Available online at www.derpharmachemica.com

Scholars Research Library

Der Pharma Chemica, 2011, 3(3):427-448
(http://derpharmachemica.com/archive.html)

ISSN 0975-413X
CODEN (USA): PCHHAX

Vibrational analysis of Two Narcotic Compounds- Codeine and Morphine - A comparative DFT study

Neeraj Misra*, Apoorva Dwivedi, Anoop Kumar Pandey and Sanjeev Trivedi

Department of Physics, Lucknow University, Lucknow, India

ABSTRACT

This work deals with the theoretical study on the molecular structure and vibrational spectra of two well known narcotics- Codeine and Morphine. The spectra were interpreted with the aid of normal mode analysis following full structure optimization based on the density functional theory and 6-311G + (d, p) basis set combination. A detailed interpretation of the infrared spectra of Morphine and codeine are reported in the present work. The similarities and differences between the vibrational analysis of the two molecules studied have been highlighted. The scaled theoretical wave numbers are in perfect agreement with the experimental values. The thermodynamic calculations related to the title compounds were also performed at B3LYP/6-311G + (d, p) level of theory. The FT-Raman and FTIR spectra of Morphine have been taken from the literature.

Keywords: Vibrational spectra, FTIR and FT-Raman spectra, Density functional theory.

INTRODUCTION

Currently available theoretical methods allow a quite precise prediction of experimental IR spectra of rigid, medium-size molecules. For most of such systems, the theoretically calculated frequencies and intensities of the IR absorption bands are close to experimental values. Hence, one may expect that the normal modes, obtained using the theoretically predicted force field, should also reflect well the forms of vibrations in a real molecule. Normal-mode analysis is commonly employed in the interpretation of the vibrational spectra [1]. Opiate molecules are major interest in classical opiate pharmacology because they show the action of analgesia, sedation and euphoria. The discovery of endogenous opiate peptides in the late 1970's developed opioid studies. Opioid peptides seem to mediate the action induced by morphine. On the other hand, opioid agonists and antagonists, who have similar molecular structures, often act differently. In this study, we have theoretically investigated the structures of some endogenous opiates and opiate molecules by molecular orbital calculations. Optimized molecular structures of two opiate molecules (morphine & codeine) are obtained by Density functional calculations [2]. Codeine is an analgesic with uses similar to morphine, but it has a mild sedative effect. It is preferable used as phosphate form and it is often administrated by mouth with aspirin or paracetamol. Therefore, it is important to investigate its structure to know the active groups and weak bonds responsible for its medical activity [3]. Morphine is isolated from crude opium, which is a resinous preparation of the opium poppy, Papaver somniferum. It can be used in symptomatic relief of moderately severe to severe pain, suppression of severe cough and suppression of severe diarrhea (e.g., that produced by cholera) [4].

Computational details

Initial geometry was generated from standard geometrical parameters and was minimized without any constraint in the potential energy surface. The gradient corrected density functional theory (DFT) [5] with the three-parameter hybrid functional (B3) [6] for the exchange part and the Lee-Yang-Parr (LYP) correlation function [7] has been employed for the computation of molecular structure, vibrational frequencies, and energies of the optimized structures, using GAUSSIAN 09 [8]. The calculated vibrational frequencies have also been scaled by a factor of 0.963 [9]. By combining the results of the GAUSSVIEW'S program [10] with symmetry considerations, vibrational frequency assignments were made with a high degree of accuracy.

RESULTS AND DISCUSSION

Geometry Optimization

The optimized structure parameters of Morphine and codeine are listed in Table 1 in accordance with the atom numbering scheme given in Fig. 1 and 2.

The morphine molecule is a five-ring structure incorporating a partially hydro-generated phenanthrene moiety. The molecule consists of two planer parts-the first part involves the atoms C4, C5, C9, to C14, O1 and O3, comprising benzene (A), oxide (B) and corbocyclic (C) rings. The second part includes the atoms C5 to C9, C13 to C7, O2 and N and contains the cyclohexenyl (D) and ethenamine (E) rings. The two planes are nearly perpendicular to each other and the molecule has T shape [11].

The morphine molecule differs from codeine in that an H replaces the C18 methyl group.

The bond lengths and angles (Table 1) are the same as those reported for morphine (Bye, 1976), within experimental error. However, there are some differences between these and those reported for codeine hydro- bromide dihydrate (Kartha *et al.*, 1962) and other morphine derivatives. The different bond distances for C9-N (1.521 A) and C16-N (1.468 A°) reported for codeine hydro bromide dihydrate (Kartha *et al.*, 1962) were not found to be different in codeine, where they were 1.477 and 1.479 A° respectively. There is no apparent chemical reason for these two bonds to be substantially different, and no differences were found in the morphine structure (Bye, 1976) which has these bond distances equal to 1.476 and 1.475 A° respectively, essentially the same as those in this work. It is interesting to note the short C3-O1 bond length of 1.367 A found in codeine and also reported in the morphine structure (Bye, 1976), where it is 1.359 A°. The O1 atom is connected to an H atom in morphine and a methyl group in codeine. It was reasoned by

Bye (1976) that this short bond distance resulted from a 'strong O-H--N hydrogen bond'. However, this short distance is also present in codeine, without the effect of hydrogen bonding. Ring A shows some deviation from planarity which would be expected with a substituted benzene ring such as this. The endocyclic torsion angles of ring B are consistent with an envelope conformation. Atoms C9-C10-C11-C12-C13 of ring C is nearly co- planar. Ring D, which is distorted by the C5-O3-C4 ether bond, takes on a distorted boat conformation. Ring E is in a characteristic chair form [12].

The main structural features of diacetyl-morphine (heroin) are very similar to those of morphine (Mackay &Hodgkin, 1955; Gylbert 1973 and Bye, 1976) and codeine (Lindsey &Barnes, 1955; Kartha, Ahmad and Barnes, 1962) and several other Morphine derivatives, eg. 6-deoxy-6azidodihydroisomorphine (Sasvari et al., 1974). The packing of diacetylmorphine appears to show some interaction between a methyl groups on one molecule with that of a neighboring carbonyl oxygen group on another molecule. This apparent interaction is supported by the relatively short interatomic distances of O5-C19=3.250 and O3-C21=3.311 A°. These distances fall into range of 3.00 to 3.28 A° listed by Donohue (1968). Such interactions have also described as polarization bonds (Dougill & Jeffrey, 1953) [13]. Jose Cotua et.al [14] has also done optimization studies of these title compounds with a lower basis set. Here, in the present work we are giving all the optimized parameters calculated with a higher basis set and also the bond lengths and bond angles of the title compounds which are found to be much closer to the experimental ones. This is the advantage of taking a higher basis set for optimization studies. The main objective of this work is to investigate in detail the vibrational spectra of the title compounds.

The optimized structural parameters of Codeine and Morphine calculated by the B3LYP method with the 6-311G (d) basis set are listed in Table 1 in accordance with the atom numbering scheme. On the basis of vibrational analysis at B3LYP/6-311G (d) levels, the standard thermodynamic functions: internal thermal energy (E), constant volume heat capacity C_v and entropy S have been calculated and are given in the Table 2. They provide helpful information for the further study on the title compounds.

Vibrational Assignments

Codeine has 43 atoms and 123 normal modes of fundamental vibration. All the 123 fundamental vibrations are IR and Raman active. Morphine has 40 atoms and 114 normal modes of fundamental vibrations. Here also all the 114 fundamental vibrations are IR and Raman active. Normal modes analysis provides detailed description of vibrational dynamics of the molecules in question. The detailed vibrational assignments have been analyzed by comparing the band positions and intensities observed in FTIR and FT-Raman spectra with the wave numbers and intensities obtained from the molecular modeling calculations given in Table 3 & 4. The FTIR spectra (Fig- 3, 4 & 5) of morphine were recorded in CsI on a Perkin-Elmer FTIR 1800 Spectrophotometer. Before recording spectra, the equipment was well purged with dry nitrogen. FT-Raman spectra (Fig-6, 7) were taken from the literature [15]. The FTIR and FT-Raman spectra of codeine were taken from the literature [16].

5.4.1.1 Spectral region over 2800 cm^{-1}

The bands located in the high frequency region of the spectra of codeine are easy to identify and belong to O–H and C–H stretching modes. The band due to O–H stretching vibration attached to the base ring is calculated at 3639 cm^{-1} having good IR intensity. The corresponding bands at 2973 and 3040 cm^{-1} are assigned to the C-H stretching mode having good IR intensity. For morphine, the band due to O–H stretching vibration attached to the base ring is calculated at 3686 cm^{-1}, which is in good agreement with the 3680 cm^{-1} in the FTIR spectra. The corresponding bands at 2971 and 3041 cm^{-1} are assigned to the C-H stretching mode, which are in good agreement with 2975 and 3050 cm^{-1} in the FTIR spectra. These are usual range of appearance for O-H and C–H stretching vibrations.

5.4.1.2 Spectral region 1750–1000 cm^{-1}

For codeine, in middle region, the C–C stretches predicted at 1486 and 1606 cm^{-1}, are in reasonable agreement with the 1500 (1500) and 1600 (1600) cm^{-1} observed in FTIR (FT-Raman) spectra. The strong stretching vibration of the C-O band is calculated at 1263 cm^{-1}, and corresponding band is observed at 1274(1280) cm^{-1} in FTIR (FT-Raman) spectrum. For Morphine, in middle region, the C–C stretches predicted at 1437 and 1613 cm^{-1}, are in reasonable agreement with the 1435(1440) and 1630(1630) cm^{-1} observed in FTIR (FT-Raman) spectra. The strong stretching vibration of the C-O band is calculated at 1302 cm^{-1}, and corresponding band is observed at 1300(-) cm^{-1} in FTIR (FT-Raman) spectrum.

5.4.1.3 Spectral region 1000–450 cm^{-1}

For codeine, as expected, the ring torsion modes along with out of plane bending modes appear in the observed low frequency range. The ring torsion and out of plane ring bend; all of them appear in the 1000-450 cm^{-1} frequency range. The ring torsion is calculated at 358 cm-1, which is in good agreement with the 355 cm^{-1} in experimental FT-Raman spectrum. In For morphine, the ring torsion is calculated at 570 cm-1, which is in good agreement with the 575 (575) cm^{-1} in experimental FTIR (FT-Raman) spectrum. Out of plane bending is calculated at 358 cm^{-1}, which is in good agreement with 358 cm^{-1} in the FTIR spectra. On comparing the computed and the experimental frequencies of codeine and morphine, one can conclude that accurate results could be achieved with scaled DFT (B3LYP).

TABLE-1 Comparison of Bond Lengths and Bond Angles of Codeine & Morphine

	Codeine			Morphine		
S. No.	**Bond Lengths & Bond Angles**	**Exp.**	**Calculated (In Literature)**	**Bond Lengths & Bond Angles**	**Exp.**	**Calculated (In Literature)**
1	C1=C2	1.380	1.400 (1.405)	C1=C2	1.41	1.396 (1.406)
2	C1-C11	1.396	1.397	C1-C11	1.39	1.403
3	C1-H23	-	1.086	C1-H22	0.90	1.086
4	C2-C3	1.394	1.403 (1.386)	C2-C3	1.39	1.400 (1.399)
5	C2-H24	-	1.083	C2-H23	1.00	1.084
6	C3=C4	1.385	1.398 (1.410)	C3=C4	1.38	1.388 (1.406)

7	C3-O20	1.367	1.362	C3-O19	1.37	1.366
8	C4-C12	1.359	1.378	C4-C12	1.37	1.376
9	C4-O22	1.386	1.364	C4-O21	1.37	1.371
10	C5-C6	1.528	1.543 (1.386)	C5-C6	1.52	1.543 (1.380)
11	C5-C13	1.547	1.557	C5-C13	1.55	1.560
12	C5-O22	1.486	1.457	C5-O21	1.47	1.460
13	C5-H25	-	1.091	C5-H24	0.90	1.090
14	C6-C7	1.489	1.514 (1.509)	C6-C7	1.49	1.513 (1.508)
15	C6-O21	1.427	1.418	C6-O20	1.46	1.420
16	C6-H26	-	1.105	C6-H25	1.00	1.105
17	C7=C8	1.332	1.332 (1.551)	C7=C8	1.36	1.332 (1.551)
18	C7-H27	-	1.087	C7-H26	1.00	1.087
19	C8-C14	1.504	1.508	C8-C14	1.51	1.508
20	C8-H28	-	1.087	C8-H27	0.90	1.087
21	C9-C10	1.555	1.564	C9-C10	1.54	1.565
22	C9-C14	1.554	1.550	C9-C14	1.55	1.553
23	C9-N19	1.477	1.474	C9-N18	1.53	1.474
24	C9-H29	-	1.095	C9-H28	1.10	1.095
25	C10-C11	1.511	1.515	C10-C11	1.52	1.515
26	C10-H30	-	1.095	C10-H29	0.90	1.095
27	C10-H31	-	1.096	C10-H30	1.00	1.096
28	C11=C12	1.392	1.385 (1.526)	C11=C12	1.36	1.383 (1.526)
29	C12-C13	1.500	1.508	C12-C13	1.5	1.508
30	C13-C14	1.536	1.551	C13-C14	1.55	1.550
31	C13-C15	1.520	1.543	C13-C15	1.54	1.542
32	C14-H32	-	1.098	C14-H31	1.00	1.098
33	C15-C16	1.492	1.529	C15-C16	1.52	1.528
34	C15-H33	-	1.096	C15-H32	1.00	1.096
35	C15-H34	-	1.094	C15-H33	1.00	1.094

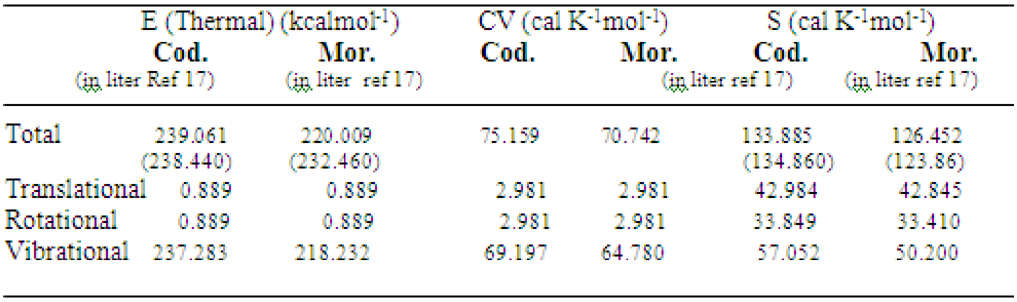
36	C16-N19	1.479	1.462 (1.502)	C16-N18	1.51	1.463 (1.502)
37	C16-H35	-	1.094	C16-H34	0.90	1.094
38	C16-H36	-	1.104	C16-H35	1.00	1.104
39	C17-N19	1.478	1.451	C17-N18	1.49	1.452
40	C17-H37	-	1.093	C17-H36	1.00	1.093
41	C17-H38	-	1.104	C17-H37	1.00	1.104
42	C17-H39	-	1.093	C17-H38	0.90	1.093
43	C18-O20	1.418	1.416	O19-40H	0.90	0.966
44	C18-H40	-	1.096	O20-H39	1.00	0.963
45	C18-H41	-	1.088			
46	C18-H42	-	1.096			
47	O21-H43	-	0.963			
48	C2=C1-C11	121.4	120.8	C2-C1-C11	-	121.0
49	C2=C1-H23	-	118.7	C2-C1-H22	-	118.8
50	C11-C1-H23	-	120.3	C11-C1-H22	121	120.0
51	C1=C2-C3	122.3	121.8	C1-C2-C3	-	121.4
52	C1=C2-H24	-	118.5	C1-C2-H23	117	120.6
53	C3-C2-H24	-	119.5	C3-C2-H23	117	117.8
54	C2-C3=C4	115.7	116.5	C2-C3-C4	124	116.6
55	C2-C3-O20	-	125.9	C2-C3-O19	119	120.6
56	C4=C3-O20	-	117.5	C4-C3-O19	121	122.6
57	C3=C4-C12	122.1	120.6	C3-C4-C12	126	121.4
58	C3=C4-022	-	126.2	C3-C4-O21	114	125.1
59	C12-C4-O22	112.8	113.0	C12-C4-O21	113	113.1
60	C6-C5-C13	114.2	112.0	C6-C5-C13	111	112.3
61	C6-C5-O22	-	111.9	C6-C5-O21	109	111.7
62	C6-C5-H25	-	108.3	C6-C5-H24	104	108.5
63	C13-C5-O22	105.8	106.7	C13-C5-O21	-	106.5
64	C13-C5-H25	-	112.5	C13-C5-H24	-	112.5

65	O22-C5-H25	-	105.0	O21-C5-H24	114	104.9
66	C5-C6-C7	114.6	113.1	C5-C6-C7	111	113.3
67	C5-C6-O21	-	108.4	C5-C6-O20	-	108.1
68	C5-C6-H26	-	104.1	C5-C6-H25	110	104.3
69	C7-C6-O21	-	113.8	C7-C6-O20	-	113.7
70	C7-C6-H26	-	107.3	C7-C6-H25	-	107.4
71	O21-C6-H26	-	109.4	O20-C6-H25	120	109.3
72	C6-C7=C8	121.6	120.4	C6-C7-C8	-	120.7
73	C6-C7-H27	-	117.4	C6-C7-H26	-	117.3
74	C8=C7-H27	-	122.0	C8-C7-H26	118	121.8
75	C7=C8-C14	119.9	119.3	C7-C8-C14	-	119.6
76	C7=C8-H28	-	121.0	C7-C8-H27	-	120.8
77	C14-C8-H28	-	119.6	C14-C8-H27	116	119.4
78	C10-C9-C14	113.0	113.3	C10-C9-C14	114	113.4
79	C10-C9-N19	-	114.9	C10-C9-N18	-	114.9
80	C10-C9-H29	-	107.4	C10-C9-H28	105	107.4
81	C14-C9-N19	106.6	106.9	C14-C9-N18	-	106.8
82	C14-C9-H29	-	107.8	C14-C9-H28	-	107.8
83	N19-C9-H29	-	105.8	N18-C9-H28	114	105.8
84	C9-C10-C11	114.1	114.5	C9-C10-C11	-	114.4
85	C9-C10-H30	-	108.8	C9-C10-H29	-	108.7
86	C9-C10-C31	-	108.5	C9-C10-H30	-	108.5
87	C11-C10-H30	-	111.3	C11-C10-H29	-	111.5
88	C11-C10-H31	-	108.0	C11-C10-H30	-	108.1
89	H30-C10-H31	-	104.9	H29-C10-H30	124	104.9
90	C1-C11-C10	-	124.7	C1-C11-C10	116	124.9
91	C1-C11=C12	115.4	116.2	C1-C11-C12	118	116.2
92	C10-C11=C12	119.2	118.4	C10-C11-C12	123	118.2
93	C4-C12=C11	122.7	123.2	C4-C12-C11	108	122.6

94	C4-C12-C13	110.3	109.4	C4-C12-C13	127	109.2
95	C11=C12-C13	126.0	126.6	C11-C12-C13	112	127.3
96	C5-C13-C12	100.1	100.2	C5-C13-C12	109	100.4
97	C5-C13-C14	115.5	116.6	C5-C13-C14	111	116.6
98	C5-C13-C15	-	111.7	C5-C13-C15	106	111.7
99	C12-C13-C14	106.6	106.2	C12-C13-C14	112	105.9
100	C12-C13-C15	-	112.7	C12-C13-C15	109	112.8
101	C14-C13-C15	108.4	108.7	C14-C13-C15	111	108.8
102	C8-C14-C9	-	115.8	C8-C14-C9	109	115.7
103	C8-C14-C13	110.4	109.8	C8-C14-C13	-	109.9
104	C8-C14-H32	-	109.4	C8-C14-H31	106	109.4
105	C9-C14-C13	106.8	106.5	C9-C14-C13	-	106.4
106	C9-C14-H32	-	105.6	C9-C14-H31	-	105.5
107	C13-C14-H32	-	109.3	C13-C14-H31	112	109.4
108	C13-C15-C16	112.3	112.3	C13-C15-C16	-	112.1
109	C13-C15-H33	-	108.3	C13-C15-H32	-	108.4
110	C13-C15-H34	-	109.8	C13-C15-H33	-	109.9
111	C16-C15-H33	-	109.2	C16-C15-H32	-	109.1
112	C16-C15-H34	-	109.5	C16-C15-H33	-	109.5
113	H33-C15-H34	-	107.3	H32-C15-H33	-	107.4
114	C15-C16-N19	110.7	111.1	C15-C16-N18	109	111.1
115	C15-C16-H35	-	109.3	C15-C16-H34	-	109.3
116	C15-C16-H36	-	109.8	C15-C16-H35	-	109.8
117	N19-C16-H35	-	108.0	N18-C16-H34	-	107.9
118	N19-C16-H36	-	111.9	N18-C16-H35	-	112.0
119	H35-C16-H36	-	106.3	H34-C16-H35	-	106.3
120	N19-C17-H37	-	109.8	N18-C17-H36	-	109.8
121	N19-C17-H38	-	114.4	N18-C17-H37	-	114.4
122	N19-C17-H39	-	109.4	N18-C17-H38	-	109.3

123	H37-C17-H38	-	107.9	H36-C17-H37	-	107.9
124	H37-C17-H39	-	107.7	H36-C17-H38	-	107.7
125	H38-C17-H39	-	107.2	H37-C17-H38	112	107.3
126	O20-C18-H40	-	111.6	C9-N18-C16	114	113.2
127	O20-C18-H41	-	105.7	C9-N18-C17	111	114.2
128	O20-C18-H42	-	111.6	C16-N18-C17	-	112.3
129	H40-C18-H41	-	109.2	C3-O19-H40	-	108.2
130	H40-C18-H42	-	109.9	C6-O20-H39	106	108.0
131	H41-C18-H42	-	109.2	C4-O21-C5	-	107.1
132	C9-N19-C16	112.5	113.1			
133	C9-N19-C17	112.5	114.2			
134	C16-N19-C17	111.4	112.3			
135	C3-O20-C18	117.9	118.0			
136	C6-O21-H43	-	108.0			
137	C4-O22-C5	105.4	107.5			

TABLE-2 Calculated Thermodynamic Properties of Codeine, Morphine (B3LYP)/ 6-311G (d) methods



	E (Thermal) (kcalmol^{-1})		CV (cal K^{-1}mol^{-1})		S (cal K^{-1}mol^{-1})	
	Cod. (in liter Ref 17)	**Mor.** (in liter ref 17)	**Cod.**	**Mor.**	**Cod.** (in liter ref 17)	**Mor.** (in liter ref 17)
Total	239.061 (238.440)	220.009 (232.460)	75.159	70.742	133.885 (134.860)	126.452 (123.86)
Translational	0.889	0.889	2.981	2.981	42.984	42.845
Rotational	0.889	0.889	2.981	2.981	33.849	33.410
Vibrational	237.283	218.232	69.197	64.780	57.052	50.200

Cod. -Codeine, Mor.-Morphine, liter- literature

TABLE-3 Comparison of the observed and calculated Vibrational spectra of Codeine with B3LYP/6-311G (d)

S.No.	B3LYP/6-311G(d,p)		Experimental		Assignment
	Sc. freq.	IR Int.	FT IR	FT Raman	
1	42	0.5981			Ring Torsion
2	56	2.8249			Ring R1R3 Torsion
3	88	1.2227			ω(CH_3)+RingR1 Torsion

4	120	2.6868		Twist(O-CH_3)adjR1+RingR3 Torsion
5	122	1.0098		Ring R1R3 Torsion
6	155	1.6789		Ring R1R3 Torsion
7	176	4.2155		ω(CH_3)adjR1+γ(ON)adjR3
8	210	0.9752		ω(CH_3)adjR1+γ(CH_2)R5+β(ON)adjR3
9	228	1.7773		τ(CH_3)adjR5&R1+τ(CCC)R1
10	234	1.5212		τ(CH_3)adjR5+γ(CH_2)R5&R4+τ(CCC)R1
11	253	0.6182		τ(CH_3)adjR1&R5+γ(CH_2)R5+τ(CCC)R1
12	257	117.0903	250	β(OH)adjR3
13	264	1.5477		Ring Torsion
14	267	0.4027		γ(CH_2)R5+τ(CH_3)adjR1+β(OH)adjR3+τ(CH)R1
15	304	0.3237		γCH_2)R5+ω(CH_3)adjR5R1+τ(CH_3)adjR1R5+γ(CH_2)R5+τ(CH_3)adjR5R3
16	317	5.8185		τ(CH_3)adjR5+β(OH)adjR3+RingR3 Bending+γ(CH_2)R5
17	336	2.1741		τ(CH_3)adjR5+γ(CH_2)R4+γ(CCC)R1
18	351	2.1837		τ(NCCH)R3+γ(CH3)adjR1+γ(CH_2)R5
19	358	5.1349	355	τ(CH_3)adjR1+γ(CCC)R1+γ(CH_2)R4
20	372	1.3275		γ(CCC)R1+γ(CH_3)adjR1R5
21	411	2.332		γ(CH_2)R5+β(14C-32H)+γ(CCC)R3
22	427	1.721		γ(CH)R3
23	449	1.2177		τ(CCCC)R1+τ(HCCC)R3
24	468	1.8507	475	β(CH)R3+bending(R5)
25	479	1.7052		β(CCC)R1+γ(CH)R3+bending(R4)
26	510	3.732		γ(CH_2)R4+γ(CH_3)adjR5+γ(CH)R3+bending(R5)
27	540	0.4029		β(CCC)R1+γ(CH)R3+γ(C-C-C)R3+γ(CH_2)R5
28	558	1.6909	550	γ(CCC)R1+τ(H-C-C-H)R1+γ(CH_2)R5
29	582	1.1981		γ(CCC)R1+γ(CH_2)R5+γ(CH)R1R3
30	603	5.2584		γ(CH_2)R4+def(R1)
31	629	2.7934	628	γ(CH)R3+Ring bending
32	634	5.9854		γ(CH)R3

33	655	17.3864		650	γ(CH)R3+defR1
34	688	9.8218			γ(CCC)R1+γ(CH)R1R3+BendingR3R4+β(OH)adjR3
35	708	5.997			β(CCC)R1+γ(CH2)R3+BreathingR4+γ(CH)R3
36	723	7.6875			γ(C-C-C)R1R3+γ(C-H)R1R3+γ(COC)R2+γ(CH_2)R4
37	759	15.9531		750	γ(CH)R1R3+γ(C-C-C)R1R3+γ(COC)R2
38	777	8.7729			γ(CH)R1+γ(C-C-C)R1+γ(CH2)R5+γ(CNC)R3
39	793	54.074	795		γ(CH)R1R3+γ(C-C-C)R3+β(O-H)adjR3
40	797	18.1226			β(CH)R1
41	797	1.5372			τ(HCCH)R5+γ(CCC)R4+γ(CH)R1
42	811	22.7548	820		RingR5R3 bending
43	850	6.1124			Ring R4 Breathing+β(14C-32H)+β(CH)R3+β(C-O-C)R2+β(CH)R1+β(C-C-C)R1
44	859	1.9847	860	850	τ(H-C-C-H)+R1
45	865	7.084			τ(H-C-C-H)+R(CH_2)R4R5+RingR4R5 bending
46	897	11.2012	895		β(C-C-C)R1+ν(O-CH_3)adjR1+β(C-C-C)R4+β(C-O-C)R2+β(CH)R2R4
47	918	8.4482			τ(HCCH)R3+τ(CH_2)R4R5
48	924	22.3192		920	RingR5 bending+β(CH)R3+R(CH2)R4+ν(C-O)R2+β(16C-30H)
49	927	14.1032	935	940	τ(HCCH)R3+R(CH_2)R4
50	959	4.4782			β(CCC)R1+γ(CCC)R3+ω(CH_2)R4
51	961	19.0453			ν(C-O)R2+β(O-H)adjR3+γ(C-C-C)R3+β(CH)R3R1
52	1009	7.804	1000		ν(C-C)R3+Ring R5 bending+β(CH)R3R4++R(CH_2)R5+β(C-C-C)R1
53	1012	15.3346			Ring R3R5 bending+ω(CH_3)adjR5
54	1021	11.1142			Ring R3R5 bending
55	1040	26.6837		1030	ν(C-O)adjR1+β(C-C-C)R1+ν(C-N)R5+R(CH_2)R5+β(CH)R5
56	1041	21.4298			ν(C-O)R3+β(C-C-C)R3+β(CH)R1
57	1053	53.3392	1055	1060	ν(O-CH_3)adjR1+β(C-C-C)R1+RingR1R5 bending+R(CH_3)R5
58	1070	57.8686			ν(C-O)adjR3+ν(C-C-C)R3+β(CH)R1
59	1080	22.9199			ν(5C-13C)+β(C-O-C)R2+β(C-C-C)R5+ν(CH_3-N)+β(CH)R1R2R3R4R5
60	1096	16.7379			ν(C-O)adjR3+β(CCC)R2R3R5+β(CH)R3+ω(CH_3)adjR5
61	1099	103.0627	1114	1100	ω(CH_3)adjR5+τ(CH_2)R5+β(CH)R1+β(C-C-C)R1+β(O-H)adjR3

62	1115	3.5441			β(CH)R1+ω(CH$_3$)adjR5
63	1131	33.6875	1130		β(CH)R1R4+β(C-C-C)R1+ν(N-CH$_3$)adjR5+β(C-N-C)R5
64	1137	0.8664			R(CH$_3$)adjR1
65	1145	24.1243			β(C-C-C)R1+ω(CH$_3$)adjR1+ν(C-C)R4+β(CH)R4R3R5
66	1154	19.1372		1150	β(CH)R3+β(OH)adjR3
67	1164	34.7501	1165		ω(CH$_3$)adjR1+β(C-C-C)R1+τ(CH$_2$)R4
68	1176	18.6144	1175		β(CH)R1+ω(CH$_3$)adjR1+β(C-C-C)R1
69	1184	89.746			ν(C-C)R1+ν(C-O)R2+β(5C-25H) +β(CH)R3 +β(OH)adjR3 +R(CH$_2$)R5+ β(CNC)R5+ ν(N-H3)R5
70	1193	7.3594			ν(C-C)R1+β(CH)R1+R(CH$_2$)R4+β(C-C)R4+ν(C-N)R5+β(14C-32H)+β(9C-25H)
71	1197	56.6501			β(CH)R3+β(O-H)adjR3
72	1206	13.9317			β(C-C-C)R1+γ(C-C-C)R3+β(CH)R1R3+ω(CH3)adjR3+β(14C-32H)
73	1221	8.2984			ν(14C-13H)+β(14C-32H)+β(13C-33H)+τ(CH$_2$)R4R5
74	1238	35.5755			β(CH)R3R5R2+ν(C-N)R5+τ(CH$_2$)R5+β(C-C-C)R1+ν(C-O)R1
75	1247	10.8768	1250		β(5C-25H)+β(6C-26H)+β(14C-32H)+β(CH)R3
76	1263	166.2121	1274	1280	ν(C-O)adjR1+R(CH$_3$)adjR1+β(C-C-C)R1+ν(C-N)R5
77	1273	22.7673			τ(CH$_2$)R5+ν(N-CH$_3$)R5+β(CH)R4R5
78	1277	14.2803			β(CH)R3R5+ν(CN)R5
79	1296	1.2621			β(CH)R3R5+β(O-H)adjR3+β(CH$_2$)R4
80	1307	16.1415	1300		ν(C-C)R1R5+β(9C-25H)+β(5C-25H)+β(5C-25H)
81	1314	15.0313	1315		ν(C-C)R1R5+β(CH)R1+β(5C-25H)+S(CH$_2$)R5
82	1320	3.5872			S(CH$_2$)R5+β(CH)R1
83	1330	0.4715			ν(C-C)R1R4+S(CH2)R4+β(9C-29H)+β(14C-32H)
84	1335	10.1523			ν(C-C)R3R4+β(CH)R3+β(5C-25H)+S(CH2)R5+ν(C-O)R5
85	1340	16.6125		1330	β(CH)R5+β(11C-32H)
86	1359	11.6596			ν(C-C)R3+β(CH)R3+β(O-H)adjR5
87	1365	16.3703	1380		s(CH$_2$)R5+s(CH$_3$)adjR5+β(CH)R5
88	1374	1.3886			β(CH)R3+β(O-H)adjR3
89	1417	19.2748			ν(C-C)R1+s(CH$_2$)R4+s(CH$_3$)adjR5+b(CH)adjR1
90	1420	7.8025			s(CH$_3$)adjR5+b(CH)R1+b(C-C)R1

91	1432	20.9443			s(CH$_3$)adjR1
92	1434	18.0811	1435	1440	s(CH$_2$)R4
93	1438	13.898			s(CH$_2$)R5
94	1447	22.6896	1445	1455	s(CH$_3$)adjR5+s(CH$_2$)R4R5
95	1451	7.45			s(CH$_3$)adjR1
96	1463	5.7641			s(CH$_2$)R5+s(CH3)adjR5
97	1465	54.0017			s(CH$_3$)adjR!
98	1475	8.0129			s(CH$_2$)R5+s(CH$_3$)adjR5
99	1486	101.9063	1500	1500	ν(C-C)R1+β(CH)R1
100	1573	23.8463	1565		ν(C-C)R1R4
101	1606	40.8866	1600	1600	ν(C-C)R1
102	1627	2.5448	1625	1632	ν(C-C)R3
103	2801	47.999			ν(CH)R3
104	2807	51.6453			ν(CH)R5adjR6
105	2817	97.3307			ν(CH)R5adjR5
106	2883	23.5328			ν(14C-32H)
107	2886	73.9222			νs(CH$_3$)adjR1
108	2901	13.3026			νs(CH$_2$)R4+ν(9C-29H)
109	2904	35.8448			νs(CH$_2$)R4
110	2921	52.8041			ν(9C-21H)+νs(CH$_2$)R4
111	2927	33.8532			νas(CH$_2$)R4
112	2933	33.815			ν(CH)R5+νs(CH$_3$) adjR5
113	2937	88.4334			ν(CH) R5adjR5
114	2938	52.4269			νas(CH$_3$)adj R1
115	2952	32.03			νas(CH$_2$)R5
116	2971	44.1308			ν(5C-25H)
117	2973	38.7659			νas(CH$_3$)R5
118	3017	30.1817			ν(CH)adj+νas(CH$_3$)
119	3018	10.1023			ν(CH)R1

120	3034	17.8069	ν(CH)R1
121	3040	30.1228	ν(CH)R3
122	3074	19.0294	ν(C-H)R1
123	3639	13.3915	ν(O-H)

w-weak; vs.-very strong; s-strong; m-middle; sh-shoulder; ν: stretching; ν_s: symmetric stretching ν_{as}: asymmetric stretching, β: -in plane bending; γ: out of plane bending, τ: torsion, F.C.: force constant.

TABLE-4 Comparison of the observed and calculated Vibrational spectra of Morphine with B3LYP/6-311G (d)

S.No.	Sc. Freq	IR Int.	Raman Act.	FT IR	FT Raman	**Assignment**
1	47	0.5786	0.9748			γ(C-O)adj R3+R(C-O-C)R2+γ(C-C-C)R3
2	67	0.3266	4.0894			Ring Torsion
3	118	0.7762	2.4211			Ring R1R3 O.P.P. Bending
4	124	1.3336	1.9014			Ring Bending
5	160	1.3722	0.5583	160		γ(C-C)R1R3+R(CH_3)adjR5+R(CH_2)R5+γ(CH)R3
6	198	1.6354	0.7889	204		Ring Bending+β(C-O)adj R3
7	232	2.4084	1.3202	232		R(CH_2)R1
8	238	1.574	0.6493	238		R(CH_3)adj R5+γ(C-C-C)R5
9	251	2.5552	0.1906	255		γ(C-O)R1+γ(C-O-C)R2+R(CH_3)adj R5
10	261	97.3183	3.4953	259		γ(OH)adj R3
11	268	3.5183	1.2347	265		R(CH_3)R5+τ(H-C-C-H)R5+γ(C-C-C)R1
12	271	5.4543	0.8788	270		R(CH_2)R4+R(CH_3)adj R5+τ(H-C-C-H)R3+γ(C-O-C)R2
13	313	5.2142	3.1397	303		τ(H-C-C-H)R3+Ring R5R3 Breathing
14	323	1.236	3.1214	323		τ(H-C-C-H)R3+R(CH_2)R5
15	335	2.7481	0.3	335		Ring R5 Bending+τ(H-C-C-H)R3
16	348	2.4344	3.1567	350		γ(C-C-C)R1R3+R(CH_2)R4+γ(CH)R1
17	358	5.6332	2.1994	358		O.O.P. R3 Bending+γ(C-O-C)R2+γ(N-N)R5+γ(CH)R1
18	382	97.8247	1.8931	375		γ(OH)adj R1
19	401	2.2698	3.6367	400	400	γ(C-C-C)R3+R(CH_2)R5
20	432	3.9304	3.6187	432		Ring R3R4 Breathing

21	449	2.2261	3.3232	458	445	γ(C-C-C)R1+τ(N-C-C-H)R5
22	468	1.3573	2.3416	465	475	Ring R3R5 Breathing
23	490	0.6395	3.337	490	490	Ring R1R4 Breathing
24	508	3.148	1.069	510		γ(C-N-C)R5+R(CH$_3$)R5+R(CH$_2$)R4+γ(CH)R3
25	538	0.3447	5.2589	535	530	γ(C-C-C)R1+γ(CH)R3+R(CH$_2$)R5
26	556	3.4645	0.303	550	560	τ(H-C-C-H)R1+γ(C-N-C)R5+R(CH$_2$)R5
27	570	4.8808	0.6631	575	575	τ(H-C-C-H)R1+γ(CH)R3+γ(C-N-C)R5
28	592	10.0897	0.1975	590	585	γ(C-C-C)R1R2R4+γ(CH)R1+γ(C-O)adj R3
29	609	2.2189	3.8056	610	600	γ(C-C-C)R4R3+τ(H-C-C-H)R1
30	629	1.6738	15.5813	635	625	γ(CH)R3+β(C-O-C)R2
31	647	21.2658	6.6594	650		γ(CH)R3+γ(C-C-C)R1
32	682	8.7261	3.1235	690		γ(C-C-C)R1R2R4+γ(CH)R2
33	713	4.8026	3.2975	715	700	β(C-C-C)R1R4+γ(CH)R3
34	721	4.8664	0.9973	725		γ(C-C-C)R1R4+γ(C-O-C)R2+γ(CH)R1R3
35	760	12.8912	0.754	750		γ(C-C-C)R1R4+γ(CH)R3+γ(C-O-C)R2
36	774	6.4181	5.3622	770	755	γ(C-C-C)R1+R(CH$_2$)R4R5+γ(C-N-C)R5
37	791	44.1356	1.2621	775		γ(C-C-C)R3+γ(CH)R1+β(OH)adj R3+β(C-C-C)R4
38	777	27.1075	1.6831	785		γ(CH)R1
39	797	1.1474	1.6121	800		γ(C-C-C)R1+γ(CH)R1+τ(H-C-C-H)R5+R(CH$_2$)R4
40	809	24.5584	2.9775	810		ν(C-C)R3+γ(CH)R3+β(OH)R3+γ(C-O-C)R2
41	846	6.436	2.6557	845	840	ν(C-C)R4+β(14C-31H)+τ(H-C-C-H)R3R5+β(C-C-C)R3
42	862	9.4538	1.1319	865		β(C-C-C)R3R5+R(CH$_2$)R3R5
43	891	0.9858	0.314	890		τ(H-C-C-H)R1
44	913	22.3502	2.6041	900		Ring Bending
45	919	19.9512	1.6377	925		Ring R5-R3 Bending
46	928	11.7416	3.2992	930	935	Twist(H-C-C-H)R1R3+β(C-O-C)R2+β(C-C-C)R1+ν(13C-12C)
47	936	5.0329	1.3703	935		Twist(26H-7C-8C-27H)R3+γ(C-C-C)R1
48	954	4.4395	2.8419	945		Twist(31H-14C-8C-27H)+β(C-C-C)R1+β(CH)R1
49	957	21.9451	1.1831	955		ν(N-C)R5+R(CH$_2$) R5+γ (C-C-C)R5

50	1005	13.7397	3.1356	1010		β(C-C-C)R1R3+ν(C-C)R5+β(CH)R5R4+β(CH$_2$)R5
51	1006	16.8971	1.3323	1015		β(CH)R1R3+β(C-C-C)R1R4
52	1018	15.976	3.7646	1020		ω(CH$_3$)adj R5+ν(CH)R5
53	1036	21.6278	3.3137	1035		ν(C-O)adj R3+ν(C-C)R3R4
54	1041	12.3857	1.2886	1045		ν(9C-14C)+ν(N-H)R5+ν(C-C)R1+R(CH$_3$)adj R5
55	1059	56.5292	3.3769	1065		β(CH)R1+γ(C-C-C)R3+β(14C-31H)+ν(C-O)adjR3+β(5C-24H)+R(CH$_2$)R5
56	1071	10.9415	8.1813	1075	1080	β(C-C-C)R1R3R5+β(CH)R1+β(14C-31H)+β(5C-24H)
57	1087	61.2323	5.2217	1085		γ(C-C-C)R3R5+β(14C-31H)+ω(CH$_3$)adjR5+β(OH)adj R3+β(CH)R1+ν(C-C)R4
58	1091	9.6575	4.7082	1095		ν(C-C)R3R5+β(CH)R3+ω(CH$_3$)adj R5+R(CH$_2$)R4
59	1105	7.7393	1.9674	1105		ω(CH$_3$)adj R5+β(CH)R1+τ(CH$_2$)R5
60	1124	50.3283	0.7958	1120	1120	β(C-C-C)R1+β(CH)R1+ν(N-CH$_3$)+ν(C-C-C)R2+β(8C-28H)
61	1133	21.0906	1.3832	1135		β(C-C-C)R1+β(CH)R1R4+ν(CO)R2
62	1141	23.5209	9.3133	1140	1140	β(C-C-C)R1+β(CH)R1R3+β(OH)adjR1+β(9C-28H)+β(14C-31H)
63	1148	5.579	4.457	1150		β(CH)R3+β(OH)adj R3
64	1165	11.4622	6.9153	1160		β(OH)adj R1+τ(CH$_2$)R4R5+β(14C-31H)+β(C-C-C)R1
65	1182	7.1508	5.9005	1175		ν(C-C)R1+R(CH$_2$)R4+β(CH)R4
66	1192	46.0831	2.4646	1190		β(CH)R3+β(OH)adj R3
67	1197	18.3082	8.5606	1200		τ(CH$_2$)R1+β(14C-31H)+β(9C-28H)+β(C-C-C)R1+β(CH)R1
68	1207	130.855	0.6516	1205	1205	β(C-C-C)R1+ν(C-O)adj R1+β(CH)R1+β(6C-25H)+β(5C-24H)
69	1211	103.8086	4.317	1215		τ(CH$_2$)R4+β(OH)adj R1+ν(C-O)adj R1+β(14C-31H)
70	1232	5.0094	2.096	1230		τ(CH$_2$)R5+β(5C-24H)+β(CH)R3
71	1235	9.137	1.7938	1240		τ(CH$_2$)R4+β(CH)R2R3R5
72	1262	8.1143	10.4676	1250	1250	β(C-H)
73	1266	20.6193	0.8707	1260		ν(N-H)R5+τ(CH$_2$)R5+β(CH)R3R5
74	1285	4.2617	3.79	1280	1280	β(CH)R1R2R3R4R5+β(OH)adj R1+R(CH$_2$)R4
75	1297	16.1225	10.2162	1295		β(OH)adj R1+ν(C-C)R1+ν(C-O)R2+β(CH)R1R2R3R4R5
76	1302	20.1968	3.0332	1300		ν(C-O)R2+β(CH)R2R3R4+R(CH$_2$)R5
77	1309	9.5525	10.2318	1310		ν(C-O)R1+β(CH)R2R3R4+β(OH)adj R1
78	1315	0.952	1.5037	1315		β(CH)R1R2R3R4R5+β(OH)adj R1

79	1327	7.315	2.8013	1325		ν(C-C)R1+β(CH)R1R3R5+ν(C-O)R2+R(CH$_2$)R3+β(OH)adj R3
80	1329	14.5436	4.0663	1330	1330	β(CH)R3R4R5
81	1339	39.0957	4.9103	1345	1340	ν(C-C)R1+β(C-H)R1R3+β(OH)adj R1R3
82	1351	3.5124	2.0966	1355		β(CH)R3+β(OH)adj R3+R(CH$_2$)R5
83	1356	13.0517	2.5487	1365		ν(N-CH$_3$)R5+R(CH$_2$)R5
84	1365	1.8802	2.6961	1370		β(OH)adj R1+β(CH)R1
85	1404	1.1868	3.1411	1395		s(CH$_3$)adj R5
86	1416	1.3777	10.657	1400		s(CH$_2$)R4+s(CH$_3$)adj R5
87	1424	0.8205	6.9713	1410		s(CH$_2$)R4+s(CH$_3$)adj R5
88	1430	39.9204	12.472	1420	1425	s(CH$_3$)adj R5+s(CH$_2$)R4+ν(C-C)R1+β(CH)R1
89	1437	76.5154	5.7785	1435	1440	ν(C-C)R1+β(CH)R1+β(OH)adj R1+s(CH$_2$)R4+s(CH$_3$)adjR5
90	1451	2.5564	4.0022	1445		s(CH$_3$)adj R5+s(CH$_2$)R5
91	1461	7.8251	14.2721	1465	1475	s(CH$_3$)adjR5+S(CH$_2$)
92	1482	67.4019	2.7723	1500		ν(C-C)R1+β(OH)adjR1
93	1589	42.1189	6.6083	1580		ν(C-C)R1+β(OH)adjR1
94	1613	38.4607	31.8245	1630	1630	ν(C-C)R1+β(CH)R1
95	1626	3.3345	18.447	1640		ν(C-C)R3
96	2805	33.3246	134.4275	2800		ν(CH)R3+ν(CH)adjR5
97	2804	58.1153	27.2911	2810		ν(CH)R5+ν(CH)adjR5+ν(CH)R3
98	2813	89.3931	111.16	2815		ν(CH)R5
99	2879	17.618	74.0127	2885		ν(14C-31H)
100	2898	9.9075	69.9213	2895		νs(CH$_2$)R4
101	2900	32.9936	78.5277	2900		νs(CH$_2$)R5
102	2916	47.9462	156.4425	2920		ν(CH)R5
103	2926	32.5933	100.8539	2930		νas(CH$_2$) R4
104	2928	31.9622	66.3058	2935		νs(CH$_3$)R5+ν(CH)R5
105	2932	69.2139	274.8601	2940		ν(CH)R5
106	2948	27.9141	68.8149	2945		νas(CH$_2$)R5
107	2969	25.9062	96.5798	2970		νas(CH$_3$)adjR5

108	2969	43.1949	125.4226	2975	ν(5C-24H)
109	3019	6.1284	54.9362	3010	ν(CH)R3
110	3038	12.173	80.9225	3035	ν(CH)adjR1
111	3041	22.4694	167.0816	3050	ν(CH)adjR3
112	3063	11.7895	215.8472	3060	ν(CH)adjR1
113	3653	71.7397	70.9766	3650	ν(OH)adjR1
114	3686	33.4209	162.0219	3680	ν(OH)adjR3

W-weak; vs.-very strong; s-strong; m-middle; sh-shoulder; ν: stretching; ν_s*: symmetric stretching* ν_{as}*: asymmetric stretching, β: -in plane bending; γ: out of plane bending, τ: torsion.*

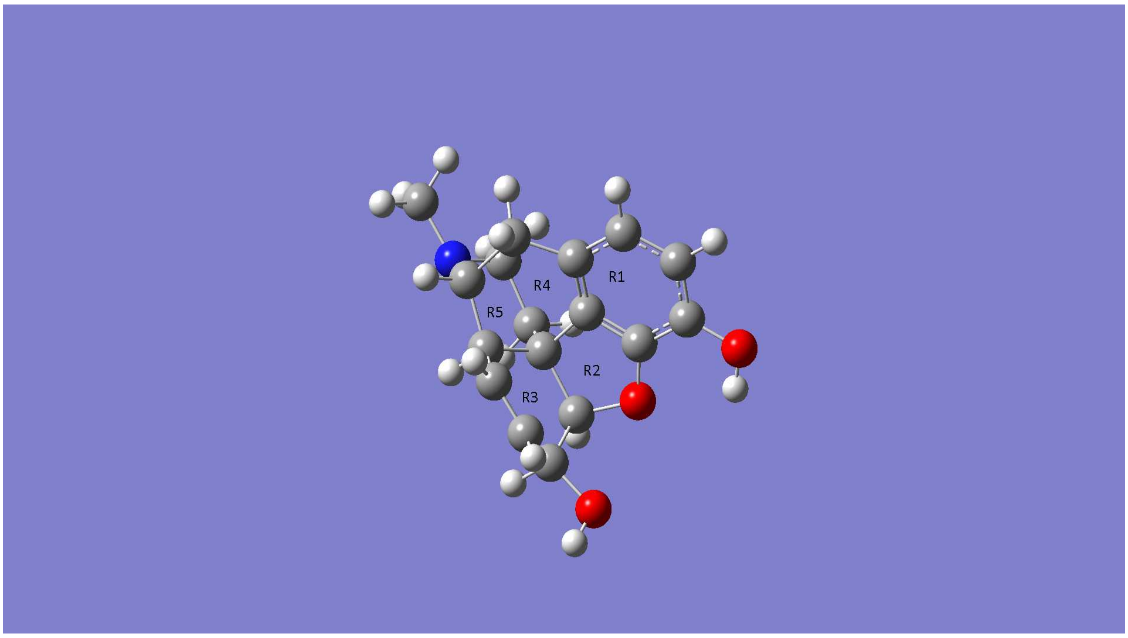


Fig.1. Model molecular structure of morphine

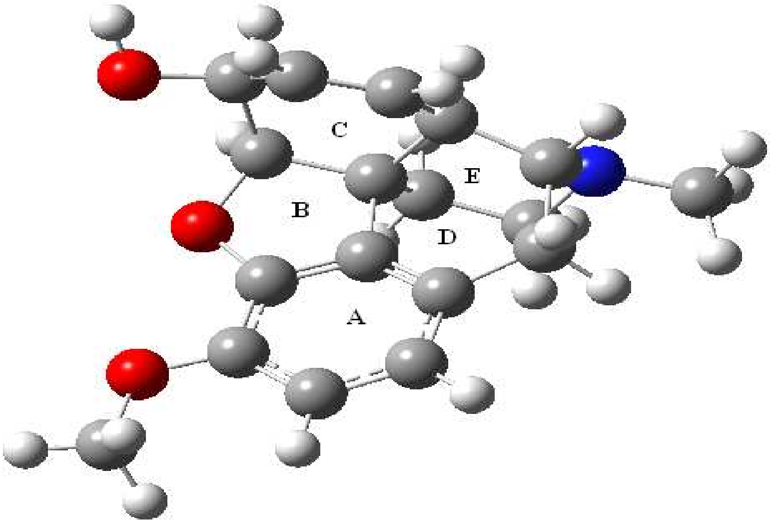


Fig.2. Model molecular structure of codeine

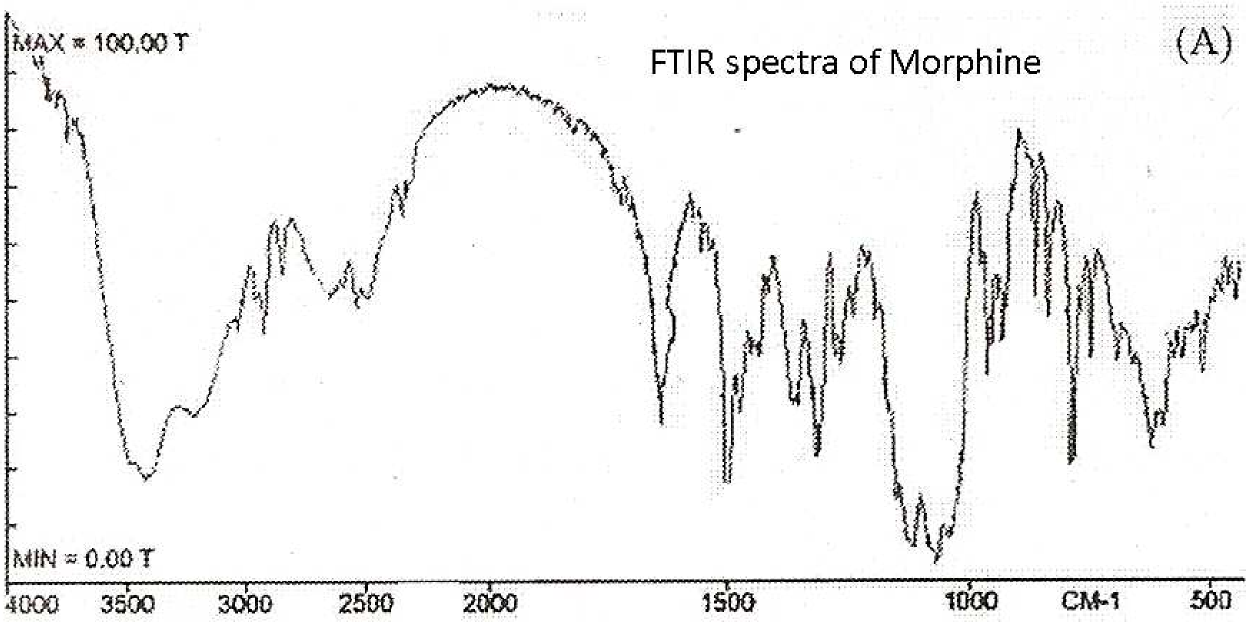


Fig.3. FT-IR spectra of morphine above 500 cm^{-1}

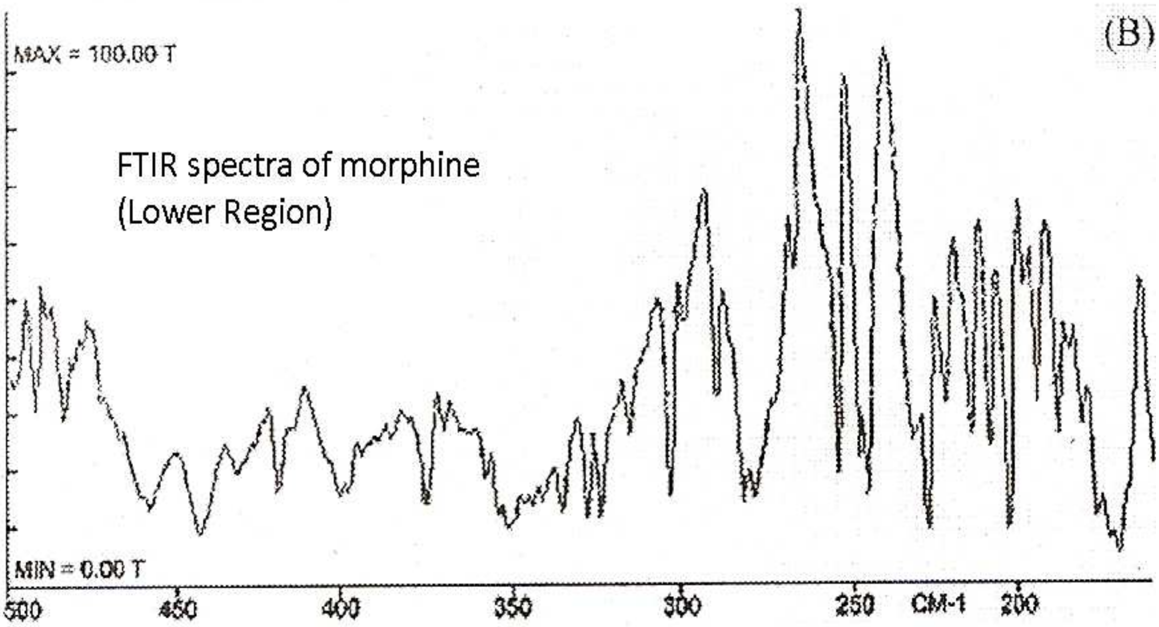
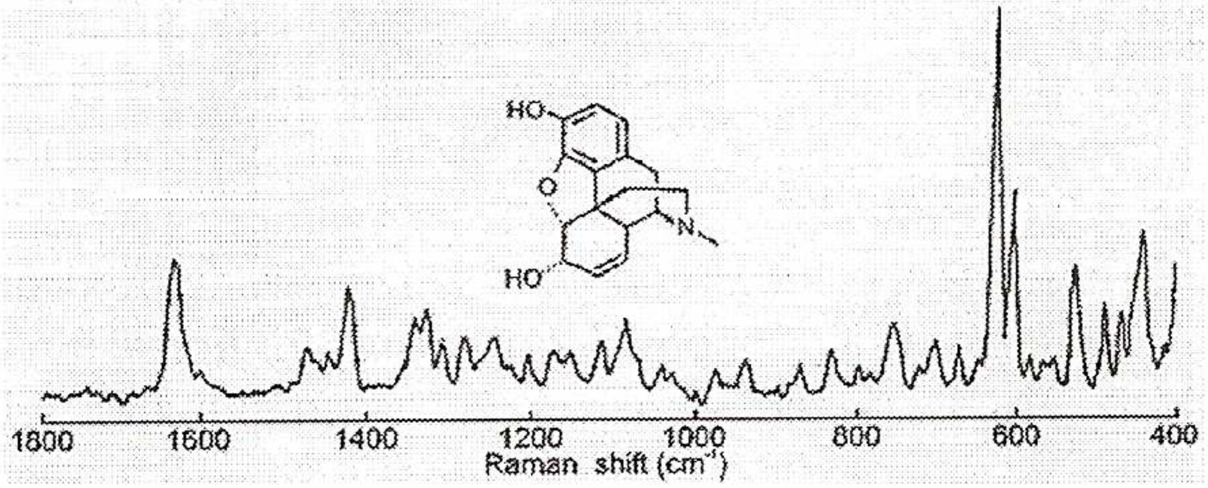


Fig.4. FT-IR spectra of morphine below 500 cm^{-1}



FT-Raman of Morphine

Fig.5. FT-Raman spectra of morphine

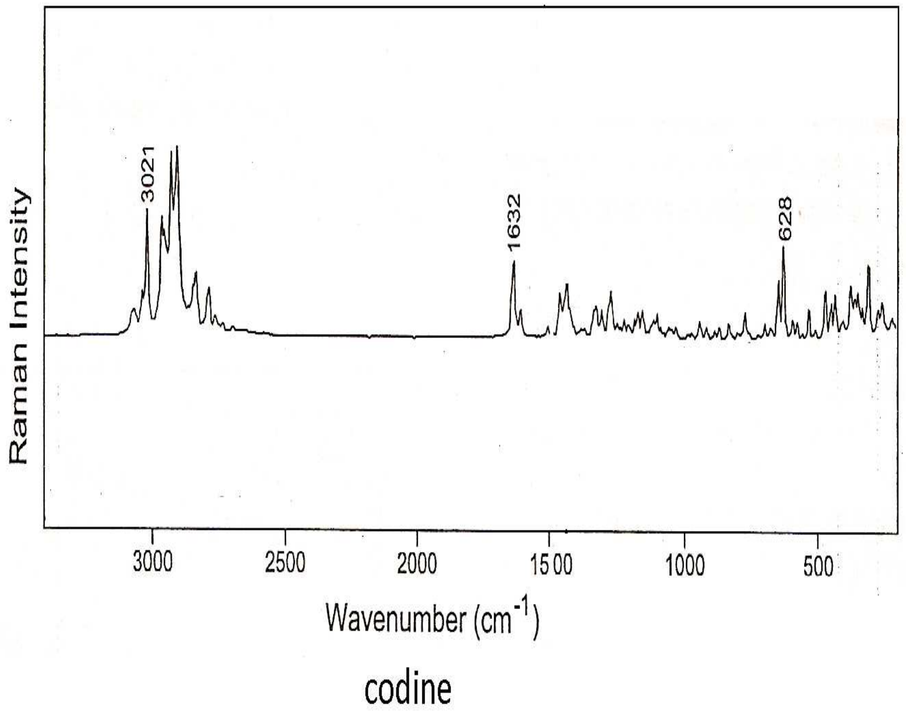


Fig.6. FT-Raman spectra of codeine

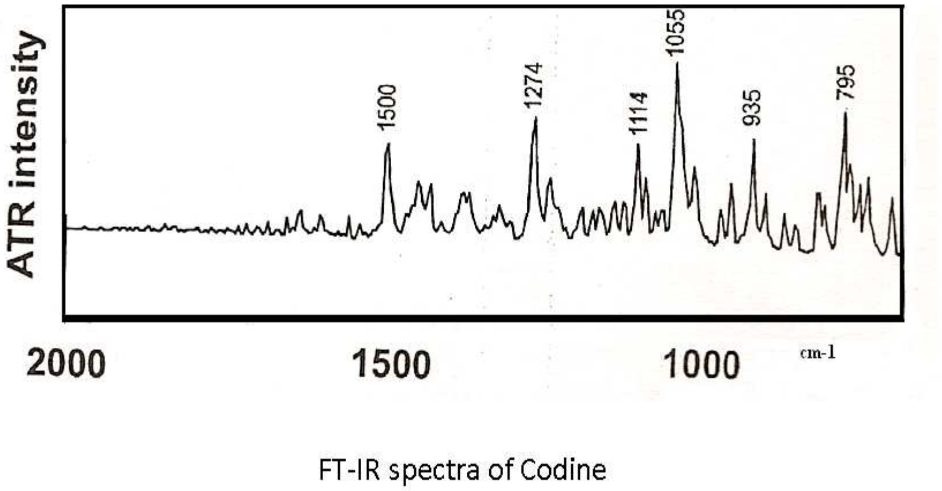


Fig.7 FTIR spectra of codeine

CONCLUSION

Attempts have been made in the present work for the proper frequency assignments for codeine and morphine from the FTIR and FT-Raman spectra. The equilibrium geometries and harmonic frequencies of codeine and morphine were determined and analyzed at DFT level of theory utilizing 6-311 + G (d) as the basis set. The vibrational frequency calculation proved that both structures are stable (no imaginary frequency). The difference between the observed and scaled wave number values of most of the fundamentals is very small. Any discrepancy noted between the observed and the calculated frequencies may be due to the fact that the calculations have been actually done on a single molecule in the gaseous state contrary to the experimental values recorded in the presence of intermolecular interactions.

Acknowledgement
The corresponding author (NM) is grateful to UGC (New Delhi) for providing the financial assistance.

REFERENCES

[1] M. Tasumi, M. Nakata, *Pure Appl. Chem*. 57, **1985**, 121.
[2] Mizukami Yoshihiro, Shimizu Erika, *J-East***,** Vol.No**.**51; **2001**, 49-55.
[3] M.A. Zayed, M.F. Hawash and M.A. Fahmey, *Spectrochimica Acta Part A: Molecular and Biomolecular Spectroscopy*, Vol. 64, Issue 2, **2006**, 363-371.
[4] Opium-The Heroin, Morphine, And Codeine Drug Family F.A.Q. Editor: Mike Hamilton.
[5] P. Hohenberg, W. Kohn, *Phys. Rev*. 136, **1964**, 13864.
[6] A.D. Becke, *J. Chem. Phys* 98, **1993**, 5648.
[7] C. Lee, W. Yang, R.G. Parr, *Phys. Rev. B* 37, **1988**, 785.
[8] Frisch, M. J. et al Gaussian 09 Gaussian, Inc., Pittsburgh, PA, **2009**.
[9] P.L.Fast, J.Corchado, M.L.Sanches, D.G.Truhlar, *J.Phys.Chem A*.103, **1999**, 3139.
[10]A.Frisch, A.B.Nelson, AJ.Holder, Gauss view, Inc.Pittsburgh PA, **2000**.
[11]Mackay M and Hodgkin D. C., *J. Chem Society*, **1955**, 3261-3267.
[12]DennisV.Canfield,James Barrick and B.C.Giessen, *Acta Cryst.*C43, **1987**, 977-979.
[13]DennisV.Canfield,JamesBarrick & B.C.Giessen,*ActaCryst.*B35, **1979**, 2806-2809.
[14]José Cotuá, Sandra Cotes, Pedro Castro, Fernando Castro, and Liadys Mora, Molecular Descriptor, *Journal of the Korean Chemical Society*, **2010**, *Vol. 54, No. 4.*
[15]Hodges C.M. and Akhavan J, *Spectrochim Acta*, 40, **1990**, 303-307.
[16]Hartiwz Schulz, Mangorzata Baranska et al., *Analyst*, 129, **2004**, 917-920.
[17]Fazlul Huq & J. Al-shuneigat, *Journal of pharmacology and toxicology*, 1 (5), **2006**, 407-417.