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Theoretical study for Synthesis Reactions of α-Alkylidene-γ-butyrolacton-2-ones (Tetronic acid Derivatives)

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Abstract

Multicomponent reaction for the synthesis of α-alkylidene-γ-butyrolacton-2-ones as Tetronic acid analogues is studied theoretically by performing Density Functional Theory calculation at B3LYP / 6-311G (d,p) levels of theory. There are two isomers of α-alkylidene-γ-butyrolacton-2-ones in different forms (E and Z). The calculation has shown that the major product (E-isomer) has highest value of nuclear repulsion energy in comparison with minor product (Z-isomer). In this study method is reported to indicate theoretically the major and the minor products for reactions before we do those reactions by using Density Functional Theory calculation at B3LYP / 6-311G (d,p) to the expected product and the major product which have highest value of nuclear repulsion energy . The MOs calculations, the energy of the highest occupied molecular orbital (HOMO) and the energy of the lowest unoccupied molecular orbital (LUMO) and HOMO-LUMO gap was also calculated at the same level.
Key words: DFT, nuclear repulsion energy, α-alkylidene-γ-butyrolacton-2-ones

1. Introduction

Tetronic acid derivatives represent an important class of oxygen 5-membered hetrocyclic compounds [1] These compounds are structural motifs in many natural products[2] and exhibiting a wide range of biological activities including antibiotic, antiviral, antineoplastic, and anticoagulant activity [3,4]. The interesting biological and structural diversity of these compounds has drawn the attention of chemists and biologists by reason of their challenging structural complexity and their high affinity to various sorts of "biological effectors" ranging from simple "metal cations" to complex enzymes[5]. They are commonly known for their cytostatic and antimicrobial [6,7] activities. Many of them have feeding deterrent activity against insects [8-10] of interest in naturally occurring.

Electronic structure methods provide useful information on the molecular structure and charge distribution, so they are useful to understand and describe systems where electronic effects and molecular orbital interactions are dominant [11]. Depending on the theoretical assumptions used for calculations, electronic structural methods belong to Density Functional Theory calculation [12].

2. Energy Representations

In the Born–Oppenheimer (BO) direct dynamics the potential energy V(q) and derivatives $\partial V/\partial q_i$ for each step of the trajectory integration are obtained by optimizing the electronic wave function. For a Born–Oppenheimer electronic structure theory calculation the electronic energy $E_e(q)$ is determined variationally from

$$E_e(q) = \frac{\langle \psi e\,(q) He(q)\psi e(q)\rangle}{\langle \psi e\,(q)\psi e(q)\rangle} \tag{2.1}$$

Adjustable parameters in the electronic wave function ψ_e (q) are varied to minimize $E_e(q)$ for the set of coordinates q. The potential energy for the system is given by

$$V(q) = E_e(q) + V_{NN}(q) \tag{2.2}$$

where $V_{NN}(q)$ is the nuclear–nuclear repulsion energy. It is straightforward to show that the derivative $\partial V_{NN}(q)/\partial q_i$ is analytical and, depending on the electronic structure theory and computer program used for the simulations, the derivative $\partial E_e(q)/\partial q_i$ may be determined directly as Ee(q) is calculated without the need for a finite difference[13].

The density functional theory (DFT) is based on the Hohenberg-Kohn theorem that the complete ground-state properties of the system are determined by the electronic density. In particular, they define a pairwise distance directed Gaussian function[14] (PDDG) to compute a contribution to the nuclear repulsion energy between atoms A and B as

$$V_N^{PDDG}(A,B) = \left(\frac{1}{n_A + n_B}\right) \sum_{i=1}^{2}\sum_{j=1}^{2} (n_A P_{i,A} + n_B P_{j,B}) e^{-[(r_{AB} - D_{I,A} - D_{J,B})2/_{10}]} \tag{2.3}$$

where n is the number of atomic valence electrons ,parameters P are preexponential factors, and parameters D are distance terms in A ˚.

3. Computational details

The energy minima for each molecule were identified in its potential energy surfaces, obtained through the Density Functional Theory. Minimum was optimized with the DFT B3LYP Method at 6-311G (d,p) basis set, available in the GAUSSIAN 03 program[15] . This level of theory Leads to accurate results[16].

The SCF MO theory on which the paper is based was developed by Roothaan (1951). In this theory the total wavefunction of a system is represented as a product of one electron molecular spin orbitals which are antisymmetrized to account for the indistinguishabitty of the electrons. The molecular Hamiltonian within the Born-Oppenheimer approximation consists of kinetic energy, electron-nuclear attraction, electron electron repulsion and nuclear-nuclear repulsion[17] .

4. Results and discussion

There are two isomers of α-alkylidene-γ-butyrolacton-2-ones in different forms (E and Z) shown in Fig. 1. The calculatation was shown that the major products (E- isomer) has highest value of nuclear repulsion energy in comparison with minor products (Z-isomer). The yield of reaction [18] show in Table 1 , the yield ratio of E-isomer is more than Z-isomer for the same R substituted in α-alkylidene-γ-butyrolacton-2-ones. (That's results for other searchers)[18]. In this study a method is reported to indicate the major and minor

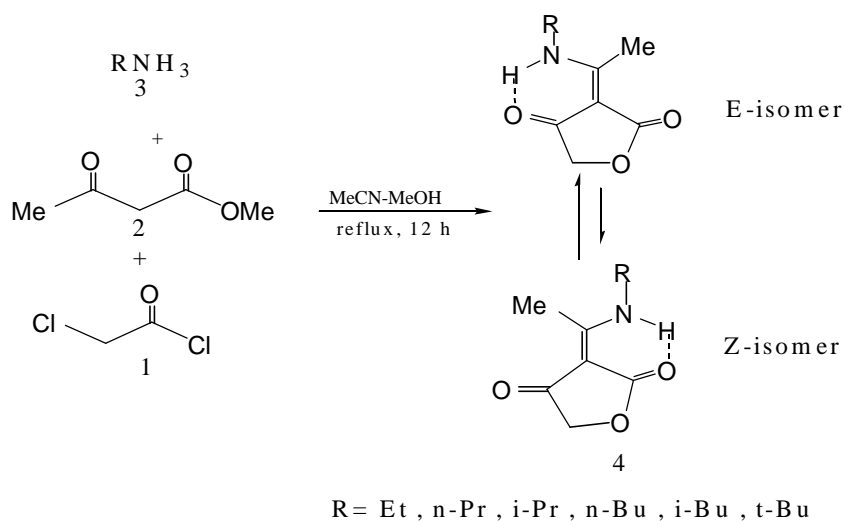products theoretically for reactions before carry out the reactions.

R = Et , n-Pr , i-Pr , n-Bu , i-Bu , t-Bu

Figure-1. Reaction between primary amines(3), Methyl Acetoacetate (2) and Chloroacetyl Chlorid (1) to give E and Z isomers of α-alkylidene-γ-butyrolacton-2-ones when R =Et,n-Pr,i-Pr,n-Bu,i-Bu,t-Bu[18]

The calculated energy values obtained by DFT ,B3LYP methods at 6-311G basis set for (E-isomer and Z-isomer) of α-alkylidene-γ-butyrolacton-2-ones are given in Table 2.

The total energy values for the products (T- Et, T- n-Pr, T- i-Pr, T- n-Bu, T- i-Bu, T- t-Bu) are almost equal in E-isomer and Z-isomer for same compounds, ΔEt are (0.011, 0.010, 0.012, 0.010, 0.013, 0.008 Haretree) respectively, that comport with the fact that is isomerization reactions are associated with a change in either the connectivity (the constitution) of the molecule or the steric arrangement of atoms or groups in the molecule. However, no change of the empirical formula is involved[19].

Table -1. Yields of reaction for synthesis of α-alkylidene-γ-butyrolacton-2-ones and the yield ratio of E-isomer and Z-isomer [18]

Products	R	Yield of α-alkylidene-γ-butyrolacton-2-ones (%)	E-isomer/Z-isomer
T- Et	Et	71	53:47
T- n-Pr	n-Pr	80	66:34
T- i-Pr	i-Pr	82	67:33
T- n-Bu	n-Bu	75	60:40
T- i-Bu	i-Bu	70	60:40
T- t-Bu	t-Bu	77	62:38

Table -2. The calculated Total Energy(Haretree) and Nuclear Repulsion Energy (a.u) of E-isomer and Z-isomer of α-alkylidene-γ-butyrolacton-2-ones with the DFT/6-311G basis set

Products	R	Total Energy(Haretree)			Nuclear Repulsion Energy (a.u)		
		E-isomer	Z-isomer	ΔE_t	E-isomer	Z-isomer	ΔE_N
T- Et	Et	-591.653	-591.664	0.011	717.637	693.189	24.448
T- n-Pr	n-Pr	-630.968	-630.978	0.010	811.466	783.462	28.004
T- i-Pr	i-Pr	-670.281	-670.293	0.012	906.801	874.287	32.514
T- n-Bu	n-Bu	-670.283	-670.293	0.010	923.848	911.988	11.860
T- i-Bu	i-Bu	-670.282	-670.295	0.013	945.253	929.405	15.848
T- t-Bu	t-Bu	-630.972	-630.980	0.008	819.280	798.664	20.616

The Nuclear Repulsion Energy values for products T- Et, T- n-Pr, T- i-Pr, T- n-Bu, T- i-Bu, T- t-Bu are the major products (E- isomer) has highest value of nuclear repulsion energy in comparison with minor products (Z-isomer)for same compound . ΔE_N are 24.448, 28.004, 32.514, 11.860, 15.848, 20.616 a.u respectively.

The results of DFT method are presented in Table-3. The eigenvalues of LUMO and HOMO and their energy gap reflect the chemical activity of the molecule. LUMO as an electron acceptor represents the ability to obtain an electron, while HOMO as an electron donor represents the ability to donate an electron.

Table 3 The calculated amounts of HOMO and LUMO energies, and (HOMO-LUMO)gap ΔE_L of E-isomer more than Z-isomer of α-alkylidene-γ-butyrolacton-2-ones with the DFT/6-311G basis set

Products	Highest Occupied Molecular Orbital Energy HOMO (a.u.)		Lowest Unoccupied Molecular Orbital Energy LUMO (a.u.)		(HOMO-LUMO)gap ΔE_{-L}	
	E-isomer	Z-isomer	E-isomer	Z-isomer	E-isomer	Z-isomer
T- Et	-0.2173	-0.2333	-0.0820	-0.1338	-0.1353	-0.0995
T- n-Pr	-0.2159	-0.2316	-0.0811	-0.1330	-0.1348	-0.0986
T- i-Pr	-0.2151	-0.2307	-0.0806	-0.1325	-0.1345	-0.0982
T- n-Bu	-0.2155	-0.2292	-0.0804	-0.1288	-0.1351	-0.1004
T- i-Bu	-0.2171	-0.2303	-0.0814	-0.291	-0.1357	0.0607
T- t-Bu	-0.2170	-0.2319	-0.0813	-0.1327	-0.1356	-0.0992

The smaller the LUMO - HOMO energy gaps, the easier HOMO electrons to be excited; the higher the HOMO energies, the easier HOMO to donate electrons; and the lower the LUMO energies, the easier LUMO to accept electrons Fig-2 shows HOMO AND LUMO plots and diagram of arrangement MOs by the energies of (E-isomer and Z-isomer) of α-alkylidene-γ-butyrolacton-2-ones. From the resulting data shown in Table-3, it is obvious that the LUMO energies of E-isomer products are lower than those of Z-isomer products and, consequently, the electrons transfer from HOMO to LUMO in E-isomer products (T- Et, T- n-Pr, T- i-Pr, T- n-Bu, T- i-Bu, T- t-Bu) is relatively easier than that in Z-isomer products. With the decrease of the LUMO energies, LUMO in E-isomers student accepts electrons easily[20]. The values HOMO-LUMO gap of studied compounds are however consistent with the well known fact that a large HOMO - LUMO gap has also been considered as an important prerequisite for the chemical stability of isomers [21].
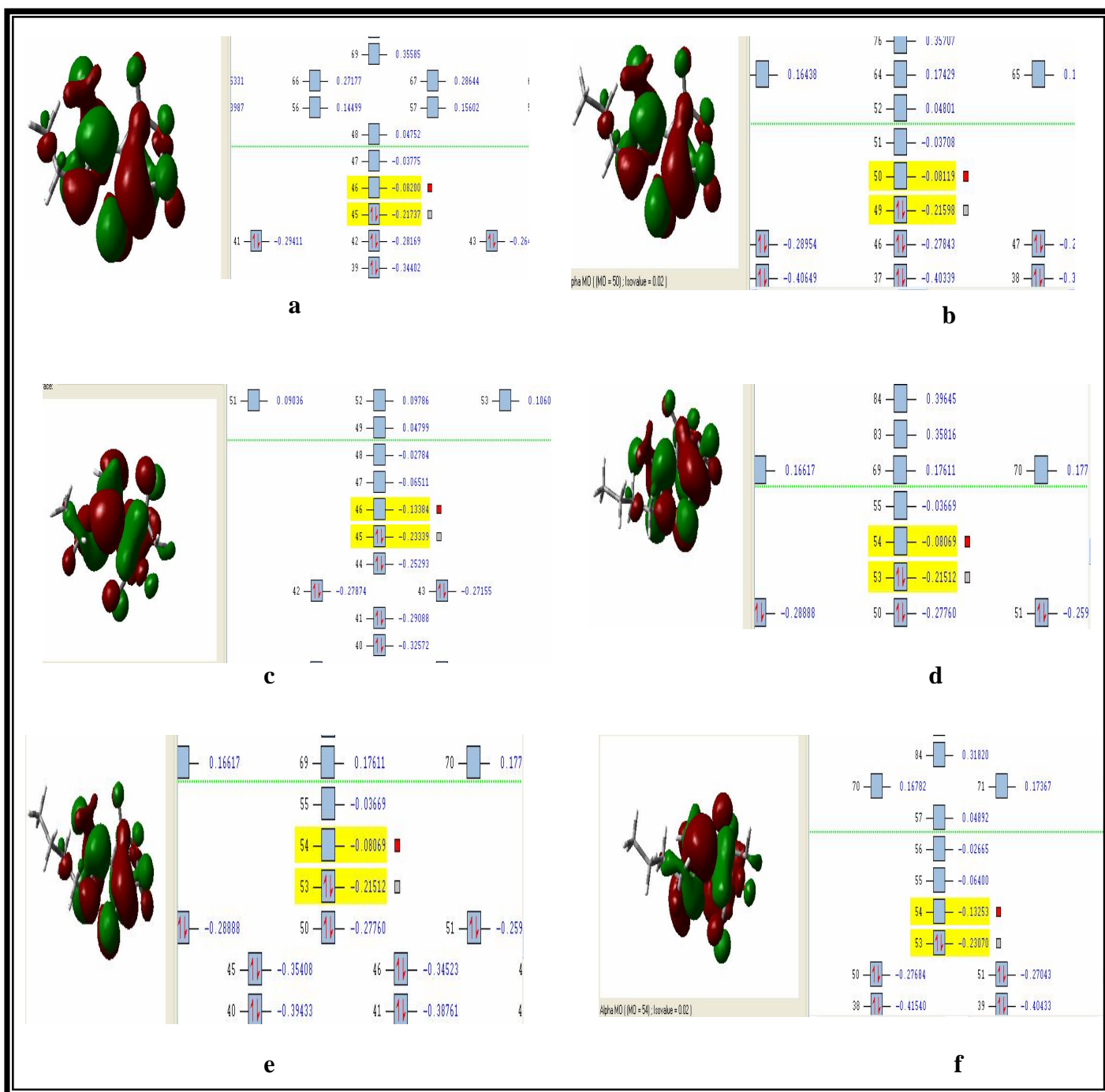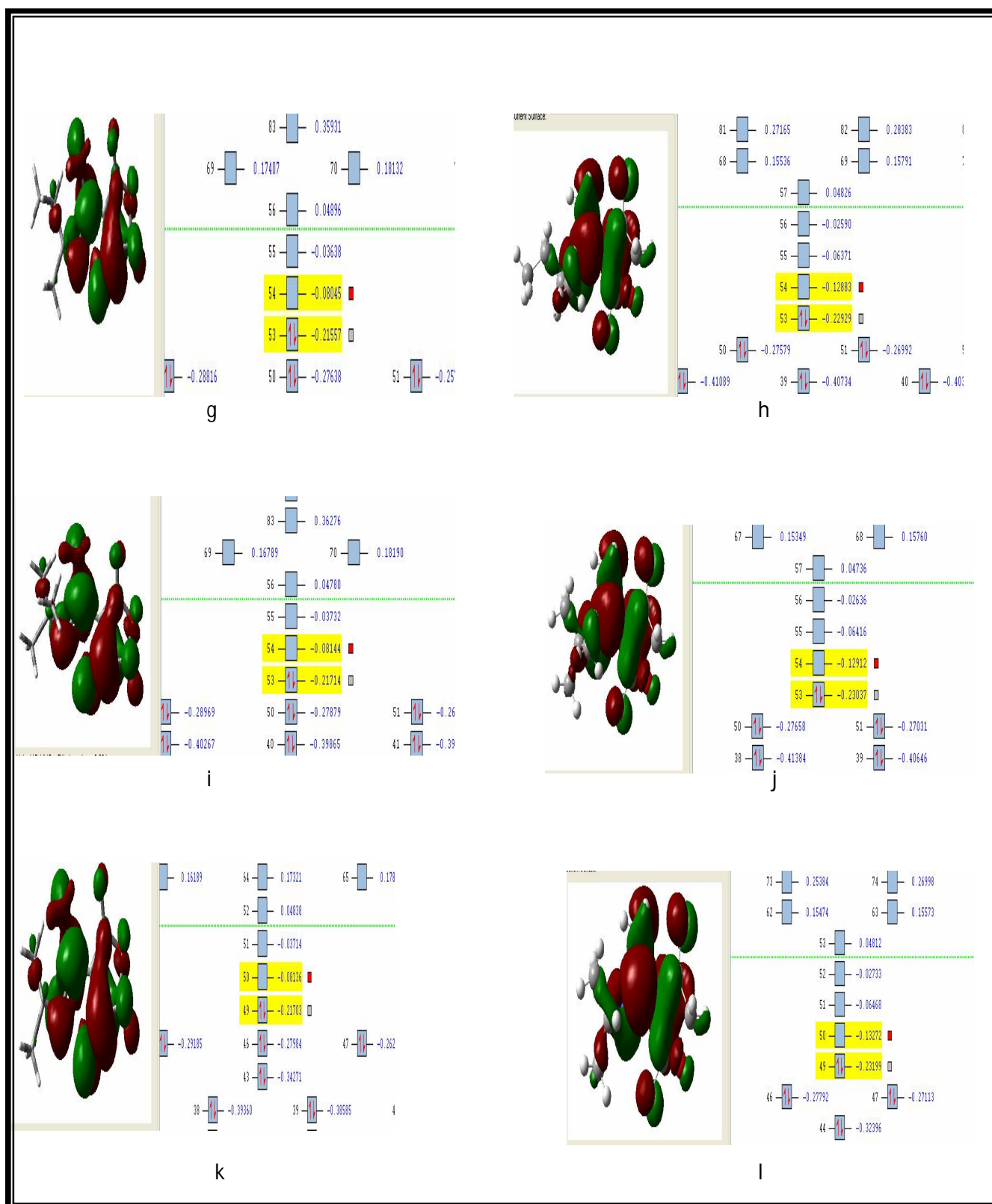
Figure-2. HOMO and LUMO plots and diagram of arrange MOs by energy of (E-isomer and Z-isomer) of α-alkylidene-γ-butyrolacton-2-ones with the DFT/6-311G basis set.[E-isomer T- Et(a), Z-isomer T- Et(b), E-isomer T- n-Pr (c), Z-isomer T- n-Pr (d), E-isomer T- i-Pr (e), Z-isomer T- i-Pr (f)]

g

h

i

j

k

l

Continue Figure-2. [E-isomer T- n-Bu (g), Z-isomer T- n-Bu (h), E-isomer T- i-Bu (i), Z-isomer T- i-Bu (j), E-isomer T- t-Bu (k), Z-isomer T- t-Bu (l)]

5. Conclusions

In the present work, we compare the experimental results for the synthesis of α-alkylidene-γ-butyrolacton-2-ones and yield ratio of two isomers form (E and Z-

isomer) with the results of Density Functional Theory (DFT) calculated with B3LYP method and 6-311G basis set the calculation showed that the major products (E-isomer) of α-alkylidene-γ-butyrolacton-2-ones have bigger value of nuclear repulsion energy in comparison with value of nuclear repulsion energy of minor products (Z-isomer) of α-alkylidene-γ-butyrolacton-2-ones. In this study a method is reported to indicate theoretically the major and minor products for reactions before carry out the reactions.

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دراسة نظرية لتفاعلات تحضير α- الكايلدين-γ - بيوتيرولكتون-2-ون (مشتقات حامض التترونيك)

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المستخلص

تمت دراسة تفاعلات تحضير مشتقات حامض التترونيك باستعمال حسابات نظرية دوال الكثافة وطريقة B3LYP وعناصر قاعدة 6-311G (d,p) . تتضمن نواتج التفاعلات تكوين ايزومرين من نوع E و Z بحصيلة تفاعل مختلفة حيث تكون حصيلة الايزومر من نوع E اكبر من الايزومر الاخر من نوع Z (حسب نتائج الباحثين المنشورة) لكل التفاعلات الستة المختلفة المدروسة لتحضير α- الكايلدين-γ - بيوتيرولكتون-2-ون (مع تغيير مجموعة الالكيل المعوضة) . اظهرت الحسابات النظرية ان طاقة التنافر النووية للايزومر E (ذو الحصيلة الاكبر في التفاعل) اكبر من طاقة التنافر النووية للايزومر Z (ذو الحصيلة الاقل في التفاعل) ولكل ازواج النواتج في التفاعلات الستة المدروسة. هذه النتيجة تسجل طريقة لتحديد ناتج التفاعل ذي الحصيلة الاكبر في التفاعلات ذات النواتج الايزومرية قبل اجراءها وذلك من خلال اجراء الحسابات النظرية للنواتج المتوقعة وتحديد اي منها ذي الحصيلة الاكبر حسب نتائج هذه الدراسة. كذلك اجريت حسابات طاقات الاوربتالات الاعلى طاقة المشغولة HOMO و الاوربيتالات الاوطأ طاقة غير المشغولة LUMO