Synthesis, spectroscopic investigation, molecular docking and DFT studies of novel (2Z,4Z)-2,4-bis(4-chlorobenzylidene)-5-oxo-1-phenylpyrrolidine-3-carboxylic acid (BCOPCA)

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Abstract

The synthesized compound (2Z,4Z)-2,4-bis(4-chlorobenzylidene)-5-oxo-1-phenylpyrrolidine-3-carboxylic acid (BCOPCA) was characterised by Ultraviolet, FT-Infra Red, 1H, 13C Nuclear Magnetic Resonance and mass spectroscopy. The compound was further subjected to quantum chemical calculations at the level of density functional theory (DFT) using 6-31G (d,p) basis sets method with B3LYP and CAM-B3LYP hybrid functionals. The intramolecular interactions, polarizability, hyperpolarizability and nonlinear optical properties of the title compound were also incorporated in the study. The total first static hyperpolarizability (β0 = 19.477 × 10−30 and 16.924 × 10−30 esu) value was also computed and indicated the title molecule as an interesting forthcoming NLO
material. The other thermodynamic properties (entropy, heat capacity and zero vibrational energy) were also discussed. The study also includes NBO computations, complete vibrational assignments, Mulliken charges, UV—Visible spectral analysis and HOMO—LUMO energies. The regions of low and high electron density were obtained from MESP and ESP maps. The calculated parameters for BCOPCA using aforementioned functions are harmonious with the experimental findings. The in-vitro antimicrobial activity and molecular docking studies of BCOPCA were also done and showed a good correlation.

Keyword: Theoretical chemistry

1. Introduction

Nitrogen based five membered heterocycle pyrrolidine, is a reassuring molecule for the design of newer drugs. It is well known from the literature that pyrrolidine, is a pharmaceutically active molecule and exhibits miscellaneous biological activities [1, 2, 3, 4, 5]. In addition, it is also apparent that certain compounds with benzylidene moiety in their structure are also important in the field of medicinal chemistry [6]. As a part of our research on the synthesis and DFT studies of novel heterocyclic molecules [7, 8], in this research article, the writers look forward to contribute a detailed account on the molecular geometry, vibrational assignments, mulliken charges, conformations and electronic features of novel (2Z, 4Z)-2,4-bis(4-chlorobenzylidene)-5-oxo-1-phenylpyrrolidine-3-carboxylic acid (BCOPCA), obtained by Claisen-Schmidt reaction of 5-oxo-1-phenylpyrrolidine-3-carboxylic acid (1) and p-chlorobenzaldehyde (2). The quantum chemical computations were investigated with the help of two hybrid functionals i.e. B3LYP and CAM-B3LYP using 6-31G (d,p) basis sets. The NBO properties of BCOPCA could be seen due to increasing interest in organic materials as non-linear optical devices which gathers the information about bonding and anti-bonding orbitals, electron affinities, bond energies, vibrational frequencies and geometries of organic compounds. The results obtained from computations establish a good agreement with the experimental results [9, 10, 11, 12, 13, 14].

2. Materials and method

The instrument used to record $^1$H and $^{13}$C-NMR spectra of BCOPCA with chemical shifts values in ppm was Bruker 400 MHz, taking CDCl$_3$ as the solvent and TMS as the internal standard. IR (KBr) and UV (200—500 nm, CHCl$_3$) spectra were recorded on a Perkin-Elmer FT-IR and UV-visible Spectrophotometer instruments. The mass spectrum (DART-MS) of BCOPCA was also recorded with the help of JEOL-AccuTOF JMS-T1100LC Mass spectrometer. 5-oxo-1-phenylpyrrolidine-3-carboxylic acid (1) was synthesized with the known procedure [15].
2.1. Synthesis of 4(2Z, 4Z)-2,4-bis(4-chlorobenzylidene)-5-oxo-1-phenylpyrrolidine-3-carboxylic acid (BCOPCA)

5-oxo-1-phenylpyrrolidine-3-carboxylic acid (1) (0.005 mol, 1.025) and p-chlorobenzaldehyde (2) (0.005 mol, 0.705) were refluxed together for 5-8 hrs in 10 mL ethanol in presence of pyridine (1 mL). The product (3) obtained on cooling the reaction mixture was filtered and recrystallized from alcohol (Fig. 1). Yield: ~ 56%; M.P. 87–89 °C, Rf value: 0.54, MS, m/z: 449 [Hexane: Ethyl acetate] (8.0:2.0 v/v) as mobile phase.

2.2. Computational details

The various DFT studies on BCOPCA were performed at B3LYP and CAM-B3LYP/6-31G (d,p) hybrid functionals respectively. The optimization of BCOPCA molecule was done with the help of GaussView5.0 and the Gaussian 09 software [16, 17, 18]. GIAO program was used for computing 1H & 13CNMR chemical shifts [19]. The Non Bonding Orbital predictions [20] were implemented at DFT/B3LYP level in further to compare the distinct second order interactions. The TD-DFT was used for Frontier orbital study by implementing IEFPCM model taking CHCl3 as solvent. The molecule BCOPCA was analysed by AIM calculation [21]. For potential energy distribution (PED) calculations vibrational problem was set up in terms of internal coordinates using GAR2PED [22] software.

3. Results and discussion

3.1. Molecular geometry

Fig. 2 shows the structure and atom numbering of BCOPCA. The optimized bond lengths and bond angles of BCOPCA are presented in Table 1. On comparing the experimental data of a similar molecule from the literature with the theoretical values of BCOPCA [23, 24], it is perceived that the values for BCOPCA are slightly larger than the data obtained from the literature.
The bond lengths of two carbonyl groups i.e. C29 – O30 and C11 – O12 and C29-O31 of acid with values of 1.192, 1.215 and 1.282 Å depicted double and single bond characters. The C-C bond lengths of benzene ring of BCOPCA are longer than standard double bond lengths and shorter than the standard single bond lengths ranging from 1.3890 to 1.4591 Å at B3LYP and CAM-B3LYP hybrid functionals. The bond angle value for C2-C1-C6 is found to be 121.5°, revealing slightly distorted hexagonal geometry. The discussed variations may be due to the following reasons: (a) lone pair (b) electronegativity of the central atom and (c) alternate double bonds in BCOPCA.

3.2. Conformational analysis

The Potential Energy Surface (PES) scan (sketched in Fig. 3), performed to determine the most energetically favourable conformer which showed three minima corresponding to the conformers I, II and III with energy values of –2163.74, –2163.76 and –2163.75, a.u. respectively.

3.3. ¹H & ¹³C NMR spectroscopy

Observed and calculated data for ¹H and ¹³C NMR spectra are displayed in Tables 2 and 3. The experimental ¹H and ¹³C NMR spectra of BCOPCA have been measured in CDCl₃ and displayed in Fig. 4(a) and (b) respectively. The aromatic ring protons in the ¹H NMR spectrum of the title molecule appeared at 7.50—7.53, 7.27—7.33 and 7.06—7.11 ppm respectively. The doublets observed at 7.71—7.74 and 7.86—7.91 ppm represent methine (–CH-) protons and the multiplet at 4.10—4.90 ppm corresponded to pyrrolidine ring. The ¹³C NMR spectrum showed signals at 172.25 and 171.66 ppm corresponding to carbonyl carbon (–C=O). In BCOPCA signals at 138.51, 131.12, 130.73, 129.21, 128.67, 128.39, 124.70, 124.60 and 119.91 ppm represented the aromatic carbons [25] of phenyl rings. The –CH carbon appeared at 61.36 ppm.
Table 1. Optimized geometrical parameters for BCOPCA calculated at B3LYP and CAM-B3LYP as 6-31Gd-p basis sets.

| Geometrical parameter calculated with | B3LYP     | CAM-B3LYP | Experimental |
|--------------------------------------|-----------|-----------|--------------|
| Bond length (Å)                      |           |           |              |
| C1-C2                                | 1.3931    | 1.3884    | 1.3927       |
| C1-C6                                | 1.3965    | 1.3913    | 1.381        |
| C1-H32                               | 1.0856    | 1.0846    | 0.93         |
| C2-C3                                | 1.4004    | 1.3926    | 1.396        |
| C2-H33                               | 1.0856    | 1.085     | 0.93         |
| C3-C4                                | 1.3982    | 1.3912    | 1.382        |
| C3-N7                                | 1.43      | 1.428     | 1.42         |
| C4-C5                                | 1.3949    | 1.3898    | 1.38         |
| C4-H34                               | 1.0826    | 1.0828    | 0.93         |
| C5-C6                                | 1.3951    | 1.3904    | 1.375        |
| C5-H35                               | 1.0856    | 1.0846    | 0.93         |
| C6-H36                               | 1.0856    | 1.0847    | 0.93         |
| N7-C8                                | 1.424     | 1.4209    | 1.472        |
| N7-C11                               | 1.412     | 1.3955    | 1.355        |
| C8-C9                                | 1.5212    | 1.5167    | 1.525        |
| C8-C14                               | 1.3473    | 1.3373    | 0.97         |
| C9-C10                               | 1.5164    | 1.5125    | 1.381        |
| C9-C29                               | 1.5475    | 1.5351    | 0.93         |
| C9-H37                               | 1.0907    | 1.0897    | 1.525        |
| C10-C11                              | 1.486     | 1.4847    | 0.97         |
| C10-C13                              | 1.3495    | 1.3391    | 0.97         |
| C11-O12                              | 1.2177    | 1.2142    | 1.215        |
| C12-C15                              | 1.4591    | 1.4618    | 0.93         |
| C13-H38                              | 1.0899    | 1.0886    | 1.38         |
| C14-C16                              | 1.4664    | 1.4685    | 0.93         |
| C14-H39                              | 1.0868    | 1.0857    | 0.93         |
| C15-C17                              | 1.4103    | 1.402     | 0.98         |
| C15-C21                              | 1.4105    | 1.4021    | 1.523        |
| C16-C22                              | 1.4103    | 1.4026    | 1.524        |
| C16-C26                              | 1.4094    | 1.4013    | 1.000        |
| C17-C18                              | 1.3895    | 1.3853    | 1.390        |
| C17-H40                              | 1.0862    | 1.0852    | 1.395        |
| C18-C19                              | 1.3951    | 1.3886    | 1.503        |
| C18-C41                              | 1.084     | 1.0833    | 1.504        |
| C19-C20                              | 1.3954    | 1.3887    | 1.392        |
| C19-C127                             | 1.7538    | 1.7469    | 1.747        |

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| Geometrical parameter calculated with | B3LYP | CAM-B3LYP | Experimental |
|--------------------------------------|-------|------------|--------------|
| C20-C21                             | 1.3913 | 1.387      | 1.375        |
| C20-H42                             | 1.0841 | 1.0834     | 1.2070       |
| C21-H43                             | 1.0831 | 1.0825     | 1.392        |
| C22-C23                             | 1.3901 | 1.3855     | 1.207        |
| C22-H44                             | 1.0865 | 1.0854     | 1.373        |
| C23-C24                             | 1.3943 | 1.3883     | 1.295        |
| C23-H45                             | 1.0842 | 1.0835     | 1.207        |
| C24-C25                             | 1.3933 | 1.3867     | 1.503        |
| C24-C28                             | 1.7574 | 1.7501     | 1.264        |
| C25-C26                             | 1.3933 | 1.3889     | 1.292        |
| C25-H46                             | 1.0842 | 1.0836     | 1.52         |
| C26-H47                             | 1.0826 | 1.0819     | 1.371        |
| C29-O30                             | 1.2085 | 1.2065     | 1.19         |
| C29-O31                             | 1.3473 | 1.3372     | 1.282        |
| O31-H48                             | 0.971  | 0.97       | 1.5          |
| Bond angle\(^\circ\)                |       |            |              |
| C2-C1-C6                            | 120.1675 | 120.0936  | 121.5        |
| C2-C1-H32                           | 119.552 | 119.634    | 119.2        |
| C6-C1-H32                           | 120.2784 | 120.2706  | 119.2        |
| C1-C2-C3                            | 119.8525 | 119.6997  | 119.9        |
| C1-C2-H33                           | 120.4564 | 120.5939  | 120.1        |
| C3-C2-H33                           | 119.6909 | 119.7062  | 120.1        |
| C2-C3-C4                            | 120.2038 | 120.5062  | 118.4        |
| C2-C3-N7                            | 119.204 | 119.1592   | 119.1        |
| C4-C3-N7                            | 120.5827 | 120.3336  | 119.1        |
| C3-C4-C5                            | 119.4649 | 119.416    | 120.9        |
| C3-C4-H34                           | 119.8178 | 119.8271  | 119.5        |
| C5-C4-H34                           | 120.7059 | 120.7519  | 119.5        |
| C4-C5-C6                            | 120.5561 | 120.3686  | 121          |
| C4-C5-H35                           | 119.3349 | 119.496    | 119.5        |
| C6-C5-H35                           | 120.1088 | 120.135    | 119.5        |
| C1-C6-C5                            | 119.7513 | 119.9117  | 118.3        |
| C1-C6-H36                           | 120.0944 | 120.0312  | 120.8        |
| C5-C6-H36                           | 120.1541 | 120.057    | 120.8        |
| C3-N7-C8                            | 124.5285 | 124.0042  | 120.4        |
| C3-N7-C11                           | 122.8067 | 122.5617  | 127.4        |
| C8-N7-C11                           | 111.7042 | 111.869    | 112          |
| N7-C8-C9                            | 106.24  | 106.1696   | 103.5        |

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Table 1. (Continued)

| Geometrical parameter calculated with B3LYP | CAM-B3LYP | Experimental |
|--------------------------------------------|-----------|--------------|
| N7-C8-C14                                  | 123.9764  | 123.8905     | 111.1       |
| C9-C8-C14                                  | 129.7058  | 129.8984     | 111.1       |
| C8-C9-C10                                  | 102.7952  | 102.6542     | 111.1       |
| C8-C9-29                                   | 111.3715  | 110.8963     | 111.1       |
| C8-C9-H37                                  | 111.7079  | 111.8358     | 109         |
| C10-C9-C29                                 | 111.1317  | 110.8401     | 104.4       |
| C10-C9-H37                                 | 113.3464  | 113.2492     | 113         |
| C29-C9-H37                                 | 106.9355  | 107.3983     | 108.1       |
| C9-C10-C11                                 | 107.8382  | 107.5884     | 114.7       |
| C9-C10-C13                                 | 132.5935  | 132.7076     | 108.1       |
| C11-C10-C13                                | 119.5053  | 119.6024     | 108.1       |
| N7-C11-C10                                 | 106.495   | 106.7195     | 104.2       |
| N7-C11-O12                                 | 125.2761  | 125.3382     | 110.9       |
| C10-C11-O12                                | 128.2287  | 127.9423     | 110.9       |
| C10-C13-C15                                | 131.9471  | 131.4343     | 110.9       |
| C10-C13-H38                                | 113.1128  | 113.5881     | 110.9       |
| C15-C13-H38                                | 114.883   | 114.9079     | 108.9       |
| C8-C14-C16                                 | 130.1969  | 129.5292     | 125.2       |
| C8-C14-H39                                 | 115.5543  | 115.9984     | 125.5       |
| C16-C14-H39                                | 114.1541  | 114.3742     | 123.4       |
| C13-C15-C17                                | 117.1306  | 117.0862     | 120.2       |
| C13-C15-C21                                | 124.9491  | 124.6486     | 116.3       |
| C17-C15-C21                                | 117.92    | 118.2641     | 111.1       |
| C14-C16-C22                                | 116.9533  | 116.9455     | 113.5       |
| C14-C16-C26                                | 125.6477  | 125.3662     | 109.5       |
| C22-C16-C26                                | 117.3968  | 117.6866     | 122.7       |
| C15-C17-C18                                | 121.7189  | 121.5305     | 120.3       |
| C15-C17-H40                                | 119.1775  | 119.3283     | 117.0       |
| C18-C17-H40                                | 119.1009  | 119.1392     | 119.0       |
| C17-C18-C19                                | 118.8788  | 118.7876     | 120.5       |
| C17-C18-H41                                | 120.8816  | 120.8289     | 120.5       |
| C19-C18-H41                                | 120.2393  | 120.3832     | 120.0       |
| C18-C19-C20                                | 120.9704  | 121.178      | 120.0       |
| C18-C19-C127                               | 119.4852  | 119.4077     | 120.0       |
| C20-C19-C127                               | 119.5417  | 119.4121     | 119.8       |
| C19-C20-C21                                | 119.6733  | 119.5158     | 123.4       |
| C19-C20-H42                                | 120.0229  | 120.1268     | 120.2       |
| C21-C20-H42                                | 120.3005  | 120.3553     | 116.3       |

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| Geometrical parameter calculated with | B3LYP  | CAM-B3LYP | Experimental |
|--------------------------------------|--------|-----------|--------------|
| C15-C21-C20                          | 120.8245 | 120.7106  | 111.1        |
| C15-C21-C43                          | 121.1407 | 121.2074  | 113.5        |
| C20-C21-H43                          | 117.9922 | 118.0484  | 109.5        |
| C16-C22-C23                          | 121.9783 | 121.8166  | 122.7        |
| C16-C22-H44                          | 119.1281 | 119.2167  | 120.3        |
| C23-C22-H44                          | 118.8904 | 118.9649  | 117.0        |
| C22-C23-C24                          | 119.0437 | 119.9541  | 119.0        |
| C22-C23-H45                          | 120.7247 | 120.6818  | 120.5        |
| C24-C23-H45                          | 120.2316 | 120.364   | 120.5        |
| C23-C24-C25                          | 120.6493 | 120.851   | 120.0        |
| C23-C24-C128                         | 119.6327 | 119.5533  | 120.0        |
| C25-C24-C128                         | 119.7147 | 119.593   | 120.0        |
| C24-C25-C26                          | 119.7834 | 119.6139  | 119.8        |
| C24-C25-H46                          | 120.0714 | 120.1907  | 123.4        |
| C26-C25-H46                          | 120.1401 | 120.1917  | 109.5        |
| C16-C26-C25                          | 121.1295 | 121.0607  | 118.4        |
| C16-C26-H47                          | 121.3002 | 121.3533  | 124.3        |
| C25-C26-H47                          | 117.5394 | 117.5642  | 124.4        |
| C9-C29-O30                           | 122.9859 | 123.0089  | 111          |
| C9-C29-O31                           | 116.4749 | 116.8521  | 119.9        |
| O30-C29-O31                          | 120.5385 | 120.1376  | 120.1        |
| C29-O31-H48                          | 110.8373 | 111.9199  | 120.1        |

Dihedral angles (°)

| C6-C1-C2-C3                          | −0.6109 | −0.5839   |
| C6-C1-C2-H33                         | 179.5494 | 179.5869 |
| H32-C1-C2-C3                         | 179.9191 | 179.9014 |
| H32-C1-C2-H33                        | 0.0794  | 0.0721    |
| C2-C1-C6-C5                          | 0.1657  | 0.2974    |
| C2-C1-C6-H36                         | −179.64 | −179.6126 | −178.80    |
| H32-C1-C6-C5                         | 179.6318 | 179.809  |
| H32-C1-C6-H36                        | −0.1738 | −0.1009   |
| C1-C2-C3-C4                          | 0.5046  | 0.2642    |
| C1-C2-C3-N7                          | 179.3026 | 179.8984 |
| H33-C2-C3-C4                         | −179.6545 | −179.9051 | −178.6     |
| H33-C2-C3-N7                         | −0.8565 | −0.2708   |
| C2-C3-C4-C5                          | 0.0471  | 0.3413    |
| C2-C3-C4-H34                         | 178.8302 | 179.5328 |
| N7-C3-C4-C5                          | −178.7342 | −179.2886 |
| Geometrical parameter calculated with | B3LYP | CAM-B3LYP | Experimental |
|--------------------------------------|-------|-----------|--------------|
| N7-C3-C4-H34                         | 0.0489| −0.0971   |              |
| C2-C3-N7-C8                          | 57.6483| 64.5247   |              |
| C2-C3-N7-C11                         | −134.5078| −130.9131 |              |
| C4-C3-N7-C8                          | −123.5584| −115.8405 |              |
| C4-C3-N7-C11                         | 44.2856| 48.7217   |              |
| C3-C4-C5-C6                          | −0.4965| −0.6307   |              |
| C3-C4-C5-H35                         | 179.6415| 179.6003  |              |
| H34-C4-C5-C6                         | −179.2686| −179.8146 |              |
| H34-C4-C5-H35                        | 0.8695 | 0.4164    |              |
| C4-C5-C6-C1                          | 0.3921 | 0.3146    |              |
| C4-C5-C6-H36                         | −179.8023| −179.7755 |              |
| H35-C5-C6-C1                         | −179.7469| −179.9179 |              |
| H35-C5-C6-H36                        | 0.0586 | −0.0079   |              |
| C3-N7-C8-C9                          | −170.5224| −173.4804 |              |
| C3-N7-C8-C14                         | 12.4116| 8.6588    |              |
| C11-N7-C8-C9                         | 20.4592| 20.5093   |              |
| C11-N7-C8-C14                        | −156.6068| −157.3515 |              |
| C3-N7-C11-C10                        | −178.8606| −175.7201 |              |
| C3-N7-C11-O12                        | 1.2808 | 4.2051    |              |
| C8-N7-C11-C10                        | −9.6219| −9.4759   |              |
| C8-N7-C11-O12                        | 170.5194| 170.4493  |              |
| N7-C8-C9-C10                         | −22.0033| −22.1493  |              |
| N7-C8-C9-C29                         | 96.8884| 96.2758   |              |
| N7-C8-C9-H37                         | −143.8611| −143.8708 |              |
| C14-C8-C9-C10                        | 154.8339| 155.536   |              |
| C14-C8-C9-C29                        | −86.2744| −86.039   |              |
| C14-C8-C9-H37                        | 32.9761| 33.8145   |              |
| N7-C8-C14-C16                        | 177.4438| 177.3122  |              |
| N7-C8-C14-H39                        | 1.234 | 1.1589    |              |
| C9-C8-C14-C16                        | 1.1063 | −0.0094   |              |
| C9-C8-C14-H39                        | −175.1036| −176.1627 |              |
| C8-C9-C10-C11                        | 16.5817| 16.8321   |              |
| C8-C9-C10-C13                        | −160.4262| −159.3659 |              |
| C29-C9-C10-C11                       | −102.2162| −101.6325 |              |
| C29-C9-C10-C13                       | 80.7759| 82.1695   |              |
| H37-C9-C10-C11                       | 137.3216| 137.5863  |              |
| H37-C9-C10-C13                       | −39.6863| −38.6117  |              |
| C8-C9-C29-O30                        | 129.7818| 131.4858  |              |
### Table 1. (Continued)

| Geometrical parameter calculated with | B3LYP    | CAM-B3LYP | Experimental |
|---------------------------------------|----------|-----------|--------------|
| C8-C9-C29-O31                         | −50.5183 | −48.9559  | −28.72       |
| C10-C9-C29-O30                        | −116.4732| −115.1709 | −158.40      |
| H37-C9-C29-O30                        | 7.7078   | 9.016     |              |
| C9-C10-C11-N7                         | −5.2282  | −5.4971   |              |
| C13-C10-C11-N7                        | 172.2412 | 171.2903  |              |
| C9-C10-C11-O12                        | 174.6249 | 174.5803  |              |
| C9-C10-C13-C15                        | 177.0893 | 176.8905  |              |
| C11-C10-C13-C15                       | −176.6912| −175.6934 |              |
| C11-C10-C13-H38                       | 0.3623   | 1.0595    |              |
| C10-C13-C15-C17                       | 165.4828 | 164.0494  |              |
| H38-C13-C15-C17                       | −11.5298 | −12.6696  |              |
| C8-C14-C16-C22                        | −158.5925| −156.846  |              |
| C8—14—C16-C26                        | 21.9495  | 23.6512   |              |
| H39-C14-C16-C22                       | 17.6601  | 19.3583   |              |
| H39-C14-C16-C26                       | −161.7979| −160.1445 |              |
| C13-C15-C17-C18                       | −178.5089| −178.3138 |              |
| C13-C15-C17-H40                       | 0.9      | 1.1686    |              |
| C21-C15-C17-C18                       | 1.332    | 1.309     |              |
| C15-C17-C18-H40                       | −179.2591| −179.2086 |              |
| C13-C15-C21-C20                       | 178.7341 | 178.509   |              |
| C13-C15-C21-H43                       | −3.689   | −3.64     |              |
| C17-C15-C21-C20                       | −1.0932  | −1.0828   |              |
| C17-C15-C21-H43                       | 176.4837 | 176.7682  |              |
| H39-C14-C16-C22                       | 176.4797 | 176.8606  |              |
| C14-C16-C26-C25                       | −179.0959| −179.1017 |              |
| C14-C16-C26-H47                       | 2.9761   | 2.6388    |              |
| C22-C16-C26-C25                       | 1.4482   | 1.3988    |              |
| C22-C16-C26-H47                       | −176.4797| −176.8606 |              |
| C15-C17-C18-C19                       | −0.5914  | −0.5794   |              |
### Table 1. (Continued)

| Geometrical parameter calculated with | B3LYP     | CAM-B3LYP | Experimental |
|--------------------------------------|-----------|-----------|--------------|
| C15-C17-C18-H41                      | 179.5982  | 179.5994  |              |
| C40-C17-C18-C19                      | 179.9992  | 179.9373  |              |
| H40-C17-C18-H41                      | 0.1888    | 0.1161    |              |
| C17-C18-C19-C20                      | −0.4198   | −0.4037   |              |
| C17-C18-C19-C27                      | −179.8184 | −179.8652 |              |
| H41-C18-C19-C20                      | 179.3919  | 179.4184  |              |
| H41-C18-C19-C27                      | −0.0067   | −0.0432   |              |
| C18-C19-C20-C21                      | 0.6457    | 0.6179    |              |
| C18-C19-C20-H42                      | −178.702  | −178.8638 |              |
| CI27-C19-C20-C21                     | −179.956  | −179.9206 |              |
| CI27-C19-C20-H42                     | 0.6963    | 0.5977    |              |
| C19-C20-C21-C15                      | 0.1344    | 0.1463    |              |
| C19-C20-C21-H43                      | −177.517  | −177.7711 |              |
| H42-C20-C21-C15                      | 179.4802  | 179.6268  |              |
| H42-C20-C21-H43                      | 1.8289    | 1.7093    |              |
| CI6-C22-C23-C24                      | 0.5254    | 0.4755    |              |
| CI6-C22-C23-H45                      | −179.5588 | −179.6161 |              |
| H44-C22-C23-C24                      | 179.8632  | 179.9829  |              |
| H44-C22-C23-H45                      | −0.2211   | −0.1087   |              |
| CI22-C23-C24-C25                     | 0.5332    | 0.5037    |              |
| CI22-C23-C24-H45                     | 179.8698  | 179.9084  |              |
| CI45-C23-C24-C25                     | −179.383  | −179.4049 |              |
| CI45-C23-C24-I28                     | −0.0463   | −0.0003   |              |
| CI23-C24-C25-C26                     | −0.5664   | −0.5021   |              |
| CI23-C24-C25-H46                     | 178.6157  | 178.803   |              |
| CI28-C24-C25-C26                     | −179.9025 | −179.9065 |              |
| CI28-C24-C25-H46                     | −0.7204   | −0.6014   |              |
| CI24-C25-C26-C16                     | −0.4575   | −0.4786   |              |
| CI24-C25-C26-H47                     | 177.5459  | 177.8447  |              |
| CI46-C25-C26-C16                     | −179.639  | −179.7837 |              |
| CI46-H25-C26-H47                     | −1.6357   | −1.4604   |              |
| CI9-C29-O31-I48                     | 1.20772   | 1.8811    |              |
| CI30-C29-O31-H48                     | −179.335  | −178.5472 |              |

### 3.4. Electronic absorption

The UV-Visible spectrum of compound was computed at the B3LYP and CAM-B3LYP hybrid functionals with 6-31G (d,p) basis sets and integral equation formalism polarizable continuum model (IEFPCM) was employed for accounting
The excitation energies, oscillator strength, and percent contributions have been tabulated in Table 4. Fig. 5 represents two intense electronic transitions at 348 and 278 nm with an oscillator strength $f = 0.269$ and $0.255$ in chloroform, complying with the observed values of 256 and 240 nm. The title compound depicted in Fig. 3.

**Table 2.** Calculated and experimental $^1$H NMR chemical shifts (δ/ppm) of BCOPCA in CDCl₃.

| δ<sub>calcd.</sub> | δ<sub>exp.</sub> | Assignment |
|------------------|----------------|------------|
|                  | B3LYP          | CAM-B3LYP  |            |
| 32H              | 7.36           | 7.82       | 7.339–7.062 m, 5H, phenyl ring |
| 33H              | 8.48           | 8.63       |            |
| 34H              | 7.08           | 7.3        |            |
| 35H              | 7.59           | 7.76       |            |
| 36H              | 7.21           | 7.35       |            |
| 37H              | 8.79           | 8.76       | 4.109–3.900 m, 1H, CH in pyrrolidine ring |
| 38H              | 7.25           | 7.65       | 7.742–7.714 m, 2H, CH between pyrrolidine and 4-chloro substituted phenyl ring |
| 39H              | 6.41           | 6.63       |            |
| 40H              | 7.21           | 7.49       | 7.533–7.507 dd, 4H, 4-chloro substituted phenyl ring |
| 41H              | 7.12           | 7.36       |            |
| 42H              | 7.65           | 7.9        |            |
| 43H              | 10.03          | 11.43      |            |
| 44H              | 6.71           | 6.93       | 7.434–7.406 dd, 4H, 4-chloro substituted phenyl ring |
| 45H              | 7.08           | 7.3        |            |
| 46H              | 7.76           | 8.09       |            |
| 47H              | 4.96           | 4.04       |            |
| 48H              | 7.51           | 7.45       | 11.45 Hydroxyl proton of carboxylic acid |

solvent effect [26]. The excitation energies, oscillator strength, percent contributions have been tabulated in Table 4. Fig. 5 represents two intense electronic transitions at 348 and 278 with an oscillator strength $f = 0.269$ and 0.255 in chloroform complying with the observed values of 256 and 240 nm. The title compound depicted
n → π* HOMO-1 to LUMO+1 with 63% and π → π* HOMO-2 to LUMO with 53% contribution as shown in Fig. 6. The HOMO-LUMO energy gaps were found to be 2.199 (B3LYP) and 3.060 (CAM-B3LYP).

### 3.5. Vibrational assignment

There are 48 atoms having C1 point group and 138 routine modes of vibrations performed on the basis of recorded FT-IR spectrum, in BCOPCA. The discard of anharmonicity in real system is responsible for higher calculated vibrational wavenumbers than the observed wavenumbers. Therefore, calculated wavenumbers are scaled.

| Atom | δ_{calc.} | δ_{exp.} | Assignment |
|------|-----------|-----------|------------|
| B3LYP | CAM-B3LYP | B3LYP | CAM-B3LYP |
| 1C  | 129.04    | 129.11    | 124.70–119.91 | Phenyl ring attached at nitrogen of pyrrolidine ring |
| 2C  | 117.29    | 116.65    |            |            |
| 3C  | 126.25    | 132.85    |            |            |
| 4C  | 115.92    | 114.78    |            |            |
| 5C  | 127.81    | 127.81    |            |            |
| 6C  | 120.83    | 119.99    |            |            |
| 8C  | 88.87     | 134.71    | 77.64–76.69 | Pyrrolidine ring |
| 9C  | 135.99    | 71.17     |            |            |
| 10C | 73.5      | 126.74    |            |            |
| 11C | 130.46    | 167.93    | 171.66     | C=O in Pyrrolidine ring |
| 13C | 167.6     | 128.88    | 61.36      | Methine group between Pyrrolidine and 4-chloro substituted phenyl ring |
| 14C | 127.71    | 103.11    |            |            |
| 15C | 102.78    | 116.93    | 129.21–128.39 | 4-chloro substituted phenyl ring |
| 16C | 117.88    | 123.98    |            |            |
| 17C | 124.37    | 133.12    |            |            |
| 18C | 133.09    | 125.55    |            |            |
| 19C | 126.2     | 140.8     |            |            |
| 20C | 142.34    | 130.01    |            |            |
| 21C | 130.56    | 146.57    |            |            |
| 22C | 145.77    | 128.51    | 138.51–130.73 | 4-chloro substituted phenyl ring |
| 23C | 128.75    | 129.7     |            |            |
| 24C | 129.75    | 134.82    |            |            |
| 25C | 136.38    | 128.23    |            |            |
| 26C | 189.63    | 188.07    |            |            |
| 29C | 149.5     | 149.38    | 172.25     | C=O group in carboxylic acid |

Table 3. Calculated and experimental $^{13}$C NMR chemical shifts (δ/ppm) of BCOPCA in CDCl$_3$-solvent.
down by a single factor 0.9679 [27] B3LYP and compared with experimental wave-numbers. The observed and computed frequencies, PED and simulated vibrational spectra of BCOPCA are presented in Table 5 and Fig. 7.

The experimental FT-IR -OH stretching vibration band appeared at 3622 cm\(^{-1}\) is in good agreement with the calculated value at 3545 cm\(^{-1}\) with a contribution of 68% [28, 29, 30, 31]. The band at 2944 cm\(^{-1}\) is assigned to C-H stretching vibrations with a calculated value of 3054 cm\(^{-1}\) and 86% contribution. The C–H in plane bending vibrations with 63% contribution and out of plane bending vibrations with 41% contribution in IR were observed at 1375, 1038 and 978, 805 cm\(^{-1}\) respectively [32, 33, 34]. The bands for C¼C and C–C stretching vibrations in the molecule appeared at 1375, 1442, and 1513 cm\(^{-1}\) depicting good correlation between theoretical and experimental values [35, 36]. The carbonyl carbons showed stretching
vibrations at 1729 and 1702 cm\(^{-1}\) [37] while it was calculated at 1716 cm\(^{-1}\). The C=O stretching vibration [38, 39] appeared at 1036 cm\(^{-1}\) complying well with the calculated value at 1020 cm\(^{-1}\). C-Cl vibration in BCOPCA appeared at 679 cm\(^{-1}\) with PED contribution of 53\% and is in good agreement with the observed wavenumber at 667 cm\(^{-1}\) [40].

### 3.6. Mulliken charge distribution

The Mulliken charges were calculated at two different levels as enumerated in Table 6 and plotted in Fig. 8. On the basis of the results performed on neutral molecule the negative charges were delocalized on O12, O30 and O31 atoms and similar positive charges were noticed on all the hydrogen atoms in the molecule. C11 and C29 attached with oxygen atoms had more positive charges due to electronegative character of oxygen atoms [41, 42, 43]. Almost like values of positive charges were

### Table 4. Experimental and theoretical absorption wavelengths \(\lambda\) (nm) and excitation energies E (eV) of BCOPCA using functional B3LYP and CAM-B3LYP 6-31G(d,p) basis set.

| Major contributing molecular orbitals | E (eV) | Calculated \((\lambda_{max})\) | Oscillatory strength (f) | Assignments \((\lambda_{max})\) | Observed \((\lambda_{max})\) |
|----------------------------------------|--------|----------------------------|--------------------------|-----------------------------|-------------------------|
| B3LYP                                  |        |                           |                          |                             |                         |
| H \(\rightarrow\) L (69\%)              | 2.19   | 523                       | 0.014                    | \(\pi \rightarrow \pi^*\)   | 288                     |
| H-1 \(\rightarrow\) L+1 (63\%)          | 2.92   | 424                       | 0.225                    | n \(\rightarrow\) \(\pi^*\) | 273                     |
| H-2 \(\rightarrow\) L (61\%)            | 3.55   | 348                       | 0.269                    | \(\pi \rightarrow \pi^*\)   | 256                     |
| H-2 \(\rightarrow\) L+2 (46\%)          | 3.77   | 328                       | 0.222                    | n \(\rightarrow\) \(\pi^*\) | 240                     |
| H-4 \(\rightarrow\) L (46\%)            | 3.99   | 310                       | 0.192                    | \(\pi \rightarrow \pi^*\)   | 227                     |
| CAM-B3LYP                               |        |                           |                          |                             |                         |
| H \(\rightarrow\) L (55\%)              | 3.06   | 405                       | 0.05                     | \(\pi \rightarrow \pi^*\)   | 288                     |
| H-1 \(\rightarrow\) L (40\%)            | 3.49   | 354                       | 0.40                     | n \(\rightarrow\) \(\pi^*\) | 273                     |
| H \(\rightarrow\) L+2 (45\%)            | 3.82   | 323                       | 0.11                     | \(\pi \rightarrow \pi^*\)   | 256                     |
| H-2 \(\rightarrow\) L (53\%)            | 4.45   | 278                       | 0.25                     | n \(\rightarrow\) \(\pi^*\) | 240                     |
| H-2 \(\rightarrow\) L+1 (52\%)          | 4.65   | 266                       | 0.14                     | \(\pi \rightarrow \pi^*\)   | 227                     |
observed for hydrogen atoms bonded to carbon atoms in the aromatic ring. It must be noted that the biggest value of charge on H48 might be due to hydrogen bonding.

### 3.7. Molecular electrostatic potential

A colour scheme depicting different values of the electrostatic potential in ascending order at the surface is as follows: red < yellow < green < light blue < blue (Figs. 9 and 10). Red colour depicts nucleophilic region while blue depicts electrophilic region [44, 45, 46, 47]. The yellow, green and light blue colours portrayed slightly electron rich; neutral and slightly electron deficient regions respectively [48, 49]. The region of maximum negative electrostatic potential with a value of $-7.648$ a.u., is around C11 & O12 and the most positive region with a value of $+7.648$ a.u., is at C47 & O30, as revealed by MEP and ESP maps. C11, O12 and C47, O30 are most preferred sites for nucleophilic and electrophilic attack respectively.

### 3.8. Non bond orbital (NBO) analysis

The hyperconjugative interactions in molecular systems [50, 51], correlation between donor (i), acceptor (j) level bonds and stabilization energy $E(2)$ are explained according to second order Fock matrix as follows:
Table 5. Experimental and calculated (selected) vibrational wavenumbers of BCOPCA using B3LYP/6-31 G (d,p) and their assignments [harmonic wavenumbers (cm$^{-1}$), IR int (Kmmol$^{-1}$)].

| Wave number unscaled | Wave number scaled | Exp. Wave numbers | Exp.IRint | Assignment (PED) ≥ 5 % |
|----------------------|-------------------|-------------------|-----------|------------------------|
| 3689.7               | 3545.064          | 3622              | 101.07    | v(O31-H48) (68.) v(O22-C20) (41.) |
| 3263.2               | 3135.283          | 3297              | 1.92      | v(C26-H47) (11.)       |
| 3241.8               | 3114.721          | 3205              | 4.65      | v(C18-H41) (37.) v(C5-C6) (32.) |
| 3239.5               | 3112.512          | 3205              | 132.76    | v(C23-H45) (31.)       |
| 3235.2               | 3108.38           |                   | 11.28     | v(C20-H42) (17.) -v(C5-C6) (34.) |
| 3223.6               | 3097.235          |                   | 26.29     | v(C25-H46) (7.) v(C25-C26) (14.) -v(C25-C21) (9.) |
| 3213.5               | 3087.531          |                   | 1.83      | v(C5-C36) (17.) -v(C5-C6) (23.) -v(C1-C2) (27.) |
| 3187.8               | 3062.838          | 3003              | 33.77     | -v(C6-H36) (34.) -v(C1-C6) (18.) v(C5-C6) (14.) |
| 3186.6               | 3061.685          |                   | 11.27     | v(C2-C3) (16.) v(C1-C6) (12.) -v(C4-H34) (7.) v(C5-C6) (13.) |
| 3179.2               | 3054.575          | 2944              | 13.35     | v(C5-H35) (86.)        |
| 3173.4               | 3049.003          | 2893              | 4.61      | v(C17-H40) (29.) v(C17-C15) (7.) |
| 3168.3               | 3044.103          |                   | 0.44      | v(C22-H44) (16.) v(C22-C23) (9.) v(C22-C16) (6.) |
| 3157.08              | 3033.322          |                   | 1.99      | v(C6-C36) (51.)        |
| 3127.25              | 3004.662          |                   | 107.24    | v(C14-H39) (39.) v(C14-C8) (32.) v(C16-C14) (19.) |
| 1827.74              | 1756.093          |                   | 0.21      | v(C2-C3) (99.)         |
| 1786.58              | 1716.546          | 1729              | 11.17     | v(C4-C20) (99.)        |
| 1710.14              | 1643.103          | 1702              | 33.06     | v(C4-H34) (60.) v(C3-N4) (15.) v(C1-H32) (12.) v(C1-H32) (6.) |
| 1692.15              | 1625.818          |                   | 154.16    | v(C1-C6) (69.) v(C4-C5) (9.) -v(C10-C11) (5.) |
| 1652.43              | 1587.655          |                   | 9.19      | v(C3-C4) (45.) v(C1-C2) (12.) -v(C1-C2) (9.) -v(C1-C2) (6.) -v(C2-H33) (5.) |
| 1643.02              | 1578.614          |                   | 101.03    | v(C1-C2) (42.) -v(C3-C4) (11.) -δ(C10-C13-H38) (7.) v(C1-C6) (7.) -v(C1-H32) (5.) -v(C10-C11) (5.) |
| 1641.62              | 1577.268          |                   | 135.99    | v(C1-C2) (24.) v(C4-C5) (22.) -v(C2-C3) (8.) -v(C5-C6) (7.) v(C4-C5) (6.) -v(C2-C3) (6.) v(C2-C3) (5.) |
| 1640.94              | 1576.615          |                   | 41.78     | v(C22-C23) (23.) v(C3-C4) (21.) -v(C4-H34) (12.) -v(C4-H34) (7.) -v(C16-C26) (7.) v(C1-C2) (7.) v(C2-H33) (5.) |
| 1611.62              | 1548.444          |                   | 15.76     | v(C1-C6) (18.) v(C3-C4) (16.) -v(C5-C6) (14.) -v(C2-C3) (12.) -v(C1-H32) (5.) -v(C1-C2) (5.) -v(C3-N4) (5.) |

(continued on next page)
Table 5. (Continued)

| Wave number unscaled | Wave number scaled | Exp. Wave numbers | Exp.\(\text{IR}_{\text{int}}\) Assignment (PED) ≥ 5 % |
|----------------------|-------------------|------------------|---------------------------------|
| 1609.97              | 1546.859          | 24.12 | ν(C1-C2) (17.) ν(C3-N4) (16.) ν(C1-H32) (8.) -ν(C3-C4) (6.) -ν(C4-N3) (6.) ν(C4-C5) (6.) -ν(C4-C5) (5.) |
| 1539.05              | 1478.719          | 11.43 | ν(C4-C5) (16.) ν(C2-C3) (15.) ν(C4-H34) (14.) -ν(C1-C2) (14.) -ν(C1-C6) (12.) -ν(C16-C26) (11.) -δ(C8-C14-C16) (6.) |
| 1535.31              | 1475.126          | 51.92 | ν(C2-H33) (21.) -ν(C1-H32) (17.) -ν(C4-C5) (17.) ν(C3-N4) (14.) -ν(C2-C3) (9.) -ν(C3-C4) (5.) |
| 1533.9               | 1473.771          | 183.64 | ν(C2-C3) (15.) -δ(C2-C1-H32) (15.) -ν(C4-C5) (14.) ν(C3-C4) (12.) ν(C3-C4) (9.) -ν(C5-C6) (8.) -ν(C1-C6) (8.) -ν(C3-N4) (7.) |
| 1494.33              | 1435.752          | 166.6 | ν(C1-H32) (14.) -ν(C3-N4) (13.) ν(C1-C6) (13.) ν(C1-C2) (12.) -ν(C4-H34) (11.) -ν(C4-H34) (11.) ν(C2-C3) (7.) -ν(C16-C26) (5.) |
| 1452.24              | 1395.312          | 16.69 | δip (C17-H40) (16.) -ν(C2-C3) (15.) ν(C1-H32) (13.) ν(C4-C5) (13.) -ν(C3-C4) (12.) ν(C2-H33) (7.) -ν(C3-N4) (7.) -ν(C4-C5) (5.) |
| 1451.23              | 1394.342          | 200.84 | ν(C1-C2) (20.) -ν(C4-C5) (19.) -ν(C2-C3) (13.) -δ(C2-C1-H32) (13.) ν(C1-C6) (10.) ν(C2-C3) (6.) -ν(C3-C4) (5.) |
| 1421.23              | 1365.518          | 9.5   | ν(C1-C2) (22.) -ν(C2-C23) (10.) ν(C3-C4) (10.) ν(C1-C2) (7.) -ν(C4-H34) (7.) -ν(C1-C2) (6.) -ν(C4-C5) (6.) |
| 1404.45              | 1349.396          | 6.13  | ν(C1-C2) (13.) -ν(C3-N4) (12.) ν(C3-C4) (9.) -ν(C1-C2) (9.) ν(C4-C5) (7.) -δ(C10-C13-H38) (6.) -δip (C17-H40) (5.) |
| 1365.65              | 1312.117          | 3.93  | ν(C1-C6) (25.) δ(C8-C14-C16) (17.) -ν(C1-C2) (17.) ν(C3-C4) (5.) ν(C2-H33) (5.) |
| 1360.93              | 1307.582          | 2.22  | δ(C10-C13-H38) (42.) -ν(C3-N4) (11.) -ν(C3-N4) (8.) ν(C3-C4) (5.) ν(C1-C2) (5.) |
| 1347.32              | 1294.505          | 31.21 | ν(C4-C5) (9.) ν(C1-C2) (8.) -ν(C3-N4) (6.) -δ(C8-C14-C16) (6.) ν(C5-C6) (6.) |
| 1343.19              | 1290.537          | 467.5 | ν(C3-C4) (13.) δ(C8-C14-C16) (9.) ν(C4-C5) (8.) ν(C1-C6) (6.) ν(C3-N4) (6.) -ν(C4-C5) (6.) ν(C1-C2) (5.) |
| 1338.76              | 1286.281          | 7.6   | ν(C3-C4) (8.) ν(C2-C3) (7.) -ν(C1-H32) (6.) δip (C17-H40) (6.) -ν(C4-C5) (6.) |
| 1337.4               | 1284.974          | 85.78 | ν(C2-C3) (13.) -ν(C3-C4) (13.) -ν(C5-C6) (7.) ν(C1-C6) (7.) ν(C2-C3) (6.) -ν(C1-C2) (6.) δ(C2-C1-H32) (6.) -ν(C3-C4) (5.) ν(C4-C5) (5.) |
| 1326.19              | 1274.203          | 21.8  | ν(C2-C3) (14.) -ν(C1-C6) (12.) ν(C4-H34) (10.) ν(C1-C2) (9.) ν(C1-H32) (7.) -ν(C4-H34) (6.) ν(C3-N4) (5.) |

(continued on next page)
Table 5. (Continued)

| Wave number unscaled | Wave number scaled | Exp. Wave numbers | Exp.IRint Assignment (PED) ≥ 5% |
|----------------------|-------------------|-------------------|--------------------------------|
| 1316.12              | 1264.528          | 43.95             |
|                      |                   | ν(C2-H33) (21.) -ν(C1-H32) (18.) ν(C4-C5) (12.) -ν(C3-N4) (11.) ν(C1-C2) (7.) ν(C4-C5) (5.) |
| 1285.83              | 1235.425          | 44.82             |
|                      |                   | ν(C4-C5) (14.) -δ(C8-C14-C16) (12.) -ν(C1-C2) (11.) -ν(C16-C26) (8.) ν(C2-H33) (6.) ν(C4-H34) (6.) -ν(C2-C3) (5.) |
| 1276.77              | 1226.721          | 104.08            |
|                      |                   | ν(C1-H32) (42.) -ν(C3-N4) (24.) -ν(C29-O31) (13.) |
| 1269.12              | 1219.37           | 50.09             |
|                      |                   | ν(C1-H32) (34.) -ν(C3-N4) (34.) -ν(C2-H33) (15.) |
| 1232.16              | 1183.859          | 111.88            |
|                      |                   | ν(C2-C3) (19.) -ν(C3-N4) (16.) ν(C1-H32) (15.) -ν(C1-H32) (6.) -ν(C2-H33) (6.) -ν(C3-N4) (5.) |
| 1222.23              | 1174.319          | 4.82              |
|                      |                   | δ(C3-N4) (10.) ν(C2-H33) (10.) -ν(C1-H32) (8.) -ν(C1-H32) (8.) δ(C8-C14-C16) (7.) -ν(C4-H34) (7.) ν(C2-C3) (7.) ν(C1-C2) (5.) |
| 1220.82              | 1172.964          | 55.32             |
|                      |                   | ν(C2-C3) (27.) ν(C1-H32) (11.) ν(C4-H34) (9.) -ν(C2-H33) (7.) -ν(C3-N4) (7.) ν(C1-C2) (6.) |
| 1206.25              | 1158.965          | 34.78             |
|                      |                   | ν(C2-C3) (16.) -ν(C3-C4) (14.) ν(C4-C5) (13.) -δ(C17-H40) (8.) -ν(C3-N4) (7.) ν(C3-N4) (6.) -ν(C3-C4) (5.) |
| 1201.85              | 1154.737          | 5.82              |
|                      |                   | ν(C3-N4) (16.) -ν(C4-H34) (13.) ν(C1-C2) (12.) -ν(C1-H32) (10.) -ν(C3-C4) (8.) -ν(C2-C3) (6.) ν(C3-C4) (5.) |
| 1194.19              | 1147.378          | 3.6               |
|                      |                   | δ(C2-C1-H32) (23.) -ν(C4-C5) (18.) ν(C3-C4) (16.) -ν(C2-C3) (16.) ν(C1-C2) (11.) ν(C4-C5) (6.) |
| 1186.58              | 1140.066          | 3.71              |
|                      |                   | ν(C3-N4) (41.) -ν(C1-H32) (23.) -ν(C29-O31) (9.) -ν(C2-H33) (8.) ν(C4-C5) (5.) |
| 1180.41              | 1134.138          | 5.73              |
|                      |                   | ν(C1-C6) (18.) δ(C8-C14-C16) (15.) ν(C2-C3) (11.) -ν(C1-H32) (10.) ν(C4-H34) (5.) -ν(C10-C11) (5.) |
| 1150.05              | 1104.968          | 2.92              |
|                      |                   | ν(C2-C3) (32.) δ(C2-C1-H32) (26.) ν(C5-C6) (11.) -ν(C1-C6) (9.) |
| 1146.19              | 1101.259          | 0.61              |
|                      |                   | ν(C3-N4) (14.) -ν(C1-H32) (8.) -ν(C10-C11) (8.) -ν(C1-C6) (8.) ν(C1-H32) (8.) δ(C8-C14-C16) (6.) -ν(C2-H33) (5.) |
| 1125.27              | 1081.159          | 0.24              |
|                      |                   | δ(C17-H40) (21.) ν(C1-C2) (14.) ν(C2-C3) (11.) -ν(C4-C5) (9.) -ν(C3-N4) (9.) -ν(C3-C4) (8.) ν(C2-C3) (6.) |
| 1109.35              | 1065.863          | 0.94              |
|                      |                   | ν(C1-C2) (25.) -ν(C1-H32) (14.) -ν(C22-C23) (11.) -ν(C3-N4) (7.) -ν(C4-C5) (7.) ν(C3-C4) (6.) ν(C1-C2) (6.) ν(C4-H34) (5.) -ν(C4-H34) (5.) |
| 1108.03              | 1064.595          | 5.41              |
|                      |                   | ν(C1-C6) (14.) ν(C3-N4) (13.) -ν(C2-C3) (11.) -ν(C3-C4) (9.) -ν(C10-C11) (5.) |

(continued on next page)
Table 5. (Continued)

| Wave number unscaled | Wave number scaled | Exp. Wave numbers | Exp. IR<sub>int</sub> | Assignment (PED) ≥ 5 % |
|----------------------|--------------------|-------------------|-----------------------|------------------------|
| 1105.37              | 1062.039           | 50.09             | v(C1-C2) (9.) -v(C2-H33) (8.) v(C1-C6) (8.) v(C2-C3) (8.) -v(C4-C5) (7.) v(C1-H32) (6.) -v(C3-C4) (5.) v(C2-H33) (5.) -v(C3-C4) (5.) |
| 1054.67              | 1013.327           | 6.53              | v(C2-H33) (17.) -v(C1-C6) (16.) -v(C2-C3) (16.) v(C1-H32) (7.) -v(C3-C4) (6.) v(C2-H33) (6.) |
| 1023.66              | 983.5325           | 50.81             | v(C2-H33) (12.) -v(C3-C4) (11.) v(C1-H32) (10.) v(C2-C3) (8.) -v(C1-C2) (7.) |
| 1021.59              | 981.5437           | 21.37             | v(C5-C6) (27.) v(C1-C6) (26.) -δ(C2-C1-H32) (6.) -v(C1-C6) (6.) v(C3-C4) (6.) v(C2-C3) (5.) |
| 1018.45              | 978.5268           | 918               | v(C1-C6) (63.) v(C4-C5) (10.) v(C3-N4) (9.) -v(C3-C4) (5.) |
| 1005.8               | 966.3726           | 32.43             | v(C4-C5) (35.) v(C4-H34) (17.) v(C16-C26) (12.) -v(C4-H34) (11.) -v(C2-H33) (8.) |
| 1001.41              | 962.1547           | 2.27              | v(C1-C6) (63.) v(C2-C3) (8.) v(C3-C4) (8.) v(C4-C5) (6.) v(C1-C2) (5.) |
| 988.26               | 949.5202           | 25.84             | v(C1-H32) (28.) -v(C2-H33) (19.) v(C1-C2) (18.) v(C2-H33) (17.) -v(C4-H34) (5.) |
| 983.9                | 945.3311           | 35.87             | v(C2-H33) (21.) -v(C3-N4) (11.) v(C1-C6) (10.) -v(C3-N4) (6.) v(C2-H33) (5.) |
| 980.18               | 941.7569           | 17.69             | v(C1-C2) (32.) v(C3-N4) (18.) -v(C2-H33) (10.) -v(C4-H34) (10.) -v(C2-H33) (9.) |
| 977.39               | 939.0763           | 25.74             | v(C3-N4) (21.) -v(C2-H33) (16.) -v(C4-H34) (13.) -v(C1-C2) (13.) -v(C10-C11) (9.) v(C1-C2) (7.) v(C4-C5) (5.) -v(C3-N4) (5.) |
| 968.88               | 930.8999           | 32.85             | v(C10-C11) (38.) -v(C4-C5) (25.) v(C3-N4) (7.) -v(C2-H33) (5.) |
| 963.22               | 925.4618           | 9.93              | v(C2-H33) (24.) -v(C1-C2) (22.) v(C4-H34) (19.) -v(C3-N4) (14.) v(C3-C4) (12.) -v(C3-N4) (8.) |
| 940.85               | 903.9687           | 17.69             | v(C1-C6) (30.) -v(C2-C3) (23.) -v(C4-C5) (22.) v(C5-C6) (20.) |
| 929.51               | 893.0732           | 18.41             | v(C1-C2) (33.) v(C1-C2) (25.) -v(C4-H34) (22.) v(C2-H33) (6.) |
| 903.87               | 868.4383           | 7.93              | v(C10-C11) (15.) -v(C4-C5) (8.) v(C1-C6) (7.) -v(C4-C5) (6.) v(C3-N4) (5.) |
| 888.87               | 854.0263           | 10.42             | v(C4-H34) (27.) v(C3-N4) (27.) -v(C3-N4) (11.) v(C2-H33) (8.) v(C1-H32) (7.) |
| 876.45               | 842.0932           | 4.24              | v(C1-C6) (49.) -τ-R2 (10.) v(C4-C5) (6.) |
| 853.77               | 820.3022           | 11.95             | τ-R2 (30.) v(C1-C6) (11.) -v(C4-C5) (10.) -v(C1-H32) (9.) -v(C29-C31) (8.) -v(C3-N4) (7.) -δ(C8-C14-C16) (6.) |

(continued on next page)
| Wave number unscaled | Wave number scaled | Exp. Wave numbers | Exp.IR<sub>int</sub> Assignment (PED) ≥ 5% |
|----------------------|-------------------|------------------|------------------------------------------|
| 850.75               | 817.4006          | 21.31 δ(C8-C14-C16) (31.) ν(C1-C6) (26.) -ν(C2-H33) (8.) ν(C3-C4) (7.) |
| 847.74               | 814.5086          | 19.72 δ(C8-C14-C16) (26.) (τ–R2) (13.) |
| 844.44               | 811.338           | 14.39 6ν(C3-N4) (31.) -ν(C4-H34) (26.) -ν(C1-C2) (20.) ν(C2-H33) (16.) |
| 838.36               | 805.4963          | 11.09 ν(C2-H33) (41.) ν(C3-N4) (23.) -ν(C3-C4) (14.) -ν(C4-H34) (9.) |
| 832.42               | 799.7891          | 0.08 ν(C4-C5) (38.) (νC10-C11) (27.) |
| 800.72               | 769.3318          | 9 ν(C1-C2) (41.) ν(C4-H34) (34.) -ν(C3-C4) (10.) -ν(C4-H34) (6.) |
| 789.41               | 758.4651          | 9.21 ν(C2-C3) (36.) ν(C1-C6) (36.) -ν(C1-C6) (6.) ν(C1-C6) (5.) |
| 762.46               | 732.5716          | 14.35 ν(C2-H33) (17.) -ν(C1-C6) (13.) -δ(C8-C14-C16) (11.) |
| 743.29               | 714.153           | 86.47 δ(C8-C14-C16) (30.) (τ–R2) (12.) ν(C1-C2) (5.) ν(C4-H34) (5.) |
| 736.17               | 707.3121          | 33.27 ν(C2-H33) (26.) -ν(C2-H33) (30.) ν(C3-N4) (8.) -ν(C1-H32) (7.) ν(C4-H34) (6.) ν(C2-H33) (5.) ν(C1-C2) (5.) |
| 724.59               | 696.1861          | 12.74 ν(C4-H34) (29.) (τ–R2) (18.) ν(C1-C2) (12.) -ν(C3-N4) (7.) |
| 716.1                | 688.0289          | 23.91 δ(C8-C14-C16) (21.) ν(C2-H33) (17.) ν(C4-H34) (10.) ν(C2-H33) (9.) ν(C1-C6) (6.) ν(C1-C2) (5.) |
| 706.81               | 679.103           | 18.21 ν(C2-H33) (25.) ν(C4-H34) (13.) ν(C1-C6) (11.) -δ(C8-C14-C16) (10.) -ν(C4-C5) (7.) -ν(C1-H32) (5.) |
| 694.6                | 667.3717          | 57.73 ν(C2-H33) (18.) -ν(C1-C6) (11.) ν(C4-H34) (8.) -δ(C8-C14-C16) (7.) ν(C4-C5) (7.) -ν(C1-C6) (5.) -ν(C3-C4) (5.) -ν(C1-C2) (5.) (τ–R2) (5.) |
| 682.25               | 655.5058          | 667 5.28 ν(C2-H33) (53.) -ν(C1-H32) (32.) -ν(C2-H33) (7.) -ν(C1-C2) (7.) |
| 675.05               | 648.588           | 17.19 ν(C4-C5) (12.) -ν(C1-C2) (12.) -ν(C1-C2) (8.) -ν(C4-H34) (7.) ν(C3-N4) (6.) -ν(C2-H33) (5.) ν(C2-H33) (5.) |
| 666.38               | 640.2579          | 23.53 δ(C8-C14-C16) (28.) ν(C1-C2) (8.) ν(C1-C6) (5.) ν(C2-C3) (5.) -ν(C3-N4) (5.) 4ν(C2-H33) (5.) |
| 641.16               | 616.0265          | 2.66 ν(C2-C3) (14.) -ν(C1-C2) (13.) ν(C4-C5) (8.) ν(C1-H32) (8.) -δ(C8-C14-C16) (7.) ν(C4-C5) (5.) |
| 631.6                | 606.8413          | 2.74 ν(C1-C2) (9.) -ν(C4-H34) (7.) ν(C3-N4) (7.) -ν(C2-C3) (7.) -ν(C1-H32) (6.) ν(C2-C3) (6.) ν(C2-H33) (5.) -ν(C1-C2) (5.) (continued on next page)
\[ E(2) = \Delta E_{ij} = q_i \left( \frac{F_{ij}}{E_j - E_i} \right)^2 \]  

(1)

Where, \( q_i \) is occupancy of donor orbital; \( E_i \) and \( E_j \) are diagonal elements; \( F_{ij} \) is off-diagonal NBO Fock matrix element. The result of the calculations is tabulated in Table 7.

The results showed 22 consecutive high energy transitions in BCOPCA. A transition from \( \pi \) (C\(_1\)-C\(_6\)) to \( \pi^* \) (C\(_2\)-C\(_3\)) and (C\(_4\)-C\(_5\)) with stabilization energies of 18.03 and 22.22 kcal mol\(^{-1}\), and an intramolecular charge transfer from \( \pi \) (C\(_2\)-C\(_3\)) to \( \pi^* \) (C\(_1\)-C\(_6\)) and (C\(_4\)-C\(_5\)) with stabilisation energies of 21.25 and 18.36 kcal mol\(^{-1}\), designating the presence of conjugation in the phenyl ring attached to the nitrogen atom of pyrrolidine ring. An intramolecular charge transfer from \( \pi \) (C\(_8\)-C\(_14\)) to \( \pi^* \) (C\(_16\)-C\(_26\)) is seen with an energy of 17.7 kcal mol\(^{-1}\). The molecule also observed four transitions showing intramolecular charge transfer from \( \pi \) (C\(_16\)-C\(_26\)) to \( \pi^* \) (C\(_29\)-C\(_9\)), (C\(_8\)-C\(_14\)), (C\(_22\)-C\(_23\)) and (C\(_24\)-C\(_25\)) with stabilisation energies of 56.27, 21.23, 17.82 and 23.43.
Another intramolecular charge transfer is observed from $\pi$(C$_{17}$-C$_{18}$) to $\pi^*$ (C$_{19}$-C$_{20}$) with a stabilisation energies of 20.40 kcal mol$^{-1}$ and from $\pi$(C$_{19}$-C$_{20}$) to $\pi^*$ (C$_{17}$-C$_{18}$) with a stabilisation energies of 18.42. Charge transfers from $\pi$(C$_{22}$-C$_{23}$) to $\pi^*$ (C$_{16}$-C$_{26}$) and (C$_{24}$-C$_{25}$), from $\pi$(C$_{24}$-C$_{25}$) to $\pi^*$ (C$_{22}$-C$_{23}$) and from nonbonding orbital of O$_{30}$ to $\sigma^*$ (C$_{26}$-H$_{47}$) with stabilisation energies of 20.12, 18.68 kcal mol$^{-1}$, 20.18 and 37.82 kcal mol$^{-1}$ are also observed for BCOPCA. Two very high energy transitions from nonbonding orbital of O$_{30}$ and O$_{31}$ to $\sigma^*$ orbitals of (C$_{29}$-C$_{9}$) and (C$_{9}$-O$_{29}$) with stabilisation of 156.15 and 77.29 kcal mol$^{-1}$ are also present in BCOPCA. In BCOPCA charge transfer is also taking place from nonbonding orbital of O$_{12}$ to $\sigma^*$ of (C$_{10}$-C$_{11}$) and $\pi^*$ (C$_{10}$-C$_{13}$), (C$_{17}$-C$_{18}$) with stabilization energies of 19.88 and 77.03, 17.15 kcal mol$^{-1}$. The intramolecular charge transfer is observed from nonbonding orbital of Cl$_{27}$and$_{28}$ to $\sigma^*$ (C$_{19}$-C$_{20}$) and $\pi^*$ (C$_{24}$-C$_{25}$) with a stabilisation energies of 13.74 and 13.07 kcal mol$^{-1}$ respectively. A very high stabilization energy of 38.35 and 26.42 kcal mol$^{-1}$ is due to the charge transfer from nonbonding orbital of N$_{7}$ to $\pi^*$ (C$_{2}$-C$_{3}$) and (C$_{11}$-O$_{12}$). All these transitions are due to high delocalisation of bonds inside the molecular system.

### 3.9. Non-linear optical (NLO) analysis

NLO studies [52, 53] find wide applications in laser technology, optical communication, optical information processing. The results of these studies when performed on BCOPCA (tabulated in Table 8), revealed that the computed dipole moment, polarizability $\alpha_{tot}$ and first hyper polarizability [54] for the BCOPCA are found to be $3.832$ D, $66.30814 \times 10^{-24}$ and $19.477 \times 10^{-30}$ esu for B3LYP functional and $3.994$ D, $61.16037 \times 10^{-24}$ and $16.924 \times 10^{-30}$ esu for CAM-B3LYP functional.
Table 6. The Mulliken charge distribution calculated at B3LYP and CAM-B3LYP/6-31G (d,p) methods of BCOPCA.

| Atom no. | Atomic charges (Mulliken) | B3LYP/6-31 G (d,p) | CAM-B3LYP/6-31 G (d,p) |
|----------|--------------------------|---------------------|------------------------|
| C1       | -0.0984                  |                     | -0.112305              |
| C2       | -0.12148                 |                     | -0.133082              |
| C3       | 0.307709                 |                     | 0.298710               |
| C4       | -0.1131                  |                     | -0.124885              |
| C5       | -0.09443                 |                     | -0.109076              |
| C6       | -0.08815                 |                     | -0.108510              |
| N7       | -0.59224                 |                     | -0.596539              |
| C8       | 0.155754                 |                     | 0.160467               |
| C9       | -0.31508                 |                     | -0.319554              |
| C10      | 0.003882                 |                     | 0.006426               |
| C11      | 0.490942                 |                     | 0.506113               |
| O12      | -0.4566                  |                     | -0.466186              |
| C13      | -0.11424                 |                     | -0.100354              |
| C14      | -0.12482                 |                     | -0.114265              |
| C15      | 0.127164                 |                     | 0.103231               |
| C16      | 0.174044                 |                     | 0.152624               |
| C17      | -0.11282                 |                     | -0.117769              |
| C18      | -0.09507                 |                     | -0.109200              |
| C19      | -0.0881                  |                     | -0.092192              |
| C20      | -0.10377                 |                     | -0.116854              |
| C21      | -0.01027                 |                     | -0.015269              |
| C22      | -0.13217                 |                     | -0.140170              |
| C23      | -0.08157                 |                     | -0.094387              |
| C24      | -0.10668                 |                     | -0.113412              |
| C25      | -0.087                   |                     | -0.094325              |
| C26      | -0.14349                 |                     | -0.144029              |
| C27      | 0.00253                  |                     | -0.016928              |
| C28      | -0.00293                 |                     | 0.021647               |
| C29      | 0.56722                  |                     | 0.554144               |
| O30      | -0.50087                 |                     | -0.512658              |
| O31      | -0.46541                 |                     | -0.470745              |
| H32      | 0.090539                 |                     | 0.105410               |
| H33      | 0.123023                 |                     | 0.122702               |
| H34      | 0.089017                 |                     | 0.106571               |
| H35      | 0.088672                 |                     | 0.105458               |

(continued on next page)
3.10. Thermodynamical analysis

Statistical thermodynamic functions mainly heat capacity and entropy were calculated for the molecule at varying temperatures (100—500 K) and summarised in Table 9. The correlation graph between these thermodynamic measurements and temperatures (T) are shown in Figs. 11(a) and (b). The calculated fitting factors ($R^2$) are 0.998 and 1 for B3LYP and CAM-B3LYP/6-31G (d,p) hybrid functionals respectively. The zero point vibrational energy (ZPVEs), thermal energy, rotational constant, molar heat capacity, entropy and enthalpy at room temperature for

| Atom no. | B3LYP/6-31 G (d,p) | CAM-B3LYP/6-31 G (d,p) |
|----------|-------------------|------------------------|
| H36      | 0.083435          | 0.097917               |
| H37      | 0.206544          | 0.232032               |
| H38      | 0.122806          | 0.142620               |
| H39      | 0.112816          | 0.132991               |
| H40      | 0.096202          | 0.119416               |
| H41      | 0.10825           | 0.124519               |
| H42      | 0.111383          | −0.112305              |
| H43      | 0.075855          | −0.133082              |
| H44      | 0.086612          | 0.298710               |
| H45      | 0.106367          | −0.124885              |
| H46      | 0.140598          | −0.109076              |
| H47      | 0.242209          | −0.108510              |
| H48      | 0.335112          | 0.596539               |

Fig. 8. Mulliken charge distribution in BCOPCA.

Table 6. (Continued)
BCOPCA were obtained and indexed in Table 10 [55, 56]. It is obvious from our observations that the calculated ZPVE energy is lower in B3LYP (225.86 kcal mol$^{-1}$) than CAM-B3LYP (228.47 kcal mol$^{-1}$) method. However, the calculated molar heat and entropy were 83.392, 140.86 and 83.029, 140.093 cal mol$^{-1}$ k$^{-1}$ respectively at B3LYP and CAM-B3LYP/6-31G (d,p) hybrid functionals.

3.11. Reactivity descriptors

3.11.1. Global reactivity descriptors

Global reactivity descriptors such as electronegativity, chemical potential ($\mu$), global hardness ($\eta$), global softness ($S$), $\Delta$Nmax and electrophilicity index ($\omega$) have been calculated and listed in Table 11. Koopman’s theorem was used to confirm chemical reactivity and site selectivity for BCOPCA [56, 57, 58].
Table 7. Second order perturbation theory analysis of Fock matrix in NBO basis of BCOPCA.

| Doner (i) | Type | Acceptor (j) | Type | ED/e | E (2)* | (Ej-Ei)* | Fij* |
|-----------|------|--------------|------|------|--------|-----------|------|
| C1-C6     | π    | C2-C3        | π*   | 1.66 | 0.409  | 18.03     | 0.28  | 0.066 |
| C1-C6     | π    | C4-C5        | π*   | 1.66 | 0.33   | 22.22     | 0.28  | 0.07  |
| C1-C3     | π    | N7-C8        | π*   | 1.96 | 0.044  | 4.99      | 1.03  | 0.068 |
| C2-C3     | π    | C1-C6        | π*   | 1.62 | 0.34   | 21.25     | 0.29  | 0.07  |
| C2-C3     | π    | C4-C5        | π*   | 1.62 | 0.33   | 18.36     | 0.29  | 0.065 |
| C3-C4     | n    | N7-C11       | π*   | 1.96 | 0.119  | 5.23      | 1.02  | 0.067 |
| C4-C5     | π    | C1-C6        | π*   | 1.69 | 0.34   | 18.01     | 0.29  | 0.065 |
| C4-C5     | π    | C2-C3        | π*   | 1.69 | 0.409  | 21.69     | 0.28  | 0.072 |
| C8-C14    | π    | C14-C16      | π*   | 1.97 | 0.025  | 5.34      | 1.43  | 0.073 |
| C8-C14    | π    | C16-C26      | π*   | 1.97 | 0.04   | 17.7      | 0.33  | 0.074 |
| C9-C29    | σ    | C21-H43      | σ*   | 1.93 | 0.07   | 8.93      | 1.23  | 0.094 |
| C9-C29    | σ    | C26-H47      | σ*   | 1.93 | 0.14   | 38.41     | 1.34  | 0.206 |
| C9-H37    | σ    | C21-H43      | σ*   | 1.91 | 0.074  | 14.96     | 1.07  | 0.114 |
| C9-H37    | σ    | C29-O31      | π*   | 1.91 | 0.12   | 5.6       | 0.84  | 0.062 |
| C10-C13   | σ    | C11-O12      | π*   | 1.82 | 0.015  | 17.43     | 0.28  | 0.064 |
| C13-C15   | σ    | C10-C13      | π*   | 1.96 | 0.192  | 5.04      | 1.4   | 0.075 |
| C13-H38   | σ    | C9-C10       | π*   | 1.96 | 0.045  | 7.6       | 0.9   | 0.074 |
| C13-H38   | σ    | C15-C21      | π*   | 1.96 | 0.035  | 5.45      | 1.11  | 0.07  |
| C14-C16   | n    | N7-C8        | σ*   | 1.96 | 0.44   | 6.73      | 1.08  | 0.076 |
| C14-C16   | σ    | C8-C14       | π*   | 1.96 | 0.22   | 5.37      | 1.39  | 0.077 |
| C14-C16   | σ    | C16-C26      | π*   | 1.96 | 0.44   | 5.42      | 1.34  | 0.076 |
| C14-H39   | σ    | C8-H9        | σ*   | 1.96 | 0.049  | 7.58      | 0.9   | 0.074 |
| C14-H39   | σ    | C16-C26      | π*   | 1.96 | 0.44   | 5.48      | 1.12  | 0.07  |
| C15-C21   | π    | C13-C15      | π*   | 1.96 | 0.024  | 5.11      | 1.35  | 0.074 |
| C16-C26   | π    | C14-C16      | π*   | 1.96 | 0.025  | 5.28      | 1.35  | 0.076 |
| C16-C26   | π    | C29-C9       | π*   | 1.58 | 0.121  | 56.27     | 1.1   | 0.071 |
| C16-C26   | π    | C8-C14       | π*   | 1.58 | 0.22   | 21.23     | 0.28  | 0.065 |
| C16-C26   | π    | C22-C23      | π*   | 1.58 | 0.3    | 17.82     | 0.28  | 0.073 |
| C17-C18   | π    | C19-C20      | π*   | 1.68 | 0.37   | 20.4      | 0.27  | 0.067 |
| C19-C20   | π    | C17-C18      | π*   | 1.66 | 0.014  | 18.42     | 0.3   | 0.067 |
| C21-C43   | σ    | C8-C9        | σ*   | 1.92 | 0.049  | 6.66      | 0.91  | 0.07  |
| C22-C23   | π    | C16-C26      | π*   | 1.68 | 0.44   | 20.12     | 0.29  | 0.07  |
| C22-C23   | π    | C24-C25      | π*   | 1.68 | 0.377  | 18.68     | 0.27  | 0.06  |
| C24-C25   | π    | C16-C26      | π*   | 1.68 | 0.44   | 15.71     | 0.31  | 0.064 |
| C24-C25   | π    | C22-C23      | π*   | 1.68 | 0.44   | 20.18     | 0.3   | 0.07  |
| C29-O30   | n    | C26-H47      | σ*   | 1.95 | 0.14   | 37.82     | 1.73  | 0.235 |

(continued on next page)
3.11.2. Local reactivity descriptors

Local reactivity descriptors such as softness (Sk), Fukui Function (FF) and electrophilicity index (\(\omega_k\)) \([59, 60]\) were enumerated in Table 12. Local softnesses (\(s_k^+\)), \(s_k^-\), \(s_k^0\)) and electrophilicity indices (\(\omega_k^+\), \(\omega_k^-\), \(\omega_k^0\)) are described with the help of following equations.

\[
s_k^+ = S_f K, \quad s_k^- = S_f K, \quad s_k^0 = S_f K
\]

\[
\omega_k^+ = \omega_f K, \quad \omega_k^- = \omega_f K, \quad \omega_k^0 = \omega_f K
\]

Where +, −, 0 signs show attack of nucleophile, electrophile and radical.

The observed values at C2, C6, C19, C23 and C25 showed that these sites are more liable to nucleophilic attack whereas the relatively enhanced values at H48, C29, O30, O31 suggested that these sites are accountable for attack of electrophiles. These explorations are helpful enough to provide more information about the chemical reactivity of the molecule.

Table 7. (Continued)

| Donor (i) | Type | ED/e | Acceptor (j) | Type | ED/e | E (2)\(^a\) | (Ej-Ei)\(^b\) | Fij\(^c\) |
|-----------|------|------|-------------|------|------|-----------|-------------|--------|
| O31-H48   | n    | 1.98 | C29-O30     | π*   | 0.04 | 8.61      | 1.31        | 0.096  |
| LP (1) N7 | n    | 1.62 | C2-C3       | π*   | 0.4  | 38.35     | 0.3         | 0.097  |
| LP (1) N7 | n    | 1.62 | C11-O12     | π*   | 0.24 | 26.42     | 0.26        | 0.076  |
| LP (1) O12| n    | 1.97 | N7-C11      | σ*   | 0.119| 34.24     | 0.6         | 0.129  |
| LP (2) O12| n    | 1.83 | C10-C11     | σ*   | 0.072| 19.88     | 0.66        | 0.105  |
| LP (1) C15| n    | 1.04 | C10-C13     | π*   | 0.192| 77.03     | 0.14        | 0.12   |
| LP (1) C15| n    | 1.04 | C17-C18     | π*   | 0.29 | 17.15     | 0.13        | 0.106  |
| LP (1) O12| n    | 0.93 | C19-C20     | π*   | 0.37 | 78.68     | 0.12        | 0.108  |
| LP (3) C127| π | 1.91 | C19-C20     | σ*   | 0.37 | 13.74     | 0.34        | 0.066  |
| LP (1) C128| π | 1.92 | C24-C25     | π*   | 0.37 | 13.07     | 0.34        | 0.065  |
| LP (1) O30 | n    | 1.94 | C16-C26     | π*   | 0.049| 5.47      | 1.32        | 0.076  |
| LP (1) O30 | n    | 1.94 | C21-H43     | σ*   | 0.074| 5.1       | 0.82        | 0.06   |
| LP (2) O30 | n    | 1.75 | C26-H47     | σ*   | 0.14 | 22.1      | 0.92        | 0.131  |
| LP (2) O30 | n    | 1.75 | C29-C9      | σ*   | 0.04 | 156.15    | 0.14        | 0.147  |
| LP (3) O30 | n    | 1.75 | C16-C26     | π*   | 0.04 | 6.32      | 0.89        | 0.071  |
| LP (2) O30 | n    | 1.75 | C26-H47     | σ*   | 0.14 | 5.95      | 0.92        | 0.068  |
| LP (1) O31 | n    | 1.96 | C9-C29      | σ*   | 0.092| 7.59      | 0.95        | 0.077  |
| LP (2) O31 | n    | 1.79 | C9-C29      | σ*   | 0.049| 77.29     | 0.21        | 0.13   |

\(^a\) Energy of hyperconjugative interactions (Kcal/mol).

\(^b\) Energy difference between donor and acceptor i and j NBO orbitals in a.u.

\(^c\) The Fock matrix elements between i and j NBO orbitals in a.u.
3.12. Atom In molecule (AIM) approach

The molecular graph of compound BCOPCA at B3LYP/6-31G (d, p) hybrid functionals is presented in Fig. 12 with help of AIM program. The strong, medium, weak H-bonds and their covalent, partially covalent and electrostatic nature can be denoted by \( V_2(r) < 0 \) and \( H_{BCP} < 0 \) and \( V_2(r) > 0 \) and \( H_{BCP} > 0 \) \[61\]. \( r_{BCP} \) and \( H_{BCP} \) are Laplacian of electron density and total electron density at bond critical point respectively. The various bond interactions and their values are provided in Table 13 and indicated that C2-H24⋯O12 and C19-H41⋯O12 are weak interactions having

![Table 8. Dipole Moment \( \mu \), Polarizability \( \alpha_{tot} \times 10^{-24} \)esu and first order static hyperpolarizability \( \beta_{tot} \times 10^{-30} \) data of BCOPCA.](image)

| Dipole moment | B3LYP-6-31G (d,p) | CAM-B3LYP-6-31G (d,p) | Hyperpolarisability | B3LYP 6-31G (d,p) | CAM-B3LYP-6-31G (d,p) |
|---------------|------------------|------------------------|---------------------|------------------|------------------------|
| \( \mu_x \)   | -3.662           | -3.828                 | \( \beta_{xxx} \)   | -2.94566         | -18.1538               |
| \( \mu_y \)   | -1.028           | -1.081                 | \( \beta_{xyy} \)   | -3.74721         | 1.572093               |
| \( \mu_z \)   | 0.465            | 0.366                  | \( \beta_{zzz} \)   | 15.26366         | 9.189278               |
| \( \mu \)     | 3.832            | 3.994                  | \( \beta_{yy} \)    | -4.18332         | -2.02151               |

Polarizability

| \( \alpha_{xx} \) | 94.94433         | 86.27759               | \( \beta_{xx} \)    | -17.1825         | -10.3637               |
| \( \alpha_{xy} \) | 0.236824         | 0.337451               | \( \beta_{xy} \)    | 4.443019         | 3.289241               |
| \( \alpha_{yy} \) | 71.67693         | 67.41914               | \( \beta_{yy} \)    | 4.662803         | -3.53805               |
| \( \alpha_{zz} \) | 2.720952         | 3.09738                | \( \beta_{zz} \)    | -0.31326         | -0.94099               |
| \( \alpha_{xz} \) | 6.916494         | 68.98265               | \( \beta_{xz} \)    | -0.81097         | -0.68121               |
| \( \alpha_{yz} \) | 32.30315         | 31.58438               | \( \beta_{yz} \)    | -0.08346         | 0.225054               |
| \( \alpha \)     | 66.30814         | 61.76037               | \( \beta_{total} \) | 19.477           | 16.924                 |

3.12. Atom In molecule (AIM) approach

The molecular graph of compound BCOPCA at B3LYP/6-31G (d, p) hybrid functionals is presented in Fig. 12 with help of AIM program. The strong, medium, weak H-bonds and their covalent, partially covalent and electrostatic nature can be denoted by \( \nabla^2\rho(BCP) < 0 \) and \( H_{BCP} < 0 \), \( \nabla^2\rho(BCP) > 0 \) and \( H_{BCP} > 0 \) \[61\]. \( \rho(BCP) \) and \( H_{BCP} \) are Laplacian of electron density and total electron density at bond critical point respectively. The various bond interactions and their values are provided in Table 13 and indicated that C2-H24⋯O12 and C19-H41⋯O12 are weak interactions having

![Table 9. Thermodynamic functions at different temperatures of BCOPCA employing B3LYP and CAM-B3LYP/6-31 G (d,p) methods.](image)

| Temperature (T) (K) | B3LYP-6-31-G (d,p) | CAM-B3LYP-6-31-G (d,p) |
|---------------------|-------------------|------------------------|
|                     | Heat capacity (CV) (Cal/mol K) | Entropy (S) (Cal/Mol K) | Heat capacity (CV) (Cal/mol K) | Entropy (S) (Cal/Mol K) |
| 100                 | 26.74             | 86.85                  | 27.35             | 87.48                  |
| 200                 | 54.27             | 115.05                 | 54.74             | 116.07                 |
| 298                 | 83.02             | 142.86                 | 83.39             | 144.04                 |
| 300                 | 83.56             | 143.39                 | 83.93             | 144.57                 |
| 400                 | 111.1             | 171.86                 | 111.54            | 173.15                 |
| 500                 | 134.49            | 199.69                 | 135.08            | 201.1                  |
\( \nabla^2 \text{(BCP)} \) and \( H_{\text{BCP}} \) values greater than zero. The total energy of intramolecular interaction was 0.0903 kcal mol\(^{-1}\) as calculated with the help of AIM. There is delocalization of \( \pi \) electrons in aromatic ring as shown by the lower values of ellipticity [62].

**Table 10.** Calculated thermodynamic parameters of BCOPCA employing B3LYP and CAM-B3LYP/6-31 G (d,p) methods.

| Parameters                             | B3LYP/6-31 G (d,p) | CAM-B3LYP/6-31 G (d,p) |
|----------------------------------------|--------------------|------------------------|
| Zero-point vibrational energy (Kcal/mol) | 225.86             | 228.47                 |
| Rotational temperatures (K)            | 0.00704            | 0.00704                |
|                                        | 0.00482            | 0.00482                |
|                                        | 0.00315            | 0.00315                |
| Rotational constants (GHZ)             |                    |                        |
| X                                      | 0.14672            | 0.14672                |
| Y                                      | 0.10047            | 0.10047                |
| Z                                      | 0.06559            | 0.06559                |
| Thermal energy (Kcal/mol)              |                    |                        |
| Total                                  | 238.10             | 240.85                 |
| Translational                          | 0.889              | 0.889                  |
| Rotational                             | 0.889              | 0.889                  |
| Vibrational                            | 236.32             | 239.07                 |
| Molar capacity at constant volume (cal mol\(^{-1}\) k\(^{-1}\)) | | |
| Total                                  | 83.392             | 83.029                 |
| Translational                          | 2.9810             | 2.9810                 |
| Rotational                             | 2.9810             | 2.9810                 |
| Vibrational                            | 77.438             | 77.068                 |
| Entropy (cal mol\(^{-1}\) k\(^{-1}\))  |                    |                        |
| Total                                  | 140.86             | 140.093                |
| Translational                          | 40.192             | 44.196                 |
| Rotational                             | 37.054             | 37.052                 |
| Vibrational                            | 61.627             | 62.804                 |

**Fig. 11.** (a) & (b) Correlation graphs of heat capacity and entropy calculated at various temperatures using B3LYP and CAM-B3LYP/6-31G (d,p) of BCOPCA.
3.13. Evaluation of antimicrobial activity

The in-vitro antimicrobial activity of BCOPCA was studied using the disc diffusion method with different strains of bacteria [Salmonella typhi (St, MTCC 537), Klebsiella pneumonia (Kp, MTCC 661), Pseudomonas aeruginosa (Pa, MTCC 424)] [63]. Chloroform was used as negative control and Vancomycin was used as standard drug. The zone of inhibition (mm) results showed that compound showed a good bactericidal activity against Salmonella typhi, Klebsiella pneumonia and Pseudomonas aeruginosa where the diameter of zone of inhibition was 12, 10 and 9.5 mm etc.

3.14. Molecular docking studies

In modern drug designing, molecular docking, which predicts the preferred orientation of one molecule to a second when bound to each other to form a stable complex, is an important tool for understanding drug-receptor interaction. The molecular docking study of BCOPCA was also carried out in the present article to come up with the rationale for the biological activity. All in silico docking experiment were carried out the using Auto Dock version 4.2 [64, 65]. Crystal structure of 3-Dehydroquinase from Salmonella typhi (PDB ID: 1GQN), Pyridoxal kinase (PDBID: 5B6A) from Pseudomonas aeruginosa and Dihydrofolate reductase enzyme from Klebsiella pneumonia (PDBID: 4oR7) for the docking studies was downloaded from Protein Data Bank (http://www.rcsb.org/pdb).
Table 12. Fukui functions ($f_k^+$, $f_k^-$), Local softnesses ($sk^+$, $sk^-$) in eV, local electrophilicity indices ($\omega_k^+$, $\omega_k^-$) in eV for specific atomic sites of BCOPCA.

| Atoms | $q_N$ | $q_{N+1}$ | $q_{N-1}$ | $f_k^+$ | $f_k^-$ | $sk^+$ | $sk^-$ | $\omega_k^+$ | $\omega_k^-$ |
|-------|-------|-----------|-----------|---------|---------|--------|--------|-------------|-------------|
| 1 C   | −0.00786 | −0.02542 | 0.033475 | −0.01756 | −0.04134 | −0.00453 | −0.01065 | −0.06428 | −0.15133 |
| 2 C   | 0.001539 | 0.048247 | 0.037914 | 0.046708 | −0.03638 | 0.01204 | −0.00937 | 0.170984 | −0.13316 |
| 3 C   | 0.307709 | 0.009798 | 0.306242 | −0.29791 | 0.001467 | −0.0768 | 0.000378 | −1.09056 | 0.00537 |
| 4 C   | −0.02409 | 0.050011 | −0.0047 | 0.074098 | −0.01939 | 0.019101 | −0.005 | 0.271251 | −0.07097 |
| 5 C   | −0.00575 | −0.02706 | 0.031592 | −0.0213 | −0.03735 | −0.00549 | −0.00962 | −0.07799 | −0.13671 |
| 6 C   | −0.00471 | 0.080973 | 0.055309 | 0.085687 | −0.06002 | 0.022088 | −0.01547 | 0.313674 | −0.21973 |
| 7 N   | −0.59224 | 0.102799 | −0.57026 | 0.695039 | −0.02198 | 0.179167 | −0.00566 | 2.544329 | −0.08047 |
| 8 C   | 0.155754 | −0.04326 | 0.153809 | −0.19901 | 0.001945 | −0.0513 | 0.000501 | −0.72853 | 0.00712 |
| 9 C   | −0.10853 | 0.003445 | −0.09773 | 0.111976 | −0.01081 | 0.028865 | −0.00278 | 0.409911 | −0.03956 |
| 10 C  | 0.003882 | 0.062521 | 0.002279 | 0.058639 | 0.001603 | 0.015116 | 0.000413 | 0.21466 | 0.005868 |
| 11 C  | 0.490942 | −0.01266 | 0.503595 | −0.5036 | −0.01265 | −0.12982 | −0.00326 | −1.84354 | −0.04632 |
| 12 O  | −0.4566 | −0.01315 | −0.42393 | 0.443457 | −0.03267 | 0.114314 | −0.00842 | 1.623363 | −0.1196 |
| 13 C  | 0.008565 | 0.002923 | 0.069755 | −0.00564 | −0.06119 | −0.00145 | −0.01577 | −0.02065 | −0.224 |
| 14 C  | −0.01201 | 0.071771 | 0.051188 | 0.083779 | −0.0632 | 0.021597 | −0.01629 | 0.30669 | −0.23134 |
| 15 C  | 0.127164 | 0.042609 | 0.134058 | −0.08456 | −0.00689 | −0.0218 | −0.00178 | −0.30953 | −0.02524 |
| 16 C  | 0.174044 | −0.01827 | 0.173628 | −0.19232 | 0.000416 | −0.04957 | 0.000107 | −0.70401 | 0.001523 |
| 17 C  | −0.01662 | −0.02564 | 0.028202 | −0.00903 | −0.04482 | −0.00233 | −0.01155 | −0.03305 | −0.16406 |

(continued on next page)
| Atoms | $q_N$ | $q_{N+1}$ | $q_{N-1}$ | $f_k^+$ | $f_k^-$ | $s_k^+$ | $s_k^-$ | $\omega_k^+$ | $\omega_k^-$ |
|-------|-------|---------|---------|--------|--------|--------|--------|----------|----------|
| 18 C  | 0.013185 | 0.043672 | 0.070556 | 0.030487 | -0.05737 | 0.007859 | -0.01478 | 0.111604 | -0.21002 |
| 19 C  | -0.0881 | -0.00617 | -0.08513 | 0.081928 | -0.00297 | 0.021119 | -0.00077 | 0.29914 | -0.01088 |
| 20 C  | 0.007614 | -0.00083 | 0.031913 | -0.00845 | -0.0243 | -0.00218 | -0.00626 | -0.03092 | -0.08895 |
| 21 C  | 0.065587 | 0.054414 | 0.040768 | -0.01117 | 0.024819 | -0.00288 | 0.006396 | -0.0409 | 0.090855 |
| 22 C  | -0.04556 | 0.075571 | 0.020497 | 0.121129 | -0.06606 | 0.031225 | -0.01702 | 0.443417 | -0.24181 |
| 23 C  | 0.024794 | -0.03624 | 0.085728 | -0.06103 | -0.06093 | -0.01573 | -0.0157 | -0.22341 | -0.22306 |
| 24 C  | -0.10668 | 0.052009 | -0.10027 | 0.158684 | -0.0064 | 0.040906 | -0.00165 | 0.580895 | -0.02343 |
| 25 C  | 0.053594 | -0.00012 | 0.098318 | -0.05372 | -0.04472 | -0.01385 | -0.01153 | -0.19663 | -0.16372 |
| 26 C  | -0.14349 | 0.138092 | -0.15236 | 0.281579 | 0.008868 | 0.072585 | 0.002285 | 1.030776 | 0.032463 |
| 27 C  | 0.00253 | 0.001909 | 0.069687 | -0.00062 | -0.06716 | -0.00016 | -0.01731 | -0.00227 | -0.24584 |
| 28 Cl | -0.00293 | 0.012659 | 0.081015 | 0.015591 | -0.08395 | 0.004019 | -0.02163 | 0.057074 | -0.3073 |
| 29 C  | 0.809429 | 0.021538 | 0.848196 | -0.78789 | -0.03877 | -0.2031 | -0.00999 | -2.88423 | -0.14191 |
| 30 O  | -0.50087 | 0.340429 | -0.40777 | 0.841299 | -0.0931 | 0.21687 | -0.02399 | 3.079743 | -0.34082 |
| 31 O  | -0.1303 | -0.00657 | -0.08558 | 0.123728 | -0.04471 | 0.031895 | -0.01152 | 0.452931 | -0.16368 |
The purpose of taking type I DHQase (3-Dehydroquinase), as a target molecule is due to the fact that the shikimate pathway for the biosynthesis of aromatic amino acids (Phenylalanine, Tyrosine and tryptophan), is absent in mammals. Pyridoxal kinase is an essential enzyme for Pyridoxal 5'-phosphate (PLP) homeostasis since PLP is required for the catalytic activity of a variety of PLP-dependent enzymes involved in amino acid, lipid, and sugar metabolism as well as neurotransmitter biosynthesis. Dihydrofolate reductase enzyme is taken as target molecule because the resistance to the antibacterial antifolate trimethoprim (TMP) is increasing in members of the family Enterobacteriaceae including *Klebsiella pneumoniae*.

Hydrogen atoms and Kollman charges were added and water molecules were removed from the molecule to execute the docking operations. The B3LYP/6-31G (d,p) functional of theory set was used to prepare minimum energy ligand for docking. Auto Dock requires pre-calculated grid maps. This grid must to include residues of the active site. In the present study the grid size was 60 Å × 60 Å × 60 Å.

**Table 13.** Topological parameters for intramolecular interactions in compound electron density ($\rho_{BCP}$), Laplacian of electron density ($\nabla^2 \rho_{BCP}$), electron kinetic energy density ($G_{BCP}$), electron potential energy density ($V_{BCP}$), total electron energy density ($H_{BCP}$), Hydrogen bond energy ($E_{HB}$) at bond critical point (BCP).

| Interactions | $\rho_{BCP}$ | $\nabla^2 \rho_{BCP}$ | $G_{BCP}$ | $V_{BCP}$ | $H_{BCP}$ | $E_{HB}/(\text{Elipticity})$ |
|--------------|---------------|-------------------|----------|-----------|----------|-----------------------------|
| C21—H43…O30 | 0.013730      | 0.040154          | 0.009933 | −0.009828 | 0.009734 | 0.063524                   |
| C26—H47…O30 | 0.011629      | 0.036157          | 0.008547 | −0.007975 | 0.016153 | 0.253943                   |
| C31—H48…N7  | 0.012850      | 0.041625          | 0.009642 | −0.008877 | 0.032226 | 0.430191                   |
| C9—H37…H47  | 0.008698      | 0.036508          | 0.006843 | −0.004559 | 0.567843 | 0.611709                   |

$\rho_{BCP}$, $\nabla^2 \rho_{BCP}$, $G_{BCP}$, $V_{BCP}$, $H_{BCP}$ in a.u. and $E_{HB}$ in (kcal/mol).
Lamarckian Genetic Algorithm (LGA) available in Auto Dock was employed for docking. The obtained docking results are stated as correct when the root mean square deviation (RMSD) value is smaller than 2 Å [66]. RMSD is used to estimate the average distance or deviation from the active site of the ligand and most important criterium for the docking results. The binding energy was taken into consideration after the RMSD values, as the molecule may also give lower binding energy with a place other than the active region. UCSF Chimera 1.10.2 program was employed to accomplish graphical representations of the docked pose. The ligand binds at the active site of the protein by H-bonding. Out of 10 conformations acquired by docking into the active site of 3-Dehydroquinase, Pyridoxal kinase and Dihydrofolate reductase, the best conformation was chosen depending on the RMSD value and

Fig. 13. (a) Schematic representation for the docked conformation at active site of the bacterial enzyme 3-Dehydroquinase (PDB ID: 1GQN) from *Salmonella typhi* with BCOPCA. (b) Schematic representation for the docked conformation at active site of the bacterial enzyme Pyridoxal kinase (PDBID: 5B6A) from *Pseudomonas aeruginosa* with BCOPCA. (c) Schematic representation for the docked conformation at active site of the bacterial enzyme Dihydrofolate reductase (PDBID: 4oR7) enzyme from *Klebsiella pneumonia* with BCOPCA.
binding energy. The ligand-target interaction of BCOPCA to 3-Dehydroquinase, Pyridoxal kinase and Dihydrofolatereductase binding site is depicted in Fig. 13(a–c). The hydrogen bond interactions and binding energy of compound to 3-Dehydroquinase, Pyridoxal kinase and Dihydrofolatereductase are presented in Table 14. Out of all docked conformations, the conformation well bonded to the active site, was chosen for detailed interactions. The docking output inferred that BCOPCA could compactly occupy the active sites of 3-Dehydroquinase, Pyridoxal kinase and Dihydrofolatereductase with binding energy $-2.26$, $-6.15$ and $-8.47$ kcal/mol respectively.

**Estimated Free Energy of Binding for compound with 3-Dehydroquinase = $-2.26$ kcal mol$^{-1}$ [= (1) + (2) + (3)-(4)]**

(1) Final Intermolecular Energy = $-2.99$ kcal mol$^{-1}$
   vdw + Hbond + desolv Energy = $-2.41$ kcal mol$^{-1}$
   Electrostatic Energy = $-0.58$ kcal mol$^{-1}$
(2) Final Total Internal Energy = $-0.64$ kcal mol$^{-1}$
(3) Torsional Free Energy = $+1.37$ kcal mol$^{-1}$
(4) Unbound System’s Energy = $+0.00$ kcal mol$^{-1}$

**Estimated Free Energy of Binding for compound with Pyridoxal kinase = $-6.15$ kcal mol$^{-1}$ [= (1) + (2) + (3)-(4)]**

(1) Final Intermolecular Energy = $-7.11$ kcal mol$^{-1}$
   vdw + Hbond + desolv Energy = $-7.14$ kcal mol$^{-1}$
   Electrostatic Energy = $+0.03$ kcal mol$^{-1}$
(2) Final Total Internal Energy = $-0.41$ kcal mol$^{-1}$
(3) Torsional Free Energy = $+1.37$ kcal mol$^{-1}$
(4) Unbound System’s Energy = $+0.00$ kcal mol$^{-1}$

**Table 14.** Hydrogen bond interactions of BCOPCA with target 3-Dehydroquinase from *Salmonella typhi* (PDB ID: 1GQN), Pyridoxal kinase (PDBID: 5B6A) from *Pseudomonas aeruginosa* and dihydrofolatereductase enzyme from *Klebsiella pneumoniae* (PDBID: 4oR7).

| Macromolecular target | Compound | Bonded residue…Ligand atom | No. of hydrogen bonds | Bond distance (Å) | Inhibition constant (µM) | Binding energy Kcal/mol |
|-----------------------|----------|-----------------------------|-----------------------|-------------------|---------------------------|-------------------------|
| 1GQN                  | ARG 48…OH | 1                           | 2.690                 | 21940             | $-4.71$                   |
| 5B6A                  | ASN 148 A…OH | 1                       | 3.554                 | 31.09             | $-6.15$                   |
| 4oR7                  | SER 49.A…O=C | 1                        | 3.427                 | 0.6196            | $-8.47$                   |
Estimated Free Energy of Binding for compound with Dihydrofolatereductase
\[ = -8.47 \text{ kcal mol}^{-1} \]  

(1) Final Intermolecular Energy = $-9.13 \text{ kcal mol}^{-1}$  
\[ \text{vdW} + \text{Hbond} + \text{desolv Energy} = -9.51 \text{ kcal mol}^{-1} \]  
\[ \text{Electrostatic Energy} = +0.38 \text{ kcal mol}^{-1} \]

(2) Final Total Internal Energy = $-0.71 \text{ kcal mol}^{-1}$

(3) Torsional Free Energy = $+1.37 \text{ kcal mol}^{-1}$

(4) Unbound System’s Energy = $+0.00 \text{ kcal mol}^{-1}$

All the three enzymes showed only one hydrogen bond interaction with the best docked conformation of compound. The residue ARG 48 of 3-Dehydroquinase from *Salmonella typhi*, residue ASN 148 A of Pyridoxal kinase (PDBID: 5B6A) from *Pseudomonas aeruginosa* has hydrogen bond interactions with the hydroxyl O atom of ligand at a distance of 2.690 Å and 3.554 Å respectively and residues SER 49 Å of Dihydrofolatereductase enzyme from *Klebsiella pneumonia*, has hydrogen bond interactions with the carbonyl oxygen atom of ligand at a distance of 3.427 Å.

It is a well known fact that, if the number of interactions is greater in the docked complex, it will enrich the bioactivity of the compound but the noteworthy part is that one hydrogen bond interaction was obtained with all three enzymes. Compound may be deemed as a capable inhibitor of 3-Dehydroquinase as compared to Pyridoxal kinase (PDBID: 5B6A) and Dihydrofolatereductase enzyme due to small distance of ligand–residue interaction which was also confirmed by experimental results.

### 4. Conclusions

The present study gives a detailed account for spectral and computational characterisation of BCOPCA. The complete vibrational analysis of novel (2Z,4Z)-2,4-bis(4-chlorobenzylidene)-5-oxo-1-phenylpyrrolidine-3-carboxylic acid was performed on two different hybrid functionals (B3LYP and CAM-B3LYP6-31G (d,p)). The observed and calculated wavenumbers agreed with each other. The stabilization energy and the calculated HOMO and LUMO energies indicated charge transfer in the molecule, which in turn indicated its bioactive properties. The title compound depicted $n \rightarrow \pi^* \text{HOMO-1}$ to LUMO+1 with 63% and $\pi \rightarrow \pi^* \text{HOMO-2}$ to LUMO with 53% contribution.

The chemical shift values, obtained by GIAO NMR calculations were in good agreement with experimental data. The results of the fundamental vibrational frequencies, calculated with the help of PED, were found satisfactory. The sites of chemical
reactivity and charge density distribution of BCOPCA were ascertained by mapping molecular electrostatic potential surface (MESP) and electrostatic potential surface (ESP) contour surface. The MEP and ESP values 7.648 a.u. and −7.648 a.u. indicated that C11, O12 and C47, O30 are most preferred sites for electrophilic and nucleophilic attack. The delocalisation of π electrons in the aromatic ring is shown by the lower values of ellipticity and four feeble hydrogen bonds were explored by AIM approach. IR showed good agreement between experimental and calculated value. Mulliken charge distribution confirmed the enhanced value of charge on H48 that can be accounted to hydrogen bonding. Molecular docking studies using in-silico analysis were done to access the interactions of BCOPCA with 3-Dehydroquinase (PDB ID: 1GQN), Pyridoxal kinase (PDBID: 5B6A) and Dihydrofolate reductase (PDBID: 4oR7) enzymes from Salmonella typhi, Pseudomonas aeruginosa and Klebsiella pneumonia and matched well with the in vitro antibacterial activity.

**Declarations**

**Author contribution statement**

Poornima Devi: performed the experiments.

Shaheen Fatma, Shraddha Shukla, Roop Kumar, Vineeta Singh: contributed reagents, materials, analysis tools or data.

Abha Bishnoi: conceived and designed the experiments; wrote the paper.

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**Competing interest statement**

The authors declare no conflict of interest.

**Additional information**

No additional information is available for this paper.

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