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Research Article

Quantum Chemical Computational Studies on 4-(1-Aminoethyl)pyridine

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Abstract

The density functional theory (DFT) method combined with B3LYP and B3PW91 hybrid functional were utilized for geometrical optimization, vibrational frequencies and electronic spectral study. The B3LYP and B3PW91 levels of the time dependent-DFT with 6–311+G(d, p) basis set have been used to determine the highest occupied molecular orbital (HOMO) – the lowest unoccupied molecular orbital (LUMO) energies, absorption wavelengths, and electronic properties (total energy and energy gap) of 4-(1-aminoethyl)pyridine. Global reactivity descriptors like ionization potential, chemical hardness and electron affinity, etc. have been estimated using the B3LYP/6–311+G (d, p) and B3PW91/6–311+G (d, p) methods. The effect of the solvent has been simulated using the integral equation formalism-polarized continuum model (IEF-PCM).

Keywords: DFT, Energy, 4-(1-aminoethyl)pyridine, Solvent effect

4-(1-Aminoetil)piridin'in Kuantum Kimyasal Hesaplamaları Üzerine Çalışmalar

Öz

Geometrik optimizasyonu, titreşim frekansları ve elektronik spektral çalışma için yoğunluk fonksiyonel teorisinin (DFT) B3LYP ve B3PW91 hibrit fonksiyonelleri kullanıldı. 4-(1-aminoetil) piridin'in en yüksek dolu moleküler orbital (HOMO) ve en düşük boş moleküler orbitallerin (LUMO) enerjileri, absorbsiyon dalga boylarının ve elektronik özelliklerinin (toplam enerji, enerji aralığı vb.) hesaplanmasında zamana bağlı-DFT ile B3LYP ve B3PW91 ve 6–311+G(d, p) baz seti kullanıldı. İyonizasyon potansiyeli, kimyasal sertlik ve elektron afinitesi gibi global reaktiflik tanımlayıcıları B3LYP/6–311+G (d, p) ve B3PW91/6–311+G (d, p) yöntemleri kullanılarak tahmin edilmiştir. Çözücü etkisi zamana bağlı yoğunluk fonksiyonel teorisine sürekli polarizasyon modeli (IEF-PCM) uygulanarak hesaplandı.

Anahtar Kelimeler: DFT, enerji, 4-(1-aminoetil)piridin, çözücü etkisi

1. Introduction

Cancer is one of the biggest health problems from past to present (Sankpal et al., 2012). The high toxicity of chemotherapeutic drugs used in the treatment and the resistance of various tumor cells to anticancer drugs pose a critical medical problem (Szakacs et al., 2006). Although the development of new and effective cancer treatments is the most important goal, new drug design and tests are of great importance. DNA has become one of the main biological targets for antitumor compounds since the development of cisplatin, the most important cancer drug (Huang et al., 2005; Pizarro et.al., 2009). Therefore, the experimental and computational study of the interaction of appropriate molecules with DNA is of great importance in drug design.

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Pyridine and its derivatives are preferred in the synthesis of different compounds because they have many pharmacological properties such as antimicrobial (Bhatt et al., 2001), antifungal (Patrick et al., 1996; Hishmat et al.,1990), and antitubercular (Doshi et al.,1999). Aminopyridines have attracted attention to the account of their potential uses in different fields, particularly in the treatment of neurologic disorders (Strupp et al., 2017). It is known that especially 4-aminopyridine (4-AP) and 3,4-diaminopyridine (3.4-DAP) are used in the treatment of diseases such as ocular motor disorders (Smith et al.,1994; Middleton et al.,1980; Dubey et al.,2010; Sedehizadeh et al., 2012; Keogh et al.,2011).

In the previous study, the coordination polymers including 4-(2-aminoethyl)pyridine were synthesized and characterized with XRD method, FTIR and Raman techniques by Karaağaç et al. (Karaağaç et al., 2019). They have also reported the FT-IR and Raman spectral data, the thermal properties and the crystal structures of some metal(II) tetracyanometalatte(II) complexes with 4-(2- aminoethyl)pyridine (Karaağaç et al. 2017). Although studies on 4-(2-aminoethyl)pyridine are limited in the literature, there is no studies on 4-(1-aminoethyl)pyridine.

Preferring computational methods to investigate many new properties while working on a molecule provides a great advantage in terms of time and cost. DFT has been increasingly used for calculating a wide variety of molecular properties that includes stability structure, charge transfer interactions, transition states, etc. DFT computations have made a significant contribution to the understanding of the quantum chemical properties of 4-(1-aminoethyl)pyridine.

Up to now, there are no theoretical and experimental studies of 4-(1-aminoethyl)pyridine in the literature. The optimized geometric parameters and vibrational frequencies have been calculated using B3LYP and B3PW91 with 6-311+G (d, p) basis set. Therefore, in this work, the ionization potential (I), electron affinity (A), electronegativity (χ), chemical hardness (η), softness (s), and electrophilic index (w) have been investigated for 4-(1-aminoethyl)pyridine. The indicator used in the computational bio-activity study of the molecule is the electrophilic index. In addition, the toxic potential of substances can be estimated by calculating the electrophilic index (Siddiqui and Javed, 2021). The electronic excitation energy and absorption wavelengths of 4-(1-aminoethyl)pyridine have been computed by using the B3LYP and B3PW91 methods with the 6-311+G (d, p) basis set. The electronic absorption spectra of 4-(1-aminoethyl)pyridine have been calculated by using DFT two different methods in water. The effect of the solvent has been simulated using the integral equation formalism-polarized continuum model (IEF-PCM).

2. Computational Details

The geometry of 4-(1-aminoethyl)pyridine molecule has been optimized by using the B3LYP (Lee et al., 1988), and B3PW91 (Perdew et al., 1996) levels of the density functional theory (DFT). The quantum chemical descriptors were calculated using GAUSSIAN 09W program packages (Frisch et al., 2009). The Gauss View 5.0 program was used to generate visual presentations (Dennington, 2009). The electronic spectral parameters of 4-(1-aminoethyl)pyridine in water and the gas phase were investigated by using DFT (B3LYP and B3PW91) method with the 6–311+G (d, p) basis set. The B3LYP and B3PW91 hybrid functional with 6–311+G (d, p) basis set were also used to calculate the chemical hardness, softness, and electronegativity.

3. Results and Discussion

3.1 Geometry optimization

The optimized geometry of 4-(1-aminoethyl)pyridine was carried out using the B3LYP and B3PW91 levels combined with 6-311+G(d, p) basis set (Fig. 1) The selected parameters of 4-(1-aminoethyl)pyridine for the two-hybrid functionals are tabulated in Table 1.

The geometric parameters (bond lengths and angles) of 4-(1-aminoethyl)pyridine are calculated slightly differently from the B3LYP method by the B3PW91 method. The C4-C7, C7-C8, and C7-N2 bond lengths are computed as 1,525Å, 1,542Å, and 1,467Å for the B3LYP level, respectively. The corresponding bond distances are calculated as 1,510Å, 1,536Å, and 1,461Å for the B3PW91 level, respectively.

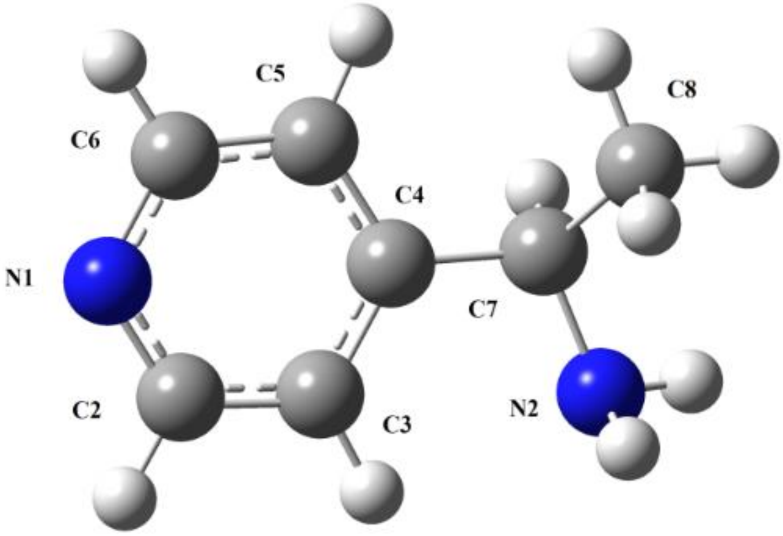

Figure 1. The optimized (with B3LYP/6-311+G (d, p) level) geometric structure of 4-(1-aminoethyl)pyridine.

The angle C4/C7/C8 is predicted as 111,62° for B3LYP hybrid functional and 111,72° for B3PW91 hybrid functional. The C4/C7/N2 angle is calculated as 111,07° for the DFT/B3LYP method, while the angle is computed as 110,89° for the DFT/B3PW91 method.

Table 1. Selected molecular structure parameters

	B3LYP	B3PW91
Bond Lengths(Å)		
N1—C2	1,334	1,332
N1—C6	1,337	1,334
C2—C3	1,397	1,392
C3—C4	1,395	1,393
C4—C5	1,399	1,397
C5—C6	1,390	1,389
C4—C7	1,525	1,520
C7—C8	1,542	1,536
C7—N2	1,467	1,461
Angles (°)		
C4—C7—C8	111,62	111,72
C4— C7— N2	111,07	110,89
C5—C4—C7	120,88	121,17
C3—C4—C7	122,44	122,15

3.2. IR Assignment

The calculated IR spectra of 4-(1-aminoethyl)pyridine was carried out using the DFT/B3LYP and DFT/B3PW91 level with 6-311+G (d, p) basis set. The theoretical data of vibration frequencies are tabulated in Table 2, as compared with experimental results (Karaağaç et al., 2017). The FT-IR spectra are displayed in Fig. 2. The computed frequencies are scaled with 0.96 for B3LYP and 0.95 for B3PW91 (Merrich et al., 2007; Sundaraganesan et al., 2005). Since there is no theoretical and experimental vibration frequencies so far in the literature of 4-(1-aminoethyl)pyridine, the vibration frequencies of 4-(2-aminoethyl)pyridine (4aepy) (Karaağaç et al., 2017) for vibration frequencies of 4-(1-aminoethyl)pyridine are used. Karaağaç et al. (2017) have reported NH_2 asymmetric and symmetric stretching frequencies of 4aepy molecule are found as 3362 cm^{-1} and 3292 cm^{-1}. The corresponding stretching frequencies are calculated as 3432-3349 cm^{-1} for B3LYP, and 3420-3334 cm^{-1} for B3PW91 levels. The in-plane NH_2 bending vibration of 4aepy molecule is observed at 1605 cm^{-1} experimentally and calculated at 1595cm^{-1} for DFT/ B3LYP and 1575 cm^{-1} for DFT/ B3PW91.

The CH stretching mode of 4aepy molecule appears at 3072 cm^{-1} experimentally (Karaağaç et al., 2017). The computed vibrations at 3077 cm^{-1} and 3053 cm^{-1} are assigned to ν(CH) mode for B3LYP and B3PW91 levels. The $\nu(CH_3)$ asymmetric and symmetric modes are computed as 2972, 2901 cm^{-1} for B3LYP, and 2951, 2880 cm^{-1} for B3PW91. The CC ring stretching mode is computed as 1568 cm^{-1} for B3LYP and 1565 cm^{-1} for B3PW91. This mode in FT-IR was observed at 1558 cm^{-1} (Karaağaç et al., 2017).

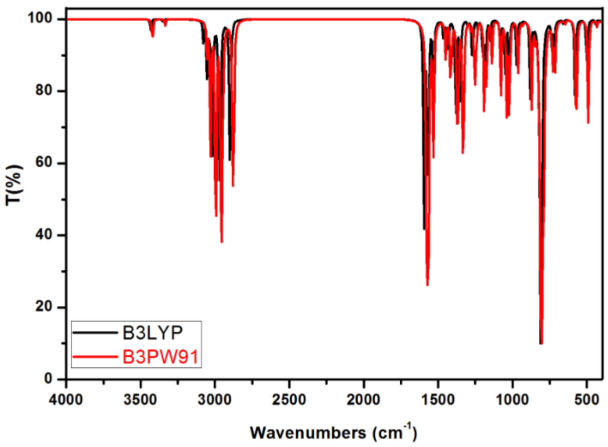

Figure 2 Calculated IR spectrum of 4-(1-aminoethyl)pyridine

The $(CH)_R$ in-plane bending vibration of 4-(1-aminoethyl)pyridine is computed as 1462 cm^{-1} for B3LYP level and 1449 cm^{-1} for B3PW91 level. This peak of the 4aepy molecule appears at 1442 cm^{-1}. The in-plane CH_3 bending vibration is calculated as 1429 cm^{-1} for B3LYP level and 1407 cm^{-1} for B3PW91 level. The $(CH)_R$ out-of-plane bending vibration of the 4aepy molecule is observed at 1386 cm^{-1} experimentally and computed at 1382cm^{-1} for DFT/ B3LYP and 1369 cm^{-1} for DFT/ B3PW91. The $(CH)_R$ out-of-plane bending mode is computed to be 962cm^{-1} and 953cm^{-1} for B3LYP and B3PW91 levels. In pyridine and substituted pyridines, the ring breathing mode is near 995 cm^{-1} (Topaçlı et al., 1999; Vural et al., 2016). The ring breathing mode of 4-(1-aminoethyl)pyridine is calculated at 971 cm^{-1} and 953 cm^{-1} for B3LYP and B3PW91 levels. It can be said that DFT/B3LYP-calculated frequencies are in good agreement with the experimental values (Karaağaç et al., 2017; Vural et. al., 2019) of the similar compounds.

Table 2 Calculated IR frequencies of 4-(1-aminoethyl)pyridine

	4aepy*	**B3LYP**	**B3PW91**
$\upsilon_{as}(NH_2)$	3362	3432	3420
$\upsilon_{s}(NH_2)$	3292	3349	3334
$\upsilon(CH)_R$	3072	3077	3053
$\upsilon(CH)_R$	3031	3050	3030
$\upsilon(CH)_R$		3021	2997
$\upsilon(CH)_R$	2993	3018	2994
$\upsilon_{as}(CH_3)$		2972	2951
$\upsilon_{s}(CH_3)$		2901	2880
$\beta(NH_2)$	1605	1595	1575
$\upsilon(CC)_R$	1558	1568	1565
$\beta(CH)_R$	1442	1462	1449
$\beta(CH_3)$		1438	1416
$\beta(CH_3)$		1429	1407
$\beta(CH)$	1386	1382	1369
γ (CH_3)		1349	1327
RB (*py*)	807-1000	971	965
γ $(CH)_R$		962	953
$\gamma(NH_2)$		811	806

s:symmetric, as: asymmetric, py: pyridine, υ: stretching, β: in-plane bending, γ: out-of-plane bending, RB: Ring breathing
*Karaağaç et al., 2017.

3.3. Electronic properties

The UV-vis spectral data for the gas phase and solvent of 4-(1-aminoethyl)pyridine were estimated using two different DFT functional. The solvent effect was computed by using TD-DFT (B3LYP and B3PW91) method and IEF-PCM model employing 6–311+G (d, p) basis set. The electronic spectral data of 4-(1-aminoethyl)pyridine are tabulated in Table 3, by using the Swizard program (Gorelsky, 2010). The B3LYP and B3PW91 hybrid functionals with 6–311+G(d, p) basis set were also used to calculate the chemical hardness (η) , softness (s), electronegativity (χ), and electrophilicity index (w) in the gas phase.

The calculated electronic spectrum of 4-(1-aminoethyl)pyridine showed different absorption maxima in the gas phase and water. According to TD-DFT/B3LYP/6–311+G (d,p) calculations (Table 3), the absorption maxima correspond to the electronic transitions from HOMO(H)→LUMO(L) (53%) and HOMO(H)→LUMO(L) (67%). These bands are predicted as $\pi \rightarrow \pi^*$ transitions. For the compound, the highest wavelength band is computed as 256 nm (f = 0.0040) for B3LYP level in the gas phase. The corresponding value is calculated at 246 nm (f = 0.0087) in the water. It is seen that the electronic transition wavelengths obtained at the gas phase are higher than the water solution. The calculated electronic transitions of 4-(1-aminoethyl)pyridine calculated by the B3PW91 functional are found to be very close to the calculations made with the B3LYP functional

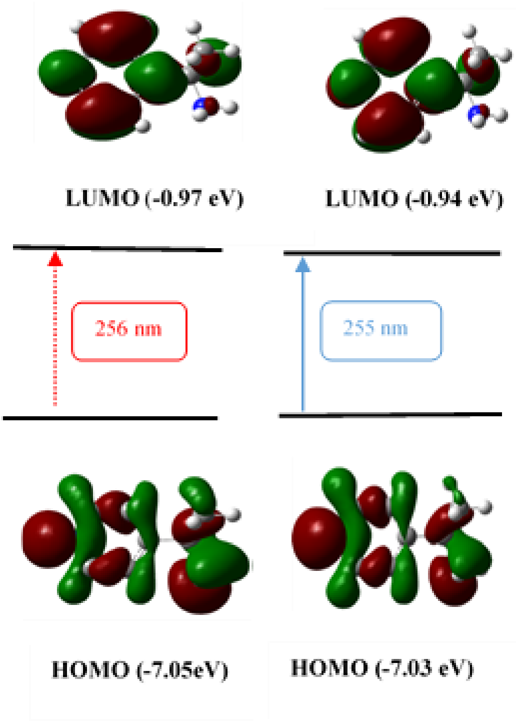

Figure 3. The FMOs of 4-(1-aminoethyl)pyridine by using the B3LYP and B3PW91 levels in the gas phase.

The HOMO and the LUMO have termed frontier molecular orbitals (FMOs). The energy gap (ΔE) between FMOs determines the energy that is very important to calculate chemical reactivity parameters (Vural et al., 2019). Figure 3 displays the energies of the FMOs for 4-(1-aminoethyl)pyridine.

Table 3. Calculated electronic transitions for 4-(1-aminoethyl)pyridine with the TD-DFT method

TD-DFT/ IEF-PCM		λ (nm)	osc. strength	major contributions
B3LYP	**gas phase**	256	0.0040	H→L (53%)
		228	0.0269	H-1→L (53%)
		187	0.0252	H-1→L+3 (26%)
		185	0.1124	H-3→L+1 (43%)
		180	0.1708	H-3→L+1 (18%)
	water	246	0.0087	H→L (67%)
		224	0.0308	H→L+1 (55%)
		185	0.0466	H-2→L+2 (78%)
		183	0.3895	H-1→L+1 (28%)
		181	0.4293	H→L+4 (19%)
B3PW91	**gas phase**	255	0.0040	H→L (83%)
		226	0.0247	H-2→L (66%)
		185	0.0071	H-2→L+2 (84%)
		180	0.1931	H-2→L+1 (19%)
		178	0.1853	H-1→L+4 (21%)
	water	246	0.0089	H→L (64%)
		228	0.0112	H→L+1 (65%)
		195	0.0395	H→L+2 (82%)
		181	0.4528	H-3→L+1 (40%)
		179	0.6549	H-2→L+1 (26%)

As given in Table 4, the I and A parameters of 4-(1-aminoethyl)pyridine are calculated by the DFT/B3LYP method are 7.05 eV and 0.97 eV, respectively. The corresponding parameters are computed at 7.03 eV and 0.94 eV for B3PW91 level. The η value is calculated at 3.04 eV for B3LYP level and 2.95 eV for B3PW91 level. The s value is calculated at 0.16 eV for the two-hybrid functionals. The w value is computed at 2.64 eV for B3LYP level and 2.60 eV for B3PW91 level. The very low chemical softness value of the title molecule indicates that it is theoretically non-toxic (Siddiqui and Javed, 2021). The ΔE is found at 6.08 eV for B3LYP level and 6.09 eV for B3PW91 level. The chemical reactivity parameters computed by the B3LYP and B3PW91 methods are close to each other.

Table 4. Calculated FMOs analysis of 4-(1-aminoethyl)pyridine and related properties obtained by the two different DFT methods in the gas phase.

Parameters (eV)	**B3LYP**	**B3PW91**
E_{HOMO}	-7.05	-7.03
E_{LUMO}	-0.97	-0.94
$\Delta E = E_{\mathrm{LUMO}} - E_{\mathrm{HOMO}}$	6.08	6.09
I	7.05	7.03
A	0.97	0.94
χ	4.01	3.98
η	3.04	3.04
s	0.16	0.16
w	2.64	2.60

4. Conclusions

In the present paper, the vibrational frequencies and global reactivity descriptors of 4-(1-aminoethyl)pyridine have been investigated by using the hybrid functional (B3LYP and B3PW91) of the DFT. The vibrational wavenumbers obtained by the B3LYP hybrid functional are in good agreement with that from FT-IR. The influence of the solvent on the electronic spectral properties of 4-(1-aminoethyl)pyridine is estimated using two different DFT hybrid functional. According to the results of the time-dependent DFT calculation, the electronic spectra of 4-(1-aminoethyl)pyridine showed different absorption maxima in the gas phase and water. The electronic transitions of 4-(1-aminoethyl)pyridine calculated by the B3PW91 functional are found to be very close to the calculations made with the B3LYP functional. The ΔE is found to be 6.08 eV which suggests that the molecule bioactive in nature. The comparatively low energy gap between FMOs suggests that the charge transfer may occur within 4-(1-aminoethyl)pyridine. The molecule and its complexes may be used as reagents or precursors in many fields such as physics, chemistry, pharmacology, and materials science.

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