

Lignin and Lignans

Advances in Chemistry

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9 Reactivity of Lignin- Correlation with Molecular Orbital Calculations

Thomas Elder and Raymond C. Fort, Jr.

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INTRODUCTION

To date, and as can be seen from the other chapters of this text, the structure and chemistry of lignin have been described in terms of results from a wide range of chemical or spectroscopic methods to construct a mosaic picture of the polymer. The current chapter continues this process by describing past, present and potential applications of electronic structure calculations to the chemistry of lignin, and correlation with experimental results. Although there may be a tendency to consider experiment and theory as two distinct approaches with little in common, the boundary is becoming increasingly blurred as calculations are extensively integrated with experiment. Improvements in algorithms can provide results with chemical accuracy, such that calculations now represent another "analytical" methodology,

and have been described as an "M.O. spectrometer" [1]. Theoretical methods represent another tool that can be used to complement other techniques, a strategy that has found extensive applications in other branches of chemistry. It is in this spirit that this chapter is written. While this chapter is concerned with the specific applications of molecular orbital calculations to lignin, a general and brief introduction to the vocabulary of computational chemistry is also in order.

COMPUTATIONAL CHEMICAL PRELIMINARIES

We are living at a very fortunate and interesting time with respect to computational chemical techniques. Until about the mid-1980s, calculations in chemistry were primarily the domain of relatively few specialists who were largely concerned with improving theoretical predictions on small molecules or even single atoms. The calculations were, to a large extent, studies of the methodology, rather than the molecules. In the recent past, however, due to the rapid improvements in capabilities of computer hardware and software, along with major improvements in accessibility, computational methods have become readily available to practicing chemists. Calculations have become an indispensable tool, similar to spectroscopic resources. A brief perusal of the major chemistry journals will reveal computational applications ranging from small molecules (both organic and inorganic) to large polymer systems and biomolecules.

The general term "molecular modeling" is usually taken to include both classical mechanical and quantum mechanical calculations, along with visualization of results. While the charge of the current chapter is to report on molecular orbital calculations as they have been applied to lignin, a short synopsis of classical mechanical methods and some references to general literature may be of some use.

MOLECULAR MECHANICS

Classical mechanical calculations, also referred to as force-field or molecular mechanics calculations treat molecular structures, as the name implies, as a classical mechanical system, in which the energy of a structure is the sum of a number of subterms that will include, but are not limited to bond stretching, angle bending, torsion, and nonbonded terms. Stretching and bending can be described as harmonic potentials, or by using the somewhat more sophisticated Morse potential. Spring constants describe the stiffness of the bond, and deviations from the specified equilibrium distance or angle, for a given group of atoms, will increase the energy of the system. Torsional energy, associated with twisting or changes in dihedral angles, depends on a parameterized barrier height, multiplicity (i.e., the number of minima encountered in a 360° rotation) and a phase factor describing the geometry at which the minimum energy is found. The simplest nonbonded terms are described by van der Waals interactions using a Lennard-Jones potential and coulombic terms for electrostatics. More sophisticated calculations will begin to include cross-terms (e.g., stretch-bend). It is important to be aware that these calculations do not address the presence of electrons, but rather concentrate only on the behavior of the nuclei.

Owing to the computational simplicity of force-field calculations, very large systems can be examined in short periods of time. These are the methods of choice for studying the structure of synthetic polymers, proteins, nucleic acids, and inorganic networks such as zeolites. Force-fields are also used to provide the energies in molecular dynamics calculations, in which the time evolution of structures can be examined.

The parameter sets, defining the bond lengths, angles, torsion, and nonbonded interactions can be very specific for a given application, such as proteins or nucleic acids. This specificity can lead to surprising failures due to missing parameters even for relatively common atom types and combinations.

Among the major parameter sets used for force-field calculations are those from the University of Georgia, the most recently released of which is MM4 [2], which has very general applicability. Other general force-fields include Sybyl from Tripos Associates [3], and Dreiding [4] and UFF [5], both of which originated at Cal Tech. Among the more specific parameter sets are Gromos [6], AMBER [7], and CHARMM [8] for proteins and nucleic acids, and Momec for inorganic systems [9]. Major references describing the parameterization details and exhaustive examples of force-field calculations include Burkert and Allinger [10], Coomba and Hambley [11], and Rappé and Casewit [12].

MOLECULAR ORBITAL CALCULATIONS

In contrast to force-field calculations in which electrons are not explicitly addressed, molecular orbital calculations, use the methods of quantum mechanics to generate the electronic structure of molecules. Fundamental to the quantum mechanical calculations that are to be performed is the solution of the Schrödinger equation to provide energetic and electronic information on the molecular system. The Schrödinger equation cannot, however, be exactly solved for systems with more than two particles. Since any molecule of interest will have more than one electron, approximations must be used for the solution of the Schrödinger equation. The level of approximation is of critical importance in the quality and time required for the completion of the calculations. Among the most commonly invoked simplifications in molecular orbital theory is the Born-Oppenheimer [13] approximation, by which the motions of atomic nuclei and electrons can be considered separately, since the former are so much heavier and therefore slower moving. Another of the fundamental assumptions made in the performance of electronic structure calculations is that molecular orbitals are composed of a linear combination of atomic orbitals (LCAO).

Molecular orbital calculations can be divided into two large categories, described as *ab initio* and semiempirical, depending on the approximations that are made. The former method is more rigorous, using only mathematical functions and natural constants to describe the atomic orbitals of which the molecular orbitals are composed, via linear combinations. The latter calculations incorporate experimental data and the neglect of the more extensive and time consuming computational details that are explicitly performed in *ab initio* calculations. At the time of this writing, and as a function of computer and basis set, *ab initio* calculations can be feasibly performed

on systems with several tens of atoms, while semiempirical calculations can handle several hundreds of atoms.

***Ab Initio* Calculations**

Ab initio calculations are defined in terms of a method or level of theory and the basis set that is used. The methods differ in how interactions between electrons are treated while the basis sets describe the shape of the orbitals. For comprehensive discussions of *ab initio* calculations see the texts by Hehre et al. [14], Leach [15], and Young [16].

The most commonly used method is the Hartree-Fock calculation in which interactions between electrons are treated as the interaction of one electron within an average field of the remaining electrons. Electron interactions are, of course, much more specific than this, and include Pauli repulsions as well as electrostatic ones. Electron correlation can be addressed by various methods, but among the most commonly used are configuration interaction and Moeller-Plesset perturbation theory.

Configuration interaction (commonly abbreviated CI) includes excited states, which, the argument goes, could become populated due to repulsion between electrons. A linear combination of the wavefunctions for the ground state and the excited states should lead to a better (lower) energy for the atom.

In Moeller-Plesset theory, the mixing in of excited states is treated as a series of perturbations with designations MP_n (usually MP2, MP3, MP4), where *n* designates the point at which the series is truncated. Moeller-Plesset theory is less laborious than CI, and thus has displaced the latter method in most *ab initio* calculations, where the computational labor is already high.

Recently, another class of calculations, density functional theory (DFT) has become quite common. This method is faster than *ab initio* calculations for similar levels of performance, and has the advantage that correlation effects are included, at least in part. According to this theory, the properties of a molecular system are functions of the electron density, rather than a wave function (as described by the Schrödinger equation). There is some degree of debate over whether DFT is an *ab initio* calculation or in a class by itself. Parenthetically, one of the recipients of the 1998 Nobel Prize for Chemistry was Walter Kohn, in recognition of his development of density functional theory.

Once a level of theory is selected, a basis set must be chosen. Basis sets are available in a large range of complexity, and the choice exerts considerable influence on the accuracy and time required for the calculation. Basis sets, with their specific and somewhat confusing nomenclature, are incorporated into comprehensive computer programs that will control the calculation and the amount of ancillary information that is reported. Among the standard packages for *ab initio* calculations are Gaussian, Gamess, Jaguar, and HyperChem.

Basis sets will differ in the number of basis functions that are included. The simplest type is a *minimal* basis set, in which each atom is represented by a single orbital of each type, as in sophomore organic chemistry. Thus, a carbon atom would have a 1s orbital, a 2s orbital, and one 2p orbital along each Cartesian axis. An example of a minimal basis set is STO-3G.

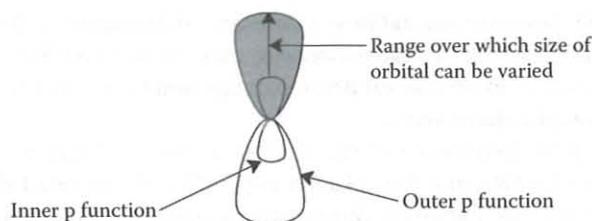


FIGURE 9.1 Split basis set showing inner and outer orbitals.

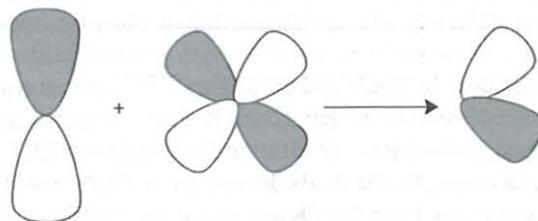


FIGURE 9.2 Polarization basis set of a p orbital by mixing with d function.

In the next level of sophistication, a *split valence* basis set, each valence orbital is described by two basis functions representing the inner and outer parts of the orbital. These two terms can be varied independently, and examples are the 3-21G, 6-31G basis sets. Similarly, a triply split basis set is 6-311G. Split valence basis sets will allow the size of the orbitals to change, while the addition of polarization functions, designated as 6-31G(d) or 6-31G*, allow the shape of the orbital to change. This is done by the addition of d-orbitals to all heavy atoms, such that now each nonhydrogen atom will have 15 basis functions (Figure 9.1).

To provide more accurate descriptions of anions, or neutral molecules with unshared pairs, basis sets may be further augmented with so-called diffuse functions. These are intended to improve the basis set at large distances from the nuclei, thus better describing the barely bound electrons of anions. For example, a p-orbital on carbon may be polarized away from the nucleus by mixing into it a d-orbital. Such a basis set will be designated with a "+" as in 6-31+G(d), adding an additional four basis functions to each heavy atom (Figure 9.2).

Increasingly complex basis sets are generated by further splitting of orbitals, and the addition of further polarization and/or diffuse functions. As basis functions are added, the number of orbitals to be evaluated is effectively increased, resulting in a simultaneous and exponential (fourth power) increase in time requirements for a given system. As a consequence, a computational study must take into account the size of the system, and computational resources to establish the feasibility of a particular effort.

Semiempirical Calculations

While *ab initio* calculations have become much more feasible for relatively large molecules, their performance in a reasonable length of time may be predicated on access to high throughput computers. Semiempirical calculations can, however, be

readily executed on small workstations or even personal computers. While still based on quantum mechanics, these calculations are more rapid to perform than *ab initio* due to the inclusion of experimental parameter sets and the exclusion of some of the more tedious computational steps.

Historically, there have been two major efforts in the development of semiempirical calculations under the direction of John Pople (Nobel Laureate 1998) and M.J.S. Dewar. The earliest calculations of this nature are, however, the Hückel (HMO) and extended Hückel molecular orbital calculations (EHMO). While not mathematically rigorous, or used extensively at the present time, these calculations can provide considerable insight into the methods and in specific applications can be quite accurate.

True Hückel molecular orbital calculations, among other limitations, only address π -electrons. All atom, semiempirical calculations that include both π - and σ -electrons were developed originally by Pople and coworkers [17] implementing the method of complete neglect of differential overlap (CNDO), followed by the increasingly rigorous method of intermediate neglect of differential overlap (INDO) [18].

For general applications, the methods developed by Pople have largely been supplanted by the calculations from the Dewar group originating at the University of Texas. The first-generation program from this group was MINDO/3 [19], and while successful had systematic errors in heats of formation and bond angles. The subsequent method, the modified neglect of diatomic overlap (MNDO) [20] has been extensively parameterized to cover a larger number of elements, and was the foundation of the more recent AM1 [21] and PM3 [22] methods.

WHAT INFORMATION CAN BE OBTAINED AND HOW IS IT USED?

The output from a molecular orbital calculation, regardless of the specific computational method used, will always report a number of results. These will include the geometry of the system, the total energy for *ab initio* calculations, heat of formation for semiempirical calculations, the energy of each molecular orbital and the coefficients of the atomic orbitals for each atom.

The geometry that is reported at the end of a calculation will depend on how the calculation is performed and what options are initially invoked. The molecular geometry is used as the basic input for all of the calculations that have been discussed thus far, and the geometry can be described in several ways. Although current technology allows the user to sketch an input structure or build it from fragments, the positions of each atom are converted to either Cartesian or internal coordinates for computational purposes. Internal coordinates, or a Z-matrix, describe the molecular structure in terms of bond lengths, bond angles, dihedral angles and connectivity, and for most computational chemistry applications are easier to use than Cartesian coordinates [23]. If diffraction data is available, fractional coordinates that define the dimensions of the unit cell will be reported, and depending on the software, can be input directly. Fractional coordinates are generally converted by the computer program into internal coordinates.

Since the geometry of a molecule will markedly affect the energy, the development of a reasonable geometry is essential. While this might be done with chemical

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intuition, geometry optimization methods are more consistent and systematic in this regard. Given that energy is a function of geometry, it is theoretically simple to determine by derivative methods the geometry at which the energy is minimized, and therefore representative of the preferred structure. Difficulties arise, however, due to the multidimensional nature of the energy surface. Determining a minimum on such a surface can be problematic, and there are usually several nonlinear optimization methods (e.g., eigenvector following, Davidon-Fletcher-Powell, and Newton-Raphson) incorporated into a computational package [24].

While energy minimizations have become routine, even for relatively sophisticated *ab initio* calculations, it must be borne in mind that the geometry that is identified will only represent a local minimum. Optimization methods are always searching for a minimum and, therefore, will not cross energy barriers, even to reach lower energy structures. As a consequence, conformational searching may be required in order to insure that a suitable geometry is found [25].

Conformational searching involves varying the molecular structure followed by energy calculations, as a means of sampling the potential energy surface and identifying low-energy structures. In theory, changes in bond lengths, angles, and dihedral angles would need to be altered in a rigorous exploration of the surface. In practice, however, changing lengths and angles require large amounts of energy in comparison to changes in dihedral angles that also impart large structural changes. Most conformational search procedures therefore concentrate on modifications to dihedral angles.

There are several methods by which conformational searches can be performed, none of which are guaranteed to identify the global minimum. The most straightforward method is the grid search, in which selected dihedral angles are systematically rotated through a specific number of increments, followed by an energy calculation or minimization. Systematic searches such as these will sample all parts of the surface, but depending on how finely the rotations are divided may miss important conformations. Furthermore, grid searches can be very time consuming, since the number of conformations to be evaluated increases exponentially with the number of bonds considered. For example, for a β -O-4 dimer in which the six rotatable bonds are examined, in 60-degree increments, over 46,000 conformations would be generated. Even at an extremely optimistic calculation rate of one conformation per minute, this calculation would take more than 30 days to complete. Clearly, if a systematic search is to be employed, the researcher must use chemical intuition to limit the scope of the search.

Alternatives to systematic searches include random searches, genetic algorithms, and simulated annealing. A random search, as the name implies, generates random variations in structure, for which energy minimizations are performed and populations of conformers identified. Genetic algorithms begin with a large population of random conformations, the individuals of which have varying levels of "fitness." The more fit members are selected and the procedure is repeated to identify low-energy structures. Simulated annealing is analogous to the annealing process in metallurgy, in that the energy of the structure is increased to a very high temperature, followed by a cooling step. At suitably elevated temperatures, all of conformational space is available (i.e., energy barriers can be crossed). Upon cooling and subsequent energy

minimization the low-energy conformers can be selected. In general, conformational searching, particularly the nonsystematic methods, generate so many possible conformations that the calculations must be performed via force-field calculations. Once a smaller set of likely conformations has been selected, molecular orbital calculations can be utilized.

The values reported for the energies of a molecule are in molar quantities and are not directly comparable for nonisomeric structures. Of greater utility are the computed energetics of reactions. The reactions for which the estimation of energetics is possible can be divided into several categories depending on the conservation of electron spin and electron pairs.

Reactions in which the numbers of paired electrons are not conserved are classified as nonisogyric reactions. Examples include homolytic bond dissociations and transition state calculations. In contrast, isogyric reactions conserve the number of paired electrons, such as in heterolytic bond dissociations and some isomerizations. Last, isodesmic reactions are bond conserving and not only maintain the division of electrons into shared and unshared pairs, but also maintain the number and type of bonds between heavy atoms (nonhydrogen).

Of considerable interest and difficulty with respect to calculations is the topic of transition state location. Strictly speaking, the transition state is the structure existing at the highest energy point (a first-order saddle point) on the reaction coordinate between reactants and products.

For reactants and products, experimental data can be developed to define both structures and energies. The energy of the transition state can be defined by an experimental difference from the reactant energy: the activation energy. Kinetic isotope effects can be used to infer structural features for the transition state, but in most cases the description of the molecular arrangement in the transition state is possible only by computation. From the reaction coordinate, the reactant, product, and transition states are all stationary points such that the derivative of the energy with respect to the reaction coordinate is zero. At the minima (reactant, product) the second derivative is greater than zero, while at the maxima (transition states) the second derivative is less than zero. Since the second derivatives of the reaction coordinate are in fact the force constants from which vibrational spectra may be calculated, the minima have all real vibrational frequencies while transition states have one imaginary (negative) frequency, allowing for the verification that a transition state has been identified.

Although defining and characterizing a transition state in this way once it has been found seems straightforward, actually locating it is more complex. For some processes, the reaction coordinate is relatively easy to define, making the transition state structure straightforward to characterize. For some reactions simple bond lengths or dihedral angles will correspond to the reaction coordinate. In many other cases, however, with multiple bonds forming and breaking, no single bond distance or angle adequately describes the process.

The simplest approach for determining the transition state might just be an initial guess at the structure based on chemical intuition or symmetry constraints. Somewhat better is using a transition state that has been obtained at the intended level of calculation for a simpler system, or alternatively saving computation time by

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locating the specific transition state at a lower level of theory, and then proceeding to the desired level. Other methods are the linear or quadratic synchronous transit (LST and QST) techniques in which the transition state is an average of reactant and product geometries. These are straightforward for unimolecular reactions but more complicated for higher order reactions, where one must create a complex of reactants and/or products. If a useful definition of the reaction coordinate can be made, one can actually follow the reaction from reactants through the transition state to products using the intrinsic reaction coordinate (IRC) approach. Optimizations are performed by sequentially constraining a given geometric term (e.g., bond length or dihedral angle) to fixed values along the reaction coordinate. Alternatively, IRC calculations may begin with a transition state structure and work backward toward reactants or forward toward products.

The atomic orbital coefficients that are printed can be used to determine electron densities, and in most computer programs are employed internally to generate graphical representations of the molecular orbitals. Furthermore, according to frontier molecular orbital theory, bond formation is dependent on overlap between the highest occupied molecular orbital of the nucleophile and lowest unoccupied molecular orbital (LUMO) of the electrophile. The magnitude of the coefficients in the appropriate molecular orbital at a particular atom provides an indication of reactivity.

Another set of values that is almost always printed in the output are the atomic charges. Due to the qualitative familiarity that chemists have with this property it is tempting to use such data as measures of reactivity as well. Charge is not, however, a quantum mechanical term and arises from an arbitrary partitioning of electron density. Among the most common of the partitioning schemes is Mulliken population analysis in which electron density is summed over orbitals centered on atoms, and between nuclei electron density is evenly divided. Due to this somewhat artificial method of assignment, charge must be used with caution. Charge is also sensitive to the basis set that is used, such that the absolute values are not particularly significant and cannot be compared between methods or structures. Relative charges can be used for limited and clearly defined purposes.

A critical part of applying computational methodology to the solution of chemical problems lies in defining the problems in such a way that the "computables" enumerated above can be related to chemical observables.

APPLICATIONS TO LIGNIN CHEMISTRY

The use of molecular orbital calculations as a tool in lignin chemistry has been reviewed in the past by Shevchenko [26], Remko [27] and Elder [28]. It will be seen from these papers that a large proportion of the early work in this area was reported in journals from the former Soviet Union and Eastern Europe. The relative unavailability of these periodicals in the west has made this branch of lignin chemistry somewhat inaccessible to many researchers.

Reports on the application of molecular orbital calculations specifically to the chemistry of lignin dates back at least as far as 1966 and the work of Lindberg and coworkers [29,30,31]. In the paper by Lindberg and Tylli [30], Hückel molecular orbital calculations were used in studies on a range of monomeric model compounds

to determine π -electron charge densities, bond orders, and free valences. A linear relationship was detected between these data and the rate of protodeuteration. Similarly, the relative ease of ether cleavage reactions involving the methoxyl group was predicted among the models. Finally, the electrochemical reduction of model aldehydes was generally related to the calculated electronic results.

The later work [31], extended the initial results and revealed an excellent correlation between pK of phenols and the change in π -electron energy between free phenolic and the phenolate anion. Also, a generally linear relationship was reported for the critical oxidation potential (COP) and the energies of the highest occupied molecular orbital for the phenolate anions.

RADICALS

Among the earliest examples of the application of molecular orbital calculations to lignin chemistry is, as might be expected, the formation and reactivity of phenoxy radicals [32]. This work described the use of Pariser-Parr-Pople molecular orbital calculations, comparing various methods to determine the π -electron spin densities for a number of model compounds. The different techniques gave similar results, with the bulk of the unpaired spin density at the phenolic oxygen, followed by the *ortho* and *para* carbons. In a cinnamaldehyde model, the β -position also exhibited considerable unpaired spin density.

In more recent work on coniferyl alcohol, using an all-electron method (MNDO) and geometry optimization [33] it was found that while the phenolic oxygen does indeed have appreciable unpaired spin density, the *ortho* and *para* carbons within the aromatic ring are considerably larger in this respect, with the β -position being about equal to the oxygen. Similarly, Russell et al. [34], using AM1 semiempirical calculations on cinnamic acids and alcohols, in concert with electron spin resonance spectroscopy, found that while relatively low, the spin density at the phenolic oxygen increased with methoxyl content. The spin densities at the β -position and the available *ortho*-carbons were about equal, and interpreted as accounting for the β - β and β -5 linkages that are reported to dominate the polymer produced from coniferyl alcohol.

The coupling of radicals to form σ -complexes and dilignols was examined from a thermodynamic standpoint with PM3 calculations [35]. All combinations of σ -complexes formed through positions with positive spin densities were completed. Among these, the products with significant steric hindrance were energetic, while the β -5, β - β , β -O were the most stable, with the 5-5 couple intermediate in energy. These results are in accord with those reported from experimental results on the initial coupling reactions [36].

PULPING AND BLEACHING

Arguably the most important reactions of lignin from an industrial perspective are those concerned with pulping and bleaching. These have also been the subject of investigation using molecular orbital calculations. Computational research of this type has included work on conventional processes, alternative pulping catalysts and enzymatic bleaching.

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Given the importance of the quinone methide in kraft pulping, the nature of this intermediate and its reactivity toward nucleophiles has been the subject of considerable scrutiny. These reactions have been interpreted in terms of hard-soft acid-base (or more generally electrophile/nucleophile) theory. In this theory, a hard acid (or electrophile) will generally have a high-energy LUMO and a positive charge, whereas a hard base (or nucleophile) will have a low-energy highest unoccupied molecular orbital (HOMO) and a negative charge. Interactions between hard reactants occur through coulombic attraction. Conversely, soft bases will have a high-energy HOMO and do not always carry a negative charge, while soft acids will have a low-energy LUMO and may or may not have a positive charge. Soft-soft reactions occur due to interactions between the LUMO of the electrophile and HOMO of the nucleophile, the frontier molecular orbitals (FMO) [37].

These phenomena, with respect to lignin chemistry were summarized by Zarubin and Kiryushina [38] who presented the results of Hückel molecular orbital (presumably EHMO) calculations for a large number of monomeric and dimeric model compounds. From this work it was proposed that the reactive sites in lignin are soft entities, and that the sulfhydryl anion is softer than the hydroxide ion, accounting for the preferential reactions of SH^- in kraft pulping.

In a closely related study, Elder et al. [39], using all-atom semiempirical calculations, found that quinone methide intermediates exhibited a small partial negative charge at the α -carbon. This result led to questions over how nucleophilic attack could occur at a negatively charged carbon. Upon examining the frontier molecular orbitals, however, they found that the LUMO of the α -carbon was quite large, indicating the participation of the molecular orbitals rather than coulombic attraction in the initial reactions of kraft pulping.

Hard-soft acid-base arguments were also advanced by Shevchenko and Zarubin [40], using the results of CNDO/S calculations to show that both quinone methides and benzyl cations are soft electrophiles. Furthermore, it was proposed that the addition of a nucleophile to the α -carbon of the quinone methide was stereospecific, due to the nonequivalence of the orbital lobes on either side of the quinone methide plane.

Alternative pulping catalysts have also been addressed through molecular orbital calculations on anthraquinone and its various reactive forms and adducts. Shevchenko and Zarubin [40] interpret the reactivity of the C-10 position and the reduced form of anthraquinone in terms of the atomic orbital contributions to the HOMO. Elder et al. [41] performed MNDO calculations on anthraquinone, its radical anion and dianion, in an attempt to distinguish between a single electron transfer or ionic-adduct mechanism, respectively. The computational results indicated that the reaction of the dianion was considerably more exothermic than the anion-radical. The electronic data were, however, at variance with the proposed adduct mechanism, in that for both of the reduced forms the oxygen atoms had a very large partial negative charge, while the C-10 position carried a partial positive charge. Additionally, the oxygen atoms have generally higher HOMO electron densities than the salient carbons.

Of similar technological importance with pulping are the reactions related to pulp brightness, its generation and reversion. Both of these topics have been the subject of theoretical studies.

Although chlorine bleaching is largely a discontinued practice, the chemistry of lignin chlorination was examined by the application of MNDO calculations to coniferyl and sinapyl alcohols [42]. It has been proposed that the chlorination reaction is an electrophilic aromatic substitution, occurring through the chloronium ion at C-6, with side-chain displacement occurring at C-1, and also attack at the β -carbon in an ethylenic side chain. From calculations, it was reported that the aromatic carbon positions exhibit the largest HOMO coefficients, while the heat of reaction associated with reaction at the β -position is the lowest.

More recently, Garver [43] presented an excellent overview of the reactions of lignin model compounds toward both electrophilic and nucleophilic bleaching agents, comparing computational results with experiment. This MOPAC-93 study was interpreted in terms of charge densities, frontier orbitals and transition state theory. For example, the presence of the γ -carbonyl in coniferaldehyde resulted in a large partial positive charge at the γ -carbon. From these data, questions were raised about the possible mechanism for peroxide attack, and it was suggested that ionized phenolate groups and methoxyl groups would tend to separate the charge rather than diminish the partial positive charge at the carbonyl carbon. Garver [43] also invoked frontier molecular orbital theory in terms of both electron density and the energetics of orbital interaction, describing the relatively small energy differences between the quinone methide LUMO and various attacking nucleophiles. Finally, the reaction between acetoguaiacone (3-methoxy-4-hydroxyacetophenone) and the hydrogen peroxide anion in a totally chlorine free (TCF) bleaching process was considered. It has been proposed in the literature that acetoguaiacone exists as a tautomeric pair, with the hydrogen peroxide anion attacking the α -carbon of the quinone methide form. Calculations indicate that, based on charge density, the reaction alternatively occurs via the acetoguaiacone tautomer.

In other work related to bleaching chemistry, the reactions of chlorine dioxide with monomeric [44] and dimeric [45] lignin model compounds have been studied computationally. These studies closely parallel experimental work in which oxidation mechanisms were proposed [46-51]. In accord with the experimental work, which reports higher reactivity of phenolic compounds, the heats of reaction for these compounds are lower than those for etherified models. The experimentally based mechanisms were generally found to be energetically feasible, but in some cases the electronic results were not consistent with the proposed mechanisms.

The chemistry of enzymatic bleaching has been addressed using calculations [52] in a study of the lignin peroxidase complex II. A relationship was detected between the HOMO energy of the substrates and the association complex. In more recent work, Elder [53] reported on the oxidation reactions of veratryl alcohol itself and its interaction with a dimeric lignin model. Veratryl alcohol is a secondary metabolite produced by *Phanerochaete chrysosporium* and is a putative mediator for lignin peroxidase. Computationally, it was found that the oxidation of veratryl alcohol to veratraldehyde is largely controlled by the initial single-electron transfer, which is quite endothermic. In the addition of water to the veratryl alcohol cation radical, a number of reaction channels may be followed, but the formation of veratraldehyde is favored, in accord with experiment. Interaction of the veratryl alcohol cation radical

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with a lignin model indicates that when in close proximity, the unpaired electron density is being transferred to the lignin model, whereas at larger separations, the single electron predominates on the veratryl alcohol. In an *ab initio* study directly concerned with the interaction of veratryl alcohol and the lignin peroxidase active site [54], a distinct shift in the unpaired spin density toward the veratryl alcohol was observed, as the interunit distance decreased. Energetically, it was also found that the oxidation of veratryl alcohol is slightly exothermic.

Mediators essential for laccase bleaching of pulp have been the subject of coupled experimental and computational research by Sealy et al. [55]. This study examined the effect of substitution on N-hydroxybenzotriazole, and the activity of phthalimides. N-hydroxybenzotriazole itself was more effective in lowering kappa numbers than any of the derivatives that were tested. Computationally, the bond dissociation energy was generally lower for N-hydroxybenzotriazole than the derivatives. Similarly, the most active of the phthalimide mediators had the lowest bond dissociation energy.

Cole et al. [56] have reported on the brightness reversion reactions of high-yield pulps that have been subjected to lignin retaining bleaching. The reactions of thio-glycerols with quinones, which have been implicated in the photoyellowing process, have been examined as a method for brightness stabilization. Computationally, a Michael addition reaction was favored over a redox reaction for the model quinones that were studied. Furthermore, HOMO-LUMO energy differences paralleled the relative reactivities of the quinones. Among the less reactive quinones, the difference in heats of reaction between the Michael addition and redox mechanism were reduced, such that the latter route could become more competitive.

SPECTROSCOPY

Theoretical calculations can be of considerable utility in interpreting, verifying or refuting mechanisms that have been proposed from experimental evidence. Given the complexity of even model compound reactions, however, the mechanisms proposed, while not unreasonable, may not be unequivocal. In contrast, spectroscopic results, while possibly open to interpretation, represent a definite dataset. While a given observation may be explained by a number of conclusions; it is the interpretation and not the spectral data that is open to debate. Given this definition of the results from spectroscopy, the ability of theoretical methods to reproduce or correlate to spectroscopic data is an important measure of their validity.

Among the pioneering work on the application of molecular orbital calculations to lignin in general and spectral data in particular is the large body of research by Milan Remko and coworkers. These efforts, beginning in 1977 [57] were largely concerned with ultraviolet spectra using CNDO/CI and CNDO/s. Beginning with work on monomeric structures [57,58] good agreement with experiment was reported. Subsequent work was performed on quinone methides [58,59]. In later work [60,61], they applied CNDO/S to condensed and β -O-4 dimers. In addition to the work on specific lignin models, flavonoid, coumarone, and stilbene structures were addressed using the π -electron method of Pariser-Parr-Pople, which agreed well with experiment, especially for the determination of absorption maxima [62].

Similar work from the former Soviet Union used Hückel calculations to predict the UV/VIS spectra of lignin substructures [63]. In later papers, all-electron CNDO/S calculations were reported which were in good agreement with experiment [64]. Shevchenko et al. [65] showed the influence of conformation on UV spectra and also reported on the agreement between calculation and experiment. In work related to that of Remko, Burlakov et al. [66] compared theoretical and experimental results for quinone methides.

Working with quinones, implicated in the photoyellowing of high-yield pulps, Cole et al. [33] showed that semiempirical methodology could generate a very good linear relationship between HOMO–LUMO gap and UV absorptions, although absolute values of λ_{max} cannot be calculated at this level of theory. Furthermore, they were capable of reproducing accurately the IR spectrum of methoxybenzoquinone, using *ab initio* calculations and an appropriate scaling factor. Vibrational spectroscopy of lignin models has also been treated using force-field calculations by Jakobsens et al. [67].

While nuclear magnetic resonance spectroscopy has become an invaluable tool in lignin analysis, relatively little effort has been directed toward the calculation of such spectra for lignin model compounds. Liptaj et al. [68] compared conformational data for cinnamaldehyde models derived from NMR to calculation, and similar work on quinone methides at both semiempirical and *ab initio* levels has been reported by Korschin et al. [69].

The calculation of NMR chemical shifts has become feasible recently with improvements in both the speed and capabilities of computational chemical methods [70]. While the bulk of the theoretical work has been directed toward the calculation of ^{13}C chemical shifts, results for ^{17}O [71], ^{31}P [72], and hyperfine coupling constants for nitrogen [73] have also been reported. Calculated ^{13}C chemical shifts for a number of monomeric lignin models have been compared to experiment, with excellent correlations [74]. The sensitivity of the calculations to geometry is highlighted by the poor ability to reproduce the chemical shifts of methoxyl groups and other rotatable structures.

Although there have been few studies of this nature directly concerned with lignin or lignin models, there is a body of work on closely related substituted aromatics. In a study combining NMR and *ab initio* calculations on 1-(p-anisyl) vinyl cations, a 6-31G basis set provided successful information on both chemical shifts and rotational barriers [75]. In subsequent work, Facelli et al. [76] used low-temperature NMR techniques to examine observable differences between the chemical shifts of carbons that are ortho to the methoxyl group in anisole. The ^{13}C chemical shift tensors were calculated with the GIAO method, using self-consistent fields (SCF) and density functional theory and SCF with MP2 electron correlation. It was found that the isotropic shifts were most accurately calculated using density functional theory, while the MP2 method gave somewhat poorer results than SCF. Vanillin and 3-4-dimethoxybenzaldehyde were addressed in a coupled computational-experimental study, in which the structures were optimized at the MNDO semiempirical level, followed by GIAO calculations with a 6-311G** basis set [77]. The calculated values are generally high except for the methoxyl carbons. Among the remaining positions, the errors range from 3.4 to 10.9 ppm. This is in contrast to the results of Facelli et al. [76] in which the calculated shifts were generally lower

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than experiment. The results of Zheng et al. [77] may arise due to the sensitivity of NMR calculations to geometric accuracy [78]. Furthermore, a recent paper [79] compares a number of *ab initio* methods for calculating NMR shielding tensors, and recommends the use of hybrid density functional-Hartree-Fock methods.

In other analytical work, Shevchenko et al. [80] found excellent agreement between theoretical and experimental ionization potentials. Semenov and Khodyreva (81) compare photoelectron spectra with CNDO/S3 calculations and found good results. Semiempirical calculations, on a number of lignin model compounds have also been used as an aid in the interpretation of ESR spectroscopy [34]. In more general research on substituted aromatic systems [82] correlated experimental $\text{p}K_{\text{a}}$ values to semiempirical heats of formation and HOMO energies, with correlations in the 0.7–0.9 range.

CONFORMATION

The final area of research on lignin that has been addressed to any large extent by the application of computational methods deals with conformation and the influence of hydrogen bonds. Until the recent appearance of such work by Simon and Erkssohn [83,84], this topic was dominated by researchers from the group in Riga, Latvia [85] and Milan Remko and coworkers in Bratislava.

Work on monomeric lignin models was initiated by Remko and Polčín in 1976, using CNDO/2 to examine intramolecular hydrogen bonding in guaiacyl and syringyl models [86], hydroxyphenyl carbonyls [87], and the conformation of *cis*-cinnamaldehyde [88]. The strengths of the hydrogen bonds are reported to be quite variable, with the guaiacyl/syringyl models being very small (0.5–6.3 kJ/mol), while the 2-hydroxyphenyl carbonyls are much larger (33–44 kJ/mole). In both cases a planar conformation was found. Qualitatively similar results were found using perturbation configuration interaction using local orbitals (PCILO) [89].

Based on the results of intramolecular hydrogen bonding, work was begun on intermolecular bonding to elucidate the nature of lignin-carbohydrate complexes. Initially, small polar molecules were used as models for carbohydrates. The complexes formed between the lignin-models and polar molecules were generally strongly hydrogen bonded [90–92]. Analogous work was done with sugar structures representing cellulose and hemicelluloses, and methanol representing the lignin, in which somewhat less energetic hydrogen bond networks were found [93]. As computing power improved, true lignin-carbohydrate complexes were modeled using monosaccharides and benzyl esters and ethers [94,95]. The latter paper indicated a large accessible potential energy surface.

Work on dimeric lignin structures began with the relatively simple biphenyls [96] in which the nonplanarity of the compounds was revealed. A comprehensive study of the conformation of various interunit linkages was published in 1983 [97]. Large, inaccessible areas were found on the potential energy surface of the β -aryl ethers. A solvation study, using PCILO found no relative changes in energies as a function of solvation [98], while within a β -aryl ether, an intramolecular hydrogen bond was detected between the α -OH and β -ether oxygen, along with the confined conformational space previously reported [99].

Using semiempirical calculations, Shevchenko et al. [100] studied the impact of conformation on charge and frontier molecular orbitals in quinone methides and benzyl cations. Charges were sensitive to conformation, while the frontier molecular orbitals were not. These data were used to interpret the stereoselectivity of quinone methides toward nucleophiles. Additional related work addressed the Z-E conformation about the C-1-C- α double bond in quinone methides. Konshcin et al. [69] reported that according to NMR results, the Z-conformation predominates a result that is in accord with their *ab initio* calculations. In similar work [101] it was proposed that the energetic barrier between the conformations was low enough to allow for interconversion at room temperature, taking issue with results from NMR reported by Ralph and Adams [102]. In subsequent work, it was reported that there is a significant barrier to rotation, as evidenced by both calculation and the resolution of both conformers by NMR [103].

In a series of recent studies, Simon and Eriksson have reported on the conformation and hydrogen bonding patterns of lignin model compounds using both force-field [83] and *ab initio* molecular orbital calculations. Among the latter papers, the first work dealt with a phenoxypropane diol, used to model the β -O-4 system in lignin and compare results from the MM3 force-field and HF/6-31G* calculations with respect to geometry, energy and hydrogen bonding [83].

The geometries obtained by the optimization of several conformers using both computational methods did not correspond well, and the force-field calculations resulted in more flexible structures. Based on the *ab initio* calculations, revised MM3 parameters were developed that improved the agreement between the methods. It was also proposed that the presence of hydrogen bonding would alter the rotation of the aromatic ring. This hypothesis was tested by the use of methoxybenzene and water, placed at varying distances from the methoxyl oxygen. As the interatomic distance increased there was a simultaneous decrease in hydrogen bonding, and increases in both the energy of the complex and rotational barrier.

A subsequent study explicitly addressed the conformation of dimeric β -O-4 structures [84], again using MM3 and HF/6-31G* in conjunction. Preliminary work on monomeric methoxylated compounds indicated the presence of an intramolecular hydrogen bond between primary alcoholic groups and the methoxyl group, stabilizing the structure. From these smaller structures, true β -O-4 dimers were constructed, in an effort to minimize computer time requirements. The most stable conformers for both *threo* and *erythro* configurations were found to be extended, rather than folded structures.

The most recent contribution from this group [104] concerned the elasticity of the β -O-4 structures, as related to the macroscopic mechanical properties of wood. Given that both elongation and compression of a molecular system are mainly concerned with torsional changes, rather than the more energetic perturbations in bond lengths and angles, the energies associated with such rotations are the principal focus of the paper. It was reported that when placed under tension, i.e., bond rotation to accommodate extension, the responses were similar between guaiacyl, syringyl, and *p*-hydroxyphenyl structures. Due to the presence of hydrogen bond networks, however, differences can be observed between *threo* and *erythro* configurations. As the methoxyl content increases, the rotational barrier and therefore stiffness increases.

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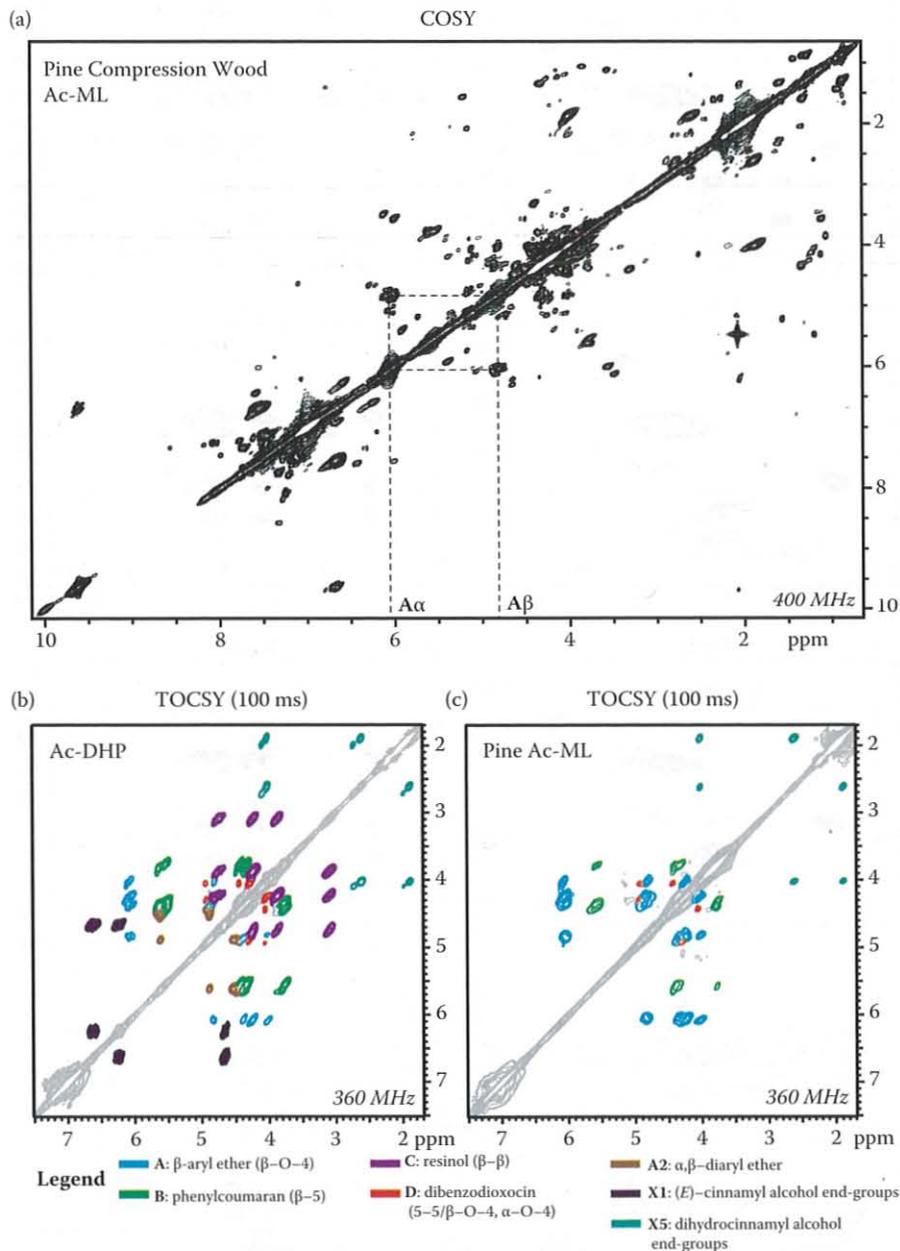
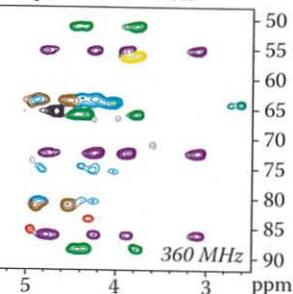
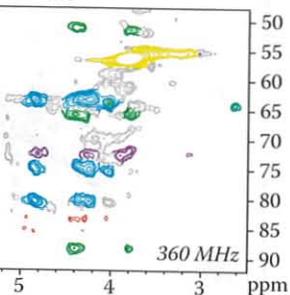


FIGURE 5.2 COSY and TOCSY spectra of acetylated lignins.

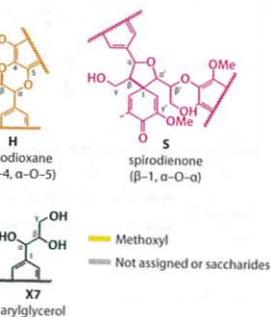
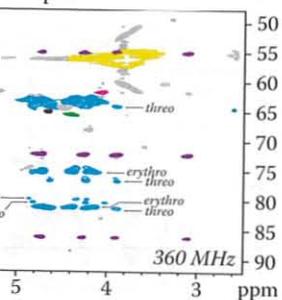
MQC-TOCSY - DHP



Pine



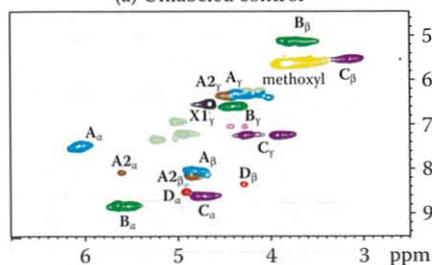
Poplar



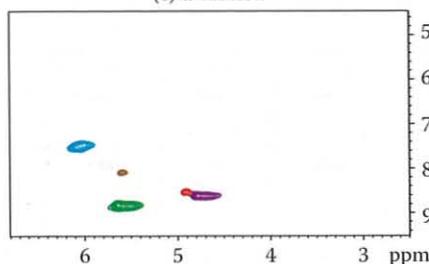
lignins.

HSQC

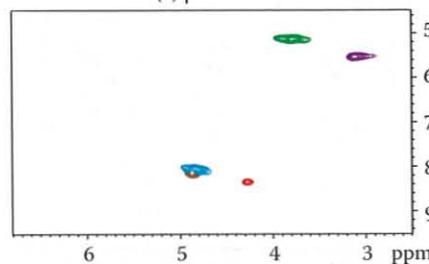
(a) Unlabeled control



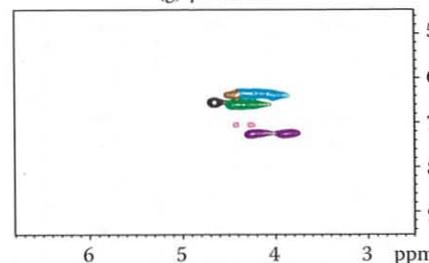
(c) α -labeled



(e) β -labeled

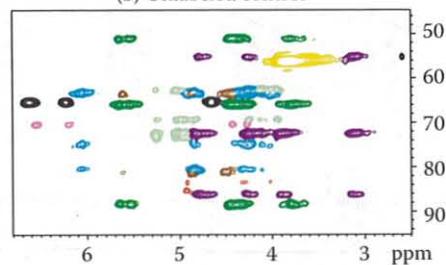


(g) γ -labeled

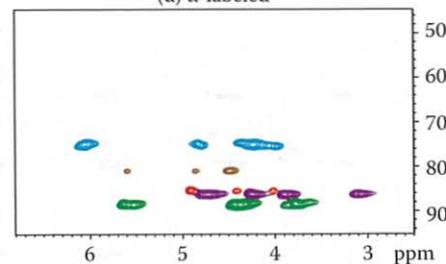


HSQC/TOCSY

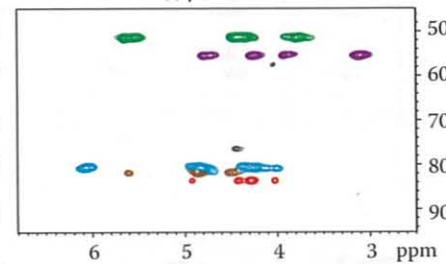
(b) Unlabeled control



(d) α -labeled



(f) β -labeled



(h) γ -labeled

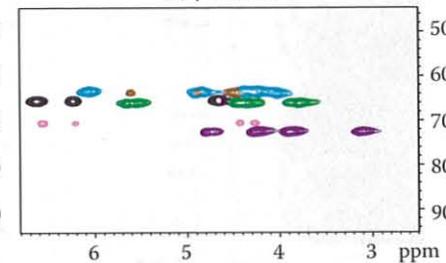


FIGURE 5.4 HSQC and HSQC-TOCSY spectra, and difference-spectra of acetylated synthetic lignins from specifically ^{13}C -enriched coniferyl alcohols.

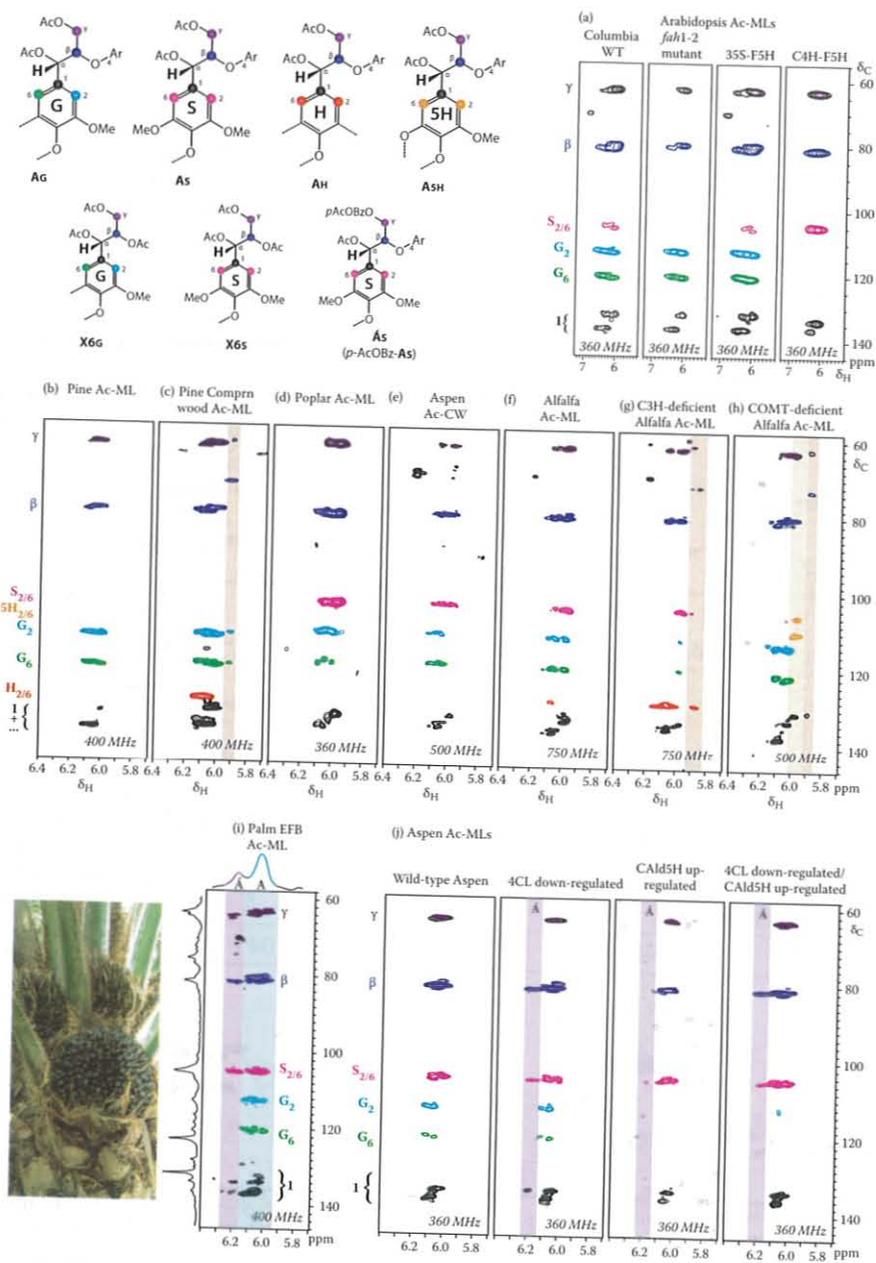
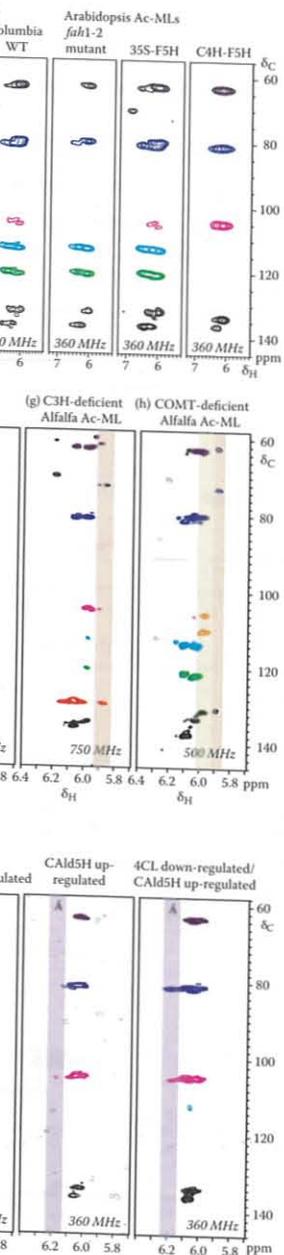


FIGURE 5.5 Heteronuclear long-range correlation (HMBC) spectra of acetylated lignins.

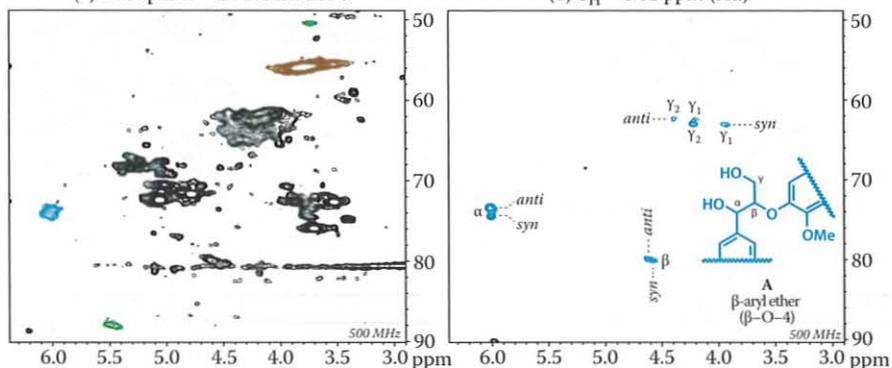


spectra of acetylated lignins.

3D TOCSY-HSQC: F_2 - F_3 planes, ^{13}C - ^1H (HSQC at a given ^1H shift)

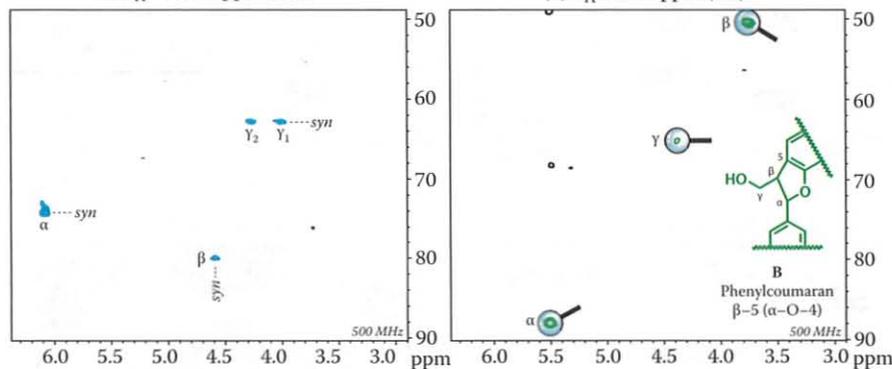
(a) First plane—all correlations

(b) $\delta_{\text{H}} = 6.01$ ppm ($\text{A}\alpha$)



(c) $\delta_{\text{H}} = 6.095$ ppm ($\text{A}\alpha$)

(d) $\delta_{\text{H}} = 5.50$ ppm ($\text{B}\alpha$)



(e-h) F_1 - F_2 planes, ^{13}C - ^1H (HSQC-TOCSY at a ^1H shift)

(i-l) F_1 - F_3 planes, ^1H - ^1H (TOCSY at a ^{13}C shift)

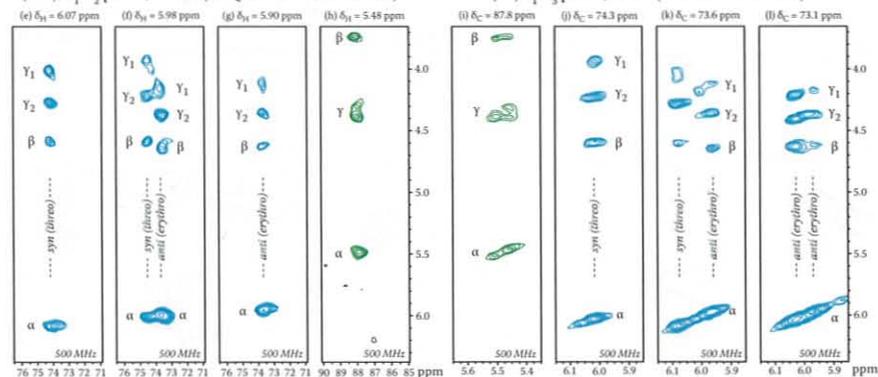
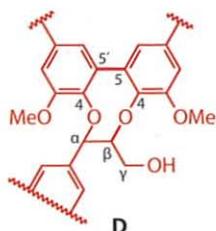
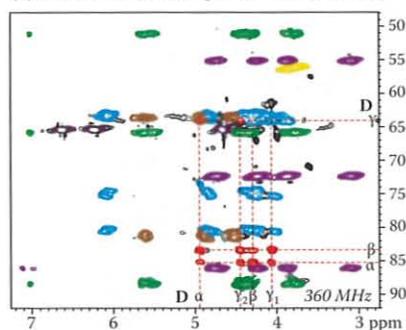


FIGURE 5.6 Slices from a 3D TOCSY-HSQC NMR spectrum of acetylated pine cell walls.

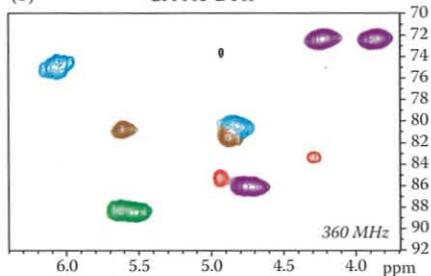


dibenzodioxocin (5-5/β-O-4, α-O-4)

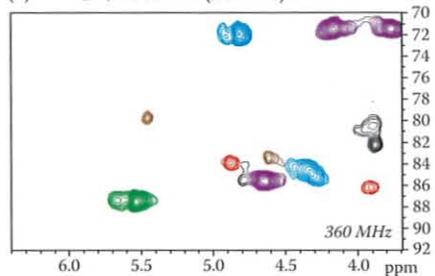
(a) CA Ac-DHP HMQC-TOCSY (125 ms)



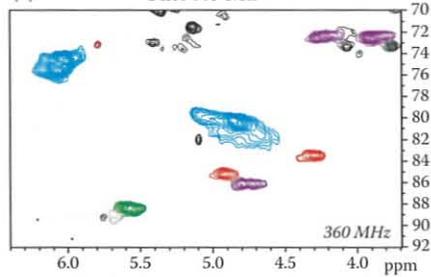
(b) CA Ac-DHP



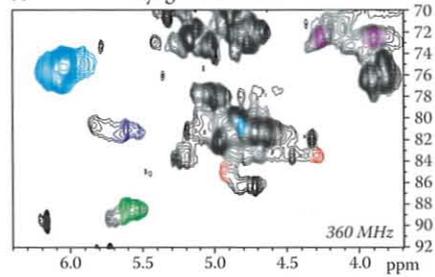
(e) CA/diFA-Ara (non-Ac) DHP



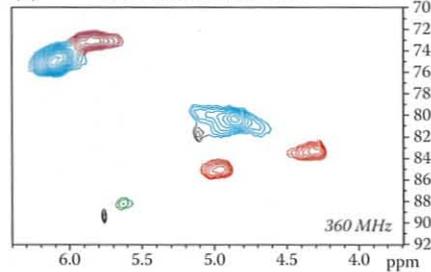
(c) Pine Ac-ML



(f) Ryegrass Ac-ML



(d) CAD-null Pine Ac-ML



(g) Aspen Ac-ML

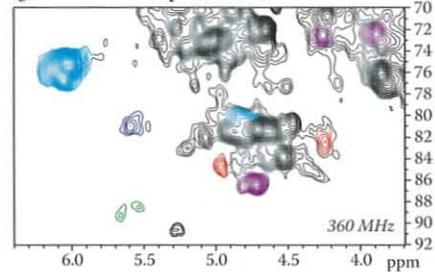
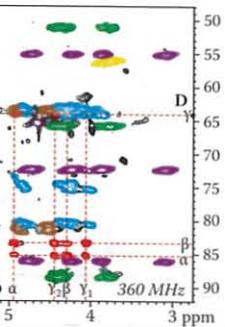
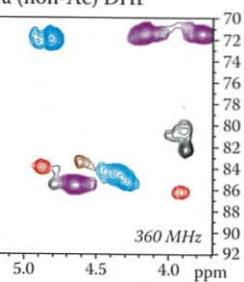


FIGURE 5.10 Dibenzodioxocins revealed in heteronuclear correlation spectra.

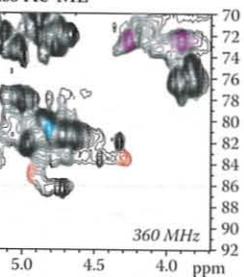
MQC-TOCSY (125 ms)



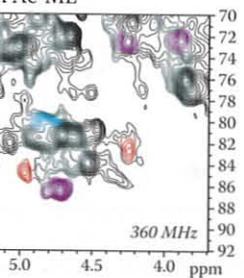
non-Ac) DHP



Ac-ML



Ac-ML



ation spectra.

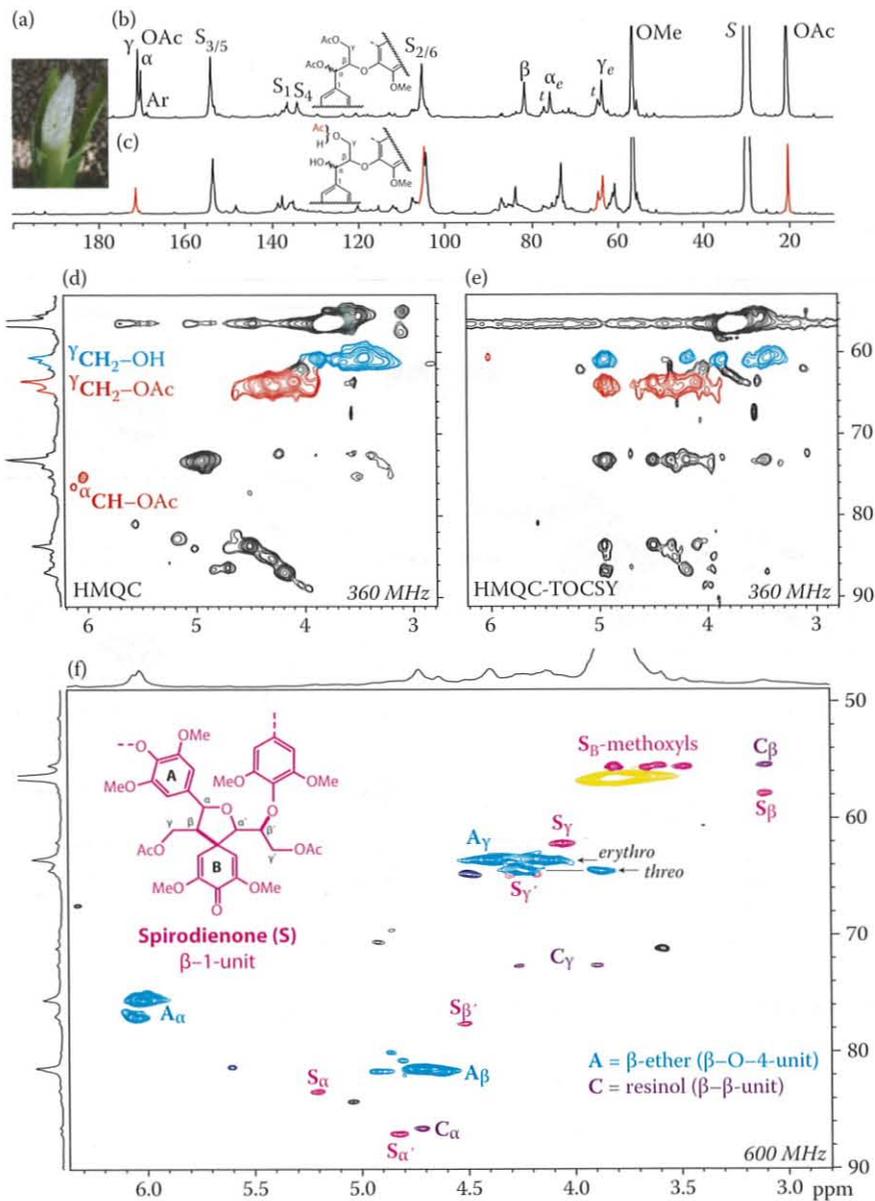


FIGURE 5.11 Spectra from Kenaf isolated lignin revealing natural γ -acetylation and spirodienone units.

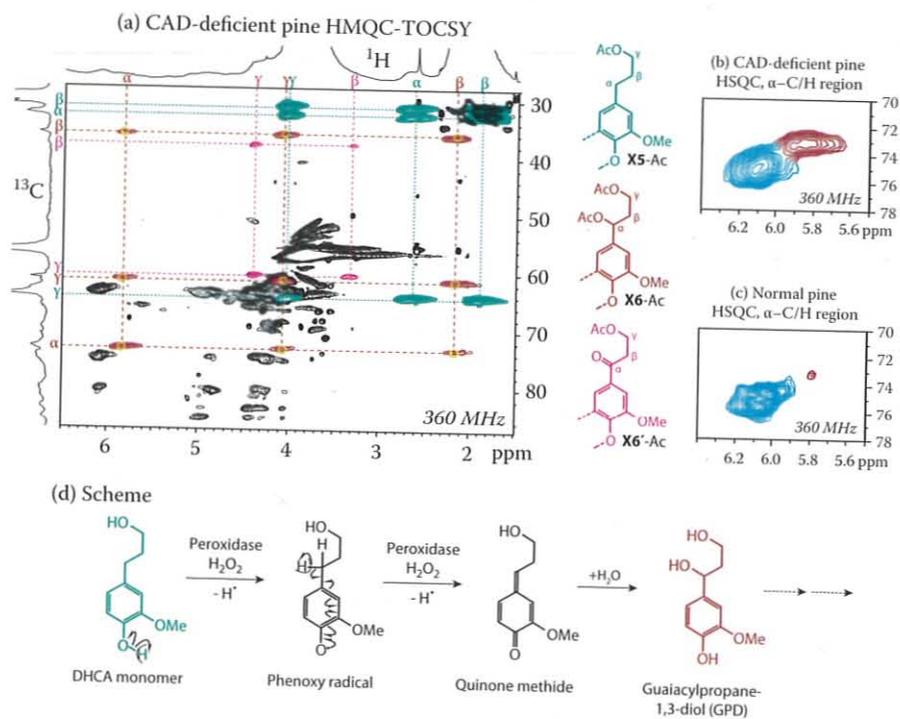
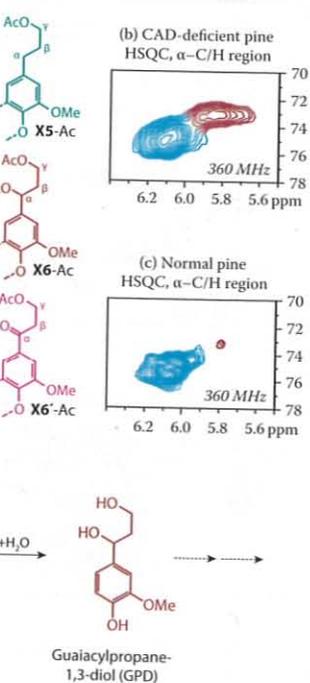


FIGURE 5.12 Dihydroconiferyl alcohol and its derived products in pine lignins.



Products in pine lignins.

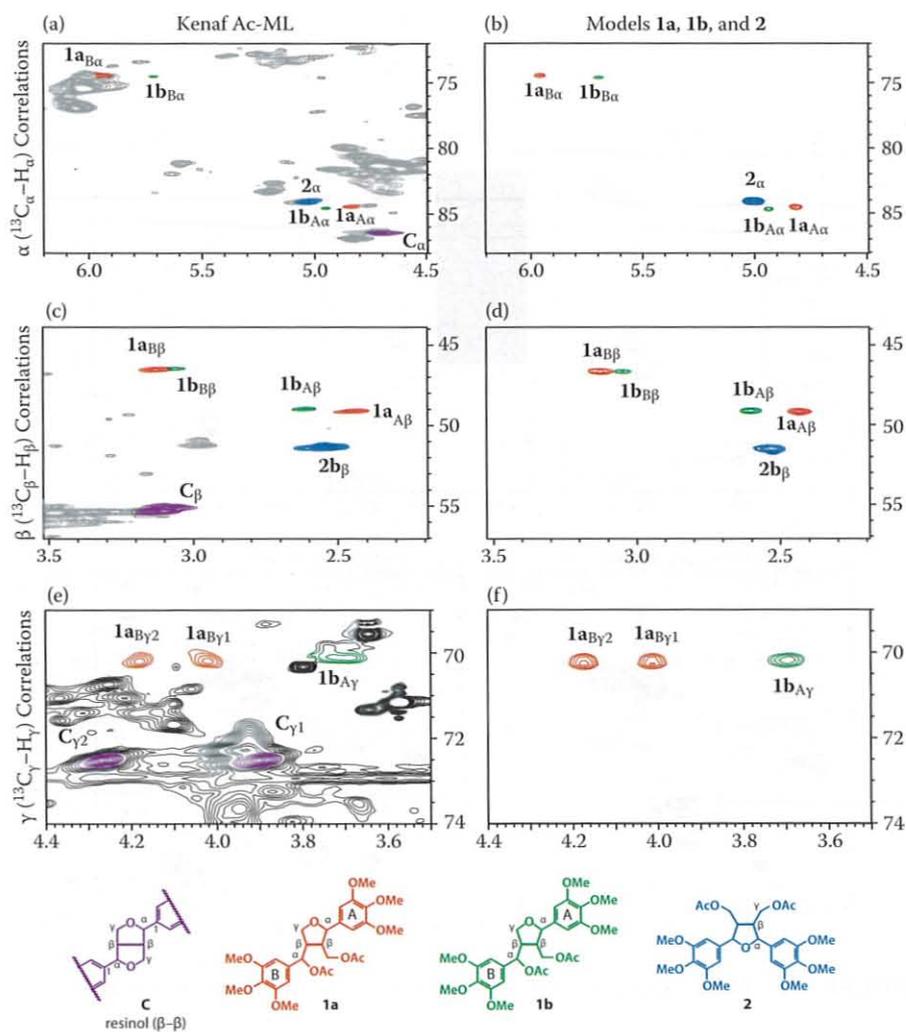


FIGURE 5.15 Novel β - β -coupled structures produced from γ -acylated sinapyl alcohol in Kenaf.

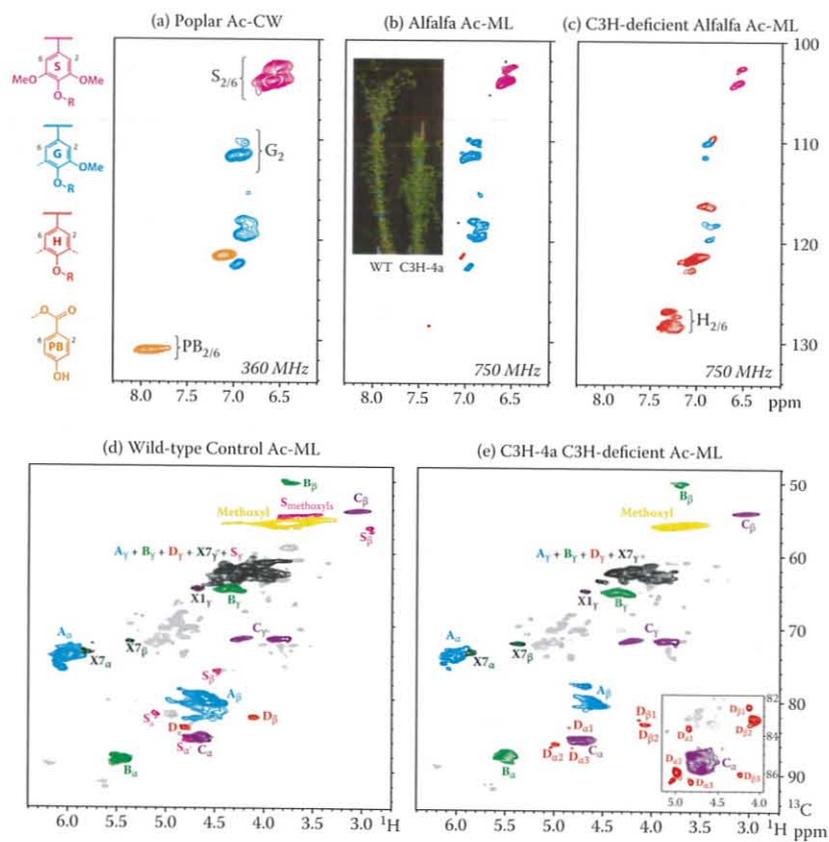
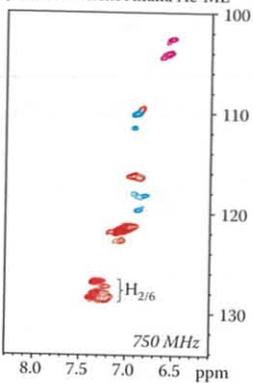
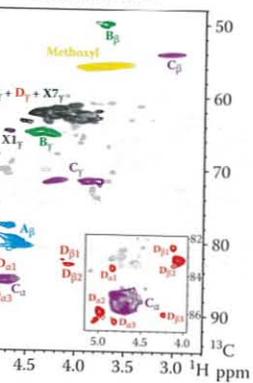


FIGURE 5.16 HSQC spectra of acetylated lignins having different H:G:S ratios.

c) C3H-deficient Alfalfa Ac-ML



C3H-deficient Ac-ML



different H:G:S ratios.

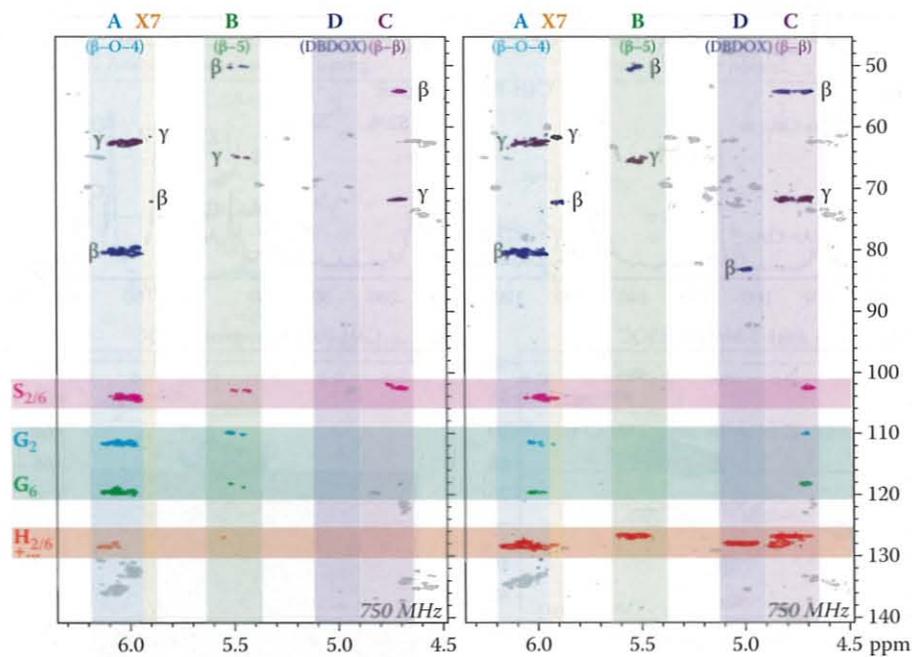


FIGURE 5.17 Partial HMBC spectra of control and C3H-downregulated alfalfa acetylated lignins.

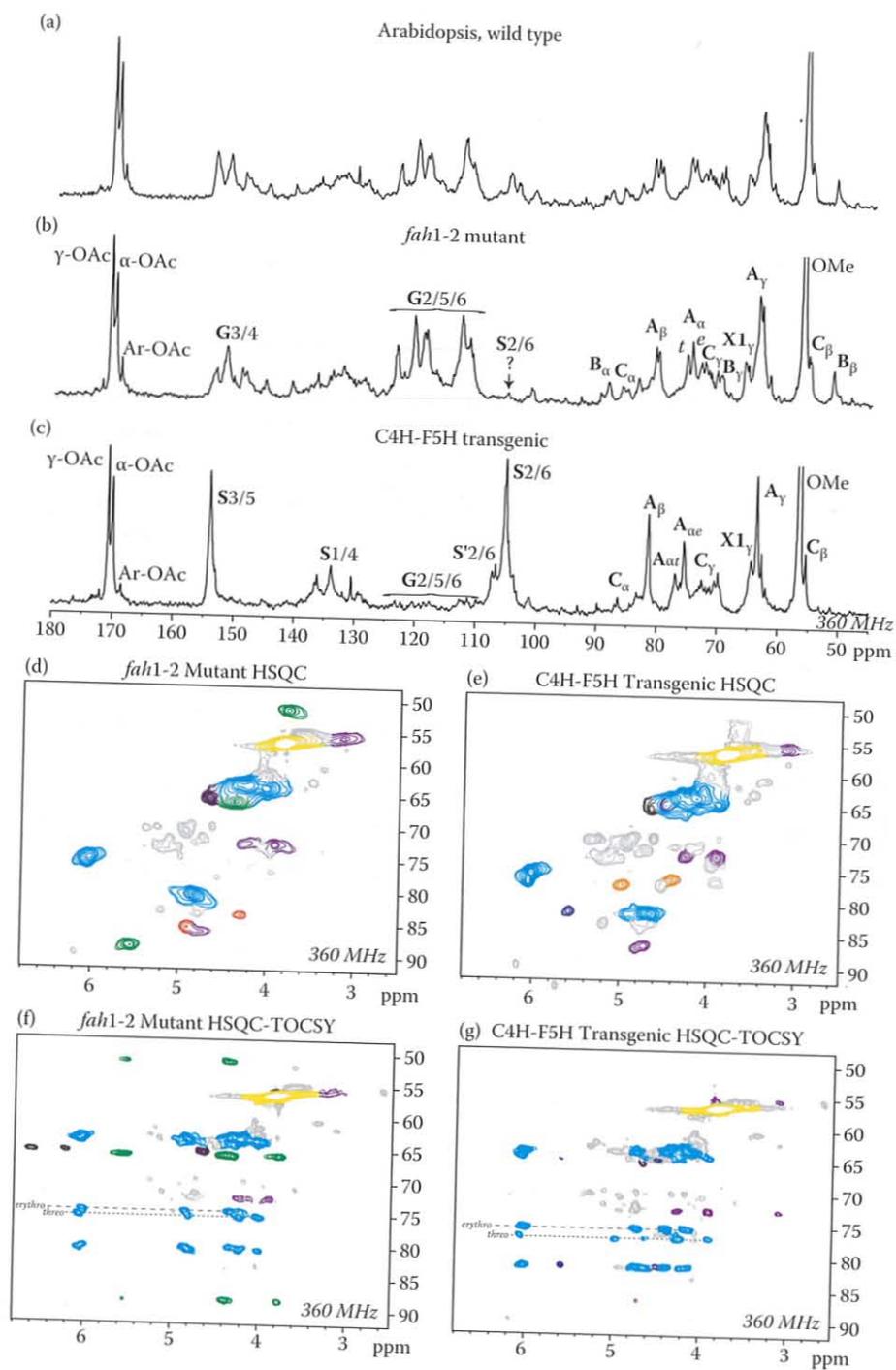
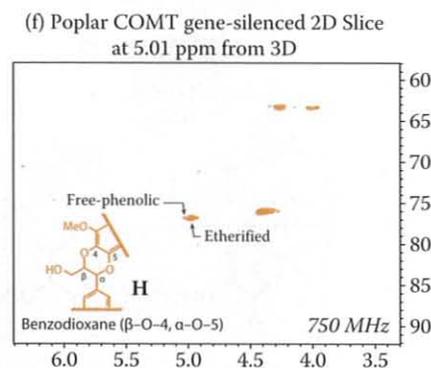
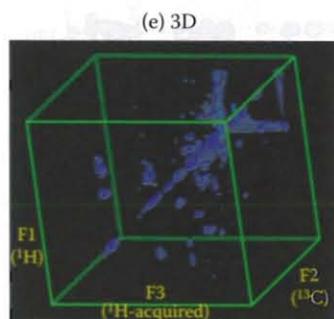
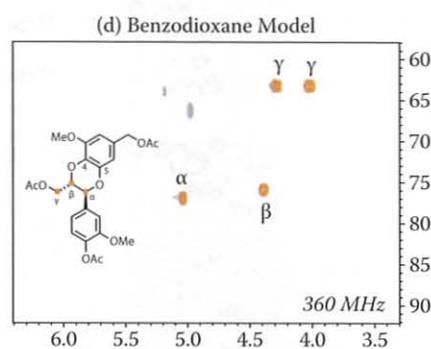
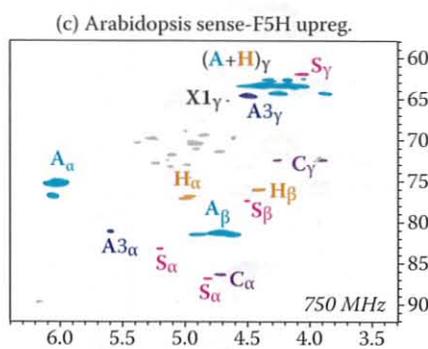
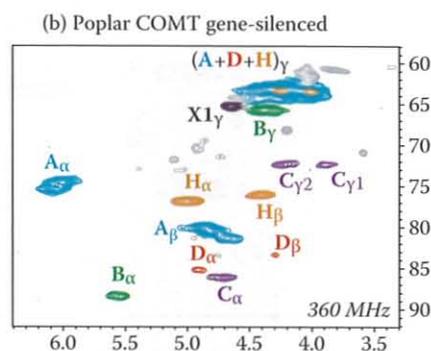
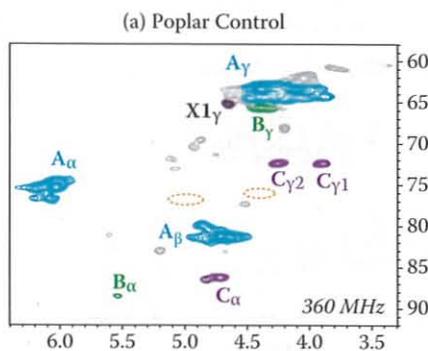
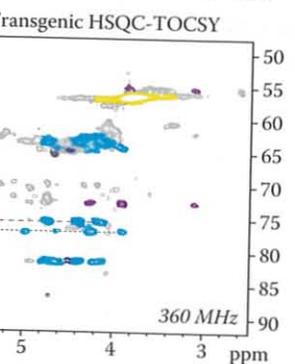
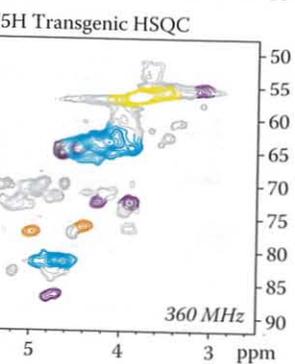
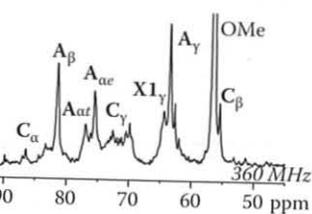
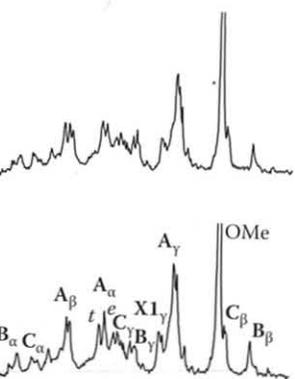


FIGURE 5.18 Spectra from wild-type and F5H-misregulated Arabidopsis lignins.



(g) Scheme for 5-hydroxyconiferyl alcohol incorporation into lignin, and benzodioxane formation

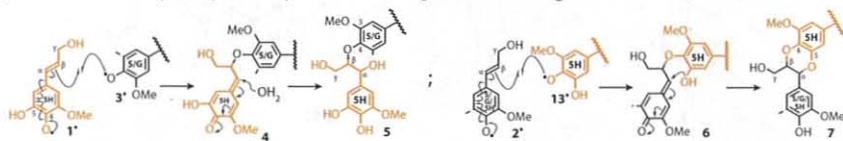


FIGURE 5.19 Partial HMQC spectra highlighting new benzodioxane units in F5H- and COMT-misregulated transgenics.

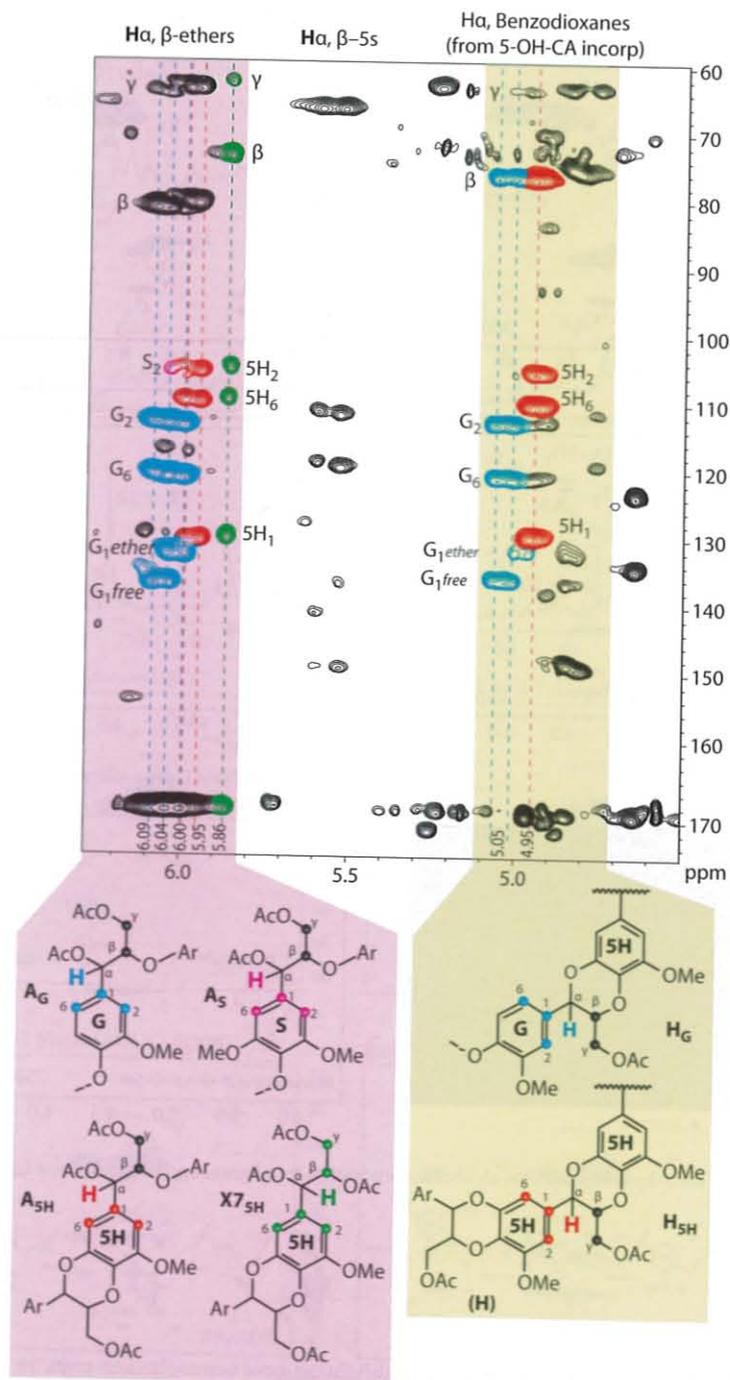


FIGURE 5.20 Partial HMBC of lignin isolated from COMT-deficient alfalfa.

cient alfalfa.

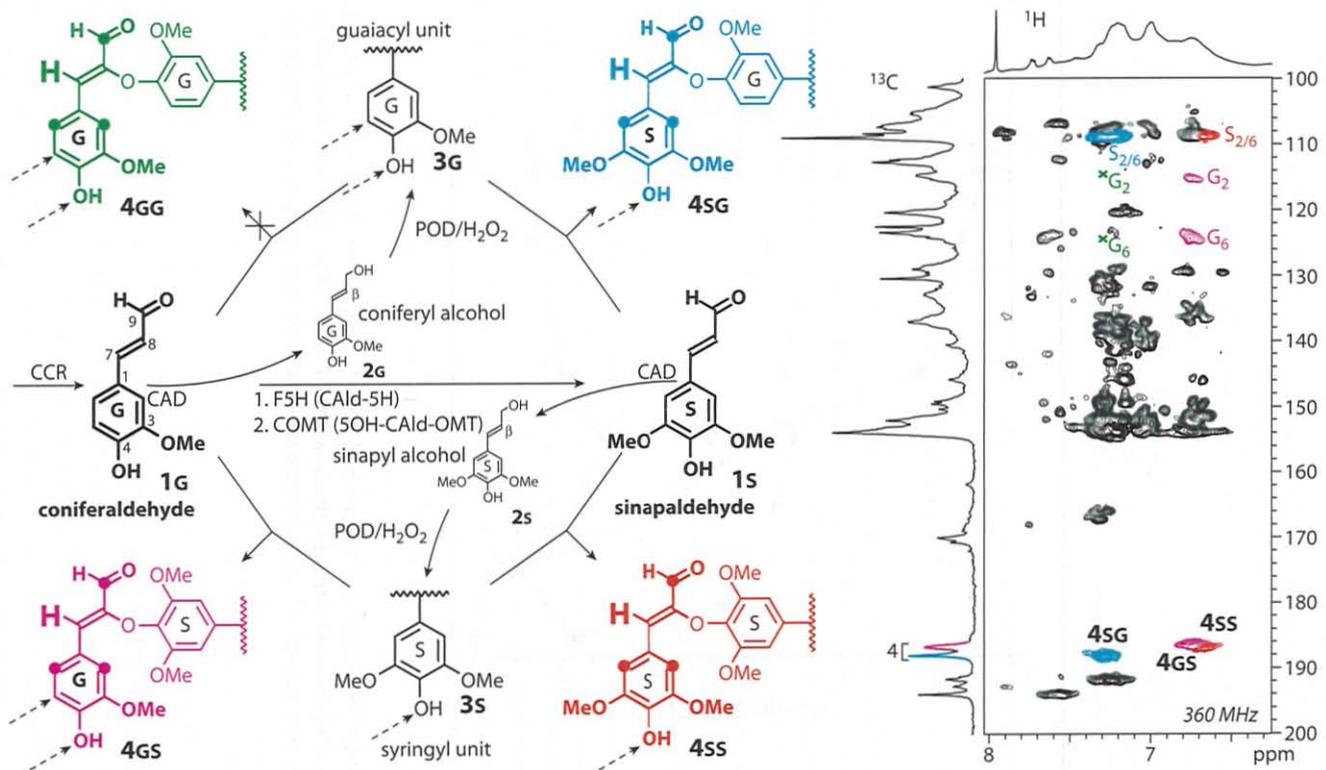
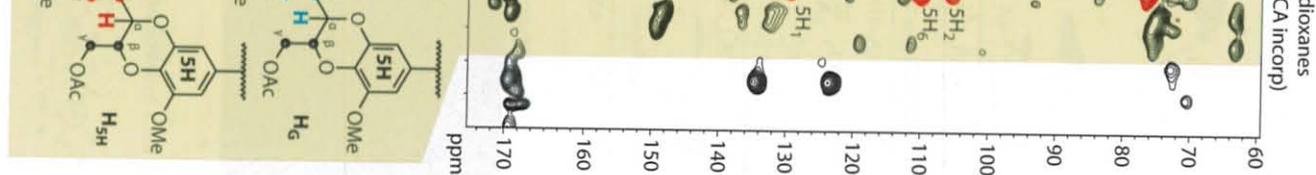
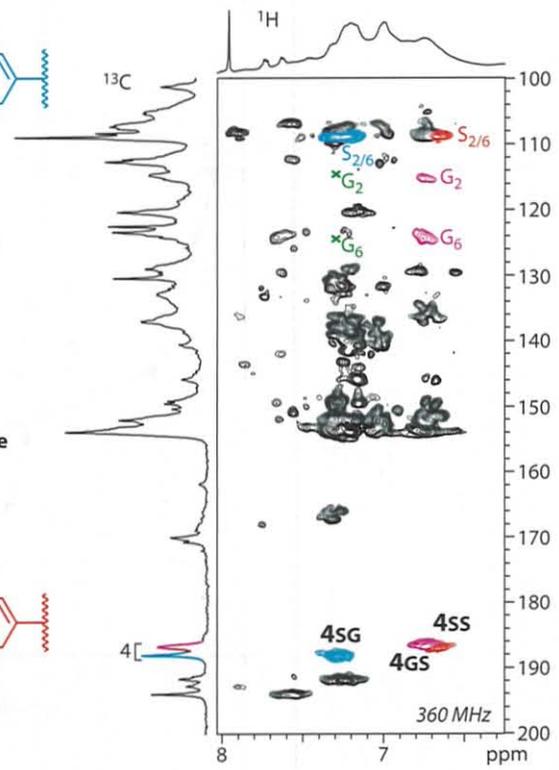


FIGURE 5.21 Cross-coupling of hydroxycinnamaldehydes with lignin units.



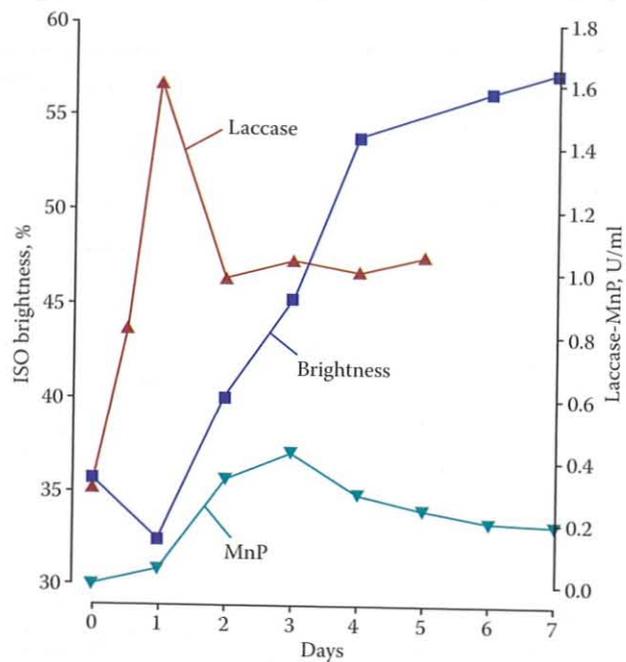


FIGURE 15.7 Production of laccase and MnP by cultures of *Trametes versicolor* during bleaching of hardwood kraft pulp. (Redrawn from Paice, M.G., Reid, I.D., Bourbonnais, R., Archibald, F.S., Jurasek, L., *Appl Environ Microbiol*, 59, 260–265, 1993. With permission.)

ADDENDUM

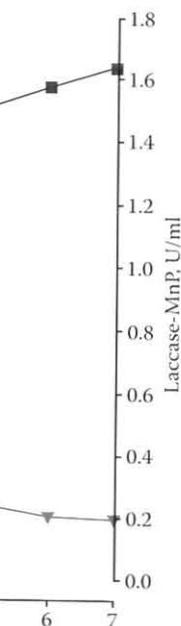
During the period between the initial preparation of this chapter and its publication, several papers have appeared in the literature that need to be noted. As might be expected, these more recent papers benefit from improvements in computer technology and software such that the methods used are generally the more sophisticated *ab initio* and density functional theory calculations. The latter offer advantages based on wide and successful application in other areas of chemistry and physics, the ability to address relatively large molecular systems, and the use of exchange correlation potentials, accounting for electron correlation effects, making these calculations more rapid to perform than the perturbation calculations that are done in conjunction with Hartree-Fock calculations.

The reactivity and coupling of lignols and the formation of the lignin polymer has been addressed at such higher levels of theory by Durbeej and Eriksson [105–108], Sarkanen and Chen [109], Elder et al. [110], Shigematsu et al. [111], and Martinez et al. [112].

The coniferyl alcohol radical and six dilignols representing the major interunit linkages present in lignin have been examined at the B3LYP/6-31G(d,p) level followed by single-point calculations using B3LYP/6-311++G(2df,p) [105]. Furthermore, the effect of conformation on spin density was determined. In accord with previous studies, polymerization was predicted to occur at positions with large, positive, unpaired spin density. The coniferyl alcohol radical, in particular, and the dimers, in general, had the highest spin density at the phenolic oxygen as would be expected based on the electronegativity of oxygen.

Durbeej and Eriksson [106] have also examined whether the subsequent dimerization reaction is under thermodynamic control by determining if the distribution of interunit linkages is correlated with the stability of the dimers. The structures studied were β -0-4, β -5, β - β , β -1, 5-5, and 5-O-4 linkages. Conformational searching for each structure was done at the PM3 level, followed by optimization with B3LYP/3-21G to identify a small number of low-energy conformers. These resultant structures were then optimized at the B3LYP/6-31G(d,p) level followed by a single-point B3LYP/6-311G(2df,p) calculation with solvation. The energetic results for the dimers indicated that the β - β structures would be dominant at room temperature, with a small amount of β -5 present. In contrast, experimental results have reported that the major coupling product is β -5, followed by β - β and β -O-4 in relatively large proportions and low levels of 5-5. It is gratifying to note that calculation finds that the β - β and β -5 structures have the lowest (albeit reversed) energies. In contradiction of the thermodynamic control theory, however, the 5-5 structure is calculated to be more stable than the β -O-4.

The β -O-4 coupling reaction has been studied using B3LYP/6-31G(d,p), and B3LYP/6-311G(2df,p) both with and without solvation at fixed C β -O4 distances from 2.52 to 1.72 Å [107]. The mechanisms evaluated were radical-radical coupling to generate a quinone methide and coupling of a phenoxy radical to coniferyl alcohol resulting in a radical dimer. Since a saddle point was not identified, these are not true transition state calculations, but energetic results were reported. Radical-radical coupling was found to be an exothermic reaction (about -23 kcal/mole) with



es of *Trametes versicolor* during
M.G., Reid, I.D., Bourbonnais, R.,
50–265, 1993. With permission.)

a maximum energy 2–5 kcal/mole greater than the isolated reactants. In contrast, the reaction between coniferyl alcohol and the phenoxy radical was only slightly exothermic with an energy maximum 6–10 kcal/mole above the reactants. While the former reaction would be favored thermodynamically, the radical formed in the latter reaction could be an important participant in lignin polymerization.

Related to this work is a paper by Shigematsu and coworkers [111] in which the PM5 semiempirical parameter set was used to evaluate the transition state for the coupling of *p*-coumaryl alcohol radicals through β -O-4 bond formation. In contrast to the density functional results [105], it was reported that the phenoxy oxygen had a lower spin density than the salient carbons. It was also found that the energy barrier from the reactants to the transition state was on the order of 10 kcal/mole, while the overall heat of reaction was approximately -18 kcal/mole. These differences are undoubtedly due to the use of semiempirical calculations rather than the more rigorous density functional methods.

In other work using higher levels of theory, Sarkanen and Chen [109] have examined the interaction of monolignols using MP2/6-31G(d) calculations. This work has been undertaken to evaluate the proposal that a preexisting macromolecular template of lignin influences subsequent polymerization reactions. Geometry optimizations indicate that an energetic minimum is obtained with a planar configuration between aromatic rings on neutral monolignols.

The addition of monolignol radicals to dilignol radicals, a reaction analogous to the endwise polymerization process proposed as a mechanism by which lignin chain growth occurs, was studied computationally by comparing the orbital energy gaps as determined by UHF/6-31g(d) optimizations followed by a single-point UB3LYP/6-311G calculation [110]. In general, the energy gaps were the lowest for combinations known from experiment to undergo cross-coupling, while those with larger energy gaps represented reactions that, based on experiment, do not occur.

The reactivity of monolignols has been examined by Martinez and coworkers [112], reporting on the application of Fukui functions to determine the susceptibility of reactive sites to nucleophilic, electrophilic, and free radical attack. Equilibrium conformations were determined at the B3LYP/6-31G(d,p) level, and electron densities at B3LYP/6-311++G(d,p) for coniferyl, sinapyl, and *p*-coumaryl alcohols. Given the importance of radical chemistry as part of the lignin polymerization process the authors focus on the results related to free radical attack, indicating that the positions with the largest magnitude of the Fukui function represent the softest and therefore most reactive sites toward radicals. The largest values occurred at the phenolic oxygen and β -carbon. Other positions within the aromatic ring, with appreciable Fukui functions were C-1 and C-4 both of which are sterically hindered and therefore not readily amenable to reaction. It is interesting to note that minimal levels of this parameter were found for the C-5 position in coniferyl alcohol and both C-3 and C-5 in *p*-coumaryl alcohol, arguing against 5-5' coupling.

Several of these papers [105–107] along with a discussion of archival reports on the application of computational methods to lignin polymerization are summarized in a review article by Durbeej et al. [108].

Calculations have also been recently applied to photochemical phenomena including the role of stilbenes [113] in photoyellowing of paper, interactions of lignin

models with singlet oxygen [114,115] and the behavior of dibenzodioxocins [116,117]. In the first paper [113], time-dependent density functional theory calculations were performed on several substituted stilbene structures and the effect on vertical excitation energy was determined. The results compare well with previously reported theoretical data as well as with experimental results. In the work on singlet oxygen reactions [114,115], using MP2/6-31G(d,p) methods and invoking frontier molecular orbital interactions it was found that for the compounds studied, the HOMO of the model would interact with the LUMO of the singlet oxygen. Furthermore, by evaluating the atomic orbital coefficients it was proposed that etherified and phenolic monomethoxyl dimers would react through the B-ring, while a dimethoxyl model would react through the A-ring, both of which are in accord with reaction products observed experimentally.

As part of a study on the photochemistry of dibenzodioxocins, time-dependent density functional and semiempirical calculations were performed on phenolic and nonphenolic model compounds [116]. Based on experimental observations the reaction coordinates for the sequential cleavage the α -O-4 and β -O-4 bonds of the first excited state were examined. It was found that the activation energy of the α -O-4 bond rupture was similar for both phenolic and nonphenolic models, while the subsequent β -O-4 cleavage was more endothermic for the phenolic model. These results are interpreted in terms of the presence of the activating ether group, which is proposed not to be capable of strengthening the β -O-4 bond. Electron densities indicate that upon α -O-4 bond breaking the phenolic model takes on a quinone-methide structure. In addition, an analysis of spin densities shows that the α -O-4 bond undergoes a homolytic cleavage reaction. The time-dependent density functional theory calculations were used to determine excitation energies and oscillator strengths, which were reported to be in accord with experimental results.

In another study on the chemistry of dibenzodioxocins, PM3 semiempirical calculations were used to assess charge distributions and heats of reactions for a phenolic model and the corresponding anion [117]. As might be expected, the largest differences in the charge distribution are centered on the phenolic and phenolate oxygen. Bond cleavage at α -O-4 and β -O-4, shifted the negative charge to the new, free oxygen site resulting from bond breaking. Furthermore, it was found that both α -O-4 and β -O-4 bond cleavage reactions were endothermic, the latter required more energy.

Computational methods coupled with experimental spectroscopy for lignin have been used by Barsberg et al. [118] and Salazar-Valencia et al. [119]. The former paper utilized density functional theory calculations to aid in the interpretation of resonance Raman spectroscopy of lignin radicals. The results from the calculations, which were in good agreement with experiment, were used to assign the vibrational bands to guaiacyl and syringyl moieties. In the latter paper, MNDO and ZINDO/S CI results were reported for dimeric and trimeric lignin models. As the size of the model increases, it is reported that the oscillator strength begins to approach experimental values.

Among the more important reactions of lignins are oxidations, associated mainly with bleaching chemistry. While some experimental oxidation potentials have been

reported for lignin model compounds, they can be difficult to perform, necessitating the use of pulse radiolytic methods. Calculated oxidation potentials may, therefore, be of utility in predicting the tendency of specific groups to undergo redox reactions of industrial importance. This has been addressed in two recent papers, the first of which [120] optimized the geometry of eight monolignols using B3LYP/6-31G(d) calculations. These geometries were subjected to single-point calculations at the B3LYP/6-311++G(2df,p) level of theory, with the determination of zero point energies and solvation. Bond dissociation energies, ionization potentials, spin densities, and charges for the phenolic oxygen were reported. Oxidation potentials were determined using a thermodynamic cycle for two possible mechanisms and compared to published results at $\text{pH} = 7.0$.

The first mechanism assumed the formation of a cation radical while the latter, beginning with a neutral phenol, had a phenoxy radical, a proton and an electron as the reaction products. The former mechanism overestimated the oxidation potential while the latter was more accurate when compared to experimental results for four models.

In a closely related paper [121] the calculated oxidation potentials for eight phenolic compounds for which experimental results are known were correlated to develop a calibration curve. From these data the oxidation potentials of coniferyl alcohol, sinapyl alcohol, anisole, guaiacol, and a pinosresinol dimer were predicted. This paper applied B3LYP/6-31G(d) optimizations to both gas phase and solvated models, and compared the results to experimental data at $\text{pH} = 0$. Based on a correlation coefficient of 0.93 for the calibration curve, the oxidation potentials of the unknowns were determined. The relative results from both of these papers are similar, with dimethoxy compounds having lower oxidation potentials than the monomethoxy compounds.

During the recent past there has been an intense renewal of interest in the use of lignocellulosic biomass as an alternative to fossil-based energy resources. As part of this effort, the thermal degradation of lignin to produce fuels or chemicals has also been a resurgent topic of research. In addition to experimental work of this type, computational methods have been employed in the elucidation of pyrolysis mechanisms of lignin [122,123]. Density functional theory calculations on a phenylethyl ether model compound indicated that the proposed homolytic cleavage reaction has a barrier of 57 kcal/mole occurring at a bond distance of 2.1 Å [122]. Additional work on the selectivity of hydrogen abstraction from the α and β carbons, also performed with density functional theory was found to be in close agreement with experiment [123].

The material properties of lignin have been examined by the calculation of Young's modulus of lignin by subjecting a dimeric model compound to strain, coupled with the determination of energy and stress [124]. The computational results, derived from semiempirical, Hartree-Fock and density functional theory calculations are in agreement with available experimental results. Changes in geometry indicate that modifications in dihedral angles occur in response to linear strain. At larger levels of strain, bond rupture is evidenced by abrupt changes in energy, structure, and charge. Based on the current calculations, the bond scission may be occurring through a homolytic reaction between aliphatic carbon atoms. These results may

difficult to perform, necessitating
ation potentials may, therefore,
roups to undergo redox reactions
n two recent papers, the first of
lignols using B3LYP/6-31G(d)
single-point calculations at the
termination of zero point ener-
ation potentials, spin densities,
Oxidation potentials were deter-
mechanisms and compared to

ication radical while the latter,
cal, a proton and an electron as
estimated the oxidation potential
o experimental results for four

oxidation potentials for eight
are known were correlated to
idation potentials of coniferyl
oresinol dimer were predicted.
o both gas phase and solvated
ata at pH = 0. Based on a cor-
the oxidation potentials of the
a both of these papers are simi-
tion potentials than the mono-

renewal of interest in the use of
ed energy resources. As part of
nce fuels or chemicals has also
perimental work of this type,
ucidation of pyrolysis mechan-
calculations on a phenylethyl
omolytic cleavage reaction has
nce of 2.1 Å [122]. Additional
the α and β carbons, also per-
o be in close agreement with

ed by the calculation of Young's
nound to strain, coupled with
computational results, derived
ctional theory calculations are
Changes in geometry indicate
nse to linear strain. At larger
changes in energy, structure,
ond scission may be occurring
oon atoms. These results may

have implications in the reactivity of lignin especially when subjected to processing methods that place large mechanical forces on the structure.

CONCLUDING REMARKS

It can be seen from the text that through dramatic improvements in computer hardware and software, computational chemical methods have become increasingly accessible to nonspecialists and have also become an integral tool in the practice of chemistry. This is, to some extent, reflected in lignin chemistry, but when compared to other analytical tools that have been brought to bear on this enigmatic polymer there are still relatively few applications of calculation. It has been the intention of the current chapter to demonstrate the feasibility, capabilities, and perhaps even more important, the limitations of these methods and how they can and have been applied to lignin.

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