to analyze chemo- and regioselectivity of these reactions. This is a significant advantage of this technique compared to LFP, PR, and LIF, because those techniques are utilized to measure reactivity, rather than selectivity. In this study, we will generate hydroxyl radical in solution, and react it with aromatic hydrocarbons. The formed radicals will be trapped or otherwise reacted with persistent aminoxyl radicals to generate closed-products. Product analysis can then be achieved by chromatographic means to yield information regarding the chemo- and regioselectivity of these reactions in organic solvents.

**1.3 Laboratory Sources of Hydroxyl Radical**

There are many sources for hydroxyl radical, ranging from an array of metal reactants, to organic nitrogen based compounds.

\[\text{H}_2\text{O}_2\] is a commonly used hydroxyl radical precursor that can be broken down by various methods: thermolysis, photolysis, Fenton chemistry, etc. To generate hydroxyl radical, typically high temperatures or very intense UV radiation must be used,
which can be detrimental to the study. Fenton chemistry supplies an alternative method for creation of hydroxyl radical.\textsuperscript{16}

Fenton reagents are composed of iron (II) reacting with hydrogen peroxide in the following manner:\textsuperscript{16}

\[
\text{Fe}^{II} + \text{H}_2\text{O}_2 \rightarrow \cdot \text{OH} + \text{Fe}^{III} + \text{OH}^- 
\]

In the presence of metal catalysts, hydrogen peroxide slowly decomposes into radical biproducts. With the presence of these metals, the degradation is rather rapid, even at low temperatures.\textsuperscript{16} When utilizing Fenton chemistry, the pH of the solution in question increases as the hydroxyl radical is formed; thus the pK\textsubscript{a} characteristics of the substrate(s) must be considered.

As an alternative method for generating hydroxyl radical at low to moderate temperatures, azohydroperoxides have been in use since the early 20\textsuperscript{th} century, and have a wide array of uses.\textsuperscript{17} Grant \textit{et al.} showed that hydroxyl radical can be formed in high yields using azohydroperoxide sources.\textsuperscript{18} In the presence of a radical trap, they have shown that up to 96\% decomposition rate into hydroxyl radical is possible. Such a high yield of hydroxyl radical from a radical source makes this method very desirable for our research. It is noteworthy, however, that other free radicals are formed during the decomposition of these peroxides (Scheme 8):

\textbf{Scheme 8}: Decomposition of \textit{tert}-Butyl Azohydroperoxide.

![Scheme 8](image)

The peroxide shown in Scheme 8 was used in this study. Based on published data,\textsuperscript{17,18} half-lives were calculated for this compound, and are shown in Table 1, overleaf.
Table 1. Calculated Half-Lives of *tert*-Butyl Azohydroperoxide.

<table>
<thead>
<tr>
<th>T (K)</th>
<th>$k_{\text{decomp}}$ (s$^{-1}$)</th>
<th>Half Life</th>
</tr>
</thead>
<tbody>
<tr>
<td>298</td>
<td>$3.93 \times 10^{-7}$</td>
<td>20 Days</td>
</tr>
<tr>
<td>308</td>
<td>$1.95 \times 10^{-6}$</td>
<td>4 Days</td>
</tr>
<tr>
<td>318</td>
<td>$8.73 \times 10^{-6}$</td>
<td>22.1 Hours</td>
</tr>
<tr>
<td>328</td>
<td>$3.57 \times 10^{-5}$</td>
<td>5.4 Hours</td>
</tr>
<tr>
<td>338</td>
<td>$1.34 \times 10^{-4}$</td>
<td>86 Minutes</td>
</tr>
<tr>
<td>348</td>
<td>$4.68 \times 10^{-4}$</td>
<td>25 Minutes</td>
</tr>
</tbody>
</table>

A useful photochemical source of hydroxyl radical, used in LFP studies, is *N*-hydroxypyridine-2-thione, which may be photolyzed in LFP at 355 nm to generate hydroxyl radical and a relatively non-reactive pyrithyyl radical, as shown in scheme 9:19

**Scheme 9**: Photolytic Decomposition of *N*-Hydroxypyrid-2-one and 2-thione.

\[
\text{N}^\text{O} \text{H} \quad \xrightarrow{h\nu} \quad \text{N}^\text{O} \text{H}^+ + \cdot \text{OH}
\]

\[X = \text{O}, \text{S}\]

The formed thiyl radical has a broad transient absorbance at 490 nm, and since hydroxyl radical is undetectable in the visible region, *trans*-stilbene is used as a reporter molecule. Similarly, *N*-hydroxypyrid-2-one can produce similar yields of HO•, and the pyridoxyl radical formed is also poorly reactive (Scheme 9).20

1.4 **Hydroxyl Radical and Polycyclic Aromatic Hydrocarbons**

Polycyclic Aromatic Hydrocarbons (PAH) are multi-ring compounds, that are very common carcinogenic toxins in the aquatic environment.21 PAH’s are a major component of crude oil, and a major product of fossil fuel combustion. This is of interest because aromatic rings are important in a wide variety of fields, including pollutant chemistry and brain chemistry.
It is believed that hydroxyl radical is electrophilic and reacts readily with aromatic compounds.\textsuperscript{22} When hydroxyl radical reacts with aromatic rings, it may follow one of three paths:

- hydrogen atom abstraction,
- addition to the aromatic ring, or
- radical substitution on the aryl ring.\textsuperscript{23}

In simple PAHs, there are typically no groups which may act as leaving groups for substitution reactions. Substitutions are more commonly observed in haloarenes, where a halogen atom may act as a leaving groups.\textsuperscript{23} Thus we may reasonably limit ourselves to abstraction and addition reactions. Using benzene as an illustrative model, these are shown in Scheme 10.

**Scheme 10.** Hydrogen Abstraction and Addition of Hydroxyl Radical with Benzene

For more complex systems, toluene for example, we find that there are multiple sites for both addition and abstraction. When considering hydrogen atom abstraction, reaction enthalpies are helpful in deciding what sites of abstraction are favorable. The Evans-Polanyi relationship\textsuperscript{24} is commonly used to predict the activation energies of reactions due to an empirical correlation between the enthalpy of activation and the enthalpy of reaction. For hydrogen abstraction reactions this may be expressed in terms of C-H bond dissociation energies as follows:
Where $E_{\text{act}}$ is the activation energy, $\alpha$ and $\beta$ are empirically determined constants, and BDE is the bond dissociation energy for the particular C-H bond. Thus, in the situation where hydroxyl radicals react with toluene, two possible extraction abstraction sites exist: the benzylic C-H bonds, which have a bond dissociation energy of 368 kJ/mol, and the aromatic C-H bonds, which have dissociation energies of 464 kJ/mol. The Evans-Polanyi relationship predicts that benzylic abstraction is dominant.

In principle, the same model may be applied to radical addition, but less is known about the relative stability of the various cyclohexadienyl radicals.

Since all the intermediates formed are free radicals, we must trap these species in such a way as to generate closed-shell species amenable to chemical analysis. We may utilize persistent aminoxyl radicals to achieve this.

### 1.4.1 The Chemistry of Aminoxyl Radicals

Aminoxyl radicals are very chemoselectively reactive towards carbon-centered radicals, and thus can be used to eliminate any sort of undesirable reactions that may arise from the presence of alkyl radicals (eg. from the decomposition of azohydroperoxides, see above). There are two major types of aminoxyl radicals: non-persistent and persistent.

Non-persistent aminoxyl radicals are called such because they have a very short lifetime, due to their rapid bimolecular disproportionation (Scheme 11). This is undesirable, because in order for the aminoxyl radicals to trap any formed carbon-
centered free radicals effectively, they must be present in the solution throughout the entire reaction.

**Scheme 11.** Disproportionation of Non-persistent Aminoxyl Radicals.

If disproportionation represents the major degradative pathway for an aminoxyl radical, then the synthesis of aminoxyl species where the attached alkyl groups contain no abstractable hydrogen atoms at the $\alpha$-position should result in long-term persistency of these species, and indeed species such as di-tert-butylamine-N-oxyl (TBNO), 2,2,6,6-tetramethylpiperidin-1-oxyl (TEMPO) and 1,1,3,3-tetramethylisoindoline-2-oxyl (TMIO) exhibit very high degrees of persistency.

Persistent aminoxyl radicals are known to react with carbon-centered radicals in two ways: by coupling and by hydrogen abstraction. The latter reaction is known to occur with cyclohexadienyl radicals. In the context of the proposed experiments (using as an example the radicals formed in Scheme 10), the reactions of TMIO with formed carbon-centered radicals are shown in Scheme 12, overleaf.
These reactions result in the formation of alkoxylamines and phenols, both of which are amenable to chromatographic analysis.

One significant limitation of this study is that it is largely dependent on gas chromatographic analysis; either GC-FID or GC-MS. It is known that the coupling reactions of persistent aminoxyl radicals are reversible at higher temperatures, and form the basis of so-called “quasi-living” free radical polymerization.\textsuperscript{28} Thus, the alkoxylamines are likely to exhibit limited stability in a GC injector port, which is heated above 500 K. The carbon radical species is released from the trap, and the breakdown products cannot be easily detected. Thus, this preliminary study is limited to the investigation of the selectivity of radical addition. It is anticipated that the question of abstraction kinetics may be amenable to liquid chromatographic methods, but this lies outside of the current study.

One other adjustment that must be made using GC as the detection method is that the alcohols must be derivatized with a silylating agent such as bis(trimethylsilyl)trifluoroacetamide (BSTFA).\textsuperscript{29} This is because the interaction of the OH groups with the stationary phase in GC columns will lead to peak broadening,
whereas silyl ethers do not cause broadening. BSTFA is used to attach TMS (trimethylsilyl) groups to the oxygen of any generated phenols (Scheme 13).

**Scheme 13. Derivatization of Phenols for GC Analysis**

1.4.2 Reaction of Hydroxyl Radical with Benzene

The simplest of the arenes is benzene. Benzene has been classified as a Group-A human carcinogen, due to increasing incidence of leukaemia.\(^{30}\) The conversion of benzene also is believed to play a significant role in tropospheric ozone formation.\(^{30}\) It is believed that the attack on benzene by hydroxyl radical leads to degradation.\(^{31}\)

Calculations on the addition of hydroxyl radical to the benzene ring indicate significant charge-transfer interactions in the transition state, which contains character that may be ascribed to a benzene radical cation/hydroxide anion pair.\(^{19}\) The reaction of benzene with hydroxyl radical (primarily addition and abstraction) can follow different mechanisms depending on the temperature and pressure. Reactions at room temperature and below are of interest to us, and typically only one dominant pathway-electrophilic addition to the aromatic ring by the hydroxyl radical is observed. Ring hydrogen abstraction becomes dominant at higher temperatures.\(^{33}\) The dominance of addition reactions at room temperature may be demonstrated in the solution phase by observed kinetic isotope effects (KIE).\(^{11}\) The absence of any significant primary KIE in the solution phase in either water or acetonitrile shows that electrophilic addition of the
hydroxyl radical is dominant. Experimentally determined rate constants for the reaction of hydroxyl radical and benzene in the gas and liquid phases are shown in Table 2.

**Table 2.** Rate Constants for Reaction of Hydroxyl Radical with Benzene

<table>
<thead>
<tr>
<th>Phase</th>
<th>Substrate</th>
<th>Solution</th>
<th>k$_{\text{OH}}$ (M$^{-1}$s$^{-1}$ sol’n, cm$^3$ molecule$^{-1}$ s$^{-1}$ gas)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Aqueous</td>
<td>Ref.</td>
</tr>
<tr>
<td><strong>Solution</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>benzene</td>
<td>7.8 x10$^9$</td>
<td>11</td>
</tr>
<tr>
<td></td>
<td>benzene-d$_6$</td>
<td>4.7 x10$^9$</td>
<td>11</td>
</tr>
<tr>
<td><strong>Gas</strong></td>
<td>benzene</td>
<td>1.24 x10$^{12}$</td>
<td>30</td>
</tr>
<tr>
<td></td>
<td>benzene-d$_6$</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

1.4.3 Reaction of Hydroxyl Radical with Toluene and Xylenes

The room temperature reaction of hydroxyl radical with toluene is in fact very similar to that of benzene. Toluene not only has the ring hydrogen atoms available for abstraction, but also benzylic hydrogens. Although this may seem like a very likely place for abstraction, the main mechanism for this reaction is believed to be dominated by radical addition to the aromatic ring. Given the charge transfer character in the transition state, and the electrophilic nature of hydroxyl radical, activation of the ring towards electrophiles is an effective way to enhance the rate of reaction, and such an enhancement is observed.

Poole *et al.*$^{11}$ used toluene and toluene-$d_3$ rates to determine a KIE value of 1.1. This indicates that abstraction of hydrogen at the benzylic position is only a minor pathway, because hydrogen abstraction from the benzylic position should exhibit a significant primary isotope effect. They also confirmed this by comparison of toluene-$d_5$
and toluene-$d_8$, showing that the KIE is barely affected by the deuteration of the benzylic position, or any other position (Table 3). Despite their potential reactivity, substitution of the ring with methyl groups does not necessarily mean that hydroxyl reactions with these substituents will become a major pathway, since adding these particular substituents also tends to increase the reactivity of the ring carbons themselves. This is one reason why the rate constant varies with the number and type of substituent groups bonded on an aromatic ring.

Table 3. Rate Constants for Reaction of Hydroxyl Radical with Methylated Benzenes at 298K

<table>
<thead>
<tr>
<th>Phase</th>
<th>Substrate</th>
<th>$k_{OH}$ (M$^{-1}$s$^{-1}$ sol’n, cm$^3$ molecule$^{-1}$ s$^{-1}$ gas)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Solution</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Aqueous</td>
</tr>
<tr>
<td></td>
<td>toluene</td>
<td>5.1 x10$^9$</td>
</tr>
<tr>
<td></td>
<td>toluene-$d_3$</td>
<td>3.8x10$^8$</td>
</tr>
<tr>
<td></td>
<td>toluene-$d_5$</td>
<td>3.5x10$^8$</td>
</tr>
<tr>
<td></td>
<td>toluene-$d_8$</td>
<td>3.6x10$^8$</td>
</tr>
<tr>
<td></td>
<td>o-xylene</td>
<td>6.7 x10$^9$</td>
</tr>
<tr>
<td></td>
<td>m-xylene</td>
<td>7.5 x10$^9$</td>
</tr>
<tr>
<td></td>
<td>p-xylene</td>
<td>7.0 x10$^9$</td>
</tr>
<tr>
<td></td>
<td>mesitylene</td>
<td>6.4 x10$^9$</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Gas</td>
</tr>
<tr>
<td></td>
<td>toluene</td>
<td>6.4x10$^{12}$</td>
</tr>
<tr>
<td></td>
<td>o-xylene</td>
<td>14.2x10$^{12}$</td>
</tr>
<tr>
<td></td>
<td>m-xylene</td>
<td>25.4x10$^{12}$</td>
</tr>
<tr>
<td></td>
<td>p-xylene</td>
<td>13.5x10$^{12}$</td>
</tr>
</tbody>
</table>

Xylenes are dimethylated benzenes, and as such may exist as three isomers: ortho-, meta-, and para-xylene. The specificity of this arrangement affects the rate
constant.\textsuperscript{11} \textit{meta}-Xylene seems to have the highest rate constant in both solution phases, because it enhances electrophilic addition to the ring.\textsuperscript{37} At temperatures below 320K, the rate constants are almost independent of temperature. The experimentally obtained rate coefficients for hydroxyl radical reaction with toluene and the xylenes are summarized in Table 3.

\textit{1.4.4 Polycyclic Aromatics: Naphthalene, Biphenyl and Anthracene}

Naphthalene is the simplest of the polycyclic aromatic hydrocarbons. The reaction of hydroxyl radical with naphthalene also occurs as radical addition on the aromatic carbons. The addition of one or more methyl groups changed the reactivity of the naphthalene drastically.\textsuperscript{11} When it came to actual experimental results on naphthalene, Biermann \textit{et al.}\textsuperscript{32} had about 5\% loss of naphthalene due to degradation, which leaves most of the mass of naphthalene to react with hydroxyl radical. They found a \( k_1/k_2 \) ratio of 0.895, where \( k_1 \) is the rate coefficient for hydroxyl radical addition to the 1-position and \( k_2 \) for addition at the 2-position.

\textbf{Table 4.} Rate Constants for Reaction of Hydroxyl Radical with Polycyclic Arenes

<table>
<thead>
<tr>
<th>Phase</th>
<th>Substrate</th>
<th>( k_{\text{OH}} ) (M\textsuperscript{-1}s\textsuperscript{-1} sol’n, cm\textsuperscript{3} molecule\textsuperscript{-1} s\textsuperscript{-1} gas)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Solution</td>
<td>Aqueous</td>
<td>Ref. Acetonitrile Ref.</td>
</tr>
<tr>
<td>naphthalene</td>
<td>9.4 x10\textsuperscript{9}</td>
<td>11 1.8x10\textsuperscript{9}</td>
</tr>
<tr>
<td>biphenyl</td>
<td>9.5 x10\textsuperscript{9}</td>
<td>11 6.8 x10\textsuperscript{8}</td>
</tr>
<tr>
<td>Gas</td>
<td>naphthalene</td>
<td>2.4x10\textsuperscript{11}</td>
</tr>
<tr>
<td>Anthracene\textsuperscript{a}</td>
<td>1.1x10\textsuperscript{12}</td>
<td>32</td>
</tr>
</tbody>
</table>

\textsuperscript{a}Measured at 373K
Anthracene is a more complex polycyclic aromatic hydrocarbon. Measurements at room temperature are not possible due to the low vapor pressure of anthracene. The lowest temperature that Anathula et al. could measure was at 373K.

Using the above described chemistry, we have investigated hydroxyl radical reactions with aromatic hydrocarbons in organic (hydrocarbon) solvents.
CHAPTER 2 – EXPERIMENTAL METHODOLOGY

Materials

All hydrocarbons used in this study were obtained from commercial sources, and used without further purification. Benzene and toluene were obtained in “spectroscopic grade”. Gases used in this study were obtained in high purity from commercial sources. Acetone t-butyl hydrazone was prepared following literature procedure.\textsuperscript{34} 1,1,3,3-Tetramethylisoindolin-2-oxyl (TMIO) was prepared following a literature procedure and recrystallized from hexanes.\textsuperscript{35}

For compounds liquid at room temperature (toluene, o-xylene, m-xylene) reactions were performed in neat aromatic solvent. Compounds such as naphthalene and biphenyl were investigated as 2 M solutions in benzene.

Preparation of 2-(tert-butylazo)-2-hydroperoxy propane (t-butyl azohydroperoxide)

60 µL of acetone t-butyl hydrazone in an NMR tube was diluted with a further 940 µL of the aromatic reaction solvent. A thin stream of oxygen gas was bubbled through the solution for 1 hour, after which argon gas was bubbled through the mixture for 15 min to cease oxidation. Conversion of the hydrazone to peroxide could be confirmed in both cyclohexane-d\textsubscript{12} and benzene-d\textsubscript{6} by \textsuperscript{1}H NMR.
Kinetic Experiments

A standard solution of 0.1M TMIO was prepared in the reaction solvent, and 815 µL was added to a reaction vial. 185 µL of t-butyl azohydroperoxide solution was added, and the resultant mixture deoxygenated by freeze-pump-thaw degassing (4 cycles). The deoxygenated solution was heated at temperature for 7 half-lives of the peroxide.

An alternative method was used for reaction temperatures above 343K, where the peroxide half life becomes comparable to the thermal equilibration time: A standard solution of 0.1M TMIO was prepared in the reaction solvent, and 815 µL was added to a reaction vial. The solution was degassed by a thin stream of bubbling argon, and equilibrated at the appropriate temperature. 185 µL of t-butyl azohydroperoxide solution was added with stirring, and the resultant solution was heated at temperature for 7 half-lives of the peroxide.

Derivatization of reaction mixtures: 150 µL of the reaction mixture and 300 µL of BSTFA were added to a reaction vial, and heated at 348 K for 2 hours. The final mixture was subjected to a combination of GC-FID and GC-MS analysis.

GC-FID/GC-MS Analysis

The GC-FID used was a Hewlett Packard 5890 using an H₂/air flame, and He carrier gas. Data acquisition and analysis was performed using Dionex Chromeleon® software. The GC-MS used was an Agilent Technologies 7890 A GC system with a 5975 C inert XL EI/CI MSD detector (1094 V), and a 7683 B Series injector and autosampler. Helium was used as the carrier gas. Data acquisition and analysis was performed using Agilent GC-MS software.
Samples were injected in 5 µL volumes with a split ratio of 80:1 in the GC-FID, and 1 µL with a split ratio of 200:1 in the GC-MS (125 mL/min on the GC-FID and 200 mL/min on the GC-MS). A temperature gradient was required to obtain acceptable resolution:

Injector temperature = 250°C (both GC-FID and GC-MS)
Detector temperature = 250°C (GC-FID)
Transfer line temperature = 230°C (GC-MS)

Oven temperature
- initial = 80°C, hold time = 2 min
- final = 200°C (10 minutes)
- ramp rate = 12°C/min

The temperature gradient was the same for both GC-FID and GC-MS experiments. Both columns used were 30m x 0.25mm with a .25µm film thickness and ZB-5 stationary phase. Relative response factors for the various aryl trimethylsilyl ethers were determined relative to the phenol ether as described in Appendix 1.
CHAPTER 3 – RESULTS & DISCUSSION

Reactions were completed by heating the azohydroperoxide at various temperatures in the presence of the persistent aminoxyl radical trap in the presence of the aromatic compound of interest. Heating was continued for the equivalent of seven half-lives of the peroxide, ensuring that less than 1% of the peroxide remains at the end of the experiment. Only hydroxyl radical addition is discussed in this chapter, as for the reasons stated earlier, abstraction is not detectable with our methods.

To be able to obtain relative concentrations, relative response factors were obtained to be able to use the peak intensities on the GC-FID to determine relative concentrations in the absence of phenol standards (Appendix 1). GC-MS was used primarily for compound identification and confirmation, so detector response factors were not determined. GC-FID quantification often relies on “effective carbon number” (ECN) models to model relative detector responses, but the ready accessibility of phenols allowed us to determine detector responses directly.
3.1. Reaction of Hydroxyl Radical with Toluene

A detailed reaction scheme for the decomposition of the azohydroperoxide in the presence of toluene and TMIO is shown in Scheme 14, below.

**Scheme 14. Decomposition of Azohydroperoxide in Toluene**

![Reaction Scheme](image)
The detected products of hydroxyl radical reaction with toluene are shown in the scheme above, and may be described as the trimethylsilyl ethers of $o$-, $m$- and $p$-cresols. Abstraction products from the aromatic ring are unable to be detected, due to the fact that they dissociate in the injector port of a GC-MS or GC-FID. Figure 2 shows a typical total ion chromatograph (TIC) of a derivatized toluene reaction mixture subjected to GC-MS analysis.

**Figure 2.** TIC from GC-MS Analysis of a Typical Toluene Reaction Mixture.

The silylated cresols elute relatively close to each other, with $o$-, $m$-, and $p$-cresol derivatives eluting at 6.01, 6.18 and 6.26 minutes in the GC-MS respectively. Baseline separation of the peaks is achievable. TMIO and TMIOH elute at 8.97 and 10.65 minutes respectively. The small peak at 8.32 minutes appears to correspond to a methylated derivative of TMIO, with m/z = 205. The possible sources of this species are discussed further below.
The product distributions can be used to determine relative rate coefficients as follows using the Arrhenius Equation,

\[ k = A e^{-\frac{E_a}{RT}} \]

An expression describing the changes in ratio of, say, o- and m-cresol is

\[ \frac{d[o]}{d[m]} = \frac{d[o]}{d[m]} = \frac{k_o[HO][tol]}{k_m[HO][tol]} \]

(Eq. 3)

where \([tol]\) is the concentration (or in principle, the activity) of toluene, and \(k_o, k_m\) are the rate coefficients for the addition of hydroxyl radical at positions ortho- or meta- to the methyl group on toluene. Thus, to good approximation:

\[ \frac{[o]}{[m]} = \frac{k_o}{k_m} \]

(Eq. 4)

A plot of natural log of the ratio of o- and m-cresol versus 1/T can be produced, where the difference in activation energies \((E_{A,o} \text{ and } E_{A,m})\) of the two competing systems is related to the slope of the line, and the intercept is the natural log of the ratio of the Arrhenius pre exponentials \((A_o \text{ and } A_m)\).

\[ \ln \left( \frac{[o]}{[m]} \right) = \ln \left( \frac{k_o}{k_m} \right) = \ln \left( \frac{A_o}{A_m} \right) + \frac{E_{A,m} - E_{A,o}}{RT} \]

(Eq. 5)

Similar expressions may be derived for \(k_p/k_m\) or any convenient ratio.

Table 5 shows the ratio of addition products at varying reaction temperatures, and Figure 4 shows the relative Arrhenius plots based on the relative rate coefficients for o-/m- and p-/m- product ratios.
Table 5. Product Distributions for Addition of Hydroxyl to Toluene

<table>
<thead>
<tr>
<th>Temperature (°C)</th>
<th>50</th>
<th>55</th>
<th>60</th>
<th>65</th>
<th>70</th>
<th>75</th>
<th>80</th>
</tr>
</thead>
<tbody>
<tr>
<td>avg(o/m)</td>
<td>4.86</td>
<td>4.31</td>
<td>4.21</td>
<td>4.07</td>
<td>3.95</td>
<td>4.21</td>
<td>3.89</td>
</tr>
<tr>
<td>avg(p/m)</td>
<td>1.13</td>
<td>1.09</td>
<td>1.12</td>
<td>1.06</td>
<td>1.10</td>
<td>1.07</td>
<td>1.10</td>
</tr>
</tbody>
</table>

Figure 3. Relative Arrhenius Plots for Hydroxyl Radical Addition to Toluene. Diamonds: ratio of o/m-cresol, Squares: p/m-cresol

Each sample was analyzed in triplicate, and the GC method was found to exhibit acceptable reproducibility. The difference in activation energies for hydroxyl radical addition are $E_{A,m} - E_{A,o} = 1.3 \pm 0.8 \text{ kcal/mol}$, $E_{A,p} - E_{A,o} = 1.1 \pm 0.9 \text{ kcal/mol}$ and $E_{A,m} - E_{A,p} = 0.2 \pm 0.4 \text{ kcal/mol}$ while the natural logarithm of the ratio of their pre-exponentials are $\ln(A_o/A_m) = 0.5 \pm 1.2$, $\ln(A_o/A_p) = -0.2 \pm 1.2$ and $\ln(A_p/A_m) = -0.2 \pm 0.6$. The uncertainties cited correspond to 90% confidence intervals based on the line of best fit.
As shown in the data, ortho and para positions are favored over meta. This is consistent with the directing effects that an electron donating group such as –CH₃ may exert on the reaction of a electrophilic species. The fact that m-cresol is detected in quantifiable amounts probably indicates that the selectivity towards hydroxyl radical is lower due to the fact that it is highly reactive, and is less electronegative than most species that undergo SEAr, which are often charged. However, when we correct for the number of sites available for attack (one p-, two each for o- and m-) we still find that the p-position is twice as reactive as the m-position, and the o-position four times as reactive.

The twofold difference of reactivity between ortho- and para-positions is noteworthy, but a definitive explanation has yet to be found, particularly as the difference appears to be largely enthalpic (ΔH°) in origin. A number of possible explanations suggest themselves:

- Proximity with respect to the methyl group. In principle, the proximity of the directing group may have an impact on kinetics. However, calculations indicate little localization of charge density at the ortho-position of toluene, and the HOMO (which would be the critical frontier orbital for reaction with an electrophilic radical) is not localized at ortho-carbons.
- ipso-Substitution is a mechanism that could possibly be occurring in our research, but is not easily determined using the current methodology. One may envisage the following reaction:

\[
\text{HO} + \cdot\text{OH} \rightarrow \text{HO} + \cdot\text{O}
\]
The cyclohexadienyl radical may be reversibly trapped by TMIO, and could rearrange to form the cyclohexadienyl radical corresponding to \( o \)-cresol. There is little evidence of 1,2-hydroxyl shifts in the free radical literature, but it is possible that the persistent radical effect allows us to access unusual reactions. Clearly further experimental and computational study is required to assess the feasibility of such a reaction. The formation of methylated trap may arise from loss of \( \cdot \text{CH}_3 \) from the intermediate radical, but it is noteworthy that no phenol is detected in these experiments.

- **Preferential Reactivity.** A preference for \( o \)-cresol may be observed where the reduction of cyclohexadienyl radical by TMIO is more favorable for \( o \)-cresol than its isomers.

Clearly, additional experimental and computational study is required to determine whether the observed preference arises from hydroxyl radical selectivity, or from other possible factors outlined above.

### 3.2. Reaction of Hydroxyl Radical with \( o \)- and \( m \)-Xylene

For \( o \)-xylene, there are only 2 potential outcomes (without considering the possibility of \( ipso \)-substitution) for mono substituted phenols: 2,3-dimethylphenol and 3,4-dimethylphenol. Similarly, addition to \( m \)-cresol may yield up to three phenol products: 2,6-dimethylphenol, 2,4-dimethylphenol, and 3,5-dimethylphenol (Scheme 15, overleaf).
The relative rate coefficients $k_{2,3}/k_{3,4}$ for addition of hydroxyl radical to $o$-xylene had values of 1.51 and 1.52 at 348 and 353K, respectively. This shows roughly a 1.5:1 reactivity ratio between these two positions, favoring the 2,3-dimethylphenol. Such an observation is consistent with the expected electrophile directing behavior of methyl groups. As noted above, the selectivity of reaction is not as marked as it is for most $S_E$Ar reactions.
In the case of \textit{m}-xylene, 2,6-dimethylphenol was found not to be a significant component of the product distribution. The relative rate coefficient ratios for the two remaining phenols, $k_{2,4}/k_{3,5}$, were found to be 1.67 and 1.62, at 348 and 353K, respectively. The absence of 2,6-dimethylphenol in \textit{m}-xylene data may be interpreted as a consequence of steric hinderance to attack, as the site lies between two methyl groups. At first glance, the ratio of 2,4-dimethylphenol to 3,5-dimethylphenol indicates that attack at the 4-position of \textit{m}-xylene is more favorable than attack at the 5-position, and this would be expected on the basis of electrophile directing effects of the two methyl groups. However, when we account for the number of possible sites of attack (two leading to the 2,4-isomer, and one leading to the 3,5-isomer), then we observe greater parity in reactivity. This is an unusual observation that requires more computational and experimental study.

3.3. Reaction of Hydroxyl Radical with Naphthalene

There are 2 possible products forming from the reaction of naphthalene with hydroxyl radical (Scheme 16).

\textbf{Scheme 16.} Reaction of Naphthalene with Hydroxyl Radical.

\[
\text{\textbullet OH} + \text{\textit{TMIO}} \rightarrow \text{\textit{1-naphthol}} + \text{\textit{2-naphthol}}
\]

The $k_1/k_2$ values for 1-naphthol/2-naphthol are 2.35 and 2.42 for 348 and 353 K respectively. This displays that as temperature increases, reactivity towards 1-naphthol increases as well, and there is a clear preference for attack at the 1-position of
naphthalene. Interestingly, these results are the opposite of those observed in the gas phase. However, the observation is consistent with the known electrophilic substitution chemistry of naphthalene, which generally favors the formation of the 1-isomer.

3.4. Reaction of Hydroxyl Radical with Biphenyl

There are three possible products forming from the reaction of biphenyl with hydroxyl radical (Scheme 17): 2-phenylphenol, 3-phenylphenol and 4-phenylphenol.

Scheme 17. Reaction of Biphenyl with Hydroxyl Radical.

As in the case of toluene, the ortho-substituted phenylphenol is much more favored than the other two phenylphenols: for 2-phenylphenol/3-phenylphenol, $k_2/k_3 = 5.07$ and $4.18$ at 348 and 353 K. For 4-phenylphenol/3-phenylphenol, $k_4/k_3 = 2.06$ and $1.74$ at 348 and 353 K, respectively. The difference in reactivity between $o$-/p- and m-substitution is enhanced from that observed in toluene, which is consistent with our general thesis, since the phenyl group is more ring activating and electron-donating. The question of ipso-substitution remains, as it did with toluene. However, in this particular case, the cyclohexadienyl radical arising from ipso-substitution will rearrange via known 1,2-phenyl shifts.
3.5 General Conclusions

Hydroxyl radical is generally considered to be an electrophilic species, and the
electrophilic nature of hydroxyl radical attack on aromatic compounds such as benzene
has been demonstrated computationally by the degree of charge transfer character in the
transition state, which has character consistent with an arene radical cation/hydroxide
complex.\textsuperscript{19} Similarly, the correlation between the kinetics of hydroxyl radical reaction
with arenes in solution and the ionization potential of the arene (a measure of the HOMO
energy where the arene acts as a nucleophile) confirms this behavior.\textsuperscript{11} Thus, it is
constructive to view the hydroxyl radical reaction as a modulated or attenuated version of
the standard S\textsubscript{E}Ar reaction.

Under such a model, one would expect the reaction selectivity to parallel to some
extent the directing effects observed in S\textsubscript{E}Ar, and thus one would expect to observe a
greater degree of ortho- and para- direction of hydroxyl radical attack. By and large, the
observed selectivites are consistent with such a model. The only two apparent
discrepancies in the data are the high preponderance of ortho-substitution over para-
in the toluene reaction, and also the product distributions observed for m-xylene. More
experimental and computational study is required to fully characterize these reactions.
APPENDIX 1 – DETERMINATION OF FID DETECTOR RESPONSES

To correctly be able to determine the concentrations of the derivitized alcohols through GC/FID methodology, relative response factors must be found. All relative response factors were determined relative to phenol.

Standard solutions (0.10M) of the aryl alcohols were prepared in benzene (10mL) and were serially diluted as indicated in the table below. 300 µL of BSTFA was added, and the resulting mixtures heated 75°C for 2 hours. The mixtures were analyzed as described in Chapter 3, and the detector response ratios for each alcohol plotted against mole ratio (in all cases, phenol served as the standard). Isomeric cresols are used as an illustrative example.

<table>
<thead>
<tr>
<th>Run #</th>
<th>v. phenol (µL)</th>
<th>v. o-cresol (µL)</th>
<th>v. p-cresol (µL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>50</td>
<td>50</td>
<td>50</td>
</tr>
<tr>
<td>2</td>
<td>50</td>
<td>40</td>
<td>40</td>
</tr>
<tr>
<td>3</td>
<td>50</td>
<td>30</td>
<td>30</td>
</tr>
<tr>
<td>4</td>
<td>50</td>
<td>25</td>
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\[
y = 1.1422x - 0.0163 \quad R^2 = 0.9998
\]

\[
y = 1.1426x - 0.0327 \quad R^2 = 0.9995
\]
BIBLIOGRAPHY


