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Pulping Catalysts from Lignin: The Diels-Alder Step

D.R. Dimmel, J.J. Bozell, D.G. von Oepen, and M.C. Savidakis

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PULPING CATALYSTS FROM LIGNIN:

The Diels-Alder Step

Donald R. Dimmel, Joseph J. Bozell, David G. von Oepen, and Michael C. Savidakis*

1. INTRODUCTION

Select anthraquinone (AQ) compounds can be used in existing kraft processes to increase pulping rates and product yields. Such catalysts could also be the focus for an industry-wide evolution of pulping from high to low to sulfur-free methodology. Catalyst pulping holds the promise of addressing problems with plant bleach effluents by producing pulps that are more easily bleached than standard kraft pulps by modifying the cooking process to reduce the amount of residual lignin present in the pulp prior to bleaching.[1]

In 1989 we first reported a new approach for an inexpensive synthesis of dimethylanthraquinone.[2] The approach involves conversion of an inexpensive pulping byproduct, lignin, to a useful AQ-type pulping catalyst using a two-stage process. In the first stage, a low molecular weight (LMW) lignin fraction is removed from a whole lignin-containing source by solvent extraction. The LMW lignin is then converted to AQ or AQ-like products in two chemical steps. First, oxidation of the LMW lignin gives a mixture of two key intermediates, monomethoxybenzoquinone (**1**, MMBQ) and dimethoxybenzoquinone (**2**, DMBQ). In the second step, isoprene is added to **1** and **2** to give a mixture of 2,6- and 2,7-dimethylanthraquinone (**3**, DMAQ) and other quinone products. While other dienes, such as butadiene, can be used in the second step, DMAQ is a more active pulping catalyst than nonmethylated AQ or more fully methylated AQ (Equation 1).[3]

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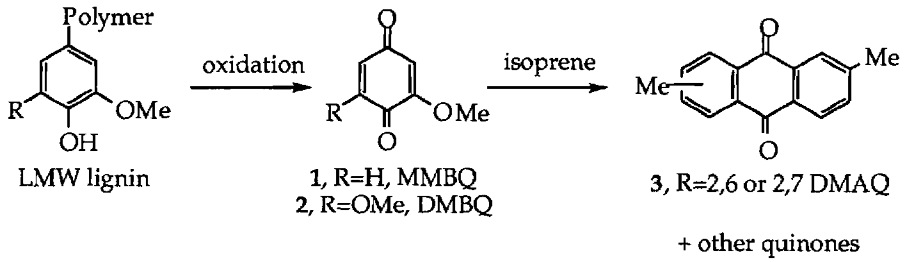
* Donald R. Dimmel, David G. von Oepen, and Michael C. Savidakis, Institute of Paper Science and Technology, 500 10th Street N. W., Atlanta, GA, 30338; Joseph J. Bozell, National Renewable Energy Laboratory, 1617 Cole Blvd., Golden, CO, 80401.



[1]

Much progress has been made on optimizing the initial oxidation step; however, the yield of **1** and **2** is still rather low.[4] Good yields are needed in the Diels-Alder step if the catalyst synthesis is to be commercially feasible. This paper describes our efforts to optimize the Diels-Alder conversion of **1** and **2** to an AQ-based pulping catalyst mixture.

2. BACKGROUND

The reaction between **1** and **2** and a diene can lead to a wide array of products. For this reason, we envisioned that the reaction would give a mixture AQ, AQ-like materials, and other quinones. This combination of quinones then acts as the pulping catalyst. As the quinone and diene components are varied, description of the various intermediates and final products can become confusing. For example, the initial products of diene addition are nonaromatic and have been categorized as either *mono-* or *bisadducts*, depending on how many molecules of diene add to the starting quinone (Figure 1).

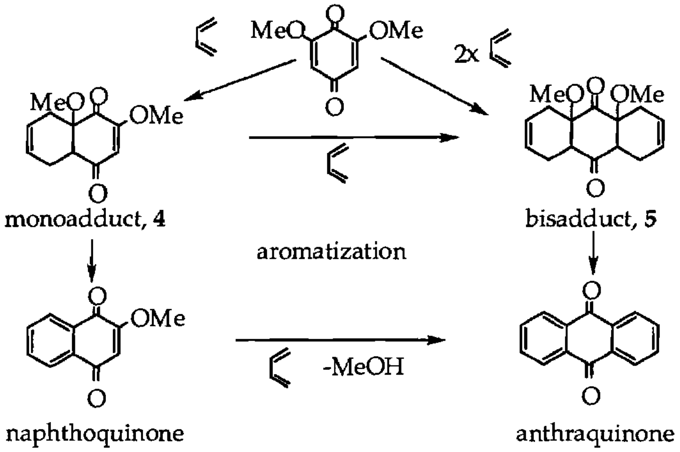
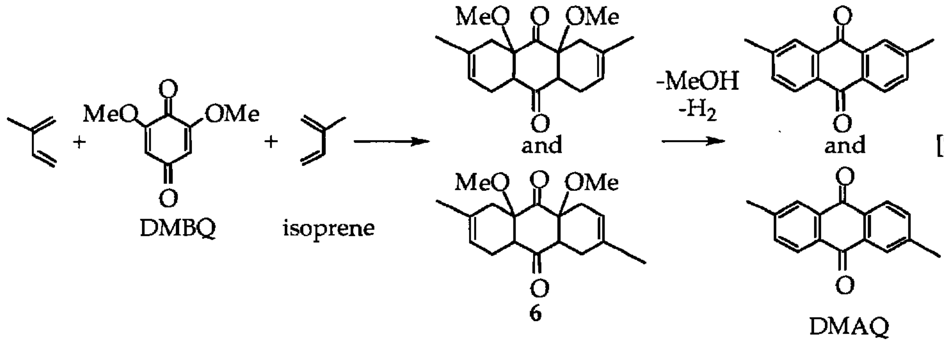


Figure 1 - Definition of Mono- and Bisadducts from Diels-Alder Addition

The most efficient approach for the synthesis of a pulping catalyst would be the simultaneous addition of two molecules of diene to the benzoquinone, initially to give bisadduct **5**, followed by aromatization of **5** to give AQ. Synthesis of anthraquinones by this type of reaction is known.[5]

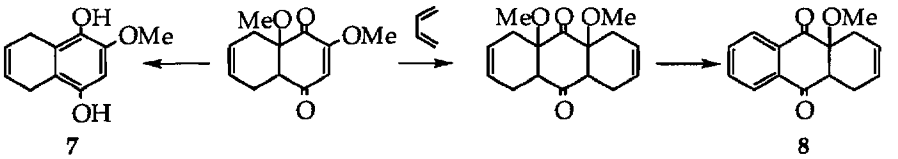
An alternate path is possible. Diene addition can also take place in a stepwise manner to give monoadduct **4**, followed by addition of a second molecule of diene to give **5**. We felt this path would most likely be successful because of the methoxy substitution on the benzoquinones obtained from lignin oxidation. In general, *para*-benzoquinones that contain electron-withdrawing substituents readily react with simple dienes to afford the corresponding adducts under mild reaction conditions. Those containing electron-donating substituents require more vigorous reaction conditions and usually give monoadducts.[6] The same aromatization processes that convert **5** into AQ would also convert **4** into naphthoquinone derivatives. These derivatives can also undergo Diels-Alder addition to afford AQ.

The catalyst mixture becomes more complex when butadiene is replaced by isoprene. In this case, Diels-Alder reaction/aromatization gives two isomeric DMAQ molecules (Equation 2) via intermediate bisadducts **6**.



[2]

Finally, it is also possible for the initial mono and bisadducts to undergo partial aromatization to give compounds such as **7** and **8** (Equation 3).



[3]

Because of the wide variety of products possible from this process, considerable effort has been devoted to clarify the course of the reaction, identify the cyclization products, and optimize the conditions necessary for the maximum production of AQ-like materials. For simplicity, nonaromatic compounds resulting from the addition of two molecules of *any* diene to the starting benzoquinone will be referred to generically as bisadducts. Nonaromatic compounds resulting from the addition of a single molecule of diene to the benzoquinone will be referred to as monoadducts. The fully aromatic compounds are generally referred to as AQ or AQ analogs. In most cases described in the following sections, only a single regioisomer will be shown for reactions involving isoprene.

3. DIELS-ALDER REACTIONS IN HOMOGENEOUS SOLUTION

Our initial experiments examined the reactivity of benzoquinone (9), a reactive quinone expected to readily form bisadducts, as well as MMBQ and DMBQ with isoprene in toluene solution (Figure 2). Benzoquinone undergoes reaction with isoprene as expected to give a mixture of mono- and bisadducts in excellent yield with the major product of the reaction being a mixture of bisadduct regioisomers.

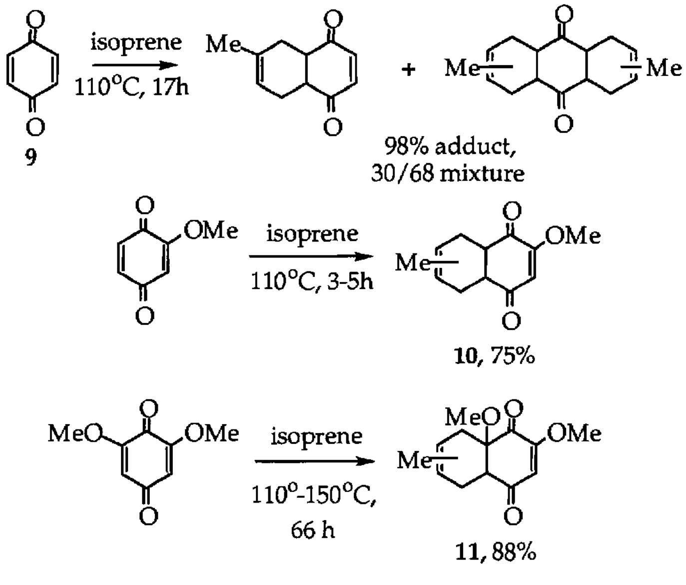
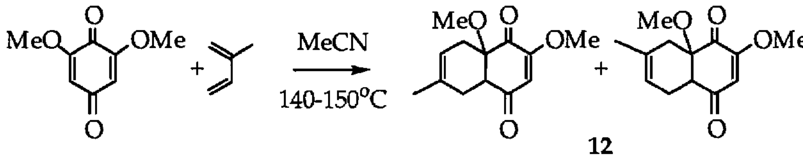


Figure 2 - Products Observed from the Reaction of Quinones in Homogeneous Solution

The presence of methoxyl groups on the quinone changed the reactivity. MMBQ underwent a rapid and high yield reaction with one equivalent of diene to give monoadduct **10**. Addition of a second equivalent of diene was not observed at moderate temperatures. DMBQ also underwent a slower reaction with a single equivalent of diene to give monoadduct **11** in high yield. The DMBQ result was important since it demonstrated that the presence of a methoxyl group on a double bond does not preclude a Diels-Alder addition. Indeed, the results from the reaction of DMBQ suggested that a second addition should be possible since the electronic nature of the remaining olefin should not differ significantly from the first. This initial adduct from DMBQ is quite stable, formed in high yield, and could serve as a useful purification point in the lignin-to-catalyst sequence.

We have performed a large number of experiments examining the reaction between DMBQ and isoprene. The optimum process treats DMBQ with excess (about 20x) isoprene in MeCN solvent in a sealed bomb at 140-150°C. The monoadduct was obtained in 90% yield or greater as a roughly 1:1 mixture of regioisomers **12** in 2.5 hours (Equation 4). NMR and GC/MS confirmed the product structure. The presence of regioisomers is difficult to discern in the NMR; however, GC/MS reveals two closely spaced peaks with almost identical MS spectra and molecular weight.



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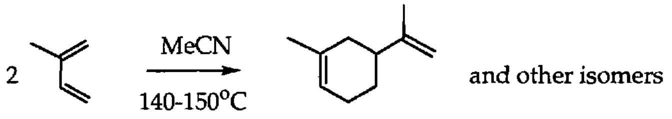
[4]

We also investigated the effect of differing amounts of isoprene on the reaction. Decreasing the amount of isoprene caused a decrease in the rate of reaction. In the presence of a 4.2 to 5-fold excess of isoprene, the conversion of DMBQ after 2.5 h dropped to 70%. At a 1.9-fold excess of isoprene, the conversion of DMBQ was 47% after 2.5 h. However, the conversion of DMBQ can be increased to >95% by allowing the reaction to proceed for 17 h at a 5:1 molar ratio of isoprene/DMBQ. We have performed this reaction on a large scale to prepare 6-7 g of material. It is preferable to run the reaction for a longer period of time rather than at higher isoprene concentrations to minimize the formation of the Diels-Alder dimer of isoprene (Equation 5), which can be a significant side reaction that results in nonproductive consumption of diene.



[5]

The monoadducts from MMBQ and DMBQ failed to undergo further reaction with diene to give a bisadduct of any kind. Since addition of the first molecule of isoprene to DMBQ occurred rapidly and in high yield, we consider this to be primarily a steric problem. We have observed that unsubstituted benzoquinone (9) exhibits a distinctly different rate of addition of the diene. The first addition to give a monoadduct was complete in 2-4 hours while addition of the second required heating overnight. Consideration of the three-dimensional structure of the adducts provides a possible explanation. Figure 3 shows the predicted transition state conformation for two modes of addition of a diene to DMBQ.

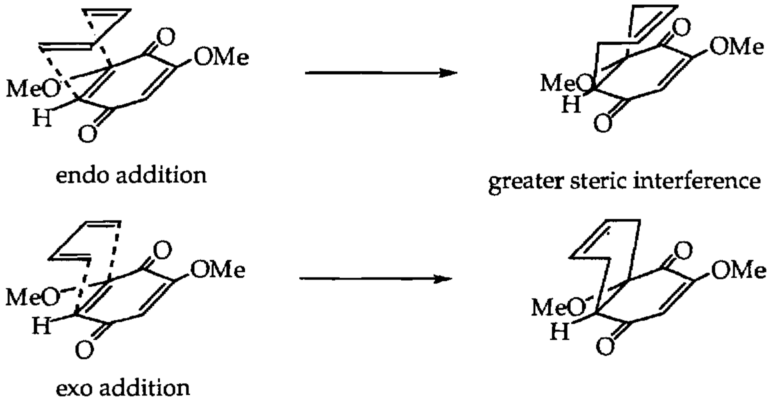


Figure 3 - Stereochemistry of the Transition State of the Diels-Alder Addition

The incoming diene has the choice of adding in either an *endo* or *exo* mode. From a steric standpoint, the *exo*-mode is preferred since there is less crowding. However, a number of reported examples exist in which *endo*-addition is observed, despite the greater steric hindrance. This observation has been attributed to a number of factors, including secondary orbital interactions in the transition state, and has been formalized as the Alder rule.[7] Certainly, once the first addition is complete, the resulting product can undergo a ring flip to the more stable *exo*-conformation. However, some fraction of the mixture will continue to exist in the *endo*-conformation. The second equivalent of diene will also attempt to adopt an *endo*-conformation in the transition state. There will be higher steric interference to the second addition regardless of the conformation of the monoadduct. This hypothesis is supported by simple molecular mechanics calculations on the monoadduct obtained from either DMBQ or MMBQ and isoprene (Figure 4). The models (hydrogens omitted) clearly show the bent nature of the monoadducts suggesting steric interference toward introduction of a second molecule of diene.

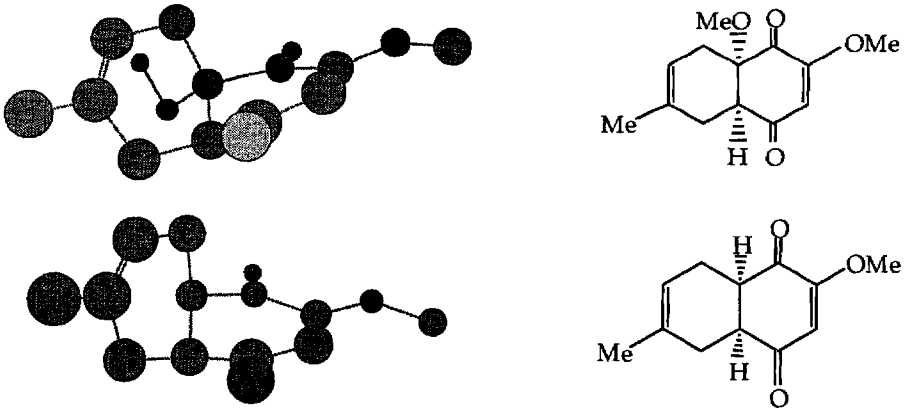


Figure 4 - Molecular Modeling of the Monoadduct from MMBQ, DMBQ and Isoprene

4. DIELS-ALDER REACTIONS IN THE PRESENCE OF LEWIS ACID PROMOTERS

If the first addition of diene gives a sterically hindered intermediate product, removal of the hindrance should make the second addition easier. A simple method of removing the hindrance is aromatization of the newly added ring to give methoxynaphthoquinone (Figure 5). This transformation would require elimination of MeOH. The intermediate triene would be expected to undergo rapid oxidation to the quinone.

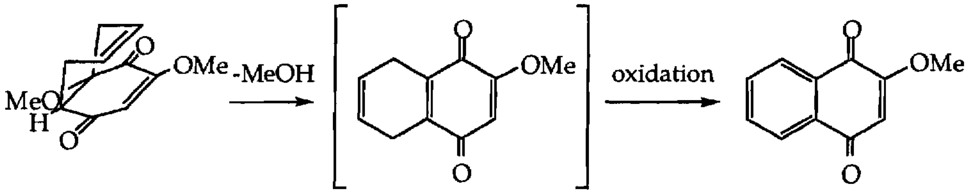


Figure 5 - Comparison of Aromatized and Nonaromatized Adducts

We envisioned that addition of a Lewis acid could promote the initial loss of MeOH from the monoadduct. In addition, the presence of a Lewis acid could also have a promoting effect on the initial Diels-Alder reaction. The literature reports many examples of the catalysis of Diels-Alder reactions in the presence of Lewis acids.[8] From a process standpoint, an added promoter should be readily available and inexpensive. Silica gel or alumina fulfills this requirement and the use of these materials as Diels-Alder promoters is widely reported.[9] We felt that a one-pot Diels-Alder addition and aromatization could be carried out *in situ* by adding either promoter to the diene/quinone mixture. Since diene is still present, a second Diels-Alder/aromatization sequence should result, eventually leading to an AQ product (Figure 6).

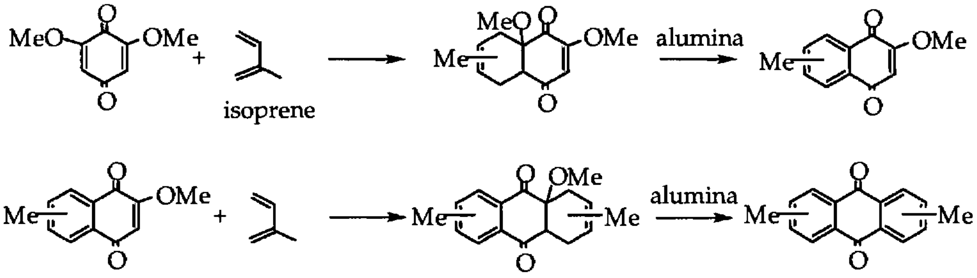
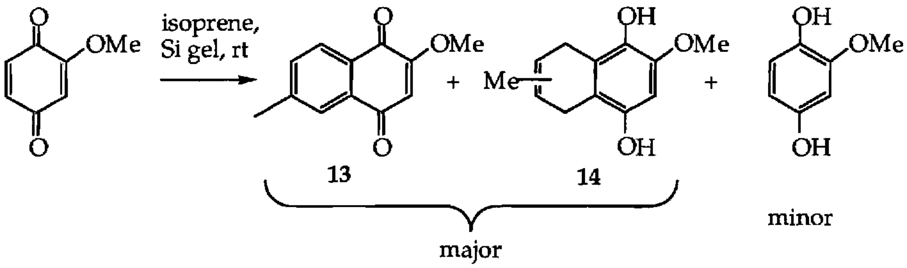


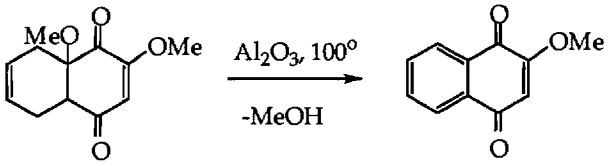
Figure 6 - One-Pot Reaction of Isoprene and Quinones with Added Alumina

Initial reactions with both alumina and silica gel were promising. Promotion of the Diels-Alder reaction was observed upon mixing of MMBQ and isoprene in the presence of silica gel for 4 hours at *room temperature*. A mixture of two aromatized Diels-Alder adducts, **13** and **14**, was obtained (Equation 6).



[6]

The diene added to the nonmethoxylated double bond. Although an exact determination of yield was not made for this reaction, the results indicated that sequential Diels-Alder cyclization and aromatization of the intermediate was possible, although the appearance of hydroquinone 14 and a small amount of reduced starting material was unexpected. The reaction was repeated with the less reactive quinone, DMBQ, and a 20% yield of the corresponding naphthoquinone was achieved upon heating at 100°C, reflecting the lower reactivity of the double bonds in DMBQ toward Diels-Alder addition. Importantly, GC/MS indicated the presence of a small amount of pure DMAQ in the mixture. We also found that the monoadduct isolated from the Diels-Alder reaction of DMBQ and butadiene underwent a facile aromatization when heated in the presence of alumina (Equation 7).



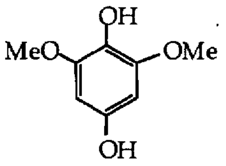
[7]

These results, achieved under very mild conditions, prompted an extensive investigation into optimization of the reaction.

4.1. Reactions on Alumina

A large number of reactions were performed using DMBQ and isoprene as the Diels-Alder reactants, and various types of alumina as the Lewis acid promoter, in the absence of solvent. The reactions were performed by mixing solid DMBQ and the promoter, adding excess diene, and heating the reaction in a sealed stainless steel vessel at 125°C for 14-18 h. The products were isolated by washing the solid support with solvent and analyzing by gas chromatography.

The reactions gave a complex mixture of quinone adducts (see Experimental section for a description of the GC/MS analysis); however, the majority of the reaction mixture contained four primary products: starting DMBQ, dimethoxyhydroquinone (15), and DMAQ regioisomers (3).



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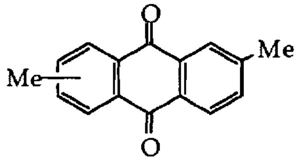

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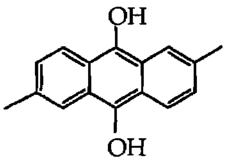
The effects of alumina type (basic, neutral, or acidic), alumina activity (Brockmann levels I through V, prepared by addition of varying amounts of water to the solid alumina), alumina amounts (between 250-1000 mg/mmole DMBQ), isoprene amounts (2-20 mmol/mmol DMBQ), and the presence of small amounts of solvent (toluene, acetonitrile, chloroform) were investigated. The large amount of data was also subjected to principal component analysis in order to deconvolute the information and discern correlations.[10] Some general trends were noted:

- Pure DMAQ can be prepared using this methodology in chemical yields of 30-40%.
- DMAQ can be prepared *directly* from DMBQ and isoprene without the intermediacy of any AQ-like materials (i. e., naphthoquinones). This is an important result from the standpoint of streamlining the process and avoiding the presence of side products in the pulping catalyst mixture.
- Acidic alumina appears to be most effective for promoting the diene addition. The most effective activity level for the alumina is less clear. Brockmann level IV appears to be the best.
- The optimum amount of alumina required (mg/mmol of quinone) is not clear. The product yields varied widely as a function of this parameter.
- The reaction proceeds most efficiently in the presence of a tenfold excess of isoprene. This observation could be a drawback because of the increased possibility of producing isoprene dimer.

4.2. Reactions on Silica Gel

In the presence of silica gel, the major products were generally DMAQ, hydroquinone **14** (Equation 6), dimethylanthrahydroquinone (**16**), and hydroquinone **17**.[11]



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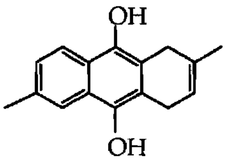

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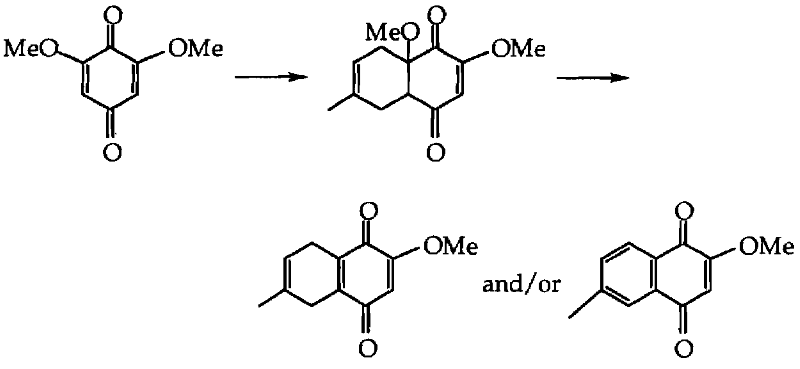
The relative proportion of AQ-like materials is about the same as on alumina, but the amount of isoprene dimer is diminished, offering an advantage for the use of silica gel.

Several additional trends were noted from reactions performed in the presence of silica gel. When a large (500 mg/mmole substrate) amount of promoter was used, the difference in reactivity between alumina and silica gel *appeared* to be minimal. However, reactions with limited (50 mg/mmole substrate) amounts of promoter showed much clearer distinctions. At this level, reactions with silica gel gave only monoadduct, as observed by GC/MS and NMR. Since DMBQ also underwent this reaction in the absence of silica gel, we concluded that the presence of silica gel is ineffective for the further aromatization of the product at these low levels.

In contrast, added alumina (basic or acidic, 50 mg/mmole substrate) clearly promoted further reaction of the first-formed adduct to give aromatization products via loss of MeOH and intermediate **18**. Alumina appeared to be a much more active catalyst under these conditions (Equation 8).



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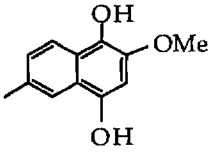
[8]

We have also investigated the question of catalysis of the reaction by the walls of the stainless steel reactor. A teflon lined reactor was prepared and parallel reactions were performed. We observed minimal difference in the reactions performed in the lined vs. the unlined reactor. At this point, we concluded that the reactor was not promoting the transformation. The silica gel promoter used in the reaction can be recycled into subsequent reactions. After three uses, silica gel still effectively promoted the formation of aromatized Diels-Alder monoadducts, e. g., **13**, but the relative amount of bisadducts dropped considerably.

4.3. Stepwise Reaction Processes

Because the normal conditions employed required the use of a large excess of isoprene, we normally observed significant amounts of isoprene dimer in the reaction product mixture. This product represented a nonproductive consumption of starting material that would be economically detrimental to the overall process. Accordingly, we examined methods to diminish the amount of this product. Our approach was based on the very efficient reaction observed between DMBQ and isoprene in MeCN in the *absence* of a promoter (Equation 4). The resulting monoadduct was isolated and then subjected to a second Diels-Alder reaction with isoprene in the presence of silica gel and in MeCN solvent. Under these conditions, the amount of isoprene present was reduced to a 5- to 8-fold excess, with a concomitant reduction (but not elimination) of the isoprene dimer. Importantly, this approach offered cleaner reaction mixtures and a much higher proportion of DMAQ than previous approaches. The primary products in the mixture as determined by GC/MS or NMR were DMAQ, **18** (more likely present as its tautomer, **19**), **13**, and hydroquinone **14**.



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The same reaction sequence was also carried out with MMBQ as a starting material. However, formation of the corresponding AQ derivative was not observed. Instead, the major product of a stepwise process was hydroquinone **19**.

4.4. Discussion

The most general result of the Diels-Alder investigation is that DMBQ can be converted to a mixture that contains a significant fraction of AQ-like materials. However, the reaction also produces a number of side products. Some could serve as catalysts, while others may be unreactive. Ideally, conditions should be such that AQ-like materials are the major reaction component. We have investigated several mechanistic aspects of the reaction in order to better understand the process and design experiments to increase the relative amounts of AQ-like materials.

Two important observations can be made that have a bearing on the reaction path. First, Diels-Alder reactions proceed to AQ-like materials much more completely with DMBQ than with MMBQ in the presence of promoters. The rationale for this observation is based on the transformations of each quinone during the Diels-Alder step. The formation of the initial monoadduct from either MMBQ or DMBQ is efficient and proceeds in high yield. Neither monoadduct proceeds to AQ-like materials in the absence of Lewis acid promoters.

However, even in the presence of promoters, only DMBQ can be easily converted to AQ-like materials. The primary difference between the two substrates is the ability of the monoadduct from DMBQ to lose a molecule of MeOH during the reaction to give a material with considerably less steric hindrance to further reaction (Equation 8). The monoadduct from MMBQ does not have this ability. The result is that the adduct formed from MMBQ will have more steric hindrance to approach of a second molecule of diene because the first ring is bent up above the plane of the quinone. Simple molecular mechanics calculations again support this hypothesis (Figure 7).

A more efficient second addition of diene is possible from the DMBQ derivatives, giving higher levels of AQ-type products.

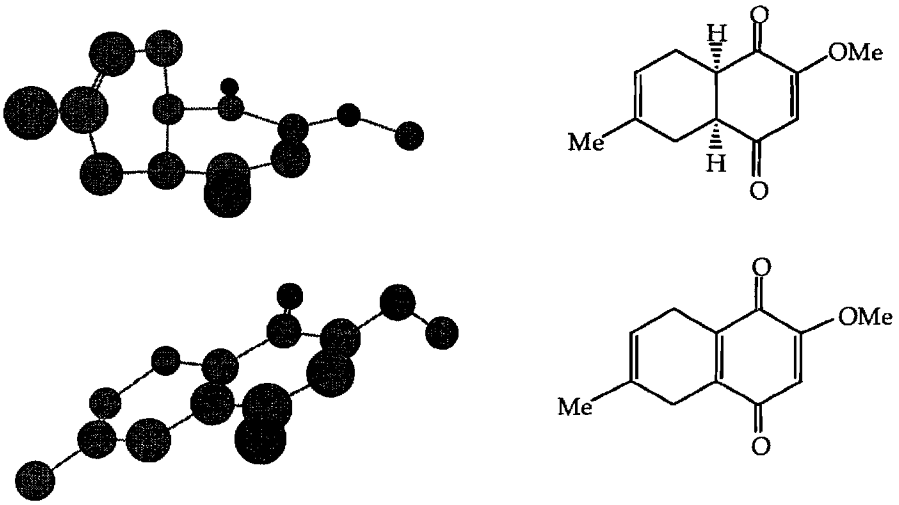


Figure 7 - Results of Molecular Mechanics Calculation on the Monoadduct from MMBQ and Isoprene

A second important mechanistic observation is the presence of hydroquinone derivatives in all of the Diels-Alder reaction mixtures. This is not a problem if one obtains only AQ and anthrahydroquinone (the reduced version of AQ), since both are reported to function as pulping catalysts. However, formation of hydroquinones from any of the starting materials or reaction intermediates is a problem, since conditions do not exist to convert them back into proper Diels-Alder intermediates. If one examines Equation 8, formation of **18** is reasonable by MeOH elimination, promoted by alumina or silica gel. However, formation of the methoxynaphthoquinone (**13**) is more difficult to explain. This product is formed by a dehydrogenation process and requires a hydrogen acceptor in the reaction medium. A mechanistic scheme that appears to account for all the intermediates observed in the reaction is shown in Figure 8.

DMBQ undergoes reaction with isoprene even in the absence of promoter to give the stable and isolable monoadduct **11**. When a promoter is present, **11** is induced to lose MeOH, giving quinone **18**. Our original hypothesis assumed that **18** was the intermediate that was subsequently converted to AQ-like materials by virtue of its flat topology and similar olefin electronics. However, we were never able to observe high concentrations of **18**, even at short reaction times. The presence of hydroquinone derivatives in the reaction mixture suggested an alternate path for **18** was available.

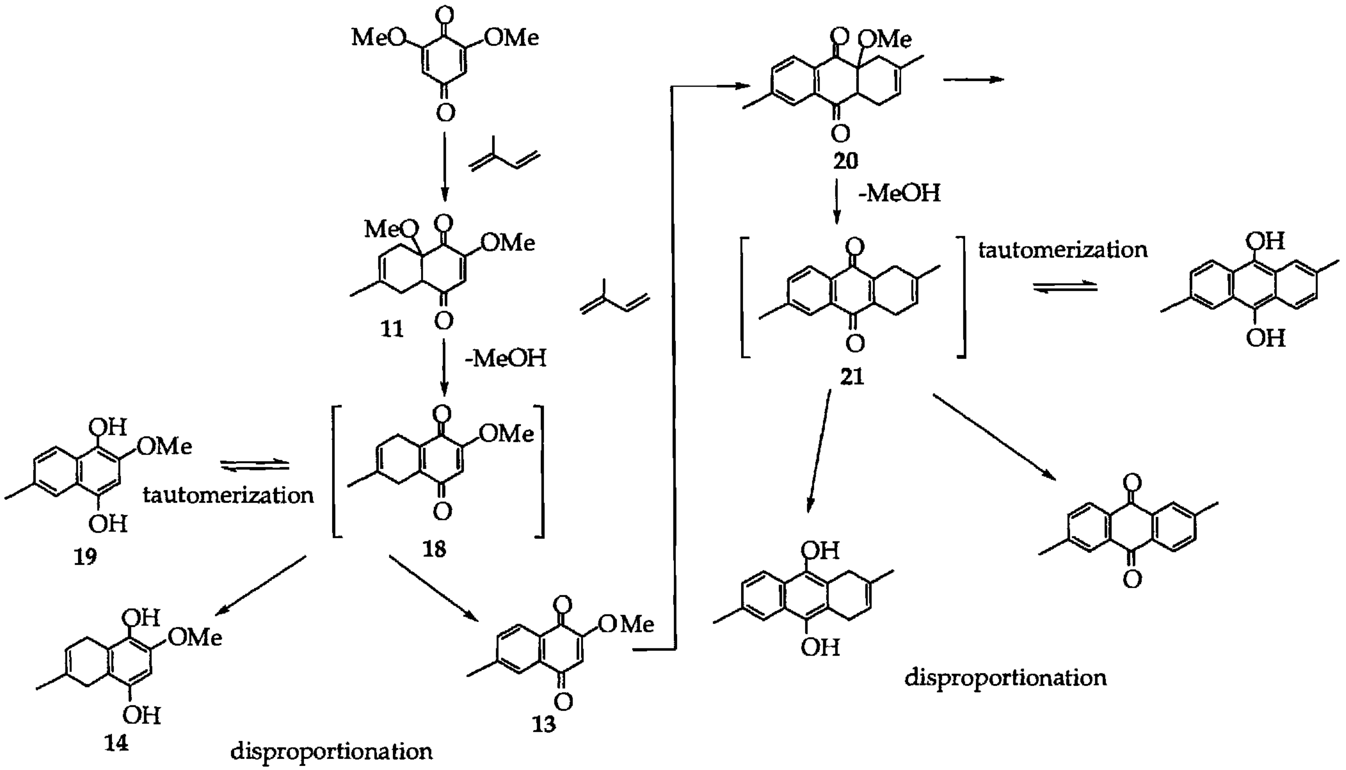
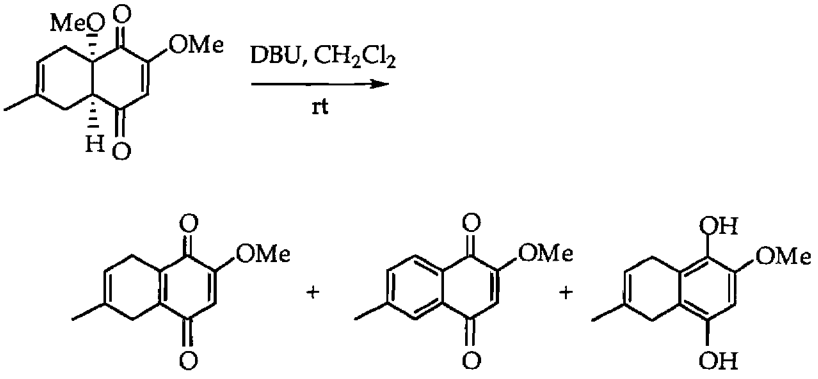


Figure 8 - Summary of Reaction Paths Available to DMBQ and Derivatives in the Diels-Alder Sequence

We now believe that **18** undergoes two different but rapid conversions. The first is a simple tautomerization, giving hydroquinone **19**. The second, which leads to an important AQ precursor, is a disproportionation, giving a second hydroquinone **14** and methoxymethylnaphthoquinone **13**. Compound **13** undergoes further Diels-Alder reaction to bisadduct **20**. This material is structurally analogous to **11** and undergoes loss of MeOH to give **21**. This compound, structurally analogous to **18**, can undergo the same pair of tautomerization/disproportionation sequences, completing identification of the product slate observed.

This hypothesis is supported by an experiment designed to form **18** exclusively (Equation 9).



[9]

18 **13** **14**

Treatment of the Diels-Alder monoadduct with DBU (1,8-diazabicyclo[5.4.0]undec-7-ene, a strong, hindered, non-nucleophilic base) caused a rapid (< 5 minutes) consumption of starting material. NMR spectroscopy showed the presence of considerable amounts of **13**. GC results also indicated that the triene **18** was a minor component in this reaction. In addition, the NMR sample for this reaction deposited an off-white precipitate after standing for a few days. This precipitate was identified as hydroquinone **14**, a compound seen in several other reactions. The disproportionation product is suggested to occur as shown in Figure 9. The initial elimination product undergoes initial base promoted elimination of MeOH to give the expected product. However, reaction of this product with base induces a hydride transfer to a second elimination product, giving MMNQ and the cyclohexadienone shown. This product can undergo tautomerization followed by proton loss to give the hydroquinone.

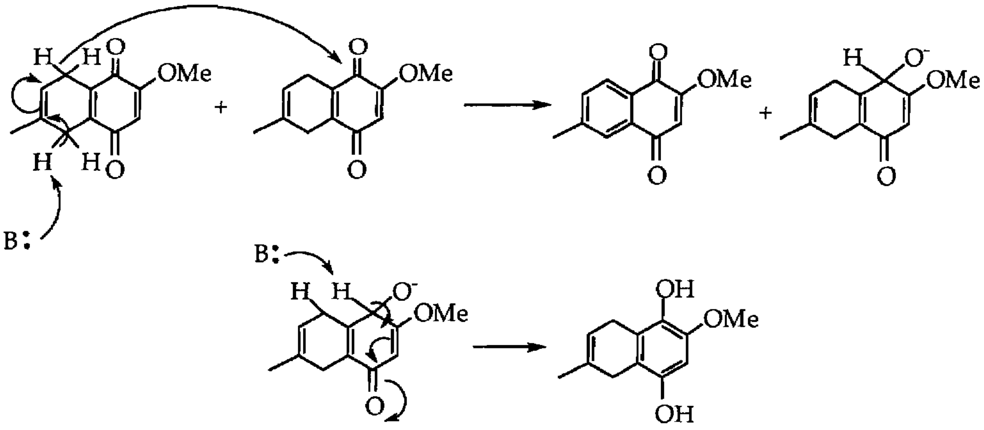


Figure 9 - Formation of Compounds 13 and 14 via Disproportionation of 18

5. DIELS-ALDER REACTIONS IN AQUEOUS SOLUTION

Changes in solvent can often have dramatic effects on the course of Diels-Alder reactions. Breslow and others have shown that the rate of Diels-Alder reactions between hydrophobic reactants can be greatly enhanced by carrying out these reactions in aqueous solvents.[12] It has been postulated that this rate enhancement occurs due to entropy effects, i.e., micellar catalysis. The Diels-Alder reaction of isoprene and DMBQ was examined in water and the results were compared to those obtained from several other solvents (Table 1).

Water proved to be the most effective solvent for directly providing a good yield of bisadducts and DMAQ. Analysis of the crude reaction mixture obtained from the aqueous DMBQ Diels-Alder reaction by GC/MS allowed for the tentative identification of several of the components (see Experimental section). Several attempts to isolate specific fractions of nonaromatic bisadducts failed; several components of the mixture are not stable to chromatography and were aromatized to DMAQ. The NMR spectra of crude reaction products agree with proposed product composition.

As the polarity of the reaction mixture decreased, the quantity of bisadducts and DMAQ in the product mixture also decreased. In many cases, the major product was MMNQ.

The modest yields of these products from reactions carried out in methanol and water suggested that increasing the molar ratio of isoprene to DMBQ should result in an increase in the amount of DMAQ formed; however; this was not observed.

Solvent	Isoprene/DMBQ Molar Ratio	DMBQ	MMNQ	Monoadducts	Bisadducts	DMAQ
Neat	3:1	31	2	0	0	0.5
Hexane	3:1	16	8	0	0	0
Ethyl ether	3:1	20	9	0	0	0
Ethyl acetate	3:1	15	11	0	0	0
Acetone	3:1	24	9	0	0	0
Isopropanol	3:1	4	17	10	0.9	0.4
Butanol	3:1	0	9	11	2	0
Acetic acid	3:1	5	8	6	12	0
Methanol	3:1	17	28	0	0	14
Methanol	6:1	3	28	8	3	18
Methanol	10:1	1	29	16	7	8
Water	3:1	0	4	0	11	22
Water	6:1	0	2	9	20	17
Water	10:1	0	0	0	18	21

Table 1 - Diels-Alder Reactions of DMBQ and Isoprene in Various Solvents[a]

[a] Reactions were carried out in steel bombs (4.0 mL capacity) at 160 °C for 16-17 h.

5.1. Aqueous Diels-Alder Optimization Reactions

The preliminary aqueous Diels-Alder reactions gave a mixture of the nonaromatized bisadduct and DMAQ in 30-40% yield. If the modest yield was a result of micellar catalysis of the cycloaddition, then more efficient micelle formation should result in an increase in the amount of bisadducts and DMAQ. To test this assertion, we performed the aqueous Diels-Alder reaction while applying ultrasonic agitation (Table 2). Good yields of monoadducts and MMNQ were observed at moderate temperature; the yields were much higher than with simple stirring at these temperatures. However, the maximum conversion to the bisadduct was only 5% at 90°C and in no cases was any AQ formed. High temperatures appear to be required for the formation of bisadducts in water. Unfortunately, the ultrasonic equipment needed to carry out these high temperature and high pressure experiments was not available. The implementation costs for such a process on an industrial scale would probably be substantial, so no further investigation into this type of process was undertaken.

Rideout and Breslow have shown that the addition of LiCl to aqueous Diels-Alder reaction of cyclopentadiene and methyl vinyl ketone causes a dramatic increase in the rate of cycloaddition.[13] They attribute this effect to the creation of a more polar reaction medium which causes the hydrophobic micelles to become even smaller. The reduced volume has a net effect of reducing the entropy change in going from two molecules to one, thus lowering the activation energy and increasing the rate of reaction. For this reason, we chose to examine the effects of LiCl on the cycloaddition of isoprene to DMBQ (Table 3). The presence of LiCl caused the yield of DMAQ to decrease by a factor of 2. A plausible explanation for the decrease is that the salt causes a reduction in the solubility of DMBQ in the reaction medium, thereby reducing the number of hydrophobic micelles that contained both reactants.

As a possible way to increase the yield of DMAQ in the aqueous Diels-Alder reaction, we examined the effects of the addition of oxidants to the DMBQ/isoprene mixture. The goal was to convert more of the monoadducts to aromatic naphthoquinones, which are key components in generating bisadducts. In general, the addition of polyoxometalates and other oxidants led to lower total combined yields of DMAQ and nonaromatic adducts. There were a few exceptions, such as V_2O_5; however, the small yield improvements probably would not offset the cost of the reagent. Several aqueous Diels-Alder reactions were also conducted in the presence of metal salts, but the yields of DMAQ did not improve.

At this point we focused our efforts on the optimization of the high temperature aqueous Diels-Alder reaction (Table 4). In general, increasing the molar ratio of isoprene:benzoquinone and the reaction time causes an increase in the combined yield of bisadducts and DMAQ; however, changing the reaction temperature had the most effect on the yield. Low temperatures (146°C) required long reaction times (75 hr) to obtain significant product yields; high temperatures (180°C) gave only DMAQ. Our optimum reaction

Temperature (°C)	Time (hr)	DMBQ	MMNQ	Monoadducts	Bisadducts	DMAQ
22	24	54	0	0.3	0	0
70	23	25	0.4	65	0	0
90	29	0.8	21	66	5	0
90[b]	25	13	6	53	0	0

Table 2 - Diels-Alder Reactions of DMBQ and Isoprene Using Ultrasonic Mixing[a]

[a]all product amounts in %

[b]Performed without ultrasonic mixing

Trial	Solvent	DMAQ (%)
1	H_2O	24
2	H_2O	28
3	H_2O	33
4	4.86 M aqueous LiCl	14
5	4.86 M aqueous LiCl	15

Table 3 - Aqueous Diels-Alder Reactions of DMBA and Isoprene in the Presence of Lithium Chloride[a]

[a]reactions carried out with 5 equivalents of isoprene at 185°C for 24 hours

Isoprene/DMBQ molar ratio	Temperature (°C)	Time (hr)	Bisadducts	DMAQ	Total
7:1	146	75	6	28	34
8:1	146	75	12	22	34
9:1	146	75	20	22	42
3:1	160	16	11	22	33
6:1	160	17	20	17	37
10:1	160	17	18	21	39
10:1	167[b]	8	19	38	57
6:1	170	23	26	22	48
8:1	170	2	4	20	24
8:1	170	17	15	30	45
8:1	170	20	26	23	49
8:1	170	41	21	21	42
5:1	180	24	0	39	39
5:1	185	24	0	28	28

Table 4 - Optimized Aqueous Diels-Alder Reactions[a]

[a] all product yields in %

[b] Reaction employed more DMBQ (6.0 mmol) in a larger (60 mL) vessel heated for 8 hr then cooled to 60°C over 16 hr

conditions, which happened to correspond to a larger scale reaction, gave the desired pulping catalyst mixture in 57% yield.

While the aqueous experiments listed in Table 4 gave modestly good DMAQ yields with large levels of isoprene, subsequent larger scale experiments often provided only ~30% direct DMAQ yield. The yield rose to ~40% after chromatography, apparently the result of reaction component aromatization. The observed large differences in DMAQ yields through the course of our aqueous Diels-Alder reaction study indicated that there may be subtleties that we do not understand.

6. HIGH BISADDUCT YIELD DIELS-ALDER REACTION

In subsequent studies we have established that the reaction of unsubstituted benzoquinone with isoprene in ethanol solvent provides the bisadduct shown in Figure 2 in 85% isolated yield.[5] We have shown that this compound is an excellent pulping catalyst and a potential candidate for commercialization.[14]

7. EXPERIMENTAL

Methods and Materials: Gas chromatography was carried out on a Hewlett-Packard 5890 chromatograph with a flame ionization detector, using one of two methods: 1) 10 m 50% crosslinked phenol methyl silicone gum phase HP-17 macrobore capillary column; helium carrier gas flow was 8 mL/min, injection temperature 250°C, detector temperature was 280°C, with a temperature program of 150°C for 1 minute, followed by ramping at 5°C/min to 275°C, and holding at 275°C for 5 min; 2) 0.5mmx30m DB-1 column, injection temperature 250°C, detector temperature was 280°C, ramping at 5°C/min between 50-250°C, and holding at 250°C until all products had come off the column. Quantitative analysis of the components is difficult because few of the Diels-Alder products are commercially available to determine response factors. Therefore, all bisadducts were assumed to have a response factor equal to that of the DMAQ internal standard. All monoadducts were assumed to have a response factor equal to the MMNQ internal standard. Standard mixtures of the two internal standards gave very good correlations. GC/MS was carried out on a 5890 Hewlett-Packard gas chromatograph using a 35 m DB-5 column and were measured at 70eV.

Product Analysis and Identification for Diels-Alder Reactions in Homogeneous Solution and in the Presence of Lewis Acid Promoters: A great majority of the products in the Diels-Alder reaction mixture have been identified by a combination of NMR and GC/MS. GC proved valuable for the rapid monitoring and analysis of the reaction mixtures obtained from both promoted and unpromoted reactions.

Table 5 summarizes the structures, retention times, and molecular weights of the products observed in these reactions. Two different instruments were used to measure the GC and the GC/MS. Because of differences in column length and carrier flow rate, the R_t for the two instruments differed slightly.

For the signal at R_t 6.7 minutes, the GC/MS revealed a clear molecular ion at m/e 136. The overall spectrum was very similar to signals at R_t 7.49 and 9.35 minutes. However, the signal at 6.7 minutes was a minor product in the spectrum and its exact structure is not yet known. In general, the assignment of specific structures to the isoprene dimers was based only on presumed steric restrictions that could exist for the Diels-Alder reaction. In some cases, two structures were assigned. The GC/MS with its longer column was sometimes able to resolve the peak into two distinct components. The compound at R_t 28.7 minutes was probably present as a mixture of regioisomers; however, GC/MS was not able to resolve the peak.

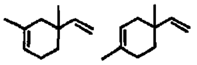
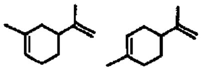
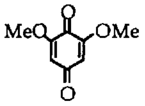
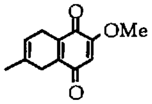
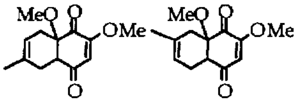
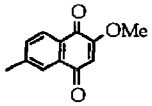
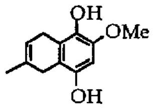
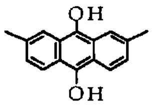
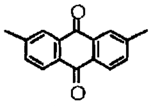
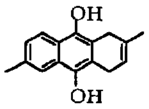
Product Analysis and Identification for Diels-Alder Reactions in Aqueous Medium: GC/MS analysis of crude reaction mixture formed in the aqueous Diels-Alder reaction of DMBQ showed the presence of many of the same products seen in nonaqueous reactions. In addition, several nonaromatic bisadducts were observed, but could not be isolated since they were not stable to chromatography. Some GC/MS assignments were confirmed by NMR. The product mixture contained three naphthoquinones (**12**, **13**, and **19**) and a gamut of AQ-related components, ranging from the expected simple bisadduct 6 to DMAQ. Molecular ions were observed for components corresponding to the structures shown in Figure 10; however, none of these structures were conclusively characterized.

General Procedure for Diels-Alder Reactions in Homogeneous Solution: A small stainless steel reaction vessel was charged with starting quinone, isoprene (1.5 - 2.0x molar excess), and solvent. The mixture was heated at the reaction temperature overnight. Solvent removal and chromatography gave the Diels-Alder products.

General Procedure for Diels-Alder Reactions in the Presence of Lewis Acid Promoters: The starting quinone was mixed with solid silica gel or alumina. The solid mixture was placed in a small stainless steel reaction vessel. Isoprene was added and the mixture was heated at the reaction temperature overnight. Solvent removal and chromatography gave the Diels-Alder products.

General Procedure for Diels-Alder Reactions in Aqueous Medium: The starting quinone was mixed with 3.5 mL of deionized water in a pressure vessel to give a 0.043 M solution.[15] Several equivalents of isoprene were added and the vessel was sealed and heated with shaking in a sand bath at 160°C. After the reaction was completed, the vessel was cooled and the reaction mixture extracted with a 3:1 mixture of chloroform and ethanol. The isolated products were analyzed by GC/MS using an internal standard.

Table 5 - GC/MS Results and Structural Assignments

GC R_t (min)	GC/MS R_t (min)	structure	GC/MS MW
6.70	10.15	isoprene dimer (?)	136
7.49	11.08		136
9.35	11.08		136
10.6		isoprene dimer(?)	136
22.04	27.78		168
28.7	36.4		204
29.04	36.6		236
29.4	37.5		202
31.9	39.7		206
33.8	41.9	unidentified	244
34.5	43.6		238
35.98	45.95		236
40.34	51.1	unidentified	242
41.03	52.5		240

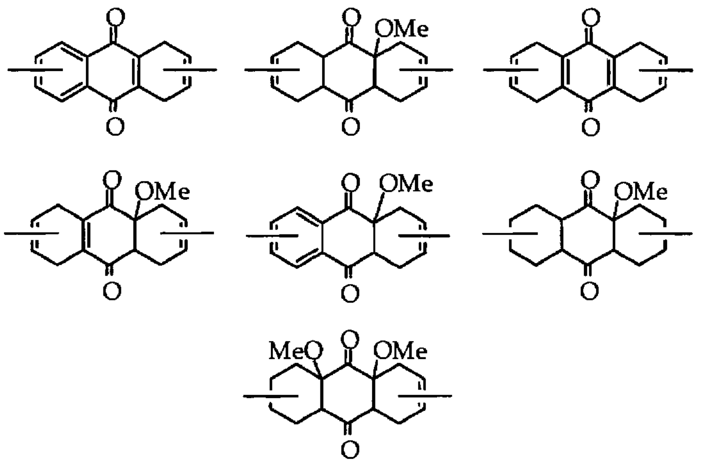


Figure 10 - Possible Structures for Additional Molecular Ions Observed in Product Mixtures from Aqueous Diels-Alder Reactions

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