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HIRSHFELD SURFACE ANALYSIS AND DFT STUDY OF ELECTRONIC STRUCTURE OF β-(N-BENZOXAZOLINE-2-THION

Abstract: *In this paper, the Hirshfeld surface analysis and DFT study of β-(N-benzoxazoline-2-thion) propionic acid was discussed. Hirshfeld surface analysis indicates that the most significant contacts in packing are H···H (30.2%), followed by H···O/O···H (29.2%), C···H/H···C (13.3.5%) and S···H/H···S (11.5%).*

By DFT calculations, electron densities on atoms and frontier MOs, as well as, MO energies and global quantum-chemical parameters based on them have been determined. Furthermore, the electron-rich and electron-deficit centers of β-(N-benzoxazoline-2-thion) propionic acid has been determined through ESP surface analysis.

Key words: *benzoxazoles, β-(N-benzoxazoline-2-thione)propionic acid, Hirshfeld surface analysis, hydrogen bonds, π–π interactions, DFT.*

Language: *English*

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Introduction

Benzoxazoline-2-thione (BT) derivatives are an important class of heterocycles and are of great interest because of their broad spectrum of biological activity. Insecticides, herbicides, fungicides and bactericides have been known among them [1]. β- (N-benzoxazoline-2-thionic) propionic acid (BTPA), which contains biologically active fragments such as BT and β-alanine, may also be a promising substance in pharmacology. This compound is also interesting from a chemical point of view due to the presence of several reaction centers in the molecule. Electrophilic exchange reactions can occur on the benzene ring. Chemical reactions characteristic to carboxylic acids can occur in the carboxyl group. In addition, the O and S atoms can participate in coordination with metal ions through their lone pair electrons.

In previous work [2], the crystal structures of the salts of β-(N-benzoxazoline-2-thione) propionic acid has been studied and showed that exocyclic active parts of benzoxazoline derivatives tended to form intra- and intermolecular hydrogen bonds in different crystal forms. In particular, in BTPA, the mobile proton of the carboxyl group is easily deprotonated and is involved in the formation of diverse organic salts.

In this regard, quantum-chemical parameters representing the electronic structure of β- (N-benzoxazoline-2-thione) propionic acid were calculated by B3LYP/6-31G(d, p) method. And also for comparison, the theoretical parameters of BT and β-alanine were calculated by the method.

Materials and methods

The XRD data (Ref Code: YEDCOC) of β- (N-benzoxazoline-2-thione) propionic acid (BTPA) has been used for Hirshfeld surface analysis by Crystal *Explorer 17* [3] program package.

The initial geometry of BTPA for DFT calculation is taken from X-Ray data (from cif file). The geometries of benzoxazoline-2-thione and β-alanine were built in Avogadro [4] program package. The geometry of all structures has been optimized by the B3LYP/6-31G(d) method using ORCA program package [5]. The results of theoretical calculations were visualized by Avogadro, MultiWFN [6] and VMD [7] program packages.

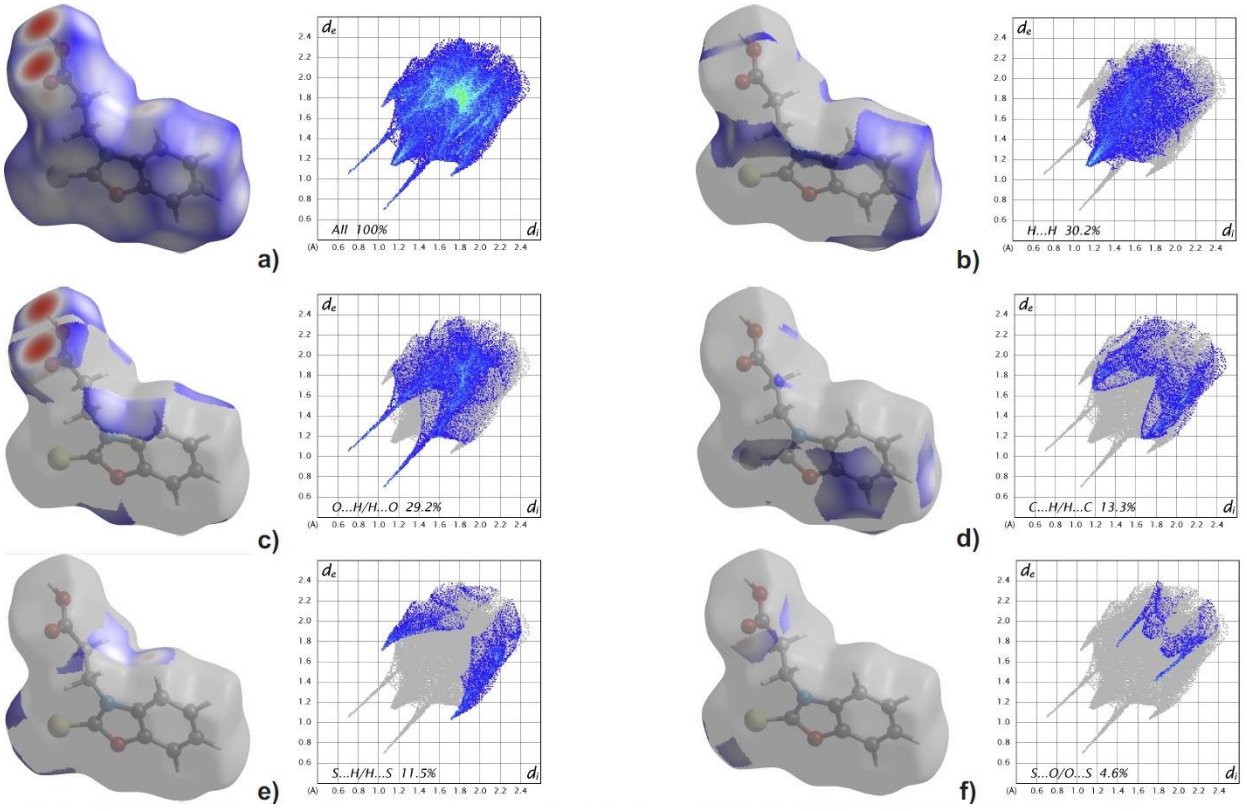

Fig. 1. Hirshfeld surface mapped over dnorm and decomposed fingerprint plots for the dominant interactions.

Results and discussion

Hirshfeld surface analysis

Herein, we report on the Hirshfeld surface analysis of β-(N-benzoxazoline-2-thion) propionic acid. To gain a better understanding of the nature of intermolecular interactions identified in compound **I**,

the Hirshfeld surface analysis was conducted through mapping the normalized contact distance (d_{norm}) as well as the calculation of interaction energies using the *Crystal Explorer 17* [3] program package. Hirshfeld surface analysis indicates that the most significant contacts in packing are H···H (30.2%), followed by H···O/O···H (29.2%), C···H/H···C (13.3.5%) and S···H/H···S (11.5) (Fig. 1).

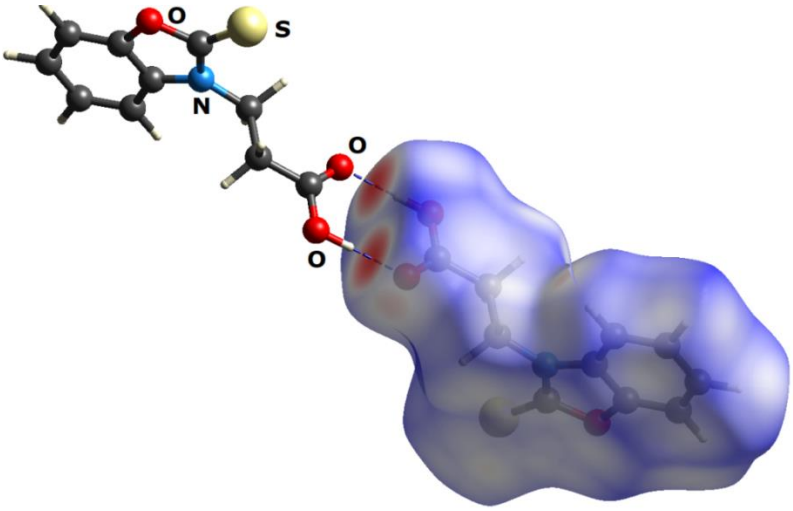

Fig. 2. The three-dimensional Hirshfeld surface showing the intermolecular interactions of (I) plotted over d_{norm}. Dotted lines (blue) signify prominent O-H…O hydrogen bonds.

The contributions of the contacts S···O/O···S, S···C/C···S,·C···C, C···O/O···C, O···O and N···H/H···N are very little and equal to 4.6%, 3.7%, 3.2%, 1.7%, 0.5 and 0.1%, respectively. Fig. 2 shows the d_{norm} mapping of (**I**) calculated in the range -0.6635 a.u. to 1.2071 a.u. The prominent hydrogen-bonded interactions are readily identified from intense red spots on the Hirshfeld surface. In Fig. 2, the intense red spots correspond to strong O–H…O hydrogen bonds whereas the diminutive red spots observed are due to strong O–H…O interactions.

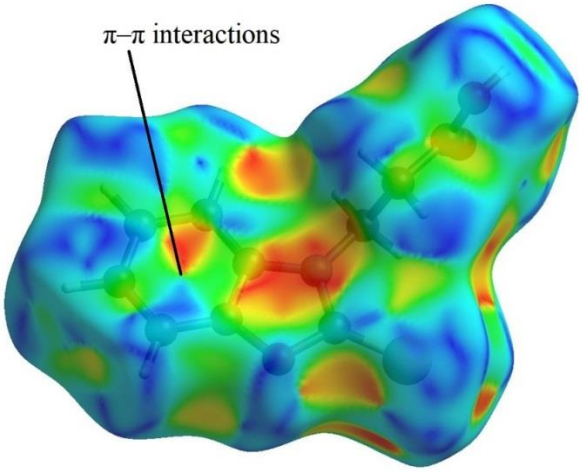

Fig. 3. Hirshfeld surface of the title compound plotted over shape-index.

The shape-index of the Hirshfeld surface is a tool to visualize π–π stacking by the presence of adjacent red and blue triangles; if there are no adjacent red and/or blue triangles, then there are no π–π interactions. Fig. 3 clearly suggests that there are π–π interactions in (**I**)

DFT study.

To study of electronic structure of BTPA, the global quantum-chemical parameters [8, 9] were determined after fully optimization of the geometry of BTPA, BT and β-alanine by B3LYP/6-31G(d,p) method.

The distribution of charge on atoms is a very useful parameter in chemistry for describing the chemical behavior of compounds - for determining the most negatively and positively charged atoms of a molecule.

Analysis of the charge distribution on atoms of

BTPA showed the localization of negative charges on the sulfur atom and oxygen atoms. It can be noted that the charge distributions on the benzoxazoline-2-thione (BT) and β-alanine atoms are almost the same as on the BTPA atoms (Fig.4).

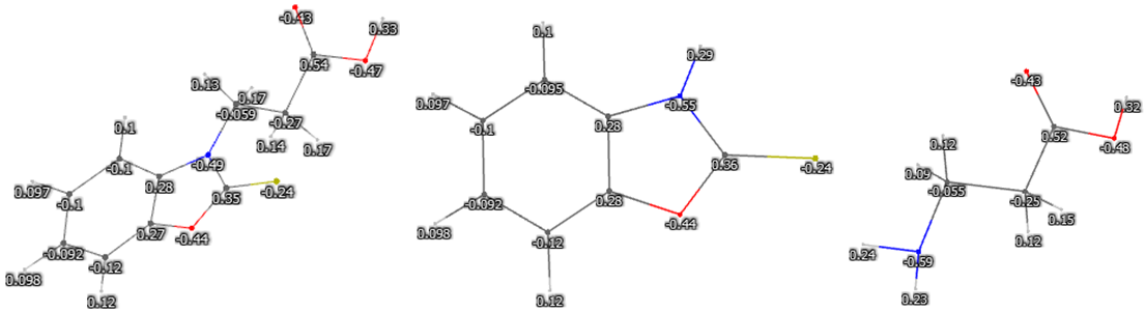

Fig.4. Charge distribution on the atoms of the BTPA, BT and β-alanine

It is known that HOMO and LUMO play an important role in chemical reactions, as well as in the manifestating of the biological activity of compounds. An analysis of the calculations showed that the electron densities in these MOs are localized in the benzoxazoline-2-part of the BTPA. (Fig.5).

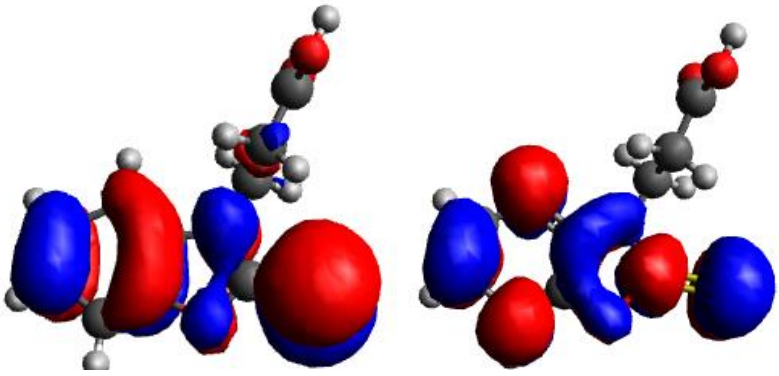

Fig.5. Distribution of electron density in the highest occupied (left) and lowest unoccupied (right) molecular orbitals of the BTPA.

Based on the energies of HOMO and LUMO, the following parameters are determined: electrophilic index (ω), stability index (|ΔE|), chemical hardness (η) and softness (σ), electronegativity (χ) and electronic chemical potential (μ_p). It turned out that the parameters calculated for the BTPA are almost identical to the BT indicators, which are its integral part.

Table-1. Quantum-chemical parameters for BTPA, BT and β-alanine

Quantum-chemical parameters	BT	β-alanine	BTPA
E_{HOMO} (eV)	-5.83	-6.37	-5.80
E_{LUMO} (eV)	-1.02	0.40	-1.02
$\|\Delta E\| = E_{HOMO} - E_{LUMO}$ (eV)	4.81	5.97	4.78
Ionization Potential, $I = - E_{HOMO}$ (eV)	5.83	6.37	5.80
Electron Affinity, $A = - E_{LUMO}$ (eV)	1.02	-0.40	1.02
Electronegativity, $\chi = (I + A)/2$ (eV)	3.43	2.98	3.41
Chemical hardness, $\eta = (I - A)/2$ (eV)	2.41	3.38	2.39
Chemical potential, $\mu_p = - (I + A)/2$ (eV)	-2.41	-3.38	-2.39
Chemical softness, $\sigma = 1/(2\eta)$ (eV^{-1})	0.21	0.17	0.21
Electrophilicity index, $\omega = \mu_p^2/2\eta$ (eV)	1.21	1.91	1.19
Dipole moment, μ (Debye)	5.49	1.35	5.22

The analysis of the surface of the electrostatic potential is widely used in the study of the electronic structure of compounds, mainly for the determination of electron-donor and electro-acceptor parts of molecule [10-12]. Consequently, the maxima and minima of the ESP surface were analyzed (Fig. 6). Red and blue colored parts in ESP surface diagram indicates maxima (a positive value) and minima (negative value), respectively. As a result of calculations, it was determined that there are 11 maxima and 5 minima for the BTPA molecule. It was found that the largest maximum (53.21 kcal/mol) is localized around the hydrogen atom of the COOH group, and the smallest minimum (-33.51 kcal/mol) is localized near the O and S atoms. The next maximum (27.50 kcal/mol) is localized on vicinity of H atoms of the N-CH2 group, and the minimum (-27.15 kcal/mol) is localized around the O atom of the C = O group.

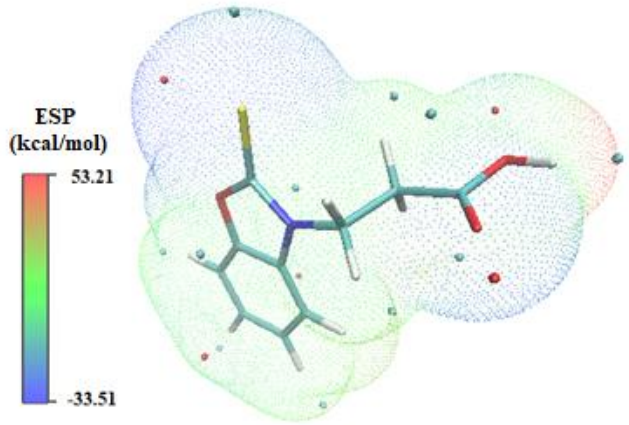

Fig.6. Ehe ESP surface maxima and minima for BTPA. The red and blue circles are minima and maxima points, respectively.

Conclusion

The Hirshfeld surface analysis of β-(N-benzoxazoline-2-thion) propionic acid has been determined using Crystal Explorer software. Hirshfeld surface analysis indicates that the most significant contacts in packing are H•••H (30.2%), followed by H•••O/O•••H (29.2%), C•••H/H•••C (13.3.5%) and S•••H/H•••S (11.5%). Furthermore, atomic charge distribution analysis, frontier electron densities, energies of frontier MOs and other parameters have been determined by DFT calculation. The electron-rich and electron-deficit centers of BTPA has been determined through ESP surface analysis.

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