Solvent and Solubility Effects on Quinone Ratios

By

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Monoquinones and diquinones are a biologically and chemically important class of compounds that can be found in numerous natural products such as: thymoquinone, oosporein, coenzyme Q, embelin and the respective dimer, biembelin. These 1, 4-benzoquinone derivatives exhibit prominent pharmacological applications such as antibiotic, anti-tumor, anti-malarial, anti-coagulant, and anti-convulsant activity.

Co-enzyme Q   Thymoquinone   Oosporein   Embelin
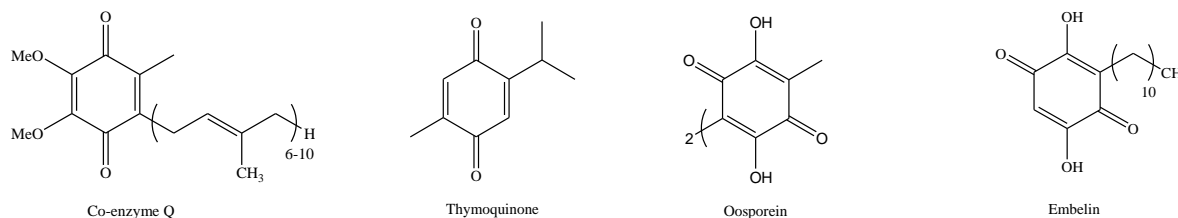
Though quinones can be prepared by a variety of processes, they are most commonly synthesized through the treatment of hydroquinone dimethyl ethers with ceric ammonium nitrate (CAN). However, this can lead to an unpredictable mixture of monoquinone and diquinone as the products. This project has investigated the effect of solvent and substrate water solubility on monoquinone / diquinone product ratios with the aim of being able to consistently and predictably favor one (monoquinone or diquinone) over the other.

Monoquinone   Diquinone
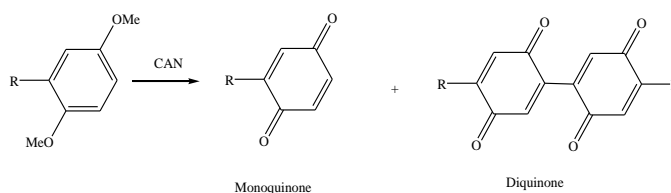
Solvent and Solubility Effects on Quinone Ratios

A Thesis
Presented To the Faculty of the Department of Chemistry
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In Partial Fulfillment of the Requirements for the Degree
Masters' in Chemistry

by

Brian Duffy

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Dedication

I would like to thank my friends, family, my wife Chelsea, and the Chemistry Department for all

of the support in this opportunity and providing me a means to succeed in life.

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List of Symbols or Abbreviations

THF - tetrahydrofuran…………………………………………………………………..…………….

n-BuLi – n-butyl-Lithium………………………………………………………………………….

min - minute……………………………………………………………………………………….

rt – room temperature……………………………………………………………………………….

°C – degree Celsius …………………………………………………………………….…………..

mmol - millimole……………………………………………………………………..…………….

mL - milliliter…………………………………………………………………………………….

M - molar……………………………………………………………………………..…………..

sat'd - saturated………………………………………………………………………………….

mp – melting point………………………………………………………………………………..

g – gram(s)…………………………………………………………………………………………

δ - chemical shift (ppm)…………………………………………………………………………….

Hz - hertz ……………………………………………………………………………………..…..

MHz - megahertz……………………………………………………………………………..…..

TMS – tetramethylsilane, used for calibrating NMR…………………………………………………

J – coupling constant……………………………………………………………………………..

br – broad………………………………………………………………………………………...

s - singlet………………………………………………………………………………..…..

d - doublet…………………………………………………………………………………..……

t - triplet………………………………………………………………………………………..

q - quartet……………………………………………………………………………………..…..

m – multiplet…………………………………………………………………………………….

Chapter 1: Introduction

Oxidation of dimethoxybenzenes is not new to the literature. Originally, nitric acid or silver oxide was used to oxidize hydroquinone dimethyl ethers into the corresponding quinones.[1] However, both reagents require harsh conditions as well as strongly acidic media.[2] In some cases, when in the presence of nitric acid, nitration of the aromatic ring occurred instead of or in addition to the oxidative demethylation.[1] Castagnoli and co-workers first introduced ceric ammonium nitrate ($[Ce(NH_4)_2(NO_3)_6]$) or commonly known as CAN, in acetonitrile for the oxidative demethylation of numerous hydroquinone dimethyl ethers.[2] They showed that the reaction can be carried out in the absence of a strong acid and generally completes oxidation readily at room temperature.[2]

Presently, the exact mechanism of this one electron oxidation[3] is uncertain; however, it appears that starting material **1** can either be oxidized directly to the monoquinone **2** or dimerize to a tetra-methoxy intermediate **3**. Work[4] has shown monoquinone **2** is not a precursor to diquinone **5.** Dimer **3** can be either partially oxidized to **4** or fully oxidized to the respective diquinone **5**.

Figure 1.1.1: Quinone Formation
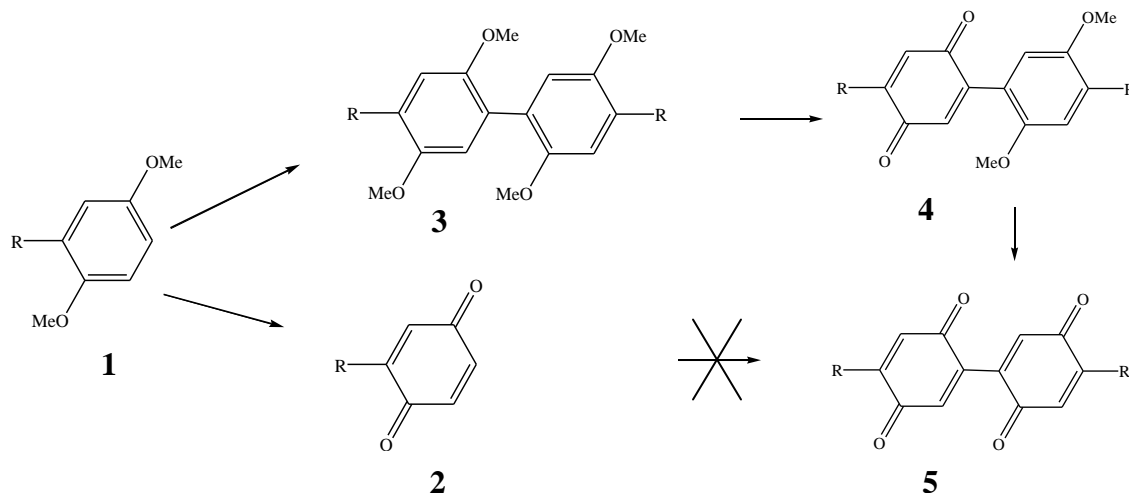
Even though the exact mechanism of the monoquinone/diquinone formation is unknown,

one possible mechanism is shown below. Please note, although many different resonance

structures are possible for the intermediates shown, only one is represented.

Figure 1.1.2: Proposed Mechanism of Monoquinone/Diquinone Formation

<u>Monoquinone Formation</u>

Oxidation/Nucleophilic Attack/ Hemiacetal Formation
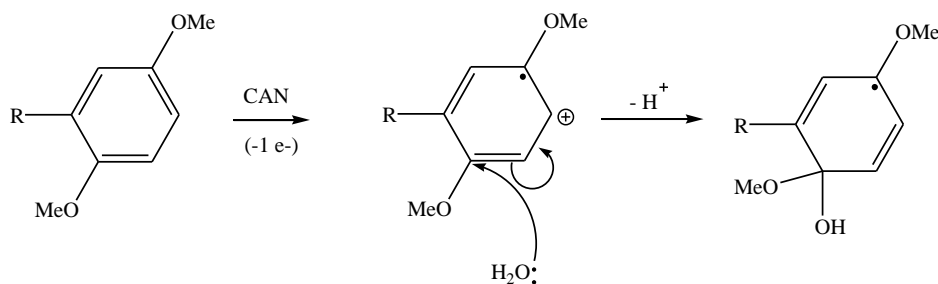
Oxidation/Nucleophilic Attack/ Hemiacetal Formation
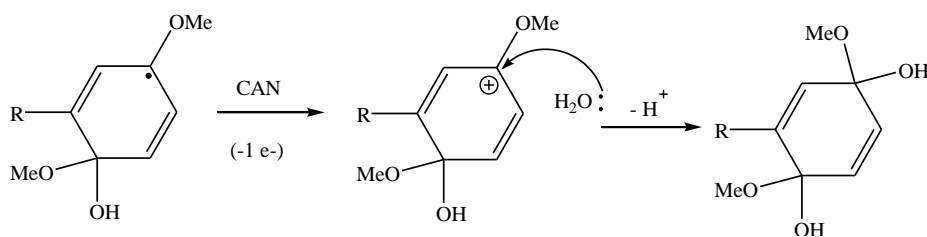
Hemiacetal Decomposition
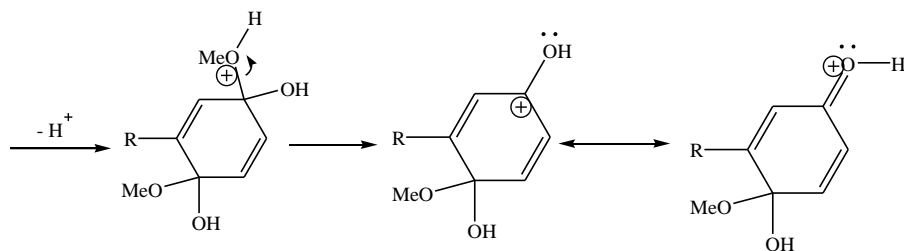
Formation of the Monoquinone
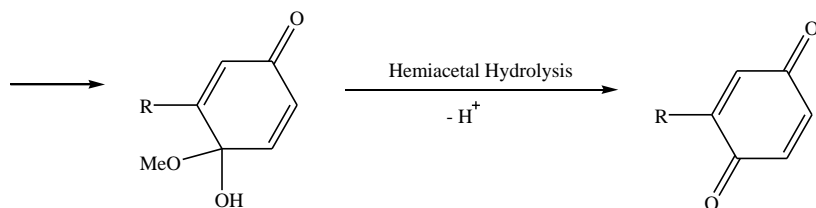
Figure 1.1.2: Proposed Mechanism of Monoquinone/Diquinone Formation continued

Diquinone Formation
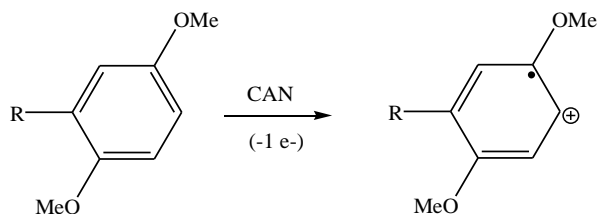
Oxidation

Electrophilic Aromatic Substitution
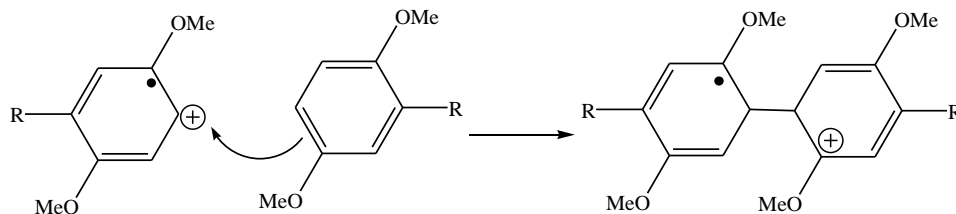
Regeneration of Aromaticity
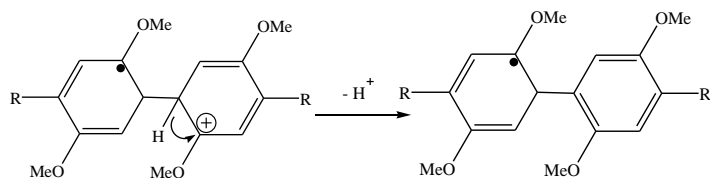
Oxidation
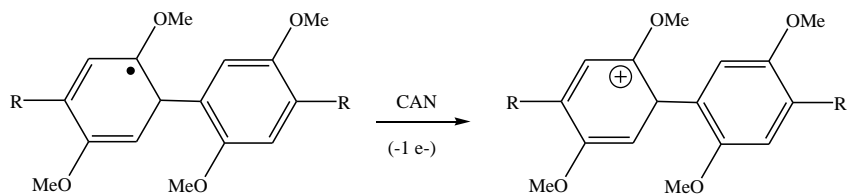
Regeneration of Aromaticity
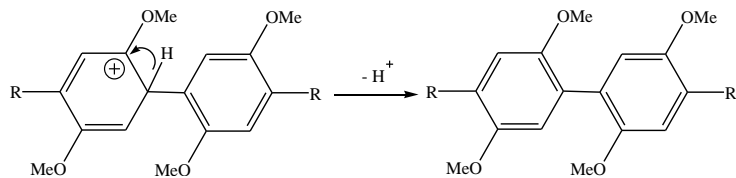
Figure 1.1.2: Proposed Mechanism of Monoquinone/Diquinone Formation continued

Hemiacetal Formation/Decomposition (mechanism shown previously) and Diquinone Formation
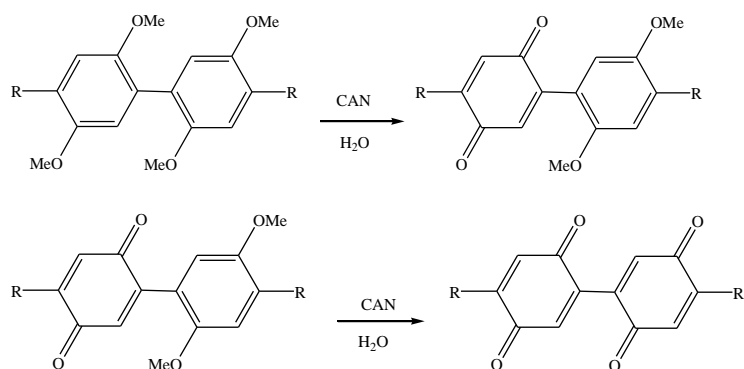
This project has examined the product outcome for two orders of addition, "traditional" and "inverse". We chose the term "traditional", because traditionally the oxidant is introduced into the stirring sample of arene which is dissolved in acetonitrile.[4] With this mode of addition, one might expect that diquinone formation would be favored, because during the initial stages of the addition the arene would be in greater excess relative to the oxidant, so the probability of the radical cation encountering unreacted arene is elevated.

Inverse addition, on the other hand, is the term we applied when the arene was introduced into a solution of aqueous ceric ammonium nitrate. One might think this would to lead to significant monomer formation because as the arene is introduced dropwise into the oxidant, it would be oxidized immediately with little present with which it could dimerize.

We found, however, that traditional addition typically produced a greater proportion of monomer than "inverse" addition, and conversely inverse addition led to a greater proportion of dimer formation than "traditional" addition. One possible explanation is that during inverse addition, when the arene solution first adds to the aqueous ceric ammonium nitrate solution, the low aqueous solubility of the arene generates a high local concentration of arene, which allows for unreacted starting material to attack the radical cation faster than a water molecule, leading to

4

dimer formation. On the other hand, during "traditional" addition, the arene is dispersed in

solvent (acetonitrile) and as the solution increases in aqueous volume, the water is then able to

do a nucleophilic attack on the cation faster than an unreacted starting material can complete an

electrophilic aromatic substitution. Since the radical cation intermediate is attacked more

quickly by water than by the arene, this leads to monomer formation. Our investigation of

addition effects on product formation will be discussed later.

1.1: Quinones in nature

Quinones are a main component in numerous naturally occurring products. They occur

predominately in plants, fungi, insects (sex and defense hormones), as well as in metabolic

processes and have numerous prominent pharmacological applications such as antibiotic,

antitumor, anti-malarial, anti-coagulant, and anti-convulsant activity.[4-9]

In addition to being useful compounds in their own right, monoquinones and diquinones

are potential synthetic precursors to biologically significant natural products. For example,

popolohuanone E **6** has shown inhibitory activity toward topoisomerase II as well as selective

cytotoxicity against the A549 nonsmall human lung cancer cell line.[5] Popolohuanone E has been

previously isolated from the Pohnpei marine sponge *Dysidea* sp.[5] To date there has been no

successful total synthesis of **6**, though in theory it could be prepared by dimerization of the

appropriate arene followed by a ring closure reaction, which is discussed later.
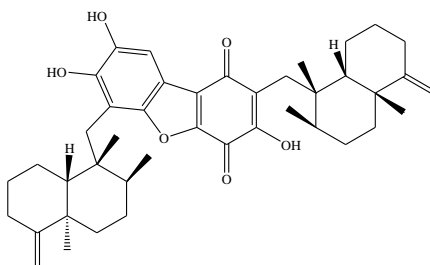
6

Another important naturally occurring quinone is thymoquinone, **7**, which is found in the plant *Nigella sativa*, which has been used for treating liver disorders and arthritis.[6]
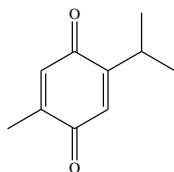
7

Oosporein, **8**, is a fungal metabolite that has been synthesized and isolated various times from several sources and has shown antifungal, antibiotic, and antiviral activities.[4]
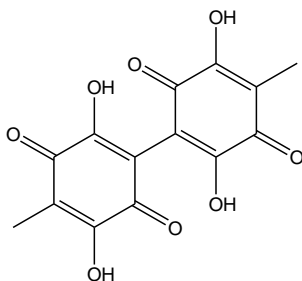
8

Coenzyme Q, **9**, also known as ubiquinone, is a main component of the electron transport chain that is present in most eukaryotic cells and assists in generating ATP (adenosine triphosphate).[7]
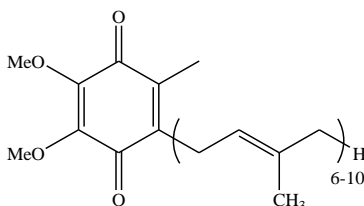
9

Embelin (2,5-dihydroxy-3-undecyl-1,4-benzoquinone), **10**, is a major constituent of *Embelia ribes* Burm. from the family Myrsinaceae. Embelin has shown antitumor, anti-inflammatory, antibacterial, and antioxidant activities.[8]

10

The respective dimer, biembelin **11**, is a known yet rare compound and, to date, we are

unaware of any attempts to synthesize this compound.
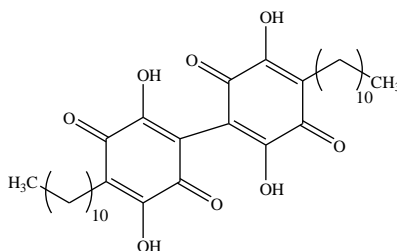
11

Numerous quinones serve as insect hormones, especially sex and defense hormones.[9]

One of particular interest is gentisyl quinone isovalerate, or commonly known as

blattellaquinone, **14**. This hormone is of interest because it can lead to consistently effective traps

without harming the environment.[9]
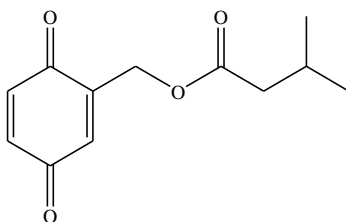
14

1.2: Synthetic challenges

Even though each of these respective quinones commands an in-depth study, the goal of

my project was to introduce a method to generate specifically the monoquinone or the diquinone

starting from the same dimethoxyarene precursor. By manipulating the mode of addition, volume

of solvent, or identity of the reaction solvent, we believed that we could influence the product distribution.

Occasionally investigators obtain either a mixture of monoquinone and diquinone or none of the desired quinone product when using ceric ammonium nitrate to oxidize dimethoxyarenes. For example, when Srikrishna[10] attempted to prepare monoquinone **16** (as part of his synthesis of Herbertenone A), by treating the dimethoxyarene precursor **15** with ceric ammonium nitrate, only the diquinone, Herbertenone B, **17** was isolated.

Figure 1.2.1: Formation of **17**

| **15** | **16** | **17** |
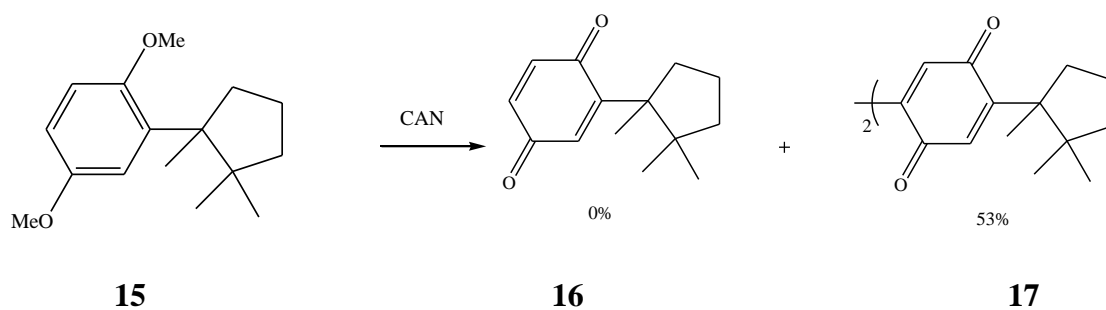
Srikrishna was able to synthesize the desired monoquinone **16**, but only by converting the starting material into **18** via BBr_3 and then subjecting **18** to oxidation with ceric ammonium nitrate[10]. Successful development of a reaction protocol which favors monoquinone formation starting from dimethoxybenzenes might make this additional step unnecessary.

18
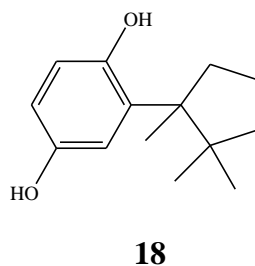
On the other hand, diquinones can occasionally be the desired product of oxidation of arenes. For example, as part of a model study related to the attempted total synthesis of popolohuanone E **6,** Anderson and co-workers were able to convert diquinone **B** into **C** by

simple treatment with potassium carbonate[5] as seen in Figure 1.2.2 below. (In this case the

neopentyl group serves as a substitute for the more complex aliphatic sidechain of **6**). The

proposed mechanism for this transformation involves an intramolecular Michael addition[5] as

shown in Scheme 1.2.1.

Figure 1.2.2: Biomimetic Diquinone Rearrangement

A   **B**   **C**
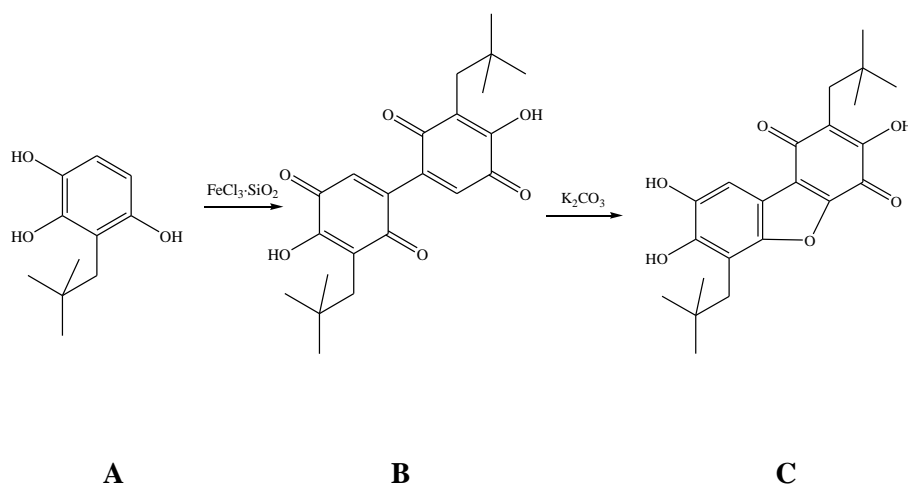
Scheme 1.2.1: Intramolecular Michael Addition
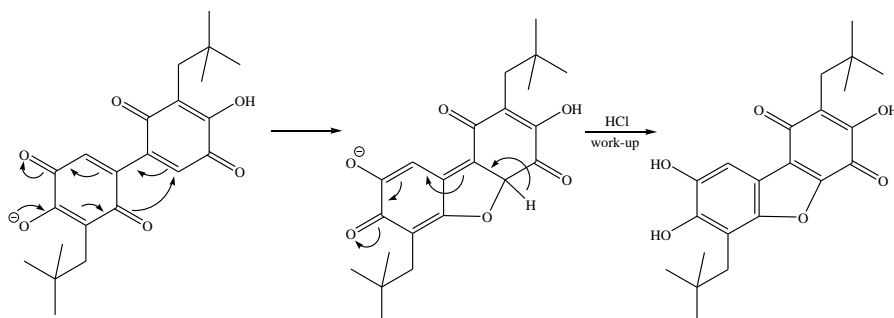
No successful synthesis of intermediate **B** has been reported using a CAN-based

oxidation, though Anderson was able to prepare **B** from **A** using iron(III) chloride on silica gel.

Unfortunately, use of this same reaction on the analogous compound in which the neopentyl

group had been replaced with the popolohuanone E sidechain failed to give any of the desired

dimer. Development of a protocol which consistently favors diquinone formation might help to solve this synthetic problem.

Another example of a synthetic challenge is seen with the generation of blattellaquinone, **14**. This quinone is a German cockroach sex pheromone and has been recently synthesized by Feist from a dimethoxyarene precursor, **13**, in poor yield as shown in Scheme 1.2.2.[9]

Scheme 1.2.2: Formation of Gentisyl Quinone Isovalerate

	2,5-dimethoxybenzyl-3-methylbutanoate	gentisyl quione isovalerate
	30-40 %	20-30 %
12	**13**	**14**
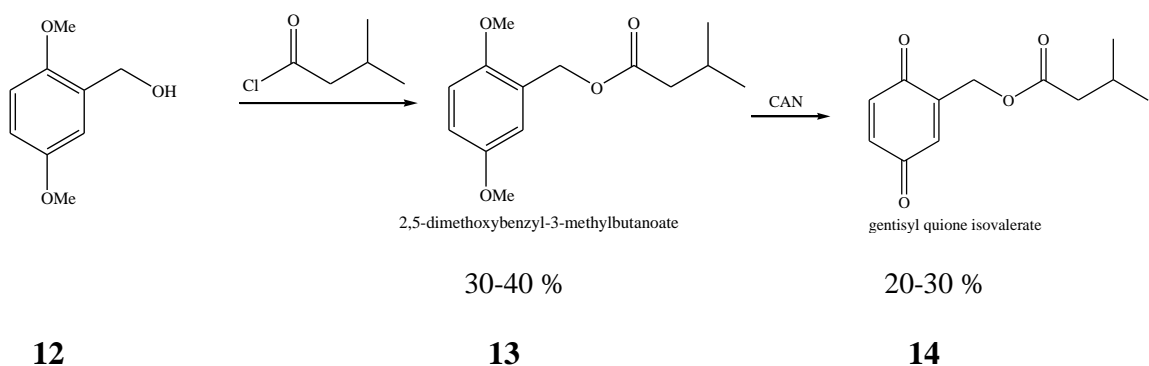
Feist reports 20-30 % yield of the desired monoquinone with the generation of a pale yellow solid precipitate; which she claims to be "reduced ceric ammonium nitrate".[9] This work and previous work[4] have shown that the pale yellow solid is actually the corresponding diquinone and not "reduced ceric ammonium nitrate" as Feist reports it to be. Once again, development of reaction conditions which favor monoquinone formation at the expense of diquinone formation would help improve the yield of this synthesis.

To our knowledge, there has not been a systematic investigation of the factors that influence the monoquinone/diquinone ratios. In this project, water solubility of the substrate, solvent composition effects, and the nature of the reaction solvent were investigated.

Chapter 2: Thesis Project Part I

One hypothesis is that there is an optimal degree of water solubility that favors diquinone formation. More specifically, if the substrate is somewhat insoluble in water, the amount of arene present may exceed its solubility in water, resulting in either micelle formation or the formation of a suspension of the arene in the aqueous reaction mixture. In either case, this would create areas of high concentration of the arene (relative to that found in solution) allowing the unreacted starting material to compete more effectively with the water in attacking the initial radical cation intermediate. This might be expected to lead to increased formation of diquinone.

Conversely, if the substrate is too water soluble, monoquinone formation takes precedence. This is because a dispersed arene in solution allows for water to compete more effectively with the arene in attack on the radical cation intermediate and allows for an increase in monoquinone formation.

2.1: Water solubility

In the early stages of this project, we wanted to modify the methoxy groups into either more hydrophobic or more hydrophilic substituents. We hypothesized that if it was made more hydrophobic, by introducing a phenyl or an aliphatic chain, this would significantly decrease the water solubility of the substrate, and lead to enhanced diquinone formation.

Conversely, by introducing a glycol chain, we hypothesized this would generate a more hydrophilic substrate and allow for a dispersed arene and lead to monoquinone formation. By allowing for a more dispersed arene in solution, the radical cation intermediate would be more accessible to water, which, according to our hypothesis, should increase monomer formation.

2.2: Investigating the Ideal Substrate

Before modifying the water solubility of the substrate, we first had to find an "ideal substrate". We deemed an "ideal substrate" one which gave both monoquinone and diquinone upon treatment with ceric ammonium nitrate, and also allowed us to readily determine the relative amounts of the monomer and dimer. By doing so, we could use the precursors to then modify the water solubility of the respective substrate and determine the change in product formation.

Numerous syntheses of precursors were attempted in order to find the "ideal substrate", as shown below. Please note, an "X" denotes an unsuccessful reaction in which only starting material was isolated, while a dashed arrow means a proposed reaction that was not run.

Scheme 2.2.1[11-14] : Precursor Formation
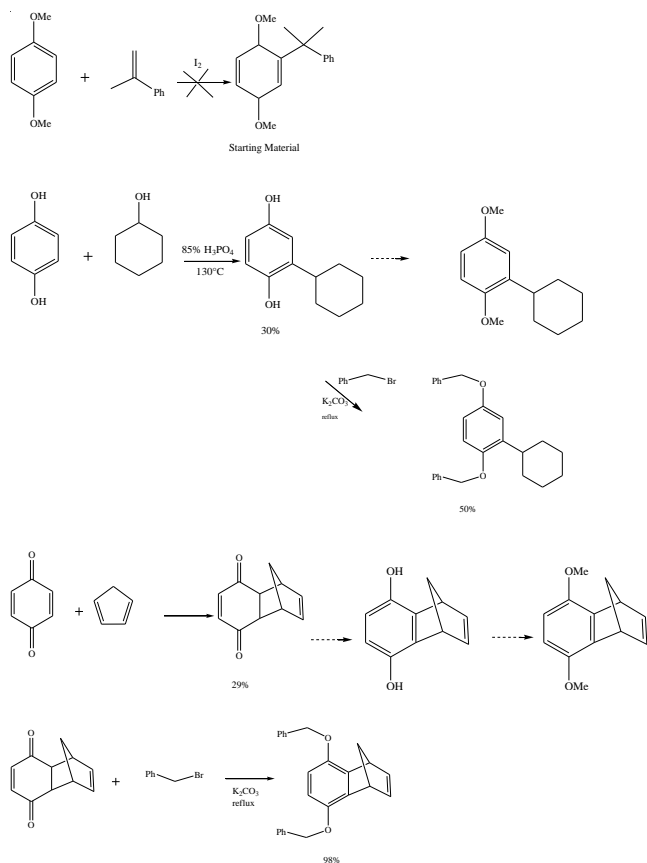
Scheme 2.2.1[11-14] : Precursor Formation Continued

23%
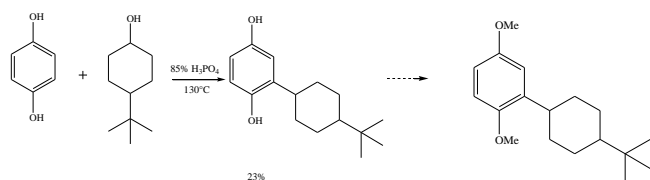
Soon after synthesizing these precursors, we investigated 2,5-dimethoxybenzyl 3-methylbutanoate, **13**, and 2-*tert*-butyl-1,4-dimethoxy-benzene, **19**.

2,5-dimethoxybenzyl 3-methylbutanoate

13

2-*tert*-butyl-1,4-dimethoxy-benzene
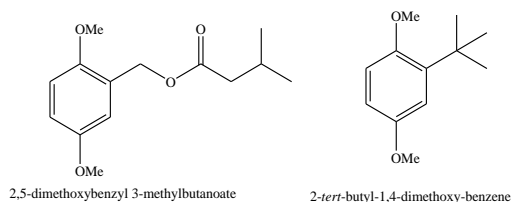
19

Products derived from these two substrates have shown complete physical separation (the diquinone precipates out of the reaction mixture, whereas the monoquinone stays in solution) and also are readily distinguishable by proton NMR spectroscopy. Furthermore, the precursors are made fairly easily and consistently in respectable yields (see experimental section). Since each of these substrates produced easily separated and distinguishable monoquinone and diquinone products upon treatment with CAN, we thus found two suitable "ideal substrates." With this observation, the previously shown precursors in Scheme 2.2.1 were no longer studied.

After synthesizing 2,5-dimethoxybenzyl 3-methylbutanoate and 2-*tert*-butyl-1,4-dimethoxy-benzene by known methods, we also added 2,5-dimethoxytoluene, **20**, to our list of potential substrates.

2,5-dimethoxytoluene
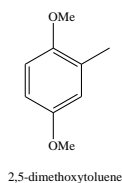
20

We added this substrate because we knew that it too generates a precipitate that is generally pure dimer.[4] We quickly saw similarities in the alkyl chain substrates, 2-*tert*-butyl-1,4-dimethoxy-benzene and 2,5-dimethoxytoluene but results varied greatly in diquinone product formation when 2,5-dimethoxybenzyl 3-methylbutanoate was used as the substrate.

We speculated that the different behavior of **13** was due to the presence of the benzylic oxygen functionality. This oxygen could be affecting the product ratio in any number of ways. For example, it could provide additional stability to benzylic radicals (resulting in additional side reactions), it could lower the electron density of the benzene ring, and thereby reduce the rate of electrophilic substitution relative to the alkyl substituted substrates, or the carbonyl group to which it is attached could help to stabilize the radical cation intermediate, making it a weaker electrophile, and thus also reducing the rate of electrophilic substitution relative to the alkyl substituted substrates. We are uncertain of which, if any, of these effects are responsible for the observed effects on product ratios.

Even though 2,5-dimethoxybenzyl 3-methylbutanoate leads to an interesting quinone in its own right, we decided to no longer study substrates with heteroatom containing sidechains. Instead, we decided to focus only on substrates with simple alkyl chains since any variation in chain length should not have any significant effect on the electronic nature of the substrates.

Since we found 2-*tert*-butyl-1,4-dimethoxy-benzene and 2,5-dimethoxytoluene to be our "ideal substrates," we then attempted to prepare other 1,4-dimethoxybenzene derivatives bearing simple alkyl chains. One of the first investigated was the compound substituted with an undecyl chain, **21**, given that this can be considered a precursor to embelin, **10**, and biembelin, **11**, which were on our list of interesting natural products. We synthesized **21** as shown in scheme 2.2.5, and then attempted to prepare the respective monoquinone and diquinone as shown below.

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Scheme 2.2.5: Formation of Undecyl Alkyl Chain Monomer and Dimer

21   **22**   **23**
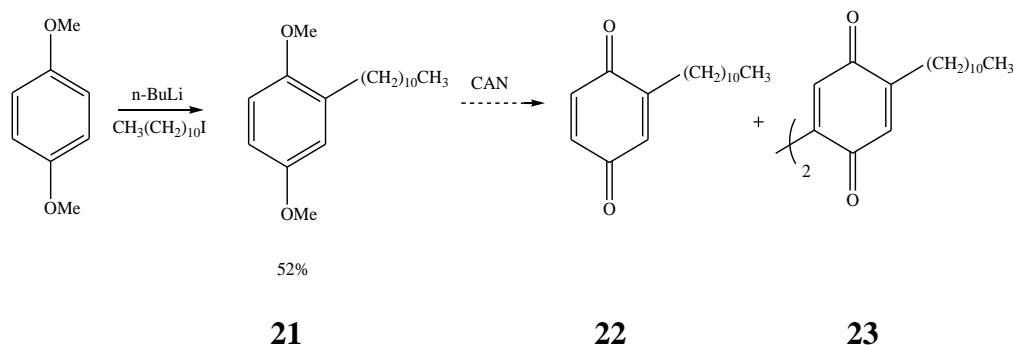
We found, however, that the undecyl substituted compound **21** was not soluble in acetonitrile and only starting material was isolated from its reaction with aqueous ceric ammonium nitrate. Because of this observation, we had to ask the question, "At what point does the alkyl chain become too hydrophobic to allow it to undergo the oxidation reaction?" This prompted us to study propyl, pentyl, heptyl, and nonyl alkyl chains to see if the increasing hydrophobicity would lead to methoxy-containing products (an indication of incomplete oxidation), greater dimer formation, or, as seen with the undecyl chain, starting material. Furthermore, we needed to develop a new method of synthesizing **22** and **23**, which will be discussed later.

These substrates (with alkyl substituents ranging from propyl to undecyl) were all prepared via ortho-lithiation with the appropriate alkyl iodide, as shown in Scheme 2.2.7. 1-iodopropane, 1-iodopentane, and 1-iodoheptane were all obtained commercially, but 1-iodononane and 1-iodoundecane were both prepared from the corresponding alcohol as shown in Scheme 2.2.6. The yields for synthesizing these alkyl iodides were 70.3% and 71.7%, respectively.

Scheme 2.2.6[23]: Formation of Alkyl Iodide Chain

Scheme 2.2.7: General Ortho-lithiation
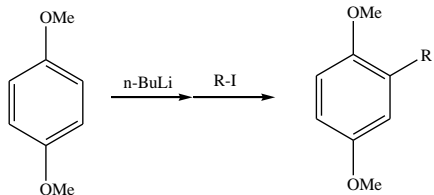
Table 2.1: Percent Yield of Precursors from Ortho-Lithiation Reaction

R=	Yield (%)
$(CH_2)_2CH_3$	71
$(CH_2)_4CH_3$	62
$(CH_2)_6CH_3$	64
$(CH_2)_8CH_3$	19
$(CH_2)_{10}CH_3$	79

As for the other two substrates used in these studies, 2,5-dimethoxytoluene was obtained commercially, and 2-*tert*-butyl-1,4-dimethoxy-benzene was prepared by alkylation of butylated hydroxyanisole with dimethyl sulfate as shown in Scheme 2.2.8.

Scheme 2.2.8[24]: Formation of 2-*tert*-butyl-1,4-dimethoxy-benzene
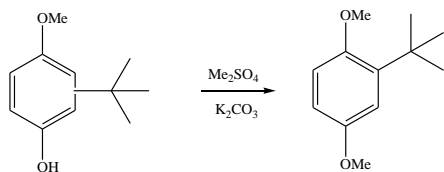
85%

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2.3: Effects of Order of Addition and Alkyl Chain Length on Product Ratios

In this portion of my project, we wanted to investigate varying effects on monoquinone /diquinone product ratios. One effect we investigated was the order of addition of the reagents

by comparing the results obtained via "traditional" and "inverse" addition. We also wanted to see if product ratios were affected by the length of the alkyl chain present on the substrate.

We originally hypothesized that with increasing length of the alkyl chain, greater dimer formation would be evident. To further support this hypothesis, we compared calculated log P values (per ChemDraw) of the starting materials, which are as follows:

Table 2.2: Starting Material Calculated log P Values
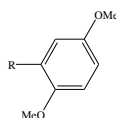
R=	Calculated Log P
t-Bu	3.49
CH_3	2.27
$(CH_2)_2CH_3$	3.10
$(CH_2)_4CH_3$	3.49
$(CH_2)_6CH_3$	4.77
$(CH_2)_8CH_3$	5.61

We look at the log P values because they give a good indication of how hydrophobic each substrate is. We see that, as expected, as the alkyl chain becomes longer, log P values for the substrate generally increase, however the differences are not necessarily dramatic.

Once we synthesized our precursors, we then completed 1:1 traditional addition for all of our alkyl chain substrates and compared the product ratios to 1:1 inverse addition. For every sample completed, we maintained a consistent volume of 10 mL for both acetonitrile and water, which we denote as "1:1". As mentioned earlier, traditional or inverse addition denotes the mode of addition that was used. Traditional addition is where an aqueous solution of ceric ammonium

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nitrate is added to the arene, which is dissolved in acetonitrile, and inverse addition is where the addition is reversed.

Moreover, as mentioned earlier, previous work[4] has shown that traditional addition leads to a greater amount of monomer formation and inverse addition leads to primarily dimer formation. The initial hypothesis would suggest that as the alkyl chain elongates, the substrate would become more hydrophobic and dimer formation would take precedence. This is based on the assumption that as the water solubility of the substrate decreases, this promotes formation of high concentrations of unreacted starting material and allows for attack of the radical cation intermediate by arene to compete effectively with hydrolysis, thereby increasing diquinone formation.

Table 2.3: Comparison of 1:1 Traditional Addition to 1:1 Inverse Addition
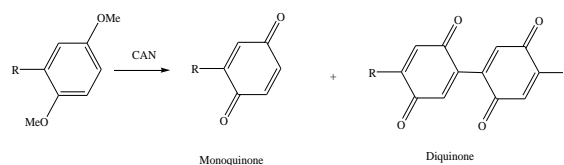
R=	1:1 Acetonitrile:Water Traditional		1:1 Acetonitrile:Water Inverse	
	Mono: Di	Total Product Yield	Mono:Di	Total Product Yield
t-Bu	1 .1: 1	67	1 : 1.4	99
CH_3	1 : 94	84	1 : 45	93
$(CH_2)_2CH_3$	2 : 1	44	1 : 6	72
$(CH_2)_4CH_3$	1 : 9	82	1 : 11	80
$(CH_2)_6CH_3$	1 : 3	80	1 : 3	57 *
$(CH_2)_8CH_3$	1 : 2	45	1 : 1.1	91*

* significant methoxy containing products

Looking at the series of substrates for a given reaction protocol (either "traditional" or "inverse") we fail to see a clear trend in the increase of diquinone ratio as the length of the alkyl

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group increases. In fact, the greatest dimer formation is found with the substrate with the shortest alkyl chain, 2,5-dimethoxytoluene.

Though a linear trend is not obvious, generally we found that the smaller alkyl chains produced higher percentages of the corresponding diquinone. One possibility is that factors which were not rigorously controlled (such as precise rate of addition of the reagent which was being added and/or the rate of stirring of the solution to which it was being added) might also affect product ratios, and thus account for the wide variance in results. Although other factors might be occurring, we are currently uncertain of the exact cause of this observation.

In comparing traditional versus inverse addition for a given substrate, we yet again fail to see a definitive trend. We did observe, however, that use of the inverse addition protocol for the most hydrophobic substrates resulted in increased formation of products which still contained methoxy groups (as evidenced by their proton NMR spectra). We suspect that these methoxy-containing compounds are products in which two aromatic rings have joined, yet the compounds have not been fully oxidized to the diquinone stage, such as the tetramethoxybiaryl and dimethoxyaryl quinone intermediates shown in Fig 1.1.2, though other methoxy-containing intermediates have also been proposed or observed in similar oxidations.[20, 21] We believe that these intermediates in which R = heptyl, nonyl or undecyl were too insoluble in the aqueous ceric ammonium nitrate solution to allow their complete oxidation to the corresponding diquinones.

We tried another variation on 1:1 traditional addition where we dissolved the ceric ammonium nitrate in a 50:50 mixture of acetonitrile:water and added it to the arene, which was also dissolved in a 50:50 mixture of acetonitrile:water. This reaction mixture was still considered "1:1" because the final reaction volume was equivalent to a normal 1:1 addition, but yet it

removed the effect of having an acetonitrile solution of the arene add to an aqueous solution of the ceric ammonium nitrate – in effect, there was no change in solvent composition as the addition progressed. This variation was complicated as the mixture being added was difficult to maintain as homogeneous. In any case, little to no variation occurred in the product ratio. For example, with the *tert*-butyl substrate, a 1 : 1.1 monomer : dimer ratio was found, which is the same ratio as was observed for the normal traditional addition protocol.

2.4: Solvent Composition Effects

In this portion of the project, we wanted to vary the solvent composition. By using an equal volume of acetonitrile to water, which we indicate as 1:1, and using traditional and inverse addition as our starting point, we wanted to try simple modifications to increase or decrease monoquinone/diquinone ratios stemming from the same dimethoxyarene precursor. We began with what we called "1 (acetonitrile): 2 (water) traditional addition". This is where we dissolved the arene in 5 mL of acetonitrile and 10 mL of the aqueous ceric ammonium nitrate was added. We decided on this ratio because we did not want to introduce diluting the ceric ammonium nitrate into this specific experiment.

Table 2.4: Comparison of 1:1 Traditional Addition to 1:2 Traditional Addition
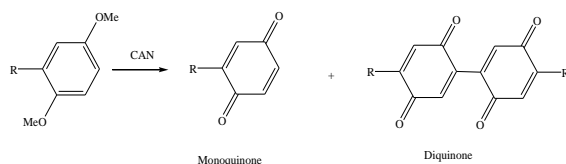
Traditional				
	1:1 Acetonitrile:Water		1:2 Acetonitrile:Water	
R=	Mono : Di	Total Product Yield	Mono : Di	Total Product Yield
t-Bu	1 .1: 1	67	1 : 2	99
CH_3	1 : 94	84	1 : 154	84
$(CH_2)_2CH_3$	2 : 1	44	1 : 16	88
$(CH_2)_4CH_3$	1 : 9	82	1 : 4	71
$(CH_2)_6CH_3$	1 : 3	80	1 : 5	40*
$(CH_2)_8CH_3$	1 : 2	45	1 : 3	71*

* significant methoxy containing products

Looking at the data for 1:2 traditional addition, we again fail to see a significant trend among the various substrates (the methyl substituted compound still gives the highest proportion of dimer). In comparing the 1:1 solvent ratio with the 1:2 ratio, however, we see that generally the 1:2 mixture led to an increase in dimer formation (with the exception of the pentyl-substituted substrate). This supports the original idea that the arene has low water solubility, which results in the formation of regions of high arene concentration as the amount of water present in the solvent mixture is increased. Thus, unreacted starting material is more accessible and this allows for an increase in dimer formation. Also, as was seen with 1:1 inverse addition, the more hydrophobic substrates (those substituted with heptyl and nonyl groups) once again gave product mixtures in which significant amounts of methoxy-containing compounds were observed. We believe once again that these methoxy-containing compounds (whatever they

might be) precipitated out of solution before being fully oxidized to the corresponding diquinones.

Next, we tried "2 (acetonitrile): 1 (water) inverse addition" where the ceric ammonium nitrate was concentrated into 5 mL of water. Originally, we thought that with utilization of the inverse addition protocol, the hydrophobic substrate would form a type of micelle (or at least some sort of region of increased arene concentration) as the arene solution first encountered the aqueous ceric ammonium nitrate and would lead towards dimer formation.

By decreasing the amount of water available, in respect to 1:1 inverse addition, we believed we would see a decrease in monoquinone formation because this would increase the ionic strength of the aqueous solution, even more so than 1:1 inverse addition. By increasing the ionic strength, we thought that we would see an increase in dimer formation because the aqueous solution would be more "inhospitable" toward the arene than the solution used in the 1:1 inverse addition reaction. By making the aqueous solution more inhospitable towards the arene, this should increase the regions of high concentration of unreacted starting material and make water less competitive with respect to attack on the radical cation intermediate.

Table 2.5: Comparison of 2:1 Inverse Addition to 1:1 Inverse Addition

Monoquinone   Diquinone
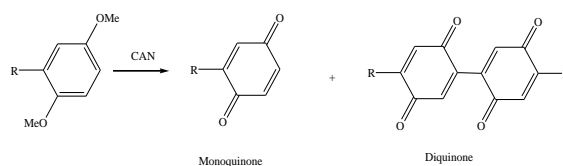
Inverse				
	2:1 Acetonitrile:Water		1:1 Acetonitrile:Water	
R=	Mono : Di	Total Product Yield	Mono : Di	Total Product Yield
t-Bu	1 : 2	56	1 : 1.4	99
CH_3	1 : 125	92	1 : 45	93
$(CH_2)_2CH_3$	1 : 9	68	1 : 6	72
$(CH_2)_4CH_3$	1: 5	75	1 : 11	80
$(CH_2)_{-6}CH_3$	1 : 4	100*	1 : 3	57 *
$(CH_2)_8CH_3$	1 : 4	79 *	1 : 1.1	91*

* significant methoxy containing products

Once again there is no obvious trend among the substrates as the chain length increases. In this solvent composition variation, we anticipated that we would see an increase in dimer formation due to the increased ionic strength of the CAN solution, and this is the general trend we see. With the exception of the pentyl-substituted substrate, greater proportions of dimer were found in the product mixtures from "2:1 inverse addition" as compared to "1:1 inverse addition", though the differences were not great. As we have seen before, starting arenes substituted with heptyl and nonyl groups once again gave product mixtures in which significant amounts of methoxy-containing compounds were observed. It seems that by varying the solvent composition by either manipulating the ionic strength or by increasing the amount of water present can increase dimer formation. This supports our hypothesis that the low water solubility

of the arene encourages dimer formation because unreacted starting material is more accessible

than water.

Chapter 3: Thesis Project Part II: Effects of Varying Solvent

3.1: DMSO

In this portion of my project, we investigated the effects of varying the reaction solvent on quinone/diquinone ratios. Acetonitrile and water are the most commonly used solvents when using ceric ammonium nitrate to oxidize a hydroquinone dimethyl ether into the corresponding quinone. This is because water solvates the ceric ammonium nitrate and the acetonitrile dissolves the arene. Once both are combined, this leads to a mixture that can lead toward monoquinone or diquinone formation as seen in Figure 1.1.2.

Originally, we investigated mode of addition and relative solvent volume to manipulate quinone formation stemming from a dimethoxyarene precursor. As part of these studies, we were able to develop reaction conditions that allowed us to produce diquinones as the major reaction product. Unfortunately, even under the reaction conditions most conducive to monomer formation (1:1 traditional addition), diquinones were still the major product in almost all cases. Because of this, we wanted to investigate if by further manipulating the solvent, we could generate significant amounts of the monomer. We chose dimethyl sulfoxide (DMSO) because it would solvate ceric ammonium nitrate and also allow for a uniformly dispersed arene in solution, thus generating a homogeneous mixture. We believed that by generating a homogeneous mixture, water would be more accessible and thereby minimize any areas of increased arene concentration, and this should lead to primarily monoquinone formation.

In the early stages of these experiments, we used only 3.3 equivalents of ceric ammonium nitrate, this being the same number of equivalents used in traditional addition. Unfortunately, we found that the product mixture obtained when 2-*tert*-butyl-1,4-dimethoxybenzene **19** was used as a substrate contained several different compounds bearing methoxy groups. As before, we were

uncertain of the identity of these methoxy-containing products. The observation of these methoxy-containing compounds was somewhat surprising, as earlier we had attributed their formation to the precipitation of intermediates from the product mixture. In the reaction run in DMSO, however, all products stayed in solution throughout the reaction. To further investigate if these methoxy-containing compounds consisted of either the tetramethoxybiaryl or aryl quinone intermediates as seen in Figure 1.1.1, we synthesized 4, 4'-di-*tert*-butyl-2,2',5,5'-tetramethoxybiphenyl, **24**, and 2-*tert*-butyl-5-(4-*tert*-butyl-2,5-dimethoxy-phenyl)-1,4-benzoquinone, **25** independently.

Scheme 3.1.1: Formation of 4, 4'-di-*tert*-butyl-2,2',5,5'-tetramethoxybiphenyl and 2-*tert*-butyl-5-(4-*tert*-butyl-2,5-dimethoxy-phenyl)-1,4-benzoquinone

19   **24**   **25**
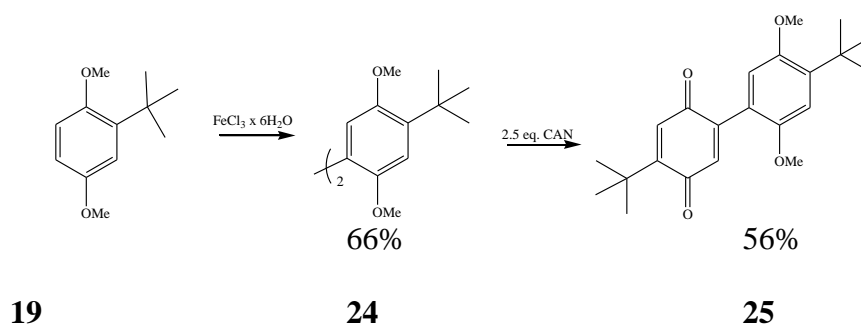
4, 4'-di-*tert*-butyl-2,2',5,5'-tetramethoxybiphenyl, **24** was prepared[16] from **19** and then was treated with 2.5 equivalents of ceric ammonium nitrate using the 1:1 traditional protocol generating the 2-*tert*-butyl-5-(4-*tert*-butyl-2,5-dimethoxy-phenyl)-1,4-benzoquinone, **25**.

After synthesizing the dimer intermediates, we were still uncertain of all the methoxy-containing products contained in our product mixture from the reaction of **19** with ceric ammonium nitrate in DMSO, however we did identify both **24** and **25** as being present in the product mixture.

Since we could not blame formation of these methoxy-containing compounds on their insolubility in the reaction medium, our next presumption was that perhaps some DMSO (or an

impurity present in the DMSO) was being oxidized by the ceric ammonium nitrate, thus reducing the amount of ceric ammonium nitrate available to oxidize the arene, and products derived from it. If this was the case and these methoxy-containing products were the diquinone precursors, then we could increase the amount of ceric ammonium nitrate used in the reaction to continue the oxidation of these intermediates on to the dimer, which we could then separate from the monomer.

Nevertheless, when we increased the amount of ceric ammonium nitrate used to 4.0 equivalents, products containing methoxy groups still remained. We then decided to try 5.0 equivalents of ceric ammonium nitrate. We did see a decrease in methoxy group-bearing products, but it was not as significant as we had hoped. Believing that the DMSO was still getting oxidized by the ceric ammonium nitrate, which was then diminishing the amount of ceric ammonium nitrate available to oxidize the arene, we decided to investigate other solvents.

3.2: DME

With the observation of methoxy groups contained in the product mixture of reactions conducted in DMSO and the belief that DMSO possibly reduced the amount of ceric ammonium nitrate available, we tried 1,2-dimethoxyethane (DME) as the reaction solvent. This was chosen because it was also expected to allow for a uniformly dispersed arene in solution, but was also able to solvate the ceric ammonium nitrate. Furthermore, we chose this solvent because it is less susceptible to oxidation than DMSO. Beginning with 4.0 equivalents of ceric ammonium nitrate, we saw a significant decrease in monoquinone formation with no reduction in the amount of products containing methoxy groups. For example, with the *tert*-butyl substrate **19**, in DMSO we saw a 13:1 monomer to dimer formation, but in DME, we saw a 2.2:1 monomer to dimer formation with an increase in methoxy-containing products.

We theorized that since DME is a known chelator, DME binds to the cerium of ceric ammonium nitrate and reduces the oxidation potential of ceric ammonium nitrate such that it is no longer able to effectively oxidize the aryl quinone and/or other methoxy containing intermediates.

3.3: Aqueous Addition

From here, we decided to move back to DMSO. We decided to break up the 5.0 equivalents of ceric ammonium nitrate into 4.0 equivalents added directly to the DMSO solution as a solid and 1.0 equivalent of aqueous ceric ammonium nitrate in an equal amount of water as DMSO. We had to generate a new hypothesis in regards to DMSO, and we considered the possibility that the DMSO coordinates to the cerium more tightly than water and reduces the oxidation potential of ceric ammonium nitrate. Thus, like the cerium chelated by DME, the cerium which is heavily solvated by DMSO might be incapable of oxidizing some of the methoxy-containing intermediates on to the final diquinone product. We theorized that by introducing water, this should reduce the complexation of the ceric ammonium nitrate by the DMSO, which then would allow it to become a better oxidant than when previously coordinated to the DMSO. We saw a significant decrease in methoxy groups contained in the products when we added 5 equivalents of ceric ammonium nitrate to the arene in this manner as compared to using straight DMSO as solvent.

From this observation we wanted to scale back the ceric ammonium nitrate from 5 equivalents to 3.3 equivalents (2.2 equivalents of solid ceric ammonium nitrate/1.1 equivalents of aqueous ceric ammonium nitrate), thinking that reduction of the ceric ammonium nitrate by solvent was not in fact an issue. Unfortunately a slight increase in methoxy products was observed. From this observation, we decided to scale up to 4 equivalents of ceric ammonium

nitrate (2.5 equivalents of solid ceric ammonium nitrate/1.5 equivalents of aqueous ceric

ammonium nitrate) and significant methoxy-containing products were observed. We have no

explanation as to why the amount of methoxy-containing products would have increased upon

using a greater amount of ceric ammonium nitrate.

From these experiments, ranging from 5.0, 4.0, and 3.3 equivalents of ceric ammonium

nitrate, we have concluded that the most efficient method of generating monomer with

minimizing any methoxy containing products is to add 4 equivalents of ceric ammonium nitrate

directly to the DMSO solution of the arene, followed by addition of 1.0 equivalent of aqueous

ceric ammonium nitrate in an equal volume of water to DMSO.

3.4: Results

Table 3.1: Comparison of DMSO to DMSO + Aqueous Addition
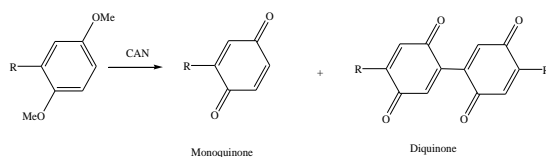
	DMSO		DMSO + Aqueous Addition	
R=	Mono : Di	Total Product Yield	Mono : Di	Total Product Yield
t-Bu	13 : 1	90*	34 : 1	79[+]
CH_3	22 : 1	100*	16 : 1	62[+]
$(CH_2)_2CH_3$	2 : 1	88*	3 : 1	77[+]
$(CH_2)_4CH_3$	10 : 1	36*	4 : 1	66[+]
$(CH_2)_6CH_3$	2 : 1	100*	4 : 1	70[+]
$(CH_2)_8CH_3$	3 : 1	56*	2 : 1	62[+]

*significant methoxy-containing products
[+]minimal methoxy-containing products

Even though some of the substrates gave an "increase" in monomer formation when compared to the aqueous addition, the total product yields were skewed due to the significant amount of methoxy-containing products in the product mixture. As mentioned earlier, utilization of a second addition of CAN (as an aqueous solution) subsequent to the initial addition of CAN to the DMSO solution of the arene has shown to significantly minimize methoxy-containing compounds in the product mixture, and so we can believe the total product yields to be fairly accurate. From this, we knew that the method we referred to as "DMSO + Aqueous Addition" was our method of generating significant amounts of monomer with minimal methoxy-containing products.

Having found our method of generating monomer by changing the solvent to DMSO + Aqueous Addition, we wanted to compare it to 1:1 traditional addition, the previous way of generating monomer stemming from a dimethoxyarene precursor. The results are shown below in Table 3.2:

Table 3.2: Comparison of 1:1 Traditional Addition to DMSO + Aqueous Addition
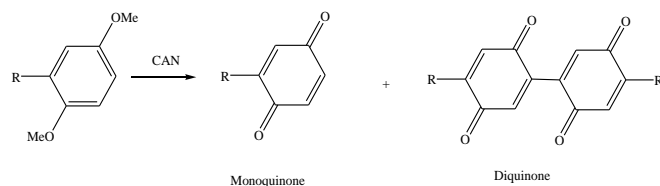

	1:1 Acetonitrile:Water Traditional		DMSO + Aqueous Addition	
R=	Mono : Di	Total Product Yield	Mono : Di	Total Product Yield
t-Bu	1 .1: 1	67	34 : 1	79^+
CH_3	1 : 94	84	16 : 1	62^+
$(CH_2)_2CH_3$	2 : 1	44	3 : 1	77^+
$(CH_2)_4CH_3$	1 : 9	82	4 : 1	66^+
$(CH_2)_6CH_3$	1 : 3	80	4 : 1	70^+
$(CH_2)_8CH_3$	1 : 2	45	2 : 1	62^+

[+]minimal methoxy-containing products

The trend we see is that significant monoquinone formation has occurred in the reactions conducted in DMSO with an aqueous addition as compared to those conducted in acetonitrile and water, thus confirming our hypothesis that by manipulating the reaction solvent we can favor significant monoquinone formation. We originally believed that DMSO allows for a uniformly dispersed arene in the reaction solvent, and that this would be sufficient to favor monoquinone formation. We now find that introducing some water via an aqueous addition of ceric ammonium nitrate is also required to generate a significant amount monomer when compared to 1:1 traditional addition, to date the most successful method of monomer formation stemming from a dimethoxyarene precursor. This result further supports our hypothesis that monoquinone formation is dependent upon the solubility of the substrate.

3.5: Other Attempts at Synthesizing 2-undecyl-1,4-benzoquinone

Scheme 3.5.1: Formation of 2-undecyl-1,4-benzoquinone and the Respective Dimer

21   **22**   **23**
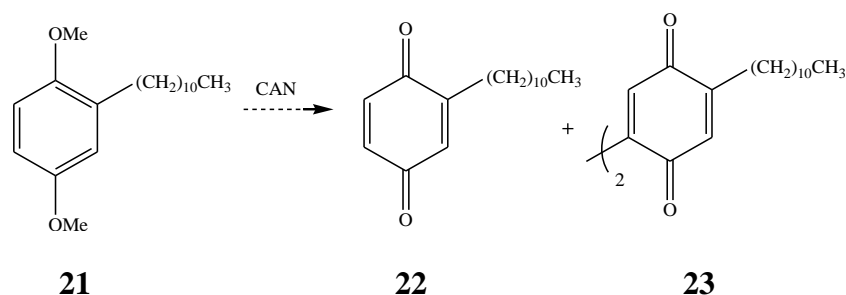
Since the 2-undecyl-1,4-benzoquinone had been consistently difficult to synthesize by

traditional means, we considered other options. In an attempt to synthesize the dimer, **23**, we first

tried use of a phase-transfer catalyst, tetra-n-butylammonium fluoride (TBAF) in diethyl ether.

We chose TBAF because this was available in our lab. Furthermore, we had to choose a catalyst

in which the anion would not be oxidized by the CAN as might be expected to occur with the

iodide or the bromide. We chose this approach because the 1,4-dimethoxy-2-undecylbenzene **21**

had been consistently insoluble in acetonitrile and even in DMSO; however, we knew that it was

soluble in diethyl ether. We used TBAF as a phase-transfer catalyst because the ceric ammonium

nitrate is not soluble in diethyl ether. We hoped that the phase-transfer catalyst would exchange

tetrabutylammonium groups for the ammonium groups associated with the CAN, and thereby

allow transfer of the oxidant into the ether layer, in which **21** was dissolved. This too was

unsuccessful as only starting material and methoxy-containing products were isolated.

In an attempt to synthesize **22**, we then tried dissolving 1,4-dimethoxy-2-undecylbenzene

in DMSO in order to allow it to react with CAN. As previously mentioned, this compound is

surprisingly not soluble in DMSO. We then added a half equivalent volume of DME. This

mixture was able to make **21** soluble. From here, we completed the general DMSO procedure,

but interestingly enough, an orange precipitate formed after the aqueous addition of ceric

ammonium nitrate and the allotted time. This precipitate was then separated and triturated with ethanol. The pale yellow precipitate thus obtained was shown to be pure 2-undecyl-1,4-benzoquinone, obtained in 17.7% yield. To date, this has been our most successful method of generating this monoquinone starting from the dimethoxyarene precursor.

Chapter 4: Discussion

To minimize the variables that could distort our results, we maintained a consistent volume of acetonitrile and water between samples, as well as use of 3.3 equivalents of ceric ammonium nitrate in the addition experiments.

At this current time, we have constructed two different modes of increasing the amount of diquinone compared to that obtained by the "traditional" reaction conditions. Traditional addition is where an aqueous solution of ceric ammonium nitrate (CAN) is added to an equal volume of acetonitrile in which the arene is dissolved. In 2 (acetonitrile) : 1 (water) inverse addition, we favored the dimer formation, perhaps by increasing the ionic strength of the CAN solution. With 1 (acetonitrile) : 2 (water) traditional addition, we were able to increase the amount of diquinone formed, perhaps by making use of the low water solubility of the arene. When compared to 1:1 inverse addition, to date the most reliable method of generating dimer from a dimethoxyarene precursor, both methods consistently gave an increase in dimer formation.

The only outlier in either trend is the pentyl substrate, for which we currently have no explanation. We ran multiple experiments in duplicate and triplicate, and most gave very similar results, so we do not believe the experiment was inconsistent. For example, in different runs using the heptyl substrate in 2:1 inverse addition, the product ratios were 1 : 4.2 and 1 : 4.6 (monomer : dimer). Another example is the pentyl substrate in 1:1 inverse addition, in which the observed product ratios were 1 : 6 and 1 : 8.

We speculate that perhaps a variation of the rate of the stirring sample or the rate of addition of reagents might distort results, but we have neither confirmed nor disproven this. We can however conclude that 2:1 inverse addition as well as 1:2 traditional addition are convenient

ways of synthesizing the dimer starting from the same dimethoxyarene precursor by varying the solvent composition.

We have shown that by increasing the ionic strength of the solution and, we perhaps, thus making the arene less soluble in the aqueous solution, that we can increase the amount of dimer formed. To further demonstrate that there is a solubility effect on dimer formation, we introduced an excessive amount of water to a concentrated arene solution. This too generated significant diquinone formation, as hypothesized.

Additionally, when we rinsed or triturated the precipitate, which is primarily dimer, with ethanol, any methoxy-containing products and monomer were removed from the precipitate, leaving only pure dimer. This has consistently shown to aid in complete separation of the dimer from all other products within the mixture.

Since we found a fairly simple way of generating dimer from the dimethoxyarene precursor but unable were to improve upon monomer formation by varying the volume or mode of addition, we then had pursue other methods.
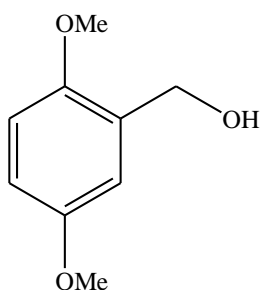
We theorized that dimethyl sulfoxide (DMSO) would generate a uniformly dispersed arene that would also able to dissolve ceric ammonium nitrate. After varying reaction solvent (DME) and amount of oxidant, we found that by adding an aqueous solution of ceric ammonium nitrate to DMSO greatly minimized the methoxy-containing products as well as lead to significant monomer formation. We believe that the ceric ammonium nitrate is a better oxidant in an aqueous solution than when dissolved in DMSO and addition of water uncoordinates the cerium from the DMSO, replacing at least some of the coordinating DMSO molecules with water. This is currently our best method of generating significant monomer starting from a dimethoxyarene precursor while minimal minimizing the amount of methoxy-containing

35

products obtained. In conclusion, we have shown that by varying the mode of addition, volume of solvent, or reaction solvent, we can generate either significant monomer or dimer formation starting from the same dimethoxyarene precursor.
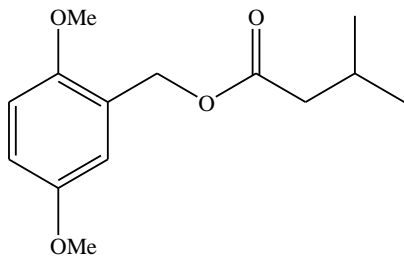
Chapter 5: Experimental

General: ^{1}H-NMR spectra were obtained on either a (Brüker Ascend ™ spectrometer operating at 400MHz, or a Varian Inova spectrometer operating at 500 MHz) and were obtained in $CDCl_3$. Chemical shifts are reported in δ (ppm) relative to an internal reference standard of tetramethylsilane (δ = 0).

12 - 2, 5-dimethoxybenzyl alcohol – 2, 5-dimethoxybenzaldehyde (8.0 g, 48.2 mmol) was dissolved in 50 mL of methanol in a round-bottom flask. This solution was placed in an ice bath and stoppered while stirring. $NaBH_4$ (3.60 g, 94 mmol) was added portion-wise over approximately 45 minutes. The mixture was removed from the ice bath and allowed to stir at room temperature for 20 hours. The mixture was opened to the air and quenched with 15 mL of sat'd NH_4Cl. Some of the solvent was removed under reduced pressure. 50 mL of diethyl ether was added and the mixture was washed with distilled water (25 mL) and sat'd NaCl (25 mL). The organic layer was dried with anhydrous magnesium sulfate and the solvent was removed under reduced pressure at room temperature. An oil product remained (7.14g, 88%). ^{1}H-NMR ($CDCl_3$): δ = 2.82 (bs, 1H), 3.74 (s, 3H), 3.77 (s, 3H), 4.62 (s, 2H), 6.75-6.77 (m, 3H).
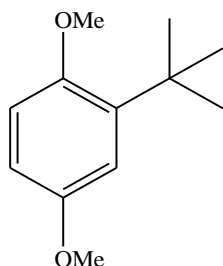
13 - 2, 5-dimethoxybenzyl-3-methylbutanoate[9] – 2, 5-dimethoxybenzyl alcohol (3.0 g, 17.8 mmol), triethylamine (2.6 g, 26 mmol) and a catalytic amount of DMAP were combined in a round-bottom flask and were dissolved in 50 mL of dichloromethane. The mixture was placed in an ice bath and stoppered while stirring. Isovaleryl chloride (3.0 g, 12.0 mmol) was dissolved in 20 mL of dichloromethane and added via
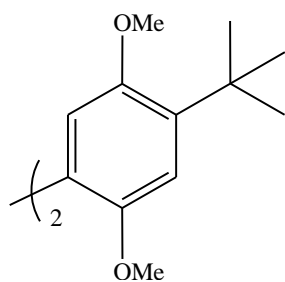
addition funnel protected by a calcium sulfate tube. The mixture was allowed to come to room temperature over 20 hours. 30 mL of dichloromethane was added and the mixture was washed with distilled water (3 x 50 mL) and sat'd NaCl (50 mL). The organic layer was dried with anhydrous magnesium sulfate and the solvent was removed under reduced pressure at room temperature. An oil product remained (4.03 g, 89.6%). ^{1}H-NMR (CDCl$_3$): δ = 0.92 (d, J= 6.5 Hz, 6H) 2.08 (m, 1H), 2.19 (d, J = 7 Hz, 2H), 3.73 (s, 3H), 3.75 (s, 3H), 6.77-6.86 (m, 3H).

19 - 2-*tert*-butyl-1,4-dimethoxy-benzene[24] –Dimethyl sulfate (4.58g, 36.3 mmol) was dissolved in 5 mL of acetone and was added to a mixture of butylated hydroxyansiole (4.38 g, 24.3 mmol) and potassium carbonate (5.40 g, 39.1 mmol) in 25 mL of acetone. This was heated at reflux in a flask equipped with a calcium sulfate tube for 20.5 hours. The mixture was allowed to cool to room temperature and 5 mL of methanol and 10 mL of 6M NaOH were added and the mixture was allowed to stir at room temperature for 20 minutes. 50 mL of diethyl ether were added and the mixture was washed with distilled water (3 x 50 mL) and sat'd NaCl (50 mL). The organic layer was dried with anhydrous magnesium sulfate and the solvent was removed under reduced pressure at room temperature. An oil product remained (3.95 g, 85%). ^{1}H-NMR (CDCl$_3$): δ = 1.36 (s, 9H), 3.86 (s, 3H), 3.89 (s, 3H), 6.79 (s, 2H), 6.89 (s, 2H), 7.01 (s, 1H).

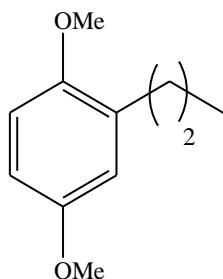**24 - 4,4'-di-*tert*-butyl-2, 5, 2', 5'-tetramethoxy-biphenyl**[16] - FeCl$_3$ x 6H$_2$O (3.93 g, 14.6 mmol) was dissolved in 40 mL of acetone and acidic alumina (15.1 g) was added and the solvent was removed. Then 2-*tert*-butyl-1, 4-dimethoxy-benzene (2.83 g, 14.6 mmol) was dissolved in 40 mL of dichloromethane and added to the mixture and the solvent was removed under reduced pressure at rt. The solid mixture was then heated to 90°C stirring open to the air.

Then 10 mL of 85% H_3PO_4 and 30 mL of methanol were added. The mixture was subjected to suction filtration and was washed with copious amounts of dichloromethane. The filtrate was washed with with distilled water (3 x 50 mL) and sat'd NaCl (50 mL). The organic layer was dried with anhydrous magnesium sulfate and the solvent was removed under reduced pressure at room temperature. A solid product remained (3.72 g, 65.9%). The product (3.45 g, 61.2%) was recrystallized using ethanol (2.49 g, 44.1%) ^{1}H-NMR (CDCl$_3$): δ = 1.36 (s, 18H), 1.41 (s, 9H), 3.75 (d, J = 16 Hz, 6H), 3.79 (d, J = 16 Hz, 6H), 6.76 (m, 2H), 6.84 (m, 2H), 6.92 (s, 2H).
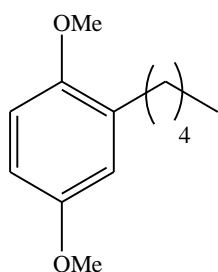
26 - 1,4-dimethoxy-2-propylbenzene 1,4-dimethoxybenzene (1.88 g, 13.6 mmol) was dissolved in approximately 10 mL of freshly distilled THF and placed under N$_2$ (g). The mixture was cooled in a dry ice/acetone bath. 8.8 mL of 1.7M n-BuLi in hexanes was added via syringe. The mixture was allowed to stir at this temperature for approximately twenty minutes. The mixture was removed and placed at room temperature to stir for one hour. 1-iodopropane (2.78 g, 16.4 mmol) was dissolved in approximately 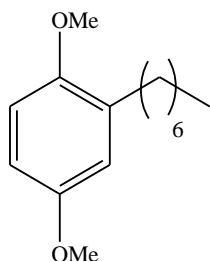10 mL of freshly distilled THF. This was added via syringe to the 1, 4-dimethoxybenzene/n-BuLi solution in a dry ice/acetone bath. This mixture was allowed to stir at this temperature for approximately twenty minutes. The mixture was then transferred to an ice bath to stir for 18 hours, slowly coming to rt. 50 mL of diethyl ether was added and the solution was washed with distilled water (3 x 50 mL) and once with sat'd NaCl (50 mL). The organic layer was dried with anhydrous magnesium sulfate and the solvent was removed under reduced pressure at room temperature. An oil residue remained (2.54 g, 104%) which was purified by kugelrohr distillation (1.75 g, 71.4 %). ^{1}H-NMR (CDCl$_3$): δ = 0.97 (t, J = 7.3 Hz, 3H), 1.63 (m, 2H), 2.58 (m, 2H), 3.72 (s, 3H), 3.73 (s, 3H), 6.81 (m, 1H), 6.72 (m, 2H).

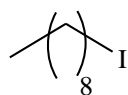**27 - 1,4-dimethoxy-2-pentylbenzene –** The procedure was exactly the same as 1,4-dimethoxy-2- propylbenzene except the 1,4-dimethoxybenzene weighed 1.53 g (11.1 mmol), 10.0 mL of 1.7M n-BuLi in hexanes was added and 1-iodopentane weighed 4.24 g (21.4mmol). An oil residue remained (2.56 g, 111%) which was purified by kugelrohr distillation (1.43 g, 62%). ^{1}H-NMR (CDCl$_3$): δ = 0.88-0.91 (m, 3H), 1.32 (m, 4H), 1.56 (m, 2H), 2.58 (m, 2H), 3.73 (s, 3H), 3.74 (s, 3H), 6.65-6.66 (m, 1H), 6.71-6.72 (m, 2H).

28 - 1,4-dimethoxy-2-heptylbenzene – The procedure was exactly the same as 1,4-dimethoxy-2-propylbenzene except the 1,4-dimethoxybenzene weighed 1.53 g (11.1 mmol) and 1-iodoheptane weighed 4.85g (21.4 mmol) An oil residue remained (3.91 g, 149%) which was purified by kugelrohr distillation (1.67 g, 64%). ^{1}H-NMR (CDCl$_3$): δ = 0.89 (t, $J = $ 5.7 Hz, 3H), 1.27-1.33 (m, 6H), 1.56-1.59 (m, 4H), 2.56-2.59 (m, 2H), 3.74 (s, 3H), 3.75 (s, 3H), 6.64-6.65 (m, 1H), 6.67-6.72 (m, 2H).

29 - 1-iodononane[23] **–** 1-nonanol (3.02 g, 21 mmol) and triethylamine (4.25 g, 42 mmol) were combined in 50 mL of dichloromethane. The mixture was placed at -5° C and methanesulfonyl chloride (2.88 g, 25 mmol) was added. The mixture was allowed to stir in a round-bottom flask at this temperature for 15 minutes while stoppered. The mixture was opened to the air and quenched with 100 mL of sat'd NH$_4$Cl. 50 mL of diethyl ether was added and the mixture was washed with sat'd NaCl (50 mL). The organic layer was dried with anhydrous magnesium sulfate and the solvent was removed under reduced pressure at room

temperature. An oil residue remained. The oil was dissolved in 100 mL of acetone. Sodium

iodide (7.93 g, 53 mmol) and sodium bicarbonate (5.32 g, 63 mmol) were added and the mixture

was allowed to stir at room temperature for 20 hours while stoppered. The mixture was opened

to the air and quenched with 100 mL of distilled water and 50 mL of diethyl ether was added.

The mixture was washed with distilled water (3 x 50 mL) and sat'd NaCl (50 mL). The organic

layer was dried with anhydrous magnesium sulfate and the solvent was removed under reduced

pressure at room temperature. An oil residue remained (3.75 g, 70.3%). ^{1}H-NMR (CDCl$_3$): δ =

0.88 (t, J = 6.7 Hz, 3H), 1.27-1.38 (m, 12H), 1.78-1.84 (m, 2H), 3.16-3.19 (m, 2H).

30 - 1,4-dimethoxy-2-nonylbenzene – The procedure was exactly the same as 1,4-

dimethoxy-2-propylbenzene except the 1-iodononane weighed 2.52 g (13 mmol). An oil residue

remained (1.18 g, 40.3%) which was purified by kugelrohr distillation (0.56

g, 19%). ^{1}H-NMR (CDCl$_3$): δ = 0.88 (t, J = 6.8 Hz, 3H), 1.25-1.31 (m,

10H), 1.54-1.58 (m, 2H), 2.54-5.59 (t, J = 7.6 Hz, 2H), 3.74 (s, 3H), 3.75 (s,

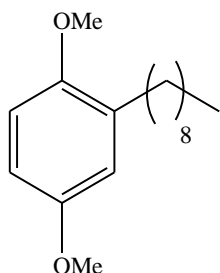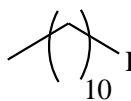3H), 6.64-6.65 (m, 1H), 6.66-6.71 (m, 2H).

31 - 1-iodoundecane[23] – 1-undecanol (3.61 g, 21 mmol) and triethylamine (4.24 g, 42

mmol) were combined in 50 mL of dichloromethane. The mixture was placed at

-5° C and methanesulfonyl chloride (2.88 g, 25 mmol) was added. The mixture

was allowed to stir in a round-bottom flask at this temperature for 15 minutes while stoppered.

The mixture was opened to the air and quenched with 100 mL of sat'd NH$_4$Cl. 50 mL of diethyl

ether was added and the mixture was washed with sat'd NaCl (50 mL). The organic layer was

dried with anhydrous magnesium sulfate and the solvent was removed under reduced pressure at

room temperature. An oil residue remained. The oil was dissolved in 100 mL of

acetone. Sodium iodide (7.93 g, 53 mmol) and sodium bicarbonate (5.32 g, 63 mmol) was added

and the mixture was allowed to stir at room temperature for 20 hours while stoppered. The

mixture was opened to the air and quenched with 100 mL of distilled water and 50 mL of diethyl

ether was added. The mixture was washed with distilled water (3 x 50 mL) and sat'd NaCl (50

mL). The organic layer was dried with anhydrous magnesium sulfate and the solvent was

removed under reduced pressure at room temperature. An oil residue remained (4.25 g, 71.7%).
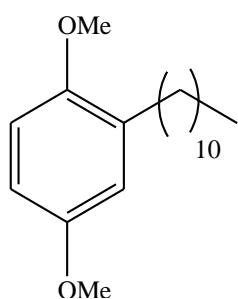
^{1}H-NMR (CDCl$_3$): δ = 0.88 (t, J = 6.8 Hz, 3H), 1.26 (m, 16H), 1.81-1.84 (m, 2H), 3.17 (m, 2H).

21 - 1,4-dimethoxy-2-undecylbenzene – The procedure was exactly the same as 1,4- dimethoxy-2-propylbenzene except the 1-iodoundecane weighed 4.25 g (15.1 mmol). An oil residue remained (3.49 g, 79.2%) which

was purified by kugelrohr distillation (0.56 g, 52.2%). ^{1}H-NMR (CDCl$_3$): δ = 0.87 (t, J = 6.6 Hz,

3H), 1.25-1.31 (m, 16H), 1.54-1.56 (m, 2H), 2.58 (t, J = 7.7 Hz, 2H), 3.74(s, 3H), 3.75 (s, 3H),

6.65-6.67 (m, 1H), 6.71-6.72 (m, 2H).

Formation of 2-*tert*-butyl-1,4-benzoquinone and 5,5'-di-*tert*-butyl-2,2'-bis-1,4-benzoquinone via

Oxidation of 1, 4-dimethoxy-2-*tert*-butylbenzene
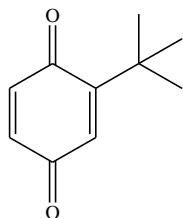
32 - 2-*tert*-butyl-1,4-benzoquinone   **33** - 5,5'-di-*tert*-butyl-2,2'-bis-1,4-benzoquinone
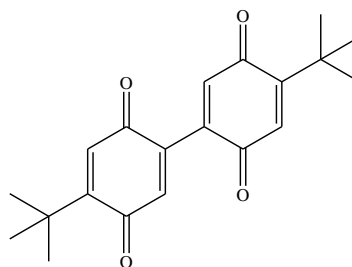
1:1 Traditional Addition Experimental Procedure –- The ceric ammonium nitrate (2.80 g, 5.1 mmol) was dissolved in 10 mL of distilled water and added dropwise to a stirred solution of 2-*tert*-butyl-1,4-dimethoxy-benzene (0.30 g, 1.55 mmol) which was dissolved in 10 mL acetonitrile. The mixture was allowed to stir at room temperature for one hour. This was then diluted with 75 mL of distilled water. A solid precipitate formed (0.12 g, 47.6%) and was separated via suction filtration. This was rinsed several times with distilled water and ethanol. 50 mL of dichloromethane was added to the filtrate. The organic layer was separated and was washed with distilled water (3 x 50 mL) and once with sat'd NaCl (50 mL). The organic layer was dried with anhydrous magnesium sulfate and the solvent was removed under reduced pressure at room temperature. A solid product formed (0.10 g, 39.4%).

Precipitate (Dimer) ^{1}H -NMR (CDCl$_3$): δ = 1.32 (s, 18H), 6.70 (s, 2H), 6.77 (s, 2H).
^{13}C -NMR (CDCl$_3$): δ = 29.1, 35.3, 131.9, 137.6, 138.0, 156.0, 185.6, 186.6. Dimer mp 190-192 °C. (lit. mp: 190-192 °C).[4]

Filtrate (Monomer) ^{1}H-NMR (CDCl$_3$): δ = 1.27 (s, 9H), 6.59 (s, 1H), 6.67 (s, 2H). ^{13}C -NMR (CDCl$_3$): δ = 29.1, 35.2, 131.5, 134.9, 138.6, 156.0, 187.4, 188.4. Monomer mp 56-58 °C. (lit. mp: 58-59 °C). [17]

1:2 Traditional Addition Experimental Procedure - The ceric ammonium nitrate (2.80 g, 5.1 mmol) was dissolved in 10 mL of distilled water and added dropwise to a stirred solution of 2-*tert*-butyl-1,4-dimethoxy-benzene (0.30 g, 1.55 mmol) which was dissolved in 5 mL acetonitrile. The mixture was allowed to stir at room temperature for one hour. This was then diluted with 75 mL of distilled water. 50 mL of dichloromethane was added, the organic layer

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was separated and was washed with distilled water (3 x 50 mL) and once with sat'd NaCl (50 mL). The organic layer was dried with anhydrous magnesium sulfate and the solvent was removed under reduced pressure at room temperature. A solid product formed (0.25 g, 98.9%). Dimer, 64.5%. Monomer, 34.5%

1:1 Inverse Addition Experimental Procedure: The 2-*tert*-butyl-1,4-dimethoxy-benzene (0.3 g, 1.55 mmol) was dissolved in approximately 10 mL Acetonitrile and added dropwise to a stirred solution of ceric ammonium nitrate (2.80 g, 5.1 mmol) dissolved in approximately 10 mL of distilled water. The mixture was allowed to stir at room temperature for one hour. This was then diluted with 75 mL of distilled water. A precipitate formed (0.16 g) and this was separated via suction filtration. 50 mL of dichloromethane was added to the filtrate. The organic layer was separated and was washed with distilled water (3 x 50 mL) and once with sat'd NaCl (50 mL). The organic layer was dried with anhydrous magnesium sulfate and the solvent was removed under reduced pressure at room temperature. A solid product formed (0.09 g). Precipitate (Mostly Dimer, 29.1%). Filtrate (Mostly Monomer, 41.4%)
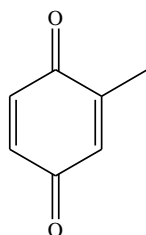
2:1 Inverse Addition Experimental Procedure: The 2-*tert*-butyl-1,4-dimethoxy-benzene (0.30 g, 1.55 mmol) was dissolved in 10 mL acetonitrile and added dropwise to a stirred solution of ceric ammonium nitrate (2.80 g, 5.1 mmol) dissolved in 5 mL of distilled water. The mixture was allowed to stir at room temperature for one hour. This was then diluted with 75 mL of distilled water. A solid precipitate formed (dimer, 0.09 g, 35.6%) and was separated via suction filtration. This was rinsed several times with distilled water. 50 mL of dichloromethane was added to the filtrate. The organic layer was separated and was washed with distilled water (3 x 50 mL) and once with sat'd NaCl (50 mL). The organic layer was dried with anhydrous

magnesium sulfate and the solvent was removed under reduced pressure at room temperature. A solid product formed (monomer, 0.05 g, 19.7%).
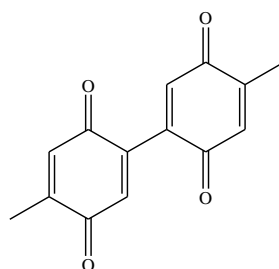
DMSO + Aqueous Addition Experimental Procedure: The 2-*tert*-butyl-1,4-dimethoxy-benzene (0.15 g, 0.77 mmol) was dissolved in 4.0 mL of DMSO and four equivalents of solid ceric ammonium nitrate (1.68 g, 3.1 mmol) was manually added portion-wise over 20 minutes. The mixture was allowed to stir at room temperature for one hour. Then, one equivalent of ceric ammonium nitrate (0.44 g, 0.82 mmol) was dissolved in 4.0 mL of distilled water, which was added via addition funnel. This was allowed to stir at room temperature for 30 minutes. The solution was then diluted with 75 mL of distilled water and 50 mL of dichloromethane. The organic layer was separated and was washed with distilled water (3 x 50 mL) and once with sat'd NaCl (50 mL). The organic layer was dried with anhydrous magnesium sulfate and the solvent was removed under reduced pressure at room temperature. An oil residue formed (0.10 g, 78.9%). (Mostly Monomer with trace dimer)

<u>Formation of 2-methyl-1,4-benzoquinone and 5,5'-di-methyl-2,2'-bis-1,4-benzoquinone via</u>

<u>Oxidation of 1, 4-dimethoxytoluene</u>

34- 2-methyl-1,4-benzoquinone   **35** - 5,5'-di-methyl-2,2'-bis-1,4-benzoquinone

1:1 Traditional Addition Experimental Procedure – The procedure was exactly the same as 1:1 traditional addition of 2-*tert*-butyl-1,4-dimethoxy-benzene except the 2, 5-

dimethoxytoluene weighed 0.30 g (1.97 mmol) and the ceric ammonium nitrate weighed 3.61 g (6.5 mmol). A solid product formed (0.20 g, 83.7%).

Precipitate (mostly dimer) ^{1}H-NMR (CDCl$_3$): δ = 1.93 (s, 6H), 6.72 (s, 2H), 6.83 (s, 2H). ^{13}C -NMR (CDCl$_3$): δ = 15.6, 133.6, 135.9, 139.5, 146.2, 184.7, 186.9. Dimer mp 186-188 °C. (lit. mp: 186-187 °C). [4]

Filtrate (monomer) ^{1}H-NMR (CDCl$_3$): δ = 1.57 (s, 3H), 6.62-6.63 (m, 1H), 6.72-6.73 (m, 1H), 6.75-6.78 (m, 2H). ^{13}C -NMR (CDCl$_3$): δ = 15.8, 133.3, 136.5, 136.6, 146.2, 184.7, 186.9. Monomer mp 62-64 °C. (lit. mp: 69 °C). [17]

1:2 Traditional Addition Experimental Procedure - The procedure was exactly the same as 1:2 traditional addition of 2-*tert*-butyl-1,4-dimethoxy-benzene except the 2, 5-dimethoxytoluene weighed 0.30 g (1.97 mmol) and the ceric ammonium nitrate weighed 3.62 g (6.5 mmol). A solid product formed (0.18 g, 75.4%). (Mostly dimer with trace monomer)

1:1 Inverse Addition Experimental Procedure – The experimental data was received from previous work[4].

2:1 Inverse Addition Experimental Procedure - The procedure was exactly the same as 2:1 inverse addition of 2-*tert*-butyl-1,4-dimethoxy-benzene except the 2, 5-dimethoxytoluene weighed 0.30 g (1.97 mmol) and the ceric ammonium nitrate weighed 3.62 g (6.5 mmol). A solid product formed (0.22 g, 92.1%). (mostly dimer with trace monomer)
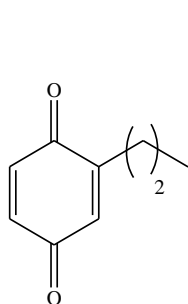
DMSO + Aqueous Addition Experimental Procedure - The procedure was exactly the same as DMSO addition of 2-*tert*-butyl-1,4-dimethoxy-benzene except the 2, 5-
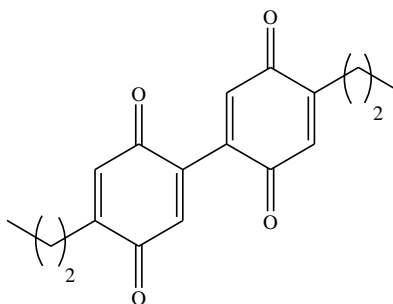
dimethoxytoluene weighed 0.12 g (0.77 mmol). An oil residue formed (0.05g, 52%). (mostly monomer with trace dimer)

Formation of 2-propyl-1,4-benzoquinone and 5,5'-di-propyl-2,2'-bis-1,4-benzoquinone via

Oxidation of 1, 4-dimethoxy-2-propylbenzene

36 - 2-propyl-1,4-benzoquinone   **37** - 5,5'-di-propyl-2,2'-bis-1,4-benzoquinone

1:1 Traditional Addition Experimental Procedure - The procedure was exactly the same as 1:1 traditional addition of 2-*tert*-butyl-1,4-dimethoxy-benzene except the 1, 4-dimethoxy-2-propylbenzene weighed 0.10 g (0.56 mmol) and the ceric ammonium nitrate weighed 1.01 g (1.83 mmol). A solid product formed (0.07 g, 84.5%).

Precipitate (Dimer, 55.5%) ^{1}H-NMR (CDCl$_3$): δ = 1.02 (t, J = 8.84 Hz, 6H), 1.57 (m, 4H), 2.44 (m, 4H), 6.55 (s, 2H), 6.81 (s, 2H). ^{13}C -NMR (CDCl$_3$): δ = 13.81, 20.99, 30.8, 132.7, 136.2, 139.2, 149.7, 184.9, 186.7. Dimer mp 152-154 °C. (lit. mp: 153-154 °C). [4]

Filtrate (Impure monomer, 24.8%) ^{1}H-NMR (CDCl$_3$): δ = 0.96-0.99 (m, 3H), 1.52-1.58 (m, 2H), 2.38-2.42 (m, 2H), 6.56-6.57 (m, 1H), 6.72-6.77 (m, 2H).[19]

1:2 Traditional Addition Experimental Procedure - The procedure was exactly the same as 1:2 traditional addition of 2-*tert*-butyl-1,4-dimethoxy-benzene except the 1, 4-

47

dimethoxy-2-propylbenzene weighed 0.15 g (0.83 mmol) and the ceric ammonium nitrate weighed 1.51 g (2.76 mmol). A solid product formed (0.11 g, 88.6%, mostly dimer).
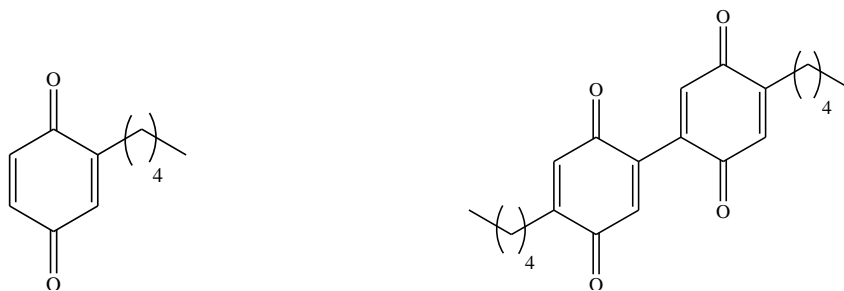
1:1 Inverse Addition Experimental Procedure - The procedure was exactly the same as 1:1 inverse addition of 2-*tert*-butyl-1,4-dimethoxy-benzene except the 1, 4-dimethoxy-2-propylbenzene weighed 0.10 g (0.56 mmol) and the ceric ammonium nitrate weighed 1.01 g (1.84mmol). A solid product formed (0.07 g, 72.4%, mostly dimer).

2:1 Inverse Addition Experimental Procedure - The procedure was exactly the same as 2:1 inverse addition of 2-*tert*-butyl-1,4-dimethoxy-benzene except the 1, 4-dimethoxy-2-propylbenzene weighed 0.10 g (0.56 mmol) and the ceric ammonium nitrate weighed 1.00 g (1.83 mmol). A solid product formed (0.07 g, 68.4%, mostly dimer).

DMSO + Aqueous Addition Experimental Procedure - The procedure was exactly the same as DMSO addition of 2-*tert*-butyl-1,4-dimethoxy-benzene except the 1, 4-dimethoxy-2-propylbenzene weighed 0.14 g (0.77 mmol). An oil residue formed (0.09 g, 77.3%, mostly monomer).

Formation of 2-pentyl-1,4-benzoquinone and 5,5'-di-pentyl-2,2'-bis-1,4-benzoquinone via

Oxidation of 1, 4-dimethoxy-2-pentylbenzene

38 - 2-pentyl-1,4-benzoquinone   **39**- 5,5'-di-pentyl-2,2'-bis-1,4-benzoquinone

1:1 Traditional Addition Experimental Procedure - The procedure was exactly the same as 1:1 traditional addition of 2-*tert*-butyl-1,4-dimethoxy-benzene except the ceric

ammonium nitrate weighed 2.60 g (4.75 mmol) and the 1, 4-dimethoxy-2-pentylbenzene weighed 0.30 g (1.44 mmol). A solid precipitate formed (0.16 g, 73.5%, mostly dimer). A solid product formed in the filtrate (0.03 g, 8.7%, mostly monomer).

Precipitate (dimer) ^{1}H-NMR (CDCl$_3$): δ = 0.88 (t, J = 3.5 Hz, 6H), 1.37 (m, 4H), 1.58 (m, 8H), 2.46-2.48 (m, 4H), 6.67 (s, 2H), 6.83 (s, 2H). ^{13}C -NMR δ = 13.9, 22.4, 27.4, 28.8, 31.4, 132.6, 136.2, 139.2, 150.1, 184.0, 185. Dimer mp 157-158 °C. (lit. mp: 158-159 °C). [4]

Mostly monomer: ^{1}H-NMR (CDCl$_3$): δ = 0.88-0.95 (m, 3H), 1.25-1.37 (m, 2H), 1.58 (m, 4H), 2.45 (m, 2H), 6.56-6.57 (m, 1H), 6.71-6.75 (m, 2H).[18]

1:2 Traditional Addition Experimental Procedure - The procedure was exactly the same as 1:2 traditional addition of 2-*tert*-butyl-1,4-dimethoxy-benzene except the ceric ammonium nitrate weighed 2.61 g (4.82 mmol) and the 1, 4-dimethoxy-2-pentylbenzene weighed 0.31 g (1.44 mmol). A solid product formed (0.18 g, 71.3%, mostly dimer).

1:1 Inverse Addition Experimental Procedure - The procedure was exactly the same as 1:1 inverse addition of 2-*tert*-butyl-1,4-dimethoxy-benzene except the 1, 4-dimethoxy-2-pentylbenzene weighed 0.30 g (1.44 mmol) and the ceric ammonium nitrate weighed 2.60 g (4.75 mmol). A solid product formed (0.19 g, 79.9%, mostly dimer).
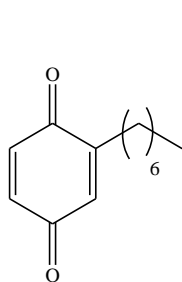
2:1 Inverse Addition Experimental Procedure - The procedure was exactly the same as 2:1 inverse addition of 2-*tert*-butyl-1,4-dimethoxy-benzene except the 1, 4-dimethoxy-2-pentylbenzene weighed 0.25 g (1.2 mmol) and the ceric ammonium nitrate weighed 2.20 g (4.01

mmol). A solid precipitate formed (0.13 g, 63.5%, mostly) and was separated via suction

filtration. A solid product formed from the filtrate (0.03 g, 11.7%, mostly monomer).
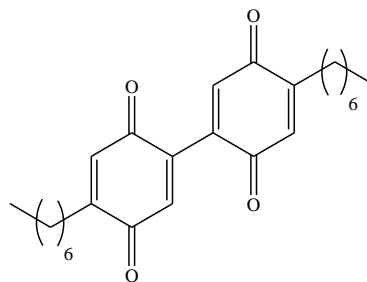
DMSO + Aqueous Addition Experimental Procedure - The procedure was exactly the

same as DMSO addition of 2-*tert*-butyl-1,4-dimethoxy-benzene except the 1, 4-dimethoxy-2-

pentylbenzene weighed 0.16 g (0.77 mmol). An oil residue formed (0.09 g, 65.8%, mostly

monomer).

Formation of 2-heptyl-1,4-benzoquinone and 5,5'-di-heptyl-2,2'-bis-1,4-benzoquinone via

Oxidation of 1, 4-dimethoxy-2-heptylbenzene

40 - 2-heptyl-1,4-benzoquinone   **41** - 5,5'-di-heptyl-2,2'-bis-1,4-benzoquinone

1:1 Traditional Addition Experimental Procedure - The procedure was exactly the

same as 1:1 traditional addition of 2-*tert*-butyl-1,4-dimethoxy-benzene except the ceric

ammonium nitrate weighed 0.77 g (1.40 mmol) and the 1, 4-dimethoxy-2-heptylbenzene

weighed 0.10 g (0.42 mmol). A solid product formed (0.07 g, 80.4%, mostly dimer).

Precipitate (dimer, 58.5%) ^{1}H-NMR (CDCl$_3$): δ = 0.86 (t, J = 13 Hz, 6H), 1.31-1.33 (m, 8H),

1.35-1.54 (m, 8H), 1.64-1.69 (m, 4H), 2.46-2.48 (m, 4H), 6.67 (s, 2H), 6.82 (s, 2H). ^{13}C -NMR δ

= 14.0, 22.6, 27.7, 28.8, 28.9, 29.2, 31.6, 132.6, 136.2, 139.2, 150.1, 184.9, 186.7. Dimer mp

152-154 °C. (lit. mp: 157-159 °C).[4]

Filtrate (impure monomer, 21.9%) ^{1}H-NMR (CDCl$_3$): δ = 0.89 (m, 3H), 1.31-1.33 (m, 4H), 1.35-1.54 (m, 4H), 1.62-1.67 (m, 2H), 2.46-2.48 (m, 2H), 6.67 (s, 1H), 6.82 (m, 2H). ^{13}C -NMR δ = 14.0, 22.5, 27.7, 28.91, 28.94, 29.2, 31.6, 132.3, 136.2, 136.7, 149.7, 187.5, 187.8.

1:2 Traditional Addition Experimental Procedure - The procedure was exactly the same as 1:2 traditional addition of 2-*tert*-butyl-1,4-dimethoxy-benzene except the ceric ammonium nitrate weighed 0.77 g (1.40 mmol) and the 1, 4-dimethoxy-2-heptylbenzene 0.10 g (0.42 mmol). A solid product formed (0.03 g, 40%, mostly dimer).
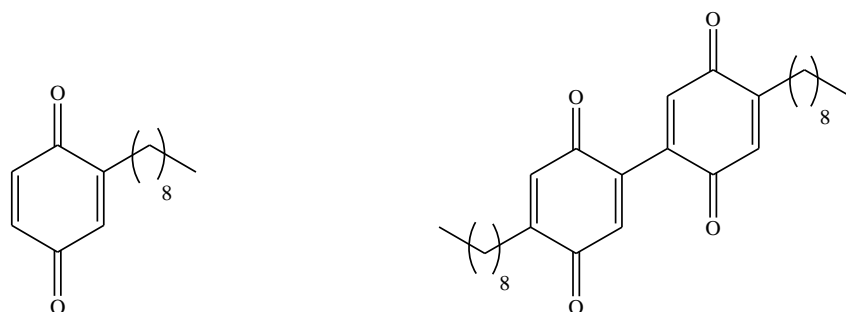
1:1 Inverse Addition Experimental Procedure - The procedure was exactly the same as 1:1 inverse addition of 2-*tert*-butyl-1,4-dimethoxy-benzene except the 1, 4-dimethoxy-2-heptylbenzene weighed 0.10 g (0.42 mmol) and the ceric ammonium nitrate weighed 0.77 g (1.40 mmol). A solid product formed (0.07 g, 57.7%, mostly dimer).

2:1 Inverse Addition Experimental Procedure - The procedure was exactly the same as 2:1 inverse addition of 2-*tert*-butyl-1,4-dimethoxy-benzene except the 1, 4-dimethoxy-2-heptylbenzene weighed 0.10g (0.42 mmol) and the ceric ammonium nitrate weighed 0.78 g (1.41 mmol). A solid product formed (0.09 g, 103.5%, mostly dimer).

DMSO + Aqueous AdditionExperimental Procedure - The procedure was exactly the same as DMSO addition of 2-*tert*-butyl-1,4-dimethoxy-benzene except the 1, 4-dimethoxy-2-heptylbenzene weighed 0.18 g (0.77 mmol). An oil residue formed (0.11g, 70.1%, mostly monomer).

Formation of 2-nonyl-1,4-benzoquinone and 5,5'-di-nonyl-2,2'-bis-1,4-benzoquinone

via Oxidation of 1, 4-dimethoxy-2-nonylbenzene

42 - 2-nonyl-1,4-benzoquinone   **43** - 5,5'-di-nonyl-2,2'-bis-1,4-benzoquinone

1:1 Traditional Addition Experimental Procedure - The procedure was exactly the same as 1:1 traditional addition of 2-*tert*-butyl-1,4-dimethoxy-benzene except the ceric ammonium nitrate weighed 0.69 g (1.25 mmol) and the 1, 4-dimethoxy-2-nonylbenzene weighed 0.10 g (0.36 mmol). A solid product formed (0.04 g, 45.3%).

Precipitate (mostly dimer, 30.9%) ^{1}H-NMR (CDCl$_3$): δ = 0.89 (t, J = 6.5 Hz, 3H), 1.27-1.34 (m, 16H), 1.35-1.59 (m, 12H), 2.46-2.48 (m, 4H), 6.67 (s, 2H), 6.82 (s, 2H). ^{13}C -NMR δ = 14.1, 22.6, 27.7, 28.9, 29.2, 29.2, 29.3, 29.4, 31.8, 132.6, 136.2, 139.2, 150.1, 185.0, 186.7. Dimer mp 155-157 °C.

Filtrate (impure monomer, 14.4%) ^{1}H-NMR (CDCl$_3$): δ = 0.88 (t, J = 8.1 Hz, 3H), 1.27-1.34 (m, 8H), 1.35-1.59 (m, 6H), 2.46-2.48 (m, 2H), 6.56 (m, 1H), 6.69-6.77 (m, 2H). ^{13}C -NMR δ = 14.1, 22.6, 27.7, 28.9, 29.2, 29.2, 29.3, 29.6, 31.8, 132.3, 136.2, 136.7, 150.1, 185.0, 187.5.

1:2 Traditional Addition Experimental Procedure - The procedure was exactly the same as 1:2 traditional addition of 2-*tert*-butyl-1,4-dimethoxy-benzene except the ceric

ammonium nitrate weighed 0.69 g (1.30 mmol) and the 1, 4-dimethoxy-2-nonylbenzene weighed 0.1 g (0.38 mmol). A solid product formed (0.05 g, 56.6%).

1:1 Inverse Addition Experimental Procedure: The procedure was exactly the same as 1:1 inverse addition of 2-*tert*-butyl-1,4-dimethoxy-benzene except the 1, 4-dimethoxy-2nonyl-benzene weighed 0.10 g (0.38 mmol) and the ceric ammonium nitrate weighed 0.69 g (1.25 mmol). A solid product formed (0.08 g, 90.5%).

2:1 Inverse Addition Experimental Procedure: The procedure was exactly the same as 2:1 inverse addition of 2-*tert*-butyl-1,4-dimethoxy-benzene except the 1, 4-dimethoxy-2-nonylbenzene weighed 0.10 g (0.36 mmol) and the ceric ammonium nitrate weighed 0.69 g (1.25 mmol). A solid product formed (0.07 g, 79.2%).

DMSO Experimental Procedure: The procedure was exactly the same as DMSO addition of 2-*tert*-butyl-1,4-dimethoxy-benzene except the 1, 4-dimethoxy-2-nonylbenzene weighed 0.20 g (0.77 mmol). An oil residue formed (0.11 g, 62.1%). (Mostly Monomer, 43.5%) (Some Dimer, 18.6%)

Formation of 2-undecyl-1,4-benzoquinone via Oxidation of 1, 4-dimethoxy-2-undecylbenzene
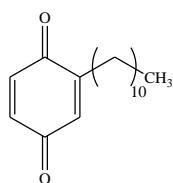
22 - 2-undecyl-1,4-benzoquinone

Experimental Procedure: The procedure was exactly the same as DMSO addition of 2-*tert*-butyl-1,4-dimethoxy-benzene except the 1, 4-dimethoxy-2-undecylbenzene weighed 0.22 g (0.77 mmol) and 3 mL of DME was added. An orange precipitate formed after the allotted time and was separated via suction filtration. This precipitate was triturated with ethanol and was separated via suction filtration, a pale yellow solid remained (0.04 g, 17.7%). (Pure Monomer)

^{1}H-NMR (CDCl$_3$): δ = 0.88 (m, 3H), 1.26 (m, 18H), 2.41 (m, 2H), 6.56 (s, 1H), 6.72 (m, 1H), 6.74 (m, 1H). ^{13}C -NMR δ = 14.1, 22.6, 27.7, 28.9, 29.2, 29.2, 29.3, 29.3, 29.4, 29.6, 31.9, 132.3, 136.2, 139.2, 149.8, 186.7, 187.3. mp 54-57 °C. (lit. mp: 57-59 °C).[20]

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