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Computational Studies of Furanone and its *5Methyl*/*5Phenyl* Derivatives

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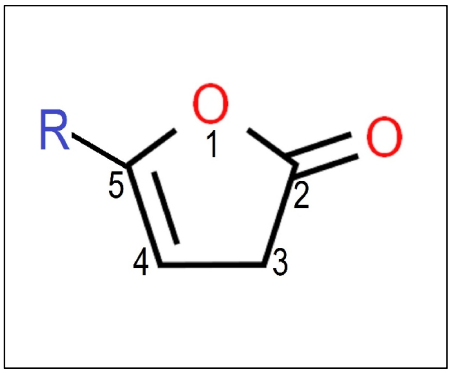

ABSTRACT

The properties for 2(*5H*)-furanone and 2(*5Methyl*)- and 2(*5Phenyl*)-furanone derivatives have been explored by computational chemistry approach. The subatomic unit calculations have been done to optimize the models and to evaluate their corresponding properties, in which several achievements have been seen for the investigated models. The energy levels of molecular orbitals indicated the importance of structural modifications for obtaining better electronic properties. To this aim, total energy, energy levels of the highest occupied and the lowest unoccupied molecular orbitals, energy gap, ionization positional, electron affinity, hardness, softness and dipole moment have been evaluated in addition to the original molecular weight and *Log*P parameters. The results revealed better reactivity and antioxidativity for 2(*5Phenyl*)-furanone in comparison with two other models proposing it for various possible applications in biological systems. Moreover, hardness and softness properties were also seen more favorable for this model. As a conclusion, the importance of furanone could be very much increased regarding structural modification, which could be very well investigated by the computational chemistry approach.

Keywords: Furanone; Structural modification; Antioxidativity; Computational chemistry.

Introduction

Starting from small organic structures is an important way to synthesize complex organic or medicinal related compounds. Furanone (Fig. 1) is among the most important mentioned small organic structures for various types of organic and bioorganic synthesis [1]. Furanone could be extracted from natural resources; however, its

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synthetic production has been also developed due to its large consumption in different chemical structure generations [2]. Based on the bioorganic purposes, several therapeutical activities have been seen for those generated structures from starting furanone including anticancer, analgesic, anticonvulsant, anti-inflammatory, antifungal, antibacterial, antimalarial, antioxidant, antimicrobial, antipsychotic, antiulcerative, antituberculosis, antiviral, vasorelaxant action and so many other applications [3-10]. The important role of furanone in therapeutics designated it as a famous pharmacophore for treatments of living systems [11]. Therefore, investigating its characteristic properties is still a formidable task to develop novel medicinal related compounds. Within this work, properties for 2(*5H*)-furanone heterocyclic structure (Fig. 1) has been investigated based computational chemistry approach. Furthermore, methyl and phenyl functionalization of *5H* position have been considered for investigating the effects of structural modification on the properties of starting and resulted structures (Table 1). The molecular orbital properties could designate the properties such as reactivity and antioxidativity very well, in which computational chemistry approach are almost the best technique to evaluate them as employed by earlier works for different theoretical and experimental purposes [12]. Structural modifications are important to generate new structures from the starting one; however, the physicochemical properties should be tracked to see what will happen after modification. To this aim, molecular properties have been evaluated for the original furanone and two of 5H derivatives to explore the effects of structural modifications in addition to molecular orbital properties of new structures (Table 1). Knowledge about subatomic unites properties for chemical structures could help to provide new structures based on desired proposes, which are very much important to introduce new compounds especially for treatments of living systems [13-25].

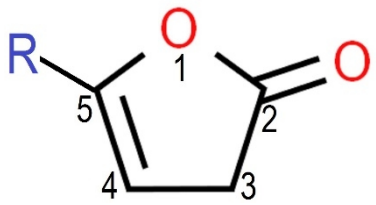


Fig. 1. 2(*5R*)-Furanone; R= *H*, *Methyl* or *Phenyl*.

Materials and Methods

Four steps have been designed to perform the computational processes to obtain the required properties for achieving the goals of this work. First, the 3D molecular models of 2(*5H*)-furanone (F), 2(*5Methyl*)-furanone (5MF) and 2*(5Phenyl*)-furanone (5PF) and the values of molecular weight (*MW*) and *Log*P have been obtained from the ChemSpider structural bank [26]. Second, all obtained 3D molecules have been optimized to reach their minimum energy structures based on density functional theory (DFT). To this aim, the B3LYP exchange-correlation functional and the 6-31G* standard basis set have been employed to perform DFT calculations by the Gaussian package of program [27]. Third, the molecular descriptors including total energy (E_T), energies of the highest occupied and the lowest unoccupied molecular orbitals (E_H and E_L) and dipole moment (*DM*) have been directly extracted from the calculation results in addition to the stabilized structures. Fourth, further molecular descriptors including energy gap (E_G), ionization potential (*I*), electron affinity (*A*), hardness (*H*) and softness (*S*) have been evaluated using the eqs. (1) - (5) [28].

$$E_G = E_L - E_H \quad (1)$$

$$I = -E_H \quad (2)$$

$$A = -E_L \quad (3)$$

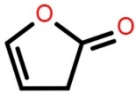
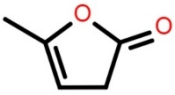
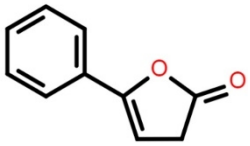
$$H = E_G/2 \quad (4)$$

$$S = 1/H \quad (5)$$

All the investigated models description including the models representation and molecular descriptors are exhibited in Table 1. It is important

to note that the computational chemistry could provide insightful information about the characteristic properties of chemical structures in both of singular and complex systems [29]. Quantum mechanical (QM) and molecular mechanical (MM) methods have been developed very well to investigate almost all chemical structures and processes prior to or parallel with experiments. Molecular graphics and computational softwares could provide the *in silico* environment for high-performance research activities [30-40]. By these benefits, this work has been done to carefully investigate the characteristic models description of F, 5MF and 5PF structures based computational chemistry approach.

Table 1: Models description*

Name	2(*5H*)-Furanone	2(*5Methyl*)-Furanone	2(*5Phenyl*)-Furanone
Symbol	F	5MF	5PF
CSID	124157	11071	249962
Figures			
***MW* (Da)**	84	98	160
***Log*P**	0.25	0.52	1.59
E_T (eV)	-8306	-9377	-14594
E_H (eV)	-6.86	-6.52	-6.20
E_L (eV)	-0.34	-0.21	-1.12
E_G (eV)	6.52	6.31	5.08
***I* (eV)**	6.86	6.52	6.20
***A* (eV)**	0.34	0.21	1.12
***H* (eV)**	3.26	3.12	2.54
***S* (eV^{-1})**	0.31	0.32	0.39
***DM* (Debye)**	3.86	3.99	3.85

*Please see Fig. 1 for starting model.

Results and discussion

The models of this work include F, 5MF and 5PF, in which the starting structure is shown in Fig. 1 and details are listed in Table 1. As mentioned earlier, the structures have been optimized to reach the minimum energy structures to obtain their properties in addition the stabilized structures. Comparing the molecular weights (*MW*) of three compounds shows than we have three levels of structures, in which F is the lightest and 5PF is the heaviest one, with 5MF in the middle. The obtained values of *Log*P, the solvation proportion of substance in oil/water media, show that the solubility of functionalized structures is leading to oil media for heavier structures. It is noted that the *5R* position of furanone (Fig .1) is an important atomic site for structural modification, in which the structures could be stabilized and their properties could be evaluated. Looking at the results of Table 1 indicates that the values of total energies (E_T) are changed for the investigated models, which is reasonable because of different numbers of atoms and their corresponding subatomic unites. Moreover, the molecular orbital properties (E_H and E_L) also indicate the effects of structural modifications on the electronic environments of corresponding structures. In addition to the exact values of E_H and E_L, their energy gaps (E_G) show the level of reactivity, in which the most reactive one could be designated

for 5PF with lower value of E_G. It is important to note here that the energy levels of the highest occupied and the lowest unoccupied molecular orbitals (HOMO and LUMO) are crucial for electronics of chemical structures, in which the electron s should be transferred into these levels to contribute to chemical reactions. Therefore, ionization potential and electron affinity (*I* and *A*) could be defined based on the values of HOMO and LUMO. Regarding the obtained results, better *I* and *A* properties have been obtained for 5PF in comparison with both of F and 5MF in agreement with the achievement on chemical reactivity. For antioxidant activity, the values of *I* and *A* are dominant to propose a chemical structure for further use in the aspects of antioxidativity. These antioxidant agents could play important roles for inhibiting the growth of cancer cells. Within current results, these properties could be seen by the structural modifications to achieve better activities. Considering no target, structural properties of chemical substances could lead them to biological activities for drug design purposes, which is called ligand-based drug design (LBDD) [41]. To this aim, computational chemistry could provide *in silico* environment for drug design processes [42-49]. In agreement with the results up to now, hardness and softness (*H* and *S*) also indicate better properties for 5PF in comparison with F and 5MF, which reveals that 5PF could be employed for the reactivity purposes better than other two models. Lower value of *H* and higher value of *S* for 5PF indicate better situation for contributing to chemical reactivity, which is an important property for various applications, especially in antioxidativity. The obtained values of dipole moments (*DM*) show different electronic balance in the investigated structures.

Conclusion

Computational chemistry approach has been employed within this work to investigate properties for furanone and its methyl and phenyl derivatives. The structural modification could significantly change the properties of structures regarding their subatomic unit calculations. The results indicated that the chemical reactivity of structures are changed based on the employed modifications, in which phenyl group plays a dominant role to evaluate characteristic properties for functionalized furanone. Moreover, the energy levels of molecular orbitals indicated that electron transfer properties could be better achieved for phenyl functionalized furanone in comparison with the original furanone and methyl functionalized one. Antioxidativity activity of furanone could be increased by phenyl functionalization, in addition to better activity. The oil/water solubility is also increased for the phenyl functionalized structure, in which this property is crucial for drug design processes. Finally, the properties of investigated structures have been very well evaluated based on the employed computational chemistry approach.

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