Geometric and Electronic Structural Features of 5, 7- Dimethyloxy-2-Phenyl-Benzopyran-4H-One and its Derivatives and Theoretical Investigation

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Abstract:- *Flavonoids are a class of polyphenolic compounds, most abundantly present in leaves and barks of the plants. Chrysin is a flavonoids widely distributed in nature and has been reported to exibit various biological activites like antibacterical, antioxidant, anti-Inflammatory and anti cancer activity. These activities are largely attributed due to the presence of α, β-unsaturated ketone and hydroxyl functional group of chrysin moiety. Interestingly, by Introducing various substituents into the two aryl rings are a subject of interest because it plays a vital role in structure activity relationship and thus motivates to synthesize pharmacologically active chrysin derivatives. Computational chemistry tools are very useful in designing the reaction and to check the stabilities of the modeled compounds. Here we have modeled various 5, 7-O-disubstituted chrysin derivatives to check their structure stability and also to evaluate their antioxidant and anticancer activites. Theoretical methods are already used successfully for understanding the structure, bonding and properties of pharmacologically important molecules. We have studied the compounds of the type 5, 7- R_2-2-phenylbenzopyran-4H-one where (R = OMe (**2**), OEt (**3**), O (nPr) (**4**), O (isoPr) (**5**), OBu (**6**), OtertBu (**7**), OAc (**8**)] by using semi empirical PM3 and DFT methods. Interestingly our results show that the possible stability of these compounds and four of the compounds are synthesized in lab with the help of our collaborators.*

Key Words: **Chrysin derivatives, PM3, DFT, HOMO, LUMO, Bonding and Stability.**

1. INTRODUCTION

chrysin are a belonging to the family of passiflorance compounds widely distributed in nature, with physicochemical properties of scientific interest. These compounds present benefits in human health because of their biological properties which include activity [1] influenza virus [2] and bacteria, Flavonoids also show antifungal, anticancer [3], anti- inflammatory [4], anti diabeties [5], antiplatelet drugs [6] and antioxidant [7] effects. Latest scientific researches confer antioxidant activity of flavonoids to their skill for linking with enzymes [8].

The structural features of these chrysin and chrysin derivatives deserve more theoretical attention. Computational chemistry tools are being used nowadays for the studying structural features of the compounds of our interest. Here we have studied the possibility of the synthesis of new chrysin derivatives 5,7-R2-2-phenylbenzopyran-4H-one obtained from computed DFT method [where R = OMe (**2**), OEt (**3**), O(nPr) (**4**), O(*iso*Pr) (**5**), OBu (**6**), O*tert*Bu (**7**), OAc (**8**)].

Scientific classification of *Passiflora caerulea*

Kingdom : Plantae

Order : Malpighi ales

Family : Passifloraceae

Genus : Passiflora

Species : *P. caerulea*

Binomial name: *Passiflora caerulea.* L.

COMPUTATIONAL METHODES

The DFT optimized geometries at BP86/TZVP level for the compounds studied are provided in **Figure.1-8.** The PM3 and DFT computed bond parameters are provided in **Tables.1–8**. The PM3 and DFT optimized metrical parameters for the compound Chrysin (1) are in good agreement with those of the experimental values obtained from X-ray crystallography **Table.1**.

The DFT computed bond distance of C=O of carbonyl carbon is 0.18 Å shorter than the experimental values. This may be due to the crystal packing effects in the solid state. The metrical parameters obtained from the semi empirical PM3 and DFT calculations on the new chrysin derivatives 5, 7-R2-2-phenyl benzopyran-4H-one (R = OMe (**2**), OEt (**3**), O (nPr) (**4**), O (*iso*Pr) (**5**), OBu (**6**), O*tert*Bu (**7**), OAc (**8**)] are in good agreement with the experimental values of similar compounds.

Compound **6** has been synthesized with the help of our collaborators and the computed bond parameters are in good agreement with those of the experimental values **Figure.6** and **Table .6**

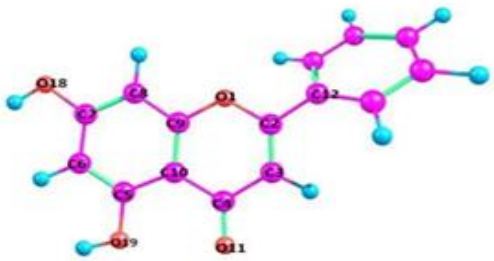

Figure.1: DFT Optimized (BP86/TZVP) geometry for Chrysin

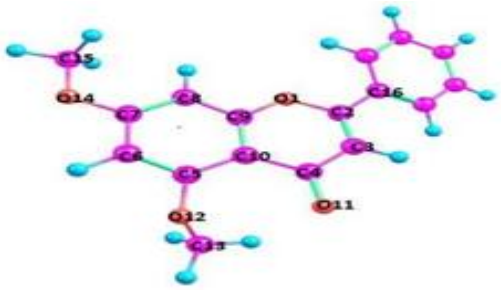

Figure .2: DFT optimized (BP86/TZVP) geometry for the compou 5,7dimethyloxy -2-phenyl benzopyran-4H-one

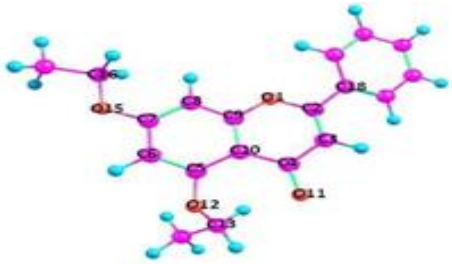

Figure.3: Optimized (BP86/TZVP) geometry for the compound 5, 7-diethyloxy-2-phenyl benzopyran 4H-one

Figure.4: DFT optimized (BP86/TZVP) geometry for the compound 5, dipropyloxy-2-phenyl benzopyran-4H-one

Figure.5: DFT optimized (BP86/TZVP) geometry for the compound 5, 7-di-*iso*propyloxy-2-phenyl benzopyran-4H-one

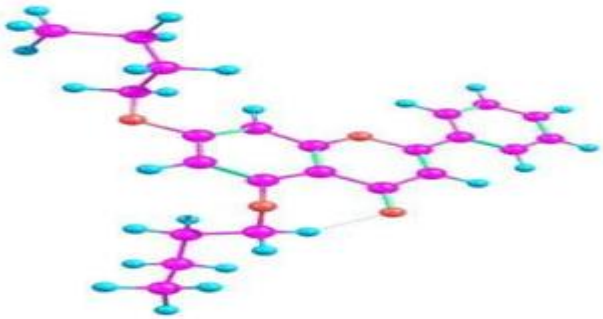

Figure.6: DFT optimized (BP86/TZVP) geometry for the compound 5, 7dibutyloxy-2-phenyl benzopyran-4H-one

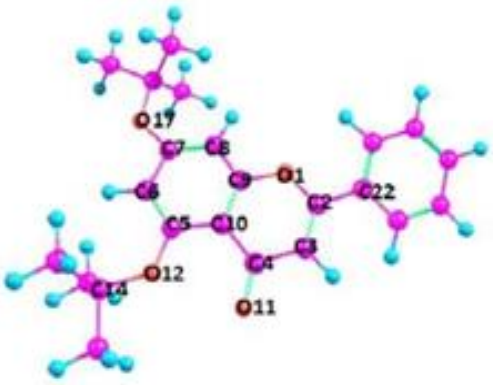

Figure.7: DFT optimized (BP86/TZVP) geometry for the compound 5, 7-*tert*-butyloxy-2-phenylbenzopyran-4H-one

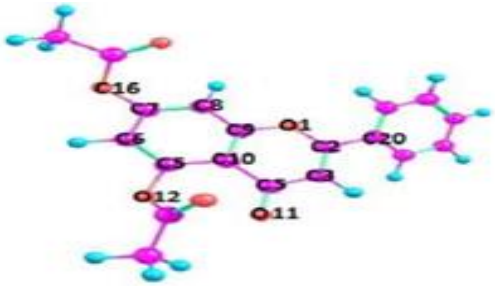

Figure.8: DFT optimized (BP86/TZVP) geometry for the compound 5, 7-diacetyloxy-2-phenyl benzopyran-4H-one

Table: 1. Metrical parameters (Å,^{0}) obtained from PM3, DFT (BP86/TZVP) calculation for the compound chrysin

S.NO	Atoms	Bond Length (Å)		Atoms	Bond Angle (0)	
		PM3	DFT		PM3	DFT
1.	C2-O1	1.374	1.374	C2-O1-C3	123.90	121.21
2.	C4-O11	1.237	1.237	C4-C10-O18	120.75	124.84
3.	C5-O19	1.360	1.360	C5-O19-C10	117.53	118.29
4.	C7-O18	1.370	1.370	C6-O18-C7	122.64	122.89
5.	C9-O11	1.378	1.378	C9-C10-O1	123.79	124.84

Table 2: Metrical parameters (Å, 0) obtained from PM3, DFT calculation for the compound 5, 7-dimethyloxy-2-phenyl benzopyran-4H-one

S.NO	Atoms	Bond Length (Å)		Atoms	Bond Angle (0)	
		PM3	DFT		PM3	DFT
1.	O1-C2	1.374	1.370	C3-C2-O1	122.87	120.92
2.	O1-C9	1.380	1.381	O1-C2-C22	113.27	112.55
3.	C4-O11	1.223	1.242	C2-O1-C9	117.75	120.22
4.	C5-O12	1.385	1.368	O12-C5-C6	113.72	120.68
5.	C7-O17	1.377	1.364	O12-C5-C10	124.68	124.00
6.	O12-C13	1.412	1.444	O17-C7-C6	114.88	115.60

Table 3: Metrical parameters (Å, 0) obtained from PM3, DFT calculation for the compound 5, 7diethyloxy-2-phenyl benzopyran-4H-one

S.NO	Atoms	Bond Length (Å)		Atoms	Bond Angle (0)	
		PM3	DFT		PM3	DFT
1.	O1-C2	1.374	1.370	C3-C2-O1	122.83	121.04
2.	O1-C9	1.380	1.382	O1-C2-C22	113.31	112.5
3.	C4-O11	1.223	1.241	C2-O1-C9	117.76	120.14
4.	C5-O12	1.384	1.364	O12-C5-C6	113.84	116.12

5.	C7-O15	1.371	1.364	O12-C5-C10	124.72	123.12
6.	O12-C13	1.421	1.456	O15-C7-C8	125.62	124.35
7.	O15-C16	1.426	1.443	C5-O12-C13	116.83	118.35

Table 4: Metrical parameters (Å, 0) obtained from PM3, DFT calculation for the compound 5, 7-di-*n*propyloxy-2-phenyl benzopyran-4H-on

S.NO	Atoms	Bond Length (Å)		Atoms	Bond Angle (0)	
		PM3	DFT		PM3	DFT
1.	O1-C2	1.374	1.371	C3-C2-O1	121.17	121.17
2.	O1-C9	1.380	1.382	O1-C2-C22	112.46	112.46
3.	C4-O11	1.223	1.364	C2-01-C9	120.1	120.11
4.	C4-O12	1.385	1.241	O12-C5-C6	116.32	116.32
5.	C7-O16	1.371	1.364	O12-C5-C10	122.90	122.90
6.	O12-C13	1.420	1.456	O16-C7-C8	124.29	124.29
7.	O16-C17	1.425	1.441	C5-O12-C13	118.26	118.26

Table 5: Metrical parameters (Å, 0) obtained from PM3, DFT calculation for the compound 5, 7-di-*iso*propyloxy-2-phenyl benzopyran-4H-one

S.NO	Atoms	Bond Length (Å)		Atoms	Bond Angle (0)	
		PM3	DFT		PM3	DFT
1.	O1-C2	1.376	1.372	C3-C2-O1	123.79	121.05
2.	O1-C9	1.379	1.381	O1-C2-C20	111.89	112.34
3.	C4-O11	1.219	1.238	C2-O1-C9	117.39	120.16
4.	C5-012	1.369	1.351	O12-C5-C6	124.09	124.91
5.	C7-O16	1.372	1.366	O12-C5-C10	114.99	115.07
6.	O12-C13	1.427	1.460	O15-C7-C8	125.03	125.04
7.	O16-C17	1.438	1.457	C5-O12-C13	121.57	124.97

Table .6: Metrical parameters (Å, ^{0}) obtained from PM3, DFT calculation for the compound 5, 7-dibutyloxy-2-phenyl benzopyran-4H-one

S.NO	Atoms	Bond Length (Å)		Atoms	Bond Angle (0)	
		PM3	DFT		PM3	DFT
1.	O1-C2	1.374	1.370	C3-C2-O1	122.84	120.91
2.	O1-C9	1.380	1.382	O1-C2-C22	113.30	125.54
3.	C4-O12	1.223	1.243	C2-O1-C9	117.71	120.23
4.	C5-O12	1.385	1.456	O12-C5-C6	114.80	115.23
5.	C7-O17	1.376	1.446	O12-C5-C10	124.70	124.2
6.	O12-C13	1.418	1.456	O17.C7-C6	114.80	115.23

Table .7: Metrical parameters (Å, 0) obtained from PM3, DFT calculation for the compound 5, 7-*tert*-butyloxy-2-phenylbenzopyran-4H-one

S.NO	Atoms	Bond Length (Å)		Atoms	Bond Angle (0)	
		PM3	DFT		PM3	DFT
1.	O1-C2	1.376	1.371	C3-C2-O1	123.06	120.99
2.	O1-C9	1.379	1.382	O1-C2-C22	113.11	112.40
3.	C4-O11	1.220	1.238	C2-O1-C9	117.76	120.7
4.	C5-O12	1.362	1.350	O12-C5-C10	114.35	114.75
5.	C7-O17	1.369	1.365	O12-C5-C6	125.04	125.45
6.	C18-C19	1.53	1.475	C7-O17-C18	212.31	125.48
7.	C7-C8	1.395	1.395	C7-C8-C9	118.34	118.02

Table. 8: DFT optimized (BP86/TZVP) geometry for the compound 5, 7diacetyloxy-2 -phenylbenzopyran-4H-one

S.NO	Atoms	Bond Length (Å)		Atoms	Bond Angle (0)	
		PM3	DFT		PM3	DFT
1.	O1-C2	1.375	1.370	C3-C2-O1	123.92	121.35
2.	O1-C9	1.379	1.378	O1-C2-C20	111.84	112.35
3.	C4-O11	1.220	1.240	C2-O1-C9	117.48	120.13

4.	C5-012	1.391	1.386	O12-C5-C6	117.01	116.95
5.	C7-O16	1.391	1.395	O12-C5-C10	120.82	121.22
6.	C17-O18	1.211	1.208	C7-O16-C18	120.00	122.11
7.	C13-O14	1.211	1.206	O16-C7-C8	121.76	123.83

Table :9 Ionization potential, Number of filled levels, Heat of formation, Elumo, Ehomo,Dipole point for the compound 5,7 dibutyloxy-R-2-phenylbenzopyran-4H-one obtained from computed PM3 method [where R = OMe (2), OEt (3), O(nPr) (4), O(isoPr) (5),OBu (6), O*ter*Bu (7), O(AC(8)]

Compound 1-4

Compounds	1	2	3	4
Ionization potential	9.260	9.299	9.268	9.305
Number of filled levels	47	53	59	65
Heat of formation (kcal/mol)	-88.918	-71.846	-82.658	-93.178
E_{LUMO}	-0.598	-0.932	-0.908	-0.738
E_{HOMO}	-9.260	-9.299	-9.268	-9.305
ELUMO-HOMO	8.661	8.366	8.360	8.566
Dipole moment	2.851	4.733	4.738	4.730

Compound 5-8

Compounds	5	6	7	8
Ionization potential	9.140	9.274	9.008	9.411
Number of filled levels	65	71	71	63
Heat of formation (kcal/mol)	-96.289	-104.57	-105.44	-160.31
E_{LUMO}	-0.534	-0.913	-0.679	-0.831
E_{HOMO}	-9.146	-9.274	-9.008	-9.411
ELUMO-HOMO	8.606	8.361	8.329	8.579
Dipole moment	3.995	4.669	4.091	3.619

Table 10: EHOMO, ELUMO, Chemical potential, Electrophilicity, Hardness, for the compound 5,7dibutyloxy-2-phenylbenzopyran-4H-one obtained from computed DFT method [where R= OMe (2), OEt (3), O(nPr) (4), O(isoPr), (5) ,OBu(6),O(Ter)7,O(AC(8)]

Compound 1-4

Compounds	**1**	**2**	**3**	**4**
EHOMO	-5.213	-5.424	-5.305	-5.303
ELUMO	-2.404	-2.767	-2.707	-2.675
ELUMO-HOM0	2.808	2.657	2.597	2.628
Chemical potential μ = ELUMO-HOM0/2	-3.808	-4.095	-4.006	-3.989
Hardness η = ELUMO-HOM0/2	1.404	1.328	1.298	1.314
Global softness S = 1/η	0.712	0.752	0.769	0.760
Electrophilicity = μ^2/ 2η	5.164	6.313	6.178	6.056

Compound 5-8

Compounds	**5**	**6**	**7**	**8**
EHOMO	-4.967	-5.383	-4.939	-5.681
ELUMO	-2.476	-2.723	-2.460	-2.961
ELUMO-HOM0	2.491	2.659	2.478	2.719
Chemical potential μ = ELUMO-HOM0/2	-3.721	-4.053	-3.699	-4.321
Hardness η = ELUMO-HOM0/2	1.245	1.329	1.239	1.359
Global softness S = 1/η	0.802	0.751	0.806	0.735
Electrophilicity = μ^2/ 2η	5.559	6.117	5.521	6.865

Result and Discussion

The PM3 computed heat of formation, energies of the HOMO, LUMO and the energy gap ELUMO-HOMO are listed in **Table.9** From the heat of formation values the possible formation and stability of the compounds are in the order – (**8**) -160.31 **>** -105.44 **(7) >** -104.57 **(6) >** -96.289 **(5) >** -93.178 **(4) >** -88.918 **(1) >** -82.658 (**3**) > -71.846 (**2**) Kcal/mol for R = OMe (**2**), OEt (**3**),O(nPr) (**4**), O(*iso*Pr) (**5**), OBu (**6**), O*tert*Bu(**7**), OAc (**8**), based on our semi empirical PM3 calculations. The higher negative values of heat of formations of these compounds are an indicator for their possible stability in room temperature, in fact compounds with heat of formation values of 18 Kcal/mol are stable in room temperature. The DFT computed energies of the HOMO, LUMO and the energy gap ELUMO-HOMO are listed in **Table 10**. It is evident that from the DFT computed energy gap ELUMO-HOMO values ranging from 2.5 to 2.8eV, the molecules **2 - 8** are stable and their possible formation in the laboratory. Next to chrysin compounds **2, 3, 6** and **8** possess the higher ELUMO-HOMO value of 2.7eV. Thus the compound **6** has been synthesized in the laboratory.

Electronic Structure: PM3 and DFT calculations were made to calculate the electronic properties of the chrysin derivatives like ionization potential, electron affinity, absolute hardness, chemical potential and electrophilicity. All these properties are calculated from the values of HOMO and LUMO energies (Koopmann's theorem) and displayed in **Tables 9** and **10**. Ionization potential is nothing but the energy required to remove an electron from the outer most orbital which is equal to the energy of the HOMO. Electronic affinity can be calculated from the orbital energy of LUMO, ie. Energy required to add an electron to the

molecule. The high value of HOMO shows the electron donating ability to an appropriate molecule of low empty molecular orbital. From the DFT computed EHOMO values of -5.0 to -5.7. eV shows the equal electron donating abilities of the compounds **2-8**. The LUMO-HOMO energy gap is an important parameter as a function of reactivity of the chrysin derivative towards free radical. As the ELUMO-HOMO increases the reactivity of the molecule decreases. The low value of ELUMO –HOMO suggests the reactive nature of the chrysin derivative. The DFT computed energy gap values of 2.5–2.8 eV for the chrysin derivatives **2-8**, suggest the equal stabilities of the modeled molecules. The hardness values are the index of stability of the molecule and the DFT computed hardness values of about 1.2 to 1.4 suggest the equal stability of the compounds **2 - 8** among which the 5, 7 –diacyloxy-2-phenyl benzopyran-4h-one shows the highest value of 1.4 **(Table.10)**. The dipole moment is a parameter arises from the electronic distribution in a molecule and is the measure of polarity of a polar covalent bond. The highest value of dipole moment (PM3) is observed for the compound **1**(2.9 D) and lowest dipole moment value is observed for the compound **3** (4.7D). The electrophilicity index (ω) is a measure of the stabilization in energy after a system accepts additional amount of electron charge from other species. The DFT computed electrophilicity values suggest the most electrophilic nature of the **8** (6.9eV) and the lowest is observed for **7** (5.5eV) (**Table.10**). These compounds possess higher electrophilicity values when compared that of chrysin.

CONCLUSION

Semi empirical PM3 and DFT calculations were carried out on the compounds 5,7-R22-phenylbenzopyran-4H-one where R= OMe (**2**), OEt (**3**), O(nPr) (**4**), O(*iso*Pr) (**5**), OBu(**6**), O*tert*Bu(**7**), OAc (**8**). The following conclusions were drawn from the present study. The present study proves the strength of DFT methods in analyzing the geometric and electronic structural features of 5,7-dimethyloxy-2-phenyl benzopyran- 4H- one and its chrysin derivatives. Semi empirical calculations at PM3 level and DFT calculations using ORCA at BP86/TZVP level predict the structural parameters for the compounds **1** - **8**, which are in good agreement with the experimental values (**6**) of the similar compounds. The computed energetics and HOMO-LUMO gap values of > 2.0 eve, confirm the stabilities of these chrysin derivatives.

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