Spectroscopic analysis and Quantum chemical calculations of 4-Acetylmorpholine: A DFT approach

T. Kavitha*, [a] and G. Velraj[b]

[a]*Department of Physics, Periyar University, Salem-636 011, Tamilnadu, India.*
[b]*Department of Physics, Anna University, Chennai-620 025, Tamilnadu, India.*
(*e-mail - [a]:kavisrianu@gmail.com, [b]:gvelraj@yahoo.co.uk)

Abstract

Acetylation is a more interesting phenomenon which enhances the effectiveness of drugs. In the present investigation, an Acetylated compound 4-Acetylmorpholine has been chosen for Density functional theory calculations. The FT-IR and FT-Raman spectra of the title compound have been recorded and the results obtained were compared with the theoretical one. All the density functional theory calculations of the title compound were carried out with Gaussian 09 software along with the Gauss view 5.0 visualization software using B3LYP/6-31++G(d,p) basis set. The experimental and theoretical spectra agree with each other. Comparing the thermodynamic properties of Morpholine with Acetylated Morpholine, ie., the title compound, it was found that the process of Acetylation increases the total energy, Heat capacity, Entropy etc., Beyond these, the Morpholine molecule on Acetylation gives raise to increase in the value of dipole moment which shows the high reactivity of the title compound. Such kind of compound is having more applications in the field of pharmaceutical chemistry.

Keywords: DFT; FT-IR; FT-Raman; Dipole moment; 4-Acetylmorpholine;

1. Introduction

Morpholine is a heterocyclic organic compound which has the characteristics of both amine and ether. The presence of amine in morpholine compound shows that it is a base and it can be reacted with acids. Since the volatility of Morpholine is same as that of water, it is used in industries as a common additive for pH adjustment in both fossil fuel and nuclear power plant steam systems. It is a corrosion inhibitor. It is commonly used as a solvent for chemical reactions. Morpholine is used as a chemical emulsifier and solubility aid for shellac in the process of waxing fruit to protect them against insects and fungal contamination. This can be lost as the fruit is being cleaned [1]. Acetyl is a functional group that contains a methyl group single bonded to a carbonyl group. The acetyl moiety is a component of many organic compounds including the neuro transmitter acetylcholine, acetyl-CoA, acetylcysteine and the analgesics acetaminophen and acetylsalicylic acid. The process of introducing an acetyl group into a molecule is called acetylation. Acetylated organic molecules exhibited increased effectiveness of a given dose [2]. In the present investigation we describe the results on an acetylated compound 4-Acetylmorpholine (4AMP) concerning the structure, vibrational assignments and thermodynamic properties at different temperatures.

2. Experimental methods

4-Acetylmorpholine with the stated purity of 99% was purchased from Sigma Aldrich Chemical Company and used for experimental analysis as such without any further purification. The FT-IR spectrum was recorded in the Mid- IR region 4000-400 cm^{-1} using KBr pellet on Bruker Tensor 27 Spectrometer. FT-Raman spectrum of the sample was recorded using Bruker RFS 27 FT-Raman Spectrometer in the range 50-4000cm^{-1} with the standard resolution of ± 2cm^{-1}. The laser source used in recording the FT-Raman spectrum is Nd: YAG at 1064 nm.

3. Computational methods

Initial geometry generated from standard geometrical parameters were minimized at DFT/B3LYP level with 6-31++G (d,p) basis set. The entire set of calculation was performed by using the Gaussian 09 program package [3] and Gauss view 5.0 graphical interfaces [4]. Along with the thermodynamic parameters for 4AMP at standard 298.15K, the thermodynamic properties such as specific heat capacity, entropy, enthalpy and Gibbs free energy were calculated for the range of different

temperatures from 100 to 700 K using DFT/B3LYP/6-31++G(d, p) basis set, and the results were tabulated.

4. Results and Discussion
4.1 Optimized Geometry

4AMP is a six-membered heterocyclic organic compound where the hydrogen atom of amine group was replaced by acetyl group through the process of Acetylation. The acetyl structure has a methyl group single bonded with a carbonyl group. The title compound 4-Acetyl morpholine exhibits C1 point group symmetry. The minimum energy obtained through structure optimization of 4AMP using B3LYP/6-31++G (d,p) basis set was found to be -440.4934 a.u. The optimized structure of 4AMP with the numbering of atoms is as shown in the Figure 1. The selected optimized structural parameters such as bond length and bond angles between various atoms of 4AMP have been listed in Table 1.
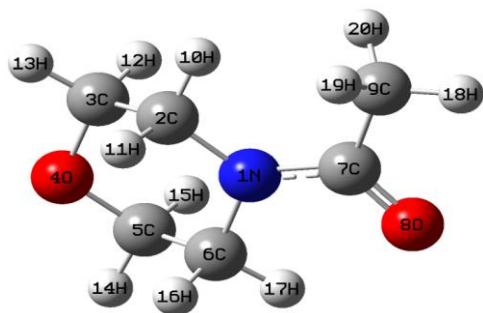

Figure 1: Optimized molecular structure of 4AMP

From the literature [5], it was found that the experimental bond lengths of 1N-2C, 2C-3C, 3C-4O, 4O-5C, 5C-6C, 6C-1N to be 1.48, 1.52, 1.43, 1.41, 1.53, 1.41Å and their corresponding theoretical values calculated using DFT/B3LYP/6-31++G(d,p) basis set were 1.46, 1.53, 1.42 , 1.43 , 1.53 and 1.47° respectively. Usually the bond length of C-H will be 1.09 Å. Here all the C-H bond lengths were found to be around 1.09 and 1.10 Å. Morpholine thus exhibits the cyclohexane geometry with chair confirmation with the H atom in equatorial position. The addition of Acetyl group does not disturb the chair position. The acetyl group was attached to the nitrogen 1N of the Morpholine structure with the N-H bond distance of 1.38 Å. In the acetyl group, the O-C bond length will be 1.214 Å and C-C will be 1.482Å. In the title compound the O-C bond length was obtained as 1.23 Å and C-C bond length as 1.52 Å which are in close agreement with the experimental one [5]. The N-C-C bond angle 109.83° was in close

Table 1: Selected Optimized geometric data for 4AMP using B3LYP/6-31++G (d,p)

Bond length	(Å)	Bond angle	(°)
1N-2C	1.46	2C-1N-7C	125.61
1N-6C	1.47	1N-2C-3C	109.81
1N-7C	1.38	1N-2C-10H	110.46
2C-3C	1.53	1N-2C-11H	109.80
2C-10H	1.09	3C-2C-10H	109.44
2C-11H	1.10	3C-2C-11H	109.12
3C-4O	1.42	10H-2C-11H	108.17
3C-12H	1.10	2C-3C-4O	111.47
3C-13H	1.09	2C-3C-12H	109.63
4O-5C	1.43	2C-3C-13H	110.41
5C-6C	1.53	12H-3C-13H	108.84
5C-14H	1.09	3C-4O-5C	111.23
5C-15H	1.10	4O-5C-6C	111.40
6C-16H	1.10	4O-5C-14H	106.27
6C-17H	1.09	14H-5C-15H	108.86
7C-8O	1.23	1N-6C-5C	109.83
7C-9C	1.52	1N-6C-16H	109.46
9C-18H	1.09	1N-6C-17H	108.08
9C-19H	1.09	16H-6C-17H	108.47
9C-20H	1.09	1N-7C-8O	121.57
		1N-7C-9C	117.74
		8O-7C-9C	120.69

agreement with the experimental value 107.71°. The C-N-C bond angle was found to be 121.03° which are also in agreement with the experimental value 119.55°. The other bond angels were listed in the table as said earlier.

4.2 Vibrational Analysis

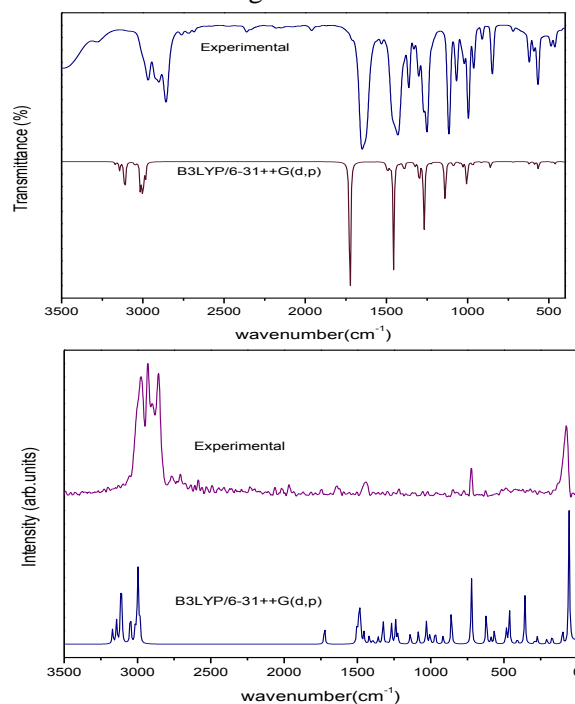The observed (FT-IR and FT Raman) wave numbers, calculated IR and Raman intensities and assigned wave numbers

Figure 2: Experimental and theoretical FT-IR(top) and FT-Raman(bottom) spectra of 4AMP

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calculated at the B3LYP level using basis set 6-31++G(d,p) were listed in Table 2. The molecule 4AMP under consideration has 20 atoms with 54 normal modes of fundamental vibrations. The experimental and theoretically predicated FT-IR, FT Raman spectra for 4AMP are shown in Figure 2. The vibrational frequency calculated at 6-31++G (d,p) level was scaled by 0.96. Fundamental modes were assigned by comparing calculated values with the experimental.

Table 2: Tentative Vibrational assignments of 4AMP

Experimental		B3LYP/6-31++G (d,p)			Vibrational Assignments
FT-IR (cm⁻¹)	FT-Raman (cm⁻¹)	Scaled freq. (cm⁻¹)	I_{IR} (km mol⁻¹)	I_{Raman} Å/amu⁻¹	
-	76(m)	54	2.80	10.8	γ (CH₂)
-	-	96	2.88	0.99	ρ (CH₃) + γ (CH₂)
-	-	165	0.57	0.43	τ (CH₃)
-	-	199	4.15	0.08	τRtrig + ρ (CH₃)
-	-	261	13.69	0.07	ρ (C-H)
-	-	278	3.84	0.62	ρ (C-H)
-	-	343	1.72	0.30	β (C-H) + β(C-O) +Rγ_S
-	-	393	1.06	0.09	τ (C-H)
-	-	444	5.39	0.23	ρ (C-H)
464(vw)	489(vw)	465	1.89	1.06	β (C-H)
-	-	542	17.59	0.08	β (C-H)
568(m)	-	565	5.12	1.06	ω (C-H)
621(w)	-	595	6.44	0.25	ρ (CH₃)
-	-	693	1.49	0.12	R γ_S
-	-	823	5.84	0.04	R γ_{AS}
-	-	824	9.77	0.06	Rtrig
849(w)	847(vw)	878	2.49	0.19	γ (C-H)
911(vw)	-	930	9.95	0.07	γ (C-H)
963(w)	-	965	64.04	0.76	γ (C-H)
996(s)	-	989	10.60	0.13	γ (C-H)
-	-	1007	2.49	0.79	ρ (CH₃)+γ (C=O)
-	-	1040	4.95	0.22	ω (C-H)+γ(C-H)
1068(m)	-	1046	7.04	0.15	τ (C-H)
-	-	1091	70.36	0.29	γ(C-O)+τ(C-H)
-	-	1096	39.61	0.10	T (C-H) + γ(C-O)+γ (C-H)
1116(vs)	-	1175	3.33	0.04	T (C-H) + γ(C-N)
-	-	1189	0.91	0.04	γ (C-H) + T(CH₂)
-	1217(vw)	1217	165.83	0.30	γ (C-H) + T(CH₂)
1251(vs)	-	1246	54.76	0.68	T(CH₂) + ν(C-N)
-	-	1272	11.35	0.72	γ (C-H) + T(CH₂)
1301(w)	-	1304	0.98	0.18	γ (C-H)
-	-	1333	20.66	1.04	ω (C-H)+ γ (C-H)
-	-	1336	1.24	0.29	ω (C-H)+γ (C-H)
-	-	1343	5.48	0.16	γ (C-H)
1363(m)	-	1362	3.15	0.24	γ (C-H)
-	-	1396	230.91	0.30	ν(C-N)+ω(C-H)+ T(CH₂)
-	-	1418	8.64	0.29	sci (CH₂) + γ (C-H)
-	-	1425	3.31	0.66	sci (CH₂)+ γ (C-H)
1429(vs)	-	1429	1.26	0.19	sci (CH₂)
-	-	1434	22.94	0.13	sci (CH₂)
-	-	1440	0.76	0.16	sci (CH₂)
-	1443(vw)	1444	3.26	0.34	sci (CH₂)
1650(vs)	1640(vw)	1655	388.01	0.00	ν (C=O)+ ω (C-H)
2858(m)	2857(vs)	2864	40.87	0.01	ν_S CH₂
-	-	2876	35.19	0.01	ν_S CH₂
-	-	2881	48.88	0.02	ν_S CH₂
-	-	2893	79.09	0.02	ν_S CH₂
2902(m)	2929(vs)	2926	7.84	0.04	ν_SCH₃
2967(m)	2976(s)	2982	35.51	2.29	ν_{AS} CH₂
-	-	2986	11.35	2.36	ν_{AS} CH₂
-	-	2990	31.50	6.28	ν_{AS} CH₂
-	-	3015	13.73	1.58	ν_{AS} CH₂
-	-	3018	7.03	1.64	ν_{AS} CH₂
-	-	3042	6.14	1.86	ν_{AS} CH₃

(ν) Stretching, (ν_S) Symmetric stretching, (ν_{AS}) Anti-symmetric stretching, (β) In plane Bending, (γ) out of plane bending, (T) twisting, (τ) torsion, (ω) wagging, (ρ) rocking, (sci) scissoring, R-ring, trig- trigonal deformation

In the present investigation, the medium peaks observed at 2902, and 2967cm⁻¹ in the FTIR spectrum and the very strong and strong peaks observed at 2929 and 2976 cm⁻¹ in the FT Raman spectrum were assigned to CH₂ asymmetric and symmetric stretching vibrations. The theoretical peaks observed in this region were in good agreement with the experimental. The Raman band at 1443cm⁻¹ was assigned to scissoring vibration and the B3LYP calculated wave numbers 1444cm⁻¹ to 1418cm⁻¹ corresponds to CH₂ scissoring[6].

The CH₃ antisymmetric and symmetric stretching occurs at the regions 3042 and 2926 cm⁻¹ respectively. The medium band observed at 2902 cm⁻¹ and the very strong band observed at 2929 cm⁻¹ of FTIR and FT-Raman spectra respectively corresponds to CH₃ symmetric stretching.

In the present study the C-H out of plane vibrations were observed in the region 878-989cm⁻¹ which is in good agreement with the literature [7]. The C=O stretching vibration occur in the region 1715-1680cm⁻¹ [8]. The strong peak observed at 1650cm⁻¹ of FTIR spectrum and the peak observed at 1640cm⁻¹ in the FT Raman spectrum were assigned to C=O stretching which is in good agreement with the theoretical value. A band appears at 1251 cm⁻¹ in FT-IR spectrum whose corresponding theoretical value 1246 cm⁻¹ may be due to the presence of C-N stretching vibrations [9]. Here, the theoretical bands observed at 199, 343, 693, 823, 824 cm⁻¹ were assigned to ring trigonal deformation, ring symmetric out of plane bending, ring symmetric out of plane bending, ring asymmetric out of plane bending and ring trigonal deformation respectively. These ring vibrations appears only in the low frequencies [10].

4.3 Thermodynamic properties

The thermodynamic properties of Morpholine and 4AMP such as specific heat capacity, zero point vibrational energy, entropy, rotational constants and dipole moment were calculated using DFT/B3LYP/6-31++G(d,p) level and given in Table 3. These values are computed for the commonly used standard ambient temperature of 298.15K. The processes of Acetylating Morpholine have made enormous changes in the thermodynamic properties of 4AMP. The dipole moment of Morpholine is 1.3518 Debye whereas the value becomes 3.1492 Debye for 4AMP. The increase in Dipole moment, vibrational energy and zero point vibrational energy may due to

Table 3: Thermodynamic parameters of 4AMP

Thermodynamic parameters (298K)	Morpholine	4AMP
SCF energy (a.u.)	-287.819	-440.49
Total energy (thermal), E_{total} (kcal mol^{-1})	88.026	113.752
Heat capacity at const. volume, C_v (cal mol^{-1} K^{-1})	20.682	32.645
Entropy, S (cal mol^{-1} K^{-1})	73.185	91.513
Vibrational energy, E_{vib} (kcal mol^{-1})	86.249	111.975
Zero–point vibrational energy, E_0 (kcal mol^{-1})	84.672	108.279
Rotational constants (GHz)		
A	4.841	3.187
B	4.571	1.185
C	2.653	0.921
Dipole moment (Debye)		
μ_x	-0.0001	-1.0983
μ_y	0.3361	2.9504
μ_z	1.3093	0.0803
μ_{total}	1.3518	3.1492

the above said process of adding acetyl group to the Morpholine structure which is responsible for the increase in effectiveness of drugs.

Table 4: *Thermodynamic parameters of 4AMP at various temperatures*

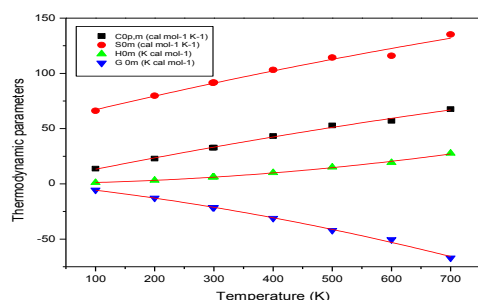| T(K)	$C^0_{p,m}$ (cal mol^{-1} K^{-1})	S^0_m (cal mol^{-1} K^{-1})	H^0_m (K cal mol^{-1})	G^0_m (K cal mol^{-1})
100	13.71	66.12	1.13	-5.48
200	22.86	79.81	3.16	-12.81
298.15	32.65	91.51	6.07	-21.22
300	32.84	91.73	6.13	-21.39
400	43.30	103.19	10.14	-31.14
500	52.81	114.34	15.16	-42.02
600	57.03	115.95	19.12	-50.45
700	67.62	135.28	27.68	-67.01

F*igure 4: The correlation graph of thermodynamic parameters of 4AMP*

Since the properties such as Specific heat (C), Entropy (S), Enthalpy (H) and Gibbs free energy (G) depends mainly on temperature, the temperature of 4AMP was increased from 100 to 700 K, varied every 100K for vibrational analysis at the 6- 31++G(d,p) level.

The thermodynamic properties at different temperatures were listed in the Table 4.

It was revealed that the thermodynamic parameter values increases with increase in temperature. It is due to the fact that the molecular vibrational intensities increase with respect to temperature. The correlation graphs of these values are plotted and are fitted by quadratic formulae as shown in Figure 4.

The corresponding equations of fit are as follows:

$C^0_{p,m} = 2.43 + 0.11 - 2 \times 10^{-5} T^2$ ($R^2 = 0.9939$) -- (1)
$S^0_m = 54.22 + 0.13 - 3 \times 10^{-5} T^2$ ($R^2 = 0.9749$) ---- (2)
$H^0_m = 0.22 + 0.01 + 4 \times 10^{-5} T^2$ ($R^2 = 0.9943$) ---- (3)
$G^0_m = 0.38 - 0.06 - 5 \times 10^{-5} T^2$ ($R^2 = 0.9959$) ----- (4)

5. Conclusions

The compound 4-Acetyl morpholine was optimized and the frequency calculations along with thermodynamic properties were carried out. The experimental FT-IR and FT-Raman spectrum were also analyzed and the results were compared with the theoretical values. The 4AMP molecule undergoes chair confirmation. The experimental vibrations were in good agreement with the theoretical findings. The Morpholine molecule on Acetylation gives raise to increase in the value of Dipole moment which shows the high reactivity of 4AMP. The thermodynamic parameters of 4AMP at different temperatures were calculated along with the standard ambient temperature and the correlation graphs were also drawn.

6. References

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