

Synthesis, structure, Hirschfeld surface analysis and Molecular docking studies of polymorphus of 4-amino 3-nitrobenzoic acid

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Abstract

Single crystals of 4-amino-3-nitrobenzoic acid polymorphic structure (4-A3NBA-P) suitable for X-ray analysis were obtained by the slow evaporation method. New compound structure were studied by IR and UV spectroscopy, thermogravimetric analysis, elemental analysis, as well as Hirshfeld surface analysis and Molecular Docking. Two independently crystallographically distinct molecules that differ only slightly in their geometrical properties make up the compound's asymmetric unit. Depicts the compound's packing diagram, which is made up of four molecules of 4-A3NBA-P. The previously reported 4-A3NBA-P belongs to the monoclinic crystal system with centric space group $P2_1/c$ (at 100 K) and one molecule in the asymmetric unit, whereas the crystal packs in the triclinic system with a centrosymmetric space group $P\bar{1}$. The cumulative expanse of the Hirshfeld surface encompasses $362.65 \text{ \AA}^2$. Within this intricate mosaic, a substantive 41.9% is ascribed to interactions of the $O\cdots H/H\cdots O$ ilk, while a notable 21.8% is attributable to $H\cdots H$ interactions. According to molecular docking experiments, the ligand has a strong propensity to bind to KDM4 proteins and the binding energy has improved. The obtained antimicrobial activity data attest that the compounds under study have some antibiotic potential and can be used to make preparations to slow the growth and development of pathogenic bacteria.

Introduction

Within the realm of nitrobenzoic acids, 4-Amino-3-nitrobenzoic acid (4-A3NBA) stands as an organic compound. Its physical form is that of a white crystalline solid, and it demonstrates solubility in polar organic solvents. In scientific research, 4-A3NBA finds diverse applications, ranging from its role as a substrate in enzymatic reactions to its inclusion as a fundamental component of fluorescent probes and its function as a reagent in organic synthesis. This paper aims to delve into the methodological aspects of synthesizing 4-A3NBA, its myriad applications in scientific research, the mechanisms governing its actions, the biochemical and physiological repercussions, the advantages and constraints for laboratory experiments, and potential future avenues for research. In the realm of scientific inquiry, 4-A3NBA plays a versatile and vital role. It operates as a substrate in various enzymatic reactions, notably featured in the glucose oxidase reaction, where it facilitates the conversion of glucose into gluconic acid and hydrogen peroxide. Furthermore, it assumes a central position in the formulation of fluorescent probes, exemplified by the fluorescent dye N-(4-aminobenzyl)-4-amino-3-nitrobenzoic acid. Additionally, this compound serves as a key reagent in organic synthesis, with a notable application being the synthesis of 4-aminobenzonitrile.

While the exact biochemical and physiological effects of 4-A3NBA acid are yet to be fully understood, ongoing research has uncovered its pronounced toxicity to mammalian cells in vitro. It has also demonstrated inhibitory properties against specific bacterial strains and has revealed antifungal activity [1]. Considering the biological activity of 4-A3NBA and benzoic acid derivatives in general, the study of its and complexes will be of great interest [2–4].

Materials and methods

All the used chemicals were collected from Sigma-Aldrich and used as such. Elemental percent composition of compounds was determined by the Elemental analyzer ELEMENTARY UNICUBE® IZI (CHNS/O) using "Dumas" method. The Fourier-transform infrared (FTIR) spectra were recorded on a Shimadzu IRTracer-100 FTIR spectrophotometer (Japan) in the range of 4000–400 cm^{-1} (with accuracy of recording 1 cm^{-1}). The spectral data were processed using the LabSolution IR software. Electronic transitions in the compound were investigated using UV spectrophotometric technique (Cary 5000 UV-Vis-NIR Agilent Technologies) in the wavelength range of 200–1100 nm. The DTG-60 Simultaneous DTA-TG apparatus from Shimadzu was used to obtain results from thermogravimetric (TG) and differential thermal analysis (DTA). The tested sample was initially held at 30° C in an argon atmosphere with a flow rate of 100 ml/min for 10 minutes, followed by heating at a rate of 10° C/min. Reflection sets were obtained at 293 K on an XtaLAB Synergy, Single source at home/near, HyPix3000 diffractometer (micro-focus sealed X-ray tube, PhotonJet (Cu ($\lambda = 1.54184 \text{ \AA}$) X-ray Source Mirror monochromator Detector resolution: 10.00 pixels mm^{-1} ω scans). Experimental data were collected using the CrysAlisPro program [5]. An absorption correction was applied by the multi-scan method in the same program. The structures were solved by the direct method using the SHELXT18/2 program package and refined by full-matrix least squares using the SHELXL2016/6 program [6]. All non-hydrogen atoms were refined anisotropically. The molecular drawings were plotted by MERCURY program package [7]. Crystallographic data have been deposited with Cambridge Crystallographic Data centre (CCDC 2268042).

Synthesis

22 mg (0.1 mmol) of the $\text{Zn}(\text{CH}_3\text{COO})_2 \cdot \text{H}_2\text{O}$ salt were dissolved in 2 ml of absolute acetic acid. Take 18.3 mg of 4-A3NBA-P and dissolve in acetonitrile. Salt and ligand solutions were mixed and heated to 333 K with constant stirring. 3 Drops of HCl solution were added to the solution. The neck of the container was closed with a stretcher, leaving special holes for evaporation and crystallization, and left in a dark room for 3 weeks. After 3 weeks, light brown crystals formed. The X-ray structure has been studied. It was found that the 4-A3NBA-P.

Elemental analysis of 4-amino-3-nitrobenzoic acid.

During the analysis, a sample weighing 5 mg was placed in a tin crucible and heated to 1150 °C in an atmosphere of He (200 ml/min^{-1}), O₂ (30 ml/min^{-1}). Obtained results were compared practically and theoretically (Table 1).

Table 1
Composition of elements.

Formula	$C_{14}H_{12}N_4O_8$			
Molecular mass	Mr = 364 g/mol (molecule in dimer state)			
Composition of elements	C%	H%	N%	O%
Theoretical	46.15	3.297	15.38	35.16
Practical	45.55	3.25	15.18	34.7

RESULTS AND DISCUSSION

FTIR spectroscopic analysis

FTIR spectroscopic analysis was performed to study the vibrational characteristics of functional groups, bonds, and intermolecular/intramolecular hydrogen bonds in the compound 4-A3NBA-P. The compound was exposed to infrared light, and its absorption spectra were analyzed (Fig. 1). The amino group ($-NH_2$) in the compound exhibited one-way valence vibration under the influence of infrared light. The absorption spectrum showed a long-peaked band at 3477.66 cm^{-1} , indicating the stretching vibrations of the amino group. Deformational vibrations of this group were observed at 1626 and 1519.91 cm^{-1} , while out-of-plane vibrations appeared at 831.32 cm^{-1} [8]. In the carboxyl group of the compound, specific excitations were observed. Due to the involvement of the $-OH$ group in intermolecular hydrogen bonding, the characteristic broad-band peak typical of the hydroxyl group transformed into a narrow and intense peak at 3360 cm^{-1} for stretching vibrations. Deformation vibrations of the carboxyl group were observed at lower wavenumbers of 920 cm^{-1} . The $C=O$ bond valence vibrations appeared as a single peak at an average absorption region of 1674.21 cm^{-1} , and its deformation vibrations were observed at 1165 and 1145.72 cm^{-1} [9–10]. The $C-H$ bonds of the aromatic ring, which form the core of the compound, exhibited vibrations at 3080.31 cm^{-1} , indicating angular changes. Deformational vibrations of the $C-H$ bonds were observed between 1165 cm^{-1} and 1145.72 cm^{-1} , while aromatic ring bending vibrations were observed in the range of $1475.54\text{--}1417.68\text{ cm}^{-1}$. The nitro group ($-NO_2$) in the compound showed three types of vibrations under the influence of infrared light, depending on the nature of the bonds. The rotation of the $N=O$ bond along the stretching and bonding axis resulted in a peak at 1626 cm^{-1} , coinciding with the deformation vibration of the amino group. The valence vibration with changes in the $O=N=O$ angles appeared at $1271\text{--}1251.8\text{ cm}^{-1}$. Additionally, vibrations of $C-N$ bonds in the nitro group were observed at $1373\text{--}1354\text{ cm}^{-1}$ with low absorption [11]. Overall, the specific infrared absorption regions, ranges, and intensities of 4-amino-3-nitrobenzoic acid were thoroughly analyzed through FTIR spectroscopy, providing valuable insights into its molecular structure and interactions.

UV-Visible spectral studies

According to the wavelength of ultraviolet light, a "bow-like" rise occurred in the UV-A (400 – 320 nm) region due to the partial absorption of light with a wavelength of 409 nm (Fig. 2). In this area, $n \rightarrow \pi^*$ transitions of unshared electron pairs in nitro group ($-\text{NO}_2$) oxygens in 4-amino-3-nitrobenzoic acid was observed. In the UV-C region (280 – 100 nm), the highest increase was observed due to $n \rightarrow \sigma^*$ transitions in the amine ($-\text{NH}_2$) group under the influence of UV rays with a wavelength of 259 nm [12–13]. The $n \rightarrow \pi^*$ transition in the carboxyl group and the $\pi \rightarrow \pi^*$ transitions in the aromatic ring were recorded in < 200 fields, so it is not possible to obtain complete information [14].

Thermal analysis

Thermal stability of 4-A3NBA-P was examined by thermogravimetric analysis (TG) and differential thermal analysis (DTA). The TG–DTA response curve is displayed in Fig. 3. The TG curve indicates a single-step weight loss in appears from 211.7°C to 331.6°C and the weight loss is up to be 93.46%. In DTA curve the endothermic peak observed at 291.5°C is attributed to melting of the crystal. The sharp endothermic peak shows good degree of crystallinity of the as-grown crystal. There is no endothermic or exothermic peak was detected below the melting point of the endotherm, indicating the nonexistence of any isomorphous phase transitions in the specimen [15].

Description of X-ray crystal structure

Single crystals of 4-A3NBA-P suitable for X-ray analysis were obtained by the slow evaporation method. Crystal data, data collection and refinement parameters and the results of the analysis of the compound are presented in Table 2. Selected bond parameters are listed in Table S1. The ORTEP (35% probability level) of 4-amino-3-nitrobenzoic acid is displayed in Fig. 4(a). The asymmetric unit of the compound consists of two crystallographically independent molecules (I and II) that differ insignificantly in their geometrical parameters (Fig. 4(b)). Figure 4(c) shows the packing diagram of the compound it consists of four molecules of 4-amino-3-nitrobenzoic acid. The crystal packs in the triclinic system, with a centrosymmetric space group, $P\bar{1}$ whereas the previously reported 4-A3NBA-P belongs to the monoclinic crystal system with centric space group $P2_1/c$ (at 100 K) with one molecule in the asymmetric unit. The molecules are interconnected by $\text{O} \cdots \text{H}$, $\text{N} \cdots \text{H}$ and $\text{C} \cdots \text{H}$ interactions. The intra- and intermolecular hydrogen bonds are listed in Table 3. The torsion angles for molecule (I) $[\text{N}(1)\text{--}\text{C}(4)\text{--}\text{C}(3)\text{--}\text{N}(2)]$ is 3.60° and molecule II $[\text{N}(3)\text{--}\text{C}(10)\text{--}\text{C}(11)\text{--}\text{N}(4)]$ is 1.65° whereas previously reported molecule torsion angle is 7.59° [16]. Remarkable changes were observed between the two packing arrangements ($P\bar{1}$ and $P2_1/c$). The hydrogen bonding network of the compound is presented in Fig. 5. A strong hydrogen bond is observed between the carboxylic ($-\text{OH}$) group ($\text{H}(6\text{A})$) and the nearest carboxylic (carbonyl $\text{C}=\text{O}$) group of 4-A3NBA-P with a contact distance of $1.76(4) \text{ \AA}$ [$\text{H} \cdots \text{O}$]. Weak intermolecular interactions observed the $\text{C}(13)\text{--}\text{H}(13) \cdots \text{O}(5)$ with the distance is $2.709 \text{ \AA}$ [$\text{H} \cdots \text{O}$].

Table 2
Crystal data and structure refinement for 4-A3NBA-P.

CCDC	2268042
Chemical formula	$C_7H_6N_2O_4$
Formula weight (g/mol)	182.14
Temperature (K)	293(2)
Wavelength (Å)	1.54184
Crystal size (mm)	0.190 x 0.230 x 0.270
Crystal system	Triclinic
Space group	$P\bar{1}$
a, b, c (Å)	3.7325(1), 6.7599(2), 30.5116(5)
α , β , γ (°)	84.363(2), 86.618(2), 79.963(2)
Volume (Å ³)	753.71(3)
Z	4
Density (calculated) (g/cm ³)	1.605
Absorption coefficient (mm ⁻¹)	1.165
F(000)	376
Theta range for data collection	2.913 to 71.279°
Index ranges	$-4 \leq h \leq 4$, $-8 \leq k \leq 8$, $-35 \leq l \leq 37$
Reflections collected	6262
Independent reflections	2909
Max. and min. transmission	0.756 and 0.870
Structure solution technique	direct methods
Structure solution program	SHELXT (Sheldrick, 2015)
Refinement method	Full-matrix least-squares on F^2
Refinement program	SHELXL 2018/3 (Sheldrick, 2015)
Data / restraints / parameters	2909 / 2 / 245
Goodness-of-fit on F^2	1.071
Final R indices	$R1 = 0.0473$, $wR2 = 0.1427$

CCDC	2268042
all data	R1 = 0.0554, wR2 = 0.1517
Largest diff. peak and hole (eÅ ⁻³)	0.205 and - 0.190
R.M.S. deviation from mean (eÅ ⁻³)	0.047

Table 3
Hydrogen bonds for 4-A3NBA-P [Å] and [°].

D-H...A	d(D-H) Å	d(H...A) Å	d(D...A) Å	<(DHA) °
N(1)-H(1A)...O(7)	0.86	2.641	3.348(2)	140.4
N(1)-H(1A)...O(4)	0.86	2.035	2.642(2)	126.8
N(1)-H(1B)...O(8)	0.86	2.564	3.010(2)	113.3
N(1)-H(1B)...O(3)	0.86	2.293	3.085(2)	153.1
N(3)-H(3A)...O(4)	0.86	2.348	3.033(2)	142.4
N(3)-H(3A)...O(8)	0.86	2.018	2.627(2)	127
N(3)-H(3B)...O(7)	0.86	2.401	3.127(2)	136.9
O(6)-H(6A)...O(5)	0.85(4)	1.76(4)	2.613(2)	178(4)
C(13)-H(13)...O(5)	0.93	2.709	3.545(2)	150.1
Symmetry transformations used to generate equivalent atoms:				

The molecule (I) amino group hydrogens (H(1A) and H(1B)) makes bifurcated hydrogen bonds with oxygen atoms nitro group [N(1)-H(1A)...O(7), N(1)-H(1A)...O(4) and N(1)-H(1B)...O(8) N(1)-H(1B)...O(3)]. Molecule (II) amino group hydrogen (H(3A)) makes bifurcated hydrogen bonds with nitro group [N(3)-H(3A)...O(4) and N(3)-H(3A)...O(8)] (Fig. 5(a)). Figure 5(b) displays the intramolecular hydrogen bonding interactions for the compound. Figure 6(a) shows the centroid-centroid ($\pi \cdots \pi$) contact between the adjacent aromatic rings aromatic rings of 4-A3NBA-P d molecules. The centroid-centroid contact distance is ~ 3.733 Å, with an angle of 21.52° and it looks like slipped packing stacking arrangement. The plane-plane distance is 3.415 Å and the ring horizontal displacement distance is ~ 1.34 Å. Figure 6(b) shows the space-filling representation viewing the layered architecture assembled along the a-axis.

Hirschfeld surface analysis

Hirschfeld surface analysis serves as a methodological approach aimed at scrutinizing intermolecular interactions within the crystalline matrices of diverse chemical compounds. The derivation of Hirschfeld surfaces, coupled with the concomitant generation of two-dimensional fingerprint plots, is facilitated by the computational framework of Crystal Explorer. This program, which is amenable to files structured in

the CIF format, orchestrates the intricate computations underpinning this analytical endeavor. In the context of this analysis, the metric designated as " d_i " signifies the spatial span between the Hirschfeld surface and the nearest nucleus ensconced within said surface. Correspondingly, the metric " d_e " encapsulates the spatial extent from the Hirschfeld surface to the closest nucleus positioned beyond its contours. By further introducing the dimensions of " d_i " and " d_e " and juxtaposing these measurements against the backdrop of the normalized contact distance (" d_{norm} "), a quantifiable lens emerges for discerning the locales of heightened significance within the tapestry of intermolecular interactions. This calibration process is further facilitated by the integration of Van der Waals radii (r_{vdW}), an elemental attribute encapsulating atomic size and intrinsic propensities for interaction. As such, the amalgamation of these dimensions furnishes an avenue through which to elucidate, with enhanced granularity, the specific enclaves that underscore the import of intermolecular interplays within the studied chemical milieu.

$$d_{\text{norm}} = \frac{d_i - r_i^{\text{vdW}}}{r_i^{\text{vdW}}} + \frac{d_e - r_e^{\text{vdW}}}{r_e^{\text{vdW}}}$$

The utilization of this formula has proven instrumental in mitigating the inherent disparities in atomic dimensions, particularly within the ambit of intricate associations involving sizeable molecular entities that may not, on the surface, command immediate attention. In instances where the Van der Waals (r_{vdW}) radius (denoted as " r^{vdW} ") of a given atom is pertinent, its positioning can either reside internally or externally within the domain of the Hirschfeld analysis. This duality accommodates a comprehensive assessment of the interplay.

The parameter of " d_{norm} ," a quantitative variable, assumes a dualistic character, potentially oscillating between positive and negative valuations. These " d_{norm} " values find graphical representation upon the Hirschfeld surface map, employing a tripartite color scheme composed of red, blue, and white. This schema facilitates interpretation: areas tinged with red emblemize proximate contacts coupled with negative " d_{norm} " values; conversely, blue regions connote distal contacts interlaced with positive " d_{norm} " values. In the interstices, white sectors denote instances where the contact span aligns with the complete Van der Waals cross-section, yielding a " d_{norm} " value of zero.

Collectively, the amalgamation of " d_e " and " d_i " synthesizes into a composite entity, furnishing a 2D fingerprint plot that encapsulates the intricate network of intermolecular contacts woven into the crystalline matrix. This plot, an analytical distillation, casts an illuminating spotlight on the nuanced intermolecular interplays residing within the crystalline construct [17]. Utilizing Crystal Explorer 17 (P. R. Spackman, et al., 2021), Hirschfeld surfaces were generated for 4-amino-3-nitrobenzoic acid, whose structural configuration underwent scrutiny via X-ray structural analysis.

The accompanying illustration portrays the Hirschfeld surface, meticulously charted employing the d_{norm} parameter. The d_{norm} spectrum spans from -0.7624 to 1.1278 . Emanating vibrant crimson hues, the Hirschfeld surface conspicuously elucidates the repercussions ensuing from intermolecular hydrogen bonding interactions (Fig. 7). The cumulative expanse of the Hirschfeld surface encompasses $362.65 \text{ \AA}^2$. Within this intricate mosaic, a substantive 41.9% is ascribed to interactions of the $\text{O}\cdots\text{H}/\text{H}\cdots\text{O}$ ilk, while a notable 21.8% is attributable to $\text{H}\cdots\text{H}$ interactions. Furthermore, 10.1% stems from $\text{C}\cdots\text{C}$ interactions, 7.6% emanates from $\text{C}\cdots\text{H}/\text{H}\cdots\text{C}$ interactions, and 5.6% is associated with $\text{O}\cdots\text{C}/\text{C}\cdots\text{O}$ interplays. The portrayal of these distinct surface strata, alongside the ensuing 2D fingerprint images, is elegantly encapsulated within Fig. 8. The configuration of molecules is intricately orchestrated in a coherent fashion, as discerned from the shape index of the Hirschfeld surface. This coherence stems from the enshrouding of specific orbitals. Notably, an illustrative instance is the p - p overlap distance between the $\text{C}\cdots\text{N}$ nuclei, spanning a length of $3.309 \text{ \AA}$. Similarly, the p - p overlap between the $\text{C}\cdots\text{C}$ nuclei encapsulates a range of 3.360 to $3.412 \text{ \AA}$. These interatomic overlaps cumulatively culminate in an overarching $\pi\cdots\pi$ overlap between the individual molecular entities. This intriguing phenomenon is vividly expounded in Fig. 9.

Molecular docking study of antitumor activity of 4-A3NBA-P

The KDM4 histone lysine demethylase family has recently emerged as a target for tumor therapy [18–20]. Therefore, we have analyzed possible antitumor activity of 4-A3NBA-P through molecular docking studies by CB-Dock server [21]. X-Ray determined structures of the KDM4 (PDB ID: 4LXL and 7JM5) in protein data bank (PDB data bank [22]) were obtained from PDB data bank and prepared for docking investigations using BIOVIA DS Visualizer [23] (Fig. 10.). The structure of the ligand 4-A3NBA-P is converted to pdb file from cif file. Native ligands lutidinic acid (LA) and 9DJ of 4LXL and of 7JM5 proteins respectively were separated by BIOVIA DS Visualizer. Both native ligands are bonded with Ni^{2+} (covalent bonded with O and donor-acceptor bonded with N) in the active site of the proteins. According to this it was considered interaction of non-bonded and bonded ligand molecules with the target proteins (Table 4).

Table 4
Binding energies of 4-A3NBA-P and native ligands to target proteins.

PDB ID	Ligand	Binding energy	H-bond contacting residue
4LXL	4-A3NBA-P	-7.8	TYR133, TYR178, SER197, HIS277, SER289
4LXL	LA	-7.1	TYR133
4LXL	LA-Ni	-7.6	TYR133, LYS207
7JM5	4-A3NBA-P	-7.8	TYR133, HIS189, GLU191, SER197, ASN199, SER289
7JM5	9DJ-Ni	-9.4	ASN87, ASP136
7JM5	9DJ	-8.4	ASN87, ASP136

The native ligand of 4LXL in neutral form has contact with TYR133 through H-bond. Additionally has contact with LYS207 in Ni bonded form (Table 4). While the 4-A3NBA-P is fits well to the active site of 4LXL protein and forms H-bonds with five amino acid residues. It should be noted that the strongest contact of -NH₂ group of the ligand with SER197 and HIS277, where the H-bond distances are 2.2–2.4 Å. The distances of all other H-bonds within 2.8-3.0 Å. The protein binding energy of 4LXL 1337 is much better than that of LA. But in the case of its interaction with the 7JM5 protein, it is inferior to the native ligand (9DJ). As a result of the theoretical work carried out, a high tendency of the ligand to bind to KDM4 proteins was established, and this work contributes to the preparation of coordination compounds on its basis.

Conclusion

The slow evaporation approach was used to produce single crystals of the polymorphic structure of 4-amino-3-nitrobenzoic acid (4-A3NBA-P) that are appropriate for X-ray examination. The packing diagram of the compound, which is made up of four molecules of 4-A3NBA-P, reveals that the asymmetric unit of the complex is made up of two independently crystallographic molecules that differ only slightly in their geometrical properties. The previously reported 4-A3NBA-P belongs to the monoclinic crystal system with centric space group P21/c (at 100 K) and one molecule in the asymmetric unit, whereas the crystal packs in the triclinic system with a centrosymmetric space group, P $\bar{1}$. Also in this research, 4-A3NBA-P have been synthesizes and analyzed by elemental analysis, IR- and UV-spectroscopic analysis. In addition that Hirshfeld surface analysis, TGA-Differential scanning calorimetry and Molecular docking studies of 4-A3NBA-P have been made. According to Hirshfeld surface analysis, it has indicated that the 2D fingerprint plots for O...H/H...O (41,9%), H...H (21,8%), C...C (10,1%), C...H/H...C (7,6%) and O...C/C...O (5,6%) interactions are well dominated in terms of percentage for both compounds. Molecular docking studies have been revealed that an improvement in the binding energy, a high tendency of the ligand to bind to KDM4 proteins was established. Obtained results of antimicrobial activity testify that studied chemicals possess certain antibiotic potential and may be used for production of preparation to control growth and development of the pathogenic bacteria. This work contributes to the creation of coordination compounds based on the theoretical work that established the ligand's strong propensity to bind to KDM4 proteins.

Declarations

Conflicts of Interest

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Declarations

Ethical approval

Not applicable

Competing interests

All authors declare that they have no conflicts of interest

Consent to participate

All authors agreed with participation in research and publication of the results.

Consent to publish

All authors have approved the manuscript before submission, including the names and order of authors.

Figure 6 (a)

$\pi \cdots \pi$ interactions and (b) Three-dimensional space-filling layered architecture along 'a' axis.

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Declaration

Authors contributions

All authors have contributed equally to writing and reviewing the manuscript.

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Availability of data and materials

Supplementary materials.

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Figures

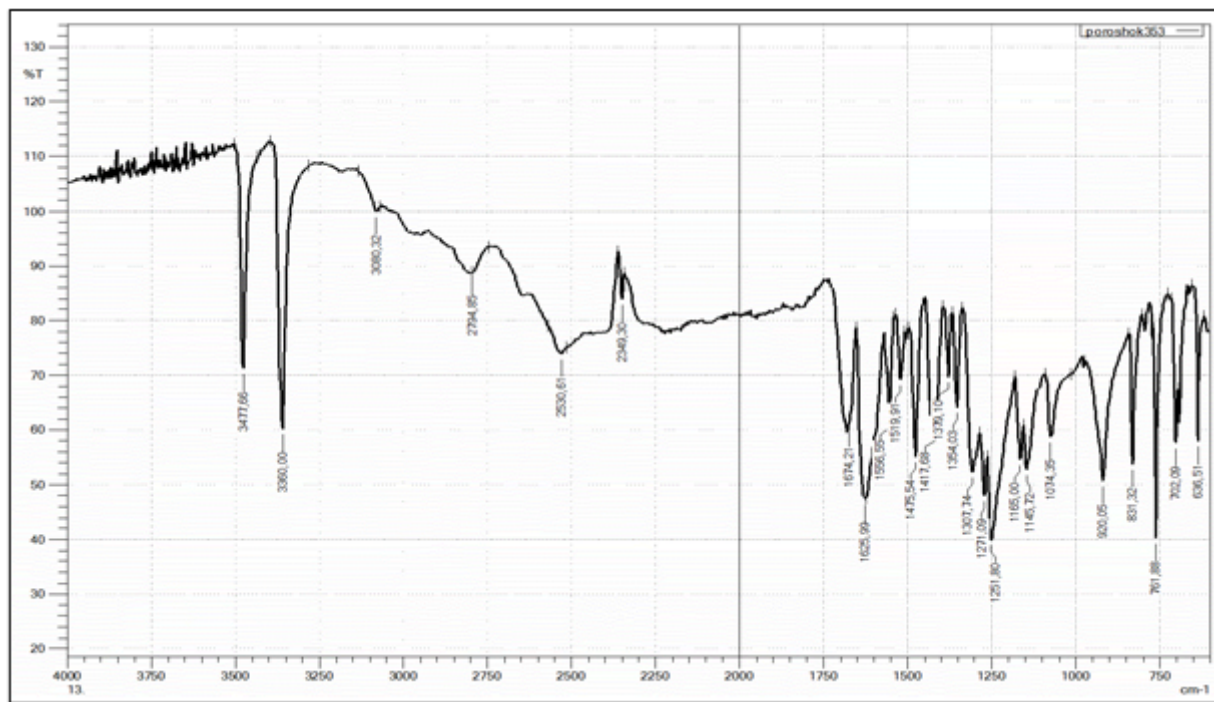


Figure 1

IR-spectroscopic analysis of 4-A3NBA-P.

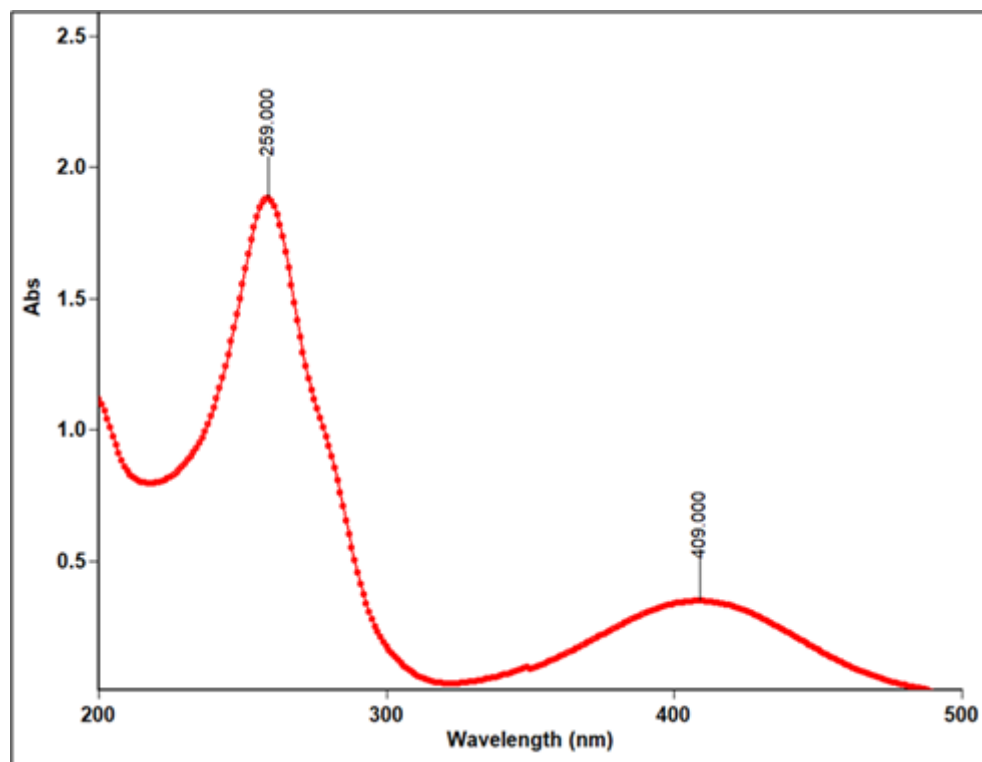


Figure 2

UV-spectroscopic analysis of 4-A3NBA-P.

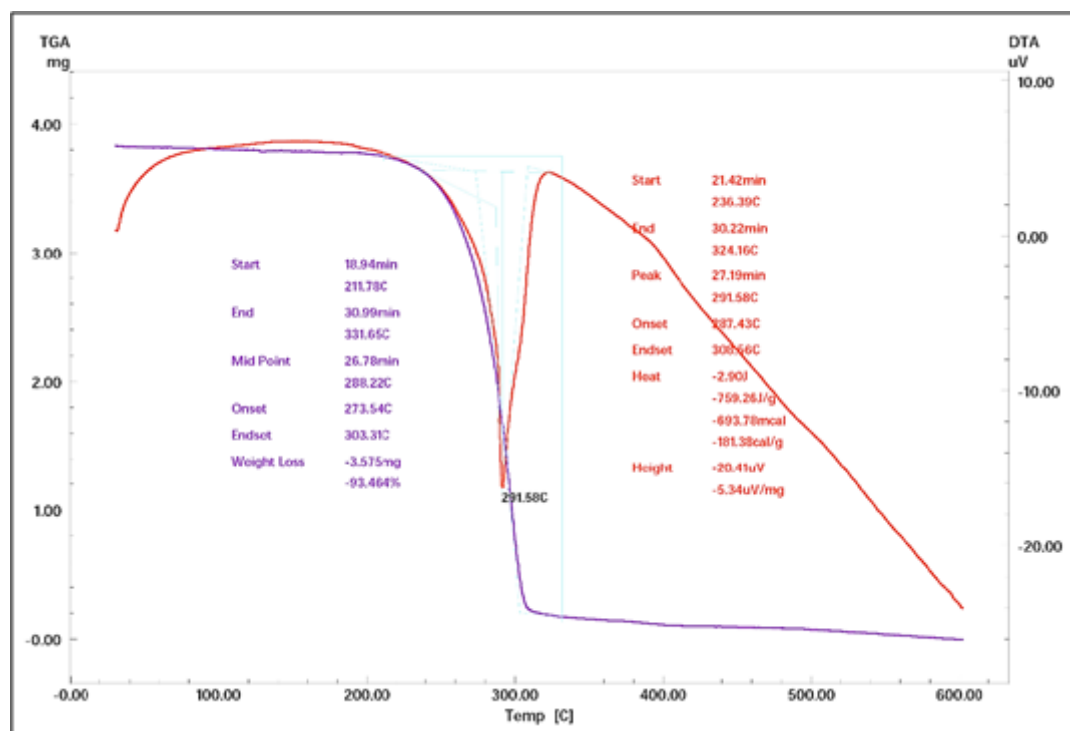


Figure 3

TG-DSC curves of 4-A3NBA-P.

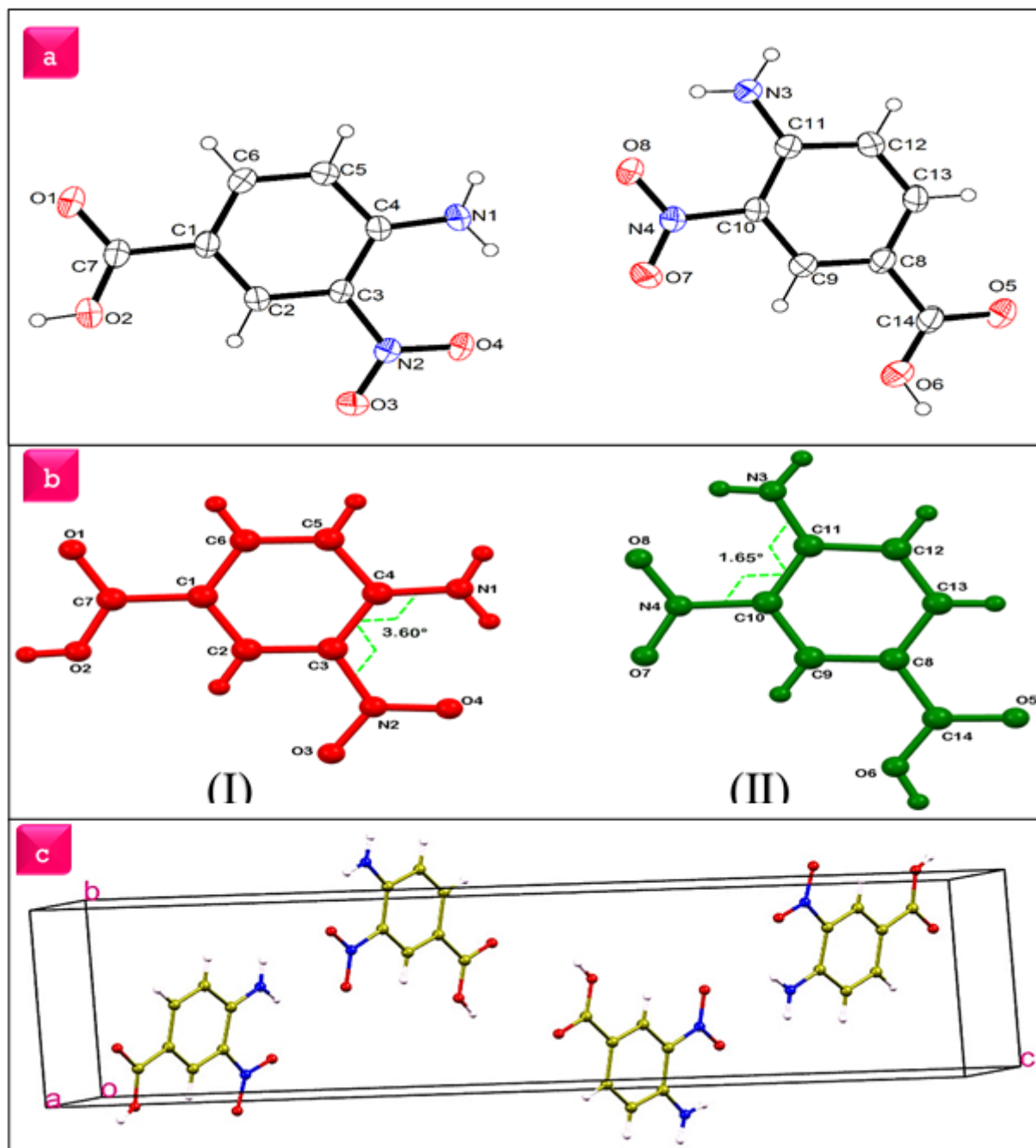


Figure 4

(a) ORTEP (35% probability level) (b) molecule I (red colour) and molecule II (green colour) and (c) packing diagram of 4-A3NBA-P.

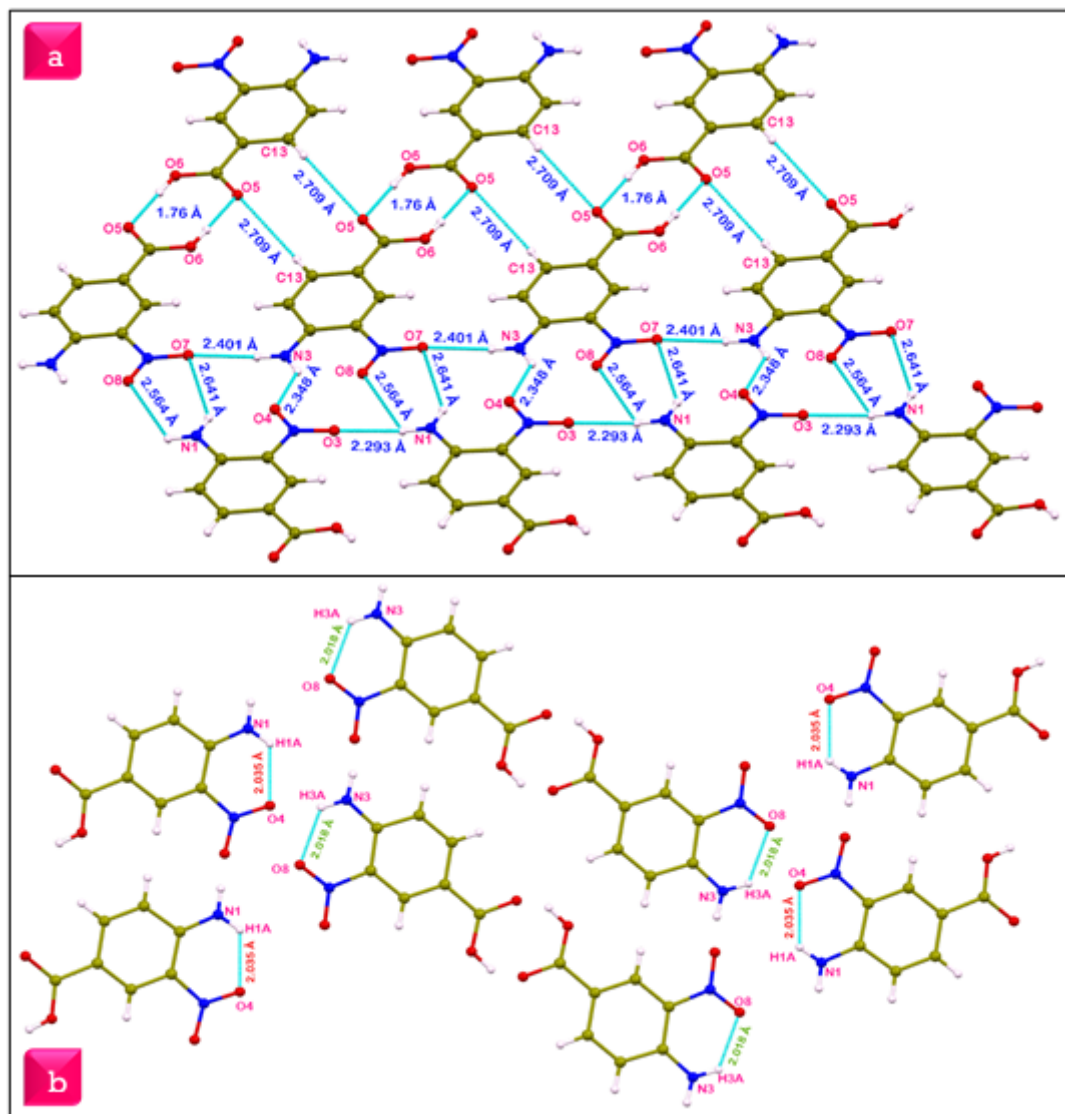


Figure 5

(a) Intermolecular and (b) Intramolecular hydrogen-bonding network for 4-A3NBA-P.

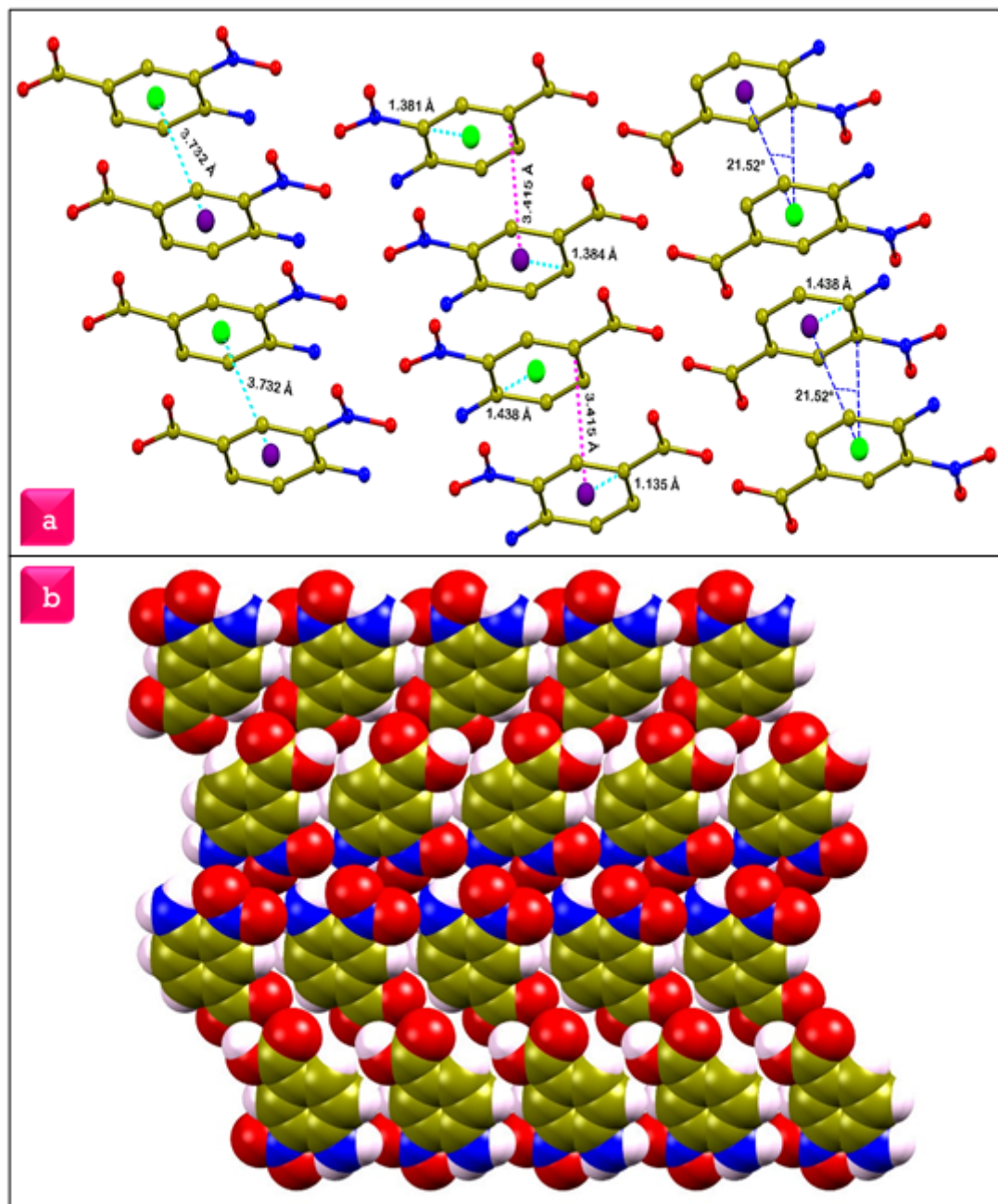


Figure 6

(a) $\pi \cdots \pi$ interactions and (b) Three-dimensional space-filling layered architecture along 'a' axis.

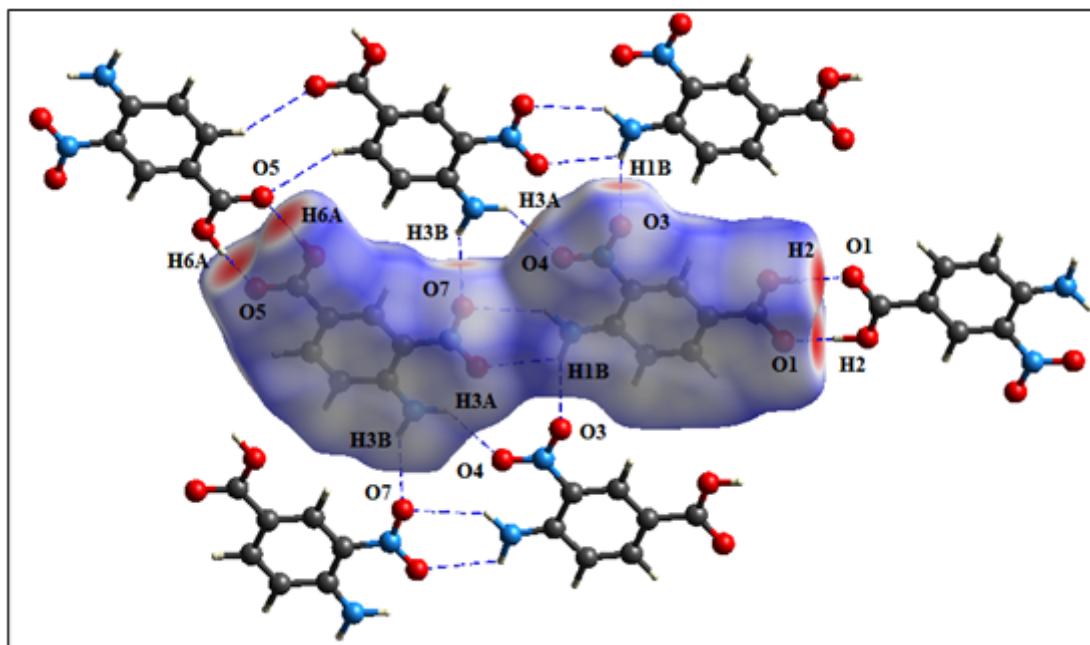


Figure 7

Hydrogen bonds in the Hirshfeld surface and boiling points of 4-A3NBA-P.

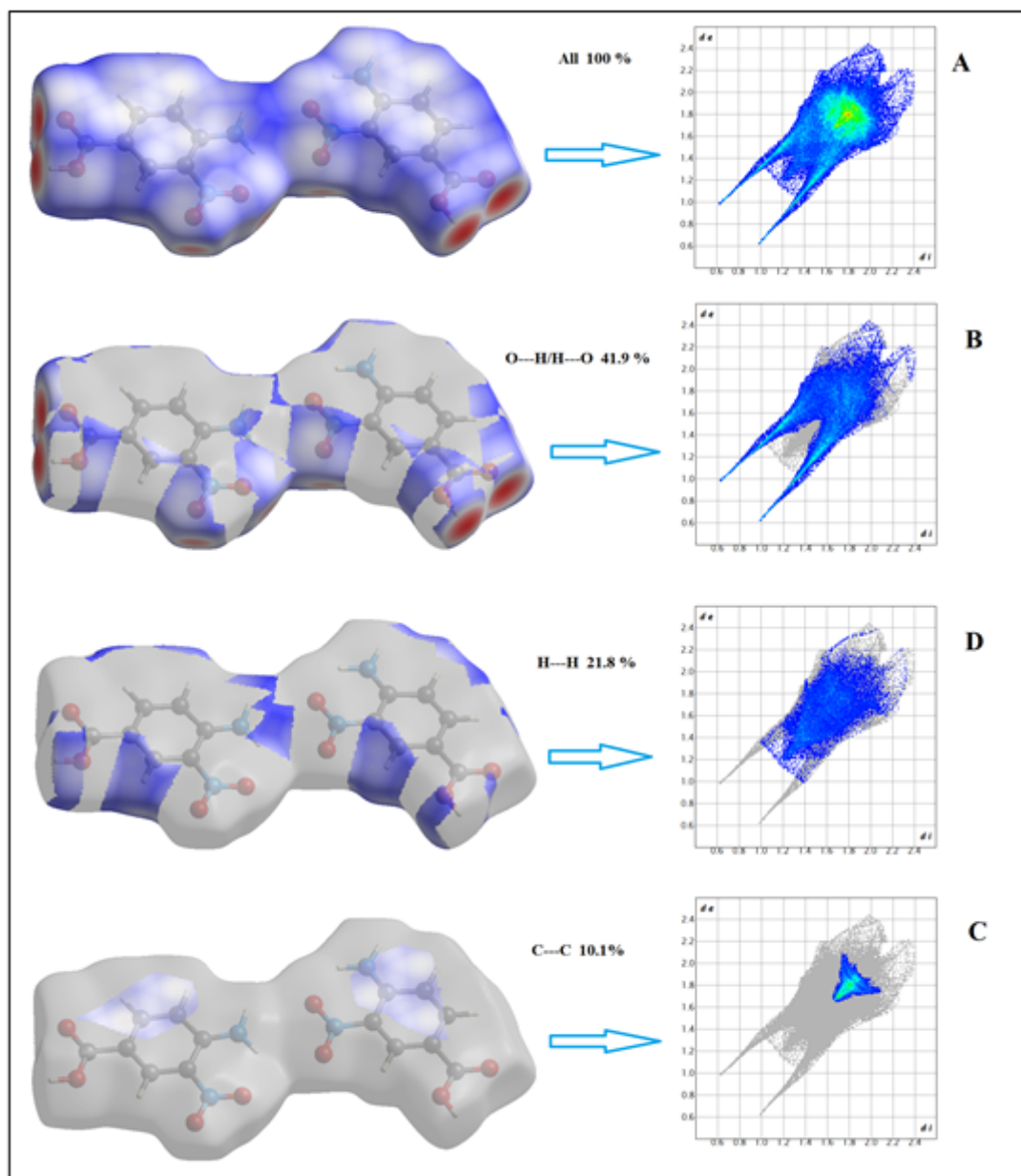


Figure 8

3D Hirshfeld surfaces and 2D fingerprint images of 4-A3NBA-P.

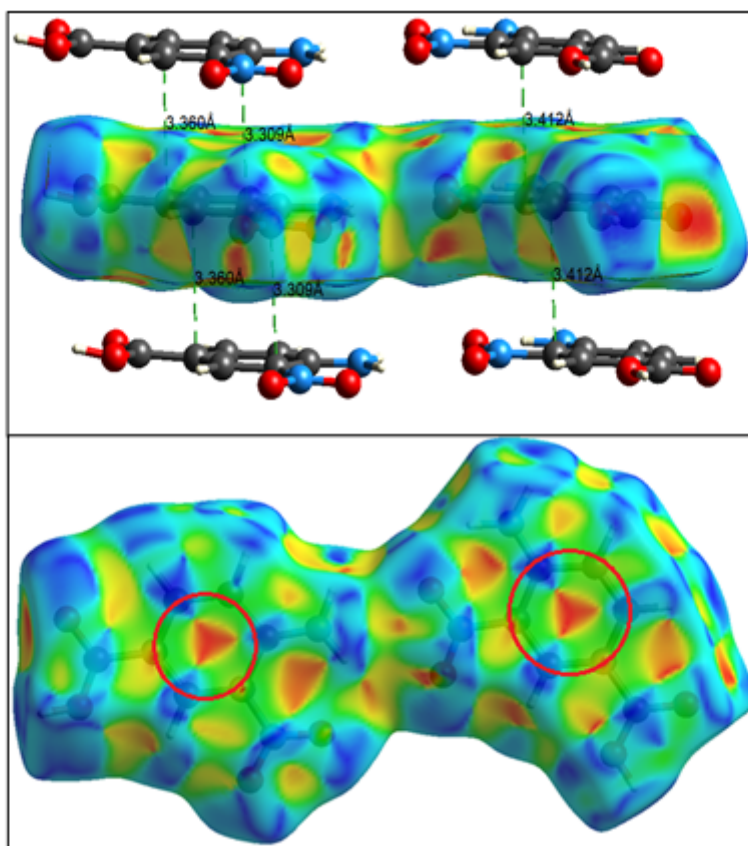


Figure 9

Shape index: p-p overlaps between molecules and its $\pi \cdots \pi$ stacking.

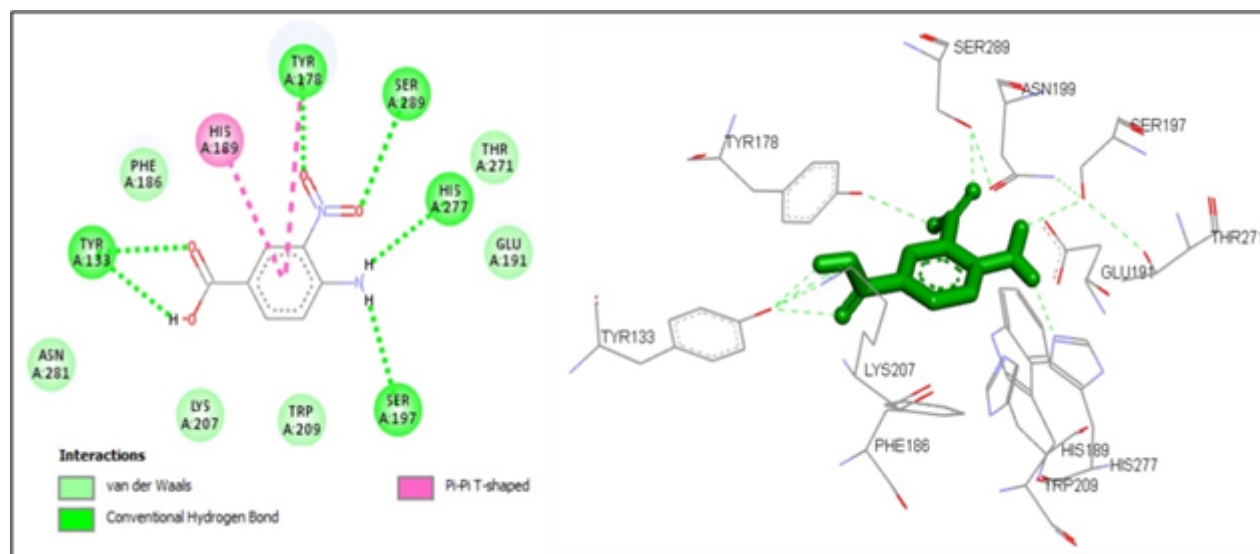


Figure 10

2D and 3D contacting residues in the active site of the 4LXL protein.

Supplementary Files

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