

CLEAVAGE OF BENZYL ARYL ETHERS

BY CHLORINE

A Thesis

by

Anne-Marie F. Fruteau de Laclos

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DEDICATION

To my family,  
especially my husband, Eric, and my son, Jean-Baptiste,  
who are my life and my strength,  
I dedicate this thesis.

They have supported me at all times, and have put up  
with my extended absences from the family scene, so that  
I might invest a part of my life and a lot of my  
strength in completing this work and achieving my goal.

**" Es irrt der Mensch so lang er strebt "**

Goethe (Faust)

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## ABSTRACT

In order to extend application of the gel-degradation mechanism of delignification, model compounds of the general structure (3,4-dimethoxyphenyl)-CH(OR)R' were treated at room temperature with increasing charges of molecular Cl<sub>2</sub> in glacial HOAc.

Catalytic amounts of Cl<sub>2</sub> cleaved benzyl aryl ether bonds (OR=2-methoxy-4-methylphenoxy) before any ring chlorination occurred. Yields of cleavage decreased in the order: R'=H; R'=-CH<sub>2</sub>-2-methoxyphenoxy; R'=-CH(CH<sub>2</sub>OH)-2-methoxyphenoxy. These results support the concept that the delignification of wood pulp by chlorine results from benzyl aryl ether cleavage. The conditions of the reaction, as well as control reactions with hydrochloric acid, suggest that the cleavage is due to conventional acid hydrolysis induced by chlorine. The experimental evidence does not rule out another possible mechanism in which the cleavage is initiated by molecular chlorine.

Benzyl ether links were generally stable in models of the benzyl alkyl type, whose primary reactions were ring chlorination. A large excess of chlorine caused side-chain displacement, hitherto considered the primary reaction in the solubilization of lignin.

## RÉSUMÉ

Afin d'étendre à la délignification l'application du mécanisme de dégradation de gel, des composés modèles de structure générale (diméthoxy-3,4 phényl)-CH(OR)R' furent traités à température ambiante dans l'acide acétique glacial par des taux croissants de chlore moléculaire.

Des quantités catalytiques de Cl<sub>2</sub> provoquent la rupture des liaisons benzyl aryl éther (OR=méthoxy-2 méthyl-4 phénoxy) avant même la chloration des noyaux aromatiques. Les rendements de la réaction de coupure diminuent dans l'ordre suivant: R'=H; R'=-CH<sub>2</sub>-méthoxy-2 phénoxy; R'=-CH(CH<sub>2</sub>OH)-méthoxy-2 phénoxy. Ces résultats étayent le concept selon lequel la délignification de la pâte de bois par le chlore résulte de la rupture des liaisons benzyl aryl éther. Les conditions expérimentales, ainsi que des réactions de contrôle avec l'acide chlorhydrique, suggèrent que la rupture est causée par l'hydrolyse acide conventionnelle induite par le chlore. Les faits expérimentaux n'excluent pas la possibilité d'un autre mécanisme dans lequel la rupture est initiée par le chlore moléculaire lui-même.

Par contre, les liaisons benzyl éther sont généralement stables dans les modèles de type benzyl alkyl; les réactions premières sont la chloration du noyau aromatique. Un large excès de chlore provoque l'élimination de la chaîne latérale, réaction qui avait été jusqu'à présent considérée comme la réaction première de la solubilisation de la lignine.

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## CHAPTER I

### GENERAL INTRODUCTION

For many years, the reaction of chlorine with lignin has constituted the first stage of the conventional commercial bleaching of chemical wood-pulps. Despite decades of research, the mechanism whereby chlorine breaks down the lignin polymer and solubilizes it has not been completely elucidated - particularly in the light of newer theories of delignification as a process of gel degradation. To this latter end, this thesis describes a series of chlorination experiments with specifically designed compounds as models for the structural units of lignin.

#### I-1- Introduction

To-day, more than 150 years after Anselme Payen discovered and defined it as "encrusting material", lignin has no unambiguous and unanimously accepted structure. From the considerable knowledge amassed since then about lignin, it has at least been possible to identify the two main factors that make its structure the *ignis fatuus* for lignin chemists.

First is the disconcerting heterogeneous character of lignin. It has actually not one single structure<sup>1a</sup>: Significant differences have been observed, not only among plant or wood species, but also between various locations within a single tree, the variations depending upon the history of growth of the tissues. Moreover, it is also well established<sup>2</sup> that the distribution and chemical nature of lignin are not homogeneous within the wood cell itself. The plural name "lignins" is therefore more appropriate.



The second major obstacle to a clear understanding of the nature of lignins is that they are virtually impossible to isolate without inducing structural changes<sup>1b</sup>.

Therefore, there is no simple and direct route towards characterizing lignins. Instead, it is necessary to combine information from four different approaches: (1) the study of lignification, i.e. biosynthesis; (2) the investigation of the properties of isolated lignins; (3) the study of delignification, starting from whole wood or isolated lignins, with analysis of the products resulting from degradative reactions; and (4) research on the reactions of relatively simple compounds that are models for segments of the lignin macromolecules. Non-degradative methods such as UV, IR, Raman<sup>3</sup>, liquid state, and CP/MAS solid state NMR spectroscopy<sup>4</sup>, and SEM- and TEM-EDXA techniques<sup>5</sup> provide useful information about the structure and distribution of isolated lignin and of the proto-lignin in the cell walls.

Despite increasingly sophisticated means of analysis, lignin structure, in many ways, maintains its enigmatic character.

For the chemical pulping industry, lignins are a troublesome material. The liberation of the cellulosic fibers from their lignin matrix, the process of delignification, is the basic aim of chemical pulping. Lignin chemistry and pulping chemistry can thus be considered as partners. On the one hand, the earliest developments in the structural chemistry of lignins were derived from their behaviour during chemical pulping processes. On the other hand, a clear understanding of the structure, properties, and reactivity of lignins

now appears essential for achieving rational control of pulping and bleaching processes. Most investigations have focussed on lignins of coniferous species -and especially of spruce-, which are economically important to the paper industry.

The environmental awareness of recent years has made these points of chemistry all the more urgent. Not only does industry need to learn how to control pollution arising from pulping (sulfur compounds) and bleaching (chlorinated compounds), but it also needs to take better advantage of the huge potential of by-product lignins as a chemical feed-stock.

Thus it is both economic and environmental interests that have given renewed impulse to lignin chemistry.

## I-2- Structure

### I-2 a- Chemical structure of lignins

Ironically, most of the effort expended for finding a well defined chemical structure for lignins has only led to providing evidence for their heterogeneous character at all levels. To our present knowledge,

(1) lignins represent about 30% of coniferous wood, a natural composite material, in which they are unevenly distributed<sup>2</sup> (Figure I-1), and physically and chemically bound to polysaccharides<sup>1c</sup>.

(2) lignins exhibit major structural differences<sup>1d</sup> depending on

a) the wood species of origin: softwood lignins are made up of guaiacylpropane units, hardwood lignins of both guaiacyl- and syringylpropane units. Lignins occur also in grasses, and are composed

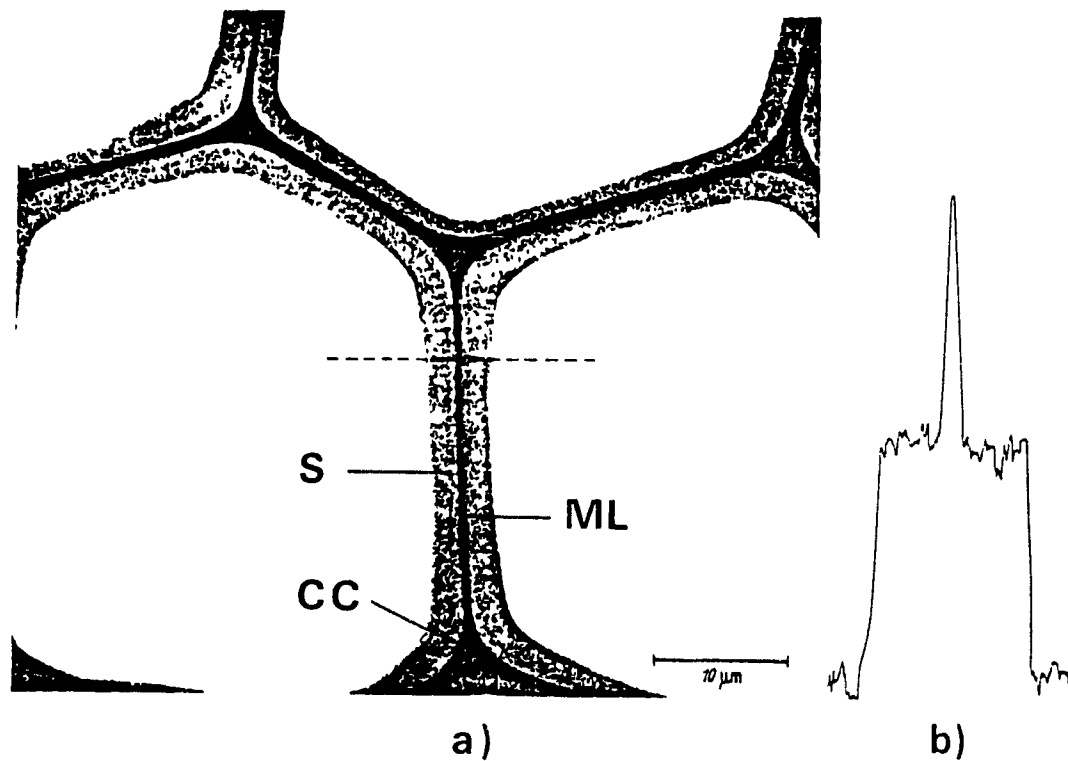


Figure I-1. Transverse section of a spruce tracheid<sup>6</sup>.

a) UV microscopy; b) UV densitometry of section indicated by - - - - in a). S: secondary wall; ML: compound middle lamella; CC: cell corner.

of guaiacyl-, syringyl-, and p-hydroxyphenylpropane units.

- b) the growth history of the tree: reaction wood differs from normal wood by its lignin content and the composition of the lignin.
- c) the location within the cell walls.
- d) the isolation procedure.

Analytical data must thus be considered for each specific type of lignin obtained by a given isolation procedure and from a given class of wood. Only if these considerations are respected do the data become a reliable link between scientific reasoning and reality. Comparing the theoretical calculation of elemental composition of a proposed structural model with the analytical results obtained from a particular type of lignin is very useful for checking the validity of the model. Examples of theoretical and experimental values are given in Table I-1, from which it is clear that the elemental composition of lignins has not yet been established.

Nevertheless, taking into account the intrinsic variations in the nature of lignins, our knowledge of the chemical structure of lignins, after several decades of thorough research, has reached a somewhat satisfactory level of exactness.

Since the 1940s<sup>7</sup>, lignins have been known to be polymers of phenylpropane (or C<sub>9</sub>) units. Coniferyl, synapyl and p-coumaryl alcohols (Figure I-2) were identified as the immediate biosynthetic precursors of lignins<sup>8</sup>.

Table I-1 . Analytical composition of spruce lignins  
 (MWL: Milled Wood Lignin; CEL: Cellulolytic Enzyme  
 Lignin).

---

|                                         |                                                                                        |                                   |
|-----------------------------------------|----------------------------------------------------------------------------------------|-----------------------------------|
| <u>Structural models:</u>               | C <sub>9</sub> H <sub>7.76</sub> O <sub>2.38</sub> (OCH <sub>3</sub> ) <sub>0.92</sub> | (Freudenberg <sup>9</sup> )       |
|                                         | C <sub>9</sub> H <sub>8.11</sub> O <sub>2.56</sub> (OCH <sub>3</sub> ) <sub>0.89</sub> | (Forss and Fremer <sup>10</sup> ) |
| =====                                   |                                                                                        |                                   |
| <u>Isolated lignins</u> <sup>10</sup> : | C <sub>9</sub> H <sub>8.83</sub> O <sub>2.37</sub> (OCH <sub>3</sub> ) <sub>0.96</sub> | (MWL; Bjorkman)                   |
|                                         | C <sub>9</sub> H <sub>8.05</sub> O <sub>2.84</sub> (OCH <sub>3</sub> ) <sub>0.96</sub> | (MWL; Chang)                      |
|                                         | C <sub>9</sub> H <sub>7.92</sub> O <sub>3.11</sub> (OCH <sub>3</sub> ) <sub>0.95</sub> | (CEL; Chang)                      |

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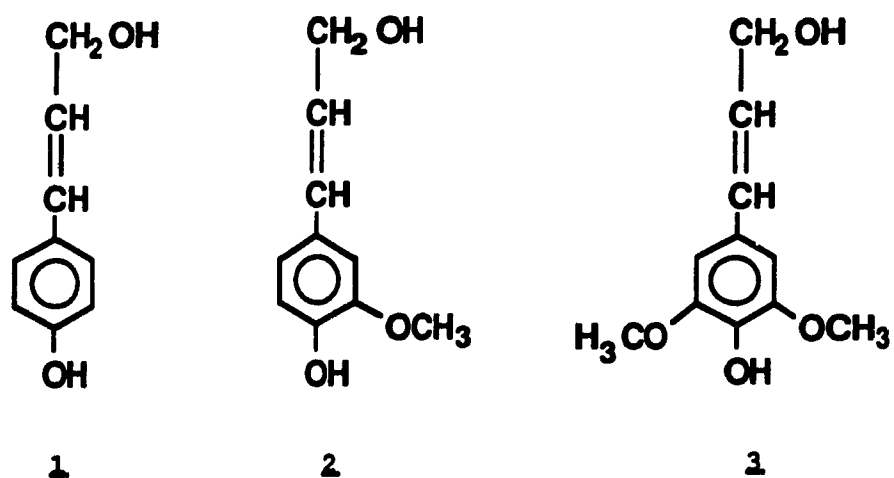


Figure 1-2. Precursors of lignins<sup>8</sup>. 1: p-Coumaryl alcohol,  
2: Coniferyl alcohol, 3: Sinapyl alcohol.

Degradative studies of lignins, and of model compounds representing both softwoods and hardwoods, gave evidence for the phenylpropane skeleton. Extensive work on the biosynthesis of lignins has revealed the nature of the C<sub>3</sub> side-chain, of the functional groups (Table I-2) and of the various types of linkages present in the polymer (Figure I-3), as well as their proportions in the structure (Tables I-3 and I-4). More than two thirds of the C<sub>9</sub> units are linked by ether bonds, and about one third by carbon-to-carbon bonds. Arylglycerol-beta-aryl ethers constitute about half of the linkages, and most of the C-C bonds link up with at least one C<sub>5</sub>, while phenylcoumaran, biphenyl, and benzyl aryl ether (alpha-aryl ether) structures are also present in non-negligible proportions.

These experimental data support and are explained by the biosynthetic mechanisms. Peroxidases initiate the polymerization process by dehydrogenating the phenolic group<sup>6</sup>. Resonance stabilized phenoxy radicals (Figure I-4) are generated, and can combine into a variety of dimers, or dilignols (Figure I-5)<sup>7</sup>. The complexity of the resulting lignin molecule is ascribable to the multiplicity of possible couplings between the various mesomeric forms. The relative occurrence of structures such as  $\beta$ -O-4 ethers, pinoresinol (C $\beta$ -C $\beta$ ) and phenylcoumaran (C $\beta$ -C<sub>5</sub>) in lignins can be accounted for by the relative frequency with which individual sites engage in a coupling reaction. This frequency depends on their relative electron densities. A considerable structural difference between lignins in various parts of the cell wall<sup>11</sup> suggests, however, that polymerization is probably not a simple statistical process governed by the stability of the phenoxyl radicals, and that the wood cells have a direct, or indirect means of controlling the polymerization<sup>12</sup>.

Table I-2. Functional groups of lignins per 100 C<sub>9</sub> units<sup>13</sup>.

| Group <sup>a</sup>       | Spruce<br>lignin | Birch<br>lignin |
|--------------------------|------------------|-----------------|
| Methoxyl                 | 92-96            | 139-158         |
| Phenolic hydroxyl (free) | 15-30            | 9-13            |
| Benzyl alcohol           | 15-20            |                 |
| Noncyclic benzyl-ether   | 7-9              |                 |
| Carbonyl                 | 20               |                 |

<sup>a</sup> The contents may vary depending the origin of the lignin (e.g. middle lamella or secondary wall lignin).



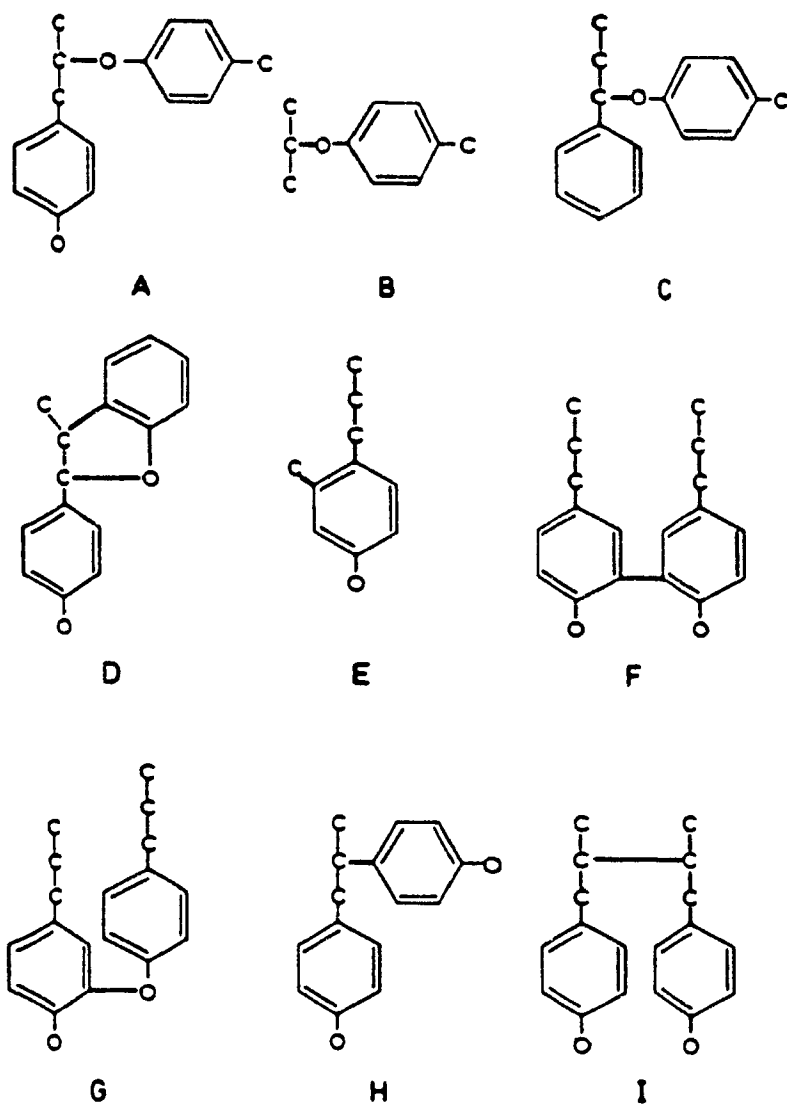


Figure I-3. The most common linkages between phenylpropane units<sup>7</sup>.

Table I-3 .Percentages of different types of bonds in Spruce (*Picea abies*) Lignin (MWL)<sup>7</sup>.

| Bond type <sup>a</sup> |                                           | Percentage |
|------------------------|-------------------------------------------|------------|
| A                      | Arylglycerol- $\beta$ -aryl ether         | 48         |
| B                      | Glyceraldehyde-2-aryl ether               | 2          |
| C                      | Noncyclic benzyl aryl ether               | 6-8        |
| D                      | Phenylcoumaran                            | 9-12       |
| E                      | Structures condensed in 2- or 6-positions | 2.5-3      |
| F                      | Biphenyl                                  | 9.5-11     |
| G                      | Diaryl ether                              | 3.5-4      |
| H                      | 1,2-Diarylpropane                         | 7          |
| I                      | $\beta,\beta$ -linked structures          | 2          |

<sup>a</sup> Letters A through I are illustrated in Figure I-3.

Table I-4 . Percentages of different types of bonds in Birch (*Betula verrucosa*) Lignin (MWL)<sup>1</sup>.

| Bond type <sup>a</sup> | Guaiacyl | Syringyl | Total   |
|------------------------|----------|----------|---------|
| A                      | 22-28    | 34-39    | 60      |
| B                      |          |          | 2       |
| C                      |          |          | 6-8     |
| D                      |          |          | 6       |
| E                      | 1-1.5    | 0.5-1    | 1.5-2.5 |
| F                      | 4.5      |          | 4.5     |
| G                      | 1        | 5.5      | 6.5     |
| H                      |          |          | 7       |
| I                      |          |          | 3       |

<sup>a</sup> Letters A through I are illustrated in Figure I-3.

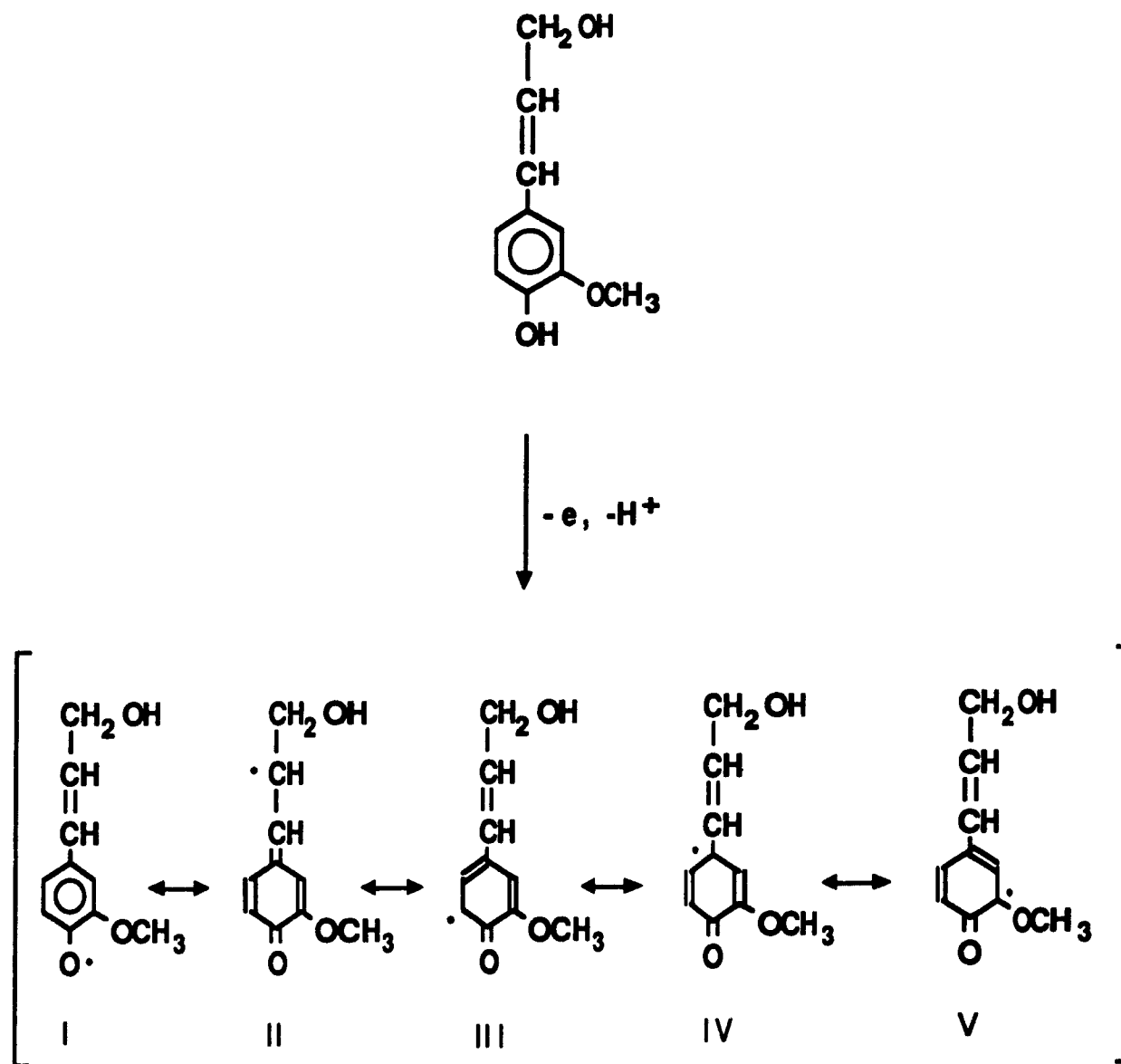


Figure I-4. Resonance-stabilized phenoxo radicals resulting from the enzymatic dehydrogenation of coniferyl alcohol<sup>7</sup>.

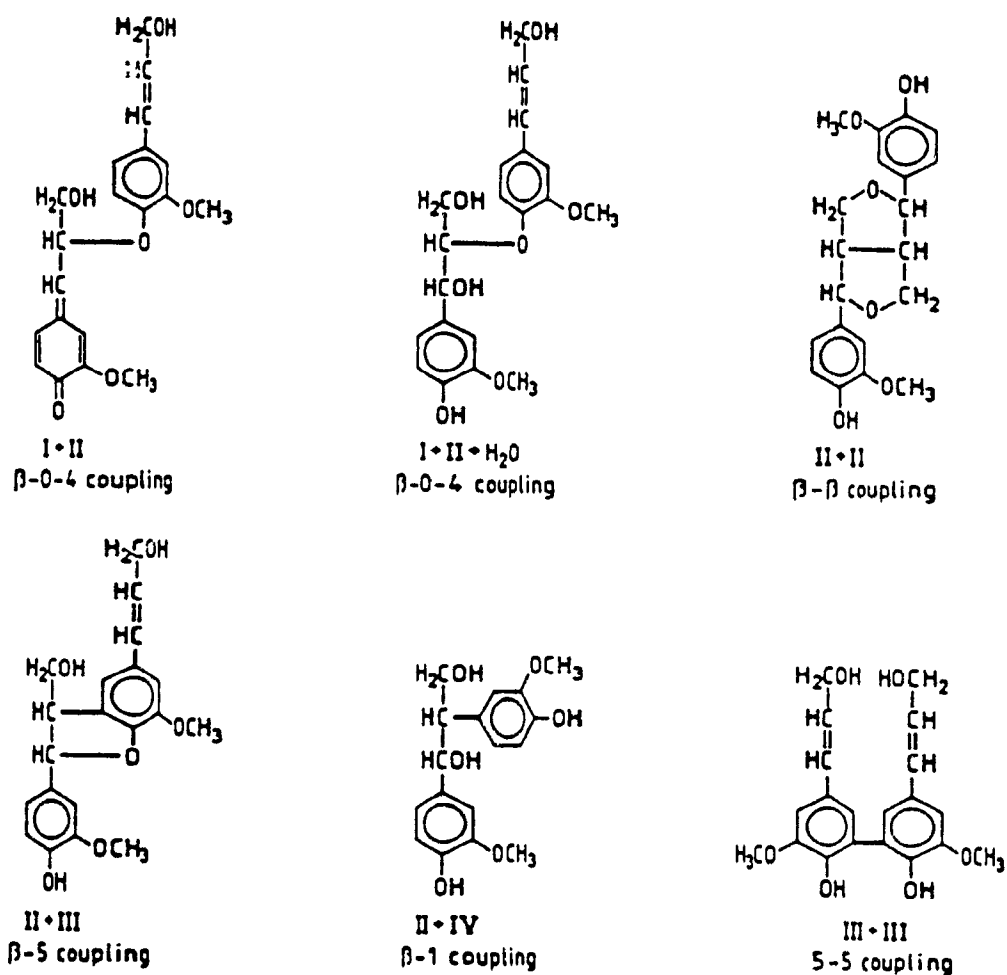


Figure I-5 . Typical dilignol structures<sup>7</sup>. Roman numerals from Figure I-4.

I + II: Quinonemethide

I + II + H<sub>2</sub>O: Guaiacylglycerol- $\beta$ -coniferyl ether

II + II: D,L-Pinoresinol

II + III: Dehydroconiferyl alcohol

II + IV: 1,2-Diguaiacylpropane-1,3-diol

III + III: Dehydrobisconiferyl alcohol

It is now generally accepted<sup>13</sup> that lignin polymer is the result of two complementary mechanisms: (1) dehydrogenative addition, in which either the radical monomers combine with oligomers ("bulk polymerization"), or add to the end of the growing polymer ("end-wise polymerization"), and (2) non-dehydrogenative addition, in which the quinone methide (Figure I-5) reacts with water, carbohydrates, or phenols, to yield  $\alpha$ -O-4,  $\beta_5$ - $\beta_5$ , and 5-O-4 linkages. While the first mechanism produces branched and linear polymers, the second includes the formation of points of cross-linking. Controversy concerning the way phenylpropane units are linked in lignins has given rise to a plethora<sup>14</sup>, of formulations for the "building block" representing typical segments of the lignin polymer, from Freudenberg's 18-unit model<sup>8</sup> (Figure I-6) based on biosynthetic evidence, to Glasser and Glasser's 81-unit model obtained by computer simulation and based on degradative experimental data<sup>14</sup> (Figure I-7). Forss and Fremer<sup>10</sup>, criticizing Freudenberg's formula for its linear character (Figure I-8) and for its failure to agree with experimental degradation data, proposed recently a more compact 18-unit block (Figure I-9) which they called a "repeating unit". The criticism of linearity in the Freudenberg model does not appear valid. Bolker and Brenner<sup>15</sup> had earlier pointed out that the structure was consistent with being a part of a cross-linked macromolecule composed of short, slightly branched chains (Figure I-10).

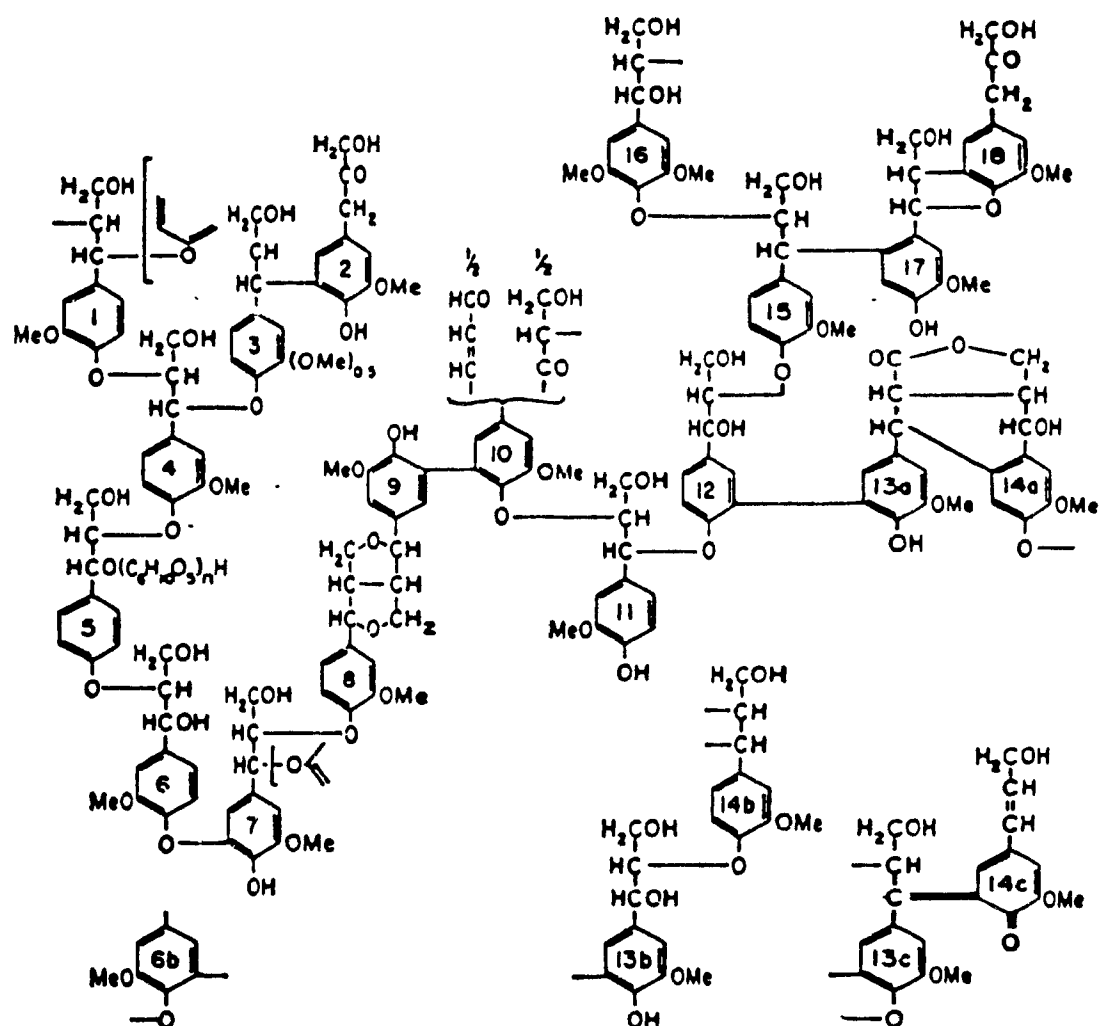


Figure I-6 . A structural representation of spruce lignin  
(Freudenberg) <sup>8</sup>.

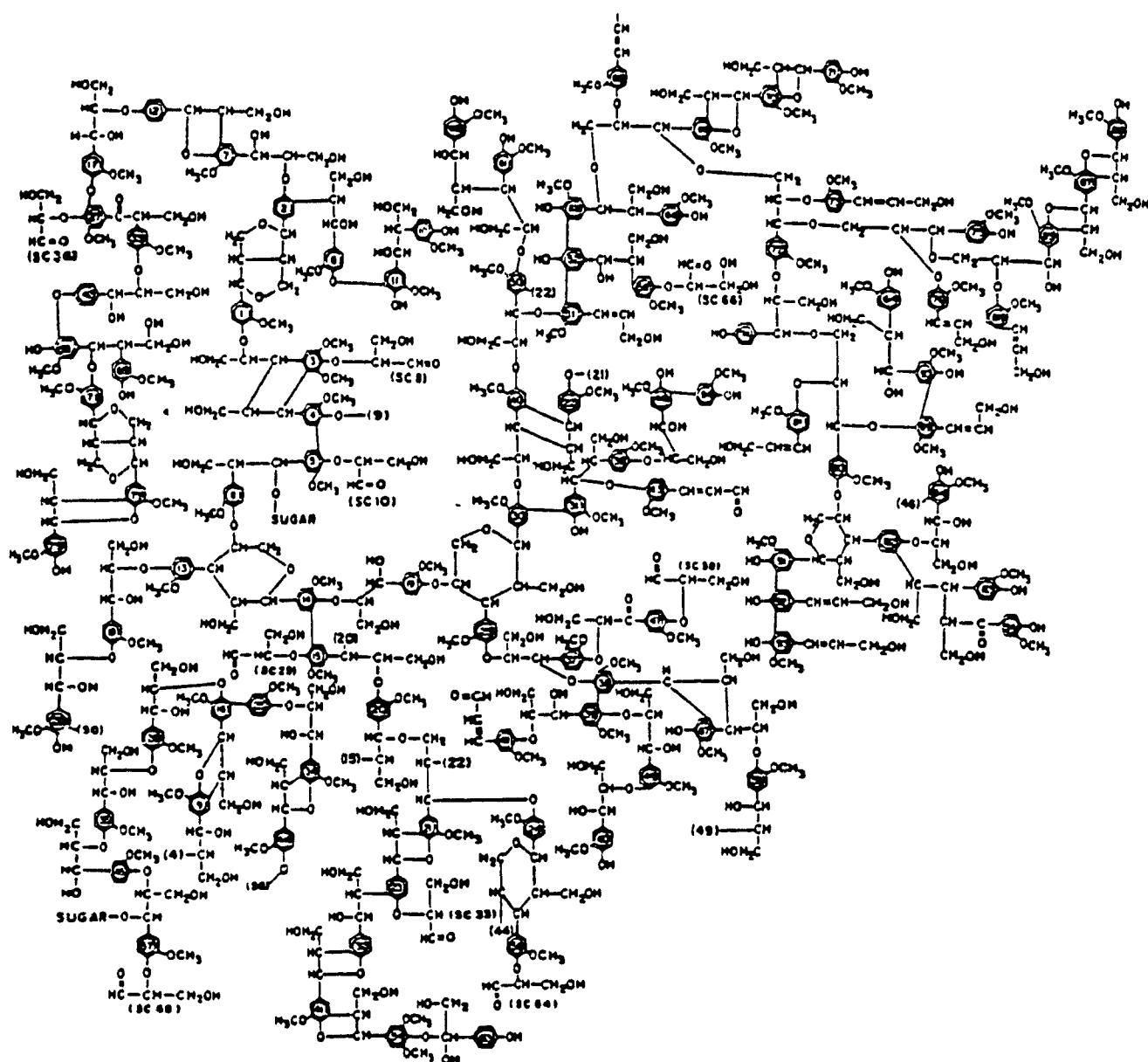


Figure I-7. Softwood lignin model designed by computer evaluation  
(Glasser and Glasser)<sup>14</sup>.



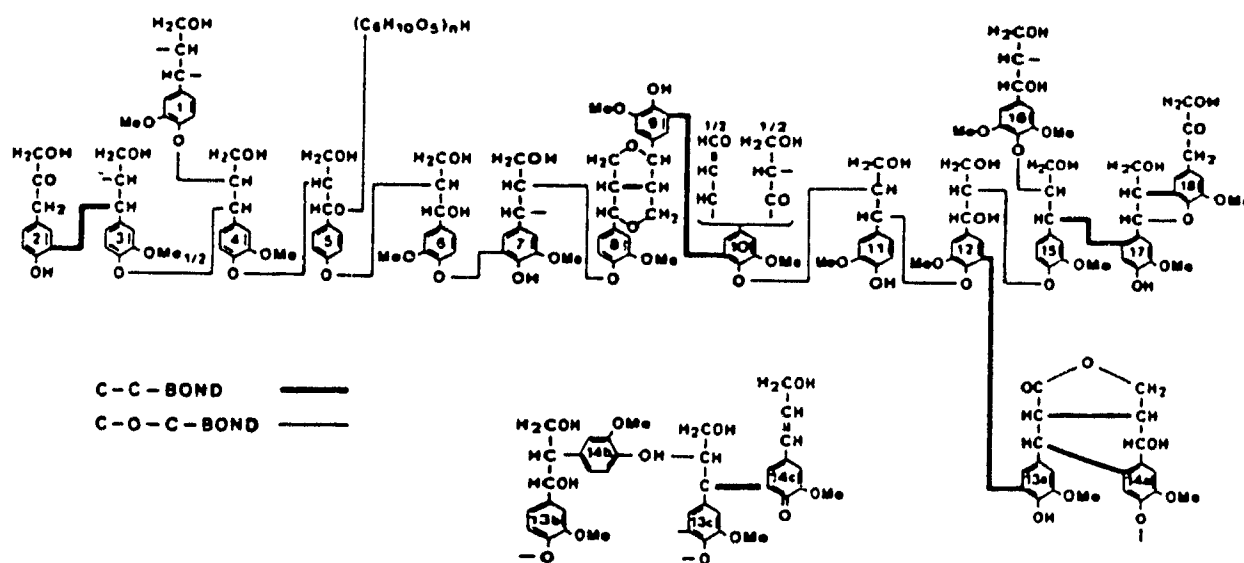


Figure I-8. Freudenberg's latest formulation of spruce lignin, rearranged in a more linear form<sup>10</sup>.

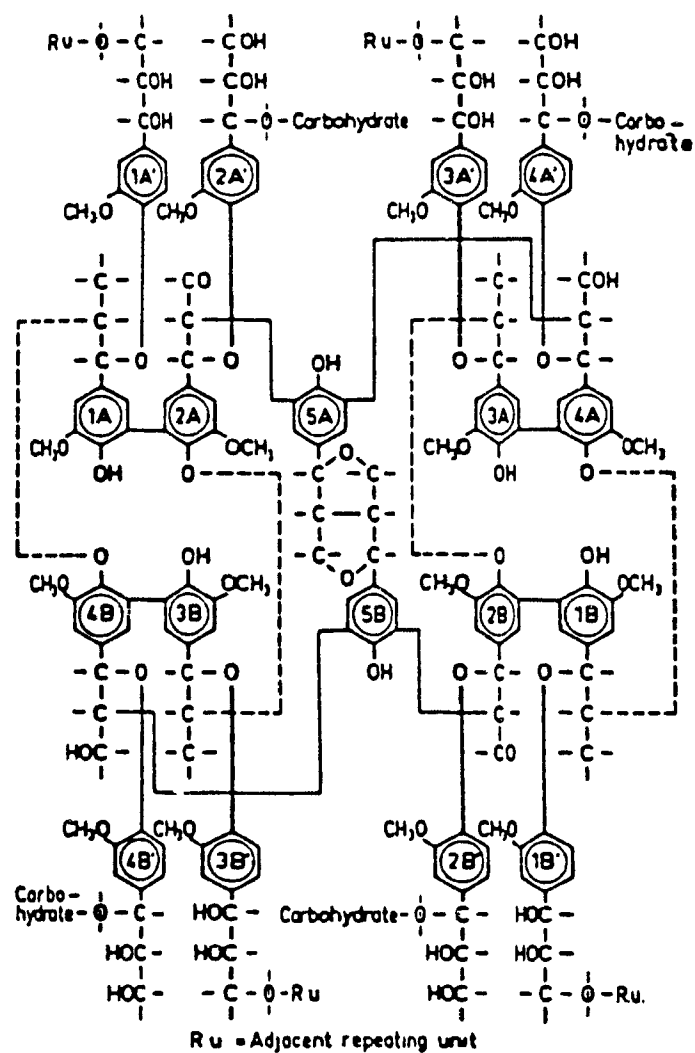
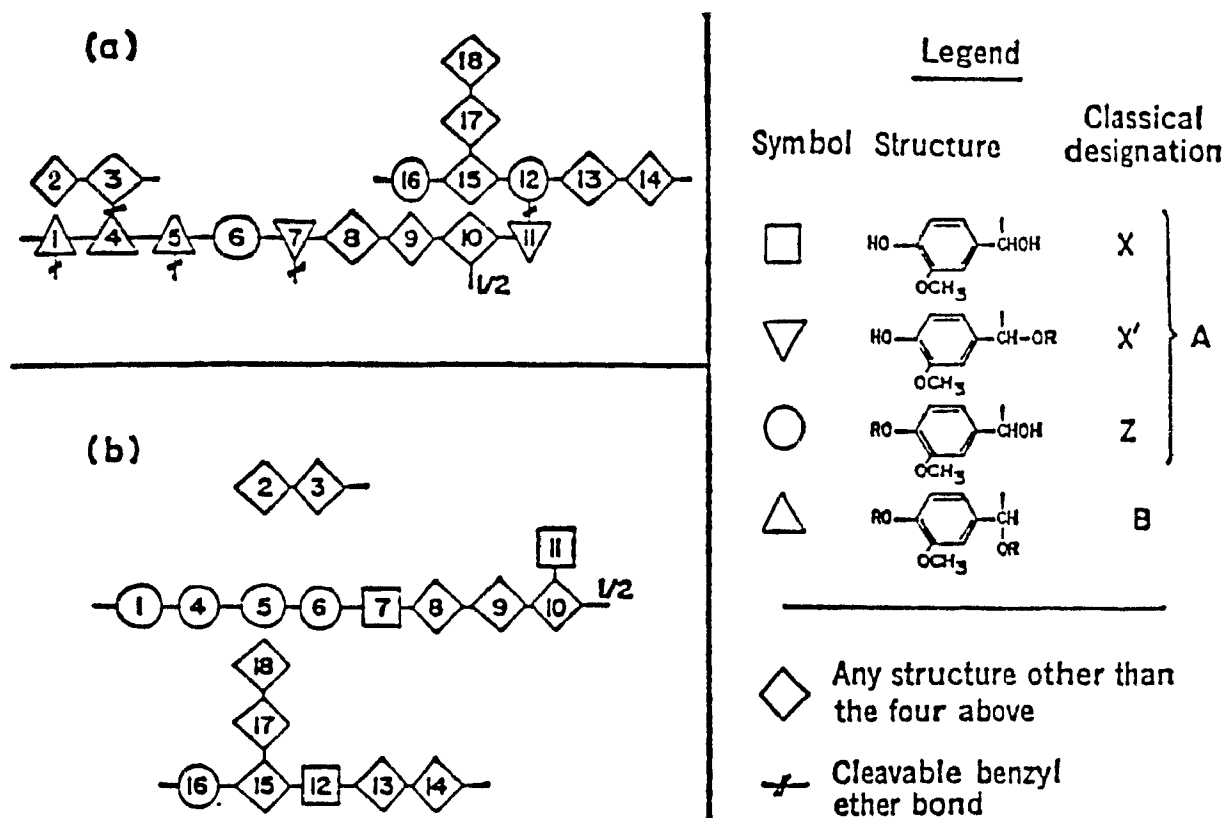


Figure I-9. Forss and Fremer's "repeating unit" of spruce lignin<sup>10</sup>.



**Figure I-10 .** Cleavage of ether bonds in cross-linked lignin macromolecule<sup>15</sup>. (a) Freudenberg model of lignin (Figure I-6), simplified, indicating the five locations of cross-links at the sites of benzyl ether groups. (b) The results of cleaving the benzyl ether bonds: formation of linear or slightly branched fragments.

In the study of delignification, much importance has been ascribed to bonds that are very frequent or have a strong influence on lignin fragmentation. Accordingly, the arylglycerol- $\beta$ -aryl ether bond and the influence of phenolic units on its cleavage, have been considered of primary importance in delignification<sup>16</sup>, and the reactivity of appropriate models has been thoroughly studied<sup>7</sup>. Such investigations, however, were generally completed in the light of organic chemistry, and ignored the polymeric nature of lignins.

#### I-2 b- Polymer properties of lignins .

X-rays diffraction<sup>17</sup> has unambiguously shown that lignins are amorphous materials, but the question of whether they are highly branched or cross-linked polymers still arouses polemics, even though much evidence supporting the idea of a cross-linked network has been advanced.

The existence of a linear structure can be readily ruled out, since the polyfunctionality of the C<sub>9</sub> units undoubtedly confers a branched character on lignins. Simple reasoning<sup>18</sup> shows that in a branched polymer, when there is no intramolecular condensation, the number of free chain-ends is always higher than the number of branch points. Now, in the model proposed by Freudenberg<sup>8</sup>, for instance, 6 to 7 units out of 18 are trifunctional, while only 2 to 3 units are chain ends. It is thus clear that intramolecular bonds do exist in the lignin structure, in sufficient number to generate a highly cross-linked network.

As early as 1952, Schuerch<sup>19</sup>, after considering the physiological inertness of lignins, their insolubility into good organic solvents, and their similarity to cross-linked rubber in swelling behaviour, proposed the possibility that they had a highly cross-linked character.

From the polydisperse nature of isolated lignins, two controversial theories were proposed, the so-called "condensation", and "gel degradation" theories<sup>20a</sup>. The former, which stated that lignin was actually composed of small reactive molecules that polymerize during any method of isolation, was eventually ruled out<sup>21</sup>. In the gel degradation theory, natural lignins are taken as a random three-dimensional infinite polymer whose fragmentation and solubilization follow the theory of Flory and Stockmayer (F-S theory)<sup>20b</sup>. A third theory of delignification<sup>22</sup>, held that a physical factor, the sieving effect of the porous cell wall, was responsible for the increasing molecular weight of degraded lignins observed as fragmentation proceeds. Delignification studies on "naked-lignin" preparations, -i.e. preparations where carbohydrates have first been removed from around the lignin, such as by cuoxam and periodate-, have proven<sup>23</sup> that this physical factor, if it exists, is not responsible for the increase in molecular weight of the degraded lignins.

Data<sup>20c</sup> from viscosity, polydispersity and molecular weight of extracted lignins has increased the acceptability of the gel degradation theory. However, all physical properties have been determined on soluble lignins preparations, which are actually degraded lignins, and this has left open to criticism any inferences concerning the in-situ polymer.

Support for the idea of a cross-linked structure of lignin was first obtained from the quantitative treatment of delignification based on F-S theory by Szabo and Goring<sup>24</sup>, then by Bolker and Brenner<sup>15</sup>.

Szabo and Goring considered lignin to be the result of cross-linking of di- and trifunctional monomers. They developed a theoretical correlation between the increasing molecular weight of the dissolved lignin and the degree of delignification, and proposed a model that could predict, at various stages of delignification, the concentration of residual lignin in different morphological regions, as well as the average molecular weight of the sol fraction. Experimental data from Kraft and sulfite delignification agreed qualitatively with their theory. However, they had made the assumption of random degradation, with all functional groups, namely all ether bonds, having identical reactivity, and this is rather unrealistic in terms of organic chemistry. Bolker and his coworkers<sup>15, 23, 25</sup> considered acid sulfite delignification in relation to model compound studies, and specifically assigned the role of cross-link to the benzyl ether bond (Figure I-10) according to its well known higher reactivity. These studies and the experimental data related to different types of delignification<sup>21, 25a, 26</sup> suggested that lignin behaves like a polymer derived from the cross-linking of primary chains (linear or branched) with an average degree of polymerization ( $\overline{DP}$ ) of 18. When degradation is conducted under different conditions<sup>25b</sup>, such as by chlorine monoxide, or on other types of lignins, such as cuoxam and periodate, the apparent  $\overline{DP}$  of the primary chain was found to be 7.

From the mathematical treatment of the degelation theory, Yan<sup>27</sup> derived a primary size distribution, and experimental data from the neutral dioxane extraction of softwood sawdust<sup>18</sup> indicated that the primary chains are polydisperse, with a high degree of branching. In the same study, soluble fractions obtained from the mild acid hydrolysis of wood sawdust exhibited increasing polydispersity as the delignification progressed, as expected from the breakdown of a gel<sup>28</sup>.

Most of the evidence for a cross-linked network has so far been derived from acidic delignification. However, recent application<sup>29</sup> of the degelation theory to alkaline delignification of soft and hardwoods suggested that softwood lignin consists of primary chains cross-linked in a tetrafunctional way (two trifunctional units may pair up to form a tetrafunctional cross-link). Interestingly, the authors found longer primary chains and lower cross-linking density in hardwood lignin than in softwood, and this may explain the faster delignification of hardwood. They also obtained quantitative evidence of the topological inhomogeneity of lignin, with a cross-linking density about twice as high in the middle lamella as in the secondary wall lignin. This finding rationalizes the distinction made earlier by Szabo and Goring<sup>24</sup> regarding the rate of delignification between these two morphological regions.

### I-3- Necessity for the study of model compounds

The elucidation of the polymer structure of lignins via the F-S theory is based on Flory's assumptions<sup>30</sup> that "...all functional groups are chemically equivalent and hence equally reactive..." and "...independent of the size or structure of the molecule (or network) to which they are attached...". This over simplification is a limitation of the F-S theory of delignification. It is therefore necessary to identify the linkages by the study of appropriate model compounds under delignifying conditions.

According to the present knowledge of lignin structure, the reactions of trifunctional, (i.e., trietherified models bearing an alkoxyl group at position 4, and an aryloxy group at the alpha and beta positions) must be examined in order to obtain information on the role of the benzyl ether linkage during lignin fragmentation. In acidic delignification, the relative instability of the benzyl ether bonds has been well substantiated<sup>31</sup>; they are often referred to as the reactive bonds in lignins, and are taken as responsible for lignin degradation in acidic media, even during the vibratory ball milling of wood<sup>32</sup>. Until recently, however, none of the trietherified models studied showed much instability in alkaline delignification<sup>33</sup>. These models contained the alpha alkyl ether bond. Recently, Mirshokraie<sup>34</sup> made an important step forward with the finding that models with alpha aryloxy groups were actually NOT stable under conditions of alkaline hydrolysis. This results suggests that the alpha alkyl ethers were not appropriate models for investigating the mechanism of alkaline delignification, and that benzyl ether bonds, rather than  $\beta$ -O-4 linkages as had been proposed earlier<sup>27,35</sup>, are responsible for lignin degradation in alkaline delignification.



It also suggests that models used for the study of the mechanism of delignification by chlorination may not have been appropriate. Although a great deal of investigation<sup>36</sup> has been conducted on the chlorination of phenylpropane models bearing an alpha alkoxy group, there is very little information on the reaction of models with an alpha aryloxy group. Accordingly, the research described in this thesis includes reactions of molecular chlorine with tri-etherified lignin model compounds bearing alpha aryloxy groups.

#### I-4- Relevance of the present work to delignification

Lignin units of the benzyl alcohol type are known<sup>37,38</sup> to be extensively cleaved by the action of an excess of chlorine. At low chlorine charge, substitution on the aromatic rings occurred, as in alpha alkyl ethers. These results, together with the observation that about 20% of the units in lignin are of the benzyl-alcohol type, conferred a remarkable importance on the side-chain electrophilic displacement in the delignification reaction by chlorine. It became generally accepted<sup>38</sup> that degradation of units of the alpha-hydroxyl type contributed significantly to lignin solubilization process. However, from the point of view of the gel degradation theory, and considering lignin as a three-dimensional cross-linked network, these particular units represent a linear part of the polymer, and their degradation, however extensive it is, and however numerous these units are, is of low efficiency in the overall network breakdown.

The stability of the benzyl-alkyl ether bond reported in the literature<sup>38</sup> confers on the initial dimeric structure a durability which does not serve the purpose of delignification. As fully etherified compounds with an alpha alkyl-ether substituent were generally taken as representative of the trietherified units in lignin, their stability seemed to bring more evidence that delignification by chlorine could proceed only through side chain cleavage, whose efficiency is restricted to structures bearing a free hydroxyl group on the alpha position. These experimental results thus stood against the view that lignin was a cross-linked network that degrades according to the gel degradation theory.

However, the extremely efficient catalytic cleavage that we have observed in the reaction of molecular chlorine with benzyl aryl ethers provided evidence that benzyl alkyl ethers were not truly representative of the tri-etherified units in lignin. The experimental results obtained here from model compounds are in perfect agreement, and give the means to rationalize the observation made by several authors more than 40 years ago<sup>39</sup>, that delignification was much more efficient at low pH, when molecular chlorine exists as the predominant species in aqueous solution. These results suggest that the primary network-breaking mechanism in chlorination is the same as in acidic and alkaline delignification: cleavage at the alpha position in a tri-etherified unit. They open the door to applying the gel-degradation theory to delignification by chlorine.

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<sup>36</sup> **DENCE C. W., ANNERGREN G. E.**

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<sup>37</sup> **SARKANEN K. V., DENCE C. W.**

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CHAPTER II

CLEAVAGE OF THE BENZYL ARYL ETHER BOND IN  
NON-PHENOLIC LIGNIN MODEL COMPOUNDS

## INTRODUCTION

The beta-0-4 linkage, as the most prominent feature in lignin<sup>1a</sup> - 48% in spruce milled-wood lignin (Table I-3) -, has been thoroughly investigated for its role in virtually every alkaline, neutral and acidic reaction in pulping and bleaching processes. By the same reasoning, the lack of attention paid by lignin chemists to non-phenolic benzyl aryl ether structures probably reflects the generally accepted view<sup>1b,2</sup> that they occur in the lignin polymer in proportions - 6 to 8 % in spruce milled-wood lignin (Table I-3) - that are too small to significantly affect its chemistry. Whereas new knowledge is indeed available on the acid hydrolysis of benzyl aryl ethers<sup>3</sup>, this type of compound has not been considered in research on chlorination. The most recent and, to our knowledge, the only piece of information on the reactivity of benzyl-aryl ether bonds towards molecular chlorine was published by Sintenis<sup>4</sup>, in 1872.

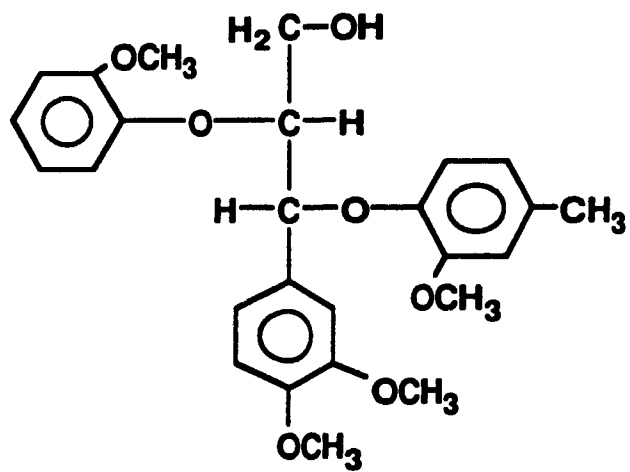
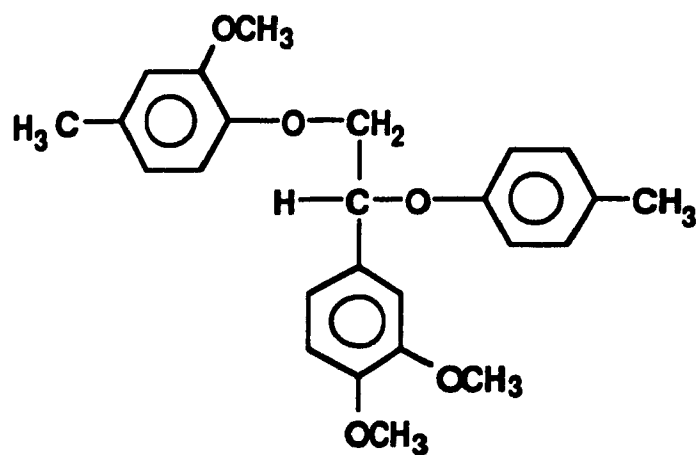
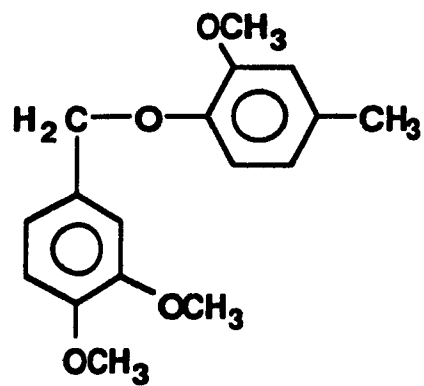
From the point of view of the degelation theory, however, trietherified trimeric structures are of primary importance, since they represent the cross-link points in the macromolecule, and hence, the key-points in the breakdown of the polymer network.

This chapter describes experiments with three model compounds representing trietherified units of the benzyl-aryl ether type in lignin, differing in the nature of their side chains. These experiments have revealed that, in glacial acetic acid, the benzyl-aryl ether bonds were cleaved by chlorine and hydrogen chloride.

## RESULTS

Compounds **2**, **6** and **9**, shown in Scheme II-1, all bear benzyl-aryl ether groups and show increasing similarity to a non-phenolic building unit in lignin; the dimer **2** is the simplest benzyl-aryl ether structure; the trimer **6** approaches the trietherified structure; finally, the trimer **9** - with a side chain bearing a hydroxyl group on the gamma carbon and an aryloxy group on the beta carbon - is the most representative of the cross-link point in the three-dimensional network of lignin.

The compounds were treated with chlorine gas dissolved in glacial acetic acid, as described in the experimental section. We chose the technique of fast addition of the chlorine charge, because a slow transfer permits a greater loss of chlorine, without, as found by Van Buren and Dence<sup>5</sup>, assuring a better homogeneity of the reaction. Sparging the reaction mixture with dry nitrogen<sup>6</sup> was a simple and clean means for removing residual chlorine at the end of the reaction. Unlike the usual method of quenching chlorine with sodium thiosulfate<sup>7</sup>, no additional chemical species were introduced into the reaction mixture, thus permitting a simpler work up procedure.



SCHEME II-1 . Compounds of the benzyl-aryl ether type. Dimer 2, trimers 6 and 9 .

Chlorination of derivatives of guaiacol and veratrole<sup>8,9</sup>, and of compounds of the beta aryl-ether type<sup>10</sup> in glacial acetic acid has revealed that in such nonaqueous solvents, aromatic substitution was virtually the sole reaction, since neither cleavage of aryl ether linkages nor oxidation of the side chains was observed. In contrast, chlorination of the same compounds<sup>6,9,11</sup> in aqueous acidic media promoted extensive dealkylation reactions, with the formation of quinonoid structures, and oxidative rupture of the aromatic rings yielding carboxylic acids. Such oxidation reactions, however, were shown to have little influence on the dissolution of lignin<sup>12</sup>. Thus, as a first step in the investigation of the chlorination of compounds with alpha aryl-ether groups, glacial acetic acid was a suitable solvent which, by decreasing the number of reactions which might take place, would let us see more clearly the effect of the alpha aryl-ether bond on the reaction with molecular chlorine.

In order to identify the products of reaction, they were first analyzed by gas- or liquid chromatography coupled with mass spectrometry. The compatibility of compound 2 with the gas chromatography technique permitted a complete and rigorous investigation. With higher molecular weights, compounds 6 and 9 were less volatile than compound 2, and this, with their greater thermolability ascribable to steric congestion, made it impossible to adequately analyze these compounds and their reaction products by gas chromatography. High performance liquid chromatography was used instead, and in a way which requires some comments.

In LC- (and GC-) MS analysis, the area of a peak appearing on the Total Ion Chromatogram (or TIC) depends on the number of ions which are

generated in the MS ion source, and which reach the detector. The term used in mass spectrometry for defining the capacity for a substance to ionize is the "Ionization Cross Section", or ICS. Fragmentation of equal amounts of different substances with different ICS, will generate a different number of ions. For instance, with an additional aromatic ring in the compound, the fragmentation may produce twice as many ions and thus yield, amount for amount, twice as big a peak area. Quantitative measurements are possible, provided standard curves are drawn for each substance.

For substances with similar structures and fragmentation patterns, one may assume that the ICS are comparable (keeping in mind, however, the difference between the fragmentation pattern, where the abundance of the ions is expressed in relative intensities, and the ICS expressing the absolute number of ions, which determines the area on the TIC), and thus that, amount for amount, the different substances will form comparable quantities of ions, and hence comparable areas on the TIC. One may then compare the peak areas from the different substances with each other, in order to draw conclusions about the relative proportions of the products in the sample, and thus on the stoichiometry of the reaction.

In short, we may say that for compounds of similar structures, and thus similar MS fragmentation patterns, separated and detected by chromatography-MS, the relative areas of the peaks appearing on the TIC (Total Ions Chromatogram) can be taken as roughly representative of the relative proportions of the compounds in the sample. Information of the semi-quantitative type may thus be obtained directly from the TIC.



Unexpectedly, the low molecular weight, phenolic type of substances resulting from the scission of the alpha ether bonds, which are usually well recorded by GC, did not appear on the TIC given by LC-MS analysis. The selectivity of detection originating from the LC-MS interface - for polar substances with a thermospray (TS) mode, and for apolar substances with a particle beam (PB) mode - cannot be the reason, since no extra peak corresponding to phenols was observed in either mode. The very low sensitivity of detection of LC-MS for guaiacyl and veratryl derivatives was confirmed by analysis of a standard mixture of 5-chlorocreosol and dichloroveratrole, but no reasonable explanation was found for this phenomenon. The possibility that such volatile compounds were lost in vacuum locks placed at the interface between LC and MS does not hold with a thermospray interface - where the ions are produced directly after vaporization of the effluent near the exit of the capillary tube-, nor with a particle-beam interface where the technique of momentum separators favors the detection of low molecular weight compounds.

Since all the products of reaction were not detected, the numbers obtained from the comparison of the respective areas on the TIC do not represent the relative proportions of the products in the sample, but must be regarded only as indicators revealing the trends of the chlorination reaction. These numbers, are nevertheless true representations of the reaction of benzyl aryl ethers with molecular chlorine.

For quantitative analyses, we found it generally easier and less misleading to express the yields in terms of "mole percent of initial C<sub>9</sub> - or monomer - unit". In this work, any aryl-ether substituent on the side chain of a model compound was understood as a "C<sub>9</sub> unit", although it was an uncomplete one. Accordingly, compound 2 is formed of two "C<sub>9</sub> units", and compounds 6 and 9 include three "C<sub>9</sub> units". The terminology "dimer" and "trimer" refers also to the number of "C<sub>9</sub> units" present in a given compound. The overall summation of the yields of all the products detected was thus based on one hundred per cent, regardless of whether the initial compound was a dimer or a trimer. Comparisons between the starting compounds were thus more straightforward. Whenever needed, however, the conversion into "mole percent of starting material" can be readily made, taking into account the structures of both the product and the initial compound.

The complete results of the chlorination of compounds 2, 6 and 9 are presented in tables II-1 to II-6. Tables II-7 and II-8 summarize the extent of aromatic substitution and cleavage reactions that take place in each compound. All three compounds behaved similarly, although with some variations inherent in their differences in structure. Their common feature is that the compounds, although quite stable in glacial acetic acid - a non dissociated medium -, readily underwent considerable cleavage of their benzyl ether linkages when treated with very low charges of chlorine.

Table II-1 . Products from the chlorination of compound 2 .

| compound    | structure                       | GC retention time <sup>a)</sup> (min) |
|-------------|---------------------------------|---------------------------------------|
| <hr/>       |                                 |                                       |
| <u>2</u>    | compound 2                      | 9.00                                  |
| <u>2-1</u>  | creosol                         | 1.40                                  |
| <u>2-2</u>  | 5-chlorocreosol                 | 2.36                                  |
| <u>2-3</u>  | veratrylchlorocarbene           | 3.00                                  |
| <u>2-4</u>  | veratrylacetocarbene            | 4.01                                  |
| <u>2-5</u>  | (6-chloroveratryl)chlorocarbene | 4.32                                  |
| <u>2-6</u>  | (6-chloroveratryl)acetocarbene  | 5.30                                  |
| <u>2-7</u>  | unknown                         | 9.48                                  |
| <u>2-8</u>  | unknown                         | 9.72                                  |
| <u>2-9</u>  | 3,5- or 5,6-dichlorocreosol     | 3.06                                  |
| <u>2-10</u> | dichloroveratrole               | 3.21                                  |
| <u>2-11</u> | 5,6- or 3,5-dichlorocreosol     | 4.17                                  |
| <u>2-12</u> | trichloroveratrole              | 4.72                                  |
| <u>2-13</u> | trichlorocreosol                | 4.76                                  |

a) GC and GC-MS conditions: carrier Helium, 1ml/min; temperature gradient: 150°C, 2 min; 270°C, 15°C/min.

Table II-2 . Yields of the products of chlorination of compound 2

under increasing charges of chlorine, x, (in mole of chlorine per C<sub>9</sub> unit). Yields, expressed in percent of initial C<sub>9</sub> unit, are obtained by GC analysis. Standard deviations are given in parentheses.

| x     | Δ         | 2-1           | 2-2           | 2-3           | 2-4           | 2-5           | 2-6          | 2-7/2-8                | 2-9           | 2-10         | 2-11         | 2-12         | 2-13          | total     |
|-------|-----------|---------------|---------------|---------------|---------------|---------------|--------------|------------------------|---------------|--------------|--------------|--------------|---------------|-----------|
| 0     | 95<br>(2) | -             | -             | -             | -             | -             | -            | -                      | -             | -            | -            | -            | -             | 95<br>(2) |
| 0.05  | 26<br>(2) | 22<br>(2)     | 1.6<br>(0.2)  | 4<br>(1)      | 22.0<br>(0.5) | -             | -            | 2.1/2.0<br>(0.2)/(0.3) | -             | -            | -            | -            | -             | 80<br>(3) |
| 0.10  | 9<br>(2)  | 32<br>(5)     | 3<br>(1)      | 8<br>(3)      | 30<br>(3)     | -             | -            | 1.1/2.4<br>(0.2)/(0.6) | -             | -            | -            | -            | -             | 85<br>(7) |
| 0.15  | 0         | 30<br>(1)     | 7.8<br>(0.4)  | 11.6<br>(0.3) | 27<br>(1)     | -             | -            | - /3.6<br>- / (0.5)    | -             | -            | -            | -            | -             | 80<br>(2) |
| 0.20  | -         | 35<br>(1)     | 11<br>(1)     | 13<br>(1)     | 22<br>(1)     | -             | -            | - /4.8<br>- / (0.4)    | -             | -            | -            | -            | -             | 86<br>(2) |
| 0.375 | -         | 23.5<br>(0.4) | 26<br>(1)     | 16.3<br>(0.3) | 13.6<br>(0.8) | -             | -            | 0                      | -             | -            | -            | -            | -             | 79<br>(2) |
| 0.5   | -         | 21.3<br>(0.4) | 28<br>(1)     | 20<br>(2)     | 13<br>(2)     | -             | -            | -                      | -             | -            | -            | -            | -             | 82<br>(3) |
| 0.625 | -         | 12            | 37<br>(1)     | 26<br>(0.6)   | 8.3<br>(0.4)  | -             | -            | -                      | -             | -            | -            | -            | -             | 83<br>(1) |
| 1.0   | -         | 0             | 39<br>(1)     | 40<br>(1)     | 3.1<br>(0.4)  | 1.2<br>(0.4)  | Tr           | -                      | -             | -            | -            | -            | -             | 84<br>(2) |
| 1.5   | -         | -             | 34.5<br>(0.3) | 22.3<br>(0.6) | 2.6<br>(0.1)  | 11.2<br>(0.6) | 2.1<br>(0.3) | -                      | -             | -            | -            | -            | -             | 73<br>(1) |
| 2.0   | -         | -             | 28.7<br>(0.5) | 11<br>(1)     | 0             | 25<br>(1)     | 4.0<br>(0.3) | -                      | -             | -            | -            | -            | -             | 69<br>(2) |
| 3.0   | -         | -             | 3.9<br>(0.3)  | 0             | -             | 41.1<br>(0.4) | 4.8<br>(0.2) | -                      | 2.7<br>(0.1)  | 1.2<br>(0.3) | 4.0<br>(0.1) | Tr           | -             | 58<br>(1) |
| 4.0   | -         | -             | 2.8<br>(0.1)  | -             | -             | 42<br>(1)     | 4.5<br>(0.1) | -                      | 8.5<br>(0.3)  | 2.0<br>(0.1) | 7.1<br>(0.2) | .9<br>(0.1)  | -             | 68<br>(1) |
| 5.0   | -         | -             | 0             | -             | -             | 42.4<br>(0.8) | 4.7<br>(0.1) | -                      | 12<br>(0.3)   | 2.9<br>(0.1) | 11<br>(0.2)  | 1.5<br>(0.1) | 3.0<br>(0.3)  | 77<br>(2) |
| 6.0   | -         | -             | -             | -             | -             | 44<br>(2)     | 4.0<br>(0.1) | -                      | 11.2<br>(0.5) | 4.0<br>(0.1) | 9.0<br>(0.4) | 1.6<br>(0.1) | 5.4<br>(0.3)  | 79<br>(2) |
| 8.0   | -         | -             | -             | -             | -             | 38<br>(2)     | 3.5<br>(0.5) | -                      | 15<br>(1)     | 6.5<br>(0.4) | 4.3<br>(0.3) | 1.6<br>(0.2) | 11.0<br>(0.1) | 80<br>(2) |

Table II-3 . Products from the chlorination of compound 6 .

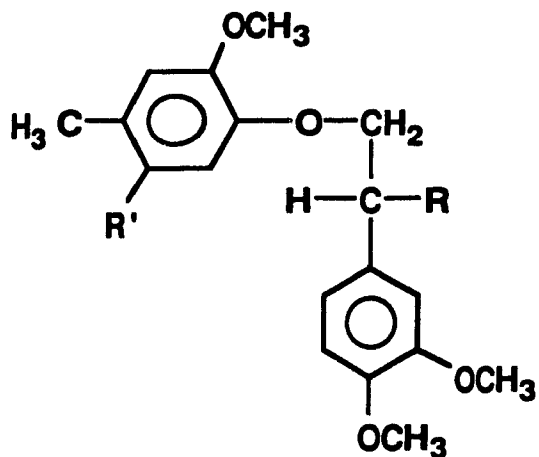
| compound   | structure                                                                                        | LC retention time <sup>a)</sup> (min) |       |       |
|------------|--------------------------------------------------------------------------------------------------|---------------------------------------|-------|-------|
|            |                                                                                                  | TS                                    | PB-CI | PB-EI |
| <u>6</u>   | compound <u>6</u>                                                                                | 14.3                                  | 13.4  | 13.5  |
| <u>6-1</u> | 1-(3,4-dimethoxyphenyl)-1-acetoxy-<br>2-(2-methoxy-4-methylphenoxy)ethane.                       | 5.1                                   | 3.9   | 3.9   |
| <u>6-2</u> | 1-(3,4-dimethoxyphenyl)-1-methoxy-2-(2-<br>methoxy-4-methylphenoxy)ethane ( <u>5</u> )           | 5.5                                   | -     | -     |
| <u>6-3</u> | 1-(3,4-dimethoxyphenyl)-1-acetoxy-2-(5-<br>chloro-2-methoxy-4-methylphenoxy)ethane.              | 7.2                                   | 6.0   | 6.2   |
| <u>6-4</u> | 1-(3,4-dimethoxyphenyl)-1-methoxy-2-(5-chloro<br>-2-methoxy-4-methylphenoxy)ethane ( <u>12</u> ) | 8.2                                   | 6.5   | 6.8   |

a) LC-MS conditions:

TS: In Thermospray mode: Eluent MeOH:Buffer 70:30 (0.005M NH<sub>4</sub>OAc); Flow rate 1.0 ml/min; column temperature 45°C.

PB-CI: In Particle Beam-methane Chemical Ionization: Eluent MeOH:H<sub>2</sub>O 60:40; Flow rate 0.4 ml/min; column temperature 65°C.

PB-EI: In Particle Beam-Electron Impact: Eluent MeOH:H<sub>2</sub>O 60:40; Flow rate 0.4 ml/min; column temperature 65°C.



| compound   | R   | R' |
|------------|-----|----|
| <u>6-1</u> | OAc | H  |
| <u>6-2</u> | OMe | H  |
| <u>6-3</u> | OAc | Cl |
| <u>6-4</u> | OMe | Cl |

SCHEME II-2 . Products from the chlorination of trimer 6 .

Table II-4 . Estimated yields of products from the chlorination of compound 6 with 0.25 moles of chlorine per C<sub>9</sub> unit. Estimates are based on area percent of the Total Ion Chromatogram, or TIC, obtained by HPLC-MS (TS mode) analysis.

| x <sup>a)</sup> | <u>6</u> | <u>6-1</u> | <u>6-2</u> | <u>6-3</u> | <u>6-4</u> | total |
|-----------------|----------|------------|------------|------------|------------|-------|
| 0               | 100      | -          | -          | -          | -          | 100   |
| 0.25            | 1.5      | 33.4       | 7.9        | 45.8       | 11.4       | 100   |

a) charge of chlorine in moles/C<sub>9</sub> unit.

Table II-5 . Products from the chlorination of compound 9 .

| compound   | structure                                                                                   | LC retention time <sup>a)</sup> (min) |       |       |
|------------|---------------------------------------------------------------------------------------------|---------------------------------------|-------|-------|
|            |                                                                                             | TS                                    | PB-CI | PB-EI |
| <u>9</u>   | compound <u>9</u>                                                                           | 31.7/33.4                             | 10.4  | 9.2   |
| <u>9-1</u> | 1-(3,4-dimethoxyphenyl)-2-(2-methoxyphenoxy)-1,3-propanediol <u>7</u>                       | 4.8                                   | -     | -     |
| <u>9-2</u> | unknown                                                                                     | 6.0                                   | -     | -     |
| <u>9-3</u> | 3-(3,4-dimethoxyphenyl)-3-acetoxy-2-(2-methoxyphenoxy)propanol.                             | 7.0/7.8                               | 3.3   | 3.0   |
| <u>9-4</u> | 3-(3,4-dimethoxyphenyl)-3-methoxy-2-(2-methoxyphenoxy)propanol.                             | 8.3                                   | -     | -     |
| <u>9-5</u> | 3-(3,4-dimethoxyphenyl)-3-(5-chloro-2-methoxy-4-methylphenoxy)-2-(2-methoxyphenoxy)propanol | 58.5/65.8                             | 17.9  | 16.2  |

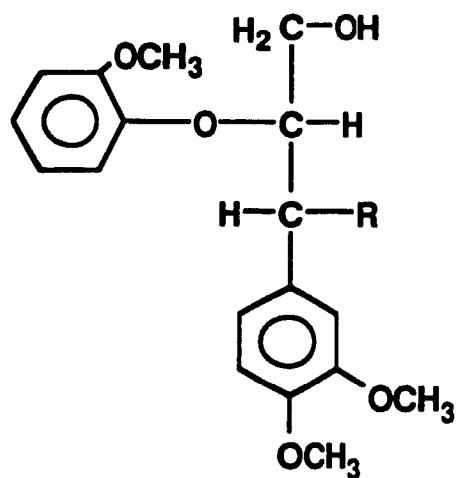
a) LC-MS conditions:

TS: In Thermospray mode: Eluent MeOH:Buffer 56:44 (0.005M NH<sub>4</sub>OAc); Flow rate 1.0 ml/min; column temperature 45°C.

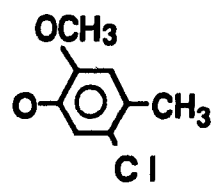
PB-CI: In Particle Beam-methane Chemical Ionization: Eluent MeOH:H<sub>2</sub>O 48:52; Flow rate 0.4 ml/min; column temperature 55°C.

PB-EI: In Particle Beam-Electron Impact: Eluent MeOH:H<sub>2</sub>O 48:52; Flow rate 0.4 ml/min; column temperature 70°C.





| compound   | R   |
|------------|-----|
| <u>9-1</u> | OH  |
| <u>9-3</u> | OAc |
| <u>9-4</u> | OMe |
| <u>9-5</u> |     |



SCHEME II-3 . Products from the chlorination of trimer 9

Table II-6 . Estimated yields of the major products from the chlorination of compound 9 with 0.10 and 0.25 moles of chlorine, x, per C<sub>9</sub> unit. Estimates are based on area percent of the Total Ion Chromatogram, or TIC, obtained by HPLC-MS (PB-CI mode) analysis. Data extracted from the TIC produced in PB-EI mode are given in parentheses.

| x    | <u>9</u>  | <u>9-1</u> | <u>9-3</u> | <u>9-4</u> | <u>9-5</u> | total |
|------|-----------|------------|------------|------------|------------|-------|
| 0    | 100 (100) | -          | -          | -          | -          | 100   |
| 0.10 | 50 (37)   | nd         | 33 (40)    | nd         | 17 (22)    | 100   |
| 0.25 | 3 (4)     | nd         | 62 (62)    | nd         | 35 (34)    | 100   |

Table II-7 . Combined yields of related products from the chlorination of compound 2 under increasing charges of chlorine, x (in mole of chlorine per C<sub>9</sub> unit): a) compound 2 recovered unaltered after the reaction, b) products from alpha aryl-ether bond cleavage, c) products from substitution on the aromatic rings. Yields are expressed in percent of initial C<sub>9</sub> unit, obtained by GC analysis. Standard deviations are given in parentheses.

| Cl <sub>2</sub><br>charge<br>x | un-<br>altered<br>2 | alpha-ether<br>cleavage<br><u>2-1, 2-2, 2-3,</u><br><u>2-4, 2-5, 2-6,</u><br><u>2-9, 2-11, 2-13</u> | substitution                                                    |       | unknown<br><u>2-7, 2-8</u> |
|--------------------------------|---------------------|-----------------------------------------------------------------------------------------------------|-----------------------------------------------------------------|-------|----------------------------|
|                                |                     |                                                                                                     | ipso-substitution<br>(side-chain cleavage)<br><u>2-10, 2-12</u> | other |                            |
| 0                              | 95<br>(2)           | 0                                                                                                   | -                                                               | -     | 0                          |
| 0.05                           | 26<br>(2)           | 50<br>(2)                                                                                           | -                                                               | -     | 4.1<br>(0.4)               |
| 0.10                           | 9<br>(2)            | 73<br>(6)                                                                                           | -                                                               | -     | 3.5<br>(0.6)               |
| 0.15                           | 0                   | 76<br>(2)                                                                                           | -                                                               | -     | 3.6<br>(0.5)               |
| 0.20                           | -                   | 81<br>(2)                                                                                           | -                                                               | -     | 4.8<br>(0.4)               |
| 0.5                            | -                   | 82<br>(3)                                                                                           | -                                                               | -     | 0                          |
| 1.0                            | -                   | 84<br>(2)                                                                                           | -                                                               | -     | -                          |
| 2.0                            | -                   | 69<br>(2)                                                                                           | 0                                                               | -     | -                          |
| 4.0                            | -                   | 65<br>(1)                                                                                           | 2.9<br>(0.1)                                                    | -     | -                          |
| 6.0                            | -                   | 73<br>(2)                                                                                           | 5.6<br>(0.1)                                                    | -     | -                          |
| 8.0                            | -                   | 72<br>(2)                                                                                           | 8.1<br>(0.4)                                                    | -     | -                          |

Table II-8. Combined yields of related products from the chlorination of compounds 2, 6 and 9 under increasing charges of chlorine,  $x$ , (in mole of chlorine per  $C_9$  unit): a) compound 2 recovered unaltered after the reaction, b) products from alpha aryl-ether bond cleavage, c) products from substitution on the aromatic rings. Estimates are expressed in percent of the TIC, obtained by HPLC analysis.

| Cl <sub>2</sub><br>charge | starting<br>compound | unaltered<br>compound<br><u>2</u> , <u>6</u> , <u>9</u> | alpha-ether<br>cleavage<br><u>6-1</u> , <u>6-2</u> , <u>6-3</u> ,<br><u>6-4</u> ;<br><u>9-1</u> , <u>9-3</u> , <u>9-4</u> | substitution                                  |                     |
|---------------------------|----------------------|---------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------|---------------------|
|                           |                      |                                                         |                                                                                                                           | ipso-substitution<br>(side-chain<br>cleavage) | other<br><u>9-5</u> |
| $x = 0$                   | <u>2</u>             | 100                                                     | 0                                                                                                                         | 0                                             | 0                   |
|                           | <u>6</u>             | 100                                                     | 0                                                                                                                         | 0                                             | 0                   |
|                           | <u>9</u>             | 100                                                     | 0                                                                                                                         | 0                                             | 0                   |
| $x = 0.10$                | <u>9</u>             | 50 (37)                                                 | 33 (40)                                                                                                                   | 0                                             | 17 (22)             |
| $x = 0.25$                | <u>2</u>             | 0                                                       | nd                                                                                                                        | nd                                            | nd                  |
|                           | <u>6</u>             | 1.5                                                     | 98.5                                                                                                                      | 0                                             | 0                   |
|                           | <u>9</u>             | 3 (4)                                                   | 62 (62)                                                                                                                   | 0                                             | 35 (34)             |

• Identification of the reaction products.

The products formed by chlorination of compound 2 were identified by GC-MS, and those from compounds 6 and 9 by LC-MS. They are listed in tables II-1, II-3, and II-5, respectively. The detailed mass spectral data are reported in Appendix II. As expected<sup>13</sup>, the mass spectra mainly exhibited peaks due to ions resulting from the combination of: i) elimination of the alpha substituent (with formation of the much more stable benzylic cation, very often present as the base peak), ii) elimination of the beta substituent (if any), and iii) cleavage of the C $\alpha$  - C $\beta$  bond, (if any). Dehydration and cleavage of the C $\beta$  - C $\gamma$  bond with elimination of formaldehyde, mentioned in the literature<sup>14</sup>, were also observed with the products derived from compound 2.

In the thermospray mode, all the effluent goes into the source, is ionized, and the compounds, taken into a matrix of ions, are also ionized. The resulting chemical ionization is responsible for the combination with NH<sub>4</sub><sup>+</sup> or H<sup>+</sup> (M+NH<sub>4</sub><sup>+</sup> being among the most abundant ions in the spectra). Addition of methanol (CH<sub>3</sub>OH), or of a second molecule of analyte was also observed in several instances. When the particle beam mode with chemical ionization with methane (CH<sub>4</sub>) was used, the expected<sup>15</sup> combination with C<sub>2</sub>H<sub>5</sub><sup>+</sup> or H<sup>+</sup> was observed. Electron impact generally promoted greater fragmentation, and the molecular ion was not always present in the spectrum.

The analysis of the products from compound 2 presented three obstacles:

a) Creosol and veratrole being structural isomers, the distinction between di- or tri-chlorocreosol and di- or tri-

chloroveratrole, respectively, could not be discerned from the nature of the molecular ions. Nevertheless, the assignment could be made from the presence of a large peak for  $[M^{+}-H^{+}]$ , characteristic<sup>16</sup> of phenols, and absent from the spectra of veratroles, combined with the comparison with the retention times and mass spectra of authentic samples of di- and tri- chloroveratrole.

b) The distinction between two positional isomers of dichlorocresol (2-9 and 2-11, in table II-1) could not be clearly made. As McLafferty has already reported in his paper on aromatic halogenated compounds<sup>17</sup>, mass spectrometry could not distinguish among isomeric positions of substitution on the ring. In their investigation of the chlorination of cresol in an aqueous medium, Gess and Dence<sup>18</sup> found the following order of reactivity for the 3 sites available for chlorine substitution on cresol ring: position 5 (para to methoxyl) > position 6 (ortho to hydroxyl) >> position 3 (ortho to methoxyl). A different order was observed however by several authors<sup>19</sup>, in which position 6 was quite unreactive compared to position 3. In our experiments, besides the expected formation of 5-chlorocresol (2-2 in tables II-1 and II-2) as the only monochlorinated cresol, a third situation was observed, with both di-substituted cresols formed in comparable yields (Table-II-2), indicating a similar reactivity for both positions 2 and 6. We have two explanations for this discrepancy:

i) As a general rule, a weaker electrophile shows higher selectivity<sup>20</sup>. Chlorine is a stronger electrophile in glacial acetic acid than in aqueous medium, and is therefore less selective in the substitution on the positions 2 and 6.

ii) The stronger activation of one site compared to another is demonstrated through the higher rate of substitution on this site. A very short reaction time (a few minutes in the experiments of Gess and Dence) will exhibit the rate difference between the two sites. In contrast, a very long reaction time (we stopped the reaction after 5 to 6 hours) will tend to mask the difference if thermodynamic equilibrium and kinetic equilibrium each favors a different site.

c) Two products, 2-7 and 2-8, could not be identified. They both displayed retention times (Table II-1) in the same time domain as 2, thus suggesting a dimeric structure. The retention times of both products remained unaltered whether or not the sample was silylated before injection. This indicates the absence of any free hydroxyl group in these products, and shows that 2-7 and 2-8 did not result from demethylation. The occurrence of m/e:151 (100), m/e 135 (5), and m/e 107 (12), in the mass spectrum of 2-8 (Appendix II), revealed the same unchlorinated benzylic moiety in the structure of 2-8 as in 2, and suggested that 2-8 may be a product of recombination formed subsequent to alpha-ether cleavage. Examples of carbon-carbon bond formation at the benzylic position with a phenyl group arising from ether cleavage, or even with beta aryl substituent (at the 6 position) were observed in acetic acid pulping<sup>21</sup>. These reactions depend on experimental conditions, and they are not always observed in HCl-catalysed acidolysis<sup>22</sup>.

The chlorination products from compound 6 were unambiguously identified by cross-checking spectral data obtained from different interface and ionization modes. The fragmentation pattern was very dependent on the structure of the molecule through the influence of the

alpha substituent. In PB-EI mode the presence of the acetyl group at the alpha position eases the elimination of the beta substituent because of the possible formation of a 5-membered ring in the resulting fragment which actually yields the base peak. Such stabilization is not possible with a methoxyl group at the alpha position, and the base peak is then the fragment resulting from the cleavage of the  $C_{\alpha}-C_{\beta}$  linkage. Under the elution conditions used with the PB mode, the separation of 6-1 and 6-2 was not achieved, but the presence of the two species under the same peak was disclosed by selective ion detection (with  $M^{+} = 360$  for 6-1 and  $M^{+} = 350$  for 6-2). The site of substitution on compounds 6-3 and 6-4 (Table II-3) was deduced from some characteristics of their mass spectra, (Tables II-9 a) and b)), and from the combination of the para-orienting conjugative influence of the methoxyl group and the ortho-directing inductive effect of the alkyl group. The preferential substitution on position 5 of the creosyl nucleus, rather than on position 6 of the veratryl nucleus suggested that the presence of an electron-withdrawing substituent on the alkyl side chain decreased its activating effect on the aromatic nucleus. As we have mentioned already, the cresyl moiety resulting from the cleavage of the alpha ether bond was not detected. Nevertheless, we can take for granted that the cresyl nucleus, lacking of the para activation of a second methoxyl group, had not undergone chlorine substitution.

Under the chromatographic conditions used with the thermospray mode but not in the particle beam mode, separation of the diastereomers of 2 and its derivatives was achieved in some instances, and more products were detected (Table II-5).



Table II-9 . Determination of the site of aromatic substitution on 6-3 and 6-4 by mass spectrometry. a) The characteristic fragments, and their m/e, of the possible positional isomers. The ring bearing the chlorine atom is named, preceded by "Cl-". "Creo" represents creosyl, and "Ver", veratryl. b) The experimental values showing that the site of aromatic substitution of 6-3 and 6-4 is on the the creosyl ring.

9 a)

| COMPOUND            | CHARACTERISTIC MS FRAGMENTS (PB-EI) |                                                                                                                  |
|---------------------|-------------------------------------|------------------------------------------------------------------------------------------------------------------|
|                     | beta subst. (m/e)                   | veratryl ring (m/e)                                                                                              |
| <u>6-1</u>          | Creosol <sup>+</sup> (138)          | (CH <sub>3</sub> O) <sub>2</sub> C <sub>6</sub> H <sub>3</sub> (CH)(OAc)CH <sub>2</sub> <sup>+</sup> (223)       |
| Cl-Creo- <u>6-3</u> | Cl-creosol <sup>+</sup> (172/174)   | (CH <sub>3</sub> O) <sub>2</sub> C <sub>6</sub> H <sub>3</sub> (CH)(OAc)CH <sub>2</sub> <sup>+</sup> (223)       |
| Cl-Ver- <u>6-3</u>  | Creosol <sup>+</sup> (138)          | Cl(CH <sub>3</sub> O) <sub>2</sub> C <sub>6</sub> H <sub>3</sub> (CH)(OAc)CH <sub>2</sub> <sup>+</sup> (257/259) |
| Cl-Creo- <u>6-4</u> | Cl-creosol <sup>+</sup> (172/174)   | (CH <sub>3</sub> O) <sub>2</sub> C <sub>6</sub> H <sub>3</sub> (CH)(OCH <sub>3</sub> ) <sup>+</sup> (181)        |
| Cl-Ver- <u>6-4</u>  | Creosol <sup>+</sup> (138)          | Cl(CH <sub>3</sub> O) <sub>2</sub> C <sub>6</sub> H <sub>3</sub> (CH)(OCH <sub>3</sub> ) <sup>+</sup> (215/217)  |

9 b)

| EXPERIMENTAL VALUES FOR m/e (PB-EI) |            |            |            |
|-------------------------------------|------------|------------|------------|
| m/e                                 | <u>6-1</u> | <u>6-3</u> | <u>6-4</u> |
| 138                                 | 98.6       | -          |            |
| 223                                 | 100        | 100        |            |
| 181                                 | -          | -          | 100        |
| 172/174                             | -          | 68.8/20.9  | -          |
| 257/259                             | -          | -          | -          |
| 215/217                             | -          | -          | -          |

One of them, 9-2, could not be identified. In compound 9-5, as in 6-3 and 6-4, the site of substitution could be unambiguously established from mass spectrometric data by considering the fragments of high relative abundance characteristic of the veratryl ring, and the alpha- and beta- substituents, respectively (Tables II-10a) and II-10b)). From the three aromatic rings present in compound 9 - veratryl, guaiacyl and creosyl - the creosyl group alone was chlorinated. This observation supported the earlier hypothesis for the chlorination of compound 6, that the departing cresyl ring had not undergone any substitution by chlorine.

• Consumption of the starting compound. (Tables II-7 and II-8).

The starting compounds were quite stable in glacial acetic acid. Dimer 2 was recovered in 95% yield (Table II-7), and none of the possible solvolysis products of the trimers 6 and 9 were detected (Table II-8).

However, 2 disappeared completely when a charge of 0.15 mole of chlorine per monomer unit was applied (Table II-7), whereas a small amount of trimer 6 was left unreacted after chlorination with 0.25 mole of chlorine per C<sub>9</sub> unit (Table II-8). Chlorination of compound 9 with 0.10 and 0.25 mole of chlorine per C<sub>9</sub> unit yielded trimeric structures which accounted for about 40 to 50%, and 40%, respectively, of the products detected (Table II-8).

Table II-10 . Determination of the site of aromatic substitution on 9-5 by mass spectrometry. a) The characteristic fragments, and their m/e, of the possible positional isomers. The ring bearing the chlorine atom is named, preceded by "Cl-". "Gu" represents guaiacyl, "Creo", creosyl, and "Ver", veratryl. b) The experimental values showing that the site of aromatic substitution of 9-5 is on the creosyl ring.

| 10 a)               |  | CHARACTERISTIC MS FRAGMENTS (PB-CI)    |                                        |                                                                                                                      |
|---------------------|--|----------------------------------------|----------------------------------------|----------------------------------------------------------------------------------------------------------------------|
| COMPOUND            |  | alpha subst (m/e)                      | beta subst (m/e)                       | veratryl ring (m/e)                                                                                                  |
| <u>9</u>            |  | Creosol+H <sup>+</sup><br>(139)        | Guaiacol+H <sup>+</sup><br>(125)       | (CH <sub>3</sub> O) <sub>2</sub> C <sub>6</sub> H <sub>3</sub> (CH)(CH)CH <sub>2</sub> <sup>+</sup><br>(195)         |
| Cl-Gu- <u>9-5</u>   |  | Creosol+H <sup>+</sup><br>(139)        | Cl-Guaiacol+H <sup>+</sup><br>(159/61) | (CH <sub>3</sub> O) <sub>2</sub> C <sub>6</sub> H <sub>3</sub> (CH)(CH)CH <sub>2</sub> <sup>+</sup><br>(195)         |
| Cl-Creo- <u>9-5</u> |  | Cl-Creosol+H <sup>+</sup><br>(173/175) | Guaiacol+H <sup>+</sup><br>(125)       | (CH <sub>3</sub> O) <sub>2</sub> C <sub>6</sub> H <sub>3</sub> (CH)(CH)CH <sub>2</sub> <sup>+</sup><br>(195)         |
| Cl-Ver- <u>9-5</u>  |  | Creosol +H <sup>+</sup><br>(139)       | Guaiacol+H <sup>+</sup><br>(125)       | (CH <sub>3</sub> O) <sub>2</sub> (Cl)C <sub>6</sub> H <sub>3</sub> (CH)(CH)CH <sub>2</sub> <sup>+</sup><br>(211/213) |

10 b)

| EXPERIMENTAL VALUES FOR m/e (PB-CI) |          |            |
|-------------------------------------|----------|------------|
| m/e                                 | <u>9</u> | <u>9-5</u> |
| 125                                 | 62.4     | 79.1       |
| 139                                 | 100      | -          |
| 195                                 | 32.67    | 38.9       |
| 159/161                             | -        | -          |
| 173/175                             | -        | 100/31.9   |
| 211/213                             | -        | -          |

• Characteristics of the products of reaction.

CLEAVAGE OF ALPHA-ETHER LINKAGE

compound 2 (Tables II-1 and II-2):

A charge of as little as 0.05 mole of chlorine per monomer unit of compound 2 effected the breakdown of about 75% of the initial dimer into two main unchlorinated products, creosol (2-1) and veratryl alcohol acetate (2-4). Two other products bearing an atom of chlorine, veratryl chloride (2-3) and 5-chlorocreosol (2-2) were also formed, in minor amount at first, and their proportions in the sample increased with the charge. At charges of between 0.15 and 1.0 mole of chlorine per C<sub>9</sub> unit, compound 2 was entirely and exclusively (except for minor amounts of two unidentified compounds) converted into compounds 2-1 and 2-4.

compound 6 (Tables II-3 and II-4):

All the products detected from the chlorination of compound 6 resulted from the cleavage of the alpha-ether bond, as denoted by the presence at the alpha position of either an acetyl group (6-1, 6-3), or - to a much lesser extent - a methoxyl group (6-2, 6-4), replacing the initial cresyl substituent. Because all the products had a similar dimeric structure, the area percent of the TIC is likely to be representative of the real proportions of products in the sample. There was no evidence, however, of any compound bearing a chlorine at the alpha position. No product from the cleavage of the beta ether bond was detected, in accordance with the literature<sup>10</sup>.

compound 9 (Tables II-5 and II-6):

One single product (9-3) from the cleavage of the benzyl ether bond in compound 9, with the replacement of the alpha substituent by an acetyl group, was detected in significant proportions. These proportions are most likely somewhat underestimated: not only dimers (9-3), but also trimers (9-1, 9-5) were present in the mixture, and fewer ions are likely to be produced by a dimer than by a trimer to contribute to the peak area on the TIC. Two minor products were also detected and identified as the alpha-hydroxy- and alpha-methoxy- derivatives of 9, (9-1 and 9-4, respectively) but occurred only as traces. As observed in the chlorination of compound 6, no product bearing a chlorine atom in alpha position was detected.

#### AROMATIC SUBSTITUTION BY CHLORINE

compounds 2 and 6 :

Unlike the analogous benzyl alkyl ethers (Chap. III and IV), compounds 2 and 6, on chlorination, did not exhibit aromatic substitution as their initial reaction. Rather, substitution occurred only on the products resulting from the cleavage of the benzyl ether bond, and its pattern followed the previously described order of reactivity of the different sites available for substitution. Tables II-1 and II-2 show that chlorination of the liberated creosol from compound 2 occurred when the charges of chlorine were less than 1.0 mole per mole of monomer, whereas substitution on the veratryl ring began only at charges higher than 1.0. At even higher charges (> 2.0) di- and tri-chlorocreosol were formed, and further substitution on the veratryl ring, taking place at the ipso position, promoted the electrophilic displacement of the alkyl side chains.

Further evidence that creosol is much more reactive towards electrophilic attack than the veratryl part is that trichlorocreosol was formed, but not trichlorinated veratryl moiety.

In the reaction of compound 6, substitution took place on the most reactive site: position 5 on the creosyl group present as beta-substituent in 6-3 and 6-4 (Table II-3).

compound 9 :

In the chlorination of compound 9 only substitution occurred in considerable proportions (even if the substitution products may be overestimated), accounting, as shown in table II-6, for about 35% of the reaction products detected at a charge of 0.25 mole of chlorine per C<sub>9</sub> unit.

We can summarize all these experimental results as follows:

Cleavage of the benzyl aryl ether bonds

- did not occur in glacial acetic acid;
- took place in significant proportion, if not quantitatively, in the presence of a minute amount of molecular chlorine , in glacial acetic acid;
- yielded mostly apha acetylated , but also alpha-chloro, or -methoxy, or hydroxy products;
- was inhibited by the presence of additional substituents on the side-chain;
- competed with aromatic electrophilic substitution by chlorine.

Effect of HCl on compounds 2, 6, and 9.

The foregoing observations suggested that the facile cleavage of the benzyl aryl ether bonds might be explicable as hydrolysis catalyzed by hydrogen chloride formed by the reaction of chlorine either with acetic acid or with the small amount of water present in it. Accordingly, compounds 2, 6, and 9 were allowed to react with a charge of 0.25 mole of anhydrous HCl per C<sub>9</sub> unit, in otherwise exactly the same conditions as in the chlorination experiments. Dry HCl was allowed to bubble into glacial acetic acid until the increase in weight corresponded to the desired amount<sup>9</sup>. Aliquots corresponding to the desired charge were withdrawn from the stock solution by syringe and injected into the reaction mixture exactly in the same manner as in the chlorination experiments. The products of reaction were analyzed by GC (compound 2 only) and HPLC.

• Identification of the reaction products.

Although most of products had already been encountered and identified in the course of the chlorination study, several compounds, accounting for a non-negligible part of the reaction products, could not be identified (Table II-11). They may be recombination products, as discussed earlier. GC-MS analysis of acidolysis products of compound 2 gave little additional information, but confirmed the presence of creosol 2-1, veratryl acetocarbene 2-4, and 2-8 as major reaction products. The detailed mass spectral data are reported in Appendix II.

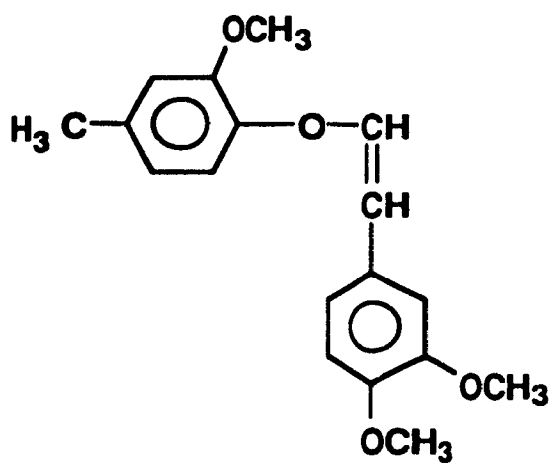
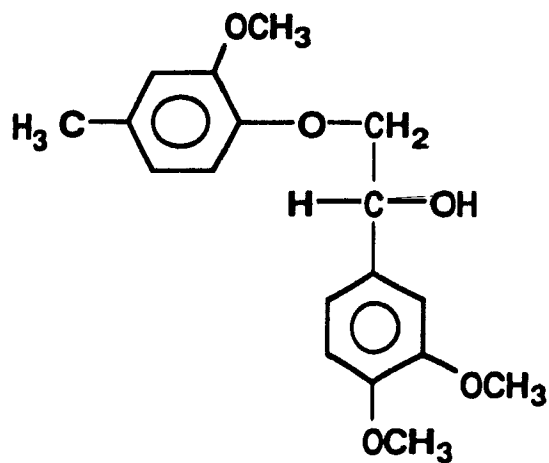
Table II-11. Products from the acidolysis of compounds 2, 6, and 9.

| compound    | structure                                                                              | LC retention time <sup>a</sup> (min) |
|-------------|----------------------------------------------------------------------------------------|--------------------------------------|
| <u>2-14</u> | veratryl alcohol                                                                       | 2.65 <sup>b</sup>                    |
| <u>2-4</u>  | veratryl-acetocarbene                                                                  | 3.61 <sup>b</sup>                    |
| <u>2-8</u>  | unknown 6.33 <sup>b</sup>                                                              |                                      |
| ***         |                                                                                        |                                      |
| <u>6-5</u>  | 1-veratryl-2-creosyl-ethylene                                                          | 2.19                                 |
| <u>6-6</u>  | unknown 3.16                                                                           |                                      |
| <u>6-7</u>  | 1-(3,4-dimethoxyphenyl)-<br>2-(2-methoxy-4-methylphenoxy)ethanol                       | 4.00                                 |
| <u>6-1</u>  | 1-(3,4-dimethoxyphenyl)-1-acetoxy-<br>2-(2-methoxy-4-methylphenoxy)ethane.             | 4.98                                 |
| <u>6-2</u>  | 1-(3,4-dimethoxyphenyl)-1-methoxy-2-(2-<br>methoxy-4-methylphenoxy)ethane ( <u>5</u> ) | 5.53                                 |
| <u>6-8</u>  | unknown 6.88                                                                           |                                      |
| <u>6-9</u>  | unknown 8.40                                                                           |                                      |
| ***         |                                                                                        |                                      |
| <u>2</u>    | compound <u>2</u> 4.95                                                                 |                                      |
| <u>9-1</u>  | 1-(3,4-dimethoxyphenyl)-2-<br>(2-methoxyphenoxy)-1,3-propanediol ( <u>7</u> )          | 2.17                                 |
| <u>9-3</u>  | 3-(3,4-dimethoxyphenyl)-3-acetoxy-<br>2-(2-methoxyphenoxy)propanol.                    | 3.05                                 |
| <u>9-4</u>  | 3-(3,4-dimethoxyphenyl)-3-methoxy-<br>2-(2-methoxyphenoxy)propanol.                    | 3.30                                 |
| <u>9-6</u>  | unknown                                                                                | 3.77/4.03                            |

a) LC-MS conditions: Thermospray mode (TS): Eluent, MeOH:Buffer 70:30 (0.005M NH<sub>4</sub>OAc); Flow rate 1.0 ml/min; column temperature 45°C.

b) Eluent, MeOH: Buffer 60:40.



6-56-7

SCHEME II-4 . Products 6-5 and 6-7 from the acidolysis of trimer 6 .

• Estimation of the reaction products. (Table II-12)

The numbers given in table II-12 are, again, only indicative. They show, however, that all three initial compounds have been totally - or quasi (only traces of 2 were detected) - consumed after the reaction. All the products identified arose from alpha ether-bond cleavage. The percentages represented by compounds 2-8, 6-6, 6-8, 6-9, and 9-6 cannot be used for analysis since their structures are not known.

The main observation from these results is that a charge of 0.25 mole of anhydrous HCl per mole of monomer unit applied on the three compounds, 2, 6, and 9, in glacial acetic acid promoted, complete disappearance of the initial compounds, and extensive cleavage of the alpha ether bond. Unidentified products were also formed, most likely due to recombination between the cleavage products.

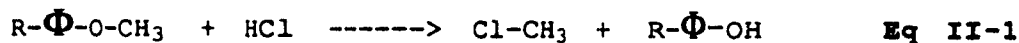
Table II-12 . Estimates of relative yields, in area percent of the TIC (TS mode), of the major products from the acidolysis of compounds 2, 6, and 9 under a charge of 0.25 mole of HCl per C<sub>9</sub> unit. .

|          | unreacted<br>compound | alpha<br>-OH | alpha<br>-OAc | alpha<br>-OMe | others     | unknowns             |
|----------|-----------------------|--------------|---------------|---------------|------------|----------------------|
| products | <u>2</u>              | <u>2-14</u>  | <u>2-4</u>    | -             | -          | <u>2-8</u>           |
| area %   |                       | 0            | 9             | 55            |            | 27                   |
| products | <u>6</u>              | <u>6-7</u>   | <u>6-1</u>    | <u>6-2</u>    | <u>6-5</u> | <u>6-6, 6-8, 6-9</u> |
| area %   | 0                     | 6            | 5             | 20            | 1          | 29, 10, 9            |
| products | <u>9</u>              | <u>9-1</u>   | <u>9-3</u>    | <u>9-4</u>    | -          | <u>9-6</u>           |
| area %   | 3                     | 29           | 28            | 18            |            | 20                   |

## DISCUSSION

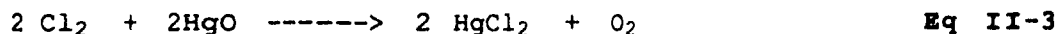
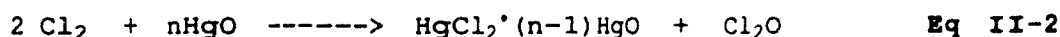
In his early study on the action of an excess of molecular chlorine on benzyl phenyl- and benzyl ethyl ethers in glacial acetic acid, Sintenis<sup>4</sup> found different responses from alkyl- and aryl benzyl ethers. Chlorination in cold ethanol ("in der Kälte") of the ethylether yielded benzaldehyde and ethylchloride, whereas the phenylether was cleaved into benzylchloride and the corresponding chlorine-substituted phenol. Yields were not reported, so that it is difficult to estimate the relative extents of the two cleavage reactions. Nevertheless, our experiments on compound 2 were in accord with Sintenis's results. When a large excess of chlorine was applied (table II-2), the main products were 6-chloroveratryl chloride and chlorinated creosols (up to about 40% and 30% yield, respectively, for charges of from 3 to 8 moles of chlorine per monomer unit). Aromatic substitution on the benzylic moiety was not observed by Sintenis. It took place, however, on the veratryl moiety of compound 2, as expected<sup>23</sup> because of the large activating effect on the aromatic ring by the two methoxyl substituents, which makes it much more reactive towards electrophilic substitution.

By analogy with the reaction of anisole derivatives with hydrochloric acid<sup>24a</sup> (Eq II-1),



Sintenis attributed the cleavage of aryl ether not to the direct action of chlorine, but rather to an acid hydrolysis subsequent to the

liberation of  $H^+$  and  $Cl^-$  species from the electrophilic substitution observed on the phenyl ring. Sintenis supported his hypothesis by setting experimental conditions that would quench the hydrogen halide produced: cleavage was then totally inhibited, and the p-chlorophenyl benzyl ether was formed, which, after isolation, was hydrolysed by HCl and split into benzyl chloride and p-chlorophenol. The conclusion that was drawn from these experiments presumably discouraged any further investigations along these lines, so that today, in contrast to the proliferation of information on acid hydrolysis, the reaction of chlorine with benzyl aryl ethers seems somehow neglected. However, the conclusion that chlorine acted on benzyl-aryl ether bonds via aromatic electrophilic substitution is seriously questionable. It is indeed well known<sup>25</sup> that mercuric oxide, HgO, used by Sintenis as an HCl quencher, reacts with molecular chlorine as well. Chlorine is quantitatively converted by HgO into chlorine monoxide,  $Cl_2O$ , and mercuric chloride  $HgCl_2$  (Eq. II-2 and II-3).

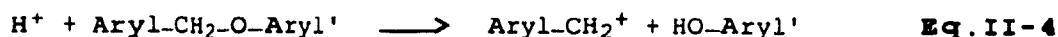


Since Sintenis stopped the reaction when the excess of mercuric oxide was almost totally converted into mercuric chloride ("Die Operation wurde ..... unterbrochen, als das im Uberschuß vorhandene Quecksilberoxyd fast vollständig in Quecksilberchlorid verwandelt war."), molecular chlorine was given no chance to act as such during the reaction,

and the substitution product - benzyl (p-chlorophenyl) ether - undoubtedly resulted from the action of  $\text{Cl}_2\text{O}$  on the initial ether. Therefore, this experiment did not actually provide evidence on the nature of the action of molecular chlorine on the benzyl aryl ether linkage.

Sintenis did demonstrate, however, that benzyl alkyl- and benzyl aryl ethers were cleaved at room temperature by a large excess of chlorine gas, and indicated the labile C-O bond of each type of ether. That the linkage cleaved was different, was not by itself evidence either for a different mechanism, or for a completely different reaction. It indicated only that the nature of the ether groups had an influence on the cleavage process.

Since the work of Sintenis, benzyl aryl ethers have indeed been commonly recognized as highly reactive compounds<sup>26a,27</sup> compared to their benzyl alkyl homologs, for reasons that are now common knowledge. When the labile bond between the benzylic carbon and the ethereal oxygen cleaves, a quite stable benzylic carbocation is generated, with a positive charge delocalized onto the aromatic ring. The liberated phenolic counterpart is a very good leaving group (Eq.II-4).



Benzyl aryl ethers have actually been found to undergo thermal degradation at lower temperatures<sup>28</sup> than their alkyl homologs<sup>29</sup>. After Sintenis described the somewhat facile cleavage of benzyl phenyl ether

by concentrated hydrochloric acid at 100°C, yielding phenol and benzyl chloride<sup>30</sup>, extensive studies provided additional experimental evidence of the highly reactive character of benzyl aryl ethers. The influence of the stability of the benzylic carbocation on the rate of hydrolysis was pointed out in 1929 by Tronov and Ladigina, who investigated the hydrolysis of a variety of ethers by hydrobromic acid in glacial acetic acid at 20°C, and found relative rates of 1 and 864 for anisole and benzyl phenyl ether, respectively<sup>31</sup>. Another example was the selective removal of both benzyl groups in 1,4-dimethoxy-2,6-dibenzyloxybenzene in a one hour reaction at 65°C with concentrated hydrochloric acid<sup>24b</sup>. Moreover, in 1972, Johansson and Miksche found that alpha aryl-ether bonds undergo sulfuric acid-catalyzed hydrolysis 100 times faster than do beta aryl ethers<sup>32</sup>. The influence of the nature of the leaving group on the rate of hydrolysis had already been demonstrated by Tronov and Ladigina with the finding that benzyl phenyl ether hydrolysed 5 times faster than dibenzyl ether. In 1978, Iakubovskii and Reznikov<sup>33</sup> observed that the acid-catalyzed hydrolysis rate constants at pH 2 and 80°C of guaiacyl ether of veratryl alcohol was about 45 times greater than that of its alpha-methyl equivalent. An investigation on the kinetics of hydrochloric-acid catalyzed hydrolysis in aqueous ethanol of benzyl aryl ethers<sup>3</sup> showed that these compounds are reactive even at room temperature. In more recent work, though, Yasuda<sup>34</sup> observed that non phenolic phenylcoumaran structures, that is to say cyclic benzyl aryl ethers, were exceptionally stable, and resisted a 3 hour treatment with 90% acetic acid at 180°C.

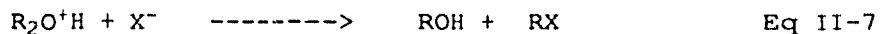
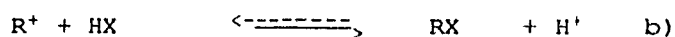
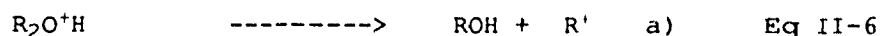
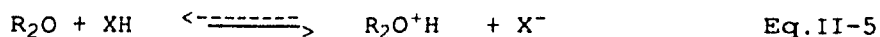
The high reactivity of benzyl aryl ethers in acid-catalyzed hydrolysis made plausible the hypothesis of Sintenis. However, our experiments with low charges of chlorine permitted us to identify the primary reaction occurring during the chlorination of benzyl aryl ethers.

When compound 2 was treated with very low charges of chlorine, ( $x = 0.10$  and  $0.05$  in table II-2), unreacted starting material and aromatic alpha-cleavage products, chlorine-substituted or not, were detected in the reaction mixture, but no uncleaved product from the aromatic substitution of chlorine on 2. Under the hypothesis that substitution induces acidolysis, chlorine substituted dimer should have cleaved faster than unreacted 2 in order to account for the above observations.

This result may suggest that ring-chlorination is not an initial source of any hydrogen chloride that would catalyze benzyl cleavage. Nevertheless, even a slight reaction of chlorine with acetic acid might generate hydrogen chloride (along with hypochlorite). Furthermore, since the acetic acid was not rigorously dried, hydrogen chloride (and hypochlorous acid) may well have been generated by aqueous hydrolysis.

The generally accepted mechanism for acid hydrolysis of ethers proceeds through two basic steps<sup>24c, 26b</sup>. The first is the formation of an oxonium salt, or something akin to one (Eq.II-5); the second is the cleavage of the ether bond either unimolecularly ( $A_1$ ) (Eq.II-6), or bimolecularly ( $A_2$ ) with the intervention of a nucleophile in the dissociation process (Eq.II-7).





The stability of the carbocation  $R^+$  determines, in theory, which one of the two mechanisms,  $A_1$  or  $A_2$ , should be followed, and which of the two carbon-oxygen bonds should be broken. In these reactions, all proton transfers are usually fast equilibria, so that the rate-determining step in both mechanisms  $A_1$  and  $A_2$  is the dissociation of the carbon-oxygen bond. It has been found, however, that changes in basicity of the ethereal oxygen affect the rate of acidolysis<sup>24d</sup>. The overall influence from its inductive and conjugative effects (electron-withdrawing and -releasing, respectively) makes chlorine an electron-withdrawing group<sup>35a</sup>. We thus expect that its presence on the aromatic nucleus decreases the electronic density on the ethereal oxygen, hence also decreases its basicity, and the rate of cleavage of the ether bond. Experimental support for this reasoning is given by the observation that the presence of an electron-releasing group (a methyl group) on the phenyl ring noticeably increased the rate of HCl-catalysed hydrolysis of benzyl aryl ethers<sup>3</sup>. So we can conclude that the acidolysis of alpha ether bond is slower in the chlorine substituted dimer. Therefore, substitution cannot be the primary reaction, and the actual numbers indicate that cleavage occurred before substitution, which took place afterwards on the phenols arising from

the cleavage, which are more reactive<sup>36</sup> than the etherified phenolic moiety present in the initial compound.

Chlorination of trimer 6 exhibited the same features (Table II-4). No chlorinated trimer was detected, whereas the starting compound was still partially recovered. We observed a different situation in the reaction of the trimer 9: the chlorinated trimer 9-5), the cleavage product 9-3, and the unreacted trimer were simultaneously present (Table II-6). The stabilization of the alpha ether bond by the side chain, already noticeable in the chlorination of compound 6, revealed the competition between cleavage and substitution reactions. Initial compound 9 almost disappeared after a treatment by 0.25 mole of chlorine per monomer unit, while a large proportion of chlorinated trimer was detected, providing additional experimental support to the conclusion drawn earlier on the slower cleavage of chlorine-substituted products.

For all the compounds, the cleavage reaction preceded aromatic substitution. Electrophilic side-chain displacement, resulting from ipso-substitution by chlorine on the benzyl ring, was a secondary reaction, and took place only when chlorine was applied in an excess large enough to first satisfy the sites that are more reactive towards aromatic substitution (Table II-2).

We conducted another type of experiment, aimed at bringing to light the difference between the chlorine-catalyzed and acid-catalyzed cleavage of the benzyl ether bond. Following Sintenis's hypothesis, substituting molecular HCl for molecular chlorine should not affect the cleavage reaction, and HCl-catalyzed acidolysis and Cl<sub>2</sub>-

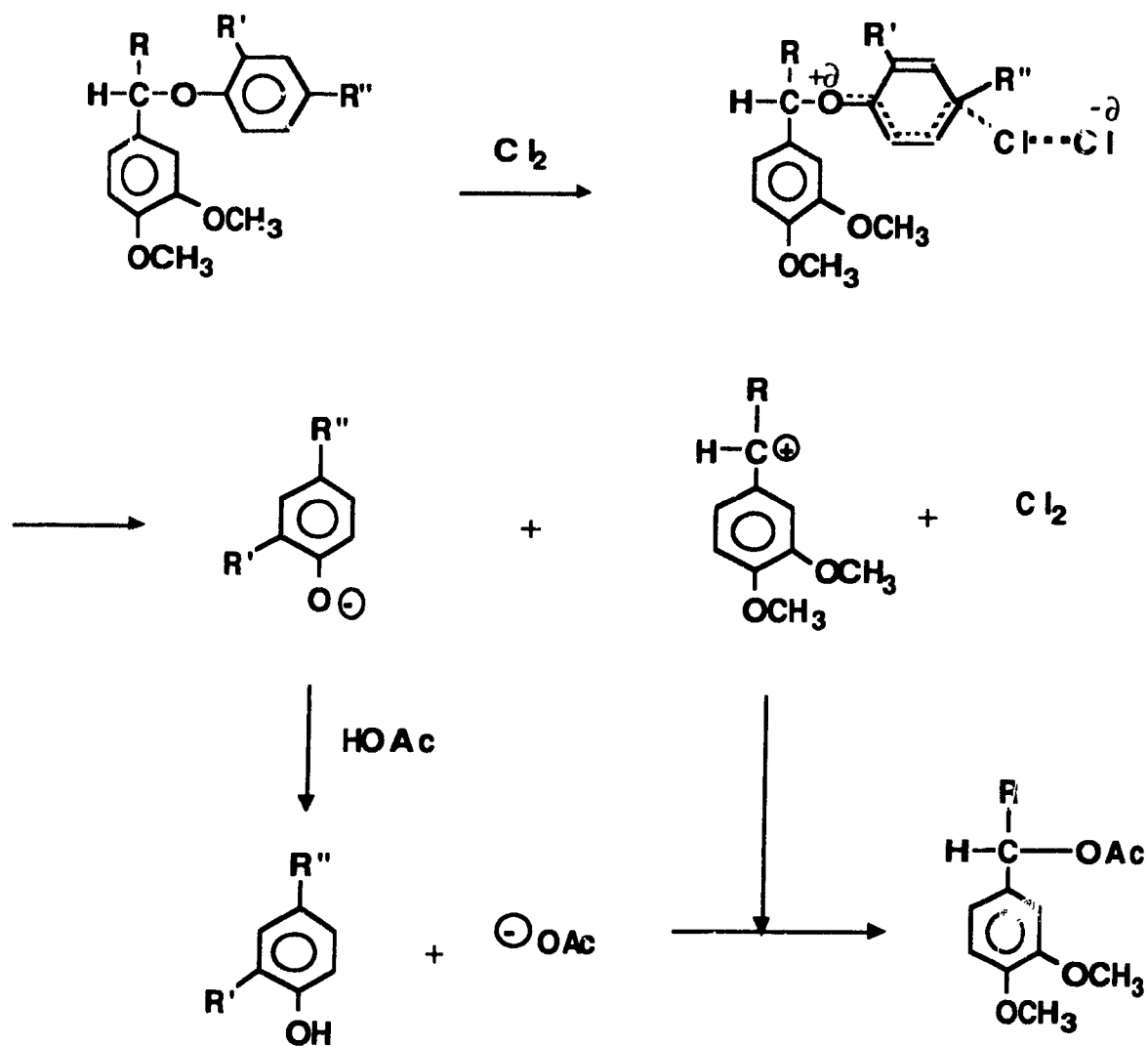
induced-acidolysis products would differ only by the presence of chlorine substituents on the aromatic rings. Compounds 2, 6, and 9 were accordingly subjected to direct acidolysis under a charge of hydrochloric acid of 0.25, under exactly the same experimental conditions as in chlorination.

The direct acidolysis was different from the chlorination in two ways (Tables II-11 and II-12): 1) the far more extensive alpha ether cleavage, 2) the nature and relative proportions of reaction products. The second point derives logically from the first: the higher reactivity of HCl is more likely to promote recombination reactions, thus explaining both the presence of additional reaction products (6-6, 6-8, 6-9, 9-6), and the modification of the relative proportions of cleavage products (Table II-12). Benzyl ether bond cleavage, although expected, was surprisingly more extensive upon treatment with HCl gas than with Cl<sub>2</sub>, in glacial acetic acid. The effect of stabilization of the alpha ether linkage by the nature of the side-chain, which was manifest in the chlorination experiments (the proportions of unaltered ether bond found in the products of 2, 6, and 9 were 0, 1.5, and 38, respectively), was here hardly noticeable: merely traces of uncleaved trimer were detected after direct-acidolysis of 9.

Despite these differences in the nature and yields of products, the evidence suggests that the course of the cleavage by chlorine is generally similar to that of hydrolysis by hydrogen chloride. Accordingly, acid hydrolysis provides a reasonable interpretation for the cleavage of the lignin model compounds by chlorine in glacial acetic acid.

### A possible role of $\text{Cl}_2$ in the cleavage process

The evidence does not permit, however, eliminating the speculative possibility that the cleavage of benzyl aryl ethers by chlorine, which does not cleave benzyl alkyl ethers, proceeds by a unique mechanism. As is well known, glacial acetic acid has some very unusual characteristics<sup>37</sup>. Despite its dielectric constant of 6.15 at 20°C, it exhibits a very low conductance (an indication of the degree of autoionization); its dipole moment is zero because of its association into symmetrical dimers, and its solvation power is very small. Such properties obviously preclude the development of charge separation and the existence of highly dissociated species in solution. Therefore, in chlorination, the reagent is molecular chlorine rather than the so-called "positive" chlorine. Although kinetics experiments have not been done, there is evidence in the literature<sup>26c, 38</sup> suggesting a mechanism in which molecular chlorine may be the initiating agent. If we consider that the cleavage occurs in the presence of very low charges of chlorine, whose contribution to the reaction was non-stoichiometric, then chlorine itself may act as a catalyst. The mechanism shown in scheme II-5 describes the chlorine-catalyzed cleavage of benzyl aryl ethers, and accounts for the formation of alpha-acetylated compounds as principal reaction products. The formation of benzyl chloride derivatives could result from two different mechanisms, either nucleophilic substitution with the displacement of the acetyl group by  $\text{Cl}^-$  ( $\text{SN}_2$ ), or competition between the solvent and  $\text{Cl}^-$  in the nucleophilic substitution subsequent to ether cleavage ( $\text{SN}_1$ ).



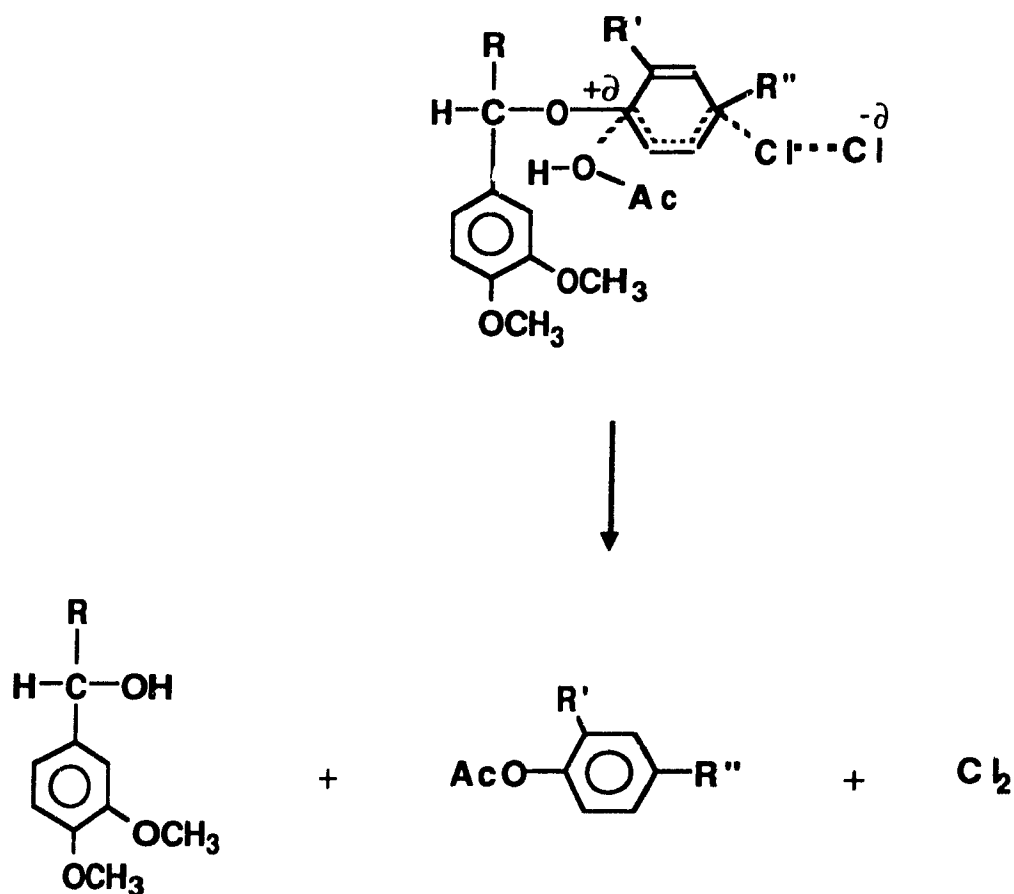
| starting compound | R                                         | R'               | R''             |
|-------------------|-------------------------------------------|------------------|-----------------|
| <b>2</b>          | H                                         | OCH <sub>3</sub> | CH <sub>3</sub> |
| <b>6</b>          | CH <sub>2</sub> OAr <sub>1</sub>          | H                | CH <sub>3</sub> |
| <b>2</b>          | CH (OAr <sub>1</sub> ) CH <sub>2</sub> OH | OCH <sub>3</sub> | CH <sub>3</sub> |

SCHEME II-5. A possible mechanism proposed for the chlorine-catalyzed cleavage of benzyl aryl ether linkage in glacial acetic acid.

The occurrence of such products only in the chlorination of compound 2 (Tables II-1, II-3 and II-5) suggests that additional aryl ether group on the side chain affected the reaction in the same way as it affected acidolysis, which follows an  $SN_1$  mechanism<sup>3</sup>, and that, by decreasing the stabilization of the benzylic carbocation, it statistically favoured the attack by the solvent in the competition between the two nucleophiles.

The analogies in the literature<sup>26c,38</sup> suggest that an alpha hydroxyl group may arise from the scission of the aryl-oxygen bond (scheme II-6). The presence of alpha methoxyl groups in some reaction products from 6 and 9 are almost certainly artefacts of the HPLC analysis. During the analysis, the reaction products were in contact with a mixture of methanol and water, in presence of a acidic buffer,  $NH_4^+OAc$ . Hence, all the benzylic halogens that appeared in the GC would now appear as acetate or methoxyl.

It may seem illogical to invoke electrophilic aromatic attack for the mechanism of a reaction which takes place faster than electrophilic aromatic substitution itself. It is not illogical, however, if we consider the well known mechanism of aromatic substitution<sup>35b</sup>: the initial step is a rapid, reversible, non specific complexation of the electrophile with the  $\pi$  electron system of the aromatic ring; the next step is the rate-determining transition of the  $\pi$ -complex into a  $\sigma$ -complex, with the formation of a cyclohexadienonium ion where the electrophile is linked to a specific carbon atom of the nucleus. In the mechanism that we propose, the chlorine molecule is only associated with the aromatic nucleus in  $\pi$ -interactions which, being rapid



SCHEME II-6. A possible mechanism of the scission of the aryl-oxygen bond<sup>26c,38</sup>. R, R', and R'' are illustrated in scheme II-5.

(the rate of formation of  $\pi$ -complexes cannot be measured even at temperatures as low as  $-80^{\circ}\text{C}$ <sup>39</sup>) and reversible, confer the catalytic character on the action of chlorine.

Shades of meaning must be brought to the notion of non-specificity of the  $\pi$ -interaction. The charge delocalized on the aromatic ring being nevertheless polarized by the inductive and conjugative effects, the electronic density will forcedly not be homogeneous all over the ring, and the interaction will be stronger with the higher electronic density. It is in that context that we call this interaction "para-attack". But it must be clear that the mechanism described in scheme II-5 does not include the formation of any para  $\sigma$ -linkage between the chlorine atom and the aromatic nucleus.

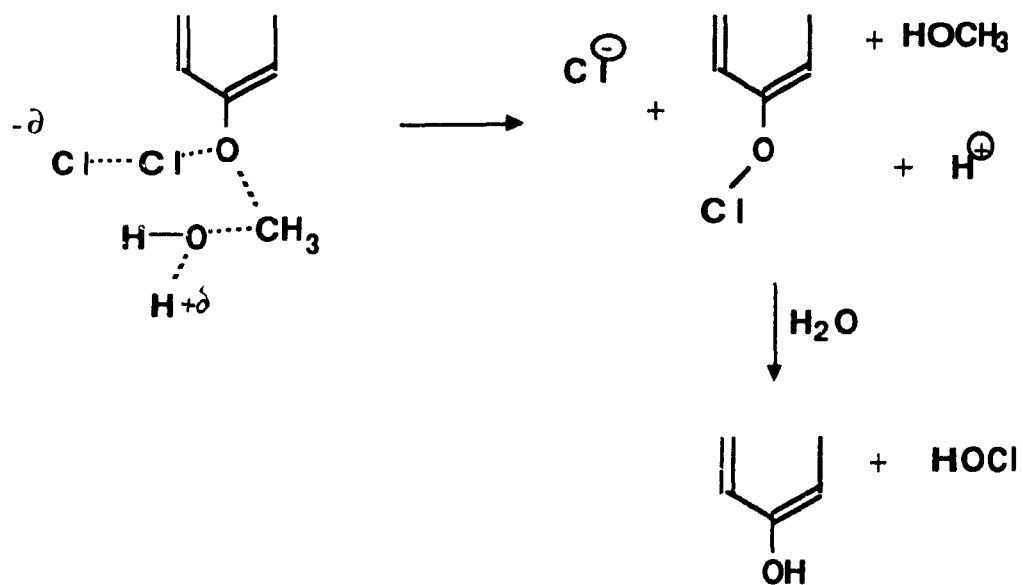
We may consider the mechanism in scheme II-5 in the light of similar chlorine-catalyzed reactions reported in the literature. In the course of investigation on the chlorination of lignin model compounds by molecular chlorine in aqueous acetic acid, Sarkanen and Dence<sup>9</sup> observed that despite the firm resistance of methyl phenylethers to acidolysis, demethylation did occur at room temperature in the presence of chlorine. They proposed two possible mechanisms:

a) In a bimolecular mechanism similar to that of the acid-catalyzed hydrolysis reaction (Eq.II-5 and II-7), the chlorine molecule assumes the usual role of the proton and forms an oxonium complex with the ethereal oxygen, while water acts as the nucleophile in the cleavage of the O-CH<sub>3</sub> bond (Scheme II-7 a)).

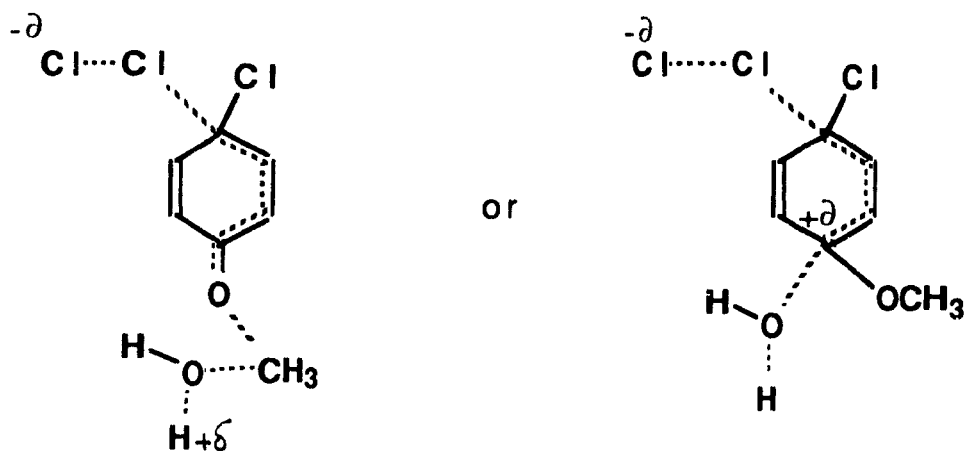
b) The second mechanism begins with the attack of the chlorine molecule at the position para to the methoxyl group (Scheme II-7 b)).



a)



b)



SCHEME II-7. Mechanisms proposed by Sarkanen and Dence for demethylation in aqueous acetic acid.<sup>9</sup> a) Attack of the polarized chlorine at the ether oxygen of the methoxyl group; b) Possible intermediates resulting from the attack at the position para to the methoxyl group.

After additional experiments, Sarkanen and Strauss<sup>40</sup> chose the first mechanism, which has since been generally considered the more probable. This mechanism, however, was not unequivocally established, but was justified by two dubious and controversial arguments:

i) the demethylation rate was not affected by the presence para to the methoxyl, of either chlorine or an aldehyde group, and

ii) the failure of demethylation when positions ortho to the methoxyl were both occupied by either a chlorine or a methoxyl group, an effect attributed to steric hindrance.

The first argument is refuted by the observation<sup>9</sup> that demethylation was much faster than aromatic substitution at a position ortho to the methoxyl groups, and slower than substitution at the para position.

Thus, since demethylation takes place on the para-substituted molecule, it should not be affected if the initial compound is already para-substituted.

The second argument was brought into question by the finding that 1,2,3-trimethoxybenzene was effectively demethylated to 2,6-dimethoxybenzoquinone by nitrous acid<sup>38</sup>. In the mechanism proposed for this reaction, demethylation was initiated by an attack of the electrophilic agent ( $\text{H}_2\text{ONO}'$ ) at the position para to the central methoxyl group. Accordingly, the observation<sup>40</sup> that demethylation of tetrachloroveratrole and 2,4,6-trichloroanisole does not occur can be attributed to the electron-withdrawing influence of the numerous chlorine atoms on the ring which was then sufficiently deactivated to be unreactive towards any kind of electrophilic interaction at the position para to the methoxyl group.

In glacial acetic acid, chlorine does not cause demethylation<sup>8,10</sup>, but does cleave benzyl aryl ether bonds. The action of chlorine in the demethylation process is conditional on the presence of a strong nucleophile and polarizing agent such as water. However, replacing the methyl group by a benzyl group (where a potential positive charge is much more stabilized) promotes this scission despite the limited solvating and polarizing properties of glacial acetic acid. This observation suggests that the rate-determining step in the cleavage process is not the attack by chlorine, but the C-O bond dissociation stage.

However, the presence of a benzyl group on one side of the ether bond is not the only condition for achieving cleavage, as shown by the stability of benzyl alkyl ethers towards chlorine, as discussed in the next chapter. This difference in reactivity may be imputable to the very good leaving-group character of phenol compared to alcohol, as it is described for acidolysis, thus supporting the mechanism favoured by Sarkanen and his coworkers for demethylation (Scheme II-7 a)). The difference can be better explained, however, by the second mechanism (Schemes II-5 and II-7 b)) in which the effectiveness of Cl<sub>2</sub> catalysis is restricted to benzyl aryl ethers, with their unique ability to interact with Cl<sub>2</sub> through  $\pi$ -complexes, and to readily form quinonoid structures.

Theoretical support was given to this latter mechanism when the two possible mechanisms proposed by Sarkanen and Dence<sup>9</sup> were examined<sup>4,1</sup> in relation to the hard and soft acids and bases concept (HSAB)<sup>42</sup> extended to electrophiles and nucleophiles, and to the frontier molecular orbital

theory<sup>43</sup>. The direct attack of  $\text{Cl}^{\delta+}$  on  $-\text{OCH}_3$  (analogous to the protonation step in acid hydrolysis) was found to be highly unstable thermodynamically, while the mechanism through an attack by  $\text{Cl}^{\delta+}$  on the ring at the position para to the methoxyl appeared as the most favoured, both kinetically and thermodynamically. The passage via a quinonoid form (Schemes II-5 and II-7 b)) was also supported by the calculations performed on the structure representing the attack of the electrophile at the position para to the methoxyl group. They show that the bond between the oxygen and the aromatic ring has increased double bond character, and the degree of bonding between the oxygen and the methyl group is lower than in the ground state. The mechanism via ortho-chlorination that is proposed in the literature<sup>44</sup> was also demonstrated to require more energy than that via an attack in para, presumably because of steric influence.

### Conclusion

From our experimental results and theoretical considerations, we conclude that the cleavage of benzyl aryl ether linkage by chlorine in glacial acetic acid is the primary reaction prior to aromatic substitution - and *a fortiori* occurs prior to electrophilic side-chain displacement. In the compounds examined in these experiments, this cleavage is readily explicable as the result of conventional hydrolysis by acid.

From the experimental evidence, however, we cannot rule out the possibility that the cleavage may be promoted by the catalytic action of molecular chlorine by a mechanism that includes an electrophilic interaction between chlorine and the site of the phenyl nucleus para to the ether bond. This conclusion is consistent with and rationalizes the observation made long ago<sup>12</sup> that rates of delignification by chlorine increase at lower pH. It also suggests that chlorine substitution, a non-beneficial reaction - in terms of delignification - with undesirable environmental fall-out, may be avoidable during the bleaching of pulp.

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### CHAPTER III

#### CLEAVAGE OF THE BENZYL ALKYL ETHER BOND IN NON-PHENOLIC LIGNIN MODEL COMPOUNDS

## INTRODUCTION

The experiments reported in chapter II on the chlorination of benzyl aryl ethers has had no precedent in the literature. Although some publications include results on the chlorination of benzyl alkyl ethers, this reaction, too, has not been extensively investigated. Generally, in the study of the chlorination of lignin<sup>1</sup>, the trietherified non-phenolic units in the polymer have been represented by benzyl alkyl ethers bearing an aryloxy group at the beta carbon of the side chain. Surprisingly, however, their reaction with molecular chlorine in glacial acetic acid has scarcely been investigated, and then only when a large excess of chlorine was applied<sup>2</sup>.

This chapter gives the results of the chlorination of four model compounds representing fully etherified units of the benzyl-alkyl ether type in lignin, and bearing different substituents on the side chain. These experiments provided evidence that in the reaction of benzyl alkyl ethers with molecular chlorine in glacial acetic acid the primary effect was aromatic substitution, and that benzyl alkyl ether bonds were generally stable.

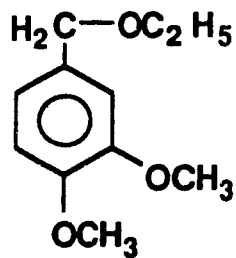
## RESULTS

Compounds 1, 4, 5 and 8 in scheme III-1 are the alkyl analogues of the benzyl aryl ethers whose reactions are reported in Chapter II (Scheme II-1). The alpha substituent was either a methyl- (compounds 1 and 5) or an ethyl ether group (compounds 4 and 8), depending on the availability of the synthesis reagents. Reactivity was not likely to be altered by such minor structural differences. However, the presence of an additional methyl substituent on the aromatic ring of the beta-aryloxy group (compound 5) was expected to influence the course of aromatic substitution and of subsequent reactions.

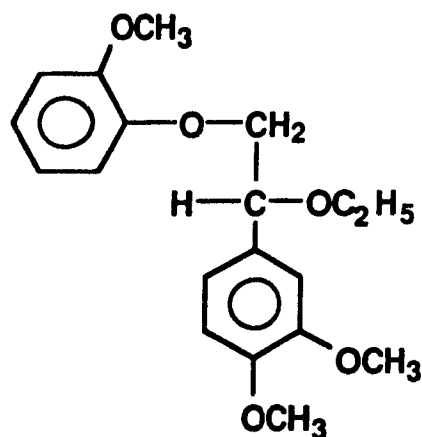
The compounds were treated in the same manner as their aryl analogues (see Experimental and Chapter II). The stability of the compounds and of their products of reaction under the conditions of analysis allowed us to proceed to identification and yield measurements by GC-MS and GC analyses, respectively.

The complete results of the chlorination of compounds 1, 4, 5, and 8 are presented in detail in the tables III-1 to III-17. Except for some minor differences, in all four compounds the benzyl-alkyl ether bonds exhibited great stability in the presence of chlorine.

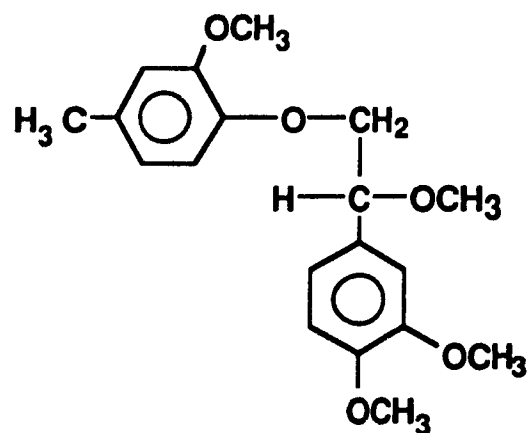




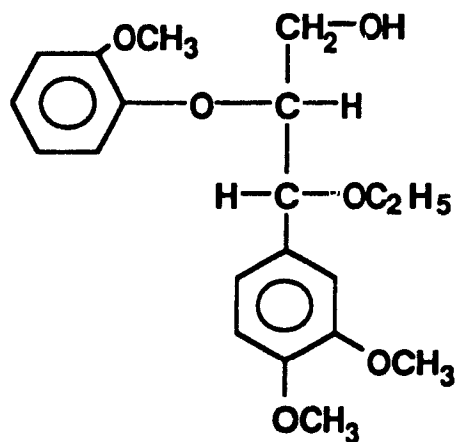
1



4



5



8

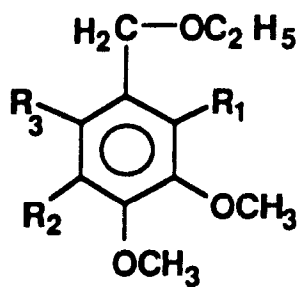
SCHEME III-1 . Compounds of the benzyl-alkyl ether type. 1, 4, 5, and 8.

Table III-1 . Products from the chlorination of compound 1.

| compound   | structure                                                  | GC retention time* (min) |
|------------|------------------------------------------------------------|--------------------------|
| <u>1</u>   | compound 1                                                 | 3.02                     |
| <u>1-1</u> | veratrylchloride                                           | 2.89                     |
| <u>1-2</u> | veratrylacetate                                            | 3.73                     |
| <u>1-3</u> | (6-chloro-3,4 dimethoxyphenyl)-ethoxymethane               | 4.16                     |
| <u>1-4</u> | (2 or 5-chloro-3,4 dimethoxyphenyl)-<br>ethoxymethane      | 3.99                     |
| <u>1-5</u> | 4,5-dichloroveratrole                                      | 3.06                     |
| <u>1-6</u> | (5 or 2, 6-dichloro-3,4 dimethoxyphenyl)-<br>ethoxymethane | 5.15                     |
| <u>1-7</u> | (2 or 5, 6-dichloro-3,4 dimethoxyphenyl)-<br>ethoxymethane | 5.34                     |
| <u>1-8</u> | (2, 5-dichloro-3,4 dimethoxyphenyl)-<br>ethoxymethane      | 4.57                     |
| <u>1-9</u> | (2,5,6-trichloro-3,4 dimethoxyphenyl)-<br>ethoxymethane    | 5.87                     |

\* GC and GC-MS conditions:

column DB5, J&W; carrier He, 1ml/min; temperature gradient:  
140°C- 270°C, 10°C/min.



| compound         | R <sub>1</sub> | R <sub>2</sub> | R <sub>3</sub> |
|------------------|----------------|----------------|----------------|
| <u>1-3</u>       | H              | H              | Cl             |
| <u>1-4</u>       | H              | Cl             | H              |
| or               | Cl             | H              | H              |
| <u>1-6 ; 1-7</u> | H              | Cl             | Cl             |
| and              | Cl             | H              | Cl             |
| <u>1-8</u>       | Cl             | Cl             | H              |
| <u>1-9</u>       | Cl             | Cl             | Cl             |

SCHEME III-2 . Substitution products from the chlorination  
of compound 1

Table III-2 . Yields of products of the chlorination of compound 1 under increasing charges of chlorine, x, (in moles of chlorine per C<sub>9</sub> unit). Yields, expressed as percent of initial C<sub>9</sub> unit, obtained by GC analysis. Standard deviations are given in parentheses.

| x    | 1             | 1-1          | 1-2          | 1-3           | 1-4          | 1-5           | 1-6          | 1-7          | 1-8          | 1-9          | total         |
|------|---------------|--------------|--------------|---------------|--------------|---------------|--------------|--------------|--------------|--------------|---------------|
| 0    | 96.0<br>(0.1) |              |              |               |              |               |              |              |              |              | 96.0<br>(0.1) |
| 0.25 | 47.9<br>(0.1) | 8<br>(2)     | 8<br>(1)     | 22<br>(1)     |              |               |              |              |              |              | 86<br>(2)     |
| 0.50 | 22.2<br>(0.1) | 12<br>(1)    | 8<br>(1)     | 47<br>(2)     | 1.1<br>(0.1) |               |              |              |              |              | 90<br>(2)     |
| 0.75 | 4.8<br>(0.2)  | 8.2<br>(0.1) | 3.6<br>(0.1) | 64<br>(1)     | 1.3<br>(0.1) |               |              |              |              |              | 82<br>(1)     |
| 1.0  | 0.8<br>(0)    | 2.0<br>(0.1) | 0            | 88<br>(2)     | 1.7<br>(0.1) |               |              |              |              |              | 92<br>(2)     |
| 1.5  | 0             | 0            | -            | 68.6<br>(0.1) | 1.6<br>(0.1) | 17.5<br>(0.1) | 3.6<br>(0.2) | 4.3<br>(0.1) |              |              | 95.6<br>(0.3) |
| 2.0  |               |              |              | 28<br>(2)     | 1.9<br>(0.4) | 42<br>(2)     | 6.7<br>(0.4) | 8.6<br>(0.3) |              |              | 87<br>(3)     |
| 2.5  |               |              |              | 1.7<br>(0.1)  | 4.5<br>(0.1) | 50.7<br>(0.1) | 6.8<br>(0.5) | 11<br>(1)    | 1.0<br>(0.1) | 2.0<br>(0.2) | 78<br>(1)     |

Table III-3. Combined yields of related products from the chlorination of compound 1 under increasing charges of chlorine, x, (in moles of chlorine per C<sub>9</sub> unit): a) compound 1 recovered unaltered after the reaction, b) products from alpha aryl ether bond cleavage, c) products from substitution on the aromatic rings. Yields, expressed as percent of initial C<sub>9</sub> unit, obtained by GC analysis. Standard deviations are given in parentheses.

| chlorine<br>charge<br>x | unaltered<br>1 | alpha-ether<br>cleavage<br><u>1-1, 1-2,</u> | substitution                                             |                                                       |
|-------------------------|----------------|---------------------------------------------|----------------------------------------------------------|-------------------------------------------------------|
|                         |                |                                             | ipso-substitution<br>(side-chain cleavage)<br><u>1-5</u> | other<br><u>1-3, 1-4, 1-6</u><br><u>1-7, 1-8, 1-9</u> |
| 0                       | 96.0<br>(0.1)  | 0                                           | -                                                        | 0                                                     |
| 0.25                    | 47.9<br>(0.1)  | 16<br>(2)                                   | -                                                        | 22<br>(1)                                             |
| 0.50                    | 22.2<br>(0.1)  | 20<br>(1)                                   | -                                                        | 48<br>(2)                                             |
| 0.75                    | 4.8<br>(0.2)   | 11.8<br>(0.1)                               | -                                                        | 65<br>(1)                                             |
| 1.0                     | 0.8<br>(0.1)   | 2.0<br>(0.1)                                | 0                                                        | 90<br>(2)                                             |
| 1.5                     | 0              | 0                                           | 17.5<br>(0.1)                                            | 78.3<br>(0.2)                                         |
| 2.0                     | -              | -                                           | 42<br>(2)                                                | 45<br>(2)                                             |
| 2.5                     | -              | -                                           | 50.7<br>(0.1)                                            | 27<br>(1)                                             |

Table III-4 . Products from the chlorination of compound 4.

| compound   | structure                                                                                      | GC retention time* (min) |
|------------|------------------------------------------------------------------------------------------------|--------------------------|
| 4          | compound 4                                                                                     | 5.38                     |
| <u>4-1</u> | 1-(6-chloro-3,4 dimethoxyphenyl)-1-ethoxy-<br>2-(2-methoxyphenoxy)ethane                       | 6.19                     |
| <u>4-2</u> | 1-(3,4 dimethoxyphenyl)-1-ethoxy-2-(4 or 5-chloro-<br>2-methoxyphenoxy)ethane                  | 6.61                     |
| <u>4-3</u> | 1-(3,4 dimethoxyphenyl)-1-ethoxy-2-(5 or 4-chloro-<br>2-methoxyphenoxy)ethane                  | 6.78                     |
| <u>4-4</u> | 1-(6-chloro-3,4 dimethoxyphenyl)-1-ethoxy-<br>2-(4 or 5-chloro-2-methoxyphenoxy)ethane         | 7.68                     |
| <u>4-5</u> | 1-(6-chloro-3,4 dimethoxyphenyl)-1-ethoxy-<br>2-(5 or 4-chloro-2-methoxyphenoxy)ethane         | 7.91                     |
| <u>4-6</u> | 1-(6-chloro-3,4 dimethoxyphenyl)-1-ethoxy-<br>2-(4,5-dichloro-2-methoxyphenoxy)ethane          | 10.14 <sup>a)</sup>      |
| <u>4-7</u> | 1-(2 or 5,6-dichloro-3,4 dimethoxyphenyl)-1-ethoxy-<br>2-(4,5-dichloro-2-methoxyphenoxy)ethane | 12.62 <sup>a)</sup>      |
| <u>4-8</u> | 1-(5 or 2,6-dichloro-3,4 dimethoxyphenyl)-1-ethoxy-<br>2-(4,5-dichloro-2-methoxyphenoxy)ethane | 12.85 <sup>a)</sup>      |

\* GC and GC-MS conditions:

column DB5, J&W; carrier He, 1ml/min; temperature gradient:  
200°C-270°C, 20°C/min.

a) Temperature gradient: 230-270°C

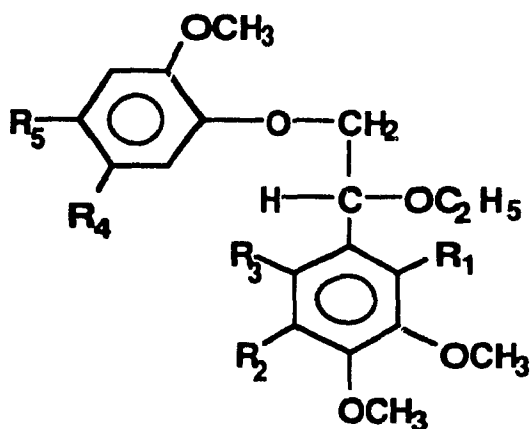
Table III-4 (cont'd) . Products from the chlorination of compound 4.

| compound    | structure                                                                                      | GC retention time* (min) |
|-------------|------------------------------------------------------------------------------------------------|--------------------------|
| <u>4-9</u>  | 4,5-dichloroveratrole                                                                          | 1.97                     |
| <u>4-10</u> | 3,4,5-trichloroveratrole                                                                       | 2.33                     |
| <u>4-11</u> | tetrachloroveratrole                                                                           | 2.43                     |
| <u>4-12</u> | (4,5-dichloro-2-methoxyphenoxy)acetaldehyde                                                    | 2.50                     |
| <u>4-13</u> | unknown. Presumably penta- and hexachloro<br>products from substitution on compound <u>4</u> . | 0.53/11.83/12.20         |

\*GC and GC-MS conditions:

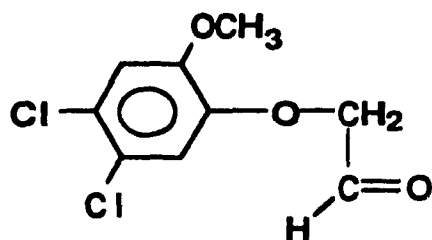
column DB5, J&W; carrier He, 1ml/min; temperature gradient:  
200°C-270°C, 20°C/min.

a)



| compound        | R <sub>1</sub> | R <sub>2</sub> | R <sub>3</sub> | R <sub>4</sub> | R <sub>5</sub> |
|-----------------|----------------|----------------|----------------|----------------|----------------|
| <u>4-1</u>      | H              | H              | Cl             | H              | H              |
| <u>4-2; 4-3</u> | H              | H              | H              | Cl             | H              |
| and             | H              | H              | H              | H              | Cl             |
| <u>4-4; 4-5</u> | H              | H              | Cl             | Cl             | H              |
| and             | H              | H              | Cl             | H              | Cl             |
| <u>4-6</u>      | H              | H              | Cl             | Cl             | Cl             |
| <u>4-7; 4-8</u> | Cl             | H              | Cl             | Cl             | Cl             |
| and             | H              | Cl             | Cl             | Cl             | Cl             |

b)

4-11

SCHEME III-3 . Products from the chlorination of compound 4.

a) Substitution products. b) Cleavage product.



Table III-5. Yields of aromatic substitution products from the chlorination of compound 4 under increasing charges of chlorine, x, (in moles of chlorine per C<sub>9</sub> unit). Yields, in percent of initial C<sub>9</sub> unit, obtained by GC analysis. Standard deviations are given in parentheses.

| Cl <sub>2</sub><br>charge | UN-           | MONO-         |               |               | DI-           |               | TRI-          | TETRA-     |              | PENTA-<br>HEXA-              |
|---------------------------|---------------|---------------|---------------|---------------|---------------|---------------|---------------|------------|--------------|------------------------------|
| x                         | 4             | <u>4-1</u>    | <u>4-2</u>    | <u>4-3</u>    | <u>4-4</u>    | <u>4-5</u>    | <u>4-6</u>    | <u>4-7</u> | <u>4-8</u>   | <u>4-13</u>                  |
| 0                         | 87<br>(1)     | -             | -             | -             | -             | -             | -             | -          | -            | -                            |
| 0.125                     | 50.0<br>(0.3) | 21.5<br>(0.1) | 5.8<br>(0.2)  | 5.7<br>(0.1)  | -             | -             | -             | -          | -            | -                            |
| 0.25                      | 32.3<br>(0.1) | 29.9<br>(0.3) | 8.5<br>(0.3)  | 8.0<br>(0.5)  | 3.9<br>(0.1)  | 3.6<br>(0.1)  | -             | -          | -            | -                            |
| 0.375                     | 19.1<br>(0.2) | 34.8<br>(0.2) | 9.8<br>(0.1)  | 8.8<br>(0.3)  | 8.0<br>(0.3)  | 7.3<br>(0.1)  | -             | -          | -            | -                            |
| 0.50                      | 10.3<br>(0.4) | 38.7<br>(0.3) | 10.7<br>(0.4) | 10.1<br>(0.4) | 9.4<br>(0.1)  | 8.8<br>(0.1)  | -             | -          | -            | -                            |
| 0.75                      | 2.6<br>(0.1)  | 27.8<br>(0.2) | 6.9<br>(0.2)  | 6.1<br>(0.1)  | 27.0<br>(0.2) | 23.1<br>(0.2) | -             | -          | -            | -                            |
| 1.0                       | 0             | 0             | 0             | 0             | 40.7<br>(0.5) | 32.5<br>(0.4) | 15.7<br>(0.4) | -          | -            | -                            |
| 1.5                       | -             | -             | -             | -             | 21<br>(1)     | 19<br>(1)     | 45<br>(5)     | -          | 1.5<br>(0.2) | -                            |
| 2.0                       | -             | -             | -             | -             | 0             | 0             | 41<br>(1)     | 5<br>(3)   | 19<br>(1)    | -                            |
| 2.5                       | -             | -             | -             | -             | -             | -             | 29<br>(2)     | 6<br>(2)   | 27<br>(1)    | 3/1<br>(1)/(1)               |
| 3.5                       | -             | -             | -             | -             | -             | -             | 3.0<br>(0.1)  | 7<br>(3)   | 50<br>(3)    | 5/4<br>(1)/(1)               |
| 4.0                       | -             | -             | -             | -             | -             | -             | -             | 7<br>(0.5) | 55<br>(2)    | 8/6.5/3.5<br>(1)/(0.2)/(0.5) |
| 6.0                       | -             | -             | -             | -             | -             | -             | -             | -          | 60<br>(3)    | 15<br>(2)                    |

Table III-6 . Yields of cleavage products (aromatic ipso-substitution) from the chlorination of compound 4 under increasing charges of chlorine, x, (in moles of chlorine per C<sub>9</sub> unit). Yields, in percent of initial C<sub>9</sub> unit, obtained by GC analysis. Standard deviations are given in parentheses.

| chlorine<br>charge<br>x | <u>4-9</u>   | <u>4-10</u>  | <u>4-11</u>  | <u>4-12</u>  |
|-------------------------|--------------|--------------|--------------|--------------|
| 1.5                     | -<br>(0.1)   | -            | -            | -            |
| 2.0                     | 4.9<br>(0.5) | 1.2<br>(0.1) | -            | 0.7<br>(0.1) |
| 2.5                     | 8.0<br>(0.3) | 1.7<br>(0.2) | -            | 5<br>(1)     |
| 3.5                     | 8.5<br>(0.1) | 2.0<br>(0.1) | 0            | 6<br>(1)     |
| 4.0                     | 6.8<br>(0.1) | 3.0<br>(0.1) | 0.5<br>(0.1) | 8<br>(1)     |
| 4.5                     | 12<br>(3)    | 2.0<br>(0.5) | 2.0<br>(0.5) | 7<br>(1)     |
| 5.0                     | 13<br>(1)    | 4.5<br>(0.5) | 3.0<br>(0.5) | 3.0<br>(0.5) |
| 6.0                     | 7.2<br>(0.2) | 4.0<br>(0.1) | 1.5<br>(0.5) | 3.0<br>(0.5) |

Table III-7 . Combined yields of related products from the chlorination of compound 4 under increasing charges of chlorine, x, (in moles of chlorine per C9 unit): a) compound 4 recovered unaltered after the reaction, b) products from alpha aryl ether bond cleavage, c) products from substitution on the aromatic rings. Yields, expressed as percent of initial C9 unit, obtained by GC analysis. Standard deviations are given in parentheses.

| Cl <sub>2</sub><br>charge<br>x | unaltered<br>4 | alpha-ether<br>cleavage | substitution                                                                         |                                                                             | Total         |
|--------------------------------|----------------|-------------------------|--------------------------------------------------------------------------------------|-----------------------------------------------------------------------------|---------------|
|                                |                |                         | ipso-substitution<br>(side-chain cleavage)<br><u>4-9, 4-10,</u><br><u>4-11, 4-12</u> | other<br><u>4-1, 4-2, 4-3,</u><br><u>4-4, 4-6,</u><br><u>4-7, 4-8, 4-13</u> |               |
| 0                              | 87<br>(1)      | -                       | -                                                                                    | 0                                                                           | 87<br>(1)     |
| 0.125                          | 50.0<br>(0.3)  | -                       | -                                                                                    | 33.0<br>(0.3)                                                               | 83.0<br>(0.4) |
| 0.25                           | 32.3<br>(0.1)  | -                       | -                                                                                    | 53.9<br>(0.7)                                                               | 86.2<br>(0.7) |
| 0.375                          | 19.1<br>(0.2)  | -                       | -                                                                                    | 68.7<br>(0.5)                                                               | 87.8<br>(0.5) |
| 0.50                           | 10.3<br>(0.4)  | -                       | -                                                                                    | 77.7<br>(0.6)                                                               | 88.0<br>(0.7) |
| 0.75                           | 2.6<br>(0.1)   | -                       | -                                                                                    | 90.9<br>(0.4)                                                               | 93.5<br>(0.4) |
| 1.0                            | 0              | -                       | -                                                                                    | 88.9<br>(0.9)                                                               | 88.9<br>(0.9) |
| 1.5                            | -              | -                       | 0                                                                                    | 86<br>(3)                                                                   | 86<br>(3)     |
| 2.0                            | -              | -                       | 6.8<br>(0.5)                                                                         | 65<br>(3)                                                                   | 72<br>(3)     |
| 2.5                            | -              | -                       | 15<br>(0.4)                                                                          | 66<br>(3)                                                                   | 81<br>(3)     |
| 3.5                            | -              | -                       | 16<br>(1)                                                                            | 69<br>(4)                                                                   | 85<br>(4)     |
| 4.0                            | -              | -                       | 18<br>(3)                                                                            | 80<br>(2)                                                                   | 98<br>(4)     |
| 6.0                            | -              | -                       | 15.7<br>(0.7)                                                                        | 75<br>(3)                                                                   | 90<br>(3)     |

Table III-8 . Products from the chlorination of compound 5.

| compound   | structure                                                                                                 | GC retention time* (min) |
|------------|-----------------------------------------------------------------------------------------------------------|--------------------------|
| -----      |                                                                                                           |                          |
| <u>5</u>   | compound <u>5</u>                                                                                         | 5.57                     |
| <u>5-1</u> | 1-(3,4 dimethoxyphenyl)-1-methoxy-2-(5-chloro-4-methyl-2-methoxyphenoxy)ethane                            | 6.78                     |
| <u>5-2</u> | 1-(6-chloro-3,4 dimethoxyphenyl)-1-methoxy-2-(4-methyl-2-methoxyphenoxy)ethane                            | 7.26                     |
| <u>5-3</u> | 1-(6-chloro-3,4 dimethoxyphenyl)-1-methoxy-2-(5-chloro-4-methyl-2-methoxyphenoxy)ethane                   | 7.83                     |
| <u>5-4</u> | 1-(6-chloro-3,4 dimethoxyphenyl)-1-methoxy-2-(3 or 6,5-dichloro-4-methyl-2-methoxyphenoxy)ethane          | 9.29                     |
| <u>5-5</u> | 1-(6-chloro-3,4 dimethoxyphenyl)-1-methoxy-2-(6 or 3,5-dichloro-4-methyl-2-methoxyphenoxy)ethane          | 10.14                    |
| <u>5-6</u> | 1-(2 or 5,6-dichloro-3,4 dimethoxyphenyl)-1-methoxy-2-(3 or 6,5-dichloro-4-methyl-2-methoxyphenoxy)ethane | 11.21                    |
| <u>5-7</u> | 1-(6-chloro-3,4 dimethoxyphenyl)-1-methoxy-2-(3,5,6-trichloro-4-methyl-2-methoxyphenoxy)ethane            | 11.39                    |
| <u>5-8</u> | 1-(2 or 5,6-dichloro-3,4 dimethoxyphenyl)-1-methoxy-2-(3,5,6-trichloro-4-methyl-2-methoxyphenoxy)ethane   | 14.33                    |
| <u>5-9</u> | 1-(2,5,6-trichloro-3,4 dimethoxyphenyl)-1-methoxy-2-(3,5,6-trichloro-4-methyl-2-methoxyphenoxy)ethane     | 16.49                    |

\*GC and GC-MS conditions:

column DB5, J&W; carrier He, 1ml/min; temperature gradient:  
200°C-270°C, 15°C/min.

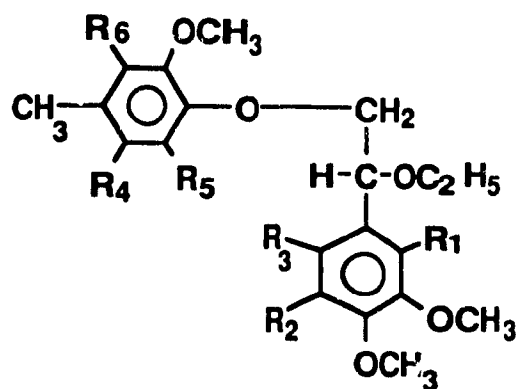
Table III-8 (cont'd) . Products from the chlorination of compound 5.

| compound    | structure                                                               | GC retention time* (min) |
|-------------|-------------------------------------------------------------------------|--------------------------|
| -----       |                                                                         |                          |
| <u>5-10</u> | 4,5-dichloroveratrole                                                   | 1.97                     |
| <u>5-11</u> | 3 or 6,5-dichlorocreosol (trimethyl)silyl ether                         | 2.33                     |
| <u>5-12</u> | 3,5,6-trichlorocreosol (trimethyl )silyl ether                          | 2.50                     |
| <u>5-13</u> | trichloroveratrole                                                      | 4.42                     |
| <u>5-14</u> | 1-(6-chloro-3,4 dimethoxyphenyl)-<br>1-methoxy-2-acetoxyethane          | 6.14                     |
| <u>5-15</u> | 1-(2 or 5,6-dichloro-3,4 dimethoxyphenyl)-<br>1-methoxy-2-acetoxyethane | 7.07                     |
| <u>5-16</u> | 1-(2,5,6-trichloro-3,4 dimethoxyphenyl)-<br>1-methoxy-2-acetoxyethane   | 7.19                     |

\*GC and GC-MS conditions:

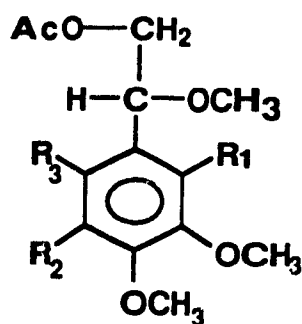
column DB5, J&W; carrier He, 1ml/min; temperature gradient:  
200°C-270°C, 15°C/min.

a)



| compound        |     | R <sub>1</sub> | R <sub>2</sub> | R <sub>3</sub> | R <sub>4</sub> | R <sub>5</sub> | R <sub>6</sub> |
|-----------------|-----|----------------|----------------|----------------|----------------|----------------|----------------|
| <u>5-1</u>      |     | H              | H              | H              | Cl             | H              | H              |
| <u>5-2</u>      |     | H              | H              | Cl             | H              | H              | H              |
| <u>5-3</u>      |     | H              | H              | Cl             | Cl             | H              | H              |
| <u>5-4; 5-5</u> |     | H              | H              | Cl             | Cl             | Cl             | H              |
|                 | and | H              | H              | Cl             | Cl             | H              | Cl             |
| <u>5-6</u>      |     | H              | Cl             | Cl             | Cl             | Cl             | H              |
|                 | or  | Cl             | H              | Cl             | Cl             | H              | Cl             |
| <u>5-7</u>      |     | H              | H              | Cl             | Cl             | Cl             | Cl             |
| <u>5-8</u>      |     | H              | Cl             | Cl             | Cl             | Cl             | Cl             |
|                 | or  | Cl             | H              | Cl             | Cl             | Cl             | Cl             |
| <u>5-9</u>      |     | Cl             | Cl             | Cl             | Cl             | Cl             | Cl             |

b)



| compound    | R <sub>1</sub> | R <sub>2</sub> | R <sub>3</sub> |
|-------------|----------------|----------------|----------------|
| <u>5-14</u> | H              | H              | Cl             |
| <u>5-15</u> | H              | Cl             | Cl             |
|             | or             | Cl             | H              |
| <u>5-16</u> | Cl             | Cl             | Cl             |

SCHEME III-4. Products from the chlorination of compound 5.

a) Substitution products. b) Cleavage products.

Table III-9. Yields of aromatic substitution products from the chlorination of compound 5 under increasing charges of chlorine,  $x$ , (in moles of chlorine per  $C_9$  unit). Yields, in percent of initial  $C_9$  unit, obtained by GC analysis. Standard deviations are given in parentheses.

| Cl <sub>2</sub><br>charge | UN-           | MONO-        |              | DI-           | TRI-          |              | TETRA-        |              | PENTA-<br>HEXA- |              |
|---------------------------|---------------|--------------|--------------|---------------|---------------|--------------|---------------|--------------|-----------------|--------------|
| $x$                       | 5             | <u>5-1</u>   | <u>5-2</u>   | <u>5-3</u>    | <u>5-4</u>    | <u>5-5</u>   | <u>5-6</u>    | <u>5-7</u>   | <u>5-8</u>      | <u>5-9</u>   |
| 0                         | 93.3<br>(0.4) | -            | -            | -             | -             | -            | -             | -            | -               | -            |
| 0.5                       | 12.9<br>(0.7) | 80<br>(1)    | 4.5<br>(0.2) | 3.1<br>(0.3)  | -             | -            | -             | -            | -               | -            |
| 1.0                       | 0             | 8.3<br>(0.3) | 0            | 89.9<br>(0.1) | -             | -            | -             | -            | -               | -            |
| 1.5                       | -             | -            | -            | 48.2<br>(0.1) | 36.5<br>(0.5) | 6.8<br>(0.1) | -             | -            | -               | -            |
| 2.0                       | -             | -            | -            | 5.7<br>(0.1)  | 55.3<br>(0.3) | 7.5<br>(0.3) | 7.3<br>(0.5)  | 5.7<br>(0.1) | -               | -            |
| 3.0                       | -             | -            | -            | -             | 13.2<br>(0.1) | 0            | 17.1<br>(0.3) | 9.4<br>(0.2) | 10.8<br>(0.2)   | -            |
| 4.0                       | -             | -            | -            | -             | -             | -            | 7.4<br>(0.4)  | 1.5<br>(0.1) | 14.1<br>(0.6)   | 1.7<br>(0.1) |
| 5.0                       | -             | -            | -            | -             | -             | -            | 3.9<br>(0.2)  | 0.5<br>(0.1) | 17.6<br>(0.6)   | 3.0<br>(0.6) |
| 7.5                       | -             | -            | -            | -             | -             | -            | 1.8<br>(0.1)  | 0.6<br>(0.1) | 16.5<br>(0.8)   | 3.2<br>(0.1) |
| 10.0                      | -             | -            | -            | -             | -             | -            | 0             | 0            | 24.4<br>(0.8)   | 9.7<br>(0.3) |
| 15.0                      | -             | -            | -            | -             | -             | -            | -             | -            | 21<br>(1)       | 12<br>(1)    |
| 20.0                      | -             | -            | -            | -             | -             | -            | -             | -            | 23<br>(4)       | 18<br>(4)    |

Table III-10. Yields of cleavage products (aromatic ipso-substitution and beta-O-4 cleavage) from the chlorination of compound 5 under increasing charges of chlorine, x, (in moles of chlorine per C<sub>9</sub> unit). Yields, in percent of initial C<sub>9</sub> unit obtained by GC analysis. Standard deviations are given in parentheses.

| chlorine<br>charge<br>x | side chain<br>cleavage |              | beta-O-4<br>cleavage |               |              |              |              |
|-------------------------|------------------------|--------------|----------------------|---------------|--------------|--------------|--------------|
|                         | <u>5-10</u>            | <u>5-13</u>  | <u>5-11</u>          | <u>5-12</u>   | <u>5-14</u>  | <u>5-15</u>  | <u>5-16</u>  |
|                         |                        |              |                      |               |              |              |              |
| 1.5                     | 0.8<br>(0.1)           | -            | 3.2<br>(0.2)         | 0.5<br>(0.1)  | 3.2<br>(0.3) | -            | -            |
| 2.0                     | 1.9<br>(0.1)           | -            | 3.0<br>(0.1)         | 3.1<br>(0.1)  | 5.5<br>(0.6) | 0.8<br>(0.1) | -            |
| 3.0                     | 5.7<br>(0.1)           | 0.6<br>(0.1) | 0.5<br>(0.1)         | 8.9<br>(0.3)  | 2.9<br>(0.3) | 4.2<br>(0.2) | 0.5<br>(0.2) |
| 4.0                     | 7.0<br>(0.1)           | 2.4<br>(0.1) | 0.6<br>(0.1)         | 11.3<br>(0.1) | 0            | 6.0<br>(0.2) | 1.0<br>(0.3) |
| 5.0                     | 5.2<br>(0.1)           | 2.8<br>(0.1) | 0.5<br>(0.1)         | 10.2<br>(0.6) | -            | 6.2<br>(0.3) | 1.1<br>(0.1) |
| 10.0                    | 3.1<br>(0.1)           | 6.4<br>(0.1) | 0.6<br>(0.1)         | 8.2<br>(0.3)  | -            | 4.2<br>(0.2) | 0.8<br>(0.2) |



Table III-11 . Combined yields of related products from the chlorination of compound 5 under increasing charges of chlorine, x, (in moles of chlorine per C<sub>9</sub> unit): a) compound 5 recovered unaltered after the reaction, b) products from beta aryl ether bond cleavage, c) products from substitution on the aromatic rings. Yields are expressed as percent of initial C<sub>9</sub> unit, obtained by GC analysis. Standard deviations are given in parentheses.

| Cl <sub>2</sub><br>charge<br><u>x</u> | unaltered<br><u>5</u> | beta-ether<br>cleavage<br><u>5-11, 5-12</u><br><u>5-14</u><br><u>5-15, 5-16</u> | substitution                                                    |                                                                          | Total          |
|---------------------------------------|-----------------------|---------------------------------------------------------------------------------|-----------------------------------------------------------------|--------------------------------------------------------------------------|----------------|
|                                       |                       |                                                                                 | ipso-substitution<br>(side-chain cleavage)<br><u>5-10, 5-13</u> | other<br><u>5-1, 5-2, 5-3</u><br><u>5-4, 5-6, 5-7</u><br><u>5-8, 5-9</u> |                |
| 0                                     | 93.3<br>(0.4)         | -                                                                               | -                                                               | 0                                                                        | 93.3<br>(0.4)  |
| 0.5                                   | 12.9<br>(0.7)         | -                                                                               | -                                                               | 87<br>(1)                                                                | 100<br>(1)     |
| 1.0                                   | 0                     | -                                                                               | -                                                               | 98.2<br>(0.3)                                                            | 98.2<br>(0.3)  |
| 1.5                                   | -                     | 7.7<br>(0.4)                                                                    | 0.8<br>(0.1)                                                    | 91.5<br>(0.5)                                                            | 100.0<br>(0.6) |
| 2.0                                   | -                     | 13.8<br>(0.7)                                                                   | 1.9<br>(0.1)                                                    | 81.5<br>(0.7)                                                            | 97<br>(1)      |
| 3.0                                   | -                     | 22.6<br>(0.8)                                                                   | 6.3<br>(0.1)                                                    | 52.3<br>(0.4)                                                            | 81<br>(1)      |
| 4.0                                   | -                     | 26.2<br>(0.6)                                                                   | 9.4<br>(0.1)                                                    | 25.9<br>(0.6)                                                            | 62<br>(1)      |
| 5.0                                   | -                     | 22.5<br>(0.6)                                                                   | 8.0<br>(0.1)                                                    | 26<br>(1)                                                                | 56.6<br>(1)    |
| 10.0                                  | -                     | 16.4<br>(0.5)                                                                   | 9.5<br>(0.1)                                                    | 34.1<br>(0.8)                                                            | 60<br>(1)      |
| 15.0                                  | -                     | nd                                                                              | nd                                                              | 33<br>(1)                                                                | nd             |
| 20.0                                  | -                     | nd                                                                              | nd                                                              | 41<br>(6)                                                                | nd             |

Table III-12 . Yields of unidentified products from the chlorination of compound 5 under increasing charges of chlorine,  $x$ , (in moles of chlorine per  $C_9$  unit), labeled by their GC retention times. Yields are expressed as percent of initial  $C_9$  unit, obtained by GC analysis. Standard deviations are given in parentheses.

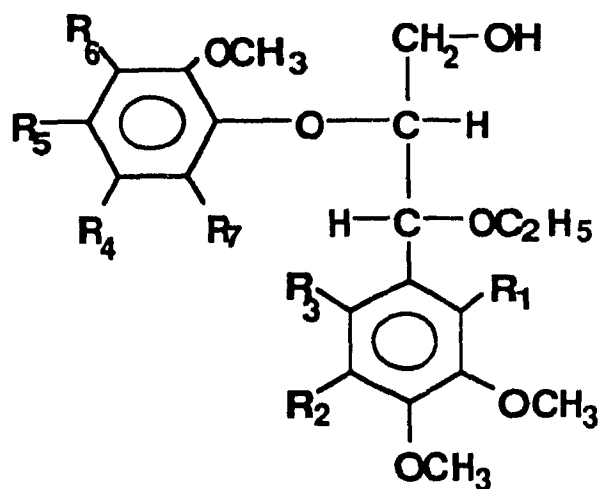
| Cl <sub>2</sub><br>charge<br>$x$ | Retention times (min) |              |              |              |              |              |              |              | Total        |
|----------------------------------|-----------------------|--------------|--------------|--------------|--------------|--------------|--------------|--------------|--------------|
|                                  | 3.97                  | 6.32         | 7.02         | 7.43         | 7.63         | 8.40         | 8.72         | 11.35        |              |
| 1.5                              | -                     | -            | -            | 0.4<br>(0.1) | -            | -            | -            | -            | 0.4<br>(0.1) |
| 2.0                              | 0.2<br>(0.1)          | -            | -            | 0.7<br>(0.1) | -            | -            | -            | -            | 0.9<br>(0.1) |
| 3.0                              | 0.8<br>(0.1)          | 1.6<br>(0.5) | 0.9<br>(0.1) | 0.5<br>(0.1) | 1.2<br>(0.5) | 0.4<br>(0.2) | 0.2<br>(0.1) | 1.8<br>(0.1) | 7.4<br>(0.8) |
| 4.0                              | 1.2<br>(0.2)          | 1.2<br>(0.5) | 0.9<br>(0.1) | 0.6<br>(0.1) | 1.3<br>(0.2) | 1.9<br>(0.2) | 0.2<br>(0.1) | 1.2<br>(0.1) | 9.5<br>(0.6) |
| 5.0                              | 1.2<br>(0.1)          | 0.9<br>(0.1) | 0.7<br>(0.1) | 0            | 0.6<br>(0.1) | 1.1<br>(0.1) | 0.2<br>(0.1) | 1.1<br>(0.2) | 5.8<br>(0.3) |
| 10.0                             | 1.3<br>(0.1)          | 0            | 0            | -            | 0            | 0.8<br>(0.3) | -            | 0            | 2.1<br>(0.3) |

Table III-13. Products from the chlorination of compound 8.

| compound    | structure                                                                                                                                     | GC retention time* (min)   |
|-------------|-----------------------------------------------------------------------------------------------------------------------------------------------|----------------------------|
| <u>8</u>    | compound 8 [2 diastereomers a) and b)]                                                                                                        | 11.92/12.01                |
| <u>8-1</u>  | 3-(6-chloro-3,4-dimethoxyphenyl)-3-ethoxy-2-(2-methoxyphenoxy)propanol [2 diastereomers a) and b)]                                            | 12.28/12.46                |
| <u>8-2</u>  | 3-(3,4-dimethoxyphenyl)-3-ethoxy-2-(4 or 5-chloro-2-methoxyphenoxy)propanol [3 isomers a), b) and c)]                                         | 12.65/12.76/12.90          |
| <u>8-3</u>  | 3-(6-chloro-3,4-dimethoxyphenyl)-3-ethoxy-2-(4 or 5-chloro-2-methoxyphenoxy) propanol [4 isomers a), b), c) and d)]                           | 13.07/13.23<br>13.29/13.42 |
| <u>8-4</u>  | 3-(6-chloro-3,4-dimethoxyphenyl)-3-ethoxy-2-(4,5-dichloro-2-methoxyphenoxy) propanol [2 diastereomers a) and b)]                              | 14.24/14.48                |
| <u>8-5</u>  | 3-(2 or 5,6-dichloro-3,4-dimethoxyphenyl)-3-ethoxy-2-(4,5-dichloro-2-methoxyphenoxy) propanol [2 diastereomers a) and b)]                     | 15.37/15.68                |
| <u>8-6</u>  | 3-(2,5,6-trichloro-3,4-dimethoxyphenyl)-3-ethoxy-2-(4,5-dichloro-2-methoxyphenoxy) propanol                                                   | 15.94                      |
| <u>8-7</u>  | 3-(2 or 5, 6-dichloro-3,4-dimethoxyphenyl)-3-ethoxy-2-(3 or 6,4,5-trichloro-2-methoxyphenoxy) propanol [2 diastereomers a) and b)]            | 16.39/16.84                |
| <u>8-8</u>  | presumably<br>3-(2,5,6-trichloro-3,4-dimethoxyphenyl)-3-ethoxy-2-(3 or 6,4,5-trichloro-2-methoxyphenoxy) propanol [2 diastereomers a) and b)] | 17.16                      |
| <u>8-9</u>  | unknown                                                                                                                                       | 3.56                       |
| <u>8-10</u> | 4,5-dichloroveratrole                                                                                                                         | 6.13                       |
| <u>8-11</u> | trichloroveratrole                                                                                                                            | 7.00                       |

\* GC and GC-MS conditions:

column DB5, J&W; carrier He, 1ml/min; temperature gradient:  
80°C-300°C, 20°C/min.



| compound   |     | R <sub>1</sub> | R <sub>2</sub> | R <sub>3</sub> | R <sub>4</sub> | R <sub>5</sub> | R <sub>6</sub> | R <sub>7</sub> |
|------------|-----|----------------|----------------|----------------|----------------|----------------|----------------|----------------|
| <u>8-1</u> |     | H              | H              | Cl             | H              | H              | H              | H              |
| <u>8-2</u> |     | H              | H              | H              | Cl             | H              | H              | H              |
|            | and | H              | H              | H              | H              | Cl             | H              | H              |
| <u>8-3</u> |     | H              | H              | Cl             | Cl             | H              | H              | H              |
|            | and | H              | H              | Cl             | H              | Cl             | H              | H              |
| <u>8-4</u> |     | H              | H              | Cl             | Cl             | Cl             | H              | H              |
| <u>8-5</u> |     | H              | Cl             | Cl             | Cl             | Cl             | H              | H              |
|            | and | Cl             | H              | Cl             | Cl             | Cl             | H              | H              |
| <u>8-6</u> |     | Cl             | Cl             | Cl             | Cl             | Cl             | H              | H              |
| <u>8-7</u> |     | H              | Cl             | Cl             | Cl             | Cl             | Cl             | H              |
|            | and | Cl             | H              | Cl             | Cl             | Cl             | H              | Cl             |
| <u>8-8</u> |     | Cl             | Cl             | Cl             | Cl             | Cl             | Cl             | H              |
|            | and | Cl             | Cl             | Cl             | Cl             | Cl             | H              | Cl             |

SCHEME III-5.

Products from the chlorination of compound 8.

Table III-14 . Yields of aromatic substitution products from the chlorination of compound 8 under increasing charges of chlorine, x, (in moles of chlorine per C<sub>9</sub> unit). Yields are expressed as percent of initial C<sub>9</sub> unit, obtained by GC analysis. Standard deviations are given in parentheses.

| Cl <sub>2</sub><br>charge | UN-                    | MONO-             |                              | DI-                                    | TRI-                  | TETRA-                 | PENTA-<br>HEXA- |                      |              |
|---------------------------|------------------------|-------------------|------------------------------|----------------------------------------|-----------------------|------------------------|-----------------|----------------------|--------------|
| <u>x</u>                  | <u>8</u>               | <u>8-1</u>        | <u>8-2</u>                   | <u>8-3</u>                             | <u>8-4</u>            | <u>8-5</u>             | <u>8-6</u>      | <u>8-7</u>           | <u>8-8</u>   |
| 0                         | 56/41<br>(1/1)         | -                 | -                            | -                                      | -                     | -                      | -               | -                    | -            |
| 0.25                      | 31.7/20.3<br>(0.5/0.5) | 10/15<br>(1/2)    | 2.0/3.4/2.8<br>(0.1/0.4/0.7) | 1.0/1.0/0.5/1.0<br>(0.1/0.3/0.1/0.6)   | -                     | -                      | -               | -                    | -            |
| 0.5                       | 14.0/7.8<br>(0.8/0.7)  | 16/28<br>(1/2)    | 3.2/5.3/3.9<br>(0.1/0.4/0.6) | 4.1/6/3.5/3.5<br>(0.7/2/0.2/0.1)       | -                     | -                      | -               | -                    | -            |
| 0.75                      | 2.9/1.3<br>(0.4/0.1)   | 13/28<br>(1/2)    | 2.1/3.2/2.8<br>(0.1/0.2/0.8) | 8.9/10/9/10.0<br>(0.8/1/1/0.2)         | 0.4/0.3<br>(0.1/0.1)  | -                      | -               | -                    | -            |
| 1.0                       | 0                      | 4.4/16<br>(0.8/2) | 0.5/0.6/0.9<br>(0.1/0.1/0.2) | 14.3/17.8/18.5/19<br>(0.2/0.7/0.5/1)   | 2.0/1.5<br>(0.5/0.2)  | -                      | -               | -                    | -            |
| 1.5                       | -                      | 0                 | 0                            | 5.5/9.6/14.3/15.8<br>(0.1/0.2/0.1/0.1) | 20.8/21<br>(0.6/1)    | 2.8/1.5<br>(0.1/0.2)   | -               | -                    | -            |
| 2.0                       | -                      | -                 | -                            | -0.7/1.6/2.5<br>(-0.1/0.1/0.1)         | 29.3/41<br>(0.2/1)    | 8.0/8<br>(0.1/1)       | -               | -                    | -            |
| 3.0                       | -                      | -                 | -                            | 0                                      | 7.2/10.8<br>(0.5/0.7) | 17.5/27.1<br>(0.2/0.5) | 2.7<br>(0.1)    | 8.1/2.5<br>(0.5/0.2) | 1.5<br>(0.2) |
| 4.0                       | -                      | -                 | -                            | -                                      | 0                     | 18.7/28<br>(0.2/1)     | 6.7<br>(0.2)    | 10/10<br>(1/2)       | 3.8<br>(0.1) |
| 5.0                       | -                      | -                 | -                            | -                                      | -                     | 10/15<br>(2/3)         | 6<br>(1)        | 7/4.5<br>(1/0.5)     | 4<br>(1)     |

Table III-15 . Combined yields of aromatic substitution products from the chlorination of compound 8 under increasing charges of chlorine, x, (in moles of chlorine per  $C_9$  unit). Yields are expressed as percent of initial  $C_9$  unit, obtained by GC analysis. Standard deviations are given in parentheses.

| $Cl_2$<br>charge | UN-           | MONO-           | DI-           | TRI-          | TETRA-        | PENTA-<br>HEXA-      |
|------------------|---------------|-----------------|---------------|---------------|---------------|----------------------|
| <u>x</u>         | <u>8</u>      | <u>8-1, 8-2</u> | <u>8-3</u>    | <u>8-4</u>    | <u>8-5</u>    | <u>8-6, 8-7, 8-8</u> |
| 0                | 97<br>(1)     | -               | -             | -             | -             | -                    |
| 0.25             | 51.0<br>(0.7) | 33<br>(2)       | 3.5<br>(0.7)  | -             | -             | -                    |
| 0.5              | 22<br>(1)     | 56<br>(2)       | 17<br>(2)     | -             | -             | -                    |
| 0.75             | 4.2<br>(0.4)  | 49<br>(2)       | 38<br>(2)     | 0.7<br>(0.1)  | -             | -                    |
| 1.0              | 0             | 22<br>(2)       | 70<br>(1)     | 3.5<br>(0.5)  | -             | -                    |
| 1.5              | -             | 0               | 45.2<br>(0.3) | 42<br>(1)     | 4.3<br>(0.2)  | -                    |
| 2.0              | -             | -               | 4.8<br>(0.2)  | 70<br>(1)     | 16<br>(1)     | -                    |
| 3.0              | -             | -               | 0             | 18.0<br>(0.8) | 44.6<br>(0.5) | 14.8<br>(0.6)        |
| 4.0              | -             | -               | -             | 0             | 47<br>(1)     | 31<br>(2)            |
| 5.0              | -             | -               | -             | -             | 25<br>(4)     | 22<br>(2)            |

Table III-16 . Yields of cleavage products (aromatic ipso-substitution) from the chlorination of compound 8 under increasing charges of chlorine,  $x$ , (in moles of chlorine per  $C_9$  unit). Yields are expressed as percent of initial  $C_9$  unit, obtained by GC analysis. Standard deviations are given in parentheses.

| chlorine<br>charge<br>$x$ | side chain<br>cleavage |              | unknown      |
|---------------------------|------------------------|--------------|--------------|
|                           | <u>8-10</u>            | <u>8-11</u>  | <u>8-9</u>   |
| 1.5                       | 0.9<br>(0.1)           | -            | -            |
| 2.0                       | 1.8<br>(0.3)           | -            | 1.8<br>(0.3) |
| 3.0                       | 9.3<br>(0.2)           | 0.6<br>(0.1) | 6.5<br>(0.2) |
| 4.0                       | 9.0<br>(0.3)           | 2.5<br>(0.2) | 6.2<br>(0.1) |
| 5.0                       | 4.6<br>(0.1)           | 4.2<br>(0.3) | 6.9<br>(0.1) |

Table III-17. Combined yields of related substitution products from the chlorination of compound 8 under increasing charges of chlorine, x, (in moles of chlorine per C<sub>9</sub> unit): a) compound 8 recovered unaltered after the reaction, b) products from ether cleavage, c) products from substitution on the aromatic rings. Yields are expressed as percent of initial C<sub>9</sub> unit, obtained by GC analysis. Standard deviations are given in parentheses.

| Cl <sub>2</sub><br>charge<br><u>x</u> | unaltered<br><u>8</u> | beta-ether<br>cleavage | substitution                                                    |                                                                              | Total     |
|---------------------------------------|-----------------------|------------------------|-----------------------------------------------------------------|------------------------------------------------------------------------------|-----------|
|                                       |                       |                        | ipso-substitution<br>(side-chain cleavage)<br><u>8-10, 8-11</u> | other<br><u>8-1, 8-2</u><br><u>8-3, 8-4</u><br><u>8-6, 8-7</u><br><u>8-8</u> |           |
| 0                                     | 97<br>(1)             | -                      | -                                                               | -                                                                            | 97<br>(1) |
| 0.25                                  | 51.0<br>(0.7)         | -                      | -                                                               | 37<br>(2)                                                                    | 88<br>(2) |
| 0.5                                   | 22<br>(1)             | -                      | -                                                               | 73<br>(3)                                                                    | 95<br>(3) |
| 0.75                                  | 4.2<br>(0.4)          | -                      | -                                                               | 88<br>(3)                                                                    | 92<br>(3) |
| 1.0                                   | 0                     | -                      | -                                                               | 95<br>(2)                                                                    | 95<br>(2) |
| 1.5                                   | -                     | -                      | 0.9<br>(0.1)                                                    | 91<br>(1)                                                                    | 92<br>(1) |
| 2.0                                   | -                     | -                      | 1.8<br>(0.3)                                                    | 90.8<br>(0.6)                                                                | 94<br>(1) |
| 3.0                                   | -                     | -                      | 9.9<br>(0.3)                                                    | 77<br>(1)                                                                    | 94<br>(1) |
| 4.0                                   | -                     | -                      | 11.5<br>(0.3)                                                   | 78<br>(2)                                                                    | 96<br>(3) |
| 5.0                                   | -                     | -                      | 8.8<br>(0.3)                                                    | 47<br>(4)                                                                    | 63<br>(4) |



• Identification of the reaction products .

The products formed during the chlorination of compounds 1, 4, 5, and 8 are listed in tables III-1, III-4, III-8, and III-13, respectively. In the experiments with compound 8, the samples were acetylated before analysis. For clarity, however, we have listed the reaction products under their initial structure, and not as acetates (Table III-13). The phenolic structures of 5-11 and 5-12 were ascertained by silylation of the samples before GC-MS analysis. These compounds are listed as their (trimethyl)silyl ethers in Table III-8.

The complete mass spectral results are given in Appendix III. When the side chain was reduced to a single carbon (in compound 1 and its reaction products), then the benzyl alkyl ether bond split, giving rise to the base peak. The other compounds exhibited characteristic fragmentation patterns that differed from those observed among the benzyl aryl ethers (Chapter II) in that the base peaks originated from the cleavage of the  $C_{\alpha}$ - $C_{\beta}$  linkage and not from the elimination of the alpha ether substituent. We found additional indication of the stability of the benzyl-alkyl ether linkage in the fragmentation pattern of compounds from the chlorination of 4: the beta aryloxy substituent was preferentially eliminated, and the rupture of the oxygen-alkyl bond in the alpha substituent occurred with elimination of a neutral ethylene molecule, while the benzyl ether bond itself was not, or scarcely, cleaved.

Given the mass values for the molecular ion on the one hand, and for the base peak arising systematically from the  $C_{\alpha}$ - $C_{\beta}$  cleavage on the other hand, we could generally determine the distribution of the chlorine atoms between the two aromatic rings present in the structure

of compounds 4, 5, and 8. Nevertheless, we could not determine the exact structure of 8-8 (Table III-13) because its molecular ion did not appear on the mass spectrum. However, the presence of the penta-chlorinated 8-6 (Table III-14) strongly suggested that 8-8 was the hexa -chlorinated derivative of 8.

The positions of the chlorine atoms on the rings were attributed according to the respective reactivities of the different sites towards electrophilic attack as given in the literature. This point is discussed in detail in chapter II. The proposed structures of the 3 isomers (1-6, 1-7, and 1-8 in table III-1) of the dichloro derivative of 1 were based on their respective order of appearance among the chlorination products and their yields, which both revealed their probability of formation. The occurrence of (2,5-dichloro-3,4-dimethoxyphenyl)-ethoxymethane 1-8, although not likely, was the only explanation for the presence of a third dichloro isomer of 1. Sometimes only one peak was detected when several positional isomers were expected, as in 1-4 and 5-6, 5-8, or 5-11 (Tables III-1, and III-8, respectively). Since we did not see any reason for one isomer to be preferentially formed, we attributed this single peak to the isomers having the same GC retention time.

The presence of the two diastereomers of compound 8 slightly complicated the GC analysis, in that the peaks for positional isomers arising from substitution and those for their diastereomers often overlapped (Table III-13). It was far beyond the scope of this work to single out each of them, therefore the same general structure was attributed to all the compounds exhibiting same mass spectral characteristics. The details of the contribution from every isomer are

given in Table III-14, and the yields are summarized for each aromatic substitution pattern in Table III-15.

Several products arising from the chlorination of compound 4 (4-13, Table III-4) exhibited GC retention times greater than that of the tetrachloro derivative of 4. No mass spectra of these products were obtained, and they were tentatively assigned as derivatives of 4 with levels of chlorine substitution higher than four.

Not all the products were identified. The retention time recorded for 8-9 (Table III-13) was close to those exhibited by chlorinated veratroles, thus suggesting that its initial dimeric structure was not intact. Approximate yields could be calculated by taking for default value the response factor found for dichloroveratrole. They suggested that 8-9 was a minor product formed in amounts increasing with the chlorine charge.

Table III-12 presents the yields and GC retention times of a series of unidentified minor products obtained from the chlorination of compound 5. Although they were all formed in negligible amounts, the overall approximate yields (calculated as for 8-9) added up to about 10% of the initial monomer units. Since these compounds were neither major nor primary reaction products, we did not try to investigate them further.

The aldehydic moiety from the elimination of the side chain was not always detected. It may not have been stable either in the reaction mixture itself or during the chromatographic analysis. Nevertheless, the extent of the cleavage reaction could be derived from the sum of the yields of the chlorinated veratroles.

The overall recovery of the reaction products was sometimes excessively small, in particular in the reaction of compound 5 (Table III-11), when charges higher than 3.0 moles of chlorine per mole of monomer unit were applied. Several factors may account for these low yields. Firstly, not all the cleavage products (aldehydic moi . ' were detected. Secondly, default values for the response factors were taken for some species for which standards were not available. Both of these factors would lead to an error in the estimation of the yields. Finally, the degree of substitution on the aromatic rings increasing with the chlorine charge, the nature of the analytes, as well as their GC retention times became more and more different from the internal standard, bringing another source of error. Other side-reactions may also have occurred, but we did not further investigate them, the scope of our work being essentially focussed on primary reactions.

• Consumption of the starting compound . (Tables III-3, III-7, III-11 and III-17)

The starting compounds were stable in glacial acetic acid. All four of them were quantitatively recovered (87 to 97% yields) after the blank reaction ( $x=0$ ). The initial compounds were progressively consumed as the applied charge increased up to 1 mole of chlorine per monomer unit. Then, they completely disappeared, except for traces of starting material 1. All compounds behaved similarly regardless of the nature of the side chain.

• Characteristics of the products of reaction

CLEAVAGE OF ALPHA-ETHER LINKAGE

We did not observe any cleavage of the benzyl-alkyl ether bond, except in the chlorination of compound 1. The alpha-chloro and alpha-aceto derivatives (1-1 and 1-2 respectively) were detected only at low charges of chlorine (up to 1 mole of chlorine per mole of monomer unit), and in moderate, though non-negligible yields (Table III-2). After a maximum accounting for 20% of the initial compound was reached (Table III-3), yields of 1-1 and 1-2 decreased to zero as higher chlorine charges were applied. No derivatives from the aromatic substitution of 1-1 and 1-2 were ever detected, that could explain the lower yields of these compounds as the chlorine charge increased. The parallel disappearance of alpha ether cleavage products and of unaltered 1 thus suggests that ether cleavage occurred on 1 only, and was inhibited after chlorine substitution on the aromatic nucleus. The absence of chlorine-substituted alpha cleavage products also indicates that the presence on the alpha carbon of a chlorine atom or an acetate group in place of the ether group noticeably deactivated the aromatic ring towards electrophilic aromatic substitution.

CLEAVAGE OF BETA-ETHER LINKAGE

Compound 5 exhibited a marginal behaviour. An excess of chlorine promoted the cleavage of the beta-aryl ether linkage to the extent of about 4 to 13% of the initial dimer (Table III-11), as indicated by the presence among the reaction products of both creosyl, and beta-acetylated moieties. The unbalanced yields observed between the two moieties (Table III-10) suggest that not all of the cleavage

products were recovered. The beta-chloro derivative of compound 5 may not even have been formed. In the reaction of elimination of the beta substituent, the solvent, rather than chlorine, is statistically more likely to be the nucleophilic agent. An elimination-addition mechanism, with the formation of a  $\alpha$ - $\beta$  double bond, is possible although we did not detect the corresponding unsaturated compound(s).

#### AROMATIC SUBSTITUTION BY CHLORINE

Aromatic substitution by chlorine was, at any chlorine charge, the most significant reaction of compounds 1 and 5 (Tables III-3 and III-11), and the sole reaction of compounds 4 and 8 (Tables III-7 and III-17). With the majority of the products arising from substitution, substitution is thus the primary reaction of benzyl alkyl ethers with molecular chlorine. When a guaiacyl group was present at the beta position, monochlorination occurred mainly on the veratryl ring, and the positional isomers of the monochlorination on the guaiacyl group were minor products (compounds 4 and 8; Tables III-5 and III-9, respectively). In compound 5, monochlorination occurred almost exclusively on the creosyl ring, more reactive (Table III-14). Among all the compounds, dichlorination began before all the starting compound had been monochlorinated, on either equivalent position on the guaiacyl ring (4 and 8), or on the veratryl ring (5). The positions were successively substituted, as more chlorine was introduced, and highly chlorinated dimers were formed in good yields.

The cleavage reaction depended solely on prior chlorination of the veratryl ring. Ipso-substitution, promoting side-chain cleavage, took place when an excess of chlorine was applied, and after all of the

most reactive sites had reacted. Even then, however, electrophilic side chain displacement was not of major significance. Under chlorine charges of 2.5 to 3.0 moles per mole of monomer unit, it affected not more than roughly 10 to 15 % of the initial dimeric structure of compounds 4, 5 and 8 (Tables III-6, III-10, III-16, respectively). These numbers are in complete agreement with the published<sup>2</sup> results obtained from the chlorination of compound 4 in glacial acetic acid with an excess of chlorine. Compound 1 exhibited noticeably higher yields of side-chain cleavage. Yields were up to 50% of the initial compound when a charge of 2.5 mole of chlorine per initial monomer unit was applied. The decrease in yields of cleaved dimer from 50 to 15 and 10% for compounds 1, 4 and 8, respectively, suggested that the nature of the side chain affected the efficiency of the ipso-substitution. This phenomenon may be explained by steric hindrance and electronic influence, both increasing with the length of the side chain.

## DISCUSSION

The experiments described by Sintenis<sup>3</sup> unambiguously demonstrated the facile cleavage by chlorine of the bond between the benzylic carbon and the oxygen in benzyl phenyl ether, and the strength of the same bond in the ethyl ether. Not benzyl chloride, but benzaldehyde was formed by treatment of benzyl ethyl ether with a large excess of chlorine either at room or high temperature, thus indicating that the rupture had occurred on the ether-alkyl bond. Unlike the simple benzyl ethyl ether studied by Sintenis, compound 1 bears two additional methoxy groups which, by inductive and conjugative effects, increase the participation of the aromatic ring in the stabilization of a positive charge on the alpha carbon. In our experiments with compound 1, we observed that alpha ether cleavage took place only at low charges of chlorine (Table III-3), forming the veratryl chloride and veratryl acetate derivatives, but no veratraldehyde (Table III-1 and III-2). This observation indicates that the stabilization of the benzylic carbocation is one of the critical factors determining the lability of the benzyl-oxygen linkage. Another piece of evidence was provided by the observation that alpha ether bond cleavage was inhibited by chlorine substituted on the veratryl ring. The deactivating action of chlorine on the aromatic ring counterbalanced the effect of the methoxy groups. We can reasonably expect that if a very large excess of chlorine was applied over the course of several hours, i.e. if the same experimental conditions as in Sintenis work were used, the perchlorinated veratraldehyde would eventually form.



Table III-18 . Yields (in percent of initial compound) of undegraded initial structures in the chlorination of compounds 1, 4, 5 and 8 under increasing charges of chlorine, x, (in mole of chlorine per  $C_9$  unit).

| Cl <sub>2</sub><br>charge | <u>1</u> | <u>4</u> | <u>5</u> | <u>8</u> |
|---------------------------|----------|----------|----------|----------|
| 0                         | 96.0     | 87       | 93.3     | 97       |
| 0.25                      | 69.9     | 86.2     | nd       | 88       |
| 0.5                       | 70.2     | 88.0     | 100      | 95       |
| 0.75                      | 69.8     | 88.9     | nd       | 92       |
| 1.0                       | 90.8     | 86       | 98.2     | 95       |
| 1.5                       | 78.3     | 65       | 91.5     | 91       |
| 2.0                       | 45       | 66       | 81.5     | 90.8     |
| 2.5                       | 27       | nd       | nd       | nd       |
| 3.0                       | nd       | 80       | 52.3     | 77       |
| 4.0                       | nd       | nd       | 25.9     | 78       |
| 5.0                       | nd       | nd       | 26       | 47       |
| 6.0                       | nd       | 75       | nd       | nd       |
| 10.0                      | nd       | nd       | 34.0     | nd       |
| 15.0                      | nd       | nd       | 33       | nd       |
| 20.0                      | nd       | nd       | 41       | nd       |

When no significant stabilization of the benzylic carbocation is available, the relative stability of the products formed governs the course of the reaction. Rather than the alpha-chloro aromatic product, the aromatic aldehyde, with the conjugation of the carbonyl group with the ring, will thus be preferentially formed.

From Table III-18, which summarizes, for the four model compounds, the yields of unbroken initial structure, it is clear that, unlike compound 1, the dimeric structure of compounds 4, 5, and 8 was barely altered by low charges of chlorine. Thus, the nature of the side chain affected the cleavage of the alpha alkyl-ether bond. Others<sup>4</sup> have already observed the same influence under conditions of acid hydrolysis, and we observed it in the chlorination (Chapter II) of benzyl-aryl ether bonds. The presence of beta and gamma carbons and substituents can inhibit the cleavage reaction in two ways, a) by simple steric hindrance which obstructs the approach of chlorine, and b) by inductive electron-withdrawing effect which decreases the stability of a possible benzylic carbocation.

The stability of the alpha alkyl ether bonds in presence of chlorine stands in striking contrast to the extremely labile character of their aryl analogues. It provides us with experimental support for the mechanism that we proposed for the chlorine-catalyzed cleavage of the benzyl aryl ether linkage (Scheme II-5), and against the mechanism advanced by Sarkanen and Strauss for the demethylation reaction (Scheme II-7 a)). That the totally different reactivities of alkyl and aryl ethers are inherent in the aromatic nature of the alpha substituent is in complete agreement with the mechanism described in scheme II-5 which holds specifically for aromatic benzyl ethers.

The efficiency of chlorine in promoting the cleavage reaction of the alpha alkyl ether bond in compound 1 was much less than the catalytic cleavage observed in the chlorination of the benzyl aryl ether 2. In all likelihood, the mechanism by which molecular chlorine promoted the cleavage of the benzyl-alkyl ether bond in compound 1 was the same as the one in the acidolysis of ether linkages, as described in the equations II-5 to II-7.

The unique behaviour of compound 1 is of great interest in the fundamental understanding of the mechanism of the cleavage of the benzyl ether by chlorine. It is, however, of limited importance in the study of delignification. On the one hand, not more than 30% of the initial structure of compound 1 was actually affected by the cleavage reaction. On the other hand, the monomeric structure of compound 1 bears little resemblance to the basic phenylpropane unit in lignin.

Chlorination of compound 5 promoted, although in moderate yields, cleavage of the beta-aryl ether linkage. Neither the cleavage of beta-aryl ether bonds nor the demethylation reaction is usually observed in non-aqueous solvents<sup>2</sup>, and the results obtained with compound 4 accorded with the literature on this point. The different behaviour of compound 5 raised the following questions:

- 1) why did beta-aryl ether cleavage occur under an excess of chlorine and not when catalytic amounts of chlorine were applied (as in benzyl-aryl ether cleavage)?
- 2) why did beta aryl ether cleavage occur and not demethylation?
- 3) why did beta aryl ether cleavage occur with compound 5 and not with compound 4?

Compound 5 differs from compound 4 by the presence of a methyl substituent on the aromatic ring para to the beta-aryl ether linkage. The mechanism proposed for the chlorine-catalyzed cleavage of benzyl aryl ethers (Scheme II-5) begins with an electrophilic interaction between the  $\pi$ -system of the aromatic ring and the chlorine molecule. It can thus be influenced by the reactivity of the aromatic ring towards electrophilic species. A methyl substituent on an aromatic ring is electron releasing both inductively and by hyperconjugation. Therefore, it usually enhances the reactivity of the ring towards electrophilic substitution, with ortho and para orientation. If cleavage of the beta-ether bond occurred in compound 5 and not compound 4 for such electronic reasons, we would have then logically expected beta-ether bond cleavage to take place when the beta aryloxy substituent was at its higher level of reactivity towards electrophilic species, i.e. before aromatic substitution. However, instead of ether cleavage, we actually observed aromatic substitution by chlorine. It's having proceeded on the beta-substituent rather than on the veratryl moiety actually demonstrated the stronger reactivity of the creosyl ring over the guaiacyl ring towards electrophilic aromatic substitution. Beta-ether bond cleavage occurred only after the creosyl ring had been substituted by a number of chlorine atoms. The products from beta-ether cleavage are present in the reaction mixture together with their precursors (Tables III-9 and III-10). These dimeric species bear one or two chlorine atoms on the creosyl ring (5-3, 5-4 and 5-5). These chlorine atoms, by their electron withdrawing inductive effect, tend to counterbalance the effect of the methyl group.

Thus cleavage occurred after a decrease of the reactivity of the creosyl ring. Furthermore, chlorination provided compound 5 with a bulkier beta-aryloxy group (5-4 and 5-5) than in compound 4 (4-6, 4-7, 4-8), so that steric interactions with the rest of the molecule are likely to ease the departure of the beta-aryloxy group. That beta-aryl ether bond cleavage occurred after aromatic substitution suggests that steric, and not electronic interactions are the driving force for bond cleavage. These interactions are not present when the bulky benzylic moiety is replaced by a single H, as in the methoxyl group. Answering thus the three questions in the previous paragraph, we believe that steric hindrance, created by the larger degree of substitution on the creosyl nucleus that is due to the presence of the methyl group, explains the instability of the alkyl aryl ether bond in compound 5, relative to that in compound 4 as well as in methyl aryl ethers.

The occurrence of the beta cleavage prompts two points of discussion regarding, first, the reactivity of the different types of ether bonds in the molecule, and, second, the significance of the reaction to lignin chlorination.

a) Since the stress was released by elimination of the beta- and not of the alpha-substituent, we can infer that the factors promoting the elimination of the beta-substituent (its nature of good leaving group, the possible catalytic interaction between the aromatic ring and chlorine) overbalanced those tending to the elimination of the alpha substituent (the possibility of stabilization of a benzylic carbocation). We have already observed in compound 1 that substitution of only one chlorine atom on the veratryl nucleus (1-3, 1-4, Table III-2,  $x=1.5$ ) very efficiently inhibited the elimination of the alpha

alkyl ether. When beta-cleavage was initiated in compound 5, the veratryl ring was also monochlorinated (5-3, 5-4, 5-5, Table III-9,  $x=1.5$ ), and it is therefore not surprising that the elimination of the alpha alkyl ether could not take place.

b) With the methyl group on the beta-aryl substituent representing the side chain of the phenylpropane unit attached at the beta-position of the side chain of another unit, compound 5 was taken as approaching the structures present in lignin better than for instance compound 4. One might therefore conclude from the behaviour of compound 5, that the cleavage of the beta-O-4 linkage, affecting about 25% of the initial compound, is one of the reactions responsible for the degradation of lignin network by chlorine. This reasoning does not hold, however. We found that the elimination of the beta substituent was the consequence of the steric hindrance due to the chlorination of the creosyl ring. Besides, the identification of the primary reaction products permitted us to establish the relative reactivities of the two veratryl and creosyl aromatic rings, or in other words, the relative activating effects of the two side chains  $-\text{CH}(\text{OALKYL})-\text{CH}(\text{OARYL})$  and  $-\text{CH}_3$  towards electrophilic aromatic substitution by chlorine. Table III-19 shows, for each of the aromatic nuclei, veratryl and creosyl in compound 5, the yields of products calculated at different levels of substitution by chlorine. This calculation was made according to the following example. At a charge  $x=1.5$  (Table III-9), the three products 5-3, 5-4, and 5-5 were formed. In 5-3, both rings are monochlorinated, whereas 5-4 and 5-5 contain a monochlorinated veratryl nucleus and a dichlorinated creosyl nucleus.

The product 5-3 accounted for about 48% of the initial monomer units, which can be decomposed into 24% of monochlorinated veratryl and 24% of monochlorinated creosyl rings. Similarly, 5-4 and 5-5 represented roughly 22% of monochlorinated veratryl and 22% of dichlorinated creosyl ring. The overall summation of both type of nucleus and each level of substitution (Table III-19) brings clear evidence for the much stronger activating power of the methyl group compared to a side chain bearing ether groups. Considering lignin structure, the beta aryloxy substituents in lignin are more likely to follow the behaviour of the veratryl ring, with monochlorination on the free position para to the methoxyl group, then ipso substitution and elimination of the side chain as observed in compound 1 (Tables III-2 and III-1), rather than extensive substitution by chlorine as in compound 5. Accordingly, compound 4, with a guaiacyl group at the beta-position, is more likely to mimic the behaviour of lignin during chlorination. The fact that cleavage of the beta-aryl ether linkage did not occur at all during the chlorination of compound 4 (Table III-7) decreases the significance of the beta-ether cleavage in the process of delignification by chlorine.

Like compound 1, the behaviour of compound 5 brings important elements to our insight into the reactivity of ether bonds in presence of chlorine, but it presents limited relevance to delignification.

Table III-19 . Yields (in percent of initial C<sub>9</sub> units) of chlorinated creosyl and veratryl moieties of compound 5 formed under increasing charge of chlorine x (in mole of chlorine per C<sub>9</sub> unit).

[Cl-, Cl<sub>2</sub>-, and Cl<sub>3</sub>- stand for mono-, di-, and tri-chlorinated respectively; "Ver" and "Creo" stand for veratryl and creosyl ring respectively].

| Cl <sub>2</sub><br>charge | VERATRYL RING |                      |                      | CREOSYL RING |                       |                       |
|---------------------------|---------------|----------------------|----------------------|--------------|-----------------------|-----------------------|
| x                         | Cl-Ver        | Cl <sub>2</sub> -Ver | Cl <sub>3</sub> -Ver | Cl-Creo      | Cl <sub>2</sub> -Creo | Cl <sub>3</sub> -Creo |
| 0.5                       | 3.7           | 0                    | 0                    | 41.5         | 0                     | 0                     |
| 1.0                       | 45            | 0                    | 0                    | 49.1         | 0                     | 0                     |
| 1.5                       | 45.8          | 0                    | 0                    | 24.2         | 21.6                  | 0                     |
| 2.0                       | 37            | 3.6                  | 0                    | 3.0          | 35                    | 2.8                   |
| 3.0                       | 11.3          | 13.9                 | 0                    | 0            | 15.1                  | 10.1                  |
| 4.0                       | 0.7           | 10.7                 | 0.8                  | 0            | 3.7                   | 8.5                   |



An additional carbon bearing an hydroxyl group on the side chain does not seem to cause any major changes in the reactivity of the molecule. Compounds 8 and 4 behaved similarly (Tables III-17 and III-7 respectively), with no cleavage of alpha or beta ether bonds. The reported<sup>5</sup> participation of the gamma-hydroxyl group in alpha-ether cleavage through intramolecular hydrogen bonding, did not take place here.

In all four compounds investigated in this research, the primary reaction, and the major reaction if not the only one, was aromatic electrophilic substitution. This reaction promoted the breakdown of the initial structure directly and principally by electrophilic side-chain displacement due to ipso aromatic substitution, and also indirectly by causing the elimination of the beta-aryl ether substituent in order to release the steric encumbrance. As substitution on the uncleaved dimer increased, the reactivity decreased, thus reducing the probability of the ipso substitution and also reducing the efficiency of the side-chain cleavage in the breakdown of the molecule. Degradation occurred only under excess of chlorine, and stoichoimetrically with chlorine. Side-chain cleavage alone was not very efficient, a chlorine charge of 4.0 mole per C<sub>9</sub> unit leaving about 80% of the dimeric structure uncleaved (compounds 4, and 2). When beta cleavage took place (compound 5), however, only 30% of the dimer survived.

In general, however, the chlorination of benzyl alkyl ethers leads to minor structure breakdown, but to extensive chlorination on the aromatic rings. In relation to the bleaching process (the industrial chlorine charge corresponds to about 4 moles of chlorine per monomer unit), not only is the application of an excess of chlorine on benzyl alkyl ethers inefficient in terms of delignification, but it is, in addition, responsible for the eventual discharge in the effluents of highly chlorinated low molecular weight aromatic compounds.

### Conclusion

The stability of alpha-alkyl ether bonds in the reaction with chlorine provided evidence that molecular chlorine did not have the same catalytic action on them as on benzyl-aryl ethers. These experimental results supported the validity of the mechanism proposed in chapter II to explain the cleavage of benzyl aryl ethers; the cleavage of the benzyl-alkyl ether bond observed in compound 1 is likely to proceed through a mechanism similar to that of the acidolysis of ether bonds.

Considering the action of chlorine on the different types of ether linkages encountered in chapters II and III, we propose the following tentative order of reactivity:

- on the unchlorinated compound:  $\alpha$  aryl  $\gg$   $\alpha$  alkyl  $>$   $\beta$  aryl.
- on the chlorinated compound:  $\beta$  aryl  $>$   $\alpha$  alkyl.

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## CHAPTER IV

### REACTION OF NON-PHENOLIC LIGNIN MODEL COMPOUNDS BEARING A BENZYLIC ALCOHOL GROUP

## INTRODUCTION

In research on the chlorination of lignin, the most widely investigated model compounds have been of the beta-aryl ether type bearing a hydroxyl group at the benzylic position, probably because they represent about one fifth of all C<sub>9</sub> units in lignin. The investigations, however, mainly dealt with reactions in aqueous media<sup>1,2</sup>, and/or with reactions of a large excess of chlorine<sup>3</sup>. Only one paper has been published on the primary reactions of veratryl alcohols with chlorine<sup>4</sup>, but conditions and yields were not clearly specified.

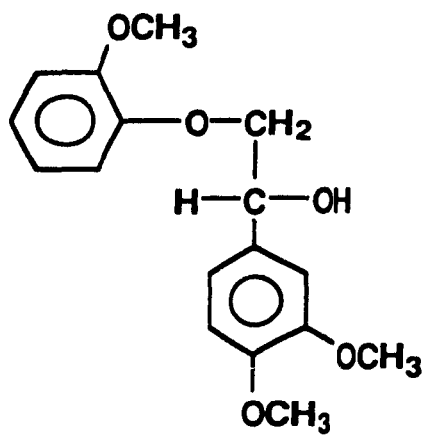
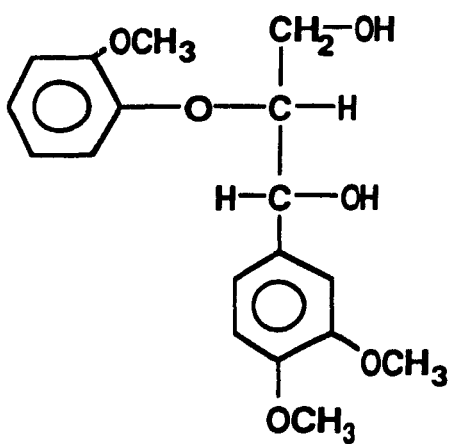
The experiments described in this chapter, with two model compounds representing linear units of the beta-aryl ether type, aimed at more precise elucidation of the influence of the alpha-hydroxyl group on the primary reaction of molecular chlorine with such compounds. These experiments brought additional support to the already known reactivity of the benzylic alcohols, and provided a detailed view of the stepwise progression of the substitution reaction leading eventually to dimer degradation.

## RESULTS

Compounds 3 and 7 are shown in scheme IV-1. Both dimers bear a benzylic alcohol function, and a beta aryloxy substituent; they are the alpha-hydroxyl analogues of compounds 4 and 8. With a carbinol group in gamma position on the side chain, compound 7 represents a more realistic dimeric unit in lignin. Unlike compound 8, which represented the mixture of the two diastereomers, compound 7 is the pure threo form of the veratryl glycerol guaiacyl ether.

The compounds were treated in the same manner as their alkyl and aryl analogues (see Experimental and Chapter II). Because of the presence of hydroxyl groups in the starting compounds and in their products, the samples from compound 3 and 7, were derivatized before GC and GC-MS analyses by methylation and acetylation, respectively.

The complete results of the chlorination of compounds 3 and 7 are shown in tables IV-1 to IV-10. Both dimers exhibited the same behaviour, and were degraded by an excess of chlorine via elimination of the side chain.

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SCHEME IV-1 . Compounds of the benzyl alcohol type. 3 and 7

Table IV-1. Products from the chlorination of compound 3.

| compound    | structure                                                                                                                      | GC retention time* (min) |
|-------------|--------------------------------------------------------------------------------------------------------------------------------|--------------------------|
| <u>3</u>    | compound <u>3</u>                                                                                                              | 7.40                     |
| <u>3-1</u>  | 1-(6-chloro-3,4-dimethoxyphenyl)-<br>2-(2-methoxyphenoxy)ethanol                                                               | 8.51                     |
| <u>3-2</u>  | 1-(3,4-dimethoxyphenyl)-2-(4 or 5 chloro-2-methoxy<br>phenoxy)ethanol [2 positional isomers a and b]                           | 9.29/9.56                |
| <u>3-3</u>  | 1-(6-chloro-3,4-dimethoxyphenyl)-2-(4 or 5 chloro-<br>2-methoxyphenoxy)ethanol<br>[2 positional isomers a and b]               | 10.70/11.05              |
| <u>3-4</u>  | 1-(6-chloro-3,4-dimethoxyphenyl)-<br>2-(4,5 dichloro-2-methoxyphenoxy)ethanol                                                  | 14.26                    |
| <u>3-5</u>  | 1-(2 or 5,6-dichloro-3,4-dimethoxyphenyl)-<br>2-(4,5 dichloro-2-methoxyphenoxy)ethanol                                         | 15.99                    |
| <u>3-6</u>  | 1-(2,5,6-trichloro-3,4-dimethoxyphenyl)-<br>2-(4,5 dichloro-2-methoxyphenoxy)ethanol                                           | 15.46 <sup>d</sup>       |
| <u>3-7</u>  | 1-(2 or 5,6-dichloro-3,4-dimethoxyphenyl)-<br>2-(3 or 6,4,5 trichloro-2-methoxyphenoxy)ethanol                                 | 16.47 <sup>d</sup>       |
| <u>3-8</u>  | 1-(2,5,6-trichloro-3,4-dimethoxyphenyl)-2-<br>(3 or 6,4,5 trichloro-2-methoxyphenoxy)ethanol<br>[2 positional isomers a and b] | 17.97/19.23 <sup>d</sup> |
| <u>3-9</u>  | 4,5-dichloroveratrole                                                                                                          | 3.25 <sup>b</sup>        |
| <u>3-10</u> | trichloroveratrole                                                                                                             | 3.69 <sup>b</sup>        |
| <u>3-11</u> | tetrachloroveratrole                                                                                                           | 3.75 <sup>b</sup>        |
| <u>3-12</u> | 2-(4,5 dichloro-2-methoxyphenoxy) acetaldehyde                                                                                 | 4.09 <sup>b</sup>        |
| <u>3-13</u> | 2-(4,5 dichloro-2-methoxyphenoxy) vinyl alcohol<br>trimethylsilyl ether                                                        | 6.62 <sup>b</sup>        |

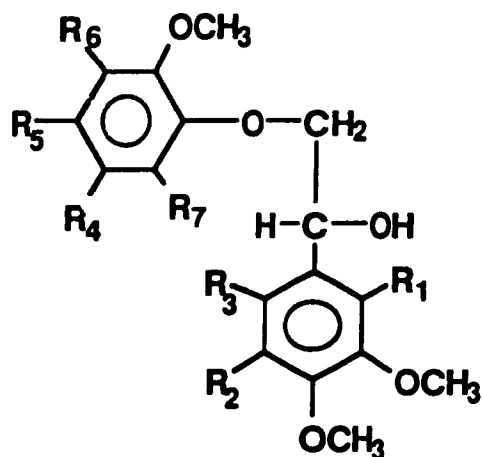
\*GC and GC-MS conditions: column DB5, J&W; carrier He, 1ml/min;  
temperature gradient: 230°C- 270°C, 5°C/min.

<sup>a</sup> temperature gradient: 80-270°C, 25°C/min.

<sup>b</sup> temperature gradient: 150-270°C, 15°C/min.

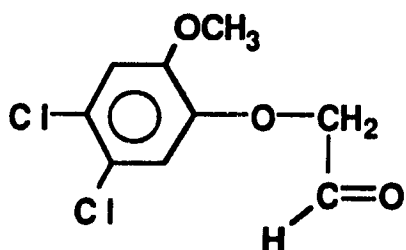
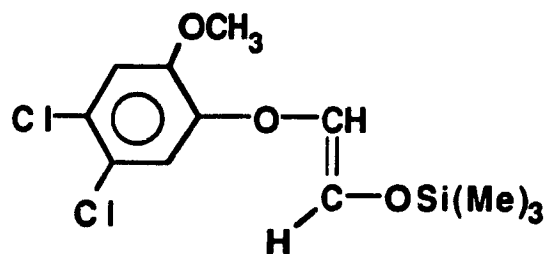


a)



| compound   | R <sub>1</sub> | R <sub>2</sub> | R <sub>3</sub> | R <sub>4</sub> | R <sub>5</sub> | R <sub>6</sub> | R <sub>7</sub> |
|------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|
| <u>3-1</u> | H              | H              | Cl             | H              | H              | H              | H              |
| <u>3-2</u> | H              | H              | H              | Cl             | H              | H              | H              |
| and        | H              | H              | H              | H              | Cl             | H              | H              |
| <u>3-3</u> | H              | H              | Cl             | Cl             | H              | H              | H              |
| and        | H              | H              | Cl             | H              | Cl             | H              | H              |
| <u>3-4</u> | H              | H              | Cl             | Cl             | Cl             | H              | H              |
| <u>3-5</u> | Cl             | H              | Cl             | Cl             | Cl             | H              | H              |
| and        | H              | Cl             | Cl             | Cl             | Cl             | H              | H              |
| <u>3-6</u> | Cl             | Cl             | Cl             | Cl             | Cl             | H              | H              |
| <u>3-7</u> | Cl             | H              | Cl             | Cl             | Cl             | Cl             | H              |
| and        | H              | Cl             | Cl             | Cl             | Cl             | H              | Cl             |
| <u>3-8</u> | Cl             | Cl             | Cl             | Cl             | Cl             | Cl             |                |
| and        | Cl             | Cl             | Cl             | Cl             | Cl             | H              | Cl             |

b)

3-123-13

SCHEME IV-2 . Products from the chlorination of compound 3 .

a) Substitution products. b) Cleavage products.

Table IV-2 . Yields of aromatic substitution products from the chlorination of compound 3 under increasing charges of chlorine,  $x$ , (in moles of chlorine per  $C_9$  unit). Yields are expressed in percent of initial  $C_9$  unit, obtained by GC analysis. Standard deviations are given in parentheses.

| Cl <sub>2</sub><br>charge | UN-       | MONO-         |                  | DI-                    | TRI-          | TETRA-        | PENTA-       |              | HEXA-                |
|---------------------------|-----------|---------------|------------------|------------------------|---------------|---------------|--------------|--------------|----------------------|
| $x$                       | 3         | <u>3-1</u>    | <u>3-2 [a/b]</u> | <u>3-3 [a/b]</u>       | <u>3-4</u>    | <u>3-5</u>    | <u>3-6</u>   | <u>3-7</u>   | <u>3-8 [a/b]</u>     |
| 0                         | 77<br>(2) | -             | -                | -                      | -             | -             | -            | -            | -                    |
| 0.125                     | 65<br>(3) | 29<br>(3)     | 2.8<br>(0.4)     | -                      | -             | -             | -            | -            | -                    |
| 0.375                     | 8<br>(2)  | 61<br>(3)     | 18<br>(4)        | 5.2/3.9<br>(0.6/0.1)   | -             | -             | -            | -            | -                    |
| 0.5                       | 0         | 67.0<br>(0.2) | 6.8<br>(0.2)     | 10.3/8.5<br>(0.3/0.1)  | -             | -             | -            | -            | -                    |
| 0.625                     | -         | 57<br>(1)     | 0                | 14/11.6<br>(1/0.8)     | -             | -             | -            | -            | -                    |
| 1.0                       | -         | 22<br>(2)     | -                | 33/27<br>(2/2)         | 2.9<br>(0.1)  | -             | -            | -            | -                    |
| 1.5                       | -         | 0             | -                | 19.3/15.4<br>(0.3/0.1) | 30<br>(1)     | -             | -            | -            | -                    |
| 2.0                       | -         | -             | -                | 2.4/-<br>(0.1/-)       | 40.5<br>(0.9) | 6.3<br>(0.1)  | -            | -            | -                    |
| 2.5                       | -         | -             | -                | 0                      | 18<br>(1)     | 15<br>(1)     | -            | -            | -                    |
| 3.0                       | -         | -             | -                | -                      | 11.4<br>(0.1) | 16.5<br>(0.3) | 2.9<br>(0.1) | -            | -                    |
| 4.0                       | -         | -             | -                | -                      | 0             | 9.9<br>(0.1)  | 6<br>(1)     | 2.9<br>(0.7) | -                    |
| 5.0                       | -         | -             | -                | -                      | -             | 3<br>(1)      | 6<br>(1)     | 2.3<br>(0.2) | 2.5/1.0<br>(0.2/0.2) |
| 6.0                       | -         | -             | -                | -                      | -             | 1.4<br>(0.1)  | 4.5<br>(0.5) | 2.0<br>(0.1) | 3.2/0.1<br>(0.3/0.1) |

Table IV-3 . Combined yields of aromatic substitution products from the chlorination of compound 3 under increasing charges of chlorine, x, (in moles of chlorine per C<sub>9</sub> unit). Yields are expressed in percent of initial C<sub>9</sub> unit, obtained by GC analysis. Standard deviations are given in parentheses.

| Cl <sub>2</sub><br>charge | UN-       | MONO-                 | DI-              | TRI-          | TETRA-        | PENTA-          | HEXA-            |
|---------------------------|-----------|-----------------------|------------------|---------------|---------------|-----------------|------------------|
| <u>x</u>                  | <u>3</u>  | <u>3-1, 3-2 [a/b]</u> | <u>3-3 [a/b]</u> | <u>3-4</u>    | <u>3-5</u>    | <u>3-6, 3-7</u> | <u>3-8 [a/b]</u> |
| 0                         | 77<br>(2) | -                     | -                | -             | -             | -               | -                |
| 0.125                     | 65<br>(3) | 32<br>(3)             | -                | -             | -             | -               | -                |
| 0.375                     | 8<br>(2)  | 79<br>(5)             | 9.1<br>(0.6)     | -             | -             | -               | -                |
| 0.5                       | 0         | 73.8<br>(0.2)         | 18.8<br>(0.3)    | -             | -             | -               | -                |
| 0.625                     | -         | 57<br>(1)             | 26<br>(1)        | -             | -             | -               | -                |
| 1.0                       | -         | 22<br>(2)             | 60<br>(3)        | 2.9<br>(0.1)  | -             | -               | -                |
| 1.5                       | -         | 0                     | 34.8<br>(0.3)    | 30<br>(1)     | -             | -               | -                |
| 2.0                       | -         | -                     | 2.4<br>(0.1)     | 40.5<br>(0.9) | 6.3<br>(0.1)  | -               | -                |
| 2.5                       | -         | -                     | 0                | 18<br>(1)     | 15<br>(1)     | -               | -                |
| 3.0                       | -         | -                     | -                | 11.4<br>(0.1) | 16.5<br>(0.3) | 2.9<br>(0.1)    | -                |
| 4.0                       | -         | -                     | -                | 0             | 9.9<br>(0.1)  | 9<br>(1)        | -                |
| 5.0                       | -         | -                     | -                | -             | 3<br>(1)      | 8<br>(1)        | 3.5<br>(0.3)     |
| 6.0                       | -         | -                     | -                | -             | 1.4<br>(0.1)  | 6.5<br>(0.5)    | 3.3<br>(0.3)     |

Table IV-4 . Yields of cleavage products (aromatic ipso-substitution) from the chlorination of compound 3 under increasing charges of chlorine,  $x$ , (in moles of chlorine per  $C_9$  unit). Yields are expressed in percent of initial  $C_9$  unit, obtained by GC analysis. Standard deviations are given in parentheses.

| chlorine<br>charge<br>$x$ | side chain<br>cleavage |               |              |                   | unknown <sup>a</sup><br>4.33, 4.88 |
|---------------------------|------------------------|---------------|--------------|-------------------|------------------------------------|
|                           | <u>3-9</u>             | <u>3-10</u>   | <u>3-11</u>  | <u>3-12, 3-13</u> |                                    |
| 1.0                       | 0.2<br>(0.1)           | -             | -            | -                 | -                                  |
| 1.5                       | 4.3<br>(0.1)           | -             | -            | 0.3<br>(0.1)      | 0.7<br>(0.1)                       |
| 2.0                       | 11.0<br>(0.2)          | 0.4<br>(0.1)  | -            | 0.7<br>(0.2)      | 1.9<br>(0.5)                       |
| 2.5                       | 17.2<br>(0.1)          | 0.3<br>(0.1)  | -            | 7.1<br>(0.2)      | 3.6<br>(0.4)                       |
| 3.0                       | 21<br>(2)              | 2<br>(1)      | -            | 17<br>(2)         | 2<br>(1)                           |
| 4.0                       | 16.9<br>(0.1)          | 8.5<br>(0.2)  | 0.4<br>(0.1) | 11.7<br>(0.5)     | 3<br>(1)                           |
| 5.0                       | 11.6<br>(0.6)          | 14.1<br>(0.6) | 1.1<br>(0.1) | 9.5<br>(0.3)      | 2.7<br>(0.1)                       |
| 6.0                       | 7.4<br>(0.1)           | 15.6<br>(1)   | 1.7<br>(0.1) | 7.0<br>(0.1)      | 2.5<br>(0.3)                       |

<sup>a</sup> Characterized by their respective GC retention times; temperature gradient: 150-270°C, 15°C/min.

Table IV-5 . Combined yields of related products from the chlorination of compound 3 under increasing charges of chlorine, x, (in moles of chlorine per C<sub>9</sub> unit): a) compound 3 recovered unaltered after the reaction, b) products from beta aryl ether bond cleavage, c) products from substitution on the aromatic rings. Yields are expressed in percent of initial C<sub>9</sub> unit, obtained by GC analysis. Standard deviations are given in parentheses.

| Cl <sub>2</sub><br>charge<br>x | unaltered<br><u>3</u> | beta<br>aryl-ether<br>cleavage | substitution                                                                        |                                                                          | Total         |
|--------------------------------|-----------------------|--------------------------------|-------------------------------------------------------------------------------------|--------------------------------------------------------------------------|---------------|
|                                |                       |                                | ipso-substitution<br>(side-chain cleavage)<br><u>3-9, 3-10</u><br><u>3-11, 3-12</u> | other<br><u>3-1, 3-2, 3-3</u><br><u>3-4, 3-5</u><br><u>3-6, 3-7, 3-8</u> |               |
| 0                              | 77<br>(2)             | -                              | -                                                                                   | 0                                                                        | 77<br>(2)     |
| 0.125                          | 65<br>(3)             | -                              | -                                                                                   | 32<br>(3)                                                                | 97<br>(4)     |
| 0.375                          | 8<br>(2)              | -                              | -                                                                                   | 88<br>(5)                                                                | 96<br>(5)     |
| 0.5                            | 0                     | -                              | -                                                                                   | 92.6<br>(0.4)                                                            | 92.6<br>(0.4) |
| 0.625                          | -                     | -                              | -                                                                                   | 83<br>(1)                                                                | 83<br>(1)     |
| 1.0                            | -                     | -                              | 0.2<br>(0.1)                                                                        | 85<br>(4)                                                                | 85<br>(4)     |
| 1.5                            | -                     | -                              | 4.6<br>(0.1)                                                                        | 65<br>(1)                                                                | 70<br>(1)     |
| 2.0                            | -                     | -                              | 12.1<br>(0.3)                                                                       | 49<br>(1)                                                                | 61<br>(1)     |
| 2.5                            | -                     | -                              | 24.6<br>(0.2)                                                                       | 33<br>(1)                                                                | 58<br>(1)     |
| 3.0                            | -                     | -                              | 40<br>(3)                                                                           | 30.8<br>(0.4)                                                            | 71<br>(3)     |
| 4.0                            | -                     | -                              | 37.5<br>(0.6)                                                                       | 18<br>(1)                                                                | 55<br>(1)     |
| 5.0                            | -                     | -                              | 36.3<br>(0.9)                                                                       | 15<br>(1)                                                                | 51<br>(1)     |
| 6.0                            | -                     | -                              | 32<br>(1)                                                                           | 11.2<br>(0.6)                                                            | 43<br>(1)     |

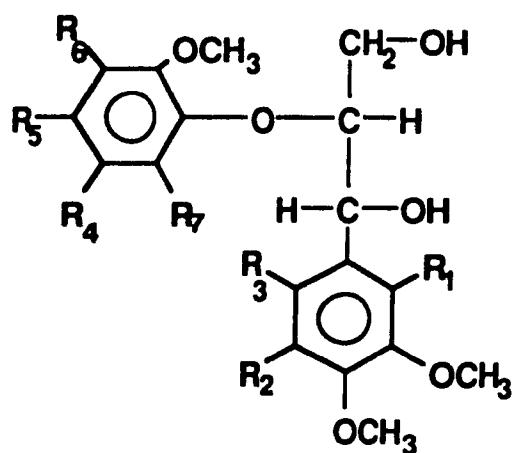
Table IV-6 . Products from the chlorination of compound 7

| compound    | structure                                                                                                         | GC retention time* (min) |
|-------------|-------------------------------------------------------------------------------------------------------------------|--------------------------|
| <u>7</u>    | compound <u>7</u> .                                                                                               | 11.28                    |
| <u>7-1</u>  | 1-(6-chloro-3,4-dimethoxyphenyl)-<br>2-(2-methoxyphenoxy)propane 1,3-diol.                                        | 11.57                    |
| <u>7-2</u>  | 1-(6-chloro-3,4-dimethoxyphenyl)-2-(4 or 5 chloro-<br>2-methoxyphenoxy)propane 1,3-diol.<br>[2 isomers a) and b)] | 12.26/12.40              |
| <u>7-3</u>  | 1-(6-chloro-3,4-dimethoxyphenyl)-2-(4, 5 chloro-<br>2-methoxyphenoxy)propane 1,3-diol.                            | 13.20                    |
| <u>7-4</u>  | 1-(2 or 5,6-dichloro-3,4-dimethoxyphenyl)-2-(4, 5 dichloro-<br>2-methoxyphenoxy)propane 1,3-diol.                 | 14.01                    |
| <u>7-5</u>  | 1-(2 or 5,6-dichloro-3,4-dimethoxyphenyl)-<br>2-(3 or 6,4,5 trichloro-2-methoxyphenoxy)propane 1,3-diol.          | 14.82                    |
| <u>7-6</u>  | 1-(2,5,6-trichloro-3,4-dimethoxyphenyl)-2-(4,5 dichloro-<br>2-methoxyphenoxy)propane 1,3-diol.                    | 15.14                    |
| <u>7-7</u>  | 1-(2,5,6-trichloro-3,4-dimethoxyphenyl)-<br>2-(3 or 6,4,5 trichloro-2-methoxyphenoxy)propane 1,3-diol.            | 16.43                    |
| <u>7-8</u>  | 4,5-dichloroveratrole                                                                                             | 6.12                     |
| <u>7-9</u>  | trichloroveratrole                                                                                                | 7.01                     |
| <u>7-10</u> | tetrachloroveratrole                                                                                              | 7.51                     |
| <u>7-11</u> | 3-hydroxy-2-(4,5 dichloro-<br>2-methoxyphenoxy)propanaldehyde                                                     | 7.56                     |

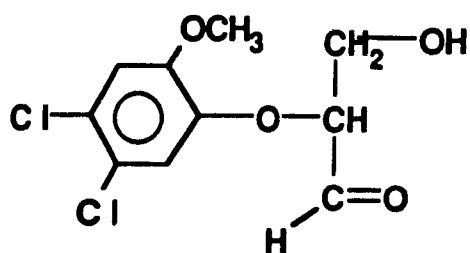
\*Conditions: column DB5, J&W; carrier He, 1ml/min;

GC-MS: Acetylation, temperature gradient: 250°C- 300°C, 5°C/min.

GC: Silylation, temperature gradient: 80°C- 300°C, 20°C/min.



| compound   | R <sub>1</sub> | R <sub>2</sub> | R <sub>3</sub> | R <sub>4</sub> | R <sub>5</sub> | R <sub>6</sub> | R <sub>7</sub> |
|------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|
| <u>7-1</u> | H              | H              | Cl             | H              | H              | H              | H              |
| <u>7-2</u> | H              | H              | H              | Cl             | H              | H              | H              |
| and        | H              | H              | H              | H              | Cl             | H              | H              |
| <u>7-3</u> | H              | H              | Cl             | Cl             | Cl             | H              | H              |
| <u>7-4</u> | H              | Cl             | Cl             | Cl             | Cl             | H              | H              |
| and        | Cl             | H              | Cl             | Cl             | Cl             | H              | H              |
| <u>7-5</u> | H              | Cl             | Cl             | Cl             | H              | H              | Cl             |
| and        | Cl             | H              | Cl             | H              | Cl             | Cl             | H              |
| <u>7-6</u> | Cl             | Cl             | Cl             | Cl             | Cl             | H              | H              |
| <u>7-7</u> | Cl             | Cl             | Cl             | Cl             | Cl             | Cl             | H              |
| and        | Cl             | Cl             | Cl             | Cl             | Cl             | H              | Cl             |

7-11

SCHEME IV-3 . Products from the chlorination of compound 7 .

a) Substitution products. b) Cleavage products.

Table IV-7. Yields of aromatic substitution products from the chlorination of compound 7 under increasing charges of chlorine, x, (in moles of chlorine per C<sub>9</sub> unit). Yields are expressed in percent of initial C<sub>9</sub> unit, obtained by GC analysis. Standard deviations are given in parentheses.

| Cl <sub>2</sub><br>charge | UN-           | MONO-         | DI-                      | TRI-       | TETRA-       | PENTA-                 | HEXA-        |
|---------------------------|---------------|---------------|--------------------------|------------|--------------|------------------------|--------------|
| <u>x</u>                  | <u>7</u>      | <u>7-1</u>    | <u>7-2</u> [a/b]         | <u>7-3</u> | <u>7-4</u>   | <u>7-5</u> <u>7-6</u>  | <u>7-7</u>   |
| 0                         | 90.8<br>(0.3) | -             | -                        | -          | -            | - -                    | -            |
| 0.25                      | 26.6<br>(0.2) | 39.8<br>(0.3) | 2.2/2.8<br>(0.7)/(0.6)   | -          | -            | - -                    | -            |
| 0.5                       | 4.0<br>(0.7)  | 40<br>(2)     | 6.2/7.5<br>(0.6)/(0.7)   | -          | -            | - -                    | -            |
| 0.75                      | 0             | 30<br>(1)     | 19.5/25.8<br>(0.2)/(0.2) | -          | -            | - -                    | -            |
| 1.0                       | -             | 5<br>(1)      | 27/36<br>(1)/(1)         | 8<br>(1)   | -            | - -                    | -            |
| 1.5                       | -             | 0             | 4.2/5.3<br>(0.2)/(0.1)   | 27<br>(1)  | 11<br>(1)    | - -                    | -            |
| 2.0                       | -             | -             | 0                        | 0          | 21<br>(1)    | - 7<br>(1)             | -            |
| 2.5                       | -             | -             | -                        | -          | 15<br>(1)    | 1.4 4<br>(0.5) (1)     | 2<br>(1)     |
| 3.0                       | -             | -             | -                        | -          | 9.3<br>(0.2) | 1.7 2.4<br>(0.2) (0.2) | 2.5<br>(0.5) |
| 4.0                       | -             | -             | -                        | -          | 4.3<br>(0.5) | 1.8 2.5<br>(0.4) (0.5) | 4<br>(1)     |
| 5.0                       | -             | -             | -                        | -          | 2.5<br>(0.5) | 0.8 0<br>(0.2)         | 6<br>(1)     |



Table IV-8 . Combined yields of aromatic substitution products from the chlorination of compound 7 under increasing charges of chlorine,  $x$ , (in moles of chlorine per  $C_9$  unit). Yields are expressed in percent of initial  $C_9$  unit, obtained by GC analysis. Standard deviations are given in parentheses.

| Cl <sub>2</sub><br>charge | UN-           | MONO-         | DI-              | TRI-       | TETRA-       | PENTA-          | HEXA-        |
|---------------------------|---------------|---------------|------------------|------------|--------------|-----------------|--------------|
| $x$                       | <u>7</u>      | <u>7-1</u>    | <u>7-2</u> [a/b] | <u>7-3</u> | <u>7-4</u>   | <u>7-5, 7-6</u> | <u>7-7</u>   |
| 0                         | 90.8<br>(0.3) | -             | -                | -          | -            | -               | -            |
| 0.25                      | 26.6<br>(0.2) | 39.8<br>(0.3) | 5<br>(1)         | -          | -            | -               | -            |
| 0.5                       | 4.0<br>(0.7)  | 40<br>(2)     | 14<br>(1)        | -          | -            | -               | -            |
| 0.75                      | 0             | 30<br>(1)     | 45.3<br>(0.2)    | -          | -            | -               | -            |
| 1.0                       | -             | 5<br>(1)      | 63<br>(1)        | 8<br>(1)   | -            | -               | -            |
| 1.5                       | -             | 0             | 9.5<br>(0.2)     | 27<br>(1)  | 11<br>(1)    | -               | -            |
| 2.0                       | -             | -             | 0                | 0          | 21<br>(1)    | 7<br>(1)        | -            |
| 2.5                       | -             | -             | -                | -          | 15<br>(1)    | 5<br>(1)        | 2<br>(1)     |
| 3.0                       | -             | -             | -                | -          | 9.3<br>(0.2) | 4.1<br>(0.2)    | 2.5<br>(0.5) |
| 4.0                       | -             | -             | -                | -          | 4.3<br>(0.5) | 4.3<br>(0.5)    | 4<br>(1)     |
| 5.0                       | -             | -             | -                | -          | 2.5<br>(0.5) | 0.8<br>(0.2)    | 6<br>(1)     |

Table IV-9 . Yields of cleavage products (ipso-substitution) from the chlorination of compound 7 under increasing charges of chlorine, x, (in moles of chlorine per C<sub>9</sub> unit). Yields are expressed in percent of initial C<sub>9</sub> unit, obtained by GC analysis. Standard deviations are given in parentheses.

| Cl <sub>2</sub><br>charge<br>x | side chain<br>cleavage |               |              |              |
|--------------------------------|------------------------|---------------|--------------|--------------|
|                                | <u>7-8</u>             | <u>7-9</u>    | <u>7-10</u>  | <u>7-11</u>  |
| 1.5                            | 8.5<br>(0.4)           | 0.8<br>(0.2)  | -            | 1.8<br>(0.5) |
| 2.0                            | 19.2<br>(0.2)          | 2.4<br>(0.4)  | -            | 9<br>(1)     |
| 2.5                            | 21<br>(1)              | 6.7<br>(0.5)  | -            | 9<br>(1)     |
| 3.0                            | 17<br>(1)              | 10.3<br>(0.5) | 0.8<br>(0.3) | 6.0<br>(0.8) |
| 4.0                            | 18<br>(1)              | 15.1<br>(0.7) | 3.1<br>(0.7) | 8.5<br>(0.5) |
| 5.0                            | 6.6<br>(0.5)           | 21<br>(1)     | 4.1<br>(0.3) | 7<br>(1)     |

Table IV-10 . Combined yields of related products from the chlorination of compound 7 under increasing charges of chlorine,  $x$ , (in moles of chlorine per  $C_9$  unit): a) compound 7 recovered unaltered after the reaction, b) products from ether cleavage, c) products from substitution on the aromatic rings. Yields are expressed in percent of initial  $C_9$  unit, obtained by GC analysis. Standard deviations are given in parentheses.

| Cl <sub>2</sub><br>charge<br>$x$ | unaltered<br><u>7</u> | $\beta$ -ether<br>cleavage | substitution                                                              |                                                            | Total         |
|----------------------------------|-----------------------|----------------------------|---------------------------------------------------------------------------|------------------------------------------------------------|---------------|
|                                  |                       |                            | ipso-substitution<br>(side-chain cleavage)<br><u>7-8, 7-9, 7-10, 7-11</u> | other<br><u>7-1, 7-2, 7-3, 7-4</u><br><u>7-5, 7-6, 7-7</u> |               |
| 0                                | 90.8<br>(0.3)         | -                          | -                                                                         | -                                                          | 90.8<br>(0.3) |
| 0.25                             | 26.6<br>(0.2)         | -                          | -                                                                         | 45<br>(1)                                                  | 72<br>(1)     |
| 0.5                              | 4.0<br>(0.7)          | -                          | -                                                                         | 54<br>(2)                                                  | 59<br>(2)     |
| 0.75                             | 0                     | -                          | -                                                                         | 75<br>(1)                                                  | 75<br>(1)     |
| 1.0                              | -                     | -                          | -                                                                         | 76<br>(2)                                                  | 76<br>(2)     |
| 1.5                              | -                     | -                          | 11.1<br>(0.9)                                                             | 47<br>(1)                                                  | 58<br>(1)     |
| 2.0                              | -                     | -                          | 31<br>(1)                                                                 | 28<br>(1)                                                  | 59<br>(1)     |
| 2.5                              | -                     | -                          | 40<br>(1)                                                                 | 22<br>(2)                                                  | 62<br>(2)     |
| 3.0                              | -                     | -                          | 34<br>(1)                                                                 | 15.9<br>(0.6)                                              | 40<br>(1)     |
| 4.0                              | -                     | -                          | 45<br>(1)                                                                 | 13<br>(1)                                                  | 58<br>(3)     |
| 5.0                              | -                     | -                          | 39<br>(2)                                                                 | 9<br>(1)                                                   | 48<br>(2)     |

• Identification of the reaction products

The products formed in the reaction of compounds 3 and 7 with chlorine are listed under their initial un-derivatized structures in tables IV-1 and IV-6, respectively. The complete mass spectral data of the derivatized products are given in Appendix IV. The fragmentation pattern was similar to that obtained from benzyl alkyl ethers, with the base peaks arising from the cleavage of the  $C_{\alpha}-C_{\beta}$  linkage. The 1,3-diacetylated structure of compound 7 and of its reaction products gave rise to a cyclic fragment after elimination of a neutral molecule of acetic anhydride. This corresponds to the 1,4 elimination of a  $H_2O$  molecule reported in the literature<sup>5</sup> in the mass spectrum of compound 7. In addition, after the guaiacyl beta-substituent was dichlorinated, the base peak resulted from the elimination of acetic anhydride and of the aryloxy radical (compounds 7-4 to 7-7). The determination of the structure of the substitution products from 3 and 7 was made as in the previous chapters from the nature of the molecular ion and that of the base peak.

In several instances where positional isomerism was possible, only one product was detected (3-5, 3-7, and 7-4, 7-5, 7-7), probably because the isomers were not separated. The positional isomers of mono- and dichlorinated products (3-2, 3-3 and 7-2) arising from the two equivalent positions 4 and 5 on the guaiacyl ring were nevertheless well separated.

Two products, arising in all likelihood from the cleavage of compound 3, could not be identified. They are listed under their GC retention times, with the other cleavage products in table IV-4, and their approximate yields indicated that they were very minor products even when large charges of chlorine were applied.

The recovery of the aldehydic moiety seemed incomplete. The aldehydes 3-12 and 7-11, but also the (trimethyl)silyl derivative of the corresponding enol 3-13 were detected (Tables IV-1 and IV-6). The poor yields, however, did not balance those of their chlorinated veratrole counterparts (Tables IV-4 and IV-9). It was also noteworthy that all detected aldehydic moieties were only dichlorinated, although substitution products with the beta guaiacyl substituent bearing 3 chlorine atoms were identified from the chlorination of both compounds 3 and 7. There are two possible explanations: either trichlorinated aldehydes have not been detected, or they have not been formed. The latter explanation seems more plausible, since the veratryl ring in the molecules bearing a trichlorinated guaiacyl ring can be sufficiently substituted to be deactivated towards further chlorine substitution and hence not to undergo side-chain cleavage.

The reaction products were poorly recovered when more than 1.5 mole of chlorine per mole of monomer unit was applied. The overall yields became lower and lower with the increasing chlorine charge (Tables IV-5 and IV-10), while at the same time, both cleavage and substitution reactions became more and more extensive. These poor yields may be explained by the incomplete recovery of the aldehydic moiety, and also by artefacts coming from the analyses: the error made on the yields of the substituted dimers as the degree of substitution increased becomes greater due to the greater difference in structure and retention time from the internal standards. The instrumental error also increased as the peak shape degraded, i.e. at larger retention time. Another source of error can be the derivatization procedure, during which evaporation may expel very volatile compounds.

Other side reactions may also have taken place, promoting partial degradation of the dimers to smaller, volatile products.

• Consumption of the starting compound (Tables IV-5 and IV-10).

Despite the presence of a reactive hydroxyl group on the benzylic carbon, compounds 3 and 7 were as stable in glacial acetic acid as their etherified analogues. Lower charges of chlorine were sufficient to consume all starting material: 3 and 7 had totally -or quasi-disappeared under a charge of 0.5 mole of chlorine per monomer unit (Tables IV-5 and IV-10) whereas a charge of chlorine of 1.0 was required with benzyl alkyl ethers (Tables III-3, III-7, III-11, III-17). At the low level of chlorine charge, the reaction responsible for the consumption of the starting compounds is the aromatic substitution on the veratryl ring. The early disappearance of the starting compounds thus suggests that the presence of a hydroxyl group at the alpha position increased the reactivity of the veratryl moiety towards substitution. As a consequence, unlike benzyl alkyl ethers, the starting compounds are much more reactive towards electrophilic aromatic substitution by chlorine than the monochlorinated compounds (3-1, 3-2, and 7-1 in tables IV-2, and IV-7, respectively).

• Characteristics of the products of reaction

AROMATIC SUBSTITUTION BY CHLORINE

No product of the cleavage of the beta-ether linkage was detected among the reaction products of either compound 3 or 7. This was in perfect agreement with the results obtained by Gierer and Huber<sup>3</sup> who investigated the stability of the glycerol side chain and of guaiacyl

glycerol ether bonds. Furthermore, we did not find any evidence of reactions on the alpha-carbon, such as acetylation or nucleophilic substitution. Aromatic substitution was the sole reaction observed in the chlorination of the compounds 3 and 7, and presented, with increasing charge of chlorine, the same stepwise substitution pattern on the aromatic rings as in the chlorination of benzyl alkyl ethers. Tables IV-3 and IV-8 show the yields of the chlorinated dimers 3 and 7, respectively, at each level of substitution. Tables IV-2 and IV-7 exhibit the detailed features of the substitution reaction on each starting compound. The yields of the two possible monochlorinated dimers (3-1, 3-2) and the fact that monochlorination of compound 7 only occurred on the veratryl nucleus, show clearly that the veratryl ring is again more reactive than the guaiacyl ring. In addition, the positional isomerism on the guaiacyl ring was better revealed by the similar yields of the two possible dichlorinated derivatives of both compounds (3-3 a/b, and 7-2 a/b).

Although traces of dichloroveratrole (3-9) were already detected after the reaction of 3 with 1 mole of chlorine, ipso-substitution (Tables IV-4 and IV-9) occurred in significant yields when charges higher than 1.5 moles of chlorine per monomer unit were applied. The summation of the yields of chlorinated veratroles from the chlorination of compound 3 levelled at charges greater than 3 moles of chlorine per monomer unit, at about 25% of the initial monomer units (Table IV-4). That is to say that roughly 50% of the dimeric structure 3 was cleaved via side-chain elimination, and yielded monomeric species, most of them bearing 2 to 3 chlorine atoms. In the reaction of chlorine with compound 7, a total of 30 to 35% yields of chlorinated veratroles was

formed (Table IV-9), thus accounting for 60 to 70% of the starting dimer. Meanwhile, 10 to 20% of the starting dimers of both compounds, heavily chlorinated, remained stable (Tables IV-5 and IV-10) however high the charge of chlorine applied. Unlike compound 3, side-chain elimination in compound 7 accounted for about all the degraded initial dimeric structure. Gierer and Huber investigated the reaction in glacial acetic acid of these same compounds 3 and 7 with an excess of chlorine of 4 moles per mole of monomer unit. They observed that 80% and 66%, respectively, of the initial dimeric structure was broken off with formation of dichloroveratrole. Although we found less extensive yields of chlorinated veratroles from compound 3, our results are consistent with theirs. The fact that we detected tri- and tetrachlorinated veratroles, while they reported yields of dichloroveratrole only, can be explained by our longer reaction time which permitted further chlorination of the dichloroveratrole after it was formed.

#### DISCUSSION

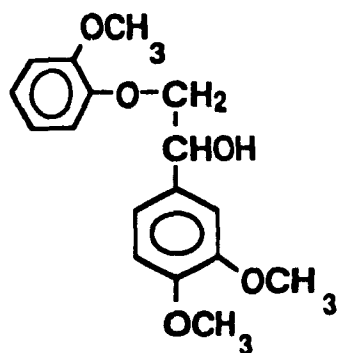
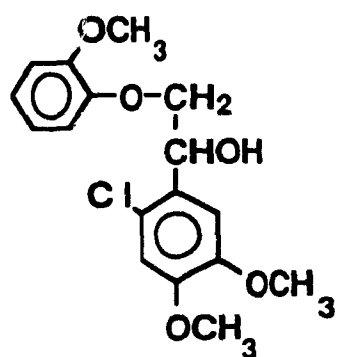
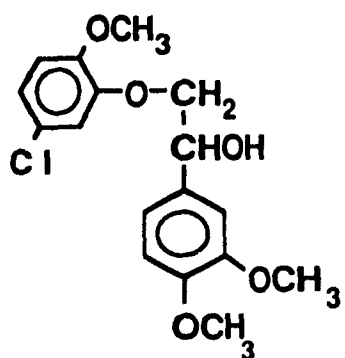
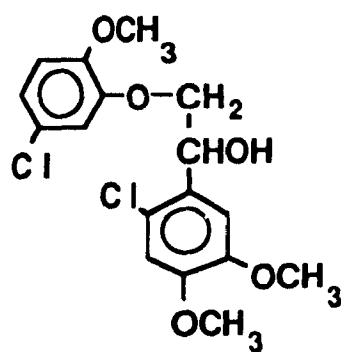
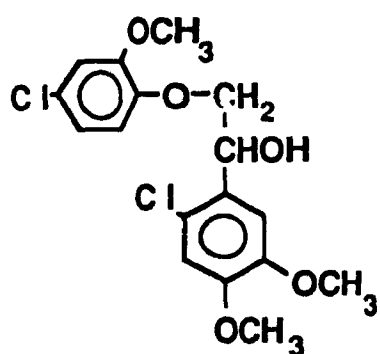
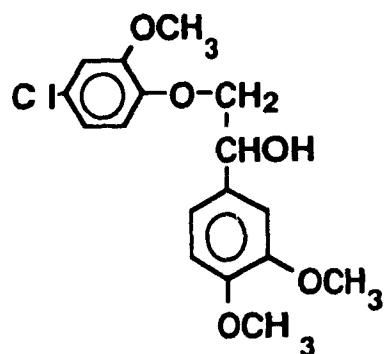
Thirty years ago, Sarkanen and Dence<sup>2</sup> reported the quasi quantitative cleavage of veratryl alcohol into dichloroveratrole after its reaction in glacial acetic acid with an excess of chlorine. A few years later, Gierer and Huber<sup>3</sup> established that the elimination of the side chain was a general reaction of the p-alkoxy and p-hydroxy benzyl alcohols, given by primary benzyl alcohols, and also by those compounds



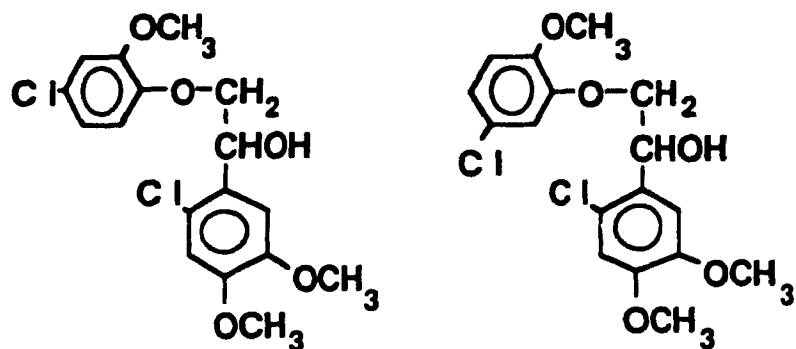
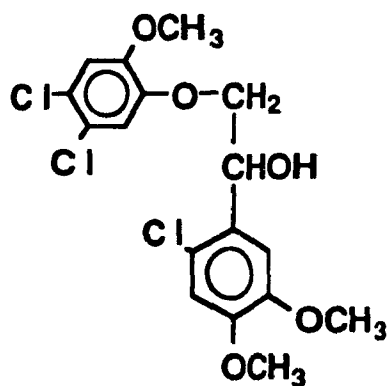
having a neighbouring oxygen-containing substituent such as an hydroxyl or an aryloxy group, with or without an hydroxyl group at the gamma position on the side chain. Under an excess of chlorine, cleavage was almost always quantitative, and dichloroveratrole was formed in high yields. They also reported the far stronger resistance to cleavage exhibited by the alpha-alkyl ethers. Our experiments at high chlorine charges were the duplication of these experiments, and our results were in good agreement.

However, our investigation at low charges of chlorine permitted the determination of the stepwise chlorination products, and of the relative reactivity of each site and ring. This led to the correction of an inexactitude in the literature. After the reaction of compound 3 dichlorinated on the positions 4 and 5 of the guaiacyl ring with an excess of chlorine, Gierer and Huber<sup>3</sup> obtained the same cleavage products, in similar yields as they had obtained from compound 3 itself. They concluded from this experiment that the 4,5-dichloroguaiacyl ether of veratrylglycol was an intermediate in the chlorination of compound 3.

However, the dichloro compound was not detected among the products formed in our experiments with low chlorine charges. Moreover, our results gave the evidence that the veratryl ring was more reactive towards aromatic substitution than the guaiacyl ring, and was thus chlorinated first, precluding the existence of the intermediate proposed by Gierer and Huber. The stepwise substitution pattern evidenced by our experiments on compound 3 is outlined in the scheme IV-4.

33-13-2 a), b)3-3 a), b)

SCHEME IV-4. Stepwise substitution sequence observed in the chlorination of 3.

3-3 a), b)3-5

SCHEME IV-4 (cont'd). Stepwise substitution sequence observed in the chlorination of 3.

The rupture of the carbon-carbon bond in compounds of the veratryl alcohol type originates from the presence of the hydroxyl group at the alpha position.

On the one hand, it activates the veratryl ring towards electrophilic substitution more than an alpha-alkoxy group does. This was demonstrated by the higher reactivity of the starting compounds **3** and **7** and their disappearance at lower charges of chlorine (Tables IV-5 and IV-10) than required by their alkyl ethers **4** and **8** (Tables III-7 and III-17). Ipso-substitution is consequently facilitated.

On the other hand, solvation of the hydroxylic proton by glacial acetic acid contributes to ease the formation of the aldehydic moiety resulting from the cleavage. This participation of solvation in the side-chain elimination process is obviously precluded when the substituent at the alpha position is an alkoxy group.

The presence of hydroxyl group at the benzylic position did not promote the elimination of the beta-aryloxy substituent. Since, as we discussed in Chapter III, beta-ether bond cleavage occurred because of steric hindrance, then an alpha-hydroxyl group, smaller than an alpha-alkoxy group, is more likely to delay the cleavage reaction.

### Conclusion

The presence of a hydroxyl group at the alpha position of the side chain of a lignin model compound causes considerable degradation of the dimeric structure by electrophilic displacement of the side chain. However, chlorination experiments with low levels of chlorine demonstrated that this reaction depends on the prior chlorination of the veratryl ring, and becomes significant only when a large excess of chlorine is applied.

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## CHAPTER V

## EXPERIMENTAL

GENERAL METHODS AND REMARKS

Melting points (uncorrected) were determined with a Fischer Johns hot-plate apparatus.  $^1\text{H}$  NMR spectra were recorded at room temperature on a Varian XL-200 FT NMR spectrometer operating at 4.75 T and with a frequency of 200.058 MHz. The solvent for all samples was  $\text{CDCl}_3$ , no internal standard being required. Mass spectrometry was performed on an HP 5980A instrument using the chemical ionization (CI) method, as well as on a Dupont 21-492B instrument using the electron impact (EI) method, and on a Kratos MS25RFA instrument equipped with a DS90 Data System. GC-MS analyses were performed on a Varian 3500 gas chromatograph equipped with a DB5 column, and coupled with a Finnigan Model 700 Ion Trap Detector mass spectrometer using the EI method. HPLC-MS analyses were performed on an Hewlett Packard 5988 A HPLC-MS instrument equipped with both thermospray and particle beam interfaces, and with a reverse phase column (length: 200mm, internal diameter: 2.1mm, packing: octodecasilane C18). When working in particle beam mode, both EI and CI with methane ( $\text{CH}_4$ ) spectra were recorded. Elemental analyses were performed by Schwarzkopf Micronalytical Laboratories (New-York).

Solvents (spectroscopic grade) and chemicals (Aldrich) were generally used as received. Solvents were dried over 4 Å molecular sieves when necessary. Thin layer chromatography was performed on small cuts of silica gel aluminium-backed plates (Merck 60F<sub>254</sub>), and preparative thick layer chromatography on glass-backed 2mm thick silica gel plates (Merck 60F<sub>254</sub>) with appropriate solvent mixtures as eluent. Column chromatography was performed on silica gel (Merck 60, 400 mesh), appropriate column sizes<sup>1</sup> and eluents.



### GAS CHROMATOGRAPHIC PROCEDURES

The gas chromatograph used throughout this research was a Hewlett Packard 5890A instrument equipped with a 30 m capillary DB5 column (internal diameter: 0.25 mm, coating: polymethyl(5% phenyl)siloxane), a split inlet, and a flame ionization detector (FID).

The usual conditions for gas chromatography were as follows:

|                            |                                            |
|----------------------------|--------------------------------------------|
| Injection port temperature | 270°C                                      |
| Detector temperature       | 280°C                                      |
| Oven temperature           | gradient depending on the compound studied |
| split ratio                | 100                                        |

In order to prepare a sample for injection, two different procedures were followed:

1) identification of the reaction products (as acetylated derivatives<sup>2</sup>): Each dried mixture was dissolved into a known volume of dry chloroform. Typically, an aliquot of sample containing 0.2 to 0.3 mmole of hydroxyl group was mixed into a Reacti-vial with 100 µl dry pyridine, 500 µl dry pyridine with acetic anhydride (250 ml/l) as acetylating agent, and 200 µl pyridine with DMAP [N,N-dimethylaminopyridine] (20 g/l) as catalyst. Each teflon-lined tightly closed vial was heated at 70°C for 10 minutes. Then the excess of acetylating reagents and solvent was carefully and slowly evaporated to dryness by allowing a gentle stream of nitrogen to sweep the surface of the mixture, and the residue was dissolved in an adequate amount of

dry chloroform. Then 0.4  $\mu$ l of the solution from each vial was directly and immediately injected into the gas chromatograph.

2) determination of the yields of the reaction products (as silylated derivatives<sup>3</sup>): Each dried mixture was dissolved in a known volume of dry chloroform. Twenty microlitres of this solution was injected into a Reacti-vial containing known amount of the appropriate internal standard(s), 30  $\mu$ l dry pyridine and 50  $\mu$  BSTFA [N-bis(trimethylsilyl)trifluoroacetamide] as silylating agent. Each teflon-lined, tightly closed vial was heated at 70°C for 10 minutes. The excess of silylating reagent and solvent was removed as described in 1), and the residue was dissolved in the adequate amount of dry chloroform. Then 0.4  $\mu$ l of the solution from each vial was directly and immediately injected into the gas chromatograph. Amounts of individual reaction products were calculated by the method of the internal standard, after calibration of the instrument.

#### Calibration procedure.

Standard mixtures containing one or several internal standards were analyzed prior any quantitative analyses, in order to

- 1) calibrate the instrument relative to the response of the internal standard(s),

- 2) determine as precisely as possible the respective relative response factors for the different compounds under study. When standards were not available, the response factor for a compound of very similar structure was taken as the best approximation.

### GENERAL CHLORINATION PROCEDURES

For each compound studied, the chlorination procedure was as follows:

A stock solution containing about 1g/l of compound in glacial acetic acid was prepared. Ten ml aliquots were pipetted and withdrawn into 100 ml round bottom flasks with magnetic stirrers; the flasks were then placed in a waterbath kept at 25°C under magnetic stirring (Lab-Line Multi-Magnestir), and allowed to reach the bath temperature. After about 30 min, the desired chlorine charge was added to each sample as a solution of chlorine gas in glacial acetic acid. Syringes of the appropriate size, fitted with a teflon needle (Hamilton) were used for the transfer of chlorine solution. The reaction was allowed to proceed 5 to 6 hours, after which the excess of chlorine - if any - was removed by bubbling nitrogen gas into the reaction mixture<sup>4</sup> for 20 min under stirring. All samples were treated in this way, even when no residual chlorine was expected. To each reaction mixture toluene was added in order to form the azeotrope (acetic acid:  $b_{760}$  , 118.1°C; toluene:  $b_{760}$  , 110.6°C; azeotrope(32%wgt acetic acid):  $b_{760}$  , 104°C) and the mixture was then evaporated to dryness under reduced pressure at low temperature (30°C). The residue was then dissolved in dry chloroform, quantitatively transferred into a volumetric flask of adequate size, and immediately used for chromatographic analyses.

For each sample the reaction was at least duplicated. For chlorination reactions aimed at the determination of yields, 20 ml of initial solution was taken.

### Preparation and titration of the chlorine solution

Freshly prepared stock solutions of similar concentration were always used.

Chlorine gas (Matheson) was allowed to bubble into glacial acetic until a strong yellow coloration appeared. Iodometric titration<sup>5</sup> was performed immediately before use.

### Alternative work-up

In order to check the adequacy of the work-up described above, another procedure was followed. After the bubbling of nitrogen, each flask was chilled and kept below the freezing temperature of glacial acetic acid (mp = 15.8°C); 10 ml of cold chloroform was added and the slurry was stirred for 10 min, then the chloroform was carefully and completely pipetted out. This operation was repeated 3 times. The respective volumes of chloroform and acetic acid were checked, and there was usually about 1 ml of acetic acid transferred together with chloroform. Therefore, the chloroform solution was washed first with slightly alkaline water, then with cold water until neutrality, and dried over magnesium sulfate. Then the solvent was distilled off under reduced pressure and low temperature (30°C). The residue was then used as described above for chromatographic measurement. Both work-up procedures provided similar results, and the first described above, easier, was used.

### SYNTHESIS OF MODEL COMPOUNDS

Unless otherwise stated all mass spectra were run on a DuPont 21-492B spectrometer by direct inlet at 70eV in electron impact mode with the ion source at 250°C.

Spectra are reported as: m/z (assignment, relative intensity).

**Veratryl alcohol ethyl ether 1 [MW = 196].**

(3,4-dimethoxyphenyl)-ethoxymethane

This and several of the following etherification procedures are adaptations of a method used for peralkylation of lignin<sup>6</sup> and cellulose<sup>7</sup>.

A solution of 30.8 mmole (5.1805 g) of veratryl alcohol [MW = 168] in 20 ml dimethylsulfoxide (DMSO) was mixed in a 100 ml round bottom flask with a four-fold excess, 125 mmole (5 g), of powdered sodium hydroxide [MW = 40], and kept for 45 min under vigorous stirring (the mixture turned from colorless to orange after 10 min). Iodoethane [MW = 156] in small excess, 38 mmole (6ml), was then added slowly, the reaction being extremely exothermal. After addition of the first ml of iodoethane, the mixture was stirred 5-10 min until the reaction started (the orange color disappeared), then the rest was added slowly. The reaction was complete after 30 min, as checked by TLC (eluent, petroleum ether: ethyl acetate (2:1); Rf starting material: 0.26; product: 0.5). The excess of iodoethane (b<sub>760</sub>, 72°C<sup>8</sup>) was evaporated under reduced pressure at 30°C; the reaction

mixture was then filtered on a sintered glass funnel in order to remove the excess of NaOH powder which was then rinsed with 10 ml pure DMSO. Water (30ml) was added to the DMSO solution, which was extracted with chloroform (50 ml, 3 times). The combined organic layers were washed twice with 100 ml distilled water. After drying over magnesium sulfate, the solvents were removed under reduced pressure, leaving a slightly yellow liquid. 5.2503 g, 26.8 mmole, 87.0%.

$^1\text{H}$  NMR:  $\delta$ (ppm) 1.22 (t, 3H,  $\text{CH}_3$  of ethyl,  $J = 8$  Hz), 3.51 (q, 2H,  $\text{CH}_2$  of ethyl,  $J$ ), 3.85, 3.87 (2s, 6H, 2  $\text{OCH}_3$ ), 4.42 (s, 2H,  $\alpha$ - $\text{CH}_2$ ), 6.82, 6.83, 6.84, 6.88 (3H, arom.H).

Anal. calcd. for  $\text{C}_{11}\text{H}_{16}\text{O}_3$ : MW 196.

Found (inlet  $30^\circ\text{C}$ ): 196 ( $\text{M}^+$ , 51.2), 167 ( $\text{M}^+ - \cdot\text{CH}_2\text{CH}_3$  i.e.  $[(\text{CH}_3\text{O})_2\text{C}_6\text{H}_3\text{CH}_2\text{O}]^+$ , 6.4), 165 (8.2), 151 ( $\text{M}^+ - \cdot\text{OCH}_2\text{CH}_3$  i.e.  $[(\text{CH}_3\text{O})_2\text{C}_6\text{H}_3\text{CH}_2]^+$ , 100), 139 (15.0), 137 ( $\text{M}^+ - \cdot\text{CH}_2\text{OCH}_2\text{CH}_3$  i.e.  $[(\text{CH}_3\text{O})_2\text{C}_6\text{H}_3]^+$ , 11.6), 121 (7.5), 107 (9.5).

**Veratryl alcohol creosyl ether 2 [MW = 288].**

(3,4-dimethoxyphenyl)-(2-methoxy-4-methylphenoxy)methane

The synthesis required two steps, the first being the preparation of the  $\alpha$ -bromo-derivative of the veratryl alcohol.

• Veratryl bromide<sup>9</sup> **2-a** [MW = 231].

To a solution of 15.3 mmole (2.57 g) of veratryl alcohol [MW = 168] in 20 ml dry chloroform ( $\text{CHCl}_3$ ) in a 100 ml round bottom

flask under continuous stirring, a three-fold excess, 49.0 mmole (7.5 ml), of bromotrimethylsilane (TMSBr) [MW = 153] was added. The reaction took place instantaneously and was complete after one minute as checked by TLC (eluent petroleum ether: ethyl acetate(2:1); Rf starting material: 0.27; product: 0.64). The excess of TMSBr was evaporated under reduced pressure at 25°C. During the evaporation, the organic solution turned from light purple to purple-blue, then to light yellow after being washed with water(30 ml, 3 times). After drying over magnesium sulfate, the solvent was removed under reduced pressure, leaving a slightly yellow oil, which crystallized readily after cooling in a dry ice-acetone mixture and subsequent addition of cold dry diethylether. The white crystals obtained were quite stable (a few days) if protected from the atmosphere by a layer of cold diethylether, and kept cool and in the dark (in a refrigerator) in a closed flask (if left in contact with the atmosphere, the crystals decomposed within a minute, into a dark purple oil.). 1.9658 g, 0.5 mmole, 56%. The unexpected<sup>9</sup> poor yield can be explained by the instability of the bromide. Moreover, a source of additional error was the multiple-step determination of the weight of the air-sensitive bromide: The bromide was dispersed in cold diethylether in a weighed round bottom flask; the solvent was removed under reduced pressure at low temperature; the bromide was then quickly redispersed in a known weight of very cold diethylether (the flask was cooled down beforehand to avoid evaporation of the added solvent), and the flask was weighed again; the weight of final product was then calculated from the total weight, the tare and the weight of added solvent.

$^1\text{H}$  NMR:  $\delta$ (ppm) 3.87, 3.89 (2s, 6H, 2 OCH<sub>3</sub>), 4.50 (s, 2H,  $\alpha$ -CH<sub>2</sub>), 6.78, 6.82, 6.9-7.0 (3H, arom.H).

Anal. calcd. for C<sub>9</sub>H<sub>11</sub>O<sub>2</sub>Br: MW 231.

Found (inlet 45°C): 230/232 (M<sup>+</sup>, 13.5/7.9), 151 (M<sup>+</sup> - Br, i.e. [(CH<sub>3</sub>O)<sub>2</sub>C<sub>6</sub>H<sub>3</sub>CH<sub>2</sub>]<sup>+</sup>, 100), 137 ([ (CH<sub>3</sub>O)<sub>2</sub>C<sub>6</sub>H<sub>3</sub>]<sup>+</sup>, 9.8), 135 (16.8).

• Veratryl alcohol creosyl ether  $2^{10}$  [MW = 288].

The procedure used to prepare compound 1 was not employed here because the benzyl bromide is extremely reactive towards nucleophiles. As a consequence, [Na·OH] ion pair present in large excess can efficiently compete with the polarized creosol, yielding a mixture of veratryl alcohol and its creosyl ether. Satisfactory yields were obtained from the procedure given in ref.<sup>10</sup>.

In a 100 ml round bottom flask, 6.8 mmole (1.5822 g) of veratryl bromide was dissolved in 40 ml of dry acetone and stirred for 10 hours at room temperature with 10.9 mmole (1.5 g) of potassium carbonate K<sub>2</sub>CO<sub>3</sub> [MW = 138], 9.0 mmole (1.5 g) of potassium iodide KI [MW = 166], and a five-fold excess, 32.5 mmole (4.5 ml), of creosol [MW = 138]. The reaction was then complete, as checked by TLC (eluent, petroleum ether: ethyl acetate (1:1); R<sub>f</sub> starting material: 0.20; product: 0.47). The work-up was done according to ref.<sup>10</sup>. The yellow oily residue crystallized readily upon cooling in a dry ice/acetone bath. White needles were obtained by recrystallization from a mixture of petroleum ether: ethyl acetate (3: 1). 1.3978 g, 4.8 mmole, 70.6%. mp = 85-86°C. (lit.<sup>11</sup>: 83-84°C, 58%).



$^1\text{H}$  NMR:  $\delta$ (ppm) 2.28 (s, 3H,  $\text{CH}_3$ ), 3.858, 3.864, 3.872 (3s, 9H, 3  $\text{OCH}_3$ ), 5.04 (s, 2H,  $\alpha\text{-CH}_2$ ), 6.6-7.0 (m, 6H, arom.H).

Anal. calcd. for  $\text{C}_{17}\text{H}_{20}\text{O}_4$ : MW 288.

Found (inlet:105°C): 288 ( $\text{M}^{+}$ , 1.2), 151 ( $\text{M}^{+} - \text{OC}_6\text{H}_3(\text{OCH}_3)(\text{CH}_3)$ , i.e.  $[(\text{CH}_3\text{O})_2\text{C}_6\text{H}_3\text{CH}_2]^+$ , 100), 137 ( $\text{M}^{+} - \text{OCH}_2\text{OC}_6\text{H}_3(\text{OCH}_3)(\text{CH}_3)$ , i.e.  $[(\text{CH}_3\text{O})_2\text{C}_6\text{H}_3]^+$ , 6.6), 135 (3.0), 123 (1.2), 108 (10.4), 107 (12.8), 91 (11.6).

### 1-(3,4-dimethoxyphenyl)-2-(2-methoxyphenoxy)ethanol **3**

[MW = 304]

•  $\omega$ -bromoacetoveratrone<sup>12</sup> **3-a** [MW = 259].

The literature method was used without any modification.

Starting material: acetovanillone [MW = 180], 55.5 mmole (10g).

Product: pink/purple crystals that crystallize easily in cold diethylether (TLC eluent petroleum ether: ethyl acetate (1:1);  $R_f$  starting material: 0.35; product: 0.42.). 10.5 g, 41.7 mmole, 75%. mp = 79.5-80.0°C (methanol). (lit.<sup>12</sup> 80-81°C, 84%; lit.<sup>13</sup> 76-78°C).

$^1\text{H}$  NMR:  $\delta$ (ppm) 3.90, 3.92 (2s, 6H, 2  $\text{OCH}_3$ ), 4.38 (s, 2H,  $\text{CH}_2\text{-Br}$ ); H arom.: 6.87 (d, 1H,  $\text{H}_{\text{meta}}$ ,  $J_{\text{meta-ortho}} = 8.39$  Hz, 7.49 (d, 1H,  $\text{H}_{\text{ortho}}$ ,  $J_{\text{ortho-ortho}} = 2.01$  Hz), 7.57 (d,d; 1H,  $\text{H}_{\text{ortho}}$ ).

Anal. calcd. for  $\text{C}_{10}\text{H}_{11}\text{O}_3\text{Br}$ : MW 259.

Found (HP 5980A spectrometer,  $\text{NH}_3$  chemical ionization ( $\text{NH}_3 - \text{CI}$ ), inlet 163°C): 276/278 ( $\text{M} + \text{NH}_4^+$ , 28.9/28.4), 259/261 ( $\text{M} + \text{H}^+$ , 99.7/100).

- 6-guaiacylacetooveratrone 3-b [MW = 302]

The procedure<sup>10</sup> for compound 2 was followed.

Starting material: 3-a [MW = 259], 10.3 mmole (2.68 g)

product: white crystals (TLC eluent, petroleum ether: ethyl acetate (2:1); Rf starting material: 0.27; product: 0.10). 2.79 g, 9.2 mmole, 72.6%. mp = 96-97°C (methanol). (lit<sup>14</sup>: 90-92°C (methanol), 76%; lit<sup>15</sup>: 93.5-94.5 (ethanol)).

<sup>1</sup>H NMR:  $\delta$ (ppm) 3.86, 3.91, 3.93 (3s, 9H, 3 OCH<sub>3</sub>), 5.28 (s, 2H, CH<sub>2</sub>); 6.81-7.68 (m, 7H, H arom.).

Anal. calcd. for C<sub>17</sub>H<sub>18</sub>O<sub>5</sub>: MW 302.

Found (HP 5980A spectrometer, NH<sub>3</sub> - CI, inlet 166°C): 320 (M + NH<sub>4</sub><sup>+</sup>, 4.6), 303 (M + H<sup>+</sup>, 100.0).

- 1-(3,4-dimethoxyphenyl)-2-(2-methoxyphenoxy)ethanol 3

The procedure described by Adler and his co-workers<sup>14</sup> for the reduction of a similar compound, modified by Chew<sup>16</sup> was used without further modification.

Starting material: 3-b [MW = 302] 6.9 mmole (2.11 g).

product: white crystals (TLC eluent, petroleum ether: ethyl acetate (2:1); Rf starting material: 0.10; product: 0.20). 1.35 g, 4.4 mmole, 64.3%. mp = 135-135.5°C (diethylether) (lit<sup>15</sup>: 129.5-131°C (ethanol); lit<sup>17</sup>: 134-135°C (acetone), 83%).

<sup>1</sup>H NMR:  $\delta$ (ppm) 3.67 (s, broad, 1H, OH), 3.87, 3.89 (2s, 9H, 3 OCH<sub>3</sub>), 5.05 (d,d; broad, 1H,  $\alpha$ -H, J $\alpha\beta$  = 8.66 Hz, J $\alpha\beta'$  = 2.71 Hz), 3.95, 4.13 (2 d,d; H $\beta$ , H $\beta'$ , J $\alpha\beta$ , J $\alpha\beta'$ , J<sub>gem</sub> = 10.02 Hz), 5.6-7.0 (m, 7H, H arom.).

**N.B.:** a) The coupling constants were determined from decoupling experiments on a sample mixed with one drop of D<sub>2</sub>O.

b) The notation "  $\beta$  " is taken for the more shielded of the two beta protons.

Anal. calcd. for C<sub>17</sub>H<sub>20</sub>O<sub>5</sub>: MW 304.

Found (GC-MS analysis was run on a sample methylated according to a literature method<sup>19</sup>; GC inlet: 230°C-270°C, 5°C/min; Rt = 5.54 min): 318 (M<sup>+</sup>, 5.8), 286 (M<sup>+</sup>-CH<sub>3</sub>OH, i.e. [(CH<sub>3</sub>O)<sub>2</sub>C<sub>6</sub>H<sub>3</sub>CH=CH(OC<sub>6</sub>H<sub>4</sub>OCH<sub>3</sub>)]<sup>+</sup>, 2.7), 181 (M<sup>+</sup> - <sup>•</sup>CH<sub>2</sub>OC<sub>6</sub>H<sub>4</sub>(OCH<sub>3</sub>), i.e. [(CH<sub>3</sub>O)<sub>2</sub>C<sub>6</sub>H<sub>3</sub>CH(OCH<sub>3</sub>)]<sup>+</sup>, 100), 165 (11.8), 151 (8.1), 123 (3.6), 121 (8.1).

Compounds **4** and **5** were prepared by etherification of the alpha-hydroxyl group of compound **3**.

**1-(3,4-dimethoxyphenyl)-1-ethoxy-2-(2-methoxyphenoxy)ethane 4**  
[MW = 332]

Two pathways were tried for the alkylation of the alpha-hydroxyl group of compound **3**: The acid-catalyzed nucleophilic substitution of compound **3** on ethanol, with p-toluene sulfonic acid (p-TsOH) as catalyst [method A]<sup>19</sup>, and the base-catalyzed\* nucleophilic substitution of iodoethane on compound **3** in the presence of NaOH powder [method B]<sup>6</sup>. Higher yields were obtained with the latter method, - about 83% versus 66% - , after a shorter reaction time -1 to 2 hours at room temperature instead of 5 to 7 days at 30-40°C.

\* N.B. : This is not true catalysis, since all the NaOH inducing the polarization of each OH bond effectively cleaved is hydrolyzed into NaI and H<sub>2</sub>O. Thus it is not regenerated as a catalyst must be.

The final product obtained from both methods crystallized easily in cold diethylether as white crystals (TLC eluent, petroleum ether: ethyl acetate (1:1); R<sub>f</sub> starting material: 0.5; product: 0.7). mp ~ 65.0-65.5°C (methanol).

Method A : The procedure described by Adler and his co-workers<sup>19</sup> for the alkylation of a similar compound was used without modification.

Starting material: **3** [MW = 304] 6.4 mmole (1.96g).

Product: 1.42g, 4.3 mmole, 66.3%.

Method B : The procedure for compound **1** was followed.

Starting material: compound **3** [MW = 304] 3.1 mmole (933mg).

Product: 852mg, 2.6 mmole, 83.6%.

<sup>1</sup>H NMR:  $\delta$ (ppm) 1.21 (t, 3H, CH<sub>3</sub> from ethyl, J = 7.0 Hz), 3.50 (q, 2H, CH<sub>2</sub> from ethyl, J), 3.84, 3.87, 3.89 (3s, 9H, 3 OCH<sub>3</sub>), 4.03 (d,d; 1H, H $\beta$ , J $\alpha\beta$  = 4.19 Hz, J<sub>gem</sub> = 10.37 Hz), 4.19 (d,d; 1H, H $\beta'$ , J $\alpha\beta$  = 7.58 Hz, J<sub>gem</sub>), 4.68 (d,d; 1H, H $\alpha$ , J $\alpha\beta$ , J $\alpha\beta'$ ), 6.80-6.95 (m, 7H, H arom.).

Anal. calcd. for C<sub>19</sub>H<sub>24</sub>O<sub>5</sub>: MW 332.

Found (GC-MS analysis; GC inlet:200°C-270°C, 20°C/min; Rt = 5.34 min): 332 (M<sup>+</sup>, 4.1), 208 (M<sup>+</sup> - HOC<sub>6</sub>H<sub>4</sub>(OCH<sub>3</sub>), 2.25), 195 (M<sup>+</sup> -

$^+\text{CH}_2\text{OC}_6\text{H}_4(\text{OCH}_3)$ , i.e.  $(\text{MeO})_2\text{C}_6\text{H}_3\text{CH}(\text{OC}_2\text{H}_5)^+$ , 100), 167  
 $((\text{MeO})_2\text{C}_6\text{H}_3\text{CH}(\text{OC}_2\text{H}_5)^+ - \text{CH}_2\text{CH}_2)$ , i.e.  $[(\text{MeO})_2\text{C}_6\text{H}_3\text{CHOH}]^+$ , 14.7), 139  
 (33.5), 124 (7.8).

**1-(3,4-dimethoxyphenyl)-1-methoxy-2-(2-methoxy-4-methylphenoxy)ethane 5 [MW = 332]**

The same synthetic scheme was followed as for compounds 3 and 4, with creosol instead of guaiacol in the substitution step on the beta carbon (compound 5-a), and methyl iodide instead of ethyl iodide for the alpha etherification (compound 5).

• **o-creosylacetoveratrone 5-a [MW = 316]**

Starting material: 3-a [MW = 259], 19.3 mmole (0.5010 g).

product: white crystals (TLC eluent, petroleum ether: ethyl acetate (1:1); Rf starting material: 0.75; product: 0.62). 0.5363 g, 16.9 mmole, 87.9%. mp = 90.5-91°C (methanol). (lit<sup>11</sup>: 88-90°C, 61%).

<sup>1</sup>H NMR:  $\delta$ (ppm) 2.27 (s, 3H, CH<sub>3</sub>), 3.85, 3.91, 3.93 (3s, 9H, 3 OCH<sub>3</sub>), 5.23 (s, 2H, CH<sub>2</sub>); 6.64-6.89, 7.57-7.68 (m, 7H, H arom.).

• **1-(3,4-dimethoxyphenyl)-2-(2-methoxy-4-methylphenoxy)ethanol 5-b [MW = 318].**

Starting material: 5-a [MW = 316] 4.67 mmole (1.4773 g).

product: white crystals (TLC eluent, petroleum ether: ethyl acetate (2:1); Rf starting material: 0.10; product: 0.05). 1.0560 g, 3.3 mmole, 71.0%. mp = 69.5-70.0°C (diethylether). (lit<sup>11</sup>: 63-68°C, 85%).

$^1\text{H}$  NMR:  $\delta$ (ppm) 2.29 (s, 3H,  $\text{CH}_3$ ), 3.70 (d, 1H, OH,  $J_{\text{OH-H}\alpha} = 2.15$  Hz), 3.82, 3.84, 3.86 (3s, 9H, 3  $\text{OCH}_3$ ), 3.92-3.97 (m, probably d of d partially overlapping with  $\text{OCH}_3$ , 1H,  $\text{H}\beta$ ,  $J_{\alpha\beta} \sim 12.8$  Hz), 4.11 (d,d; 1H,  $\text{H}\beta'$ ,  $J_{\alpha\beta'} = 3.13$  Hz,  $J_{\text{gem}} = 10.05$  Hz), 4.99 (m, 1H,  $\text{H}\alpha$ ,  $J_{\alpha\beta}, J_{\alpha\beta'}, J_{\text{H}\alpha-\text{OH}}$ ), 6.65-7.0 (m, 6H, H arom.).

Anal. calcd. for  $\text{C}_{18}\text{H}_{22}\text{O}_5$ :  $M^+$  318.

Found (GC-MS analysis was performed on a methylated sample as in the analysis of compound 3; GC inlet:  $250^\circ\text{C}$ ;  $R_t = 6.21$  min): 332 ( $M^{++}$ , 5.5), 194 ( $M^{++} - \text{HOC}_6\text{H}_3(\text{OCH}_3)(\text{CH}_3)$ , i.e.  $(\text{MeO})_2\text{C}_6\text{H}_3\text{CH}(\text{OCH}_3)\text{CH}_2]^+$ , 23.8), 181 ( $M^{++} - ^\circ\text{CH}_2\text{OC}_6\text{H}_3(\text{OCH}_3)(\text{CH}_3)$ , i.e.  $(\text{MeO})_2\text{C}_6\text{H}_3\text{CH}(\text{OCH}_3)]^+$ , 100), 165 ( $[(\text{MeO})_2\text{C}_6\text{H}_3\text{CO}]^+$ , 15.9).

• 1-(3,4-dimethoxyphenyl)-1-methoxy-2-(2-methoxy-4-methylphenoxy)ethane  
5 [MW = 332]

Starting material: 5-b [MW = 318] 0.6043 g, 1.9 mmole.

product: white crystals (TLC eluent, petroleum ether: ethyl acetate (1:1);  $R_f$  starting material: 0.39; product: 0.61). 0.4858 g, 1.5 mmole, 78.9%. mp =  $96.5-97^\circ\text{C}$  (methanol).

$^1\text{H}$  NMR:  $\delta$ (ppm) 2.28 (s, 3H,  $\text{CH}_3$ ), 3.34 (s, 3H, alpha  $\text{OCH}_3$ ), 3.82, 3.87, 3.89 (3s, 9H, 3  $\text{OCH}_3$ ), 3.98 (d,d; 1H,  $\text{H}\beta$ ,  $J_{\alpha\beta} = 3.69$  Hz,  $J_{\text{gem}} = 10.45$  Hz), 4.15 (d,d; 1H,  $\text{H}\beta'$ ,  $J_{\alpha\beta'} = 7.88$  Hz,  $J_{\text{gem}}$ ), 4.56 (d,d; 1H,  $\text{H}\alpha$ ,  $J_{\alpha\beta}, J_{\alpha\beta'}$ ), 6.66-6.93 (m, 6H, H arom.).

Anal. calcd. for  $\text{C}_{19}\text{H}_{24}\text{O}_5$ : MW 332.

Found (inlet  $220^\circ\text{C}$ ): 332 ( $M^{++}$ , 11.4), 195 ( $M^{++} - ^\circ\text{OC}_6\text{H}_3\text{CH}_3$ , 18.4), 194 ( $M^{++} - \text{HOC}_6\text{H}_3\text{CH}_3$ , 21.4), 182 (18.4), 181 ( $M^{++} - ^\circ\text{CH}_2\text{OC}_6\text{H}_3\text{CH}_3$ , 100), 166 (21.6), 165 (22.9), 164 (18.6), 151 (20.0).

1-(3,4-dimethoxyphenyl)-1-(4-methylphenoxy)-2-(2-methoxy-4-methylphenoxy)ethane 6 [MW = 408]

The synthetic pathway was the same as in the preparation of compound 2, with 1-(3,4-dimethoxyphenyl)-2-(2-methoxy-4-methylphenoxy)ethanol as starting material, and p-cresol (p-methylphenol) as alpha substituent. The last step was performed through the procedure proposed by Meshgini and Sarkanen<sup>11</sup> (except that p-cresol was taken instead of creosolate); the method used for compound 2 was inefficient, probably because of steric hindrance. A third method<sup>20</sup>, taking ethanolic sodium hydroxide as a polarizing medium was also tested, but the ethyl ether, instead of the cresyl ether was formed. The high reactivity of our substrate, and the steric hindrance around the reacting site might be responsible for polarized ethanol competing successfully with polarized cresol as a nucleophile.

• 1-(3,4-dimethoxyphenyl)-2-(2-methoxy-4-methylphenoxy)ethylbromide 6-a [MW = 381].

The same procedure as for the synthesis of compound 2-a was followed.

Starting material: 5-b [MW = 318] 3.5 mmole, 1.1191g.

product: white powder, relatively stable in contact with air (TLC eluent, petroleum ether: ethyl acetate (2:1), Rf starting material: 0.21, product: 0.61). 1.2433g, 3.3 mmole, 92.7%. mp = 88-90°C (diethylether). (lit<sup>11</sup>: 90-92°C; 77%).

In large scale experiments, the completion of the reaction was determined by TLC, and the next step was performed directly on the reaction mixture, without any work-up.

$^1\text{H}$  NMR:  $\delta$ (ppm) 2.29 (s, 3H,  $\text{CH}_3$ ), 3.78, 3.87, 3.88 (3s, 9H, 3  $\text{OCH}_3$ ), 4.47, 4.48 (2 d, 2H,  $\text{H}_\beta$ ,  $J_{\alpha\beta} = 7.02$  Hz), 5.25 (t, 1H,  $\text{H}_\alpha$ ,  $J_{\alpha\beta}$ ), 6.65-7.05 (m, 6H, H arom.).

Anal. calcd. for  $\text{C}_{18}\text{H}_{21}\text{O}_4\text{Br}$ : MW 381.

Found (inlet  $140^\circ\text{C}$ ): 380/382 ( $\text{M}^{++}$ , 0.7/0.6), 301 ( $\text{M}^{++} - \text{Br}^+$ , 15.2), 300 ( $\text{M}^{++} - \text{HBr}$ , 65.1), 285 (13.1), 271 (9.9), 240 (31.2), 225 (3.1), 205 (5.0), 165 (52.8), 164 ( $\text{M}^{++} - \text{Br}^+ - \text{OC}_6\text{H}_3(\text{OCH}_3)(\text{CH}_3)$ , i.e.  $[\text{CH}_2=\text{CHC}_6\text{H}_3(\text{OCH}_3)_2]^{++}$ , 100), 151 (36.8), 149 (56.9), 138 ( $[\text{HOC}_6\text{H}_3(\text{OCH}_3)(\text{CH}_3)]^{++}$ , 65.6), 137 ( $[\text{OC}_6\text{H}_3(\text{OCH}_3)(\text{CH}_3)]^+$ , 12.3), 121 (34.9).

•1-(3,4-dimethoxyphenyl)-1-(4-methylphenoxy)-2-(2-methoxy-4-methylphenoxy)ethane 6 [MW = 408]

Starting material: 6-a [MW = 381] 3.4 mmole, 1.3g.

product: white crystals, (TLC eluent, petroleum ether: ethyl acetate (2:1),  $R_f$  starting material: 0.25, product: 0.37). 1.14 g, 2.8 mmole, 82%. mp =  $93.5-94.0^\circ\text{C}$  (methanol).

$^1\text{H}$  NMR:  $\delta$ (ppm) 2.22, 2.28 (2s, 3H, 3H, 2  $\text{CH}_3$ ), 3.78, 3.84, 3.85 (3s, 9H, 3  $\text{OCH}_3$ ), 4.16 (d,d; 1H,  $\text{H}_\beta$ ,  $J_{\alpha\beta} = 3.95$  Hz,  $J_{\text{gem}} = 10.72$  Hz), 4.36 (d,d; 1H,  $\text{H}_\beta$ ,  $J_{\alpha\beta} = 7.70$  Hz,  $J_{\text{gem}} = 10.77$  Hz), 5.43 (d,d; 1H,  $\text{H}_\alpha$ ,  $J_{\alpha\beta} = 3.90$  Hz,  $J_{\alpha\beta} = 7.67$  Hz), 6.4-7.0 (m, 10H, H arom.).



Anal. calcd. for  $C_{25}H_{28}O_5$ : MW 408.

Found (inlet 175°C): 301 ( $M^{++} - ^\bullet OC_6H_4CH_3$ , 11.4), 164 ( $M^{++} - ^\bullet OC_6H_4CH_3 - ^\bullet OC_6H_4(OCH_3)CH_3$ , 13.2), 151 ( $((CH_3O)_2C_6H_3CH_2^+$ , 11.2).

Found (HPLC-MS, particle beam, methane chemical ionization ( $CH_4$ -CI); column temperature: 65°C; eluent, methanol (MeOH): water ( $H_2O$ ) (60: 40); flow rate 0.4ml/min,  $R_t$  = 13.7 min): 437 ( $M + C_2H_5^+$ , 1.9), 329 ( $M + C_2H_5^+ - HOC_6H_4(CH_3)$ , 2.18), 301 ( $M^{++} + H^+ - HOC_6H_4(CH_3)$ , 100), 271 ( $M^{++} + H^+ - HOC_6H_3(OCH_3)(CH_3)$ , 2.7), 163 ( $[(OCH_3)_2C_6H_3CHCH]^+$ , 27.2), 137 ( $[(OCH_3)_2C_6H_3]^+$ , 21.1).

Anal. calcd. for  $C_{25}H_{28}O_5$ : C: 73.53%; H: 7.11%;  $OCH_3$ : 22.79%.

Found (elemental analysis): C: 73.29%; H: 6.97%;  $OCH_3$ : 24.11%; 23.93% (duplicate).

**1-(3,4-dimethoxyphenyl)-2-(2-methoxyphenoxy)-1,3-propanediol**  
**7** [MW = 334].

Compound **7** was first synthesized according to the literature methods<sup>(10,12,14)</sup>, from which a mixture of diastereomers was obtained. However, the pure threo diastereomer was obtained by hydrolysing a sample of pure threo diastereomer diacetate that had been prepared by a previous researcher. Compounds **8** and **9** were prepared by etherifying compound **7** at the alpha position. Both diastereomers were again formed in unequal amount during the bromination step, and chlorination experiments were performed on the mixtures of isomers.

- 3-hydroxy-2-(2-methoxyphenoxy)propioveratrone 7-a [MW = 332.

The procedure described by Adler and his co-workers<sup>14</sup> was used without modification.

Starting material: 3-b [MW = 302] 4.1 mmole, 1.2538 g.

product: white crystals (TLC eluent, 5% methanol in chloroform; Rf starting material: 0.62, product: 0.45). 1.048 g, 3.1 mmole, 76.0%. mp = 68-70°C (methanol). (lit<sup>14</sup>: 114-116°C; 84%; lit<sup>16</sup>: 67.5-69°C, the lower melting temperature was explained by the presence of water of crystallization).

<sup>1</sup>H NMR:  $\delta$ (ppm) 3.24 (s, broad, 1H, OH), 3.85, 3.92, 3.95 (3s, 9H, OCH<sub>3</sub>), 4.10 (d, 2H, H <sub>$\gamma$</sub> , J <sub>$\gamma\beta$</sub>  = 6.06 Hz), 5.40 (t, 1H, H <sub>$\beta$</sub> , J <sub>$\gamma\beta$</sub> ), 6.80-7.07, 7.61-7.83 (m, 7H, arom).

Anal. calcd. for C<sub>18</sub>H<sub>20</sub>O<sub>6</sub>: MW 332.

Found (HP5980 A, NH<sub>3</sub> - CI, 210°C ion source, direct inlet, 178°C): 350 (M+NH<sub>4</sub><sup>+</sup>, 8.0), 333 (M+H<sup>+</sup>, 100), 315 (M+H<sup>+</sup>- H<sub>2</sub>O, 9.9), 303 (M+H<sup>+</sup>- CH<sub>2</sub>O (McLafferty rearrangement<sup>21</sup>), 12.1).

- 1-(3,4-dimethoxyphenyl)-2-(2-methoxyphenoxy)-1,3-propanediol 7 [MW = 334].

The procedure described by Adler and his co-workers<sup>14</sup>, modified by Chew<sup>16</sup>, was used.

Starting material: 7-a [MW = 332] 2.9 mmole, 0.9765 g.

product: colorless oil (2 diastereomers), (TLC eluent, dichloromethane: ethyl acetate (4:1); Rf starting material: 0.35; product: 0.24 and 0.16). 0.5521 g, 1.6 mmole, 56.2 %.

$^1\text{H}$  NMR:  $\delta$ (ppm) 2.97-3.13 (2d of d overlapping, 1H,  $\gamma$  - OH), 3.40-3.73 (m, overlapping, 2H,  $\text{H}_\gamma, \text{H}_\gamma'$ ), 3.85-3.90 (several s, 10H, 3  $\text{OCH}_3$ , and  $\alpha$ -OH), 4.0-4.2 (m, overlapping, 1H,  $\text{H}_\beta$ ), 4.95-5.0 (m overlapping, 1H,  $\text{H}_\alpha$ ), 6.78-7.14 (m, 7H, arom).

Anal. calcd. for  $\text{C}_{18}\text{H}_{22}\text{O}_6$ : MW 334.

Found (HP5980 A,  $\text{NH}_3$  - CI,  $210^\circ\text{C}$  ion source, direct inlet,  $178^\circ\text{C}$ ): 352 ( $\text{M} + \text{NH}_4^+$ , 26.1), 335 ( $\text{M} + \text{H}^+$ , 19.1), 334 ( $\text{M} + \text{NH}_4^+ - \text{H}_2\text{O}$ , 100.0), 317 ( $\text{M} + \text{H}^+ - \text{H}_2\text{O}$ , 56.4), 304 ( $\text{M} + \text{NH}_4^+ - \text{H}_2\text{O} - \text{CH}_2\text{O}$ , 2.96), 299 ( $\text{M} + \text{H}^+ - 2 \text{H}_2\text{O}$ , 43.0), 287 ( $\text{M} + \text{H}^+ - \text{H}_2\text{O} - \text{CH}_2\text{O}$ , 12.4), 210 ( $\text{M}^{++} - \text{HOC}_6\text{H}_4\text{OCH}_3$ , 24.5), 176 (8.9), 161 (3.5), 151 (10.6), 150 ( $[(\text{CH}_3\text{O})\text{C}_6\text{H}_4\text{OCH}=\text{CH}_2]^{++}$ , 10.4).

#### •• Hydrolysis of the threo -diacetate

A suspension of 3.1 mmole (477.4 mg) anhydrous barium oxide  $\text{BaO}$  [MW = 153] in 25 ml methanol  $\text{MeOH}$  was stirred vigorously for 10 min in a stoppered erlenmeyer flask, then filtered and added immediately to a suspension of 1.2 mmole (494.8 mg) of starting material in  $\text{MeOH}$  maintained at  $-5^\circ\text{C}$ . As the acetate groups hydrolyzed, the product dissolved, and the solution became clear after 5 min stirring. The reaction was complete after 20 min (TLC eluent petroleum ether: ethyl acetate (1:1);  $R_f$  diacetate: 0.5, diol: 0.19). The solvent was evaporated under reduced pressure at low temperature ( $25^\circ\text{C}$ ) and the residue was dissolved in 50 ml of chloroform. The organic phase was washed with distilled water until neutral, dried over magnesium sulfate, filtered, and the solvent was evaporated under reduced pressure ( $T = 25^\circ\text{C}$ ), yielding a slightly yellow oil. 367.4 mg, 1.1mmole, 91.6%.

Diacetate: mp = 103.0-103.5°C. (lit<sup>17</sup>: 96-97°C)

<sup>1</sup>H NMR:  $\delta$ (ppm) 2.00, 2.01 (2s, 6H, 2 CH<sub>3</sub> of acetyl groups), 3.82, 3.86 (2s, 9H, 3 OCH<sub>3</sub>), 3.99 (d,d; 1H, H<sub>γ</sub>, J βγ = 5.80 Hz, J<sub>γγ'</sub> = 11.86 Hz), 4.27 (d,d; 1H, H<sub>γ'</sub>, J βγ' = 3.93 Hz, J<sub>γγ'</sub> = 11.87 Hz), 4.62 (m, 1H, H<sub>β</sub>), 6.08 (d, 1H, H<sub>α</sub>, J<sub>αβ</sub> = 6.85 Hz).

[ lit<sup>22, 23</sup>: 4.01 (H<sub>γ'</sub>, J βγ = 5.7 Hz, J<sub>γγ'</sub> = 11.8 Hz), 4.28 (H<sub>γ</sub>, J βγ' = 4.0 Hz, J<sub>γγ'</sub> = 11.8 Hz), 6.08 (H<sub>α</sub>, J<sub>αβ</sub> = 7.0 Hz)].

Diol:

<sup>1</sup>H NMR:  $\delta$ (ppm) 2.81 (d,d; 1H, γ-OH, J<sub>γ-OH</sub> = 6.08 Hz, J<sub>γ'-OH</sub> = 7.69 Hz), 3.38-3.68 (m, 2H, H<sub>γ</sub>, H<sub>γ'</sub>, J<sub>γγ'</sub>; J βγ; J βγ'; J<sub>Hγ-OH</sub>; J<sub>Hγ'-OH</sub>), 3.73 (d, 1H, α-OH, J<sub>Hα-OH</sub> = 1.90 Hz), 3.85, 3.88 (2s, 9H, 3 OCH<sub>3</sub>), 3.97 (d,d,d; 1H, H<sub>β</sub>, J βα; J βγ; J βγ'), 4.96 (d,d; 1H, H<sub>α</sub>, J<sub>Hα-OH</sub>, J<sub>αβ</sub> = 7.94 Hz), 6.80-7.16 (m, 7H, arom.).

The coupling constants were determined for a sample mixed with one drop of D<sub>2</sub>O. J βγ = 3.3 Hz; J βγ' = 3.9 Hz; J<sub>γγ'</sub> = 12.5 Hz.

The GC-MS was performed on a re-acetylated sample<sup>2</sup>.

Anal.calcd, for C<sub>22</sub>H<sub>26</sub>O<sub>8</sub>: MW = 418.

Found ( GC-MS; GC inlet:250°C-300°C, 5°C/min; Rt = 6.17 min): 418 (M<sup>+</sup>, 56.9), 299 (M<sup>+</sup>- HOAc - <sup>18</sup>OAc, 54.7), 298 (M<sup>+</sup>- 2 HOAc, 27.0), 235 (M<sup>+</sup>- HOAc - <sup>18</sup>OC<sub>6</sub>H<sub>4</sub>OCH<sub>3</sub>, 58.4), 220 (12.4), 209 ([ (CH<sub>3</sub>O)<sub>2</sub>C<sub>6</sub>H<sub>3</sub>CH(OAc) ]<sup>+</sup>, 100), 193 (36.5), 192 (31.4), 167 (76.6), 161 (40.9), 149 (33.6), 139 (51.1), 133 (14.6), 124 (37.2), 121 (16.1).

3-(3,4-dimethoxyphenyl)-3-ethoxy-2-(2-methoxyphenoxy)propanol 8, and 3-(3,4-dimethoxyphenyl)-3-(2-methoxy-4-methylphenoxy)-2-(2-methoxyphenoxy)propanol 9 .

The reaction of TMSBr is much faster on a benzylic alcohol group (10 min) than on aliphatic primary alcohol group (300 hours)<sup>4</sup>. Both functions are present in compound 7. The NMR spectrum obtained from the product of bromination gave evidence that the alpha carbon was actually selectively brominated in the reaction of TMSBr on the diol 7, and that the mechanism of attack of the bromide ion on the alpha-carbon was characteristic of the formation of a benzylic carbocation since the pure threo isomer of 7 was transformed into a mixture of the two diastereomeric bromides. Subsequent etherification at the alpha position with ethoxy or cresolate groups yielded compounds 8 and 9 (respectively), as mixtures of diastereomers.

• 3-bromo-3-(3,4-dimethoxyphenyl)-2-(2-methoxyphenoxy)propanol 8-a [MW = 397].

Starting material: diol 7, 1 mmole (334.0 mg) [MW = 334], i.e 2 mmole OH.

product: unstable in the open air, 340.5 mg, 0.86 mmole, 86%.

<sup>1</sup>H NMR:  $\delta$ (ppm) 3.27, 3.54 (2 d,d; 2H, H<sub>γ</sub> and H<sub>γ'</sub>, threo isomer, J<sub>γβ</sub> = 3.07 Hz, J<sub>γ'β</sub> = 3.10 Hz, J<sub>γγ'</sub> = 12.34 Hz), 3.77, 3.82, 3.86, 3.87, 3.88 (5s, 18H, 2\* 3 OCH<sub>3</sub> [threo and erythro]), 3.83, 3.84 (2s, 2H, 2\* γ-OH [threo and erythro]), 4.0, 4.1 (2 d,d; 2H, H<sub>γ</sub> and H<sub>γ'</sub>, erythro isomer, J<sub>γβ</sub> = 3.10 Hz, J<sub>γ'β</sub> = 3.98 Hz, J<sub>γγ'</sub> = 12.42 Hz), 4.40 (m, 1H, H<sub>β</sub> threo isomer, J<sub>αβ</sub> = 9.03 Hz, J<sub>γβ</sub> = 3.07 Hz, J<sub>γ'β</sub> = 3.10

Hz), 4.56 (m, 1H,  $H_\beta$  erythro isomer,  $J_{\alpha\beta} = 8.82$  Hz,  $J_{\gamma\beta} = 3.10$  Hz,  $J_{\gamma'\beta} = 3.98$  Hz), 5.26 (d, 1H,  $H_\alpha$  erythro,  $J_{\alpha\beta} = 8.82$  Hz), 5.34 (d, 1H,  $H_\alpha$  threo,  $J_{\alpha\beta} = 9.03$  Hz), 6.75-7.15 (m, 2\* 7H, arom. both isomers).

N.B.: 1- The notation " $\gamma$ " is taken for the more shielded of the two gamma carbons.

2- The distinction between the signals of the threo and erythro isomers for the aliphatic protons was based on the analogy (in chemical shifts and coupling constants) between the signals given by the erythro isomer of the bromide and the diol for the protons  $\gamma$  and  $\gamma'$ . The assignment of the other sets of signals (alpha and beta protons) to threo and erythro isomers was inferred from the values observed for the coupling constants between the gamma and the beta protons.

• 3-(3,4-dimethoxyphenyl)-3-ethoxy-2-(2-methoxyphenoxy)propanol 8 [MW = 362]

The same etherification procedure as in the synthesis of compound 1 was used.

Starting material: 8-a, 1.1 mmole, 438.7 mg.

NaOH [MW = 40], 12 mmole, 0.5 g, and ethanol [MW = 46], 11 mmole, 0.5 g, were left 3 hours under stirring in 25 ml DMSO, then the bromide was added. The reaction was complete after 45 min as checked by TLC (TLC eluent, petroleum ether: ethyl acetate (2:1.5),  $R_f$  starting material: 0.11, product: 0.35. The residue after work-up was a yellow oil. 281.4 mg, 0.78 mmole, 70.7%.

The product was converted into its acetate according to a literature method<sup>2</sup>, for easier purification. The NMR spectrum was run on both the acetate and compound 8, while mass spectrometry was run on

unacetylated compound **8** only.

N.B.: As long as the 2 diastereomers were present in a 1 to 1 ratio (as in compound **8-a**), the integration of the NMR signals could be calculated for each isomer by taking the total number of protons as twice the number of protons in the compound. For compound **8**, the proportion in which the two isomers were present were not precisely known. The total number of protons in the compound was thus taken into account, and the integration considered for each signal was the sum of the integration of the signals from both isomers.

Acetate:

$^1\text{H}$  NMR:  $\delta$ (ppm) 1.15, 1.17 (2 t overlapping [threo and erythro isomers], 3H,  $\text{CH}_3$  from ethyl group,  $J = 7.00$  Hz and 7.02 Hz respectively), 1.97, 2.01 (2s, 3H,  $\text{CH}_3$  [threo and erythro isomers] from acetate group), 3.35-3.55 (2 q overlapping [threo and erythro isomers], 2H,  $\text{CH}_2$  from ethyl group), 3.74, 3.81, 3.82, 3.85, 3.87 (5s, 9H, 3  $\text{OCH}_3$  [threo and erythro isomers]), 3.96-4.60 (m, 4H,  $\text{H}_\alpha$ ,  $\text{H}_\beta$ ,  $\text{H}_\gamma$ ,  $\text{H}_{\gamma'}$  for both isomers. For threo isomer, the following values could be determined:  $J_{\beta\gamma} = 6.13$  Hz,  $J_{\beta\gamma'} = 3.56$  Hz,  $J_{\gamma\gamma'} = 11.75$  Hz;  $\delta(\text{H}_\gamma) = 4.00$  ppm,  $\delta(\text{H}_{\gamma'}) = 4.23$  ppm.), 6.78-7.08 (m, 7H, arom.).

compound **8** :

$^1\text{H}$  NMR:  $\delta$ (ppm) 1.19, 1.20 (2 t overlapping [threo and erythro isomers], 3H,  $\text{CH}_3$  from ethyl group,  $J = 7.00$  Hz and 7.02 Hz respectively), 3.38-4.22 (several multiplets overlapping with each other and with  $\text{OCH}_3$  signals, 7H,  $\text{CH}_2$  from ethyl group,  $\text{H}_\beta$ ,  $\text{H}_\gamma$ ,  $\text{H}_{\gamma'}$ , and OH, for both isomers), 3.81, 3.83, 3.85, 3.86, 3.87 (5s, 9H, 3  $\text{OCH}_3$

[threo and erythro isomers]], 4.49, 4.53 (2 d, 1H,  $H_\alpha$  for both isomers;  $J_{\alpha\beta}$  = 6.73 Hz and 7.09 Hz, respectively), 6.80-7.05 (m, 7H, arom.).

Anal. calcd. for  $C_{20}H_{26}O_6$ : MW 362.

Found (Kratos spectrometer, direct inlet 80°C): 362 ( $M^{++}$ , 6.2), 286 ( $M^{++}$  -  $CH_3CH_2OH$  -  $CH_2O$ , i.e.  $[C_6H_3(OCH_3)_2CH=CH(OC_6H_4(OCH_3))]$  $^{++}$ , 6.3), 208 ( $M^{++}$  -  $CH_3OC_6H_4OH$  -  $CH_2O$ , i.e.  $[C_6H_3(OCH_3)_2CH(OCH_2CH_3)CH]$  $^{++}$ , 4.2), 196 (35.8), 195 ( $[C_6H_3(OCH_3)_2CH(OCH_2CH_3)]^+$ , 100), 167 (34.5), 165 (16.8), 151 (30.7), 144 (9.5), 139 (41.4), 124 (18.4).

• 3-(3,4-dimethoxyphenyl)-3-(2-methoxy-4-methylphenoxy)2-(2-methoxyphenoxy)propanol 9 [MW = 454]

Etherification was performed according to the method of Meshgini and Sarkanen<sup>11</sup>, with sodium creosolate as nucleophilic species.

Starting material: 8-a [MW = 397], 0.16 mmole, 65.8 mg.

product: yellow oil (TLC eluent, petroleum ether: ethyl acetate (2:1);  $R_f$  starting material: 0.2; product: 0.35). 58.5 mg, 0.13 mmole, 77.7%.

A sample of product was acetylated, and the two isomers were separated by thick layer chromatography using the TLC eluent described above. The compounds were then deacetylated and NMR spectrum was recorded for each pure isomer.

isomer #1:  $^1H$  NMR:  $\delta$ (ppm) 2.22 (s, 3H,  $CH_3$  from creosyl group), 3.40-3.61 (m, 3H,  $H_\gamma$ ,  $H_\gamma'$ , OH), 3.81, 3.84, 3.85, 3.86 (4s, 12H, 4  $OCH_3$ ), 4.40-4.49 (m, 1H,  $H_\beta$ ), 5.35 (d, 1H,  $H_\alpha$ ,  $J_{\alpha\beta}$  = 6.68 Hz), 6.47-7.08 (m, 10H, arom.).



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isomer #2:  $^1\text{H}$  NMR:  $\delta$ (ppm) 2.24 (s, 3H,  $\text{CH}_3$  from creosyl group), 3.95-4.05 (m, 3H,  $\text{H}_\gamma$ ,  $\text{H}_\gamma'$ , OH;  $J_{\text{gem}} = 12.2$  Hz), 3.78, 3.82, 3.83, 3.86 (4s, 12H, 4  $\text{OCH}_3$ ), 4.35 (d,d,d; 1H,  $\text{H}_\beta$ ,  $J_{\alpha\beta} = 7.69$  Hz,  $J_{\beta\gamma} = 4.6$  Hz,  $J_{\beta\gamma'} = 3.9$  Hz), 5.23 (d, 1H,  $\text{H}_\alpha$ ,  $J_{\alpha\beta} = 7.66$  Hz), 6.55-7.02 (m, 10H, arom).

Anal. calcd. for  $\text{C}_{26}\text{H}_{30}\text{O}_7$ : MW 454.

Found (HPLC-MS, particle beam,  $\text{CH}_4$ -CI, column temperature:  $55^\circ\text{C}$ , eluent MeOH:  $\text{H}_2\text{O}$  (48: 52), flow rate 0.4ml/min,  $R_t = 10.37$  min): 483 ( $\text{M} + \text{C}_2\text{H}_5^+$ , 3.3), 345 ( $\text{M} + \text{C}_2\text{H}_5^+ - \text{HOC}_6\text{H}_3(\text{OCH}_3)(\text{CH}_3)$ , 1.3), 317 ( $\text{M} + \text{H}^+ - \text{HOC}_6\text{H}_3(\text{OCH}_3)(\text{CH}_3)$ , 52.3), 299 ( $\text{M} + \text{H}^+ - \text{HOC}_6\text{H}_3(\text{OCH}_3)(\text{CH}_3) - \text{H}_2\text{O}$ , 47.1), 287 ( $[(\text{CH}_3\text{O})_2\text{C}_6\text{H}_3\text{CH}(\text{OC}_6\text{H}_4\text{CH}_3)]^+$ , 63.1), 195 ( $\text{M} + \text{H}^+ - {}^*\text{OC}_6\text{H}_3(\text{OCH}_3)(\text{CH}_3) - {}^*\text{OC}_6\text{H}_4(\text{OCH}_3)$ , 32.6).

**Table V-1.**  $^1\text{H}$ -NMR chemical shifts  $\delta$  (ppm) and coupling constants  $J$  (Hz) for aliphatic protons for compounds 7, 7 diacetate, 8-a, 8, 8 acetate, and 9.

|                                | compound <u>7</u> |           | compound <u>7 diacetate</u> |       | compound <u>8-a</u> |           |
|--------------------------------|-------------------|-----------|-----------------------------|-------|---------------------|-----------|
|                                | erythro           | threo     | erythro                     | threo | erythro             | threo     |
| $J_{\alpha\beta}$              | -                 | 7.94      | -                           | 6.85  | 8.82                | 9.03      |
| $J_{\beta\gamma}$              | -                 | 3.3       | -                           | 5.80  | 3.10                | 3.07      |
| $J_{\beta\gamma'}$             | -                 | 3.9       | -                           | 3.93  | 3.95                | 3.10      |
| $J_{\gamma\gamma'}$            | -                 | 12.5      | -                           | 11.87 | 12.42               | 12.34     |
| $J_{\text{H}\gamma\text{OH}}$  | -                 | 6.08      |                             |       | -                   | -         |
| $J_{\text{H}\gamma'\text{OH}}$ | -                 | 7.69      |                             |       | -                   | -         |
| $J_{\text{H}\alpha\text{OH}}$  | -                 | 1.90      |                             |       |                     |           |
| $\delta_\alpha$                | -                 | 4.96      | -                           | 6.08  | 5.26                | 5.34      |
| $\delta_\beta$                 | -                 | 3.97      | -                           | 4.12  | 4.56                | 4.40      |
| $\delta_\gamma$                | -                 | 3.38-3.68 | -                           | 4.09  | 4.0                 | 3.27      |
| $\delta_{\gamma'}$             | -                 | 3.38-3.68 | -                           | 4.27  | 4.1                 | 3.54      |
|                                | compound <u>8</u> |           | compound <u>8 acetate</u>   |       | compound <u>9</u>   |           |
|                                | isomer #1         | isomer #2 | erythro                     | threo | isomer #1           | isomer #2 |
| $J_{\alpha\beta}$              | 6.73              | 7.09      | -                           | -     | 6.68                | 7.69      |
| $J_{\beta\gamma}$              | -                 | -         | -                           | 6.13  | -                   | 4.6       |
| $J_{\beta\gamma'}$             | -                 | -         | -                           | 3.56  | -                   | 3.9       |
| $J_{\gamma\gamma'}$            | -                 | -         | -                           | 11.75 | -                   | 12.2      |
| $J_{\text{H}\gamma\text{OH}}$  | -                 | -         |                             |       | -                   | -         |
| $J_{\text{H}\gamma'\text{OH}}$ | -                 | -         |                             |       | -                   | -         |
| $J_{\text{H}\alpha\text{OH}}$  |                   |           |                             |       |                     |           |
| $\delta_\alpha$                | 4.49              | 4.53      | 3.96-4.60                   |       | 5.35                | 5.23      |
| $\delta_\beta$                 | 3.38-4.22         |           | 3.96-4.60                   |       | 4.40-4.49           | 4.35      |
| $\delta_\gamma$                | 3.38-4.22         |           | 3.96-4.60                   | 4.00  | 3.40-3.61           | 3.95-4.05 |
| $\delta_{\gamma'}$             | 3.38-4.22         |           | 3.96-4.60                   | 4.23  | 3.40-3.61           | 3.95-4.05 |

# SYNTHESIS OF CHLORINATED REFERENCE COMPOUNDS

Authentic samples of chlorinated compounds were prepared and used to confirm the identity of several of those compounds found by GC-MS, and to determine the FID response factor for quantitative analysis.

N.B.: In all cases, the NMR signals assigned to OH disappeared upon addition of D<sub>2</sub>O to the sample, while a broad signal appeared at 4.8 ppm.

## **4,5-dichloroguaiacol<sup>24</sup> [MW = 193]**

About 0.4 mole (50 g) of sulfuryl chloride [MW = 135] was added dropwise to 0.16 mole (20 g) of guaiacol [MW = 124] over half an hour. The mixture was then left stirring for several hours, and solidified. The solid was washed with and recrystallized from petroleum ether yielding white needles. 18.3g, 0.09 mole, 58.8%. mp = 72.0-72.5°C (lit.<sup>24</sup>: 72-73°C, 51.8%).

<sup>1</sup>H NMR:  $\delta$ (ppm) 3.84 (s, 3H, OCH<sub>3</sub>), 5.68 (s, 1H, OH), 6.86, 6.97 (2s, 2 \* 1H, arom.).

Anal.calcd. for C<sub>7</sub>H<sub>6</sub>O<sub>2</sub>Cl<sub>2</sub> : MW 193

Found (GC-MS, GC inlet 200°C, Rt = 3.58 min): 192/194/196 (M<sup>+</sup>, 100/65.0/6.9), 177/179/181 (M<sup>+</sup> - <sup>•</sup>CH<sub>3</sub>, 46.1/23.8/4.9), 149/151/153 (M<sup>+</sup> - <sup>•</sup>CH<sub>3</sub> - CO, 41.2/25.1/7.7), 121/123/125 (M<sup>+</sup> - <sup>•</sup>CH<sub>3</sub> - 2\*CO, 10.2/9.2/2.5).

**4,5,6-trichloroguaiacol<sup>25a)</sup> [MW = 227.5]**

A stream of dry chlorine gas was left bubbling gently for about half an hour into a 25% solution of guaiacol [MW = 124] 0.040 mole (5 g) in glacial acetic acid (15 ml) maintained at +5°C and under vigorous stirring. The mixture turned yellow and crystallized. The white solid was filtered, washed with and recrystallized from petroleum ether. 8.1 g, 0.036 mole, 89.0%. mp = 109.5-110°C (lit<sup>25a)</sup>: 110°C).

<sup>1</sup>H NMR:  $\delta$ (ppm) 3.93 (s, 3H, OCH<sub>3</sub>), 5.87 (s, 1H, OH), 6.90 (s, 1H, arom.).

Anal.calcd. for C<sub>7</sub>H<sub>5</sub>O<sub>2</sub>Cl<sub>3</sub> : MW 227.5

Found (HP 5980A spectrometer, NH<sub>3</sub> - CI, inlet 246°C): 243/245/247/249 (M + NH<sub>4</sub><sup>+</sup>, 28.3/30.0/10.2/0.8), 226/228/230/232 (M + NH<sub>4</sub><sup>+</sup>-H<sub>2</sub>O, 93.0/100/32.8/2.2).

**tetrachloroguaiacol<sup>25</sup> [MW = 262]**

The same procedure as for the synthesis of trichloroguaiacol was followed except that the reaction mixture was maintained at 30°C. The solution turned deep red, and a precipitate formed after 15 to 20 min. White, cotton-like material recrystallized from petroleum ether. 8.5 g, 0.032 mole, 81%. mp = 121-121.5°C (lit<sup>25</sup>: 121°C).

<sup>1</sup>H NMR:  $\delta$ (ppm) 3.95 (s, 3H, OCH<sub>3</sub>), 6.01 (s, 1H, OH), 7.25 (s, 1H, arom.).

Anal.calcd. for C<sub>7</sub>H<sub>4</sub>O<sub>2</sub>Cl<sub>4</sub> : MW 262

Found (HP 5980A spectrometer,  $\text{NH}_3$  - CI, inlet  $246^\circ\text{C}$ ):  
 278/280/282/284 ( $\text{M}+\text{NH}_4^+$ , 20.6/25.3/11.5/2.9), 260/262/264/266 ( $\text{M}+\text{NH}_4^+-\text{H}_2\text{O}$ , 84.2/100/65.1/7.2).

**4,5-dichloroveratrole<sup>26</sup> [MW = 207]**

An excess, 0.35 mole (48 g), of sulfuryl chloride [MW = 138,  $d = 1.68$ ] was added slowly to 0.15 mole (21 g) of veratrole in 50 ml carbon tetrachloride at room temperature. After refluxing for 1 hr, the reaction was complete as checked by TLC. The mixture was then evaporated to dryness under reduced pressure, and the crystals that formed were washed with petroleum ether and recrystallized from methanol. 26.4 g, 0.13 mole, 83.8%. mp =  $83.0-83.5^\circ\text{C}$  (lit<sup>26</sup>:  $83.5^\circ\text{C}$ , 80%).

$^1\text{H}$  NMR:  $\delta$ (ppm) 3.78 (s, 6H,  $2 \times \text{OCH}_3$ ), 6.89 (s, 2H, arom.).

Anal. calcd. for  $\text{C}_8\text{H}_8\text{O}_2\text{Cl}_2$ : MW 207

Found (HP 5980A spectrometer,  $\text{NH}_3$  - CI, inlet  $223^\circ\text{C}$ ):  
 206/208/210 ( $\text{M}^+$ , 100/65.1/9.9), 191/193/195 ( $\text{M}^+ - \text{CH}_3$ , 22.0/13.9/2.0), 163/165/167 ( $\text{M}^+ - \text{CH}_3 - \text{CO}$ , 7.5/4.2/0.8).

Found (GC-MS, inlet  $200^\circ\text{C}$ , Rt = 2.67 min): 206/208/210 ( $\text{M}^+$ , 100/75.8/7.6), 191/193/195 ( $\text{M}^+ - \text{CH}_3$ , 70.7/45.5/8.1), 163/165/167 ( $\text{M}^+ - \text{CH}_3 - \text{CO}$ , 29.8/18.7/5.0), 128/130 ( $\text{M}^+ - \text{CH}_3 - \text{CO} - \text{Cl}$ , 79.3/22.2), 127/129 ( $\text{M}^+ - \text{CH}_3 - \text{CO} - \text{HCl}$ , 43.9/24.2).

**trichloroveratrole [MW = 241.5]**

Dimethylsulfate [MW = 126] in slight excess, 0.016 mole (2.0 g), was added under vigorous stirring to 0.011 mole (2.6 g) of 3,4,5-trichloroguaiacol [MW = 227.5] dissolved in 25 ml sodium hydroxide 1N solution. A precipitate formed rapidly after stirring for one hour. The solid was filtered, washed with distilled water, and recrystallized from methanol. 2.4 g, 0.010 mole, 90.3%. mp = 68-68.5°C (lit<sup>25</sup>: 68°C).

<sup>1</sup>H NMR:  $\delta$ (ppm) 3.85, 3.86 (2s, 6H, 2\*OCH<sub>3</sub>), 6.95 (s, 2H, arom.).

Anal.calcd. for C<sub>8</sub>H<sub>7</sub>O<sub>2</sub>Cl<sub>3</sub> : MW 241.5

Found (inlet 40°C): 240/242/244/246 (M<sup>+</sup>, 11.5/12.5/3.4/0.4), 225/227/229/231 (M<sup>+</sup> - \*CH<sub>3</sub>, 8.8/8.8/3.2/0.3).

**Tetrachloroveratrole [MW = 276]**

The same procedure as for the preparation of trichloroveratrole was followed, with tetrachloroguaiacol [MW = 262], 0.010 mole (2.6 g), instead of trichloroguaiacol. The product formed white needles upon recrystallization from methanol. 2.5 g, 0.009 mole, 90.5%. mp = 87.5-88°C (lit<sup>25</sup>: 88°C).

<sup>1</sup>H NMR:  $\delta$ (ppm) 3.47 (s, 6H, 2 OCH<sub>3</sub>).

Anal.calcd. for C<sub>8</sub>H<sub>6</sub>O<sub>2</sub>Cl<sub>4</sub> : MW 276

Found (GC-MS, inlet 80°C-270°C, 20°C/min, Rt = 7.50 min): 274/276/278 (M<sup>+</sup>, 25.8/43.5/18.6), 259/261/263 (M<sup>+</sup> - CH<sub>3</sub>, 15.3/25.1/7.5).

**5-chlorocreosol [MW = 172.5]**

(5-chloro-2-methoxy-4-methylphenol)

The same procedure as for the synthesis of 4,5-dichloroguaiacol was followed, with this time nearly equimolar amounts of creosol [MW = 136], 0.145 mole (20 g) and sulfuryl chloride [MW = 138], 0.18 mole (25 g). The mixture solidified after mixing for several hours, and was washed with and recrystallized from petroleum ether, yielding white crystals. 13.1g, 0.076 mole, 52.4%. mp = 71-72°C.

$^1\text{H}$  NMR:  $\delta$ (ppm) 2.28 (s, 3H,  $\text{CH}_3$ ), 3.85 (s, 3H,  $\text{OCH}_3$ ), 5.47 (s, 1H, OH), 6.68, 6.91 (2s, 2\*1H, arom.)

Anal. calcd. for  $\text{C}_8\text{H}_9\text{O}_2\text{Cl}$  : MW 172.5

Found (GC-MS, inlet 180°C (2min)-270°C, 15°C/min, Rt = 2.29 min): 172/173 ( $\text{M}^{++}$ , 100/30.3), 157/159 ( $\text{M}^{++}$  -  $\cdot\text{CH}_3$ , 79.8/24.5), 137 ( $\text{M}^{++}$  -  $\cdot\text{Cl}$ , 14.1), 129/131 ( $\text{M}^{++}$  -  $\cdot\text{CH}_3$  - CO, 58.4/13.5).

**1-(3,4-dimethoxyphenyl)-2-(2-methoxy-4,5-dichlorophenoxy)ethanol<sup>27</sup> 10 [MW = 373].**

The same procedure as for the preparation of compound 3 was followed, except that 4,5-dichloroguaiacol was taken instead of guaiacol.

• **10-(4,5-dichloroguaiacyl)acetoveratrone 10-a [MW = 371]**

Starting material: 3-a [MW = 259], 3.3 mmole (1.0 g).

Product: White crystals (TLC eluent, petroleum ether: ethyl acetate (1:1); Rf starting material: 0.60; product: 0.35), which formed



readily after the work-up, and recrystallized from a mixture of chloroform: methanol (1:1). 1.0 g, 2.7 mmole, 71.0%. mp = 132-132.5°C (lit<sup>27</sup>: 130-131°C, 89%).

<sup>1</sup>H NMR:  $\delta$ (ppm) 3.86, 3.92, 3.95 (3s, 9H, 3 OCH<sub>3</sub>), 5.29 (s, 2H,  $\beta$ -CH<sub>2</sub>), 6.86-6.93, 7.53-7.61 (m, 5H, arom.H).

Anal. calcd. for C<sub>17</sub>H<sub>16</sub>O<sub>5</sub>Cl<sub>2</sub>: MW 371.

Found (inlet 200°C): 370/372/374 (M<sup>+</sup>, 10.3/6.6/1.0), 255 (4.9), 192/194 ([[(OCH<sub>3</sub>)Cl<sub>2</sub>C<sub>6</sub>H<sub>2</sub>OH]<sup>+</sup>, 6.7/3.6), 180 (6.1), 171 ([CH<sub>2</sub>OC<sub>6</sub>H<sub>2</sub>(OCH<sub>3</sub>)Cl<sub>2</sub>]<sup>+</sup> - Cl<sup>+</sup>, 6.7, 166 [(CH<sub>3</sub>O)<sub>2</sub>C<sub>6</sub>H<sub>3</sub>CHO]<sup>+</sup>, 23.8), 165 (M<sup>+</sup> - <sup>1</sup>CH<sub>2</sub>OC<sub>6</sub>H<sub>2</sub>(OCH<sub>3</sub>)Cl<sub>2</sub> i.e. [(CH<sub>3</sub>O)<sub>2</sub>C<sub>6</sub>H<sub>3</sub>CO]<sup>+</sup>, 100), 151 (18.5).

• 1-(3,4-dimethoxyphenyl)-2-(2-methoxy-4,5-dichlorophenoxy)ethanol 10  
[MW = 373]

Starting material: 10-a [MW = 371] 1.3 mmole (0.4992 g).

The product crystallized readily (TLC eluent, petroleum ether: ethyl acetate (1:1); R<sub>f</sub> starting material: 0.36, product 0.28).

Recrystallization from toluene/petroleum ether gave white needles.

0.4464 g, 1.2 mmole, 88.9%. mp = 145-145.5°C (lit<sup>27</sup>: 144-145°C, 85%)

<sup>1</sup>H NMR:  $\delta$ (ppm) 3.33 (s, broad, 1H, OH), 3.82, 3.87, 3.89 (3s, 9H, 3 OCH<sub>3</sub>), 3.95, 4.07 (2 d, d, 2 \* 1H, H $\beta$ , H $\beta$ , J $\alpha\beta$  = 8.92 Hz, J $\alpha\beta$  = 3.17 Hz, J<sub>gem</sub> = 9.77 Hz), 5.06 (m, broad, 1H,  $\alpha$ -CH), 6.82-6.99 (m, 5H, arom.H).

Anal. calcd. for C<sub>17</sub>H<sub>18</sub>O<sub>5</sub>Cl<sub>2</sub>: MW 373.

Found (inlet 205°C): 372/374/376 ( $M^{+}$ , 6.4/3.8/0.8), 354/356 ( $M^{+}$  -  $H_2O$ , 1.5/1.0), 255 (6.1), 192/194 ( $[(CH_3O)Cl_2C_6H_2OH]^{+}$ , 29.1/10.7), 180 ( $M^{+}$  -  $HOC_6H_2Cl_2(OCH_3)$ , 167 ( $M^{+}$  -  $CH_2OC_6H_2(OCH_3)Cl_2$  i.e.  $[(CH_3O)_2C_6H_3CHOH]^{+}$ , 100), 165 ( $[(CH_3O)_2C_6H_3CO]^{+}$ , 35.6), 151 (48.3), 139 (52.9).

**1-(3,4-dimethoxyphenyl)-1-ethoxy-2-(2-methoxy-4,5-dichlorophenoxy)ethane 11 [MW = 401]**

The same method as for the synthesis of compound 1 was used.  
 Starting material: 10 [MW = 373], 2.9 mmole (1.0763 g).  
 Product: brown oil (TLC eluent, petroleum ether: ethyl acetate (2:1);  
 Rf starting material: 0.15, product: 0.49, by-product: 0.41). After  
 purification through chromatographic column (petroleum ether: ethyl  
 acetate (3:1)), white crystals were obtained from cold diethylether.  
 0.9303 g, 2.3 mmole, 80.4%. mp = 62.5-63°C.

$^1H$  NMR:  $\delta$ (ppm) 1.20 (t, 3H,  $CH_3$  from ethyl,  $J = 7.05$  Hz), 3.48 (q, 2H,  $CH_2$  from ethyl,  $J$ ), 3.81, 3.87, 3.89 (3s, 9H, 3  $OCH_3$ ), 3.99, 4.13 (2 d,d; 2 \* 1H,  $H\beta$ ,  $H\beta'$ ,  $J_{\alpha\beta} = 4.0$  Hz,  $J_{\alpha\beta'} = 7.6$  Hz,  $J_{gem} = 10.3$  Hz), 4.64 (d,d; 1H,  $\alpha$ -CH,  $J_{\alpha\beta}$ ,  $J_{\alpha\beta'}$ ), 6.87-6.96 (m, 5H, arom.H).

Anal. calcd. for  $C_{19}H_{22}O_5Cl_2$ : MW 401.

Found (inlet 175°C): 400/402/404 ( $M^{+}$ , 7.6/3.8/1.0), 209 ( $M^{+}$  -  $OC_6H_2(OCH_3)Cl_2$ , 18.4), 208 ( $M^{+}$  -  $HOC_6H_2(OCH_3)Cl_2$ , 19.8), 196 (23.4), 195 ( $M^{+}$  -  $CH_2OC_6H_2(OCH_3)Cl_2$  i.e.  $[(CH_3O)_2C_6H_3CHOEt]^{+}$ , 100), 166 ( $[(CH_3O)_2C_6H_3CHOEt]^{+}$  -  $Et^{+}$  i.e.  $[(CH_3O)_2C_6H_3CHO]^{+}$ , 29.8), 165 ( $[(CH_3O)_2C_6H_3CO]^{+}$ , 36.4).

1-(3,4-dimethoxyphenyl)-1-methoxy-2-(2-methoxy-4-methyl-5-chlorophenoxy)ethane 12 [MW = 366.5]

The same procedure as for 3 was followed, with 5-chlorocreosol instead of guaiacol.

• O-(5-chlorocreosyl)acetoveratrone 12-a [MW = 350.5]

Starting material: 3-a [MW = 259] , 4.2 mmole (1.1013 g).

5-chlorocreosol: 4.6 mmole (0.8 g).

Product: The reaction was complete after 10 hrs (TLC eluent, petroleum ether: ethyl acetate (1:1); Rf starting material: 0.50; product: 0.35), and yielded yellow crystals, which formed readily after the work-up, and recrystallized from a mixture of chloroform: methanol (1:1). 1.2355 g, 3.5 mmole, 82.9%. mp = 120-120.5°C.

<sup>1</sup>H NMR:  $\delta$ (ppm) 2.29 (s, 3H, CH<sub>3</sub>), 3.85, 3.93, 3.95 (3s, 9H, 3 OCH<sub>3</sub>), 5.26 (s, 2H,  $\beta$ -CH<sub>2</sub>), 6.74-6.92, 7.56-7.60 (m, 5H, arom.H).

Anal. calcd. for C<sub>18</sub>H<sub>19</sub>O<sub>5</sub>Cl: MW 350.5.

Found (inlet 200°C): 350/353 (M<sup>+</sup>, 15.0/5.7), 172/174 ([Cl(CH<sub>3</sub>)C<sub>6</sub>H<sub>2</sub>(OCH<sub>3</sub>)Cl]<sup>+</sup>, 7.8/2.8), 166 ([ (CH<sub>3</sub>O)<sub>2</sub>C<sub>6</sub>H<sub>3</sub>CHO]<sup>+</sup>, 7.4), 165 ([ (CH<sub>3</sub>O)<sub>2</sub>C<sub>6</sub>H<sub>3</sub>CO]<sup>+</sup>, 100).

• 1-(3,4-dimethoxyphenyl)-2-(2-methoxy-4-methyl-5-chlorophenoxy)ethanol 12-b [MW = 352.5]

Starting material: 12-a [MW = 350.5] 3.2 mmole (1.1145 g).

Product: The reaction was complete after 2 hrs (TLC eluent, petroleum ether: ethyl acetate (1:1); Rf starting material: 0.36, product: 0.21), and yielded white crystals. 1.0070 g, 2.8 mmole, 87.5%. mp = 134.5-135°C.

$^1\text{H}$  NMR:  $\delta$ (ppm) 2.30 (s, 3H,  $\text{CH}_3$ ), 3.69 (s, 1H, OH), 3.84, 3.87, 3.89 (3s, 9H, 3  $\text{OCH}_3$ ), 3.97, 4.12 (2 d,d; 2 \* 1H,  $\text{H}_\beta$ ,  $\text{H}_{\beta'}$ ,  $J_{\alpha\beta} = 9.2$  Hz,  $J_{\alpha\beta'} = 3.0$  Hz,  $J_{\text{gem}} = 10.0$  Hz), 5.03 (d,d; 1H,  $\alpha$ -CH,  $J_{\alpha\beta}$ ,  $J_{\alpha\beta'}$ ), 6.82-6.99 (m, 5H, arom.H).

Anal. calcd. for  $\text{C}_{18}\text{H}_{21}\text{O}_5\text{Cl}$ : MW 352.5.

Found (inlet  $230^\circ\text{C}$ ): 352/354 ( $\text{M}^+$ , 0.9/0.3), 334/336 ( $\text{M}^+ - \text{H}_2\text{O}$ , 0.2/0.1), 182 (5.2), 180 ( $\text{M}^+ - \text{HOC}_6\text{H}_2(\text{OCH}_3)(\text{CH}_3)\text{Cl}$ , 4.1), 172/174 ( $[\text{HOC}_6\text{H}_3\text{Cl}(\text{CH}_3)(\text{OCH}_3)]^+$ , 13.3/2.3), 167 ( $[(\text{CH}_3\text{O})_2\text{C}_6\text{H}_3\text{CHOH}]^+$ , 25.3), 165 ( $[(\text{CH}_3\text{O})_2\text{C}_6\text{H}_3\text{CO}]^+$ , 12.8), 157/159 (4.7/1.7), 149/151 ( $(\text{CH}_3\text{O})_2\text{C}_6\text{H}_3\text{C}^+$ , 5.9/5.2).

• 1-(3,4-dimethoxyphenyl)-1-methoxy-2-(2-methoxy-4-methyl-5-chlorophenoxy)ethane 12 [MW = 366.5]

The same method as for the synthesis of compound 1 was used.

Starting material: 12-b [MW = 352.5], 2.9 mmole (1.0502 g).

Product: white crystals (TLC eluent, petroleum ether: ethyl acetate (2:1);  $R_f$  starting material: 0.13, product: 0.39) were obtained from cold diethylether. 0.8877 g, 2.4 mmole, 81.3%. mp =  $110.5-111^\circ\text{C}$ .

$^1\text{H}$  NMR:  $\delta$ (ppm) 2.29 (s, 3H,  $\text{CH}_3$ ), 3.33 (s, 3H,  $\alpha$ -C- $\text{OCH}_3$ ), 3.80, 3.87, 3.88 (3s, 9H, 3  $\text{OCH}_3$ ), 3.96, 4.11 (2 d,d; 2 \* 1H,  $\text{H}_\beta$ ,  $\text{H}_{\beta'}$ ,  $J_{\alpha\beta} = 3.6$  Hz,  $J_{\alpha\beta'} = 7.9$  Hz,  $J_{\text{gem}} = 10.4$  Hz), 4.55 (d,d; 1H,  $\alpha$ -CH,  $J_{\alpha\beta}$ ,  $J_{\alpha\beta'}$ ), 6.68-6.95 (m, 5H, arom.H).

Anal. calcd. for  $\text{C}_{19}\text{H}_{23}\text{O}_5\text{Cl}$ : MW 366.5.

Found (inlet  $175^\circ\text{C}$ ): 366/368 ( $\text{M}^+$ , 4.0/1.8), 239 (1.2), 195 ( $\text{M}^+ - \text{OC}_6\text{H}_2(\text{CH}_3)(\text{OCH}_3)\text{Cl}$ ), 15.8), 194 ( $\text{M}^+ - \text{HOC}_6\text{H}_2(\text{CH}_3)(\text{OCH}_3)\text{Cl}$ ), 17.6), 182 (27.7), 181 ( $\text{M}^+ - \text{CH}_2\text{OC}_6\text{H}_2(\text{OCH}_3)(\text{CH}_3)\text{Cl}$ , 100), 166 ( $[(\text{CH}_3\text{O})_2\text{C}_6\text{H}_3\text{CHO}]^+$ , 22.2), 165 ( $[(\text{CH}_3\text{O})_2\text{C}_6\text{H}_3\text{CO}]^+$ , 27.5), (151 (21.3).

1-(3,4-dimethoxyphenyl)-2-(2-methoxy-tetrachlorophenoxy)ethanol 13 [MW = 442].

The same procedure as for the preparation of compound 3 was followed with tetrachloroguaiacol instead of guaiacol.

• 0-(tetrachloroguaiacyl)acetoveratrone 13-a [MW = 440]

Starting material: 3-a [MW = 259], 1.2 mmole (0.3021 g).

Tetrachloroguaiacol [MW = 262]: 1.5 mmole (0.4 g).

The reaction was complete after 2 hrs, and yielded red crystals. Recrystallization from a mixture of petroleum ether: methanol (1:1) gave a white powder. 0.2158 g, 0.5 mmole, 40.8 %. mp = 138.5-139°C.

<sup>1</sup>H NMR:  $\delta$ (ppm) 3.85, 3.89, 3.90 (3s, 9H, 3 OCH<sub>3</sub>), 5.31 (s, 2H,  $\beta$ -CH<sub>2</sub>); H arom. : 6.85 (d, 1H, H<sub>meta</sub>, J<sub>meta-ortho</sub> = 8.40 Hz, 7.50 (d, 1H, H<sub>ortho</sub>, J<sub>ortho-ortho</sub> = 2.04 Hz), 7.54 (d of d, 1H, H<sub>ortho</sub>).

Anal. calcd. for C<sub>17</sub>H<sub>14</sub>O<sub>5</sub>Cl<sub>4</sub>: MW 440

Found (inlet 225°C): 438/440/442/444/446 (M<sup>+</sup>, 2.9/3.4/1.4/0.3/0.1), 403/405/407 (M<sup>+</sup> - Cl<sup>+</sup>, 1.0/1.1/0.3), 260/262/264 ([ (CH<sub>3</sub>O)Cl<sub>4</sub>C<sub>6</sub>OH]<sup>+</sup>, 3.6/4.2/1.7), 245/247/249 ([ (CH<sub>3</sub>O)Cl<sub>4</sub>C<sub>6</sub>OH]<sup>+</sup> - <sup>+</sup>CH<sub>3</sub>, 3.8/4.5/2.1), 217/219/221 ([ (O)Cl<sub>4</sub>C<sub>6</sub>OH]<sup>+</sup> - CO, 1.7/2.1/1.0), 180 (11.5), 165 ([ (CH<sub>3</sub>O)<sub>2</sub>C<sub>6</sub>H<sub>3</sub>CO]<sup>+</sup>, 100), 151 (21.1).

• 1-(3,4-dimethoxyphenyl)-2-(2-methoxy-tetrachlorophenoxy)ethanol 13 [MW = 442]

Starting material: 13-a [MW = 440] 0.5 mmole (0.2102 g).

Product: White crystals. 0.1144 g, 0.3 mmole, 54.2%. mp = 339.5-340°C.

$^1\text{H}$  NMR:  $\delta$ (ppm) 3.51 (d, 1H, OH,  $J_{\text{H}\alpha\text{-OH}} = 2.61$  Hz), 3.87, 3.89, 3.90 (3s, 9H, 3  $\text{OCH}_3$ ), 4.02, 4.32 (2 d,d; 2 \* 1H,  $\text{H}\beta$ ,  $\text{H}\beta'$ ,  $J_{\alpha\beta} = 8.99$  Hz,  $J_{\alpha\beta'} = 2.93$  Hz,  $J_{\text{gem}} = 10.40$  Hz), 5.03 (d,d,d; 1H,  $\alpha\text{-CH}$ ,  $J_{\alpha\beta}$ ,  $J_{\alpha\beta'}$ ,  $J_{\text{H}\alpha\text{-OH}}$ ), 6.86-6.95 (m, 3H, arom.H).

Anal. calcd. for  $\text{C}_{17}\text{H}_{16}\text{O}_5\text{Cl}_4$ : MW 442.

Found (inlet  $120^\circ\text{C}$ ): 440/442/444/446 ( $\text{M}^{+\cdot}$ , 2.6/2.8/1.7/0.3), 279 (4.3), 260/262/264/266 ( $[(\text{CH}_3\text{O})\text{Cl}_4\text{C}_6\text{OH}]^{+\cdot}$ , 7.7/8.9/3.1/1.0), 245/247/249/251 ( $[(\text{CH}_3\text{O})\text{Cl}_4\text{C}_6\text{OH}]^{+\cdot} - \cdot\text{CH}_3$ , 6.9/8.3/3.4/0.9), 217/219/221/223 ( $[(\text{O})\text{Cl}_4\text{C}_6\text{OH}]^+ - \text{CO}$ , 2.9/3.9/1.5/1.2), 181 (9.0), 180 (14.3), 167 ( $[(\text{CH}_3\text{O})_2\text{C}_6\text{H}_3\text{CHOH}]^+$ , 83.1), 165 ( $[(\text{CH}_3\text{O})_2\text{C}_6\text{H}_3\text{CO}]^+$ , 14.0), 151 (81.3), 149 (74.0), 139 (56.2), 129 (41.6).

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## APPENDIX I

### INTERNAL STANDARDS

Ideally, in the method of internal standard, the material taken as the standard must have a retention time close to that of the analyte, whose response factor to the specific detector must be known.

In our work, the GC traces of the products of reaction were typically divided into two domains of retention times: the early eluting, low molecular weight products arising from the cleavage reactions, and the late eluting, higher molecular weight whole di- or trimeric structures, substituted or not. In order to approach ideal conditions of analysis, one internal standard was chosen for each of the time domains. Whenever possible, the response factor was determined on an authentic sample of the analyte; otherwise, the response factors of compounds with similar structures were determined and used as default values. Frequently, this approximation was made for highly chlorine-substituted di- or trimers. The contribution to the effective carbon number of a chlorine atom on an olefinic carbon being, according to Grob<sup>1</sup>, quite small, and positive, the error introduced should not be large. More likely to worsen the error in the determination of the yield of these highly chlorinated compounds, is their increasing retention time with the degree of substitution,

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<sup>1</sup> GROB R. L.

"Modern practice of gas chromatography". 2<sup>nd</sup> Ed., John-Wiley & Son, New York, 1985. p151.

not only because it tends to increase the distance between them and the internal standard, but also because, at such high retention times, the shapes of the peaks degrade, and thus diminish the precision of the determination of the peak area.

The compounds used as internal standards for each of the lignin model compounds studied in this work are listed below.

| compound | early eluting standard | late eluting standard |
|----------|------------------------|-----------------------|
| 1        | piperonal              | <u>4</u>              |
| 2        | piperonal              | -                     |
| 3        | piperonal              | <u>10, 13</u>         |
| 4        | piperonal              | <u>11</u>             |
| 5        | piperonal              | <u>11</u>             |
| 6        | -                      | -                     |
| 7        | piperonal              | <u>10</u>             |
| 8        | piperonal              | <u>10</u>             |
| 9        | -                      | -                     |

APPENDIX IIMASS SPECTRA OF THE PRODUCTS OF CHLORINATION AND OF  
ACIDOLYSIS OF COMPOUNDS 2, 6, AND 9

The spectra are reported as : m/z (assignment, relative intensity)

2 1-(3,4-dimethoxyphenyl)-1-(2-methoxy-4-methylphenoxy)methane.

[MW=288]:

288 ( $M^{+}$ , 10.5), 151 ( $[(OMe)_2C_6H_3CH_2]^+$ , 100), 138  
( $(CH_3O)(CH_3)C_6H_3OH^{+}$ , 14.5); and comparison with authentic sample  
of 2.

2-1 creosol. [MW=138]:

138 ( $M^{+}$ , 100), 137 ( $M^{+}-H^{+}$ , 14.4), 123 ( $M^{+}-CH_3^{+}$ , 30.6), 122  
(8.1), 95 ( $M^{+}-CH_3^{+}-CO$ , 42.3), 94 ( $M^{+}-H^{+}-CH_3^{+}-CO$ , 10.8), 77  
(26.1), 67 (61.3), 66 (24.3), 65 (18.9), 55 (31.0); and comparison  
with authentic sample of creosol.

2-2 5-chlorocreosol. [MW=172.5]:

172/174 ( $M^{+}$ , 100/26.2), 171 ( $M^{+}-H^{+}$ , 10.7), 157/159 ( $M^{+}-CH_3^{+}$ ,  
78.0/24.2), 137 ( $M^{+}-Cl^{+}$ , 9.9), 129/131 ( $M^{+}-Me^{+}-CO$ , 54.9/17.7),  
94 (12.1), 93 (14.4), 77 (11.8), 65 (67.6); and comparison with  
authentic sample of 5-chlorocreosol.

2-3 veratrylchlorocarbene. [MW=186.5]:

186/188 ( $M^{+}$ , 24.0/8.2), 171 ( $M^{+}-CH_3^{+}$ , 1.4), 151 ( $M^{+}-Cl^{+}$ , i.e.  
 $[(CH_3O)_2C_6H_3CH_2]^+$ , 100), 135 ( $M^{+}-CH_3^{+}-HCl$ , 4.0), 107 ( $M^{+}-CH_3^{+}-HCl$   
- CO, 17.0).

2-4 veratrylacetocarbene. [MW=210]:

210 ( $M^{+}$ , 49.7), 168 ( $M^{+}-CH_2CO$ , 23.8), 151 ( $M^{+}-^{\circ}OCOCH_3$ , 100),  
137 (7.3), 135 (6.8), 107 (14.5).

2-5 (6-chloroveratryl)chlorocarbene. [MW=221]:

220/222/224 ( $M^{+}$ , 18.4/12.8/2.9), 205 ( $M^{+}-CH_3^{\circ}$ , 1.2), 185/187  
( $M^{+}-Cl^{\circ}$ , 100/30), 169/171 ( $M^{+}-CH_3^{\circ}-HCl$ , 3.4/1.9), 141/143  
( $M^{+}-CH_3^{\circ}-HCl-CO$ , 16.6/6.0), 107 ( $M^{+}-CH_3^{\circ}-Cl^{\circ}-CO-Cl^{\circ}$ ,  
18.4).

2-6 (6-chloroveratryl)acetocarbene. [MW=244.5]:

244/246 ( $M^{+}$ , 51.0/15.0), 209 ( $M^{+}-Cl^{\circ}$ , 13.1), 202/204 ( $M^{+}-CH_2CO$ ,  
27.5/8.6), 185/187 ( $M^{+}-^{\circ}OCOCH_3$ , 100/43.1), 167 ( $M^{+}-CH_2CO-Cl^{\circ}$ ,  
43.4), 166 ( $M^{+}-CH_2CO-HCl$ , 11.6), 141/143 ( $M^{+}-HOCOCH_3-CO^{\circ}-CH_3^{\circ}$ ,  
18.0/7.6), 107, ( $M^{+}-HOCOCH_3-CO^{\circ}-CH_3^{\circ}-Cl^{\circ}$ , 18.1).

2-7 unknown: 288 (100), 273 (20), 257 (25), 225 (18), 150 (80),  
138 (40), 107 (20) This compound could not be identified.

2-8 unknown: 151 (100), 135 (5), 107 (12). This compound could  
not be identified.

2-9 3,5- or 5,6-dichlorocresol. [MW=207]:

206/208/210 ( $M^{+}$ , 51.5/31.9/4.9), 205 ( $M^{+}-H^+$ , 3.3), 191/193/195  
( $M^{+}-CH_3^{\circ}$ , 100/61.6/8.1), 172 ( $M^{+}+H^+-Cl^{\circ}$ , 7.2), 163/165 ( $M^{+}-CH_3^{\circ}-CO$ ,  
39.4/31.6), 157 ( $M^{+}+H^+-Cl^{\circ}-CH_3^{\circ}$ , 8.5), 128/130 ( $M^{+}-CH_3^{\circ}-CO-Cl^{\circ}$ ,  
28.6/6.5), 127/129 ( $M^{+}-CH_3^{\circ}-CO-HCl$ , 20.2/16.9),  
99/101 ( $M^{+}-CH_3^{\circ}-CO-HCl-CO$ , i.e.  $[C_5H_4Cl]^+$ , 70.0/20.2

**2-10** dichloroveratrole. [MW=207]:

206/208/210 ( $M^{+}$ , 88.8/56.5/6.1), 191/193/195 ( $M^{+}-CH_3^{\cdot}$ , 53.1/61.1/7.3), 163/165 ( $M^{+}-CH_3^{\cdot}-CO$ , 39.2/24.2), 157 ( $M^{+}+H^{+}-Cl^{\cdot}-CH_3^{\cdot}$ , 5.4), 128/130 ( $M^{+}-CH_3^{\cdot}-CO-Cl^{\cdot}$ , 60.4/25.4), 127/129 ( $M^{+}-CH_3^{\cdot}-CO-HCl$ , 55.4/40.0), 99/101 ( $[C_5H_4Cl]^+$ , 100/35.8); and comparison with authentic sample of 4,5-dichloroveratrole.

**2-11** 5,6- or 3,5-dichlorocreosol. [MW=207]:

206/208/210 ( $M^{+}$ , 94.8/51.6/6.3), 205 ( $M^{+}-H^{+}$ , 8.7), 191/193/195 ( $M^{+}-CH_3^{\cdot}$ , 100/59.5/7.5), 171/173 ( $M^{+}-Cl^{\cdot}$ , 12.2/5.5), 163/165/167 ( $M^{+}-CH_3^{\cdot}-CO$ , 40.5/35.2/5.5), 157 ( $M^{+}+H^{+}-Cl^{\cdot}-CH_3^{\cdot}$ , 6.4), 135/137 ( $M^{+}-CH_3^{\cdot}-CO-CO$ , 23.6/16.1), 128/130 ( $M^{+}-CH_3^{\cdot}-CO-Cl^{\cdot}$ , 19.2/6.5), 127/129 ( $M^{+}-CH_3^{\cdot}-CO-HCl$ , 22.0/7.1), 111 (9.1), 99/101 ( $[C_5H_4Cl]^+$ , 54.3/24.8).

**2-12** trichloroveratrole. [MW=241.5]:

240/242/244/246 ( $M^{+}$ , 33.8/35.8/11.3/5.8), 225/227/229 ( $M^{+}-CH_3^{\cdot}$ , 68.5/65.7/14.7), 197/199 ( $M^{+}-CH_3^{\cdot}-CO$ , 22.5/25.5), 191/193 ( $M^{+}+H^{+}-CH_3^{\cdot}-Cl^{\cdot}$ , 20.6/16.7), 185/187 (36.8/7.2), 172 ( $M^{+}+H^{+}-Cl^{\cdot}+H^{+}-Cl^{\cdot}$ , 35.3); and comparison with authentic sample of trichloroveratrole.

**2-13** trichlorocreosol. [MW=241.5]:

240/242/244/246 ( $M^{+}$ , 100/90/30/2), 239/241/243/245 ( $M^{+}-H^{+}$ , 30/65/38/15), 225/227/229 ( $M^{+}-CH_3^{\cdot}$ , 15/12/5), 205/207/209 ( $M^{+}-Cl^{\cdot}$ , 3/7/1.5), 162/164 ( $M^{+}-CH_3^{\cdot}-Cl^{\cdot}-CO$ , 4/8/1).

**2-14** veratryl alcohol. [MW=168]:

**TS:** 218 ( $M + NH_4^{+} + CH_3OH$ , 16.2), 186 ( $M + NH_4^{+}$ , 88.6), 168 ( $M + NH_4^{+} - H_2O$ , 13.0), 151 ( $M + H^{+} - H_2O$ , 100).

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6 1-(3,4-dimethoxyphenyl)-1-(4-methylphenoxy)-2-(2-methoxy-4-methylphenoxy)ethane. [MW = 408]

TS: 426 ( $M+NH_4^+$ , 42.6), 318 ( $M+NH_4^+ - (CH_3)C_6H_4OH$ , 42.2), 301 ( $M+H^+ - (CH_3)C_6H_4OH$ , 100), 195 (8.6), 180 ( $M+NH_4^+ - (CH_3O)(CH_3)C_6H_3OH - (CH_3)C_6H_4OH$ , 4.2), 163 ( $M+H^+ - (CH_3O)(CH_3)C_6H_3OH - (CH_3)C_6H_4OH$ , 8.5)

PB-CI: 437 ( $M+C_2H_5^+$ , 1.9), 329 ( $M+C_2H_5^+ - (CH_3)C_6H_4OH$ , 2.2), 301 ( $M+H^+ - (CH_3)C_6H_4OH$ , 100), 271 ( $M+H^+ - (CH_3O)(CH_3)C_6H_3OH$ , 2.7), 191 ( $M+C_2H_5^+ - (CH_3O)(CH_3)C_6H_3OH - (CH_3)C_6H_4OH$ , 1.0), 163 ( $M+H^+ - (CH_3O)(CH_3)C_6H_3OH - (CH_3)C_6H_4OH$ , 27.3), 137 (21.2), 109 (8.2);

PB-EI: 301 ( $M^{+*} - (CH_3)C_6H_4O^*$ , 26.4), 270 ( $M^{+*} - (CH_3)(CH_3O)C_6H_4OH$ , 0.9), 257 ( $M^{+*} - (CH_3)(CH_3O)C_6H_4OCH_2^*$ , 3.2), 241 (.9), 179 (1.2), 165 (4.4), 164 ( $M^{+*} - (CH_3)(CH_3O)C_6H_4O^* - (CH_3)C_6H_4O^*$ , 27.9), 163 (29.9), 151 ( $(CH_3O)_2C_6H_3CH_2^+$ , 7.1), 149 (8.1), 137 (100), 109 (14.6); and comparison with authentic sample of model 6.

6-1 1-(3,4-dimethoxyphenyl)-1-acetoxy-2-(2-methoxy-4-methylphenoxy)ethane. [MW = 360]

TS: 378 ( $M+NH_4^+$ , 78.8), 318 ( $M+NH_4^+ - CH_3CO_2H$ , 41.4), 301 ( $M+H^+ - CH_3CO_2H$ , 100), 195 (9.8), 180 ( $M+NH_4^+ - (CH_3O)(CH_3)C_6H_3OH - CH_3CO_2H$ , 5.4), 163 ( $M+H^+ - (CH_3O)(CH_3)C_6H_3OH - CH_3CO_2H$ , 8.5);

PB-CI: 389 ( $M+C_2H_5^+$ , 2.3), 360 (3.9), ( $M+C_2H_5^+ - CH_3CO_2H$ , 2.3), 301 ( $M+H^+ - CH_3CO_2H$ , 100), 223 ( $M+H^+ - (CH_3O)(CH_3)C_6H_3OH$ , 13.9), 165 (13.7), 163 ( $M+H^+ - (CH_3O)(CH_3)C_6H_3OH - CH_3CO_2H$ , 33.4), 151 (6.2), 137 (30.6);

PB-EI: 360 ( $M^{+*}$ , 3.9), 300 ( $M^{+*} - CH_3CO_2H$ , 4.7), 271 (1.7), 240 (2.7), 223 ( $M^{+*} - (CH_3)(CH_3O)C_6H_4O^*$ , 100), 181 (62.6), 180 (34.4),



167 (24.7), 166 (13.7), 165 (13.7), 164 ( $M^{+} - (CH_3)(CH_3O)C_6H_4O^{\cdot-} - CH_3CO_2^{\cdot-}$ , 35.2), 151 ( $(CH_3)(CH_3O)C_6H_4OCH_2^+$ , 63.8), 149 (18.2), 138 ( $(CH_3)(CH_3O)C_6H_4OH^{+}$ , 98.6), 123 (34.2).

**6-2** 1-(3,4-dimethoxyphenyl)-1-methoxy-2-(2-methoxy-4-methylphenoxy)ethane [MW = 332].

**TS:** 350 ( $M+NH_4^+$ , 100), 335 ( $M+NH_4^+ - CH_3^{\cdot}$ , 10.6), 318 ( $M+H^+ - CH_3^{\cdot}$ , 22.5), 301 ( $M+H^+ - CH_3OH$ , 62.3);

**6-3** 1-(3,4-dimethoxyphenyl)-1-acetoxy-2-(5-chloro-2-methoxy-4-methylphenoxy)ethane [MW = 394.5]

**TS:** 412/414 ( $M+NH_4^+$ , 78.0/33.8), 352/354 ( $M+NH_4^+ - CH_3CO_2H$ , 30.9/9.8), 335/337 ( $M+H^+ - CH_3CO_2H$ , 100/28.3), 197/199 (59.7/22.9), 195 (9.5), 180 ( $M+NH_4^+ - Cl(CH_3)(CH_3O)C_6H_2OH - CH_3CO_2H$ , 6.0).

**PB-Cl:** 423/425 ( $M+C_2H_5^+$ , 3.2/1.3), 394/396 (6.4/2.5), 375 (1.2), 363/365 ( $M+C_2H_5^+ - CH_3CO_2H$ , 2.2/.8), 335/337 ( $M+H^+ - CH_3CO_2H$ , 100/33.9), 307/309 (3.8/1.1), 223 ( $M+H^+ - Cl(CH_3)(CH_3O)C_6H_2OH$ , 23.2), 197/199 (12.0/27.8), 173 (12.2), 171 (17.0), 165 (11.9), 164 (21.9);

**PB-EI:** 394 ( $M^{+}$ , 3.9), 335 ( $M^{+} - CH_3CO_2^{\cdot}$ , 1.2), 270 (2.6), 223 ( $M^{+} - Cl(CH_3)(CH_3O)C_6H_2O^{\cdot}$ , 100), 181 (58.2), 180 (34.23), 172/174 ( $Cl(CH_3)(CH_3O)C_6H_2OH^{+}$ , 68.8/20.9), 167 (77.5).

**6-4** 1-(3,4-dimethoxyphenyl)-1-methoxy-2-(5-chloro-2-methoxy-4-methylphenoxy)ethane [MW = 366.5]

**TS:** 384/386 ( $M+NH_4^+$ , 100/37.1), 335/337 ( $M+H^+ - CH_3OH$ , 51.0/20.7), 197 (6.9).

**PB-Cl:** 395 ( $M+C_2H_5^+$ , 3.4), 366/368 (6.3/2.5), 335/337 ( $M+H^+ - CH_3OH$ , 100/33.0), 229 (4.8), 223 ( $M+C_2H_5^+ - Cl(CH_3)(CH_3O)C_6H_2OH$ , 8.5),

197/199 (37.1/15.9), 195 (15.3), 181 (11.5), 173/175

(Cl(CH<sub>3</sub>)(CH<sub>3</sub>O)C<sub>6</sub>H<sub>2</sub>OH+H<sup>+</sup>, 26.1/5.9), 171 (27.5), 165 (22.7), 164 (31.8),  
151 (14.3);

PB-EI: 366 (M<sup>+</sup>, 2.1), 223 (7.9), 195 (M<sup>+</sup> -  
Cl(CH<sub>3</sub>)(CH<sub>3</sub>O)C<sub>6</sub>H<sub>2</sub>O<sup>+</sup>, 5.9), 194 (M<sup>+</sup> - Cl(CH<sub>3</sub>)(CH<sub>3</sub>O)C<sub>6</sub>H<sub>2</sub>OH, 5.2), 181  
( (CH<sub>3</sub>O)<sub>2</sub>C<sub>6</sub>H<sub>3</sub>(CH)(OCH<sub>3</sub>)<sup>+</sup>, .100), 151 (18.9), 135 (3.0).

6-5 1-veratryl-2-creosylethylene. [MW=300]

TS: 318 (M + NH<sub>4</sub><sup>+</sup>, 31.7), 301 (M + H<sup>+</sup>, 100), 180 (M + NH<sub>4</sub><sup>+</sup> -  
(CH<sub>3</sub>)(CH<sub>3</sub>O)C<sub>6</sub>H<sub>3</sub>OH, 19.8), 163 (M + H<sup>+</sup> - (CH<sub>3</sub>)(CH<sub>3</sub>O)C<sub>6</sub>H<sub>3</sub>OH, 62.9).

6-7 1-(3,4-dimethoxyphenyl)-2-(2-methoxy-4-methylphenoxy)ethanol.

[MW=318]

TS: 336 (M + NH<sub>4</sub><sup>+</sup>, 100), 318 (M + NH<sub>4</sub><sup>+</sup> - H<sub>2</sub>O, 6.0), 301 (M + H<sup>+</sup>  
- H<sub>2</sub>O, 19.8).

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2 3-(3,4-dimethoxyphenyl)-3-(2-methoxy-4-methylphenoxy)-2-(2-  
methoxyphenoxy)propanol [MW = 454]

TS: 472 (M+NH<sub>4</sub><sup>+</sup>, 100), 334 (M+NH<sub>4</sub><sup>+</sup> - (CH<sub>3</sub>O)(CH<sub>3</sub>)C<sub>6</sub>H<sub>3</sub>OH, 16.1),  
317 (M+H<sup>+</sup> - (CH<sub>3</sub>O)(CH<sub>3</sub>)C<sub>6</sub>H<sub>3</sub>OH, 30.1), 299 (M+H<sup>+</sup> - (CH<sub>3</sub>O)(CH<sub>3</sub>)C<sub>6</sub>H<sub>3</sub>OH -  
H<sub>2</sub>O, 14.1), 287 (M+H<sup>+</sup> - (CH<sub>3</sub>O)(CH<sub>3</sub>)C<sub>6</sub>H<sub>3</sub>OH - CH<sub>2</sub>O, 5.7), 242 (2.0), 228  
(3.8), 225 (8.9), 210 (M+NH<sub>4</sub><sup>+</sup> - (CH<sub>3</sub>O)(CH<sub>3</sub>)C<sub>6</sub>H<sub>3</sub>OH - (CH<sub>3</sub>O)C<sub>6</sub>H<sub>4</sub>OH, 4.5);

PB-CI: 483 (M+C<sub>2</sub>H<sub>5</sub><sup>+</sup>, 3.3), 345 (M+C<sub>2</sub>H<sub>5</sub><sup>+</sup> - (CH<sub>3</sub>O)(CH<sub>3</sub>)C<sub>6</sub>H<sub>3</sub>OH,  
1.4), 327 (M+C<sub>2</sub>H<sub>5</sub><sup>+</sup> - (CH<sub>3</sub>O)(CH<sub>3</sub>)C<sub>6</sub>H<sub>3</sub>OH - H<sub>2</sub>O, 3.0), 317 (M+H<sup>+</sup> -  
(CH<sub>3</sub>O)(CH<sub>3</sub>)C<sub>6</sub>H<sub>3</sub>OH, 52.4), 299 (M+H<sup>+</sup> - (CH<sub>3</sub>O)(CH<sub>3</sub>)C<sub>6</sub>H<sub>3</sub>OH - H<sub>2</sub>O, 47.2),  
288 (12.3), 287 (M+H<sup>+</sup> - (CH<sub>3</sub>O)(CH<sub>3</sub>)C<sub>6</sub>H<sub>3</sub>OH - CH<sub>2</sub>O, 63.1), 223 (M+C<sub>2</sub>H<sub>5</sub><sup>+</sup> -  
(CH<sub>3</sub>O)(CH<sub>3</sub>)C<sub>6</sub>H<sub>3</sub>O<sup>+</sup> - (CH<sub>3</sub>O)C<sub>6</sub>H<sub>4</sub>O<sup>+</sup>, 5.0), 195 (M+H<sup>+</sup> - (CH<sub>3</sub>O)(CH<sub>3</sub>)C<sub>6</sub>H<sub>3</sub>O<sup>+</sup> -

$(\text{CH}_3\text{O})\text{C}_6\text{H}_4\text{O}^+$ , 32.7), 193 ( $\text{M}+\text{C}_2\text{H}_5^+$  -  $(\text{CH}_3\text{O})(\text{CH}_3)\text{C}_6\text{H}_3\text{O}^+$  -  $(\text{CH}_3\text{O})\text{C}_6\text{H}_4\text{O}^+$  -  $\text{CH}_2\text{O}$ , 20.7), 177 ( $\text{M}+\text{H}^+$  -  $(\text{CH}_3\text{O})(\text{CH}_3)\text{C}_6\text{H}_3\text{O}^+$  -  $(\text{CH}_3\text{O})\text{C}_6\text{H}_4\text{O}^+$  -  $\text{H}_2\text{O}$ , 41.3), 139 ( $(\text{CH}_3\text{O})(\text{CH}_3)\text{C}_6\text{H}_3\text{OH} + \text{H}^+$ , 100), 125 ( $(\text{CH}_3\text{O})\text{C}_6\text{H}_4\text{OH} + \text{H}^+$ , 62.4).

PB-EI: 330 ( $\text{M}^{++}$  -  $(\text{CH}_3\text{O})\text{C}_6\text{H}_4\text{OH}$ , 1.6), 317 ( $\text{M}^{++}$  -  $(\text{CH}_3)(\text{CH}_3\text{O})\text{C}_6\text{H}_4\text{O}^+$ , 13.2), 299 ( $\text{M}^{++}$  -  $\text{H}_2\text{O}$  -  $(\text{CH}_3)(\text{CH}_3\text{O})\text{C}_6\text{H}_4\text{O}^+$ , 13.9), 287 (24.1), 286 ( $\text{M}^{++}$  -  $\text{CH}_2\text{O}$  -  $(\text{CH}_3)(\text{CH}_3\text{O})\text{C}_6\text{H}_4\text{OH}$ , 30.9), 271 (7.9), 257 (9.1), 226 (11.1), 194 (55.5), 193 (37.9), 176 (28.8), 166 (12.6), 165 (28.1), 164 (28.5), 163 (22.4), 162 (12.3), 161 (12.3), 151 ( $(\text{CH}_3\text{O})_2\text{C}_6\text{H}_3\text{CH}_2^+$ , 100), 138 ( $(\text{CH}_3)(\text{CH}_3\text{O})\text{C}_6\text{H}_4\text{OH}^{++}$ , 69.5), 123 ( $(\text{CH}_3\text{O})\text{C}_6\text{H}_4\text{O}^+$ , 62.5), 109 (39.9); and comparison with authentic sample of **2**.

**9-1** 1-(3,4-dimethoxyphenyl)-2-(2-methoxyphenoxy)-1,3-propanediol  
[MW = 334]

TS: 352 ( $\text{M}+\text{NH}_4^+$ , 100), 334 ( $\text{M}+\text{NH}_4^+$  -  $\text{H}_2\text{O}$ , 19.4), 317 ( $\text{M}+\text{H}^+$  -  $\text{H}_2\text{O}$ , 40.4), 299 ( $\text{M}+\text{H}^+$  -  $2\text{H}_2\text{O}$ , 12.4), 287 (8.9), 225 (9.6), 193 (4.1), 161 (4.2).

**9-2** unknown TS: 389 (3.9), 299 (6.8), 223 (2.3), 181 (100)

**9-3** 3-(3,4-dimethoxyphenyl)-3-acetoxy-2-(2-methoxyphenoxy)propanol  
[MW = 376]

TS: 394 ( $\text{M}+\text{NH}_4^+$ , 100), 359 ( $\text{M}+\text{H}^+$  -  $\text{H}_2\text{O}$ , 1.4), 334 ( $\text{M}+\text{NH}_4^+$  -  $\text{CH}_3\text{CO}_2\text{H}$ , 12.7), 317 ( $\text{M}+\text{H}^+$  -  $\text{CH}_3\text{CO}_2\text{H}$ , 11.8), 299 ( $\text{M}+\text{H}^+$  -  $\text{H}_2\text{O}$  -  $\text{CH}_3\text{CO}_2\text{H}$ , 5.1), 225 (4.5), 210 ( $\text{M}+\text{NH}_4^+$  -  $\text{CH}_3\text{CO}_2\text{H}$  -  $(\text{CH}_3\text{O})\text{C}_6\text{H}_4\text{OH}$ , 2.2).

PB-CI: 405 ( $\text{M}+\text{C}_2\text{H}_5^+$ , 3.2), 376 (3.2), 359 ( $\text{M}+\text{H}^+$  -  $\text{H}_2\text{O}$ , 6.8), 339 (1.6), 327 ( $\text{M}+\text{C}_2\text{H}_5^+$  -  $\text{H}_2\text{O}$  -  $\text{CH}_3\text{CO}_2\text{H}$ , 4.3), 317 ( $\text{M}+\text{H}^+$  -  $\text{CH}_3\text{CO}_2\text{H}$ , 13.2), 299 ( $\text{M}+\text{H}^+$  -  $\text{H}_2\text{O}$  -  $\text{CH}_3\text{CO}_2\text{H}$ , 100), 287 ( $\text{M}+\text{H}^+$  -  $\text{CH}_2\text{O}$  -  $\text{CH}_3\text{CO}_2\text{H}$ ,

20.5), 236 ( $M+H^+ - H_2O - (CH_3O)C_6H_4O^+$ , 5.3)

PB-EI: 376 ( $M^{+}$ , 4.4), 316 ( $M^{+} - CH_3CO_2H$ , .6), 286 ( $M^{+} - CH_2O - CH_3CO_2H$ , 5.3), 210 (10.9), 181 (26.8), 167 (69.9), 150 ( $(CH_3O)_2C_6H_3CH^+$ , 100), 124 ( $(CH_3O)C_6H_4OH^+$ , 27.5), 109 (25.9).

9-4 3-(3,4-dimethoxyphenyl)-3-methoxy-2-(2-methoxyphenoxy)propanol  
[MW = 348]

TS: 366 ( $M+NH_4^+$ , 100), 334 ( $M+NH_4^+ - CH_3OH$ , 54.8), 317 ( $M+H^+ - CH_3OH$ , 53.9), 299 ( $M+H^+ - H_2O - CH_3OH$ , 16.7), 225 (36.6), 210 ( $M+NH_4^+ - CH_3OH - (CH_3O)C_6H_4OH$ , 6.9).

9-5 3-(3,4-dimethoxyphenyl)-3-(5-chloro-2-methoxy-4-methylphenoxy)-2-(2-methoxyphenoxy)propanol [MW = 488]

TS: 506/508 ( $M+NH_4^+$ , 100/24.9), 458 (4.6), 334 ( $M+NH_4^+ - Cl(CH_3O)(CH_3)C_6H_2OH$ , 53.6), 317 ( $M+H^+ - Cl(CH_3O)(CH_3)C_6H_2OH$ , 79.7), 299 ( $M+H^+ - H_2O - Cl(CH_3O)(CH_3)C_6H_2OH$ , 38.5), 287 ( $M+H^+ - CH_2O - Cl(CH_3O)(CH_3)C_6H_2OH$ , 19.9), 225 (18.3), 210 ( $M+NH_4^+ - Cl(CH_3O)(CH_3)C_6H_2OH - (CH_3O)C_6H_4OH$ , 8.8).

PB-Cl: 317 ( $M+H^+ - Cl(CH_3O)(CH_3)C_6H_3OH$ , 24.1), 299 ( $M+H^+ - Cl(CH_3O)(CH_3)C_6H_3OH - H_2O$ , 27.0), 287 ( $M+H^+ - Cl(CH_3O)(CH_3)C_6H_3OH - CH_2O$ , 35.2), 223 ( $M+C_2H_5^+ - Cl(CH_3O)(CH_3)C_6H_3O^+ - (CH_3O)C_6H_4O^+$ , 5.9), 195 (38.9), 177 (15.2), 173/175 ( $Cl(CH_3O)(CH_3)C_6H_3OH + H^+$ , 100/31.9), 151 (17.4), 125 ( $(CH_3O)C_6H_4OH + H^+$ , 79.1).

PB-EI: 317 ( $M^{+} - Cl(CH_3)(CH_3O)C_6H_4O^+$ , 15.3), 299 ( $M^{+} - H_2O - Cl(CH_3)(CH_3O)C_6H_4O^+$ , 16.6), 287 ( $M^{+} - CH_2O - Cl(CH_3)(CH_3O)C_6H_4O^+$ , 21.0), 286 ( $M^{+} - CH_2O - Cl(CH_3)(CH_3O)C_6H_4OH$ , 28.2), 257 (8.0), 226 (10.3), 194 (59.2), 172/174 ( $Cl(CH_3)(CH_3O)C_6H_4OH^+$ , 43.2/13.7), 157 (52.7), 151 ( $(CH_3O)_2C_6H_3CH_2^+$ , 100), 123 ( $(CH_3O)C_6H_4O^+$ , 21.2), 109 (26.9).

APPENDIX III

MASS SPECTRA OF THE PRODUCTS OF CHLORINATION OF  
COMPOUNDS 1, 4, 5, AND 8

The spectra are reported as : m/z (assignment, relative intensity).

- 1 (3,4 dimethoxyphenyl)-ethoxymethane. [MW=196]:  
 196 ( $M^{+}$ , 71.1), 181 ( $M^{+}-CH_3$ , 1.2), 165 (6.3), 151 ( $M^{+}-OCH_2CH_3$ ,  
 i.e.  $[(OMe)_2C_6H_3CH_2]^+$ , 100), 139 (9.4), 137 ( $M^{+}-CH_2OCH_2CH_3$ , i.e.  
 $(CH_3O)_2C_6H_3^+$ , 9.1), 121 (6.5), 107 (9.3); and comparison with  
 authentic sample of compound 1.
- 1-1 veratrylchloride. [MW=186.5]:  
 186/188 ( $M^{+}$ , 11.2/5.3), 151 ( $M^{+}-Cl^+$ , i.e.  $[(OMe)_2C_6H_3CH_2]^+$ , 100),  
 135 ( $M^{+}-CH_3^+-HCl$ , 6.9), 107 ( $M^{+}-CH_3^+-HCl-CO$ , 29.3).
- 1-2 veratrylacetate. [MW=210]:  
 210 ( $M^{+}$ , 55.3), 168 ( $M^{+}-CH_2CO$ , 21.7), 151 ( $M^{+}-OCOCH_3$ , 100),  
 139 (6.1), 137 ( $M^{+}-CH_2OCOCH_3$ , i.e.  $[(OMe)_2C_6H_3CH_2]^+$ , 8.6), 135  
 (10.3), 107 (27.0).
- 1-3 (6-chloro-3,4 dimethoxyphenyl)-ethoxymethane. [MW=230.5]:  
 230/232 ( $M^{+}$ , 72.9/22.3), 195 ( $M^{+}-Cl^+$ , 20.5), 185/187 ( $M^{+}-OCH_2CH_3$ ,  
 i.e.  $[(Cl)(CH_3O)_2C_6H_3CH_2]^+$ , 100/34.9), 167 (2.5), 151 ( $M^{+}-Cl^+-$   
 $OCH_2CH_3$ , 17.1), 139 (13.3), 107 (8.2).
- 1-4 (2 or 5-chloro-3,4 dimethoxyphenyl)-ethoxymethane: [MW=230.5]:  
 230/232 ( $M^{+}$ , 35.5/12.1), 201 (6.5), 195 ( $M^{+}-Cl^+$ , 35.5), 185/187  
 $(M^{+}-OCH_2CH_3$ , i.e.  $[(Cl)(CH_3O)_2C_6H_3CH_2]^+$ , 100/29.9), 167 (9.7), 151  
 $(M^{+}-Cl^+-OCH_2CH_3$ , 41.2), 138 (24.2), 129 (7.3), 107 (39.5).

1-5 4,5-dichloroveratrole. [MW=207]:

206/208/210 ( $M^{+}$ , 100/65.4/8.6), 191/193/195 ( $M^{+}-CH_3^{\cdot}$ , 18.5/8.6/2.3), 163/165/167 ( $M^{+}-CH_3^{\cdot}-CO$ , 8.4/5.2/1.2), 128 ( $M^{+}-CH_3^{\cdot}-CO-Cl^{\cdot}$ , 7.6); and comparison with authentic sample of 4,5-dichloroveratrole.

1-6 (5 or 2, 6-dichloro-3,4 dimethoxyphenyl)-ethoxymethane. [MW=265]:

264/266 ( $M^{+}$ , 33.3/19.4), 229/231 ( $M^{+}-Cl^{\cdot}$ , 12.4/9.3), 219/221 ( $M^{+}-^{\cdot}OCH_2CH_3$ , 100/65.9), 205 ( $M^{+}-^{\cdot}CH_2OC_2H_5$ , 5.4), 201 (8.5), 185 ( $M^{+}-CH_3CHO-^{\cdot}Cl$ , 34.9), 173 (11.6), 141 (31.0), 138 (16.3), 133 (11.6).

1-7 (2 or 5, 6-dichloro-3,4 dimethoxyphenyl)-ethoxymethane. [MW=265]:

264/266/268 ( $M^{+}$ , 81.7/54.9/11.3), 229/231 ( $M^{+}-Cl^{\cdot}$ , 36.6/14.1), 219/221/223 ( $M^{+}-^{\cdot}OCH_2CH_3$ , 100/53.5/9.9), 205 ( $M^{+}-^{\cdot}CH_2OC_2H_5$ , 14.1), 201 (45.1), 185/187 ( $M^{+}-CH_3CHO-^{\cdot}Cl$ , 64.8/14.1), 173 (15.5), 141 (22.5), 138 (26.8), 133 (21.2).

1-8 (2, 5-dichloro-3,4 dimethoxyphenyl)-ethoxymethane. [MW=265]:

264/266 ( $M^{+}$ , 21.7/21.7), 229 ( $M^{+}-Cl^{\cdot}$ , 27.7), 219/221 ( $M^{+}-^{\cdot}OCH_2CH_3$ , 57.8/43.4), 201 (18.1), 185/187 ( $M^{+}-CH_3CHO-^{\cdot}Cl$ , 100/30.2), 173 (16.9), 141 (21.7), 138 (13.3).

1-9 (2,5,6-trichloro-3,4 dimethoxyphenyl)-ethoxymethane. [MW=299.5]:

298/300 ( $M^{+}$ , 50.0/20.4), 263/265 ( $M^{+}-Cl^{\cdot}$ , 18.6/11.1), 253/255/257 ( $M^{+}-^{\cdot}OCH_2CH_3$ , 100/93.2/27.2), 239 ( $M^{+}-^{\cdot}CH_2OC_2H_5$ , 10.2), 235 (16.1), 219/221 ( $M^{+}-CH_3CHO-^{\cdot}Cl$ , 67.8/31.4).

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4 1-(3,4 dimethoxyphenyl)-1-ethoxy-2-(2-methoxyphenoxy)ethane.

[MW=332]:

332 ( $M^{+}$ , 4.1), 292 (0.9), 229 (1.2), 208 ( $M^{+}-(CH_3O)C_6H_4OH$ , 2.2),

195 ( $M^{+} - ^\bullet CH_2OC_6H_4(CH_3O)$ , i.e.  $[(OMe)_2C_6H_3CH(OC_2H_5)]^+$ , 100), 167 ( $M^{+} - ^\bullet CH_2OC_6H_4(CH_3O) - C_2H_4$ , i.e.  $[(OMe)_2C_6H_3CH(OH)]^+$ , 14.7), 139 ( $[(OMe)_2C_6H_3CH(OH)]^+ - CO$ , 33.5), 124 ( $(OMe)C_6H_4OH^{+}$ , 7.8); and comparison with authentic sample of compound 4.

**4-1** 1-(6-chloro-3,4 dimethoxyphenyl)-1-ethoxy-2-(2-methoxyphenoxy)ethane. [MW=366.5]:

366/368 ( $M^{+}$ , 5.9/1.9), 315 (1.9), 281 (0.9), 242 ( $M^{+} - (CH_3O)C_6H_4OH$ , 15.6), 229/231 ( $M^{+} - ^\bullet CH_2OC_6H_4(CH_3O)$ , i.e.  $[Cl(OMe)_2C_6H_2CH(OC_2H_5)]^+$ , 100/42.8), 215 (3.6), 201/203 ( $M^{+} - ^\bullet CH_2OC_6H_4(CH_3O) - C_2H_4$ , i.e.  $[Cl(OMe)_2C_6H_2CH(OH)]^+$ , 30.3/10.1), 173 ( $[Cl(OMe)_2C_6H_2CH(OH)]^+ - CO$ , 21.9), 138 (32.9), 122 ( $(OCH_2O)C_6H_4^{+}$ , 10.3).

**4-2** 1-(3,4 dimethoxyphenyl)-1-ethoxy-2-(4 or 5-chloro-2-methoxyphenoxy)ethane. [MW=366.5]:

366 ( $M^{+}$ , 2.1), 355 (1.1), 285 ( $M^{+} - HOCH_2CH_3 - HCl$ , 1.1), 207 ( $M^{+} - Cl(CH_3O)C_6H_3OH$ , 2.1), 195 ( $M^{+} - ^\bullet CH_2OC_6H_3(CH_3O)(Cl)$ , i.e.  $[(OMe)_2C_6H_3CH(OC_2H_5)]^+$ , 100), 191 (1.6), 181 (1.4), 167 ( $M^{+} - ^\bullet CH_2OC_6H_3(CH_3O)(Cl) - C_2H_4$ , i.e.  $[(OMe)_2C_6H_3CH(OH)]^+$ , 21.2), 156/158 ( $(OCH_2O)(Cl)C_6H_3^{+}$ , 4.5/1.7), 139 ( $[(OMe)_2C_6H_3CH(OH)]^+ - CO$ , 39.0), 121 ( $(OCH_2O)C_6H_3^{+}$ , 6.8).

**4-3** 1-(3,4 dimethoxyphenyl)-1-ethoxy-2-(5 or 4-chloro-2-methoxyphenoxy)ethane. [MW=366.5]:

366 ( $M^{+}$ , 3.1), 355 (1.6), 321 ( $M^{+} - HOCH_2CH_3$ , 1.9), 207 ( $M^{+} - Cl(CH_3O)C_6H_3OH$ , 4.6), 195 ( $M^{+} - ^\bullet CH_2OC_6H_3(CH_3O)(Cl)$ , i.e.  $[(OMe)_2C_6H_3CH(OC_2H_5)]^+$ , 100), 191 (2.7), 181 (2.8), 167 ( $M^{+} - ^\bullet CH_2OC_6H_3(CH_3O)(Cl) - C_2H_4$ , i.e.  $[(OMe)_2C_6H_3CH(OH)]^+$ , 16.3), 156/158 ( $(OCH_2O)(Cl)C_6H_3^{+}$ , 3.7/2.0), 139 ( $[(OMe)_2C_6H_3CH(OH)]^+ - CO$ , 36.7), 121 ( $(OCH_2O)C_6H_3^{+}$ , 6.4).

**4-4** 1-(6-chloro-3,4 dimethoxyphenyl)-1-ethoxy-2-(4 or 5-chloro-2-methoxyphenoxy)ethane. [MW=401]:

400 ( $M^{+}$ , 2.4), 378 (1.9), 327/329 (2.0/1.2), 281 (2.6), 229/231 ( $M^{+}-\cdot CH_2OC_6H_3(CH_3O)(Cl)$ ), i.e.  $[Cl(OMe)_2C_6H_2CH(OCH_2CH_3)]^{+}$ , 100/31.4), 215 (3.2), 207/209 (9.7/3.0), 201/203 ( $M^{+}-\cdot CH_2OC_6H_3(CH_3O)(Cl) - C_2H_4$ ), i.e.  $[(Cl)(OMe)_2C_6H_2CH(OH)]^{+}$ , 36.2/9.9), 173/175 ( $[(Cl)(OMe)_2C_6H_2CH(OH)]^{+} - CO$ , 15.4/4.7), 156/158 ( $(OCH_2O)(Cl)C_6H_3^{+}$ , 8.3/3.6), 138 (27.5).

**4-5** 1-(6-chloro-3,4 dimethoxyphenyl)-1-ethoxy-2-(5 or 4-chloro-2-methoxyphenoxy)ethane. [MW=401]:

400 ( $M^{+}$ , 2.2), 355/357 ( $M^{+}-HOCH_2CH_3$ , 6.4/3.1), 281 (4.5), 243 ( $M^{+}-Cl(CH_3O)C_6H_3O^{+}$ , 8.35), 229/231 ( $M^{+}-\cdot CH_2OC_6H_3(CH_3O)(Cl)$ ), i.e.  $[Cl(OMe)_2C_6H_2CH(OCH_2CH_3)]^{+}$ , 100/32.5), 215/217 (8.1/2.6), 207/209 (9.3/2.6), 201/203 ( $M^{+}-\cdot CH_2OC_6H_3(CH_3O)(Cl) - C_2H_4$ ), i.e.  $[(Cl)(OMe)_2C_6H_2CH(OH)]^{+}$ , 27.5/4.1), 173/175 ( $[(Cl)(OMe)_2C_6H_2CH(OH)]^{+} - CO$ , 20.8/4.5), 156/158 ( $(OCH_2O)(Cl)C_6H_3^{+}$ , 6.4/5.2), 138 (25.3).

**4-6** 1-(6-chloro-3,4 dimethoxyphenyl)-1-ethoxy-2-(4,5-dichloro-2-methoxyphenoxy)ethane. [MW=435.5]:

434 ( $M^{+}$ , 3.3), 390 ( $M^{+}-CH_3CHO$ , 1.7), 281 (1.5), 243 ( $M^{+}-\cdot OC_6H_2(CH_3O)(Cl)_2$ , 2.9), 229/231 ( $M^{+}-\cdot CH_2OC_6H_2(CH_3O)(Cl)_2$ , 100/29.7), 207/209 (5.4/1.9), 201/203 ( $M^{+}-\cdot CH_2OC_6H_2(CH_3O)(Cl)_2 - C_2H_4$ ), i.e.  $[(Cl)(OMe)_2C_6H_2CH(OH)]^{+}$ , 21.5/8.0), 173/175 ( $[(Cl)(OMe)_2C_6H_2CH(OH)]^{+} - CO$ , 14.9/5.2), 138 (20.0).

**4-7** 1-(2 or 5,6-dichloro-3,4 dimethoxyphenyl)-1-ethoxy-2-(4,5-dichloro-2-methoxyphenoxy)ethane. [MW=470]:

468/470/472 ( $M^{+}$ , 6.0/9.0/5.2), 452 (1.9), 443 (2.6), 429 (12.0), 355 (10.1), 328 (4.5), 295/297 (4.5/4.1), 281/283



(19.5/7.9), .263/265/267 ( $M^{+} - ^\bullet CH_2OC_6H_2(CH_3O)(Cl)_2$ , 100/53.2/8.3), 253 (13.1), 235/237 ( $M^{+} - ^\bullet CH_2OC_6H_2(CH_3O)(Cl)_2 - C_2H_4$ , i.e.  $[(Cl)_2(OMe)_2C_6HCH(OH)]^+$ , 10.9/16.9), 207/209 ( $[(Cl)_2(OMe)_2C_6HCH(OH)]^+ - CO$ , 43.1/12.0), 172 (13.1).

**4-8** 1-(5 or 2,6-dichloro-3,4 dimethoxyphenyl)-1-ethoxy-2-(4,5-dichloro-2-methoxyphenoxy)ethane. [MW=470]:

468/470/472 ( $M^{+}$ , 8.8/10.8/3.7), 429 (3.9), 355 (5.9), 281 (4.3), 263/265/267 ( $M^{+} - ^\bullet CH_2OC_6H_2(CH_3O)(Cl)_2$ , 100/57.2/6.8), 235/237 ( $M^{+} - ^\bullet CH_2OC_6H_2(CH_3O)(Cl)_2 - C_2H_4$ , i.e.  $[(Cl)_2(OMe)_2C_6HCH(OH)]^+$ , 22.2/6.8), 207/209 ( $[(Cl)_2(OMe)_2C_6HCH(OH)]^+ - CO$ , 16.2/8.1), 172 (21.5).

**4-9** 4,5-dichloroveratrole. [MW=207]:

206/208/210 ( $M^{+}$ , 100/49.4/10.4), 191/193/195 ( $M^{+} - CH_3^\bullet$ , 63.5/41.9/5.8), 175 (3.9), 163/165/167 ( $M^{+} - CH_3^\bullet - CO$ , 38.1/11.9/3.9), 157 (2.7), 145/147 (10.8/7.7), 148/150 ( $M^{+} - CH_3^\bullet - CO - CH_3^\bullet$ , 6.9/6.9), 127/129 ( $M^{+} - CH_3^\bullet - CO - HCl$ , 50.8/16.9), 99/101 ( $M^{+} - CH_3^\bullet - CO - HCl - CO$ , i.e.  $[C_5H_4Cl]^+$ , 76.5/23.1); and comparison with authentic sample of 4,5-dichloroveratrole.

**4-10** 3,4,5-trichloroveratrole. [MW=241.5]:

240/242/244 ( $M^{+}$ , 68.7/48.8/16.3), 225/227/229 ( $M^{+} - CH_3^\bullet$ , 66.8/100/11.3), 197/199/201 ( $M^{+} - CH_3^\bullet - CO$ , 20.9/19.3/9.7), 182/184/186 ( $M^{+} - CH_3^\bullet - CO - CH_3^\bullet$ , 11.3/16.7/5.4), 175 (5.4), 162/164 ( $M^{+} - CH_3^\bullet - CO - Cl^\bullet$ , 51.5/20.9), 147/149 ( $M^{+} - CH_3^\bullet - CO - Cl^\bullet - ^\bullet CH_3$ , 133/135 (45.9/25.3); and comparison with authentic sample of trichloroveratrole.

**4-11** tetrachloroveratrole. [MW=235]:

234/236/238 ( $M^{+}$ , 94.6/77.8/12.6), 206/208 ( $M^{+} - CO$ , 25.9/17.3), 205/207 ( $M^{+} - ^\bullet CHO$ , 17.4/18.4), 191/193/195 ( $M^{+} - ^\bullet CH_2CHO$ , i.e.  $[(Cl)_2C_6H_2OCH_3O]^+$ , 88.7/58.7/9.8), 190/192/194 ( $M^{+} - CH_3CHO$ , i.e.

$[(Cl)_2C_6H_2OCH_2O]^+$ , 198.4/100/24.4), 176/178 ( $[(Cl)_2C_6H_2O_2]^+$ , 17.4/9.7), 145/147/149 (20.2/14.3/11.8), 133/135 (25.7/15.9), 128/130 ( $[(Cl)_2C_6H_2OCH_3O]^+-CO-\cdot Cl$ , 83.8/22.5), 127/129 (56.9/25.6), 113/115 (62.3/18.5)

**4-12** (4,5-dichloro-2-methoxyphenoxy) acetaldehyde. [MW=276]:

274/276/278 ( $M^{+\cdot}$ , 29.7/40.8/19.7), 259/261/263 ( $M^{+\cdot}-\cdot CH_3$ , 16.4/27.1/5.9), 231/233/235 ( $M^{+\cdot}-\cdot CH_3-CO$ , 20.5/18.4/10.2).

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**5** 1-(3,4 dimethoxyphenyl)-1-methoxy-2-(4-methyl-2-methoxyphenoxy)ethane. [MW=332]:

332 ( $M^{+\cdot}$ , 6.1), 300 ( $M^{+\cdot}-HOCH_3$ , 1.6), 194 ( $M^{+\cdot}-(CH_3O)(CH_3)C_6H_3OH$ , 34.9), 181 ( $M^{+\cdot}-\cdot CH_2OC_6H_3(CH_3)(CH_3O)$ , i.e.  $[(CH_3O)_2C_6H_3CH(OCH_3)]^+$ , 100), 166 ( $M^{+\cdot}-\cdot CH_2OC_6H_3(CH_3)(CH_3O)-\cdot CH_3$ , i.e.  $[(CH_3O)_2C_6H_3CH(O)]^+$ , 4.2), 165 (8.3), 164 (2.3), 163 (7.5), 151 ( $(CH_3O)_2C_6H_3CH_2^+$ , 4.7); and comparison with authentic sample of compound 5.

**5-1** 1-(3,4 dimethoxyphenyl)-1-methoxy-2-(5-chloro-4-methyl-2-methoxyphenoxy)ethane. [MW=366.5]:

366/368 ( $M^{+\cdot}$ , 3.1/1.5), 300 (1.6), 271 (1.3), 240 (1.3), 195 ( $M^{+\cdot}-\cdot OC_6H_2(OCH_3)(CH_3)Cl$ , 9.2), 194 ( $M^{+\cdot}-HOC_6H_2(OCH_3)(CH_3)Cl$ , 11.2), 181 ( $M^{+\cdot}-\cdot CH_2OC_6H_2(CH_3)(CH_3O)Cl$ , i.e.  $[(CH_3O)_2C_6H_3CH(OCH_3)]^+$ , 100), 166 (8.1), 165 (11.2), 151 ( $(CH_3O)_2C_6H_3CH_2^+$ , 8.5).

**5-2** 1-(6-chloro-3,4 dimethoxyphenyl)-1-methoxy-2-(4-methyl-2-methoxyphenoxy)ethane. [MW=366.5]:

366/368 ( $M^{+\cdot}$ , 2.7/0.9), 229/231 ( $M^{+\cdot}-\cdot OC_6H_2(OCH_3)(CH_3)$ , 15.3/7.2), 215/217 ( $M^{+\cdot}-\cdot CH_2OC_6H_2(CH_3)(CH_3O)$ , i.e.  $[(CH_3O)_2(Cl)C_6H_2CH(OCH_3)]^+$ , 100/37.3), 185 ( $(CH_3O)_2(Cl)C_6H_3CH_2^+$ , 10.3).

- 5-3** 1-(6-chloro-3,4 dimethoxyphenyl)-1-methoxy-2-(5-chloro-4-methyl-2-methoxyphenoxy)ethane > [MW=401]:  
 400/402 ( $M^{+}$ , 11.1/5.4), 270 (1.8), 229/231 ( $M^{+}$ - $^{\circ}OC_6H_2(OCH_3)(CH_3)Cl$ , 13.7/5.4), 228/230 ( $M^{+}$ - $HOC_6H_2(OCH_3)(CH_3)Cl$ , 23.9/7.0), 215/217 ( $M^{+}$ - $^{\circ}CH_2OC_6H_2(CH_3)(CH_3O)Cl$ , i.e.  $[(CH_3O)_2(Cl)C_6H_2CH(OCH_3)]^{+}$ , 100/38.9), 207 (2.35), 200/202 (12.3/2.2), 199/201 (10.1/5.6).
- 5-4** 1-(6-chloro-3,4 dimethoxyphenyl)-1-methoxy-2-(3 or 6,5-dichloro-4-methyl-2-methoxyphenoxy)ethane. [MW=435.5]:  
 434/436/438 ( $M^{+}$ , 6.2/4.3/1.5), 229/231 ( $M^{+}$ - $^{\circ}OC_6H(CH_3)(CH_3O)(Cl)_2$ , 5.4/2.3), 215/217 ( $M^{+}$ - $^{\circ}CH_2OC_6H(CH_3)(CH_3O)(Cl)_2$ , i.e.  $[Cl(OMe)_2C_6H_2CH(OCH_3)]^{+}$ , 100/31.7), 200 (9.4).
- 5-5** 1-(6-chloro-3,4 dimethoxyphenyl)-1-methoxy-2-(6 or 3,5-dichloro-4-methyl-2-methoxyphenoxy)ethane. [MW=435.5]:  
 434/436/438 ( $M^{+}$ , 3.1/2.0/0.7), 229/231 ( $M^{+}$ - $^{\circ}OC_6H(CH_3)(CH_3O)(Cl)_2$ , 45.3/14.8), 215/217 ( $M^{+}$ - $^{\circ}CH_2OC_6H(CH_3)(CH_3O)(Cl)_2$ , i.e.  $[Cl(OMe)_2C_6H_2CH(OCH_3)]^{+}$ , 100/36.0), 200 (15.3).
- 5-6** 1-(2 or 5,6-dichloro-3,4 dimethoxyphenyl)-1-methoxy-2-(3 or 6,5-dichloro-4-methyl-2-methoxyphenoxy)ethane. [MW=470]:  
 468/470/472/474 ( $M^{+}$ , 12.5/10.0/8.0/2.1), 263/265 ( $M^{+}$ - $^{\circ}OC_6H(CH_3)(CH_3O)(Cl)_2$ , 14.2/6.5), 249/251/253 ( $M^{+}$ - $^{\circ}CH_2OC_6H(CH_3)(CH_3O)(Cl)_2$ , i.e.  $[Cl_2(OMe)_2C_6HCH(OCH_3)]^{+}$ , 100/88.7/9.0), 234/236 ( $[Cl_2(OMe)_2C_6HCH(OCH_3)]^{+}$ - $^{\circ}CH_3$ , 5.6/1.9), 233/235 ( $[Cl_2(OMe)_2C_6HCH(OCH_3)]^{+}$ - $CH_4$ , 5.2/2.1), 219/221 ( $[Cl_2(OMe)_2C_6HCH(OCH_3)]^{+}$ - $CH_2O$ , i.e.  $[Cl_2(OMe)_2C_6HCH_2]^{+}$ , 6.7/3.8).
- 5-7** 1-(6-chloro-3,4 dimethoxyphenyl)-1-methoxy-2-(3,5,6-trichloro-4-methyl-2-methoxyphenoxy)ethane. [MW=470]:  
 468 ( $M^{+}$ , 10.5), 238/240 (6.5/3.0), 229/231 ( $M^{+}$ - $^{\circ}OC_6(CH_3)(CH_3O)(Cl)_3$ ,

23.6/10.2), 215/217 ( $M^{+} - ^\bullet CH_2OC_6(CH_3)(CH_3O)(Cl)_3$ , i.e.  
 $[Cl(OMe)_2C_6H_2CH(OCH_3)]^+$ , 100/34.7).

5-8 1-(2 or 5,6-dichloro-3,4 dimethoxyphenyl)-1-methoxy-2-(3,5,6-trichloro-4-methyl-2-methoxyphenoxy)ethane. [MW=504.5]:  
 502/504 ( $M^{+}$ , 13.0/8.0), 457 (7.0), 263/265/267 ( $M^{+} - ^\bullet OC_6(CH_3)(CH_3O)(Cl)_3$ , 53.0/28.0/6.0), 249/251/253 ( $M^{+} - ^\bullet CH_2OC_6(CH_3)(CH_3O)(Cl)_3$ , 100/83.0/15.0), 228/230 ( $M^{+} - ^\bullet OC_6(CH_3)(CH_3O)(Cl)_3 - Cl$ , 11.0/8.0), 219/221 ( $M^{+} - ^\bullet CH_2OC_6(CH_3)(CH_3O)(Cl)_3 - CH_2O$ , 19.0/23.0), 207 (13.0), 168/170 (7.0/10.0).

5-9 1-(2,5,6-trichloro-3,4 dimethoxyphenyl)-1-methoxy-2-(3,5,6-trichloro-4-methyl-2-methoxyphenoxy)ethane. [MW=539]:  
 536/538 ( $M^{+}$ , 8.5/15.3), 429 (13.6), 355 (21.2), 297/299/301 ( $[Cl_3(OMe)_2C_6CH(OCH_3)CH_2]^+$ , 53.0/51.5/21.2), 283/285/287 ( $[Cl_3(OMe)_2C_6CH(OCH_3)]^+$ , 100/74.3/19.8), 269 (15.2), 251 (21.2).

5-10 4,5-dichloroveratrole. [MW=207]:  
 206/208 ( $M^{+}$ , 98.6/50.4), 191/193 ( $M^{+} - CH_3^\bullet$ , 57.8/40.2), 163/165 ( $M^{+} - CH_3^\bullet - CO$ , 33.4/20.8), 128/130 ( $M^{+} - CH_3^\bullet - CO - ^\bullet Cl$ , 60.3/19.8), 127/129 ( $M^{+} - CH_3^\bullet - CO - HCl$ , 60.3/21.0), 113 ( $M^{+} - ^\bullet CH_3 - ^\bullet CO - ^\bullet Cl - ^\bullet CH_3$ , 20.3), 99/101 ( $M^{+} - CH_3^\bullet - CO - HCl - CO$ , i.e.  $[C_5H_4Cl]^+$ , 100/28.7);  
 and comparison with authentic sample of 4,5-dichloroveratrole.

5-11 3 or 6,5-dichlorocreosol (trimethyl)silyl ether. [MW=279]:  
 278/280 ( $M^{+}$ , 41.2/19.2), 263/265 ( $M^{+} - ^\bullet CH_3$ , 19.2/11.8), 250/252 ( $M^{+} - ^\bullet CO$ , 100/17.6), 248 ( $M^{+} - ^\bullet CH_3 - ^\bullet CH_3$ , 52.9), 213/215 ( $M^{+} - ^\bullet CH_3 - ^\bullet CH_3 - ^\bullet Cl$ , 23.5/17.6), 183 (13.2), 73 ( $HOSi(CH_3)_3$ , 88.2).

5-12 3,5,6-trichlorocresol (trimethyl )silyl ether. [MW=313.5]:

312/314/316 ( $M^{++}$ , 16.0/11.0/5.0), 297/299/301 ( $M^{+}$  -  $\cdot CH_3$ ,  
 24.3/22.1/6.1), 284/286 ( $M^{++}$  -  $\cdot CO$ , 100/30.0), 282 ( $M^{+}$  -  $\cdot CH_3$  -  
 $\cdot CH_3$ , .88.0), 247/249/251 ( $M^{++}$  -  $\cdot CH_3$  -  $\cdot CH_3$  -  $\cdot Cl$ , 17.7/8.3/5.0), 217  
 (3.9), 189 (3.3), 73 ( $HOSi(CH_3)_3$ , 60.0).

5-13 trichloroveratrole. [MW=241.5]:

240/242/244 ( $M^{++}$ , 65.7/47.2/16.0), 225/227/229 ( $M^{++}-CH_3^{+}$ ,  
 70.1/100/15.3), 197/199/201 ( $M^{++}-CH_3^{+}-CO$ , 18.5/15.4/9.2), 182/184/186  
 ( $M^{++}-CH_3^{+}-CO-CH_3^{+}$ , 12.5/16.2/7.9), 162/164 ( $M^{++}-CH_3^{+}-CO-Cl^{+}$ ,  
 47.0/18.3), 147/149 ( $M^{++}-CH_3^{+}-CO-Cl^{+}-\cdot CH_3$ , 25.2); .and comparison  
 with authentic sample of trichloroveratrole.

5-14 1-(6-chloro-3,4 dimethoxyphenyl)-1-methoxy-2-acetoxyethane.

[MW=288.5]:

273 ( $M^{++}$  -  $\cdot CH_3$ , 5.6), 271 (5.6), 215/217 ( $M^{+}$  -  $\cdot CH_2O(CO)CH_3$ ,  
 100/38.2), 185 ( $M^{+}$  -  $\cdot CH_2O(CO)CH_3$  -  $CH_2O$  i.e.  $[Cl(CH_3O)_2C_6H_2CH_2]^+$ ,  
 5.1), 152 (5.6).

5-15 1-(2 or 5,6-dichloro-3,4 dimethoxyphenyl)-1-methoxy-2-acetoxyethane.

[MW=323]:

249/251/253 ( $M^{++}$  -  $\cdot CH_2O(CO)CH_3$ , 100/80.7/11.2), 234/236 ( $M^{+}$  -  
 $\cdot CH_2O(CO)CH_3$  -  $\cdot CH_3$ , 6.4/5.6), 219 ( $M^{+}$  -  $\cdot CH_2O(CO)CH_3$  -  $CH_2O$ , 7.3),  
 213 ( $M^{+}$  -  $\cdot CH_2O(CO)CH_3$  -  $HCl$ , 7.7), 151 (2.6).

5-16 1-(2,5,6-trichloro-3,4 dimethoxyphenyl)-1-methoxy-2-acetoxyethane.

[MW=357.5]:

283/285/287 ( $M^{++}$  -  $\cdot CH_2O(CO)CH_3$ , 100/63.8/24.2), 255 (6.9),  
 247/249/251 ( $M^{++}$  -  $\cdot CH_2O(CO)CH_3$  -  $HCl$ , 13.8/13.8/12.1), 207 (6.9),  
 175 (4.3), 164 (5.2), 147 (8.6).

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8 3-(3,4-dimethoxyphenyl)-3-ethoxy-2-(2-methoxyphenoxy)propanol.

[MW=404]:

a) 404 ( $M^{+}$ , 0.8), 299 ( $M^{+}$ -  $^{\circ}O(CO)CH_3 - ^{\circ}OC_2H_5$ , 5.5), 221 ( $M^{+}$ -  $HO(CO)CH_3 - ^{\circ}OC_6H_4(OCH_3)$ , 1.0), 195 ( $[(CH_3O)_2C_6H_3CH(OC_2H_5)]^{+}$ , 100), 175 (1.0), 167 ( $[(CH_3O)_2C_6H_3CH(OH)]^{+}$ , 6.0), 139 (15.5), 124 (6.1).

b) 299 ( $M^{+}$ -  $^{\circ}O(CO)CH_3 - ^{\circ}OC_2H_5$ , 6.7), 221 ( $M^{+}$ -  $HO(CO)CH_3 - ^{\circ}OC_6H_4(OCH_3)$ , 1.5), 195 ( $[(CH_3O)_2C_6H_3CH(OC_2H_5)]^{+}$ , 100), 167 ( $[(CH_3O)_2C_6H_3CH(OH)]^{+}$ , 9.6), 139 (18.2), 124 (7.3); and comparison with an authentic sample of compound 8.

8-1 3-(6-chloro-3,4-dimethoxyphenyl)-3-ethoxy-2-(2-methoxyphenoxy)propanol. [MW=438.5]:

a) 378 ( $M^{+} - HOCOCH_3$ , 1.5), 333 ( $M^{+}$ -  $HO(CO)CH_3 - ^{\circ}OC_2H_5$ , 2.5), 255 ( $M^{+}$ -  $HO(CO)CH_3 - ^{\circ}OC_6H_4(OCH_3)$ , 2.4), 229/231 ( $[(Cl)(CH_3O)_2C_6H_2CH(OC_2H_5)]^{+}$ , 100/30.3), 209 (8.13), 192 (2.2), 161 (10.7), 138 (2.9).

b) 402 ( $M^{+} - HCl$ , 1.1), 333 ( $M^{+}$ -  $HO(CO)CH_3 - ^{\circ}OC_2H_5$ , 31.6), 255 ( $M^{+}$ -  $HO(CO)CH_3 - ^{\circ}OC_6H_4(OCH_3)$ , 2.4), 229/231 ( $[(Cl)(CH_3O)_2C_6H_2CH(OC_2H_5)]^{+}$ , 100/44.4), 209 (15.6), 192 (5.2), 161 (15.4), 138 (2.9).

8-2 3-(3,4-dimethoxyphenyl)-3-ethoxy-2-(4 or 5-chloro-2-methoxyphenoxy)propanol. [MW=438.5]:

a) 229 (15.1), 195 ( $[(CH_3O)_2C_6H_3CH(OC_2H_5)]^{+}$ , 100), 167 ( $[(CH_3O)_2C_6H_3CH(OH)]^{+}$ , 8.7), 152 (3.2), 139 (20.1), 123 (5.5).

b) 438 ( $M^{+}$ , 2.3), 341 (2.7), 195 ( $[(CH_3O)_2C_6H_3CH(OC_2H_5)]^{+}$ , 100), 167 ( $[(CH_3O)_2C_6H_3CH(OH)]^{+}$ , 13.1), 139 (27.9), 124 (3.5).

c) 225 (4.0), 195 ( $[(CH_3O)_2C_6H_3CH(OC_2H_5)]^{+}$ , 100), 167

$[(\text{CH}_3\text{O})_2\text{C}_6\text{H}_3\text{CH}(\text{OH})]^+$ , 15.2), 151 (4.0), 139 (31.4), 124 (2.9).

**8-3** 3-(6-chloro-3,4-dimethoxyphenyl)-3-ethoxy-2-(4 or 5-chloro-2-methoxyphenoxy)propanol. MW=473]:

**a)** 472 ( $\text{M}^{++}$ , 8.4), 253 (3.6), 229/231 ( $[(\text{Cl})(\text{CH}_3\text{O})_2\text{C}_6\text{H}_2\text{CH}(\text{OC}_2\text{H}_5)]^+$ , 100/21.6), 207 (9.0), 201 ( $[(\text{Cl})(\text{CH}_3\text{O})_2\text{C}_6\text{H}_2\text{CH}(\text{OH})]^+$ , 24.0), 138 (21.6).

**b)** 472 ( $\text{M}^{++}$ , 4.5), 255 ( $\text{M}^{++} - \text{HO}(\text{CO})\text{CH}_3 - ^\circ\text{OC}_6\text{H}_3(\text{OCH}_3)(\text{Cl})$ , 10.2), 229/231 ( $[(\text{Cl})(\text{CH}_3\text{O})_2\text{C}_6\text{H}_2\text{CH}(\text{OC}_2\text{H}_5)]^+$ , 100/28.7), 201 ( $[(\text{Cl})(\text{CH}_3\text{O})_2\text{C}_6\text{H}_2\text{CH}(\text{OH})]^+$ , 33.4), 138 (26.9).

**8-4** 3-(6-chloro-3,4-dimethoxyphenyl)-3-ethoxy-2-(4,5-dichloro-2-methoxyphenoxy)propanol. [MW=507.5]:

**a)** 506 ( $\text{M}^{++}$ , 6.5), 489 (5.8), 332 (5.8), 281 (5.8), 229/231 ( $[(\text{Cl})(\text{CH}_3\text{O})_2\text{C}_6\text{H}_2\text{CH}(\text{OC}_2\text{H}_5)]^+$ , 100/38.7), 207 (17.5), 201 ( $[(\text{Cl})(\text{CH}_3\text{O})_2\text{C}_6\text{H}_2\text{CH}(\text{OH})]^+$ , 28.4), 138 (32.9).

**b)** 506 ( $\text{M}^{++}$ , 3.4), 365 (2.8), 331 (3.5), 295 (2.1), 229/231 ( $[(\text{Cl})(\text{CH}_3\text{O})_2\text{C}_6\text{H}_2\text{CH}(\text{OC}_2\text{H}_5)]^+$ , 100/34.7), 207 (28.5), 201 ( $[(\text{Cl})(\text{CH}_3\text{O})_2\text{C}_6\text{H}_2\text{CH}(\text{OH})]^+$ , 19.2), 138 (34.2).

**8-5** 3-(2 or 5,6-dichloro-3,4-dimethoxyphenyl)-3-ethoxy-2-(4,5-dichloro-2-methoxyphenoxy)propanol. [MW=542]:

**a)** 540 ( $\text{M}^{++}$ , 1.0), 510 (0.8), 437 (3.8), 399 (2.4), 359 (5.4), 289 ( $\text{M}^{++} - \text{HO}(\text{CO})\text{CH}_3 - ^\circ\text{OC}_6\text{H}_2(\text{OCH}_3)\text{Cl}_2$ , 10.2), 263/265/267 ( $[(\text{Cl}_2)(\text{CH}_3\text{O})_2\text{C}_6\text{HCH}(\text{OC}_2\text{H}_5)]^+$ , 100/65.3/8.2), 229/231 (10.2/7.6), 172 (6.5).

**b)** 540 ( $\text{M}^{++}$ , 3.5), 289 ( $\text{M}^{++} - \text{HO}(\text{CO})\text{CH}_3 - ^\circ\text{OC}_6\text{H}_2(\text{OCH}_3)\text{Cl}_2$ , 6.6), 263/265/267 ( $[(\text{Cl}_2)(\text{CH}_3\text{O})_2\text{C}_6\text{HCH}(\text{OC}_2\text{H}_5)]^+$ , 100/68.2/9.4), 229/231 (9.1/6.7), 172 (5.6).

8-6 3-(2,5,6-trichloro-3,4-dimethoxyphenyl)-3-ethoxy-2-(4,5-dichloro-2-methoxyphenoxy)propanol. [MW=576.5]:

575/577 ( $M+H^+$ , 12.8/7.3), 523 (7.3), 471 ( $M+H^+ - HO(CO)CH_3 - ^*OC_2H_5$ , 3.4), 433 (3.4), 355 (3.0), 323 ( $M^{++} - HO(CO)CH_3 - ^*OC_6H_2(OCH_3)Cl_2$ , 6.8), 297/299/6301 ( $[(Cl_3)(CH_3O)_2C_6CH(OC_2H_5)]^+$ , 100/62.4/17.1), 277/279 (46.6/23.1), 263/265 (28.2/15.4), 229/231/233 (30.7/23.1/6.4).

8-7 3-(2 or 5, 6-dichloro-3,4-dimethoxyphenyl)-3-ethoxy-2-(3 or 6,4,5-trichloro-2-methoxyphenoxy)propanol. [MW=576.5]:

a) 574 ( $M^{++}$ , 10.2), 263/265/267 ( $[(Cl_2)(CH_3O)_2C_6HCH(OC_2H_5)]^+$ , 100/70.4/10.9), 235 ( $[(Cl_2)(CH_3O)_2C_6HCH(OH)]^+$ , 19.7).

b) 489 (4.5), 453 (4.2), 409 (6.2), 263/265/267 ( $[(Cl_2)(CH_3O)_2C_6HCH(OC_2H_5)]^+$ , 100/64.6/7.2), 235 ( $[(Cl_2)(CH_3O)_2C_6HCH(OH)]^+$ , 15.4).

8-8 presumably: 3-(2,5,6-trichloro-3,4-dimethoxyphenyl)-3-ethoxy-2-(3 or 6,4,5-trichloro-2-methoxyphenoxy)propanol. [MW=576.5 or 611]:

577 (18.0), 483 (25.6), 450/452 (18.4/15.6), 324 (25.8), 297/299/301 ( $[(Cl_3)(CH_3O)_2C_6CH(OC_2H_5)]^+$ , 100/56.7/14.8), 263/265 (55.2/30.4). It was not possible to determine whether this compound was penta or hexa chlorinated.

8-9 Mass spectrum was not recorded.

8-10 4,5-dichloroveratrole. [MW=207]:

206/208/210 ( $M^{++}$ , 87.5/73.2/10.3), 191/193 ( $M^{++} - CH_3^+$ , 39.3/36.4), 163/165 ( $M^{++} - CH_3^+ - CO$ , 20.3/27.6), 143 (15.8), 128/130 ( $M^{++} - CH_3^+ - CO - ^*Cl$ , 100/29.3), 127/129 ( $M^{++} - CH_3^+ - CO - HCl$ , 43.5/35.2); and comparison with authentic sample of 4,5-dichloroveratrole.



8-11trichloroveratrole. [MW=241.5]:

240/242/244 ( $M^{+}$ , 100/62.4/19.3), 225/227 ( $M^{+}-CH_3$ , 80.1/98.4), 210 (18.4), 197/199/201 ( $M^{+}-CH_3-CO$ , 40.2/17.3), 162/164 ( $M^{+}-CH_3-CO-Cl$ , 68.2/20.4), 149 ( $M^{+}-CH_3-CO-Cl-CH_3$ , 27.3); .and comparison with authentic sample of trichloroveratrole.

## APPENDIX IV

MASS SPECTRA OF THE PRODUCTS OF CHLORINATION OF COMPOUNDS 3 AND 7

The spectra are reported as : m/z (assignment, relative intensity).

3 1-(3,4-dimethoxyphenyl)-2-(2-methoxyphenoxy)ethanol. [MW=318]:  
 318 ( $M^{+}$ , 3.5), 286 ( $M^{+}$  - HOCH<sub>3</sub>, 1.6), 195 ( $M^{+}$  - (CH<sub>3</sub>O)C<sub>6</sub>H<sub>4</sub>O<sup>•</sup>, 3.9),  
 194 ( $M^{+}$  - (CH<sub>3</sub>O)C<sub>6</sub>H<sub>4</sub>OH, 5.1), 181 ( $M^{+}$  - <sup>•</sup>CH<sub>2</sub>OC<sub>6</sub>H<sub>4</sub>(CH<sub>3</sub>O), i.e.  
 [(CH<sub>3</sub>O)<sub>2</sub>C<sub>6</sub>H<sub>3</sub>CH(OCH<sub>3</sub>)]<sup>+</sup>, 100), 166 ( $M^{+}$  - <sup>•</sup>CH<sub>2</sub>OC<sub>6</sub>H<sub>4</sub>(CH<sub>3</sub>O) - <sup>•</sup>CH<sub>3</sub>, i.e.  
 [(CH<sub>3</sub>O)<sub>2</sub>C<sub>6</sub>H<sub>3</sub>CHO]<sup>+</sup>, 14.9), 151 ([ (CH<sub>3</sub>O)<sub>2</sub>C<sub>6</sub>H<sub>3</sub>CH(OCH<sub>3</sub>)]<sup>+</sup> - CH<sub>2</sub>O, i.e.  
 (CH<sub>3</sub>O)<sub>2</sub>C<sub>6</sub>H<sub>3</sub>CH<sub>2</sub><sup>+</sup>, 8.5); and comparison with authentic sample of 3.

3-1 1-(6-chloro-3,4-dimethoxyphenyl)-2-(2-methoxyphenoxy)ethanol.  
 [MW=352.5]:  
 352 ( $M^{+}$ , 4.5), 317 ( $M^{+}$  - Cl<sup>•</sup>), 229/231 ( $M^{+}$  - <sup>•</sup>OC<sub>6</sub>H<sub>4</sub>(OCH<sub>3</sub>), 8.0/3.7),  
 228/230 ( $M^{+}$  - HOC<sub>6</sub>H<sub>4</sub>(OCH<sub>3</sub>), 16.5/8.0), 215/217 ( $M^{+}$  - <sup>•</sup>CH<sub>2</sub>OC<sub>6</sub>H<sub>4</sub>(CH<sub>3</sub>O),  
 i.e. [Cl(CH<sub>3</sub>O)<sub>2</sub>C<sub>6</sub>H<sub>2</sub>CH(OCH<sub>3</sub>)]<sup>+</sup>, 100/30.6), 199/201 ([Cl(CH<sub>3</sub>O)<sub>2</sub>C<sub>6</sub>H<sub>2</sub>CO]<sup>+</sup>,  
 5.5/5.0), 194 ( $M^{+}$  - <sup>•</sup>OC<sub>6</sub>H<sub>4</sub>(OCH<sub>3</sub>) - <sup>•</sup>Cl, 5.5), 185/187  
 ([Cl(CH<sub>3</sub>O)<sub>2</sub>C<sub>6</sub>H<sub>2</sub>CH(OCH<sub>3</sub>)]<sup>+</sup> - CH<sub>2</sub>O, i.e. [Cl(CH<sub>3</sub>O)<sub>2</sub>C<sub>6</sub>H<sub>2</sub>CH<sub>2</sub>]<sup>+</sup>, 8.0/1.3),  
 149/151 ([Cl(CH<sub>3</sub>O)<sub>2</sub>C<sub>6</sub>H<sub>2</sub>CH(OH)]<sup>+</sup> - HCl, 2.0/4.8).

3-2 1-(3,4-dimethoxyphenyl)-2-(4 or 5 chloro-2-methoxyphenoxy)ethanol.  
 [MW=352.5]:  
 a) 352 ( $M^{+}$ , 4.3), 320/322 ( $M^{+}$  - HOCH<sub>3</sub>, 7.4/4.1), 279/281 (7.4/3.3),  
 256 (6.9), 207 (4.1), 181 ([ (CH<sub>3</sub>O)<sub>2</sub>C<sub>6</sub>H<sub>3</sub>CH(OCH<sub>3</sub>)]<sup>+</sup>, 100), 167  
 ([ (CH<sub>3</sub>O)<sub>2</sub>C<sub>6</sub>H<sub>3</sub>CH(OH)]<sup>+</sup>, 18.8), 166 ([ (CH<sub>3</sub>O)<sub>2</sub>C<sub>6</sub>H<sub>3</sub>CHO]<sup>+</sup>, 13.3), 165  
 ([ (CH<sub>3</sub>O)<sub>2</sub>C<sub>6</sub>H<sub>3</sub>CO]<sup>+</sup>, 10.2), 137 ([ (CH<sub>3</sub>O)<sub>2</sub>C<sub>6</sub>H<sub>3</sub>]<sup>+</sup>, 5.9).  
 b) 352 ( $M^{+}$ , 4.8), 320/322 ( $M^{+}$  - HOCH<sub>3</sub>, 19.4/4.2), 281 (15.3), 256

(8.4), 207 (3.4), 181 :  $[(CH_3O)_2C_6H_3CH(OCH_3)]^+$ , 100), 166  
 $[(CH_3O)_2C_6H_3CHO]^{++}$ , 15.3), 165  $[(CH_3O)_2C_6H_3CO]^+$ , 16.8), 137  
 $[(CH_3O)_2C_6H_3]^+$ , 12.5).

**3-3** 1-(6-chloro-3,4-dimethoxyphenyl)-2-(4 or 5 chloro-2-methoxyphenoxy)ethanol. [MW=387]:

a) 386/388 ( $M^+$ , 4.8/3.7), 355 ( $M^+ - ^\bullet OCH_3$ , 1.4), 269 (1.2), 229/231 ( $M^+ - ^\bullet OC_6H_3(CH_3O)Cl$ , 4.5/3.2), 228/230 ( $M^+ - HOC_6H_3(CH_3O)Cl$ , 4.0/3.3), 215/217 ( $M^+ - ^\bullet CH_2OC_6H_3(CH_3O)Cl$  i.e.  $[Cl(CH_3O)_2C_6H_2CH(OCH_3)]^+$ , 100/36.9), 200 ( $[Cl(CH_3O)_2C_6H_3CHO]^{++}$ , 15.6).

b) 386/388 ( $M^+$ , 3.2/2.0), 354 ( $M^+ - HOCH_3$ , 1.6), 256 (3.0), 229/231 ( $M^+ - ^\bullet OC_6H_3(CH_3O)Cl$ , 15.2/3.4), 228/230 ( $M^+ - HOC_6H_3(CH_3O)Cl$ , 15.2/6.4), 215/217 ( $[Cl(CH_3O)_2C_6H_2CH(OCH_3)]^+$ , 100/36.3), 200 ( $[Cl(CH_3O)_2C_6H_2CHO]^{++}$ , 14.2).

**3-4** 1-(6-chloro-3,4-dimethoxyphenyl)-2-(4,5 dichloro-2-methoxyphenoxy)ethanol. [MW=421.5]:

420/422 ( $M^+$ , 2.3/3.2), 229/231 ( $M^+ - ^\bullet OC_6H_2(CH_3O)Cl_2$ , 7.4/3.7), 228/230 ( $M^+ - HOC_6H_2(CH_3O)Cl_2$ , 7.1/3.2), 215/217 ( $M^+ - ^\bullet CH_2OC_6H_2(CH_3O)Cl_2$ , i.e.  $[Cl(OMe)_2C_6H_2CH(OCH_3)]^+$ , 100/31.7), 200/202 ( $[Cl(OMe)_2C_6H_2CHO]^{++}$ , 9.4), 199/201 ( $[Cl(OMe)_2C_6H_2CO]^+$ , 7.9/2.8).

**3-5** 1-(2 or 5,6-dichloro-3,4-dimethoxyphenyl)-2-(4,5 dichloro-2-methoxyphenoxy)ethanol. [MW=456]:

454/456/458 ( $M^+$ , 21.9/13.7/9.8), 263/265/267 ( $M^+ - ^\bullet OC_6H_2(CH_3O)Cl_2$ , 16.8/12.5/7.5), 262/264 ( $M^+ - HOC_6H_2(CH_3O)Cl_2$ , 4.3/6.6), 249/251/253 ( $M^+ - ^\bullet CH_2OC_6H_2(CH_3O)Cl_2$ , i.e.  $[Cl_2(OMe)_2C_6HCH(OCH_3)]^+$ , 73.4/67.9/9.4), 207 (17.6).

3-6 1-(2,5,6-trichloro-3,4-dimethoxyphenyl)-2-(4,5 dichloro-2-methoxyphenoxy)ethanol. [MW=490.5]:

488/490/492 ( $M^{+}$ , 5.3/8.4/3.2), 297/299/301 ( $M^{+}-^{\bullet}OC_6H_2(CH_3O)Cl_2$ , 13.4/13.0/5.2), 296/298 ( $M^{+}-HOC_6H(CH_3O)Cl_2$ , 6.7/8.0/4.9), 283/285/287 ( $M^{+}-^{\bullet}CH_2OC_6H_2(CH_3O)Cl_2$ , i.e.  $[Cl_3(OMe)_2C_6CH(OCH_3)]^{+}$ , 100/89.9/24.3).

3-7 1-(2 or 5,6-dichloro-3,4-dimethoxyphenyl)-2-(3 or 6,4,5 trichloro-2-methoxyphenoxy)ethanol. [MW=490.5]:

1488/490/492 ( $M^{+}$ , 4.5/2.9/1.0), 263/265/267 ( $M^{+}-^{\bullet}OC_6H(CH_3O)Cl_3$ , 14.5/12.3/3.8), 262/264 ( $M^{+}-HOC_6H(CH_3O)Cl_3$ , 4.9/5.2/1.9), 249/251/253 ( $M^{+}-^{\bullet}CH_2OC_6H(CH_3O)Cl_3$ , i.e.  $[Cl_2(OMe)_2C_6HCH(OCH_3)]^{+}$ , 89.3/69.0/10.2).

3-8 1-(2,5,6-trichloro-3,4-dimethoxyphenyl)-2-(3 or 6,4,5 trichloro-2-methoxyphenoxy)ethanol. [MW=526]:

a) 522/524 ( $M^{+}$ , 3.2/3.8), 297/299/301 ( $M^{+}-^{\bullet}OC_6H(CH_3O)Cl_3$ , 8.9/9.0/4.1), 296/298/300 ( $M^{+}-HOC_6H(CH_3O)Cl_3$ , 3.4/5.0/2.4), 283/285/287 ( $M^{+}-^{\bullet}CH_2OC_6H(CH_3O)Cl_3$ , 90.4/100/35.6).

b) 522 ( $M^{+}$ , 2.0), 297/299/301 ( $M^{+}-^{\bullet}OC_6H(CH_3O)Cl_3$ , 6.4/6.0/3.1), 296/298 ( $M^{+}-HOC_6H(CH_3O)Cl_3$ , 2.6/3.0), 283/285/287 ( $M^{+}-^{\bullet}CH_2OC_6H(CH_3O)Cl_3$ , 75.6/80.2/50.2).

3-9 4,5-dichloroveratrole. [MW=207]:

206/208/210 ( $M^{+}$ , 100/63.4/10.3), 191/193 ( $M^{+}-CH_3^{\bullet}$ , 30.3/22.8), 163/165 ( $M^{+}-CH_3^{\bullet}-CO$ , 35.2/11.3), 133/135 (6.2/5.0), 128/130 ( $M^{+}-CH_3^{\bullet}-CO-^{\bullet}Cl$ , 34.3/4.6), 127/129 ( $M^{+}-CH_3^{\bullet}-CO-HCl$ , 15.8/4.3); and comparison with authentic sample of 4,5-dichloroveratrole.

**3-10** trichloroveratrole. [MW=241.5]:

240/242/244 ( $M^{+}$ , 98.0/100/35.0), 225/227/229 ( $M^{+}-CH_3^{\cdot}$ , 30.8/51.2/17.3), 197/199/201 ( $M^{+}-CH_3^{\cdot}-CO$ , 15.9/18.0/14.2), 182/184/186 ( $M^{+}-CH_3^{\cdot}-CO-CH_3^{\cdot}$ , 2.5/6.2/5.4), 162/164 ( $M^{+}-CH_3^{\cdot}-CO-Cl^{\cdot}$ , 43.6/25.3), 161/163 ( $M^{+}-CH_3^{\cdot}-CO-HCl$ , 24.2/24.3), 147/149 ( $M^{+}-CH_3^{\cdot}-CO-Cl^{\cdot}-CH_3^{\cdot}$ , 38.7/18.5), 133/135 (37.8/21.6); .and comparison with authentic sample of trichloroveratrole.

**3-11** tetrachloroveratrole. [MW=:276]

274/276/278/280 ( $M^{+}$ , 90.3/100/56.7/25.3), 259/261/263/265 ( $M^{+}-CH_3^{\cdot}$ , 25.6/30.2/14.5/8.0), 231/233/235 ( $M^{+}-CH_3^{\cdot}-CO$ , 18.8/20.4/9.6), 196/198/200 ( $M^{+}-CH_3^{\cdot}-CO-Cl^{\cdot}$ , 45.3/46.8/15.2), 195/197/199 ( $M^{+}-CH_3^{\cdot}-CO-HCl$ , 30.8/29.0/9.5).

**3-12** 2-(4,5 dichloro-2-methoxyphenoxy) acetaldehyde. [MW=235]:

234/236/238 ( $M^{+}$ , 100/55.4/10.2), 206 ( $M^{+} - CO$ , 18.4), 205 ( $M^{+} - ^{\cdot}CHO$ , 20.9), 191/193/195 ( $M^{+} - ^{\cdot}CH_2CHO$ , i.e.  $[Cl_2(OCH_3)C_6H_2O]^{\cdot}$ , 89.7/36.5), 190/192/194 ( $[Cl_2(OCH_2)C_6H_2O]^{\cdot}$ , 7.8/8.5/7.2), 163/165 ( $M^{+} - ^{\cdot}CH_2CHO - CO$ , 54.3/26.8), 160/162 ( $M^{+} - ^{\cdot}CH_2CHO - CH_2O$ , 20.8/11.9), 128/130 ( $[Cl_2(OCH_3)C_6H_2O]^{\cdot} - CO - ^{\cdot}Cl$ , 51.3/27.9), 127/129 ( $[Cl_2(OCH_3)C_6H_2O]^{\cdot} - CO - HCl$ , 48.4/16.4).

**3-13** 2-(4,5 dichloro-2-methoxyphenoxy)vinyl alcohol trimethylsilylether.

[MW=307]:

306/308 ( $M^{+}$ , 2.6/0.9), 217/219 ( $M^{+} - ^{\cdot}OSi(CH_3)_3$ , 15.6/7.9), 191/193/195 ( $[Cl_2(OCH_3)C_6H_2O]^{\cdot}$ , 3.1/2.7/0.5), 103 ( $^{\cdot}CH_2OSi(CH_3)_3$ , 100).

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**7** 1-(3,4-dimethoxyphenyl)-2-(2-methoxyphenoxy)propane 1,3-diol.

[MW=418]:

418 ( $M^{+}$ , 56.9), 299 ( $M^{+}$  -  $^{\circ}\text{OCOCH}_3$  -  $\text{HOCOCH}_3$ , 54.7), 298 ( $M^{+}$  - 2  
 $\text{HOCOCH}_3$ , 27.0), 235 ( $M^{+}$  -  $\text{HOCOCH}_3$  -  $^{\circ}\text{OC}_6\text{H}_4(\text{OCH}_3)$ , 58.4), 209  
 $([\text{C}(\text{CH}_3\text{O})_2\text{C}_6\text{H}_3\text{CH}(\text{OCOCH}_3)]^{+}$ , 100), 193 (36.5), 167 ( $[\text{C}(\text{CH}_3\text{O})_2\text{C}_6\text{H}_3\text{CH}(\text{OH})^{+}$ ,  
 76.6), 149 ( $[\text{C}(\text{CH}_3\text{O})_2\text{C}_6\text{H}_3\text{CH}]^{+}$ , 33.6), 139 (51.1), 124 (37.2).

**7-1** 1-(6-chloro-3,4-dimethoxyphenyl)-2-(2-methoxyphenoxy)propane 1,3-diol.

[MW=452.5]:

452/454 ( $M^{+}$ , 61.1/18.2), 350/352 ( $M^{+}$  -  $\text{CH}_3(\text{CO})\text{O}(\text{CO})\text{CH}_3$ , 50.2/8.9),  
 333/335 ( $M^{+}$  -  $\text{CH}_3\text{CO}_2\text{H}$  -  $\text{CH}_3\text{CO}_2^{\circ}$ , 48.9/10.4), 268/270 ( $M^{+}$  -  $\text{CH}_3\text{CO}_2^{\circ}$  -  
 $^{\circ}\text{OC}_6\text{H}_4(\text{OCH}_3)$ , 25.2/7.8), 269/271 ( $M^{+}$  -  $\text{CH}_3\text{CO}_2\text{H}$  -  $^{\circ}\text{OC}_6\text{H}_4(\text{OCH}_3)$ ,  
 63.4/25.2), 243/245 ( $[\text{Cl}(\text{CH}_3\text{O})_2\text{C}_6\text{H}_2\text{CH}(\text{OCOCH}_3)]^{+}$ , 100/37.6), 201/203  
 $([\text{Cl}(\text{CH}_3\text{O})_2\text{C}_6\text{H}_2\text{CH}(\text{OH})]^{+}$ , 50.2/15.8)

**7-2** 1-(6-chloro-3,4-dimethoxyphenyl)-2-(4 or 5 chloro-2-methoxyphenoxy)propane 1,3-diol. [MW=487]:

**a)** 486/488 ( $M^{+}$ , 47.6/19.5), 367 ( $M^{+}$  -  $\text{CH}_3(\text{CO})\text{O}(\text{CO})\text{CH}_3$ , 14.6), 329  
 $(M^{+}$  -  $^{\circ}\text{OC}_6\text{H}_3(\text{OCH}_3)\text{Cl}$ , 22.0), 269/271 ( $M^{+}$  -  $\text{CH}_3\text{CO}_2\text{H}$  -  $^{\circ}\text{OC}_6\text{H}_3(\text{OCH}_3)\text{Cl}$ ,  
 47.8/18.3), 243/245 ( $[\text{Cl}(\text{CH}_3\text{O})_2\text{C}_6\text{H}_2\text{CH}(\text{OCOCH}_3)]^{+}$ , 100/26.8), 227/229  
 (59.8/25.6), 201/203 ( $[\text{Cl}(\text{CH}_3\text{O})_2\text{C}_6\text{H}_2\text{CH}(\text{OH})]^{+}$ , 52.4/19.5), 195/197  
 (85.4/52.4).

**b)** 486/488 ( $M^{+}$ , 34.5/40.3), 367 ( $M^{+}$  -  $\text{CH}_3(\text{CO})\text{O}(\text{CO})\text{CH}_3$ , 22.8), 329  
 $(M^{+}$  -  $^{\circ}\text{OC}_6\text{H}_3(\text{OCH}_3)\text{Cl}$ , 69.6), 269/271 ( $M^{+}$  -  $\text{CH}_3\text{CO}_2\text{H}$  -  $^{\circ}\text{OC}_6\text{H}_3(\text{OCH}_3)\text{Cl}$ ,  
 43.9/20.5), 243/245 ( $[\text{Cl}(\text{CH}_3\text{O})_2\text{C}_6\text{H}_2\text{CH}(\text{OCOCH}_3)]^{+}$ , 100/36.8), 227/229  
 (45.0/14.0), 201/203 ( $[\text{Cl}(\text{CH}_3\text{O})_2\text{C}_6\text{H}_2\text{CH}(\text{OH})]^{+}$ , 14.04/5.1), 195/197  
 (59.6/40.3).

7-3<sup>a</sup> 1-(6-chloro-3,4-dimethoxyphenyl)-2-(4,5-chloro-2-

methoxyphenoxy)propane 1,3-diol. [MW=581.5]:

580 ( $M^{+}$ , 8.6), 430 (12.4), 345 (7.2), 307 (2.6), 273/275

( $[Cl(CH_3O)_2C_6H_2CH(OCOCH_3)]^{+}$ , 100/38.2).

7-4 1-(2 or 5,6-dichloro-3,4-dimethoxyphenyl)-2-(4,5-dichloro-2-

methoxyphenoxy)propane 1,3-diol. [MW=556]:

554 ( $M^{+}$ , 8.9), 492 (7.8), 477 (18.9), 429 (6.7), 363/365 ( $M^{+}$  -

$^{\circ}OC_6H_2(OCH_3)Cl_2$ , 20.0/11.1), 277/279 ( $[Cl_2(CH_3O)_2C_6HCH(OCOCH_3)]^{+}$ ,

56.7/18.9), 261/263 ( $M^{+}$  -  $CH_3(CO)O(CO)CH_3$  -  $^{\circ}OC_6H_2(OCH_3)Cl_2$ ,

100/45.6), 235/237 ( $[Cl_2(CH_3O)_2C_6HCH(OH)]^{+}$ , 53.3/22.5).

7-5 1-(2 or 5,6-dichloro-3,4-dimethoxyphenyl)-2-(3 or 6,4,5-trichloro-2-

methoxyphenoxy)propane 1,3-diol. [MW=590.5]:

588/590/592 ( $M^{+}$ , 25.8/33.3/30.2), 363/365 ( $M^{+}$  -  $^{\circ}OC_6H(OCH_3)Cl_3$ ,

41.0/35.2), 277/279 ( $[Cl_2(CH_3O)_2C_6HCH(OCOCH_3)]^{+}$ , 70.2/30.1), 261/263

( $M^{+}$  -  $CH_3(CO)O(CO)CH_3$  -  $^{\circ}OC_6H(OCH_3)Cl_3$ , 100/64.8), 235/237

( $[Cl_2(CH_3O)_2C_6HCH(OH)]^{+}$ , 87.2/46.2).

7-6 1-(2,5,6-trichloro-3,4-dimethoxyphenyl)-2-(4,5-dichloro-2-

methoxyphenoxy)propane 1,3-diol. [MW=:590.5]

588/590 ( $M^{+}$ , 10.3/20.0), 397/399/401 ( $M^{+}$  -  $^{\circ}OC_6H_2(OCH_3)Cl_2$ ,

52.6/60.3/30.2), 311/313 ( $[Cl_3(CH_3O)_2C_6CH(OCOCH_3)]^{+}$ , 59.6/40.3),

295/297/299 ( $M^{+}$  -  $CH_3(CO)O(CO)CH_3$  -  $^{\circ}OC_6H_2(OCH_3)Cl_2$ , 100/88.5/10.4),

269/271 ( $[Cl_3(CH_3O)_2C_6CH(OH)]^{+}$ , 25.3/30.6).

<sup>a</sup> identified by GC-MS, after silylation.

7-7 1-(2,5,6-trichloro-3,4-dimethoxyphenyl)-2-(3 or 6,4,5 trichloro-2-methoxyphenoxy)propane 1,3-diol. [MW=625]:

622/624/626 ( $M^{+}$ , 10.2/31.2/10.3), 504 ( $M^{+} - 2 CH_3CO_2H$ , 397/399 ( $M^{+} - ^\bullet OC_6H(OCH_3)Cl_3$ , 27.1/68.7), 398/400 ( $M^{+} - HOC_6H(OCH_3)Cl_3$ , 66.7/35.4), 337/339 ( $M^{+} - ^\bullet OC_6H(OCH_3)Cl_3 - CH_3CO_2^\bullet$ , 15.6/45.8), 311/313/315 ( $[Cl_3(CH_3O)_2C_6CH(OCOCH_3)]^+$ , 95.8/79.2/18.7), 295/297/299 ( $M^{+} - CH_3(CO)O(CO)CH_3 - ^\bullet OC_6H(OCH_3)Cl_3$ , 100/95.8/35.4).

7-8 4,5-dichloroveratrole. [MW=207]:

206/208 ( $M^{+}$ , 55.3/37.2), 191/193 ( $M^{+} - CH_3^\bullet$ , 64.2/24.8), 163/165 ( $M^{+} - CH_3^\bullet - CO$ , 21.4/20.0), 148 (8.9), 133 (18.4), 128/130 ( $M^{+} - CH_3^\bullet - CO - ^\bullet Cl$ , 50.2/14.2), 127/129 ( $M^{+} - CH_3^\bullet - CO - HCl$ , 40.8/20.2), 99/101 (54.2/21.3); and comparison with authentic sample of 4,5-dichloroveratrole.

7-9 trichloroveratrole. [MW=241.5]:

240/242/244 ( $M^{+}$ , 48.6/54.2/17.6), 225/227/229 ( $M^{+} - CH_3^\bullet$ , 91.3/40.3/23.2), 197 ( $M^{+} - CH_3^\bullet - CO$ , 19.4), 181 (17.4), 162/164 ( $M^{+} - CH_3^\bullet - CO - Cl^\bullet$ , 64.5/44.6); and comparison with authentic sample of trichloroveratrole.

7-10 tetrachloroveratrole. [MW=276]:

274/276 ( $M^{+}$ , 47.4/50.8), 259/261 ( $M^{+} - CH_3^\bullet$ , 15.6/54.3), 218/220 ( $M^{+} - CH_3^\bullet - CO$ , 17.2/8.6), 196/198 ( $M^{+} - CH_3^\bullet - CO - Cl^\bullet$ , 19.8/17.2); and comparison with authentic sample of tetrachloroveratrole.

7-11<sup>a</sup> 3-hydroxy-2-(4,5 dichloro-2-methoxyphenoxy)propanaldehyde.

[MW=337]:

262 ( $M^{+} - HSi(OCH_3)_3$ , 32.1), 246/248 ( $M^{+} - HOSi(OCH_3)_3$ , 100/48.6), 176 ( $M^{+} - HOSi(OCH_3)_3 - 2 Cl^\bullet$ , 75.9).

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<sup>a</sup> identified by GC-MS, after silylation.



### CLAIMS TO ORIGINAL RESEARCH

Previous studies of the reactions of non-phenolic lignin model compounds with a large excess of chlorine in glacial acetic acid at room temperature had led to the conclusion that side-chain displacement was the primary reaction in the solubilization of lignin. Until now, however, the reaction of non-phenolic benzyl aryloxy model compounds had not been investigated.

In this work, a number of appropriate non-phenolic alpha-aryloxy model compounds, differing in the nature of their side chains, were prepared. Chlorine at various levels, from low to large excess, was reacted with the model compounds in glacial acetic acid at room temperature. This study, which has had no precedent in the literature, has revealed that, unlike benzyl alkyl ether bonds, benzyl aryl ether bonds were cleaved by catalytic amounts of chlorine before aromatic substitution occurred. Thus this research has demonstrated the unique property of benzyl aryl ethers, and reinforces the concept of their key-role, as cross-link points in the polymer, in the degradation of lignin network. Our finding of the catalytic action of molecular chlorine is also important to the problem of minimizing the formation of chlorinated compounds during pulp bleaching.

An appropriate mechanism was proposed for the ether cleavage, consistent with the observation that the catalysis occurs only with aryl ethers, and not alkyl ethers.

Non-phenolic alpha-alkoxy and alpha-hydroxy model compounds were also prepared and examined, and some published experiments were repeated in which chlorine was used in large excess. The new feature is that in the reactions with low levels of chlorine all major reaction products were identified. This permitted an unambiguous and precise insight in the nature of the primary substitution products and led to the correction of an inexactitude in the literature. The influence of the various ring substituents on ring chlorination could be rationalized.

The reaction of benzyl aryl ethers with molecular HCl in glacial acetic acid was also investigated for the first time. It was found that the compounds cleaved, not by the expected hydrolysis, but by a mechanism analogous to that of cleavage by chlorine.

Finally, appreciable improvements were made in the synthesis and etherification of lignin model compounds.

### SUGGESTIONS FOR FUTURE STUDIES

- 1) Investigate the reaction of molecular chlorine in 100% anhydrous glacial acetic acid with selected benzyl aryl ether lignin model compounds of lower reactivity, and in which aromatic substitution by chlorine cannot take place. A compound having the structure of compound 2, and chlorinated at the most aromatic sites - i.e para to each methoxyl group - might be suitable.
  - 2) Re-investigate the reaction of alpha-aryloxy models such as 1-(3,4-dimethoxyphenyl)-1-(2-methoxy-4-methylphenoxy)-2-(2-methoxyphenoxy)-3-propanol (2), so that precise yields can be obtained in the analysis of the products. The results will permit fitting the chlorine degradation of lignin to the Flory-Stockmayer theory.
  - 3) Investigate the chlorination of alpha-aryloxy model compounds in aqueous acetic acid, under controled pH conditions. This study will provide additional information on the mechanism of ether cleavage by chlorine.
  - 4) Investigate the reaction of molecular chlorine with CUOXAM lignin from spruce wood under the same conditions as for the model compounds. The initial lignin preparation and both the solubilized and residual lignin can be characterized by conventional methods such as IR spectroscopy, determination of the OMe content, and elemental analysis; the results will be compared with the data existing in the literature for other methods of lignin degradation.
- In the investigation on residual lignin, more modern methods can also

be used, in particular solid state Cross Polarization/Magic Angle Spinning (CP/MAS)  $^{13}\text{C}$  NMR spectroscopy, paying particular attention to the chemical shift domain of the carbons from the side chain (located between those of the methoxy and the aromatic carbons). Dipolar dephasing experiments, which permit to distinguish the signals produced by methyl and quaternary carbons from the other signals, may help for the determination of the signals of interest. Preliminary solid-state NMR study of appropriate model compounds will also be necessary.

Gel Permeation Chromatography coupled to Low Angle Light Scattering (GPC-LALLS) will be used in order to determine the evolution of the Mw distributions of the solubilized and residual lignins as a function of the charge of chlorine applied and to correlate the results with the gel-degradation theory. Examination of the effect of reaction time on the degradation process may be also necessary if the heterogeneity of the reaction medium lowers the efficiency of the catalysis of the cleavage benzyl aryl ether bonds present in lignin.