

# UNIVERSIDAD DE INVESTIGACIÓN DE TECNOLOGÍA EXPERIMENTAL YACHAY

Escuela de Ciencias Químicas e Ingeniería

# TÍTULO: Theoretical Approach on the Comparison between the Oxidative Dehydrogenation of Amines and MOF Mediated Amine Oxidation

Trabajo de integración curricular presentado como requisito para la obtención del título de Químico

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Urcuquí, Abril 2022



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# DEDICATION

To my family and friends, especially to my mother Nena.

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#### RESUMEN

La deshidrogenación oxidante juega un papel importante en la producción de materias primas para la industria química, petroquímica, polímeros, farmacológica y agroquímica. Se han realizado estudios en diferentes investigaciones relacionadas con la producción de formaldehído, heterociclos de nitrógeno, iminas y en sistemas bioquímicos como la alcohol deshidrogenasa, la galactosa oxidasa y la amina oxidasa. La deshidrogenación oxidante de aminas para producir iminas ha generado un gran interés en la comunidad científica ya que las iminas pueden participar en diversas reacciones químicas como reducciones, condensaciones, adiciones y reacciones de cicloadición electrófilas. Una de las características más importantes de la deshidrogenación oxidante es su alta selectividad para formar iminas a partir de aminas y por ello se han utilizado diferentes catalizadores, disolventes, condiciones ambientales, estructuras metal-orgánicas (MOF) y complejos metálicos en combinación con diferentes metales de transición con el fin de aumentar los rendimientos de la reacción. El cobre(II) en Cu-BTC y el hierro(III) en tetraciano(1,2-diamina)ferrato(III) se han utilizado como centros metálicos en la deshidrogenación oxidativa de aminas debido a que estos metales son abundantes, baratos y de fácil acceso.

En este trabajo se ha realizado un estudio comparativo entre los mecanismos de reacción para la formación de iminas a través la deshidrogenación oxidante promovida por la coordinación del ligante amínico al hierro(III) y la oxidación de aminas catalizada por un MOF de cobre(II) mediante la optimización de las geometrías, frecuencias y las cargas de Mülliken basadas en cálculos computacionales DFT. La presencia de Fe(III) y Cu(II) como metales de transición en el tetraciano(1,2-diamina)ferrato(III) y Cu-BTC respectivamente, son los responsables de promover la oxidación de la amina coordinada que lleva a la formación de iminas. Los resultados obtenidos de las simulaciones DFT para cada paso del mecanismo de reacción del tetraciano(1,2-diamina)ferrato(III) y el Cu-BTC revelan que se requieren altas energías para formar la imina para cada paso del mecanismo de reacción, pero el mecanismo del Cu-BTC para la formación de iminas fue más favorecido termodinámicamente.

**Palabras clave:** Deshidrogenación oxidante, MOF, DFT, complejos de hierro, mecanismo de reacción.

# ABSTRACT

Oxidative dehydrogenation play an important role in the production of raw materials for chemical, petrochemical, polymers, pharmacological and agrochemical industry. Moreover, studies in different investigations have been performed in relation to the production of formaldehyde, nitrogen heterocycles, imines, and biochemical systems such as alcohol dehydrogenase, galactose oxidase, and amine oxidase. The oxidative dehydrogenation of amines to produce imines have attracted a great interest within the scientific community because imines can react as electrophiles in reductions, condensations, additions and cycloadditions reactions. One of the most important characteristics of oxidative dehydrogenation is its high selectivity to form imines from amines and for that reason several solvents, environmental conditions, metal organic frameworks and metal complexes in conjunction with different transition metals have been used as catalysts for the purposes of increasing the reaction yields. Copper(III) in Cu-BTC and iron(III) in tetracyano(1,2-diamine)ferrate(III) have been used as metallic center in oxidative dehydrogenation of amines because these metals are abundant, cheaper and easily accessible.

In this work, a comparison study between the reaction mechanisms to the imine formation through oxidative dehydrogenation promoted by the coordination of the amine ligand to iron(III) and the catalyzed oxidation of amines by a Cu(II)-MOF was carried out by using geometry optimizations, frequencies and Mülliken charges based on DFT computational calculations. The presence of Fe(III) and Cu(III) as transition metals in tetracyano(1,2-diamine)ferrate(III) and Cu-BTC respectively are the responsible to promote the oxidation of the coordinate amine which influence the imine formation. The results obtained from the DFT simulations for each step of the reaction mechanism of tetracyano(1,2-diamine)ferrate(III) and Cu-BTC reveal that high energies are required to form the imine for each step of the reaction mechanism but Cu-BTC mechanism for the formation of imines was more thermodynamically favored.

**Key words:** oxidative dehydrogenation, MOF, DFT, iron complexes, reaction mechanism.

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#### **Chapter 1. Background**

#### 1.1 The importance of amines and imines

Amines are nitrogen compounds and have been found in various processes of organisms that employ amines or amine-derivatives as a part of their reaction mechanism, for example, glycolysis and amino acid metabolism<sup>1</sup>. Primary amines are usually used to form imines which have been the construction blocks of a great variety of applications such as catalyzers and chemosensors<sup>2–4</sup>. Moreover, imines have also been known to play a crucial role in the agrochemical and pharmaceutical industry<sup>5,6</sup> due to their electronic structures, imines can acts as an electrophile in several reactions of reduction, addition, condensation, and cycloaddition<sup>7,8</sup>.

The functionality of imines is known as Schiff base, and it is named after the Italian chemist Hugo Schiff, the preparation of imines by condensation of a carbonyl compound with an amine under azeotropic distillation<sup>9</sup>. Imines are one of the organic compound families more used in coordination chemistry due to their ability to bond metallic ions in complexes. Chakraborti *et al.*<sup>10</sup> proposed a new method (Scheme 1) to synthesize imines by the use of Lewis acids to activate the carbonyl group of aldehydes and catalyze the nucleophilic attack by amines with the aim of improving the efficiency of Schiff bases.



Scheme 1. Synthetic route for imine formation proposed by Chakrabort et al. in 2004<sup>10</sup>

Currently, the great interest in the coordination complexes derived from the Schiff bases is due to the enrichment of their biological and therapeutic properties<sup>11</sup>. 4-aminoantipyrine is a heterocycle compound and has been profoundly studied for its antipyretic and biological activities. Mohamed and coworkers<sup>12</sup> have reported the synthesis, antibacterial, cytotoxic, and anti-tumor studies of 4-aminoantipyrine derived from Schiff bases (Scheme 2).



Scheme 2. Synthesis of Schiff bases derived from 4-aminoantipyene proposed by Mohamed et al. in 2015<sup>12</sup>

These coordination compounds are formed because of the strong affinity to the chelation of the Schiff bases towards transition metal ions<sup>13</sup>. The Schiff base metal complexes (Scheme 3) synthesized with 4-aminoantipyrine derivatives with some aldehydes and ketones show a more remarkable improvement in the biological, pharmacological, clinical, and analytical applications<sup>14</sup>.



Scheme 3. Octahedral complex resulting from coupling reaction between 4-aminoantipyrine and 2-clorofenol with metal salt proposed by Mohamed et al. in 2004<sup>15</sup>

#### 1.2 Coordination complexes based on amines

One of the pharmacological applications with more potential is the synthesis of Platinum amine coordination compounds such as *cis*-dichlorodiammineplatinum(II), which is used as an active anti-tumor agent thanks to their interaction with the cell membrane, which allows the inhibition of DNA-Polymerase<sup>16</sup>. On the other hand, Abdelhamid *et al.*<sup>17</sup> proposed imidazole compounds that contain Cr, Fe, or Cu because they possess a high antimicrobial and antifungal activity own to the chelate effect of the ligands, the total charge on the complex ion, nature of the donor atoms, metal ion, counter ions, and the geometrical structure of the complex. Amines are also used to polymerize copralactone and 1-hexene and ethane by using amine bis(phenolate) lanthanide methyl complexes and

cyclopentadienyl phenoxy-imine and phenoxy-amine complexes of titanium and zirconium<sup>18</sup>.

## 1.3 The role of amines in MOF compounds

The coordination complexes that involve transition metal ions and multidentate organic ligands are also known as MOFs (metal-organic frameworks). The study of MOF began in 1990 because of the great interest in developing materials with polymeric and porous structures from metal ions and organic ligands<sup>19–23</sup>. MOFs are commonly used for gas adsorption, separations, a new generation of batteries, medical drug, and catalysis<sup>24–29</sup>. The wide variety of particular uses in different reactions is due to their distinctive characteristics such as high values of porosity, good thermal stability, magnetic, electronic, and thermal properties<sup>30</sup>. All chemical and physical properties are attributed both to the transition metal and to the organic bridging groups.

Recent studies showed that MOFs with pendant amines could be used for biomedical applications in the controlled release of nitric oxide, which is crucial in the cardiovascular, nervous, and immune system<sup>31,32</sup>. On the other hand, iron-based oxalate-phosphate-amine MOFs could be used in agriculture to help reduce soil fertility own to their high oxalate solubility, mainly attributable to the largest possible pore sizes<sup>33</sup>. Furthermore, the MOF oxalate solubility is required to initiate bacterial mineralization, and, at the same time, it is essential for a more efficient control for releasing the plant nutrient in soil<sup>33</sup>. More recently Jinlin *et al.*<sup>34</sup> have reported an amine-functionalized zirconium MOF(UiO-66-NH<sub>2</sub>) as visible-light photo-catalyst for aerobic organic transformations such as alcohols, olefins, and cyclic alkanes with a high efficiency and high selectivity.

There are different studies carried out on the oxidative dehydrogenation of amines to produce imines with MOFs, but there is only one investigation where copper is the transition metal used and which, in addition, the mechanism is proposed<sup>35</sup>. Cu-BTC is the MOF used as catalyst thanks its Lewis acid sites to the oxidative dehydrogenation of benzylamine as one can see in the Scheme 5.



Scheme 4. Reaction mechanism of benzylamine oxidative dehydrogenation for the synthesis of the corresponding imine by using Cu-BTC MOF as catalyst proposed by Boosa et al.<sup>36</sup>

#### 1.4 Evolution of theories to understand the behavior of the coordinative bonds

In 1923, G.N. Lewis proposed an alternate theory to explain the coordinate covalent bonds that cannot be explained by the Arrhenius and Brönsted-Lowry theories that are limited to substances in aqua dissolutions and proton transfers, respectively<sup>37</sup>. Lewis's acid-base theory is based on electron sharing and defines an acid as a species able to accept or share one electron pair donated by a base and a base as a species able to donate or share an electron pair donated by an acid<sup>37</sup>.

In coordination compounds, the metals are the Lewis acids which means that they are the electron attracting due to their lowest unoccupied molecular orbital (LUMO). In contrast, the ligands are the Lewis bases that have lone electron pairs in the highest occupied molecular orbital (HOMO)<sup>38</sup>. The coordinate covalent bonds are formed when the lone

electron pair in HOMO fill the Lewis acid's LUMO because of the Lewis base's nucleophilicity and electrophilicity of the Lewis acid.

The hybridization, geometry, and the magnetic character of coordination complexes are justified with the valence bond theory which affirms that the coordination bonds are formed when the ligand electrons fill the hybrid orbitals of the metal. However, this theory has a problem justifying the color and the electronic spectra of the complexes.

The limitations of the valence bond theory were solved with the crystal field theory because this theory is based on an electrostatic model, and the bond between the metal (positive point charge) and the ligand (negative point charge) is considered as a "ionic" bond<sup>39</sup>. The formation of coordination bonds occurs when the punctual charges of the ligands interact with the ungerade d-orbital of metal by electrostatic attraction and repulsion of the charges<sup>39</sup>. This interaction produces crystal field splitting of the metal and redistribution in the space of the d orbitals to achieve maximum energetic stability. The factors that influence the crystal field splitting are the oxidation state of the metal ion, geometry of ligands, nature of ligands, and the metal ion that produces that metal can be weak field-high spin or strong field-low spin<sup>40</sup> as can be seen in the Figure 1.

The crystal field theory allows it to predict the stability of an oxidation state of a particular complex, degenerate of d orbitals, and the ligands' type. Moreover, the spectroscopic (color) and magnetic (paramagnetic or diamagnetic) properties also can be explained. However, one of the problems of this theory is found in the interpretation of some organometallic complex spectral based only on the crystal field theory<sup>41</sup>.



Figure 1. High spin and low spin diagram energy for 3d<sup>5</sup> orbital

The ligand field theory is an adaptation of the molecular orbital theory based on the crystal field theory in which the bonds are covalent and allows it to explain the limitation of the crystal field theory. The antibonding orbitals are taken into account, and the ligand field theory affirms that the overlapping forms the covalent bond between the central ion and ligand orbitals with an adequate symmetry, and as a consequence, the molecule orbitals are formed<sup>42</sup> as can be seen in the Figure 2.

In 3d orbitals, the complex can have a high spin or low spin configuration in comparison with the metals that have 4d and 5d orbitals which always will be low spin. This is due to a significantly energy decrease in orbitals with bigger size and therefore, the electrons will prefer the orbitals with low energy. The molecular orbitals formed can have sigma, sigma\*, or pi interaction<sup>42</sup>. The pi interaction between the ligand and the metal depends on whether the orbital is full or empty. This interaction gives it information about the order of the spectrochemical series, the trend, the bond strength, and the crystal field splitting<sup>42</sup>.



Figure 2. Ligand field energy diagram for an octahedral complex with pi-donorligands<sup>43</sup>

# **1.5 Oxidative Dehydrogenation**

Several methods have been employed to synthesize imines (Scheme 5). Condensation is one of the traditional methods that presents several problems, such as using odorous and unstable aldehydes that also require *in situ* purification prior to use<sup>44,45</sup>. Another method that suffers limitations is hydrogenation because the reactions require high temperatures and active, sensitive, expensive, and not easily accessed novel metal complexes<sup>46,47</sup>. In contrast, the methods used to form imines by oxidative dehydrogenation have been proved to be efficient, cheaper, and environmentally friendly.



Scheme 5. Organic synthesis of imines as different intermediates<sup>48</sup>

Oxidative dehydrogenation began to be studied in 1960 in the conversion of secondary amine groups to azomethine linkages<sup>49</sup>. The studies affirm the relevance of this type of reaction because they can be applied in the production of formaldehyde, nitrogen heterocycles, imines, and biochemical systems such as alcohol dehydrogenase, galactose oxidase, and amine oxidase<sup>50,51,52</sup>.

High selectivity performance in the formation of formaldehyde has been reported in the oxidation of methanol with a MoO<sub>3</sub> catalyst prepared on the surface of  $F_2O_3$  at 275°C<sup>53</sup>. The presence of molybdenum oxide on the surface plays a vital role and it improves the reaction by a 5-fold increase with a 90% conversion of formaldehyde and reduction in the amount of produced CO<sub>2</sub>.

Therapeutic potential in diverse disease models, natural products, organic dyes, and pharmaceutical intermediates are the most plausible applications for nitrogen heterocicles<sup>51</sup>. Several oxidants have been used to obtain significant yields, but one with the greatest potential in the oxidative dehydrogenation of tetrahydroquinazolines with aldehydes in acetonitrile is the o-Iodoxybenzoic conducted at room temperatures<sup>54</sup>. The reaction involves an attack by nitrogen tetrahydroquinazolines on the iodine center of o-Iodoxybenzoic followed by a reduction to generate the dihydroquinazoline.

Through the years, the selective oxidation of amines into imines has been studied with different methodologies, and catalysts. Many of these studies have achieved good yields by the use of catalysts based on metals such as  $Ru^{48}$ ,  $Co^{55}$ ,  $Cu^{56}$ ,  $Au^{57}$ ,  $Ni^{58}$ ,  $Pd^{59}$ ,  $Zn^{60}$  and  $V^{52}$ . In addition, photocatalytic systems based on  $TiO_2^{61}$ ,  $NB_2O_5^{62}$  and mesoporous graphite carbon nitride<sup>63</sup> under visible light irradiation also have been reported in the amine oxidation.

The growing interest in the oxidative dehydrogenation reactions by metal complexes has allowed the study of different metal transitions because they have proven to be a more sustainable, economical, and highly effective method in the oxidative dehydrogenation of amines. Polyethylene glycol clicked-immobilized Co(II) Schiff base is used as a catalyst, and in oxidative dehydrogenation tert-butylhydroperoxide as oxidant of secondary amines<sup>64</sup>. The catalytic activity presents high product yields and it can be easily recovered by precipitation of diethyl ether.

Another promising metallic complex catalyst reported (Scheme 6) is the octa-aza macrocyclic dinucleating ligand coordinated to Cu(II) in which the amine groups in one macrocycle is oxidized, and the Cu(II) centers are reduced<sup>65</sup>. The novelty of this investigation lies in the spontaneity of the oxidative dehydrogenation reaction and the absence of oxidants or external bases for the synthesis of imines.



Scheme 6. Reaction proposed for the cooper catalyzed amine to imine where L is octaazamacrocyclic dinucleating ligand by Gemma et al.<sup>65</sup>

Moreover, one of the most studied transition metal that promotes oxidative dehydrogenation is iron because its versatility in oxidation states, affordable redox potentials and their ability to promote both one-electron and two-electron reaction mechanisms. Fe(NO<sub>3</sub>)<sub>3</sub>/2,2,6,6-tetramethylpiperidin-1-yl)oxyl (TEMPO) system was used as the first method based on Fe to catalyze the oxidative dehydrogenation reaction of primary and secondary amines to obtain imines<sup>45</sup>. The addition of TEMPO to Fe(NO<sub>3</sub>)<sub>3</sub> improve the efficiency of the reaction from 66% to 85% of yield. Zhang and Coworkers<sup>45</sup> a biofriendly method as the main objective in which proved Fe(NO<sub>3</sub>)<sub>3</sub>/TEMPO with air as oxidant. Byproducts such as nitriles and amides was not observed, revealing the high imine selectivity and allowing to reach a 98% of yield reaction at 80°C in toluene as solvent.

Tetracyano (1,2-diamine) ferrate(III) is a metal complex that has been studied in the oxidative dehydrogenation reaction to produce imine. Goto *et al.*, proposed a mechanism in which tetracyano(1,2-diamine)ferrate(III) is reduced to the corresponding tetracyano(1,2-diimine) ferrate(II) under neutral or basic pH with different solvents such as  $H_2O_2$ ,  $ClO_2^-$ ,  $[Fe(CN)_6]^{3-}$  and  $O_2^{35}$ . In the oxidative dehydrogenation reaction mechanism of amine there are two proton transfers and one electron transfer to form the first imine as it can be seen in Scheme 7.



Scheme 7. Reaction mechanism of Tetracyano (1,2-diamine) ferrate(III) oxidative dehydrogenation for the formation of Tetracyano (1,2-diimine) ferrate(II) proposed by Goto et al.<sup>35</sup>

A similar study about oxidative dehydrogenation of amines conducted by Lopez<sup>66</sup> was made with the primary goal of evaluating the reactivity of Fe(III) against two pyridinic ligands (L2 and L3) substituted in positions 2 and 3 of the pyridine ring. Experimental analysis of magnetic susceptibility, cyclic voltammetry, IR, NMR, and UV-Vis spectroscopy was performed to characterize and study the kinetics of the reaction product (Figure 3) obtained from the interaction between the ligands and [Fe(DMSO)<sub>6</sub>](NO<sub>3</sub>)<sub>3</sub>. Even though the structure of the two ligands is almost identical, the results show that the acidity of the proton presents a considerable difference in the pyridinic ligand substituted in position 2 when it is removed.



Figure 3. Formation of  $[Fe(II)(L2)(DMSO)]^{2+}$  complex in presence of oxygen<sup>66</sup>

Jimenez<sup>67</sup> made a theoretical study about the investigation mentioned above to corroborate and compare the stability of both pyridinic ligands when an iron complex is added. Density functional theory was used to perform the theoretical calculations and compare the energies involved in each step of the reaction mechanism showed in the Figure 4. In addition, different solvents and basis sets were probed to establish the influence on the behavior of the oxidative dehydrogenation reaction. As a result, higher stability of the system was obtained by using methanol and def2-SVP (split valence polarization) as solvent and basis set, respectively, for the formation of imines by oxidative dehydrogenation of amines.



 $\mathbf{R}$ = H, CH<sub>3</sub>, CH<sub>3</sub>CH<sub>2</sub>

Figure 4. Proposed mechanism for oxidative dehydrogenation of amine<sup>67</sup>

# 1.6 Computational chemistry fundamentals

Computational chemistry simulate structures and chemical reactions based on physical theories<sup>68</sup>. The development of technology and computational tools applied to chemistry have allowed it to study the electronic interactions in molecular systems.

The obtained results from computational simulations can solve chemical problems that save time and money from experimental activities. One example of this is the possibility of modeling a molecular system in which there are short-lived compounds prior to use them in the laboratory computing can be done to analyze the electronic behavior and predict if it is possible to carry out the reaction in real life.

Two different physical principles support computational chemistry, the molecular mechanic based on classical mechanics, and the other principle is the quantum mechanics based on electronic structure methods classified in three groups: ab initio, density functional theory, and semi empirics<sup>68</sup>.

The wave function calculation is not required directly for the DFT method in comparison with ab initio and semi empiric methods due to all molecular properties are described as a function of electronic density. DFT is the method most reliable and widely used in chemistry, biology, and physics to compute efficiently and accurately the electronic structure of atoms, molecules, and solids<sup>69</sup>.

# 1.6.1 DFT basis

DFT was developed with the main goal of solving the Schrödinger equation in a simple way. An easy and appropriate description of the matter's quantum nature is achieved with the DFT technique because the Schrödinger equation was considered from a different philosophically and computationally point of view. DFT is supported by the Hohenberg-Kohn theorem<sup>70</sup>, in which the electron density,  $\rho_s(\vec{r})$ , is used to determine the groundstate properties for a system with 2N electrons that do not interact with each other, and it is described to  $\psi_i$  orbitals so that the electron density coincide with the real system  $\rho(\vec{r})$ , which is formulated as follows in the equation 1:

$$\rho_s(\vec{r}) = 2\sum_{i=1}^N |\psi_i|^2 = \rho(\vec{r})$$
(1)

Hohenberg-Kohn theorems are the basis for the Kohn-Sham theory<sup>71</sup> that allows it to reduce the difficulty in the electron-electron interaction term where the electrons interact with an external potential it is simplified to a problem where the electrons have an effective potential and do not present interaction<sup>72</sup>. The N electrons of the wave function in the Schrödinger equation are reduced by a simpler function (electron density) that only depends on three space coordinates independent of the electron numbers and allows it to significantly decrease the computational costs. The DFT according to the equation 2 and Kohn-Sham theory is given by:

$$E_{KS}(\rho) = T_{s}(\rho) + E_{en}(\rho) + J(\rho) + E_{xc}(\rho)$$
(2)

Kohn-Sham electronic energy,  $E_{KS}$  is dependent of electron density,  $\rho$ , and also  $T_s$ ,  $E_{en}$ , J, and  $E_{xc}$ . These terms represent the system kinetic, potential and Coulombic energy, respectively. Finally, the correlation and interchange term of electrons represented by  $E_{xc}$  is considered as an electron density functional and the kinetic energy that is not taken into account in  $T_s$  is added in order to have an independent particle system<sup>73</sup>. This theory presents a difficulty when looking expressions for  $E_{xc}$  of an accurate way and for that reason a great variety of functionals have been developed.

#### 1.6.2 B3LYP

Currently, there are different functionals to calculate an approximation to the exchangecorrelation term and are classified in density local, generalized gradient, and hybrid approximation<sup>72</sup>. Although, density local and generalized gradient approximation present good results, the remarkable performance in many areas of chemistry was achieve with the addition of a fraction of Hartree-Fock exchange in the functional also known as B3LYP functional.

B3LYP is a hybrid functional because its terms depend on the local spin density, gradient, and 20% of Hartree-Fock interchange terms. The functional is formed by the interchange functional of three parameters Becke (B3)<sup>74</sup> and Lee, Yang, and Parr (LYP) correlation functional<sup>75</sup>. The B3LYP functional is expressed as follows in the equation 3:

$$E_{XC} = E_{XC}^{LSDA} + a_0 (E_{XC}^{exact} - E_X^{LSDA}) + a_X \Delta E_X^{B88} + a_c \Delta E_C^{PW91}$$
(3)

where:

 $E_X^{exact}$  is the exact interchange energy

 $E_X^{B88}$  is the gradient correction for the Becke interchange reported in 1988

 $E_c^{PW91}$  is the gradient correction for the Perdew and Wang correlation reported in 1991

The optimal values determinate values for the semi empiric coefficients are  $a_0 = 0,02$ ,  $a_x = 0,72$  and  $a_c = 0,81$ 

B3LYP is one of the most used functional in different investigations because of the low computational costs, reasonable results in the predictions of barrier heights, bonds energies, and geometries, especially for organic systems<sup>76</sup>. The disadvantages of this method relies on the appearance of transition metals.

#### 1.6.3 Programs used for computational simulations

# 1.6.3.1 Avogadro

Avogadro is a free molecular editor and visualizer available for all operating systems, and it is used widely in computational chemistry to build 3D chemical structures, format input files, and analyze the output of different computational program packages<sup>77</sup>. Moreover, Avogadro included an option to prepare an input file for DFT calculations in ORCA that expresses in 3N Cartesian coordinates the constructed molecule.

#### 1.6.3.2 ORCA

ORCA is a program package that allows it to obtain information about electronic interactions from different electronic structure methods. The main advantage of ORCA relies on their wide range of computational chemistry applications as well as on their powerful, reliable, flexible, graphical, and user-guide interfaces<sup>78</sup>. ORCA is considered a modern quantum chemistry program that uses standard Gaussian, effective core potential, and auxiliary basis sets (def2)<sup>79</sup>. The applications more used in ORCA are the transition states and geometry optimization and computing of the vibrational frequencies and free energy of solvation that are usually corroborated with the computational results of different spectroscopic properties. Additionally, the Cartesian coordinates from the input file generated for Avogadro are converted into internal coordinates (bond lengths and valence angles) for ORCA because, in geometry optimization, the Cartesian coordinates do not reflect the chemical structure and bonding of a molecule<sup>80</sup>.

### 1.6.4 Basis set

The basis set is commonly used in computational chemistry in combination with DFT, HF, or ab-initio methods because it allows it to obtain reliable results. The Ahlrichs def2 basis set family, which covers most of the periodic table, can be recommended for DFT calculations<sup>81</sup>. Def2 basis is a set of polarization functions of the elements from H to Rn with the main goal of reducing the computational work and, as a consequence improving the electronic structure approximation. Def2-SVP basis set contains polarizing p functions for the H and an f function for the d-elements that reduce the errors of the B3LYP method for d-compounds<sup>82</sup>.

#### **1.6.5 Potential energy surface**

The relationship between the energy and geometry of a molecule is possible to determine by calculating the potential energy surface (PES). The PES concept is based on the Born-Oppenheimer approximation which affirms that the movement of the electrons is faster than the nuclei and therefore the nuclei position is considered as fix<sup>83</sup>. The calculation of the energy of every atomic arrangement are classified according to the first and second derivate of the energy in relation with the atomic position<sup>83</sup>. In addition, the plot of the all single point energies for all atomic arrangements allows it to obtain the PES diagram. The most important points are the stationary points (zero gradient) because they are involve in the physical behavior as one can see in the Figure 5.



Figure 5. Potential Energy Surface diagram illustrating transitions states, saddle points, reaction paths, valley-ridge inflection point and minimum for product A, B, and reactant adapted from Bernhard 2002<sup>84</sup>

# 1.6.6 Geometry optimization

The geometry optimization is used to find the geometry of the current molecule with the lowest possible energy conformation through a process where atoms of the molecule are arranged until the most energy-stable structure is achieved. A gradient method (quasi-Newton optimizer) is used for the ORCA program, by default, to achieve the geometry optimization using only the first derivate of the potential (gradient) energy in internal coordinates and an approximate Hessian<sup>85</sup>. Then, the software iteratively uses algorithms until the number of gradient evaluations reaches certain criteria established for convergence which is required to locate true global minima on the PES, as shown in the Figure 6.



Figure 6. Flow chart for quasi-Newton algorithms for geometry optimization proposed by Bernhard 1995<sup>86</sup>

# 1.6.7 The conductor-like polarizable continuum model (CPCM)

A large proportion of the reactions are carried out in an aqueous medium, and therefore, solvents play an important role in the reactions and influence the structural, electronic, and spectroscopic properties both for inorganic and organic complexes<sup>87</sup>.

The natural choice to incorporate the solvent effects would be the addition of the solvent molecules into the DFT simulation but this process represents a highly computational costs due to the great number of electrons.

One of the most successful solvation models is CPCM which it is used for the computation of the solvent effects on the system by using algorithms that describe electrostatic solute-solvent interactions<sup>88</sup> and reduces significantly the computational costs. In the solvent approach, the interaction between de solute and the solvent is represented by a dielectric polarizable continuum<sup>89</sup>.

#### **1.6.8 Frequency calculation**

Each bond length in the molecule oscillates with a characteristic vibrational frequency. The procedure to calculate the vibrational frequency starts by determining the second derivatives of the potential energy from a stationary point of the Cartesian coordinates and then transforming to mass-weighted coordinates<sup>90</sup>. The frequency calculation must be performed at a stationary point on the potential surface<sup>91</sup> (geometry optimization). Positive frequencies indicate a local minimum, one negative frequency represents a transition state, and two or more negative frequencies represent stationary points<sup>68</sup>.

# 1.6.9 Mülliken charges

The Mülliken charges arises from the Mülliken population analysis obtained in the output file of the geometry optimization. These charges give information about the excess or deficiency of the charges in the atoms that make up the molecules. The regions where electronic charge accumulates are susceptible to electrophile attacks, and the other hand, in the depopulated regions of electronic charges are susceptible to nucleophile attacks<sup>92</sup>.

# **Chapter 2. Problem statement**

# 2.1 General problem statement

Through the years, the great interest in the synthesis of imines has constantly grown and it is due to their wide range of applications such as synthesis of dyes, coordination polymers, alkaloids, nitrogen heterocyclic, precursors of biologically active compounds, and their important role in the agrochemical industry, especially in pesticides. There are many methods to synthesize imines from amines, from which, oxidative dehydrogenation is one of the most promising method.

The reaction mechanism proposed for oxidative dehydrogenation have been profoundly studied and analyzed with different oxidants, solvents, temperatures, and catalysts based on transition metals principally with iron, copper, cobalt, gold, ruthenium, and vanadium because of their physicochemical characteristics. The production of imines from amines with iron and copper has demonstrated promising experimental results, particularly in the selectivity and efficiency of oxidizing amines. However, most of these investigations do not have a computational approach to the electronic interactions that allows it to propose the best candidate. For this reason, it is crucial a computational analysis on the reaction mechanism of the oxidation of amines to imines promoted by using metal promoted oxidative dehydrogenation and MOF-amine oxidation to compare the efficiency in the selectivity between both reaction mechanisms.

# 2.2 Objectives

# 2.2.1 General objective

- To perform a comparative analysis on the selectivity of the reaction mechanisms to form imine by oxidative dehydrogenation of tetracyano(1,2-diamine)ferrate(III) and by using of Cu-BTC.

# 2.2.2 Specific objectives

- To compute the single point energy of each reaction mechanism step for amine oxidative dehydrogenation of tetracyano(1,2-diamine) ferrate(III) by DFT simulations in ORCA.

- To compute the single point energy of each reaction mechanism step for the formation of imine by using Cu-BTC DFT simulations in ORCA.

-To analyze the computed energies to establish the most efficient reaction mechanism to oxidase amines to imines.

# Chapter 3. Methodology

# 3.1 Experimental section

# **3.1.1 Materials and equipment**

# 3.1.1.1 Reactants

Iron(III) Nitrate Nonahydrate, Fe(NO<sub>3</sub>)<sub>3</sub>.9H<sub>2</sub>O- MP =  $47^{\circ}$ C, MW = 404.02 g/mol, J. T. Baker 98%.

Cupric sulfate pentahydrate, CuSO<sub>4</sub>.5H<sub>2</sub>O - MP: 110°C, MW: 249.685 g/mol, SIGMA-ALDRICH 99%.

Ethanol,  $C_2H_5OH - BP = 78.3^{\circ}C$ , MW = 46.07 g/mol,  $\rho 25^{\circ} = 0.793 \text{ g/mL}$ , Merck. Ethylenediamine  $-BP = 199-209^{\circ}C$ , MW = 78.13 g/mol,  $\rho 20^{\circ} = 0.955 \text{ g/mL}$ , Aldrich

99%.

2-pyridinecarboxaldehyde – BP =  $181^{\circ}$ C, MW = 107.11 g/mol,  $\rho 25^{\circ} = 1.122$  g/mL, Aldrich.

# 3.3.1.2 Equipment

UV-Vis spectroscopy- UV-Vis measurements were performed with an Analytic-Jena Specord S200 diode array spectrophotometer in the range from 820 to 190 nm.

Imbabura's computational cluster.

# 3.1.2 Synthesis of the ligand L3

The polyamine ligand L3 (scheme 8) was synthetized following the method previously reported for other similar ligands<sup>93</sup>. In a round flask 30 mL of ethanol were added, then 2-pyridinecarboxaldehyde (0.24 mol) and ethylendiamine (0.12 mol) were added in a ratio of 2:1. The reaction was carried out in a reflux system at 78 °C and constant stirring for 5 h ensuring an acidic pH to promote the condensation reaction. The reaction was followed by thin layer chromatography (TLC) tests using ethyl acetate as eluent. Change in color was an evident of the diimine formation. In order to confirm the end of the reaction TLC test was performed until the disappearance of the aldehyde spot.



Scheme 8. Schiff base condensation of 2-pyridinecarboxaldehyde and ethylenediamine

In a second step, catalytic hydrogenation of L3 was performed. 100 mg of 10% of Pd/C catalyst was added to the mixture obtained in the previous step. A closed system with a hydrogen generator based on the oxidation of metallic zinc with concentrated HCl was constructed. After 4 h, the evident change in color, from dark brown, of the diimine to yellow, of the diamine was used as evidence of the end of the reduction reaction of the diimine (scheme 9).



Scheme 9. Catalytic hydrogenation (pd/C, H<sub>2</sub>) of the Schiff base to obtain the L3 ligand

# 3.1.3 Synthesis of [Fe(L3)(en)]<sup>3+</sup>

In order to perform the synthesis of the hexacoordinate  $[Fe(L3)(en)]^{3+}$  firstly the trisquelate  $[Fe(en)_3]^{3+}$  was synthesized. 411 mg (0.58 mmol) of  $[Fe(DMSO)_6](NO_3)_3$  and (1.74 mmol) of ethylenediamine were added to a round flask containing 50 mL of ethanol. After 1 h the well-known violet tris-chelate  $[Fe(en)_3]^{3+}$  was obtained. In order to incorporate the L3 ligand, stoichiometric mixture of the tris-chelate with L3 led it to obtain the desired complex. The reaction was followed until the change in color has stopped.

# 3.1.4 Synthesis of [Fe(L4)(en)]<sup>3+</sup>

The synthesis used for the hexacoordinate  $[Fe(L4)(en)]^{3+}$  was the same that  $[Fe(L3)(en)]^{3+}$  but in this case 400 mg (0.58 mmol) of  $[Fe(DMSO)_6](NO_3)_3$  and (0.174 mmol) of ethylenediamine were added to a round flask containing 50 mL of ethanol.

# 3.1.5 Kinetics of the oxidative dehydrogenation of [Fe(L4)(en)]<sup>3+</sup>

The kinetic study of the oxidative dehydrogenation of  $[Fe(L4)(en)]^{3+}$  was performed in a sealed 1 cm quartz cell and monitored by the Uv-vis spectrophotometric in a range of 280 to 650 nm during 36000 s. In addition, it was observed that the absorbance variations between each spectrum are more significant at 385 nm. Therefore, the variations in absorbance at this wavelength were analyzed

# 3.1.6 Synthesis of Cu-BTC MOF

Synthesis of Cu-BTC was previously reported<sup>36</sup>. Initially, 5 g of benzene-1,3,5tricarboxylic acid was dissolved in ethanol to obtain the solution A. To obtain the solution B, 11 g of Cu(NO<sub>3</sub>)<sub>2</sub>\*3H<sub>2</sub>O was added in 25 mL of dimethylformamide (DMF) to then be mixed in 25 mL of water. Next, solution A was added to solution B drop by drop and mixed thoroughly on a magnetic stir at 90°C for 12 hours. Once the mother liquor is filtered and washed with DMF and ethanol, heat-treatment at 180°C for 1 hour was necessary. Finally, the blue solid obtained was weighed and labeled. Several attempts of the oxidation of benzilamine by the direct exposition with Cu-BTC were performed without good results.

# **3.2 Theoretical section**

# 3.2.1 Search of mechanism information

An exhaustive well detailed search of the mechanisms is the previous work and also absolutely crucial to obtain a step-by-step guide for correct simulation. Besides, it is important to consider that there are many investigations about oxidation of amines to imines in which catalysts based on iron and copper transition metal were employed, but the major problem relies on the insufficient information about the proposed reaction mechanisms in these works. In this thesis, the mechanisms were collected from <sup>35,36</sup>, in which the reaction mechanisms used as models for this thesis are the most relevant in the literature and can be seen in the Scheme 4 and 6.

# 3.2.2 Preparation of the input files for ORCA

Once the mechanism was selected is necessary to obtain a reliable structure of the reactants from literature. The structures involved of amine oxidation reaction mechanism of tetracyano(1,2-diamine)ferrate(III) (Scheme 8) were drawn in the open-source software Avogadro as well as the structures of benzilamine oxidation reaction mechanisms because of the small size. However, in the case of the Cu-BTC structure,

CCDC ref. no. 987873 was used as a reference and opened with Avogadro. Then, launch the simple optimizer function in Avogadro was necessary to obtain a good starting geometry by arranging the atoms. Once drawing and saving the initial structure in Avogadro, the selection of "Extensions"  $\rightarrow$  "Orca"  $\rightarrow$  "Generate Orca Inputs" were necessary to create the first input file for ORCA simulations. The corresponding functional, basis set, charge and multiplicity for each molecule of the reaction mechanism for tetracyano (1,2-diamine) ferrate(III) oxidative dehydrogenation were introduced, as shown in Table 1. In the case of benzylamine oxidative dehydrogenation the multiplicities and charges were 1 and 0 respectively for each step of the mechanism.



Scheme 10. Reaction mechanism of oxidative dehydrogenation of tetracyano( 1,2-diamine)ferrate(III) adapted from Boosa et al.<sup>36</sup>

Step	Total spin	Multiplicity (2S+1)	Charge
1	1/2	2	-1
2	1/2	2	-2
2'	1/2	2	-2
3	0	1	-1
4	0	1	-2

 Table 1. Parameters used in DFT calculations for each step of mechanism reaction of the tetracyano (1,2-diamine)

 ferrate(III) oxidative dehydrogenation

# 3.2.3 Geometry optimization

The fundamental quantum chemical calculations of the present thesis were performed with ORCA available in the School of Physical Sciences cluster of Yachay Tech University. ORCA software was used to optimize the geometry of reactants and products of each mechanism step by locating the structures with minimum potential energies.

The geometry optimizations were performed with the hybrid density functional method B3LYP with the Def2-SVP basis set in conjunction with the D3BJ as the Grimme's dispersion correction factor. The input files for geometry optimization with Orca were created from the modeling structures established in Avogadro with their respective Cartesian coordinates. B3LYP D3BJ OPT def2-SVP PAL4 were the parameters introduced in the input file corresponding for geometry optimization as one can see in the Figure 7.

#	avogad	ro genera	ated ORCA	input file	
#	Basic	Mode			
#					
!	B3LYP	D3BJ OPT	def2-SVP	PAL4	
*	xyz -1	1			
	Fe	-3.44	179	1.94671	-0.00204
	С	-3.462	283	3.37302	-1.45295
	С	-4.87	998	2.97920	0.98784

Figure 7. Parameters used for functional, basis set and dispersion correction factor in the input file for geometry optimization

# 3.2.4 Conductor-like polarizable continuum model

Once the optimizations have been obtained, the output files obtained are opened with Avogadro with the goal to get a new ORCA input file to each of the optimized structures to introduce solvation factors with CPCM method at the same level of theory to ensure the minimum and compute the interaction of aqueous solvation free energy of water (solvent in the system proposed in this work) against the reactants by using a conductor-like polarizable continuum model (Figure 8). The command for the introduction of solvation factor in the input file was CPCM(WATER) with a dielectric constant of 80.4 in order to simulate the aqueous environment.

#	avogadr	o generated ORC	A input file	
# #	Basic M	ode		
!	B3LYP D	3BJ CPCM (WATER)	def2-SVP PAL4	
*	xyz -2	2		
	Fe	-3.55627	2.04518	0.06152
	С	-3.42087	3.31827	-1.47606
	С	-4.90191	3.01419	1.06152

Figure 8. Input for the calculation of the solvation effects in the reaction of oxidative dehydrogenation

#### 3.2.5 Verification of the geometry optimization with frequency calculations

After the geometry optimization calculations have converged with the maximum number of cycles, it is necessary to perform harmonic vibrational frequency calculations at the same level of theory using the output files of the optimized geometries in order to confirm the reliability of the results by verifying the absence of any negative frequencies, which means that the optimized structure was successfully converged to a minimum.

# 3.2.6 Determination of the Mülliken charges

The Mülliken charges were calculated independently for each molecule that its geometry has been optimized. The last with the aim of determining the total charges of the atoms involved for each step of the reaction mechanisms.

### Chapter 4. Results and discussion

# 4.1 Experimental part

For the experimental part it is important to mention some interesting conclusions before presenting the results. In the case of oxidative dehydrogenation of the  $[Fe(L3)(en)]^{3+}$  complex, spectroscopic evidence (NMR) of mixed imines present in the final complex indicates that both L3 and ethylenediamine were oxidized in the process. As the interest of this work is the study of the oxidative dehydrogenation of ethylenediamine, this reaction was discarded. The strategy to avoid the presence of mixed multi-imines was use the complex  $[Fe(L4)(en)]^{3+}$  instead of  $[Fe(L3)(en)]^{3+}$  because the presence of the imines in L4 at the start of the reaction makes possible to exclusively follow the oxidative dehydrogenation of ethylenediamine with Cu-BTC the experimental results were not satisfactory since it was not possible to identify the presence of the imine moiety in the final mixture.

# 4.1.2 Kinetics of the oxidative dehydrogenation of [Fe(L4)(en)]<sup>3+</sup>

 $[Fe(L4)(en)]^{3+}$  is an iron complex that exhibits an octahedral geometry with a strong d6 field configuration. From the kinetic studies we demonstrate the change in the reduction state of iron from Fe(III) to Fe(II) confirming the oxidative dehydrogenation in the complex. At the end of the reaction, the UV-vis spectrum reveals three absorption bands (385 nm, 505 and 560 nm) located in the visible region and according to the Tanabe-Sugano diagram the corresponding electronic transitions are  ${}^{1}T_{2g} \in {}^{1}A_{1g}$ ,  ${}^{1}T_{1g} \in {}^{1}A_{1g}$  and  ${}^{1}E_{1g} \in {}^{1}A_{1g}$  as can be seen in Figure 9.



Figure 9. UV-Vis spectra at different times for the oxidative dehydrogenation of  $[Fe(L4)(en)]^{3+}$ 

# **4.2 Theoretical part**

## 4.2.1 Optimization of geometries with Avogadro

The initial three-dimensional structures of the study molecules shown in Figures 10 and 11, for both reaction mechanisms were the starting points to perform computational simulations. As it was mentioned in the methodology by using the molecule editor Avogadro.



Figure 10. Structures drawn in Avogadro program for tetracyano (1,2-diamine) ferrate(III) and OH



Figure 11. Structures drawn in Avogadro program for Cu-BTC and benzylamine

# **4.2.2** Geometry optimization oxidative dehydrogenation reaction mechanism of tetracyano (1,2-diamine) ferrate(III)

The study of the reaction mechanism starts with the geometry optimization of the molecules involved in the reaction. Moreover, for this reason, a series of DFT calculations using the ORCA program was performed for the compounds involved in the first step of the mechanism (tetracyano (1,2-diamine) ferrate(III) and OH<sup>-</sup>) showed in the Scheme 8 to find the structure with the most stable ground state. Energy values were collected in Table 2.

Step	Energy (Hartree)	Energy (KJ/mol)
1	-2127.13	0
2	-2126.62	1350.35
2'	-2126.62	1350.35
3	-2126.38	1970.99
4	-2126.07	2795.62

Table 2. Energies in Hartree and KJ/mol units for each step of reaction mechanism

The visualization of the output file in Avogadro from the energy differences obtained in the geometry optimization in conjunction with B3LYP functional, D3BJ dispersion correction factor and def2-SVP basis set, indicates a convergence toward an octahedral geometry for tetracyano (1,2-diamine) ferrate(III). This result is expected because Fe(III) presents a low-spin d<sup>5</sup>, i.e.,  $(t_{2g})^5$  electronic configuration according to the ligand field theory. Figure 12 represents the optimized geometry of the reactant. The multiplicity and charge used for the geometry optimization for the complex were 2 and -1, respectively. The structure with the most stable-energy (minimum) resulted in a value of -2127.13 (Hartree).



Figure 12. Optimized structure for the first step of the reaction mechanism

The geometry structures involved in the second proposed step for the mechanism was optimized considering the same oxidation state of the first step and a change of the charge in the molecular system. This was due to only one proton was removed (deprotonation) from the coordinated amine group in tetracyano (1,2-diamine) ferrate(III), and which was carried out by a base-assisted OH<sup>-</sup>. The optimized geometry of the compound is depicted in Figure 13. For this geometry optimization, the energy obtained was -2126.62 (Hartree). In this step, despite the fact that octahedral geometry of the complex is maintained, there is an increase of energy as one can see in Table 2 which is attributed to the N-H's asymmetry in axial geometry<sup>94</sup>. The amine deprotonation in step one was a requirement to facilitate the intramolecular electron transfer from the amine anion to the Fe(III) center<sup>35</sup> to produce the aminyl radical in the prime second step.



Figure 13. Optimized structure for the second step of the reaction mechanism

The aminyl radical formed in the prime second step was taken as identical to the second step in multiplicity and charge due to the unpaired electron of the free radical, and furthermore, there was no change in the energy calculated by using ORCA geometry optimization. It is crucial to take into account, that in this step was carried out one electron transfer from the amine anion to Fe(III) center, which would cause the aminiyl radical and the reduction of Fe(III) to Fe(II). This charge transfer was carried out thanks to the empty orbitals lying at relatively low energy levels in low-spin Fe(III)<sup>35</sup>.

For the third step, there is an oxygen molecule that acts as an oxidant and induces the intermolecular electron transfer of aminyl radical to dioxygen, causing the formation of the amine cation. In this step, the multiplicity of the complex is 1, and the charge is -1 own to the amine cation formed. Moreover, the oxidation of the amine occurs. The energy obtained from geometry optimization showed an increase of -2126.38 (Hartree) for this DFT simulation. Figure 14 represents the optimized geometry of the reactant.



Figure 14. Optimized structure for the third step of the reaction mechanism

For the fourth step, there is an electron-deficiency that facilitates the proton transfer from  $CH_2$ -group, next to the amine cation, to the  $OH^-$ . The free electrons of carbon anion obtained from deprotonation are responsible for establishing the C=N double bond formation with the amine cation and, therefore, the first imine. The multiplicity and charge taken for the input file in geometry optimization were 1 and -2, respectively. The resulting energy from this simulation was -2126.07 (Hartree), which is stabilized by the formation of the C=N double bond. The optimized geometry of the fourth step is shown in Figure 15.

According to the obtained energies from the geometry optimization and recollected in Table 2, the most stable structure is the first step because it has the lowest energy between the reaction mechanism steps in the formation of the first imine. Moreover, according to the energies in KJ/mol units of Table 2, the highest energy showed concerning to the first step in the geometry optimization, means that the reaction could not be carried out because to achieve these steps, it is necessary to provide a large amount of energy.



Figure 15. Optimized structure for the fourth step of the reaction mechanism

# **4.2.3 Analysis of single point energy about amine oxidation mechanism by Cu-BTC** The geometry optimizations for each molecule involved in the mechanism showed in the Scheme 9 were performed by using the ORCA program in conjunction with B3LYP functional, D3BJ dispersion correction factor, and def2-SVP basis set. Energy values are collected in Table 3.



Scheme 11. Reaction mechanism used as computational model for the geometry optimizations

Step	Energy (Hartree)	Energy (KJ/mol)
1	-4764.39	0
2	-4762.53	4887.56
3	-4764.49	-269.98
4	-4764.15	642.46

Table 3. Energies in Hartree and KJ/mol units for each step of reaction mechanism

According to Boosa<sup>36</sup> et al., the oxidative dehydrogenation mechanism starts with the interaction between Cu-BTC MOF and benzylamine. However, for practical application and in order to justify the number of total electrons was necessary to start with the second step where Cu-BTC and benzylamine interact because of the Lewis acid nature of the Cu-BTC. Therefore, in this work, the first step started with the participation of the MOF-benzylamine and oxygen as an oxidant environmental to enhance the dehydration in the second step. The charge and multiplicity parameters were 0 and 1, respectively, in order to perform the geometry optimization for each structure. The energy obtained for the first step was -4764.39 (Hartree). Optimized geometry for the first step is shown in Figure 11.

In the second step, the formation of the imine intermediate is due to the oxidative dehydrogenation caused by oxygen in the first step, in which a molecule of  $H_2O$  was eliminated because of the removal of two hydrogen atoms from benzylamine. The charge and multiplicity are 0 and 1, respectively. The energy obtained from this step was - 4762.53 (Hartree), and the optimized geometry is shown in Figure 16. The energy difference between steps 1 and 2 is 4887.55 KJ/mol, and therefore the energy required to the formation of step 2 would be very high and practically impossible to carry out according to the DFT calculations. The increase in the system energy was necessary to release two hydrogen atoms by breaking N-H and C-H single bonds and, consequently, the formation of the imine intermediate.



Figure 16. Optimized structure for the second step of the reaction mechanism

In the third step, the formation of the benzaldehyde that is homo-coupled from the amine to the Cu-BTC catalyst is caused by the nucleophilic addition of benzylamine with the imine intermediate<sup>36</sup>. The charge and multiplicity used in this DFT calculation were 1 and 0, respectively, and the resulting single point energy was -4764.49 (Hartree). Figure 17 represents the optimized geometry of the molecules in the third step. The energy difference between the first and third steps is -269.97 KJ/mol, which is more reasonable and could feasibly be carried out in the formation of benzaldehyde with respect to the second step. The decrease in the energy for this step concerning to the first step was possibly due to the bond formation between benzylamine with imine intermediate to form the benzaldehyde as the product.



Figure 17. Optimized structure for the third step of the reaction mechanism

In the last step, the formation of N-benzylbenzaldimine on the catalytic surface was due to the loss of an NH<sub>3</sub> molecule. The charge and multiplicity were 0 and 1, respectively, and the single point energy obtained in the fourth step as a result of the geometry optimization was -4764.15 (Hartree). Optimized geometry of the fourth step is shown in Figure 18. In addition, the energy difference between the first and fourth steps is 642.46 KJ/mol, which was required for the disruption of the N-C single bond and the release of the NH<sub>3</sub> and N-benzylidenebenzylamine.



Figure 18. Optimized structure for the fourth step of the reaction mechanism

There are no redox reactions as in the previous mechanism because Cu(II) from Cu(BTC) MOF in the mechanism proposed to the benzylamine aerobic oxidation is used as a catalyst due to its Lewis acid sites.

# 4.2.4 Analysis of CPCM and frequency vibrational calculation

The obtained solvation energies show a slight difference after addition of the dielectric constant for the water,  $\epsilon = 80$ , as a solvent by using a conductor-like polarizable continuum model in comparison with the energy of geometry optimizations in each step of the two reaction mechanisms. In addition, each geometry optimization after CPCM application was verified with a harmonic vibrational frequency calculation at the same level of the theory. The obtained results showed zero imaginary frequencies, which means that the optimized geometry structures have been successfully converged to the local minimum on the PES for each molecule involved, in each oxidative dehydrogenation reaction mechanism.

# 4.2.5 Mülliken charges

The Mülliken charges are used to assign the charges to each atom of the molecule of interest. The negative Mülliken charges obtained for Fe(III) and Fe(II) in step 1,2 and 2,3 respectively, reveals possible mistakes in the calculation of the geometry optimization

because it is expected to obtain positive Mülliken charges in metal centers due to its metallic nature. The Mülliken charges are summarized in Table 4.

Step	Atom	Mülliken charges
1	Fe (III)	-0.626136
2	Fe (III)	-0.494437
3	Fe (II)	-0.505749
4	Fe (II)	-0.431137

Table 4. Mülliken charges of iron atom corresponding for the optimized structures

In the case of Cu-BTC, there are two copper atoms, but it does not present a redox reaction in comparison with the iron atom in the mechanism above. A small charge variation was detected in the copper atom near to nitrogen atom of benzylamine in the first, second, and third step with regard to the fourth step own the influence of nitrogen negative charge (-2.47432) shown in the Mülliken population analysis. A more significant positive charge variation can be seen in the fourth step because, as mentioned above, Cu-BTC has an interaction with benzylamine through Lewis acid sites<sup>36</sup>. In the case of the fourth step, the participation of the copper atom, with a Mülliken charge of 0.517841, closest to the benzylamine as a Lewis acid site has already completed, and therefore there are no alterations in the charge of other copper atoms. The Mülliken charges are recollected in Table 5.

Step	Cu (III)	Cu (III)
1	0.412192	0.511396
2	0.458670	0.508193
3	0.412192	0.511396
4	0.517841	0.516941

Table 5. Mülliken charges of copper atom corresponding for the optimized structures

# 4.2.6 Analysis of the energy diagrams

The energies calculated by DFT simulation in ORCA program for each step of the reaction mechanisms were plotted to perform an analysis of the process efficiency when the imine is formed as final product.

The comparison between the energies in the step 4 showed in the energy diagrams (Figure 19 and 20) resulting from the imine formation for both mechanisms reveals that the oxidative dehydrogenation reaction of Cu-BTC require less energy for the synthesis of the imine than tetracyano (1,2-diamine) ferrate(III). More energy is necessary for removing a hydrogen for the formation of C=N double bond in the tetracyano (1,2-diamine) ferrate(III) possibly due to there is a greater attraction over the hydrogen adjacent to carbon atom.

# B3LYP D3BJ OPT def2-SVP



*Figure 19. Energy diagram for the reaction mechanism of the oxidative dehydrogenation of tetracyano (1,2-diamine) ferrate(III) in presence of oxygen* 



Figure 20. Energy diagram for the reaction mechanism for the synthesis of imine by using Cu-BTC as catalyst

# **Chapter 5. Conclusions**

The lack of experimental investigations that proposes reaction mechanisms in the amines oxidative dehydrogenation to synthesize imines by using copper atom in MOF causes considerable limitations in obtaining reaction mechanism proposals from different points of view and, therefore, a low level of understanding regarding the steps involved in the reaction mechanism.

Geometry optimization for each reaction mechanism was successfully obtained through DFT calculations in the ORCA program using hybrid density functional method B3LYP with the Def2-SVP basis set in conjunction with the D3BJ as the Grimme's dispersion correction factor.

The geometry observed from geometry optimization for tetracyano (1,2-diamine) ferrate(III) was octahedral, which is in accordance with the literature.

The frequencies obtained after geometry optimization was positive, which means that the system achieved a local minimum in the PES and the optimized structure is not a transition state.

The Mülliken charges for Fe(III) in the first and second step and Fe(II) in the third and fourth step indicated a possible error in the calculations due to the negative charges obtained. In the case of Cu(II) atoms, all Mülliken's charges obtained were positive, which is in accordance with the literature and the significant change for the Mülliken charges recorded in the fourth step was possible because of the non-interaction between the Cu(II) of Cu-BTC and Nitrogen of benzylamine.

For each reaction step in the imine formation by Cu-BTC and tetracyano (1,2-diamine) ferrate(III) oxidative dehydrogenation, the system energy considerably increases, indicating that the two deprotonation reactions would not carried out spontaneously.

The imines proposed as products in the mechanism are experimentally viable, but the calculated energies according to the DFT calculations in ORCA reveal that very high energies are required to achieve the formation of imines, and therefore, the mechanisms to synthesize imines from amines should be different from those proposed in the literature.

Finally, if the final energies obtained from the two mechanism for the formation of the corresponding imines were taken into account to decide the reaction more thermodynamically favored, it can be said that using of Cu-BTC as MOF is more energy-efficient which favors the reaction due to less energy is necessary to carried out the synthesis of the imine.

# **Perspectives and future work**

The study of the oxidative dehydrogenation reaction of amines by using a Fe-complex and Cu-MOF for the formation of imines was possible through DFT calculations in ORCA program. The laboratory access limitations only allow to carry on the electron absorption spectroscopy analysis. However, it is necessary to perform more experimental studies of characterization by using of NMR, cyclic voltammetry and EPR to complement the computational results obtained in this work.

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