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Theoretical Study of Some Physical and Thermodynamic Properties for some Diclofenac Derivatives by using Semi-Empirical Calculations (PM3 Method)

Nidaa A. Jasim

MSc in Physical Chemistry, Karbala Education Directorate, Iraq.

ABSTRACT

In this study , a Gaussian (09) program was selected using semi-experimental calculations (PM3 Method Where some thermodynamic properties were calculated, along with some kinematic properties At equilibrium Thermodynamic of the inhibitors - acetic acid] 2-(2,6- Dichloro- phenylamino)-phenyl] acetic acid Shown the results of theoretical calculations that (COOH-R-CH2COOCH3) has the highest values of thermodynamic functions H0, G0, A0, CV ,CP ,S0) compared to the rest of the study compounds COOH-R-CH2COOC R-CH2COOCH3 COOH-R-CH2COOH , R-CH2COOH) , Where some physical properties were calculated such as orbital energies (EHOMO , ELUMO in eV), (dipole moment μ in Debye) , orbital energies (EHOMO , ELUMO in eV), IP (in e V) , (measurement stability ΔE) , hardness η and Electron Affinity EA) . Plus, its formation enthalpy (ΔHr0) of these compounds were calculated by using (semi-empirical method model in AM1 MOPAC). The results showed that the compound (COOH-R-CH2COOH) Have the least value of the formation enthalpy (the more Stability) Compared to other compounds At the same time it has the most reduced value (EHOMO, ELUMO, ΔE) , that is implies it's the most elevated active between the Studied compounds and have highest IP. Also The results showed that compound [R- CH2COOCH3] have lower electronegativity ,higher hardness(η), lower energy gap (ΔE), and lower dipole moment which might be clarified the highest anti-inflammatory The reason for this discrepancy in the results is due to the nature of the replaced group

Keywords: Physical and Thermodynamic Properties, Diclofenac Dervatives by using Semi-Empirical Calculations (PM3 Method)

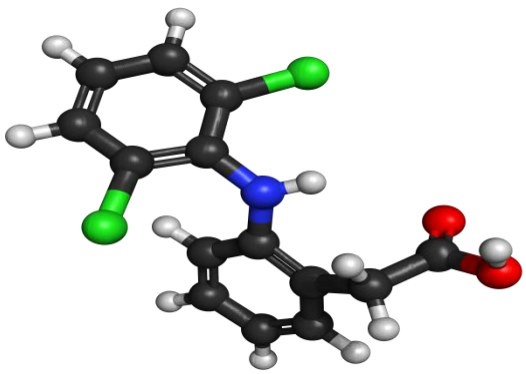
Correspondence:
Nidaa A. Jasim
MSc in Physical Chemistry, Karbala Education Directorate, Iraq.

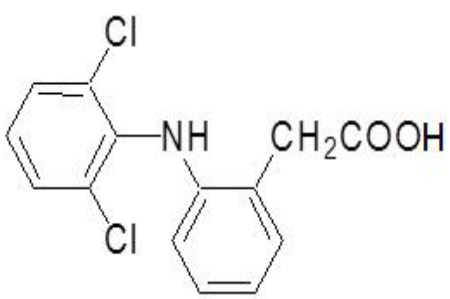
الخلاصة

في هذه الدراسة ، تم اختيار برنامج(Gaussian 09) باستخدام حسابات شبه تجريبية (طريقة PM3 حيث تم حساب بعض الخصائص الديناميكية الحرارية مع بعض الخصائص الحركية عند التوازن الديناميكا الحرارية للمثبطات - حمض الأسيتيك
2-(2,6- Dichloro- phenylamino)-phenyl]acetic acid أظهرت نتائج الحساب النظرية أن المركيب $COOH\text{-}R\text{-}CH_2COOCH_3$ لديه أعلى قيمة للدوال الديناميكية الحرارية (E^0, H^0, G^0, A^0, C_V ,C_P ,S^0) لهذه المركبات $COOH\text{-}R\text{-}CH_2COOCH_3$, $R\text{-}CH_2COOCH_3$, $COOH\text{-}R\text{-}CH_2COOH$, ($R\text{-}CH_2COOH$) بنما تم حساب بعض الخصائص الفيزيائية مثل طاقة المدارات(E_{HOMO} E_{LUMO}) , عزم ثنائي القطب (μ in Debye) طاقة التأين ((IP in eV) طاقة التأين (IP in eV) , فجوة الطاقة(ΔE(in eV) , الألفة الالكترونية و الصلابة (E_A, in eV) η بالإضافة لانثالبي التكوين التي حسبت للمركبات باستخدام برنامج (MOPAC لاستخدام الطريقة الشبه تجريبية AM1 اشارت النتائج المحسوبة ان المركب($COOH\text{-}R\text{-}CH_2COOH$) له قيمة أقل من ا لمحتوى الحراري للتكوين (المزيد من الاستقرار) بالمقارنة مع المركبات الاخرى ، وفي الوقت نفسه لديه القيمة الأقل (E_{HOMO}, E_{LUMO}, ΔE) وذلك يعني أنه الأكثر نشاطًا بين المركبات المدروسة ولديه أعلى IP. كما أظهرت النتائج أن المركب [R-CH_2COOCH_3] له كهرسلبية أقل ، وصلابة أعلى (η) ، وفجوة طاقة أقل (ΔE) ، وعزم ثنائي القطب أقل يمكن توضيحه بأعلى مضاد للالتهابات والسبب في تباين النتائج يعود الى طبيعة المجموعة المعوضة

INTRODUCTION

Diclofenac, one of the most frequently used anti-inflammatory drugs, is decarboxylation. It is supplied as or contained in medications under a variety of trade names. The name "diclofenac" derives from its chemical name: **2-(2,6-dichloranilino) phenyl acetic acid**[1]
Diclofenac sodium is a synthetic, nonsteroidal, anti-inflammatory and analgesic compound with the following formula:





[Diclofenac (DF)]

Figure (1): Structure of diclofenac

$C_{14}H_{11}Cl_2NO_2$ Molar Mass = 296.148 g/mol g·mol^{-1}

In 1973 diclofenac was developed by Ciba-Geigy (presently Novartis) but in 1979 it was introduced for the first time by the United States [2,3] In most cases, Diclofenac is used in the form of sodium or potassium salt. Now it is used in China as sodium salt. Diclofenac is often used to treat pain associated with cancer [4], Diclofenac has been seen as successful against all strains of multi medicate safe E. coli, with a MIC of 25 micrograms/ml. In this manner, it might be recommended that diclofenac has the ability to treat uncomplicated urinary tract infections (UTI) brought about by E. coli additionally been demonstrated to be powerful in treating Salmonella infections in rats what's more, is under scrutiny for the treatment of tuberculosis . It is an anti-inflammatory drug that is used regularly for people suffering from osteoporosis in knee and delicate tissue wounds. Oral treatment with diclofenac has negative effects as it affects the digestive and renal system. These negative effects are accepted to be limited with topical diclofenac formulations without loss of effectiveness Especially if the inflammation treatment is planned for chronic pain specifically if inflammation treatment of chronic pain[5 , 6, 7] . It has no odor , white powder, Crystalline structure,slightly hygroscopic substance .Its crystals are fused at 283-285°C , Diclofenac sodium is slightly soluble in water and acetone; insoluble in ether While it soluble in alcohol [8 , 9]. Diclofenac sodium is an inhibitor of prostaglandin synthetize. It helps reduce inflammation and relieve pain such as Ankylosing Spondylitis arthritis and osteoporosis, Acute gout and the results of some major surgery. The usual oral dose is 75-150 mg daily individed doses [10]. Diclofenac Potassium is believed to dissolve faster, So its absorption is faster, than the sodium salt It is recommended for treatments That need a faster effect, , Because it is considered a painkiller using for the treatment of primary dysmenorrheal For mild to moderate pain. As with other NSAIDs, diclofenac [11].

G 09 PROGRAME

Computational chemistry is a modern section of chemistry that depends on solving mathematical equations and approximations that help in understanding the movement and positioning of an electron.

computational chemistry has turned into one of the most powerful scientific tools used in theoretical calculations, as it has been widely used to interpret, and compare calculated results. It was used to define molecular formulas and molecular structures, calculate vibrational frequencies as well as magnetic resonance, and because of this wide application of computational chemistry, time and effort to access information requiring significant effort in practice have been reduced. [12] . The significant and continuous advancement in computers has contributed to the development and improvement of computer software packages [13] . Computer simulations are used regularly to interpret experimental results and prediction Material properties. Gaussian09 is capable of predicting many properties of molecules and reactions. Gaussian09 program is general purpose algorithm chemical package originally released in 1970 by John Poble. It is a program that uses a set of derivative relationships GAUSSIAN- studied using the 09 program from statistical thermodynamics, which is based on the Boltzmann concept and molecular dependencies [14]. In order to determine (S^0, H^0, G^0). Gaussian 09 Program is a new release for the computer operating system, which works with the Windows system, through which the electronic structure and energy are recognized and used by chemists, engineers, and physicists around the world to access information about the electronic structure, Characteristics of electronic and partial properties[15] . The Gaussian 09 program can achieve the properties of stable vehicles on which it is difficult to record information in experimental terms such as short-lived intermediaries and transitional structures[14]The Gaussian 09 program can use the most advanced modeling program today and has made many improvements To predict a wide range of spectra in the ultraviolet / visible and infrared region, Raman, NMR and to explore different chemical fields addition to thermochemistry and photochemistry[16,17]
.

MINDO (Modified Intermediate Neglect of Differential Overlap)

MINDO it is a Semi-Empirical - method used in the quantum calculations of electronic molecular structures in quantum computational chemistry, a group of things on the modified average neglect of differential interference, John Bebel Parametric Method number 3 (PM3 continues to be widely used. This method uses NDDO, which is a powerful model It is more accurate than that, especially in calculating the bounding angles, AM1, approximately the same equations used in Hydrogen [18]. It is also used to calculate structural properties, total energy, free formation and may result To abnormal behaviors that are still under treatment PM3 some group characteristics .It is a semi-empirical method for the quantum calculationin quantum calculations of the electronic molecular structure in computational chemistry. The principle of the work of this method is based on the neglect of the integrative, differential, and integrative convergence. The PM3 method uses the same formalism and equations as the AM1 method [19]. PM3 utilizes two Gaussian functions for the essential repulsion function, rather than the variable number utilized by AM1 which is used between one and four Gaussians per element. These methods rely on experimental measurements in the calculations to find the physical properties of organic and inorganic compounds, as the semi-experimental methods depend on the approximation of the Schruddinker equation during the calculation process i.e. in the sense of compensating the values of some integrals with practical values instead of calculating them[20]. There are several methods including (AM1, PM3, MNDO, CNDO), and the AM1 method or what you know (Austin method) and (PM3) method The difference between the two methods is that each method has the ability to calculate some elements within the periodic table compared to the other, for example, we find that the AM1 method has the ability to calculate the elements located in the elements of the second group while the method of (PM3) is for heavy group elements , The semi-experimental methods contrast from the Ab initio strategy as far as information exactness and speed and precision, therefore it is called (semi-exploratory, as are semi- experimental techniques, for example, CNDO/1, INDO), CNDO, MNDO, PM3 and AM1) when determined for some physical properties For example, (the length of the bond, the polarization force, and dipole moment in the technique . Mathematical derivations and equations are used in the processing of calculations We find that most data resulting from the theoretical calculation process Computational differ from

the practical calculations (Experimental) at a rate of (7-10) %. choosing the best method for carrying out a specific research requires several factors, these factors include: the nature of the molecule to be studied, the type of data required in the study, the availability of some practical data that some methods may require, as well as the availability of practical capabilities and calculations that have specifications so that they can The work is done in the shortest possible time, bypassing some limitations such as the size and number of its atoms and the availability of data on them[21,22,23]. In the MNDO method, two important changes were made to determine the repulsion charge of the nucleus of about five angstroms Anyway , in MNDO, two-electron, two-center ⟨sAsA|sBsB⟩⟨sAsA|sBsB⟩ integrals and core-electronic interactions do not converge with the point charge interactions do not While that, They are always a little smaller. Net repulsion between two uncharged atoms the core-core expression ⟨sAsA|sBsB⟩⟨sAsA|sBsB⟩ integrals Has been replaced by the exact $1/R_{AB}$ term , the additional term is needed for Increasing core-core of small distances Because of the core of polarization. Two changes can be expressed as the core MNDO dissonance term as defined in [24,25]

$$En(A,B) = ZAZB\langle sAsA|sBsB\rangle (1+ e^{-\alpha ARAB}+e^{-\alpha BRAB})$$

Approximation of 1- Electron integral

$H_{uu} = U_{uu} - \sum_{B\neq A} V_{AB}$ U_{uu} From atomic spctra

V_{AB} value per atom pair

$Huv = 0$ uv on th same atom

$Huv = \beta_{AB} Suv$ $\beta_{AB=1/2}(\beta A + \beta B)$ One β parameter per electron

The simplest method that can be used for correction is to add characteristic values for specific atoms such as atomic polarization correction **(α_a)** [23] In calculating polarization by Dewar et al. (23). Parameters for the atomic correction units were determined for eight elements (H, C, O, F, Cl, Br, I, N) by least-square fitting based on calculated polarizabilities, using52 chemical compounds by MINDO method.α_a can be found in matrix form as follows [26, 27]

$(N^t. N). \alpha_a = N^t. \Delta\alpha$

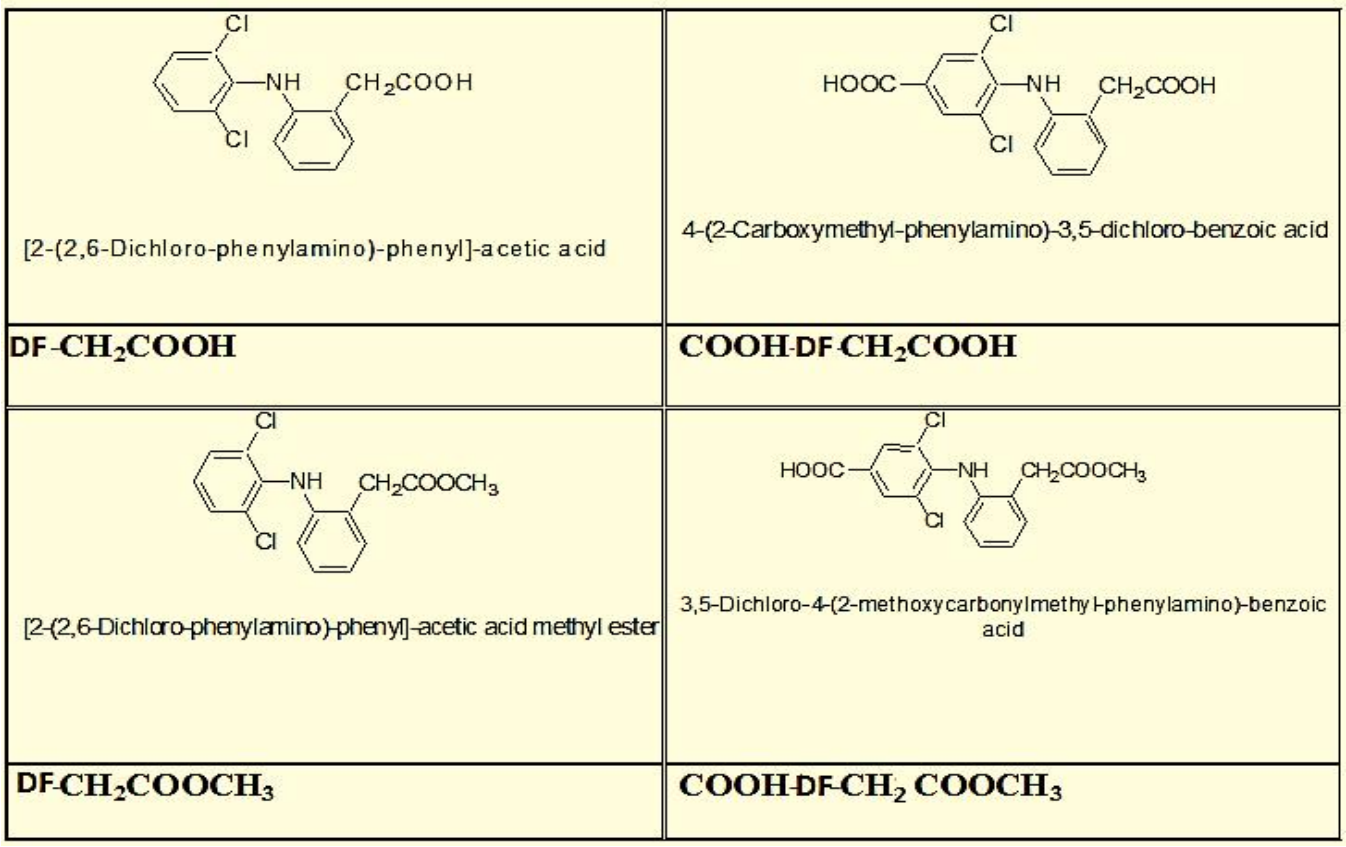


Fig. 2: The geometric equilibrium for the derivatives of] 2-(2,6- Dichloro- phenylamino)-phenyl] acetic acid

***Methods of calculation*.**

Computations were applied via the Gaussian 09 package program [28], the geometry optimization of the structures have been performed by the application the Semi-Empirical calculations(PM3 Method) [29,30]

RESULTS AND DISCUSSION GEOMETRICAL PARAMETER

In this research calculated the geometry (bond lengths and bond angels) of the four molecules of [2-(2,6-dichloro-anilino) phenyl] acetate DF-CH_2COOH derivatives COOH-DF-CH_2COOH, DF-CH_2COOCH_3, COOH-DF-CH_2COOCH_3), using the semi-empirical PM3 methods. According to the results calculated and recorded in the(table1 and fig. 2) .Show that each the bonds C_{15}-X_{16} [X=CH_2COOH ,CH_2COOCH_3] in compounds DF-CH_2COOH and DF-CH_2COOCH_3 have high value compared to other compounds COOH -DF-CH_2COOH and COOH-DF- CH_2COOCH_3 may be caused by the less electro negative of (Carboxyl group) of groups. Where the bond C_1-X_{20} [X=H,COOH] in compounds

COOH -DF- CH_2COOH and COOH-DF -CH_2COOCH_3 have high value compared to other compounds .Also the change of the group substituted had effect on the value of the angles of the compounds studied in this research , have shown calculation in the (table 1and fig.1). That the angle ($\angle C_4\ C_5\ C_6$) showed that in COOH -DF-CH_2COOH and COOH-DF-CH_2COOCH_3 have high value compared to other compounds. When the angle ($\angle C_2\ C_1C_6$) in DF-CH_2COOH and DF-CH_2COOCH_3 have high value compared to others. May be due big size of substitution groups on the angles.

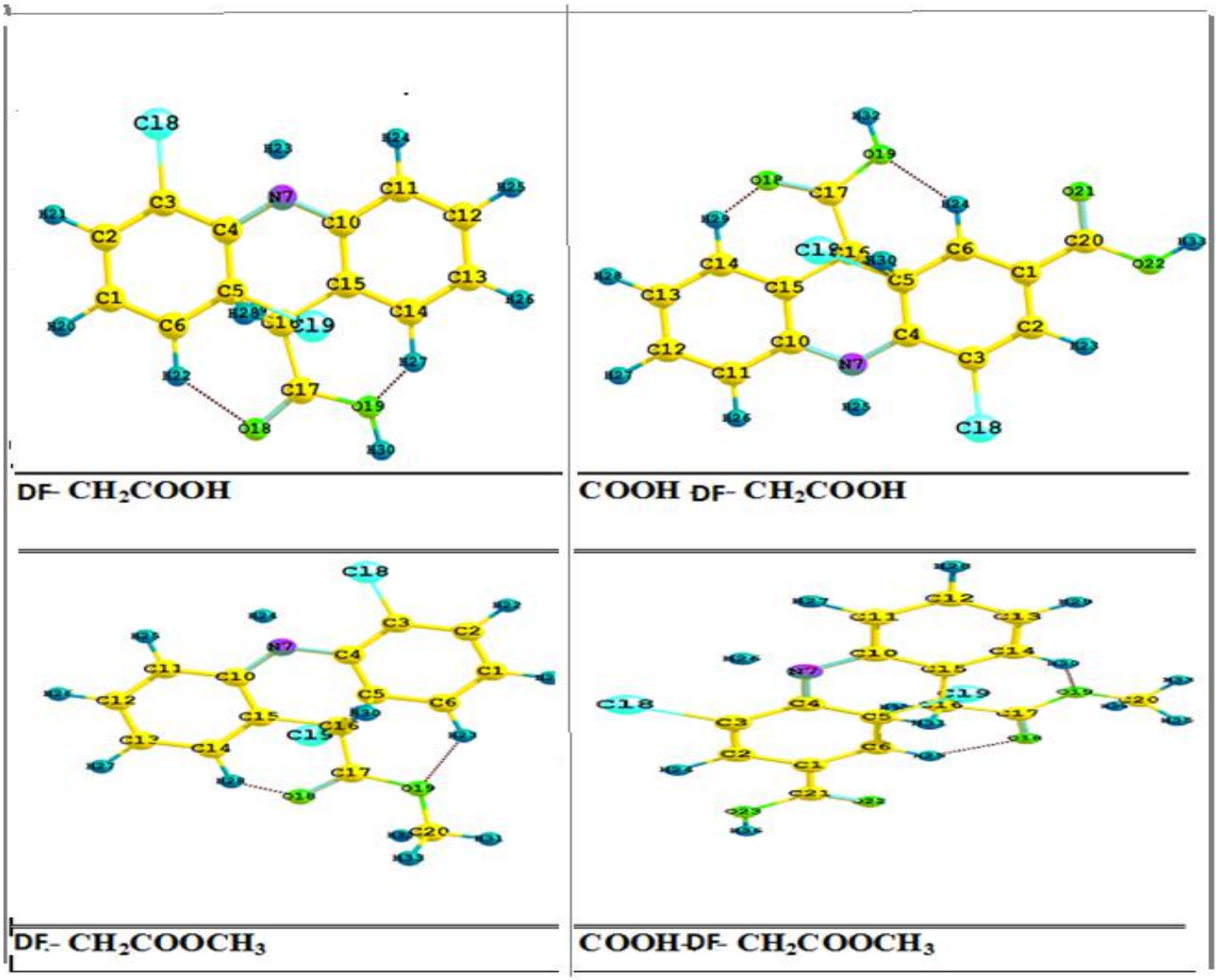


Fig. (3): The geometric equilibrium for the derivatives of [2-(2,6-dichloro-anilino) phenyl] acetate

Table 1: Calculated geometric parameters (bond lengths in Angstrom length angles in degree) of the derivatives [2-(2,6-dichloro-anilino) phenyl] acetate.

DF- CH_2COOH		COOH-DF- CH_2COOH		DF- CH_2COOCH_3		COOH-DF- CH_2COOCH_3	
Para. Geo.	**Bond length and Angle**	**Para. Geo.**	**Bond length and Angle**	**Para. Geo.**	**Bond length and Angle**	**Para. Geo.**	**Bond length and Angle**
R(1-2)	1.448	R(1-2)	1.453	R(1-2)	1.448	R(1-2)	1.453
R(1-6)	1.339	R(1-6)	1.347	R(1-6)	1.339	R(1-6)	1.347
R(1-20)	1.095	R(1-20)	1.483	R(1-21)	1.095	R(1-21)	1.483
R(2-3)	1.343	R(2-3)	1.343	R(2-3)	1.343	R(2-3)	1.343

R(2-21)	1.096	R(2-23)	1.098	R(2-22)	1.096	R(2-24)	1.098
R(3-4)	1.471	R(3-4)	1.469	R(3-4)	1.471	R(3-4)	1.468
R(3-8)	1.685	R(3-8)	1.687	R(3-8)	1.685	R(3-8)	1.688
R(4-5)	1.600	R(4-5)	1.598	R(4-5)	1.599	R(4-5)	1.597
R(4-7)	1.476	R(4-7)	1.479	R(4-7)	1.476	R(4-7)	1.479
R(4-9)	1.795	R(4-9)	1.800	R(4-9)	1.797	R(4-9)	1.804
R(5-6)	1.478	R(5-6)	1.478	R(5-6)	1.478	R(5-6)	1.479
R(5-16)	1.519	R(5-16)	1.517	R(5-16)	1.519	R(5-16)	1.517
R(5-29)	1.110	R(5-31)	1.110	R(5-30)	1.110	R(5-32)	1.110
R(6-22)	1.096	R(6-24)	1.099	R(6-23)	1.096	R(6-25)	1.099
R(7-10)	1.377	R(7-10)	1.382	R(7-10)	1.378	R(7-10)	1.382
R(7-23)	0.988	R(7-25)	0.990	R(7-24)	0.989	R(7-26)	0.990
R(9-15)	1.500	R(9-15)	1.498	R(9-15)	1.500	R(9-15)	1.499
R(9-16)	1.406	R(9-16)	1.406	R(9-16)	1.406	R(9-16)	1.407
R(10-11)	1.413	R(10-11)	1.411	R(10-11)	1.413	R(10-11)	1.411
R(10-15)	1.435	R(10-15)	1.434	R(10-15)	1.435	R(10-15)	1.434
R(11-12)	1.371	R(11-12)	1.372	R(11-12)	1.371	R(11-12)	1.372
R(11-24)	1.096	R(11-26)	1.096	R(11-25)	1.096	R(11-27)	1.096
R(12-13)	1.416	R(12-13)	1.415	R(12-13)	1.415	R(12-13)	1.415
R(12-25)	1.097	R(12-27)	1.097	R(12-26)	1.096	R(12-28)	1.097
R(13-14)	1.365	R(13-14)	1.365	R(13-14)	1.365	R(13-14)	1.365
R(13-26)	1.096	R(13-28)	1.096	R(13-27)	1.096	R(13-29)	1.096
R(14-15)	1.424	R(14-15)	1.424	R(14-15)	1.423	R(14-15)	1.424
R(14-27)	1.098	R(14-29)	1.098	R(14-28)	1.098	R(14-30)	1.098
R(16-28)	1.087	R(16-30)	1.088	R(16-29)	1.087	R(16-31)	1.088
R(17-18)	1.218	R(17-18)	1.218	R(17-18)	1.216	R(17-18)	1.216
R(17-19)	1.339	R(17-19)	1.339	R(17-19)	1.348	R(17-19)	1.349
R(19-30)	0.953	R(19-32)	0.953	R(19-20)	1.410	R(19-20)	1.410
A(2-1-6)	121.5	R(20-21)	1.220	R(20-31)	1.093	R(20-33)	1.093
A(2-1-20)	117.2	R(20-22)	1.354	R(20-32)	1.095	R(20-34)	1.095
A(1-2-3)	121.8	R(22-33)	0.952	R(20-33)	1.095	R(20-35)	1.095
A(1-2-21)	117.9	A(2-1-6)	121.3	R(19-31)	1.963	R(21-22)	1.220

A(6-1-20)	121.3	A(2-1-20)	119.1	A(2-1-6)	121.5	R(21-23)	1.355
A(1-6-5)	122.7	A(1-2-3)	121.5	A(2-1-21)	117.2	R(23-36)	0.952
A(1-6-22)	121.9	A(1-2-23)	118.5	A(1-2-3)	121.8	R(19-33)	1.962
A(3-2-21)	120.2	A(6-1-20)	119.6	A(1-2-22)	117.9	A(2-1-6)	121.3
A(2-3-4)	123.5	A(1-6-5)	122.6	A(6-1-21)	121.3	A(2-1-21)	119.1
A(2-3-8)	120.8	A(1-6-24)	121.8	A(1-6-5)	122.7	A(1-2-3)	121.5
A(4-3-8)	115.8	A(1-20-21)	128.1	A(1-6-23)	121.8	A(1-2-24)	118.5
A(3-4-5)	114.4	A(1-20-22)	116.6	A(3-2-22)	120.3	A(6-1-21)	119.6
A(3-4-7)	111.8	A(3-2-23)	119.9	A(2-3-4)	123.5	A(1-6-5)	122.6
A(3-4-9)	122.0	A(2-3-4)	123.9	A(2-3-8)	120.8	A(1-6-25)	121.8
A(5-4-7)	114.6	A(2-3-8)	120.5	A(4-3-8)	115.8	A(1-21-22)	128.1
A(5-4-9)	84.7	A(4-3-8)	115.6	A(3-4-5)	114.4	A(1-21-23)	116.6
A(4-5-6)	115.9	A(3-4-5)	114.3	A(3-4-7)	111.8	A(3-2-24)	119.9
A(7-4-9)	106.8	A(5-4-7)	112.1	A(5-4-9)	84.6	A(4-3-8)	115.6
A(4-7-10)	109.7	A(5-4-9)	84.5	A(4-5-6)	115.9	A(3-4-5)	114.3
A(4-7-23)	122.1	A(4-5-6)	116.0	A(4-5-16)	88.0	A(3-4-7)	113.4
A(4-9-15)	94.2	A(4-5-16)	88.2	A(4-5-30)	113.4	A(3-4-9)	122.8
A(4-9-16)	84.3	A(4-5-31)	113.7	A(7-4-9)	106.8	A(5-4-7)	112.1
A(6-5-16)	113.8	A(7-4-9)	106.6	A(4-7-10)	109.7	A(5-4-9)	84.4
A(6-5-29)	110.9	A(4-7-10)	109.2	A(4-7-24)	122.0	A(4-5-6)	116.0
A(5-6-22)	115.5	A(4-7-25)	120.9	A(4-9-15)	94.1	A(4-5-16)	88.3
A(5-16-9)	103.0	A(4-9-16)	84.2	A(6-5-16)	113.8	A(7-4-9)	106.5
A(5-16-28)	115.9	A(6-5-16)	113.1	A(6-5-30)	110.8	A(4-7-10)	109.3
A(9-15-10)	116.6	A(5-16-30)	116.1	A(10-7-24)	124.2	A(6-5-32)	110.6
A(9-15-14)	127.3	A(10-7-25)	123.1	A(7-10-11)	125.4	A(5-6-25)	115.7
A(9-16-28)	141.1	A(7-10-11)	125.3	A(7-10-15)	112.2	A(16-5-32)	113.7
A(11-10-15)	122.3	A(7-10-15)	112.3	A(15-9-16)	120.3	A(5-16-9)	103.1
A(10-11-12)	118.4	A(15-9-16)	122.2	A(9-15-10)	116.6	A(5-16-31)	116.1
A(10-11-24)	120.2	A(9-15-10)	116.8	A(9-15-14)	127.3	A(10-7-26)	123.1
A(10-15-14)	116.1	A(9-15-14)	127.1	A(9-16-29)	141.1	A(7-10-11)	125.3
A(11-12-13)	120.9	A(11-10-15)	122.3	A(10-11-12)	118.4	A(15-9-16)	122.0
A(11-12-25)	120.1	A(10-11-12)	118.5	A(10-11-25)	120.2	A(9-15-10)	116.8

A(13-12-25)	119.0	A(10-11-26)	120.2	A(10-15-14)	116.1	A(9-15-14)	127.1
A(12-13-14)	120.8	A(10-15-14)	116.1	A(12-11-25)	121.3	A(9-16-31)	140.9
A(12-13-26)	119.0	A(12-11-26)	121.3	A(11-12-13)	120.9	A(11-10-15)	122.3
A(14-13-26)	120.2	A(11-12-13)	120.8	A(11-12-26)	120.1	A(10-11-12)	118.5
A(13-14-15)	121.5	A(11-12-27)	120.1	A(13-12-26)	119.0	A(10-11-27)	120.2
A(13-14-27)	121.3	A(13-12-27)	119.0	A(12-13-14)	120.7	A(10-15-14)	116.1
A(15-14-27)	117.2	A(12-13-14)	120.7	A(12-13-27)	119.0	A(12-11-27)	121.3
A(18-17-19)	114.2	A(12-13-28)	119.1	A(14-13-27)	120.2	A(11-12-13)	120.8
A(17-19-30)	111.2	A(14-13-28)	120.2	A(13-14-15)	121.5	A(11-12-28)	120.1
		A(13-14-15)	121.5	A(13-14-28)	121.3	A(13-12-28)	119.0
		A(13-14-29)	121.3	A(15-14-28)	117.1	A(12-13-14)	120.7
		A(15-14-29)	117.2	A(18-17-19)	117.6	A(12-13-29)	119.1
		A(18-17-19)	114.3	A(17-19-20)	120.2	A(14-13-29)	120.2
		A(17-19-32)	111.2	A(17-19-31)	153.1	A(13-14-15)	121.6
		A(21-20-22)	115.3	A(19-20-31)	102.6	A(13-14-30)	121.3
		A(20-22-33)	109.3	A(19-20-32)	111.7	A(15-14-30)	117.2

PHYSICAL PROPERTIES

Depending on the Semi-empirical method of calculation according to the (PM3) is calculate some physical properties of the molecules studied in this research; Dipole moments (μ in Debye) , energies (e V) of the high occupied Molecular Orbital (E_{HOMO}) and the lower unoccupied molecular orbital (E_{LUMO}) . The higher HOMO energy value shows the molecule is a good electron donor, on the other hand the lower HOMO energy values indicated that a weaker ability of the molecules donating electron. LUOM presents

The ability of a molecule for receiving electron .The negative E_{HOMO} is equal to the ionization potential .Also energy difference (**ΔE) ,** was calculated , and finally molecular hardness (**η**=1/2(E_{HOMO} −E_{LUMO}) , electron affinity (EA= -E_{LUMO}) were calculate[25,27] .The HOMO and LUMO of a molecule play important role intermolecular interaction through the interaction between the HOMO of the drug with the LUMO of the receptor and versa . The interaction stabilized inversely proportional with energy gap between the interaction orbitals, Increasing HOMO energy and decreasing LUMO in the drug molecules lead to enhancement stabilizing interactions, and hence, binding with the receptor with the receptor. The results have shown that compound

(**COOH-DF- CH_2COOH**) has high value for each of (Dipole moments , IP, Electron Affinity E_A),And less value (E_{LUMO}) , this means that this compound has more ability to lose electrons and be easier ionization compared to other compounds .and also results showed **DF- CH_2COOCH_3** compound has higher electrophilic , higher Ha(dness(η) , lower energy gap (**ΔE)** and lower dipolmoment **(Table 2) ,** which may be explained the highest anti-inflammatory compound

The MOPAC computational packages (semi-empirical method , AM1 model) employed to compute physical properties; heats of formation (ΔH_f KJ / mol) .The results showed **COOH-DF-CH_2COOH** compound has lower heat of formation (more stability), Whereas the compound (**DF-CH_2COOH**)has a higher heat formation (less stability) perhaps due this result to the effect of the group substitutes for the stability the compound , as previously mentioned reason.

Table 2:Values of ΔHf (KJ.mol^{-1}), μ (in Debye) , Orbital energies (E_{HOMO}, E_{LUOM}, ΔE in eV) , IP (in eV) , E_A (in eV) , and η (in eV) for the derivatives of [2-(2,6-dichloro-anilino) phenyl] acetate .

Comp.	ΔH_f KJ/mol	μ Debye	E_{HOMO}	E_{LOMO}	ΔE	IP	E_A	η

DF-CH_2COOH	-530.218	4.716	-9.1341	-1.5211	7.6130	9.1341	1.5211	-3.8065
COOH-DF- CH_2COOH	-568.357	6.1287	-9.4288	-1.7083	7.7205	9.4288	1.7083	-3.8602
DF- $CH_2COOCH3$	-83.454	4.4360	-9.1003	-1.4972	7.6031	9.1003	1.4972	-3.8015
COOH-DF-$CH_2COOCH3$	-517.886	5.9405	-9.3948	-1.6737	7.7211	9.3948	1.6737	-3.8606

Thermodynamics functions

Thermodynamics functions for the studied molecules were listed in **Table 3**. Compared with the (R- CH_2COOH, COOH-R- CH_2COOH, R-$CH2COOCH_3$, COOH-R-CH_2COOCH_3) molecules along with the rotational constants, obtained in this study, where used to calculate the vibration and rotation contributions to the thermodynamic functions according to the statistical thermodynamic equations[32,33]

$$U_{vib}^{0} = \sum_{i=1}^{3N-6} \frac{R T X_i}{e^{X_i} - 1} \quad \text{----------(1)}$$

$$X_i = \frac{1.44\bar{\nu}}{T} \quad \text{----------(2)}$$

$$S_{vib}^{0} = R \sum_{i=1}^{3N-6} \left[\frac{X_i}{e^{X_i} - 1} - \ln\left(1 - e^{-X_i}\right) \right] \quad \text{----------(3)}$$

$$S_{rot}^{0} = R \left[\frac{3}{2} + \ln \frac{8\pi^2 \left(8\pi^2 I_X I_Y I_Z\right)^{\frac{1}{2}} (KT)^{\frac{3}{2}}}{\sigma \hbar^3} \right] \quad \text{----------(4)}$$

[34,35]

Both -COOH, $COOCH_3$ substituent's in same compound causes an increase in all thermodynamics functions [E^o, H^o, G^o, A^o, C_V, C_P, S^o] due to its stabilization by resonance effect. COOH-DF- CH_2COOCH_3> DF- CH_2COOCH_3> COOH-DF- CH_2COOH > DF- CH2COOH, The deferent thermodynamics functions values due to deferent substituted groups.

Table 3: ***The calculated standard thermodynamics functions at 298.15oK of the derivatives of [2-(2,6-dichloro-anilino) phenyl] acetate.***

Comp.	E^0 KJ/mol	H^0 kJ/mol	G^0 kJ/mol	S^0 kJ/mol.deg	A^0 KJ/mol	Cp KJ/mol.deg	Cv K J/mol.deg
R- CH2COOH	629.528	3107.1	2943.15	0.5501	2779.20	8.5793	0.2653
COOH-R- CH2COOH	679.185	3156.75	2971.88	0.6205	2787.03	8.6225	0.3085
R- CH2COOCH3	703.033	3180.61	3006.59	0.5839	2832.58	8.6007	0.2867
COOH-R-CH2COOCH3	752.630	3230.20	3034.58	0.655	2839.55	8.6439	0.3299

THE CHARGES

The Calculated for all charges atoms of the molecules studied according to the method (PM3) have shown calculation results of the charges **(Table: 4)**are each of the (O_{19}) has higher value of charge in the case of compound (DF-CH2COOH) as result of this difference in electrical negative and molecular weight as:

DF-CH_2COOH > COOH-DF- CH_2COOH > DF- CH_2COOCH_3 > COOH-DF-CH_2COOCH_3

Where the atom (C_{11}, C_{13}) have the highest value than the other atoms in the first rings **fig 1** , that means the group substitutes prefer to direct towards the site meta ,while the second substituted prefer to direct towards the site ortho on C_1.

Table:4 Calculated charge for the derivatives of [2-(2,6-dichloro-anilino) phenyl] acetate.

R- CH_2COOH		COOH-DF- CH_2COOH		DF- CH_2COOCH_3		COOH-DF-CH_2COOCH_3	
Atom	Charge	Atom	Charge	Atom	Charge	Atom	Charge
C1	-0.1120	C1	-0.1296	C1	-0.1121	C1	-0.1298
C2	-0.0570	C2	-0.0265	C2	-0.0591	C2	-0.0286
C3	-0.1273	C3	-0.1381	C3	-0.1254	C3	-0.1363
C4	-1.0725	C4	-1.0633	C4	-1.0713	C4	-1.0611
C5	0.2682	C5	0.2554	C5	0.2677	C5	0.2547
C6	-0.0940	C6	0.0006	C6	-0.0942	C6	0.0009
N7	0.2863	N7	0.2733	N7	0.2856	N7	0.2741
Cl8	0.0901	Cl8	0.0874	Cl8	0.0902	Cl8	0.0871
Cl9	4.1579	Cl9	4.1596	Cl9	4.1582	Cl9	4.1603
C10	0.2100	C10	0.2107	C10	0.2099	C10	0.2107
C11	-0.2190	C11	-0.2161	C11	-0.2187	C11	-0.2163
C12	0.0918	C12	0.0938	C12	0.0912	C12	0.0930
C13	-0.2095	C13	-0.2051	C13	-0.2098	C13	-0.2056
C14	0.1935	C14	0.1931	C14	0.1936	C14	0.1929
C15	-1.6751	C15	-1.6757	C15	-1.6722	C15	-1.6739
C16	-2.1413	C16	-2.1378	C16	-2.1405	C16	-2.1373
C17	-0.5934	C17	-0.5981	C17	-0.6145	C17	-0.6201
O18	-0.2674	O18	-0.2626	O18	-0.2549	O18	-0.2504
O19	-0.2625	O19	-0.2624	O19	-0.2184	O19	-0.2182
H20	0.1112	C20	0.4306	C20	0.0605	C20	0.0613
H21	0.1210	O21	-0.3981	H21	0.1108	C21	0.4307
H22	0.1172	O22	-0.2989	H22	0.1208	O22	-0.3987
H23	0.0952	H23	0.1375	H23	0.1168	O23	-0.2991
H24	0.1305	H24	0.1331	H24	0.0945	H24	0.1374
H25	0.1027	H25	0.0968	H25	0.1303	H25	0.1328
H26	0.1257	H26	0.1321	H26	0.1025	H26	0.0964
H27	0.1179	H27	0.1042	H27	0.1254	H27	0.1318
H28	0.3022	H28	0.1270	H28	0.1171	H28	0.1039
H29	0.0848	H29	0.1180	H29	0.3018	H29	0.1266
H30	0.2246	H30	0.3031	H30	0.0843	H30	0.1168
		H31	0.1006	H31	0.0470	H31	0.3027
		H32	0.2268	H32	0.0438	H32	0.1001
		H33	0.2284	H33	0.0386	H33	0.0481

Aim of research

Aim of research

Diclofenac it is one of the pain medications used to treat the chronic pain of some diseases. Defolac is considered an anti-uric acid solution when using medicines that raise

the level of acid in the blood**.** So the aim of this theoretical study:

1) To help with analysis and interpretation of experimental data of **Diclofenac**
2) To help solve problems and hint solutions before doing experiments
3) To predict the properties of diclofenac derivatives, some quantities are difficult or impossible to calculate experimentally
4) To know molecular structures of Diclofenac derivatives: closely tied to energy (best structure - one for which the energy is minimum)
5) To know which compound, have more activty and the best compound using as anti-inflammatory drugs.

Recommendations

1) Future studies should focus on function of Diclofenac to reduce inflammation.
2) More studies must be carried out to determine the importance of o increase the blood pressure in patients with diabetes and Shy-Drager syndrome
3) Further investigations are necessary to understand the relationships between cancer and Diclofenac
4) Studies must be permanent that these matches to the active site of adrenergic receptors in order to determine any persistence that has a biological effect

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