



Treball Final de Grau

The electric field and the chemical reactions: A new catalyst or an inhibitor?

El camp elèctric i les reaccions químiques: Un nou catalitzador o un inhibidor?

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Nada es demasiado maravilloso para ser cierto si obedece a las leyes de la naturaleza.

Michael Faraday

Este trabajo va dedicado a toda mi familia: mi madre, mis hermanas, mis abuelos y demás que tanto tiempo han tenido que aguantarme con mi estudio de la Química y han visto como subía y bajaba como las olas hasta llegar a este trabajo que es la culminación de todo mi esfuerzo y sacrificio.

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REPORT

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1. SUMMARY

The catalysis is one of the most important areas for the reaction synthesis and mechanisms. Actually, there are thousand types of different catalysts. As we all know, a catalyst is a substance that increases the reaction rate but without reacting with the reagents and without modifying the course of the reaction. According to this definition, there is a new type of catalyst that we will probably use in the future: an Oriented External Electric Field (OEEF).

In this research we study the general effects of an OEEF on the reactions and applied to different types of bonds. From this first application of the OEEF we extracted the Shaik rules, which are general rules about the OEEF effects in all type of bonds we know about.

Secondly, we look at the Valance Bond (VB) diagrams, what they are and how to build them. This is a really good tool to understand which are all the structures involved in a reaction, plus the reagents and products, how intermediates appear and how we obtain the energy profile of any reaction (which we all know and have studied). Furthermore, we study the effect of the dipole moment in the opposite direction to the OEEF. The VB diagram model is the basic model to understand the Shaik rules for OEEF.

We applied all this knowledge in four reactions: Diels-Alder reaction, Menshutkin reaction (S_N2), benzene nucleophilic aromatic substitution (S_NAr) and cyclobutene ring opening reaction by conrotatory rotation. We study the effects of the OEEF and how the reagents substituents can affect on this reactions, resulting in catalysis or inhibition.

With all the initial knowledge and the new one acquired we study the cyclobutene ring opening reaction by disrotatory rotation and how the OEEF affects this reaction. We propose how to apply them so that the reaction goes from forbidden to allowed, something that no one has done before.

Finally, we can say that we study the OEEF and its applications, a new type of catalyst that has many possibilities despite its possible negative effects.

2. RESUMEN

La catálisis es uno de los campos más importantes en la reactividad y el mecanismo de las reacciones. Actualmente, hay cientos de catalizadores diferentes. Como todos sabemos, un catalizador es una sustancia que aumenta la velocidad de la reacción pero sin reaccionar con los reactivos y sin modificar el curso de la reacción. De acuerdo con esta definición, hay un nuevo tipo de catalizador que probablemente utilicemos en el futuro: un Campo Eléctrico Externo Orientado (OEEF, acrónimo en inglés).

En esta investigación hemos estudiado los efectos generales del OEEF en las reacciones y aplicado a diferentes tipos de enlace. De esta primera aplicación del OEEF hemos obtenido las reglas de Shaik, que son definiciones generales de los efectos del OEEF en todos los tipos de enlaces que conocemos.

En segundo lugar, hemos visto los diagramas de enlace valencia (VB, acrónimo en inglés), que son y como construirlos. Esta es una muy buena herramienta para entender cuales son todas las estructuras implicadas en una reacción, además de los reactivos y los productos, como aparecen los intermedios y como obtenemos los perfiles de energía (que todos conocemos y hemos estudiado). Además, hemos estudiado el efecto del momento dipolar en oponerse a la dirección del OEEF aplicado.

Hemos aplicado todo este conocimiento a cuatro reacciones: Diels-Alder, reacción de Menshutkin (S_N2), sustitución nucleofila aromática del benceno (S_NAr) y la obertura de anillo del ciclobuteno por giro conrotatorio. Hemos estudiado los efectos generales del OEEF y de los sustituyentes en estas reacciones, dando lugar a la catálisis o a la inhibición.

Con todo el conocimiento inicial y todo el adquirido en el estudio de estas reacciones hemos estudiado la obertura de anillo del ciclobuteno por giro disrotatorio y como el OEEF le afecta. Hemos propuesto como aplicarlo a la reacción para que pase de estar prohibida a estar permitida, algo que nadie ha hecho antes.

Por último podemos decir que hemos estudiado el OEEF y sus efectos, un nuevo tipo de catalizador con muchas posibilidades, a pesar de sus efectos negativos.

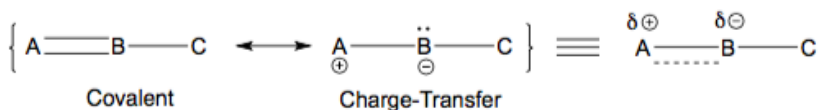
3. INTRODUCTION

3.1. Phenomena presentation

The catalysis is one of the most important areas for the reaction synthesis and mechanists. Actually, there are thousand types of different catalysts. But before all this, the first thing we have to know is what is a catalyst.

As we all know, a catalyst is a substance that increases the reaction rate but without reacting with the reagents and without modifying the course of the reaction. According to this definition, there is a new type of catalyst that we will probably use in the future and that we are going to talk about it on this research. That new catalyst is an External Electric Field.

Normally, to represent the molecules we use the Lewis structures (Scheme 1). From these structures, we can find two complementary ways: covalent structures and charge-transfer structures. Along this research, we will see that when we apply an External Electric Field the charge-transfer structures will be more important than the covalent structures and we will see how this can change the reaction selectivity, reaction profile or reaction mechanism.



Scheme 1: Generic valence-bond forms between brackets. The resulting molecular electronic structure is a hybrid of two valence-bond forms, namely, covalent and charge-transfer.

Basically, when we apply an electric field on the molecules and the reactions, the reactivity and/or selectivity of the reaction can change. For example, we can do that some prohibited reactions turn into allowed reactions. Thus, the effects of electric field on molecular systems are important in chemistry and for this reason this study is focused on this phenomena. Now, we are going to see different types of Electric Fields:

- **External Electric Field (EEF):** Uniform in space and generated by a bias current. This field affect many of the properties of the molecules, like the spectroscopy of molecules, promote electron transfer and redox reactions, change molecular geometries, etc.
- **Designed-Local Electric Field (D-LEF):** It changes the dissociation energy of distant bonds and improves H-transfer reactivity.
 - **Internal Electric Field (IEE):** It is a field generated by the molecule. It induces selectivity and gives rise to a desired mechanism.
 - **Oriented External Electric Field (OEEF):** Uniform and oriented in a given direction respect to the molecule. It is important that one element is deficient in electrons and another rich in electrons.

From all this type of fields, we focus the attention on OEEF, how it can change the reactivity and selectivity of the reactions. In addition to this, we are going to introduce the dipole effect in the reaction.

If we study the energy profile of any reaction, we will have the shape that we can see on the Scheme 2, where the progress of reaction corresponds to Z-axis. For this profile we can define the next equation for the energy barrier:

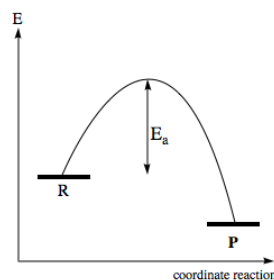
$$\Delta E_a = E(TS) - E(R)$$

And if we apply an electric field on the same direction of the reaction progress, we should have to change the previous expression for the next one:

$$\begin{aligned} \Delta E_a(e) &= E(TS) - E(R) = (E_e(TS) + \mu_{TS}F_z) - (E_e(R) + \mu_R F_z) \\ &= (E_e(TS) - E_e(R)) + F_z (\mu_{TS} - \mu_R) = \Delta E_a(e) + F_z (\mu_{TS} - \mu_R) \end{aligned}$$

Where μ_R and μ_{TS} are the dipole moments of the reagents and the transition state, respectively and the well-known expression, $E(e) = E + \mu F_z$, is applied on both reagents and transition state. In spite of the electric field is opposite to the dipole moment we are using the Shaik et al.¹³ agreements, and that is why we use $+\mu F_z$, instead $-\mu F_z$.

On this equation, we can see a relationship between the activation energy with and without electric field. Thus, in the case that the external electric field points in an opposite



Scheme 2: Energy profile of a standard reaction $R \rightarrow P$. We can see the energy barrier (E_a) too.

direction to the dipole moment of the transition state and this is greater than the dipole moment of reactants the energy barrier will fall. The best orientation of the electric field is through the bond axis to be break.

3.2. Experimental evidences

An example of the experimental application of an Oriented Electric Field, we are going to check the experimental evidences presented by Aragonés et al.¹

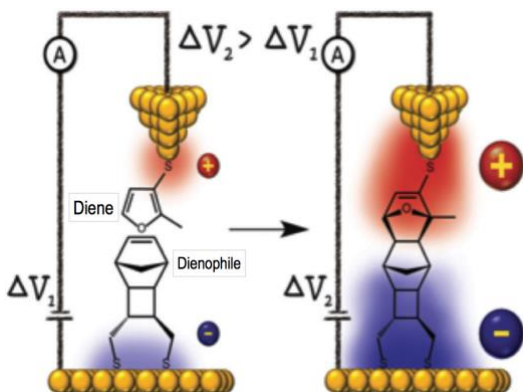


Figure 1: Use of an OEEF to catalyze a Diels-Alder reaction employing an STM tip and a gold surface to orient the reaction along the field vector. (Reproduced from ref. 1 with permission from the Nature Publishing Group, copyright 2016)

Aragonés et al.¹ used the electric field on a Diels-Alder reaction supported in STM-based experimental study. As we can see on Figure 1, they connected the diene and the dienophile, oriented in the direction of the OEEF, to a STM tip and a gold surface and then they applied the field.

The effect of the OEEF is to attract the electrons from the dienophile to decrease its electronic density, and take the electrons to the diene to increase its electronic density. Thanks to this, we benefit that π bond from dienophile will

break easily and will form a new σ bond with the diene forming the final compost.

This action of the OEEF benefits the ionic structures and stabilizes the transition state, which involves a failure of the energy barrier and an increase on the reaction rate.

4. OBJECTIVES

The main aim of this research is to present a review on the studies of the OEEF applied to some chemical reactions and to examine all the effects and changes that it produces in the reactions. As we will see, we can use the electric field as a catalysts or an inhibitor, it depends on the reactions and the reagents that we will use. We also analyse the OEEF effect on the thermally forbidden disrotatory ring opening of cyclobutene that as far as we known has not yet been studied.

For this purpose, first we will introduce the Valance Bond (VB) diagrams model,^{1,2,3} what they are and how can we build it, and we will use them to characterize the different reactions that we will see along the present study.

Second, with the help of this diagrams we will see that the charge-transfer species are more important than the neutral species (Scheme 1) and how this affects to the transition state, and consequently, to the energy barrier specially under an external electric field.

Third, at the end of this research, we will see that not all the systems where we apply an OEEF as that proposed by Shaik⁴ are adequate. Also, Shaik⁴ proposed some rules to know how will affect the OEEF to all the bonds that we already know. This rules will appear depending on the different facts and results that we are going to study.

5. RESULTS AND DISCUSSION

5.1. Initiation to the electric field applied to chemical reactions

Let us start with the Stark Effects explained on the Shaik et al.⁶ experimental evidences from a theoretical point of view using an ease and simple molecular system.

This one consists in a hydrogen atom on its second quant energy level ($n=2$). At this level, the hydrogen possesses four degenerates orbitals, one 2s and three

2p ($2p_x$, $2p_y$ and $2p_z$) as we can see on Figure 3.

With only on electron we can have the following electronic configurations: $2s_1$, $2p_{x1}$, $2p_{y1}$ and $2p_{z1}$. When we don't apply the field (Figure 2a), the states and the corresponding orbitals are mutually orthogonal and cannot mix with one another due to they have different symmetry.

But, when we apply the field along the Z-axis (Figure 2b) we can see how the $2p_{x1}$ and the $2p_{y1}$ states remain unchanged, whereas the $2s_1$ and $2p_{z1}$ states mix and split widely in energy, one below and one above the $2p_{x1}$ and $2p_{y1}$ states. This can be explained by the Stark effect, which says that in presence of an OEEF some orbitals stabilize, in particular the orbitals that describe the electronic density located in the direction of the applied OEEF. This result permits to explain why some forbidden reactions under OEEF are allowed.

From all this we can extract the first rule extracted from Shaik et al.⁶, that we will have to be taken in future cases:

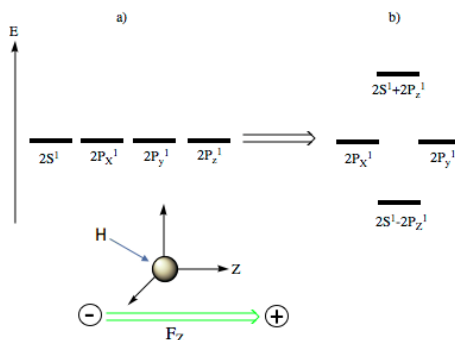


Figure 2: (a) The four degenerate states of H in its $n=2$ level. (b) The levels when we apply and OEEF on the Z-axis (Z-OEEF). This one undergoes splitting of $2S_1$ and $2P_{z1}$, shown in the drawing along with the corresponding hybridized orbitals. The energies appears in eV units. The image below shows the coordinate axes with H in the origins.

Rule 1: Two orbitals or two states, which cannot be mixed by symmetry, will mix when we orient an external electric field along the axis, which has the same symmetry as the product of the two states or the two orbitals. Thus, the field will remove the forbiddance of orbital and state mixing in molecular species and their reactions.

5.1.1. General effects of the Oriented External Field

The general effects of an OEFF have been studied by several groups⁷⁻¹¹ and they concluded that the effects that this type of field produces are the next one:

1. Changes on the bonds lengths.
2. Stretching frequencies
3. Bond dissociation energies

How we have seen on the previous section there are studies that prove the bond breaking/formation under the influence of an STM tip and a charged metallic surface (Figure 1) or between two ends. But they are not definitive because the breaking can take place in different mechanisms: ^{12,13}

- 1- Due to an OEFF through an area without current.
- 2- Involving tunnels basis mechanisms:
 - a) Introducing STM tip electrons to the molecule taking this to temporary charge states, which dissociate easily.
 - b) Collision events where part of the electron kinetic energy goes to the bond, which gets excited by vibration and a homolytic-bond breaking (we do not consider the heterolytic-bond breaking).

At the electron tunnel from the STM tip and towards the metallic surface on which the molecule is adsorbed, the electrons can be momentarily caught on the molecule or on the bond.

In this case the STM tip acts as an electrode that can give electrons to the molecule and create a radical anion; or accept electron from the molecule and create a radical cation.¹⁴ These radical species created had weaker bonds than the original molecules and they dissociate easily. This is specifically for radical anions with σ bonds.

It has been proven that in cases where an OEFF causes bond breaking; this is more effective for polar bonds and/or bonds having highly polarizable groups/atoms.^{15,16}

Now we are going to examine different types of bond and how they can break under the effect of an OEEF:

Homonuclear bonds in OEEF

The rule n°1, that we have seen above and talks about the remove of the forbidden-orbital-mixing, is transferred to the bonds. The direction of hybridization and the charge of polarization depend of the OEEF vector's direction on the e.g. Z-axis, independently if it's goes to the positive or negative direction. The orbital mixing is forbidden in the absence of an OEEF.

On Figure 3 we can see how the bond-ionicity increases with the polarisability of the atoms in the bond. This trend confirms the easy bond-breaking observed in STM-based experiments.¹ Now we are going to check the origins of the ionicity of homonuclear bond (X_A-X_B):

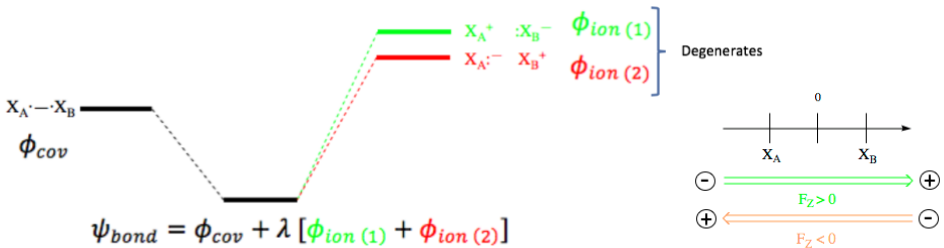


Figure 3: Ionicity in homonuclear bonds using VB-mixing diagrams: Here we can see the VB mixing for a homonuclear bond in a field-free situation. The bond-wave has degenerate inactive ionicity.

Without an OEEF the bond-wave function (ψ_{bond}) depends of the mix of the covalent structure (ϕ_{cov}) and the two degenerated ionic structures ($\phi_{ion(1)}$ and $\phi_{ion(2)}$). This mix of the ionic structures has the correct symmetry to mix into one covalent structure. The covalent homonuclear bond do not have a static ionicity, it has a degenerate inactive ionicity.

When we apply an OEEF (F_z) the degenerate inactive ionicity has its role favouring one of the ionic structures. Now we are going to see what happens when we apply an OEEF in the negative direction ($F_z < 0$) and in the positive direction ($F_z > 0$):

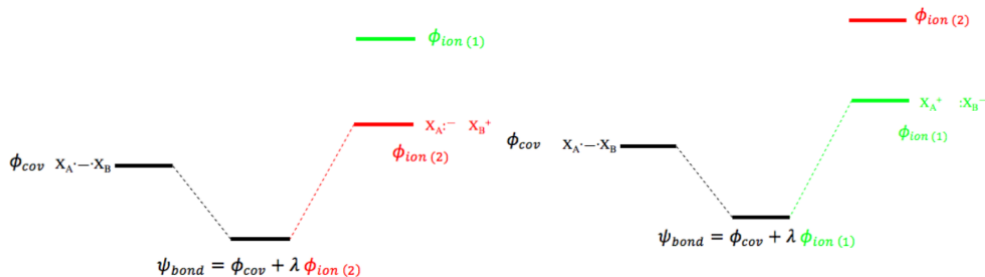


Figure 4: Ionicity in homonuclear bonds using Valence Bond-mixing diagrams: Here we have the VB-mixing diagrams in positive- and negatively-oriented field, b and c respectively, along the Z-axis. The field stabilizes the ionic structure whose ionicity is opposite to the field's ionicity, and leads to mixing of this particular structure with the covalent structure.

As we can see the negative orientation of the field ($F_z < 0$) stabilizes $\phi_{ion(2)}$ and destabilizes $\phi_{ion(1)}$. On the contrary, when we apply a field on the positive direction ($F_z > 0$) it stabilizes $\phi_{ion(1)}$ and destabilizes $\phi_{ion(2)}$.

In addition, the covalent structure mixes with the favoured ionic structure and gives to the bond wave function of the static ionicity. The OEEF oriented along Z-axis breaks the symmetry of the $\phi_{ion(1)} + \phi_{ion(2)}$ and gives the static ionicity in relation to the direction of the stabilized ionic structure.

Homonuclear bonds breaking in OEEF

As we saw before, for a field with a certain force and with an orientation on the Z-axis, the ionic structure turns every time more stable, thanks to the field effect, than the covalent structure. Also, we know that the ϕ_{ion} stabilization is proportional to the dipole moment of the ion pair:

$$\Delta E = \vec{F} \cdot \frac{\vec{\mu}}{4,8} \left[\frac{eV}{mol}, D \text{ units} \right] \quad (\text{Eq. 1})$$

The ionic structure will deeply change its geometry to increase the interaction with the field. While there is no field, the ionic pair electrostatic interaction creates a short-range minimum, when the field acts on the interaction with the dipole moment of the ionic pair separates the positive and negative ions into long distances. As the field increases it will do the distance between the ions.

This will continue happening until we will arrive to a critical F_z where the bond of the ionic structure will stretch, we will lose the minimum, and the bond will dissociate into the respective ions. (X^+ and X^-).

All the homonuclear bonds X_A-X_B under the effect of an increasing OEEF along the bond axis, gives place to a heterolysis ($A - B \rightarrow A^+ + B^-$) as a general mechanism.

Since the moment that the bond dissociates into ions, the most reliable magnitude that determinates the dissociation ease is the difference between the ionization energy (IE) and electron affinities (EA) of the atoms/fragments that form the bond. The difference IE-EA determines the polarisability of the bond. All this is resumed on rule n°26:

Rule 2: An OEEF oriented along the bond axis elongate homonuclear bonds (X_A-X_B) and sometimes will dissociate the specie into two ions.

The critic field that we need for the heterolytic breaking of the bond decreases when decrease the IE-EA of the constituent atom/fragment, or equivalently when the polarisability of the bond increases.

π bonds in OEEF

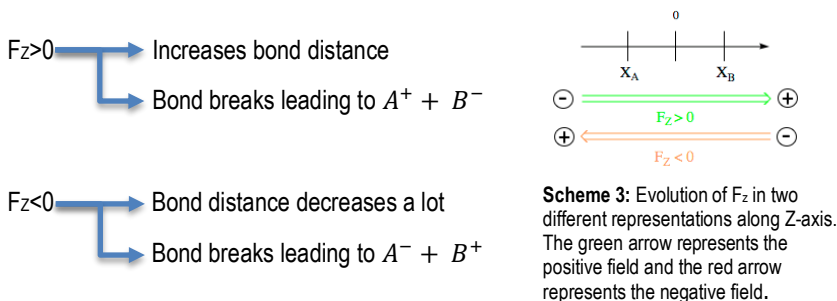
Break π -bonds under the OEEF effect is different than for σ -bonds, due to the π -bond has a σ -bond under it that confines the structure π ionic to short distances. In the case of $\text{CH}_2=\text{CH}_2$ while the weight of the ionic structure ($^-\text{CH}_2-\text{CH}_2^+$) increase moderately due to the OEEF effect on the $\text{C}=\text{C}$, the bond is still covalent even for fields $>1\text{V}/\text{\AA}$. If we change the H for other type of substituents, which stabilise the π -positive/negative charges, will make the role of the ionic structure π more relevant.

The effects of an OEEF in a π -bond are summarized on rule n° 36:

Rule 3: Unlike the for σ -bonds, which dissociate into ions with an OEEF, the π -bonds stay covalent for more time during the bond breaking via $\text{C}=\text{C}$ bon rotation and, thus are not much affected by OEEF.

Heteronuclear bond in OEEF

Heteronuclear bonds under an OEEF exhibit duality, with results that depend of the orientation of the field-vector along the bond axis. Overall, for a molecule $\text{A}-\text{B}$ (where $\text{A} \neq \text{B}$) we can see the following happens:



On the first case, we can see the dependence with the IE, the lower the IE (A) the lower the field that leads to dissociation, as it is established on rule n°2. But on the second case is less sensible to the field strength.

Has been shown that polar bonds dissociate in STM/charge-surface or STM/STM set ups, more easily than weaker homonuclear bonds. The field-induced dissociation generally generates ions with greater facility than radicals. Using the IE-EA relation of the bond, leads to understand this trend. Results for heteronuclear bonds are summarized on rule n°4e:

Rule 4: Heteropolar σ -bonds, with small IE-EA values of the fragments that form it, elongate in presence of an OEEF along the bond axis and eventually will dissociate into the two ions. The bond heterolysis shows a direct relation with the OEEF orientation. In theory, just turning the field vector for the bond axis will reduce the bond and this will be less polar; and as the field increases this will dissociate the bond to opposite ionic products.

Reaction axis rule

We can expect a bigger impact on the reactivity when the OEEF orients to the reaction axis. This is the direction in which the electrons of the bond reorganization from reagents to products are paired. In general, the reaction axis is the TS section along which the electrons are delocalized on all interchangeable bonds.

From this we can extract the last rulee:

Rule 5: The reaction axis is the direction through which the electrons get paired in the bond reorganization when we go from reagents to products.

If we apply an OEEF with the correct polarity the TS will stabilize and this will catalyse the reaction. But if we turn the OEEF in the opposite direction the inhibition will take place.

All the rules that we have been seen in all this part are basic rules that we can and we will apply on all type of bonds that we know. These rules are based on the VB mode, and that's why we'll explain them in the next section.

5.1.2. Valance bond diagrams: definition and how can we build it

Typically, we use the representation that we can see on Scheme 2 to see the energies of the reagents and products and conclude, in a qualitative analysis, if the reaction will happen or not based on the total energy of the reaction.

On this type of plots, we represent the valance bond structures, based on VB theory, of the reagents and the products in terms of energy. But we have to add the molecular orbitals of the molecules to these basic structures.

During a lot of years scientist tried to mix the Molecular Orbitals (MO) theory with the VB theory. On one hand, MO theory, which was the conceptual basis, could not offer a mechanism for the barrier formation. On the other hand, the VB theory, which could give us that mechanism, was considered obsolete and reserved to a selected group of scientists.

Hence, the MO-VB relationship was essential to create bridges between both theories to create a reactivity paradigm which had the qualitative advantages of both theories: these are the locality of the bond reorganization (best described by VB structures) and the orbital symmetry and nodal features (best described by MO theory).^{2,17}

The best way to connect both theories is a VB correlation diagram, which represents the energy of the VB states along the reaction coordinate, and by mixing of the configurations, projects the origin of the energy barrier, the transition state and the appearance of the intermediates.

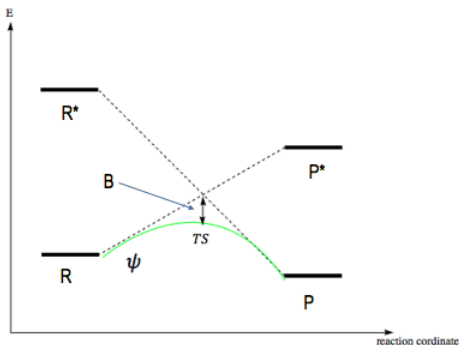
From all this we can extract the next definition of a VB diagram:

Valance Bond diagram: It is a representation of the energy of the VB structures of reagents and products along the reaction axis that connects Valance Bond theory with the Molecular Orbitals theory. These diagrams provide us information about the energy barrier of the reaction, the transition state and the appearance of the intermediates

As we will see later, we are going to use these diagrams to predict the evolution of the reaction, the role of the transition state, the influence of the charge-transfer structures and why we have intermediates on the reactions.

But before all that we have to know how build a VB diagram and what are the different parts of these. For that we are going to study the VB diagram of a generic reaction in a field-free situation:

Figure 5: VB diagram for a generic reaction $R \rightarrow P$, showing energy curves plotted along the reaction coordinate, where we can see the diabatic (in dotted lines) and adiabatic (in green) energy curves connecting the reagents to the products. The covalent-structures ϕ_{cov} describe the covalent bond of reagents (R) and products (P). On the plot (green line) below we can see the mixing of both VB structures and the VB states. Ψ_{TS} belong to the transition state and B is the resonance energy stabilization.



On the plot of Figure 5 we can see the basic states for the reagents and products, which correspond to R and P, and their excited states, which correspond to R^* and P^* . Now we are going to explain more deeply what are R^* and P^* :

- R^* : This is the excited electronic state of reagents. Corresponds to the reagents with the electronic structure of products.
- P^* : This is the excited electronic state of products. Corresponds to the products with the electronic structure of reagents.

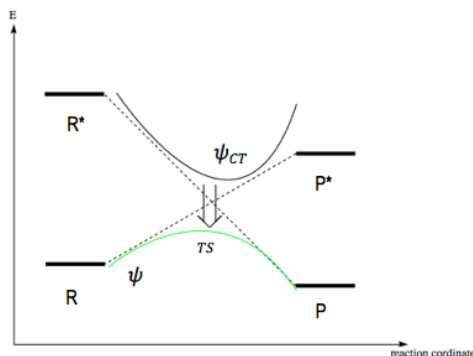
These four states represents the VB structures of the reaction. Furthermore, in the plot we can see that R and P^* are connected, as well as P and R^* are connected. That connection represents the energy increasing that takes place when we go from one state to another. This connection is represented by a wave function: ϕ_R for the R- P^* connection, and ϕ_P for the P- R^* connection.

This connection are the dotted line in Figure 5 and they are the diabatic energy curves, which means that these curves do not change their electronic structure over time and the reaction evolution. On the other hand we have the green line, which represents the connection between reagents and products, and is the adiabatic energy curve, which means that this curve changes its electronic structure over time and the reaction evolution.

Also, we can see on this plot the crossing point between both diabatic curves, under this one on the diabatic curve we can find the Transition State (TS). The adiabatic curve is what we typically know as reaction profile like the example on Scheme 2 and we use this curve to define the energy barrier. The energy difference between the crossing point and the TS it's the resonance energy stabilization (B).

But there is one more thing that we have to add to the VB diagram. We have to keep in mind that for all the chemistry reactions there is a charge-transfer (CT) contribution. On the next VB diagram, we are going to see that contribution:

Figure 6: It is the same plot of Figure 5 but now adding all the ionic and charge-transfer (CT) structures (ϕ_{ion}/Ψ_{CT}). The downward arrow indicates the interaction between these structures with the adiabatic energy curve.

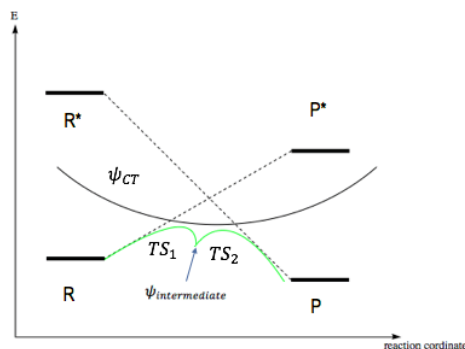


In the CT structures we are representing the structures where the species are exchanging electrons. If we apply an OEEF to any reaction de CT es will be stabilized and the CT wave function will fall. Before the crossing point nothing will happens, the reaction will follow the natural course.

But when that function continues falling to below the crossing point, we can arrive to the conclusion that the course of the reaction will change. That is because when that happens the CT wave function interacts with the adiabatic curve and changes the energy barrier of the reaction causing a kinetically stable intermediate and more than only one TS appears.

With this instead only one hill on the black line along the reaction axis that connects reagents and products we will observe a double dip profile, as we can see on Figure 7:

Figure 7: It is the same plot of Figure 7 and 8 but now adding the Ψ_{CT} curve, that falls below the crossing point. Here an intermediate is formed at the middle of the reaction coordinate instead a TS. As we can see on the black curve, the reaction mechanism has gone from a concerted mechanism to one step by step



5.1.3. Agreements adopted

Thanks to all what we have seen before and the Shaik et al.⁶ we obtain some of the agreements that we have been applying on the previous systems and that we will apply on the next sections.

First, we will define the units of the electric field and interaction energies. The field magnitude generated by a Q charge at a distance R in the Z-axis is:

$$\vec{F} = \frac{k_e \cdot Q}{R^2} \left[\frac{V}{\text{\AA}} \right] \quad (\text{Eq. 2})$$

Where Q has e units and R has Å. If we put K_e in the V/Å units we will arrive to the next equation:

$$\vec{F} = \frac{14,4 \cdot Q}{R^2} \quad (\text{Eq. 3})$$

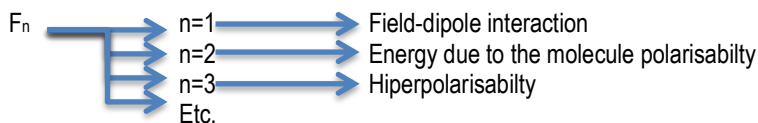
The field interaction with a Q' charge located at R in some direction is:

$$\Delta E = \vec{F} \cdot Q' \cdot \vec{R} \quad (\text{Eq. 4})$$

When Q and Q' are parallels and both are opposite Eq.4 changes on the next way:

$$\Delta E = -0,144 Q'R(eV) \quad (\text{Eq. 5})$$

A common interaction is that between the field and the molecular dipolar moment. The interaction that corresponds to energy is given by the sum of a compilation of field strength:



If we consider the n=1 case, on the Eq.4 we will use the dipole moment:

$$\vec{\mu} = 4,8 \cdot Q' \cdot \vec{R} \text{ Debye } (R \text{ in } \text{Å} \text{ and } Q' \text{ in } e \text{ units}) \quad (\text{Eq. 6})$$

Now we are going to substitute Eq. 6 on Eq.4 and we will obtain the next equation:

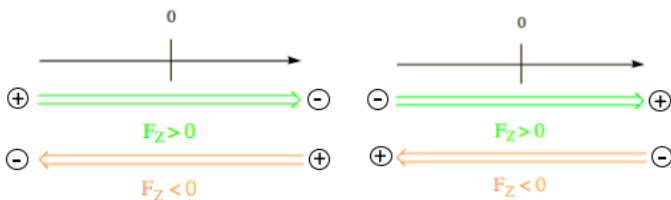
$$\Delta E = \vec{F} \cdot \frac{\vec{\mu}}{4,8} \left[\frac{eV}{mol}, D \text{ units} \right] \quad (\text{Eq. 1})$$

Since both \vec{F} and \vec{R} are vectors, when both will be parallel the sign of the interaction energy will depend of the relative orientation of the vectors. Their opposition will lead to stabilization.

In a chemistry reaction, with a field applied, the reagent-cluster (RC) and the corresponding transition state will have a dipolar moment. In this case, we will use in Eq.1 the difference between the dipoles and the net stabilization energy, becomes:

$$\Delta\Delta E = 4,8 \cdot \vec{F} \cdot \Delta\vec{\mu} \quad (\text{Eq. 7})$$

Now, we are going to establish the reference system that we will use on all the reactions that we will examine from now to the end of this study:



Scheme 4: Evolution of F_z in two different representations along Z-axis. The green arrow represents the positive field and the red arrow represents the negative field.

There are a lot of studies that use the reference system that we can see on the left of Scheme 4, but for this study we will use the reference system that we can see on the right. We will use this system because is easier to understand and the reactions that we study are based on that system.

On the physical agreement the forces goes from + to - values, system on the left in Scheme 4, but we will use the agreement where the forces goes from - to + values, system on the right.

5.2. Case study

In this section we are going to study different types of reactions in which we will apply everything that we have seen before:

5.2.1. Pericyclic reaction: Diels-Alder

As an example of a pericyclic reaction we are going to check the Meir et al.¹⁸ to examine how an OEEF can affect on the rate, mechanism, stereospecificity and endo/exo selectivity of the next Diels-Alder (DA) reaction:

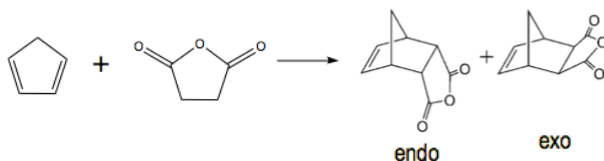


Figure 8: Moderately polar DA reaction of cyclopentadiene and maleic anhydride.

The analyses of this reaction show that an OEEF can be a “catalyst” or an accessory reagent. As we will see later, an OEEF oriented along the reaction axis, where it will take place the electrons reorganization, can affect to the reaction rate by orders of magnitude, speeding it up or slowing it down in changing the direction of the field.

At the same time, we can change the endo/exo selectivity in applying a perpendicular field to reaction axis. We will analyse the origins of the field and its effects on chosen selectivity.

Reaction: Cyclopentadiene and Maleic Anhydride

Meir et al. studied the reaction between cyclopentadiene and maleic anhydride because it is really well studied by experimentalists. On Figure 9 we can see the energy profile, in gas phase, of the endo and exo pathways, with the geometrics details for different structures:

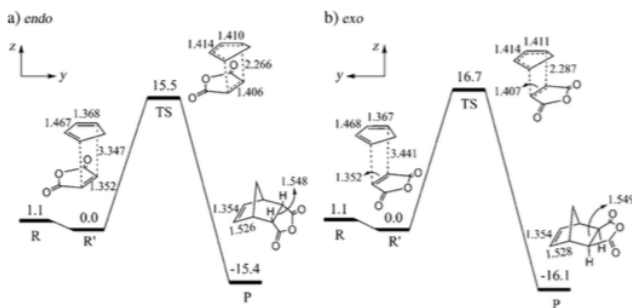


Figure 9: Energy profile of endo and exo pathways with the structures of R' and TS. (Image obtained from Meir et al., ref.18 Copyright 2010 Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim).

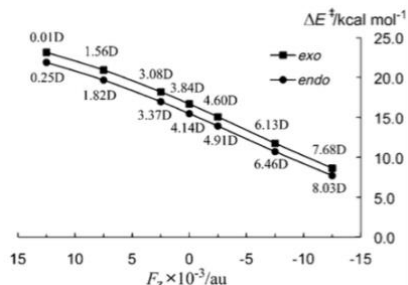
We can find the effects of an OEEF on the energy barrier for the endo and exo pathways in different oriented field on Table A2 of the Appendix 2, this data is taken from ref. 18. These values vary depending on the orientation of the field:

- **X-axis:** The energy barrier remains practically constant along the positive and negative direction.
- **Y-axis:** It difference between endo and exo pathways, and induces different selectivity than in a field-free situation.
- **Z-axis:** In the negative direction there is a huge effect in the reduction of the energy barrier at the highest field in both pathways, the decrease is around 8 Kcal/mol. On the contrary, when there is a positive field, the energy barrier increases in both pathways, the effect is around 7 Kcal/mol for the strength field.

Therefore, this information demonstrates that the catalysis or inhibition of the moderately polar DA reaction can be achieved orienting the field along the “reaction axis”; while if we want choose one of the endo/exo pathways we can achieve it with y-oriented fields along the dipoles of the diene and dienophile.

Now we are going to check Figure 10 that show changes in the energy barrier and the dipole moment for the TS of the endo and exo pathways with the field applied along the Z-axis.

Figure 10: Variation of the energy barrier and the TS dipole moment for the endo and exo pathways with the applied field strength along Z-axis (Image obtained from Meir et al., ref.18 Copyright 2010 Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim).



We see how, compared with the field-free situation, the OEEF change the energy barrier and constantly polarize the TSs affecting their dipoles. From that plot we can extract the next conclusions:

- $F_z > 0$: The energy barrier increases and the dipole decreases gradually while the field increases.
- $F_z < 0$: The energy barrier decreases and the dipole increases.

As a representation of these results we can check Figure 11, where we can see the direction of the dipole moment and the field in the positive and negative direction. Only the negative field has an opposite direction to the dipole moment.

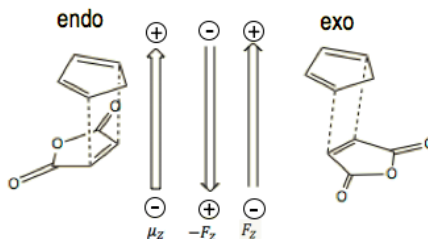


Figure 11: TS of the endo and exo pathways next to the direction of the dipole moment along Z-axis (μ_z), the direction of the field along Z-axis (F_z) and the direction of the charge transfer.

That means that the negative field will stabilize the TS and the energy barrier will decrease as we said before. But for the positive field, how its goes on the same direction than the dipole moment, this field will destabilize the TS and the energy barrier will increase.

As conclusions of this reaction we can say that when we apply an OEEF along the reaction axis in the natural direction of the electron flow the energy barrier will decrease and the field will catalyse the process. Anyway, the effects of the $\pm F_z$ does not changes the endo/exo selectivity and the net effects of the field on the species R' and TS remain unchanged to the reaction pathway.

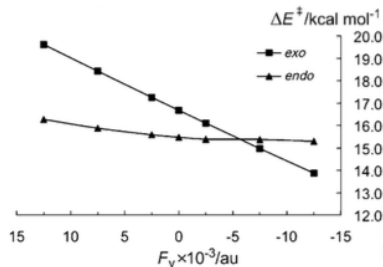
Endo/exo selectivity when we apply an OEEF

Now we are going to check how we can change the endo/exo selectivity on the cyclopentadiene and maleic anhydride reaction. The maleic anhydride has a dipole moment oriented along the Y-axis and that orientation is different for the endo and exo pathways.

Considering this, Meir et al. applied a field along the Y-axis, in the positive and negative direction, to see how could change the energy barrier. We can see the results of that application in Figure 12:

Figure 12: Variation of the energy barrier for the endo and exo pathways with the applied field strength along Y-axis (Image obtained from Meir et al., ref.18, Copyright 2010 Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim).

We see that the energy barrier for the endo pathway stays practically constant. But for the exo pathway we can observe a big difference between the positive and negative field. That variation is at least 6 Kcal/mol.



From this plot, we can conclude that when we apply a negative field, and every time more negative, the exo pathway is favoured in front of the endo pathway. On the contrary, when we apply positive field, and every time more positive, the exo pathway will be much more favoured than the endo pathway.

Thus, when we apply a field in the Y-axis, depending on its direction, we could have a first approximation of the preference between the endo and exo pathway. Another reason for that difference between the two routes when we apply the Y-oriented field is the interaction of the dipole moment with that field.

As we can see on Figure 13a, for both structures the y component of the dipole gives rise to a stabilizing interaction with the negative direction of the field ($F_y < 0$), because the dipole and the field had opposite directions.

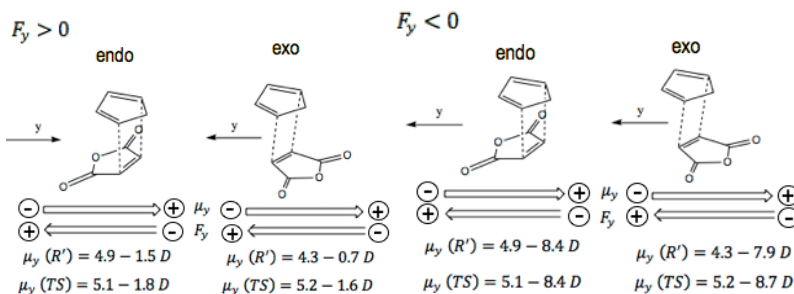


Figure 13: TS of the endo and exo pathways next to the direction of the dipole moment along Y-axis (μ_y) and the direction of the field along Y-axis (F_y): a) $F_y < 0$ and b) $F_y > 0$ (Image obtained from Meir et al., ref.18, Copyright 2010 Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim).

Also the dipole of the TS in the exo pathway (TS_{exo}) has a bigger dipole and is more polarizable than the TS in the endo pathway (TS_{endo}) so the first one stabilizes more than the second one. An extra contribution is due to the stabilization of the R'_{endo} versus R'_{exo} (see Figure 11). The decrease of the energy barrier, bigger for the exo route, cancel initial preference for endo route and gives a preference for the exo selectivity.

Furthermore, we can see the effect of the positive field ($F_y > 0$) on Figure 13b. Now, both structure are destabilized by the OEEF effect, due to the dipole moment goes on the same direction than the field. In this case R'_{endo} , which has the greatest value, is destabilized more

than R'_{exo} , and the same happens with the TSs. Also, we can see the importance of the reaction axis and how the orientation of the OEEF can change the course of the reaction.

VB diagram for a DA reaction

On Figure 14 there is a VB diagram for the pristine DA reaction. On this diagram we can see all the parts that we explained on section 5.1.2 of this review.

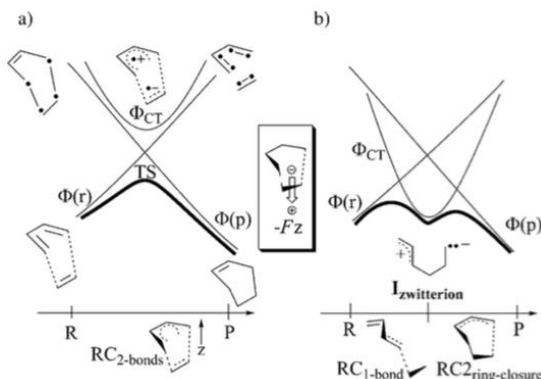


Figure 14: VB diagram describing the formation of the energy profile and all the species involved in this reaction. a) Field-free situation, b) Under the effect of an OEEF. (Image obtained from Meir et al., ref.18, Copyright 2010 Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim).

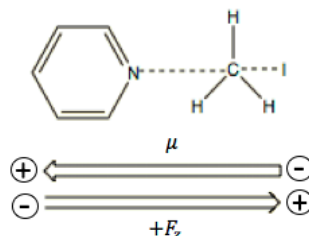
On Figure 14a we can see the field-free situation and all the species involved in the reaction. We can see how the two lines that connects R with P^* and P with R^* are called Φ_R and Φ_P , respectively. These two lines create the crossing point, below which we can find the TS. The black line that connects R and P is the energy profile that we all know and gives us the energy barrier. And the line that we can see above the crossing point corresponds to the CT species.

These two lines, in a field-free situation, do not interact, but when we apply an OEEF that changes. How we can see on Figure 14b, when we apply a field the CT curve goes down and stabilizes the TS. That stabilization causes the formation of intermediate specie, which is a zwitterion form, two TSs and a decrease of the energy barrier. Because of this, is necessary this VB diagram with respect to the one we have in Figure 9. This agrees with what we saw when we applied a field along the Z-axis, a decrease of the energy barrier due to a stabilization of the TS, what involves and increasing of the rate.

5.2.2. Substitution reaction: Menshutkin

The second reaction that we are going to study, the Menshutkin reaction explained on Ramanan et al.¹⁹ is an example of a substitution reaction (S_N2). We are going to explore the role of the OEEF on the control of the nucleophilic methyl transference with one purpose:

Scheme 5: Interaction between pyridine and alkyl halide with a field applied along the Z-axis and the dipole moment of the TS.



1. Explore the catalyst/inhibitor power of the OEEF in the reaction axis and establish the relation between the structure and the reactivity of the Menshutkin reaction.

During the reaction, the nucleophile likes the substituted pyridines shown in Scheme 5 move the halogen from the alkyl halide. In general, the gas phase of this reaction is endothermic and very slow.

OEEF effects on Menshutkin Systems

In Figure 15a we can see the energy barriers for the reaction of the different pyridines with methyl iodide in a field-free situation. We are going to start by the effect of an OEEF when we apply it along the three axes on the positive and negative direction.

As we can see on the middle of Figure 15, the reaction axis is the Z-axis, which goes through the N-C-I bond. If we check Figure 15b clearly we can see that for $F_z > 0$ the field catalyze the reaction, due to a decrease of the energy barrier, but for a $F_z < 0$ the field applied inhibits the reaction due to an increase of the energy barrier.

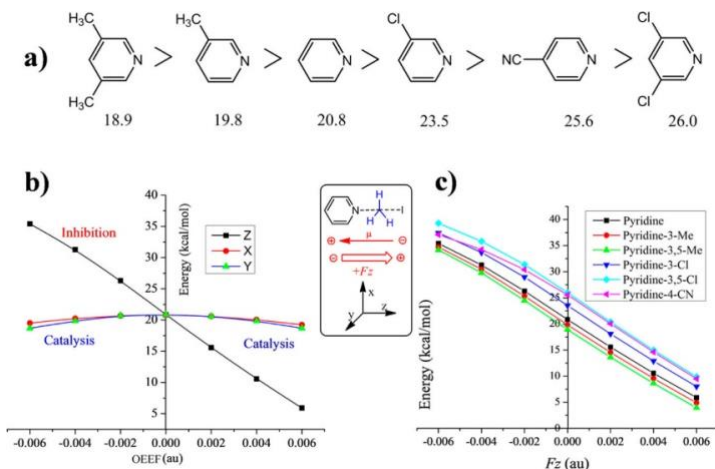


Figure 15: a) Energy barrier of the different pyridines in the reaction with alkyl halide in a field-free situation, b) Changes of energy barrier along the three axes when we apply an OEEF and c) Evolution of the energy barrier of the reaction in a) when we apply an OEEF. (Image obtained from Ramanan et al., ref.19 Copyright 2019 American Chemical Society).

The energy change is really big, which was to be expected for a field applied on the reaction axis. Also, we can see that the process of catalysis/inhibition starts to establish at weak fields, around ± 0.001 au.

In regards to X and Y-axes, we can see that for both the positive and negative direction the field decreases around 2.2 Kcal/mol. That happens because the field deforms TS away from linearity. On the Z-axis the N-C-I angle is 180° while for the X and Y-axes it is 167° , when we apply the field. Then, as we can see, the field on the X and Y-axes has a little catalyst effect.

We have seen that if we orient the molecule along the Z-axis and we apply a positive field, bigger every time, the catalyst effect is bigger. But if we apply an OEEF along the X and Y-

axes we will also have a catalyst effect and without having to orient the molecule or apply a specific field.

One of the most important components of the OEEF effect is due to the polarization that is very independent of the field direction. This polarization effects are maximum on the TS due to the electronic density offshoring. Moreover, if we apply an OEEF powerful enough it will orient the molecule so that the reaction takes place by the fastest route, in which the OEEF points in the positive directions of the reaction axis.

Then, we can expect that the catalysis take place without orient the molecules. In the other hand, if we want to inhibit the reaction we have to orient the molecules. On Figure 15c we can see the OEEF effect along Z-axis on the different types of pyridines in reacting with CH₃I, which ends up giving pyridines with different substituents. We can see how the different pyridines generate parallel lines that preserve the same distribution of $F_z=0$.

Also, we can observe how the pyridines which was less reactive (3,5-dichloro and 4-cyano) and has the higher energy barrier in a field-free situation, become much more reactive when we apply a $F_z > 0$ due to a great decrease of the energy barrier.

That changes is thanks to the substituents, because methyl gives electron density to the ring, what stabilizes the TS and the energy barrier decreases. On the contrary, if we have a substituent electron-acceptor agents, like Cl or CN, they will take electron from the ring, what destabilize the TS and the energy barrier increases. This plot is really useful to see the effect of the substituents on the energy barrier.

If we check again Scheme 5 we will see that the direction of the dipole moment and the positive field ($F_z > 0$) are opposite, we can conclude the OEEF stabilizes TS, decrease the energy barrier and catalyses the reaction. Therefore when we apply a negative field ($F_z < 0$), both vectors had the same direction and, as a result of the repulsion, destabilize TS and inhibit the reaction.

In addition to OEEF catalytic effects, this one causes changes in the TS geometry too. On Table 1 we can see changes that occurs on the bonds N-C and C-I on the TS when we apply different field strength.

Table 1: Variation of the bond distances in the pyridine with alkyl halide reaction when we apply different field strength. (Data taken from Shaik et al., ref.19, Copyright 2019 American Chemical Society).

| F_z (au) | N-C (Å) | C-I (Å) |
|------------|---------|---------|
| -0.006 | 1.81 | 2.84 |
| -0.004 | 1.82 | 2.85 |
| -0.002 | 1.84 | 2.85 |
| 0.000 | 1.89 | 2.83 |
| 0.002 | 1.96 | 2.78 |
| 0.004 | 2.03 | 2.74 |
| 0.006 | 2.11 | 2.69 |

When we go from negative to positive values of the field the N-C bond increases while the C-I bond decreases. Then, when we apply positive fields ($F_z > 0$) we are in the catalytic zone and the OEEF creates TS more similar to reagents. While when we apply a negative field ($F_z < 0$) we are in the inhibition zone and the OEEF creates TS more similar to products.

VB diagram of Menshutkin reaction

If we want to explain all the changes that occur in the energy barrier and the TS geometry under the OEEF effect, we are going to use a VB diagram. The VB diagram for the Menshutkin reaction, extracted from Ramanan et al.¹⁹:

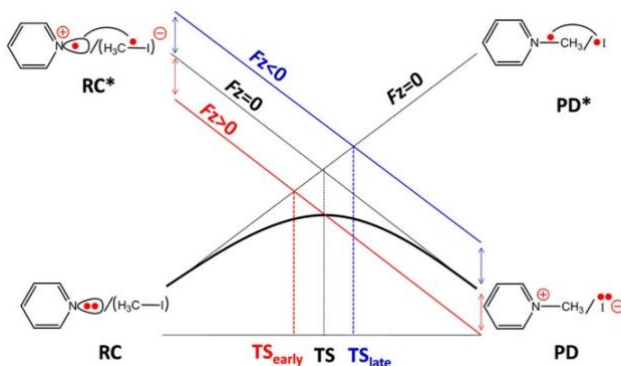


Figure 16: VB for a generic Menshutkin reaction when we apply different values of OEEF. The curve that connects RC and PD signify spin pairing of these electrons to singlet pairs. (Image obtained from Ramanan et al., ref.19, Copyright 2019 American Chemical Society).

In this VB diagram, the RC and PD structures correspond to reagents and products respectively. And RC* and PD* structures correspond to the excited reagents state and excited products state, respectively. And as we said before, the black line below the crossing point correspond to the energetic profile which appears due to the avoided crossing of the two curves, joining reagents and products and giving rise to the TS.

All the black lines that we can see on Figure 16 represents the situation of field-free that we have already studied, but we can see two more field values that changes this VB diagram:

- $F_z > 0$: As we can see the curve that connects PD and RC* is lower, which means that it is a more stable situation than the $F_z = 0$ situation. This involves that the crossing point will move to the left and, consequently, the TS will move to the left too. If that happens the energy barrier will fall, the reaction rate will increase and the OEEF will catalyse the reaction.
- $F_z < 0$: In this case, the curve that connects PD and RC* goes to the right, which means it is destabilizing when we apply the OEEF. This involves that the crossing point will move to the right and TS will move to the same direction. With this the energy barrier will increase, the reaction rate will decrease and the OEEF will inhibit the reaction.

All the changes we have seen are in line with the Bell-Evans-Polanyi principle²⁰ and the Leffler-Hammond postulate²¹, which establish that a more exothermic reaction will have a lower energy barrier and TS more similar to reagents. On the contrary, a more endothermic reaction will have a bigger energy barrier and TS more similar to products.

Therefore, the OEEF effects follow the principles of the physical organic chemistry: the catalysis with a $F_z > 0$ is more similar to a exothermic reaction, because it has a lower

energy and TS more similar to reagents. While the inhibition with a $F_z < 0$ is more similar to an endothermic reaction, because it has a bigger energy barrier and TS is more similar to products.

Moreover, the catalysis of the Menshutkin reaction thanks to OEEF effect follows the rule of the reaction axis (rule n° 5): "An OEEF oriented along the axis, where the electronic reorganization in the changeover from reagents to products takes place, will catalyse the reaction improving the stability of the ionic structures that contributes to TS and changing the energy barrier".

The importance of catalysis has often been equated with that of inhibition, and how we have seen an OEEF allows you go from one process to the other only changing the field direction. The reaction rate is bigger in the $+z$ direction than in the $-z$ direction, like in the $\pm x$ and $\pm y$ where the reaction has a better rate (See Figure 15b).

In a lot of reactions, if we apply a weak OEEF and without orient the reagents the reaction may not show any better due to the free rotation of the molecules that made the effect of the applied field equal to 0. But in the Menshutkin reaction we have a special situation because we only have one direction where the reaction rate will decrease ($F_z < 0$) while the other 5 directions that could have the field present an increasing, which can be bigger or lower.

5.2.3. Benzene nucleophilic aromatic substitution (S_NAr)

Now we are going to check the Stuyver et al.²² review that talks about the electrophilic aromatic substitution reactions (EAS) that are really important in organic chemistry. A general EAS is the next one:

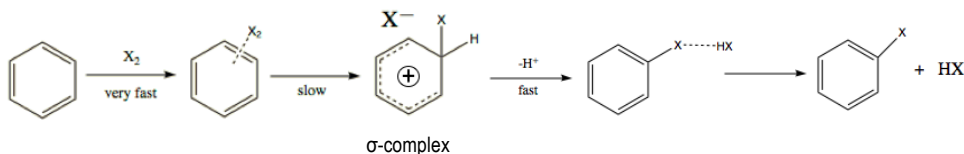


Figure 17: Representation of a general EAS involving a dihalogen (X_2) electrophile

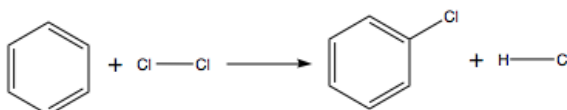
In this mechanism we can see the σ -complex, Wheland intermediate, it is the specie where the charge-transfer takes place. Now we are going to use the VB diagrams to discuss the general conditions under a transition from concerted to step by step mechanism can take place and we will use it to know the existence of σ -complexes in the EAS reaction.

Benzene + Cl_2 reaction

Figure 18 show up the reaction between the benzene and chlorine:

In this reaction, as we can

Figure 18: Representation of EAS reaction between benzene and chlorine



see above, C-H and Cl-Cl bonds will break and new bonds will form: C-Cl and H-Cl. Then, we can propose the VB diagram for this reaction:

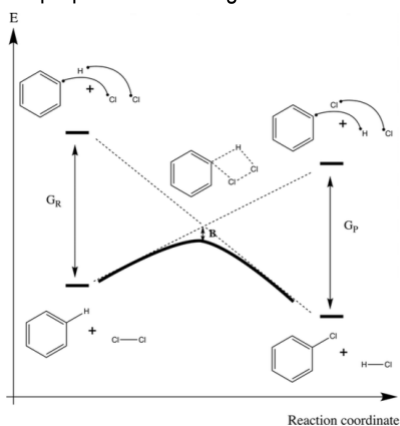


Figure 19: VB diagram for the reaction in Figure 18. We can see the structures of the reagents and products, underneath, and the structures of excited reagents and excited products, on top. Also, we can see the TS structure, the resonance energy stabilization (B) and the adiabatic line (black line) (Image obtained from Stuyver et al., ref.22, Copyright 2019 American Chemical Society).

If we leave aside for a moment the TC structures in the crossing point the reagents and products are degenerated. Apart of a completely dissociated structure the only TS structure that can accomplish this goal is what we see above the crossing point in Figure 19. This is an intermediate of four membered-ring.

We can expect that the TS structure will involve a little resonance energy stabilization (B) between reagents and products, so the black line will only pass slightly below the crossing point. It is important to keep in mind that competitive TS, with a very similar structure, involving the concerted addition of a Cl₂ molecule to the π -system of the benzene molecule instead the direct substitution of H for a Cl atom, could exist. This alternative structure is part of an alternative reaction pathway with several steps, described by Van Lommel et al (Figure 20).²³

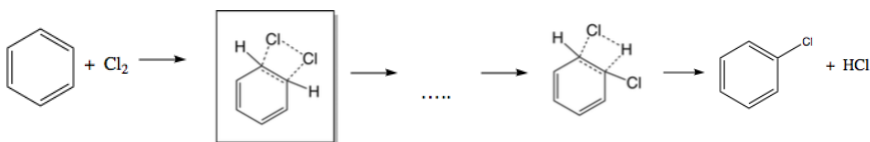


Figure 20: Representation of the electrophilic chlorination reaction in several steps. The framed structure is the TS which is similar to TS of Figure 24 (Image obtained from Stuyver et al., ref.22 Copyright 2019 American Chemical Society).

We can expect that this second TS is lower in energy than the TS that we saw on Figure 19. But, Stuyver et al.²² were in doubt if there would be 2 TS or, due to the similarity of their geometry, they would combine to give 1 single TS. According to their calculation the two TS will be mixed in only 1. Also, how TS on Figure 20 is lower in energy than TS on Figure 19, the geometry of the mixed TS will be more similar to the second TS than to the first TS.

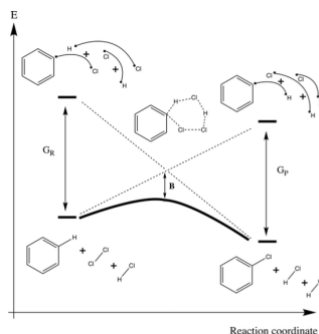
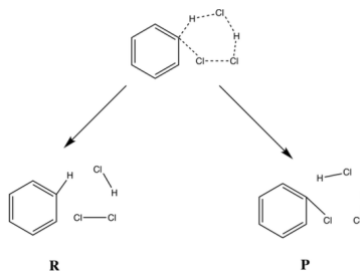
Both reactions pathways discussed above involve a 4 members TS in the concerted mechanism. We said above that we can expect a small B due to limited orbitals interactions between reagents. But, there is an alternative way to mitigate the unfavourable overlap of the orbitals in the TS geometry: adding other species, such as a molecule of the EAS product (an HCl in this case). In this mechanism in the TS we will form an hexagon instead a square in the TS geometry.^{2,17}

Due to the reagents and products should be degenerated on the TS geometry, the TS for the autocatalytic direct concerted reaction should be what we can see on Figure 21:

Figure 21: Representation of the TS of the reaction in Figure 18 in the presence of HCl (Image obtained from Stuyver et al., ref.22 Copyright 2019 American Chemical Society).

A

As we can see, with the addition of the HCl molecule we obtain a six membered-ring TS. We can expect that the participation of the HCl molecule on the reaction mechanism involves a decreasing of the energy barrier of the concerted reaction of this reaction due to a stabilization of the TS as we can see on Figure 22:



This reaction is autocatalytic in nature, and this has been corroborated by Scheler and co-workers and Van Lommel et al.²³

Due to this autocatalytic effect we go from a single-valley-shaped form to a hill-shaped form.

Figure 22: Full VB diagram of the reaction of Figure 18 in the presence of HCl. (Image obtained from Stuyver et al., ref. 22, Copyright 2019 American Chemical Society)

The importance of σ -complex

Until now, we have not taken into account the CT species, although they didn't appear in the previous reaction either, they could be directly related with the σ -complexes (Figure 22). How these structures will mix with the adiabatic curve along the reaction coordinate, in the VB diagram, will determine the role of these complexes on the EAS.



Figure 23: CT state involving electron transfer from benzene to Cl_2 , forming a σ -complex that we can see on the right. (Image obtained from Stuyver et al., ref.22, Copyright 2019 American Chemical Society).

If the CT state stays above the crossing point we obtain the same VB diagrams that we obtained previously: every step on the mechanism is concerted and there is no σ -complexes. But if the CT state stabilizes by the action of an OEEF and this curve on the VB diagram goes below the crossing point, the TS geometry will change and it will look more like the σ -complexes (Figure 23).

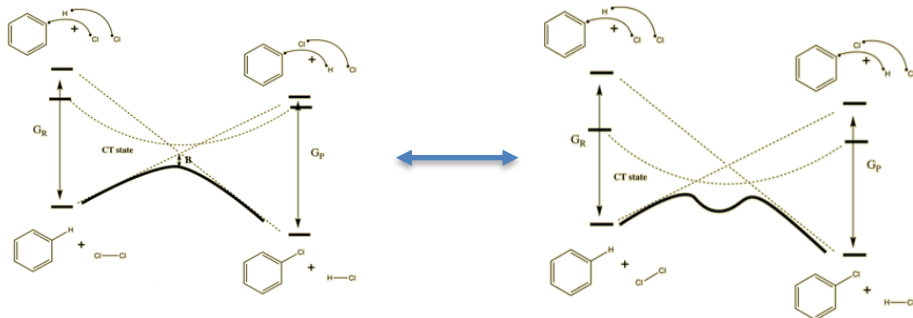


Figure 24: Same VB diagram of Figure 22 but now with the interaction of the CT curve. On the left we can see the VB diagram before the CT curve passes the crossing point. On the right we can see that the CV curve has passed the crossing point and causes the appearance of the σ -complex intermediate. G_R and G_P represent the energy needed to go from the basic state to the excited state (Image obtained from Stuyver et al., ref.22, Copyright 2019 American Chemical Society).

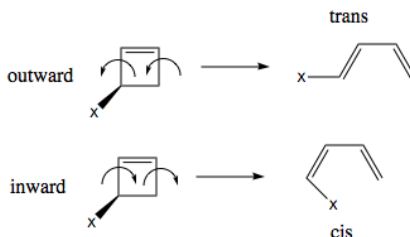
But while the CT state does not cross below the crossing point only one energy barrier will determine the reaction. The moment it crosses the crossing point and interacts with the adiabatic curve, the energy barrier will split in two, leading to the formation of the σ -complex intermediate. From this point on we will not observe any more direct concerted mechanism; the original saddle point in the adiabatic curve has sunk to a local minimum.

5.2.4. Cyclobutene ring opening by conrotatory applying an electric field

Let's go over Mattioli et al.³ that talks about the OEEF effect in the conversion reaction of 3-substituted cyclobutene to butadiene and in the stereochemistry of the reaction. This electrolytic reaction is concerted and understanding its mechanism is one of the most important discoveries of Woodward-Hoffman (WH) rules.²⁴

The basic concept of WH rules, the conservation of orbital symmetry when we pass from reagents to products, establishes that the cyclobutene ring opening has to take place by a conrotatory rotation. By this way, the bond characteristics of all the reagents occupied orbitals are maintained when we go from reagents to products. That does not happen in the disrotatory rotation (forbidden reaction) due to a really high-energy barrier.

In the case of 3-substituted cyclobutenes, the mechanism has really important stereochemical consequences due to the allowed way for the conrotatory rotation at C3, it can be both: inward (cis product) and outward (trans product), as we can see on Scheme 6:



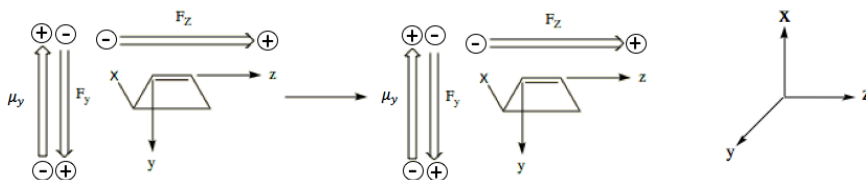
Scheme 6: Conrotatory rotation allowed inward and outward for 3-substituted cyclobutenes, leading to cis and trans products, respectively ($X = \text{H}, \text{CH}_3, \text{NH}_2, \text{CHO}, \text{NO}, \text{BH}_2$).

At the beginning they observed that for the outward rotation in many cases, trans product, was preferentially formed in such a way that it was thought to be normal, and extended to minimize steric effects in the transition state. But, in various studies, Houk²⁵⁻²⁹ made investigation into the opening of 3- and 3,4-cyclobutenes by conrotatory rotation and came to the conclusion that donor substituents favoured outward rotation, while the acceptor substituents favoured inward rotation. With this results Houk concluded that the electronic effects and not the steric effects are dominant in determining the final stereochemistry of the substituted cyclobutene rings.

In this review Mattioli et al.³ examined the OEEF effects on the reactivity for different 3-substitued cyclobutenes (C_4H_5C with $X= H, CH_3, NH_2, CHO, NO, BH_2$). They chose these substituents because they are clear examples of electron-donor and electron-acceptor for which there is both computational and experimental data.

Axes orientation and dipole effect

We can see the orientation of the axes in the 3-substitued cyclobutenes for the reagents and the TS in Scheme 7:



Scheme 7: The opposite orientation of the field with the dipole moment stabilizes the system. The dipole increasing when we go from reagents to products stabilizes the products. On the right we can see the three axes.

To understand the OEEF effects on the molecular energy (E), we can use the next equation that we extract from the perturbational theory:

$$E = E(0) - \mu_0 F - \frac{1}{2} \alpha F^2 \quad (\text{Eq. 7})$$

Where $E(0)$ is the energy in a field-free situation, μ_0 is the permanent dipole in the direction of the applied field F , and α is the polarity on the same direction. In the presence of an OEEF the electron cloud moves and distorted, causing a change in the dipole called the induced dipole (μ). We could express this as the product of the polarity and the electric field:

$$\mu = \mu_0 + \alpha F \quad (\text{Eq. 8})$$

If we replace Eq.8 on Eq.7 we obtain:

$$E = E(0) - \mu F + \frac{1}{2} \alpha F^2 \quad (\text{Eq. 9})$$

As we can see on Eq.8, if we keep the first order contribution, we can use the induced (μ) to predict the effects of the field applied to E. The μ is a general parameter that reflects the general total polarization effect of the molecular charge due to the applied field. This parameter takes into account:

1. Field effect on the energy difference between HOMO-LUMO orbitals and the change it causes in the transfer of charge between the two orbitals. What involves the stabilization/destabilization of TS (Orbital contribution).
2. Field effect in the electrons exchange between reagents and the TS (electrostatic contribution).

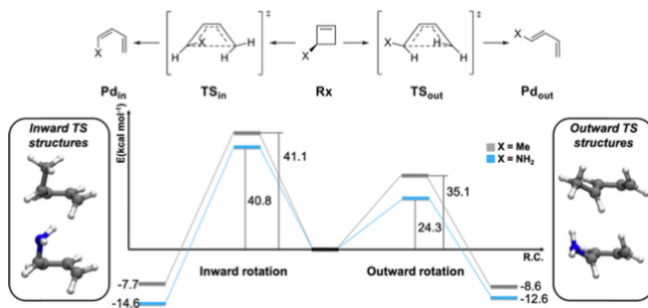
With this we can see how the final global effect of the applied field is a complex interaction of orbital and electrostatic contributions, so it is often very difficult to predict what the dominant factor will be.

Scheme 7 shows a positive field along Y-axis ($F_y > 0$) and the dipole moment along the same axis (μ_y) that goes to the opposite direction. This orientation stabilizes the molecular system. Also, if the dipole moment increases when we go from reagents to TS, the TS will stabilize due to the OEEF effect and the energy barrier will decrease (catalysis). In contrast, a decrease in dipole moment will cause an increase of the energy barrier (inhibition).

Electron-donor substituents (X=CH₃, NH₂)

In a field-free situation, both for CH₃ and NH₂ the outward rotation is favoured and the energetic preference of this rotation increases when the π -donator character of the substituent increases. On Figure 25 we can see the energy barrier on the outward and inward rotation for both substituents.

Figure 25: Energy barrier for the opening by conrotatory rotation (inward and outward rotation) of 3-methylcyclobutene and 3-aminocyclobutene in a field-free situation. Also, we can see the structures of the TS for both pathways. (Image obtained from Mattioli et al., ref.3 Copyright 2019 American Chemical Society).



As an example of this type of substituents, we are going to check X=NH₂ and its effects on the energy barrier and μ :

X=NH₂

In absence of an OEEF the energy barrier for this substituent in the outward and inward rotation are 24.3 and 40.8 Kcal/mol, respectively. We are going to study the outward rotation, favoured, on Table A2 (Appendix 2).

In this case the OEEF effect is bigger due to the big donator character of this substituent and the resulting increase of the electron density on the cyclobutene ring, resulting in greater polarization when we apply the field. The conclusions we have reached, after comparing the table with the field-free situation are:

- **X-axis:** For the positive direction ($F_x > 0$) we can observe an increasing of the energy barrier that causes an inhibition, while the negative direction we only know that is a small catalysis effect due to a small decrease of the energy barrier.
- **Y-axis:** For the $F_y > 0$ happens the same like in X-axis. And for $F_y < 0$ there is a catalysis effect due to an increase of the μ_y .
- **Z-axis:** In this case, when we apply a $F_z > 0$ the energy barrier decreases and the dipole increases, therefore, there is a catalysis due to the increase of the μ_z that stabilizes the TS.

But when we apply a $F_z < 0$ the energy barrier increases and the dipole decreases (oriented to the positive direction) which causes an inhibition due to the increase of the μ_z that destabilizes the TS.

As we have seen this trends can be explained by the difference in the dipole moment when we go from reagents to TS. The OEEF effect is more important along the Y- and Z-axis than along the X-axis, due to the dipole moment changing, when we pass from reagent to TS, involves Y- and Z-axis. The polarization along the X-axis depends of the substituent position at reagents and TS.

Electron-acceptor substituents (X=CHO, NO, BH₂)

Next, we are going to check the OEEF effect when we have electron-acceptor substituents. For this type of substituents we can see how the inward rotation can compete with the outward rotation unlike what happened to electron-donor substituents. We can see this trends on the calculates from Mattioli et al. on Table A3 (Appendix 2). We can see the difference between the energy barriers for the three substituents on Figure 26.

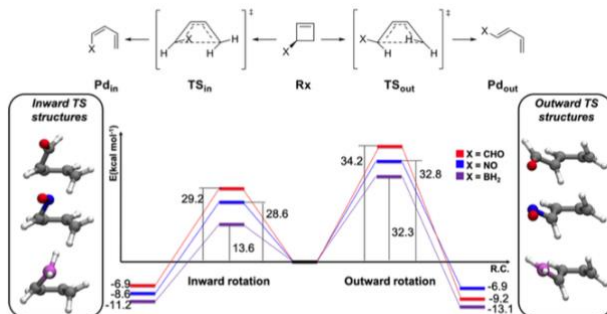


Figure 26: Energy barrier for the opening by conrotatory rotation (inward and outward rotation) of 3-formylcyclobutene and 3-nitrosocyclobutene and cyclobut-2-en-1-ylborane in a field-free situation. Also, we can see the structures of the TS for both pathways. (Image obtained from Mattioli et al., ref.3, Copyright 2019 American Chemical Society).

As an example of this type of substituents, we are going to check X=CHO and its effects on the energy barrier and μ .

X=CHO

How for this substituent the inward rotation competes outward rotation we have to study both rotations. We are going to start with the inward rotation, see Table A4 (Appendix 2). If we compare the results on this table with the energy barrier in a field free situation (Table 4) we can arrive to the following conclusions:

- **X-axis:** When we apply a positive field ($F_x > 0$) the OEEF effect is negligible. But, when we apply a $F_x < 0$ the energy barrier increases and the μ_x decreases. This causes an inhibition due to the decrease of the dipole moment.
- **Y-axis:** For the $F_y > 0$ the energy barrier decreases, which is why catalysis occurs. On the contrary, when apply a $F_y < 0$ the energy barrier increases and the μ_y (positive direction) decrease, what causes an inhibition due to the μ_y decrease.
- **Z-axis:** For both directions of the field ($F_z > 0$ and $F_z < 0$) the energy barrier increases, what causes an inhibition.

Now we are going to compare with the outward rotation. The data is on Table A5 (Appendix 2). At first glance we can see how for the Z-axis and the positive direction of the field for X-axis and Y-axis we have no data, we cannot say what kind of process will take place in these. For the axes that we have the data, we can see how in both cases the energy barrier decreases and the μ (oriented to positive direction) increase, so we can say that the catalysis will take place due to the increase of the μ .

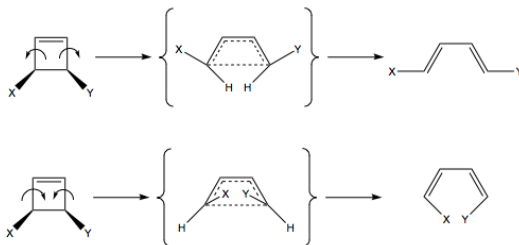
As we can see, all the effects that produce on the different axes is due to changes on the μ . Specifically, we can see how for X- and Z-axes in outward rotation are strongly inhibited. But, for $F_x < 0$ the outward rotation catalysis occurs due to the increase of μ_y in applying the field.

For the Y-axis we can see how the inward rotation with a $F_y > 0$ results in a catalysis and for a $F_y < 0$ an inhibition due to a decrease of the μ_y . On the other hand, for the outward rotation with a $F_y < 0$ catalysis occurs due to an increase of the μ_y . On Table A6 (Appendix 2) we can see a summary of the trends for X=CHO in each one of the directions in the different axes.

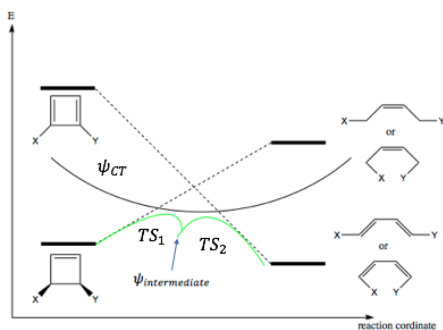
5.3. Cyclobutene ring opening by disrotatory rotation applying an electric field

Next we are going to examine the cyclobutene ring opening by disrotatory reaction applying an OEEF. More specifically, we will examine a cyclobutene 3,4-disubstituted. The first step is to look at the reaction that takes place.

Figure 34: Cyclobutene ring opening reaction by disrotatory rotation. Where we see the TS obtained for each rotation and the products, respectively. The product in the above reaction is the double trans product. The product in the reaction below is the double cis product.



Here we can see how the disrotatory rotation leads to a TS structure and products that are different with respect to the conrotatory motion. One thing we have to take into account is that in going from reagents to products all the elements of symmetry of the reagent disappear except one: the plane of symmetry. The second step is to examine the VB diagram of Figure 35.



In this we can see all the elements that we have been discussing along all this review and we explained more deeply on point 5.1.2. In this we can see the structures of reagents, products, excited reagents, R^* , and excited products, P^* . Also the diabatic curves and the adiabatic curves are shown.

Figure 35: VB diagram of cyclobutene ring opening reaction by disrotatory rotation. We can see all the structures involved in the reaction, the diabatic and the adiabatic curves.

When the reaction process takes place without an external electric field there is not an adiabatic curve. Thus the process goes to the excited product, as is very well known. Due to the substituents the sigma bond is highly polarized, for this reason this bond is σ^* characterizing the CT state. When the external electric field is applied then this state takes lower energy going to below the crossing point.

Thus, the system achieves an adiabatic curve with two transition states. The first one until the intermediate preserves the plane symmetry perpendicular to the four-membered carbon ring. The intermediate still preserving the same symmetry the sigma bond is completely broken. The second transition state connects this intermediate to the product through the disrotatory motion, also preserving the symmetry.

What we know is that the energy barrier for this reaction is too high to take place, because they cannot be mixed by symmetry. This prohibition comes from the σ bond that we have to break due to this one has a symmetric orbital and as it passes into the π bond is antisymmetric, respect to the plane, and that is why they cannot mix. Our purpose is applying an OEEF for this mixture to be produced (Shaik rule $n^{\circ}1$).

If we apply an OEEF along the reaction axis (Shaik rule n°5) we will stabilize the CT curve causing it to come down from the crossing point and interact with the adiabatic curve which represent the energy profile (green line). This will stabilize the TS and the energy barrier will decrease making reaction possible. The OEEF transform the electronic structure in such a way that the peryclic can be effective (Shaik rule n°2 and n°3). Thanks to the effect of the substituents the reaction can take place (Shaik rule n°4). It is expected that the disrotatory motion will compete with the conrotatory rotation in the ring opening under the OEEF effect.

We expect that in the future this theoretically results will be justified experimentally.

6. CONCLUSIONS

After this study and all the knowledge that it entails we can obtain the following conclusions as a definitive summary of this work:

1. We have studied the effects of OEEF applied in chemical reactions and we have seen that it can perform as both a catalyst or an inhibitor.
2. We have optimized these effects on the basis of Shaik's model and rules, a study based on the theory of VB. For this reason we have also introduced ourselves to this theory and to the VB diagrams, which are widely used by Shaik.
3. We have applied all this knowledge in four reactions: Diels-Alder reaction, Menshutkin reaction (S_N2), benzene nucleophilic aromatic substitution (S_NAr) and cyclobutene ring opening reaction by conrotatory rotation. The latter reaction is a counterexample to the perfect model of the Shaik (5.2.4).
4. We have proposed, at a very elementary level, the reaction of cyclobutene ring opening by disrotatory rotation.

Because of all this, the OEEF and the VB diagrams should be more studied because both are good tools to catalyse and for a better understanding of the reactions, respectively.

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APPENDICES

APPENDIX 1: SCANNING TUNNELING MICROSCOPE

If we check the Mzougi T.³⁰ The Scanning Tunneling Microscope (STM) is one of the first apparatuses called scanning probe microscopes (SPMs). The SPM are equipped with a probe that scans from one side to another in a raster fashion the surface of the sample. The differences between the different types of SPM are the types of interactions allowed between the sample and the probe.

As a result of this analysis, we obtain an image of the surface of the sample thanks to the correct analysis of this interaction. All the SPM are equipped with a probe, a scanning mechanism and an electronic control system.

The main component of an SPM is the probe, which size is crucial for the resolution in an atomic scale. Ideally, the end of the probe should be formed by only one atom or a precisely defined geometry.

The second most important feature of the SPM is the precision that changes the position of the probe in relation to the sample. To achieve this resolution in an atomic scale, the position must change with a 3D precision of about 1 nm. We obtain this resolution taking advantage of the ability of some crystals, called piezoelectric crystals, to change in a reproducible way when they are subjected to a voltage. The degree of expansion or contraction of the crystal depends on the voltage and can be calibrated to obtain the desired level.

STM offers many advantages over previous microscope techniques. The STM was the first apparatus that could obtain images in a non-destructive way with a high resolution in the atomic scale. And it was the first one with the capacity to identify the different atoms that are on the surface of the sample.

The SPMs had an application in design and quality control. In the manufacturing of diffraction grating masters, for example, the SPM have been used to guide a machine to cut the grooves and examine the quality of the final product.

APPENDIX 2: TABLES

Table A1: Variation of the energy barrier along the three axes for the endo and exo pathways with different field values applied (Data obtained from Meir et al., ref.17).

| | ΔE^\ddagger (Kcal/mol) | | | | | |
|---------|--------------------------------|------|------|------|------|------|
| | exo | | | endo | | |
| F (au) | x | y | z | x | y | z |
| -0.0125 | 15.8 | 15.3 | 7.7 | 17.0 | 13.9 | 8.6 |
| -0.0075 | 15.6 | 15.4 | 10.7 | 16.8 | 15.0 | 11.8 |
| -0.0050 | 15.5 | 15.3 | 12.3 | 16.7 | 15.5 | 13.4 |
| -0.0025 | 15.5 | 15.4 | 13.9 | 16.7 | 16.1 | 15.1 |
| 0.0000 | 15.5 | 15.4 | 15.5 | 16.7 | 16.7 | 16.7 |
| 0.0025 | 15.5 | 15.6 | 17.0 | 16.7 | 17.3 | 18.2 |
| 0.0050 | 15.5 | 15.7 | 18.4 | 16.7 | 17.8 | 19.6 |
| 0.0075 | 15.6 | 15.9 | 19.7 | 16.8 | 18.4 | 20.9 |
| 0.0125 | 15.8 | 16.3 | 21.9 | 17.0 | 19.6 | 23.2 |

Table A2: Variation of the energy barrier in the three axes for the cyclobutene ring opening reaction, by the outward rotation, applying different fields with NH₂ as a substituent. (Data obtained from Mattioli et al., ref.3).

| F (au) | X-axis | | Y-axis | | Z-axis | |
|----------------------|---------------------|-------------------------------------|---------------------|-------------------------------------|---------------------|-------------------------------------|
| | E_a (kcal/mol) | μ (D) from reagents to TS | E_a (kcal/mol) | μ (D) from reagents to TS | E_a (kcal/mol) | μ (D) from reagents to TS |
| +15·10 ⁻³ | 26.4 | | 30.2 | | 17.7 | -3.16 → -5.39 |
| -15·10 ⁻³ | 22.9 | | 20.6 | 3.02 → 4.05 | 30.1 | 3.84 → 2.92 |

Table A3: Variation of the energy barrier for three electron-donor substituents (CHO, NO and BH₂) in a field-free situation. (Data obtained from Mattioli et al., ref.3)

| | X=CHO | X=NO | X=BH ₂ |
|-------------------------------------------|-------|------|-------------------|
| E_a (Kcal/mol) for the inward rotation | 29.2 | 28.6 | 13.6 |
| E_a (Kcal/mol) for the outward rotation | 34.2 | 32.8 | 32.3 |

Table A4: Variation of the energy barrier in the three axes for the cyclobutene ring opening reaction, by inward rotation, applying different fields with CHO as a substituent. (Data obtained from Mattioli et al., ref.3).

| F (au) | X-axis | | Y-axis | | Z-axis | |
|---------------------|------------------|-------------------------------|------------------|-------------------------------|------------------|-------------------------------|
| | E_a (kcal/mol) | μ (D) from reagents to TS | E_a (kcal/mol) | μ (D) from reagents to TS | E_a (kcal/mol) | μ (D) from reagents to TS |
| $+15 \cdot 10^{-3}$ | Negligible | | 25.3 | | 34.2 | |
| $-15 \cdot 10^{-3}$ | 33.7 | 2.20 → 0.79 | 35.2 | 3.44 → 3.18 | 32.7 | |

Table A4: Variation of the energy barrier in the three axes for the cyclobutene ring opening reaction, by outward rotation, applying different fields with CHO as a substituent. (Data obtained from Mattioli et al., ref.3).

| F (au) | X-axis | | Y-axis | | Z-axis | |
|---------------------|------------------|-------------------------------|------------------|-------------------------------|------------------|-------------------------------|
| | E_a (kcal/mol) | μ (D) from reagents to TS | E_a (kcal/mol) | μ (D) from reagents to TS | E_a (kcal/mol) | μ (D) from reagents to TS |
| $+15 \cdot 10^{-3}$ | | | | | | |
| $-15 \cdot 10^{-3}$ | 30,6 | 2.20 → 3.19 | 33.0 | 3.44 → 3.60 | | |

Table A4: Summary of the trends of the X=CHO substituent when we apply a field in positive and negative direction for each one of the axes.

| | X-axis | Y-axis | Z-axis |
|---------|---------------------------|---------------------------|-------------------------|
| $F > 0$ | No rotation is favoured | Inward rotation favoured | No rotation is favoured |
| $F < 0$ | Outward rotation favoured | Outward rotation favoured | No rotation is favoured |

