Electronic structure and vibrational analysis of Benperidol 1-{1-[4-(4-fluorophenyl)-4-oxobutyl]piperidin-4-yl}-1,3-dihydro-2H-benzimidazol-2-one

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Abstract

Benperidol is a relatively old antipsychotic drug that has been marketed since 1966. It has been used in Germany for 30 years but is also available in Belgium, Greece, Italy, the Netherlands and the UK. Benperidol used to treat anti-social sexual behaviour which may cause offence to others. have movement problems such as twitching, muscle stiffness, trembling or restlessness. Benperidol is a butyrophenone antipsychotic, with the highest neuroleptic potency in terms of D2 receptor blockade. Those taking it are therefore reputed to be at high risk of extrapyramidal side-effects, but benperidol's unusual profile may render it valuable to certain subgroups of people with schizophrenia. The structure and the ground state energy of the molecules under investigation has been analyzed employing DFT / B3LYP level. The optimized geometry and their properties such as equilibrium energy, frontier orbital energy, dipole moment and vibrational frequencies have been used to understand the activity of Benperdiol. The calculated highest occupied molecule orbital or HOMO and the lowest un-occupied molecular orbital or LUMO energies shows that charge transfer within the molecule. The vibrational spectra of IR and Raman have been interpreted with the help of B3LYP level of theory with the 6-31G basis set from the Density function theory

Keywords: *vibrational spectroscopy, DFT, HOMO, LUMO, antipsychotic*

INTRODUCTION

Benperidol, sold under the trade name **Anquil** among others, is a drug which is a highly potent butyrophenone derivative. Benperidol is a relatively old drug that is used for the treatment of schizophrenia in several European countries. We identified only one small, poorly reported, unpublished, randomised trial comparing benperidol with another antipsychotic. Unfortunately the quality of reporting is so poor that the results cannot be considered reliable. Although benperidol was first marketed in 1966, more trials on this drug are justified as with the advent of new compounds there is a danger that inexpensive drugs such as benperidol remain under-researched and overlooked.

Benperidol is a relatively old antipsychotic drug that was formulated in the 1960s and has been marketed since 1966. It is usually taken orally but can also be given by intramuscular injection for rapid treatment of acutely disturbed psychotic people. Early uncontrolled studies (Fluegel 1967) suggest that benperidol is effective in the treatment of schizophrenia, especially for those with recent onset delusions (fixed, false beliefs out of keeping with the

person's education or cultural background) and hallucinations (perceptions with no cause). Benperidol has been associated with a high risk of adverse effects such as rigidity, mask-like appearance, tremor, stooped shuffling gait and other so called extrapyramidal effects such as inner feeling of restlessness (akathisia), acute spinal and ocular rigidity (the acute dystonias) and the slow onset of repetitive movements of the face and body (tardive dyskinesia) (Nedopil 1979).

DFT is a computational quantum mechanical modeling method used in physics, chemistry and material sciences. In the present contribution, the properties that can be calculated with DFT, such as geometries, energies, spectroscopic properties. Density functional theory (DFT) calculations have been performed to predict the IR and Raman spectra for the molecule. Fourier transform infrared (FTIR) and Raman spectra of the compound have been obtained experimentally. All FTIR and Raman bands of the compound obtained experimentally were assigned based on the modeling results obtained at the B3LYP/6-31G level. Calculations were performed using the Gaussian 09. Gaussan is a general purpose computational chemistry software package. A basis set in theoretical and computational chemistry is a set of functions (called basis functions) that is used to represent the electronic wave function in the density-functional theory The DFT methods with 6-31G basis set calculations were made first to optimize the structures. The vibrational frequencies and non-linear optical properties were calculated by means of DFT methods at the corresponding optimized geometries. All the calculations converged to an optimized geometry which corresponds to a true energy minimum as revealed by the lack of imaginary values in the calculate vibration frequencies. Vibration frequencies are calculated using B3LYP/6-31G.

Optimized geometrical structure of Benperidol is shown in figure1.

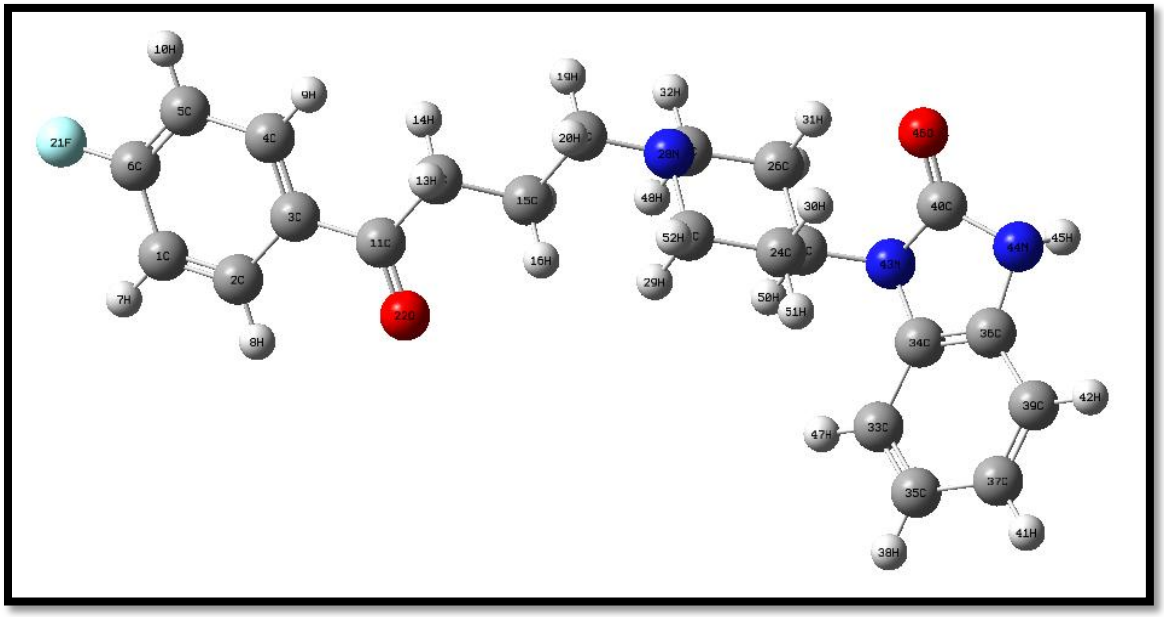


Fig 1

IR AND RAMAN FREQUENCY

IR SPECTRA-Infrared spectroscopy involves the interaction of infrared radiation with matter. It

covers a range of techniques, mostly based on absorption spectroscopy. An IR spectrum can be visualized in a graph of infrared light absorbance (or transmittance) on the vertical axis vs. frequency or wavelength on the horizontal axis.

RAMAN SPECTRA- RAMAN spectrum is a plot of the intensity of RAMAN scattered radiation as a function of its frequency difference from the incident radiation (usually in units of wavenumbers, cm^{-1}). This difference is called the *RAMAN shift,* because it is a difference value, the Raman shift is independent of the frequency of the incident radiation. Figure 2 and 3 show the calculated IR and Raman of Benperidol.

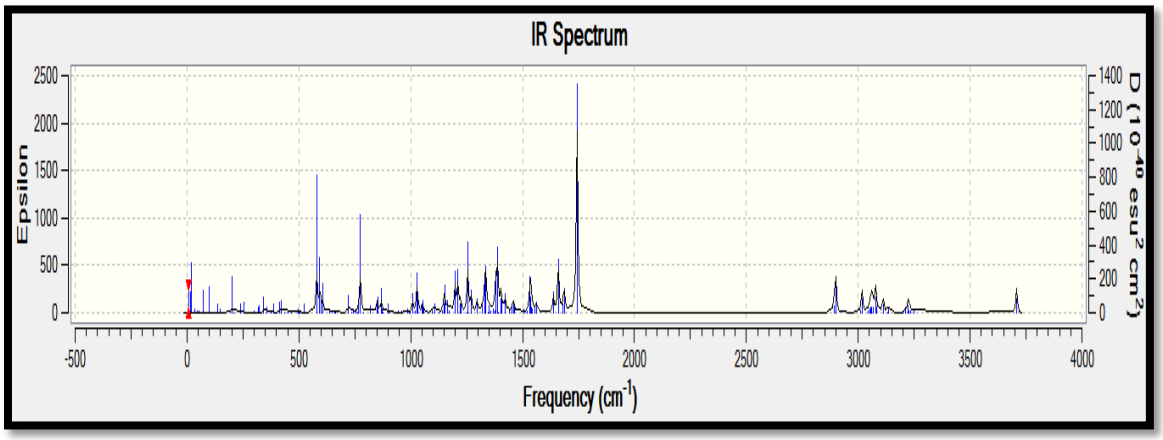


Fig 2

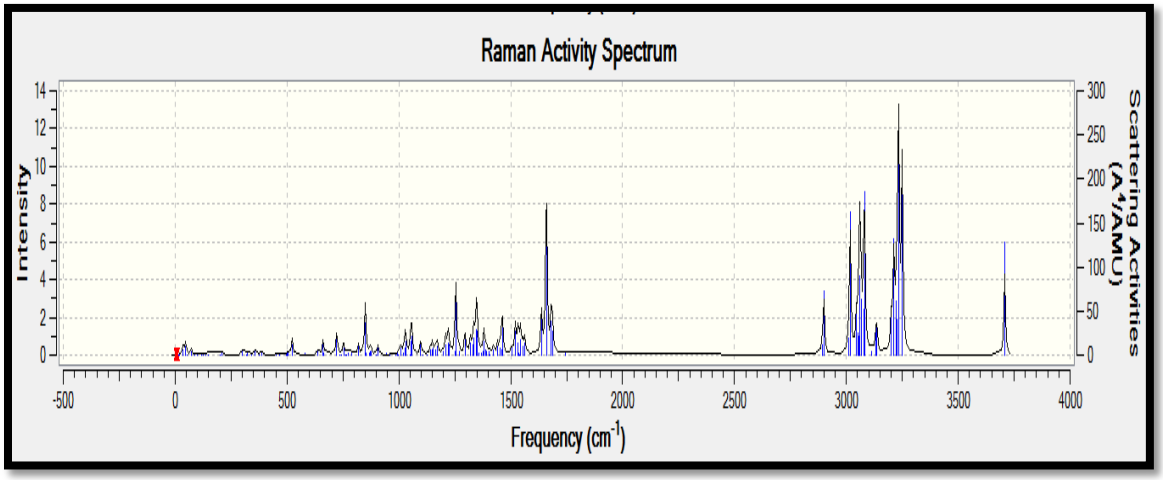


Fig 3

DEPOLARIZATION SPECTRA

The depolarization ratio is the intensity ratio between the perpendicular component and the parallel component of the raman scattered light. Two polarization occur i.e. p- polarization and u-polarization.

The optimised spectra of p-depolarization and u-depolarization is shown in the fig-4 and fig-5.

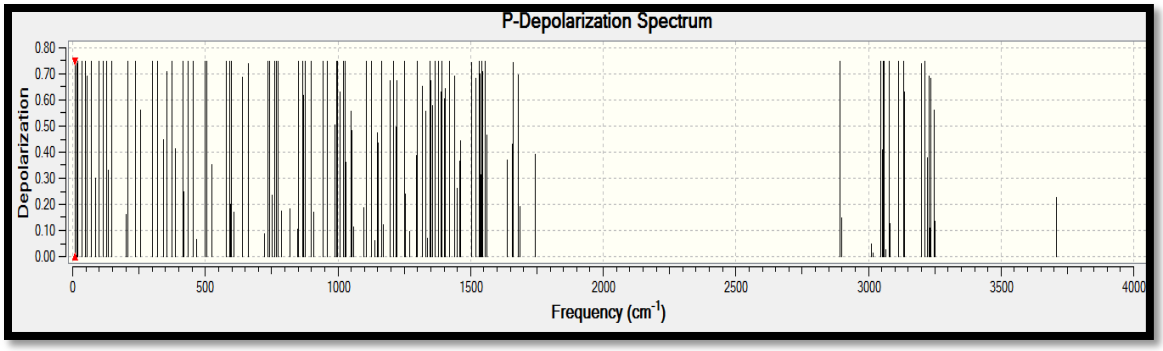


Fig 4

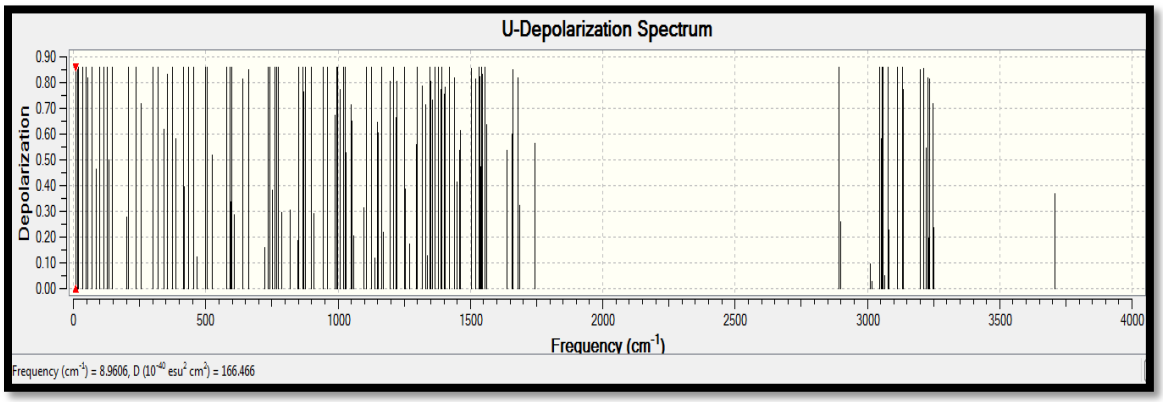


Fig 5

Theoretically computed ground state optimized parameters

Parameters	Benperidol (B3LYP/6-31G)
Energy	-1267.03336165 a.u.
Dipole moment (in Debye)	0.8989Debye

ELECTRONIC PROPERTIES

The most important orbitals in a molecule are the frontier molecular orbitals, called highest occupied molecular orbital (HOMO) and lowest unoccupied molecular orbital (LUMO).These orbitals determine the way the molecule interacts with other species. HOMO-LUMO orbitals are also called frontier orbitals as they lie at the outermost boundaries of the electrons of the molecules. The frontier orbital gap helps the chemical reactivity and kinetic stability of the molecule. A molecule with a small frontier orbital gap is generally associated with a high chemical reactivity, low kinetic stability and is also termed as soft molecule. The difference in energy between these two frontier orbitals can be used to predict the strength and stability of transition metal complexes, as well as the colors they produce in solution.

The HOMO and LUMO energy calculated by B3LYP /6-31G method –

HOMO Energy	-0. 19615a.u.
LUMO Energy	-0.06774 a.u.
ENERGY GAP	0.12841a.u.

The 3D plots of the frontier orbitals HOMO, LUMO are shown in Figure 6 and 7

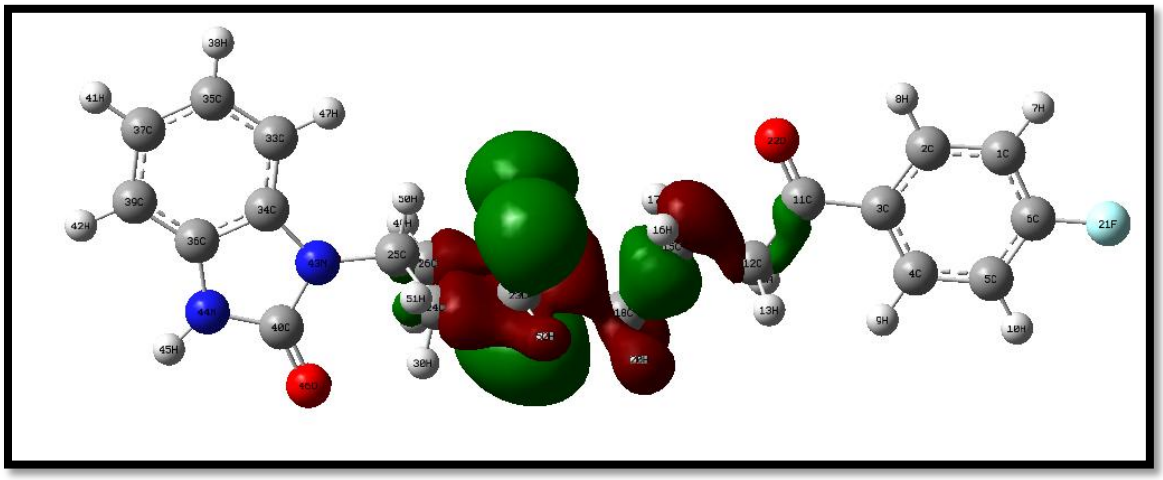


Fig 6

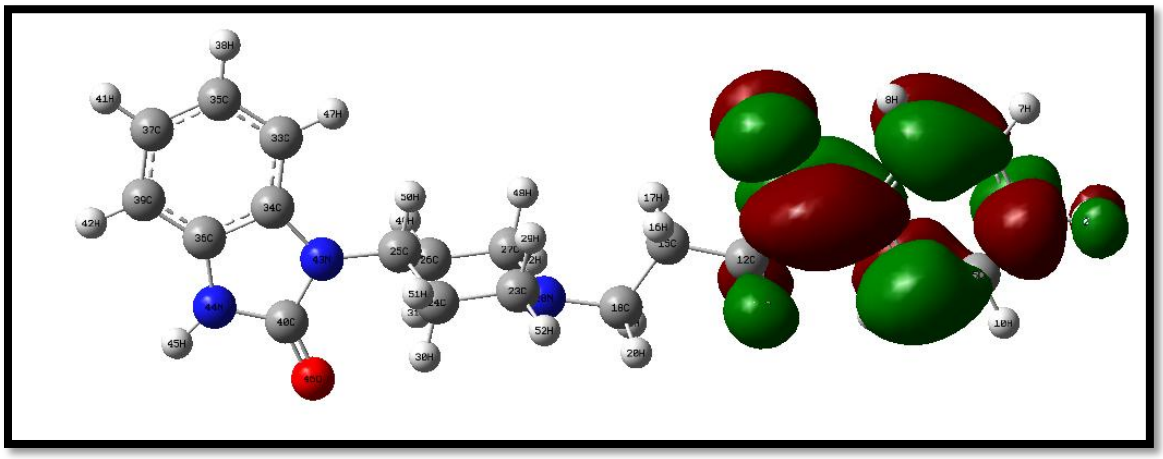
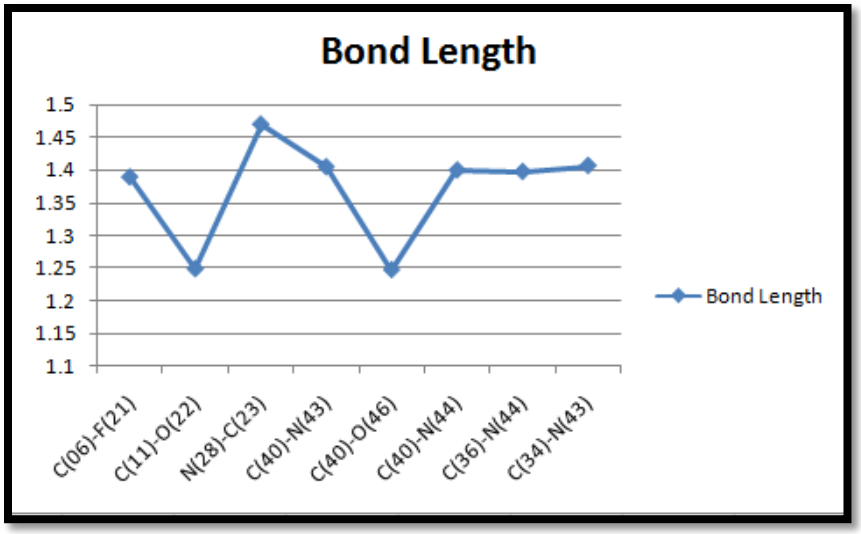


Fig 7

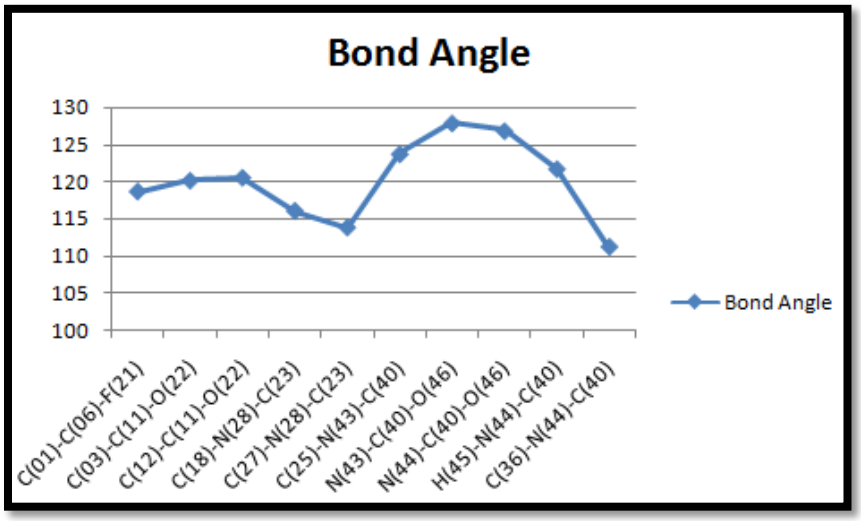
BOND LENGTH AND BOND ANGLE

In molecular geometry, bond length or bond distance is the average distance between nuclei of two bonded atoms in a molecule. It is a transferable property of a bond between atoms of fixed types, relatively independent of the rest of the molecule. Molecular geometries can be specified in terms of bond lengths and bond angles. The bond length is defined to be the average distance between the nuclei of two atoms bonded together in any given molecule. A bond angle is the angle formed between three atoms across at least two bonds. Such as bond lengths and bond angle are the optimized structural parameters, so these parameters were determined at B3LYP level theory with 6-31G basis set and they are presented in a table. Bond length and Bond angle table of Benperidol given below

Atom	Bond Length
C(06)-F(21)	1.38891
C(11)-O(22)	1.24872
N(28)-C(23)	1.46944
C(40)-N(43)	1.40444
C(40)-O(46)	1.24720
C(40)-N(44)	1.39953
C(36)-N(44)	1.39712
C(34)-N(43)	1.40635



Atom	Bond Angle
C(01)-C(06)-F(21)	118.697
C(03)-C(11)-O(22)	120.155
C(12)-C(11)-O(22)	120.549
C(18)-N(28)-C(23)	116.045
C(27)-N(28)-C(23)	113.800
C(25)-N(43)-C(40)	123.752
N(43)-C(40)-O(46)	127.927
N(44)-C(40)-O(46)	126.879
H(45)-N(44)-C(40)	121.727
C(36)-N(44)-C(40)	111.186



CONCLUSION

Simulation work of Benperidol is in the process. Simulation report of Benperidol we will reported very soon.

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