

1972

# The total synthesis of carpanone

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The total synthesis of carpanone

by

Michael Roy Engel

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The Requirements for the Degree of  
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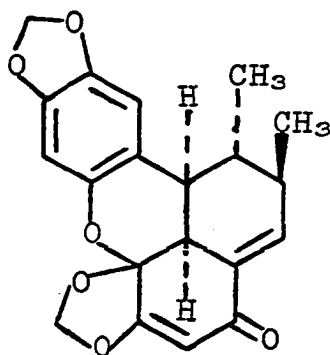
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## INTRODUCTION

Highly substituted o-quinone methides had been reported as early as 1903<sup>1-7</sup> and have been the subject of a great deal of investigation since that time. The o-quinone methide moiety, however, has not been exploited for synthetic purposes. The reason for this is lack of efficient methods for generating and handling the quinone methides.

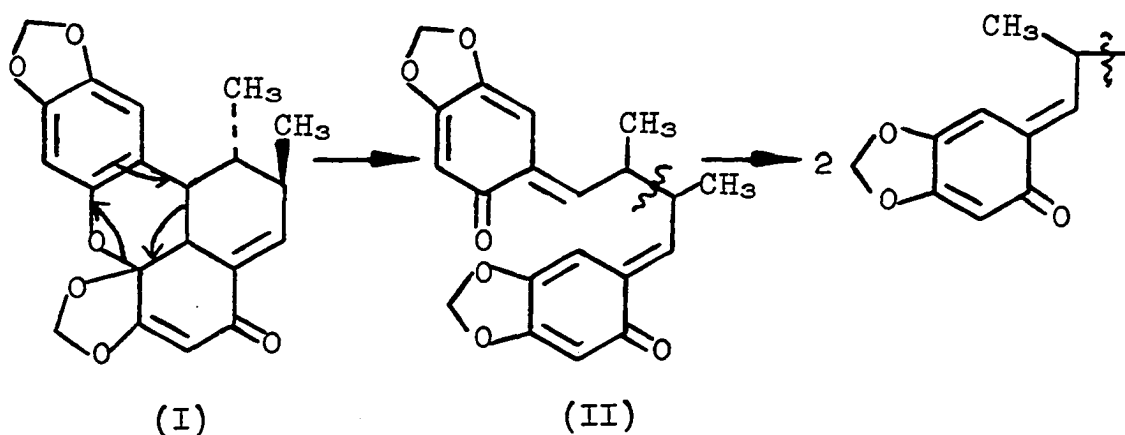
The discovery of carpanone in late 1969<sup>8</sup> supplied a good example of a molecule built up by quinone methide reactions. The carpanone molecule (I) was isolated from the bark of the carpano tree which is indigenous to Australia.



(I)

Because of its size and complexity, carpanone presents a significant synthetic challenge. The molecule contains five contiguous asymmetric centers and has no elements of symmetry. The compound as isolated, however, is racemic.

The clue to understanding the synthesis of carpanone is contained in the mass spectrum. The base peak was found to be at  $m/e = 177$  which corresponds to one-half of the molecular weight. The most reasonable explanation is that the molecule undergoes a reverse Diels-Alder type reaction (I $\rightarrow$ II) to give a species which can then cleave one bond to give two identical fragments.



The realization that carpanone is a dimeric molecule greatly clarified the synthetic approaches to it. The initial goal would be the bis-o-quinone methide (II) which would then thermally close to give carpanone. This route has the disadvantage that one must generate a "two-headed", highly reactive intermediate with proper stereochemistry. The advantage is that (II) contains two asymmetric centers rather than the five in carpanone. The intermediate has a  $C_2$  axis of symmetry which passes through the midpoint of the bond

joining the two halves. The bis-o-quinone methide, once formed, would generate the remaining three centers stereoselectively via the ensuing Diels-Alder reaction.

We therefore took this approach to the synthesis of carpanone.

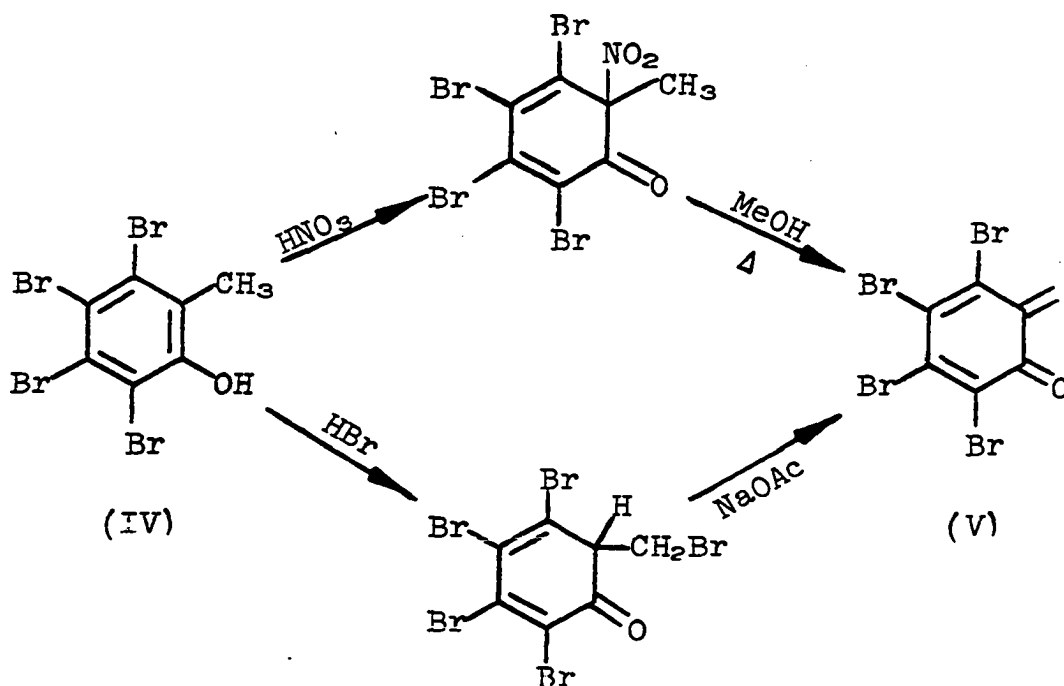
## HISTORICAL

The synthesis of carpanone is essentially synthesis using o-quinone methides; therefore, a review of their known properties is in order. Much of the work is redundant and therefore reviews will be cited and only pertinent and characteristic experiments will be mentioned in detail.

The same approach will be used with phenol oxidations.

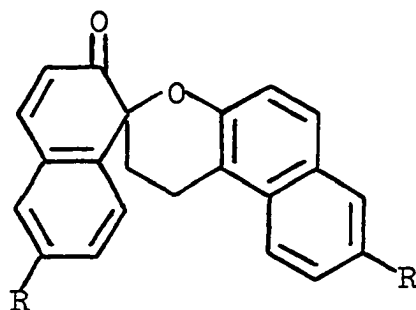
Ortho quinone methides

Zincke<sup>1-5</sup> and coworkers reported the first known quinone methides. These were obtained from completely substituted phenols such as (IV) by nitration with nitric acid in acetic acid or hydrobromination followed by elimination. Fries and Kann<sup>6</sup> and Fries and Huber<sup>7</sup>





reduced to cresols, their oxidation equivalence was only half of what would be expected for the monomers. The molecular weight determinations were believed to be unreliable due to decomposition or dissociation of (VIII) or (IX) in solution. Refluxing of (IX) in xylene gave equal amounts of (VI) and a dimer (X) of 1,2-naphthoquinone-1-methide (VII). This work



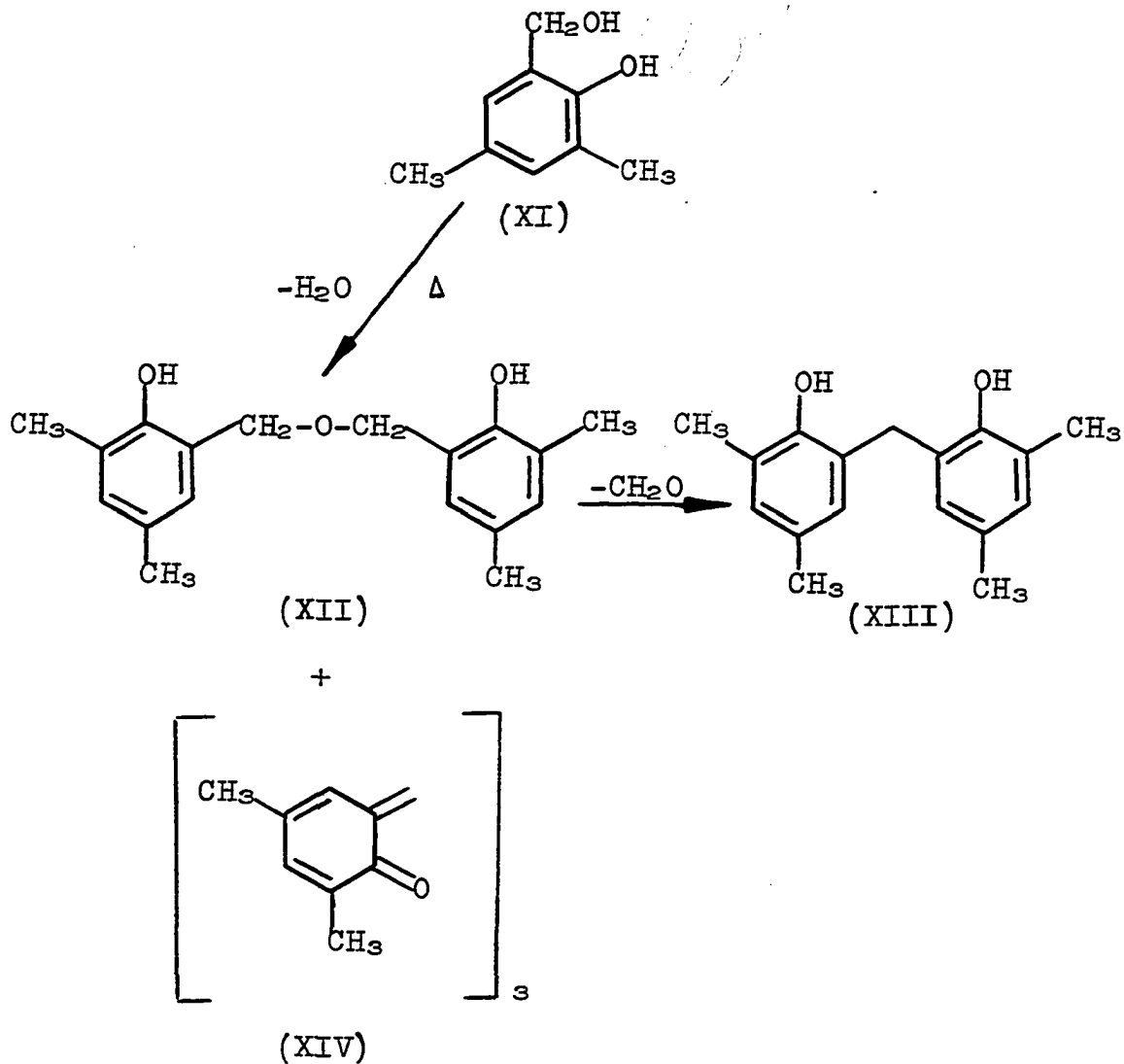
(X)

was repeated by Smith and Horner<sup>13</sup> with similar results.

Heating phenolic alcohols gives polymers which are similar to those obtained on heating mixtures of phenols and formaldehyde. Because of the importance of phenol-formaldehyde plastics, a large amount of work was done on phenolic alcohols. Several reviews on the subject of phenolic resins and the role of quinone methides are available.<sup>14,15,16</sup>

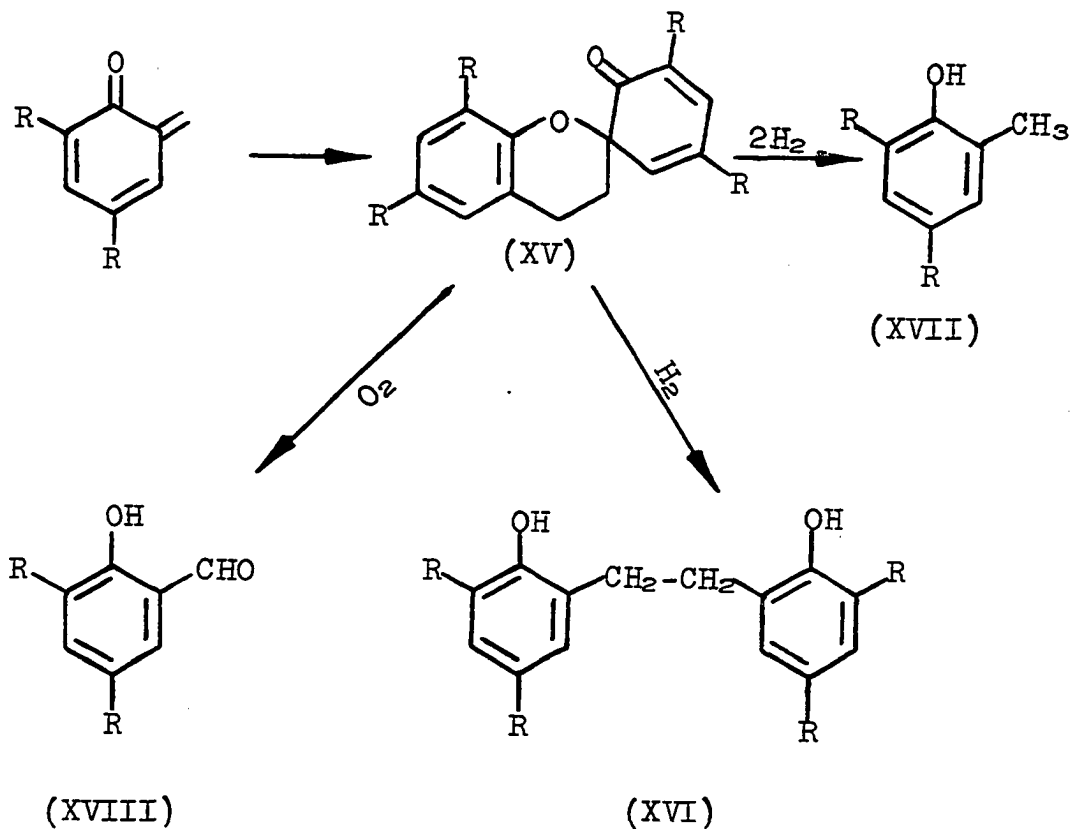
Euler and coworkers<sup>17</sup> attempted to explain the hardening of phenolic resin using a "model" system. Heating 3,5-dimethyl-2-hydroxybenzyl alcohol (XI) caused loss of water yielding a mixture of the ether (XII), the methylene bridged

compound (XIII), and a trimer of the quinone methide (XIV).



Further work showed<sup>18</sup> that the ether (XII) on continued heating loses water to give more of the trimer. Euler and coworkers<sup>19</sup> also found that a trimer could be produced by the treatment of 5-methyl-2-hydroxybenzyl bromide with sodium bicarbonate. Hultzsch<sup>20,21</sup> and Hultzsch and Schieman<sup>22</sup> did similar work and noted that bulky substituents

on the phenolic alcohols led to production of dimers or mixtures of dimers and trimers. The structure of the dimer was shown to be (XV) by hydrogenation to the ethylene bridged compound (XVI) or to the corresponding cresol (XVII) and oxidation to the corresponding aldehyde (XVIII). The

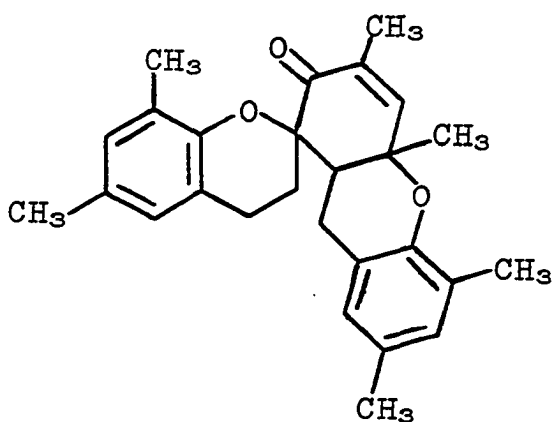


structure (XV) was consistent with results obtained by Mannich<sup>23</sup> for the dimerization of methylene cyclohexanone.

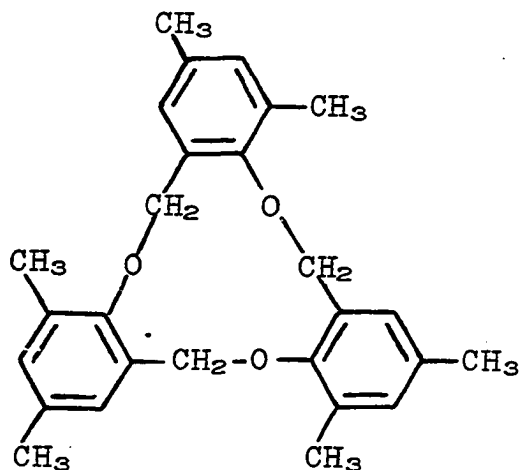




The structure of the trimer of *o*-quinone methide was not established until Cavitt *et al.*,<sup>24</sup> proved it to be (XIX). The structure (XX) had been favored by Euler. The trimer is



(XIX)

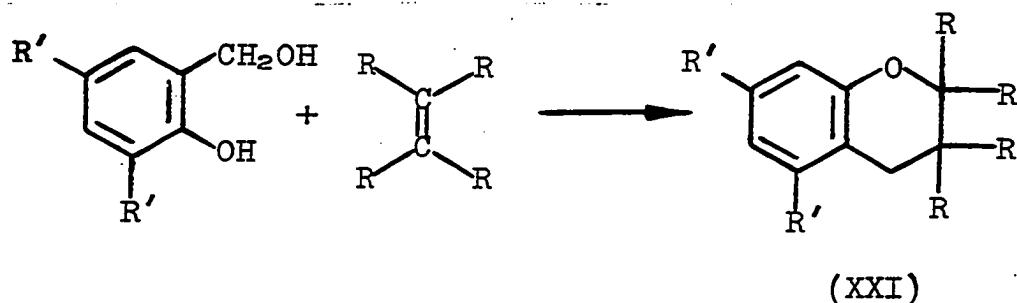


(XX)

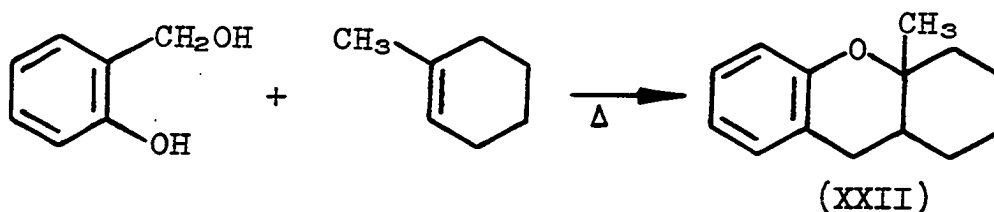
formed by a Diels-Alder addition of one quinone methide unit to the methylene double bond of a second molecule. The first quinone methide unit has, at this point, regained aromatic character while the second unit is now a dienone system. A third molecule of quinone methide can then add to one of the dienone double bonds to give the observed trimer.

The ability of *o*-quinone methides to act as dienes in Diels-Alder type reactions has been demonstrated many times. Hultsch<sup>25,26</sup> heated substituted hydroxybenzyl alcohols with styrene and a large number of other olefins to give

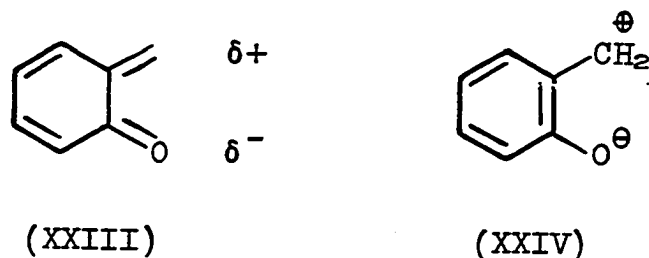
reasonable yields of chroman derivatives (XXI). Cuneen



et al.,<sup>27</sup> heated 2-hydroxybenzyl alcohol with methylcyclohexene and obtained the chroman derivative (XXII).

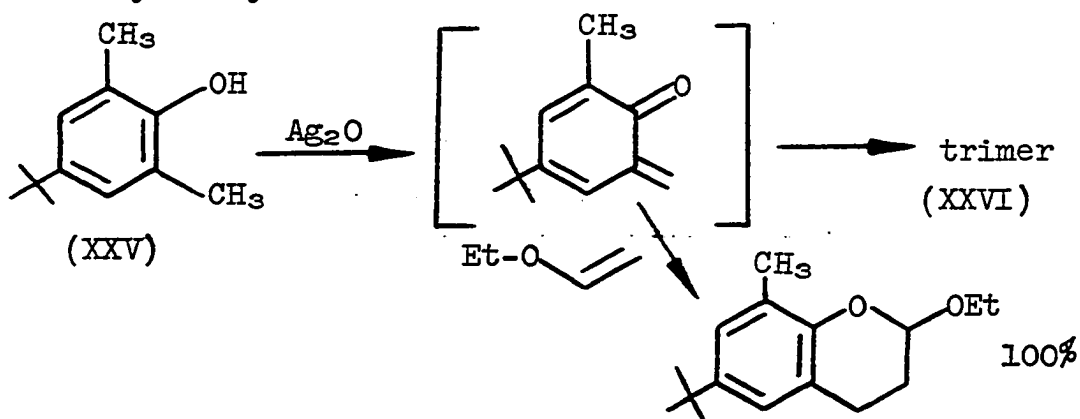


The fact that only one of two possible isomers was formed pointed to the existence of charge separation in the quinone methide molecule (XXIII). This is as expected because of the analogy to enone systems in general. Besides this, charge separated resonance forms such as (XXIV) are more likely to be important in quinone methides than in enones because of the added stabilization of the benzene unit which is generated.

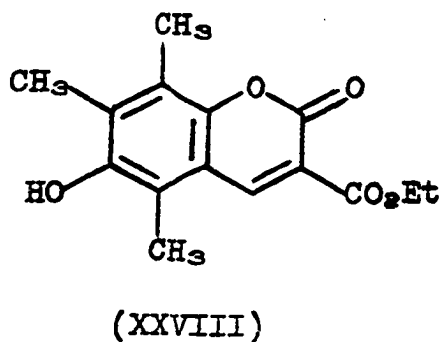
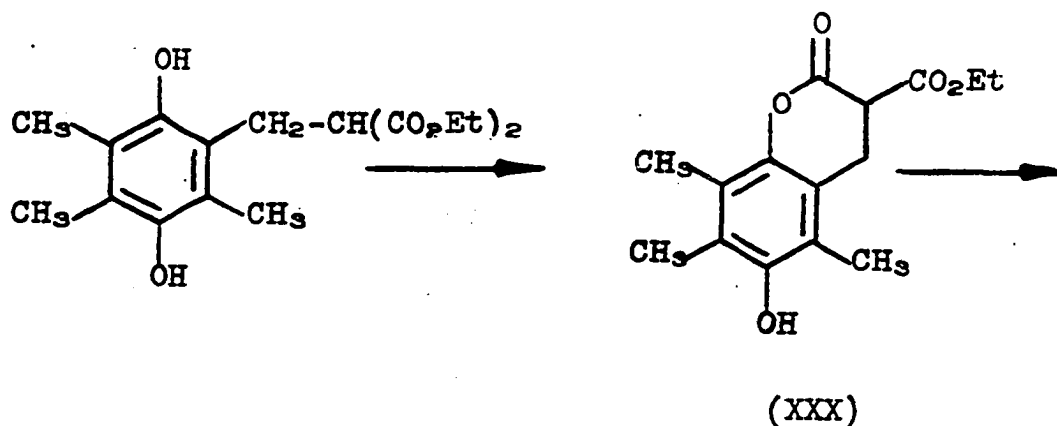
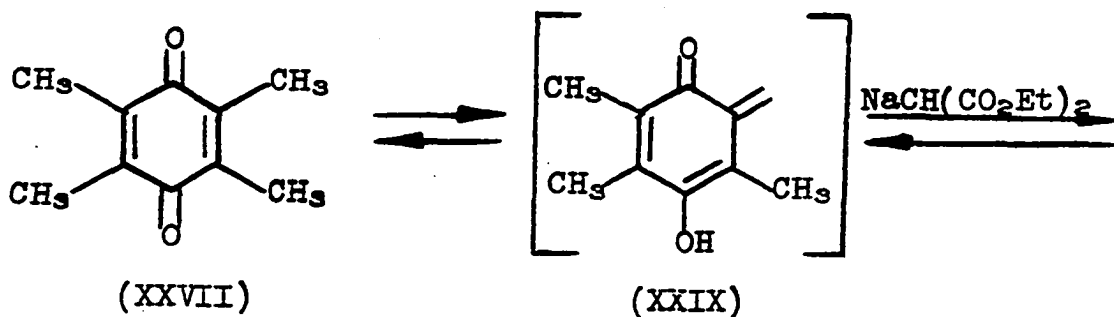


In all cases of o-quinone methide addition to olefins, the correct orientation can be predicted on the basis of polarized or charge separated species. In a situation such as addition to oleic acid<sup>28</sup> where no preference is expected, one obtains mixtures of the possible isomers. Ortho-quinone methides have also been generated by heating hydroxybenzylamines and hydroxybenzylammonium salts in the presence of base.<sup>29,30</sup>

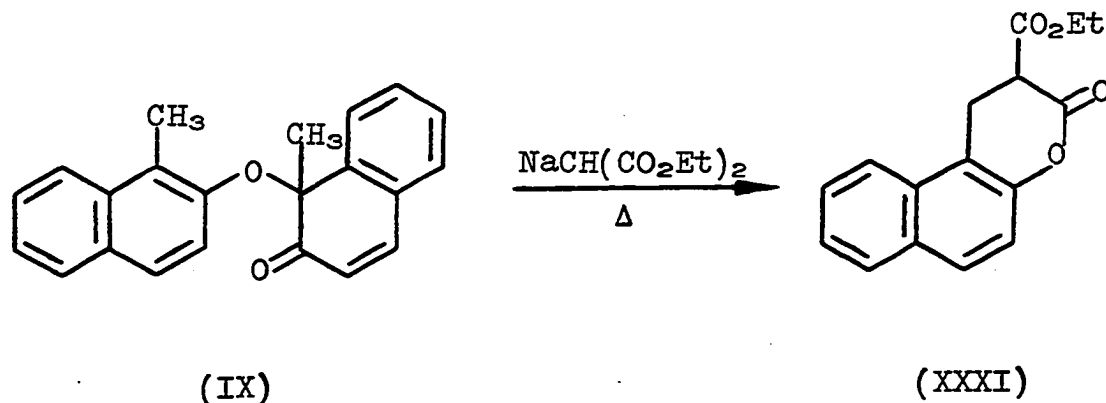
Bolon<sup>31,32</sup> has generated o-quinone methides by an oxidative route and added them to a range of olefins. On treatment with silver oxide, trisubstituted phenols such as 2,6-dimethyl-4-t-butylphenol (XXV) are oxidized to yield trimers of the corresponding quinone methide (XXVI). It is necessary that the group in the 4 position have no alpha hydrogens or else the p-quinone methide will form preferentially. Bolon found that in the presence of olefins, the quinone methide would add to give chroman derivatives and that the best yields are obtained with electron rich olefins such as ethyl vinyl ether.



Ortho-quinone methides also react with nucleophiles, usually at the methylene carbon, to yield phenols substituted at the benzyl position. Smith and Dobronolny<sup>33</sup> discovered that tetramethyl-*p*-benzoquinone (XXVII) reacted with sodium diethyl malonate to yield a coumarin derivative (XXVIII). Fuson<sup>34</sup>

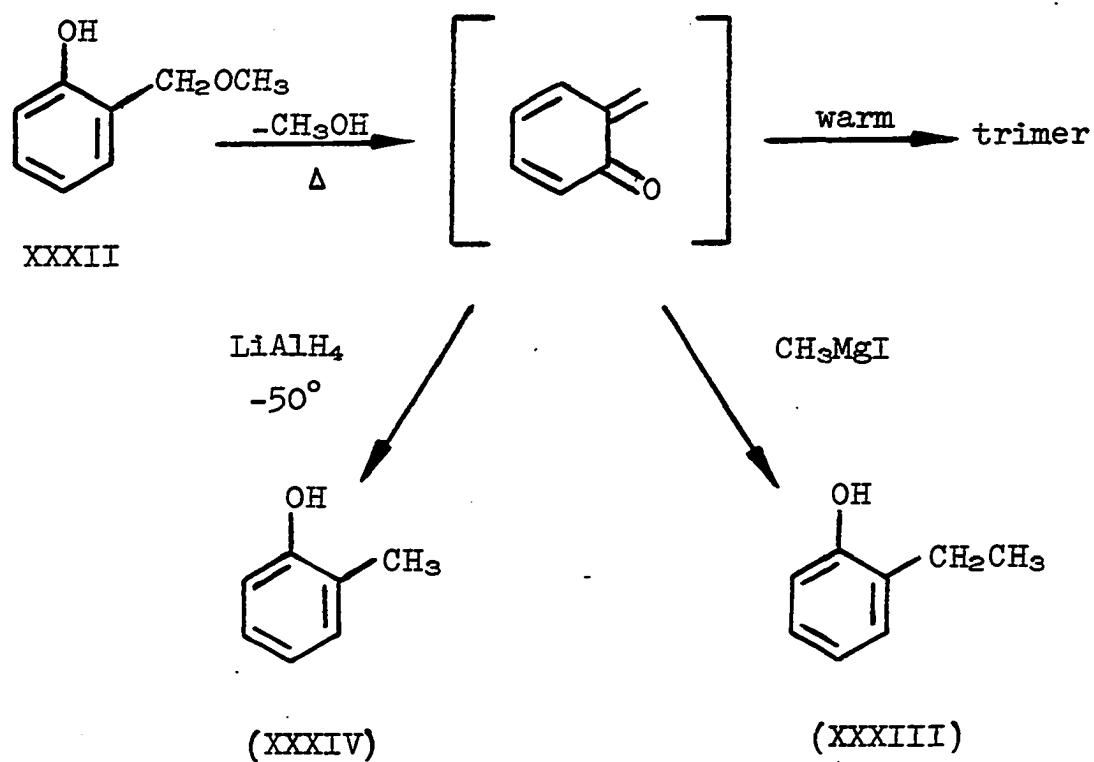


suggested that the mechanism involved isomerization of the benzoquinone to the o-quinone methide (XXIX) followed by nucleophilic addition of the malonate anion. A transesterification would then give the dihydrocoumarin (XXX). This is then oxidized to the coumarin (XXVIII) by excess benzoquinone. Smith and Kaiser<sup>35</sup> obtained similar results with one carboethoxy group replaced by a nitrile group, and Smith and Horner<sup>36</sup> produced naphthocoumarin (XXXI) by heating Fries' "naphthoquinone methide" (IX) with sodium diethyl malonate.



The actual existence of o-quinone methide monomer was demonstrated by Gardner and coworkers<sup>37,38</sup> and Cavitt<sup>39,40</sup>. The quinone methide was produced by the pyrolysis of 2-hydroxymethoxybenzyl ether (XXXII) at 500-650° in the vapor phase. The monomer was then condensed by Dry Ice temperatures as a bright yellow solid. Warming to room temperature produced white crystals of the trimer, reaction at -50° with

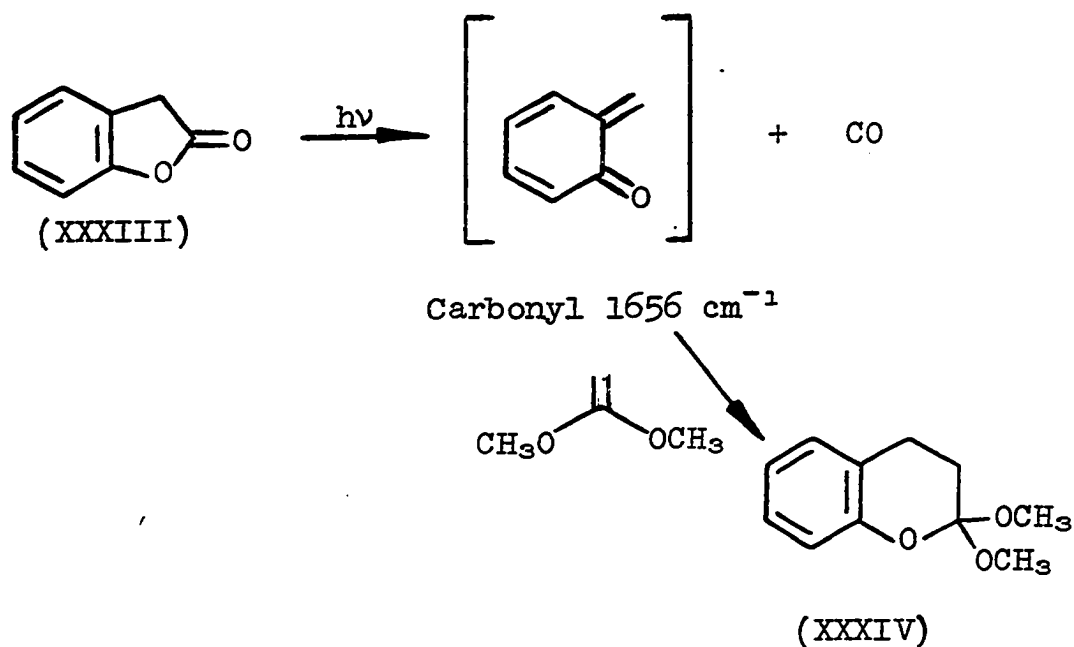
methylmagnesium iodide gave 2-ethylphenol (XXXIII), and reduction at  $-50^{\circ}$  with lithium aluminum hydride gave 2-methylphenol (XXXIV). McIntosh and Chapman<sup>41</sup> obtained further



evidence by generating *o*-quinone methide through the pyrolysis of 2-hydroxybenzyl alcohol, trapping it at liquid nitrogen temperatures, and taking the infrared spectrum. The carbonyl band was located at  $1656\text{ cm}^{-1}$ .

McIntosh and Chapman<sup>42</sup> have also discovered what is probably the most convenient method of *o*-quinone methide

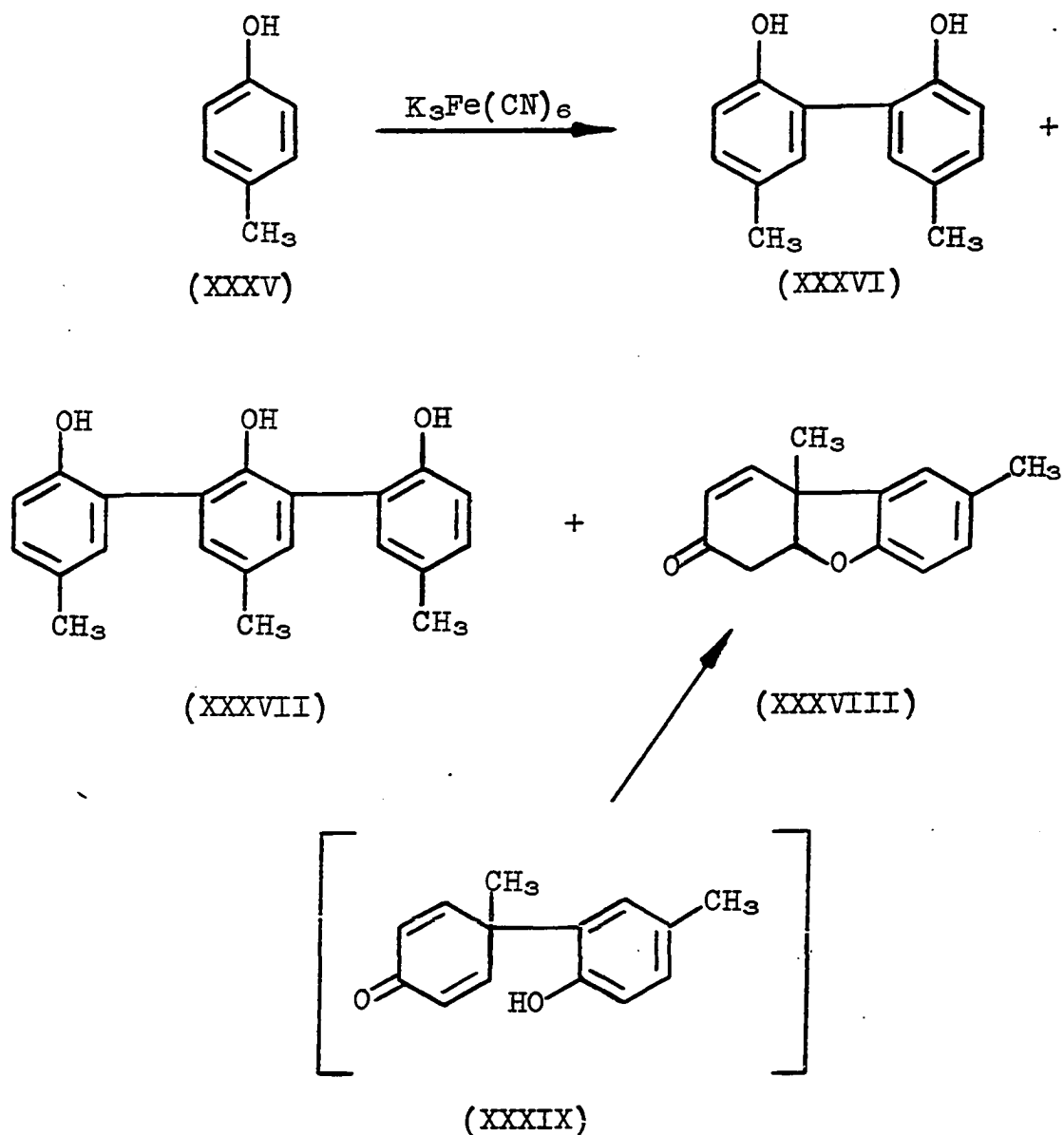
generation under neutral conditions. Photolysis of 2-coumaranone (XXXIII) proceeds with loss of carbon monoxide to yield *o*-quinone methide. The presence of the quinone methide has been shown by low temperature infrared and by trapping it with dimethoxyethylene to give the adduct (XXXIV).



### Phenol oxidation

Phenols are subject to ready oxidation by a wide range of oxidizing agents. It is well known, however, that the use of reagents such as permanganate or chromic acid constitutes a convenient synthesis of asphalt. The use of milder agents, on the other hand, gives products which are synthetically useful.

Para-cresol (XXXV)<sup>43</sup> is oxidized by potassium ferricyanide to give the dimer (XXXVI), the trimer (XXXVII), Pummerer's ketone (XXXVIII), and polymers. The formation of



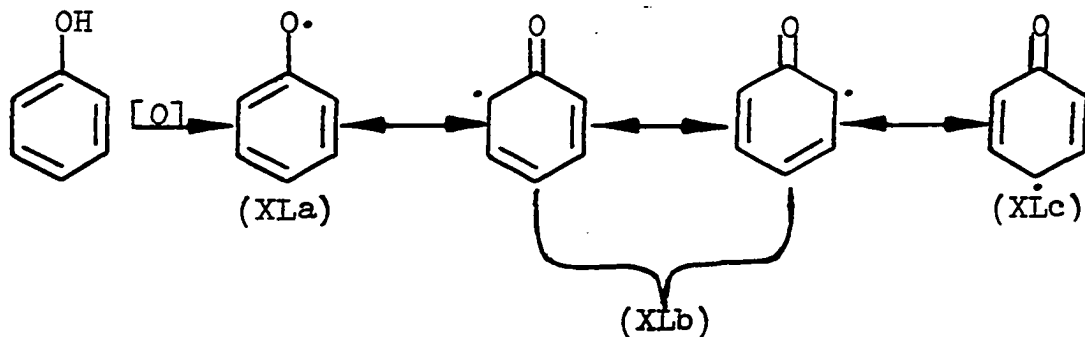
Pummerer's ketone is believed to involve the generation of dienone (XXXIX) followed by Michael addition of the phenol to



the dienone system. All the observed products are built up by carbon-carbon bond formation at the ortho positions of the phenols. In p-cresol, the para position is blocked which disfavors coupling para, but this possibility is amply demonstrated by the oxidation of alpha-naphthol<sup>44</sup> which gives all possible o-p, o-o, and p-p coupling products. It is also possible to have carbon-oxygen coupling in cases where steric considerations disfavor carbon-carbon coupling.

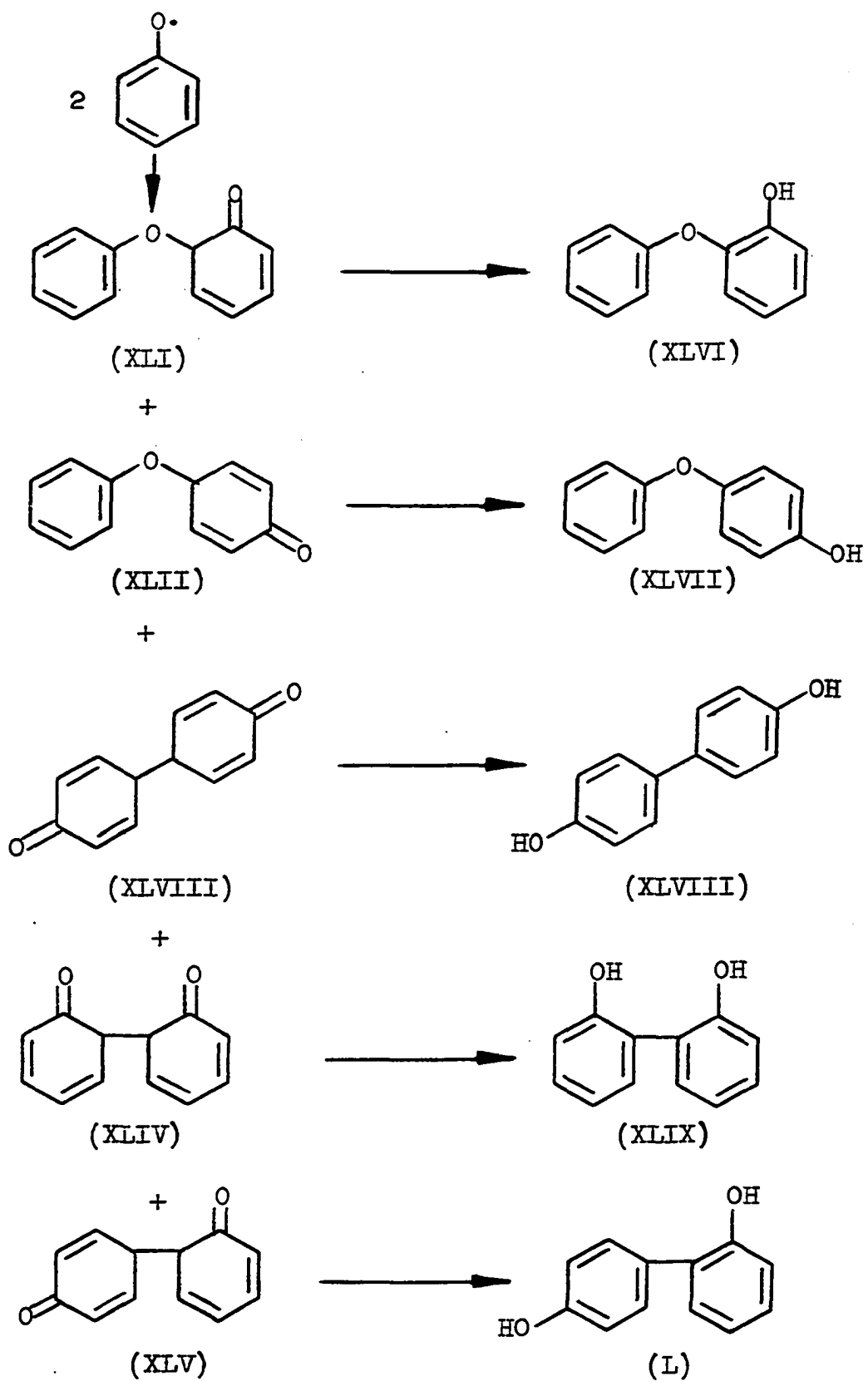
A very good review of the work in this area is contained in a collection of monographs edited by Taylor and Battersby.<sup>45</sup> The amount of work which has been done is clearly shown in the section by Musso entitled "Phenol Coupling", which contains 424 references.

The mechanism which best explains the observed products in phenol oxidations is free radical combination. The first step is oxidation of the phenol anion to the free phenoxy radical (XL). The possible resonance forms a-c indicate that the density of the unpaired electron should be greatest at the oxygen and the ortho and para ring positions. Esr studies back up this expectation.<sup>46</sup>

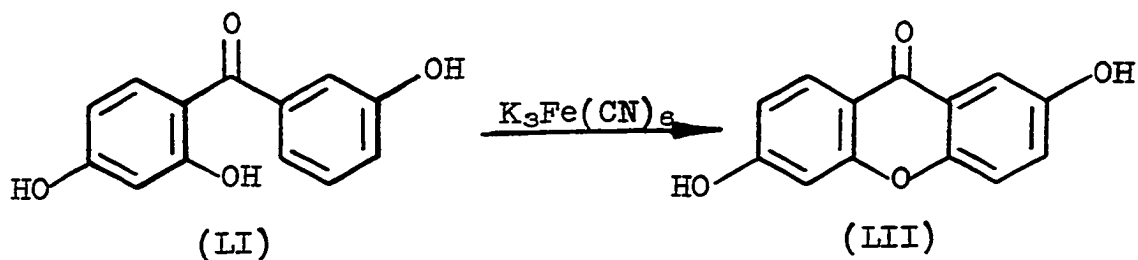


Two of these radicals may then dimerize using any one of the four possible positions on each. In the case of unsubstituted phenols, the enone type products produced (XLI-XLV) will quickly isomerize to phenolic materials (XLVI-L). This is shown on the following page. The possibility not shown, that of oxygen-oxygen coupling, has never been observed. The dimers can be further oxidized to give polymeric material.

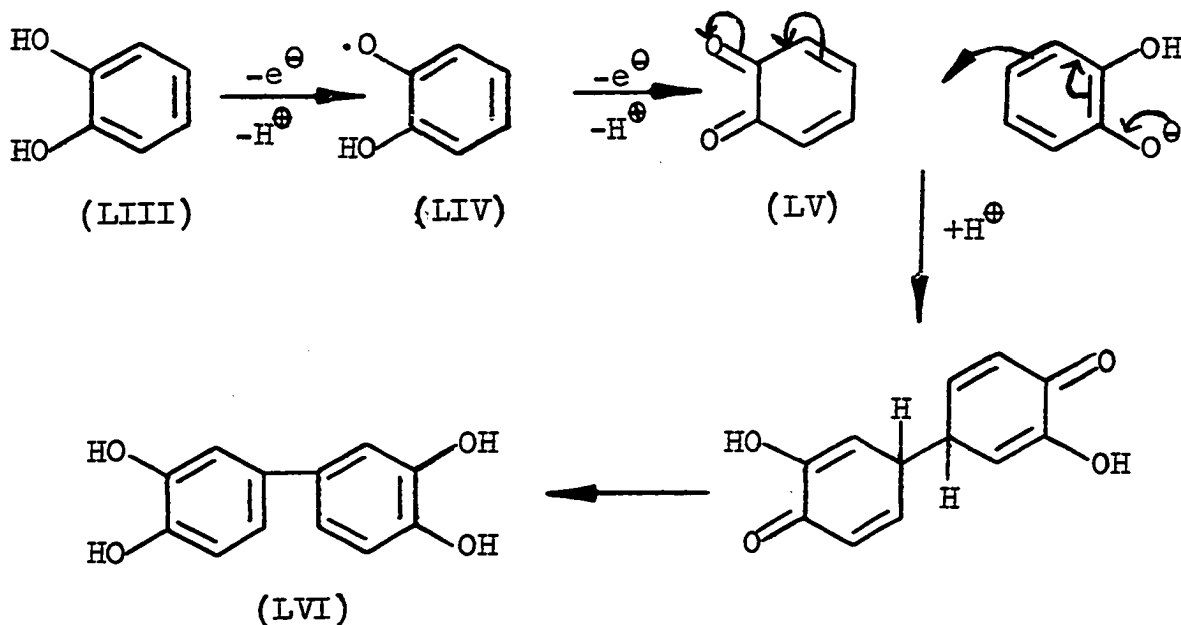
There are two other possible mechanisms which have been proposed, the first is oxidation to the phenoxy radical followed by radical addition to a molecule of phenol or phenolate anion to give a dimeric radical which could then be oxidized further to the product. Although this mechanism seems plausible, there is no evidence which would favor it over the radical coupling route. Also, the lack of any dihydro products which would be expected from a free radical addition disfavors this mechanism. The second possibility is a two electron oxidation of a phenol anion to yield the corresponding cation which then adds to a phenol or phenolate anion to give the products. There is one clear cut example where this mechanism has been shown to be operating.<sup>47</sup> The oxidation of (LI) by ferricyanide to give intramolecular coupling product (LII) displays the following characteristics: 1) the reaction is first order in the substrate (LI). 2) The reaction is first order



in ferricyanide. 3) Ferrocyanide inhibits the reaction. 4) An increase in ionic strength yields a large increase in rate. 5) Different cations give different rates in the order  $Cs > K > Na$ . These are all consistent with an electrophilic substitution mechanism involving positively charged oxygen.



In the case of polyhydroxy aromatic compounds, a fourth mechanism is possible. Catechol (LIII) can be oxidized to the radical (LIV) and then further oxidized to the quinone (LV). The quinone (LV) then reacts with another catechol molecule to form the dimer (LVI).

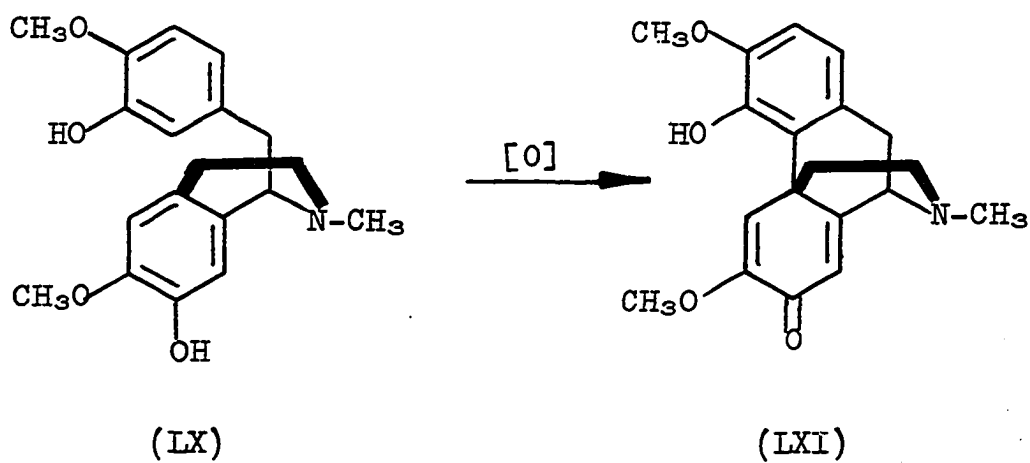
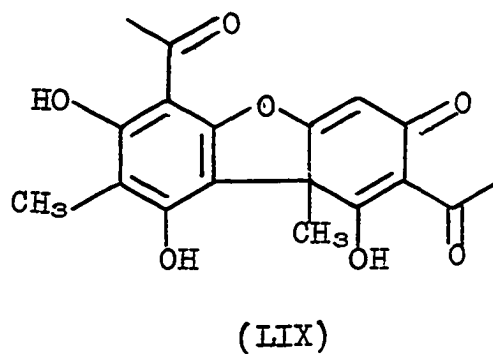
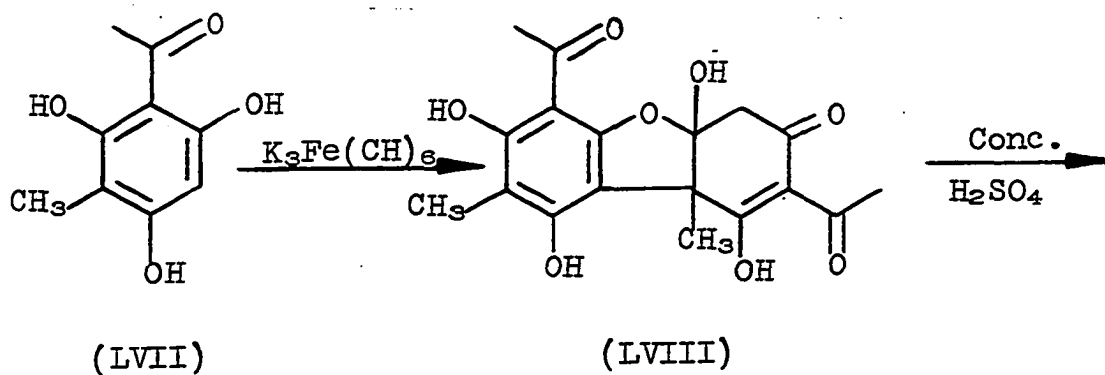


Nucleophilic addition of a phenoxy anion followed by tautomerism yields the observed product (LVI). The fact that this mechanism takes place to some extent is shown by experiments in which mixtures of polyhydroxy aromatics and phenols are oxidized under conditions where only the polyhydroxy compound should react. The recovery of mixed products in moderate yield points to the quinone mechanism.

The importance of phenol oxidations is due to the large number of natural products which appear to have been synthesized in nature by an oxidative route. Even if this is not true in the plant, oxidative phenolic coupling is in many cases the only workable synthetic route to these compounds. The classic example is Barton's and coworkers<sup>48</sup> elegant synthesis of usnic acid. The problem seemed baffling until Barton saw the resemblance of usnic acid to Pummerer's ketone. Oxidation of methylphloracetophenone (LVII) with potassium ferricyanide yielded usnic acid hydrate (LVIII) which could then be dehydrated with concentrated sulfuric acid to yield usnic acid (LIX). This is shown on the following page.

An example of phenolic coupling in the alkaloid field is the conversion of reticuline (LX) to salutaridine (LXI).<sup>49</sup> This is also shown on the following page. In the plant, salutaridine is the precursor to thebaine which is converted to codeine and then to morphine. The only drawback

to these oxidative syntheses is the yields. In the conversion of reticuline to salutaridene the yield was 0.02%. This is somewhat less than commercially useful.



## Lignin

Lignin is an amorphous methoxylated phenolic polymer which makes up 20-30% of the dry weight of the woody tissues of plants.<sup>50</sup> Unfortunately, ever since wood pulp has been used, the lignin content has become wasted material which serves only to pollute streams running by paper mills.

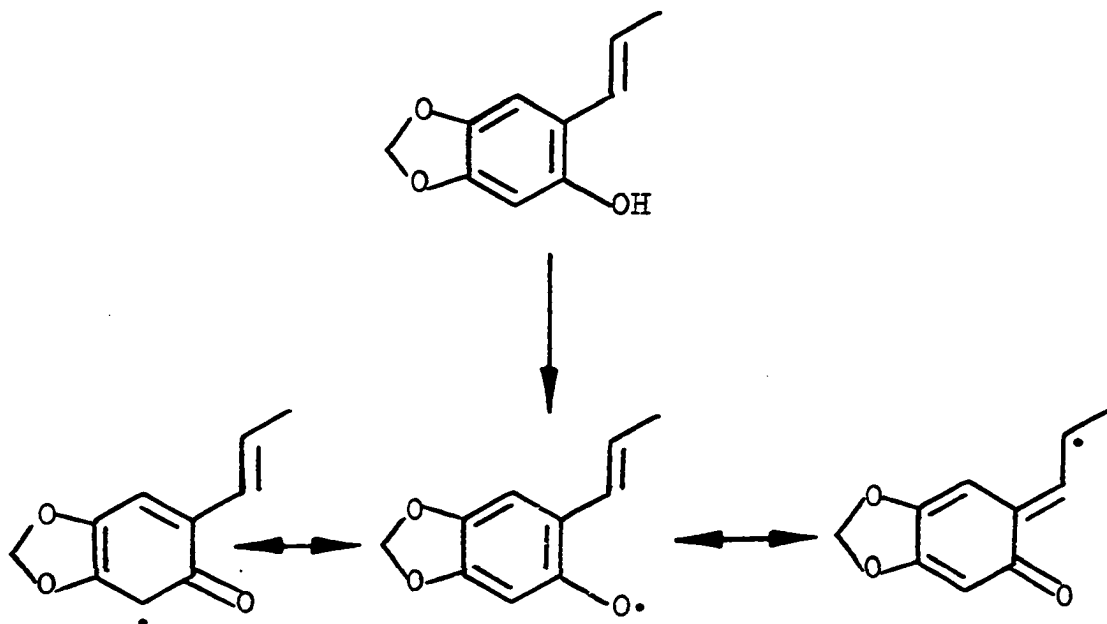
The structure of lignin had been explored as early as 1893,<sup>50</sup> but it is not fully understood to the present time. It is predominantly a polymer of coniferyl alcohol and related phenolic alcohols. It is believed to be built up by phenol oxidations followed by *p*-quinone methide reactions. Oxidative coupling of a coniferyl alcohol at the beta position yields a *p*-quinone methide which can then be attacked by nucleophiles such as other phenolic units.

Carpanone may be a novel type of lignin in that the quinone methide formed is ortho and can therefore undergo Diels-Alder type reactions which are impossible with *p*-quinone methides. An understanding of the biosynthesis of carpanone may shed some light on the lignification process in general.

## RESULTS AND DISCUSSION

The synthesis of carpanone

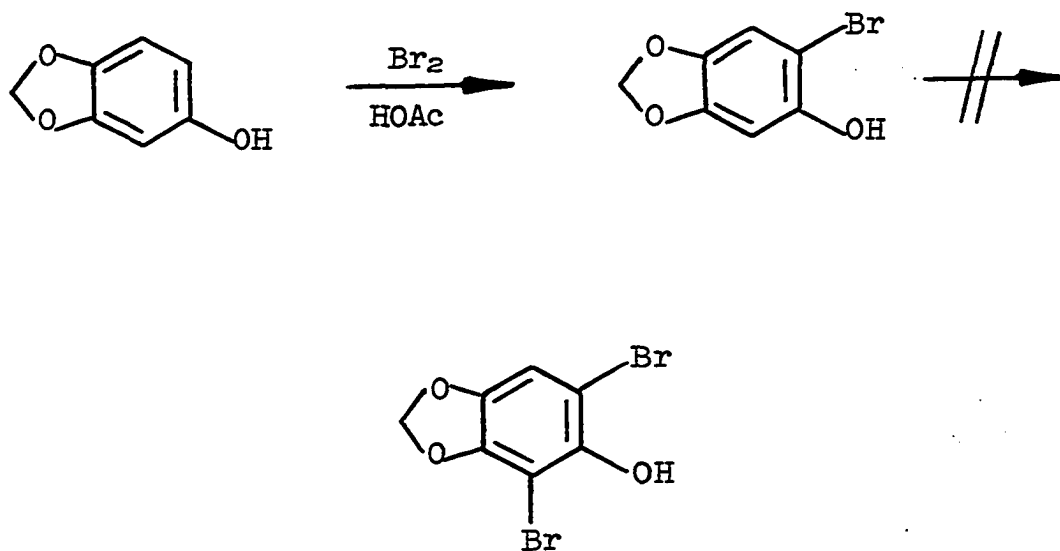
Our approach to carpanone was an oxidative one. One electron oxidation of propenylsesamol would be expected to yield initially the phenol radical which ought to dimerize. The reactive positions on the radical are the ortho and



beta positions. The ortho position was not expected to be particularly reactive since it is not so in sesamol itself. Treatment of sesamol with bromine in acetic acid yields the monobromo derivative rather than the dibromo as expected.<sup>51</sup> The beta position, however, is sterically open and beta

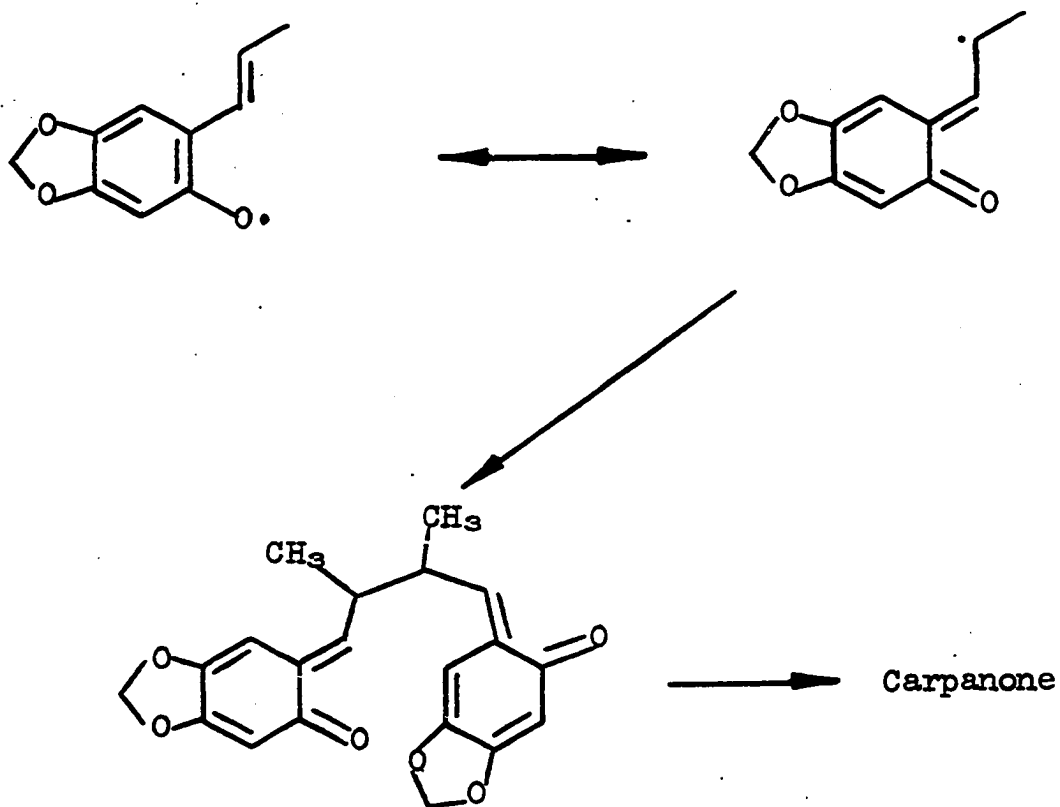


coupling has been observed previously in the oxidation of coniferyl alcohol.<sup>52</sup>



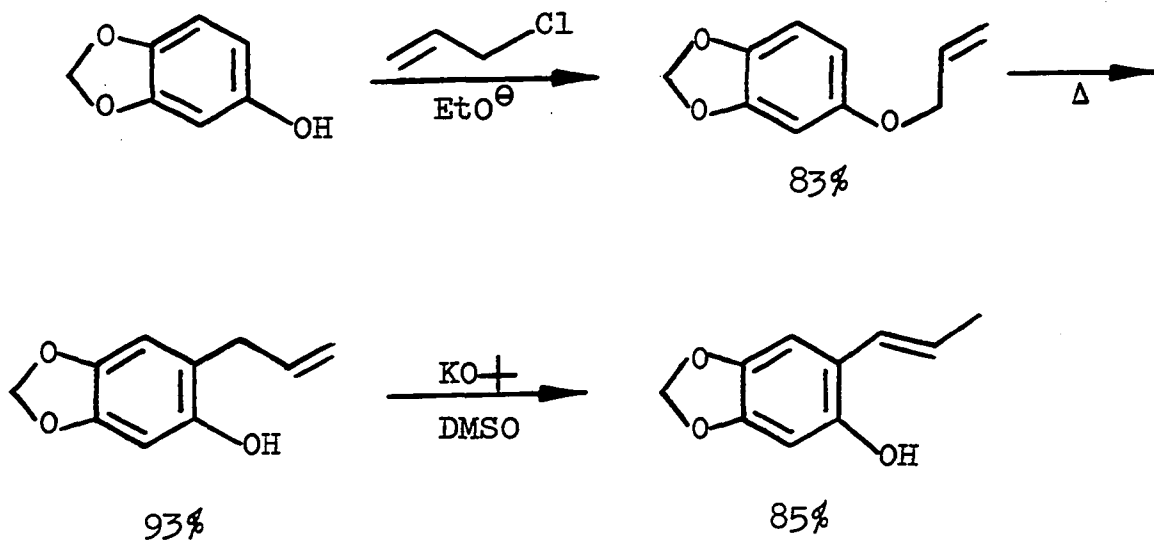
The significant point about beta coupling is that the initial product is an o-quinone methide. Furthermore, beta coupling of two propenylsesamol units gives the correct bis-o-quinone methide precursor to carpanone. This

analysis, however, ignores the stereochemistry of the two methyl groups and one would expect to get a mixture of several isomers.



Propenylsesamol was prepared from sesamol by making the allyl ether with allyl chloride, heating the ether to give the 2-allylsesamol by a Claisen rearrangement, and isomerizing the allyl derivative to the propenyl compound with potassium *t*-butoxide in dimethylsulfoxide. The propenylsesamol obtained was 95% trans and 5% cis. The trans isomer could be obtained pure by crystallization

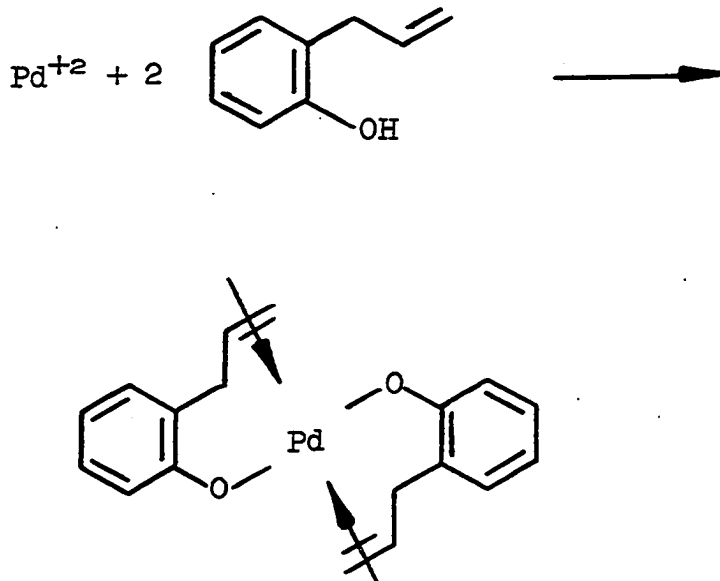
from carbon tetrachloride, but the 95-5 mixture was used for all the oxidations. The main problem with phenol oxidations



is that the radicals are generated throughout the solution at random and then must find each other in order to dimerize. This allows side reactions to predominate, i.e., reactions with starting material and polymerization. Also, there can be no control over the orientation of dimerization. A better situation would be to have an oxidizing agent which could "complex" two molecules of phenol and then oxidize them in close proximity to one another. One could then go to more dilute solutions to minimize polymerization. This would, of course, require a two electron oxidizing agent.

Palladium ion is such a two electron oxidant. Nyholm,<sup>53</sup> in a seminar at Iowa State, reported the formation of

complexes containing allylphenol and palladium. It was



evident from the examples given that it should be possible to form complexes of propenylphenol and palladium ion. We felt that if we could form such a complex it would decompose on heating to yield palladium metal plus carpanone. It is well documented<sup>54</sup> that palladium ion is readily reduced to the metal in the presence of oxidizable material. We would have the ideal situation in that the two molecules of propenylsesamol would be held close to each other at the time they were oxidized.

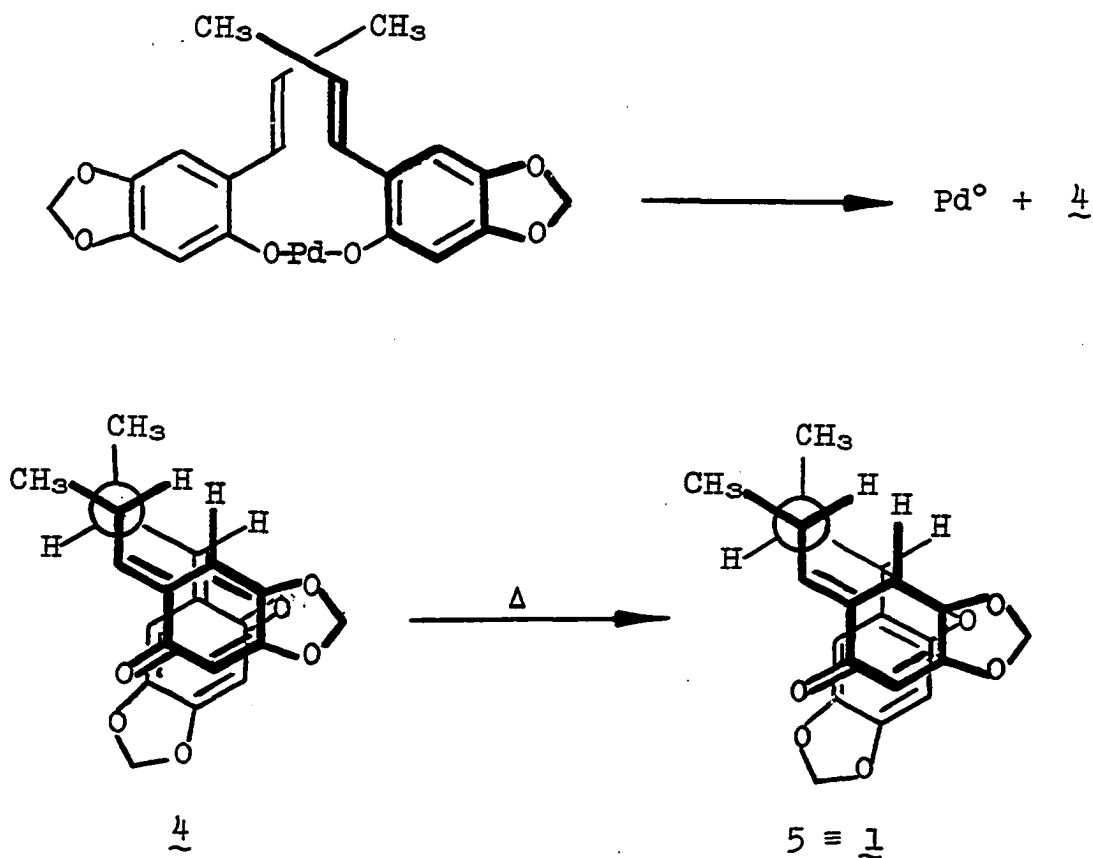
We were unable to prepare and isolate a complex such as Nyholm's. When we stirred a solution of propenylsesamol, sodium acetate, and palladium chloride in methanol/water, the palladium fell out as the metal and the only major

product was carpanone. The carpanone obtained in this way checked with the literature report as far as nmr, infrared, mass spec, and UV, but it was a glass rather than a crystalline solid as reported. Many attempts were made to crystallize the material, and finally it was crystallized from carbon tetrachloride. The crystals were clean, clear, water white needles, but the melting point ( $185^{\circ}$ ) was almost  $30^{\circ}$  lower than that of the natural product ( $212^{\circ}$ ). Furthermore, the density of the crystals (1.5 g/cc) was unreasonable for a molecule containing only carbon, hydrogen, and oxygen. A single crystal X-ray structure showed that the structure reported in the literature<sup>8</sup> based on nmr data was correct for our compound, and that a molecule of carbon tetrachloride had co-crystallized with each molecule of carpanone. This readily explained the low melting point and the density. The product was also sent to the discoverers and compared to the natural product in solution. All spectral data checked out correctly. The crude yield was 64%, and the carpanone could be crystallized directly from carbon tetrachloride giving pure carpanone- $\text{CCl}_4$  in 46% yield.

Palladium salts are expensive and we decided to try the reaction using "Wacker"<sup>54</sup> type conditions. Propenyl-sesamol was air oxidized in the presence of a catalytic amount of palladium chloride and cupric acetate. After two hours of rapid stirring in air, the reaction produced

carpanone in yields comparable to those from straight palladium chloride oxidation. We then tried cupric acetate as the oxidizing agent as a check on the "Wacker" reaction. Cupric acetate oxidation of propenylsesamol yields carpanone in 49% yield with a reaction time of only 5 minutes. The cupric ion is reduced to metallic copper in the process.

Our model of the mechanism of both the palladium and copper oxidations is shown below. The metal ion initially



bonds to two molecules of the propenylsesamol and then departs as the metal with formation of the bond as shown.

The bond formation could take place either concurrently with the loss of the metal or very soon thereafter. The trans orientation of the methyl groups is seen to be a natural outcome of the stereochemistry of the intermediate complex. The mode of dimerization shown is the only mode which can give carpanone. The conformation of the double bond at the time of oxidative dimerization must be such that it is oriented away from the phenolic hydroxyl group. If the double bond were oriented toward the hydroxyl group, the o-quinone methide unit formed would have the wrong stereochemistry. There is evidence, though, that the desired orientation is the one which predominates in o-propenylphenols.<sup>55</sup> Given the proper conformation of the double bond in both of the 2-(trans-1-propenyl)-4,5-methylene-dioxyphenol units, it is still possible to put them together so that the bis-o-quinone methide has either a C<sub>2</sub> axis of symmetry or a plane of symmetry. Only the bis-o-quinone methide with C<sub>2</sub> symmetry can give carpanone. In this case, the geometry is extremely favorable for nucleophilic attack by the enol ether function of one o-quinone methide unit on the other to give carpanone. The process of getting into position for the nucleophilic attack merely involves a rotation of approximately 60° about the bond formed in the dimerization step. Once the carpanone molecule is formed, it equilibrates with a

conformer in which the methyl groups occupy pseudoaxial positions. This is the conformation observed in the crystal.

The nature of the oxidizing agents presents evidence for the proposed mechanism. The fact that palladium ion is reduced to the metal is not surprising regardless of the mechanism since palladium in the +1 oxidation state is not common. The fact that copper is reduced to the metal, however, is quite unusual since copper is commonly reduced to the +1 state. Even in the presence of a 2:1 excess of cupric acetate, copper metal is the reduction product. The oxidation with cupric ion also tends to point to a concerted reaction. Reaction of 2-allylsesamol with cupric acetate under the same conditions gives no reaction. The oxidation potential of allyl and propenylphenol are probably very similar and the propenylphenol may be oxidized because there is a low energy path (i.e., the concerted reaction) which the reaction can take. The allylphenol, on the other hand, has no such option.

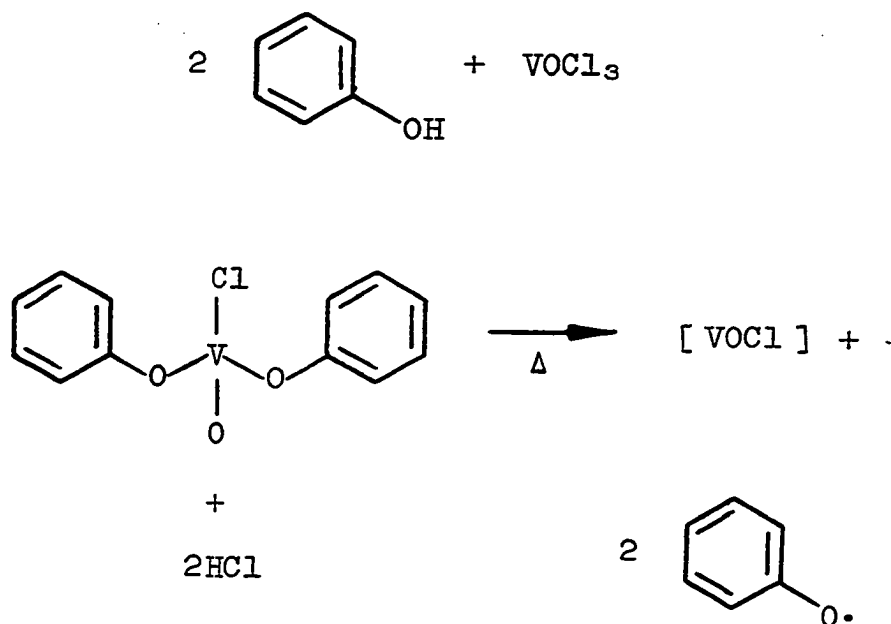
A number of other oxidizing agents were tried. The most generally successful oxidizing reagent for phenol oxidations has been potassium ferricyanide.<sup>56</sup> We therefore tried the propenylsesamol oxidation with basic aqueous ferricyanide. The reaction yielded a mixture of at least six components (tlc) and a large amount of polymer. A two phase system was tried using chloroform as the organic phase



with identical results. We were able, however, to separate a small amount (~5%) of carpanone by successive column chromatography on silica-gel. The other products were inseparable by chromatography, but an nmr of the mixture contained peaks which appeared to be from stereoisomers of carpanone. Silver oxide in basic aqueous solution gave results comparable to those obtained with ferricyanide. Silver carbonate on celite, however, gave a very clean reaction with yields of carpanone similar to those obtained from palladium or copper oxidation. The explanation may be that in the case of silver carbonate on celite the reaction is done in a non-polar solvent (benzene), and the  $\text{Ag}_2\text{CO}_3$  molecule acts as a unit which behaves like a monatomic divalent metal ion. The reaction is heterogeneous and two molecules of propenylsesamol are probably complexed on the surface of the silver salt. A recent improvement on ferricyanide, the ferric chloride-DMF complex, was also tried. The yield of carpanone after the usual work-up was 17% which was a substantial improvement over ferricyanide, but far short of the palladium or copper result.

The most interesting oxidizing agent tried was vanadium oxytrichloride. This agent was developed by Schwartz and coworkers<sup>57</sup> recently. The idea behind its use is very similar to our reasoning in the divalent metal case. The vanadium oxytrichloride is expected to form a complex with two molecules of the phenol with the loss of two

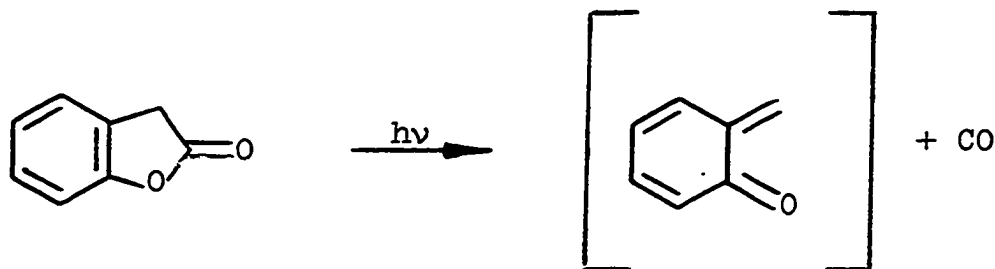
molecules of hydrochloric acid. The complex, on heating, will then lose the elements of  $\text{VOCl}$ , thus oxidizing the two phenol units in close proximity to one another. The complex



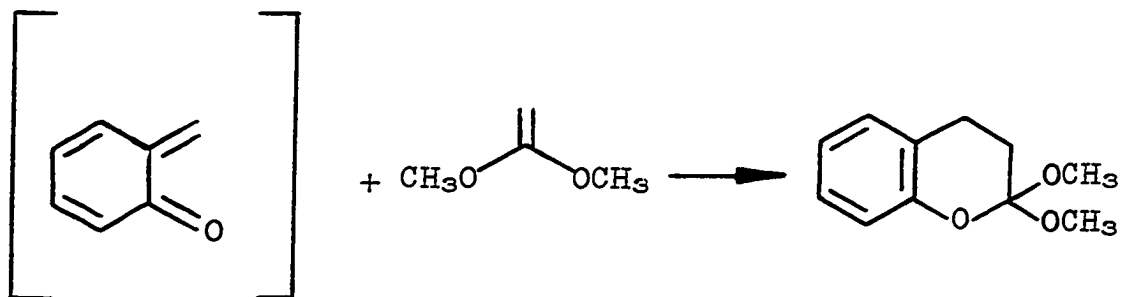
is formed at Dry Ice-acetone temperature in ether and then kept at reflux overnight to decompose it. Schwartz has obtained excellent results in some phenol oxidations with this reagent. Oxidation of propenylsesamol under these conditions gave a fair yield (36%) of neutral product. None of the product, however, was carpanone. Treatment of carpanone with vanadium oxytrichloride under the same conditions gave no reaction. The reaction of propenylsesamol with vanadium oxytrichloride is at this time not understood.

The palladium and copper oxidations were all stirred in the presence of air and, therefore, it was necessary to find out if the air played any part in it. A solution of propenylsesamol plus sodium acetate in methanol/water was stirred in air for 2 hours with no subsequent reaction occurring. This eliminated the possibility that it was not the metal salt doing the oxidations. Much longer reaction times, however, gave some reaction. If a solution of propenylsesamol and sodium acetate in methanol/water has air bubbled through it for 18 hours at room temperature, the oxidation goes to about 90% completion and the yield of carpanone based on reacted starting material is about 14%. The product mixture is composed of a large number of components (tlc) and resembles that from the ferricyanide oxidation.

There were two alternate routes to carpanone which we pursued. McIntosh and Chapman<sup>42</sup> reported a facile method of generating o-quinone methide by the photochemical decarbonylation of 2-coumaranone. The quinone methide

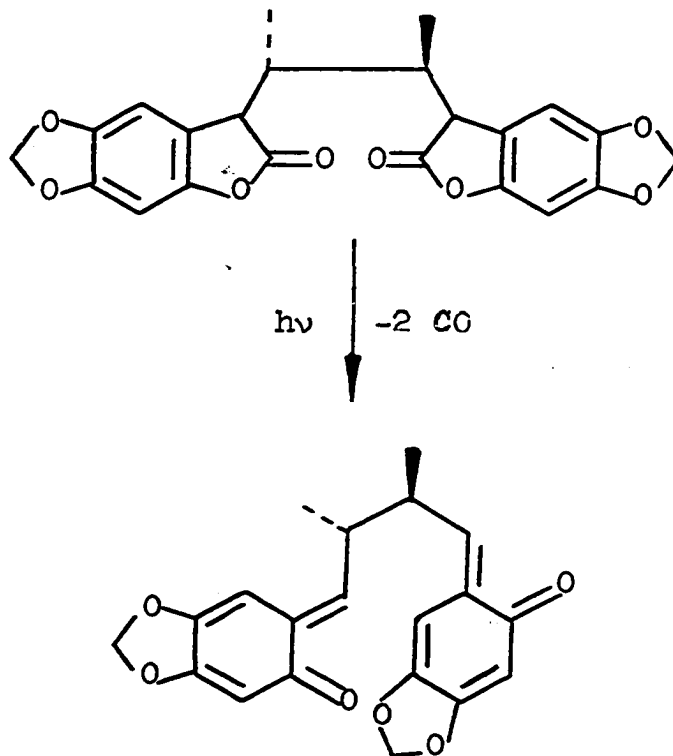


was trapped in high yield by an electron rich olefin such as dimethoxyethylene to give coumarin derivatives. We



decided to utilize this photochemical reaction in one synthesis of carpanone.

The bis-quinone methide which would be a precursor to carpanone could then be generated from the corresponding dilactone.

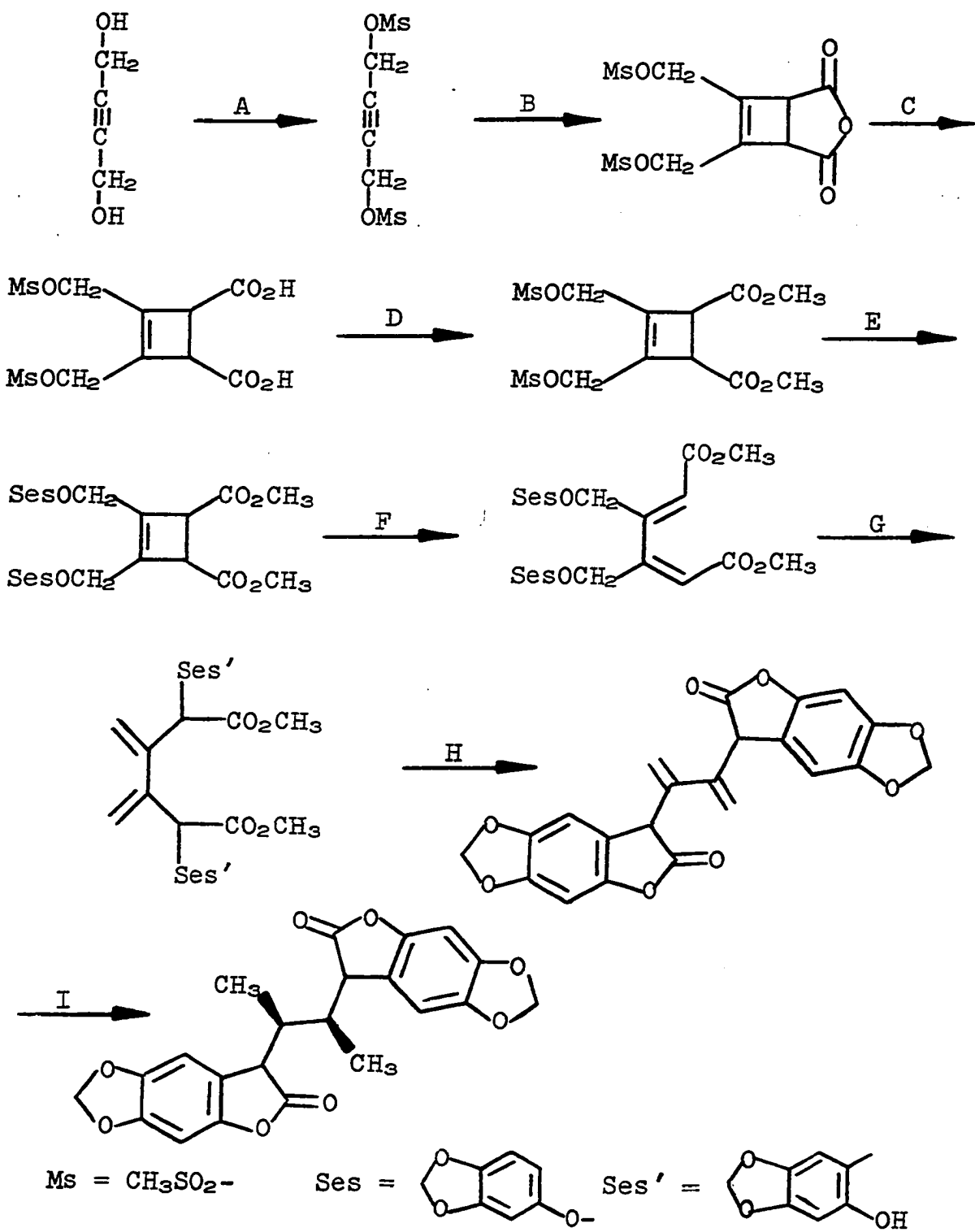


Our proposed route to the dilactone precursor is outlined in Scheme I.

Step (A) is the conversion of the diol to the dimesylate which was accomplished with methanesulfonyl chloride in the presence of triethylamine.<sup>58</sup> Step (B) is the photochemical addition of maleic anhydride to the acetylene. This was accomplished in acetone with benzophenone as the sensitizer. Step (C) is the hydrolysis of the acid anhydride which took place in the work-up of step (B). Step (D) is the esterification of the diacid with diazomethane. Step (E) is the displacement of the mesylate group by sesamol anion which did not work. Two sesamol units were incorporated into the molecule but the cyclobutene ring was destroyed in the process. Step (F) is the thermal opening of the cyclobutene ring.<sup>59</sup> Step (G) is a double Claisen rearrangement. Step (H) is acid catalyzed transesterification. Step (I) is catalytic hydrogenation of the two double bonds. The predominant conformation of the diene is expected to be as shown because of the bulk of the coumaranone type residues. Cis addition of two moles of hydrogen from one side of the molecule then yields the product stereochemistry as shown.

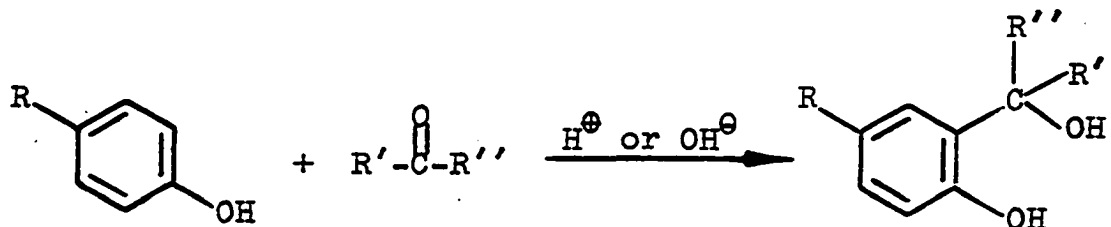
We attempted to sidestep reaction (E) by displacing the mesylates prior to the photoaddition of maleic anhydride. The displacement worked well in dimethylsulfoxide but the subsequent photoaddition failed, probably because most of

Scheme 1.

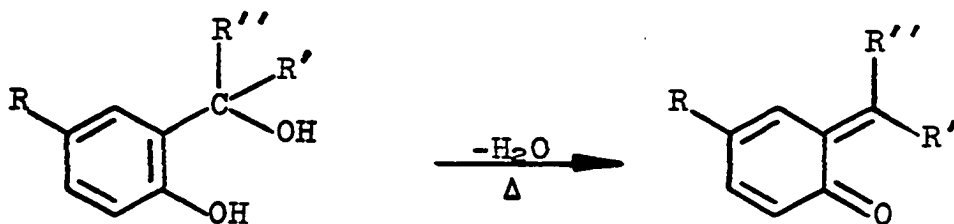


the light was absorbed by the sesamol systems. It was then decided to abandon this approach to carpanone.

Our second alternate approach to carpanone centered on the hydroxyalkylation reaction with phenols. Treatment of a phenol with an aldehyde or ketone under acidic or basic conditions yields initially a hydroxyphenol product which can then undergo further substitution reactions.<sup>60</sup>



Hydroxyphenols, however, are known to thermally lose water to yield the corresponding quinone methides.<sup>40</sup> The

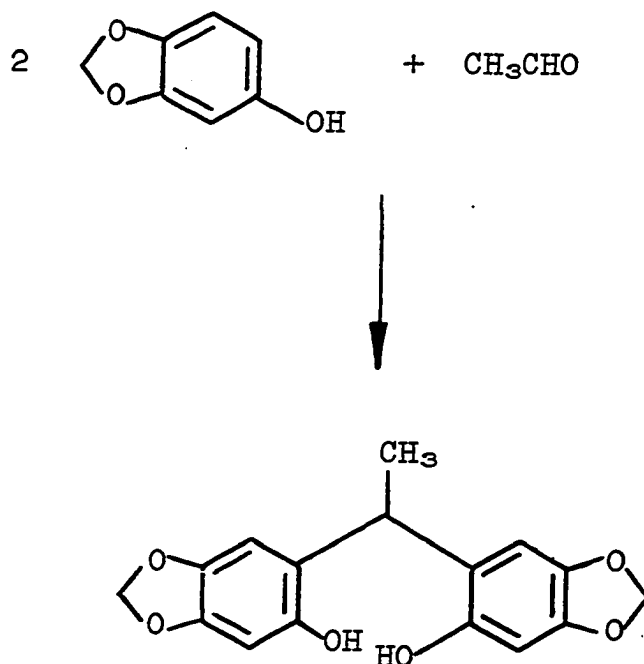


quinone methide formation would also be acid or base catalyzed and is likely to be a major route in all further reactions of the hydroxyphenol, especially in systems where the quinone methide would be stabilized.

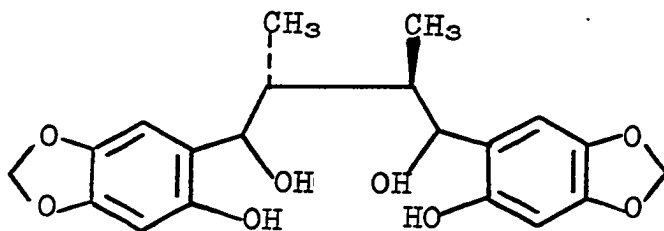
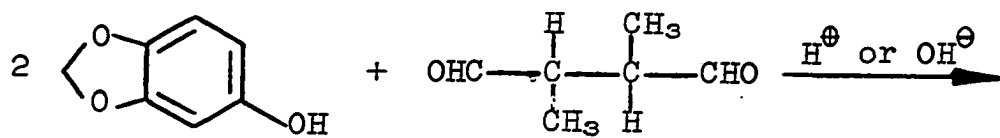
This approach would conceivably allow a one step synthesis of carpanone from sesamol. Reaction of sesamol

with dl-2,3-dimethylsuccinaldehyde could yield the bis-hydroxyphenolic intermediate which could lose two molecules of water to yield the bis-quinone methide precursor to carpanone. This is shown on the next page.

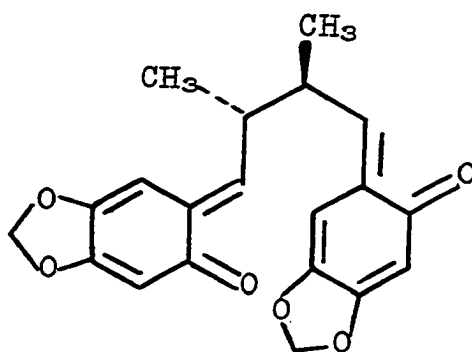
The success of this approach hinges on the formation of the hydroxyphenolic moiety on each end of the succinaldehyde without further reaction of either end with more sesamol. In order to investigate this aspect, we reacted sesamol with acetaldehyde. We found that even with a large (>20:1) excess of acetaldehyde it was impossible to stop the reaction at the hydroxyphenol stage. The main product isolated was the condensation product of two sesamol units with one acetaldehyde.







-2H<sub>2</sub>O



Carpanone

Many similar reactions were attempted such as the Mannich reaction, chloroalkylation, and cyanoalkylation. In each case the only product was the doubly condensed compound.

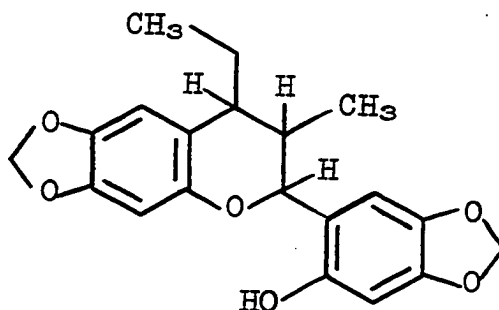
#### The dimerization of propenylsesamol

In the process of trying to purify propenylsesamol, we discovered an interesting dimerization. Sublimation of propenylsesamol was unsuccessful due to the disappearance of starting material and the formation of a mixture of dimers. Column chromatography on silica-gel gave the same result. The purification problem was solved by using sublimed allyl-sesamol in the base catalyzed isomerization. In this case the propenylsesamol is pure enough as formed.

It was decided to further investigate the thermal dimerization. Propenylsesamol was heated in diphenyl ether at 190° for 2 hours. At this point, an nmr spectrum showed no starting material remaining. The product mixture was separated on silica-gel to yield two products in roughly equal amounts. The second component to come off the column was converted to the first product on prolonged heating or on prolonged contact with silica-gel.

The gross structure of the two dimers was evident from the spectral data. Mass spectrometry indicated that they were indeed dimers, and the base peak corresponded to dissociation back to the monomer. The nmr spectrum clearly showed all the ring and methylenedioxy protons from the

sesamol units plus an ethyl and a methyl group. The methyl group was split by one proton. There was also a proton at 4-5 ppm which was apparently alpha to an oxygen and was split by one proton. The infrared showed the presence of a hydroxyl group. The structure which best fits the data is given below.

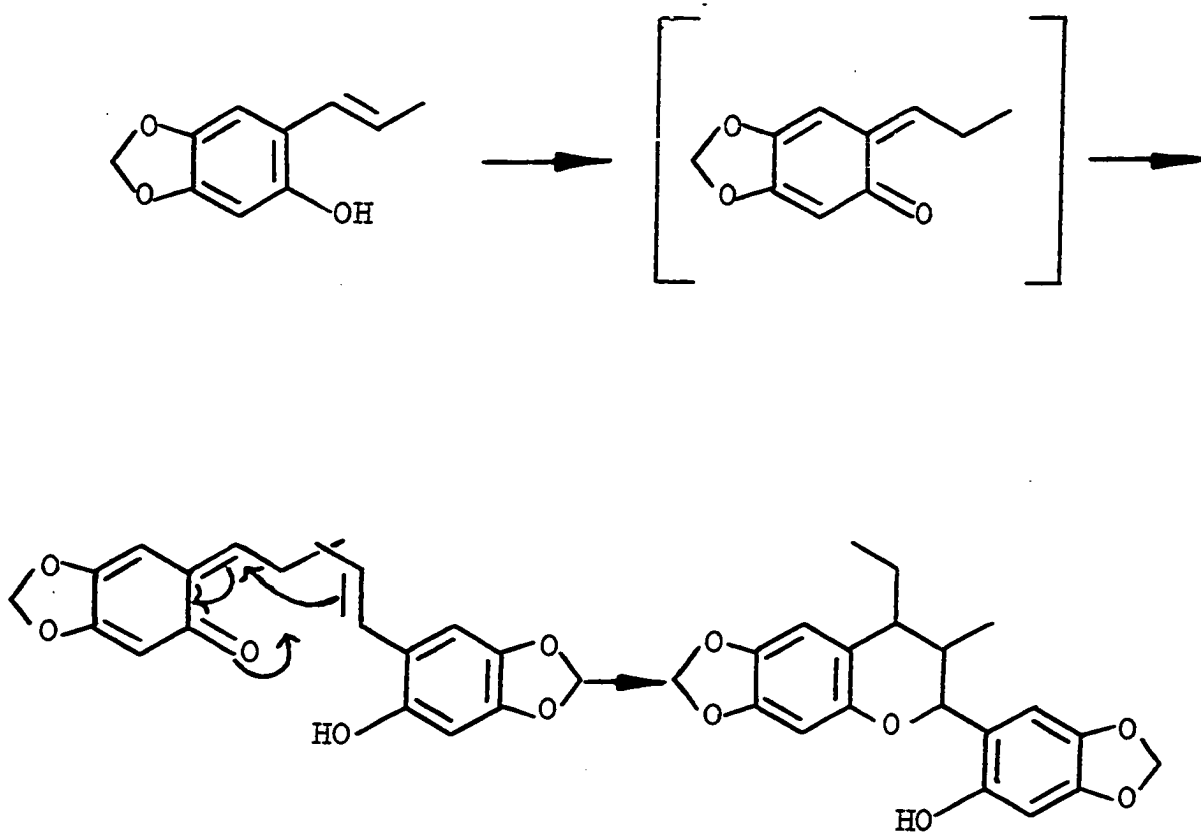


The stereochemistry at the three asymmetric centers is unknown.

The photochemistry of propenylsesamol was then investigated. Irradiation of a chloroform solution of propenylsesamol in a Rayonette Reactor with 3100 Å lamps gives an extremely facile dimerization reaction. The reaction is complete in less than 5 minutes. The quantum yield was measured to be approximately 1000. There were two products formed which were identified as dimers by the same evidence as mentioned for the pyrolysis products. One of the photolysis products was, in fact, identical to one of the pyrolysis dimers. Hereafter, the dimers will be referred to as dimers A, B, and C - where A and B are the products of the pyrolysis and B and C are the photolysis products. Irradiation of propenylsesamol in ether solution under the same

conditions required several days to effect any change. The photolysis was therefore performed in a Pyrex immersion well with a Hanovia 550 watt medium pressure lamp. Irradiation for 30 minutes gave a 95% conversion of trans-propenylsesamol to cis-propenylsesamol. Continued irradiation gave, after 2 hours, conversion to dimer C plus a small amount of dimer B. The cis-propenylsesamol could be isolated from the 30 minute irradiation, dissolved in chloroform, and irradiated for 5 minutes in the Rayonette Reactor to give complete conversion to dimer C.

Our model of the reaction mechanism for the dimerization



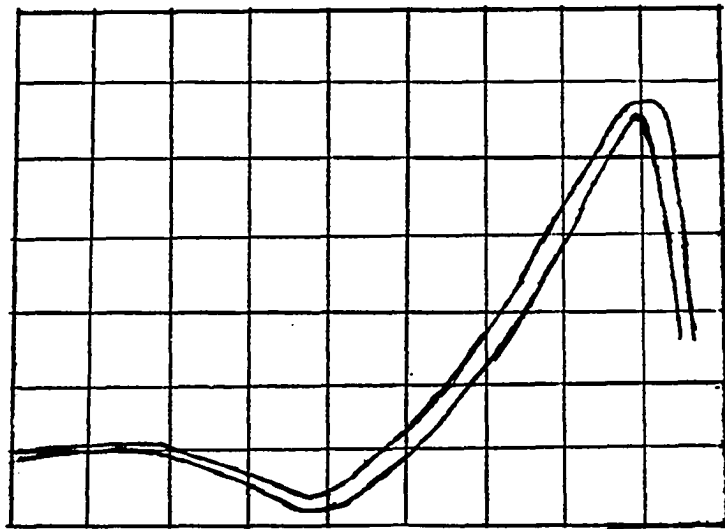
involves formation of an o-quinone methide followed by Diels-Alder type addition to a molecule of propenylsesamol.

There are several points which favor the intermediacy of an o-quinone methide. The base peak in the mass spectrum of the dimers corresponds to the reverse Diels-Alder reaction. Intermediates similar to quinone methides have been generated photochemically, i.e., the conversion of o-methylbenzaldehyde to the corresponding hydroxyquinonedimethide.<sup>61</sup> A flash



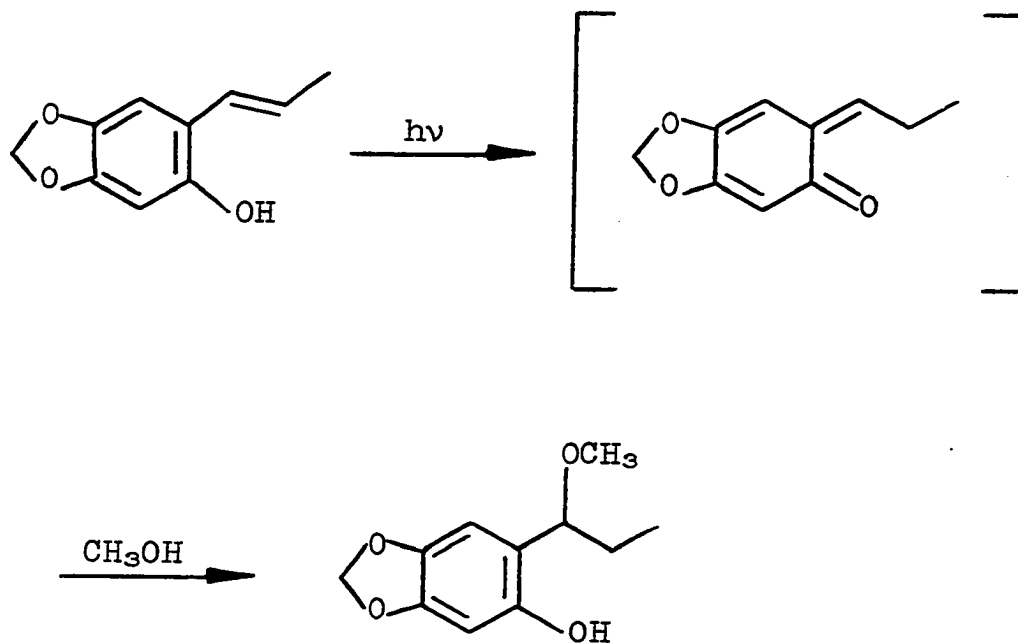
photolysis experiment showed an intermediate which looks like an o-quinone methide. Irradiation of propenylsesamol in chloroform or hexane solution in a flash photolysis apparatus showed an intermediate with a UV absorption centered at 3800 Å and with a lifetime of ~4 milliseconds (Figure 1). A similar experiment with 2-coumaranone, which is known to decarbonylate to o-quinone methide, gave the same UV maximum but a lifetime of >1 second. The explanation is that the propenylsesamol can act as its own trapping agent through formation of the dimers. The o-quinone methide can also dimerize but this is apparently a much slower reaction. Irradiation of propenylsesamol in methanol gave (2-methoxy-propyl)sesamol as the major product of a large number of

Figure 1. Flash photolysis trace for 4,5-methylenedioxy-  
2-(trans-propenyl)phenol at 3850 Å.



4 msec.

products. This was probably formed by the nucleophilic attack of methanol on an o-quinone methide intermediate.



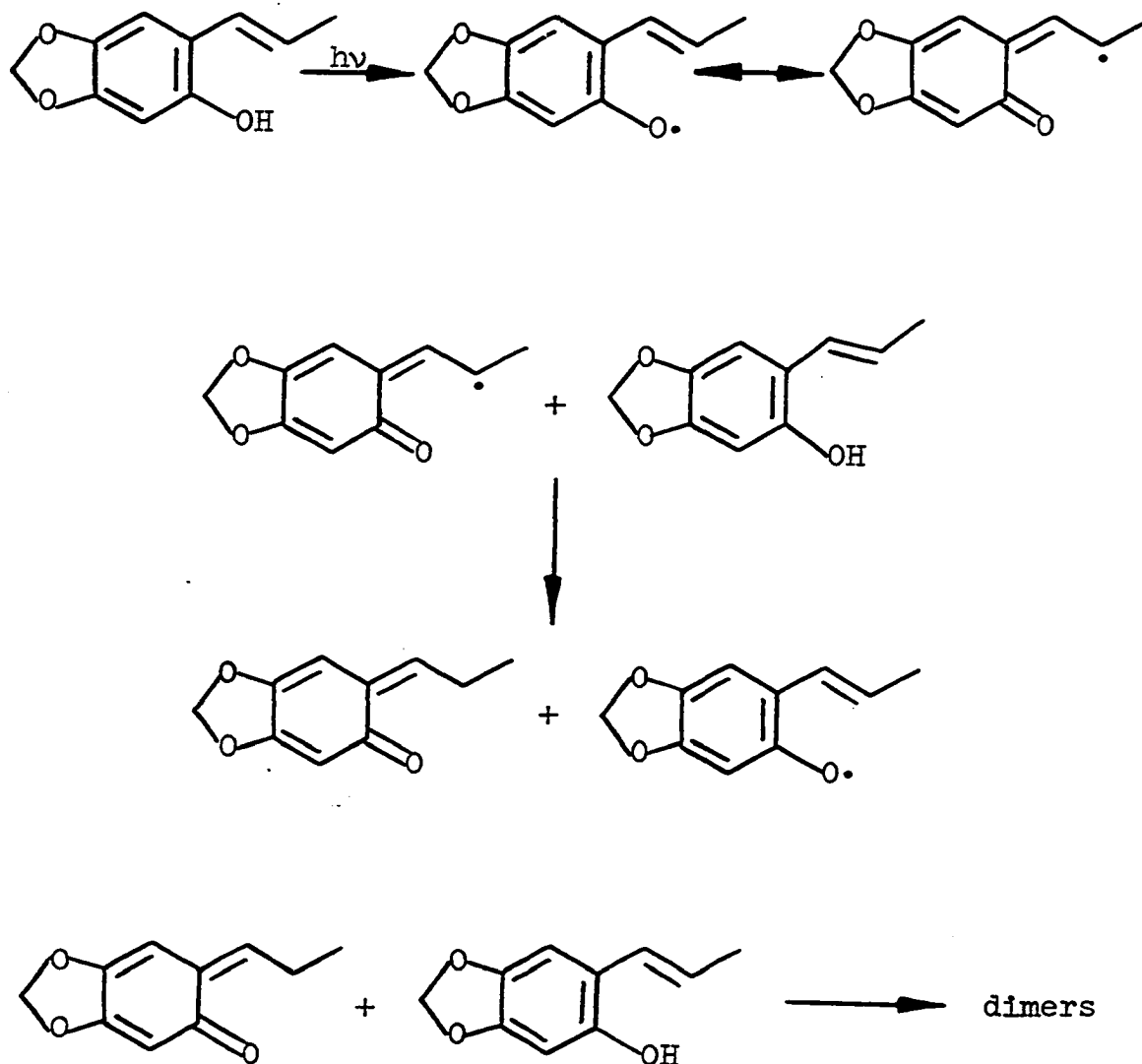
Irradiation of (2-methoxypropyl)sesamol itself gave a rapid conversion to many products, indicating that the low yield in the first photolysis corresponded to a stationary state concentration.

The next question, however, is the method in which the quinone methide is generated. The mechanism in the pyrolysis can be envisioned as intramolecular or intermolecular proton transfer of the phenolic hydrogen to the styryl double bond. Some evidence for the intramolecular transfer is provided by studies of hydrogen bonding in propenylphenol systems. A large amount of interaction is evident from infrared and UV data.<sup>55</sup> This should facilitate the intramolecular transfer.



Furthermore, the interaction is much greater in the case of cis-propenylphenols. This is in agreement with our observation that cis-propenylsesamol dimerizes at room temperature overnight while trans-propenylsesamol must be heated.

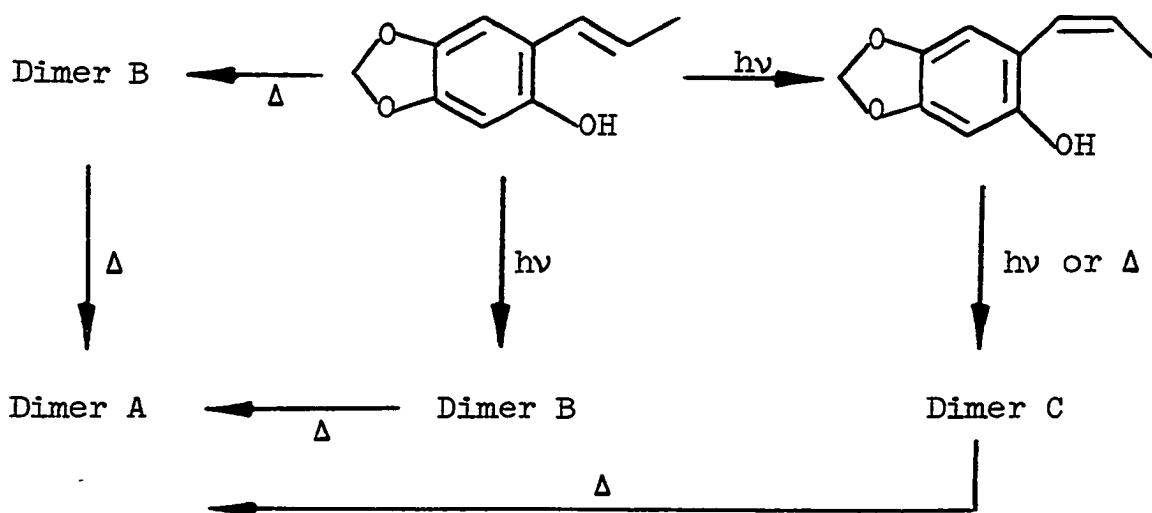
The photolysis in chloroform has a complication in that the quantum yield of  $\gg 1$  indicates a chain mechanism. The fact that the fast reaction only works in solvents such as chloroform and carbon tetrachloride points to a free radical



chain. There is evidence in the literature for the photochemical generation of phenoxy radicals from phenols.<sup>62</sup> Our model of the mechanism involves a free radical chain which produces the o-quinone methide, followed by a Diels-Alder reaction to give the dimers.

Photolysis in ether, however, shows no signs of a chain mechanism. The ether effectively quenches the radical mechanism and the initial photoproduct is the cis-propenylsesamol. Further irradiation produces dimer C. The photoreactions of coniferyl alcohol exhibit similar characteristics in that a free radical mechanism is evident in solvents such as carbon tetrachloride and a polar mechanism predominates in ether.<sup>63</sup>

Both dimers B and C are thermally unstable with respect to isomerization to dimer A and, therefore, the possibility exists that dimer A is not a primary product in the thermal reaction. With this thought in mind, we propose the following scheme for the thermal and photochemical dimerization of



propenylsesamol. The photochemical dimerization is envisioned as being a competition between dimerization and trans-cis isomerization. This explains the production of dimers B and C from trans-propenylsesamol and only dimer C from the cis isomer.

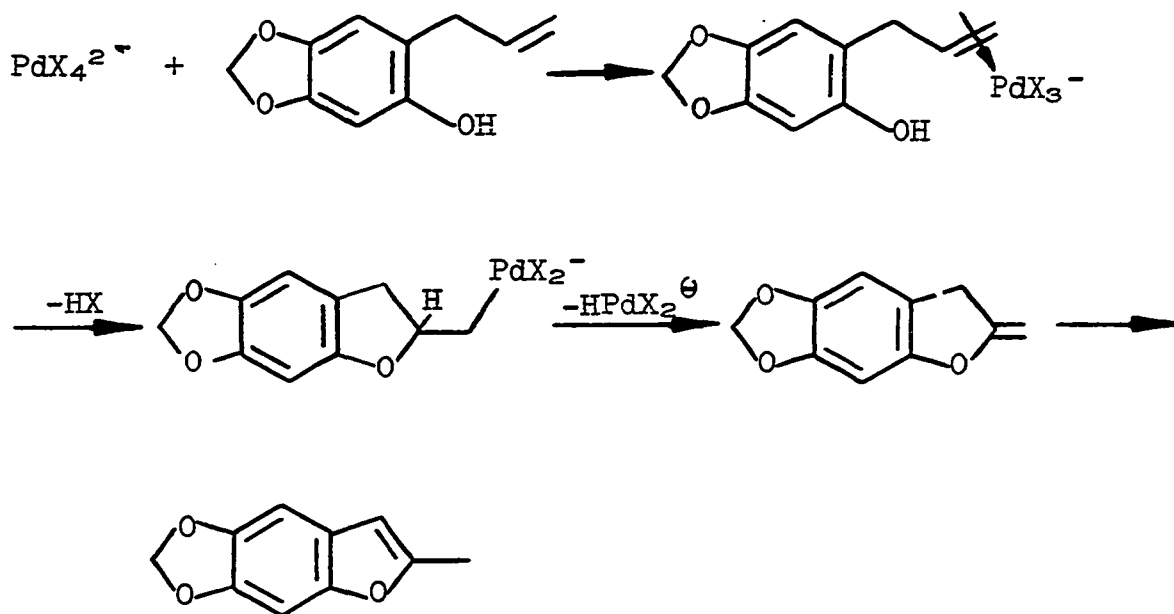
A similar study was then done with propenylphenol. One would expect that the o-quinone methide would be less stable than in the sesamol system since there are no oxygens to stabilize it by resonance. This prediction is borne out in the results. The reactions are all similar to those of propenylsesamol but much slower. The thermal reaction takes 8 hours as compared to 2 hours for propenylsesamol, and the photolysis in chloroform requires 25 minutes as compared to <5 minutes. The same three types of dimers are formed, dimers D, E, and F. The nmr spectra of these dimers are strikingly similar to those of the corresponding dimers in the sesamol series.

Ortho-quinone methides are known to add to electron rich olefins. We, therefore, attempted to trap the intermediate in the propenylsesamol irradiation with olefins such as ethyl vinyl ether. Irradiation of a chloroform solution of propenylsesamol and ethyl vinyl ether succeeded in polymerizing the ether with no change in the propenylsesamol. The phenol dimerized only after all the ethyl vinyl ether was gone. This is not difficult to understand if the reaction is

indeed a free radical chain. A chloroform solution of ethyl vinyl ether alone gives no reaction on irradiation. In ether solution, propenylsesamol isomerizes to the cis isomer and then dimerizes even in the presence of ethyl vinyl ether. This is less easily understood since it suggests that there may be some association of the propenylsesamol units which allows them to dimerize to the exclusion of other possible reactions.

#### Related reactions

The failure of cupric acetate to oxidize allylsesamol was mentioned earlier in connection with the mechanism of carpanone formation. The palladium ion oxidation was also tried. The oxidation was conducted under the same conditions as in the carpanone work, and yielded 2-methyl-6,7-methylene-dioxybenzofuran in 84% yield. Similarly, 2-allylphenol gave 2-methylbenzofuran in 86% yield. The mechanism is probably related to the "Wacker"<sup>54</sup> process for converting ethylene to acetaldehyde. The palladium ion forms a  $\pi$  complex with the double bond which is then attacked by the phenolic oxygen to give a  $\sigma$  complex. This can then lose the elements of HPdX to give the exocyclic double bond which will readily isomerize to the benzofuran structure. This represents a convenient and efficient route to methylbenzofurans from the corresponding phenol, since the two steps to the allylphenol are trivial.



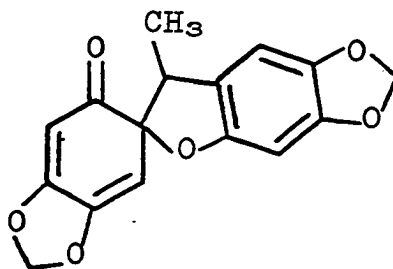
Bolon's work<sup>32</sup> on the oxidative generation of o-quinone methides led us to try that approach in our system. Propylsesamol was prepared from allylsesamol by catalytic hydrogenation and then oxidized under various conditions. Palladium chloride oxidation in methanol/water gave a quantitative yield of (2-methoxypropyl)sesamol. The phenol is oxidized to the o-quinone methide which then adds methanol. Silver oxide (Bolon's reagent) in methanol gave a 93% yield of the same product.

Bolon was able to trap the o-quinone methide intermediates with olefins such as ethyl vinyl ether. Many attempts to do this in our system failed, however. Styrene, ethyl vinyl ether, and the methyl ether of propenylsesamol were tried using palladium chloride or silver oxide as the oxidant. It would have been very informative if the

propenylsesamol methyl ether had worked since the product would have been a derivative of the dimers of propenylsesamol. This might have shed some light on the stereochemistry of the o-quinone methide. The failure of the oxidatively produced o-quinone methide to add to electron rich olefins is consistent with our negative results with the photochemically generated species, but does not give any evidence as to why it doesn't work.

We had synthesized 1,1-bis(2-hydroxy-4,5-methylene-dioxyphenyl)ethane in one of our approaches to carpanone. It appeared that the oxidation of this compound with palladium chloride would be instructive since it would show if palladium ion had a propensity to oxidize one of the phenol units to a quinone methide rather than each one to radicals. The oxidation yielded what appeared to be one product (tlc) in high yield (92%). The product could be purified on silica-gel, but it was not very stable at room temperature. The mass spectrum gave a parent ion at  $m/e = 300$ , indicating that a net two electron oxidation had occurred. The infrared spectrum showed a conjugated carbonyl group ( $1650\text{ cm}^{-1}$ ), and the UV spectrum fit a dienone type system. The methyl group was a doublet in the nmr spectrum and the proton adjacent to it looked like a very rough quartet. Double resonance centered at the methyl frequency collapsed the quartet to a rough singlet. A structure which fits the data

is given below. The nmr data fits well except for the



broadening of the quartet from the proton adjacent to the methyl and the fact that the proton delta on the enone system is a doublet. Both of these points are explained by assuming that the product is actually a mixture of two isomers depending on the stereochemistry at the asymmetric center with the methyl group. The proposed structure agrees with results obtained by other workers on ferricyanide oxidations of bisphenols of similar structure.<sup>64</sup> Ferricyanide oxidation of 1,1-bis(2-hydroxy-4,5-methylenedioxyphenyl)ethane gave the same product but in much lower yield. The structure shown could be produced by simple ortho-oxygen phenolic coupling.

Figure 2. 60 MHz nmr spectrum of carpanone.



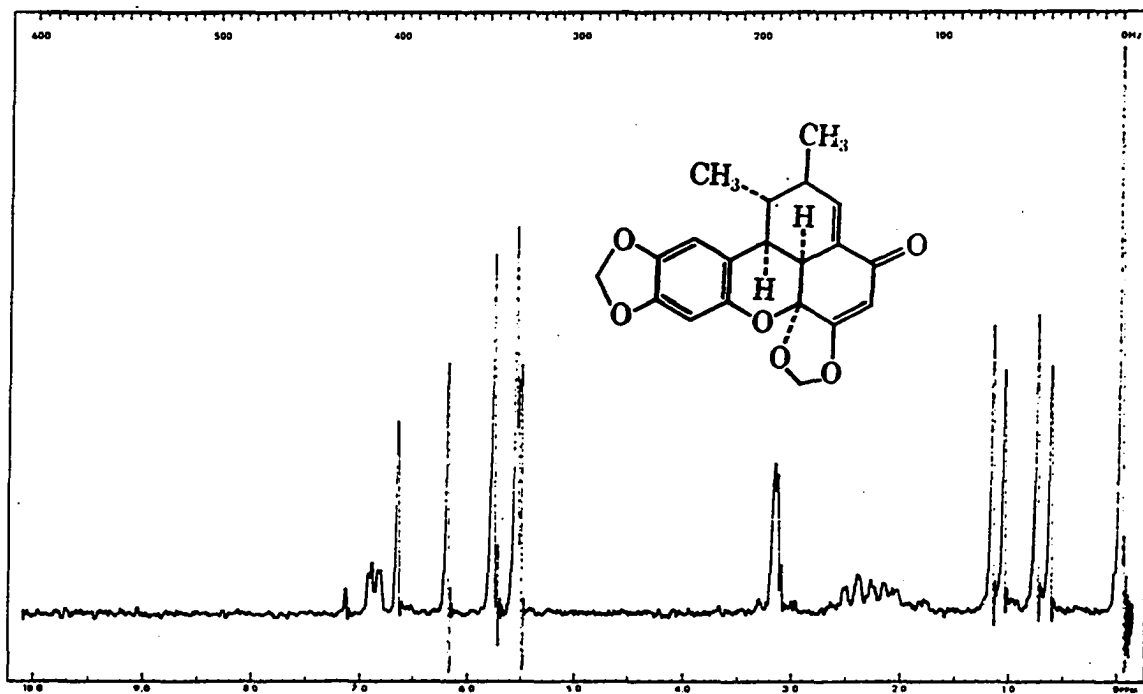


Figure 3a. 60 MHz nmr spectrum of 2-(2-hydroxy-4,5-methylenedioxyphenyl)-3-methyl-4-ethyl-6,7-methylenedioxychroman.  
(Dimer A)

Figure 3b. 60 MHz nmr spectrum of 2-(2-hydroxy-4,5-methylenedioxyphenyl)-3-methyl-4-ethyl-6,7-methylenedioxychroman.  
(Dimer B)

Figure 3c. 60 MHz nmr spectrum of 2-(2-hydroxy-4,5-methylenedioxyphenyl)-3-methyl-4-ethyl-6,7-methylenedioxychroman.  
(Dimer C)

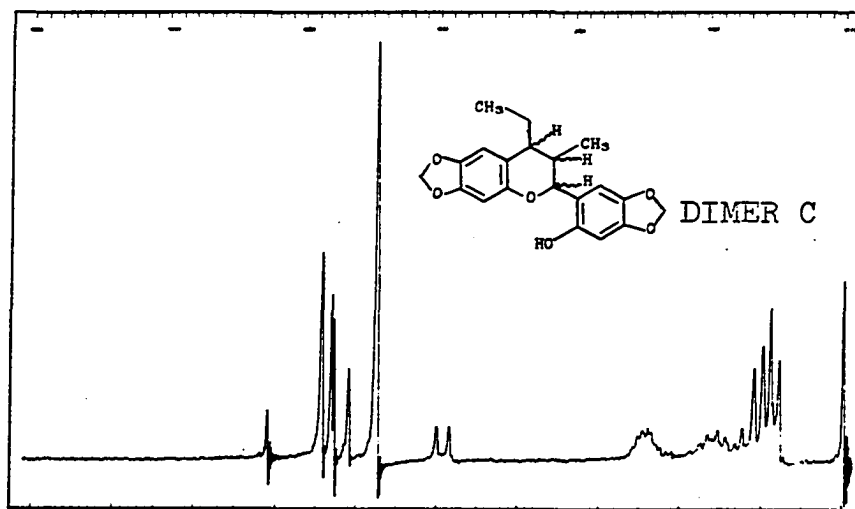
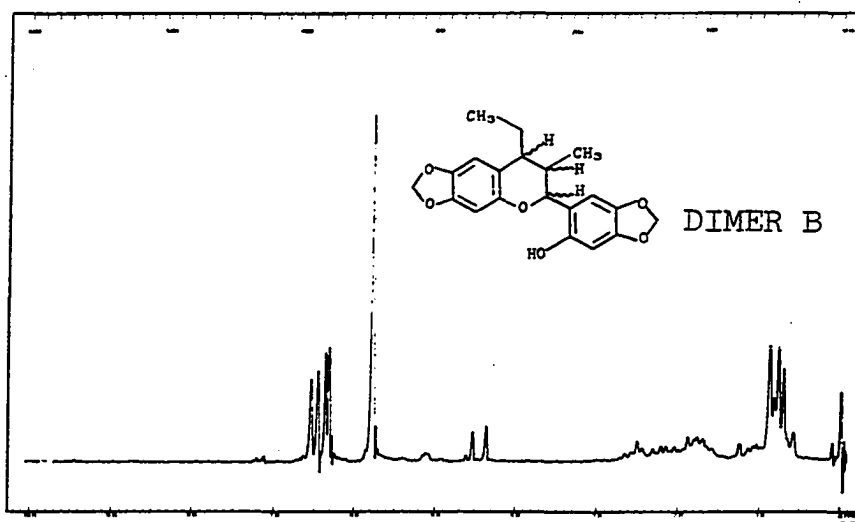
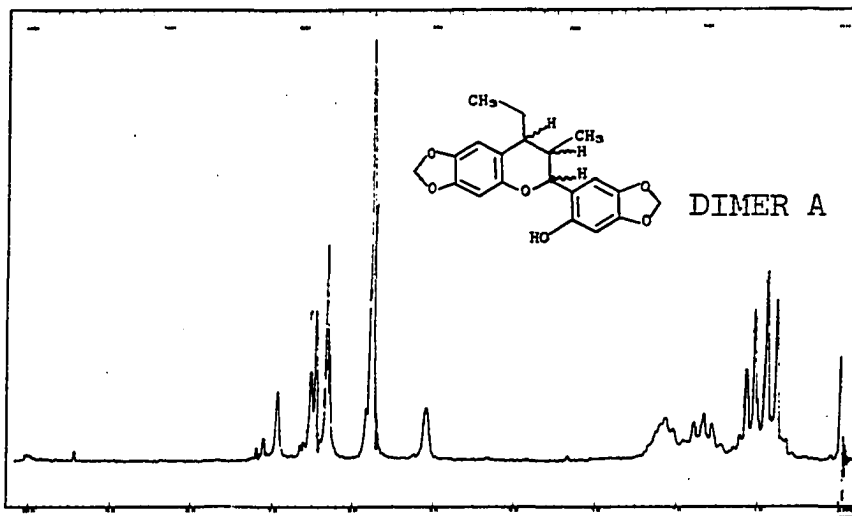


Figure 4a. Infrared spectrum of 2-(2-hydroxy-4,5-methylenedioxyphenyl)-3-methyl-4-ethyl-6,7-methylenedioxychroman.  
(Dimer A)

Figure 4b. Infrared spectrum of 2-(2-hydroxy-4,5-methylenedioxyphenyl)-3-methyl-4-ethyl-6,7-methylenedioxychroman.  
(Dimer B)

Figure 4c. Infrared spectrum of 2-(2-hydroxy-4,5-methylenedioxyphenyl)-3-methyl-4-ethyl-6,7-methylenedioxychroman.  
(Dimer C)

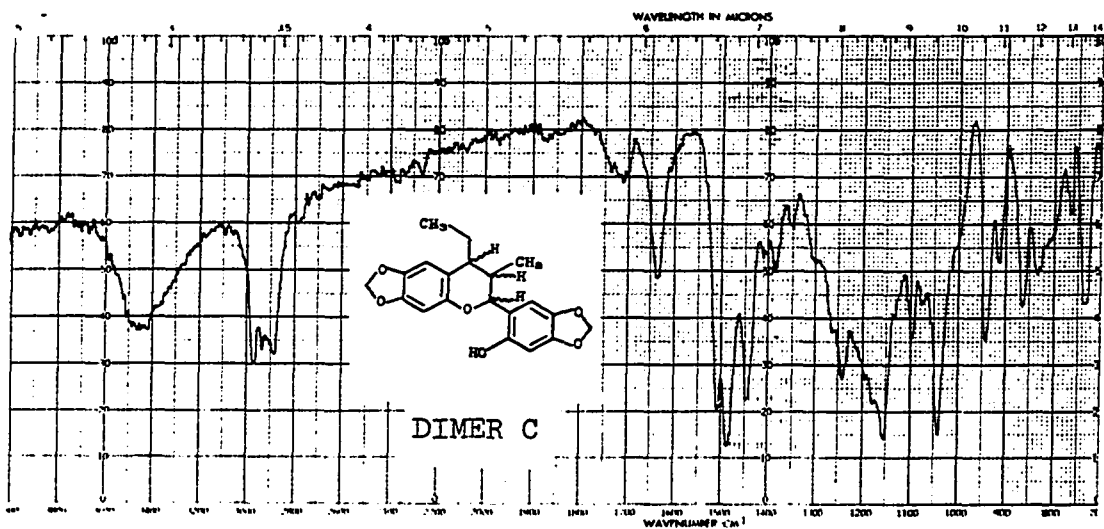
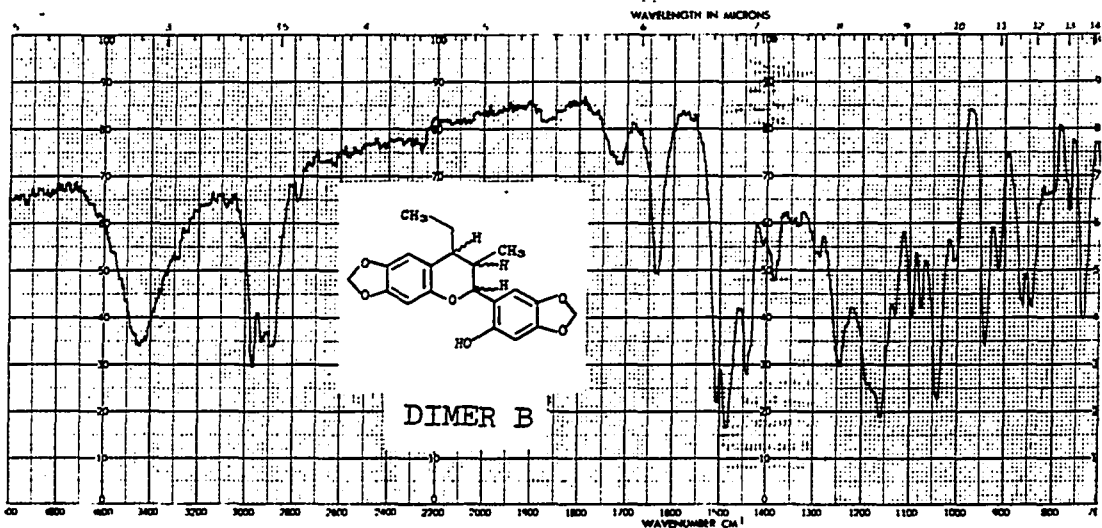
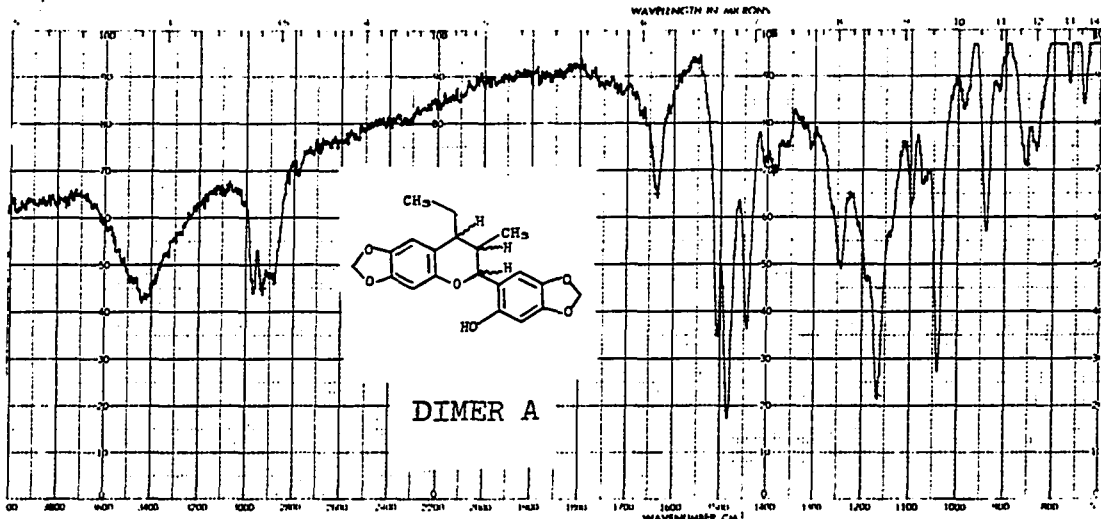


Figure 5a. 60 MHz nmr spectrum of 2-(2-hydroxyphenyl)-  
3-methyl-4-ethylchroman.  
(Dimer D)

Figure 5b. 60 MHz nmr spectrum of 2-(2-hydroxyphenyl)-  
3-methyl-4-ethylchroman.  
(Dimer E)

Figure 5c. 60 MHz nmr spectrum of 2-(2-hydroxyphenyl)-  
3-methyl-4-ethylchroman.  
(Dimer F)

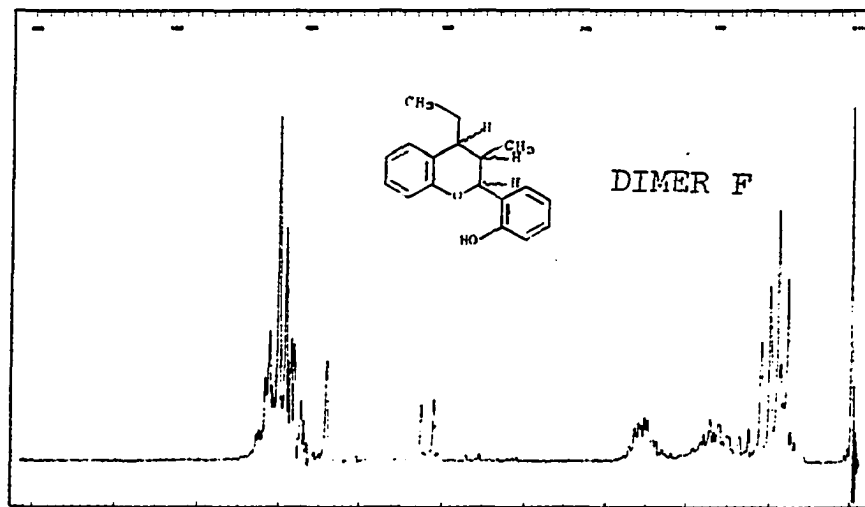
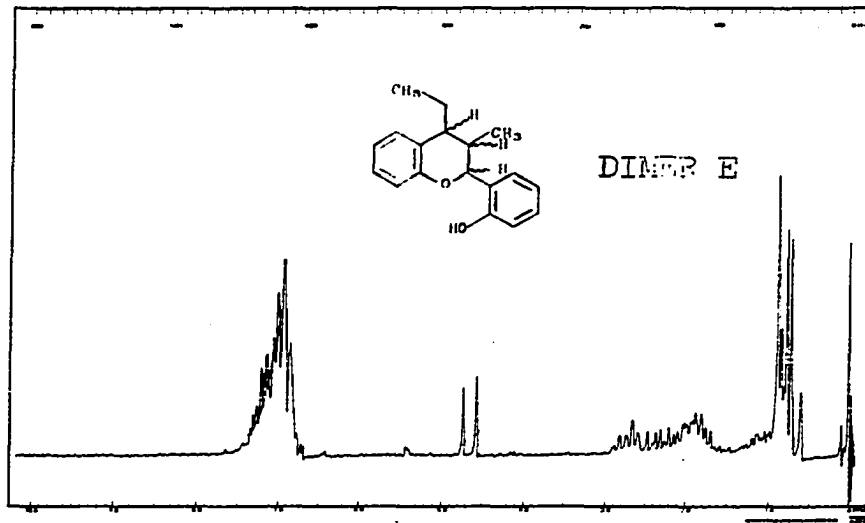
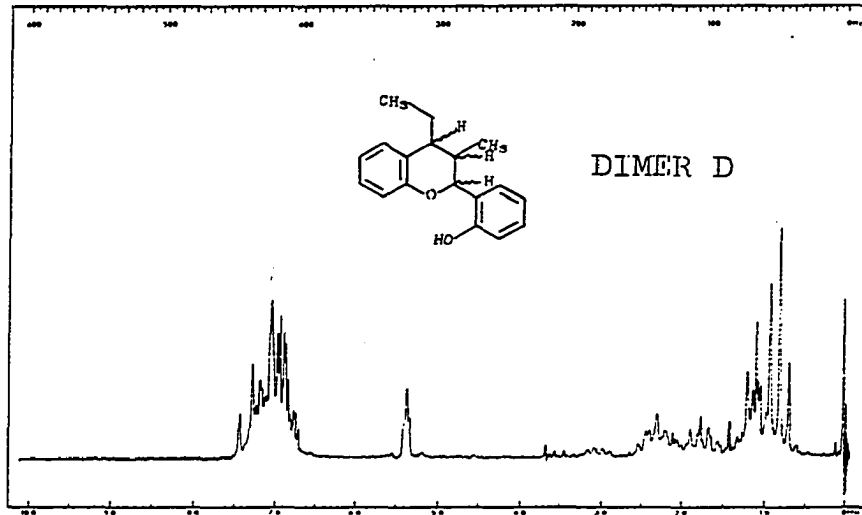
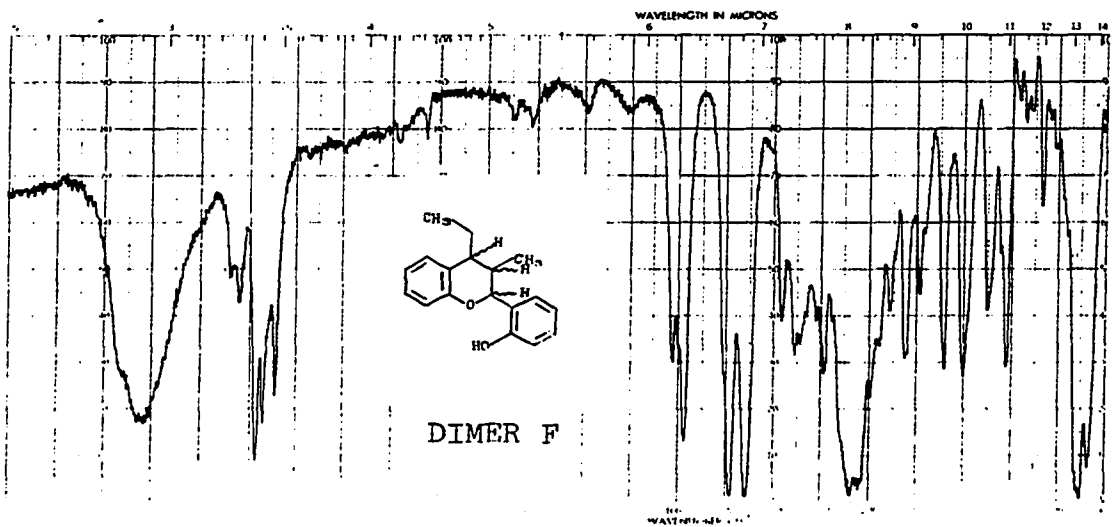
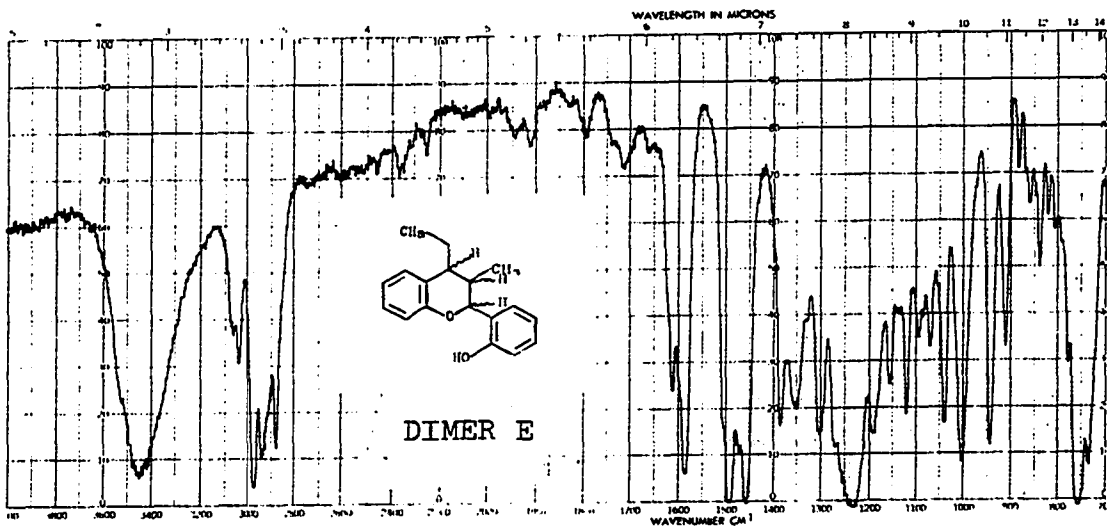
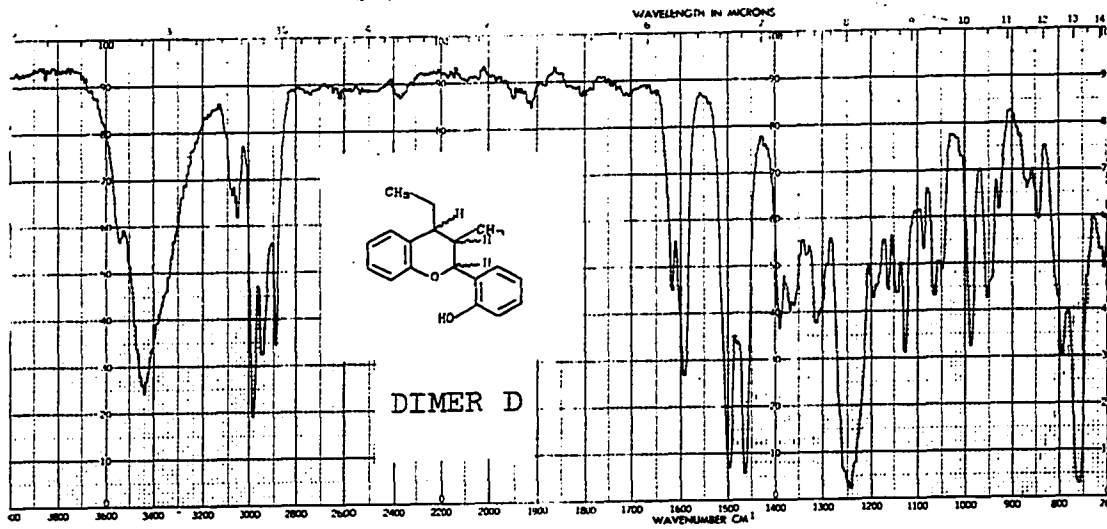


Figure 6a. Infrared spectrum of 2-(2-hydroxyphenyl)-  
3-methyl-4-ethylchroman.  
(Dimer D)

Figure 6b. Infrared spectrum of 2-(2-hydroxyphenyl)-  
3-methyl-4-ethylchroman.  
(Dimer E)

Figure 6c. Infrared spectrum of 2-(2-hydroxyphenyl)-  
3-methyl-4-ethylchroman.  
(Dimer F)





## EXPERIMENTAL

General instruments and methods

Infrared spectra were recorded on a Beckman IR-12. Nuclear Magnetic Resonance spectra were recorded on a Perkin-Elmer Hitachi Model R-20B or a Varian Associates Model A-60 or HA-100. Mass spectra were recorded on an Atlas CH-4 mass spectrometer. High resolution mass spectra were recorded on an AEI MS-902. Microanalyses were performed by Schwartzkopf Microanalytical Laboratories. Ultraviolet spectra were recorded on a Beckman DK-2A or Cary 14 spectrometer.

3,4-Methylenedioxyphenyl allyl ether. Sodium (4.2 g) was dissolved in ethanol (125 ml) and a solution of 3,4-methylenedioxyphenol (25 g, Aldrich) in ethanol (30 ml) was added. Allyl chloride (17 g) was added slowly with stirring (magnetic stirrer), and the solution was kept at reflux for 3 hours. Most of the ethanol was evaporated and water (200 ml) plus ether (200 ml) were added. The ether layer was separated and washed with dilute sodium hydroxide solution, water, dilute sulfuric acid, and water and dried over magnesium sulfate. Evaporation of the ether gave the liquid product in sufficient purity (yield 27 g, 83.4%). The product had identical infrared and nmr spectra to an authentic sample prepared by the method of Beroza.<sup>65</sup>

2-Allyl-4,5-methylenedioxyphenol. 3,4-Methylene-dioxyphenyl allyl ether (27 g) was heated under nitrogen at 170° for 2 hours. The dark liquid solidified on cooling and was purified by sublimation at 80° and 0.05 mm Hg (yield 25 g, 93%). The infrared and nmr spectra of the product were identical to those of an authentic sample prepared by the method of Beroza.<sup>65</sup>

4,5-Methylenedioxy-2-(trans-propenyl)phenol. 4,5-Methylenedioxy-2-allylphenol (5.0 g) was added with stirring to a solution of potassium t-butoxide (8.0 g) in dimethylsulfoxide (150 ml). The solution was kept at 80° for 1 hour under nitrogen and then poured over 300 ml of ice. This was then acidified with concentrated hydrochloric acid and extracted with two 100 ml portions of ether. The ether was combined and washed three times with water to remove the dimethylsulfoxide and dried over magnesium sulfate. Evaporation of the ether yielded 4.3 g (85%) of the product. The nmr spectrum (CDCl<sub>3</sub>) of the product showed bands at 1.8 (d, 3H), 5.1 (s, 1H, D<sub>2</sub>O→OH), 5.75 (s, 2H), 6.25 (s, 1H), 6.66 (s, 1H), 5.8-6.6 (m, 2H). The infrared (film) showed bands at 3320, 2900, 1634, 1510, 1490, 1300, 1248, 1172, 1040, 960, 930, 870, 835, and 760. The mass spectrum had a parent ion at m/e = 178. The UV maxima (ethanol) were at 248(7.22 x 10<sup>3</sup>), and 310(4.85 x 10<sup>3</sup>).

Anal. Calcd for C<sub>10</sub>H<sub>10</sub>O<sub>3</sub>: C, 67.41; H, 5.62. Found: C, 67.07; H, 5.78.

Palladium chloride oxidation of 4,5-methylenedioxy-2-(trans-propenyl)phenol. Palladium dichloride (0.8 g) was added to a rapidly stirred (magnetic stirrer) solution containing 4,5-methylenedioxy-2-(trans-propenyl)phenol (1.6 g) and sodium acetate (6.0 g) in methanol (150 ml) and water (30 ml). The solution was stirred for 2 hours (~38° and then left to settle for 1 hour at room temperature. After filtration and dilution with water, the resultant suspension was extracted twice with ether. The ether solution was washed with 10% sodium hydroxide solution and then distilled water. Evaporation after drying over magnesium sulfate gave the crude product (1.0 g, 62%). Carbon tetrachloride (5 ml) was added, and the product crystallized overnight. The crystals (0.98 g, mp 185°) thus obtained contained one molecule of carbon tetrachloride per molecule of carpanone (X-ray crystal structure). Chromatography of the mother liquor gave additional carpanone-CCl<sub>4</sub> (0.08 g). The total yield of crystalline carpanone is 46%. Comparison of the nmr spectra of synthetic and natural carpanone in carbon tetrachloride established their identity. The discoverers of natural carpanone<sup>8</sup> have reported the physical data including 220 MHz nmr, and therefore we will not repeat it here. A 60 MHz spectrum of carpanone is shown in Figure 2, however.

Catalyzed air oxidation of 4,5-methylenedioxy-2-(trans-propenyl)phenol. A solution of 4,5-methylenedioxy-2-(trans-propenyl)phenol (0.25 g), methanol (40 ml), water (5 ml), palladium chloride (0.009 g, .05 eq), sodium acetate (1.0 g), and cupric acetate (0.03 g, .07 eq) was stirred rapidly (magnetic stirrer) in air for 2 hours. After the same work-up as in the palladium chloride oxidation (above), the crude yield of carpanone was 0.156 g, 62.5% which corresponded closely to that obtained with palladium chloride. Crystallization from carbon tetrachloride gave pure carpanone-CCl<sub>4</sub> (yield 0.16 g, 46%). The identity of the product was established by comparison of nmr data with that from the palladium chloride oxidation.

Cupric acetate oxidation of 4,5-methylenedioxy-2-(trans-propenyl)phenol. A solution of cupric acetate (0.56 g) in water (5 ml) was added over a period of 5 minutes to a stirred solution of 4,5-methylenedioxy-2-(trans-propenyl)phenol (0.5 g), sodium acetate (2.0 g), methanol (50 ml), and water (10 ml). The resulting suspension was stirred for an additional 5 minutes and filtered. The filtrate was diluted with water and extracted with ether. The ether solution was washed with dilute sodium hydroxide solution and water and dried over magnesium sulfate. Evaporation of the ether gave the product (crude yield 0.35 g, 71%). Crystallization from carbon tetrachloride gave 0.34 g, 49% of carpanone-CCl<sub>4</sub>.

Ferricyanide oxidation of 4,5-methylenedioxy-2-(trans-propenyl)phenol. Potassium hydroxide (0.2 g) was dissolved in water (50 ml) and the solution was degassed with nitrogen. 3,4-Methylenedioxy-2-trans-propenylphenol (0.5 g) was then added and warmed under nitrogen until solution was complete. The solution was cooled in an ice bath and potassium ferricyanide (1.0 g) in water (25 ml) was added dropwise over a period of 30 minutes. The mixture was stirred at 0° for 30 minutes more and then poured into dilute sulfuric acid (300 ml). Ether (200 ml) was added, separated, washed with water, and dried over magnesium sulfate. After evaporating the ether, the product was chromatographed on silica-gel using chloroform as the eluent. The third of six components (tlc) was identified by comparison of its nmr spectrum with that reported for carpanone.<sup>8</sup> It was necessary to chromatograph the fraction two more times to completely separate it from adjacent fractions (yield 0.025 g, 5%).

Silver oxide oxidation of 4,5-methylenedioxy-2-(trans-propenyl)phenol. Silver oxide (0.67 g) was added to a stirred solution of 4,5-methylenedioxy-2-(trans-propenyl)-phenol (0.5 g) in 10% sodium hydroxide solution (150 ml). The suspension was stirred at room temperature for 1 hour and extracted three times with ether. The ether extracts were combined, washed with dilute sodium hydroxide solution and water and dried over magnesium sulfate. Evaporation of

the ether gave the crude product (yield 0.19 g, 38%). Chromatography on silica-gel with chloroform as the eluent gave pure carpanone (yield 0.09 g, 18%).

Silver carbonate on celite oxidation of 4,5-methylenedioxy-2-(trans-propenyl)phenol. Silver carbonate on celite (5.0 g) was added to benzene (200 ml) and any water present was azeotroped out. 4,5-Methylenedioxy-2-(trans-propenyl)-phenol (0.27 g) was added to the hot stirred solution. The stirring was continued for 10 minutes and the suspension was filtered. The filtrate was washed with dilute sodium hydroxide solution and water and dried over magnesium sulfate. Evaporation of the benzene gave the crude product (yield 0.20 g, 74%). Crystallization from carbon tetrachloride gave pure carpanone-CCl<sub>4</sub> (yield 0.18 g, 47%).

Oxidation of 4,5-methylenedioxy-2-(trans-propenyl)phenol with ferric chloride-dimethylformamide complex [Fe(DMF)<sub>3</sub>Cl<sub>2</sub>][FeCl<sub>4</sub>]. A solution of 4,5-methylenedioxy-2-(trans-propenyl)phenol (0.54 g) in ether (50 ml) was stirred and refluxed for 1 hour with a solution of [Fe(DMF)<sub>3</sub>Cl<sub>2</sub>][FeCl<sub>4</sub>]<sup>66</sup> (5.0 g) in water (100 ml). The ether layer was then separated, extracted with dilute sodium hydroxide solution and water, and dried over magnesium sulfate. The crude product (yield 0.19 g, 35%) was chromatographed on silica-gel with chloroform as the eluent to give pure carpanone (yield 0.09 g, 17%).

Vanadium oxytrichloride oxidation of 4,5-methylenedioxy-2-(trans-propenyl)phenol. Vanadium oxytrichloride (1.2 g) in ether (30 ml) was cooled in a Dry Ice-acetone bath, and 4,5-methylenedioxy-2-(trans-propenyl)phenol (1.0 g) was added slowly with stirring. The mixture was stirred at Dry Ice temperature for 2 hours and then kept at reflux for an additional 10 hours. The solution was worked up by extraction with water, dilute sodium hydroxide solution, and water again. The ether was dried over magnesium sulfate and evaporated to give the neutral products (yield 0.46 g, 46%). An nmr spectrum of the mixture (tlc) showed that no carpanone was present (no methyl doublet at 0.7 ppm).

Air oxidation of 4,5-methylenedioxy-2-(trans-propenyl)-phenol. Sodium acetate (8.0 g) and 4,5-methylenedioxy-2-(trans-propenyl)phenol (1.73 g) were dissolved in methanol (200 ml) and water (40 ml). Air was passed through the solution for 18 hours with a gas dispersion tube. The methanol was evaporated and ether (100 ml) was added. The ether solution was washed with dilute sodium hydroxide solution and water and dried over magnesium sulfate. Evaporation of the ether gave the crude neutral product (yield 0.48 g, 28%). An nmr spectrum of the mixture showed that it contained less than 50% carpanone (comparison of total integral to the integral of the methyl doublet at 0.7 ppm).



Attempted oxidation of 4,5-methylenedioxy-2-allylphenol with cupric acetate. Cupric acetate (0.56 g) in water (5 ml) was added slowly to a stirred solution of 4,5-methylenedioxy-2-allylphenol (0.5 g) in methanol (50 ml) and water (10 ml) at room temperature. The solution was stirred for 5 minutes and allowed to sit overnight. The blue-green solution did not change color. The solution was poured into water (100 ml) and extracted with ether (150 ml). The ether was dried over magnesium sulfate and evaporated to give starting material (comparison of nmr and ir spectra) (yield 0.47 g, 94%).

1,4-Bismethanesulfonylbutyne. Methanesulfonyl chloride (15 g) was added over a period of 10 minutes to a cooled solution ( $-10^{\circ}$ ) of 2-butyne-1,4-diol (5.0 g, Aldrich) and triethylamine (18 g) in methylene chloride (250 ml).<sup>58</sup> During the addition the temperature was maintained below  $-5^{\circ}$ . The mixture was allowed to stir (magnetic stirrer) and warm to room temperature for 20 minutes and then extracted with water, dilute hydrochloric acid, dilute sodium bicarbonate solution, and saturated sodium chloride solution. The methylene chloride was dried over magnesium sulfate and evaporated. The product was recrystallized from ethanol (yield 5.6 g, 40%). The nmr and infrared spectrum were identical to those of an authentic sample of 1,4-bismethanesulfonylbutyne prepared by the method of Haslinger and Soloway.<sup>67</sup>

The photoaddition of maleic anhydride to 1,4-bismethane-sulfonoxybutyne. Maleic anhydride (1.0 g), 1,4-bismethane-sulfonoxybutyne (5.0 g), and benzophenone (1.0 g) were dissolved in acetone (100 ml) and irradiated for 3 hours in a Pyrex immersion well using a Hanovia 550 watt, medium pressure lamp. Water (0.25 ml) was added and the solution was allowed to sit at room temperature overnight. The acetone was then evaporated, and the residue was chromatographed on silica-gel with a 1:4 mixture of ethyl acetate and benzene. After the unreacted butyne had been eluted, the product was washed from the column with pure ethyl acetate. Evaporation of the ethyl acetate gave the pure product (yield 2.8 g, 80%). The nmr spectrum (acetone-D<sub>6</sub>) had peaks at 3.1 (s, 6H), 4.0 (s, 2H), 5.0 (s, 4H), 9.0 (s, 2H, D<sub>2</sub>O→OH). The infrared spectrum (film) gave bands at 3700-2400, 1740, 1360, 1268, 1180, 945, and 819. The mass spectrum gave a parent ion at m/e = 358.

High resolution mass spectrum: Calcd for C<sub>10</sub>H<sub>14</sub>S<sub>2</sub>O<sub>6</sub>: 358.002837. Found: 358.002691.

Generation of diazomethane. Sodium hydroxide solution (60 ml, 40%) and ether (200 ml) were placed in a 300 ml Claisen flask equipped with a condenser and cork joints. The mixture was cooled to 0° in an ice bath and EXR-101 (7.2 g) was added slowly. A receiver was set up so that the distillate could be collected at 0° under ether. The

mixture was warmed slowly and an ether solution of diazomethane was collected over a period of 1 hour.

1,2-Bis-(methanesulfonylmethyl)-3,4-dicarbomethoxycyclobutene. A solution of diazomethane in ether (as prepared above) was added dropwise to a cold (ice bath) solution of 1,2-bis-(methanesulfonylmethyl)-3,4-dicarboxycyclobutene (1.0 g) in methanol (20 ml) until the yellow color persisted. The solution was then evaporated to yield the pure diester (yield 1.1 g, 100%; mp 85-86°). The nmr spectrum (CDCl<sub>3</sub>) had peaks at 3.09 (s, 6H), 3.72 (s, 6H), 3.93 (s, 2H), and 4.9 (s, 4H). The ir spectrum (film) gave peaks at 3040, 2960, 1749, 1450, 1360, 1180, 950, and 822. The mass spectrum gave a parent ion at m/e = 322.

Anal. Calcd for C<sub>12</sub>H<sub>18</sub>O<sub>10</sub>: C, 37.30; H, 4.66. Found: C, 37.48; H, 4.74.

Reaction of sodium 3,4-methylenedioxyphenolate with 1,2-bis-(methanesulfonylmethyl)-3,4-dicarbomethoxycyclobutene. A solution of 1,2-bis-(methanesulfonylmethyl)-3,4-dicarbomethoxybutene (0.5 g) and sodium 3,4-methylenedioxyphenolate (0.5 g) in dimethylsulfoxide (30 ml) was allowed to stand at room temperature overnight. The solution was then poured into water (200 ml) and extracted with ether. The ether was washed 3 times with water, dried over magnesium sulfate, and evaporated. An nmr spectrum of the product gave peaks at 3.0 (s, ~2H), 3.6-3.7 (m, ~5-6H),

5.8 (s, ~4H), and 6.0-6.7 (m, ~9H). Comparison with nmr spectra of the starting materials showed that the methoxyl peak had decreased substantially as had the peak from the methanesulfonyl groups. The peak at 5.8 and the multiplet at 6.0-6.7 checked with the spectrum of 3,4-methylenedioxyphenol.

1,1-Bis-(3,4-methylenedioxyphenoxy)butyne. Sodium metal (1.0 g) was dissolved in absolute ethanol (50 ml) and 3,4-methylenedioxyphenol (5.7 g) in absolute ethanol (20 ml) was added slowly. 1,4-Bismethanesulfonylbutyne (5.0 g) was added and the mixture was stirred at reflux for 3 hours. The mixture was poured into water (400 ml) and extracted with ether (150 ml). The ether was washed with dilute sodium hydroxide solution, dilute hydrochloric acid, and water and dried over magnesium sulfate. Evaporation of the ether gave the product as a light brown solid (yield 6.0 g, 89%).

Anal. Calcd for  $C_{18}H_{14}O_6$ : C, 66.25; H, 4.29. Found: C, 66.28, H, 4.43.

Attempted photoaddition of maleic anhydride to 1,1-bis-(3,4-methylenedioxyphenoxy)butyne. Maleic anhydride (1.0 g), 1,1-bis-(3,4-methylenedioxyphenoxy)butyne (5.0 g), and benzophenone (1.0 g) were dissolved in acetone (100 ml) and irradiated for 3 hours in a Pyrex immersion well using a Hanovia 550 watt, medium pressure lamp. The acetone was

then evaporated and a comparison of the nmr spectrum of the mixture to that of the mixture before irradiation showed that there had been no change. Prolonged irradiation gave an intractable solid on the surface of the immersion well.

1,1-Bis(2-hydroxy-4,5-methylenedioxyphenyl)ethane.

Acetaldehyde (3 g) and 3,4-methylenedioxyphenol (10 g) were dissolved in ethanol (100 ml), and concentrated hydrochloric acid (1 ml) was added. The solution was kept at reflux for 3 hours. Most of the ethanol was evaporated, and ether (100 ml) was added. The ether was extracted several times with dilute sodium bicarbonate solution, dried over magnesium sulfate, and evaporated. The product was recrystallized from carbon tetrachloride (yield 9.1 g, 81%). The nmr spectrum ( $\text{CDCl}_3$ ) had bands at 1.48 (d, 3H), 4.5 (q, 1H), 5.75 (m, 4H), 6.3 (s, 2H), 6.7 (s, 2H), 7.12 (s, 2H,  $\text{D}_2\text{O} \rightarrow \text{OH}$ ). The infrared spectrum ( $\text{CHCl}_3$ ) showed bands at 3620, 3350, 1640, 1516, 1325, 1225, 1060, 948, and 870. The mass spectrum gave a parent ion at  $m/e = 302$ . The UV spectrum (ethanol) had a maxima at  $302(1.12 \times 10^4)$ ,  $229(6.8 \times 10^3)$ , and strong end absorption.

Anal. Calcd for  $\text{C}_{16}\text{H}_{14}\text{O}_6$ : C, 63.58; H, 4.64. Found: C, 63.58; H, 4.61.

Attempted Mannich reaction with 3,4-methylenedioxyphenol. Acetaldehyde (1.3 g), dimethylamine hydrochloride (2.4 g), and 3,4-methylenedioxyphenol (4.0 g) were

dissolved in 95% ethanol (50 ml) and kept at reflux for 3 hours. The solution was then poured into water (300 ml) and extracted with ether (200 ml). The ether was dried over magnesium sulfate and evaporated. The products were separated on a silica-gel column with methylene chloride as the eluent. This yielded starting phenol (comparison of nmr and ir spectra) (2.6 g) plus a single product whose nmr and infrared spectra were the same as that of 1,1-bis(2-hydroxy-4,5-methylenedioxyphenyl)ethane (yield 1.2 g, 27%) based on starting phenol.

Pyrolysis of 4,5-methylenedioxy-2-(trans-propenyl)-phenol. Diphenyl ether (4 ml) and 4,5-methylenedioxy-2-(trans-propenyl)phenol (1.0 g) were heated under nitrogen at 190° for 2 hours. The resulting solution was chromatographed on silica-gel using benzene as the eluent. The diphenyl ether came off first followed by dimer A and then by dimer B. The isolated yield of dimer A was 0.46 g (46%) and dimer B was 0.45 g (45%). The nmr spectrum (CDCl<sub>3</sub>) of dimer A (Figure 3a) had peaks at 0.83 (d, 3H), 1.02 (t, 3H), 1.67 (t, 2H), 2.13 (m, 2H), 5.1 (m, 1H), 5.75 (s, 4H), 6.29 (s, 1H), 6.31 (s, 1H), 6.45 (s, 1H), 6.5 (s, 1H), 6.92 (s, 1H, D<sub>2</sub>O→OH). The infrared spectrum (film) (Figure 4a) had bands at 3400, 2984, 2930, 1635, 1505, 1483, 1444, 1240, 1168, 1040, 940, 855, and 832. The mass spectrum had a parent ion at m/e = 356. The UV maxima (ethanol) are 301(1.7 x 10<sup>4</sup>), 233(1.14 x 10<sup>4</sup>), and strong end absorption.

High resolution mass spectrum: Calcd for  $C_{20}H_{20}O_6$ :  
356.12598. Found: 356.12763.

The nmr spectrum ( $CDCl_3$ ) of dimer B (Figure 3b) had peaks at 0.70 (t, 3H), 0.85 (d, 3H), 1.75 (m, 2H), 2.2 (m, 1H), 2.6 (m, 1H), 4.38 (d, 1H), 5.8 (s, 4H), 6.3 (s, 1H), 6.35 (s, 1H), 6.4 (s, 1H), 6.51 (s, 1H,  $D_2O \rightarrow OH$ ). The infrared spectrum (film) (Figure 4b) had bands at 3440, 2970, 2930, 2890, 1668, 1505, 1487, 1442, 1245, 1160, 1040, 940, 860, 842, and 733. The mass spectrum gave a parent ion at  $m/e = 356$ . The UV maxima (ethanol) are  $300(1.3 \times 10^4)$ ,  $233(8 \times 10^3)$ , and strong end absorption.

Anal. Calcd for  $C_{20}H_{20}O_6$ : C, 67.42; H, 5.62. Found: C, 67.29, H, 5.61.

Photolysis of 4,5-methylenedioxy-2-(trans-propenyl)-phenol in chloroform. A solution of 4,5-methylenedioxy-2-(trans-propenyl)phenol (4.0 g) and chloroform (50 ml) in a Pyrex tube was irradiated in a Rayonette Reactor with 3100 Å lamps for 5 minutes. The chloroform was evaporated to yield 4.0 g of a mixture of two components (tlc). These were separated on a silica-gel column with benzene as the eluent. The nmr and infrared spectra of the first component identified it as dimer B previously obtained in the pyrolysis of 4,5-methylenedioxy-2-(trans-propenyl)phenol (yield 1.9 g, 45%). The second component, dimer C, (yield 1.88 g, 44%) had nmr ( $CDCl_3$ ) (Figure 3c) peaks at 0.84

(d, 3H), 1.0 (t, 3H), 1.55 (m, 2H), 2.4 (m, 2H), 4.9 (d, 1H), 5.75 (s, 4H), 6.3 (s, 2H), 6.43 (s, 2H), 6.5 (s, 1H, D<sub>2</sub>O→OH). The infrared spectrum (film) (Figure 4c) had bands at 3400, 2970, 2880, 1637, 1508, 1489, 1448, 1240, 1155, 1040, 940, 865, and 730. The mass spectrum gave a parent ion at  $m/e = 356$ . The UV spectrum (ethanol) had maxima at  $300(1.4 \times 10^4)$ ,  $233(8 \times 10^3)$ , and strong end absorption.

Anal. Calcd for C<sub>20</sub>H<sub>20</sub>O<sub>6</sub>: C, 67.42; H, 5.62. Found: C, 67.16; H, 5.62.

Photolysis of 4,5-methylenedioxy-2-(trans-propenyl)-phenol in ether. A solution of 4,5-methylenedioxy-2-(trans-propenyl)phenol (1.0 g) in ether (150 ml) was irradiated for 20 minutes in a Pyrex immersion well with a 550 watt Hanovia medium pressure lamp. An nmr integral showed that 95 percent of the starting material had been destroyed. The product was a mobile liquid which dimerized overnight at room temperature. The dimer was identified as dimer C by comparing its nmr and ir spectra to the reference spectra for dimer C. Further irradiation of the product in ether (2 hours) gave dimer C as the product. The monomer gave nmr peaks (CDCl<sub>3</sub>) at 1.66 (d, 3H), 5.77 (s, 2H), 6.32 (s, 1H), 6.46 (s, 1H), and 5.5-6.3 (m, 3H, D<sub>2</sub>O→2H). The infrared spectrum had bands at 3490, 3000, 2960, 2870, 1623, 1502, 1483, 1442, 1298, 1220, 1040, 938, 860, and 765. The mass spectrum gave a parent ion at  $m/e = 178$ . The UV spectrum



(ethanol) had maxima at  $311(5.6 \times 10^3)$ ,  $255(6.7 \times 10^3)$ , and strong end absorption.

Flash photolysis of 4,5-methylenedioxy-2-(trans-propenyl)phenol. A solution of 4,5-methylenedioxy-2-(trans-propenyl)phenol ( $10^{-3}$  M) in chloroform was flashed in a commercial (Xenon Corp.) flash photolysis apparatus. The UV absorption at a particular wavelength was observed on an oscilloscope. The wavelength control in the sensing unit was varied from flash to flash to locate the maximum. An intermediate was observed which absorbed at  $3850 \text{ \AA}$  and had a lifetime of approximately 4 msec. (Figure 1) The lifetime was taken to be the time required for the absorption to fall to zero on the oscilloscope trace. The same results were obtained in hexane solution. The experiment was repeated using 2-(trans-propenyl)phenol with similar results. The intermediate from 2-coumaranone gave the same maximum but the lifetime was almost 1 second.

Photolysis of 4,5-methylenedioxy-2-(trans-propenyl)phenol in methanol. A solution of 4,5-methylenedioxy-2-(trans-propenyl)phenol (1.0 g) in methanol (150 ml) was irradiated for 1 hour in a Pyrex immersion well with a 550 watt Hanovia medium pressure lamp. Evaporation of the methanol gave the product which was mainly 4,5-methylenedioxy-2-cis-propenylphenol (comparison of nmr spectra) plus several other compounds (tlc). The mixture was chromatographed on silica-gel with benzene as the eluent.

The products separated were shown by nmr spectra to be dimers of the propenylphenol (yield 0.8 g, 80%) and 4,5-methylenedioxy-2-(1-methoxypropyl)phenol (yield 0.1 g, 10%). The infrared and nmr spectra of the methoxy compound were identical to those of the product of palladium chloride oxidation of 4,5-methylenedioxy-2-propylphenol in methanol.

Photolysis of 4,5-methylenedioxy-2-(trans-propenyl)-phenol in the presence of ethyl vinyl ether. Ethyl vinyl ether (0.5 g) and 4,5-methylenedioxy-2-(trans-propenyl)-phenol (0.25 g) were dissolved in chloroform (1.0 ml). A sample of this solution was placed in an nmr tube and irradiated in a Rayonette Reactor with 3100 Å lamps. After 5 minutes irradiation, an nmr showed that none of the phenol had been affected, but that ~15% of the ethyl vinyl ether had gone to products. After 15 minutes more irradiation, ~10% of the phenol had disappeared and all of the ethyl vinyl ether was gone. Irradiation of a chloroform solution of only ethyl vinyl ether for 30 minutes under the same conditions gave no reaction.

Allyl phenyl ether. Sodium (12.2 g) was dissolved in ethanol (300 ml) and a solution of phenol (50 g) in ethanol (100 ml) was added. Allyl chloride (41 g) was added slowly with stirring and the solution was kept at reflux for 2 hours. The solution was then filtered, and the ethanol was evaporated and replaced with ether (200 ml). The ether

was washed with dilute sodium hydroxide solution, water, and dried over magnesium sulfate. Evaporation of the ether gave the product (yield 64 g, 90%). The infrared and nmr spectra of the product were identical to those of an authentic sample prepared by an Org. Reactions<sup>68</sup> procedure.

2-Allylphenol. Phenyl allyl ether (25 g) was placed in a flask equipped with a condenser and a nitrogen inlet. The flask was kept at 205° for 6 hours. Ether (100 ml) was added and the solution was extracted with dilute sodium hydroxide solution. The aqueous phase was separated, acidified with concentrated hydrochloric acid and extracted with ether (100 ml). The ether layer was dried over magnesium sulfate and evaporated (yield 19 g, 76%). Phenyl allyl ether (5 g, 20%) was recovered from the first ether solution. The infrared and nmr spectra of the 2-allylphenol matched those of an authentic sample prepared by an Org. Reactions<sup>68</sup> procedure.

2-(Trans-propenyl)phenol. Potassium t-butoxide (7.0 g) was dissolved in dimethylsulfoxide (150 ml) and o-allylphenol (4.0 g) was added. The solution was heated under nitrogen for 1 hour at 80° and then poured over ice (200 g). The resulting solution was acidified with concentrated hydrochloric acid and extracted with ether (150 ml). The ether layer was separated, washed with three portions of water (200 ml each), and dried over magnesium sulfate.

The ether was evaporated to give the product (yield 3.62 g, 90%). The nmr and infrared spectra of the product were identical to those of an authentic sample of 2-(trans-propenyl)phenol prepared by an Org. Reactions<sup>68</sup> procedure.

Pyrolysis of 2-(trans-propenyl)phenol. A solution of 2-(trans-propenyl)phenol (1.0 g) in diphenyl ether (4.0 ml) was heated at 180° for 7 hours. The solution was then chromatographed on silica-gel with benzene as the eluent. This yielded a mixture of two compounds (nmr) which could not be separated chromatographically (yield 0.89 g, 89%). The mixture was then dissolved in pyridine (10 ml) and acetic anhydride (8 ml) was added. The solution was allowed to sit at room temperature overnight and then diluted with water (200 ml) and extracted with ether. The ether layer was washed with dilute hydrochloric acid, dilute sodium hydroxide solution, and water, and dried over magnesium sulfate. Evaporation of the ether gave a mixture of the two acetates (yield overall 0.85 g, 85%) which were separated on a silica-gel column with benzene as eluent. They were each then saponified by dissolving each in a 10% methanolic potassium hydroxide solution and allowing it to sit overnight. Dilution with water (100 ml), acidification with dilute hydrochloric acid, and extraction with ether gave on evaporation of the ether dimer D (yield 0.38 g, 38%) and dimer E (yield 0.40 g, 40%). Dimer E was shown by its

ir and nmr spectra to be identical to one of the two isomers produced in the photolysis of 2-(propenyl)phenol in chloroform. The nmr spectrum ( $\text{CDCl}_3$ ) of dimer D (Figure 5a) had peaks at 0.82 (t, 3H), 1.15 (d, 3H), 1.78 (m, 2H), 2.30 (m, 2H), 5.37 (s, 1H), 6.7-7.3 (m, 9H,  $\text{D}_2\text{O} \rightarrow 8\text{H}$ ). The infrared spectrum (film) (Figure 6a) had bands at 3440, 2980, 2950, 2890, 1592, 1498, 1464, 1245, and 760. The mass spectrum gave a parent ion at  $m/e = 268$ . The UV maxima (ethanol) were 277( $4.8 \times 10^3$ ), 218( $1.44 \times 10^4$ ), and strong end absorption.

Anal. Calcd for  $\text{C}_{18}\text{H}_{20}\text{O}_2$ : C, 80.60; H, 7.46. Found: C, 80.40; H, 7.52.

The nmr spectrum ( $\text{CDCl}_3$ ) of dimer E (Figure 5b) had peaks at 0.72 (t, 3H), 0.85 (d, 3H), 1.6-2.9 (m, 4H), 4.65 (d, 1H), 6.9 (m, 9H,  $\text{D}_2\text{O} \rightarrow 8\text{H}$ ). The infrared (film) (Figure 6b) had bands at 3450, 2975, 1585, 1490, 1460, 1240, and 760. The mass spectrum gave a parent ion at  $m/e = 268$ . The UV maxima (ethanol) were 277( $4.35 \times 10^3$ ), 218( $1.38 \times 10^4$ ), and strong end absorption.

Anal. Calcd for  $\text{C}_{18}\text{H}_{20}\text{O}_2$ : C, 80.60; H, 7.46. Found: C, 80.61; H, 7.43.

Photolysis of 2-(trans-propenyl)phenol in chloroform.

2-(Trans-propenyl)phenol (1.0 g) was dissolved in chloroform (25 ml) and irradiated in a Pyrex tube with a Rayonette Reactor using 3100 Å lamps. The photolysis was followed by nmr. After 25 minutes no starting phenol remained, and

the chloroform was evaporated to yield a mixture of two products (tlc). The two components were separated on a silica-gel column using benzene as the eluent. The first component was identified by its spectra to be dimer E as prepared in the pyrolysis of 2-(trans-propenyl)phenol (yield 0.42 g, 42%). The second component, dimer F, (yield 0.41 g, 41%) had nmr peaks ( $\text{CDCl}_3$ ) (Figure 5c) at 0.83 (d, 3H), 1.0 (t, 3H), 1.65 (m, 2H), 2.5 (m, 2H), 5.18 (d, 1H), 6.4 (s, 1H,  $\text{D}_2\text{O} \rightarrow \text{OH}$ ), 7.0 (m, 8H). The infrared spectrum (film) (Figure 6c) had bands at 3440, 2985, 1586, 1490, 1460, 1240, and 750. The mass spectrum gave a parent ion at  $m/e = 268$ . The UV maxima (ethanol) were 276( $5.1 \times 10^3$ ), 218( $1.55 \times 10^4$ ), and strong end absorption.

High resolution mass spectrum: Calcd for  $\text{C}_{18}\text{H}_{20}\text{O}_2$ : 268.146320. Found: 268.150232.

Photolysis of 2-(trans-propenyl)phenol in ether. An ether solution (150 ml) of 2-(trans-propenyl)phenol (1.0 g) was irradiated for 2 hours in a Pyrex immersion well with a 550 watt Hanovia medium pressure lamp. The conversion had gone approximately 90 percent to completion as measured by comparing the nmr integral of the methyl doublet of starting material with the total integral. The product was separated from starting material on a silica-gel column using benzene as the eluent (yield 0.86 g, 86%). The nmr

and ir spectra of the product were identical with those of an authentic sample of 2-(cis-propenyl)phenol prepared by the method of Baker and Shulgin.<sup>55</sup>

Palladium chloride oxidation of 4,5-methylenedioxy-2-allylphenol. Palladium chloride (0.4 g) was added with stirring (magnetic stirrer) to a solution of 4,5-methylenedioxy-2-allylphenol (0.5 g) and sodium acetate (2.0 g) in methanol (50 ml) and water (10 ml). The mixture was stirred for 1 hour and filtered. The filtrate was diluted to twice its volume with water and extracted twice with ether. The ether layers were combined and washed with dilute sodium hydroxide solution and water. After drying over magnesium sulfate, the ether was evaporated to give one product (yield 0.338 g, 84.5%). The product was identified by its spectra as 2-methyl-6,7-methylenedioxybenzofuran. The nmr spectrum (CDCl<sub>3</sub>) had peaks at 2.29 (s, 3H), 5.75 (s, 2H), 6.0 (s, 1H), 6.6 (s, 1H), 6.7 (s, 1H). The infrared spectrum (film) gave bands at 2900, 1465, 1315, 1278, 1160, 1036, 932, 855, and 778. The mass spectrum gave a parent ion at m/e = 176. The UV maxima (ethanol) were 305(7.54 x 10<sup>3</sup>), 245(9.06 x 10<sup>3</sup>), and strong end absorption.

Anal. Calcd for C<sub>10</sub>H<sub>8</sub>O<sub>3</sub>: C, 68.30; H, 4.55. Found: C, 68.10; H, 4.73.

Palladium chloride oxidation of 2-allylphenol. Palladium chloride (0.5 g) was added with stirring (magnetic stirrer) to a solution of 2-allylphenol (0.5 g) and sodium acetate

(2.0 g) in methanol (50 ml) and water (10 ml). The mixture was stirred for 1 hour and filtered. The filtrate was diluted to twice its volume with water and extracted twice with ether. The ether layers were combined and washed with dilute sodium hydroxide solution and water. After drying over magnesium sulfate, the ether was evaporated to give one product (yield 0.32 g, 86.5%). The product was identified by its ir spectrum<sup>69</sup> as 2-methylbenzofuran. The nmr spectrum (CDCl<sub>3</sub>) had peaks at 2.26 (s, 3H), 6.09 (s, 1H), 7.0 (m, 4H). The infrared spectrum (film) had bands at 3080, 2940, 1620, 1463, 1258, 1190, 948, 805, and 756. The mass spectrum gave a parent ion at m/e = 132. The UV maxima (ethanol) were 282(2.9 x 10<sup>3</sup>), 275(2.9 x 10<sup>3</sup>), 245(1.16 x 10<sup>4</sup>) and strong end absorption.

4,5-Methylenedioxy-2-propylphenol. An ethanol (100 ml) solution of 4,5-methylenedioxy-2-allylphenol (1.0 g) was hydrogenated at atmospheric pressure over pre-reduced platinum oxide. The solution was filtered and evaporated to give the product (yield 1.01 g, 100%; mp 70°, lit 70-71°).<sup>70</sup> The nmr (CDCl<sub>3</sub>) had peaks at 0.90 (t, 3H), 1.52 (sextuplet, 2H), 5.5 (s, 1H, D<sub>2</sub>O→OH), 5.70 (s, 2H), 6.28 (s, 1H), 6.47 (s, 1H). The infrared spectrum (CHCl<sub>3</sub>) gave bands at 3630, 3380, 2980, 1512, 1250, 1185, 1080, 946, and 870. The mass spectrum had a parent ion at m/e = 180. The UV spectrum (ethanol) had maxima at 301(5.05 x 10<sup>3</sup>), 233(3.5 x 10<sup>3</sup>), and strong end absorption.



Palladium chloride oxidation of 4,5-methylenedioxy-2-propylphenol. Palladium chloride (0.2 g) was added to a stirred solution of 4,5-methylenedioxy-2-propylphenol (0.25 g) and sodium acetate (2.0 g) in methanol (50 ml) and water (10 ml). The mixture was stirred at room temperature for 4 hours and then filtered. The filtrate was diluted to twice its volume with water and extracted with ether. The ether was washed with water and dried over magnesium sulfate. Evaporation of the ether gave one product (yield 0.29 g, 99%) which was identified by its spectra as 4,5-methylenedioxy-2-(1-methoxypropyl)phenol. The nmr spectrum ( $\text{CDCl}_3$ ) had peaks at 0.9 (t, 3H), 1.75 (m, 2H), 3.35 (s, 3H), 4.02 (t, 1H), 5.83 (s, 2H), 6.4 (s, 2H), 7.7 (s, 1H,  $\text{D}_2\text{O} \rightarrow \text{OH}$ ). The infrared spectrum (film) had bands at 3370, 2970, 2940, 2890, 1636, 1510, 1491, 1182, 1080, 1040, 943, 867, 795, and 770. The mass spectrum did not give a parent ion; the highest peak was at  $m/e = 178$  which could correspond to loss of methanol to give the quinone methide. The UV maxima (ethanol) were  $300(5.0 \times 10^3)$ ;  $234(4.2 \times 10^3)$ ; and strong end absorption.

High resolution mass spectrum: Calcd for  $\text{C}_{11}\text{H}_{14}\text{O}_4$ : 210.089200. Found: 210.088827.

Silver oxide oxidation of 4,5-methylenedioxy-2-propylphenol. Silver oxide (0.32 g) was added to a stirred solution of 4,5-methylenedioxy-2-propylphenol (0.25 g) in

methanol (20 ml). The mixture was stirred at room temperature for 30 minutes, filtered, and the methanol was evaporated to give one product (yield 0.27 g, 93%). The product was identified as 4,5-methylenedioxy-2-(1-methoxypropyl)phenol by comparing its spectra to that from the palladium chloride oxidation of 4,5-methylenedioxy-2-propylphenol.

4,5-Methylenedioxy-2-(trans-propenyl)phenyl methyl ether. Methyl iodide (2.0 g) and 4,5-methylenedioxy-2-(trans-propenyl)phenol (1.5 g) were dissolved in acetone (100 ml) and anhydrous potassium carbonate (4 g) was added. The mixture was stirred and kept at reflux for 6 hours. It was then filtered and the filtrate was evaporated. The residue was dissolved in ether, washed with dilute sodium hydroxide solution and water, and the ether was dried over magnesium sulfate and evaporated. The product was purified by column chromatography on silica-gel with benzene as the eluent (yield 1.2 g, 74%, mp 47-48°; lit 48-49°).<sup>71</sup>

Silver oxide oxidation of 4,5-methylenedioxy-2-propylphenol in the presence of ethyl vinyl ether. Silver oxide (0.32 g) was added to a stirred solution of 4,5-methylenedioxy-2-propylphenol (0.25 g) in ethyl vinyl ether (10 ml). The suspension was stirred for 30 minutes at room temperature and filtered. The ethyl vinyl ether was evaporated, and an nmr spectrum showed a complex mixture of products which had no peaks indicative of an ethoxy group.

Palladium chloride oxidation of 1,1-bis(2-hydroxy-4,5-methylenedioxyphenyl)ethane. Sodium acetate (1.0 g) and 1,1-bis(2-hydroxy-4,5-methylenedioxyphenyl)ethane (0.25 g) were dissolved in methanol (25 ml) and water (5 ml). Palladium chloride (0.18 g) was added and the mixture was stirred at room temperature for 3 hours. The mixture was filtered, diluted to twice its volume with water, and extracted twice with ether. The ether extracts were combined, washed with dilute sodium hydroxide solution and water, and dried over magnesium sulfate. Evaporation of the ether gave one product (yield 0.23 g, 92%). The product was further purified by chromatography on silica-gel with methylene chloride as the eluent. The nmr spectrum ( $\text{CDCl}_3$ ) had peaks at 1.13 (d, 3H), 3.6 (m, 1H), 5.4 (d, 1H), 5.42 (s, 1H), 5.75 (s, 4H), 6.17 (s, 1H), 6.35 (s, 1H). The infrared spectrum (film) had peaks at 2980, 2920, 2900, 1650, 1480, 1412, 1390, 1308, 1227, 1155, 1043, 945, 850, 840, and 790. The mass spectrum gave a parent ion at  $m/e = 300$ . The UV spectrum (ethanol) had maxima at 250( $9.45 \times 10^3$ ), 310( $7.76 \times 10^3$ ), and strong end absorption. The compound was too unstable to get an element analysis.

Potassium ferricyanide oxidation of 1,1-bis(2-hydroxy-4,5-methylenedioxyphenyl)ethane. A solution of 1,1-bis(2-hydroxy-4,5-methylenedioxyphenyl)ethane (2.0 g) in benzene (100 ml) was stirred at room temperature for 1 hour with a

solution of potassium ferricyanide (20 g) and potassium hydroxide (11 g) in water (150 ml). The benzene layer was separated, washed with water, dried over sodium sulfate, and evaporated to give the product (yield 1.06 g, 50%). Comparison of the nmr spectrum of the product to that of the product from the palladium chloride oxidation showed the two to be the same compound.

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