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In silico evaluation of Molecular Structure, Vibrational Spectra and Substitution Effect of Hydantoin.

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ABSTRACT

In this study the Molecular geometry optimization, vibrational frequencies, energy gaps, net charges, dipole moments and heats of formation Hydantoin at the ground state, in present work, we have been calculated and performed by using the Molecular Mechanics, PM3, ab initio/HF and DFT/B3LYP methods basis set in order to obtain optimized geometrical parameters are in good agreement with experimental values. Comparison of the obtained fundamental vibrational frequencies of hydantoin result by DFT/B3LYP (6-311G++ (d, p)) method, are in a close agreement with the experimental data. Ab initio/HF with 6-31G basis set was used to investigate the effects of a variety of substituants (methyl ,dimethyl, trimethyl ,and chloride ,dichloride ,trichloride) on the electronic properties of hydantoin derivatives. Detailed vibrational wave number shifts and vibrational mode analyses were reported.

Keywords: in silico**,** hydantoin, imidazolinide-2, 4-dione, vibrational frequencies, substituent effect.

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INTRODUCTION

Hydantoin (2, 4-imidazolidinedione, glycol urea) was first discovered by Bayer in 1861 as a hydrogenation product of all Antoin and its derivatives are important intermediates in the synthesis of several amino acids [1] and are also used as anticonvulsants [2] or antibacterial. The hydantoin, also known2, 4-imidazolidinedione is a saturated heterocyclic imidazole derivative compound. It has two functions lactams (cyclic amide).

The Hydantoin can be obtained from urea or glycine. It can be seen as the product of the condensation of urea twice and glycolic acid. Hydantoin properties are relatively similar to those of the imidazolidine (completely saturated derivative of imidazole), although having carbonyl functions on carbons 2 and 4 of the cycle. Cases of inflammatory syndromes induced by Hydantoin (lymphadenopathy, self-anticorps) [3] are reported. We called Hydantoins substituted Hydantoin derivatives. These compounds shave relatively similar properties to that of imidazolidines, saturated derivatives of imidazoles. They are used in pharmacy as antiepileptic these include among pharmaceutical compounds Hydantoin category ethotoin, phenytoin, mephenytoin and fosphenytoin. Hydrations are biologically active molecules widely used in medicine as antiepileptic, antischisto_somal, antiarythmic, antibacterial and tuberculostatic drugs [4, 5]. It is also an effective medication for the treatment of metastatic prostate cancer. It is the parent compound of antiepileptic drug biphenyl hydantoin [6]. A Hydantoin derivative shows biological activity against human parasites like trematodeos [7].

Beside its medical usage it's also used as herbicides and fungicides [8, 9]. In recent years, the theoretical study of geometry and electronic structures has proved to be very efficient to predict the physical-chemistry properties of large systems [10-11]. The theoretical calculation of vibrational properties is used to understand the spectra's of large number of donor-acceptor systems [12-13]. Consequently, these calculations can be performed at different accuracy levels depending on the aim of the theoretical study. The substituants attached to the molecular framework can enhance or diminish the reactivity. The mechanistic conclusions based on the linear relationships with free energy have been extremely fruitful. The substituants were variable donating and withdrawing to study the effect of such change on the geometric, electronic and vibrational properties of the studied molecules. Accordingly, changes in reactivity in one reaction series caused by changes in substitution are related to changes in equilibrium or reactivity in another series caused by the same changes in substitution [14-15].Accordingly, objective of the present research is to study the geometric, electronic and vibrational spectra will characterize and predict the molecular and spectroscopic properties of hydantoin. Thus, in this work we have studied of the substituent groups effects at different positions in the hydantoin ring.

In this study, we have calculated the structure of hydantoin and derivatives by using ab initio/HF and DFT/B3LYP methods [16-17].

COMPUTATIONAL DETAILS

Initial calculations were optimized using HyperChem 8.03 software [18]. The geometries of hydantoin and its derivatives; were first fully optimized by molecular mechanics, with MM+ force-field (rms = 0.001 Kcal/Å). Further, geometries were fully re-optimized by using PM3 method [19]. In the next step, a parallel study has been made using Gaussian 09 program package [20-21], at various computational levels, HF/6-31G+, 6-31G++ (d,p), 6-311G++ (d,p),and B3LYP/6-31G+, 6-31G++ (d,p), 6-311G++ (d,p). The calculated results have been reported in the present work.

RESULTS AND DISCUSSION

Molecular geometry of Hydantoin:

The molecular structure of hydantoin is shown in (Figure 1). With this structural model, hydantoin belongs to Cs point group symmetry. The optimized geometrical parameters of hydantoin by ab initio/HF and DFT method have been depicted and compared with experimental parameters [22] obtained from the crystal structure analyses of hydantoin in (Table 1).

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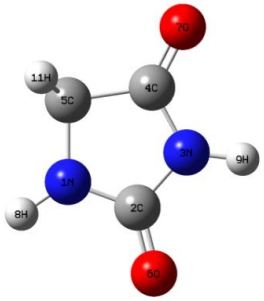

Fig 1: Conformation 3D of molecular structure and atom numbering adopted in this study for hydantoin (GaussView 09)

Thus, in this work was revealed good between the experimentally obtained values data are in good agreement with the theoretical calculations for bond lengths, bond angles and dihedral angles. The nearly of the calculated geometries from the experimental parameters are 1,364A° (C2–N1) at B3LYP/DFT, 1,39A°(C2–N3) and 1,517A°(C4-C5) at ab initio/HF ,and 1,367A°(N3-C4)at B3LYP/DFT or ab initio/HF for the bond lengths and 128,373°(O6-C2-N1),105,77°(C5-C4-N3) at ab initio/HF basis sets for the bond angles. On the other hand dihedral angles 4° (C5-N1-C2-N2) and 176,978° (O4-C4-C5-N1) which is close to the currently accepted experimental values.

Vibration frequencies of Hydantoin:

IR spectroscopy can give a great deal of information on small ring heterocyclic, because of the effects of ring strain on the frequencies of vibration of substituants attached to the ring, and because the ring vibrations fall into a readily accessible region of the IR spectrum [23, 33 and34].Experimental and theoretical (DFT_B3LYP/6–31G++ (d, p)) vibrational wave numbers of Hydantoin were given in Table 2. Hydantoin consists of 11 atoms, which has 27 normal modes. These normal modes of the title molecule have been assigned according to the detailed motion of the individual atoms.

All normal modes assigned to one of 21 types of motion

(C–H, C=O, C–H, and N–H stretching's; HCH, CCN, CCH, NC=O, CC=O, NCN, CNC, CNH, and NCH bindings, and HNC=O, OCCH, HCNH, NCNH, CNC=O, NCCN, CNCC, and NCNC twisting)The asymmetric C-H stretching frequency decreases with increasing ring size, predicted by a calculation analysis. The results obtained from the calculations show that, while the harmonic corrections of wave numbers are closer to the experimental ones rather than wave numbers of forms gave the best fit to the experimental ones. The vibrational wave numbers of the forms of hydantoin obtained fr

om the DFT calculations are almost the most the same except one value 429,743$Cm^{-1}$of mode 4at ab-initio.

The diatomic molecules have only one link, which can be stretched. The more complex molecules have many connections, and vibration maybe combined, leading to the infrared absorption at the characteristic frequencies which can be linked to chemical groups. For example, atoms ofCH2, which is commonly found in organic compounds, can vibrate in six different ways: stretching and skew symmetric, scissoring, and rocking, agitation outside plane waggingandtwistingv_1 (NH) stretching mode for monomer was observed at (moderate intensity) (3599,8–3570,24 cm–1),v_2 CH2 group (C5-H10,C5-H11) wave numbers symmetric and asymmetric stretching mode was observed at (2979,43 and 3023,23Cm^{-1}) with twisting ,waging and scissoring the absorption in the large 428Cm^{-1}, 429,743428Cm^{-1} ,429,7797428$Cm^{-1}$and 433,4412428Cm^{-1} the experimental values in good agreement with that obtained from ab-initio/HF theory using basis 6-31G+(d,p)set and 6-311G++(d,p) .

v_3 C2=O6 and ν C4=O7 stretching modes were observed with I-R intensity at 200, 371623Cm^{-1} and frequency 1864,9723Cm^{-1}These considerations thus provide additional support. Cyclic imides represent an important class of compounds in medicinal chemistry due to its large spectrum of biological activities [23, 35].

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Table 1: Comparison of the experimental and calculated values of bond lengths and bond angles of Hydantoin

Parameters	Exp.	ab initio/HF			DFT(B3LYP)		
Bond Length (A°)	[22]	6-31G+(d,p)	6-31G++(d,p)	6-311G++(d,p)	6-31G+(d,p)	6-31G++(d,p)	6-311G++(d,p)
C2-O6	1,222	1,19183	1,19188	1,18516	1,21581	1,21583	1,20705
C2-N1	1,371	1,3556	1,35556	1,35568	1,36382	1,36379	1,36137
C2-N3	1,393	1,3899	1,38991	1,39025	1,40388	1,40390	1,40267
N3-C4	1,367	1,3662	1,3662	1,36635	1,36987	1,36987	1,36775
C4-O7	1,225	1,18847	1,18850	1,18216	1,21483	1,21482	1,20641
C4-C5	1,460	1,5218	1,52188	1,52148	1,51962	1,51967	1,51714
C5-N1	1,457	1,4433	1,44329	1,44259	1,43253	1,43253	1,43006
Bond angle(°)							
O6-C2-N1	128,2	128,3769	128,373	128,438	128,646	128,649	128,752
O6-C2-N3	124,4	125,744	125,745	125,761	126,085	126,083	126,115
N3-C2-N1	107,4	105,879	105,883	105,801	105,269	105,268	105,133
C4-N3-C2	111,67	113,309	113,310	113,406	113,430	113,432	113,578
O7-C4-C5	125,3	127,070	127,075	127,089	127,121	127,120	127,125
C5-C4-N3	106,8	105,770	105,768	105,655	105,259	105,257	105,117
N1-C5-C4	104,7	101,820	101,823	101,919	102,843	102,842	102,926
C2-N1-C5	109,4	113,221	113,217	113,219	113,199	113,202	113,246
Dihedral angles(°)							
C5-N1-C2-N2	4,1	4,5	4,6	5,4	4,0	4,0	3,0
N1-C2-N2-C4	6,7	3,6	3,7	4,3	1,9	1,9	3,0
O2-C2-N1-C5	176,1	179,985	179,984	176,984	179,978	179,978	176,979
O4-C4-C5-N1	176,0	179,989	179,991	179,985	176,0	179,987	179,987

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Table 2: Comparison of the experimental and calculated vibrational spectra of hydantoin.

Mode N^0	Symmetry	EXP. IR [24]	ab- initio/HF			DFT(B3LYP)			Assignment
			6-31G+(d,p)	6-31G++ (d,p)	6-311G++ (d,p)	6-31G+ (d,p)	6-31G++ (d,p)	6-311G++ (d,p)	
1	A		-10.2319	-15.0455	-97.6155	122.4518	123.4995	128.5824	ν N1_H8
2	A		150.6568	151.1778	138.5342	148.0355	148.3966	144.7564	νN3_H9
3	A		386.5634	387.9254	378.1519	380.9977	380.9031	385.3754	νasC5_H10 andνasC5_H11
4	A	428	429.7797	429.743	433.4412	382.4965	385.0823	389.9752	νsymC5_H10 and C5_H11
5	A	554	598.0108	598.9993	588.1646	534.4869	534.4075	540.4346	νN1_H8,νC2=o6 and νC4=o7
6	A		602.3857	602.405	606.8822	542.3242	542.2391	545.114	ωC5_H10,ωC5_H11and νN1_H8,N3_H9and τ C2=O6,C4=O7
7	A	580	650.0336	649.6981	646.1346	596.9489	597.2729	601.288	δC5_H10,δC5_H11 and ν N1_H8
8	A	632	687.2993	687.323	686.8045	622.5079	622.4737	624.1676	δC5_H10,δC5_H11 and ν N1_H8
9	A	670	766.4352	766.4259	766.2077	766.4014	698.4869	701.9823	δC5_H10,δC5_H11 and ν N1_H8
10	A	719	842.3027	842.9322	852.636	728.4884	728.9946	746.5964	τ N3_H7 and νC5_H10
11	A	785	956.7526	956.6458	953.9418	884.0849	883.9607	882.9414	ωC5_H10,ωC5_H11and νN1_H8,N3_H9andτC2=O6,C4=O7
12	A	899	1063.4758	1063.4445	1059.8529	969.6732	969.365	968.2432	ωC5_H10,ωC5_H11and νN1_H8,N3_H9and νC4=O7
13	A		1122.0938	1121.9287	1119.2377	971.2799	971.2526	968.2617	τC5_H10, τ C 5_H11
14	A	990	1165.4106	1165.3967	1162.911	1073.971	1074.1322	1072.2072	ωC5_H10,ωC5_H11 and ν N1_H8
15	A	1075	1304.8551	1304.5813	1301.5487	1144.4085	1143.4119	1147.0616	ωC5_H10,ωC5_H11,ωN1_H8and ωN3_H9
16	A		1313.5705	1313.393	1303.747	1182.4483	1182.6149	1175.6719	τ C 5_H10,τC5_H11and νC4=O7
17	A	1197	1455.1549	1455.3184	1450.1199	1269.5502	1269.5006	1265.0279	ωC5_H10,ωC5_H11,νN1_H8andνN3_H9
18	A	1287	1455.1532	1506.7196	1502.0856	1313.136	1312.9686	1307.5245	νC2=O7
19	A	1377	1529.991	1581.9712	1522.1306	1363.731	1363.6334	1361.2266	ωC5_H10,ωC5_H11and νN1_H8,νN3_H9
20	A	1429	1582.1884	1581.9712	1575.1308	1400.1721	1399.7912	1392.09	ω C5_H10,ω C5_H11andνC2=O6,νN3_H9,νC4=O7
21	A		1632.6486	1633.0206	1627.3155	1434.5981	1434.5353	1426.929	τC5_H10,τC5_H11and νN3_H9
22	A	1696	1994.0682	1993.8253	1986.6061	1826.3929	1826.2343	1822.838	ρC5_H10,ρC5_H11andνN3_H9
23	A	1774	2038.8534	2038.7555	2031.0495	1865.0979	1864.9699	1863.2827	ωC5_H10,ωC5_H11andνN1_H8,νN3_H9
24	A	2944	3225.3185	3225.3719	3207.6462	2979.6648	2979.4272	2966.5839	νN1_H8,νC5_H10and νC5_H11
25	A		3271.4889	3271.475	3249.9602	3023.3671	3023.2278	3006.1303	ωN1_H8, ωC5_H10,ωC5_H11and νC2=O6,νC4=O7
26	A	3130	3892.6359	3892.586	3875.3775	3570.2473	3570.2409	3554.3144	νC5_H10,νC5_H11andνN3_H9
27	A	3257	3925.6805	3925.4852	3907.0397	3600.002	3599.8007	3584.495	τ N 1_H8,ρC5_H10,ρC5_H11and ωN3_H9

IR_{exp}: Experimental Infrared; asym: asymmetric; sym: symmetric; ν: bond stretching δS: scissoring; τ: twisting; ω: wagging; ρ: rocking;

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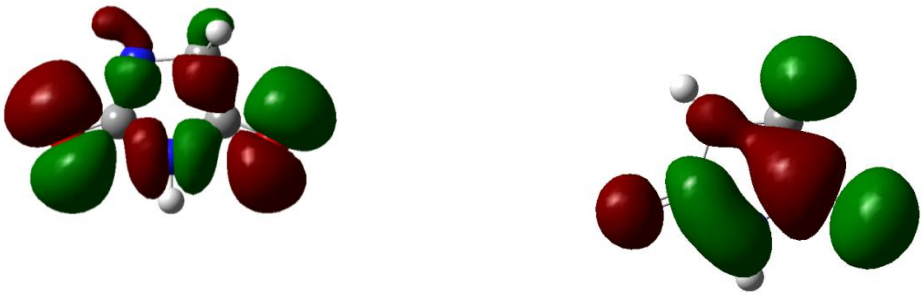
Electronic properties of Hydantoin:

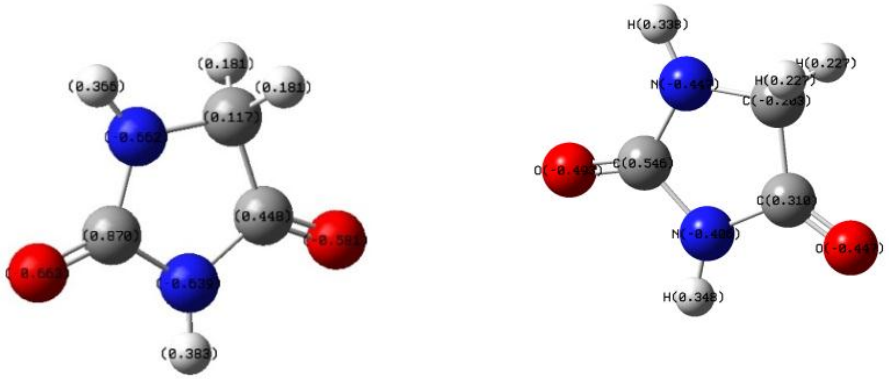
Highest occupied molecular orbital (HOMO) and lowest unoccupied molecular orbital (LUMO) are very important parameters for quantum chemistry. We can determine the way the molecule interacts with other species; hence, they are called the frontier orbitals [25]. Energies of the HOMO and the LUMO are very popular quantum chemical descriptors. The HOMO represents the ability to donate an electron; their energy is directly related to the ionization potential and characterizes the susceptibility of the molecule to attack by electrophiles. On the other hand, the LUMO as an electron acceptor; their energy is directly related to the electron affinity and characterizes the susceptibility of the molecule to attack by nucleophiles [26]. HOMO and LUMO energies, energy gap (ΔE = EHOMO-ELUMO) and dipole moments of Hydantoin calculated at ab initio/HF and B3LYP/DFT in 6-31G basis set is given in (Figure 2).The value of energy gap (ΔE) between HOMO and LUMO energies is -0, 1662 a.u. obtained at DFT/B3LYP (6-311G) whereas the (ΔE) is -0,36899a.u. Obtained at HF/ab initio (6-31G) .Atomic charges of hydantoin, which have been calculated by Mullikan method at the ab initio/HF (6–31G), and DFT/ B3LYP (6–31G) levels of calculation are shown in below (Figure 3).



(b) (a)

Fig 2: 3D plot of (a) LUMO and (b) HOMO of the hydantoin (DFT/B3LYP (6-311G (d,p)

Atomic charges of Hydantoin, which have been calculated by Mullikan method at the ab initio/HF (6–31G) and DFT/ B3LYP (6–31G) levels of calculation are shown in below (Figure 3).



ab initio/HF (6-31G(d,p)) DFT/B3LYP(6-31G(d,p))

Fig 3: The Mulliken charges (Q_M) of hydantoin

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Shows that the atoms N1, N2, C5 and O6,O7 have negative Mullikan charges which leads to electrophilic substitution, whereas at the atom C2,C3 have positive Mullikan charge which lead to preferential site nucleophilic attack.

Substituent effects on the electronic structure in hydantoin and derivatives:

Substituent effects play a fundamental role in a variety of observed physical and chemical phenomena. For example, substituent effects influence the rates of nucleophilic substitutions and the molecule's reactivity, [27] vibrational specter, [28] acid-base properties, [29] the conformations of molecules, and so forth. The calculated values of (methyl, chloride) substituted hydantoin are given in Table 4, Table 5, Table 6, Table 7, Table 8 and Table 9. The chemical structures of the compounds studied of hydantoin and derivatives are shown in (Figure 4)/ (Table 3). In (Table 4), Table 6 and Table 8, HOMO and LUMO energies, energy gaps ΔE, heat of formation and dipole moments are reported for hydantoin and its derivatives. In Table 5, Table 7 and Table 9 net atomic charges are also reported.

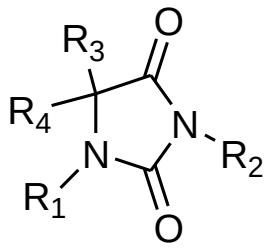

Fig 4: Structure of hydantoin derivatives

Table 3: Series of hydantoin and group's substituted hydantoin

Compound	R_1	R_2	R_3	R_4
Hydantoin	H	H	H	H
Series 1				
A1	CH3	H	H	H
A2	H	CH3	H	H
A3	H	H	CH3	H
A4	H	H	H	CH3
A5	CH3	CH3	H	H
A6	CH3	H	CH3	H
A7	H	CH3	CH3	H
A8	H	CH3	H	CH3
A9	H	H	CH3	CH3
A10	CH3	H	H	CH3
A11	CH3	CH3	CH3	H
A12	CH3	H	CH3	CH3
A13	H	CH3	CH3	CH3
A14	CH3	CH3	H	CH3
Series 2				
B1	Cl	H	H	H
B2	H	Cl	H	H
B3	H	H	Cl	H
B4	H	H	H	Cl
B5	Cl	Cl	H	H
B6	Cl	H	Cl	H

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B7	Cl	H	H	Cl
B8	H	Cl	Cl	H
B9	H	H	Cl	Cl
B10	H	Cl	H	Cl
B11	Cl	Cl	Cl	H
B12	H	Cl	Cl	Cl
B13	Cl	H	Cl	Cl
B14	Cl	Cl	H	Cl
Series 3				
C1	CH3	Cl	H	H
C2	Cl	CH3	H	H
C3	CH3	H	Cl	H
C4	CH3	H	H	Cl
C5	Cl	Cl	CH3	CH3
C6	Cl	Cl	Cl	CH3
C7	CH3	CH3	CH3	Cl
C8	CH3	CH3	Cl	Cl
C9	CH3	Cl	Cl	Cl
C10	Cl	CH3	CH3	CH3
C11	CH3	CH3	CH3	Cl
C12	Cl	Cl	Cl	CH3
C13	CH3	Cl	CH3	CH3
C14	Cl	CH3	Cl	Cl

Table 4: Energies of hydantoin and derivatives (series1):

Compound	System	Heat of formation Kcal/mol	HOMO(a.u)	LUMO(a.u)	ΔE(a.u)	μ(D)
Hyd	Hydantoin	-78,79776133	-0,42345	0,05446	0,36899	3,2857
A1	1-methyl hydantoin	-78,7978101	-0,39690	0,05901	0,33789	3,6195
A2	2-methyl hydantoin	-77,6590342	-0,40865	0,0552	0,35345	2,4968
A3	3-methyl hydantoin	-86,3483048	-0,42878	0,05919	0,36959	3,3385
A4	4-methyl hydantoin	-86,3483048	-0,4287	0,05920	0,36959	3,3380
A5	1-2 dimethyl hydantoin	-79,4127366	-0,38677	0,06152	0,32525	2,8278
A6	1-3 dimethyl hydantoin	-79,4127357	-0,38676	0,06153	0,32523	2,8271
A7	2-3 dimethyl hydantoin	-87,1501982	-0,41630	0,05935	0,35695	2,6060
A8	2-4 dimethyl hydantoin	-87,1596230	-0,41630	0,05937	0,35693	2,6038
A9	3-4 dimethyl hydantoin	-92,6008067	-0,42509	0,06196	0,36313	3,4735
A10	1-4 dimethyl hydantoin	-87,2730850	-0,40393	0,06122	0,34271	3,5864
A11	1-2-3 trimethylhydantoin	-88,0193806	-0,39734	0,06158	0,33576	2,8173
A12	1-3-4 trimethylhydantoin	-88,0220162	-0,39031	0,06157	0,32874	3,9191
A13	2-3-4 trimethylhydantoin	-93,3863432	-0,41430	0,06244	0,35186	2,7222
A14	1-2-4 trimethylhydantoin	-88,0325819	-0,39748	0,06157	0,33591	2,8123

Heat of formation by PM3/HOMO, LUMO, ΔE and μ by ab initio/HF (6-31G+ (d,p)

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Table 5: Mullikan charges of hydantoin and derivatives (series1):

Comp.	Hydantoin	A1	A2	A3	A4	A5	A6	A7	A8	A9	A10	A11	A12	A13	A14
1N	-0,662	-0,436	-0,658	-0,565	-0,565	-0,437	-0,437	-0.560	-0.560	-0.506	-0.356	-0.354	-0.300	-0.510	-0.354
2C	0,869	0,845	0,826	0,774	0,774	0,709	0,709	0.722	0.722	0.790	0.766	0.654	0.871	0.727	0.653
3N	-0,639	-0,657	-0,441	-0,603	-0,603	-0,482	-0,482	-0.405	-0.405	-0.614	-0.606	-0.420	-0.660	-0.396	-0.420
4C	0,447	0,447	0,378	0,462	0,462	0,337	0,337	0.397	0.398	0.498	0.448	0.350	0.545	0.442	0.350
5C	0,116	0,062	0,098	0,250	0,250	0,088	0,088	0.256	0.256	0.297	0.146	0.223	-0.176	0.312	0.225
6O	-0,663	-0,660	-0,661	-0,470	-0,635	-0,646	-0,646	-0.634	-0.634	-0.638	-0.643	-0.638	-0.655	-0.632	-0.638
7O	-0,581	-0,585	-0,583	0,339	-0,582	-0,584	-0,584	-0.577	-0.577	-0.577	-0.582	-0.576	-0.585	-0.571	-0.576
8C	0,366	0,177	0,176	0,186	0,470	-0,122	-0,122	-0.170	-0.170	-0.387	-0.425	-0.165	-0.406	-0.171	-0.166
9C						-0.093	-0,093	-0.476	-0.476	-0.481	-0.206	-0.445	0.090	-0.411	-0.152
10C										0.375	0.181	0.173	0.163	0.168	-0.446

Net charge calculated by ab initio/HF (6-31G+ (d, p))

We note that the heat of formation decrease approximately 8, 55 kcal/mole at addition of methyl group, 13, 8 Kcal/mole at addition dimethyl/mole group and 14, 59 Kcal/mole at addition trimethyl. In the mono-substituted alkyl group category, the hydantoin showing maximum positive charge on 2th position carbon (0, 8669996) which leads to nucleophile substitution (Table 5). The compound A1 is further supported by the smaller HOMO-LUMO energy gap (0.33789a.u) (Table 5) which depicts the chemical reactivity of the compound; higher is the HOMO-LUMO energy gap, lesser is the flow of electrons to the higher energy state, making the molecule hard and less reactive. On the other hand in smaller HOMO-LUMO gap, there is easy flow of electrons to the higher energy state making it softer and more reactive (HSAB principle: hard and soft acids and bases). Hard bases have highest-occupied molecular orbitals (HOMO) of low energy, and hard acids have lowest-unoccupied molecular orbitals (LUMO) of high energy [30, 31, and 32]. In the case of dimethyl substituted of hydantoin the C-2 position compound (A5) shows, smaller HOMO-LUMO energy gap (0,32525a.u) (Table 5). We also note that the methyl substituent (donor effect) has the effect of increasing the energy of the HOMO, with little change in the LUMO (Table 5). The presence of a donor groups in the C2 and C4 positions causes the decrease in dipole moment (compound A1), the compound (A12) shows maximum dipole moment value (3,9191D) (Table 5) . In the present work, we have studied chloride of substituted hydantoin long the same line of methyl substituted hydantoin for a comparative study.

Table 6: Energies of hydantoin and derivatives (series2):

Compound	System	Heat of formation (Kcal/mol)	HOMO (a.u)	LUMO (a.u)	ΔE (a.u)	μ (D)
B1	1Chloro hydantoin	-74,1649614	-0,42345	0,05446	0,37004	2,4138
B2	2-Chloro hydantoin	-72,8548642	-0,41660	0,04702	0,36958	4,3353
B3	3-Chloro hydantoin	-82,9777505	-0,44696	0,05759	0,389201	1,8814
B4	4-Chloro hydantoin	-82,9777505	-0,44696	0,05759	0,389201	1,8817
B5	1-2-Dichloro hydantoin	-70,0553113	-0,41043	0,05824	0,35219	3,3234
B6	1-3-Dichloro hydantoin	-79,8009974	-0,43018	0,05451	0,37567	1,2144
B7	1-4-Dichloro hydantoin	-79,8009974	-0,43019	0,05450	0,37569	1,2151
B8	2-3 Dichlorohydantoin	-79,0124588	-0,43441	0,05017	0,38424	2,8990
B9	3-4 Dichlorohydantoin	-85,7464978	-0,44976	0,05919	0,27219	1,1926
B10	2-4 Dichlorohydantoin	-79,0124587	-0,43441	0,05017	0,38424	2,8998
B11	1-2-3 Trichlorohydantoin	-75,9042986	-0,43540	0,04971	0,38569	3,2857
B12	2-3-4 Trichlorohydantoin	-81,4208831	-0,43682	0,05758	0,37924	2,0732
B13	1-3-4 Trichlorohydantoin	-81,1562699	-0,43097	0,05710	0,37387	0,3099
B14	1-2-4 Trichlorohydantoin	-74,9048532	-0,43547	0,04970	0,38577	2,1185

Heat of formation by PM3/HOMO, LUMO, ΔE and μ by ab initio /HF (6-31G+ (d, p)

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Table 7: Mullikan charges of hydantoin and derivatives (series 2)

Comp.	B1	B2	B3	B4	B5	B6	B7	B8	B9	B10	B11	B12	B13	B14
1N	-0.475	-0.659	-0.526	-0.526	-0.502	-0.331	-0.331	-0.515	-0.501	-0.515	-0.322	-0.514	-0.252	-0.322
2C	0.870	0.857	0.771	0.770	0.781	0.796	0.796	0.744	0.860	0.744	0.727	0.848	0.918	0.726
3N	-0.652	-0.494	-0.590	-0.589	-0.568	-0.606	-0.607	-0.419	-0.614	-0.420	-0.429	-0.507	-0.642	-0.428
4C	0.438	0.408	0.418	0.418	0.362	0.396	0.396	0.363	-0.640	0.363	0.319	0.431	0.532	0.319
5C	0.093	0.112	0.143	0.143	0.129	0.076	0.076	0.161	0.482	0.161	0.155	0.009	-0.349	0.155
6C									0.002	-0.643	-0.638	-0.656		
6O	-0.628	-0.631	-0.616	-0.616	-0.589	-0.587	-0.587	-0.586	-0.629	-0.586	-0.576	-0.598	-0.596	-0.554
7O	-0.569	-0.549	-0.544	-0.544	-0.537	-0.531	-0.532	-0.508	-0.508	-0.508	-0.493	-0.473	-0.496	-0.493
8Cl	0.153	0.217	-0.015	-0.015	0.240	0.122	0.122	-0.007	0.079	0.184	0.199	0.239	0.222	0.199
9Cl					0.293	0.039	0.039	0.184	0.079	-0.007	0.029	0.088	0.135	0.131
10Cl									0.375	0.182	0.132	0.088	0.136	0.029

Net charge calculated by ab initio/HF(6-31G+(d,p))

The heat of formation is increased approximately 4, 18 Kcal/mol for each addition of chloride group. In mono-substituted chloride derivatives, 2chloro hydantoin (compound B2) is predicted to be more chemically reactive on the basis of least HOMO-LUMO energy gap (0.36958a.u) (Table 6) and shows maximum positive charge (0,87) in carbon C-2 leading to favored site for nucleophilic attack (Table 7). In di-substituted chloride derivatives, the carbon C-2 in 3-4-dichloro-hydantoin (compound B9) shows maximum positive charge (0,861) leading to favored site for nucleophilic attack (Table 7). The compound3-4 -dichloro-hydantoin (B9) is more reactive than2-chloro hydantoin (B2), this is due to smaller HOMO-LUMO energy gap (0.27219) which reflects a chemical stability (Table 6). The tri-substituted hydantoin (compound B13) is predicted to be the most reactive with smaller HOMO-LUMO energy gap (0.37387a.u) (Table 6) and these considerations thus Provide additional support maximum positive charge (0.91795) in carbon C-2 leading to favored site for nucleophilic attack (Table 6) of all hydantoin systems. We note also that the chloride substituent (attractor effect) lowers the energies of HOMO and LUMO, his influence on the energy of the LUMO is more important. The compound B2 shows the maximum dipole moment value (4,3353D), it would be originate from an attractor effect in position C2.

Table 8: Energies of hydantoin and derivatives (series3):

Comp.	System	Heat of formation (Kcal/mol)	HOMO (a.u)	LUMO (a.u)	ΔE (a.u)	μ (D)
C1	2Chloro1methyl Hydantoin	-74,7661312	-0,39908	0,05525	0,34383	4,7539
C2	1Chloro2methyl Hydantoin	-78,6613821	-0,41525	0,06578	0,34978	1,5690
C3	3Chloro1methyl Hydantoin	-84,2207686	-0,42377	0,05962	0,36415	2,3295
C4	4Chloro1methyl Hydantoin	-84,2198834	-0,42374	0,05966	0,36408	2,3270
C5	1-2-Dichloro3-4dimethyl hydantoin	-85,8826626	-0,41802	0,05947	0,35855	3,8543
C6	1-2-3Trichloro 4methyl hydantoin	-83,9253767	-0,43186	0,05459	0,37727	3,0007
C7	4Chloro1-2-3trimethyl hydantoin	-93,0151461	-0,41105	0,06193	0,34501	2,6604
C8	3-4 Dichloro1-2 dimethyl hydantoin	-87,4553305	-0,41403	0,06446	0,34957	1,3357
C9	1Methyl 2-3-4Trichloro hydantoin	-82,3525281	-0,42287	0,05874	0,36413	2,8458
C10	1Chloro 2-3-4 Trimethylhydantoin	-90,5357157	-0,40556	0,06515	0,34041	2,2414
C11	2Chloro 1-3-4 Trimethylhydantoin	-89,7065127	-0,40760	0,05819	0,34941	5,0247
C12	2Methyl1-3-4 Trichlorohydantoin	-82,1378200	-0,42148	0,06047	0,36101	0,7206

Heat formation by PM3/HOMO, LUMO, ΔE and μ by ab initio/HF (6-31G+ (d, p))

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Table 9: Mullikan charges of hydantoin and derivatives (series3)

Comp.	C1	C2	C3	C4	C5	C6	C7	C8	C9	C10	C11	C12
1N	-0.432	-0.351	-0.335	-0.335	-0.224	-0.173	-0.195	-0.226	-0.223	-0.235	-0.238	-0.627
2C	0.749	0.707	0.775	0.776	0.757	0.755	0.683	0.738	0.790	0.723	0.722	0.785
3N	-0.563	-0.413	-0.601	-0.602	-0.434	-0.439	-0.422	-0.466	-0.563	-0.411	-0.434	-0.464
4C	0.373	0.348	0.392	0.393	0.441	0.429	0.412	0.386	0.449	0.404	0.446	0.381
5C	0.097	0.067	0.102	0.102	0.001	-0.138	0.008	-0.215	-0.254	0.071	0.115	-0.243
6C									0.002			
6O	-0.618	-0.592	-0.627	-0.627	-0.565	-0.555	-0.621	-0.602	-0.579	-0.592	-0.606	-0.580
7O	-0.550	-0.562	-0.544	-0.544	-0.525	-0.483	-0.528	-0.507	-0.474	-0.560	-0.537	-0.494
8C	-0.121	-0.162	-0.227	-0.227			-0.169	-0.127	-0.132		-0.173	
8Cl	0.153	0.081	-0.009	-0.009	0.124	0.152				0.111		0.259
9C							-0.154			-0.155	-0.441	-0.108
9Cl	0.270				0.193	0.201			0.294		0.173	
10Cl						0.115		0.090	0.109			0.122
11Cl							0.018	0.089	0.109			0.121
10C					-0.335		-0.448			-0.343	-0.371	
11C					-0.388					-0.414	-0.371	

Net charge calculated by ab- initio/HF (6-31G+(d,p))

The heat of formation is decreased for each addition of methyl group and increased for each addition of chloride group. In the mono-substituted methyl group, the (compound C3 and C4) showing positive charge on 2th position carbon (0,776) and in the mono-substituted chloride group, the (compound C2) showing positive charge on 2th position carbon (0,79) which leads to nucleophilic substitution (Table 9). In mono-substituted chloride derivatives the compound (C1) are predicted to be more chemically reactive on the basis of least HOMO-LUMO energy gap (0,34383a.u) and maximum dipole moment value (4,753D)(Table 8).The di-substituted hydantoin (compound C8) is predicted to be the most reactive with smaller HOMO-LUMO energy gap (0,34957a.u) (Table 8) and positive charge (0, 4428) in carbon C-2 leading to favored site for nucleophilic attack (Table 9). In tri-substituted chloride derivatives, the compound (C10) is more reactive due to smaller HOMO-LUMO energy gap (0,34041a.u) which reflects a chemical stability of all tri-substituted hydantoin systems (Table 8),the compound (C11) with the maximum dipole moment value (5,024D) and more lest smaller HOMO-LUMO energy gap (0,34941a.u) table (8).The different substitutions shown the best small energy(0,27219a.u) compared with all compounds is 3-4 dichlorohydantoin is predicted to be most reactive and the maximum dipole moment value(5,024D) is 2Chloro1-3-4 trimethyl hydantoin involve asymmetric compound and positive charge to best favored site for nucleophilic attack is compound 1chloro hydantoin.

CONCLUSIONS

The present study has confirmed previous conclusions that the aim of this work was qualitative, we are trying to clarify the characterization of hydantoin, throw computational methods. Bond lengths and angles have been calculated by using HF/6-31(G+), 6-31G++(d,p) and 6-311G++(d,p) and B3LYP/6-31(G+), 6-31G++(d,p) and 6-311G++(d,p)methods and compared with experimental values. All compared data have been shown to have a good agreement with each other. We have carried out ab initio and density functional theory calculation on the vibrational spectrum of hydantoin. The vibrational frequencies of infrared intensities with the stretching wave numbers calculated by DFT/B3LYP (6-311++G (d, p)) method agree satisfactorily with experimental results. On the basis of agreement between the calculated and experimental results, assignments of all the fundamental vibrational modes of hydantoin were examined and proposed in this investigation. This study demonstrates that scaled DFT/B3LYP calculations are powerful approach for understanding the vibrational spectra of medium sized organic compounds. In the substituted chloride group, 3-4 dichlorohydantoin is predicted to be the most reactive with least HOMO-LUMO energy gap of all methyl-hydantoin derivatives. The tri-chloroo-hydantoin is predicted to be the most reactive with all chloro and methyl derivatives. The presence of acceptor in B9(3-4dichloro hydantoin) group position causes the decrease

in energy gaps, which reflects a chemical stability and show the maximum dipole moment value in B4(4-Chloro hydantoin) derivatives. Hydantoins constitute an important class of heterocyclic in medicinal chemistry because many derivatives thus can identify activities that offer interesting against a wide range of biological targets.

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