Geometry optimization, electronic structure IR frequencies HOMO-LUMO of a molecule (DNA Minor Groove Binder)

2,5-bis{[4-(N-Ethylamidino)]phenyl}furan molecule

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ABSTRACT: DNA minor groove binders have numerous applications. According to crystal structure that 2,5-bis{[4-(N-Ethylamidino)]phenyl} furan molecule is minor groove binder. Geometry optimization, dipole moment, HOMO-LUMO and IR assignments using the B3LYP/6-31G method. A comparison has been done between optimized parameters with crystallographic structure there is a very small variations in the conformations of the ethylamidino groups. There is very small gap between HOMO-LUMO means the high chemical reactivity and inter molecule charge transferability. Several vibrational spectra of the molecule calculated are in range of 300–4000 cm−1 , reproduce reliable IR spectra Bearing in mind the highl pharmaceutical significance of minor groove binders and a long numbers of flexible options accessible for lead optimization .**

Keywords: Geometry optimization, HOMO-LUMO . IR Frequencies

INTRODUCTION

A large pof the presently used chemotherapy antitumour agents are into DNA-binding medication . thanks to the appliance potential of such medication to cancer and on the far side, the event and delineation of such compounds are substantial. useful intercalators, to disrupt desoxyribonucleic acid metabolism, bind to desoxyribonucleic acid duplex in between 2 base-pairs through a non-covalent stacking interaction that necessitates as a minimum of partial planarity, that is assisted by the conclusion at least one chemical bond , the implications of embolism are the decrease of desoxyribonucleic acid voluted twist and enlargement of the desoxyribonucleic acid duplex . the soundness of ligand-DNA complexes is predicted to be improved by multiple interactions. Combining covalent-binding with non-covalent recognition signifies AN entropic advantage over molecules that don't don't to the desoxyribonucleic acid. In vigorous cells, most of the desoxyribonucleic acid is efficiently hold on and not approachable to foreign agents. On the opposite hand, the desoxyribonucleic acid of briskly dividing cancer cells is unendingly being retrieved, modified, and replicated, with concomitant changes in structure, which may be anticipated to desoxyribonucleic acid duplex in distinct forms, desoxyribonucleic acid junctions, loops, bulges, etc. desoxyribonucleic acid recognition by medication doesn't appear to be contingent straight on the genetic codes of the four bases however slightly on the mode the development of the desoxyribonucleic acid is customized action started everywhere the globe. it had been observed by the crystallographers that the method of embolism and groove binding will turn out deep alterations within the ester secondary structure

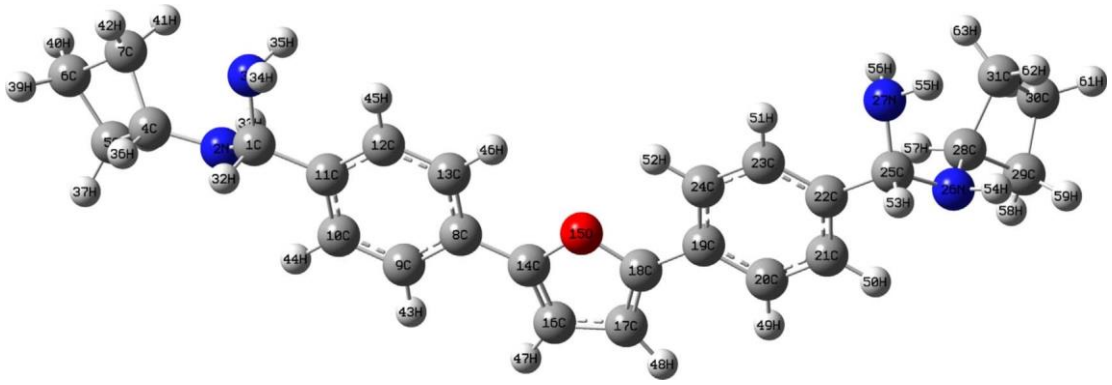

fig1

environmental conditions . Groove binders are stabilised through unit interactions and naturally have higher association constants than intercalators since a price in free energies isn't needed for the creation of binding sites . Minor Groove binders have established as clinical utility as antitumour, antiviral, and medicinal drug agents . Compounds with the flexibility of binding among the minor groove will hinder body condensation in cellular division beside the result modification in organic phenomenon. Plausibly, the foremost illustrious ANti-microbial desoxyribonucleic acid minor groove binding agent is pentamidine that demonstrates activity against an assortment of protozoa, for example, Pneumocystis jiroveci. Though, like alternative antimicrobial minor groove binding medication, penta amidines have notable toxicity as well as nephrotoxicity, cardiotoxicity, and hepatotoxicity that have angry analysis for harmless agents to delicate pneumocytosis. Pentamidine is additionally acknowledged to inhibit oncogenic PRL phosphatases , that play necessary roles in several cancers and clinically usable in ailments, as an example, carcinoma. Footprinting experiments and molecular modeling studies have

incontestable that pentamidines bind by selection among the minor groove of the AT-rich desoxyribonucleic acid duplex . Experiments conjointly show that the cis conformations of pentamidines are the foremost favored conformation for binding with the duplex . Pentamidine compounds are obtained by the substitution of amidino-nitrogens by hydrophobic chemical group teams of the furamidine, that will increase the binding affinity with desoxyribonucleic acid against pneumocystis carinii respiratory disorder . although the detection of desoxyribonucleic acid binding and therefore the effects on biological functions are well studied, an entire understanding of the mechanism of binding or the causes of affinity, etc are nevertheless to be accomplished. within the gift work molecular properties & electronic structure, of a ethylamidino substituent specifically2,5-bis{[4-(N-Ethylamidino)]phenyl} furan have done and therefore the assignment of traditional modes of vibration have out among the 300–4000 cm−1 wavenumber vary, victimization GAUSSIAN03 program

2. Methodology

The crystallographic geometry of this molecule has been taken from the PBD . The optimization of the geometry of the molecule without any constraint, in vacuum, has been carried out through the B3LYP/6-31G** DFT
as implemented in GAUSSIAN03 software . with the help of optimized coordinates of the molecule various parameters are calculated with the help of optimised Coordinates such as Mullikan's charge , HOMO LUMO , dipole moment, thermodynamic properties and IR spectra has been done.

3. Results and discussion

3.1. Geometry optimization

The molecular geometry of 2,5-bis{[4-(N-Ethylamidino)]phenyl} furan, isoptimized by B3LYP/6- 31G** method, true minima indicat negative IR wavenumber. Study of geometrical parameters indicates that the core rings have robust conformations substituents conformations have very small variation in Bond lengths of the optimized geometry of the molecule .

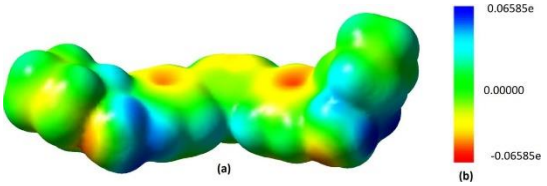

Fig 2

In crystallographic structure, the most change being for C–N bonds. Changes in bond angles have been observed at both terminal carbon atoms where the methylamidino group is attached. The dihedral angles of methylamidino rings show change i.e. the conformation of methylamidino rings is slitely change in crystallographic and gas- phase states..

3.2

HOMO-LUMO

Higher the gap between LUMO and HOMO showes greater hardness as well as a higher stability of the molecule. Not only Symmetry plays a role in chemical reactivity but also HOMO and LUMO are also involved. Value of total electronic energy of the molecule is −1304.2450 Hartree . HOMO energies of the molecule are −0.1903 and LUMO energy of the molecule is −0.0351 Hartree, . very Small value of the gap between HOMO-LUMO gap shows very high chemical reactivity of the molecule. HOMO lobes are highly intense on carbon atom of phenyle ring while less intense on nitrogen and oxygen atoms .virtual orbitals, delocalized in LUMO, are highly concentrated around single bonds in the central region (figure 3). These results clearly suggest

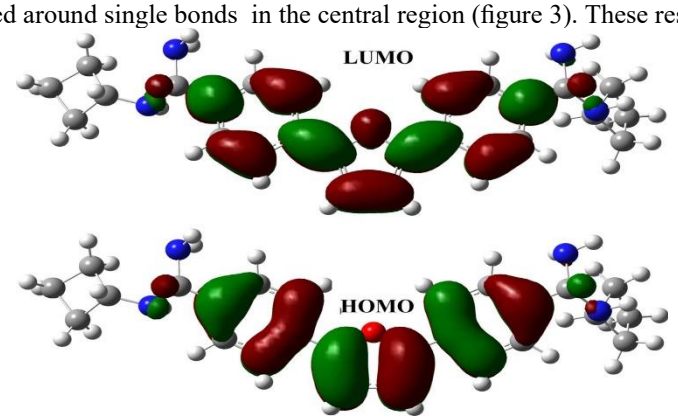

Fig 3

that the molecule is bioactive and intermolecular charge transfer can take place easily. The zero-point vibrational energy of the molecule is 339.578 cal mol−1.

3.2. IR SPECTRA

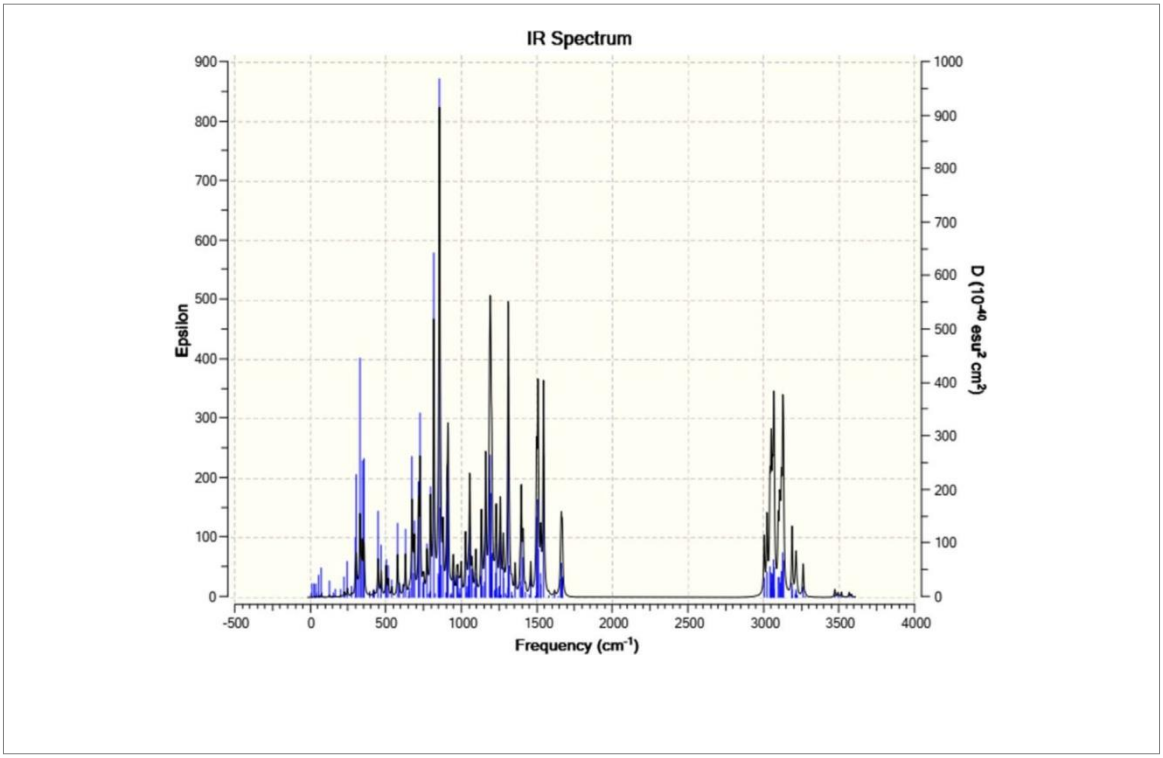

Fig 4

wavenumbers In large molecules, IR spectra are used to ascertain the specific groups present in the molecules. The absorption peaks of the molecule in the wavenumber range 300 to 4000 cm−1 calculated at B3LYP/6-31G** level have been a done. . molecule is structurally symmetric which show syn conformation with no imaginary wavenumbers exhibiting very small difference wavenumbers at the two sides of the molecule. peaks observed in the IR spectrum ring deformation, is symmetric and asymmetric stretching,. NH2 twisting is observed at 347.92 and 356.86 cm−1 while the molecule as a whole shows vibration at 394.87 cm−1. The ring out of plane deformations has been observed at 417.30 and
419.41 cm−1 wavenumbers though. the experimental value, average value is 412 cm−1 C–H out-of-plane bending vibrational value from experimental value around 474 cm−1 , in contrast, to theoretically observed values at
577.89 and 589.45 cm−1. The oxygen atom of the central furan ring show out of plane deformation at
687.07 cm−1. C–C–C and C–H out of plane distortions are observed at a small bit more wavenumbers than experimentally reported tenets. Aromatic C–C stretching modes have been found in the range 996 to 1034 cm−1 whereas furan ring C–H twisting at 972.39 cm−1. The normal modes at 1053.04, 1058.00, 1246.12, and 1336.89 cm−1 are done as C–H scissoring and rocking, C–N stretching, and C–H wagging. In- plane H–C–C bending is displaying by the molecule at 1096.82 and 1098.21 cm−1 while ring –CH–C–C stretching is observed in the range 1305 to 1317 cm−1. CH2 scissoring modes are detected at 1355.61, 1388.56, 1488.52, and 1489.62 cm−1. Asymmetric and symmetric C–H stretching vibration modes of CH2-groups of the molecule are exhibited in the range 3042 to 3067 and 3069 to 3120 cm−1 while asymmetric and symmetric aromatic C–H stretching vibrations in the range 3189 to 3208 and 3214 to 3224 cm−1 respectively. NH2 groups in the molecule
exhibit three types of vibrational modes: symmetric NH2 stretching at 3472.26 and 3492.66 cm−1, asymmetric NH2 stretching at 567.78 and 3582.82 cm−1 and N–H stretching at 3506.63 and 3515.98 cm−1 respectively.

4. Conclusion

The geometrical parameters of 2,5-bis{[4-(N-Ethylamidino)]phenyl} furanhas been calculated from the B3LYP/ 6-31G** technique are compared with the crystallographic structure that is slightly differnt. The conformation of core rings is strong enough whereas the conformation of Ethylamidino rings has significant deviations. HOMO-LUMO energy calculations clearly is that the molecule is bioactive with straightforward unit chargetransference. smart correlation is additionally discovered with the infrared(IR) assignments of the traditional wave modes of the computed and experimental wavenumbers with a multiplier of zero.96 as reportable by molecul it's been proved that the molecule had each strands of the duplex binding at intervals the minor groove . seeable of the high pharmaceutical significance of the molecule and additionally the vary of flexible choices of the molecule for lead optimization, these computations are a productive ground for the development of drugs targeting minor Grooves.

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