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The Sapience

DFT of Naphazoline

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Abstract

In this paper structure of Naphazoline is optimized with help of combination DFT/B3LYP method and 6-31G (d) basis set. Structure is fully optimized to minima without any symmetry constrains. Stability of Naphazoline can be analyses by zero-point energy, vibrational analysis and some other parameter. Chemical reactivity can be calculated with help of HOMO-LUMO gap. This gap of title molecule is lies on 13.54eV.Normal mode analysis can be calculated with animated view on gauss-view. It should noticed that calculated value lies some higher region than experimental ones so to remove this difficulty scaling factor use in this study. NLO properties state that this molecule shows optical behavior. Hyperpolarizibility of title molecule is 137 times higher than urea.

Keywords: DFT, Hyperpolrizibility, NLO, HOMO, LUMO.

1. Introduction

Naphazoline (in the hydrochloride form) is the common name for 2-(1-naphthylmethyl)-2-imidazoline hydrochloride. It is a sympathomimetic agent with marked alpha adrenergic activity. It is a vasoconstrictor with a rapid action in reducing swelling when applied to mucous membrane. It acts on alpha-receptors in the arterioles of the conjunctiva to produce constriction, resulting in decreased congestion. It is an active ingredient in several over-the-counter formulations including Clear Eyes and Naphcon eye drops [1]. It has the molecular formula C14H14N2 and a molar mass of 246.73 g/mol. A few warnings and contraindications that apply to all naphazoline-containing substances intended for medicinal use are: Hypersensitivity to naphazoline, Patients taking MAO inhibitors can experience a severe hypertensive crisis if given a sympathomimetic drug such as naphazoline HCl, Use in infants and children can result in central nervous system depression, leading to coma and marked reduction in body temperature, Should be used with caution in patients with severe cardiovascular disease including cardiac arrhythmia and in patients with diabetes, especially those with a tendency toward diabetic ketoacidosis, Drug interactions can occur with anaesthetics that sensitize themyocardium to sympathomimetics e.g. cyclopropane or halothanecautiously. Exercise caution when applying prior to use of phenylephrine. Extended use may cause rhinitis medicamentosa, a condition of reboundnasal congestion.

A possible association with stroke has been suggested.[2]Naphazoline is a decongestant used to relieve redness, puffiness, and itchy/watering eyes due to colds, allergies, or eye irritations (smog, swimming, or wearing contact lenses). It is known as a sympathomimetic (alpha receptor agonist) that works in the eye to decrease congestion. Some brands of naphazoline eye drops also contain other ingredients. Lubricants (such as glycerin, hypromellose, or polyethylene glycol 300) help protect the eyes from more irritation. Zinc sulfate, an astringent, helps reduce redness and irritation.Naphazoline have a lot of chemical biological and other physical application we choose this molecule for study.

2. Computational Details

The quantum chemical calculations were carried out with Gaussian 03 program package [3] utilizing gradient geometry optimization [4].To predict the molecular structure, vibrational wave numbers and energies of the optimized structures using combination of DFT/B3LYP[5] method and 6–31G(d) basis set, The gradient corrected Density Functional Theory (DFT) with the three-parameter hybrid functional (B3) [6] for the exchange part and the Lee-Yang-Parr (LYP) correlation function [7] has been employed, Electronic structure are analysis with help of HOMO-LUMO surfaces .Some thermodynamical parameter are also calculated.. The optimized structural parameters of Title molecule calculated by B3LYP method with the 6-31G (d) basis set are listed in table-1.

3. Results and Discussions

The optimized Structure parameters of Naphazoline calculated by B3LYP method with the 6-31G (d) basis set are listed in Table 1 and are in accordance with the atom numbering scheme as shown in Figure 2, respectively. After geometry optimization local minimum energy obtained for structured optimization of Naphazoline with 6-31G (d) basis set is approximately -638.11838 (a.u.). for B3LYP method. The optimized bond parameters of molecule calculated by various methods are listed in Table 1.

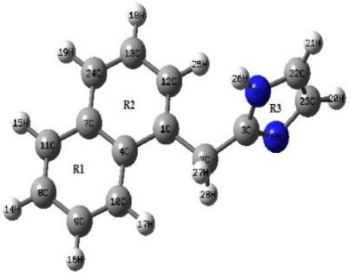


Fig. 1: Model molecular structure of Naphazoline

Naphazoline contains three ring in which two ring are benzene ring lies on one plane however on pentane ring deflected -175^0 out of plane .Two carbon of pentene ring are replaced by nitrogen. This pentene ring is connected with other benzene ring by methylene group. All carbon of benzene ring are sp^2 hybridize so all C-C bond are lies on same value but the angular changes in benzene ring geometry have also proved to be a sensitive indicator of the interaction between the substituent and the benzene ring [8]. The basic changes in the carbon essential involvement of both, the bond length and bond angles The (C-N) bond length varies between the values 1.3194Å- 1.4096Å, while (N-H) bond length varies between 1.0208Å- 3.0634Å while (C-H) bond length is 1.0824 Å. The average bond length of C-C in ring benzene rings are lies in between 1.42 Å -1.53 Å .The bond length of methylene group of both C-H are not lies on same value they differs to each other by a value $.01A^0$ .The bond length of C-H lies in plane of adjacent ring are lies $.01A^0$lower value than other which is deflected from plane of ring. The bond angle between CCC of ring R1 lies nearly120^0 however bond angle of CCC in ring R2 lies nearly 119^0. NBO analysis shows that antibonding electron of nitrogen creates repulsion in ring R_3 consequently ring R_3 distorted from planer structure. The (C-N-C) bond angle varies from 104.79^0- 126.10^0 and (C-N-H) lies at 149.53^0.

Atomic Charge, Polarizibility, Hyper Polarizibility and Thermodynamic Properties

The Mulliken atomic charges for all the atoms of the of is calculated by DFT/B3LYP method with 6-311G (d) as basis set in gas phase and are presented in Table 2.

The first hyperpolarizability (β) of this molecule and other properties (α, β, Δα) related to this hyperpolarizability of the given molecule are calculated by using combination of B3LYP/6-31G(d) method and basis set based on finite field approach. By applying electric field system energy is function of applied electric field. Hyperpolarizability and Polarizability describe the reply of a system in an functional electric field [9]. Theses Hyperpolarizability and Polarizability are determined strength of molecular interaction and collision process as well as nonlinear optical properties (N.L.O) of the system [10,11]. Hyperpolarizability of First order described by 3×3×3 matrix of is a third rank tensor. The 3D matrix contain 27 components can be reduced to 10 components due to the Kleinman symmetry [12]. It can be given in the lower tetrahedral format. The components of β are coefficients in the Taylor series expansion of the energy in the external electric field. When the external electric field is weak and homogeneous, this expansion becomes:

$E = E^0 – \mu_\alpha F_\alpha – 1/2_{\alpha\alpha}\beta F_\alpha F_\beta – 1/6\beta_\alpha\beta_\gamma F_\alpha F_\beta F_\gamma$

Where E^0 is the energy of the unperturbed molecules, $F\alpha$ the field at the origin $\mu_{\alpha,}$ $_{\alpha\alpha\beta}$, and $\beta_{\alpha\beta}$ are the components of dipole moment, polarizability and the first hyperpolarizabilities respectively

Dipole moment (μ), polarizibility $<\alpha>$and total first static hyperpolarizlbility β[13-16] are also calculated (In Table 3) by using density functional theory. They can be expressed in terms of *x*, *y*, *z* components and are given by following equations 1, 2 and 3-

$\mu= (\mu_x^2 + \mu_y^2 + \mu_z^2)^{1\backslash 2}$---------------------- (1)

$<\alpha>= 1\backslash 3\ [\alpha_{xx} + \alpha_{yy} + \alpha_{zz}]$ ---------------- (2)

$\beta_{\text{Total}} = (\beta_x^2 + \beta_y^2 + \beta_z^2)^{1\backslash 2}$

$= [(\beta_{xxx} + \beta_{xyy} + \beta_{xzz})^2 + (\beta_{yyy} + \beta_{yxx} + \beta_{yzz})^2 + (\beta_{zzz} + \beta_{zxx} + \beta_{zyy})^2]^{1\backslash 2}$--- (3)

The β components of Gaussian output are reported in atomic units.

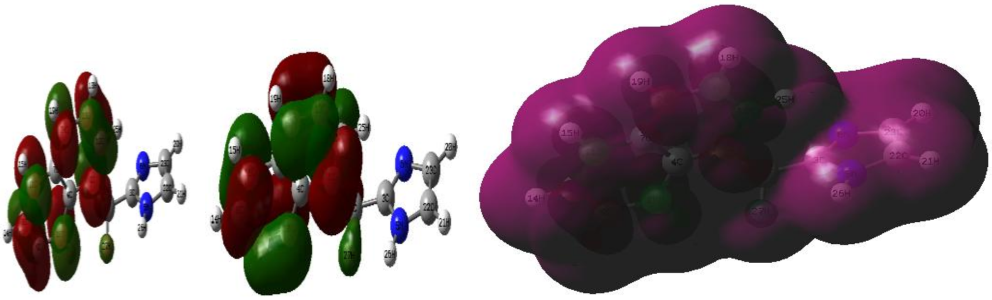
Where (1 a.u. = $8.3693X10^{-33}$ e.s.u.). For Naphazoline the calculated dipole moment value is 3.3970Debye. Having higher dipole moment than water (2.16 Debye),Naphazoline can be used as better solvent. As we see a greater contribution of α_{ZZ} in molecule which shows that molecule is elongated more towards Z direction and more contracted to Y direction. $\beta_{xxx,}$ β_{xxz} contribute larger part of hyperpolarizibity in the molecule. This shows that X-axis and XZ plane are more optical active in these directions. The value of hyperpolarizibily of title molecule is137 times greater than that of urea. These results indicate that the title molecule is a good applicant of NLO material. Urea is one of the Ideal molecule used in the study of the NLO properties of molecular systems. Therefore it was used frequently as a threshold value for comparative reference.

Several calculated thermodynamic properties based on the vibrational analysis at B3LYP and 6-311G (d, p) level, like internal thermal energy (E), constant volume heat capacity (C_v), and entropy (S), have been calculated and listed in Table 4. At the room temperature, conduction band is almost empty so electronic contribution in total energy negligible. Thermodynamic parameters clearly indicate that vibration motion plays a crucial role in assessing thermodynamical behavior of title compounds. The calculated dipole moments at B3LYP/6-311G (d, p) level are 6.6832 of Naphazoline.

Electronic Properties

The interaction with other species in a chemical system is also determined by frontier orbitals, HOMO and LUMO. It can also be determined by experimental data. The frontier orbital gape helps to distinguish the chemical reactivity and kinetic stability of the molecule. A molecule which has a larger orbital gape is more polarized having reactive part as far as reaction is concerted [17]. The frontier orbital gape in case of the given molecule is -12.34e.V for Naphazoline given in Table 5.

The contour plots of the HOMO, LUMO structure of the molecules are shown in Figure 4, 5. The importance of MESP lies in the fact that it simultaneously displays molecular size, shape as well as positive, negative, and neutral electrostatic potential region in terms of grading and is very useful in the investigation of molecular structure with its physiochemical property relationship [18, 19]. The MESP diagram is shown inFigure 6.Gap between HOMO-LUMO orbital indicates the chemical reactivity of given system. HOMO acts as primarily acceptor and LUMO acts as primary donor. From fig we see that both HOMO and LUMO are localized over whole molecule except ring R3 in which both nitrogen exist. According to mullion charge Nitrogen contains highest negative charge so acts more favorable site for nucleophile charge center. Both HOMO-LUMO orbital does not contain nitrogen occupied ring.



Fig, 2: HOMO-LUMO and MESP plot of Naphazoline Molecule.

Assignment of Fundamentals

Naphazoline has 28 atoms 78 normal modes of vibration. We made a reliable one-to-one correspondence between the fundamentals and the frequencies calculated by combination of DFT/ B3LYP method and 6-31G(d) basis set . The relative band intensities are also vary satisfactory along with their positions. The assignments are based on animated view of normal mode of vibration .The calculated and experimental frequency are not lies on same wave number because in our calculation we ignore molecular interaction ,electron-electron correlation [20],anharmonic[21] effect ,basis set deficiencies and also calculated frequencies represent vibrational signatures of the molecules in its gas phase on compression with experimental one. So calculated harmonic force constants and frequencies are usually higher than the corresponding experimental quantities; [22] So we scaled calculated frequency by a factor 0.986 to simulate with experimental one. Some important modes of vibration are disuse below one by one

N-H Vibration

N-H stretching vibrations are generally observed in the region 3500-3700 cm^{-1}.One of intense polarized along ring R_3 lies on 3552 Cm^{-1} which is corresponding to stretching of N-H bond .Some of in plane and out of plane bending modes are lies lower region of spectra of title molecule.

C-H Vibration

Change in geometry reflected by change in frequency .Noteworthy variations in intensity and frequency take place in the H–X stretching. As the amount of the change in H–X stretching frequency is known to represent a measure of the intermolecular interaction, the difference in frequency is in good agreement with the interaction energy. The aromatic structure of title molecule shows that C–H stretching vibrations in the region 2800–3200 cm^{-1}, which is the characteristic region for the ready identification of the C–H stretching vibration [23] A intense polarized peak appears at 3229 cm^{-1} corresponding to C-H stretching are obtained .Two less intense polarized mode are obtained at3261 cm^{-1},3204 cm^{-1} are also lies in this range. Some of in plane and out of plane bending mode are also obtained which are listed in table given below

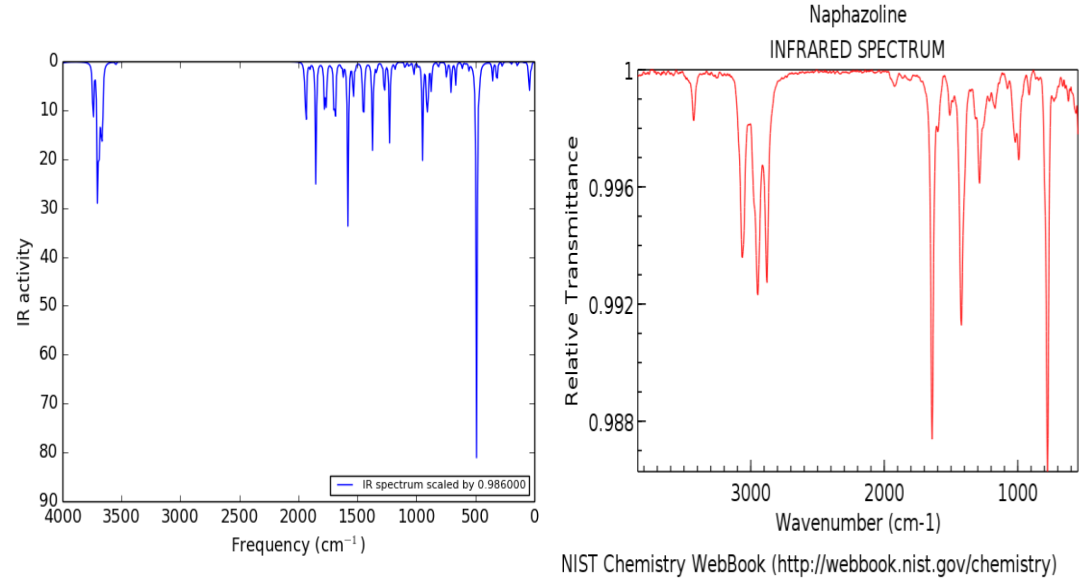
C-C Vibration

A intense polarized mode corresponding to stretching C-C are obtained at 1658Cm^{-1}.Two less polarized peak corresponds to C-C stretching mode are obtained at1614 Cm^{-1},1688 Cm^{-1}.The theoretically calculatedC–C–C bending modes and C–C torsional modes have also been found to be consistent with the recorded spectral values and the literature [24].

Some other modes of Vibration

Out of plane bending as well inplane bending are obtained at lower side spectra. Ring Torsion shown in the region 252 cm^{-1} while Twisting in C-H bond is shown in

502,1401,1500, 1529 cm$^{-1.}$ Ring breeding modes are also lies on lower region of this band. Due to mixing of band at lower region intensity as well other properties not well defined in this region. The lower region vibration has unique characteristics which is fingerprint of title molecule so this region is also called fingerprint region.



NIST Chemistry WebBook (http://webbook.nist.gov/chemistry)

Fig,3:Comprision between Calculated and experimental IR spectra of Title molecule

Where The Symbols are

μ=Stretching, β=In Plane Banding, ω=Wagging, R=Rocking,

4. Conclusions

Quantum chemical study, which involves full geometry optimization, entropy, total energy and vibrational frequency calculation, for this molecule has been carried out. All these studies are based on certain assumptions and as such have their own limitations. HOMO-LUMO and MESP picture shows that ring three is a attractive center for nucleophile charge center. NLO properties show that hyperpolarizibility of this molecule 137 times greater than urea. Combination of DFT/B3LYP method and 6-31G (d) basis set well discuss the geometry, vibrational as well as thermal properties of above molecule.

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