



ENGINEERING

EXPERIMENTAL AND THEORETICAL INVESTIGATIONS OF SPECTROSCOPIC PROPERTIES OF CLOBAZAM

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Abstract

Ab initio and density functional theory methods have been employed to study the vibrational (IR) spectrum, molecular geometry, and chemical shifts of clobazam (CLB). Experimental studies were conducted on these parameters, including FTIR, FTRaman and ¹H- and ¹³C NMR spectroscopy. The FTIR and FTRaman spectra of Clobazam have been recorded in the region 4000-400cm⁻¹ and 3500-100 cm⁻¹ respectively. On the basis of the comparison between calculated and experimental results and the comparison with related molecules, assignments of fundamental vibrational modes are examined. A detailed interpretation of the infrared spectrum of CLB is reported. Moreover, the complete assignment of ¹H- and ¹³C-NMR signals was achieved using DFT/GIAO calculated isotropic magnetic shielding at the B3LYP/6-31G(d) basis set. Theoretical values were compared to the experimental data's.

Keywords: FTIR & FTRaman spectra, HF & DFT methods, molecular geometries, vibrational analysis, Clobazam, Chemical shifts

Introduction

Clobazam (C₁₆H₁₃ClN₂O₂) is chemically known as 7-Chloro-1-methyl-5-phenyl-1, 5-benzodiazepine-2,4(3H)-dione. Clobazam (CLB) is a new antiepileptic drug that is the first 1, 5-benzodiazepine (BZP) having nitrogen atoms in the 1 and 5 positions of the heterocyclic ring, whose chemical structure was designed to give it a different pharmacological profile from that of 1, 4-BZPs. CLB had a wide spectrum of anticonvulsive actions against seizures in several animal models induced by chemical convulsants and maximal electroshock. Clobazam is approved for adjunctive therapy in complex partial seizures [1] certain types of status epileptics, specifically the myoclonic, myoclonic-absent, simple partial, complex partial, tonic varieties and non-status absence seizures [2]. From both experimental and clinical observations, CLB was proven to possess a wide spectrum of activity, high effectiveness and good tolerability in several types of epilepsies.

For the proper understanding of IR and Raman spectra, a reliable assignment of all vibrational bands is essential. For this purpose, the quantum chemical methods, ranging from HF to DFT approaches, are invaluable tools [3-5], each method having its own advantages. The Hartree-Fock, ab-initio methods are able to give good results provided a reasonable basis set and an appropriate correlation treatment are taken into account. On the other hand, DFT methods have

evolved to a powerful quantum chemical tool for the determination of the electronic structure of molecules. In the frame work of DFT approach, different exchange and correlation functions are routinely used. Among these, the B3LYP combination [6, 7] is the most used since it proved its ability in reproducing various molecular properties, including vibrational spectra. In this study, an attempt has been made to interpret the vibrational spectra of clobazam by applying ab initio and density functional theory calculations based on Hartree-Fock and Becke3- Lee-Yang-Parr (B3LYP) level using 6-31G (d,p) basis set. In addition to these ¹H and ¹³C- chemical shifts were calculated with GIAO method [8, 9] using corresponding TMS shielding calculated at the B3LYP/6-31G(d) level.

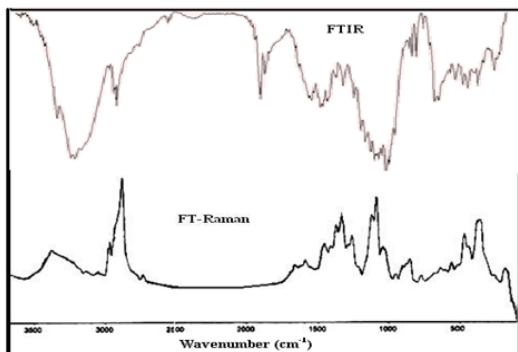
Experimental

The compound Clobazam was purchased from sigma-Aldrich chemical company, USA with more than 98% purity and was used as such without further purification to record Fourier transform infrared (FTIR) spectrum in the region 4000 – 400cm⁻¹ at a accuracy of ± 4cm⁻¹ on a bruker model IFS 66V spectrophotometer using the KBr pellet technique. The FT-Raman spectrum of TMHQ was recorded using 1064 nm line of Nd:YAG laser as excitation wavenumber in the region 100-3500 cm⁻¹ on the BRUCKER IFS-66 V spectrophotometer equipped with

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FRA 106 Raman module. The observed FTIR and FT Raman spectrum of clobazam is shown in Fig.1.

Fig. 1 Expt FTIR and FT-Raman spectrum of Clobazam



Computational Details

The entire calculations were performed using the G03 [10] package of programs. Initial geometry generated from standard geometrical parameters [11] and full optimization was carried out at Hartree-Fock level of theory employing 6-31G(d,p) basis set. All the geometries were then reoptimized using 6-31G(d,p) basis set using density functional theory (DFT)[12] employing the Becke's three – parameter hybrid functional [6] combined with Lee-Yang-Parr correlation [7] functional (B3LYP) method. The optimized structural parameters were used in the vibrational frequency calculations at the HF and DFT levels to characterize all stationary points as minima. Vibrationally averaged positions of CBZ were used for harmonic frequency calculations resulting in IR frequencies together with intensities. By combining the results of the Chemcraft program [13] with symmetry considerations, vibrational frequency assignments were made. The Raman activities (S_i) calculated with the GAUSSIAN 2003 program and adjusted during the scaling procedure with chemcraft were subsequently converted to relative Raman intensities (I_i) using the following relationship derived from the basis theory of Raman scattering [14, 15].

$$I_i = \frac{f(u_0 - u_i)^4 S_i}{u_i [1 - \exp(-hc u_i / kT)]} \quad \text{--- (1)}$$

where u_0 is the exciting frequency (in cm^{-1} units), u_i is the vibrational wave number of the i^{th} normal mode; h , C and k are fundamental constants and f is a suitably chosen common normalization factor for all peak intensities. ^1H - and ^{13}C - chemical shifts were calculated with GIAO method using corresponding TMS shielding calculated at the B3LYP/6-31G(d) level.

Results and Discussion

Molecular Geometry

The optimized structure parameters of clobazam calculated by ab initio HF and DFT-B3LYP levels with the 6-31G(d,p) basis set are listed in the Table.1 in accordance with the atom numbering scheme given in Fig.2. Table 1 compares the calculated bond lengths and angles for clobazam with the experimentally obtained data [11]. From the theoretical values, we can find that most of the optimized bond angles are slightly larger than the experimental values, due to the theoretical calculations belong to isolated molecules in gaseous phase. Comparing bond angles and lengths of B3LYP with those of HF, as a whole the formers are on higher side than the later and the HF calculated values correlates well with the experimental results. In spite of the differences, calculated geometric parameters represent a good approximation and they are the bases for calculating other parameters, such as vibrational frequencies and thermodynamic properties.

CBZ is a non-planar molecule and possesses C_1 point group symmetry. The molecule has 34 atoms and 96 normal modes of fundamental vibrations [16]. All the 96 vibrations are active in both IR and Raman. The harmonic vibrational frequencies calculated at HF and B3LYP level using 6-31G(d,p) basis set have been collected in Table 2. Comparison of the frequencies calculated at B3LYP with experimental assignments (present in Table 2) reveals the overestimation of the calculated vibrational modes due to the neglect of anharmonicity in the real system. Reduction in the computed harmonic vibrations, though basis set sensitive are only marginal as observed in the HF and B3LYP values using 6-31G(d,p) basis set. Anyway notwithstanding the level of calculations, it is customary to scale down the calculated harmonic frequencies in order to improve the agreement with the experiment. In our study, we have followed the scaling factors 0.903 for HF and 0.961 for B3LYP and those values are entered in Table 2. The computed spectra at B3LYP level, using 6-31G(d,p) has been shown in Fig. 3. In order to investigate the performance and vibrational frequencies for the title molecule, root mean square value and correlation coefficient(s) between calculated harmonic and observed fundamental vibrational frequencies for HF and B3LYP method using 6-31G(d,p) basis set were also calculated. The small difference between the experimental and calculated vibrational modes is observed. This discrepancy can come from the formation of intermolecular hydrogen bonding. Also we note that the experimental results belong to the solid phase and the theoretical calculations belong to the gaseous phase. The frequency values computed at B3LYP level

contains known systematic error. Therefore, linearity between the experimental and calculated vibrational frequency can be estimated by plotting the calculated values against experimental frequency (shown in Fig. 4). Certain values obtained between the two methods, are strongly underestimated. If the variations are omitted, B3LYP calculations provide good linearity between the calculated and experimental frequencies (correlation coefficient for HF is 0.997 and for B3LYP is 0.999).

Figure 2 Geometry of the Clobazam optimized at the B3LYP/6-31G(d,p)

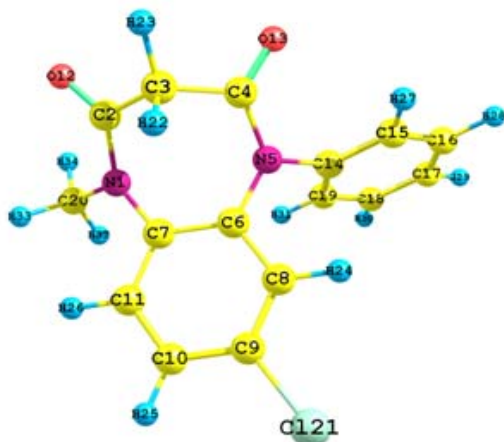


Fig. 3 Calculated IR and Raman spectra of Clobazam using B3LYP/6-31G(d,p)

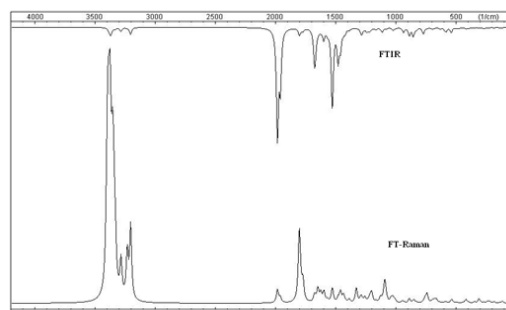


Fig. 4. Graphic correlation between the experimental and calculated wavenumber obtained by DFT HF/6-31G(d,p) and B3LYP/6-31G(d,p) methods for Clobazam

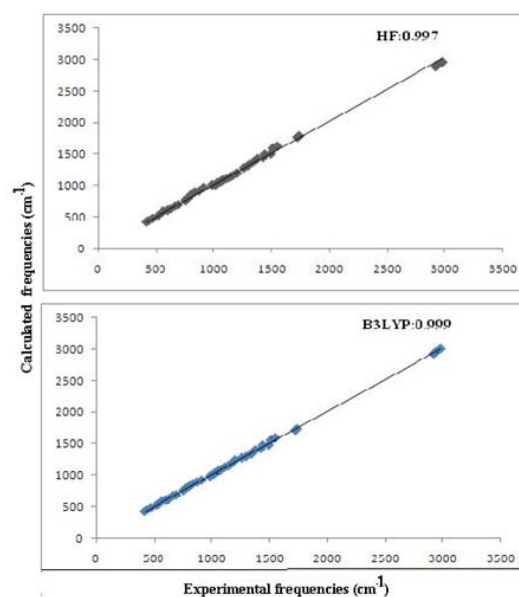


Table 1 Optimized geometrical parameters of Clobazam molecules, bond length (Å), interfacial angles (°)

| Parameters | Expt | HF/6-31G(d,p) | B3LYP 6-31G(d,p) |
|---------------------------------|-------|---------------|------------------|
| Bond Length | | | |
| N ₁ -C ₂ | 1.462 | 1.369 | 1.388 |
| N ₁ -C ₇ | 1.462 | 1.414 | 1.417 |
| N ₁ -C ₂₀ | 1.470 | 1.459 | 1.466 |
| C ₂ -C ₃ | 1.509 | 1.517 | 1.523 |
| C ₂ -O ₁₂ | 1.208 | 1.195 | 1.219 |
| C ₃ -C ₄ | 1.509 | 1.517 | 1.523 |
| C ₃ -H ₂₂ | 1.113 | 1.085 | 1.096 |
| C ₃ -H ₂₃ | 1.113 | 1.077 | 1.088 |
| C ₄ -N ₅ | 1.462 | 1.377 | 1.398 |
| C ₄ -O ₁₃ | 1.208 | 1.192 | 1.216 |
| N ₅ -C ₆ | 1.462 | 1.420 | 1.425 |
| N ₅ -C ₁₄ | 1.462 | 1.436 | 1.442 |
| C ₆ -C ₇ | 1.420 | 1.393 | 1.413 |
| C ₆ -C ₈ | 1.420 | 1.393 | 1.404 |
| C ₇ -C ₁₁ | 1.420 | 1.393 | 1.405 |

| | | | |
|---|---------|-------|-------|
| C ₈ -C ₉ | 1.420 | 1.376 | 1.387 |
| C ₈ -H ₂₄ | 1.100 | 1.072 | 1.083 |
| C ₉ -C ₁₀ | 1.420 | 1.384 | 1.395 |
| C ₉ -Cl ₂₁ | 1.719 | 1.741 | 1.756 |
| C ₁₀ -C ₁₁ | 1.420 | 1.378 | 1.389 |
| C ₁₀ -H ₂₅ | 1.100 | 1.073 | 1.084 |
| C ₁₁ -H ₂₆ | 1.100 | 1.074 | 1.084 |
| C ₁₄ -C ₁₅ | 1.420 | 1.386 | 1.398 |
| C ₁₄ -C ₁₉ | 1.420 | 1.385 | 1.398 |
| C ₁₅ -C ₁₆ | 1.420 | 1.384 | 1.395 |
| C ₁₅ -H ₂₇ | 1.100 | 1.074 | 1.083 |
| C ₁₆ -C ₁₇ | 1.420 | 1.385 | 1.396 |
| C ₁₆ -H ₂₈ | 1.100 | 1.075 | 1.086 |
| C ₁₇ -C ₁₈ | 1.420 | 1.385 | 1.396 |
| C ₁₇ -H ₂₉ | 1.100 | 1.075 | 1.086 |
| C ₁₈ -C ₁₉ | 1.420 | 1.385 | 1.394 |
| C ₁₈ -H ₃₀ | 1.100 | 1.075 | 1.086 |
| C ₁₉ -H ₃₁ | 1.100 | 1.075 | 1.085 |
| C ₂₀ -H ₃₂ | 1.113 | 1.081 | 1.091 |
| C ₂₀ -H ₃₃ | 1.113 | 1.085 | 1.096 |
| C ₂₀ -H ₃₄ | 1.113 | 1.078 | 1.089 |
| Bond angle | | | |
| C ₂ -N ₁ - C ₇ | 124.000 | 122.3 | 123.1 |
| C ₂ -N ₁ - C ₂₀ | 108.000 | 116.9 | 116.5 |
| N ₁ -C ₂ - C ₃ | 118.000 | 116.2 | 115.6 |
| N ₁ -C ₂ - O ₁₂ | 122.600 | 122.0 | 121.8 |
| C ₇ -N ₁ - C ₂₀ | 108.000 | 119.4 | 119.3 |
| N ₁ -C ₇ - C ₆ | 120.000 | 121.8 | 122.2 |
| N ₁ -C ₇ - C ₁₁ | 120.000 | 119.4 | 119.2 |
| N ₁ -C ₂₀ - H ₃₂ | 109.500 | 108.9 | 109.2 |
| N ₁ -C ₂₀ - H ₃₃ | 109.442 | 112.1 | 112.2 |
| N ₁ -C ₂₀ - H ₃₄ | 109.462 | 108.7 | 108 |
| C ₃ -C ₂ - O ₁₂ | 122.500 | 121.8 | 122.6 |
| C ₂ -C ₃ - C ₄ | 110.200 | 110.3 | 110.1 |
| C ₂ -C ₃ - H ₂₂ | 108.800 | 110.6 | 110.6 |
| C ₂ -C ₃ - H ₂₃ | 108.800 | 107.6 | 107.6 |
| C ₄ -C ₃ - H ₂₂ | 108.800 | 110.9 | 110.9 |
| C ₄ -C ₃ - H ₂₃ | 108.800 | 107.5 | 107.5 |
| C ₃ -C ₄ - N ₅ | 118.000 | 116.0 | 115.2 |
| C ₃ -C ₄ - O ₁₃ | 122.500 | 121.4 | 122.2 |
| H ₂₂ -C ₃ - H ₂₃ | 109.400 | 109.9 | 110 |
| N ₅ -C ₄ - O ₁₃ | 122.600 | 122.6 | 122.6 |
| C ₄ -N ₅ - C ₆ | 124.000 | 122.6 | 122.9 |
| C ₄ -N ₅ - C ₁₄ | 124.000 | 119.2 | 119.2 |
| C ₆ -N ₅ - C ₁₄ | 124.000 | 118.1 | 117.8 |
| N ₅ -C ₆ - C ₇ | 120.000 | 122.1 | 122.7 |
| N ₅ -C ₆ - C ₈ | 120.000 | 118.4 | 118 |
| N ₅ -C ₁₄ - C ₁₅ | 120.000 | 120.9 | 121.1 |
| N ₅ -C ₁₄ - C ₁₉ | 120.000 | 118.9 | 118.8 |
| C ₇ -C ₆ - C ₈ | 120.000 | 119.5 | 119.3 |
| C ₆ -C ₇ - C ₁₁ | 120.000 | 118.8 | 118.6 |
| C ₆ -C ₈ - C ₉ | 120.000 | 120.4 | 120.6 |
| C ₆ -C ₈ - H ₂₄ | 120.000 | 119.4 | 119.2 |
| C ₇ -C ₁₁ - C ₁₀ | 120.000 | 121.7 | 122 |
| C ₇ -C ₁₁ - H ₂₆ | 120.000 | 119.1 | 118.9 |
| C ₉ -C ₈ - H ₂₄ | 120.000 | 120.1 | 120.3 |
| C ₈ -C ₉ - C ₁₀ | 120.000 | 120.8 | 120.9 |
| C ₈ -C ₉ - Cl ₂₁ | 118.800 | 119.5 | 119.4 |

| | | | |
|--------------|---------|-------|-------|
| C10-C9- Cl21 | 118.800 | 119.7 | 119.7 |
| C9-C10- C11 | 118.823 | 118.8 | 118.7 |
| C9-C10- H25 | 120.589 | 120.5 | 120.6 |
| C11-C10- H25 | 120.589 | 120.7 | 120.8 |
| C10-C11- H26 | 120.000 | 119.2 | 119.1 |
| C15-C14- C19 | 120.000 | 120.2 | 120.1 |
| C14-C15- C16 | 120.000 | 119.7 | 119.6 |
| C14-C15- H27 | 120.000 | 119.8 | 119.8 |
| C14-C19- C18 | 120.000 | 119.9 | 119.9 |
| C14-C19- H31 | 120.000 | 119.6 | 119.5 |
| C16-C15- H27 | 120.000 | 120.5 | 120.6 |
| C15-C16- C17 | 120.000 | 120.3 | 120.5 |
| C15-C16- H28 | 120.000 | 119.6 | 119.4 |
| C17-C16- H28 | 120.000 | 120.1 | 120.1 |
| C16-C17- C18 | 120.000 | 119.8 | 119.7 |
| C16-C17- H29 | 120.000 | 120.1 | 120.1 |
| C18-C17- H29 | 120.000 | 120.1 | 120.1 |
| C17-C18- C19 | 120.000 | 120.1 | 120.1 |
| C17-C18- H30 | 120.000 | 120.2 | 120.3 |
| C19-C18- H30 | 120.000 | 119.7 | 119.6 |
| C18-C19- H31 | 120.000 | 120.5 | 120.6 |
| H32-C20- H33 | 109.000 | 109.5 | 109.5 |
| H32-C20- H34 | 109.000 | 109.6 | 110.2 |
| H33-C20- H34 | 109.000 | 108.1 | 107.8 |

Table 2 Calculated Scaled IR wavenumbers & relative intensities for Clobazam using HF/6-31G(d,p) and B3LYP/6-31G(d,p) [for a clear view of Table 2, please see supplementary file supplied with the article]

| Index | FTIR | Computed wavenumbers (cm ⁻¹) | | | | IR Intensity | Raman Activity | Vibrational Assignments | |
|-------|------|--|------------------|--------------|----------------|--------------|----------------|------------------------------|--------------------------|
| | | HF/6-31G(d,p) | B3LYP/6-31G(d,p) | IR Intensity | Raman Activity | | | | |
| W(1) | | 39 | 39 | 39 | 33 | 0.920 | 0.028 | ring bending | |
| W(2) | | 42 | 39 | 43 | 42 | 0.042 | 0.029 | ring bending | |
| W(3) | | 64 | 72 | 63 | 62 | 1.182 | 1.028 | C-H bending, C-H rocking | |
| W(4) | | 74 | 67 | 69 | 67 | 1.945 | 0.828 | ring flexing | |
| W(5) | | 84 | 76 | 87 | 84 | 1.276 | 1.112 | ring flexing | |
| W(6) | | 118 | 109 | 107 | 102 | 0.288 | 0.288 | C-H rocking | |
| W(7) | | 136 | 132 | 139 | 134 | 0.259 | 0.095 | C-H bending | |
| W(8) | | 151 | 162 | 133 | 147 | 0.221 | 0.001 | C-H bending | |
| W(9) | | 182 | 185 | 171 | 164 | 1.806 | 1.480 | C-C bending, ring flexing | |
| W(10) | | 219 | 197 | 207 | 198 | 1.282 | 0.242 | C-H bending | |
| W(11) | | 224 | 211 | 218 | 210 | 1.104 | 0.297 | ring flexing | |
| W(12) | | 270 | 244 | 255 | 245 | 3.198 | 1.328 | N-H bending | |
| W(13) | | 288 | 278 | 288 | 275 | 2.439 | 0.208 | Sp ² out-of-plane | |
| W(14) | | 315 | 283 | 293 | 287 | 1.299 | 0.931 | C-C bending, C-H rocking | |
| W(15) | | 348 | 314 | 322 | 310 | 0.528 | 0.058 | C-H bending | |
| W(16) | | 392 | 359 | 368 | 352 | 4.000 | 0.000 | C-H bending | |
| W(17) | | 418 | 313 | 336 | 374 | 0.473 | 0.425 | C-C bending, C-H rocking | |
| W(18) | | 438 | 394 | 398 | 383 | 1.139 | 0.087 | ring flexing | |
| W(19) | | 459 | 415 | 420 | 404 | 0.413 | 0.290 | ring flexing | |
| W(20) | | 474 | 428 | 434 | 417 | 4.007 | 0.158 | ring flexing | |
| W(21) | | 495 | 450 | 450 | 442 | 3.483 | 1.341 | ring flexing | |
| W(22) | | 487 | 512 | 481 | 492 | 4.719 | 0.226 | C-H bending | |
| W(23) | | 542 | 542 | 481 | 499 | 4.719 | 0.226 | ring flexing | |
| W(24) | | 579 | 522 | 531 | 510 | 20.719 | 0.007 | ring flexing | |
| W(25) | | 622 | 592 | 618 | 544 | 10.887 | 1.028 | C-H bending | |
| W(26) | | 661 | 654 | 672 | 661 | 0.842 | 0.019 | ring flexing | |
| W(27) | | 687 | 687 | 698 | 678 | 1.061 | 0.232 | ring flexing | |
| W(28) | | 692 | 676 | 676 | 667 | 1.745 | 4.505 | ring flexing | |
| W(29) | | 697 | 624 | 636 | 611 | 1.169 | 0.207 | ring flexing | |
| W(30) | | 709 | 627 | 642 | 617 | 1.169 | 0.207 | C-H bending | |
| W(31) | | 740 | 660 | 664 | 658 | 2.082 | 10.257 | C-C bending, C-H bending | |
| W(32) | | 870 | 798 | 802 | 800 | 0.882 | 0.140 | N-H bending | |
| W(33) | | 896 | 774 | 809 | 769 | 37.774 | 1.075 | Phenyl ring bending | |
| W(34) | | 927 | 747 | 758 | 750 | 10.084 | 0.168 | C-C bending | |
| W(35) | | 943 | 768 | 774 | 742 | 8.077 | 0.279 | Phenyl ring bending | |
| W(36) | | 958 | 857 | 774 | 782 | 46.866 | 1.741 | C-C bending | |
| W(37) | | 978 | 888 | 858 | 814 | 42.250 | 0.243 | C-C bending | |
| W(38) | | 928 | 847 | 829 | 797 | 30.553 | 1.027 | C-C bending | |
| W(39) | | 807 | 847 | 858 | 847 | 0.271 | 0.234 | C-C bending | |
| W(40) | | 859 | 1008 | 908 | 882 | 0.200 | 0.217 | C-H rocking | |
| W(41) | | 876 | 1019 | 920 | 892 | 0.217 | 0.180 | C-C bending | |
| W(42) | | 1029 | 920 | 928 | 889 | 0.739 | 0.799 | C-H rocking | |
| W(43) | | 1038 | 928 | 948 | 909 | 0.083 | 0.401 | C-H bending | |
| W(44) | | 918 | 1078 | 978 | 935 | 0.18 | 0.144 | C-C bending | |
| W(45) | | 1060 | 984 | 970 | 932 | 0.441 | 0.398 | ring flexing | |
| W(46) | | 1092 | 987 | 978 | 939 | 1.200 | 0.000 | C-H bending | |
| W(47) | | 1100 | 994 | 987 | 958 | 0.122 | 1.081 | C-H rocking | |
| W(48) | | 1111 | 1003 | 1017 | 971 | 0.238 | 0.040 | C-H rocking, N-H bending | |
| W(49) | | 1034 | 1184 | 1081 | 1078 | 1024 | 10.017 | C-H rocking | |
| W(50) | | 1058 | 1172 | 1084 | 1108 | 1089 | 2.229 | 0.140 | C-H rocking |
| W(51) | | 1072 | 1201 | 1098 | 1116 | 1073 | 3.009 | 10.809 | C-H bending |
| W(52) | | 1062 | 1210 | 1099 | 1122 | 1068 | 4.188 | 8.726 | C-H bending |
| W(53) | | 1222 | 1102 | 1190 | 1109 | 30.828 | 0.419 | C-H bending | |
| W(54) | | 1115 | 1239 | 1119 | 1170 | 1124 | 21.761 | 1.175 | C-H rocking |
| W(55) | | 1284 | 1284 | 1182 | 1182 | 1182 | 1.328 | 0.180 | C-H bending |
| W(56) | | 1142 | 1285 | 1142 | 1188 | 1142 | 0.995 | 1.824 | C-H bending |
| W(57) | | 1288 | 1181 | 1203 | 1198 | 28.433 | 0.001 | C-H bending | |
| W(58) | | 1187 | 1287 | 1188 | 1203 | 1178 | 0.929 | 4.747 | ring flexing |
| W(59) | | 1328 | 1199 | 1272 | 1222 | 0.732 | 0.129 | C-H bending | |
| W(60) | | 1202 | 1222 | 1202 | 1208 | 0.082 | 1.028 | C-H bending | |
| W(61) | | 1262 | 1262 | 1262 | 1262 | 11.145 | 4.205 | C-H bending | |
| W(62) | | 1261 | 1422 | 1284 | 1324 | 1273 | 22.472 | 2.484 | C-H bending |
| W(63) | | 1426 | 1261 | 1324 | 1261 | 21.860 | 10.319 | C-H bending | |
| W(64) | | 1261 | 1421 | 1324 | 1261 | 10.040 | 14.022 | C-H bending | |
| W(65) | | 1469 | 1322 | 1380 | 1307 | 12.682 | 1.916 | C-C bending, C-H bending | |
| W(66) | | 1467 | 1328 | 1360 | 1300 | 12.680 | 0.000 | C-H bending | |
| W(67) | | 1342 | 1329 | 1381 | 1387 | 1333 | 0.1220 | 0.1227 | C-H bending, C-H bending |
| W(68) | | 1368 | 1387 | 1415 | 1442 | 1388 | 28.670 | 0.999 | C-H bending |
| W(69) | | 1379 | 1384 | 1440 | 1458 | 8.474 | 1.008 | C-H bending | |
| W(70) | | 1423 | 1602 | 1448 | 1478 | 1478 | 60.189 | 4.902 | C-H bending |
| W(71) | | 1615 | 1458 | 1498 | 1428 | 2.824 | 1.201 | C-H bending | |
| W(72) | | 1622 | 1455 | 1498 | 1441 | 11.819 | 12.258 | C-H bending | |
| W(73) | | 1649 | 1459 | 1500 | 1471 | 18.429 | 19.271 | C-H bending | |
| W(74) | | 1440 | 1688 | 1505 | 1534 | 1474 | 34.242 | 1.020 | C-H bending |
| W(75) | | 1462 | 1679 | 1512 | 1528 | 1472 | 10.073 | 0.913 | C-H bending |
| W(76) | | 1711 | 1599 | 1618 | 1633 | 15.015 | 27.835 | C-H bending | |
| W(77) | | 1788 | 1642 | 1642 | 1678 | 4.228 | 1.916 | C-H bending | |
| W(78) | | 1800 | 1628 | 1648 | 1681 | 20.479 | 23.484 | C-H bending | |
| W(79) | | 1847 | 1608 | 1631 | 1655 | 1691 | 10.114 | 53.970 | C-H bending |
| W(80) | | 1781 | 1781 | 1781 | 1781 | 1781 | 0.000 | 0.000 | C-H bending |
| W(81) | | 1756 | 1889 | 1792 | 1803 | 1733 | 60.007 | 18.779 | C-H bending |
| W(82) | | 2016 | 2004 | 2002 | 2040 | 2007 | 43.214 | 104.880 | C-H bending |
| W(83) | | 2025 | 2025 | 2025 | 2025 | 2025 | 0.000 | 0.000 | C-H bending |
| W(84) | | 2071 | 2071 | 2071 | 2071 | 2071 | 0.000 | 0.000 | C-H bending |
| W(85) | | 2071 | 2071 | 2071 | 2071 | 2071 | 0.000 | 0.000 | C-H bending |
| W(86) | | 2071 | 2071 | 2071 | 2071 | 2071 | 0.000 | 0.000 | C-H bending |
| W(87) | | 2071 | 2071 | 2071 | 2071 | 2071 | 0.000 | 0.000 | C-H bending |
| W(88) | | 2071 | 2071 | 2071 | 2071 | 2071 | 0.000 | 0.000 | C-H bending |
| W(89) | | 2071 | 2071 | 2071 | 2071 | 2071 | 0.000 | 0.000 | C-H bending |
| W(90) | | 2071 | 2071 | 2071 | 2071 | 2071 | 0.000 | 0.000 | C-H bending |
| W(91) | | 2071 | 2071 | 2071 | 2071 | 2071 | 0.000 | 0.000 | C-H bending |
| W(92) | | 2071 | 2071 | 2071 | 2071 | 2071 | 0.000 | 0.000 | C-H bending |
| W(93) | | 2071 | 2071 | 2071 | 2071 | 2071 | 0.000 | 0.000 | C-H bending |
| W(94) | | 2071 | 2071 | 2071 | 2071 | 2071 | 0.000 | 0.000 | C-H bending |

Vibrational assignments

C-H vibrations

The hetero cyclic aromatic compounds and its derivatives are structurally very close to benzene. The C-H stretching frequency of such compounds falls very nearly in the region of 3100- 2900 cm^{-1} for asymmetric stretching and 2980 - 2900 cm^{-1} for symmetric stretching modes of vibration. This permits the ready identification of the structure. Further in this region, the bands are not much affected by the nature and position of the substitutions [17]. Hetero cyclic compound C-H vibration absorption bands are usually weak; in many cases it is too weak for detection. In general, the aromatic C-H stretching vibrations calculated theoretically in the region 3109 - 3061 cm^{-1} for B3LYP and 3073 - 3021 cm^{-1} for HF predicts the CH stretching bands, which supports the literature values[18,19].

Methyl group vibrations

The molecule CLZ consists of CH_3 group attached in the diazepine(7 membered ring) ring. For the assignment of CH_3 group frequencies one can expect that there are nine fundamentals, viz., the symmetrical stretching in CH_3 (CH_3 sym. stretch) and asymmetrical stretching (in plane hydrogen stretching mode), the symmetrical (CH_3 sym. deform) and asymmetrical (CH_3 asym. deform) deformation modes; the in-plane bending (CH_3 ipb), out of plane bending (CH_3 opb), twisting (t CH_3) and bending modes. The FTIR bands observed 2977, 2918 cm^{-1} represent symmetric CH_3 stretching vibrations in CLZ. The theoretically computed values of CH_3 asymmetric stretching gives calculated at 3055 cm^{-1} and CH_3 symmetric stretching calculated at 3008,2927 cm^{-1} for B3LYP shows an excellent agreement with experimental results. The identified asymmetric in-plane bending vibration at 1440 cm^{-1} , symmetric in-plane bending vibration at 1368 cm^{-1} and rocking vibration (mode no:51) of CH_3 at 1034 cm^{-1} are well comparable with theoretically calculated values. These assignments find support within the frequency intervals given by Varsanyi [18]. The CH_3 torsional modes are assigned at 102 and 147 cm^{-1} .

C=O stretching vibrations

The structural unit C=O has an excellent group frequency, which is described as a stretching vibration. Since the C=O group is a terminal group, only the carbon is involved in a second chemical bond. This reduces the number of force constants determining the spectral position of the vibration. The C=O stretching

vibration usually appears in a frequency range that is relatively free of other vibrations. For, example, in many carbonyl compounds the double bond of the C=O has a force constant different from those of such structural units such as C=C, C-C, C-H, etc.; only structural units such as C=C have force constants of magnitudes similar to that of the C=O group. The C=C vibration could interact with the C=O if it were of the same species, but generally it is not. Almost all carbonyl compounds have a very intense and narrow peak in the range of 1800 - 1600 cm^{-1} . This is why this region is considered as a very important region by organic chemists. In this present study the C=O stretching vibration observed at 1736 cm^{-1} is in excellent agreement with theoretically predicted frequency obtained in B3LYP/6-31G(d,p) value [20,21]

Charge density

The gross atomic charges of clobazam with chemical shifts are given in Tables 3. This data would be used to explain the preferred position of nucleophilic attack of this molecule. In the present study, we employed Hartree-Fock and DFT levels to calculate the atomic charges. The gross atomic charges at the carbon C_2 attached to nitrogen and oxygen atoms are electron deficient compared to other carbon atoms. In general, electron deficient atoms have the higher δ value than an electron rich atom. The chemical shift at δ 165.9 was assigned to the carbonyl carbon (C-2) and the presence of a carbonyl group was confirmed through the IR absorption at 1736 cm^{-1} . With increase in the electron density of the hydrogen atom the shielding increases and hence δ values for such proton decrease as show in Table 3. We attempted to correlate the total charge density on the hydrogen and carbon atoms with the chemical shifts obtained in NMR spectrum [22, 23]. The ^1H - and ^{13}C - chemical shifts were calculated with the B3LYP/6-31G(d,p) optimized geometries by GIAO method [24]. In order to obtain the calculated results comparable with the experimental data, we have transformed the absolute shieldings returned by the program in chemical shifts subtracting to the absolute shielding of TMS and the absolute shieldings of the molecule in exam. $\sigma_{\text{rel.}} = \sigma_{\text{rel.}} - \sigma_{\text{abs.}}$. In particular, each value of the absolute shieldings of the TMS was obtained with the same level of the absolute shieldings of the TMS, which was found with the same level of theory used in the determination of absolute shielding of the compound. There is satisfactory correlation between the total charge density and chemical shifts (exp & Theoretical).

Table 3 Gross atomic charge density and chemical shift (Experimental and Theoretical) of Clobazam

| Atom | Atomic Charge density | | ¹ H & ¹³ C NMR Expt | B3LYP/6-31G (d,p) |
|-------|-----------------------|------------------|---|-------------------|
| | HF/6-31G(d,p) | B3LYP/6-31G(d,p) | | |
| 1 N | -0.730946 | -0.49301 | | |
| 2 C | 0.68138 | 0.482982 | 165.9 | 182.2828 |
| 3 C | -0.36207 | -0.29139 | 44.7 | 61.4293 |
| 4 C | 0.55376 | 0.352528 | 165.3 | 186.5421 |
| 5 N | -0.68685 | -0.46892 | | |
| 6 C | 0.305218 | 0.308148 | 137.2 | 122.2198 |
| 7 C | 0.255843 | 0.234942 | 130.5 | 110.8562 |
| 8 C | -0.06518 | -0.01139 | 119.7 | 134.5799 |
| 9 C | -0.1852 | -0.17016 | 130.8 | 127.6228 |
| 10 C | -0.14931 | -0.10179 | 118.6 | 117.7686 |
| 11 C | -0.11856 | -0.08872 | 123.9 | 120.6818 |
| 12 O | -0.51515 | -0.41493 | | |
| 13 O | -0.50325 | -0.4126 | | |
| 14 C | 0.326712 | 0.273712 | 140.7 | 123.8544 |
| 15 C | -0.19482 | -0.04674 | 119.1 | 127.4104 |
| 16 C | -0.12438 | -0.14209 | 129.7 | 122.9138 |
| 17 C | -0.17203 | -0.07154 | 118.3 | 114.9895 |
| 18 C | -0.14106 | -0.1052 | 129.7 | 122.2732 |
| 19 C | -0.2053 | -0.12493 | 119.1 | 104.9685 |
| 20 C | -0.15327 | -0.19554 | 29.8 | 56.0128 |
| 21 Cl | 0.009195 | -0.01642 | | |
| 22 H | 0.185784 | 0.150877 | 3.17 | 5.7529 |
| 23 H | 0.199171 | 0.162263 | 3.17 | 5.3819 |
| 24 H | 0.127187 | 0.065957 | 7.70 | 32.8006 |
| 25 H | 0.168292 | 0.093899 | 7.06 | 7.3109 |
| 26 H | 0.1796 | 0.100147 | 7.02 | 7.8618 |
| 27 H | 0.227481 | 0.167283 | 7.64 | 33.3832 |
| 28 H | 0.157613 | 0.084288 | 7.24 | 8.0799 |
| 29 H | 0.143092 | 0.072426 | 7.00 | 7.3904 |
| 30 H | 0.158756 | 0.086294 | 7.24 | 7.7522 |
| 31 H | 0.172315 | 0.101984 | 7.64 | 7.4163 |
| 32 H | 0.155864 | 0.142861 | 2.78 | 4.1822 |
| 33 H | 0.152963 | 0.139958 | 2.78 | 4.9626 |
| 34 H | 0.147165 | 0.134801 | 2.78 | 3.8922 |

Table 4. Calculated polarizabilities for Clobazam

| Basis set | Dipole moment | Polarizabilities (α) | | | | | | (a) |
|------------------|---------------|-------------------------------|---------------|---------------|---------------|---------------|---------------|---------|
| | | α_{xx} | α_{xy} | α_{yy} | α_{xz} | α_{yz} | α_{zz} | |
| B3LYP/6-31G(d,p) | 4.0514 | 231.255 | 4.932 | 210.553 | -12.659 | 12.589 | 141.702 | 194.503 |
| HF/6-31G(d,p) | 4.4836 | 203.998 | 6.448 | 183.134 | -13.098 | 3.991 | 136.522 | 174.551 |

Table 5. Theoretically computed energies (a.u.), zero-point vibrational energies (Kcal mol⁻¹), rotational constants (GHz) entropies (cal mol⁻¹K⁻¹) and heat capacity (Kcal mol⁻¹K⁻¹)

| Parameters | HF/ 6-31G(d,p) | B3LYP/ 6-31G(d,p) |
|-------------------------------|----------------|-------------------|
| Total energy | -1331.3 | -1337.4 |
| Zero point vibrational energy | 175.76674 | 163.77832 |
| Rotational constants | | |
| | 0.30272 | 0.30070 |
| | 0.28838 | 0.28435 |
| | 0.17664 | 0.17282 |
| Entropy | | |
| Total | 131.575 | 135.995 |
| Translational | 42.993 | 42.993 |
| Rotational | 34.299 | 34.341 |
| Vibrational | 54.282 | 58.661 |

Other molecular properties

One of the objectives of this investigation is to study the effect of the basis set on molecular polarizability of clobazam using Gaussian 03W. In this study the computation of molecular polarizability of CLZ with different levels are reported. Here, α is a second rank tensor property called the dipole polarizability and mean polarizability (α) are evaluated using Eq. (1) [25].

$$\langle \alpha \rangle = 1/3(\alpha_{xx} + \alpha_{yy} + \alpha_{zz}) \quad (1)$$

The calculated polarizabilities using different basis sets for CLZ molecule are summarized in Table 4.

Several calculated thermodynamic parameters are presented in Table 5. Scale factors have been recommended [26] for an accurate prediction in determining zero-point vibrational energies (ZPVE) and the entropy S . The variation in ZPVEs seems to be insignificant.

Conclusion

From the before described results, the following conclusions can be drawn:

1. On the basis of calculated results, assignments of the entire fundamental vibrational Frequencies have been made.
2. The optimized geometry parameters calculated at B3LYP/6-31G(d,p) are slightly larger than those calculated at HF/6-31G(d,p) level and the HF calculated values correlates well compared with the experimentally obtained data on the whole.
3. Comparison between the calculated vibrational frequencies and the experimental values (FTIR and FT-Raman spectral data) indicates that both the

methods of B3LYP/6-31G(d,p) and HF/6-31G(d,p) can predict the vibrational spectra of the title compound well.

4. Atomic charges and chemical shifts of CBZ were calculated and results are discussed.
5. Molecular polarizability of CBZ were discussed and reported.

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