Research article

Detailed molecular structure (XRD), conformational search, spectroscopic characterization (IR, Raman, UV, fluorescence), quantum mechanical properties and bioactivity prediction of a pyrrole analogue

Katta Eswar Srikanth, A. Veeraiah, T. Pooventhiran, Renjith Thomas, K. Anand Solomon, Ch.J. Soma Raju, J. Naveena Lavanya Latha

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ABSTRACT
Pyrroles are an exciting class of organic compounds with immense medicinal activities. This manuscript presents the structural and quantum mechanical studies of 1-(2-aminophenyl) pyrrole using X-Ray diffraction and various spectroscopic methods like Infra-Red, Raman, Ultra-violet and Fluorescence spectroscopy and its comparison with theoretical simulations. The single-crystal X-ray diffraction values and optimized geometry parameters also were within the agreeable range. A fully relaxed potential energy scan revealed the stability of the possible conformers of this molecule. We present the density functional theory results and assignment of the vibrational modes in the infrared spectrum. The experimental and scaled simulated vibrations matched when density functional theory simulations (B3LYP functional with 6–311++G**). The electronic spectrum was simulated using time-dependent density functional theory with CAM-B3LYP functional in dimethylsulphoxide solvent. The fluorescence spectrum of the compound was studied at different excitation wavelengths in the dimethylsulphoxide solvent. The stability of the molecule by intramolecular electron transfer by hyperconjugation was studied with the natural bond orbital analysis. Frontier molecular orbitals and molecular electrostatic potentials of the compound gave an idea about the reactive behaviour of the compounds. Prediction of activity spectral studies followed by docking analysis indicated that the molecule is active against arylacetoniitrilase inhibitor.

1. Introduction
Pyrrole is one of the most important among aromatic five-membered heterocyclic compounds as it is present in diverse bioactive compounds like porphyrin in heme, chlorines in chlorophyll, and corrin ring in vitamin B12. Phenylpyrrole derivatives are used as precursors of poly-N-phenylpyrroles, a type of conducting polymer used in electrochemical capacitors [1], sensors [2], coating materials used in solid-phase micro-extraction [3] batteries and different energy storage devices [4]. Computational study of the high energy density pyrrole compounds also was reported [5]. Microwave structural investigation represents that the molecular geometries like bond lengths and angles are similar within a few per cent. So, the pyrrole is very identical to an oblate symmetric top with a meagre degree of asymmetry (κ = 0.94). Pyrrole belongs to the C₂ᵥ point group, which has 24 normal modes of vibration. Its vibrational spectrum was available a long time ago. Lord et al. published Infrared and Raman spectroscopic experimental data and gave complete assignments to 24 normal modes in 1942 [6]. IR spectra of a pyrrole-pyridine complex in CCl₄ and its quantum chemical studies were also reported [7]. Raman spectroscopy is an important method to do the structure elucidation of PPy (polypyrrole) in various physical states [8]. The N-heterocyclic benzimidazole compound shows inter/intramolecular hydrogen bonding and charge transfers from the N–H bond of pyrrole ring [9]. Pyrrole-2-carboxylic acid (PCA) is a biologically active

* Corresponding author.
** Corresponding author.
E-mail addresses: avru@rediffmail.com (A. Veeraiah), renjith@sbcollege.ac.in (R. Thomas).

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compound that behaves as a ligand. The spectroscopic analysis helped to evaluate the amount of effect of metal ions on the electronic charge circulation of pyrrole-2-carboxylic acid [10]. Liu has shown using theoretical studies that, pyrrole of pyrrole gives hydrogen radical from hydrogen cyanide [11]. Among many experimental techniques of laser spectroscopy, IR spectroscopy is an excellent method to probe intermolecular interactions like H-bonds and Vander Waals interactions. Recently, Y. Matsumoto et al. [12] reported the IR cavity ring-down spectroscopy (IR-CRDS) of the pyrrole (C₄H₅N) clusters in the NH stretching region. The first infrared spectrum of pyrrole was published in the first decade of the 20th century [13]. The work of Lord et al. [6] was the major comprehensive work on vibrational spectroscopy of pyrrole. La Regina reported some pyrrole derivatives which can be used as tubulin polymerization inhibition activity [14].

We present the detailed study of 1-(2-aminophenyl) pyrrole(2APP) in this manuscript. It is used in organic semiconductors [15] and the synthesis of compounds with interesting biological and pharmacological properties [16]. In this connection, we were enthused to examine the spectroscopic properties of the investigated compound. In this manuscript, we describe the detailed structural and spectroscopic properties of 1-(2-aminophenyl) pyrrole(2APP) using experimental methods (XRD, FT-IR, UV-Vis, and Fluorescence spectrum) and theoretical simulations. Different theoretical tools like molecular mechanics, density functional theory etc. are used whenever appropriate. We also aimed to study in detail the various physicochemical properties of this compound with particular reference to its non-linear optical properties and biological activities.

2. Methodology

2.1. Synthesis of single crystals

The starting material of the 1-(2-aminophenyl) pyrrole was obtained from Sigma Aldrich (USA). 20 mg of the compound was dissolved in 20 ml of methanol and warmed to heating in a 25 ml conical flask. After slow evaporation, the needle-shaped crystal formed after two days of which we took single crystal XRD and other spectral measurements are given below.

2.2. Spectral measurements

The Fourier transform Infrared spectrum of the compound 1-(2-aminophenyl) pyrrole was measured in the range 4000 to 400 cm⁻¹ using a GX Fourier transform spectrometer fitted with an IR Nicolet microscope and KBr beam splitter by powder method at the resolution 1 cm⁻¹. FT-Raman spectrum of 2APP was determined using Nicolet Magna 750 Raman spectrometer at the resolution of 4 cm⁻¹ in range 400–400 cm⁻¹ equipped with an InGaAs detector. Neodymium: Yttrium Aluminium Garnet Laser (1064 nm line and typical laser power of 500 mW) excitation source. UV-Vis absorption spectra from a Cary 5000 UV-VIS-NIRspectrophotometer and Cary Eclipse fluorescence spectrophotometer gave further experimental insights.

2.3. XRD-crystallography

Single crystal X-ray diffraction measurements of the compound were carried by taking a block shape crystal with dimension 0.60 × 0.25 × 0.20 mm out on Brukeraxs kappa apex2 CCD diffractometer with Mo Ka radiation (0.71073) at 293 K Table S1 (Supplementary). We performed data reduction with the SAINT program [17], and structure solving with using the SIR92 program [18]. With the help of SHELXL97 program, we refined the structure [19]. Structure-invariant direct methods were used for primary atom site locations, and secondary atom site locations were found from the difference Fourier map. The software used to prepare the material for publication was Mercury 2.3 (Build RC4) and ORTEP-3 [20,21]. The complete set of structural parameters of a molecule in the CIF format is available from the Cambridge Crystallographic Database Centre under no CCDC 1825686. The packing was stabilized by van der Waals interaction shown in supplementary Figure S1.

3. Computational methodology

All theoretical calculations were performed using the Gaussian 09 program package within the framework of density functional methods [22]. The most optimized structural parameters, energy, and vibrational frequencies of 2APP have been calculated in the gas phase using B3 [23] exchange functional combined with LYP [24] correlation functional resulting in the B3LYP density functional method at 6-311++G** level of theory with no symmetry constraints imposed. Optimized geometries are subjected to vibrational analysis to ensure the global minima on the potential energy surface with no imaginary frequency. The results of the quantum chemical calculations were visualized using Gauss-View [25] and Chemcraft molecular visualization programs [26]. To enhance the coincidence between the calculated and experimental wavenumbers, the theoretical harmonic wavenumbers were scaled down for a better matching. For this purpose, the scaling of the force fields was performed based on the SQMFF procedure [27]. The Cartesian representation of the theoretical force constants has been calculated at the optimized geometry by considering a molecule under C₂ point group symmetry. The transformation of the force field from Cartesian to internal-local-symmetry coordinates analysis calculation of total energy distribution (TED) with the version V7.0-G77 of the MOLVIB program [28]. The NBO measurements were performed using the NBO 3.1 program package, as developed in the Gaussian 09W.

4. Results and discussion

4.1. Molecular structure

The crystal structure examines of 2APP showed that the material was crystalized in the monoclinic space group with a Z value of 4 with unit cell dimensions a = 19.8514(16) Å, b = 5.7268(4) Å, c = 7.7715(6) Å and α = γ = 90°, β = 105.812° (see Table S1). The structural examination of the compound revealed that the compound was unsymmetrical with the point group C₂. The structural parameters like bond lengths, bond angle, and dihedral angles of the investigated molecule were calculated by the B3LYP method with a 6–311++G** basis set and compared with the experimentally determined crystallography data. Theoretical values, along with XRD values of the molecular structure, were summarized in Table S2. Optimized geometrical structure of the compound 2APP viewed from the Gauss view Software was shown in Figure 1. The molecular structure of the 2APP, the scheme was drawn at 30% probability displacement ellipsoid, is depicted in (XRD ORTEP diagram) Figure 1. From Table S2, it can be seen that there are some deviations in the computed geometric parameters and from the experimental values. These differences are because the crystalline state involves the intermolecular hydrogen bonding, whereas the results of the calculations apply to the gas phase. The experimentally measured XRD data of a substituent phenyl ring, we noticed that all the C–C bond lengths were found to be small deviations approximately 1.37 Å in B3LYP. In the case of the pyrrole ring, the C–C bond lengths were 1.40 Å for C₁–C₂, 1.35 Å for C₂–C₃, C₁–C₅. Further, N–C bond lengths were 1.38 Å for both N₄–C₃ and N₄–C₅. After that, it was observed that the maximum deviation in the bond lengths when compared to experimental data was 0.157 Å for N₁2–H₂2. The order of the observed bond angles follows the trend C₁–C₅–H₁₆ > C₂–C₃–H₁₅ > C₁–C₂–H₁₄ > C₁–C₂–H₁₃, which shows a small deviation with the theoretical values. The maximum variation in the torsional angle for C₇–C₆–N₄–C₃ was 9.14°, which shows a significant difference due to the attachment of pyrrole and substituted benzene ring.
4.2. PES scan study

Molecules can form in finite number of conformers as a result of free rotation about single bonds. The most stable conformer can be determined by conducting a relaxed potential energy scan using the B3LYP/6-311+G** level of theory. The relation between the potential energy and molecular geometry can be expressed as the potential energy surface (PES) diagram, which will help to ascertain the possible conformations of the 2APP and its relative stability. From the XRD data, the torsional angle of H22–N12–C11–C6 was -1.00°, and in the simulated optimized geometry, it was -0.7580° for the B3LYP. It indicates an unexpected bent conformation of the molecule, in contrary to the expected pyramidal structure. The scan was performed at a scan-interval of 10° in 36 steps from the dihedral of 0–360°. The potential energy surface scan for the selected torsional angle H22–N12–C11–C6 was shown in Figure 2. The H22–N12–C11–C6 torsional angle was increased by 10° from 0° to 360°, where other geometrical parameters have been concurrently relaxed. According to the figure, the global minimum energy was observed at 0° with an energy value of -496.70564 Hartrees, which shows the least energy (stable conformation) of 2APP and the global maximum was at 200°.

4.3. Vibrational analysis

Based on the calculations, 1-(2-Aminophenyl) pyrrole has a planar structure of C\textsubscript{6} point group symmetry. 2APP contains 22 atoms and hence 60 normal modes of vibrations which can be distributed among the symmetry species as \Gamma= 41A\text{'} (in-plane) + 19A\text{''} (out-of-plane) \[29\].

All the vibrational modes are identified in the recorded FT-IR spectrum. The investigated compound has been tested to be Raman in-active vibrations. We compared the experimentally recorded FT-IR spectra and the theoretically simulated spectra (Figure 3). The internal coordinates of the compound have been presented in Table S3 (Supplementary). Further, the local symmetry coordinates, which are non-redundant, were represented in Table S4 (Supplementary). The calculated frequencies by the B3LYP/6-311++G** basis set were scaled using available scaling factors and compared with the experimentally recorded frequencies \[30\]. The scaled and un-scaled frequencies, along with PED (potential energy distribution), are presented in Table 1.

4.3.1. C–H vibrations

We observed aromatic C–H stretching frequencies in the region 3000-3100 cm\textsuperscript{-1}, which can be used for quick identification of C–H stretching wavenumbers \[31\]. If there is any substituent in any position of the compound, they cannot influence the C–H vibrations. Most of the cases, the aromatic compounds have four vibrational wavenumbers in the region 3010-3080 cm\textsuperscript{-1}. Now coming to the present work, the bands scaled at 3258 cm\textsuperscript{-1}, 3252 cm\textsuperscript{-1}, 3232 cm\textsuperscript{-1}, 3220 cm\textsuperscript{-1}, 3187 cm\textsuperscript{-1} were assigned to CH stretching with mode numbers from 1 to 8. These values

![Figure 1](image1.png)

**Figure 1.** a) Optimised geometry of 1-(2-aminophenyl) pyrrole along with numbering of atoms b) ORTEP diagram with basic skeleton.

![Figure 2](image2.png)

**Figure 2.** Relaxed potential energy surface scan for dihedral angle H22–N12–C11–C6 of 1-(2-aminophenyl)pyrrole.
show a good agreement with the observed values at 3114 cm\(^{-1}\) and 3130 cm\(^{-1}\) and corresponding PED was shown in Table 1. Further, the C–H in-plane bending vibrations appeared in the range of 1000–1550 cm\(^{-1}\), and C–H out of plane bending vibrations appear in the range 700–1000 cm\(^{-1}\). In the present work, the vibrations scaled at 1381 cm\(^{-1}\), 1313 cm\(^{-1}\), 1187 cm\(^{-1}\), 1157 cm\(^{-1}\), 1127 cm\(^{-1}\), 1086 cm\(^{-1}\), 1066 cm\(^{-1}\) and 921 cm\(^{-1}\) were assigned to CH in-plane bending vibrations. The corresponding modes are observed at 1153 cm\(^{-1}\) and 1141 cm\(^{-1}\), show a good agreement. Similarly, the vibrations scaled at 963 cm\(^{-1}\), 932 cm\(^{-1}\), 869 cm\(^{-1}\), 850 cm\(^{-1}\), 823 cm\(^{-1}\), 758 cm\(^{-1}\), 738 cm\(^{-1}\) and 693 cm\(^{-1}\) were assigned to CH out of plane vibrational modes as depicted in the table whose correspondence may be found at 823 cm\(^{-1}\), 756 cm\(^{-1}\), 735 cm\(^{-1}\) in the FTIR spectrum.

4.3.2. C–C ring vibrations

The C–C stretching vibrations normally occur in the region 1650-1350 cm\(^{-1}\), which are not much influenced by substitution in the ring [32]. In the present work, the C–C stretching vibrations scaled at 1669 cm\(^{-1}\), 1625 cm\(^{-1}\), 1586 cm\(^{-1}\), 1576 cm\(^{-1}\), 1549 cm\(^{-1}\), 1408 cm\(^{-1}\), 1395 cm\(^{-1}\), 1321 cm\(^{-1}\), 1297 cm\(^{-1}\) were assigned to C–C stretching modes. The modes observed at 1620 cm\(^{-1}\), 1510 cm\(^{-1}\) and 1320 cm\(^{-1}\) in the FTIR spectrum shows a good relevance with the calculated data. The modes scaled at 873 cm\(^{-1}\) and 668 cm\(^{-1}\) were assigned to C–C in-plane bending vibrations, and the modes scaled at 659 cm\(^{-1}\) and 633 cm\(^{-1}\) were assigned to C–C out of plane bending vibrations which are not observed in the FT-IR spectrum. The bands scaled at 837 cm\(^{-1}\), 555 cm\(^{-1}\) and 298 cm\(^{-1}\) were assigned to C–C in-plane bending vibrations, and the bands scaled at 729 cm\(^{-1}\), 657 cm\(^{-1}\) and 639 cm\(^{-1}\) were assigned to C–C out of plane bending vibrations in the benzene ring.

4.3.3. NH2 group vibrations

NH2 group shows two stretching frequencies, i.e., asymmetric and symmetric stretching frequencies. Further, the asymmetric stretching frequency will be higher than the symmetric stretching frequency [33]. In the present work, the investigated compound has one NH2 group, and hence it contains one asymmetric and one symmetric stretching wave-numbers. The scaled frequencies at 3482 cm\(^{-1}\) and 3376 cm\(^{-1}\) were assigned to NH2 asymmetric and symmetric modes, respectively. The influential bands observed at 3380 cm\(^{-1}\) and 3310 cm\(^{-1}\) show a good agreement with the calculated values as it can be noticed from Table 1. Furthermore, the NH2 group has scissoring (NH2), rocking (NH2), wagging (NH2) and torsion (NH2) modes. The internal deformation vibrations known as NH2 scissoring frequency obtained at 1523 cm\(^{-1}\) is ideal within the range (1500–1650 cm\(^{-1}\)) reported for aniline by Jesson and Thompson [33], and this observation conforms with the experimental value of 1538 cm\(^{-1}\) in FT-IR spectrum. The NH2 wagging mode has been identified with the frequency at 635 cm\(^{-1}\) in FTIR, and this is in ideal coincidence with the reported region of 600–909 cm\(^{-1}\). The theoretical scaled value at 615 cm\(^{-1}\) by B3LYP/6-311++G** shows ideal agreement with experimental data. The rocking mode at 1491 cm\(^{-1}\) has not been observed experimentally, so we predicted theoretically. The torsional mode has been assigned at 351 cm\(^{-1}\).

4.3.4. C-N vibrations

Generally, the C–N stretching frequencies are observed in the region 1300 - 1100 cm\(^{-1}\). The identification of C-N stretching bands is complicated since this region contains a mixture of bands. However, in the present work, the scaled values at 1239 cm\(^{-1}\) and 1074 cm\(^{-1}\) were assigned to C–N stretching, which shows a good agreement with the observed value at 1075 cm\(^{-1}\) in the FT-IR spectrum. These assignments find support from the work of Lord et al. in the case of related molecules [6].

4.4. NBO. Analysis

The natural bond orbital (NBO) studies give practical information about the intra and inter-molecular interaction, charge transfer of the molecule. The most crucial successful interaction with their second-order perturbation energies E(2) is presented in Table S5, which gives valuable information about the calculation of delocalization and hyper-conjugation. The second-order Fock matrix analysis was performed to 2APP under investigation to know the different types of donor and acceptor interactions and energies in the molecule based on NBO analysis. The donor NBO. (i) and acceptor NBO. (j) and the stabilization energy E(2) can be represented as

\[
E(2) = - \frac{n_\alpha \langle \sigma F \sigma \rangle}{\varepsilon_\alpha - \varepsilon_\sigma} = - \frac{n_\alpha F_{ij}^2}{\Delta E}
\]  
(1)
### Table 1. Detailed assignments of fundamental vibrations of 1-(2-Amisophenyl) pyrrole by normal mode analysis based on SQM force field calculations using B3LYP/6-311++G**.

| No. | Experimental (cm⁻¹) FT-IR | Scanned Frequencies (cm⁻¹) | Un-scanned frequencies (cm⁻¹) | Intensity $I_0$ | Characterization of normal modes with PED (%) |
|-----|---------------------------|-----------------------------|-------------------------------|--------------|-----------------------------------------------|
| 1   | 3380s                     | 3482                        | 3675                          | 13.50        | sNHAS (99)                                     |
| 2   | 3310s                     | 3376                        | 3562                          | 13.38        | sNHSS (99)                                     |
| 3   | 3258                      | 3286                        | 1.23                          | sCH (99)     |                                               |
| 4   | 3252                      | 3280                        | 0.73                          | sCH (99)     |                                               |
| 5   | 3232                      | 3260                        | 3.19                          | sCH (98)     |                                               |
| 6   | 3205s                     | 3220                        | 3.29                          | sCH (99)     |                                               |
| 7   | 3187                      | 3214                        | 8.40                          | sCH (99)     |                                               |
| 8   | 3130s                     | 3172                        | 13.22                         | sCH (99)     |                                               |
| 9   | 3164                      | 3191                        | 3.42                          | sCH (98)     |                                               |
| 10  | 3113w                     | 3146                        | 6.60                          | sCH (97)     |                                               |
| 11  | 1620s                     | 1669                        | 1674                          | 100          | sCCAR(28), sCNR2(22), [NH2SC(19), [CH (12), |
| 12  | 1625                      | 1649                        | 67.36                         | sCNR2(32),  [CH (14),  [R2SYM (12) |
| 13  | 1580s                     | 1586                        | 1636                          | 9.97         | sCNR2(39), [NH2SC(28), [NH2TW (10) |
| 14  | 1510s                     | 1576                        | 1579                          | 61.45        | sCCAR(27), [CH (25), [NH2SC (20), [CNSUB (10) |
| 15  | 1549                      | 1554                        | 0.47                          | sCCAR(63), [CH (31) |
| 16  | 1538s                     | 1523                        | 1523                          | 11.14        | [NH2SC(36), sCCAR (21), [CH (13) |
| 17  | 1491                      | 1504                        | 7.45                          | [NH2BO (53), sCCAR (26), |
| 18  | 1408                      | 1442                        | 0.25                          | sCCAR (61), [CH (21), [CNSUB (10) |
| 19  | 1395                      | 1367                        | 19.30                         | sCCAR(37), [CH (33), [R1SYM (15) |
| 20  | 1381                      | 1360                        | 3.66                          | [CH (36), sCNR2 (23), [R2TRI (13), sCCAR (11) |
| 21  | 1320s                     | 1321                        | 1358                          | 4.60         | sCCAR (39), [CH (32), [NH2RO (11) |
| 22  | 1313                      | 1335                        | 3.00                          | [CH (59), sCCAR (20), [CNR1 (14) |
| 23  | 1297                      | 1298                        | 5.59                          | sCCAR (58), [CH (23) |
| 24  | 1239                      | 1275                        | 2.72                          | sCNR1 (60), [CH (16), [CNSUB (10) |
| 25  | 1187                      | 1188                        | 2.68                          | [CH (74), sCCAR (25) |
| 26  | 1153s                     | 1157                        | 1169                          | 3.53         | [CH (44), sCCAR (35), [NH2RO (12) |
| 27  | 1141s                     | 1127                        | 1140                          | 8.20         | [CH (41), sCCAR (39) |
| 28  | 1086                      | 1101                        | 9.09                          | [CH (56), sCCAR (24), [CNR1 (10) |
| 29  | 1075s                     | 1074                        | 1096                          | 8.78         | sCNR1 (43), sCCAR (26), [CH (20) |
| 30  | 1066                      | 1084                        | 7.37                          | [CH (40), sCCAR (40) |
| 31  | 1036s                     | 1039                        | 1062                          | 1.13         | [CNSUB (27), [CH (21), sCCAR (17), [CNR1 (17), [R1SYM (15) |
| 32  | 1013s                     | 1006                        | 1036                          | 8.46         | sCNSUB (27), [CH (21), sCCAR (17), [CNR1 (17), [R1SYM (15) |
| 33  | 963                       | 969                         | 0.02                          | sCH (79), [R2TRI (13) |
| 34  | 932                       | 940                         | 1.17                          | sCH (90)     |
| 35  | 924w                      | 921                         | 939                           | 13.18        | [CH (42), [R2SYM (36) |
| 36  | 873                       | 884                         | 0.08                          | [R1SYM (58), [R1ASY (29) |
| 37  | 869                       | 874                         | 0.08                          | sCH (85), [R1SYM (10) |
| 38  | 850                       | 859                         | 1.00                          | sCH (65), [R2TRI (12) |
| 39  | 833m                      | 837                         | 842                           | 0.57         | [R2TRI (34), [CH (31), sCCAR (13) |
| 40  | 823m                      | 823                         | 827                           | 1.56         | sCH(83), |
| 41  | 756w                      | 758                         | 764                           | 28.22        | sCH(92) |
| 42  | 735sw                     | 738                         | 743                           | 45.54        | sCH(84) |
| 43  | 729                       | 727                         | 739                           | 4.59         | [R2TRI (54), sCNR2 (15), [R2ASY (12), [CNSUB (10), |
| 44  | 693                       | 698                         | 4.81                          | sCH (92)     |
| 45  | 668                       | 682                         | 8.03                          | [R1ASY (28), [R2TRI (24), [CH (19), [R1SYM (18), |
| 46  | 659                       | 646                         | 4.54                          | [R1ASY (33), [R2SYM (15), [R1SYM (14), [CH (14), [CNSUB (10) |
| 47  | 633                       | 625                         | 3.75                          | [R1SYM (50), [R1ASY (24), [CH (14) |
| 48  | 625m                      | 615                         | 595                           | 86.55        | [NH2WA (45), [R2TRI (10), [R1SYM (10) |
| 49  | 558                       | 566                         | 0.21                          | [R2SYM (25), [R2ASY (14), sCNR2 (12), [CNSUB (12), [R1TRI (10), [R1SYM (10) |
| 50  | 555                       | 562                         | 51.29                         | [R2ASY (53), [R2SYM (27) |
| 51  | 489m                      | 486                         | 500                           | 0.78         | [CNR2 (21), [R2ASY (15), sCNR2 (13) |
| 52  | 467w                      | 466                         | 472                           | 12.53        | sCNR2 (33), [R2ASY (14), [CNSUB (12), [CNR2 (11), [R2SYM (10) |
| 53  | 370                       | 371                         | 20.91                         | [NH2TW (60) |
| 54  | 351                       | 352                         | 4.73                          | [NH2TW (18), [R2ASY (15), [R2SYM (14), [CH (13), [CNSUB (11) |
| 55  | 327                       | 335                         | 5.65                          | [R2ASY (44), [CH (13), [CNSUB (13), [NH2WA (11) |
| 56  | 298                       | 300                         | 0.28                          | [R2SYM (34), [CNR2 (21), [CH (13), [CNSUB (10) |

(continued on next page)
Here, $\xi ij$ or $\beta ij$ is the Fock matrix element $i$ and $j$ NBO orbitals, $\sigma^*$ and $\sigma$ are the energies of $\sigma$ and $\sigma^*$ Natural bond orbitals and $\pi$ is the population of the donor $\sigma$ orbital. More substantial is the $\xi ij$ value; the high intensive is the interaction between electron donors and electron acceptors, i.e., the more donating tendency from electron donors to electron acceptors and the higher the extent of conjugation of the entire system. The NBO calculations have been performed on 2APP by using NBO 3.1 program as developed in the Gaussian 09W package at B3LYP/6-311++G** level of theory to determine the intramolecular interaction, hyperconjugation and the delocalization of electron density. The most critical interactions in the heterocyclic pyrrole molecule with lone pair N4 with that of antibonding C1–C5 and C2–C3, stabilization energy of 33.24 and 33.69 kJ/mol respectively which denotes large delocalization. The maximum energy occurs from $\pi^*$ of C6-C11 to $\pi$ of C7–C8 (311.39 kJ/mol), as listed in Table 5 (Supplementary).

4.5 UV-vis & fluorescence spectra and frontier molecular orbital analysis

The UV-visible absorption of the compound is recorded in DMSO at the concentration of $1 \times 10^{-5}$ M under ambient conditions. The computed and experimental UV-Visible spectrum of 2APP was shown in Figure 4. Theoretically, the maximum absorption $\lambda_{\text{max}}$ was calculated by using the TD-DFT/CAMB3LYP method with a 6-311++G** basis set to get more accurate values. Generally, $\lambda_{\text{max}}$ is resulting from the electronic transition from HOMO to LUMO. However, in the present study, the computed $\lambda_{\text{max}}$ of the investigated compound in the gas phase was 446 nm. Its counterpart, i.e., the experimental $\lambda_{\text{max}}$ of the compound in DMSO was found to be 461 nm, which shows a moderate agreement with the theoretical spectrum. Another peak was computed at 435 nm, whose counterpart was observed at 440 nm. The calculated visible absorption maxima, $\lambda_{\text{max}}$ along their experimental wavelengths with a significance of HOMO, LUMO, and oscillator strength ($f$) of the compound have been listed in Table 2. We recorded the fluorescence emission spectrum of 2APP (1 $\times 10^{-5}$ M) in DMSO at three exciting wavelengths 250, 285, and 300 nm, and they were presented in Figure 6. Further, we addressed the question of whether fluorescence spectroscopy can be used to identify differences in the stability and conformation of the compound under study. The emission spectra were measured at excitation wavelengths at 250 nm, 285 nm 300 nm, and a slit width of 5 nm. Upon excitation at 250 nm, 285nm, and 300 nm, we observed a strong emission band at 350 nm, 380 nm, and 400 nm. These are corresponding to the origin of the $S_1$ electronic transition. An evaluation of the normalized emission spectra at 250 and 300 nm excitation indicates that there are no differences in the line shape; however, at 285 nm excitation, there are differences in the line shape of the spectra. It can be noticed that the excitation maxima follows redshift, which indicates that the compound is a beneficial source of interaction with visible light (see Figure 5).

The highest occupied molecular orbital (HOMO) and lowest unoccupied molecular orbital (LUMO) are the orbitals which denote the chemical stability of the molecule. The HOMO, which indicates the ability to donate an electron and LUMO, shows the ability to accept an electron [34]. Molecular orbitals (HOMO and LUMO) give useful information for physicists and chemists. They also give information about the most reactive position in the $\pi$-electron molecule and explain several types of reactions in the conjugated systems [35]. Figure 6 represents the HOMO and LUMO orbitals of the compound. The different molecular orbitals [MO: 37 – MO: 48] of 2APP, under Cs symmetry, were shown in Supplementary Figure S2. This figure depicts various MOs and their deeds at different levels. Positive and negative charges are equally distributed in both HOMO and LUMO levels. Also, a more negative charge is distributed around the benzene ring in MO-46. It can be noticed from the figure that a minimal amount of charge is distributed on the benzene ring in MOs 41, 47, and 48. Quantum chemical descriptors were used to study the biological activity of the quantitative structure-activity relationship for the molecule. The HOMO-LUMO energy gap, Ionization potential (I), Electron affinity (A), Chemical potential ($\mu$), Electrolicity index ($\omega$), Global Softness ($\sigma$), Total energy change ($\Delta E_t$), and Dipole moment(D) of 2APP have been calculated using DFT/B3LYP-6-311++G** basis set. The results were summarized in Table 3. Nowadays, the HOMO – LUMO energy gap between has been used to prove the bioactivity from intramolecular charge transfer (ICT) [36, 37]. Due to the low value of the HOMO-LUMO energy gap, these compounds have a high softness nature. The low value of the electrophilicity index around -1.0593 eV, suggests the biological activity of the compounds, as that can easily bound with the target proteins or enzymes, which is evident from docking studies.

4.6 Nonlinear optical (NLO) properties

NLO properties of any compound give valid information, i.e., they provide properties of optical modulation, optical switching, optical logic, and optical memory for the prominent technologies in the region of telecommunications, signal processing, and interconnections [38]. To know NLO properties of the compound, by DFT/B3LYP method to the investigated molecule, the dipole moment ($\mu$), the mean first hyperpolarizability ($\beta$), the mean polarizability ($\sigma_0$), the anisotropy of the
polarizability ($\Delta \alpha$) using $x, y, z$ elements can be calculated by using Gaussian 09W in finite-field approach is presented in Table 4 and equated as follows [39, 40].

$$\mu = \mu_x + \mu_y + \mu_z$$  \hspace{1cm} (2)

$$\alpha_x = \frac{\alpha_{x\alpha} + \alpha_{x\beta} + \alpha_{x\gamma}}{3}$$  \hspace{1cm} (3)

$$\Delta \alpha = 2^{1/2}[(\alpha_x - \alpha_\gamma)^2 + (\alpha_y - \alpha_\gamma)^2 + 6\alpha_z^2]^{1/2}$$  \hspace{1cm} (4)

$$\beta = (\beta_x^2 + \beta_y^2 + \beta_z^2)^{1/2}$$  \hspace{1cm} (5)

and

$$\beta_x = \beta_{xx} + \beta_{xy} + \beta_{xz}$$  \hspace{1cm} (6)

$$\beta_y = \beta_{yx} + \beta_{yy} + \beta_{yz}$$  \hspace{1cm} (7)

$$\beta_z = \beta_{zx} + \beta_{zy} + \beta_{zz}$$  \hspace{1cm} (8)

The above values, i.e., mean polarizability and mean first-order hyperpolarizability values of the Gaussian 09 output, are showed in atomic units (a.u.). Therefore, the measured values have been converted into electrostatic units (esu) ($\alpha$: 1 a.u. = $0.1482 \times 10^{-12}$esu, $\beta$: 1 a. u. = $8.6393 \times 10^{-33}$esu) [41]. Urea is an ideal compound used for understanding the NLO properties of the investigated molecules. Therefore, the NLO properties of urea are utilized for comparative purposes. The values of the mean polarizability ($\alpha_0$) and the mean first hyperpolarizability ($\beta_0$) of the investigated molecule were $15.74341 \times 10^{-12}$esu and $1.730348 \times 10^{-30}$esu. These values are approximately 4 and 9 times, respectively, greater than the values of urea. The dipole moment of the compound is 0.5685 Debye, which indicates the non-uniform distribution of atomic charges. Thus it could be a potential molecule for future studies of non-linear optical properties.

### 4.7. Molecular electrostatic potential (MEP)

MEP investigation gives information about the electrophilic and nucleophilic sites in a reaction and also shows that the hydrogen bonding interactions [42]. The molecular electrostatic potential $V(r)$ is mainly related to the electron density in a molecule. To know the MEP values in a molecule, the following expression is used to calculate the MEP values [43].

$$V(r) = N \sum_{j} (Z_{j}/|r - R_{j}|) - \int \rho(r')d^3r'/|r - r'|$$  \hspace{1cm} (9)

Here, $N$ represents the total number of nuclei; $Z_\alpha$ represents the charge of the nucleus placed at $R_\alpha$, $\rho(r')$ represents electron density function of the molecule, and $r'$ is the dummy integration variable. Further to know the positive, negative, and neutral electrostatic potential areas of the molecule understudied, MEP was calculated by using B3LYP/6-311++G** level of theory. The MEP mapping of the investigated compound represented in

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**Table 2.** The UV-Vis excitation energy and oscillator strength for 1-(2-aminophenyl)pyrrole calculated by TD-DFT/BSLYP/6-311++G**Method.

| Wavelength (nm) | Energy (eV) | Abs. | Wavelength (nm) | Energy (eV) | $f$ | Major contribs |
|----------------|-------------|------|----------------|-------------|-----|----------------|
| 311            | 4.5341      | 0.4245 | 446            | 4.6865      | 0.1119 | HOMO- $\rightarrow$ LUMO (81%) |
| 441            | 5.1683      | 0.1128 | 435            | 5.2335      | 0.1126 | H-2 $\rightarrow$ LUMO (32%), H-1 $\rightarrow$ L+1 (11%), HOMO $\rightarrow$ L+1 (41%) |
| 431            | 4.8733      | 0.0053 | 431            | 5.2075      | 0.004  | H-1 $\rightarrow$ L+1 (84%), HOMO- $\rightarrow$ L+1 (10%) |

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**Figure 5.** Fluorescence spectra of 1-(2-aminophenyl) pyrrole in different excitation wavelengths.
Supplementary Figure S3. From the figure, it can be seen that the nitrogen labelled N12 is surrounded by red colour (negative) and two hydrogens atoms H21 and H22 represents a nucleophilic portion of the molecule. The blue colour is located over the benzene ring, which indicates the positive portion, i.e., electrophilic area of the molecule.

4.8. Mulliken atomic charge analysis

Mulliken atomic charge analysis is very important because atomic charges in fluence polarizability, dipole moment, geometric structure, and much more properties of the compound under investigation [44]. In the present work, the Mulliken atomic charge analysis was carried out to the compound understudied by using the B3LYP method with a 6–311++G** basis set. The calculated atomic charges are tabulated in Supplementary Table S6 and Fig. S4. From table S6, it was observed that the atoms C1, C2, N4, C7, C8, C9, C10, and N12 have negative charges with the corresponding values 0.142, 0.140, 0.559, 0.121, 0.103, 0.082, 0.130 and 0.668 respectively. The remaining atoms were positively charged. The molecular structure, along with their charges, was represented in Table S6(Supplementary).

4.9. Molecular docking studies

The pyrrole derivatives are usually medicinally active. Prediction of the structure-activity spectra called PASS analysis was to predict the potential medicinal activity using an online tool [45]. The results of the analysis were shown in Table S7 and Fig. S5 of the supplementary information, which indicated that the compound shows a high association towards the activity as arylacetonitrilase inhibitor. We downloaded the protein responsible for this action from the protein data bank with id PDB ID: 3hkx [46]. The ligand, our pyrrole derivative, was docking with the above macromolecule using the Patchdock docking server [47, 48, 49, 50]. The score of the molecular docking between pyrrole derived compound, and the protein (PDB ID: 3hkx) was 2660, full fitness energy is -1263.77 kcal/mol, estimated \( \Delta G \) (docking score) is -6.18 kcal/mol, and total molecular solvent accessibility is 2695.32 \( \text{Å}^2 \). The docking studies help to evaluate the interaction pattern of the ligand with the studied proteins [51, 52, 53, 54, 55, 56]. The following passage gives an idea about the various interactions between the guest and the host. There are several interactions between protein (PDB ID: 3hkx) and pyrrole derived compounds. The pi-alky interactions between pyrrole ring and alanine (A:25) and leucine (A:21) represents a nucleophilic portion of the molecule. The blue colour is located over the benzene ring, which indicates the positive portion, i.e., electrophilic area of the molecule.

### Table 3. The calculated quantum chemical parameters for 1-(2-aminophenyl) pyrroleobtained by B3LYP/6–311++G** calculations.

| Property                        | B3LYP/6–311++G** |
|--------------------------------|-----------------|
| Total energy (eV)              | -13512.95       |
| \( \epsilon_{\text{HOMO}} (eV) \) | -5.506871       |
| \( \epsilon_{\text{LUMO}} (eV) \) | -0.15864        |
| Ionization potential (I) (eV)  | -5.506871       |
| Electron Affinity (A) (eV)     | -0.15864        |
| Chemical potential (\( \mu \)) (eV) | -2.833405 |
| Electronegativity (\( \chi \)) (eV) | 2.833405      |
| Chemical hardness (\( \eta \)) (eV) | -0.373864   |
| Global Softness (\( \sigma \)) (eV) | -1.059309   |
| Total energy change(\( \Delta E \)) (eV) | 0.668691     |
| Dipole moment(D)              | 1.9413          |

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Table 4. Calculated all β components and β tot value of (2-aminophenyl)pyrroleB3LYP/6-311++G** method.

| Component | B3LYP/6-311++G** | β components | B3LYP/6-311++G** |
|-----------|----------------|--------------|-----------------|
| μ_x       | 0.5240832      | μ_xx         | 111.4655101    |
| μ_y       | 0.5020414      | μ_yy         | -17.9044683    |
| μ_z       | 0.1525503      | μ_zz         | 80.022578      |
| μ(D)      | 0.5688590      | μ_νν         | -33.3158682    |
| θ_x       | 153.2053703    | θ_xx         | 20.6075202     |
| θ_y       | -2.2506453     | θ_yy         | -55.9881151    |
| θ_z       | 79.34518       | θ_zz         | 40.5048559     |
| θ_νν      | 1.8711959      | θ_νν         | 9.5072421      |
| θ_νν      | -24.7250373    | θ_νν         | -35.3795389    |
| θ_νν      | 86.1419551     | θ_νν         | 29.694309      |
| Δν        | 40.82122 × 10⁻³ esu | β(total) (esu) | 1.730348 × 10⁻³ esu |
| α (esu)   | 15.74341 × 10⁻³ esu |                  |                |

The pyrrole derivative 1-(2-aminophenyl) pyrrole was optimised for the stable geometry and compared with the molecular/atomic parameters from the XRD data. The structural data were found in agreement within the acceptable limits. The experimental FT-IR, UV-Visible and Fluorescence spectra were recorded and compared with the scaled simulated IR spectra and UV spectra using TD-DFT and are also found to be in close agreement. The detailed, potential energy distribution of the IR vibrations and assignment of the electronic transitions were also presented. The absorption wavelengths were observed at 461 and 435 nm in the UV-Visible spectrum. Fluorescence spectrum of the compound at different exciting wavelengths shows the redshift for the emission maxima in the compound that represents a good source for the visible spectrum. NBO studies indicated that the molecule is intrinsically stable from hyper conjugative interactions. The most important interactions were the one between lone pair of N4 and antibonding C2-C3, whose stabilization energy was 33.69 kJ/mol indicating large delocalization. NLO prediction with hyperpolarizability (β) indicates that the molecule possesses activity more than urea. Quantum mechanical studies of the frontier molecular orbitals and other various energy descriptors were also presented in the manuscript. MESP reports reactive sites of the compound towards electrophilic and nucleophilic agents. Docking studies show that the molecule is a potential bioactive compound with therapeutic activity. Thus it can be concluded that the presented molecule is having immense physical and biological applications.

Declarations

Author contribution statement

Katta Esvar Srikanth: Performed the experiments; Wrote the paper.
A Veeraiah: Contributed reagents, materials, analysis tools or data.
T. Pooventhiran: Analyzed and interpreted the data; Wrote the paper.
Renjith Thomas: Conceived and designed the experiments; Contributed reagents, materials, analysis tools or data; Wrote the paper.
K. Anand Solomon: Performed the experiments.
Ch. J. Soma Raju, J Naveenalavanya Latha: Analyzed and interpreted the data.

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Competing interest statement

The authors declare no conflict of interest.

Additional information

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