DFT STUDY ON CYCLOPENTA-2,4-DIENONES AND CYCLOPENTA-2,4-DIENETHIONES AS DIENOPHILES FOR REACTIVITY PREDICTION IN DIELS-ALDER REACTIONS

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Abstract. The reactivity of both cyclopenta-2,4-dienones and cyclopenta-dienethiones were discussed with special emphasis on the use of cyclopentadienethione dienophiles in Diels-Alder type reactions. The ω values obtained for the molecules with electron-donating group ($–CH_3$) increased the nucleophilicity power whereas substitution with electron-withdrawing groups (such as $–NO_2$ and $–CO_2CH_2CH_3$) increased the electrophilicity power, indicating an increase of reactivity towards a nucleophiles. The cyclopentadienethiones would be more reactive towards nucleophiles than the cyclopentadienone analogues due to low values of η and high values of ω. This was supported by local ionization potential energy surfaces and Mulliken's charges on the cardonyl carbon and oxygen on cyclopentadienone and thienyl carbon and sulphur on cyclopentadienethiones. A relationship was established for the C-S bond and electrophicity index (ω) of cyclopentadienethiones.

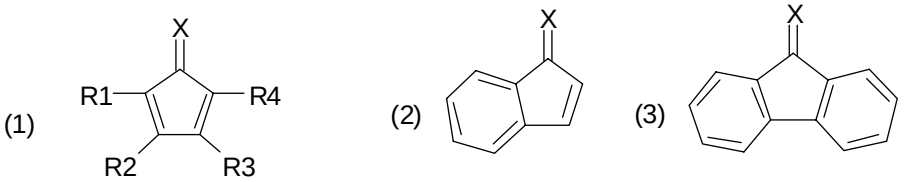
Keywords: cyclopenta-2,4-dienones, cyclopenta-2,4-dienethiones, reactivity prediction

Introduction

Cyclopentadienones have been widely recognized as having a high degree of synthetic potential [1-5]. Unfortunately, their propensity to dimerize [1,2] has limited their use in synthesis to masked cyclopentadienones or to those containing multiple aromatic rings [3-5]. A new method has been developed for the synthesis of cyclopentadienes, which involved (3+2) cycloaddition of cyclopropenones and alkynes

[6]. Variously substituted cyclopentadienones undergo in the first reaction step [4π+2π] Diels-Alder reaction yielding bridged polycyclic structures. If the reaction is conducted under vigorous conditions, loss of carbon monoxide is often observed, resulting in the production of the corresponding dienes [7-9]. Synthetic methodology based on this behavior has been exploited in preparation of various polycyclic compounds [10]. Little or information is known about cyclopentadienethiones, however molecular geometry, harmonic vibrational frequencies and absolute intensities of cyclopentadienethione has been theoretical examined and compared to that cyclopentadienone [11].

In this work, as a contribution to the understanding of the reactivity of heteroaromatic dienophiles in Deals-Adler (D-A) reactions, the electronic properties of some substituted cyclopenta-2,4-dienones and cyclopenta-2,4-dienethiones will be studied from a theoretical point of view. The substituents used are $–CH_3$, fused benzo-, $–NO_2$ and $–COOCH_2CH_3$ to examine the effect of dienophile substitution on the reactivity in order to select suitably the substituents leading to the most favourable reaction conditions.



X = O and S

(a) R1= R2 = R3 = R4 = H

(b) R1= R4 = CH_3, R2 = R3 = H

(c) R1= R4 = H, R2 = R3 = CH_3

(d) R2= R3 = H, R1 = NO_2, R4 = $COOCH_2CH_3$

(e) R1= R4 = H, R2 = NO_2, R3 = $COOCH_2CH_3$

Fig. 1. The molecules studied

The global electrophilicity index (ω) introduced by Parr et al. [12], allows to predict the trend of electron-acceptors (electrophiles) to acquire additional electronic charges from the environment. This index involves the electronegativity of the electron acceptor ($\chi = -\mu$) and its chemical hardness (η), that is to say, resistance to electron charge exchange with the environment. As Domingo et al. [13] have shown that the diene/dienophile classification is a single electrophilicity scale which a powerful tool to predict the feasibility of a cycloaddition approach and the type of mechanism involved The global electrophilicity index was evaluated using Eq. (1). Chemical potential and chemical hardness were calculated from the energies of the highest occupied molecular orbital (HOMO) and the lowest unoccupied molecular orbital (LUMO) in the ground state for N-electrons system with total energy (*E*) using Eqs. (2) and (3), respectively [14]:

$$\omega = \mu^2 / 2\eta \quad (1)$$

$$\mu = \left(\frac{\partial E}{\partial N}\right)_{v(r)} \approx -\frac{1}{2}(I + A) \approx \frac{1}{2}(E_{HOMO} + E_{LUMO}) \quad (2)$$

$$\eta = \left(\frac{\partial^2 E}{\partial N^2}\right)_{v(r)} \approx (I - A) \approx (E_{LUMO} - E_{HOMO}) \quad (3)$$

Computational details

Geometric optimizations were carried on studied molecules out without using symmetry or other structural restrictions. The geometries were fully optimized at the DFT/B3LYP level of theory with a 6-31G* basis set. The basis set 6-31G* was used for all atoms in ab initio methods, this has been used by several researchers in studying heterocycles [15-19]. However, initial geometries used for further calculations were from semi-empirical AM1 [20] method. All calculations were performed using Spartan.

Results and discussion

Reactivity descriptors

The properties calculated were the chemical potential (μ), chemical hardness (η) and chemical electrophilicity index (ω) in order to predict both the feasibility of the reaction and to evaluate the best dienophiles. The effect of dienophile substitution on the reactivity in order to select suitably the substituents leading to the most favourable reaction conditions was also examined. The calculated η, μ and ω for cyclopentadienones and cyclopentadienethiones at the B3LYP 6-31G* level of theory were shown in Tables 1 and 2. The cyclopentadienethiones would be more reactive towards nucleophiles (i.e., better dienophiles) than the cyclopentadienone analogues due to low values of η and high values of ω. Analysis form of Tables 1 and 2 also revealed that molecules 4 and 5 are more electrophiles, therefore they are expected to be more reactive towards nucleophiles in both cyclopenta-2,4-dienone and cyclopentadienethione series.

Table 1. Calculated HOMO, LUMO and global properties of substituted cyclopenta-2,4-dienone (eV)

	Studied molecule			Global properties		
		HOMO	LUMO	η	μ	ω
1	Cyclopenta-2,4-dienone	-6.64	-2.73	3.91	-4.69	2.81
2	2,5-Dimethylcyclopenta-2,4-dienone	-6.00	-2.41	3.59	-4.21	2.47
3	3,4-Dimethylcyclopenta-2,4-dienone	-6.25	-2.33	3.92	-4.25	2.30
4	2-Nitro-5-ethoxylcarbonylcyclopenta	-7.66	-4.17	3.49	-5.92	5.02
5	-2,4-dienone	-7.50	-4.14	3.36	-5.82	5.04
6	3-Nitro-4-ethoxylcarbonylcyclopenta	-6.41	-2.46	3.95	-4.44	2.50
7	-2,4-dienone	-6.23	-2.24	3.99	-4.24	2.25
	Indenone					
	Fluorenone					

The electroattractors/electron withdrawing groups ($–NO_2$ and $–CO_2CH_3$) substituents on both cyclopenta-2,4-dienone and cyclopentadienethione have profound effect on LUMO than HOMO as compared to the unsubstituted (Tables 1 and 2). Likewise, upon substitution of either cyclopenta-2,4-dienone or cyclopentadienethione with electron donating groups, the nucleophilicity power further increases, thus indicating an increase of reactivity towards a electrophile, however the position of the substituents also affect the reactivity. For instance, a molecule with substituents at positions 3 and 4 (especially electron donating groups) are more nucleophiles than s molecule with substituents at positions 2 and 5.

Table 2. Calculated HOMO, LUMO and global properties of substituted cyclopenta-2,4-dienethione (eV)

	Studied molecule			Global properties		
		HOMO	LUMO	η	μ	ω
1	Cyclopenta-2,4-dienethione	-6.29	-3.44	2.85	-4.17	4.16
2	2,5-Dimethylcyclopenta-2,4-dienethione	-5.96	-3.22	2.74	-4.59	3.85
3	3,4-Dimethylcyclopenta-2,4-dienethione	-5.90	-3.07	2.83	-4.49	3.56
4	2-Nitro-5-ethoxylcarbonylcyclopenta	-6.63	-4.48	2.15	-5.56	7.19
5	-2,4-dienethione	-7.11	-4.62	2.49	-5.89	6.92
6	3-Nitro-4-ethoxylcarbonylcyclopenta	-6.10	-3.16	2.94	-4.63	3.65
7	-2,4-dienethione	-6.00	-2.96	3.04	-4.48	3.30
	Indene-1-thione					
	Fluorene-1-thione					

The general reactivity of cyclopenta-2,4-dienethiones better towards nucleophiles is supported by local ionization potential (LIP)energy surface, which is an overlaying of the energy of electron removal (ionization) onto the electron density. The regions with red color represent regions in the molecular surface where electron removal goes (with minimal energy) most easily. The LIP energy surfaces for cyclopenta-2,4-dienones revealed that electron density cloud are greater on the molecular surface than on cyclopenta-2,4-dienethiones (Figs. 2 and 3). This result suggests the possibility of greater aromaticity and stability of cyclopenta-2,4-dienones over cyclopenta-2,4-dienethiones as reflected in the values of η (Tables 1 and 2).

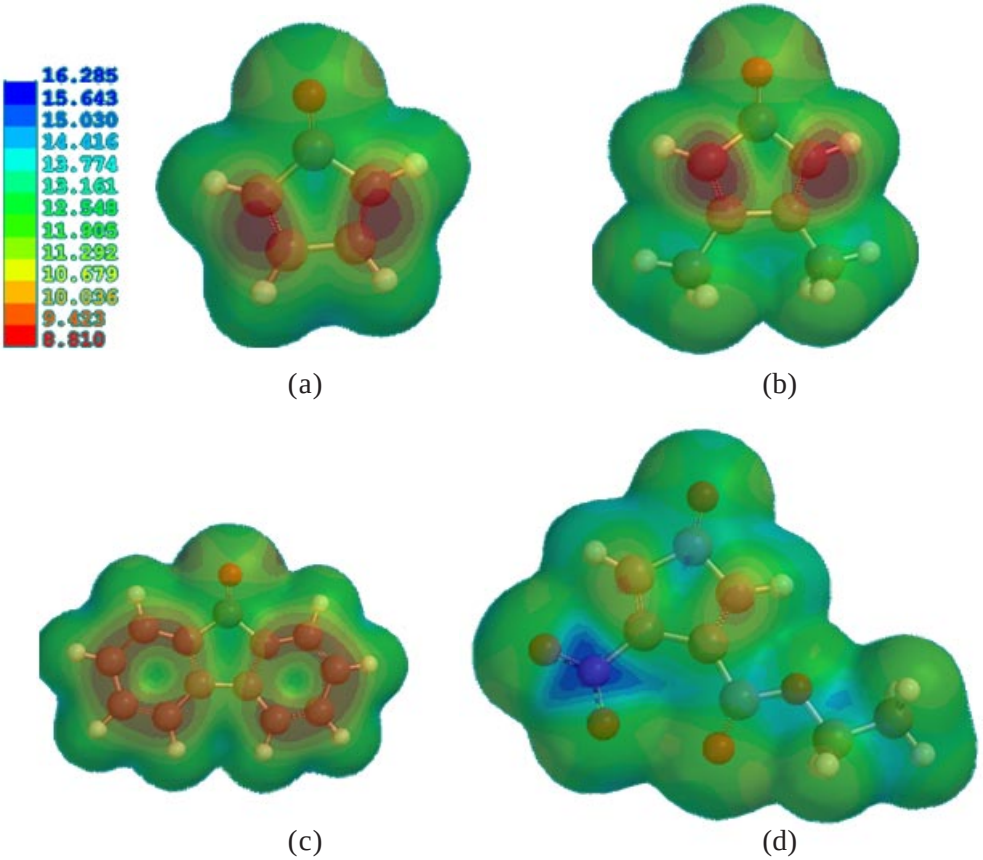


Fig. 2. Calculated local ionization energy surfaces on the molecular surfaces of cyclopenta-2,4-dienones with B3LYP/6-31G*: color ranges, in kJ/mol: from red 8.10 to blue 16.29: (a) cyclopenta-2,4-dienone, (b) 3,4-dimethylcyclopenta -2,4-dienone, (c) fluorenone and (d) 3-nitro-4-ethoxylcarbonylcyclopenta -2,4-dienone

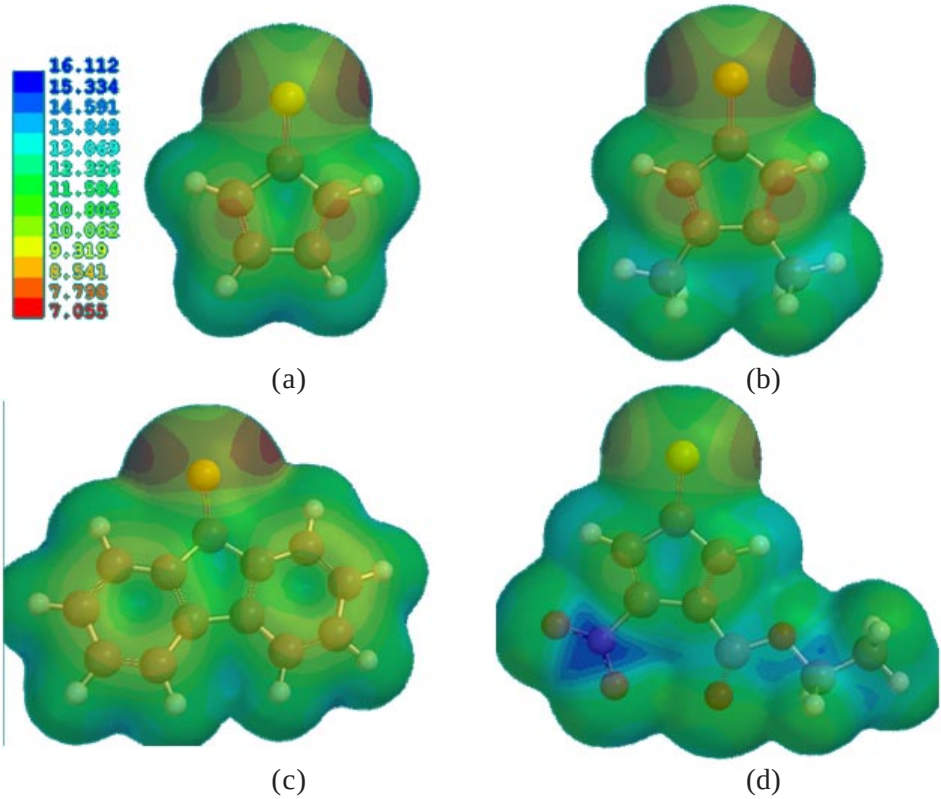


Fig. 3. Calculated local ionization energy surfaces on the molecular surfaces of cyclopenta-2,4-dienethione with B3LYP/6-31G*: color ranges, in kJ/mol: from red 7.06 to blue 16.12: (a) cyclopenta-2,4-dienethione, (b) 3,4-dimethylcyclopenta-2,4-dienethione, (c) fluorene-1-thione and (d) 3-nitro-4-ethoxylcarbonylcyclopenta-2,4-dienethione

The calculation of Mulliken's charge population (MCP) led to the same qualitatively and quantitatively similar description of the chemistry and reactivity of the cyclopenta-2,4-dienethiones better towards nucleophiles over cyclopenta-2,4-dienones (Table 3). The MCP values for carbonyl carbon on cyclopenta-2,4-dienones are positives and that of oxygen are negative suggested polar bond whereas MCP values on thienyl carbon and sulphur are all negatives (except on molecule 4). This suggested that C-S bond would extract more electrons form the molecules than C-O bond thereby leads to less electron density and stability in cyclopenta-2,4-dienethiones which is agreement with global index and LIP energy surfaces results. There is fair relationship between electrophilicity index (ω) and C-S bond in cyclopenta-2,4-dienethiones as shown in Fig. 4. The most reactive electrophile is the cyclopenta-2,4-dienethione with shortest C-S bond.

Table 3. Mulliken's charges and bond distance (Å) of cyclopenta-2,4-dienones and cyclopenta-2,4-dienethiones

Cpd	Cyclopenta-2,4-dienone			Cyclopenta-2,4-dienethione		
	Mulliken charges		Bond distance	Mulliken charges		Bond distance
	C*	O	C-O	C*	S	C-S
1	0.397	-0.434	1.214	-0.036	-0.084	1.638
2	0.343	-0.441	1.216	-0.091	-0.106	1.637
3	0.403	-0.455	1.217	-0.030	-0.122	1.641
4	0.397	-0.374	1.204	-0.076	0.046	1.629
5	0.421	-0.414	1.214	-0.048	-0.009	1.635
6	0.373	-0.451	1.217	-0.058	-0.127	1.643
7	0.341	-0.463	1.218	-0.090	-0.152	1.645

*Carbon atom that bonded to oxygen and sulphur atoms in cyclopenta-2,4-dienones and cyclopenta-2,4-dienethiones respectively.

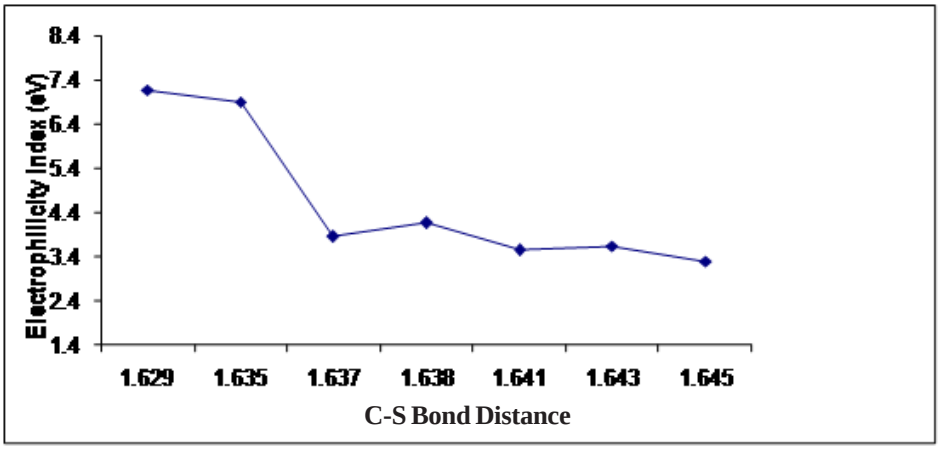
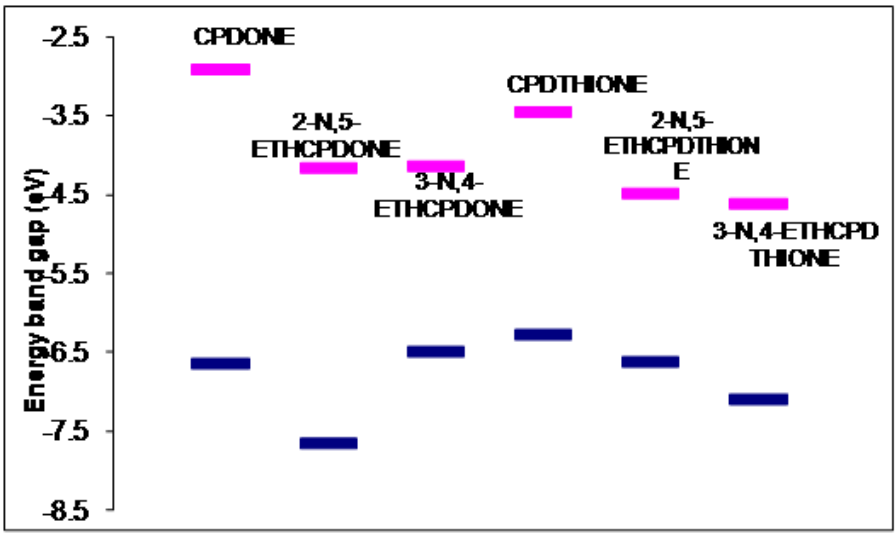


Fig. 4. Relationship between ω and C-S bond of cyclopenta-2,4-dienethiones

The reactivity of the D-A process depends on the energy separation between frontier molecular orbitals (FMO) of reagents, HOMO of the diene, and LUMO of dienophile. A small energy difference between interacting FMO would contribute to a higher stabilization of the transition state, therefore, all factors that decrease HOMO-LUMO distance will increase reaction rate. Then, from the energy point of view, the most favourable HOMO-LUMO interaction will be that of fewer ΔE. The Fig. 5

show FMO energies for some selected cyclopenta-2,4-dienones and cyclopenta-2,4-dienethiones. It could be clearly observed that electron-attractor substituents decrease LUMO energy, which would result in an acceleration of the reaction rate. These results are in agreement with those obtained by analysing the global electrophilicity index (ω).



Conclusion

Global electrophilic index is a useful tool for explaining the effect of substituents in the diene/dienophile interacting pair. Upon substitution of cyclopenta-2,4-dienones and cyclopenta-2,4-dienethiones with electron-withdrawing groups, there is an increase in ω index, thus reflecting a higher electrophilic character. On the other hand, substitution the molecules with electron-donating groups there is a decrease in ω index, thus reflecting a higher global nucleophilic nature. The cyclopentadienethiones are expected to be more reactive towards nucleophiles (i.e. better dienophiles) than the cyclopentadienone analogues due to low values of η and high values of ω . Therefore, with cyclopentadienethiones as dienophiles more suitable reaction mechanisms could be developed in designing possible precursor to be integrated in synthetic sequences/ routes for the synthesis of new class of organic compounds containing sulphur.

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