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Vibrational assignment, NBO analysis and molecular docking studies ofButyrophenone by Density functional theory

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Abstract : The Fourier-transform infrared spectrum and Fourier-transform Raman Spectrum of Butyrophenone were recorded in the region 4000-400 cm^{-1}and 4000-100 cm^{-1}respectively. A complete vibrational assignment and analysis of the fundamental vibrational modes of the molecule have been compared with the harmonic vibrational frequencies computed using HF and DFT (B3LYP) method by employing 6-311 +G(d, P) basis sets. UV-Visible spectrum of the compound was recorded and the electronic properties, such as HOMO and LUMO energies, The calculated HOMO and LUMO energies show that, the charge transfer occurs within the molecule Stability of the molecule arising from hyper conjugative interations, chare delocalization have been analyzed using natural bond orbital analysis (NBO). Molecular electrostatic otential studies were performed at DFT/B3LYP method using 6-311 +G (d, p) basis sets. Inclusion complex of Butyrophenone with β-cyclodextrin (β-CD) has been investigated by molecular docking method. The other molecular properties like Mulliken population analysis and themodynamic properties of the title compound have been calculated.

Keywords: Butyrophenone, DFT; FT-IR; FT-Raman, HOMO-LUMO; NBO.

1. Introduction

Butyrophenoneis a chemical compound some of its derivatives (called commonly Butyrophenones). Its molecular formula is $C_{10}H_{12}O$. It is a colourless liquid and insoluble in water. Its molecular weight is 148.20g/mol and its melting and boiling point is 12^0C, 229^0C respectively. Butyrophenone is a class of pharmaceutical drugs derived from butyrophenone. Haloperidol, melperone, domperidone, tenperone, benperidol, and droperidol are representatives of this class. These compounds have a functional ketone group and are often clinically used to treat various psychiatric disorders, including schizophrenia, organic psychosis, paranoid syndrome, acute idiopathic psychotic illnesses, and the manic phase of manic depressive illness [1-2]. Other uses include treatment of aggressive behaviour, delirium, acute anxiety, nausea, and vomiting, pain, organic brain syndrome, and Tourette's syndrome.

2. Experimental details

The sample was obtained from M/s. Sigma Aldrich Co., with a stated purity of 99%and was used as such without further purification. The Fourier transform infrared spectrum was recorded using Perkin Elmer spectrometer in KBr dispersion in the range of 4000–450cm^{-1}. The FT-Raman spectrum was recorded using the 1064 nm line of an Nd: YAG laser as excitation wavelength in the region 4000–100cm^{-1} on a Bruker model IFS

66 V spectrophotometer equipped with an RFS 27 FT-Raman module accessory. The UV–visible spectrum of the compound was recorded in the range of 190–900nm with Perkin Elmer-Lambda 950-UV–visible spectrometer.

3. Computational details

The entire calculations were performed at Hartree Fock (HF) and Density Functional (DFT) levels on a Pentium IV personal computer using Gaussian 09W [3] program package invoking gradient geometry optimization [4]. The geometry was optimized at B3LYP/6-311++ G (d, p) level. We have used HF and DFT/B3LYP approach for the computation of molecular structure, vibrational frequencies and energies of optimized structures in the present work using GAUSSVIEW program with symmetry considerations along with available related molecules, vibrational frequency assignments were made with a high degree of accuracy. Next the spectra were analyzed in terms of the Potential Energy Distribution (PED) contributions by using the Vibrational Energy Distribution Analysis program (VEDA) written by Michal H. Jamroz[5-6]. The natural bonding orbital (NBO) calculations [7] were performed using NBO 3.1 program as implemented in the Gaussian 03W package at the above said level in order to understand various second order interaction between the filled orbital of one subsystem and vacant orbital of another subsystem, which is measure of the intermolecular and intra molecular delocalization or hyper conjugation

4. Result and discussion

4.1 Molecular geometry

The optimized structure of Butyrophenone with atom labelled in it is shown in Fig 1. The optimized geometrical parameters (bond lengths and bond angles) were calculated by using DFT/B3LYP method with 6-311 +G (d,p) basis set and were listed in Table 1. The global minimum energy obtained for the titled compound was observed to be -463.6573 a.u. The calculated bond distance of O1-C4 is found to be 1.223**Å** (B3LYP/6-311+G(d,p)), 1.1911**Å** (HF/6-311+G(d,p). The bond length experimentally found at 1.229**Å.** The difference in bond length reflects the intermolecular hydrogen bonding interactions. The calculated bond length for C2-C4 and C5-C4 at B3LYP/6-311+G(d, p) is found to be 1.5285 Å and 1.5012 Å respectively. Experimentally it is found at 1.5212 Å and 1.4927 Å for C2-C4 and C5-C4 respectively. This difference occurs as C5 is attached to ring. The bond angle O1-C4-C5 calculated to be 120.1963 Å (B3LYP/6-311+G(d,p) and experimentally found as 119.222 Å due to the influence of electronegative atom (O1).

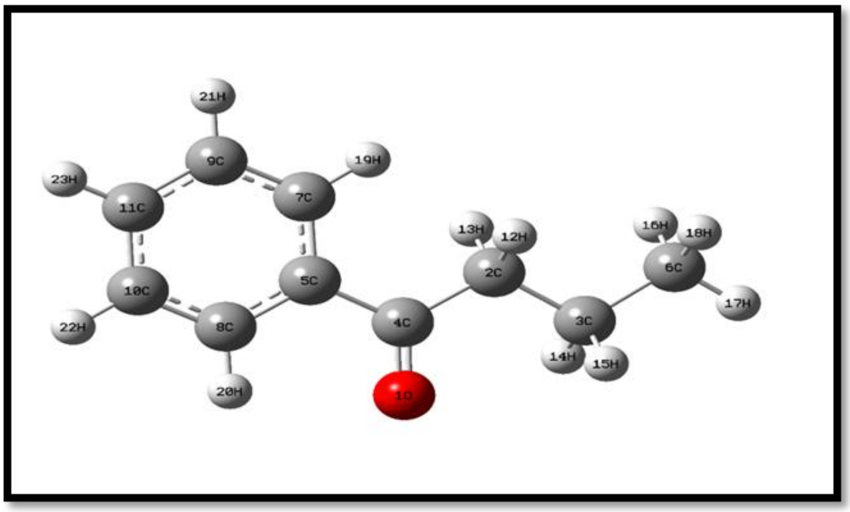


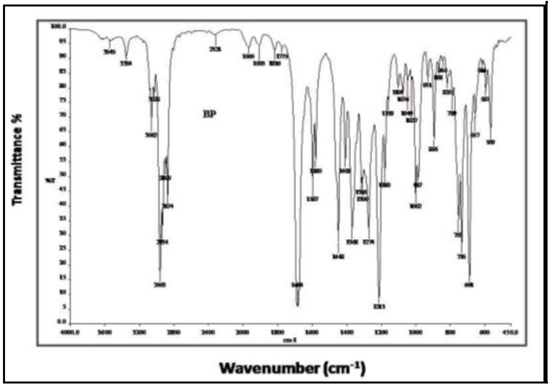
Fig 1. Optimized structure of Butyrophenone at DFTB3LYP/6-311 +G (d,p)

Table 1. Optimized parameters (bond angle and bond length) of Butyrophenone

Optimized parameters	Experimental	DFT/B3LYP/ 6-311+G(d,p)	HF/6-311+G(d,p)
Bond length(Å)			
R(1,4)	1.2290	1.223	1.1911
R(2,3)	1.5288	1.5189	1.5257
R(2,4)	1.5212	1.5285	1.5182
R(2,12)	1.0958	1.0971	1.0885
R(2,13)	1.0958	1.0971	1.0884
R(3,6)	1.5200	1.5314	1.5277
R(3,14)	1.0965	1.0941	1.0851
R(3,15)	1.0966	1.0941	1.0851
R(4,5)	1.4927	1.5012	1.506
R(5,7)	1.3759	1.4026	1.3899
R(5,8)	1.3759	1.4033	1.3927
R(6,16)	1.0947	1.0841	1.0874
R(6,17)	1.0945	1.0933	1.0857
R(6,18)	1.0946	1.0946	1.0874
R(7,9)	1.3949	1.3935	1.3863
R(7,19)	1.0837	1.0825	1.0737
R(8,10)	1.3948	1.39	1.3816
R(8,20)	1.08551	1.0829	1.0732
R(9,11)	1.39477	1.3945	1.3837
R(9,21)	1.0861	1.0838	1.0751
R(10,11)	1.3949	1.3969	1.3878
R(10,22)	1.0860	1.084	1.0752
R(11,23)	1.0861	1.084	1.0756
Bond angle(^{0})			
A(3,2,4)	112.200	114.5495	113.7062
A(3,2,12)	108.791	110.2781	110.2873
A(3,2,13)	108.642	110.278	110.2914
A(4,2,12)	108.622	108.0062	108.106
A(4,2,13)	108.816	108.0071	108.1104
A(12,2,13)	109.751	105.2751	106.0179
A(2,3,6)	111.506	112.2504	112.1128
A(2,3,14)	109.929	109.3064	109.2835
A(2,3,15)	109.982	109.3062	109.2828
A(6,3,14)	109.336	109.7824	109.9186
A(6,3,15)	109.150	118.6022	109.9182
A(14,3,15)	106.816	106.2308	106.1443
A(1,4,2)	122.077	121.0965	121.1883
A(1,4,5)	119.222	120.1963	120.0424
A(2,4,5)	118.701	118.7072	118.7693
A(4,5,7)	118.614	122.4693	122.8302
A(4,5,8)	118.607	118.6022	118.1481
A(7,5,8)	122.779	118.9285	119.0217
A(3,6,16)	110.998	111.3197	111.4043
A(3,6,17)	110.259	110.9725	110.8381
A(3,6,18)	111.011	111.319	111.4039
A(16,6,17)	108.076	107.6986	107.6474
A(16,6,18)	108.317	107.6561	107.7204
A(17,6,18)	108.073	107.6987	107.6473
A(5,7,9)	118.611	120.4152	120.5151
A(5,7,19)	123.933	120.5735	120.6882
A(9,7,19)	117.456	119.0112	118.7967
A(5,8,10)	118.616	120.6481	120.5354
A(5,8,20)	122.572	118.7658	118.7737
A(10,8,20)	118.616	120.5861	120.6909
A(7,9,11)	122.572	120.1115	119.9671
A(7,9,21)	118.811	119.7764	119.829
A(11,9,21)	119.996	120.1121	120.204
A(8,10,11)	119.993	119.9683	120.0056
A(8,10,22)	120.024	119.9674	119.9173

A(11,10,22)	119.983	120.0643	120.0772
A(9,11,10)	120.004	119.9284	119.9552
A(9,11,23)	120.003	120.0152	120.0001
A(10,11,23)	119.993	120.0564	120.0448

The FTIR and FTRaman spectra of the title compound has been recorded experimentally and shown in Fig. 2 and Fig. 3.



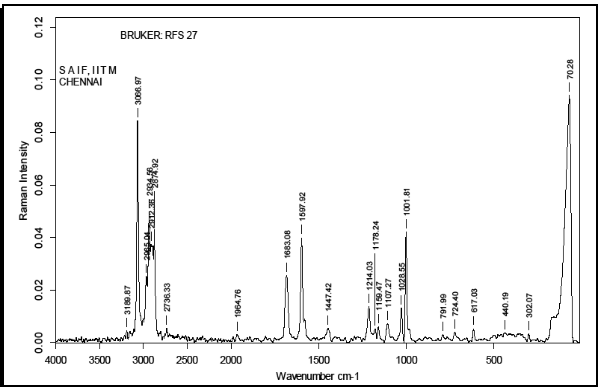


Fig 2 . FT-IR spectrum of Butyrophenone **Fig 3.FT-Raman spectrum of Butyrophenone**

4.2 Vibrational assignments

The molecule Butyrophenone has 23 atoms and it has 63 normal modes of vibration. All the 63 fundamental vibrations are IR and Raman active. The harmonic vibrational frequencies calculated for Butyrophenone and the experimental frequencies have been compared in Table 2. Vibrational assignments are based on the observations of the animated modes in Gauss View 5.1 and assignments reported in literature.

4.2.1 C-H Vibration

The presence of C-H stretching vibration is expected in the region 3100-3000 cm^{-1} [8] which is the characteristic region for the ready identification of C-H stretching vibration. The observed FTIR frequencies for this vibration is found at 3062, 3028 cm^{-1} and for FT-Raman, a band is observed at 3067cm^{-1}. In this region the bands are not affected appreciably by the nature of the substitute [9]. The calculated frequencies for C-H vibrations is 3069 cm^{-1} at HF 6-311 +G(d,p) method and 3062 cm^{-1} at DFT/B3LYP/6-311 +G (d,p) levels respectively

4.2.2 C=O Vibration

The characteristic IR frequency of carbonyl group has been investigated earlier and the C=O stretching vibration are expected in the region 1715-1680 cm^{-1}. The observed FTIR frequency for C=O vibrations is found at 1684 cm^{-1} and for FT-Raman the band is observed at 1683 cm^{-1}.The carbon oxygen band is formed by pπ-pπ* between carbon and oxygen and the lone pair of electron on oxygen also determine the nature of carbonyl group. The calculated frequencies for C=O vibrations is 1771 cm^{-1} at HF 6-311 +G(d,p) method and 1633 cm^{-1} at DFT/B3LYP/6-311 +G (d,p) levels respectively [10].

4.2.3 C-C Vibration

Aromatic C-C stretching vibrations occur in the region 1625-1430 cm^{-1}. The observed FTIR frequency for C-C vibration is found at 1597 cm^{-1} and FTRaman band is observed at 1598 cm^{-1}.These vibrations are in good agreement with the calculated values. The calculated values of C-C stretch is 1599 cm^{-1} at HF/6-311+G (d,p) level and it is observed at 1543 cm^{-1} in the DFT/B3LYP/6-311+G (d,p) level. The observed values are in good agreement with the calculated values [10].

Table 2: Vibrational Assignments of Butyrophenone

Symmetry species	Observed wavenumber (cm^{-1})		Calculated wavenumber (cm^{-1})		Assignments	IR intensity		Raman activity	
	FTIR	FT Raman	HF	DFT		HF	DFT	HF	DFT
A	3062	3067	3069	3062	$\nu(C_7H_{19})\ \nu(C_9H_{21})$	4.02	6.13	94.15	630.64
A	-	-	3052	3059	$\nu(C_7H_{19})\ \nu(C_8H_{20})$	10.11	20.87	113.44	68.99
A	-	3190	3039	3050	$\nu(C_9H_{21})\ \nu(C_{11}H_{23})$	26.08	22.62	113.86	191.51
A	-	-	3028	3041	$\nu(C_9H_{21})\ \nu(C_{10}H_{22})$	11.96	12.08	97.81	252.33
A	-	-	3016	3032	$\nu(C_9H_{21})\ \nu(C_{10}H_{22})\ \nu(C_8H_{23})$	0.08	0.14	48.02	108.18
A	-	-	2937	2949	$\nu(C_6H_{17})$	78.12	68.99	7.91	203.15
A	-	-	2924	2947	$\nu(C_3H_{14})\ \nu(C_3H_{15})\ \nu(C_6H_{16})\ \nu(C_6H_{18})$	66.06	115.98	116.16	14.89
A			2904	2927	$\nu(C_3H_{14})\ \nu(C_3H_{15})\ \nu(C_6H_{16})\ \nu(C_6H_{18})$	11.40	0.92	50.65	122.85
A	-	-	2896	2906	$\nu(C_2H_{12})\ \nu(C_2H_{13})$	12.21	3.78	84.73	256.53
A	-	-	2895	2902	$\nu(C_3H_{14})\ \nu(C_3H_{15})$	9.81	43.45	81.51	169.11
A	3028	-	2871	2885	$\nu(C_6H_{16})\ \nu(C_6H_{17})\ \nu(C_6H_{18})$	19.65	35.42	142.82	613.70
A	2963	2965	2861	2882	$\nu(C_2H_{12})\ \nu(C_2H_{13})$	38.97	35.59	83.43	87.10
A	1684	1683	1771	1633	$\nu(O_1C_4)$	266.43	417.99	37.11	210.02
A	-	-	1622	1561	$\nu(C_8C_{10})$	16.19	61.57	81.85	370.42
A	1597	1598	1599	1543	$\nu(C_{11}C_9)$	8.20	29.33	8.03	38.86
A	-	-	1497	1452	$\beta(H_{19}C_7C_9)\ \beta(H_{21}C_9C_{11})\ \beta(H_{22}C_{10}C_{11})$	0.63	1.99	0.42	12.55
A	-	-	1476	1434	$\beta(H_{15}C_3H_{14})\ \beta(H_{16}C_6H_{18})$	5.90	15.30	0.30	1.38
A	-	-	1467	1424	$\beta(H_{17}C_6H_{16})\ \beta(H_{18}C_6H_{17})\ \tau(H_{17}C_6C_3C_2)$	6.93	11.13	9.14	14.77
A	-	-	1460	1414	$\beta(H_{15}C_3H_{14})\ \beta(H_{16}C_6H_{18})$	2.39	7.35	12.43	17.39
A	-	-	1447	1410	$\beta(H_{23}C_{11}C_{10})$	21.54	23.94	3.96	9.50
A	1448	1447	1441	1381	$\beta(H_{13}C_2H_{12})$	4.86	22.26	5.47	17.39
A	1408	-	1404	1344	$\beta(H_{16}C_6H_{18})\ \beta(H_{17}C_6H_{16})\ \beta(H_{18}C_6H_{17})$	31.13	1.16	1.31	0.68
A	1368	-	1391	1333	$\beta(H_{13}C_2H_{12})\ \tau(H_{15}C_3C_2C_4)\ \omega(C3H14H_{15})$	18.23	67.30	0.43	1.31
A	-	-	1324	1290	$\beta(H_{19}C_7C_9)\ \beta(H_{20}C_8C_{10})$	15.22	5.87	2.57	6.27
A	-	-	1311	1277	$\nu(C_5C_7)\ \omega(C_3H_{14}H_{15})\ \omega(C_2H_{13}H_{12})$	23.89	38.06	2.08	12.44
A	1316	-	1304	1266	$\tau(H_{15}C_3C_2C_4)\ \omega(C_3H_{14}H_{15})\ \omega(C_2H_{13}H_{12})$	0.28	35.06	11.96	8.19
A	1309	-	1234	1264	$\beta(H_{12}C_2C_3)\ \beta(H_{14}C_3C_6)\tau(C_3H_{14}H_{15})\tau(C_2H_{13}H_{12})$	0.00	0.30	0.15	25.00
A	1274	-	1213	1197	$\beta(H_{12}C_2C_3)\tau(C_3H_{14}H_{15})\tau(C_2H_{13}H_{12})$	21.94	0.16	1.16	1.05
A	1213	1214	1198	1167	$\nu(C_4C_5)\omega(C_2H_{13}H_{12})$	113.56	199.20	21.98	124.68
A	1180	-	1170	1141	$\beta(H_{19}C_7C_9)\ \beta(H_{21}C_9C_{11})$	14.79	72.12	2.90	29.60
A	1159	1178	1103	1126	$\beta(H_{22}C_{10}C_{11})\ \beta(H_{23}C_{11}C_{10})$	7.26	10.13	7.70	18.10
A	-	-	1099	1075	$\nu\ (C_3C_2)$	1.17	1.23	16.19	41.84
A	-	1107	1095	1058	$\tau(H_{12}C_2C_4C_5)$	0.13	0.38	1.35	2.75
A	1104	-	1064	1055	$\nu\ (C_7C_9)\beta(H_{20}C_8C_{10})$	0.45	9.38	1.20	3.49
A	1049	-	1019	1002	$\nu\ (C_6C_3)$	0.02	6.29	0.08	16.17
A	-	-	1017	999	$\nu\ (C_6C_3)$	0.37	1.46	13.25	40.94
A	1027	1029	1011	977	$\tau(H_{22}C_{10}C_{11}C_9)\tau(H_{23}C_{11}C_{10}C_8)\tau(C_8C_{10}C_{11}C_9)$	4.51	0.01	7.68	0.12
A	-	-	1007	970	$\beta(C_7C_9C_{11})\ \beta(C_{10}C_{11}C_9)\ \beta(C_8C_{10}C_{11})$	0.26	11.58	0.12	106.36
A	-	-	986	961	$\nu\ (C_2C_4)$	14.51	63.98	23.92	22.56
A	1002	1002	975	961	$\tau(H_{20}C_8C_{10}C_{11})\tau(H_{21}C_9C_{11}C_{10})\tau(H_{22}C_{10}C_{11}C_9)$	25.31	0.20	28.28	0.20
A	987	-	959	916	$\tau(H_{20}C_8C_{10}C_{11})\tau(H_{19}C_7C_9C_{11})\tau(H_{23}C_{11}C_{10}C_8)$	1.37	2.65	0.12	0.89
A	931	-	875	863	$\nu\ (C_3C_2)$	14.75	35.85	9.38	9.98
A	-	-	874	849	$\beta(H_{14}C_3C_6)\tau(H_{17}C_6C_3C_2)$	0.09	0.02	1.85	4.47
A	895	-	864	825	$\tau(H_{19}C_7C_9C_{11})\tau(H_{20}C_8C_{10}C_{11})\ \tau\ (H_{21}C_9C_{11}C_{10})\ \tau\ (H_{22}C_{10}C_{11}C_9)$	0.21	0.16	0.91	4.88
A	868	-	776	763	$\beta(C_{10}C_{11}C_9)\nu(C_2C_4)$	10.21	4.78	7.98	23.57
A	789	792	769	747	$\tau(H_{21}C_9C_{11}C_{10})\ \rho(C_2H_{12}H_{13})\rho(C_6H_{18}H_{16})$	33.73	24.47	1.02	2.96
A	753	724	728	709	$\beta(H_{14}C_3C_6)\rho(C_2H_{12}H_{13})\rho(C_3H_{14}H_{15})$	37.34	65.40	0.10	0.90
A	735	-	687	670	$\tau(H_{23}C_{11}C_{10}C_8)\tau(C_8C_{10}C_{11}C_9)\tau(C_5C_7C_9C_{11})\tau(C_5C_7C_9C_{11})$	33.94	62.16	0.01	0.36
A	691	-	649	638	$\beta(O_1C_4C_2)\ \beta(C_{10}C_{11}C_9)$	23.11	23.54	3.07	5.35

A	657	617	611	603	$\beta(C_7C_9C_{11})$	0.19	0.20	6.39	16.17
A	616	-	575	554	$\tau(C_3C_2C_4C_5)\gamma(O_1C_2C_5C_4)\rho(C_2H_{13}H_{12})$	10.74	10.61	0.43	0.69
A	569	-	461	457	$\beta(C_2C_4C_5)$	3.24	2.42	1.24	2.74
A	-	440	423	409	$\tau(C_{10}C_{11}C_9C_7)\gamma(O_1C_2C_5C_4)\rho(C_2H_{13}H_{12})$	0.27	0.88	0.13	0.20
A	-	-	408	393	$\tau(C_8C_{10}C_{11}C_9)\tau(C_{10}C_{11}C_9C_7)\tau(C_5C_7C_9C_{11})$	0.01	0.01	0.01	0.01
A	-	-	367	361	$\beta(O_1C_4C_2)$ $\beta(C_6C_3C_2)$	3.90	3.62	0.96	1.63
A	-	302	287	285	$\nu(C_4C_5)$	1.09	1.45	5.62	6.81
A	-	-	249	243	$\beta(C_4C_5C_8)$ $\beta(C_3C_2C_4)$	8.56	12.37	0.15	0.51
A	-	-	239	238	$\tau(H_{16}C_6C_3C_2)\tau(H_{17}C_6C_3C_2)\tau(H_{18}C_6C_3C_2)$	0.04	0.16	0.03	0.09
A	-	-	161	154	$\gamma(C_4C_7C_8C_5)$	0.07	0.07	2.63	6.00
A	-	-	108	106	$\beta(C_4C_5C_8)$ $\beta(C_2C_4C_5)$ $\beta(C_3C_2C_4)$	0.54	0.98	0.22	0.58
A	-	-	97	88	$\tau(C_2C_4C_5C_7)\tau(C_6C_3C_2C_4)$	2.66	4.76	0.15	0.52
A	-	70	71	58	$\tau(C_3C_2C_4C_5)\tau(C_6C_3C_2C_4)$	0.04	0.16	0.13	0.38
A	-	-	28	27	$\tau(C_2C_4C_5C_7)$	1.29	1.44	1.92	5.82

Abbreviation : ν=stretching, β=bending, τ=torsion/twisting, γ=out of plane bending, ρ=rocking, ω=wagging

4.3 UV-Vis Spectral Studies:

On fully optimized structure of molecule, TDDFT/B3LYP/ 6-311 +G (d, p) level has been employed to determine excited states of Butyrophenone. Fig 4 shows the recorded spectrum of Butyrophenone. The calculated results involving vertical excitation energies, oscillator strength (f) and wavelength are tabulated in Table 3. The calculated excitation energies of p–p* transition with experimental values are compared and results are in good agreement with calculated values. The calculations of molecular orbital geometry show that visible absorption maxima of molecule correspond to electron transition between frontier orbitals such as transition from HOMO to LUMO. As can be seen from UV–vis spectrum, maxima absorption values have been found to be 315.56, 275.18 and 236.69 nm [10]. The λmax is a function of substitution, stronger the donor character of substitution, more the electrons are pushed into molecule, and the larger is λmax.

Table 3. Calculated parameter of Butyrophenone using TDDFT/B3LYP6-311+G(d,p) level

Excited state	Cl expansion coefficient	Wavenumber(λnm)		Oscillator strength (f)	Energy (eV)
		Experimental	Calculated		
Excited state→1					
40→41	0.69544	315.56	322.54	0	3.8440
40→45	-0.11718				
Excited state→2					
38→41	-0.39980	275.18	266.79	0.0281	4.6472
38→42	-0.18205				
39→41	0.53198				
39→42	-0.15270				
Excited state→3					
38→41	0.54221	236.69	247.40	0.3331	5.0115
39→41	0.42278				
39→42	0.12204				

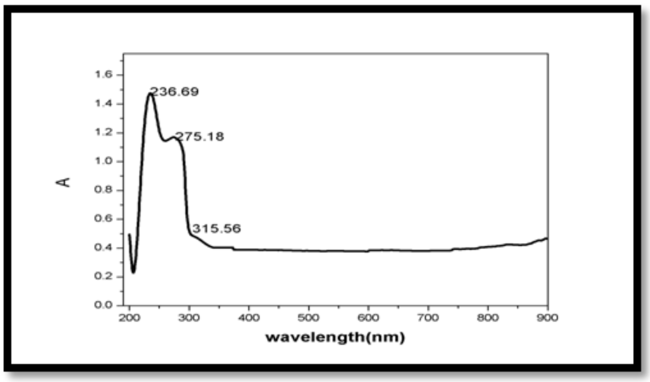
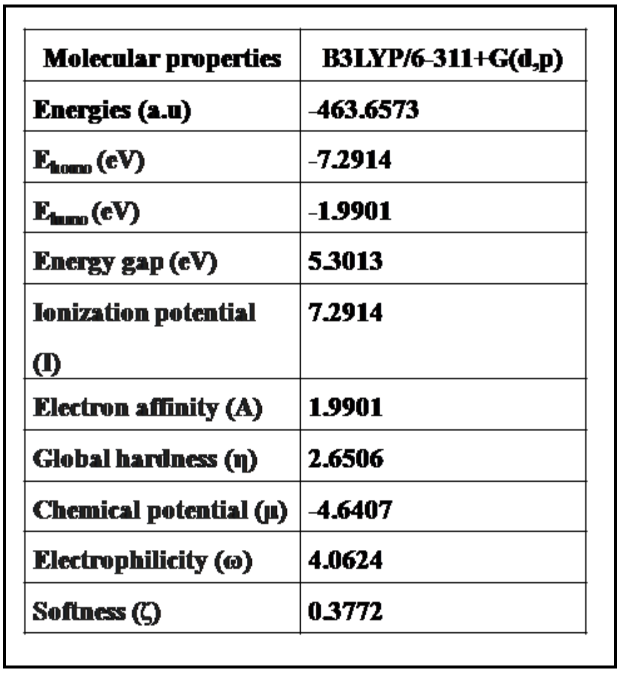


Fig 4. UV-Vis spectrum of Butyrophenone

4.4 Frontier molecular orbitals

Highest occupied molecular orbital (HOMO) and lowest unoccupied molecular orbital (LUMO) are very important parameters for quantum chemistry. The HOMO is the orbital that acts as an electron donor and LUMO is the orbital that largely act as electron acceptor. The energy of HOMO, LUMO, LUMO+1 and HOMO-1 and their orbital energy gaps of Butyrophenone are calculated using B3LYP/6-311+G (d,p) method and their positive, negative region are shown in Fig 5. The Frontier orbital energy gap (E_L-E_H) for Butyrophenone is found to be 5.3013eV.Based on density functional descriptors, global chemical reactivity descriptors of compounds such as hardness (η), softness (ζ), chemical potential (μ), and electrophilicity index (ω). Using Koopman's theorem for closed-shell compounds, symbols can be defined as: $\eta = (I-A)/2$, $\mu = -(I+A)/2$, $\zeta = 1/\eta$, $I = -E_H$, $A = -E_L$where, I and A are the ionization potential and electron affinity of the compounds. Electron affinity refers to the capability of a ligand to accept precisely one. Softness is the property of the compound that measures the extent of chemical reactivity [11]. It is the reciprocal of hardness. The global electrophilic index of the compound is defined as follows: $\omega = \mu^2/2\eta$. and shown in Table 4.

Table 4. Comparison of HOMO-LUMO energy gaps and related molecular properties of the title compound



Molecular properties	B3LYP/6-311+G(d,p)
Energies (a.u)	-463.6573
E_{homo} (eV)	-7.2914
E_{lumo} (eV)	-1.9901
Energy gap (eV)	5.3013
Ionization potential (I)	7.2914
Electron affinity (A)	1.9901
Global hardness (η)	2.6506
Chemical potential (μ)	-4.6407
Electrophilicity (ω)	4.0624
Softness (ζ)	0.3772

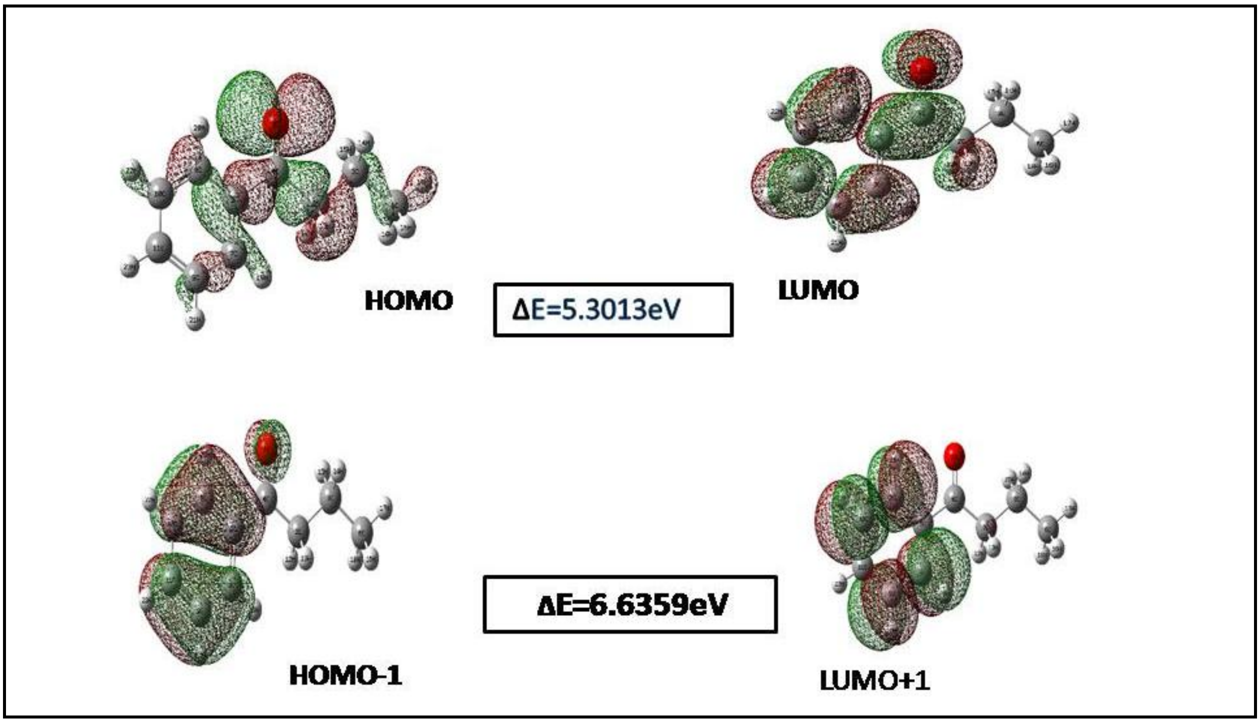


Fig 5. Frontier molecular orbital of Butyrophenone

4.5 Natural Bonding Orbital

Natural Bond Orbital (NBO) analysis is an effective tool for determining the above mentioned factors. For the titled compound Butyrophenone, in order to investigate the inter and intra molecular charge transfer takes place within the molecule. NBO analysis has been performed using NBO 4.1 program as implemented in the Gaussian 09 package at the DFT-B3LYP/6-311+G (d,p) level. For the titled compound, the donor-acceptor interactions in the NBO analysis were calculated by second order perturbation theory analysis. In the anti-bonding orbitals (σ*, π*), the electron density(ED) changes and their energies E(2) has been calculated by NBO analysis at DFT-B3LYP/6-311+G (d,p) level in order to create a clean evidence for stabilization of energy emerging from molecular interactions.

The interactions between electron donors and electron acceptors will be more intensive when the E (2) value is larger. The strength of the delocalization interaction can be estimated by the second-order energy lowering E (2);

$E\ (2) = \Delta E_{ij} = qiF(i,j)^2/E_j - E_i$

Where, E (2) is the stabilization energy, qi is the donor orbital occupancy, Ei and Ej are the diagonal elements and F (i, j) is the off diagonal NBO Fock matrix element reported or Kohn–Sham Matrix element.

Table 5 shows the possible interactions with donors, acceptors and their electron densities.A strong interaction between bonding and anti-bonding (π→π*) electron with greater energy contribution are : π(C9-C11)→π*(C5-C7)having energy (22.50Kcal/mol), π(C8-C10)→π*(C9-C11) having energy (21.38 Kcal/mol), π(C5-C7)→π*(C8-C10) having energy (20.08 Kcal/mol), π(C5-C7)→π*(O1-C4) having energy (19.35 Kcal/mol). The stabilization energy is higher for the interaction between π*(O1-C4) →π*(C5-C7) which is found to be 144.24 Kcal/mol [11].

The lone pair interactions were prominent in the titled compound as expected due to the charge transfer that taking place from lone pair atoms into the ring. The lone pair interaction with the following $E^{(2)}$ value : Lp(O1)→σ*(C2-C4) (18.84 Kcal/mol) , Lp(O1)→σ*(C4-C5) (18.36 Kcal/mol).

Table 5. Natural bonding orbital of Butyrophenone

Donor (i)	Acceptor (j)	$E^{(2)}$ k cal/mol	$E_{(j)}$-$E_{(i)}$ a.u	F(i,j) a.u
$\pi(O_1$-$C_4)$	$\pi^*(C_5$-$C_7)$	144.24	0.01	0.071
$\pi(C_9$-$C_{11})$	$\pi^*(C_5$-$C_7)$	22.50	0.28	0.071
$\pi(C_8$-$C_{10})$	$\pi^*(C_9$-$C_{11})$	21.38	0.28	0.070
$\pi(C_5$-$C_7)$	$\pi^*(C_8$-$C_{10})$	20.08	0.29	0.069
$\pi(C_5$-$C_7)$	$\pi^*(O_1$-$C_4)$	19.35	0.27	0.068
$\pi(C_8$-$C_{10})$	$\pi^*(C_5$-$C_7)$	19.02	0.28	0.066
Lp(O_1)	$\sigma^*(C_2$-$C_4)$	18.84	0.67	0.102
Lp(O_1)	$\sigma^*(C_4$-$C_5)$	18.36	0.70	0.102
$\pi(C_5$-$C_7)$	$\pi^*(C_9$-$C_{11})$	18.28	0.28	0.065
$\pi(C_9$-$C_{11})$	$\pi^*(C_8$-$C_{10})$	17.99	0.28	0.065
$\sigma(C_2$-$H_{13})$	$\sigma^*(O_1$-$C_4)$	5.32	0.51	0.048
$\sigma(C_2$-$H_{12})$	$\sigma^*(O_1$-$C_4)$	5.33	0.51	0.048
$\sigma(C_8$-$H_{20})$	$\pi^*(C_5$-$C_7)$	4.49	1.08	0.062
$\pi(O_1$-$C_4)$	$\pi^*(C_5$-$C_7)$	4.45	0.41	0.042
$\sigma(C_7$-$H_{19})$	$\pi^*(C_5$-$C_8)$	4.29	1.08	0.061

4.6 Mulliken charges

In order to investigate charges on atoms and their changes the Mulliken population analysis of the Butyrophenone has been carried out by B3LYP/6-311+G (d,p) level and values are shown in Table 6. The graphical representation of the atomic charges is shown in Fig. 6.

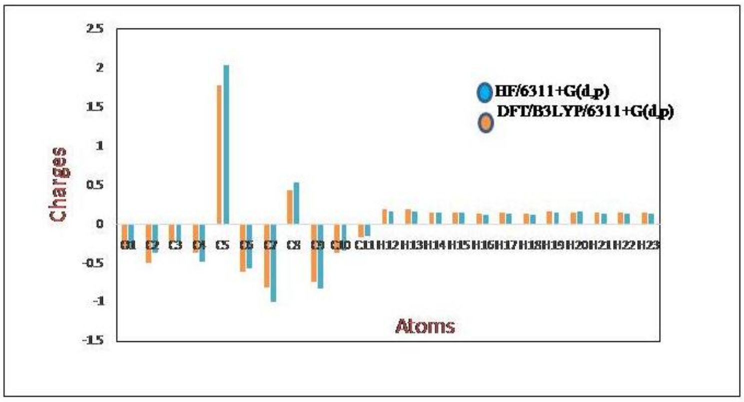


Fig 6..Mulliken atomic charge plots of Butyrophenone

Table 6. Mulliken charges of Butyrophenone

Atoms	Charges DFT/B3LYP/ 6-31 + G(d,p)	Charges HF/6-311 + G(d,p)
O_1	-0.31279	-0.31193
C_2	-0.4991	-0.37307
C_3	-0.23503	-0.22481
C_4	-0.3635	48832
C_5	1.783736	2.041258
C_6	-0.61358	-0.56896
C_7	-0.81165	-0.99996
C_8	0.429111	0.534896
C_9	-0.73804	-0.8223
C_{10}	-0.36352	-0.34142
C_{11}	-0.15991	-0.151
H_{12}	0.193325	0.167838
H_{13}	0.19331	0.167899
H_{14}	0.14988	0.142657
H_{15}	0.149876	0.142685
H_{16}	0.137568	0.116041
H_{17}	0.144307	0.131266
H_{18}	0.137568	0.116021
H_{19}	0.165907	0.147344
H_{20}	0.151762	0.162389
H_{21}	0.153426	0.136156
H_{22}	0.152511	0.13796
H_{23}	0.15484	0.137358

4.7 Electrostatic potential and molecular electrostatic potential:

In the present study, the electrostatic potential (ESP), and the molecular electrostatic potential (MEP) map figures for Butyrophenone calculated at DFT/B3LYP/ 6-311 +G(d,p) level are shown in Fig. 7(a) and 7(b) respectively. It can be seen from the ESP figures, that while the negative ESP is localized more over the oxygen atoms and is reflected as a yellowish blob, the positive ESP is localized on the rest of the molecules. Molecular electrostatic potential (MEP) is related to the electronic density and is very useful descriptor in understanding sites for electrophilic attack and nucleophilic reactions as well as hydrogen bonding interactions where the negative region is mainly localized on oxygen atoms [12].

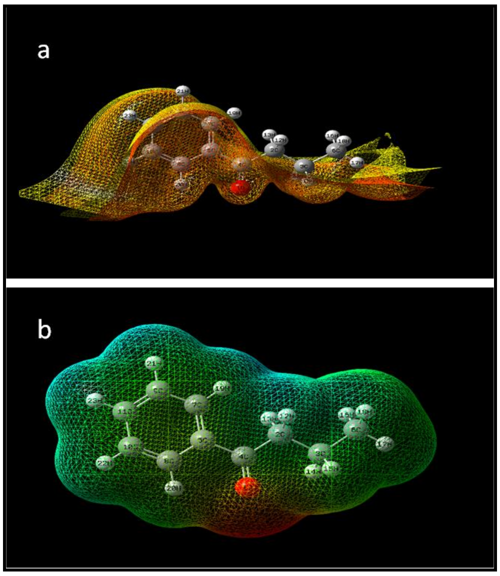


Fig. 7(a)**Electrostatic Potential map (b) Molecular Electrostatic Potential map of Butyrophenone at B3LYP/6-311+G(d,p) level**

4.8 Molecular docking studies

Molecular docking studies are used to determine the interaction of two molecules and to find the best orientation of the ligand which would form a complex with overall minimum energy. The small molecule, known as ligand usually fits within proteins cavity which is predicted by the search algorithm.

Molecular docking study of inclusion process The Patch Dock server program gave several possible docked models for the probable structure based on the energetic parameters; geometric shape complementarily scoreapproximate interface area size and atomic contact energy [13] of the Butyrophenone-CD inclusion complex. The docked Butyrophenone: β-CD model is shown in Fig 8**.**with the highest geometric shape complementarily score 2616, approximate interface area size of the complex 279.30 $Å^2$ and atomic contact energy −183.66 kcal mol^{-1} was the highly probable and energetically favourable model.

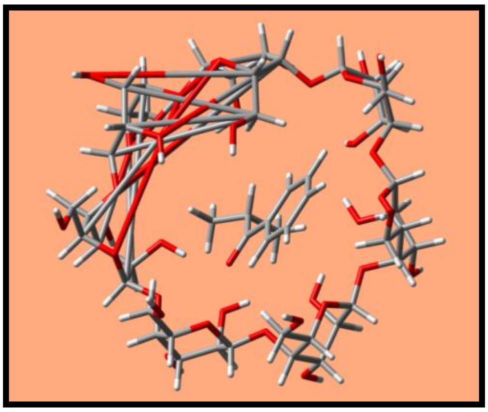


Fig 8. Docked β CD: Butyrophenone

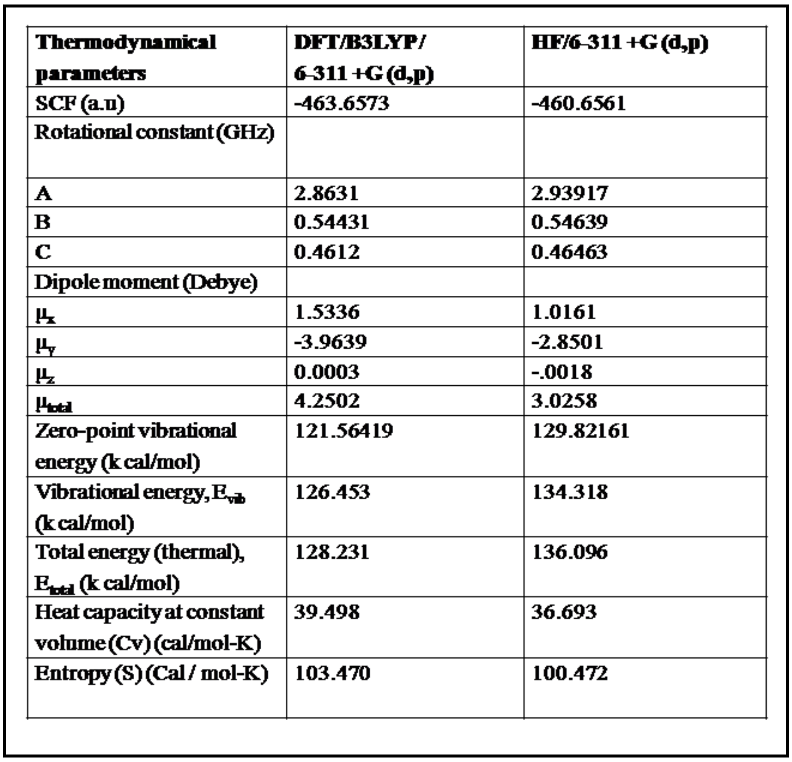
4.9 Thermodynamic Parameters

The thermodynamic parameters namely heat capacity, entropy, rotational constants, dipole moments. Vibrational and vibrational zero point energies of the compound have also been computed at DFT-B3LYP level using 6-311 +G(d,p) basis set and are presented in Table 7.The Thermodynamic data provides useful information for further study on the title compound, when this may be used as a reactant to take part in a new reaction. The dipole moment and its principal inertial axes are strongly depending upon the conformation of the molecule.

The temperature dependence of the thermodynamic properties heat capacity at constant pressure(Cp), entropy(S) and enthalpy change ($\Delta H_{0\text{-}>T}$) for Butyrophenone were also determined by B3LYP/6-311+G(d,p) method and listed in Table 8 and are shown in Fig.9. It is seen that the heat capacities, entropy, enthalpy changes are increasing with temperature ranging from 100 to 1000 K due to the fact that the molecular vibrational intensities increase with temperature. These observed relations of the thermodynamic functions vs. temperatures were fitted by quadratic formulas:

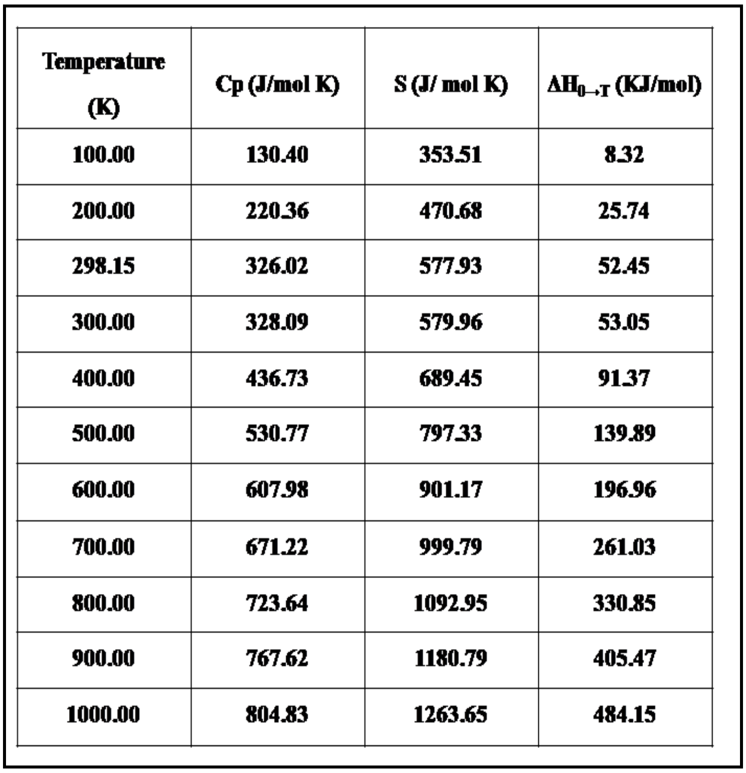
$S = 217.0465 + 0.5\,T - 1.3609 \times 10^{-4}\,T^2$
$Cp = 21.6815 + 0.3858\,T - 1.5329 \times 10^{-4}\,T^2$
$\Delta H = -4.1855 + 0.0587\,T + 1.1077 \times 10^{-4}\,T^2$

Table 7 .Thermodynamic parameter of Butyrophenone



Thermodynamical parameters	DFT/B3LYP/ 6-311 +G (d,p)	HF/6-311 +G (d,p)
SCF (a.u)	-463.6573	-460.6561
Rotational constant (GHz)		
A	2.8631	2.93917
B	0.54431	0.54639
C	0.4612	0.46463
Dipole moment (Debye)		
μ_x	1.5336	1.0161
μ_y	-3.9639	-2.8501
μ_z	0.0003	-.0018
μ_{total}	4.2502	3.0258
Zero-point vibrational energy (k cal/mol)	121.56419	129.82161
Vibrational energy, E_{vib} (k cal/mol)	126.453	134.318
Total energy (thermal), E_{total} (k cal/mol)	128.231	136.096
Heat capacity at constant volume (Cv) (cal/mol-K)	39.498	36.693
Entropy (S) (Cal / mol-K)	103.470	100.472

Table 8.Temperature dependence of thermodynamic properties



Temperature (K)	Cp (J/mol K)	S (J/ mol K)	$\Delta H_{0\rightarrow T}$ (KJ/mol)
100.00	130.40	353.51	8.32
200.00	220.36	470.68	25.74
298.15	326.02	577.93	52.45
300.00	328.09	579.96	53.05
400.00	436.73	689.45	91.37
500.00	530.77	797.33	139.89
600.00	607.98	901.17	196.96
700.00	671.22	999.79	261.03
800.00	723.64	1092.95	330.85
900.00	767.62	1180.79	405.47
1000.00	804.83	1263.65	484.15

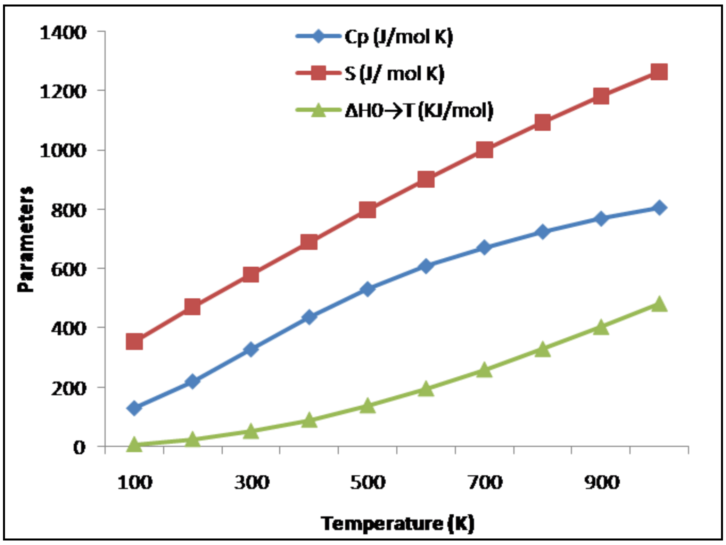


Fig 9. Effect of temperature on heat capacity, entropy and enthalpy

5 Conclusion

The geometry of Butyrophenone was optimized with HF and DFT-B3LYP methods using 6-311 +G(d,p). The complete molecular structural parameters of the compound have been obtained from ab initio and DFT calculations. The bond order and atomic charges of the title molecule have been studied by both HF and DFT methods. The vibrational frequencies of the compound have been precisely assigned and analyzed and the theoretical results were compared with the experimental vibrations. The present investigation provides the complete vibrational assignments, structural information and electronic properties of the compound which may be useful to upgrade the knowledge on Butyrophenone. The energies of MO’s, absorption wavelength (λmax), oscillator strength and excitation energies of the compound were also determined from TD-DFT method and compared with the experimental values. The NBO analysis reflects the charge transfer mainly due to C-C group of the molecule. The calculated electronic properties are compared with experimental electronic spectrum. The calculated HOMO and LUMO energies show that, the charge transfer occurs within the molecule and helped in analyzing the chemical reactivity of the molecule. The molecular electrostatic potential analysis have also been studied to explain the activity of the molecule. The inclusion complex formation which was also confirmed by molecular docking studies. The molecular docking study confirms the formation of inclusion complex of Butyrophenone with*β*-CD where the enhanced absorption confirm the entrapment of benzene ring of Butyrophenone into the *β*-CD nano cavity and –OH group containing benzene ring in the upper part of β-CD cavity.Several thermodynamical parameters were obtained and analyzed with HF and DFT methods using the same basis set. The atomic charges of the molecule were studied by both the HF and DFT methods. On comparing the experimental results with the theoretically predicted values, it was found that the B3LYP method was more accurate, proving that DFT is a reliable method for molecular vibrational analysis.

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