Quantum chemical and spectroscopic investigations of 3-methyladenine
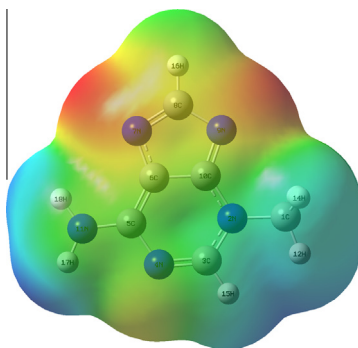
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HIGHLIGHTS

- Anharmonic frequencies were computed by PT2, VSCF and CC-VSCF methods.
- Mode–mode coupling strengths were computed using 2MR-QFF.
- Vibrational and electronic spectra of 3-methyladenine were analyzed.

GRAPHICAL ABSTRACT

ARTICLE INFO

ABSTRACT

FTIR, FT-Raman and UV–Vis spectra of 3-methyladenine have been recorded and investigated using quantum chemical calculations. The molecular geometry and vibrational spectra of 3-methyladenine in the ground state are computed by using HF and DFT methods with 6-311G(d,p) basis set. VSCF, CC-VSCF methods based on 2MR-QFF and PT2 (Barone method) have been utilized for computing anharmonic vibrational frequencies. These methods yield results that are in remarkable agreement with the experimental data. The magnitudes of coupling between pair of modes have been also computed. Vibrational modes are assigned with the help of visual inspection of atomic displacements. The electronic spectra, simulated at TD-B3LYP/6-311++G(d,p) level of theory, are compared to the experiment. The global quantities: electronic chemical potential, electrophilicity index, chemical hardness and softness based on HOMO and LUMO energy eigenvalues are also computed at B3LYP/6-311++G(d,p) level of theory.

Introduction

Adenine is a most widespread nucleic acid base found in the DNA and RNA that are involved in the storage and transfer of the genetic information [1–3]. Adenine is a key component in adenosine triphosphate (ATP), which is a primary energy carrier in all living organisms. The purine bases, adenine and guanine, are important structural constituents of the second messengers cAMP and cGMP, and are often involved in mutations leading to carcinogenesis [4]. In addition, these are the preferred biological targets of platinum-based drugs mediating the cytotoxic effect of these anticancer agents [1,2,4]. Therefore, the knowledge of structures and spectra of nucleic acids and their derivatives are helpful in understanding the biological processes and mechanisms of action of drugs. The present investigations have been carried out on 3-methyladenine (3-MA) using vibrational and UV–Vis spectroscopy with aid of HF and DFT calculations. The compound, 3-methyladenine is widely used as an inhibitor of autophagy. It inhibits P13K activity [5]. 3-MA has been shown to stimulate cell death of tumour cells under nutrient-starved conditions by inhibiting autophagy [6]. It also inhibits autophagy in tobacco culture cells under sucrose starvation conditions [7]. 3-Methylation of adenine does not influence base pairing, rather, the methyl

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group blocks replication by interfering with the interactions of DNA polymerase [8].

A critical survey of the most recent quantum chemical studies on nucleic acids and their constituents was carried out [9]. Extensive studies have been done on adenine along with its hydrogen-bonded dimers, derivatives, base pairs and tautomers by using various spectroscopic techniques and theoretical approaches [10–45]. 9-Methyladenine and its tautomers as well as complexes have been thoroughly studied using vibrational spectroscopy and quantum chemical calculations [11,15,24,25,35,39,43,44]. The polarized Raman scattering measurements were done for monoclinic crystal of 1:1 hydrogen bonded complex between 9-methyladenine and 1-methylthymine [45]. The base pair formation energy of the pair between 1-methyluracil and 9-methyladenine was obtained at HF and MP2 level of theory [46]. The electronic spectra of 9-methyladenine were investigated using UV photoelectron spectroscopy [18,29,33], resonantly enhanced multiphoton ionization spectroscopy [47], UV resonance Raman spectroscopy [48], polarization spectroscopy [37] and theoretical approaches [18,41,45]. The molecular structures of platinum-9-methyladenine complex [49], 3-ethyladenine [50], 3-methyladenine hydrochloride [51], tautomers of 1-methyladenine [52,53], 9-methyladenine [54], 9-methyladenine dihydrobromide [55] and 1:1 complex of 3-methyladenine and 9-methyladenine have been also reported [49,56]. Orbell et al. [56] computed electrostatic potential maps for 3-methyladenine and 9-methyladenine using INDO molecular orbital approximation. The IR spectra of 1-methyladenine tautomers were investigated using argon matrix [52], quantum chemical calculations [57], normal coordinate analysis [52], SQM force field [53] and PM3 method [57]. Moreover, the vibrational spectra of 8-azaadenine [58] and 2-chloroadenine [13,59] were analysed using quantum chemical computations. Many workers have performed vibrational analysis of molecules in the harmonic approximation and used various empirical scaling factors for compensating discrepancies between calculated and experimental results [60–63]. To the best of our knowledge the anharmonic force field computations, mode–mode coupling strengths and electronic spectra in different phases and vibrational spectroscopy of 3-methyladenine have not been reported so far. Therefore, there is a scope of study of the electronic and vibrational spectra of this molecule, which is of biological importance.

The vibrational calculations at harmonic level do not represent nature of anharmonic part of the potential that is itself of great interest. Some successful efforts have been made to carry out anharmonic calculations [64,65,66–74] in order to get reliable results without any scaling. Barone introduced an efficient algorithm, PT2, based on quadratic, cubic and semidiagonal quartic force constants [64,75]. Other efficient method is VSCF developed by Gerber and Ratner [65], Carney et al. [76] and Bowman [77,78]. Recently, many workers have reported anharmonic vibrational frequencies of various polyatomic molecules [79–86] using anharmonic force field methods.

In the present work, the optimized structural parameters and vibrational spectra of 3-methyladenine have been computed using the ab-initio HF and DFT (B3LYP, B3PW91) methods with 6-311G(d,p) basis set. For treating anharmonic effects, the second order perturbative (PT2) approach given by Barone [64], vibrational self-consistent field (VSCF) [65,77,78] based on 2MR-QFF potential energy function and correlation corrected vibrational self-consistent field (CC-VSCF) [87,88] methods are employed. Anharmonicity, which causes coupling between different vibrational modes, shifts the frequencies of the modes. In order to understand the coupling behaviour between pair of modes in 3-methyladenine, the magnitude of two-mode coupling for the ground state are computed and discussed [89]. NLO properties, MEP mapping and HOMO–LUMO analysis have been presented. The electronic absorption spectra in gaseous and solution phase (using PCM model) were also simulated at TD-B3LYP/6-311++G (d,p) level of the-

ory. The theoretical results are compared with experiment (FTIR, FT-Raman, UV–Vis spectra, XRD) and are found in good agreement.

Experimental details

The compound 3-methyadenine was obtained from Sigma Aldrich chemicals company, USA and was used as such for recording of FTIR, FT-Raman and ultraviolet–visible (UV–Vis) spectra. FTIR spectrum of the compound was recorded at room temperature on Tensor 37 Spectrometer (Bruker) in the spectral region of 400–4000 cm^{-1} with a spectral resolution of 2 cm^{-1} using KBr pellet technique. To increase the signal-to-noise ratio, a minimum of 32 scans were accumulated. FT-Raman spectrum was recorded on FT-Raman spectrometer (Bruker RFS 27) in the spectral region 50–4000 cm^{-1} with a spectral resolution 2 cm^{-1}. The Nd:YAG laser (1064 nm, 100 mW) was used as excitation source. UV–Vis spectra of 3-methyadenine in ethanol, water and DMSO solution were recorded in the region 175–800 nm on Lamda 950 UV–Vis–NIR spectrophotometer (Perkin Elmer).

Computational details

The calculations on 3-methyadenine molecule were performed at HF and DFT methods using Gaussian 03W software package [90]. In DFT calculations, the functional B3LYP [91,92] and B3PW91 [93–96] were used. The optimized structural parameters of the molecule in the ground state were obtained under tight convergence criterion using both HF and DFT methods with 6-311G(d,p) basis set. Subsequently, vibrational frequencies (harmonic and anharmonic) along with infrared intensities and Raman activities were calculated. Anharmonic corrections in vibrational frequencies were computed using Barone PT2 approach with Gaussian 03W package as well as VSCF/2MR-QFF and CC-VSCF (PT2-VSCF) methods implemented into Gamess-US package [97]. The PT2 method is used within the HF and DFT framework while VSCF and CC-VSCF approaches are adopted only for DFT. Gaussian program does not provide Raman intensities. Therefore, Raman intensities were computed using RAINT program [98]. The assignments were made with a high degree of accuracy using literature [42] and visual inspection of atomic displacements with the help of Gauss-View program. In general, the vibrational frequencies shift due to mode–mode coupling. In order to know the coupling between pair of modes, the magnitude of mode–mode coupling for the ground state has been estimated. 2MR-QFF potential energy function was used for calculating anharmonic mode–mode coupling strength [89,99]. The natural atomic charges were calculated with the NBO 3.1 program [100]. Electronic spectra of optimized molecule were calculated using PCM model at TD-B3LYP/6-311++G(d,p) level of theory in solution phase. For the plots of simulated IR and Raman spectra, pure Lorentzian band shapes were used with full width half maxima (FWHM) of 8 cm^{-1} [101]. The chemical behaviour and the reactivity of the 3-methyladenine were investigated using HOMO (ionization potential) and LUMO (electron affinity) energy eigenvalues calculated at DFT level. These values have been used to compute chemical reactivity descriptors such as chemical potential (μ), electronegativity (χ), chemical hardness (η), chemical softness (S) and electrophilicity index (ω). These so-called global quantities describe the reactivity of the molecule [102–108].

Results and discussion

Molecular geometry

The optimized molecular geometry of 3-methyladenine has been calculated using HF and DFT (B3LYP and B3PW91) methods