

# Teaching Thermodynamic, Geometric and Electronic Aspects of Diels-Alder Cycloadditions by Using Computational Chemistry – An Undergraduate Experiment

Norberto K. V. Monteiro\*, Caio L. Firme

Institute of Chemistry, Federal University of Rio Grande do Norte, Natal-RN, Brazil

\*Corresponding author: [norbertokv@gmail.com](mailto:norbertokv@gmail.com)

**Abstract** We have applied an undergraduate minicourse of Diels-Alder reaction in Federal University of Rio Grande do Norte. By using computational chemistry tools (Gaussian, Gaussview and Chemcraft) students could build the knowledge by themselves and they could associate important aspects of physical-chemistry with Organic Chemistry. They have performed a very precise G4 method for the quantum calculations in this 15-hour minicourse. Students were taught the basics of Diels-Alder reaction and the influence of frontier orbital theory on kinetics. They learned how to use the quantum chemistry tools and after all calculations they organized and analyzed the results. Afterwards, by means of the PhD student and teacher guidance, students discussed the results and eventually answered the objective and subjective questionnaires to evaluate the minicourse and their learning. We realized that students could understand the influence of substituent effect on the electronic (and kinetic indirectly), geometric and thermodynamic aspects of Diels-Alder reactions. Their results indicated that Diels-Alder reactions are exergonic and exothermic and that although there is an important entropic contribution, there is a linear relation between Gibbs free energy and enthalpy. They learned that electron withdrawing groups in dienophile and electron donating groups in diene favor these reactions kinetically, and on the other hand, the opposite disfavor these reactions. Considering thermodynamically controlled Diels-Alder reactions, the EDG decrease the equilibrium constant, in relation to reference reaction, unlike the EWG. We believe that this minicourse gave an important contribution for Chemistry education at undergraduate level.

**Keywords:** Diels-Alder reaction, diene, dienophile, computational chemistry, G4, frontier orbital theory

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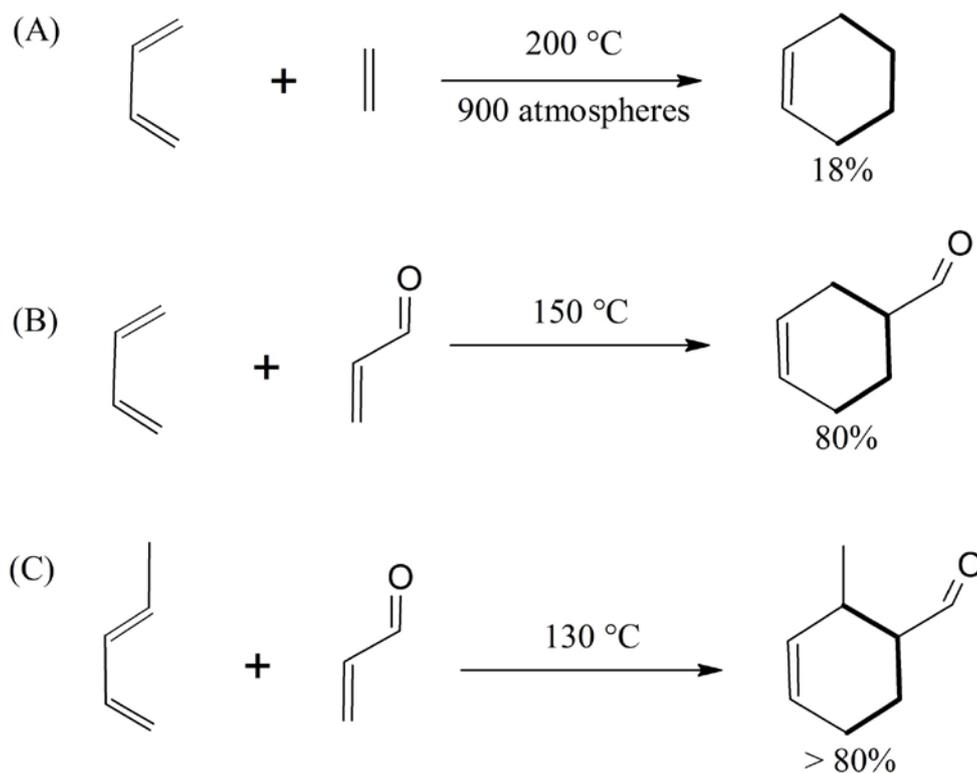
## 1. Introduction

Pericyclic reactions [1,2] are one of three major types of reactions, together with polar and radical reactions. Pericyclic reactions can be divided into four classes, *cycloadditions*, *electrocyclic reactions*, *sigma-tropic rearrangements* and the less common *group transfer reactions*. All these categories share a common feature that is a concerted mechanism involving a cyclic transition state with a concerted movement of electrons. Concerted pericyclic cycloaddition involves the reaction of two unsaturated molecules resulting in the formation of a cyclic product with two new  $\sigma$ -bonds [3]. Examples of cycloaddition reactions include the 1,3-dipolar cycloaddition (also referred as Huisgen cycloaddition), [4] nitron-olefin cycloaddition [5] and cycloadditions like the Diels-Alder reaction which is the most studied of all pericyclic reactions (Scheme 1). The number of  $\pi$ -electrons involved in the components characterizes the cycloaddition

reactions, and for the three abovementioned cases this would be [2+3], [3+2] and [4+2] respectively.

In 1950 the Nobel Prize of chemistry was granted to Otto Diels and Kurt Alder by describing an important reaction that involves the formation of C-C bond in a six membered ring with high stereochemical control, named Diels-Alder reaction [6]. Since 1928, the Diels-Alder reaction has been used in the synthesis of new organic compounds, providing a reasonable way for forming a 6-membered systems [7-13].

The simplest Diels-Alder reaction involves the reagents butadiene and ethane (dienophile), but it needed 200°C under high pressure although it has low yield [14] (about 18%) (Scheme 1A). Butadiene reacts more easily with acrolein [15], (Scheme 1B). A methyl substituent on the diene, on C1 or C2, the reaction rate increases, e.g. *trans*-piperylene reacting with acrolein [16,17] at 130°C (Scheme 1C). These last two reactions achieved a yield close to 80%.

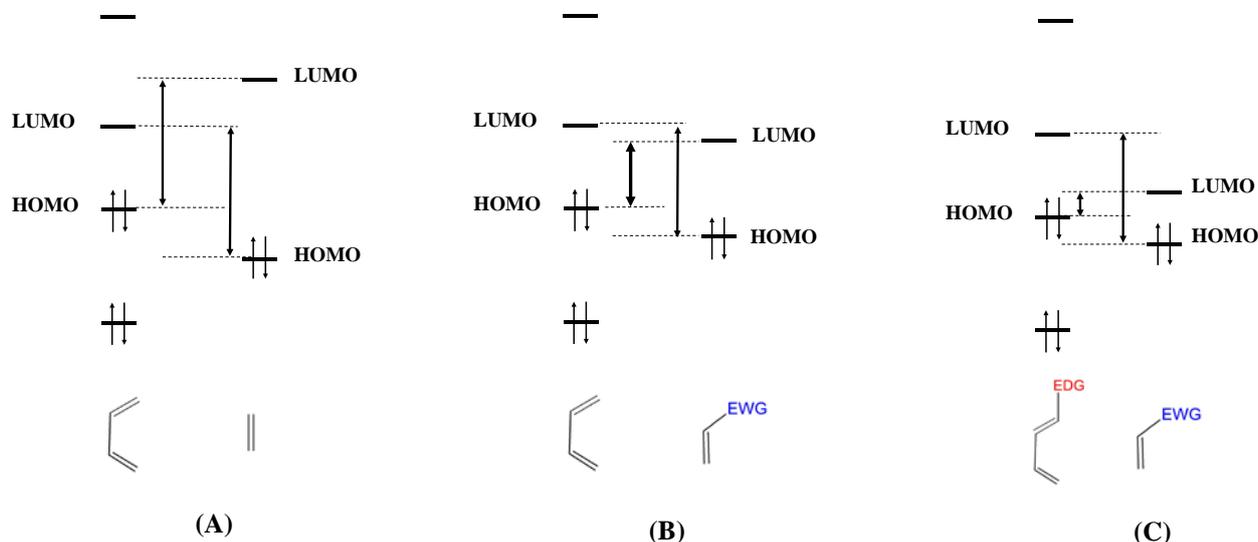


Scheme 1.

The standard state thermodynamic functions for Diels-Alder reactions are represented by enthalpy change, Gibbs free energy change and entropy. The exothermic nature of these reactions are the result of converting two weaker  $\pi$ -bonds into two stronger  $\sigma$ -bonds [18]. Because it is an addition reaction it has negative entropy change but Diels-Alder reactions are exergonic due to the high negative enthalpy change.

The reactivity of Diels-Alder reactions can be reasoned by molecular orbital (MO) theory [19] in which the HOMO of diene donates electrons to the LUMO of the dienophile by overlapping these orbitals. The addition of an EDG to the diene results in a better electron donor (and a better nucleophile) by increasing its HOMO energy. Likewise, a EWG-substituted dienophile generates a better

electron acceptor (and a better electrophile) by decreasing its LUMO energy [20]. As a consequence, the frontier molecular orbital theory accounts for the dependence of the Diels-Alder reaction rate on the substituent effect [21]. In the transition state of the Diels-Alder reactions, the HOMO of diene interacts with LUMO of dienophile. The Scheme 2A shows the energy diagram of butadiene and ethene. The Scheme 2B shows the energy diagram of butadiene and a substituted dienophile with an EWG whose energy gap is lower than that in Scheme 2A. Even lower energy gap is reached when an EDG is attached to the C1 or C2 of diene (Scheme 2C). It is well-known that the lower the energy gap between HOMO and LUMO from diene and dienophile, respectively, the faster the corresponding reaction rate.



Scheme 2.

One great challenge for chemistry education research is to improve students' understanding of physical chemical properties of chemical reactions. One very important tool for chemistry education practice is computational chemistry which improves the understanding of microscopic properties and/or provides macroscopic properties more easily. Several successful chemistry education papers focused on using computational chemistry as the main tool for the study of organic reactions. Hessley [22] used the molecular modeling to study reaction mechanisms for the formation of alkyl halides and alcohols in order to prevent the students from memorizing these reactions. Other works used computational chemistry for obtaining the Hammett plots [23]; for studying the controversial Wittig reaction mechanism [24]; for analyzing the origin of solvent effects on the rates of organic reactions [25]; and for investigating the kinetic and thermodynamic aspects of *endo* vs *exo* selectivity in the Diels-Alder reactions [26]. However, except for ref. 26 none of these studies have associated the aspects of physical-chemistry of organic reactions of these reactions.

In this work, we used the computational chemistry tool in an undergraduate minicourse in order to provide chemistry undergraduate students from Federal University of Rio Grande do Norte better understanding of the influence of substituent groups on the kinetic and thermodynamic properties of Diels-Alder reactions. All results from this minicourse were obtained by the students. Due to relatively short time of the minicourse, each student or pair of students calculated just one reaction out of seven selected reactions and afterwards all results were collected and analyzed as it is presented in this work.

## 2. Computational Details

Seven Diels-Alder reactions were previously selected and the geometries of all studied species were optimized by using standard techniques [27]. Frequency calculations were performed to analyze vibrational modes of the optimized geometry in order to determine whether the resulting geometries are true minima or transition states. The geometry optimization, frequency calculations and the generation of the HOMO and LUMO molecular orbitals of all studied species were calculated by G4 method [28] from Gaussian 09 package [29]. Every molecule's initial geometry was done with Gauss View 5 [30] and final geometry was taken from Chemcraft [31]. The G4-based computational method has been successfully used in the study of pericyclic reactions before [32].

## 3. Description of the Computational Chemistry Minicourse

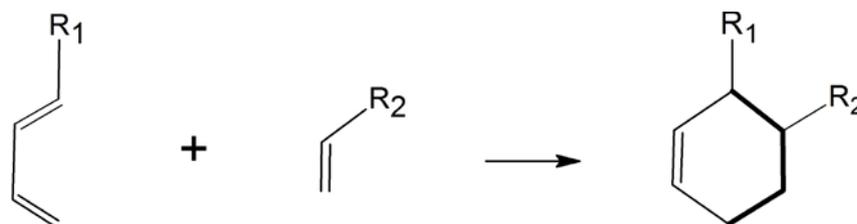
We offered a 15-hour minicourse (divided into 3 hours per day) in July, 2015. Ten students participated in the minicourse and according to pre-minicourse questionnaire (see Supporting Information) all participants were undergraduate chemistry students in different grades from Institute of Chemistry of Federal University of Rio Grande do Norte. All students have completed Organic

Chemistry 1 which is the main prerequisite for this minicourse. About 50% of students did not have any experience with computational chemistry. This minicourse was part of a teaching project in the Institute of Chemistry in which the first week at the beginning of the every semester is devoted to a series of minicourses where all chemistry students must attend and can choose the minicourse(s) that is (are) most convenient. This minicourse is taught once a year at the beginning of the first or second semester. This project can be part of a regular Organic Chemistry discipline which includes Diels-Alder reaction or it can be similarly given as minicourse. All data shown in this paper were provided by the students from calculations performed in the minicourse. Some time-consuming calculations have lasted nearly one day.

In the first class, the students received a pre-minicourse questionnaire with short-answer questions (Supporting information) in order to obtain student's academic background prior to the minicourse. After pre-minicourse questionnaire, the students were taught the theoretical content about the Diels-Alder reactions; the thermodynamic and kinetic properties for analyzing the Diels-Alder reactions; and they were presented Gaussian 09, GaussView 5 and Chemcraft software. In the second class, the students were grouped (five pairs of students) and each group performed the optimization and frequency calculations of the reagents and products of one selected Diels-Alder reaction shown in Scheme 2 (The G4 calculations occurred during the second class and in the interval between the second and third classes). In the third class the students analyzed all thermodynamic data in order to obtain student-generated data in Tables 1-2 and the plots in Figures 1 and 3. In the first half of fourth class the students generated the HOMO and LUMO molecular orbitals in order to obtain similar MO representations as shown in Figure 2 and to get their energy values and corresponding energy gaps as it is shown in Table 3. In the second half of fourth class the students analyzed the bond lengths of all reagents and products of the Diels-Alder reactions in order to obtain data in the Table 4 and Figure 4. In the fifth class, all the results were discussed as presented in sections 5 to 8 and the students answered the post-minicourse questionnaire (objective and subjective questions) and the evaluation which are shown in Supporting Information. Eventually, a statistics (in Supporting Information) were generated with the rates for answers given by the students for objective questions and student's evaluation. Three filled post-minicourse subjective questionnaire forms are shown in Supporting Information.

## 4. Results

The Scheme 3 shows all studied Diels-Alder reactions where  $R_1$  and  $R_2$  represent the substituents of the diene and dienophile respectively and the products cyclohexene derivatives formed which resulted in seven Diels-Alder reactions. We used two substituents: one electron donating group (EDG) ( $-NH_2$ ) and one electron withdrawing group (EWG) ( $-NO_2$ ).

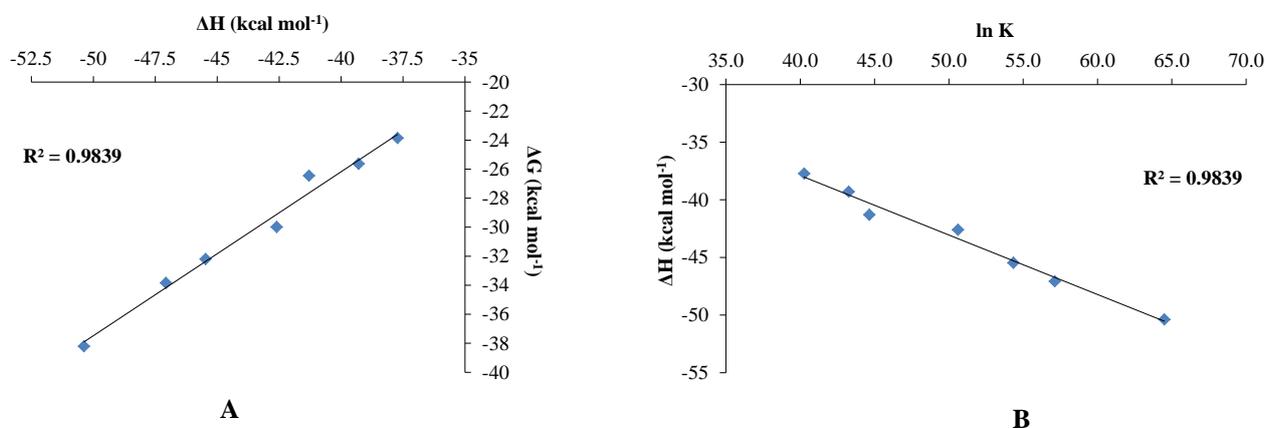


1.  $R_1 = R_2 = H$ ;
2.  $R_1 = NH_2$  and  $R_2 = H$
3.  $R_1 = H$  and  $R_2 = NO_2$
4.  $R_1 = NH_2$  and  $R_2 = NO_2$
5.  $R_1 = NO_2$  and  $R_2 = H$
6.  $R_1 = H$  and  $R_2 = NH_2$
7.  $R_1 = NO_2$  and  $R_2 = NH_2$

Scheme 3.

In Table 1 it is depicted the absolute values of enthalpy (H), Gibbs free energy (G) and entropy (S) of all reagents (dienes and dienophiles) and products (cyclohexene and cyclohexene derivatives) and the corresponding values of enthalpy change ( $\Delta H$ ), Gibbs free energy change ( $\Delta G$ ), temperature and entropy change product ( $T\Delta S$ ) and

logarithm of equilibrium constant ( $\ln K$ ) for Diels-Alder reactions(1)-(7) are shown in Table 2. In Figure 1A it is shown the linear relation involving  $\Delta H$  and  $\Delta G$  for Diels-Alder reactions (1)-(7) whereas in Figure 1B there is the linear relation of  $\ln K$  and  $\Delta H$  for Diels-Alder reactions (1)-(7).



**Figure 1.** (A) Plot of enthalpy change,  $\Delta H$ , versus Gibbs free energy change,  $\Delta G$ , of Diels-Alder reactions(1)-(7). (B) Plot of  $\ln K$  versus  $\Delta H$  of Diels-Alder reactions (1)-(7)

**Table 1.** Values of enthalpy, H, Gibbs free energy, G, in kcal mol<sup>-1</sup>, and entropy, S, in cal mol<sup>-1</sup>K<sup>-1</sup> of all studied molecules

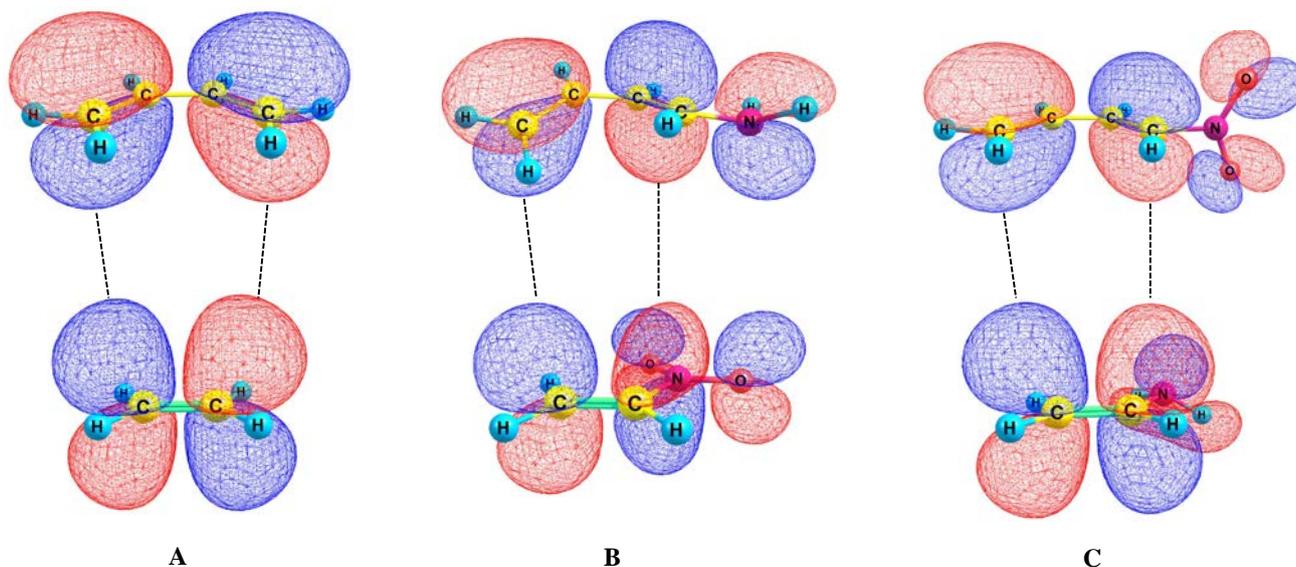
Molecule	G/kcal mol <sup>-1</sup>	H/kcal mol <sup>-1</sup>	S/cal mol <sup>-1</sup> K <sup>-1</sup>
Ethene	-49286.36	-49270.75	52.31
Ethenamine	-84010.42	-83991.90	62.02
nitroethene	-177588.33	-177567.34	70.25
Buta-1,3-diene	-97825.36	-97806.25	63.98
Buta-1,3-dien-1-amine	-132549.78	-132527.46	74.63
1-nitrobuta-1,3-diene	-226121.56	-226098.50	77.14
Cyclohexene	-147141.70	-147119.59	73.92
Cyclohex-2-en-1-amine	-181859.99	-181835.93	80.38
Cyclohex-3-en-1-amine	-181861.41	-181837.44	80.09
4-nitrocyclohexene	-275447.53	-275420.66	89.78
3-nitrocyclohexene	-275446.12	-275419.62	88.53
6-nitrocyclohex-2-en-1-amine	-310164.56	-310136.10	95.04
2-nitrocyclohex-3-en-1-amine	-310164.17	-310135.86	94.52

**Table 2.** Gibbs free energy change,  $\Delta G$ , enthalpy change,  $\Delta H$ , entropy change and temperature product, in  $\text{kcal mol}^{-1}\text{K}^{-1}$ ,  $T\Delta S$ , entropy change, in  $\text{kcal mol}^{-1}$ ,  $\Delta S$ , and equilibrium constant logarithm,  $\ln K$ , of Diels-Alder reactions (1)–(7)

Reaction	$\Delta G/\text{kcal mol}^{-1}$	$\Delta H/\text{kcal mol}^{-1}$	$T\Delta S/\text{kcal mol}^{-1}$	$\Delta S/\text{kcal mol}^{-1}\text{K}^{-1}$	$\ln K$
(1) Buta-1,3-diene + Ethene $\rightarrow$ Cyclohexene	-29.98	-42.59	-12.63	-0.0424	50.61
(2) Buta-1,3-dien-1-amine + Ethene $\rightarrow$ Cyclohex-2-en-1-amine	-23.85	-37.72	-13.88	-0.0466	40.26
(3) Buta-1,3-diene + Nitroethene $\rightarrow$ 4-nitrocyclohexene	-33.84	-47.07	-13.25	-0.0445	57.12
(4) Buta-1,3-dien-1-amine + Nitroethene $\rightarrow$ 6-nitrocyclohex-2-en-1-amine	-26.45	-41.29	-14.86	-0.0498	44.65
(5) 1-nitrobuta-1,3-diene + Ethene $\rightarrow$ 3-nitrocyclohexene	-38.21	-50.37	-12.20	-0.0409	64.49
(6) Buta-1,3-diene + Ethenamine $\rightarrow$ Cyclohex-3-en-1-amine	-25.63	-39.29	-13.69	-0.0459	43.26
(7) 1-nitrobuta-1,3-diene + Ethenamine $\rightarrow$ 2-nitrocyclohex-3-en-1-amine	-32.19	-45.46	-13.31	-0.0446	54.34

Figure 2 depicts the HOMO of buta-1,3-diene, buta-1,3-dien-2-amine and 2-nitrobuta-1,3-diene and LUMO of ethene, nitroethene and ethenamine (Figure 2A, Figure 2B and Figure 2C respectively). The energy values of

HOMO and LUMO of the reagents of the Diels-Alder reactions (1)–(7), along with the corresponding energy gap values, are shown in Table 3.

**Figure 2.** HOMO and LUMO of buta-1,3-diene and ethene (A); buta-1,3-dien-2-amine and nitroethene (B); and 2-nitrobuta-1,3-diene and ethenamine (C)**Table 3.** Energy values of HOMO ( $E_{\text{HOMO}}$ ) and LUMO ( $E_{\text{LUMO}}$ ) and energy gap between HOMO and LUMO orbitals,  $|E_{\text{HOMO}} - E_{\text{LUMO}}|$ , in a.u., of the reagents of the Diels-Alder reactions (1) – (7)

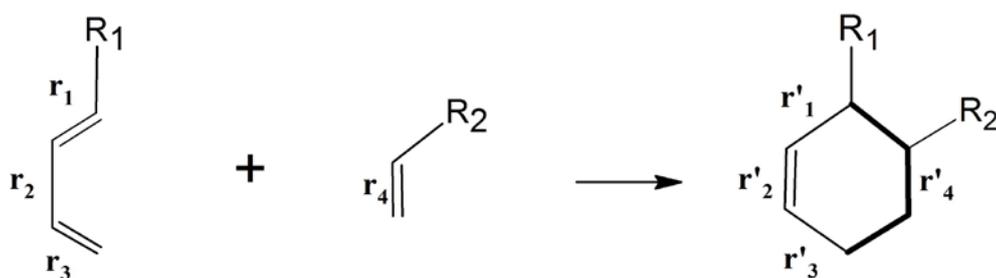
Reaction	$E_{\text{HOMO}}/\text{a.u.}$	$E_{\text{LUMO}}/\text{a.u.}$	$ E_{\text{HOMO}} - E_{\text{LUMO}} /\text{a.u.}$
(1)	-0.2293	0.0173	0.2466
(2)	-0.1867	0.0173	0.2040
(3)	-0.2293	-0.0923	0.1370
(4)	-0.1867	-0.0923	0.0944
(5)	-0.2522	0.0173	0.2695
(6)	-0.2293	0.0509	0.2801
(7)	-0.2522	0.0509	0.3031

Figure 3 shows the C-C bond length of the diene and C-C bond length of the dienophile of reactions (4) (Figure 3A) and (7) (Figure 3B) in which these bond lengths are

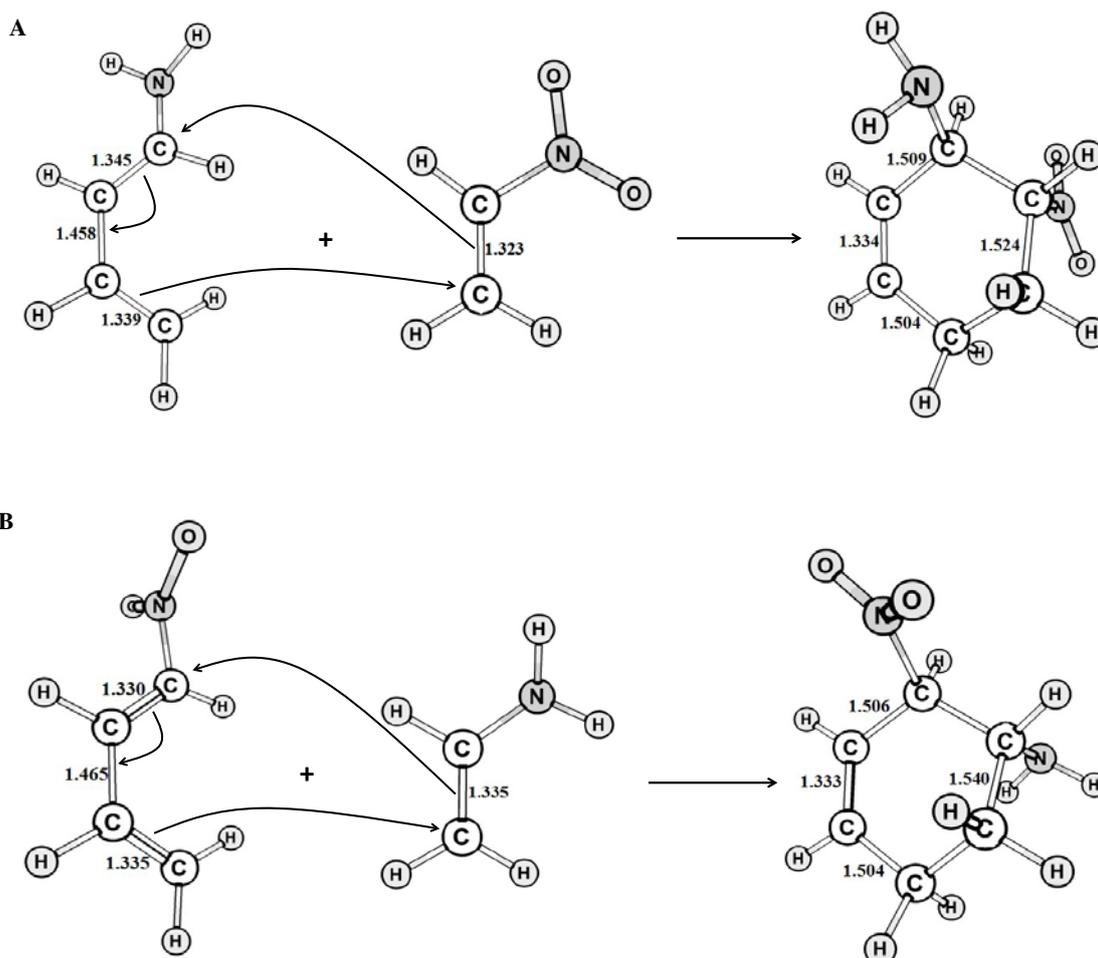
represented in the Scheme 4 ( $r_1, r_2, r_3, r_4, r'_1, r'_2, r'_3$  and  $r'_4$ ). The values of C-C bond length for Diels-Alder reactions (1)–(7) are listed in Table 4.

**Table 4.** Bond lengths of reagents ( $r_1, r_2, r_3$  and  $r_4$ ) and products ( $r'_1, r'_2, r'_3$  and  $r'_4$ ), in Angstroms, of the studied Diels-Alder reactions

Reaction	$r_1/\text{\AA}$	$r_2/\text{\AA}$	$r_3/\text{\AA}$	$r_4/\text{\AA}$	$r'_1/\text{\AA}$	$r'_2/\text{\AA}$	$r'_3/\text{\AA}$	$r'_4/\text{\AA}$
(1)	1.336	1.468	1.336	1.327	1.507	1.333	1.507	1.534
(2)	1.345	1.458	1.339	1.327	1.510	1.332	1.506	1.532
(3)	1.336	1.468	1.336	1.323	1.508	1.332	1.506	1.532
(4)	1.345	1.458	1.339	1.323	1.509	1.334	1.504	1.524
(5)	1.330	1.465	1.335	1.327	1.506	1.333	1.504	1.533
(6)	1.336	1.468	1.336	1.335	1.507	1.332	1.507	1.532
(7)	1.330	1.465	1.335	1.335	1.506	1.333	1.504	1.540



Scheme 4.



**Figure 3.** Optimized geometries of corresponding reactants and products from Diels-Alder reactions 4 (A) and 7 (B). Selected bond lengths, in Angstroms, are depicted

## 5. Thermodynamic Data and Equilibrium Constant

Enthalpy change values from Table 2 indicate that all reactions are exothermic because two weaker  $\pi$  bonds in reactants are converted to two stronger  $\sigma$  bonds in the product. Cycloaddition reactions have negative entropy change owing to the smaller translational and rotational contributions of entropy in cyclohexene adducts compared to those values from reactants (diene and dienophile). The negative entropy does not contribute to the spontaneity of Diels-Alder reaction. However, according to Gibbs free energy change values in Table 2 these reactions are exergonic due to low entropy change values in modulus (see Table 2) and high enthalpy change values in modulus

and one can see that the modulus of  $T\Delta S$  is nearly three times smaller than the modulus of  $\Delta H$ , in average. Experimental data show that Diels-Alder reactions are exothermic and exergonic, e.g., the reaction of buta-1,3-diene and ethene to form cyclohexene [33] which has an  $\Delta H$  and  $\Delta G$  of  $-40.0$  and  $-27.0$  kcal mol<sup>-1</sup> respectively; the reaction of cyclopentadiene with itself to form dicyclopentadiene ( $\Delta H$  and  $\Delta G$  of  $-18.4$  and  $-8.2$  kcal mol<sup>-1</sup> respectively) [34]; and the reaction of cyclopentadiene and maleic anhydride ( $\Delta H = -24.8$  kcal mol<sup>-1</sup>) [35]. Although the reactions are not the same as those students have calculated, their thermodynamic data is within the same range.

The tendency for a reaction to reach equilibrium at the standard conditions is driven by the standard Gibbs free energy,  $\Delta G^\circ$ , which is related to the equilibrium constant [36] according to Eq. 1.

$$\Delta G^\circ = -RT \ln K \quad (1)$$

There is no relationship between the kinetics and thermodynamics for most of chemical reactions, except for some electron transfer and some radical reactions [37,38,39]. As previously described, an EDG attached to the diene and a dienophile substituted with a EWG result in an increase in the rate of a Diels-Alder reaction. However, these effects are not observed for the thermodynamic properties as shown in Table 2. The EDG (amino group) thermodynamically disfavors the Diels-Alder reactions (2), (4) and (6) resulting in less exothermic and exergonic reactions and hence lower  $\ln K$  values compared to the reaction (1). On the other hand, the reactions with EWG (nitro group) substituent [reactions (3), (5) and (7)] have more negative values of  $\Delta G$  and  $\Delta H$  and higher values of  $\ln K$  which thermodynamically favor these reactions.

The plot from Figure 1A has a very good correlation coefficient indicating that the trend in enthalpy change for formation of cyclohexene and derivatives is nearly the same as that from corresponding Gibbs free energy change, which means that entropy change for these cycloaddition reactions does not alter significantly both trends, though  $T\Delta S$  values are not negligible (see Table 2).

Since  $\Delta G$  for all reactions is negative, there is a direct relation between modulus of  $\Delta G$  and equilibrium constant,  $K$ , according to expressions in Eq. 2.

$$K = e^{\frac{\Delta G}{RT}} \quad \therefore \Delta G < 0 \quad \therefore K = e^{\frac{-\Delta G}{RT}} \quad \therefore K = e^{\frac{\Delta G}{RT}} \quad (2)$$

Then, for exergonic Diels-Alder reactions, there is a direct relation between  $K$  and  $|\Delta G^\circ|$ , i.e., the smaller  $\Delta G^\circ$  (in modulus) the smaller  $K$ . Moreover, there is direct relation between  $K$  and reaction yield.

The very good correlation coefficient of the Figure 1B indicates that  $\Delta H$  can be associated with the  $K$  as well. Thus, we can associate  $K$  with stability factors instead of exergonicity. Then, there is a direct relation between modulus of  $\Delta H$  (in modulus) and  $K$ .

The data in Table 2 indicate that reaction (5) has the highest  $K$  value and hence the highest negative values of  $\Delta G$  and  $\Delta H$ . On the other hand, the reactions (2) and (6) have the lowest  $K$  values and the lowest negative values of  $\Delta G$  and  $\Delta H$ . The direct proportionality between  $K$  and  $|\Delta G|$  and between  $K$  and  $|\Delta H|$  can be observed in the decreasing order of  $K$ ,  $|\Delta G|$  and  $|\Delta H|$ : (5) > (3) > (7) > (1) > (4) > (6) > (2).

## 6. Yield and Kinetic Properties

The efficiency of a chemical reaction is usually related to reaction yield. In a thermodynamically controlled reaction, the reaction yield depends on the equilibrium constant and not on the reaction rate. In a kinetically controlled reaction, yield depends on the reaction rate and the reaction time. In Diels-Alder reactions, according to frontier molecular orbital theory, the electron-rich diene acts as a nucleophile. The most important orbital in the diene is the Highest Occupied Molecular Orbital (HOMO). For the formation of chemical bond, this orbital interacts with the Lowest Unoccupied Molecular Orbital (LUMO) of the dienophile, which acts as an electrophile. As most

Diels-Alder reactions are kinetically controlled, the smaller the HOMO-LUMO energy difference, the greater the charge transfer, the faster the reaction and the higher its yield.<sup>2</sup> The energy diagram (Figure 2A) shows the interaction between the HOMO of the diene and the LUMO of the dienophile. The energies of HOMO and LUMO depend on the nature of the substituents in the diene and in the dienophile, in which an EWG decreases the LUMO energy of the dienophile (Figure 2B) bringing it closer to the HOMO energy of the diene. An EDG-substituted diene (Figure 2C) further decreases the energy gap between HOMO and LUMO. Thus, EWG-substituted dienophiles and EDG-substituted dienes result in faster reactions and higher yields in comparison with unsubstituted dienophiles and dienes.

The Table 3 shows the energy values of HOMO ( $E_{\text{HOMO}}$ ) and LUMO ( $E_{\text{LUMO}}$ ) of the reagents of the Diels-Alder reactions (1)-(7), and the energy gap between HOMO and LUMO ( $|E_{\text{HOMO}} - E_{\text{LUMO}}|$ ). The reference reaction (1) has 0.2466 a. u. energy gap. The reactions with EDG in diene [reaction (2)] or EWG in dienophile [reaction (3)] have lower energy gaps as expected and additive effect of both EDG in diene and EWG in dienophile [reaction (4)] imparts further decrease in energy gap. From the analysis of energy gaps in Table 3 and assuming that frontier molecular orbital theory can indicate relatively faster or slower reactions, we could predict lower energy barriers for reactions (2), (3) and (4) which would provide higher yields for these reactions in comparison with reaction (1). On the other hand, reactions (5), (6) and (7) have the highest  $|HOMO-LUMO|$  values (0.2695, 0.2801 and 0.3031 a.u. respectively) due to *inverse electron demand*, i.e. EWG-substituted dienes and/or EDG-substituted dienophiles. Since these reactions have the highest energy gap, they are the slowest reactions. Therefore, the decreasing order of  $|HOMO-LUMO|$  is: (7) > (6) > (5) > (1) > (2) > (3) > (4).

Figure 2 shows the HOMO of buta-1,3-diene, buta-1,3-dien-2-amine and 2-nitrobuta-1,3-diene and LUMO of ethene, nitroethene and ethenamine (Figures 2A, 2B and 2C respectively). According to Figures 2B (HOMO of buta-1,3-dien-2-amine and LUMO of nitroethene) and 2C (HOMO of 2-nitrobuta-1,3-diene and LUMO of ethenamine) some changes occur in the size and shape of their corresponding HOMO and LUMO in comparison with those orbitals of their parent molecules depicted in Figure 2A (HOMO of buta-1,3-diene and LUMO of ethene). When an EDG ( $-\text{NH}_2$ ) is attached to the diene, its HOMO includes the nitrogen lone pair participation resulting in a better nucleophile while LUMO in nitroethene includes oxygen lone pair participation and  $-\text{NO}_2$  vicinal carbon orbital distortion towards nitrogen atom (Figure 2B). On the other hand, HOMO of 2-nitrobuta-1,3-diene (Figure 2C) has no nitrogen lone pair participation and 2-nitrobuta-1,3-diene is probably a weaker nucleophile than buta-1,3-dien-2-amine.

## 7. Geometric Changes

Scheme 4 represents a general Diels-Alder reaction in which selected bond lengths of reactants and product are assigned ( $r_1, r_2, r_3$  for dienes,  $r_4$  for dienophiles, and  $r'_1, r'_2, r'_3, r'_4$  for cyclohexenes). Figure 3 depicts the optimized

geometries of reactants and product of reactions (4) (Figure 3A) and (7) (Figure 3B). Surprisingly, data from Table 4 indicate that amino group increases the double bond length of reactants more than nitro group. Moreover, data from Table 4 also confirm that double bonds  $r_1$ ,  $r_3$  and  $r_4$  in reactants become single bonds in products while the single bond  $r_2$  becomes double bond in products.

Except for  $r_4$  in reactions (4) and (7), no other selected bond length of all cyclohexene derivatives is significantly affected by substituent group. Then, the variations of enthalpy change in the reactions (1) to (7) are probably accounted for by the reactants than the product. Figure 3 also shows that cyclohexane derivatives lost the carbon chain planarity from their precursors due to the loss of  $\pi$  bonds in the product.

## 8. Conclusions

The computational chemistry allowed to teach the thermodynamic, electronic (indirectly kinetic) and geometric aspects of Diels-Alder reactions. All of these reactions were exergonic and exothermic. Entropy change has an important contribution on the Gibbs free energy change, however it did not affect the linear relation between the latter and enthalpy change. Then, the thermodynamics of these reactions can be reasoned by the influence of electronic effects on the stability of reactants and product. However, from the analysis of geometrical parameters, stability is more affected by reactants than by products because the bond lengths of reactants vary more significantly in comparison with reference compound due to the substituent effect than those in the corresponding product.

Students could also understand that substituent effects on thermodynamics and kinetics (indirectly from frontier orbital theory) are distinguished. The EDG in diene makes Diels-Alder reaction less favorable thermodynamically, whereas EWG substituent in diene results in more favorable reaction in thermodynamics. On the other hand, EDG in diene and EWG in dienophile favor the Diels-Alder reaction kinetically.

From the statistics of post-minicourse questionnaire and students evaluation (Supporting information) of these minicourse we realized that students could better understand thermodynamic and kinetic aspects of a reaction from the use of computational chemistry. This minicourse also contributed for the Organic Chemistry knowledge by giving students practical and simple tools to develop the knowledge by themselves, in which these tools can also be employed in the teaching of Diels-Alder reactions in the classroom. This minicourse also contributed for the association between physical-chemistry knowledge (quantum chemistry, thermodynamics and kinetics, indirectly) with organic chemistry by means of Diels-Alder reaction.

## Associated Content and Supporting Information

Pre-minicourse, Post-minicourse questionnaires (objective and subjective questions) and students evaluation. This material is available via the Internet at

[http://www.sciepub.com/portal/downloads?doi=10.12691/wjce-3-6-3&filename=Supporting Information\\_diels-alder.docx](http://www.sciepub.com/portal/downloads?doi=10.12691/wjce-3-6-3&filename=Supporting%20Information_diels-alder.docx)

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## References

- [1] Sankaraman S. *Pericyclic reactions: a textbook: reactions, applications and theory*. Wiley-VCH, 2005.
- [2] Woodward RB, Hoffmann R. Conservation of Orbital Symmetry, *Angew Chem Int Ed*, 1969, 8, 781-853.
- [3] Carey FA, Sundberg RJ. *Advanced Organic Chemistry Part A: Structure and Mechanisms*. 2007.
- [4] Huisgen R. 1,3-Dipolare Cycloadditionen Rückschau und Ausblick, *Angew Chemie*, 1963, 75, 604-37.
- [5] Confalone PN, Huie EM. The [3+2] Nitrone-Olefin Cycloaddition Reaction. *Org. React.*, John Wiley & Sons, Inc., 2004.
- [6] Mehta G. Molecular design of compounds via intermolecular Diels-Alder reactions, *J Chem Educ*, 1976, 53, 551.
- [7] Brockson TJ, Nakamura J, Ferreira ML, Brockson U. The Diels-Alder reaction: an update, *J Braz Chem Soc*, 2001, 12, 597-622.
- [8] Nicolau KC, Snyder S a, Montagnon T, Vassilikogiannakis G. The Diels-Alder reaction in total synthesis, *Angew Chemie - Int Ed*, 2002, 41, 1668-98.
- [9] Juhl M, Tanner D. Recent applications of intramolecular Diels-Alder reactions to natural product synthesis., *Chem Soc Rev*, 2009, 38, 2983-92.
- [10] Sample TE, Hatch LF. 3-Sulfolene: A butadiene source for a Diels-Alder synthesis: An undergraduate laboratory experiment, *J Chem Educ*, 1968, 45, 55.
- [11] Baar MR, Wustholz K. Diels-Alder Synthesis of endo-cis-N-Phenylbicyclo[2.2.2]oct-5-en-2,3-dicarboximide, *J Chem Educ*, 2005, 82, 1393.
- [12] Parsons BA, Dragojlovic V. Demonstration of a Runaway Exothermic Reaction: Diels-Alder Reaction of (2 E ,4 E )-2,4-Hexadien-1-ol and Maleic Anhydride, *J Chem Educ*, 2011, 88, 1553-7.
- [13] Celiu TC. Fast Hetero-Diels-Alder Reactions Using 4-Phenyl-1,2,4-triazoline-3,5-dione (PTAD) as the Dienophile, *J Chem Educ*, 2010, 87, 10-1.
- [14] Joshel LM, Butz LW. The Synthesis of Condensed Ring Compounds. VII. The Successful Use of Ethylene in the Diels-Alder Reaction1, *J Am Chem Soc*, 1941, 63, 3350-1.
- [15] Olah GA, Molnár Á. *Hydrocarbon Chemistry*. Wiley, 2003.
- [16] Anh NT. *Frontier Orbitals: A Practical Manual*. 2007.
- [17] Fleming I. *Molecular Orbitals and Organic Chemical Reactions*. Wiley, 2010.
- [18] Williamson K, Masters K. *Macroscale and microscale organic experiments*. Cengage Learning, 2011.
- [19] Palmer DRJ. Integration of Computational and Preparative Techniques To Demonstrate Physical Organic Concepts in Synthetic Organic Chemistry: An Example Using Diels-Alder Reactions, *J Chem Educ*, 2004, 81, 1633.
- [20] Fleming S a., Hart GR, Savage PB. Molecular Orbital Animations for Organic Chemistry, *J Chem Educ*, 2000, 77, 790.
- [21] Houk KN. Frontier molecular orbital theory of cycloaddition reactions, *Acc Chem Res*, 1975, 8, 361-9.
- [22] Hessley RK. Computational Investigations for Undergraduate Organic Chemistry: Modeling Markovnikov and anti-Markovnikov Reactions for the Formation of Alkyl Halides and Alcohols, *J Chem Educ*, 2000, 77, 794.
- [23] Ziegler BE. Theoretical Hammett Plot for the Gas-Phase Ionization of Benzoic Acid versus Phenol: A Computational Chemistry Lab Exercise, *J Chem Educ*, 2013, 90, 665-8.

- [24] Albrecht B. Computational Chemistry in the Undergraduate Laboratory: A Mechanistic Study of the Wittig Reaction, *J Chem Educ*, 2014, 91, 2182-5.
- [25] Lim D, Jenson C, Repasky MP, Jorgensen WL. Solvent as Catalyst: Computational Studies of Organic Reactions in Solution. *Transit. State Model. Catal.*, vol. 721, American Chemical Society, 1999, p. 6-74.
- [26] Rowley CN, Woo TK, Mosey NJ. A Computational Experiment of the Endo versus Exo Preference in a Diels–Alder Reaction, *J Chem Educ*, 2009, 86, 199.
- [27] Fletcher R. *Practical Methods of Optimization*. vol. 53. 2000.
- [28] Curtiss L a, Redfern PC, Raghavachari K. *Gaussian-4 Theory*, *J Chem Phys*, 2007, 126, 84108.
- [29] Frisch MJ, Trucks GW, Schlegel HB, Scuseria GE, Robb MA, Cheeseman JR, et al. *Gaussian 09, Revision A.02*, Gaussian Inc Wallingford CT, 2009, 34, Wallingford CT.
- [30] Roy Dennington TK and JM. *GaussView, Version 5*, Semichem Inc, Shawnee Mission KS, 2009.  
[http://www.gaussian.com/g\\_tech/gv5ref/gv5citation.htm](http://www.gaussian.com/g_tech/gv5ref/gv5citation.htm).
- [31] Zhurko GA, Zhurko DA. *Chemcraft Program, Academic version 1.5 (2004)* 2004.
- [32] Karton A, Goerigk L. Accurate reaction barrier heights of pericyclic reactions: Surprisingly large deviations for the CBS-QB3 composite method and their consequences in DFT benchmark studies, *J Comput Chem*, 2015, 36, 622-32.
- [33] Uchiyama M, Tomioka T, Amano A. Thermal decomposition of cyclohexene, *J Phys Chem*, 1964, 68, 1878-81.
- [34] Fox MA, Whitesell JK. *Organic Chemistry*. Jones and Bartlett Publishers, 2004.
- [35] Breslauer KJ, Kabakoff DS. Enthalpy of the Diels-Alder reaction of cyclopentadiene and maleic anhydride, *J Org Chem*, 1974, 39, 721-2.
- [36] Isaacs NS. *Physical organic chemistry*. Longman Scientific & Technical, 1995.
- [37] Marcus RA. On the Theory of Oxidation-Reduction Reactions Involving Electron Transfer. I, *J Chem Phys*, 1956, 24, 966.
- [38] Marcus RA. Free Energy of Nonequilibrium Polarization Systems. III. Statistical Mechanics of Homogeneous and Electrode Systems, *J Chem Phys*, 1963, 39, 1734.
- [39] Ebersson L. Electron-Transfer Reactions in Organic Chemistry, *Adv Phys Org Chem*, 1982, 18, 79-185.