

paper is to suggest the mechanism of the studied reaction using DFT method. The mechanism of the reaction is shown in Scheme 1.

II. COMPUTATIONAL METHODS

All calculations in the present work have been done using Gaussian 09 package (Frisch, et al., 2009). DFT method has been proven to be a suitable method for the study of cycloaddition reactions and is achieved in this work as well (Khabashesku, Kudin and Margrave, 2001; Lemal, 2017; Parr and Weitao, 1989). B3LYP functional is used throughout in combination with 6-311++G(d,p) basis set (Ditchfield, Hehre and Pople, 1971; Lee, Yang and Parr, 1988). We also considered the D3 correction to take into account for the role of dispersion energies in the stability of the complexes and intermediates (Grimme, et al., 2010). Frequency calculations were performed to ensure that a transition state has only one negative frequency and a local minimum has no negative frequencies. Intrinsic reaction coordinate computations were carried out to confirm that the reactants and products are connected through the transition states (Fukui, 1970). All energies and thermodynamic parameters reported in this paper were obtained from the frequency calculations at the same level of theory. The CYLview software was used as a graphical interface (Legault, 2009).

The global electrophilicity index (ω) is obtained in terms of the electronic chemical potential (μ) and the chemical hardness (η) using the following simple expression (Parr, Szentpály and Liu, 1999):

$$\omega = \frac{\mu^2}{2\eta} \quad (1)$$

The chemical hardness (η) and the electronic chemical potential (μ) quantities may be approached in terms of the one electron energies of highest occupied molecular orbital (HOMO) and lowest unoccupied molecular orbital (LUMO), ϵ_H and ϵ_L , as (Parr and Pearson, 1983; Parr and Weitao, 1994):

$$\eta \approx \epsilon_L - \epsilon_H \quad (2)$$

$$\mu \approx \frac{\epsilon_H + \epsilon_L}{2} \quad (3)$$

The relative nucleophilicity index (N) obtained based on the energies of HOMO within the scheme of Kohn-Sham (Kohn and Sham, 1965). This quantity can be defined using Equation (4). Where TCE is tetracyanoethylene and is chosen due to its lowest HOMO energy as a reference (Domingo, Chamorro and Pérez, 2008).

$$N = E_{HOMO(Nu)} - E_{HOMO(TCE)} \quad (4)$$

III. RESULTS AND DISCUSSION

The D-A reaction of hexa-1,2,4-trien (R1) with but-3-en-2-one (R2) gives the corresponding products P1a, P1b, P2a, and P2b passing through TS1a, TS1b, TS2a, and TS2b, respectively, as sketched in Scheme 1. Fig. 1 shows the energy profiles of studied reactions. These energy profiles were determined at the B3LYP-D3/6-311++G(d,p)

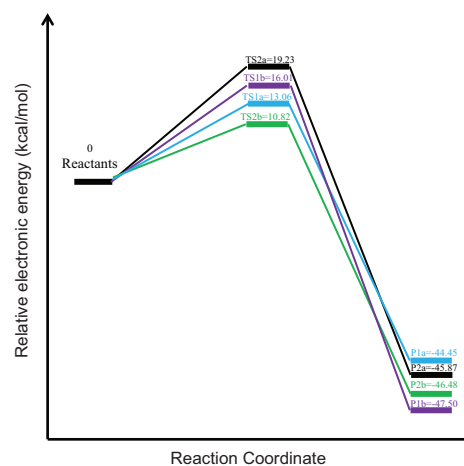


Fig. 1. Energy profile for the [4+2] cycloaddition reaction of hexa-1,2,4-trien (R1) with but-3-en-2-one (R2) using B3LYP-D3/6-311++G(d,p) level of theory. The energies are given relative to reactants (kcal/mol).

level of theory. The reactions occur through a concerted mechanism.

Fig. 1 shows that there is a significant lowering of the activation energy from cis transition state TS2a to trans TS2b, around 9 kcal/mol, and moderate lowering from trans transition state TS1b to cis TS1a, about 3 kcal/mol. It is notable to that the cycloadducts from trans conformer, P1b and P2b, have the lower relative energies as compared to the cis conformer of cycloadducts, P1a and P2a. This indicated that the trans cycloadducts are more stable than the cis cycloadducts.

Four transition states, TS1a, TS2a, TS1b, and TS2b, as sketched in Scheme 1, were obtained from the reaction of R1 with R2. The geometries of these transition states are given in Fig. 2. The studied reactions undergo cycloaddition through highly asynchronous transition states. In all cases, the length of the formed C-C bond with the ketone function is longer than the other formed C-C bond. This is due to the presence of carbonyl group in the dienophile as an electron-withdrawing group. The transition state TS1a has smaller degree of asynchronicity and TS2a has the larger degree of asynchronicity among the other transition states.

The thermodynamic parameters for the reaction of R1 with R2 in the gas phase at 1 atm and 298.15 K with B3LYP-D3/6-311++G(d,p) method are collected in Table I. The activation enthalpies range from 9.85 to 18.11 kcal/mol. It is worth to realize that the activation enthalpies reached the lower value for trans transition state TS2b and highest value cis TS2a, whereas opposite trends were found for TS1a and TS1b this is due to the stereoselectivity in transition states and products. The Gibbs free energies for all products are found to be negative and very close to each other, which indicate that pathways have the same route and no side reactions were found (Kaka, et al., 2019). The enthalpies for products were also found to be negative that indicate that the reactions are possible to occur. The enthalpies for trans products P1b and P2b are lower than the cis products, which refer to the more stability of trans products than cis products.

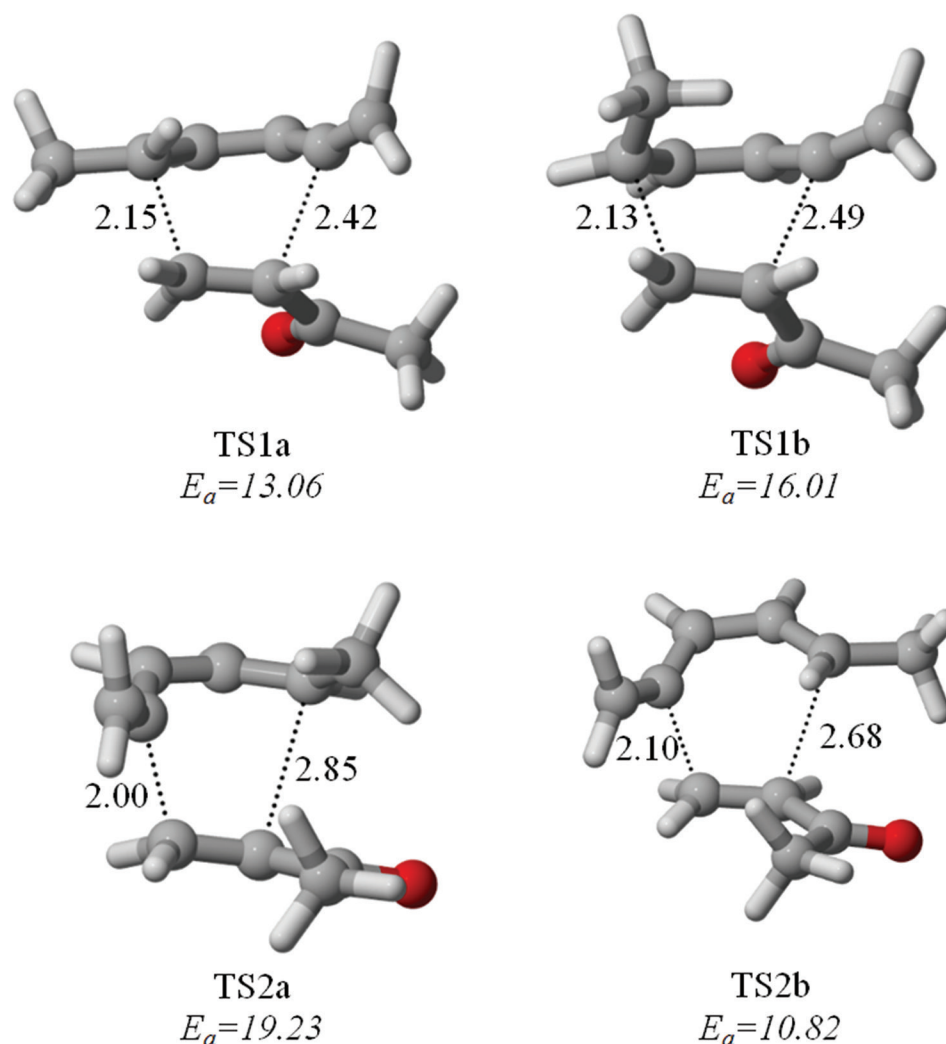


Fig. 2. Optimized geometries of the transition states involved in the [4+2] cycloaddition reactions of hexa-1,2,4-trien (R1) with but-3-en-2-one (R2) using B3LYP-D3/6-311++G(d,p) level of theory. The energy (E_a), in kcal/mol, is given relative to reactants.

TABLE I
THERMODYNAMIC PARAMETERS FOR TRANSITION STATES AND PRODUCTS AT B3LYP-D3/6-311++G(D,P) LEVEL OF THEORY IN (KCAL/MOLE) FOR ΔH AND ΔG AND IN (CAL/MOL.K) FOR ΔS

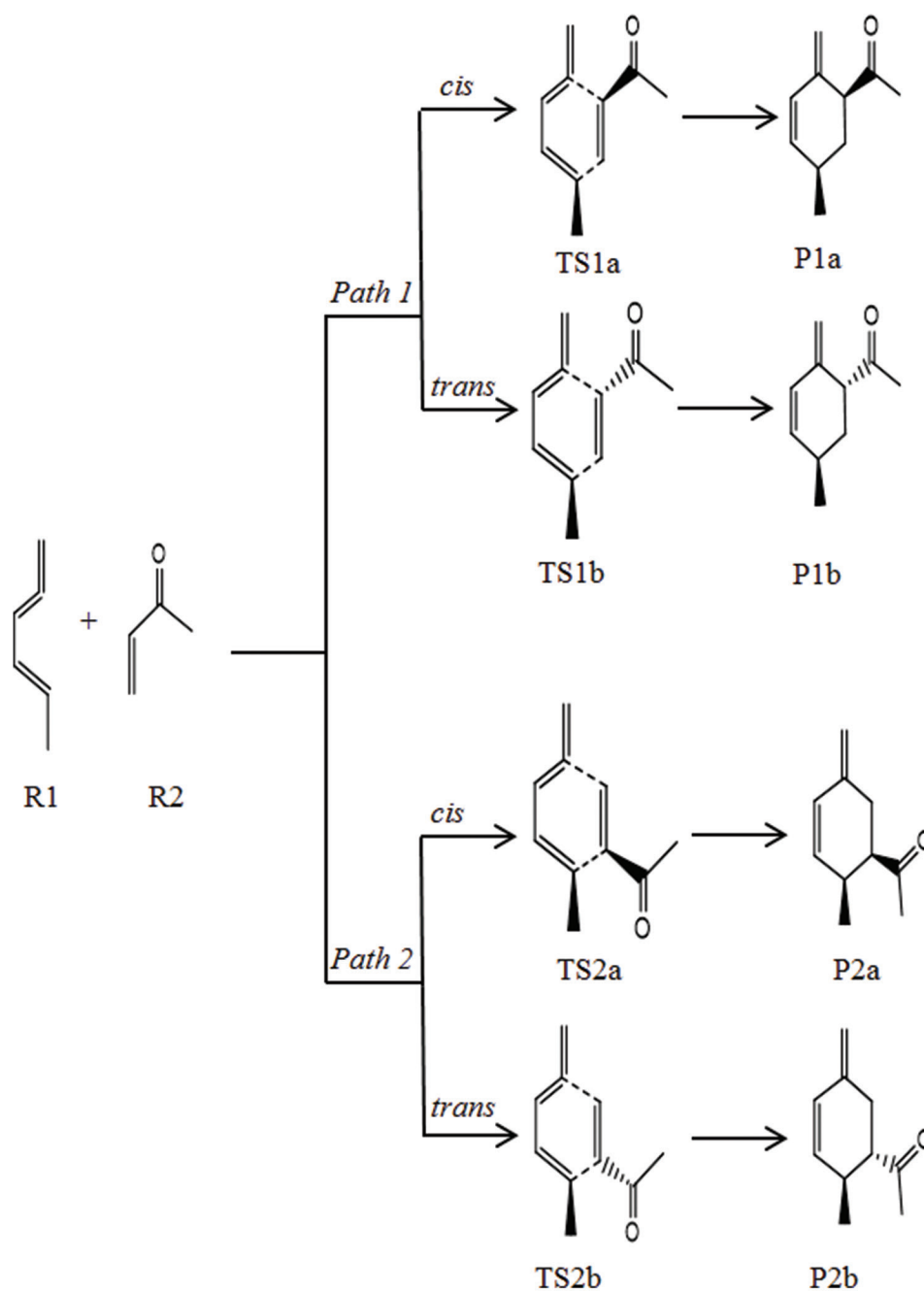
Compound	ΔH	ΔG	ΔS
P1a	-46.19	-29.40	-56.31
P1b	-49.16	-33.09	-53.93
P2a	-47.54	-31.15	-54.96
P2b	-48.20	-32.05	-54.14
TS1a	12.07	27.15	-50.58
TS1b	15.04	30.26	-51.05
TS2a	18.11	33.73	-52.39
TS2b	9.85	24.74	-49.94

From the observed thermodynamic results that the P1b is preferred thermodynamically, whereas P2b is preferred kinetically since it has lower activation energy.

In the D-A reaction, predictions of reactivity and selectivity are normally based on the strength of a single FMO interaction between the diene and the dienophile, dienophiles with conjugating groups are usually good for D-A reactions. Dienes react rapidly with electrophiles because

their HOMOs are relatively high in energy, but simple alkenes have relatively high-energy LUMOs and do not react well with nucleophiles. The most effective modification is to lower the alkene LUMO energy by conjugating the double bond with an electron-withdrawing group such as carbonyl or nitro. This type of D-A reaction, involving an electron-rich diene and an electron-deficient dienophile, is referred to as a D-A reaction with normal electron demand. The HOMO and LUMO energies for all products at B3LYP-D3/6-311++G(d,p) level of theory are listed in Table II. The table shows that cis products have narrower energy gaps than trans products. This indicates that the trans products are more stable than the others. The trans product P1b has wider energy gap than trans product P2b. Such results indicate that the trans product P1b is more stable among trans products. The results from the analysis of molecular orbitals were found to be consistency with the results obtained from the thermodynamic parameters.

The global reactivity indices defined within the conceptual DFT are a powerful tool to study the reactivity in polar cycloaddition reactions (Mohammad-Salim,



Scheme 1. Proposed reaction mechanism paths for the [4+2] cycloaddition reaction of but-3-en-2-one (R2) and hexa-1,2,4-trien (R1).

TABLE II
HOMO ENERGIES, LUMO ENERGIES, AND ENERGY GAP (IN eV UNIT) FOR
REACTANTS AND PRODUCTS AT B3LYP-D3/6-311++G(D,P) LEVEL OF THEORY

Compound	HOMO	LUMO	Energy gap
P1a	-6.41	-1.21	5.19
P1b	-6.44	-0.99	5.45
P2a	-6.36	-1.17	5.20
P2b	-6.37	-1.08	5.29

TABLE III
THE CHEMICAL HARDNESS (η), ELECTRONIC CHEMICAL POTENTIAL (μ), GLOBAL
ELECTROPHILICITY (ω), AND GLOBAL NUCLEOPHILICITY (N) FOR R1 AND R2 IN eV

Compound	η	μ	ω	N
R1	5.16	-3.56	1.23	3.35
R2	5.14	-4.61	2.06	2.31

et al., 2020). The static global properties, namely, chemical hardness (η), global nucleophilicity (N), global electrophilicity (ω), and electronic chemical potential (μ) for all reactants in eV are listed in Table III. The electronic chemical potential of R1 ($\mu=-3.56$) is higher than R2,

which indicates that the net charge transfer will be from R1 towards the electron-deficient R2 reactant. The ω for R1 is 1.23 eV that falls in the range of moderate electrophiles. However, the N for R1 is 3.35 eV, which falls in the range of strong electrophiles within the global nucleophilicity and electrophilicity.

IV. CONCLUSION

DFT method is used to investigate the Diels-Alder reaction between hexa-1,2,4-trien (R1) with but-3-en-2-one (R2) at B3LYP-D3/6-311++G(d,p) level of theory. The concerted mechanism was studied and the geometries of the transition states were determined. The electronic energetic results show that the cycloadducts from trans conformer are more stable than the cis cycloadducts. The global reactivity indices were analyzed at the ground state of reactants to predict the reactivity of the studied organic molecules in the cycloaddition reactions and the results indicate that the net charge transfer will be from hexa-1,2,4-trien toward the electron-deficient but-3-en-2-one reactant.

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