Theoretical Investigations of C–O Activation in Biomass

Pemikar Srifa
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Academic dissertation for the Degree of Doctor of Philosophy in Organic Chemistry at Stockholm University to be publicly defended on Wednesday 22 May 2019 at 10.00 in Magnelisalen, Kemiska övningslaboratoriet, Svante Arrhenius väg 16 B.

Abstract

This thesis focuses on using computational chemistry approaches to study how biobased molecules interact with both homo- and heterogeneous catalysts. The reaction mechanisms of such transformations have also been studied.

The first section comprises studies of interactions between organic molecules and a heterogeneous catalyst in the palladium-catalyzed depolymerization of models of lignin derivatives. From experiments, it was proposed that a keto intermediate and its enol tautomer play a significant role in the β-O-4′ bond cleavage. The study in the first section of this thesis has been divided into three parts. First, simplified models of the keto intermediate and its enol tautomer were used to investigate the adsorption to a Pd(111) surface. By using a combination of periodic density functional theory (DFT) calculations and a constrained minima hopping method, the most stable adsorption which is the so-called global minimum, was found to be an enol adsorbed to the surface.

In the second part, the study was expanded to cope with models of lignin which were used in experiments. In addition, we studied the effect of adsorbate coverage, where two different Pd(111) super cells were compared. The optimizations were performed via dispersion-corrected density functional theory (DFT-D3). The molecules were found to bind more strongly to the surface at low coverages. These results support the experimental data and show that the tautomerization has an important role during lignin depolymerization.

The third part relates to using a multilevel procedure to study the interaction of fragments derived from lignin depolymerisation with a palladium catalyst in a solvent mixture. Specifically, QM calculations and MD simulations based on the ReaxFF approach were combined to explore the reaction mechanisms occurring on Pd surfaces with lignin derivatives obtained from a solvolysis reaction. The strongest adsorptions were found to be between the aromatic rings and the Pd surfaces.

The second section focuses on a Brønsted acid-catalyzed nucleophilic substitution of the hydroxyl group in alcohols. Experimentally, phosphinic acid (H₃PO₂) was found to be an excellent catalyst for the direct intramolecular substitution of non-derivatized alcohols proceeding with good to excellent chirality transfer. In this section, benzylic alcohols with internal O-, N-, and S-centered nucleophiles were used in the calculations. By using a hybrid functional method, we found a bicyclic transition state where the proton of the H₃PO₂ protonates the leaving hydroxyl group, and the oxo-group of the same catalyst partially deprotonates the nucleophile. The transition state energies for the reactions were determined computationally. The calculations support an S₈2 mechanism, which corresponds to the experimental data where inversion of the stereogenic carbon was observed.

Keywords: DFT calculations, global minima hopping, reactive force field, lignin, palladium, nucleophilic substitution.

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Thanks for all lessons in my life...
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Populärvetenskaplig Sammanfattning

I den här avhandlingen har jag studerat hur molekyler som finns i biomassa interagerar och reagerar med olika typer av katalysatorer. I tre av arbetena har jag studerat hur lignin, som är en makromolekyl som finns i nästan all biomassa, interagerar och reagerar med en heterogen katalysator. Experimentellt är detta svårt att studera, särskilt på en molekylär nivå. Därför har jag använt beräkningskemi. Att kunna klyva denna makromolekyl selektivt skulle möjliggöra en förnybar källa till aromater som är viktiga i nästan all kemi-industri.

I det sista arbetet i denna avhandling har jag studerat hur hydroxylgruppen kan substitueras på en enantiomert ren alkohol. Eftersom de flesta alkoholer i naturen är optiskt rena skulle det vara oerhört gynnsamt om hydroxylgruppen kunde substitueras på ett selektivt sätt. Vi beskriver en metod där endast vatten bildas som en biprodukt. Även här har jag använt beräkningskemi för att förstå hur reaktionen går till i detalj.

Jag hoppas att denna avhandling kommer att inspirera andra forskare att fortsätta studera och utveckla metoder för att möjliggöra att vi kan övergå till ett biobaserat samhälle.
List of Publications

This thesis is based on the following publications and unpublished results, which are referred to in the text by their Roman numerals. The contribution by the author to each publication is clarified in Appendix A. Reprints were made with permission from the publishers, as listed in Appendix B.

I. Detecting Important Intermediates in Pd Catalyzed Depolymerization of a Lignin Model Compound by a Combination of DFT Calculations and Constrained Minima Hopping
Srifa, P., Galkin, M.V., Samec, J. S. M., Hermansson, K., Broqvist, P.*

II. Lignin intermediates on the Pd surface: Factors for structural and energetic changes
Srifa, P., Broqvist, P., Hermansson, K.*
Manuscript

III. ReaxFF Simulations of Lignin Fragmentation on a Palladium-Based Heterogeneous Catalyst in Methanol–Water Solution
Monti, S.*, Srifa, P., Kumaniaev, I., Samec, J. S. M.*

IV. Brønsted Acid-Catalyzed Intramolecular Nucleophilic Substitution of the Hydroxyl Group in Stereogenic Alcohols with Chirality Transfer
## Abbreviations

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>AIMD</td>
<td>Ab Initio Molecular Dynamics</td>
</tr>
<tr>
<td>ASE</td>
<td>Atomic Simulation Environment</td>
</tr>
<tr>
<td>B3LYP</td>
<td>Becke, three-parameter, Lee-Yang-Parr</td>
</tr>
<tr>
<td>BEs</td>
<td>Binding energies</td>
</tr>
<tr>
<td>C–C</td>
<td>Carbon–carbon single bond</td>
</tr>
<tr>
<td>C=O</td>
<td>Carbon–oxygen double bond</td>
</tr>
<tr>
<td>DFT</td>
<td>Density Functional Theory</td>
</tr>
<tr>
<td>DFT-D3</td>
<td>DFT with Grimme’s D3 correction</td>
</tr>
<tr>
<td>E_{ads}</td>
<td>Adsorption energy</td>
</tr>
<tr>
<td>eV</td>
<td>electron volt</td>
</tr>
<tr>
<td>FF</td>
<td>Force field</td>
</tr>
<tr>
<td>GGA</td>
<td>Generalized gradient approximation</td>
</tr>
<tr>
<td>IEFPCM</td>
<td>Integral equation-polarized continuum model</td>
</tr>
<tr>
<td>kcal/mol</td>
<td>kilocalories per mol</td>
</tr>
<tr>
<td>LCAO</td>
<td>Linear combination of atomic orbitals</td>
</tr>
<tr>
<td>M06</td>
<td>Minnesota 2006 DFT functionals</td>
</tr>
<tr>
<td>MD</td>
<td>Molecular dynamics</td>
</tr>
<tr>
<td>MM</td>
<td>Molecular mechanics</td>
</tr>
<tr>
<td>MO</td>
<td>Molecular orbital</td>
</tr>
<tr>
<td>NMR</td>
<td>Nuclear magnetic resonance</td>
</tr>
<tr>
<td>NVE</td>
<td>Microcanonical ensemble (moles (N), volume (V), and energy (E) are constant)</td>
</tr>
<tr>
<td>NVT</td>
<td>Canonical ensemble (moles (N), volume (V), and temperature (T) are constant)</td>
</tr>
<tr>
<td>OH</td>
<td>Hydroxyl</td>
</tr>
<tr>
<td>PAW</td>
<td>Projector-Augmented-Wave</td>
</tr>
<tr>
<td>PES</td>
<td>Potential energy surface</td>
</tr>
<tr>
<td>Pd</td>
<td>Palladium</td>
</tr>
<tr>
<td>Pt</td>
<td>Platinum</td>
</tr>
<tr>
<td>PBE</td>
<td>Perdew–Burke–Ernzerhof functional</td>
</tr>
<tr>
<td>Ph</td>
<td>Phenyl</td>
</tr>
<tr>
<td>p-TSA</td>
<td>para-toluenesulfonic acid</td>
</tr>
<tr>
<td>QM</td>
<td>Quantum Mechanics</td>
</tr>
<tr>
<td>Abbreviation</td>
<td>Description</td>
</tr>
<tr>
<td>--------------</td>
<td>-------------</td>
</tr>
<tr>
<td>RFF</td>
<td>Reactive force field</td>
</tr>
<tr>
<td>RMD</td>
<td>Restrained molecular dynamics</td>
</tr>
<tr>
<td>SCF</td>
<td>Self-consistent field</td>
</tr>
<tr>
<td>STOs</td>
<td>Slater-type orbitals</td>
</tr>
<tr>
<td>GTOs</td>
<td>Gaussian-type orbitals</td>
</tr>
<tr>
<td>SMD</td>
<td>Solvation Model based on Density</td>
</tr>
<tr>
<td>VASP</td>
<td>The Vienna Ab initio simulation package</td>
</tr>
<tr>
<td>ps</td>
<td>picosecond</td>
</tr>
<tr>
<td>ZPE</td>
<td>Zero-point energy</td>
</tr>
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1. Introduction

1.1 Renewable carbon based feedstock

Fossil energy resources such as crude oil, coal, and natural gas are considered to be key sources of carbon for energy and chemical production.

In 1769, Watt invented the steam engine. In 1875, the first coal-fired power plant in the world was built in France. The progress of human civilization was accelerated by the development of the coal industry, and coal accounted for the largest share in primary energy mix in the 1780s, surpassing wood for the first time. This was the first transformation – from wood to coal. In 1876, Otto and coworkers invented the internal combustion engine, stimulating a great increase in the demand for oil and gas as efficient energy resources. Progress in geological theory, drilling, and refining technologies drove oil and gas production to increase substantially. Accordingly, the share of oil and gas in the primary energy mix grew rapidly to more than 50% in 1965. These energy resources replaced coal as the largest energy in the world, recording the second transformation from coal to oil and gas.\(^1\)

The recoverable amount of conventional oil and gas in the world is estimated to \(471 \times 10^{12} \text{ m}^3\). The deposits are mainly concentrated in four regions: the Middle East (35%), Russia (14%), North America (13%) and South America (9%).\(^2\,^3\)

Our modern society is highly dependent on fossil resources such as crude oil, coal, and natural gas. Starting with food production and transportation continuing to pharmaceuticals, these raw materials are the main carbon sources for both energy and chemical production.

However, there are two main concerns when using fossil fuels; the depletion of finite resources and carbon dioxide emission. These issues have become one of the driving forces for worldwide organizations to search for alternative sources to fossil fuels, which is the third transformation.

Emission of carbon dioxide is associated with global warming and The International Energy Agency estimates a decrease in fossil fuels consumption from 80 to 75% worldwide by 2035.\(^4\,^5\) The European Union is committed to reduce its greenhouse gas emissions by 80–95%, that is, below 1990 levels by 2050. In these scenarios, renewables will have an important role with the potential to provide 30% of the total EU energy consumption already by 2030.\(^6\) Due to that the main renewable carbon source – biomass – differs widely from fossil fuels, fundamental studies on the molecular level to unlock its potential.
are required. In addition, methods and chemical transformations developed for fossil fuels can hardly be applied to biomass or its derivatives and therefore new approaches are needed.

Biomass is mainly composed of large molecules or macromolecules, which consists of repeating subunits: starch or cellulose such as glucose polymers, pectin (galacturonic acid), and lignin (monomllignols) (chapters 3 and 4). One of the valorization pathways for biomass polymers is depolymerization to monomeric building blocks. It is logical to perform such depolymerization at the most reactive sites, targeting the weakest inter-linkages of the structures (i.e., C–O bonds). The polymeric nature of biomass is not the only difference to fossil fuels: the functional groups found in biomass consist of ethers, esters, and alcohols and these are not present in crude oil. Consequently, there is a need to study transformations of biomass from a fundamental perspective, which is the main motivation of the present work.

1.2 Catalysis

Most chemical transformations make use of catalysts. The action of a catalyst is to reduce the activation energy and this leads to a rate increase of the chemical reaction (Figure 1.1.). This is the reason why catalysis plays an important role in chemical transformations. During a chemical reaction, the catalyst can react with a reactant to form temporary intermediates. This can lead to several elementary steps along the reaction pathway. Subsequently, the intermediates are transformed into products. However, the catalyst is not consumed during the process and its chemical structure remains unaffected at the end of the reaction.

![Figure 1.1. Illustration on how a catalyst can accelerate a chemical reaction.](image-url)

The entire array of catalysts available on the market can be classified according to the phase of the reaction in which they are involved. In homogeneous catalysis the catalyst and reactants are in the same phase while they are separated into at least two different phases in heterogeneous catalysis.
Homogeneous catalysis can further be divided. One type of homogeneous catalysis is organocatalysis, which is non-metallic process based on an acidic or basic organic catalyst. For example, Brønsted acid-base catalysis comprises only acidic and basic sites. Hydrogen bonding is commonly involved in organocatalysis and Brønsted acid-base catalysis. The last chapter of this thesis deals with Brønsted acid-base catalysis (Paper IV). Another type is organometallic catalysis in which metal-carbon bonds play key roles. Usually, metal complexes composed of a central metal atom that coordinates to one or more molecular fragments called ligands are used. The organometallic processes are strikingly different from the non-metallic ones, since their catalytic cycles usually involve redox chemistry.

Heterogeneous catalysis uses a catalyst in solid phase where the reactant is dissolved in a liquid or gas phase. The catalytic process relies on the ability of the catalyst surface to allow the reactants to adsorb and desorb to/from it. So, the adsorption stage is crucial for heterogeneous catalyzed reactions. As mentioned before, the reactivity of organic compounds is strongly dependent on their particular functional groups. These moieties constitute the preferential bonding sites when adsorbing to the catalyst. On the surface, a strong interaction which leads to bond-breaking of the molecule and bond-forming between the molecule and the surface can occur. This process is termed “chemisorption”. If only van der Waals forces contribute to the adsorption of the substrate, the phenomenon is termed “physisorption”. Heterogeneous catalysts can be recycled more easily than homogeneous catalysts. However, it is more challenging to study the reaction mechanism. In this thesis, the study of a heterogeneous catalyzed reactions are described in chapters 3 and 4 (Papers I-III).

1.3 Functional groups in biomass

Whereas crude oil is mainly built up by hydrocarbons, biomass consists of also oxygen. Therefore, abundant functional groups in biomass comprise alcohols, ethers, and esters (Figure 1.2.). Many of the polymers in biomass are interlinked by ether bonds. Therefore, development of selective transformations to cleave ether bonds is a key to depolymerize biomass into monomeric species. Chapters 3 and 4 focus on how key intermediates in lignin interact with a heterogeneous catalyst prior to an ether bond cleavage. Alcohols are abundant in biomass of which many are optically pure. To efficiently transform alcohols, without prior derivatization, is still a challenge in organic synthesis, especially when taking advantage of the chiral information. In chapter 5 of this thesis, we have studied a Brønsted acid-base catalyzed substitution of the hydroxyl (OH) group in enantioenriched alcohols where the chirality is transferred to the product.
1.4 Computational Chemistry

Computational chemistry is today a complementary methodology used to shed light on complex reaction mechanisms in chemistry, with the aim to be able to predict chemical reactions. The main tools for this field are computer modelling and simulations. Most of the methods in this thesis are based on quantum chemistry, empirical approaches, or multilevel combination of various theories. It is important for computational chemists to carefully select an appropriate technique to a specific chemical question. By using the right technique, we can study the change in structural properties and even discover intermediates and reaction pathways that are not trivial to monitor experimentally. Early versions of computational models contained only few atoms that could be computed by ab-initio calculation techniques. Various outcomes from the ab-initio calculations had a huge impact on the subsequent method development including the Kohn–Sham formulation of density functional theory (DFT). Up until now, DFT approaches have been able to treat large chemical systems comprising over 1,500 atoms. Today, almost all computations are based on DFT.

In recent decades, research on catalysis has been growing. The study of catalysis using computational chemistry requires high performance computing facilities. In order to create powerful tools for computational chemistry, reliable chemical software should be established. The combination of theories, accurate computations, and experimental data are mandatory in order to develop such calculation software.

There are many types of calculations available and useful in catalysis, depending on the principles and limitations of the calculation methods. The most important application is probably to calculate molecular structural changes and their corresponding energies. Predicting these changes are the main use of computational chemistry because the results can be applied, for example, to build up a potential energy surface (PES), which is important to illustrate a reaction mechanism. Here both DFT methods and a force field (FF) method have been used to explore the potential energy surfaces.
In heterogeneous catalysis, adsorption is a key step in the reaction mechanism. To investigate the interaction between molecules and these catalysts, which typically consist of semiconductor and metal surfaces, methodology based on electron density functionals, pseudopotentials, and plane-wave basis sets have recently made it possible to achieve reasonable adsorption energies ($E_{\text{ads}}$). The detailed discussion of theories behind the methodologies will be provided in chapter 2.

When calculating a reaction where solvent and temperature play roles in the mechanism, it is important to at least add some correction functions for the solvation effect. In these specific cases, a simulation technique with explicit solvent molecule can be used. In chapter 4, molecular dynamics (MD) simulations have been used in order to explore the effect of a solvent mixture in the study of lignin models on a catalyst surface.

In homogeneous catalysis (chapter 5), the linear combination of atomic orbitals (LCAO) based-DFT methods are suitable for this type of catalysis because of their well descriptive functionals for atomic orbitals. In this chapter, an implicit solvent correction function was used. This choice of computational models used will be discussed in this chapter.
2. Theory and Methods

Studies of reaction mechanisms in organic chemistry are often performed experimentally by analyzing results from kinetic studies, isotopic labelling approaches, or in-situ spectroscopic methods, combined with existing know-how within the research field. Some catalytic reaction mechanisms are complicated and additional theoretical methods are required to gain insight into the atomic (and electronic) level. One example is reactions that include catalytic C–O bond cleavages, as the mechanism could occur through many possible pathways depending on the nature of catalyst and type of intermediate being formed. Consequently, advanced theoretical methods to analyze different reaction pathways are needed to fully understand what governs the mechanism and the reaction kinetics. Here, computational chemistry provides useful tools to understand the interplay between molecular structures and energies.

Computationally, the most frequently used theoretical method for studies in catalysis is DFT, which is a quantum mechanics (QM) method. Some key features of the DFT will briefly be explained in section 2.2. Two different types of catalysis have been investigated in this thesis; heterogeneous catalysis (chapters 3 and 4) and homogeneous catalysis (chapter 5). With respect to each of these cases, different computational aspects and approaches have been used in this thesis to shed light on the reaction mechanisms. These approaches are discussed briefly in the following sections, namely, geometry minimizations and transition state theory. Finally, additional corrections such as solvation effect and dispersion are discussed in the following sections.

2.1 The Hartree–Fock approximation

One branch of computational chemistry is the study of chemical systems based on quantum mechanics, which is governed by the Schrödinger equation (1).

\[ \hat{H} \psi = E \psi \]  

(1)

In this thesis, the wave function \( \psi \) is the solution of the time-independent Schrödinger equation. This function describes all the properties of a particular system. The Hamiltonian operator \( \hat{H} \) is an energy operator. By applying this operator on the wave function, the total energy of the system (\( E \)) can be obtained. However, in the case of a many electron system, it is not possible to find the exact solution for the Schrödinger equation, so approximations need to be applied for the \( \hat{H} \).
The Born-Oppenheimer approximation assumes that since the electrons move much faster than the nuclei because they are much lighter, the motion of electrons and nuclei can be separated from each other. This makes it possible to solve the Schrödinger equation for the electrons only placed in a static potential of the nuclei, as shown in equation (2).

$$\hat{H}_e \psi_e = E_e \psi_e$$  \hspace{1cm} (2)

Equation (2) represents the electronic part of the Schrödinger equation with the Hamiltonian $\hat{H}_e$:

$$\hat{H}_e = -\sum_{i=1}^{N} \frac{1}{2} \nabla_i^2 - \sum_{i=1}^{N} \sum_{A=1}^{M} \frac{Z_A}{r_{iA}} + \sum_{i=1}^{N} \sum_{j>i}^{N} \frac{1}{r_{ij}}$$  \hspace{1cm} (3)

The first term in Eq. (3) is the kinetic energy of all electrons. The second and third terms correspond to electron-nuclei attractions and electron-electron repulsions, respectively. One problem with this is how to construct the electronic wave functions $\psi_e$.

One approach utilizes that the many-body electronic wave function $\psi_e$ can be written as a combination of single electron wave functions $\chi_i$, constructed in the form of a Slater determinant. This is known as the Hartree-Fock (HF) approximation.

For an N electron system, the Slater determinant will be written as:

$$\psi_{HF} (x_1, x_2, \ldots, x_N) = \left| \begin{array}{cccc} \chi_1 (1) & \chi_2 (1) & \ldots & \chi_N (1) \\ \chi_1 (2) & \chi_2 (2) & \ldots & \chi_N (2) \\ \vdots & \vdots & \ddots & \vdots \\ \chi_1 (N) & \chi_2 (N) & \ldots & \chi_N (N) \end{array} \right|$$  \hspace{1cm} (4)

The terms $\chi_i (j)$ for the i\textsuperscript{th} molecular orbital (MO) includes spatial and spin coordinates of the j\textsuperscript{th} electron. Note that placing any two electrons in the same orbital $\chi_i$ (for example $\chi_1 (1) = \chi_2 (1)$), the determinant solution will be zero. This ensures that the formulation fulfils the requirement of the Pauli exclusion principle, stating that two electrons with the same spin state cannot occupy the same orbital. The linear combination approach further satisfies the antisymmetry requirement with respect to the interchange of any two electron coordinates. By thereafter employing the variational theorem on the normalized wave function, we obtain the famous HF equation:
\[ h(x_1) \chi(x_1) + \sum_{j \neq i} \int dx_2 |\chi_j(x_2)|^2 r_{1,2} \chi_i(x_1) - \sum_{j \neq i} \int dx_2 \chi_j^*(x_2) \chi_i(x_2) r_{1,2} = \varepsilon_i \chi_i(x_1) \quad (5) \]

where \( h \) refers to a single electron integral describing the kinetic energy of the electron and \( \varepsilon_i \) is the energy eigenvalue of the function \( \chi_i \). The second term refers to the electron-electron coulomb interaction and the third term denotes the exchange energy of the electron. The electron-nuclei interaction has been excluded for simplicity. The HF equation can be solved by a self-consistent field (SCF) approach. Furthermore, the same electron wave function is applied to all the electrons and therefore they cannot be distinguished. The solution for this is to introduce density functional theory and some other post-HF approaches to the approximation.

### 2.2 Density functional theory and exchange correlation functions

Hohenberg and Kohn showed in 1965 that the total energy of a chemical system can be calculated from the electron density alone rather than the individual electron wavefunctions, see Eq. (6).

\[ E = E[\rho(r)] \quad (6) \]

Kohn and Sham proposed thereafter a scheme similar to the Hartree-Fock method described above utilizing single electron wavefunctions to obtain the electron density \( \rho(r) \), through the so-called Kohn-Sham equation (8).

\[ \hat{H}_{\text{eff}}(r) \Psi_i(r) = \left[ -\frac{1}{2} \nabla^2 + V_{\text{eff}}(r) \right] \Psi_i(r) e_i \Psi_i(r) \quad (7) \]

where the following equation relates the electronic wavefunctions to the electronic density

\[ \rho(r) = e \sum_i N_i \rho_i(r^2) \quad (8) \]

Eq. (7) is based on the principle that the total energy is composed of the energy of non-interacting electrons at the ground state in the sense that the electrons move with respect to an effective potential of all other electrons in the system. According to this formalism, the total energy can be written as:

\[ E[\rho(r)] = T_s[\rho] + J[\rho] + E_{ne}[\rho] + E_{xc}[\rho] \quad (9) \]

The first \( T_s \) term is the kinetic energy of the non-interacting electron. The second term \( J \) denotes the electron repulsion (Coulomb interaction). The third term \( E_{ne} \) is electron-nuclei interaction. The last term which represents the exchange-correlation function can be the limiting factor for the accuracy of the computed results. This is because, without the exact form of the \( E_{xc} \), it is not possible to get the exact solution to the total energy \( E[\rho(r)] \).
The exchange-correlation function has subsequently been developed based on various approximations to come as close as possible to the exact form. Here we discuss only the Generalized Gradient approximation (GGA) and the hybrid methods because they are used in this thesis. They add different types of corrections to the local density approximation (LDA), which was the first approximation for the exchange-correlation function.\textsuperscript{11}

While the exchange-correlation energy in the LDA formulation is calculated by knowing the exact value for a uniform electron gas, the exchange-correlation energy in GGA also takes into account the gradient of electron density. In this thesis, we have used the GGA developed by Perdew-Burke-Ernzerhof (PBE) for the calculations presented in chapter 3.

Hybrid GGA functionals combine the possibility of including some exact exchange from the Hartree-Fock equation together with GGA exchange-correlation. In this thesis, I have used the Becke, three-parameter, Lee-Yang-Parr (B3LYP) functional\textsuperscript{12} and the meta-hybrid-GGA called Minnesota 2006 (M06) functional\textsuperscript{13} for the calculations reported in chapter 5. A well-known drawback of DFT is that it neglects long-range London dispersion interactions. However, this can be corrected later, as will be discussed in section 2.6.

2.3 Basis sets

A basis set is a set of functions used to describe the electron wave functions in the Kohn-Sham equation (7). MO states that a molecular orbital can be constructed from the LCAO. A molecular orbital basis set $\chi_j$ is a linear combination of all basis functions.

$$\chi_j(x) = \sum_i C_{ij} \phi_{ij}(x)$$  \hspace{1cm} (10)

The coefficient $C_{ij}$ is obtained by minimizing the total energy based on the variational principle in the SCF cycle. This coefficient tells us how large portion of each basis function $\phi_{ij}$ will take part in the $\chi_j$. In this thesis, I have used two types of spin orbital basis sets, one is the split valence basis set and the other is a correlation-consistent basis set.

Even though the first developed Slater-type orbitals (STOs) are close to the actual wave function solution for an H atom, they are computationally expensive. A simplified formulation has therefore been developed which instead uses a number of Gaussian functions, the so-called Gaussian-type Orbitals (GTOs) basis set, to build the electronic wave functions. The general formula for these can be written as equation (11).

$$G_{ijk}^{\alpha \beta} = N_{ijk} \alpha^\beta (x - R_1)^i (y - R_2)^j (z - R_3)^k e^{-\alpha (r - R)^2}$$  \hspace{1cm} (11)
The GTOs add a normalization factor $N_{ijk}^\alpha$ to the exponent of the central coordinate $R$. The exponential variable $r$ is squared which is the main difference to the STOs.

For the calculations presented in chapter 5, Pople’s triple-zeta basis sets which are extended versions of GTOs,\textsuperscript{14} was used. More specifically, the 6-31G(d,p) and 6-311+G(2d,2p) basis sets, were used. The split valence basis set 6-31G(d,p), contains 6 STO primitive functions for the core electron shell, 3 primitives for the inner part of the valence shell, and only 1 primitive in the outer valence shell, respectively. The polarization function (d,p) is included to add the $d$ orbital character to any set of atoms with $p$ valence (for instance the lithium atom) and add $p$ orbital character to any sets of atoms with $s$ valence (for example the hydrogen atom). To make the calculations more reliable, the larger 6-311+G(2d,2p) adds extra polarization functions to the valence electrons. It also augments a single diffuse function (+) to improve the solution of the wave function in the distant region from an atomic nucleus. This leads to a more realistic description in anionic systems and when weak bonds appear (for example, hydrogen bonds). These basis sets are combined with the hybrid functional methods B3LYP and M06 to study homogeneous catalysis in chapter 5.

Heterogeneous catalysis, which is the topic of chapters 3 and 4, requires larger model systems including organic molecules and a metal surface. In this study, we used two different types of basis sets, depending on the model; (i) LCAO-MO based method for the bare molecules, and (ii) a plane wave basis set method for the metal surface and the adsorption studies.

In the LCAO-MO part, the cc-pVTZ basis set was used. This basis set is one of the correlation-consistent basis sets developed by Dunning and coworkers.\textsuperscript{15} The Dunning basis sets are designed for solving the complete basis set limit. The cc-pVTZ basis set will be combined with the PBE functional throughout the calculations of isolated molecules in chapter 3.

In chapter 3, most of the calculations performed are for adsorbed molecules on the catalytically active metal surface. In these calculations, a DFT method with the implementation of a plane wave basis set and pseudopotentials, was used. This further implies that all calculations were performed using the supercell approach, i.e. by applying periodic boundary conditions. A crystalline solid is considered indefinite. Such a system can be represented by a unit cell, which only explicitly contains the smallest repeating unit in our system, however, this unit repeated periodically throughout space. Taking this into account, the effective potential $V_{\text{eff}}$ in the Kohn-sham equation (7) can be represented as a periodic potential (12).

$$V_{\text{eff}}(r + R) = V_{\text{eff}}(r)$$ (12)
Where \( r \) is a position in the central cell and \( R \) is a lattice vector of the crystal.

According to Bloch's theorem,\(^{16}\) the single electron wave function \( \Psi_i \) is written in the form of a plane wave times a periodic function of the lattice \( (u_{i,k}) \). The wave function in the Kohn-sham equation results in:

\[
\Psi_{i,k} = e^{ik \cdot r} u_{i,k}(r)
\]  

(13)

In this formulation, there is an infinite number of \( k \) wave vectors in the unit cell. However, the \( u_{i,k} \) can be simplified when expressed as a Fourier series. Thus, it is enough to evaluate the wave function at a few special k-points in the Brillouin zone of the reciprocal space in the unit cell. The wave function used in the calculations using a plane wave basis set will be expanded to:

\[
\psi_{i,k}(r) = \sum_G c_{i,k} + Ge^{i(k+G) \cdot r}
\]

(14)

The \( c_{i,k} \) are the plane wave expansion coefficients and \( G \) is a wave vector in the reciprocal space.

With a plane wave basis set, in order to simplify the calculations, it is necessary to separate the valence electrons from the inactive (and computationally costly) core electrons. This assumes that, under the effect of nuclear charge, the core electrons are more strongly bound, as compared to the valence electrons. Therefore, the core part can be pre-treated by a so-called pseudopotential instead of the exact coulomb potential and kept fixed for the rest of the calculations. Additionally, the rapid oscillations of electrons close to the core can be problematic because of the computational cost to calculate accurate nodal wave functions. Consequently, nodeless smooth wave functions outside the pseudopotential region replace the single electron wave function in equation (13). In the work presented in chapters 3 and 4, pseudopotentials of the Projector-Augmented-Wave (PAW) type as proposed by Blöchl,\(^{17}\) were used.

2.4 Transition state theory

The theory to describe the reaction barrier in terms of chemical equilibrium between the reactant and an activated complex was originated by Arrhenius.\(^{18}\) In the kinetic Arrhenius equation (15), the rate constant \( k \) can be expressed by an exponential of activation energy \( E_a \) at a particular temperature \( T \).

\[
k = Ae^{-E_a/RT}
\]

(15)

Based on this equation, the transition state theory has been further developed. By including thermodynamic consideration in the pre-exponential factor \( (A) \) and the activation energy \( (E_a) \), equation (15) can be written as the so-called Eyring–Polanyi equation (16).
\begin{align*}
  k = \frac{k_B T}{h} e^{-\Delta G^\ddagger / RT}
\end{align*}

where \( k_B \) is the Boltzmann's constant, \( h \) is the Planck's constant, and \( R \) is the universal gas constant.

The standard Gibbs free energy \( \Delta G^\ddagger \) of an activated complex (transition state complex) can be calculated from the relation between the standard enthalpy of activation (\( \Delta H^\ddagger \)) and the standard entropy of activation (\( \Delta S^\ddagger \)).

Computationally, a transition state is defined as the saddle point (lowest energy point on the highest energy path) of a three dimensional PES.

The movement of a polyatomic molecule leads to its possible geometries with respect to Cartesian coordinates (xyz). Each geometry is associated with a unique potential energy. The lowest energy of a geometry is a point on the PES surface in which the gradient (the first derivative of energy) is zero. This is known as a stationary point and can be obtained by geometry optimization. Then, the three-dimensional PES can be landscaped by collecting these stationary points along any possible reaction path. The transition state is the first-ordered saddle point (deepest) of the PES in which its force constant (the second derivative of energy) has only one negative value. This point represents the lowest possible energy path of the reaction coordinate.

While an actual PES is explored from all paths in a three-dimensional space, the reaction energy profile is a one-dimensional slice of the 3D-PES and is often in the form of free energy plot.\(^{19}\)

It is proved that the transition state energy (barrier) of \( \approx 17 \) kcal/mol corresponds to a 1 s\(^{-1}\) rate constant. This example provides the link between transition state theory and experimental results.\(^{20,21}\)

### 2.5 Dispersion function

The reactant structures in some parts of this thesis contain aromatic or other functional groups that can form intermolecular hydrogen bonds to the catalyst. Therefore, taking into account the noncovalent interaction in this system is essential for these calculations. We considered that dispersion corrected functions can significantly improve the accuracy of the adsorption configuration, energy in adsorption, and transition state energies of bulky molecules, such as lignin on palladium (Pd). Therefore, the dispersion-corrected DFT of the Grimme\(^{22}\) type (D3) in chapter 3 was used for the all optimizations. The PBE-D3 was selected to use in this chapter in order to be compatible with periodic boundary conditions.
As mentioned previously, the hybrid DFT method (B3LYP) used in the chapter 5 fails to describe the van der Waals interactions, resulting in an over-estimation of the repulsion between molecules. A dispersion function, which includes atom-atom long-range interaction corrections was included here. Also the D3 dispersion correction of Grimme was used. A single point calculation was thus performed after the normal wave function had been optimized. Even though the force contributions in the D3 can affect the geometrical changes during the optimization, we found that this was not applicable because the structures of organic molecules were small.

2.6 Molecular Dynamics

The energies obtained by locating the minima and saddle points on the PES, in section 2.4, correspond to gas phase systems modelled at a temperature of 0 K. These conditions keep all molecules at their ground electronic states.

However, properties of molecules in the actual experiments are sensitive to their surrounding environment. Most of the chemical reactions are carried out in a solution at non-zero temperature. These factors affect both structures and energies as compared to the reactions that are performed in the gas phase. For example, at a finite temperature, the QM calculations can be effected by the statistical mechanics procedures. The macroscopic values that are derived from the partition function must be estimated from a representative sample. Therefore, one may incorporate temperature and solvent approaches. Simulation refers to methods which are used to generate representative averages of a system at a statistical finite temperature. In solutions, simulations are needed to describe an interaction between solute and solvent. In chapter 4, MD simulations were used to simulate the newly developed reactive FF to explain heterogeneously catalyzed reactions in a solvent mixture. MD methods are also generally performed for conformational searches when the starting geometry is known from experimental data, such as X-ray crystallography or nuclear magnetic resonance (NMR) spectroscopy. A quasi-Newton molecular dynamic method was used to find the most stable adsorption complexes in chapter 3.

In classical MD simulations, the quantum aspects of the nuclear motion are separated from the electronic part. The Schrödinger equation can be divided into a time-dependent equation for the nuclei and a time-independent equation for the electron movements. So, classical mechanics can be used to describe the motion of atoms through Newton’s second law.

\[ F_i = m_i \frac{d^2 r_i}{dt^2} = -\frac{dU}{dr_i} \]  \hspace{1cm} (17)
Where $F_i$ is the atomic force on atom $i$, $m$ is the mass of the atom, $U$ is the potential energy of the system at a specific time, and $r$ is the coordinates of the atom.

MD simulations create trajectories which are series of time-dependent points in phase space. Each trajectory of the molecular system contains the coordinate, velocity, and the potential energy, $U(r_1, r_2, ..., r_n)$, of all $N$ atoms, as a function of time.

### 2.7 Force field

Even for small systems, electronic structure calculations require a powerful computer and a lot of computational time, to perform. The particular systems studied here contain large numbers of degrees of freedom. Consequently, the Hamiltonian needs to be simplified.

In FF methods, the calculation of the electronic energy for nuclear parts (to get a PES) is avoided by writing the energy as a function of the atomic coordinates obtained by the parameters to higher level computational methods or experimental data. Electrons in FF models are not considered as individual particles, so the bonding information is not used to solve the electronic Schrödinger equation.

In addition, the quantum character of the nuclear motion is also neglected. Instead, this part is treated by classical mechanics. FF methods, which are a subset of molecular mechanics (MM) methods, are often used to find stable geometries or conformations of molecules.

The energy of FF is written as a sum of internal molecular energies;

$$E_{\text{FF}} = E_{\text{str}} + E_{\text{bend}} + E_{\text{tors}} + E_{\text{vdw}} + E_{\text{el}} + E_{\text{cross}}$$

Where $E_{\text{str}}$ is the energy term for stretching a bond between two atoms, $E_{\text{bend}}$ is the energy for bending a bond angle, $E_{\text{tors}}$ is the torsional energy for rotation around a bond or in other words, a dihedral angle energy. Two terms for non-bonding interactions in the system are $E_{\text{vdw}}$ and $E_{\text{el}}$, and $E_{\text{cross}}$ defines the coupling between the first three terms.\(^{23}\)

The two main types of FF are classical and reactive FFs. The latter can be used to describe bond cleavage and bond formation in a chemical reaction. It is important to select a suitable FF for a particular system in order to get reasonable and reliable results from MD simulations. So, the development of a new FF for a specific structure is often needed. In chapter 4 we used a reactive FF (ReaxFF)\(^{27}\) combined with MD simulations to investigate the interaction
of aromatic molecules and a catalyst surface in the presence of a solvent mixture. QM calculations of selected molecular segments were also used for the FF parametrization in order to try to develop a reliable FF for the lignin molecules studied.
The aims of this thesis

The main objective of the performed research in this thesis is to develop computational approaches to investigate how biobased molecules interact with different types of catalysts. More specifically, we want to:

1. Develop a computational scheme for investigating how organic molecules interact with a heterogeneous surface catalyst.

2. Use multiple DFT approaches to study the effect of different experimental parameters, i.e. temperature and adsorbent coverage, to the change in adsorption of lignin derivatives on a Pd surface, which is an important step in lignin depolymerization.

3. Develop a reactive force field and perform MD simulations to study the catalytic fractionation, and how lignin fragments adsorb/desorb to/from a Pd surface in the presence of a solvent mixture.

4. Use LCAO-MO based DFT methods to study enantiospecific intramolecular substitution of the OH group in enantioenriched alcohols.
3. Computational Exploration of Important Intermediates in Pd-catalyzed Lignin Depolymerization (Paper I-II)

3.1 Background

The second most abundant polymer in plants is lignin. This polymer has the potential to become a renewable raw material in chemical transformations. The depolymerization of lignin is a key to convert the polymer to smaller derivatives for further valorization. Efficient and selective lignin depolymerizations have been reported using metal catalysts to cleave the polymer through its interlinkages.\textsuperscript{28,29,30} Among these, the $\beta$-O-4' bond which is the most abundant interlinkage (more than 50%) in lignin and is a common target. Therefore, many reports use model compounds of this motif in their studies (Figure 3.1.).

**Figure 3.1.** Representation of the native lignin polymer (the $\beta$-O-4' bonds are indicated in blue).

Our group has previously performed experimental studies of the reaction mechanism in the transfer hydrogenolysis of lignin models. It was found that the reaction mechanism proceeds through ketone intermediate 2 (Figure 3.2.). In the Pd-catalyzed transformation of 1 to 4 and 5, intermediates 2 and 3 have been suggested as a result of an initial transfer dehydrogenation of the OH group in the benzylic position of the $\beta$-O-4' ether linkage (1).

**Figure 3.2.** The Pd/C catalyzed redox neutral cleavage of model 1 to products 4 and 5, via an initial transfer dehydrogenation to generate intermediate tautomers 2 and 3.
To understand the significance of the keto intermediate and its sensitivity to undergo tautomerization, our group has previously performed several experiments. Maxim et. al. found that the ketone intermediate reacted faster than its corresponding alcohol. The observation is different from a reaction mechanism proposed by Rauchfuss and co-workers where the β-O-4′ ether linkage was cleaved without prior dehydrogenation.31

Tautomerization can only occur when a substrate contains hydrogen(s) at the β-position of the benzylic alcohol. Our model structure 2 can undergo tautomerization. In synthesized models without β-hydrogens, no reactivity in the Pd/C-catalyzed transfer hydrogenolysis reaction was observed.32 The results supported the hypothesis that our real β-O-4′ model undergoes tautomerization during the reaction.

In this chapter, several different computational methods were developed to gain a better understanding of the role of the keto-to-enol tautomerization in this transformation. Until now, only a few theoretical studies on related homogeneously and heterogeneously catalyzed reactions of lignin have been reported.33,34,35

To explore the interaction of the organic molecules representing lignin with the heterogeneous Pd catalyst, the calculations here have been divided into two sections. Firstly, simplified models of the keto (2) and enol (3) lignin tautomers (2′ and 3′ in Figure 3.3.), which represent only the reactive part of β-O-4′ ether linkage, have been used to identify the most stable structures of both tautomers on the Pd(111) surface and to confirm whether our previous experimental interpretations were correct. At this point, DFT was combined with the constrained minima hopping algorithm by Goedecker36 to perform the calculations.

The minima hopping is a quasi-newton molecular dynamics method used to find the most stable ground state of a complex (other methods include; simulated annealing,37,38 basin hopping,39 or Monte Carlo minimization40). Computationally, this is the first time that the minima hopping is combined with Hookean constraints to study interactions between organic molecules and a metal surface. By using this technique, we can guarantee the true global minimum structures while minimizing computational cost. The most stable adsorption complexes of lignin intermediates have been found by this method (see Paper 1) and were used in the next section of this chapter, where more realistic models 2 and 3 have been studied.

In the second section, we expanded the study to more realistic models of lignin, by including aryl rings to the intermediate models. In this case, the coverage-sensitive effect, which probably arises from the intermolecular van der Waals interaction between the aromatic fragments, has been investigated. This coverage-induced conformation has been proven to reflect differences in
energies \(^{41,42,43}\) and is proposed to apply also for our models. To perform the study, two Pd(111) models \(i.e.\) a \(p(6 \times 6)\) and a \(p(6 \times 4)\), were selected to represent different coverages. These surface models have been demonstrated theoretically to be able to preserve the reactive region in our lignin models in contact with the catalyst surface.

Furthermore, the effect in adsorption of the molecular models with several geometric isomers \(i.e.\) \((E)\)- and \((Z)\)-configuration for enol, and eclipsed and staggered conformers for keto) was also studied. For all calculations, a method of DFT with Grimme’s D3 correction for dispersion (DFT-D3), was applied to study how the adsorbate coverage and intermolecular repulsion influence \(E_{\text{ads}}\). We aim to find appropriate model systems for the interaction between the palladium and the inter-linkage atoms of the \(\beta-O-4'\) bond, which is a first step in the interlinkage C–O bond cleavage leading to depolymerization.
3.2 Methodology

3.2.1 Models of lignin derivatives and palladium surfaces

*Lignin models*

As discussed in the introduction, we focus on the important keto intermediate 2 and its enol tautomer 3.

The theoretical study in the first section corresponds to the search of the most stable adsorption complex of lignin intermediates on the Pd catalyst surface. The keto and enol tautomers were represented by methoxypropan-2-one (2'), and 1-methoxyprop-1-en-2-ol (3'), respectively. These molecules are simplified structures from the experimental models, where the terminal aryl rings have been excluded. By choosing the appropriate calculation tools, we can investigate the interaction between β-O-4' interlinkage region in both the keto-enol tautomers, with the Pd surface.

The models of keto and enol in the second calculation section were represented by 2-phenoxy-1-phenylethanone, and 2-phenoxy-1-phenylethanol, respectively (2 and 3 in Figure 3.10.). Several geometrical isomers have been taken into account in order to find the ground state structures of the lignin intermediates (2a and 2b for keto; 3a and 3b for enol). These include staggered and eclipsed conformers of the keto tautomer and (E)- and (Z)-isomers of the enol tautomer.

*Pd catalyst surfaces*

The C–O bond cleavage of lignin molecules is catalyzed by palladium metal particles on a carbon support in the experimental system. The most stable palladium surface, *i.e.* the close-packed Pd(111) surface is used to model the catalyst.

In the first section, we performed global minima search through a combination of DFT approaches and a quasi-newton molecular dynamics. In order to compromise with computational time and cost of the MD simulations, the Pd(111) model contains a $p(4 \times 4)$ supercell structure with the lattice parameter of 3.94 Å at the PBE level (experiment was 3.89 Å), was used. An additional vacuum gap of 10 Å between the surfaces in each periodic cell was set to ensure a minimal interaction between the repeating slabs. The metal surface model was used for all the calculations including two different DFT implementations and the global minima finding for the most stable adsorption complex structure.
In the second section, two different Pd(111) super cells; $p(6 \times 4)$ and $p(6 \times 6)$ were used to represent the surface catalyst in high coverage and low coverage unit cells, respectively, in order to investigate how the $E_{\text{ads}}$ (eq. (3.1)) are affected by adsorbate coverage (Figure 3.10.). We used two different Brillouin-zones with a $2 \times 2 \times 1$ Monkhorst-Pack grid for the adsorption system on the larger orthogonal $p(6 \times 6)$ Pd(111) model and a $2 \times 3 \times 1$ for the smaller non-orthogonal $p(6 \times 4)$.

3.2.2 Electronic structure optimization

For the global minimum structure search, all the isolated adsorbates were optimized by two different DFT implementations. First of all, in order to search for the most stable structure of the bare organic molecules in gas phase, the different conformers were calculated using the PBE exchange correlation functional\(^{11}\) with the triple-$\zeta$ cc-pVTZ basis set which are implemented in the Gaussian 09 package.\(^{46}\) It was confirmed that increasing the basis set to a quadrupole on $e$ did not affect the results.

Then, a plane-wave expansion of the electron wave functions in Vienna ab initio simulation package (VASP)\(^{47,48,49,50}\) with an implementation with pseudopotentials, was used to calculate all the conformers from the first calculation. The PAW type as proposed by Blöchl et.al.\(^{17}\), was used at this stage. The wave functions were truncated using a plane-wave energy cutoff of 500 eV. The metal catalyst Pd(111) surface was optimized separately using the same parameters. In the VASP calculation, the valence electrons were treated explicitly as follows; 10 electrons for Pd ($5s^04d^{10}$), 4 electrons for C ($2s^22p^2$), 1 electron for H ($1s^1$), and 6 electrons for O ($2s^22p^4$), respectively. After that, all selected adsorption complexes were also calculated using this supercell calculation with the same parameters.

In terms of elucidation of the coverage effect in the second section, the molecular models contain aromatic groups. Therefore, van der Waals interaction could significantly influence the outcome of the calculations. To handle this effect, the calculations in this section were treated by the electron–electron exchange and the correlation energies were determined using the dispersion correction, PBE-D3. Instead of the DFT method used in the global minimum search, this PBE-D3 method was used to optimize all the isolated structures in the gas phase and the selected adsorption complexes. The treatment of valence electrons was similar to the previous calculations. However, the wavefunctions were truncated using a plane-wave energy cut-off of 400 eV.
3.2.3 Constrained minima hopping for searching the most stable adsorption complex using lignin simple models

There are many computational methods to find the global minimum of a molecular structure.\textsuperscript{51,52} In this study, the minima hopping method developed by Goedecker\textsuperscript{36} was used to find the most stable adsorption complexes in the system. The method includes an ab initio molecular dynamics (AIMD) method with geometry optimizations to screen different probable locations on the surface for the keto or enol to be adsorbed. Firstly, we performed the optimization of an initial adsorption complex structure using VASP. Then, an MD simulations method with the microcanonical (NVE) ensemble was performed at a high temperature (up to 3500 K). After the MD had been equilibrated, the resulting geometrical structure was re-optimized by the same periodic calculation to get a new local minimum and to compare its energy to the previous minima. The routine will be repeated again until no other local minima are found (maximum 0.05 eV).

To keep the molecular identity at the high temperature, we introduced the Hookean constraints which has been proven to complement well with the minima hopping method.\textsuperscript{51} The constraints keep together the Pd–Pd bonds in the metal surface, and the C–C/H/O bonds of the adsorbates. The parameters are given in Table 3.1. All the calculations were performed in the Atomistic Simulation Environment (ASE, version 3.7.0).\textsuperscript{52}

3.2.4 Energy consideration

Related energies reported in both calculation sections were considered according to the following equations.

\[ E_{\text{ads}} = [E_{\text{molecule/Pd slab}} - E_{\text{Pd slab}} - E_{\text{keto}}] \]  \hspace{1cm} (3.1)

where \( E_{\text{Pd slab}} \), \( E_{\text{keto}} \), and \( E_{\text{molecule/Pd slab}} \) are the total energies of optimized structures of the bare Pd(111) surfaces, the isolated keto molecules (the most stable structure in each set), and the combined adsorption system (particular molecule + slab), respectively. All energies are obtained by the same periodic box dimensions and the same calculation parameters in each section.

The charge density difference (\( \Delta \rho_s \)) was obtained by:

\[ \Delta \rho_s = \rho_{\text{molecule/Pd slab}} - \rho_{\text{Pd slab}} - \rho_{\text{molecule}} \]  \hspace{1cm} (3.2)

The charge transfer between the adsorbates and the surface can be analyzed by calculating the charge differences between them to give electron relocation.
details during their interaction. In the charge densities (ρ) calculations, all atomic coordinates for the three terms in the equation (3.2) were set to be the same as in the optimized structure for the adsorbed molecule on the surface.

All reported energies are given without zero-point energy (ZPE) contributions. We considered the difference in $E_{\text{ads}}$ between ZPE corrected adsorption complexes and the one without the correction, the difference in energies is 1.7 kcal/mol in case of enol, while in the case of keto, the $E_{\text{ads}}$ difference is 2.1 kcal/mol. Thus, the inclusion of the ZPE will not considerably affect our results.

<table>
<thead>
<tr>
<th>Moiety</th>
<th>element-element</th>
<th>Identity Constraint</th>
</tr>
</thead>
<tbody>
<tr>
<td>CH$_3$(terminal)</td>
<td>3 x (C–H)</td>
<td>1.59</td>
</tr>
<tr>
<td>O2CH$_3$(terminal)</td>
<td>C–O</td>
<td>1.79</td>
</tr>
<tr>
<td></td>
<td>3 x (C–H)</td>
<td>1.40</td>
</tr>
<tr>
<td>CβH$_2$O2(keto)</td>
<td>C–O</td>
<td>1.58</td>
</tr>
<tr>
<td></td>
<td>2 x (C–H)</td>
<td>1.59</td>
</tr>
<tr>
<td>Cα=O1(keto)</td>
<td>C=O</td>
<td>1.58</td>
</tr>
<tr>
<td>CβHO2 (enol)</td>
<td>C–O</td>
<td>1.58</td>
</tr>
<tr>
<td></td>
<td>C–H</td>
<td>1.59</td>
</tr>
<tr>
<td>Cα-O1H(enol)</td>
<td>C–O</td>
<td>1.79</td>
</tr>
<tr>
<td></td>
<td>O–H</td>
<td>1.40</td>
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<tr>
<td>Pd surface</td>
<td>Pd–Pd</td>
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</tr>
</tbody>
</table>

Table 3.1. Set up parameters for the Hookean constraints used in the minima hopping calculation. $r_t$ is the threshold distance and $k$ is the spring constant used in each moiety.
3.3 Results and Discussion

We found one relevant report by Willock et al. In their DFT study, the hydrogenation of acetone to propan-2-ol over a Pt(111) surface was investigated. They found that the keto form of acetone first tautomerized to its enol form before adsorbing to the surface by the C=C bond instead of the C=O bond. Then, the hydrogenation occurred as a subsequent step. This report inspired us to study whether a similar tautomerization process also occur in our system.

3.3.1 Study of interaction between simplified models of lignin and a Pd catalyst, by a combination of DFT calculations and constrained minima hopping.

3.3.1.1 Isolated keto and enol tautomers in gas phase

All the stable structures (local minima) of simplified keto and enol conformers were calculated by DFT calculations in the gas phase and are illustrated in Figure 3.3. The conformation search was set based on the rotation of the dihedral angle between O1 and O2 around the Cα-Cβ bond. As highlighted in the figure, 2’a and 3’a are the global minimum structures of the gas phase keto and enol tautomer. A staggered conformer 2’a corresponds to the conformer in which the oxygen O1 and the oxygen of the ether linkage (O2) are trans to each other with a perfect dihedral angle of 180°. In contrast, the most stable structure 3’a was found to have a (Z)-configuration with an intramolecular hydrogen bond between O1H⋯O2CH3 with a distance of 2.163 Å.

Figure 3.3. Structures obtained using DFT with the implementation with plane-waves and pseudopotentials. All bond lengths are in Å.
As explained in the methodology section, the electronic optimizations were performed by a Gaussian orbital-based and a wavefunction-based calculation method. Here, the relative energies between the different local minima from both methods are given in Table 3.2. As can be seen from the table, the results from the two different DFT implementations are in agreement with each other for all the bare conformers with the energy differences less than 1.2 kcal/mol. The minimum configuration and the PES for the water dimer when compared to CCSD(T) calculations was reported using PBE functionals. Consequently, the energetic data of hydrogen bonds in our calculations are supposed to be sufficient by using the same functional.

To sum up, only two conformers of keto are found to be stable in the gas phase whereas there are seven stable variations of enol conformers. The most stable keto isomer (2’a) is 5.1 kcal/mol more stable than the most stable enol form (3’a). This is in accordance to theory, and also corresponds to experimental observations.

<table>
<thead>
<tr>
<th>Stable Conformer</th>
<th>Gaussian calculation</th>
<th>VASP calculation</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>E_{diff} (kcal/mol)</td>
<td>E_{diff} (kcal/mol)</td>
</tr>
<tr>
<td>2’a</td>
<td>0.0</td>
<td>0.0</td>
</tr>
<tr>
<td>2’b</td>
<td>2.3</td>
<td>2.3</td>
</tr>
<tr>
<td>3’a</td>
<td>6.1</td>
<td>5.1</td>
</tr>
<tr>
<td>3’b</td>
<td>10.2</td>
<td>9.6</td>
</tr>
<tr>
<td>3’c</td>
<td>11.1</td>
<td>10.4</td>
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<td>3’d</td>
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<tr>
<td>3’f</td>
<td>13.1</td>
<td>12.4</td>
</tr>
<tr>
<td>3’g</td>
<td>15.9</td>
<td>15.1</td>
</tr>
</tbody>
</table>

Table 3.2. Relative energies of the stable keto and enol conformers in gas phase.

3.3.1.2. Modelling Pd(111) for keto and enol adsorption

The convergence test for determining the suitable number of Pd layers for our models was performed. The keto (3’a) and enol (2’a) were selected to be the tested adsorbates on variable numbers of Pd layers in the slab. The molecules were adsorbed only on one side of the slab. The bottom Pd layer in the supercell was always kept fixed at bulk positions while all other Pd atoms were allowed to relax during the calculations.

The results from the test demonstrate a strong odd–even dependence in the E_{ads} for the enol form as illustrated in the Figure 3.4. (compare 1 and 3 to 2
and 4 layers of Pd in the Figure 3.4.). However, the effect is much less for the keto form. Interestingly, the $E_{\text{ads}}$ for the 1- and 2-layer slabs in the enol system are strikingly different while the energies for the keto are similar. These slab thickness sensitivities are then more clarified when analyzing the integrated charge difference in Figure 3.5.

**Figure 3.4.** Convergence test for the $E_{\text{ads}}$ of 2'a and 3'a adsorption on Pd slabs with varying number of Pd layers. The bottom layer is always kept fixed at bulk distances. For the one-layer slab, the Pd surface is kept fixed at bulk distances.

As seen in Figure 3.5., the charge reorganization is much larger in the case of enol adsorption when the molecule adsorbed on 1 and 2 layers of Pd in Figure 3.5. a). For 1 Pd layer, the di-$\sigma$ bond forming between the enol and two Pd atoms with a large amount of charge gain on the metal surface in the $z$-direction was observed. This effect led to the breakage of the Cα=Cβ bond in the molecule and this further explains why the 1-layer slab overestimates the $E_{\text{ads}}$. However, the feature is obviously much smaller for the 2-layer slab.

The results for the keto adsorption were found to be quite different from those of the enol molecule. As illustrated in Figure 3.5. b), the main interaction between the molecule and the Pd surface is electrostatic. There is no significant difference between the adsorption on 1 and 2 Pd layers. This is clearly seen from a comparison of the upper and lower panels of the Figure 3.5. b).

This suggests that the two molecules interact very differently with the surface. We can conclude that the bonding behavior of the enol is chemisorption while that of the keto is physiosorption. The odd–even convergence behavior diminishes sharply beyond three layers of Pd atoms.

We now return to the main goal of the surface screening; to determine the minimum number of layers needed in our models. This convergence test suggests that the 2-layer slab is able to qualitatively describe the energetic properties of both the adsorbed keto and enol tautomers on the surface. In addition,
in the constrained minima hopping study, it is necessary to have as small model as possible but still capable to describe the relative energetics between the different adsorption structures. We consequently use the $p(4 \times 4)$ 2 layer of Pd slab (32 Pd atoms) as the metal surface model to explore the potential energy landscape and search for stable adsorption on Pd(111).

Figure 3.5. Charge difference analysis for a) enol $3'$ adsorption and b) keto $2'$ adsorption on one and two layer slabs of Pd(111). The left figures show structural models and isosurface ($0.08 \text{ e/Å}^3$), where pink and yellow isosurface signals charge depletion and charge gain, respectively. The right figures show the integrated charge differences along the $z$-axis, in relation to the surface. In the structural model, various color codes represent different atoms; grey for carbon, red for oxygen, white for hydrogen, and blue for palladium.

To ensure that each calculation is accurate, we decided to use a thicker model Pd(111) $p(4 \times 4)$ 4-layer slab (64 Pd atoms) to refine the calculations of the most stable structures. At this point, the most stable adsorption complexes found from the global minima searching were subsequently optimized.
on this larger slab model to obtain accurate $E_{\text{ads}}$. For direct comparison of reported energies, all $E_{\text{ads}}$ were calculated with respect to the total energy of the most stable keto molecule in the gas phase.

![Initial adsorption configurations for enol and keto tautomers on Pd(111).](image)

Figure 3.6. Initial adsorption configurations for enol and keto tautomers on Pd(111). a)-d) are different enol conformers and e) and f) are different keto conformers to adsorb on the surface.

3.3.1.3 Global minimum search

The constrained minima hopping method was applied to search for the global minima adsorption complex structure of a single keto or enol molecule on the surface model. As discussed in the methodology section, the starting temperature was 3500 K so the Hookean constraints as seen in Table 3.1. were also employed at this stage.
Six initial adsorption complexes, including two keto and four of enol adsorbed molecules to the surface, were used as initial structures for this MD simulations (Figure 3.6.). These complexes were chosen based on the stable isolated gas phase conformers (2’a and 3’a) and Polanyi’s theory. The organic molecules prefer to adsorb to a metal catalyst surface through their reactive regions, which are the Ca=Cb bond and the hydroxyl O1–H group, in case of the enol, and the Ca=O in case of the keto.

For the enol, we further hypothesized that the (E)-configuration 3’a can bind at a bridging site on the surface by using either its Ca=Cb bond (so called, position 1: P1) or O1–O2 linkage pointing up (position 2: P2) or down (position 3: P3) to any two adjacent Pd atoms (3’a–P1, 3’a–P2, and 3’a –P3, respectively). For the (Z)-configuration 3b, the Ca=Cb was positioned across two Pd atoms on the surface (3’b–P1). The 2’a–P1 and 2’b–P1 are characterized according to their different rotations to the surface.

3.3.1.4 Enol adsorption

After the global minima hopping search, 53 different search steps were performed by MD and geometry optimizations. Among these steps, 31 different local minima were found. This is in accordance with the energy criterion that states that energy differences between steps should be larger than 1.2 kcal/mol. The E_{ads} for all these structures are given in the left panel of Figure 3.7. These structures were found to correspond to two different adsorption cases, either as an (E)- or a (Z)-enol binding across a Pd–Pd bridge on the Pd(111) surface as illustrated in Figure 3.8. a)–d).

The structure which contains the lowest E_{ads} (−10.0 kcal/mol) in the case of enol adsorption is an (E)-enolate 3’a–M1. In this energy minimum structure, the Ca=Cb bond cleavage occurred and two new C–Pd bond formed. This result can be confirmed by a bond elongation between the Ca and Cb atoms (from 1.345 Å in the isolated molecule to 1.503 Å in the adsorption complex), which defines the cleavage of the double bond and formation of a C–C single bond. The distances of Ca–Pd and Cb–Pd are 2.118 and 2.111 Å, respectively.

Additionally, the intramolecular hydrogen bond between O2 and the hydrogen atom at O1, as we found in the isolated 3’a, was still present in the adsorbed complex 3’a–M1 with a distance of 2.060 Å (Figure 3.8.). The other (E)-enolate minima 3’a–M2 and 3’a–M3 were also found to have this kind of hydrogen bond. Interestingly, the adsorption (Z)-conformer 3’b–M1 (Figure 8.d) without the hydrogen bond has a slightly less negative E_{ads} than that of 3’a–M1 by 1.89 kcal/mol. This shows that the hydrogen bonding might have a small effect on the enol adsorption complex.
3.3.1.5 Keto adsorption

In case of keto adsorption, 21 different local minima were found from 28 steps of global minima search. The energies for all these structures are given in the right panel of Figure 3.7, and their configurations correspond to the ones shown in Figure 3.8, e) and f). Even though they look similar, their $E_{ads}$ are different by 1.4 kcal/mol. The global minimum of keto corresponds to the complex $2'a-M1$ shown in Figure 3.8, e) with the $E_{ads}$ of $-9.1$ kcal/mol. Furthermore, a self-rotation of the initial structure $(E)-2'b-P1$ to form its $(Z)$-conformer $2'b-M1$ (Figure 3.8, f)) around the Cα=Cβ bond was observed.

Both $2'a-M1$ and $2'b-M1$ complexes were found to physisorb via the oxygen of the carbonyl pointing towards one Pd atom on the surface with an O1–Pd distance of 2.246 and 2.237 Å, respectively. Another study on adsorption of aldoses to metal surfaces, has been reported. The molecules were adsorbed to the surface through the π orbitals of the carbonyl group. This structure was not observed in this study. Optimizations of initial geometries of the keto molecule always returned to the stable O1–Pd adsorption complex.
3.3.1.6 The most stable structures on four layers of Pd

In the final step, the $3'a$–M1 (Figure 3.8. a)) and $2'a$–M1 (Figure 3.8. e)), which are the most stable adsorption complexes for the enol and keto tautomers from the screening process, were fully optimized using a four-layer Pd(111) slab with the bottom layer kept frozen at bulk distances. To verify our calculations, the most stable structures were also optimized using four layers of Pd. As expected, there were no dramatic changes in the $E_{ads}$ (Figure 3.9.). The adsorption complexes undergo only small changes in structure compared to the ones using two Pd layers. The hydrogen bond in the $3'a$–M1 complex was elongated from 2.060 to 2.109 Å in $3'a$–G. For the keto and the enol adsorption on the four-layer slab, we found that the enol form was negligibly more stable than the keto form by 1.9 kcal/mol.
3.3.2 Study of lignin model compounds with aromatic groups on the palladium surface: factors for structural and energetic changes.

3.3.2.1. Isolated aromatic models in gas phase

The simplified models from the previous section were subsequently expanded to the more representative models used in experiments in the transfer hydrogenolysis of lignin models (Figure 3.2). Two phenyl rings were introduced to the model in the terminal positions. The calculations started with finding the lowest energy structures for all isolated compounds in the system in order to find the most suitable references for energy calculations in equation (3.1) and (3.2).

The most stable structures after the optimization of their possible conformations in the gas phase, as shown in Figure 3.10, were studied using the all-electron DFT with a local and plane-wave basis sets. The total energy differences (keto vs enol) between the two DFT implementations was only 0.1 kcal/mol. In terms of the keto tautomer, the most stable structure corresponded to the staggered conformer, which is 2.0 kcal/mol more stable than the eclipsed one. In case of the enol, an isomer with (Z)-configuration has the lowest energy. In this structure, we found an intra-molecular hydrogen bond between O1H…O2Ph with a distance of 2.153 Å in analogy to the previous section. In Figure 3.10., the staggered **Keto** (2a) isomer is 5.1 kcal/mol more stable than the most stable **Enol** (3a) form in the gas phase. This relative order is in agreement with experimental observations. 57

The next step was to search for stable structures of two different Pd(111) super cells; \( p(6 \times 4) \)-Pd(111) and \( p(6 \times 6) \)-Pd(111), which represent catalyst
in high and low coverage unit cells, respectively. The most stable models of the heterogeneous catalyst are shown in Figure 3.10. The geometries were constructed from Pd bulk with the geometry optimized from the crystallographic lattice parameter of 3.94 Å at the PBE level (experimental data is 3.89 Å)\cite{45} with an additional vacuum gap of 10 Å to ensure a minimal interaction between periodically repeated slabs and adsorbates. Increasing this gap to 15 Å was tested but we did not observe any noticeable changes in $E_{\text{ads}}$.  

![Figure 3.10. Theoretical isolated models of keto and enol intermediates and Pd(111) surfaces. All bond lengths are in Å.](image)

### 3.3.2.2 Adsorption of the adsorbates to the Pd(111) models.

To analyze the intermolecular interactions between the tautomers and the catalyst, the adsorption configurations performed in this study were based on two types; higher and lower molecular coverage. The scheme to find the preliminary search of adsorption properties of the intermediates on two layers of Pd(111) is demonstrated in Figure 3.11. In the case of higher coverage complexes, Keto and Enol models were adsorbed on a “small model” $p(6 \times 4)$ Pd(111) (denoted as H), which was chosen from the literature.$^{58}$ The adsorption complexes which represented lower molecular coverage (denoted as L) were built up by placing the molecules on a “large model” $p(6 \times 6)$ of Pd surface. All $E_{\text{ads}}$ were calculated with the total energy of these surface models using Staggered Keto (2a), as references.
In order to get reasonable results, we selected two layers of the palladium surface to explore the potential energy landscape and to perform a preliminary search for the most stable adsorption. Previously, we have shown that the energetic properties from two-layer palladium complexes, reasonable represent the larger systems (see section 3.3.1.2). The bottom Pd–layer in the supercell was fixed at bulk positions while all other atoms were allowed to relax. The **Keto** and **Enol** conformers were positioned on different adsorption sites of Pd(111). Both (E)– and (Z)–conformers of each **Enol** and staggered and eclipsed forms of the **Keto** were allowed to place on atop (T) or bridge (B) positions of the surface. It was found that the (E)–**Enol** (3b) and the staggered conformer of the **Keto** (2a) have weak interactions to the surface compared to the (Z)–conformer of the enol (3a) and the eclipsed form of the **Keto** (2b). For example, the $E_{\text{ads}}$ of (3b) on an atop site of the L-Pd is $-91.9$ kcal/mol, which is less negative than the one of (3a) at the same position by $11.2$ kcal/mol. The adsorption of 2a is less stable than the one of 2b. ($E_{\text{ads}}$ is $-95.5$ vs $-101.3$ kcal/mol). Thereby, 3b gives stronger adsorption to the L-Pd as compared to the H-Pd. The $E_{\text{ads}}$ in the lower coverage case (both **Keto** and 3a) are in the range of $-91.9$ to $-103.0$ kcal/mol while the energies in the case of higher coverage are between $-71.5$ to $-75.4$ kcal/mol. This implies that the (E)–conformer of enol 3b and eclipsed form of the 2b are more prone to adsorb on a less dense palladium surface.

However, there are no significant differences in the $E_{\text{ads}}$ of 3b on atop and bridge site positions. All the preliminary adsorption results are listed in Figure 3.11.

The weak interaction to the surface of 3b and 2a and the lack of selectivity in adsorption to various sites led us to consider to only study interactions of the catalyst with 3a and 2b, by adding two more layers of palladium to refine the accuracy in the adsorption results.

In the next step, we used two different four-layer palladium surface models for adsorption studies of structures 3a and 2b to ensure accuracy in the calculations. In section 3.3.1.2, we tested the convergence of this calculation system by using different Pd slab thicknesses. At this point, eight initial adsorption complexes (Figure 3.12.) were chosen based on the reactive regions (Cα–O1; Cα–Cβ) of the molecules and possible adsorption sites of palladium surfaces.
All the calculations of the adsorption complexes were performed using the dispersion-corrected DFT-D3 in the implementation with plane waves and pseudo-potentials, in order to treat the van der Waals interactions between species on the catalyst surface.

**Figure 3.11.** Schematic searching approach for the preliminary adsorption of the intermediates on 2 layers of Pd(111). All $E_{\text{ads}}$ are in kcal/mol.

**Eclipsed-keto(2b) adsorption on 4 Pd layers**

All calculations were based on two adsorption sites between the Cα and Cβ of the molecules to the catalyst surface (atop or bridge). In case of the smaller Pd supercell, the chemisorption of keto was found on both adsorption sites. In case of higher coverage, Cα=O1 bond was broken and new Cα–Pd and O1–Pd bonds were formed. This chemisorption was not observed in the previous calculation where simplified models were used. On the atop site, these two new bonds were found to be shorter than on the bridge position. This corresponds to the more negative $E_{\text{ads}}$ (-95.9 kcal/mol on atop site vs -88.3 kcal/mol on bridge site). In terms of the lower coverage cell, the $E_{\text{ads}}$ of ketone are -104.0 kcal/mol and -100.7 kcal/mol for atop and bridge sites, respectively. The energies reflect that the molecule preferred to adsorb on this lower adsorbate coverage cell. For example, on the bridge site, the energy decreased by 11.5 kcal/mol (from -88.3 in smaller cell to -100.7 kcal/mol in larger cell). Concerning of geometrical changes after keto adsorption, the terminal phenyl rings adsorb strongly to the palladium lying parallel to the palladium surface. The inter-linkage area of the molecules lies non-flat to the surface because Cα of the 2b does not interact with the surface. The most stable adsorption structure of all 2b adsorptions was when the molecule adsorbed on an atop position in the lower coverage case.
When the number of layers of Pd(111) was increased from two to four layers, the $E_{\text{ads}}$ of 3a on the atop site increased by 1.8 kcal/mol (from $-95.0$ to $-93.2$ kcal/mol) in the higher coverage, but decreased by 8.7 kcal/mol (from $-82.9$ to $-91.6$ kcal/mol) in terms of the lower coverage. The reactive region in the middle of the molecule was more flattened as compared to the molecule on the bridge site, in which the O2 positioned away from the surface. In both smaller and larger supercells, the 3a adsorption complexes on both the atop and bridge sites aligned in a similar way in which the Cα=Cβ bond was broken to form two new single Pd–C bonds, leading to a chemisorption. On the higher coverage cell, the $E_{\text{ads}}$ on the atop site was $-93.2$ kcal/mol (Figure 3.12. c)) which is more negative than on the bridge site by 7.6 kcal/mol. The opposite was found in case of the lower coverage cell, where the $E_{\text{ads}}$ of 3a on bridge site is slightly more negative compared to the ones on the atop site (Figure 3.12. g) vs Figure 3.12. h)). The difference in $E_{\text{ads}}$ energy between the two adsorption sites is 2.5 kcal/mol. The most stable adsorption complex was found for 3a on the bridge site, where the calculated energy was $-105.7$ kcal/mol (Figure 3.12. h)).

3.3.2.3 Comparison of factors for structural and energetic changes between keto and enol.

It can be seen clearly that both 2b and 3a tautomers adsorb strongly to the Pd(111) surface through their phenyl rings which align parallel to either a bridge-30 configuration or on a hcp-0 position which also have been reported to be the most stable adsorption sites for benzene.$^{59}$

Despite the strong binding of the terminal phenyl groups, the intermediates still adsorb to the surface through the cleavage of the unsaturated bond at the linkage region, i.e. chemisorption. We also found that both keto and enol tautomers preferred to adsorb on to the lower adsorbate coverage surface to avoid intermolecular repulsions between molecules. The chemisorption of this linkage to the surface can therefore be considered as a first step in the depolymerization to form the cleaved products 4 and 5 in Figure 3.2.

In both keto and enol adsorption to the surface, there are two modes depending on the position of the newly formed molecule–Pd sigma ($\sigma$) bonds. Pi ($\pi$)-adsorption mode was found when two new bonds were formed over the same palladium while di-$\sigma$ mode was considered when the new sigma bonds was positioned across the Pd–Pd bridge.$^{60}$ In this study, the chemisorption of the 2b does not lead to a productive route in the desired depolymerization. Instead, an undesired Cα–O1 bond cleavage leads to a species that is not as reactive in the desired Cβ–O2 ether bond cleavage. Our results correspond to a related study in which the adsorption of ethylene and formaldehyde on a
gold cluster was investigated, in which the strength of bonding interaction between the adsorbate and cluster follows the order; \( \text{di-} \sigma > \pi > \text{O-} \sigma \) mode.\(^6\)

In the calculations for finding the global minimum, the \( E_{\text{ads}} \) of 2’\( a \) and 3’\( a \) tautomers were approximately 10\% of the ones in this study. However, we still see a similar adsorption mode (\( \text{di-} \sigma \) mode and \( \pi \)-adsorption) around the reactive region (O1–C\( \alpha \)–C\( \beta \)–O2) on both tautomers. The strong adsorption supports that the interaction of this region to the catalyst is important for further transformation i.e. depolymerization.

**Figure 3.12.** Selected geometrical parameters and \( E_{\text{ads}} \) of lignin intermediates on 4 layers of Pd (1 1 1). Keto and enol adsorption on higher coverage supercell are represented on a), b), c), d). The adsorption of species on lower coverage supercell are shown in e), f), g), h). Top and Bridge refer to the initial positions which were designed before optimization.
3.4 Conclusions

A key step in the Pd/C-catalyzed lignin depolymerization has been investigated.

In this work, the adsorption of models of important intermediates in lignin depolymerization to different Pd(111) surface models has been investigated by multiple computational approaches. In the first section we studied the simplified molecule of the intermediates on a \( p(4x4) \) Pd(111) supercell. We used DFT-based calculations combined with global minima hopping criteria as tools for the calculations. The results show that on the Pd surface, the enol tautomer adsorbed stronger than the keto (\(-11.3 \text{ vs } 9.4 \text{ kcal/mol for enol and keto, respectively}\)), which is different from the gas phase where the keto tautomer is more stable by 5.1 kcal/mol.

In the second section, different geometric isomers of keto and enol tautomers having aryl rings, have been optimized in the gas phase using LCAO-based DFT and corrected by the DFT-D3. By considering the coverage effect on the \( E_{\text{ads}} \), we probed the intermediates with possible adsorption sites to the Pd(111) in a small \( p(6x4) \) and large \( p(6x6) \) super cell of Pd(111). In the gas phase, staggered conformer of the keto tautomer was found to have the most stable geometry. However, when these conformers were adsorbed to the palladium, the calculated energies were different. Due to the \( E_{\text{ads}} \), the intermediates prefer to adsorb to the lower coverage cell (bigger supercell) by \( \sim 10 \text{ kcal/mol} \). The most stable adsorption complex agrees with a low-coverage enol structure with the \( E_{\text{ads}} \) of -105.7 kcal/mol. In this adsorption complex, the enol chemisorbed to the palladium through the \( \text{C}_\alpha=\text{C}_\beta \) bond in the same way as in the previous section. The bond is vicinal to the \( \text{C}_\beta=\text{O}_2 \) bond that can easily be cleaved in a subsequent step leading to depolymerization. These results could be important for experimental design purposes to perform related reactions at lower concentrations. The calculations also support that the DFT methodology can be used to analyze reactions including metal surfaces and organic molecules.
4. ReaxFF Simulations of Lignin Derivatives on a Pd Catalyst under Organic Solvent Condition

4.1 Background

In chapter 3, we investigated the adsorption of lignin intermediates on a Pd catalyst in gas phase. DFT calculations and a quasi-Newton MD method were used to study the interaction between the molecules and catalyst surface. It should be noted that all of those calculations were performed in the gas phase. In this chapter, we were interested in studying the interaction of larger lignin models on the Pd surface. The effect of solvent was experimentally found to be important and we therefore wanted to include it in the calculations. Computationally, this solvent effect is difficult to study by DFT as it requires long calculation times as mentioned in chapter 2. Therefore, a reactive FF method complemented with MD simulations, was selected.\textsuperscript{60} Due to the efficiency of this comprehensive procedure, chemical reactions on the surface can be simulated.

Catalytic fractionation is a process in which an organosolv pulping is combined with a (transfer) hydrogenolysis.\textsuperscript{62} In such a process, the lignocellulose is fractionated by solvolysis and a transition metal operates in the lignin depolymerization. Such processes are usually performed in batch, however, lately our group has succeeded in performing a catalytic fractionation in a continuous flow.\textsuperscript{63} Thereby, this transformation is different from the one described in the previous chapter. The process of lignin fractionation using a continuous flow includes two processes that occur in two separate reactors. The first reactor is a percolation chamber which is filled with the lignocellulose-based biomass. Partial depolymerization of the lignin by solvolysis was experimentally found to occur in this chamber to yield short oligomers, dimers, and phenolic monomers. The second reactor is filled with a heterogeneous Pd/C catalyst. The main reactions in this reactor are the cleavage of the $\beta$-O-4$'$ bond, the reduction reaction of the double bond in the allylic alcohol, and the transfer hydrogenolysis reaction of the same molecule.

The efficiency of the catalytic procedure is highly dependent on the flowrate, reaction time, temperature, and solvent. These parameters can be optimized experimentally. The reaction is performed in methanol and water (ratio 7:3 v/v). In order to get the optimal performance of the cleavage reaction, the mentioned factors should be tuned properly.
It is challenging to study the interaction between organic molecules and a heterogeneous catalyst in the presence of a solvent. Therefore, computational chemistry methods could have an important role in understanding intermolecular interactions in such systems.

In order to simulate a large chemical system containing significant numbers of atoms, multilevel computational methods are needed. In recent years, the combination between MD simulations of ReaxFF, and QM calculations, has shown very promising results in systems which contain organic molecules and metal heterogeneous catalysts.\textsuperscript{64,65,66} In 2016, a method combination by Monti et al, has been used to demonstrate the two-consecutive binding steps of cysteine molecules to a gold catalyst surface.\textsuperscript{64} The same multiscale method has been specially developed for the multi-molecular system containing Cu(II)-ion, (2,2,6,6-tetramethylpiperidine-1-oxylradical)-mediated oxidized cellulose nanofibers, and graphene oxide membranes. The combination of multiple calculation techniques can, for example, illustrate the layered structure of the nanofibers and membranes from their self-assembly, which corresponds to the structure investigated by advanced microscopic techniques. Thus, combinations of such calculations would be a promising approach to study metal-catalyzed organic reactions, such as lignin depolymerization.

In this study, the interactions of two species from the Pd/C catalyzed fractionation have been investigated. The computational models for those species were specially designed according to the optimal reaction conditions from experiments. The interaction between derivatives having the β-O-4’ bond and a palladium surface model has been simulated in a model of mixed solution between methanol and water under high temperature and pressure. The first dimeric species 1” (Figure 4.1.) which consist of the β-O-4’ bond has been used and we were able to study both adsorption as well as the C–O bond cleavage event. The second species 6 is a highly reactive monophenolic compound found in the product mixture from solvolysis. With the conjugate bond in the structure, the reduction of the double bond has been possible to study. The two main conversions are crucial for the catalytic fractionation of lignocellulose.
4.2 Methodology

4.2.1 The collection of training set

To identify all of the different conformations of lignin derived species, QM calculations (energy minimization at the M06-2X/6-31G(d) level) combined with a molecular mechanics FF have been used to perform a conformational search. A series of conformational search were performed and data was collected and used as a training set to parametrize a reactive force field (RFF) for depicting the behavior of these molecules in the gas phase (Paper III).

4.2.2 Molecular dynamic simulations

The primary RFF was created by gathering parameters, which can describe the intermolecular interactions between the lignin model and the solvent molecules, as well as the organic molecules with palladium substrates. The initial values of these parameters were taken from well-tested ReaxFF FFs available in the literature. A computational model system of mixed methanol–water solution has been used to perform the MD simulations, in order to explore solvation effects on the molecules. The conformational studies were firstly done in the gas phase and were used to retune the RFF parameters.

Other periodic QM calculations of the representative fragments adsorbed on small palladium slabs have also been performed. The resulting configurations were added to the training set in order to reparametrize the existing RFF.
4.2.3 Validation of the RFF

The final RFF was subsequently validated against external QM data. The reproduced geometries, binding energies (BEs), and relative stability were achieved. It was found that only minor values in energy differences were overestimated by the FF. This was owing to the presence of several intramolecular hydrogen bonds in the system.

4.2.4 The simulation models

4.2.4.1 Lignin derived models

Two selected species from the Pd catalyzed fractionation have been modelled (Figure 4.1). Structure 1” represents dimeric species containing the β-O-4’ bond. This molecule has been used to study the C–O bond cleavage. The other molecule 6 is a reactive monophenolic compound used to study the reduction of the double bond. The transformations of both species are key reactions in the catalytic fractionation of lignocellulose.

4.2.4.2 The model reactor

To mimic the fixed bed reactor in experiment, the simulation was done in a model reactor box (82 × 82 × 76 Å^3) filled with an equilibrated solvent mixture molecules (methanol-water). Eight solute molecules of 1” and 6 were placed in the reactor together with the ones which were extracted from the restrained molecular dynamics (RMD) trajectories of 1” and 6 in the methanol–water solution. A Pd(111) slab of 10 layers (90 atoms, box sizes: 25.9×25.9 × 70 Å^3) or Pd(100) slab of 15 layers (50 atoms, box sizes:19.4 × 25.9 × 70 Å^3) were used in the simulations. Then, the solvent (methanol–water solution) + solute boxes were positioned on top of the slabs at a distance of ~3.5 Å, to avoid long sampling times.

Subsequently, the combined boxes were suitably cut and adjusted to match the proportion of metal slabs. RMD simulations were carried out in the canonical ensemble (NVT) at T = 453 K by using the ReaxFF/ADF program.\textsuperscript{58}

Configurations were saved every 0.05 ps for a maximum simulation time of ~200 ps. In this case, Berendsen’s thermostat was used for temperature control with a relaxation constant of 0.1 ps, and the time step was set to 0.25 fs. The adsorption of 1” and 6 on both slabs in the solution mixture were captured with more than 200 simulations for describing the adsorption properties of the lignin species on both slabs. Only the most proper results will be reported and discussed in the following section.
4.3 Results and Discussion

4.3.1 Interaction of species in the system

When the catalyst surfaces (both Pd(111) and Pd(100)) were not occupied by solvent, the most favorable posture for 1'' and 6 to adsorb was through the chemisorption of their terminal aromatic rings. When the system includes solvent, i.e. water and methanol, the adsorption of 1'' and 6 competes with the solvent molecules. This is due to the fact that both water and methanol molecules were adsorbed rapidly on the catalyst surface using their hydrogen and oxygen atoms. It has been revealed that methanol molecule can adsorb faster than water with respect to both chemisorption and physisorption. The competition of the reactions may reveal why a proper choice of the solvent mixture ratio for obtaining high yields in products, is needed.

Several significant effects have been observed. It was clearly seen that only 18% of the surface area was occupied by the adsorbates (1'' or 6) whereas most of the surface area was covered by the solvent molecule (82-95%) (considering number of adsorbate molecules in contact with the surface and the solvent that accessed the top layer of Pd surfaces).

Another noticeable effect is that the solute/solvent molecules can release their hydrogen atoms to the surface. It is known that some of those released hydrogens can transfer to the second and third metal layer. In this study, the migration was found to be approximately 5% in the case of Pd(111) and only ~2% in terms of Pd(100). The atomic transfer is known for catalytic surfaces and has broadly been studied both experimentally and theoretically. In this project, the penetration of these atoms into the subsurfaces and their ability to re-emerge to the surface has been confirmed.

4.3.2 The mechanism of 1''

After placing 1'' onto the Pd(111), the molecule was found to be rapidly chemisorbed (a few picoseconds). Figure 4.2. shows selected adsorption structures extracted from the calculations. At the initial adsorption stage, the molecule physisorbed to the surface by pointing the lone pair electrons of Cα–OH to the surface (1''A). Then, the hydroxyl hydrogen is released to a Pd atom on the top surface, leading to the chemisorption of the molecule. This process has been confirmed by plotting of the potential energy of each adsorption complex against time (Figure 4.2., bottom right). The potential energy of 1''D was rapidly increased because of extra energy of two new bonds (Pd–O and Pd–H).

The chemisorption of the molecule was strong enough to support an elongation of the C–O bond at the interface. This has been confirmed by an effect on the bond-breaking, as can be seen from Figure 4.2. The cleavage time is
slightly longer in the case of the Pd(111) (∼0.6 ps longer). This time difference is not sufficient to distinguish the catalytic efficiency of the two surfaces. However, it is possible that the species can adsorb more strongly on Pd(100) according to the more open surface.76

Figure 4.2. Selected structures relevant for the various steps of transformation of structure 1”. The potential energy of the Pd(111)+ 1” and solvent–system as a function of the simulation time is shown at the bottom right.

The whole adsorption process is approximately 10 ps. Subsequently, Figure 4.2. 1”I clearly shows the cleavage of the lignin ether linkage (β-O-4’ linkage) as the following step. This cleavage was slow, and resulted in two fragments, namely, FRAG1, which desorbed from the surface and emerged into the solvent, and FRAG3, which retained the original strong adsorption to the support. After the bond breaking, it is evident that the resulting fractions positioned themselves in a stacking direction before they departed from each other (Figure 4.2., 1”I to 1”J). The result is also confirmed in Figure 4.3. (black and blue dots).
The mechanism of 1'' on the Pd(100) surface as well as its energy changes are very similar to the process on Pd(111). The final products can be found as adsorption complexes on the surface or mixed in the solution in various arrangements depending on local conditions and solvent effects.

4.3.3 The reduction of 6

The main focus in the investigation of 6 is the reduction mechanism of the double bond. The simulations began with a set of various orientations of molecules on top of Pd(100) and Pd(111) slabs. On Pd(100), several alignments of the molecule were found to stimulate the hydrogen transfer to the double bond. In these structures, both their aryl and propenyl chain coordinate strongly to the palladium surface. The elongation of the C–C double bond as a function of the simulation time is displayed in Figure 4.4.

During the adsorption process (Figure 4.4.), the molecule firstly adsorbed the Pd surface through a chemisorption of the phenyl ring, leading to the adjustment of other atoms in the chain. The hydrogen of the terminal OH is abstracted by the palladium and the resulting alkoxide oxygen binds in between
two rows of palladium atoms joined with the C–C bond chemisorption to induce the pyramidalization of the carbons. Once the substrate adjusted in an appropriate adsorption configuration, the hydrogen atoms at the subsurface re-emerged to the surface and formed new bonds to the C–C site. The whole mechanism was found to be quite fast (~30 ps).

Figure 4.4. Distance of the C–C bond in 6 as a function of the simulation time.

BEs of the initial (double bond) and final (single bond + hydrogen) species have been calculated in order to compare the strength of molecule-surface interaction. To do this, selected stable adsorption complexes were calculated through periodic QM. All of the solvent molecules were removed and the Pd slabs were replaced by the ones used in the parametrization step. The calculated BEs are around −101 and −47 kcal/mol, for the original molecule and the hydrogenated products, respectively. Such a huge difference in energy revealed the higher possibility of the product to be found in solution.

However, the BEs could be greatly overestimated because short-range intermolecular interactions between the adsorbate and the nearby species were not taken into account.

By using the ReaxFF approach, the calculated BEs of both corresponding species are −109.4 and −99.8 kcal/mol, respectively. The BE of final species is considered to be overestimated. This is most probably due to perturbations from some important effects found only in the FF calculations. These include
self-aggregation of species on the surface, nearby interactions with the adsorbed solvent molecules, and the effect of surrounding solution. Unfortunately, these BEs have not been studied experimentally yet.

The BEs of other adsorbed fragments were also calculated and found to be fit in a large range of values (−150 to −24 kcal/mol) subject to variations of the structures and their environment. Computationally, these energies are in accordance with the energies of the ones in the parametrization step, confirming the correct behavior of the FF to reproduce the adsorption on Pd surfaces.

4.4 Conclusions

We have developed a multilevel computational method based on ReaxFF MD simulations to describe compounds derived from lignin in the presence of a solvent and a heterogeneous Pd catalyst represented by Pd(111) and Pd(110) surfaces. The results not only reproduce the experimental data obtained from continuous flow but also deepen the understanding of the adsorption dynamics. The C–O bond cleavage of a model oligomer (1”) has been investigated as well as the reduction of a reactive monomer (6). We have shown that the computational approach presented in this chapter can be used to study a complex system comprising of a heterogeneous catalyst, organic molecules, and solvent.
5. Theoretical Study of Stereospecific Nucleophilic Substitution of the Hydroxyl Group in Enantioenriched Alcohols

5.1 Background

The direct substitution of the OH group in alcohols is an ideal procedure in synthetic organic chemistry. However, it is difficult to get the desired reaction because of the poor leaving group ability of the OH group. Consequently, the OH group needs to be changed to a better leaving group before performing the substitution. Furthermore, preservation of the chirality of a starting enantioenriched alcohol to the product is even more challenging.

There are previous reports of direct intramolecular substitution of alcohol to promote chirality transfer from starting allylic alcohol to final product\(^{77,78}\). Among these, Aponick and co-workers have discovered that gold and palladium can be used to effectively catalyze such reactions. They performed a computational study where a bicyclic transition state was found in the reaction mechanism (Figure 5.1).\(^{79}\) The nucleophile both attacks the carbon as well as protonates the leaving OH group at the same time. An intramolecular hydrogen bonding interaction is crucial to stabilize this unique transition state.\(^{80}\)

However, the substrate scope for this methodology is limited because no reactivity was observed when changing the position of OH and olefin in the starting allylic alcohol.

![Figure 5.1. The unique transition state in the activation of an allylic alcohol by Aponick et. al.](image)

The research in this chapter encloses the development of stereospecific nucleophilic substitution of the OH group in alcohols. This project includes two parts; an experimental investigation, and a theoretical study. The latter part has the aim to analyze the reaction mechanism of the developed reaction.
In the experimental part, a method for the direct intramolecular and stereospecific substitution of the OH in alcohols has been developed. The selected substrate for catalyst screening was the O-centered (S)-1-phenylbutane-1,4-diol (7a in Table 5.1). It has been found that phosphinic acid (H₃PO₂) shows an outstanding catalytic performance to generate the enantioenriched five-membered tetrahydrofuran product 8a with high stereospecificity (Table 5.1).

To expand the study, N-, and S-centered nucleophiles (7b and 7c in Table 5.2) were used as reactants to generate the cyclic pyrrolidine 8b and tetrahydrothiophene derivatives 8c respectively. The products were obtained in excellent yield and with high chirality transfer.

This catalyst was reactive also for non-benzylic alcohols such as allylic, propargylic, and alkyl alcohols (Paper IV).

<table>
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</tr>
</tbody>
</table>

**Table 5.1.** Optimization of reaction conditions. Reaction condition: 7a (1 mmol), solvent (2 ml) and catalyst (10 mol%) were heated in an oil bath. aNMR Yield. bBy chiral HPLC analysis.
Table 5.2. Experimentally performed intramolecular substitution of benzylic alcohols with O-, N-, and S-centered nucleophiles.

In this theoretical study, DFT at B3LYP/6-311+G(2d,2p)/6-31G(d,p) level of theory, has been used to investigate the detailed mechanism of H$_3$PO$_2$ catalyzed direct intramolecular substitution of the nucleophilic series (Table 5.2). Molecular models of benzylic alcohols using the three different nucleophiles were used to understand the Brønsted acid catalyzed reaction. All the transition states and isolated structures during the mechanism will be discussed in terms of their energies and geometries.

5.2 Methodology

All the DFT calculations were performed using the Gaussian 09 package.$^{42}$

5.2.1 Geometrical optimization

The isolated structures of substrates, catalysts, intermediates and transition states were optimized in gas phase in order to find the most stable structure of each species in the reaction. The electronic structure calculations were done by using the B3LYP functional with the 6-31G(d,p) basis set. To compare the results between two different hybrid methods, geometrical optimizations were also performed by the M06 functional with the same basis set. Details of these functionals are described in chapter 2. The Gibbs free energy calculations for these structures began with carrying out their frequency calculations at a temperature of 353.15 K (the optimized temperature from experiment) at the same level of theory as the geometry optimizations. These calculations yield the free energy corrections for PES calculations.

5.2.2 Transition state calculations

A transition state structure can be defined by a maximum activation energy, with only one imaginary frequency. All possible transition state geometries were calculated at B3LYP/6-31G(d,p) level of theory. Each TS structure is defined by a negative force constant, which corresponds to an imaginary frequency.
5.2.3 Basis set superposition error (BSSE)

DFT calculations using small basis sets may overstabilize the model structure more than the bigger basis sets due to the BSSE. To overcome this issue and obtain better accuracy in all calculations, the optimized geometries were recalculated to get their single-point energies. The calculations were carried using the 6-311+G(2d,2p), a larger basis set which allows more space for electron delocalization.

5.2.4 Correction of solvation effect

The effect of solvent used in the experiment has been taken into account in all calculations. The solvation energy was calculated as a single-point energy correction using an implicit solvation model, the Solvation Model based on Density (SMD), with the dielectric constant for dichloroethane, which is the actual solvent used in the experiment.

This model is based on the Polarizable Continuum Model (PCM) using the integral equation formalism polarized continuum model (IEFPCM). The SMD method generates the cavity containing a substrate molecule encapsulated by polarizable continuum which is continuously created from the dielectric constant. A change in the polarization of the continuum around a substrate reflects the effect of solvent on the active site of the molecule. The correction calculations have been done using the same method and basis set as all previous calculations.

5.2.5 Dispersion correction

The energies to correct for dispersion effects were performed using an add-on B3LYP-D3 function as explained in chapter 2.
5.3 Results and Discussion

5.3.1 Optimization of isolated structures in gas phase

The structural models of the substrates with three different nucleophiles containing oxygen, nitrogen, and sulfur, have been optimized in order to search for the most stable structure for each reactant. The conformational search was performed taking into account the rotation around each single bond in the substrates. Some experimentally optimized parameters were used. These include the temperature of 353.15 K and the dichloroethane solvation model. The stable structures shown in Figure 5.4. as 7a, 7b, and 7c, refer to O-, N-, and S-nucleophiles, respectively.

The most stable structure of the O-nucleophile 7a is shown in Figure 5.4. In this structure, we have found the important role of van der Waals interactions in the model containing an oxygen nucleophile. Interestingly, the relative energy of 7a without the dispersion correction is considered as half of the one which involves the effect (0.93 kcal/mol). In 7a, the strong hydrogen bonding between the hydrogen of the benzylic OH group and the oxygen of the terminal OH group (Figure 5.4.) helps to stabilize the conformation by ≈ 1.9 kcal/mol compared to the other structures without the hydrogen bond.

Structures containing the similar hydrogen bond are also found for N-, and S-nucleophiles with a longer bond distance (from 2.050 to 2.304 Å). However, these structures are not the most stable ones. In case of N-nucleophile, the dispersion in the compounds which contain intramolecular hydrogen bonds, has been found to destabilize the structures by around 20% compared to the other linear structures. The most stable structure for this nucleophile was a linear structure in which one terminal phenyl ring is perpendicular to the other (7b). The most stable structure of the S-nucleophile was also found to be linear (7c). Furthermore, the relative free energies in products showed negative values which indicates that the substitution reactions are exothermic. The most thermodynamically stable product was 8c.
5.3.2 Transition state calculations for the H$_3$PO$_2$ catalyst

From experimental data, it was proposed that the reaction mechanism could not proceed through an S$_{N}$1 mechanism. Consequently, the saddle point calculations were considered from all feasible structures based on an S$_{N}$2 pathway. All calculated transition states were clearly found to be bridge-like configurations with two hydrogen bonds connected between H$_3$PO$_2$ and the nucleophile in one side, and between the catalyst and oxygen of substrate on the other side. These transition state structures were confirmed by an imaginary frequency (with a negative value of the force constant) presented in a mode of vibrational outputs.

In these cyclic transition states, the oxo group of H$_3$PO$_2$ attracts the proton from the nucleophile while its acidic proton protonates the leaving OH group of the substrate, resulting in a water molecule at the end of process. The bridging transition state structure demonstrates the bifunctional role of H$_3$PO$_2$ and it is considered as the key to support an S$_{N}$2 mechanism in the intramolecular substitution.
Figure 5.5. Transition state structures for the intramolecular nucleophilic substitution by the oxygen nucleophile using H$_3$PO$_2$ as a catalyst. All the interatomic distances are in Å.

Figure 5.6. Transition state structures for the intramolecular nucleophilic substitution by the nitrogen nucleophile using H$_3$PO$_2$ as a catalyst. All the interatomic distances are in Å.
For the oxygen nucleophile, two transition states have been found with similar energies of 27.3 and 27.5 kcal/mol (Figure 5.5.). The main difference between these structures is the rotations of the catalyst over the substrate.

For the nitrogen nucleophile, three different structures have been found (Figure 5.6.). The differences between them are the position of second sp\(^2\) carbon next to the nitrogen and the direction of the leaving water molecule. The lowest saddle point for the nitrogen nucleophile was TS\(_{1b-8b}\) with the energy of 23.1 kcal/mol. Four possible transition states were found for the sulfur nucleophile.

Two twist bridge-like (TS\(_{1c-8c}\) and TS\(_{2c-8c}\)) and the other direct bridge-like (TS\(_{3c-8c}\) and TS\(_{4c-8c}\)) structures were demonstrated in Figure 5.7. The TS\(_{1c-8c}\) has the lowest transition state energy of 26.8 kcal/mol.

For all transition states, the C–O bonds at the benzylic position of 7a, 8a, and 9a, were noticeably elongated from around 1.4 to be 2.2 Å.

Figure 5.7. Transition state structures for the intramolecular nucleophilic substitution of the sulfur nucleophile using H\(_3\)PO\(_2\) as a catalyst. All the interatomic distances are in Å.
A bifunctional role of the phosphinic acid to promote an $S_N2$-type reaction mechanism by an activation of both the C–O bond of the nucleofuge (the leaving OH group) and the nucleophile, was revealed. The bridging transition states lead to an inversion of configuration at the carbon center in the product.

The energy barriers for transition states for the O-, N- and S-centered nucleophiles were 27.3, 23.1, and 26.8 kcal/mol, respectively, as can be seen in Figure 5.8. These values are in agreement with the experimental findings that only the N-centered nucleophiles were reactive at 60 °C, while the reactions containing S- or O-centered nucleophiles only proceed at a higher temperature (80 °C).

![Figure 5.8](image)

**Figure 5.8.** PES of the stereospecific nucleophilic substitution of the OH group in selected benzylic alcohols. The provided $E_{\text{ads}}$ are in kcal/mol.

5.3.3 Transition state calculations for other catalysts

Finding transition states for other catalysts, which have a similar motif to phosphinic acid, was also performed. These include para-toluenesulfonic acid ($p$-TSA), $\text{Ph}_2\text{HPO}_2$, and $\text{CH}_3\text{COOH}$. As shown in Figure 5.9., the activation energy of $p$-TSA is lower than that of $\text{H}_3\text{PO}_2$, and the distance of the C–O activation site is slightly longer. The weaker interaction in the bridging tran-
Transition state might reflect the lower chirality transfer in product. In case of acetic acid (\(\text{CH}_3\text{COOH}\)), the activation energy of 36.6 kcal/mol was found. This high barrier corresponds to no reactivity being observed experimentally.

The results of using seemingly similar Ph\(_2\)HPO\(_2\) as a catalyst were more intriguing since a reasonable transition state energy was found (27.6 kcal/mol). Experimentally, the reaction was observed after heating up to 120 °C. Thereby, these transition state calculations can also be correlated to the experimental results.

![Figure 5.9. Transition state structures for the intramolecular nucleophilic substitution of the oxygen nucleophile using \(p\)-TSA, Ph\(_2\)HPO\(_2\) and CH\(_3\)COOH. All the inter atomic distances are in Å.](image-url)
5.4 Conclusions

A bifunctional role of the phosphinic acid (H₃PO₂) as a catalyst for the intramolecular nucleophilic substitution of the OH group in benzylic alcohol, has been revealed. Here, hybrid DFT calculations demonstrate that the catalyst can promote a unique bridging transition state which leads to an S₅₂-type reaction mechanism.

The substitution of the OH in alcohols was promoted by, on one side, H₃PO₂ protonating the oxygen of OH group, while, on another side, by the catalyst deprotonating the nucleophile, leading to a full inversion of configuration of the carbon in the product. The transition state energies correlates to the temperature at which the reactions can be experimentally performed.

Transition state structures of other Brønsted acids (p-TSA, Ph₂HPO₂ and AcOH) with the O-centered nucleophilic substrate, were also studied. The TS calculated for p-TSA (21.1 kcal/mol) was lower than the one in the H₃PO₂ case (27.3 kcal/mol). This result corresponds to the experimental outcome in which the stronger acid promotes the reaction at a lower temperature (at 40°C).

In addition, we found that acetic acid which is a weaker acid than other catalysts, was not reactive enough to promote the intramolecular reaction. This is due to its high energy barrier (36.6 kcal/mol). Lastly, the transition state for Ph₂HPO₂, which has a similar structural motif to H₃PO₂, has been calculated to 27.6 kcal/mol. The energy barrier is slightly higher than the one of H₃PO₂. This can be a reason for a higher reaction temperature was required when Ph₂HPO₂ was used as a catalyst in the reaction.
6. Concluding Remarks

In this thesis, interactions between bioorganic molecules with a metal-based (palladium surface) catalyst, and a non-metal acidic catalyst (H$_3$PO$_2$), were investigated and elucidated by using computational chemistry approaches.

The first section describes the possibility of tautomerization as an important step in palladium-catalysed lignin depolymerisation through the β-O-4' bond (model 1) cleavage. Here, computational techniques were used to explore the most stable structures of adsorption complexes between molecular models and a palladium surface. By comparing adsorption properties of the intermediates 2 (keto) and 3 (enol), to the Pd surface, the importance of the tautomerization was revealed. The study in this section has been divided into three parts.

In the first part of the section (Paper I and chapter 3), DFT approaches combined with AIMD were able to give insights into the adsorption of simplified structures 2' and 3' to the catalyst surface. In the second part, the models were expanded by having aryl groups (Paper II and chapter 3). The results from using DFT-D3 revealed a strong adsorption of the aryl groups of the lignin models to the palladium. The molecules interacted more strongly to the surface at low coverages especially in case of the enol tautomer. The results from these calculations confirm that the cleavage of the β-O-4' bond can occur through the tautomerization of the keto intermediate 2.

In the third part (Paper III and chapter 4), molecules from a catalytic fractionation were investigated by using a reactive force field (ReaxFF) combined with MD simulations. Important reactions of the lignin models throughout the fragmentation including chemisorption, C–O bond breaking, and reduction of a C=C bond, were explored. The multilevel method provided good results with acceptable accuracy in a reasonable calculation time. Effects of real solvent mixture used in experiment were also analyzed.

The second section focuses on a theoretical investigation of Brønsted acid-catalyzed nucleophilic substitution of alcohols (Paper IV and chapter 5). Benzylic alcohols with internal O-, N-, and S-centered nucleophiles, were used in these calculations. The catalyst is H$_3$PO$_2$, which was experimentally proven to give excellent yields and chirality transfers. The calculations support an S$_{N}$2 mechanism proceeding through a bicyclic transition state in agreement with the experimental results. Reasonable reaction barriers have also been found.

We hope that the approaches used in this thesis will be used by and inspire other researchers in this field.
Appendix A: Contribution List

The author wishes to clarify her contribution to the publications and manuscripts in this thesis.

I. Major contribution to planning the calculations including the selection of calculation methods. Major contribution to writing computer scripts for the molecular dynamics simulations. Performed all the calculations. Wrote the manuscript and prepared the supporting information.

II. Major contribution to planning the calculations including the selection of calculation methods. Performed conformational search for molecules and surfaces and performed all adsorption calculations. Wrote the manuscript and analyzed all the data.

III. Major contribution to the conformational search calculations of substrates and preparations of the main training set for the FF. Minor contribution on validation of FF. Minor contribution to the molecular dynamics simulations and mechanistic studies but involved in all the discussions. Minor contribution to the preparation of manuscript and the supporting information.

IV. Moderate contribution to the optimization of all molecular models. Performed all transition state calculations. Interacted with experimental chemists for discussions on the reaction mechanisms. Minor contribution to the preparation of the manuscript, however, major contribution to the supporting information.
Appendix B: Reprint Permissions

Reprint permissions were kindly granted for each publication by the following publishers:

I. **Detecting Important Intermediates in Pd Catalyzed Depolymerization of a Lignin Model Compound by a Combination of DFT Calculations and Constrained Minima Hopping**
   Srifa, P., Galkin, M.V., Samec, J. S. M., Hermansson, K., Broqvist, P.*
   Copyright © 2016 American Chemical Society

II. -

III. **ReaxFF Simulations of Lignin Fragmentation on a Palladium-Based Heterogeneous Catalyst in Methanol–Water Solution**
    Monti, S.*, Srifa, P., Kumaniaev, I., Samec, J. S. M.*
    Copyright © 2018 American Chemical Society

IV. **Brønsted Acid-Catalyzed Intramolecular Nucleophilic Substitution of the OH Group in Stereogenic Alcohols with Chirality Transfer**
    Copyright © 2015 American Chemical Society
Acknowledgements

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