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A Computational Study Of The Mechanism Of Transfer Hydrogenation Using An Iridium(III) Catalyst

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Abstract

Hydrogenation is an important step in the synthesis of many pharmaceuticals, and transfer hydrogenation, where a renewable source for hydrogen is used, is a green and efficient method for this process. It has been shown experimentally that alcohols can be used as a source of hydrogen with iridium (III) catalyst affecting the transfer hydrogenation. The mechanism of this process is unknown. In this research study the mechanism of transfer hydrogenation is investigated computationally, using a model system that includes carbonyl (CO), amine (NH_3), and cyclopentadiene (CP) ligands with methanol as the source of hydrogen. Density Functional Theory (DFT) calculations, using the M06 and APFD functionals, along with an effective core potential on the iridium atom and a correlation consistent basis set in the rest of the atoms. These functionals are used to determine initial, transition state, and intermediate geometries for proposed mechanisms of transfer hydrogenation including stepwise, concerted, and ion pair mechanisms. The concerted mechanism was found to be feasible and has an energy barrier of 16 Kcal/mol with a favorable exothermic process. However, the ion pair mechanism did not show promising results, concluding that it is not a favorable mechanism. The intermediate geometries of stepwise mechanisms were found and BSSE was eliminated from their energies. The pathways and energies of the mechanisms, stepwise and concerted were not compared since there is not a counterpoint calculation for the concerted mechanism. The counterpoint pairs energies for the stepwise mechanism were compared to each other obtaining counterpoise 2 as the lowest in energy.

1. Introduction

1.1 Background

The urge of novel renewable alternatives to hydrogenate or dehydrogenase a variety of ketones and alcohols, has increased dramatically over the course of the years involving them in industrial, medical, and environmental chemical fields[10]. Organometallics is the chemistry that studies reactions involving metals that are bound covalently to at least one carbon atom from an organic molecule. The involvement of transition metals are of critical importance, as they are used as catalysts in many organic synthesis[9] . The platinum group of precious noble metals are mainly involved in these types of reactions. There are 6 metals in this group including Iridium, osmium, palladium, platinum, rhodium, and ruthenium; located in groups 8-10 and periods 5 and 6. Majority of these metals have similar physical and chemical properties as they come from the same mineral deposits on earth. Asymmetric transfer hydrogenation has shown to be a fundamental piece of synthetic chemistry, as its effectiveness on reduction of carbonyls to alcohols and nitriles to amines has shown relevant results[5].

Transfer hydrogenation is the process where hydrogen is added or removed from saturated or unsaturated compounds and vice versa, these compounds are typically hydrocarbons used in the chemical industry to produce fuels. These metallic elements contain ligands that are covalently bound to the metal, typically the type of ligands are arene molecules, that coordinate the dynamics of the metal, and nitrogen and oxygen based groups that act as hydrogen

donors[5] on the transition phases of the reaction. Most of these elements have different ionic states[2] that allow them to catalyze reactions differently, depending on the conditions.

There are three major hydrogen transfer mechanistic routes to take in account, which are concerted hydrogen transfer, migratory insertion, and direct hydrogen transfer[4] . These different pathways were recommended to be studied by Noyori in 2003 in order to understand that experimentally there's not much information[4] given about the mechanistic transition phases of the metals during a reaction, as they have extremely short half-lives and typically are followed by H-NMR(Hydrogen -Nuclear Magnetic Resonance) and IR(Infrared Resonance) spectroscopy procedures[9]. This is a difficulty that computational simulations don't suffer from, and makes it a great candidate to study their intermediate phases[4].

Iridium(I) and (III) system mechanisms should be studied since poor evidence of the mechanistic aspects are shown in the literature[4,5]. Iridium was discovered in 1803 by the English chemist Smithson Tennant, naming Iridium the rainbow metal as the different salts show different colors. The most important Ir compounds to be in starting reactions are its salts and acids[2]. Compounds in the oxidation state of (II) and (III) like, Iridium, Rhodium, and Ruthenium[8] have been highly studied as metal catalysts involved in hydrogen transfer. Suitable information is provided by the literature that could serve as a guide for this study. Iridium is one of the rarest elements and the second most dense natural element with a density of 22.56 g/cm^3 after osmium, its high melting point that reaches the 2000 degrees celsius, anti-corrosive resistance to many halogens and acids , and its good mechanistic properties at room temperature makes this metal a good candidate for many reactions involving the production of drugs, biochemical processes, and even for modern engineering[1,2,4,5].

The ultimate goal for this study is to computationally simulate mechanisms of Ir(III) metal complexes to provide information about transition phases in order to determine important steps in hydrogen transfer reactions. This would be done using DFT (Density Functional Theory) Calculations M06 (Minnesota Functionals)[3] to study the potential energy surface of these complexes. DFT is a computational quantum mechanical modeling that investigates the electronic structures of different molecules[3]. Many transfer hydrogenation reactions involving a transition metal are carried on basic conditions. This experiment is proposing the conditions of neutral pH (pH of 7.0) and at room temperature (~25°C) and to study the chirality of different reaction pathways.

This computational study is interested in studying Iridium (III) complexes containing covalently bound a negatively charged nitrogen based group and carbonyl. There is also a cyclopentadiene that represents an arene group that gives the metal catalyst compound a plus one charge. Having these groups as ligands are of great importance, the carbonyl would act as hydrogen donor, the amino as hydrogen acceptor, and the arene would be used as the coordinator of electrons in the system. Literature demonstrates that iridium organometallic compounds are successfully used in transfer hydrogenation[4], but there's a lack of information about the mechanistic properties and behavior of these compounds[4]. Typically, these types of reactions are started with metal salt complexes and treated with strong bases to add or remove ligands, literature refers to the use of 2-propanol[1] as a hydrogen source.

Previously discussed there have been 4 hypothetical routes this Ir (III) mechanism could undergo of neutral pH and room temperature conditions. The first one (Figure1.a) the amino ligand would covalently bond to the proton coming from the oxygen of the alcohol making the Ir (II) compound. The second one (Figure1.b) is a nucleophilic addition to the metal of a hydride[3] coming from the alpha carbon of the alcohol and making the system neutral. The third (Figure1.c) would be a combination of the first and the second mentioned before, maintaining an Ir(I), and the fourth is the ion pair reaction that would give an active Ir(III) catalyst. In 2006 a study carried by Eyal Ben-Ari and coworkers investigated the C-H cooperation on H_2 activation. It was found that an Ir (I) and (III) systems were in equilibrium at one point of the reaction to get to a neutral product, this information could potentially provide useful information to further be investigated.

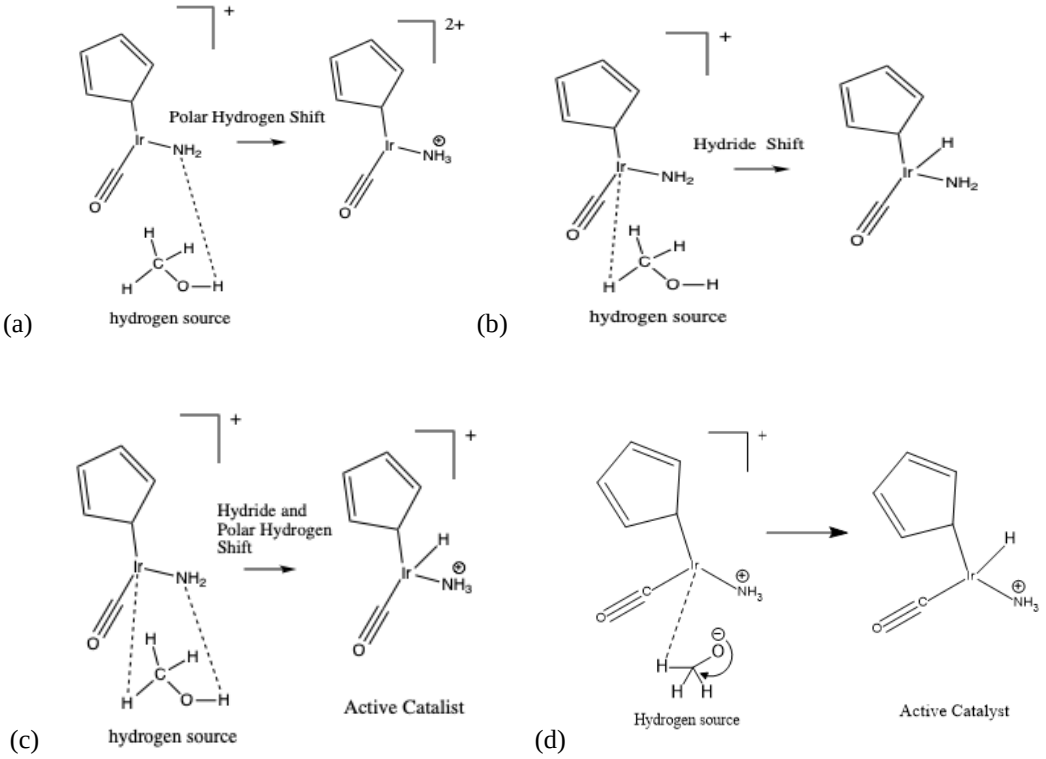


Figure 1: Proposed mechanisms (Figure1 (a) and (b) stepwise mechanism. Figure1 (c) Concerted mechanism. Figure1 (d) Ion pair mechanism.)

Previously, similar reactions were computationally studied involving rhodium as a metal catalyst in the dehydrogenation of different alcohols for molecular hydrogen (H_2 gas) production as biodegradable fuel. Many aspects of the information extracted from this experiment were provided to be physically tested and analyzed by Abby O'Connor, a chemistry professor from the College of New Jersey that studies the development of energy efficient ways to produce fuels. O'Connor focuses on stabilizing highly energetic transition states of organometallic compounds. In her latest publication she worked on the synthesis and characterization of rhodium (I) chloride organometallic complexes, containing COD (cyclooctadiene), NBD (norbornadiene) and a 2-(dicyclohexylphosphino)biphenyl (PCy2-biPh) as ligands. COD and NBD are bulky compounds that were treated in the same conditions giving different results but was proved and traced by NMR spectroscopy that these two compounds at low temperature have similar activity. As these compounds experienced intermediate or transition phases, it was found that at one point the compounds were the same. At room temperature COD was treated with molecular hydrogen and it was hydrogenated, substituting the COD with hydrogen (s), however; NBD was partially hydrogenated[6].

A goal of green chemistry is to look for solutions for the impacts caused by massive pollution, which has been a problem since the industrial revolution. However, this study would use green chemistry for safe reaction conditions; In a recent study, glycerol has been used as hydrogen source in transfer hydrogenation using a in a NHC (N-Heterocyclic carbene) based Iridium (III) catalyst and classified as a green solvent[1],which could potentially be tested on the final model of Iridium(III). The urge of new energy alternatives is critical as the sources of fossil fuels are being exploited for many reasons. The great thermodynamic and kinetic potential[10] along with the ability to easily dissolve many organic compounds proposes that glycerol is a good eco-friendly solvent that could be used as a source of hydrogen in transfer hydrogenation synthesis[1,9].

Chemistry is involved in many other sciences, and its contribution is significant for the development of new techniques and solutions. The lack of information about the transfer hydrogenation mechanism using Iridium(III) as catalyst is needed, as data in the literature shows that Ir(III) systems actually are faster and more efficient in transfer hydrogenation processes[7]. Although considering green solvents like glycerol, might influence this study in a complete different way, this study mainly would be focused on DFT calculations to investigate the geometries of different

transitions phases of Ir(III) complexes, using M06 which was specially designed for transition metals interactions and effective core potential (EPC) ideologies. EPC is used in quantum mechanical calculation, where the core electrons are replaced by an effective potential to just treat the valence electrons in reactions.

2. Computational Methods

2.1 Basis Sets And Correlation Basis Sets

All the calculations were acquired using Gaussian16 computer software. M06 functional was used to calculate the relative conformer energies and geometries of ionic compounds[11]. Since DFT methods cannot account for dispersion altercations, the functional APFD was introduced to the calculations to be used in the mechanisms proposed in Figure 1.

The APFD (Austin-Frisch-Petersson Dispersion) uses an empirical dispersion correction and spherical atom model (SAM) serves as a general corrector for DFT or HF models. Such was used as a dispersion corrector in combination with APF functional to create the APF-D dispersion corrected density functional[12].

LANL2DZ was used as the basis set for the effective core potential which replaced the core potential valence electrons with a charge and cc-pVDZ serves as correlation basis set, having multiple and different polarization functions by definition [13] for atoms used in this study, excluding Iridium.

2.2 Calculations

QST3 is a transition state optimization that requires 3 input geometries that are organized in the same order, reactants and products should be fully optimized and the transition state guess should work as a starting point.

Intrinsic reaction coordinate (IRC) command is used after a QST3 result to follow a specific path by integrating the IRC. There are two paths, the forward and reverse direction, after the initial geometry specification the calculation can follow the same path of the reaction so it can work backwards or forward at a certain point.[14,15]

Counterpoise correction calculation energy would be used to correct the basis set superposition error (BSSE); This is calculated by re-performing the previous calculations.[16]

3. Results and Discussion

3.1 Geometry calculations

3.1.1 Geometry of catalyst and alcohol

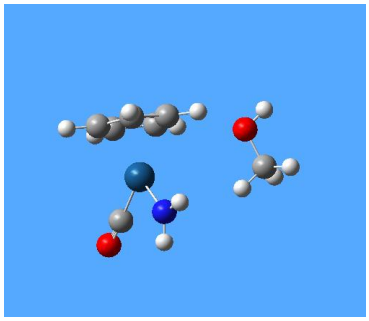


Figure 2: Input chanel complex

The fully optimized and converged geometry for the reactants in Figure 2 was achieved by using the level of theory and basis sets M06, LANL2DZ, cc-pVDZ. The distance between the alcohol O to Ir metal center catalyst was

4.032Å, O to N was 4.560Å, and H to Ir was 4.950Å . Distance between alcohol C and Ir metal center catalyst was 4.317Å and H to Ir was 3.379Å.

3.1.2 Geometry of catalyst and formaldehyde

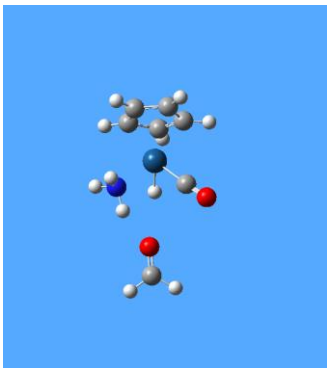


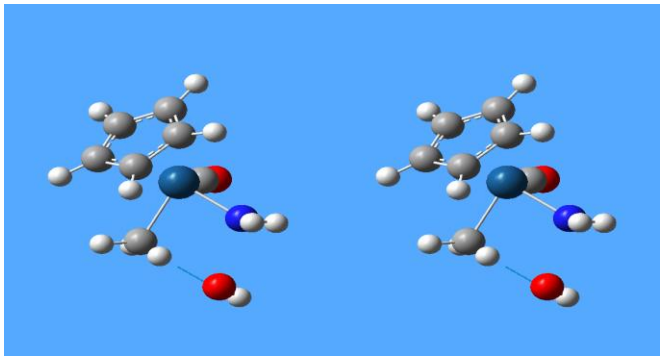
Figure 3: Output channel complex

The fully converged and optimized geometry for the products was achieved by using the level of theory and basis sets M06, LANL2DZ, cc-pVDZ. This reaction was concrete with the proposed mechanism 1.c on Figure 1, a concerted theoretical product that was later used to complete the QST3 calculations.

After using APFD functional as a level of theory, it was found that the energy and geometry changes of the system were not big. The change in total energy was -0.0604 kJ, after comparing the two levels of theory. After obtaining this information, a qst3 calculation was done to obtain a transition state geometry.

3.2 Transition state calculations

3.2.1 Elimination of water



(a) Start (b) End

Figure 4: Formation of water

After completing a QST3 calculation using M06 functional, starting with the reactant (Figure.2), product (Figure.3), and a starting transition guess. IRC calculations on the forward and reverse directions were done. The elimination of water was the result, instead of the elimination of hydrogen gas as it was expected. Figure 4 (a-b) shows the displacement vector pointing towards the hydroxide compound. However, this step is important because it can be used as a reference point to look for the desired lowest energy transition state that has been proposed in the study.

After the elimination of water, it was necessary to account for dispersion (Van der Waal forces), and the APFD functional was then introduced. After optimizing and getting new geometries for the Input and output channels, a qst3

calculation was made obtaining a promising geometry to study the transition state of the concerted mechanism on Figure.1.

3.2.2 Transition geometry for concerted mechanism

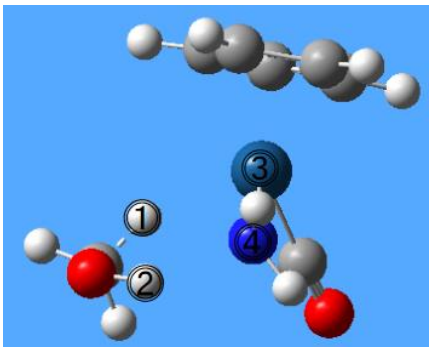


Figure 5: Intermediate complex

Table1: Important distances for intermediate complex

From Atom	To Atom	Distance in Armstrongs (Å)
1	3	2.125
1	2	2.273
2	4	1.914

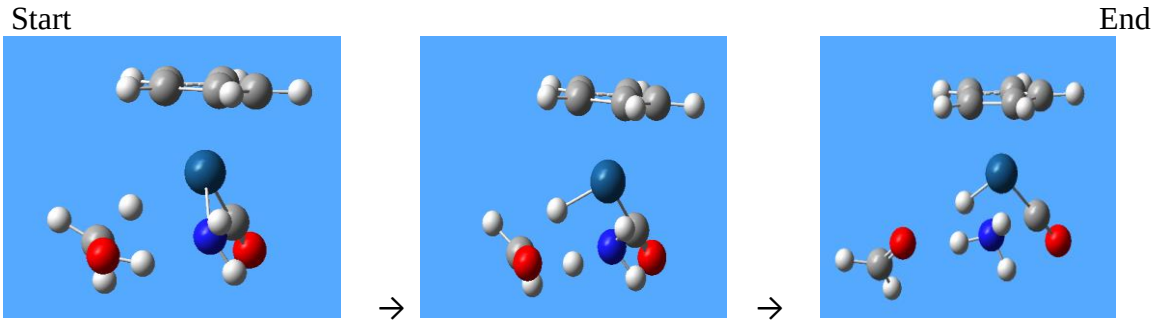
This step is of great importance, as it correlates to the position previously proposed for the transition state geometry of concerted mechanism. After collecting useful information about distances, an IRC calculation had to be executed to study the nature of this transition complex in the forward and reverse directions.

3.3 IRC calculations

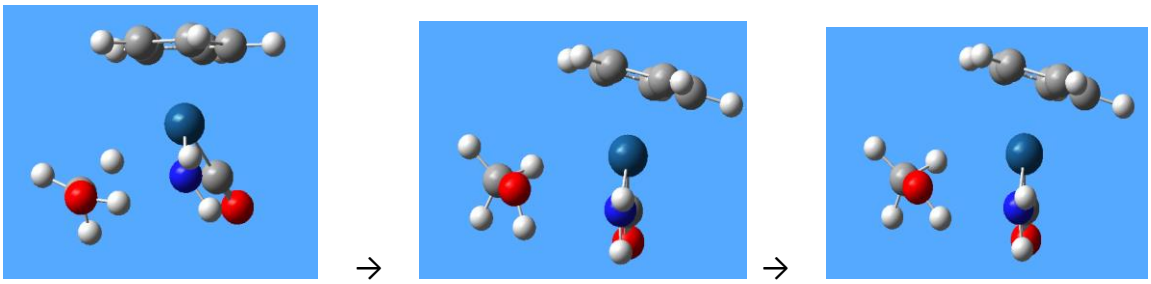
3.3.1 M06 IRC calculations

After obtaining a promising transition state complex using APFD, it was decided to use that geometry on the M06 functional. Unfortunately using M06 functional did not show feasible results as in the forward and reverse directions formed the starting material.

3.3.2 APFD IRC calculations



(a) Forward Direction



(b) Reverse Direction

Figure6: IRC calculation for the concerted mechanism transition complex using APFD.

After obtaining these results, it was concluded that a feasible mechanism for the concerted mechanism proposed in Figure.1 was found. After using two different levels of theory, the two levels of theory were used to compare energies on the potential energy surface.

3.4 Ion-pair calculations

Ion pair calculations did not converge the catalyst system. It was decided that this mechanism was not worth pursuing further.

3.5 Potential Energy surface for Concerted mechanism

3.5.1 M06 and APFD Potential Energy Surface (PES)

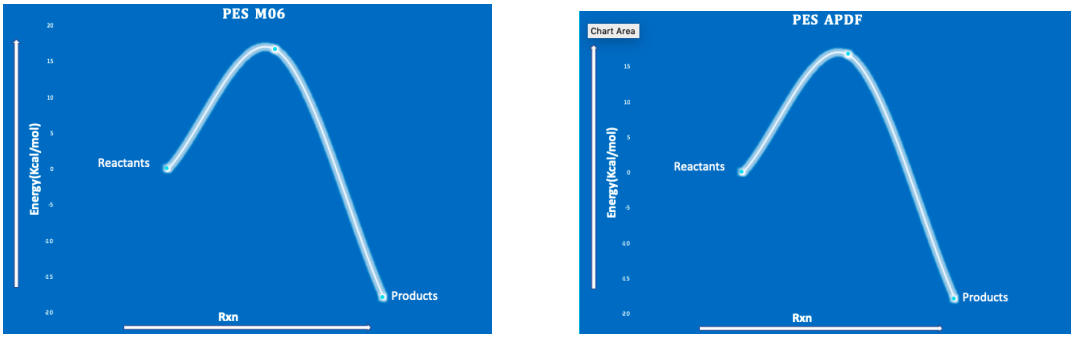


Figure.7: Comparison between the two levels of theory for concerted mechanism.

After obtaining results on Hartree units, these values were converted to Kcal/mol in order to investigate the energy barrier. After concluding that the energy barrier was approximately 16 Kcal/mol, it was determined that this was a favorable exothermic reaction. The products are lower in energy compared to the reactants. The change in energy for APFD was-74.8230kJ and M06 was -74.7626 kJ.

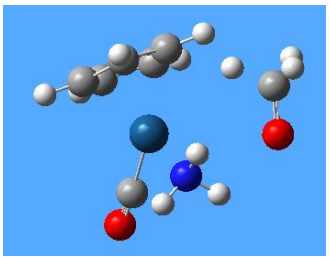
3.6 Stepwise Mechanism

3.6.1 Counterpoise calculations

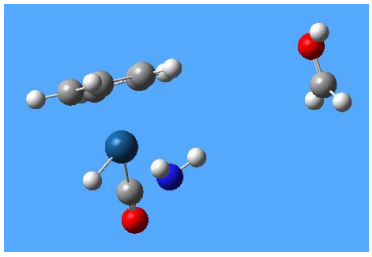
The counterpoise calculation fixes the Basis Set Superposition Error(BSSE) energy, although results shown here are only for the APFD functional. Since the M06 functional did not account for dispersion, some of the counterpoise pairs did not converge, which means that the energy was not corrected.

3.6.2 Counterpoise Pairs

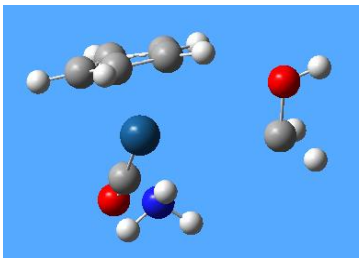
Here is the illustration of geometry and designated charges for fragments. . All of the pairs have a overall charge of +1.



Counterpoise Pair 1



Counterpoise Pair 2



Counterpoise Pair 4

Figure.7: Counterpoise pairs geometries and identification.

Table2: Counterpoise pairs fragments and its charge.

Counterpoise Pair	Alcohol fragment Charge	Iridium fragment Charge	Total Charge	Relative Energies (kcal/mol)
1	1-	2+	+1	+24.6
2	1+	0	+1	0
4	1-	2+	+1	+16.8

After obtaining the energies of the converged counterpoise pairs the values were compared to each other to obtain the lowest pair in energy. This could tell us which hydrogen gets on the catalyst first. Counteroise pairs 1 and 4 were compared to pair 2, in order to rank their energies pair 2 was assigned the lowest energy. With these results, the desired mechanism to follow was determined. On table 2, pair 1 in the alcohol fragment charge column, the 1- charge was placed on the oxygen atom. On pair 2 the carbon was assigned an 1+, making it a carbocation. On Pair 3 the oxygen has an 1+ charge, unfortunately this pair was unsuccessfully achieved. And for pair 4 a negative 1- charge was placed on the carbon. However, relatives energies on Table2 just show the method that was used to choose the best mechanism which was assigned to counteroise air 2, the migration of a hydride to the iridium metal center.

4. Conclusion

Concerted, stepwise, and ion pair reactions were performed by using Gaussian 16 with M06 and APFD Functionals. Unfortunately, ion pair calculations did not show any type of convergence between the two molecules as ion pairs, it was concluded that this mechanism was not going to be investigated. However, the concerted mechanism showed positive results with the formation of formaldehyde and an active catalyst with the hydride atom attached to the metal center. QST3 and IRC calculations were carried to investigate the behavior of transition state obtained, although the water elimination was not the desired result. APFD was introduced and a promising transition complex for concerted mechanism was found. M06 did not present useful information, as well as the IRC calculations were not effective. For the stepwise mechanism, pairs 1, 2, and 4 were optimized by correcting the BSSE Energy. Unfortunately, pair 3 was discarded, but most of the pairs are lower in energy than the starting geometry for the concerted mechanism, acquired as a feasible exothermic mechanism. Although these pairs were analyzed using just APFD, because M06 don't possess the ability to count for dispersion. With these results we have investigated stepwise and concerted mechanisms as proposed on the hypothetical routes of the mechanism. Counterpoise pair 2 was designated as the mechanism to be followed. Work continues in order to investigate in depth the behavior of transfer hydrogenation, future work would include: ligand exchange, hydride insertion, and investigation with different olefins.

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