Research Article

Spectroscopic Investigations, DFT Calculations, and Molecular Docking Studies of the Anticonvulsant (2E)-2-[3-(1H-Imidazol-1-yl)-1-phenylpropylidene]-N-(4-methylphenyl)hydrazinecarboxamide

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Drug discovery for the management of neurological disorders is a challenging arena in medicinal chemistry. Vibrational spectral studies of (2E)-2-[3-(1H-imidazol-1-yl)-1-phenylpropylidene]-N-(4-methylphenyl)hydrazinecarboxamide ((2E)-IPPMP) have been recorded and analyzed to identify the functional groups and intermolecular/intramolecular interactions of the title molecule. The blue shift of the C-H stretching wavenumber reveals the presence of improper C-H...O hydrogen bonding. The equilibrium geometry, harmonic vibrational wavenumbers, Frontier orbital energy, and natural bond orbital analyses have been carried out using density functional theory with a B3LYP/6-311++G(d,p) level of the basis set. The vibrational modes have been unambiguously assigned using potential energy distribution analysis. The scaled wavenumbers are in good agreement with the experimental results. Natural bond orbital analysis has confirmed the intermolecular/intramolecular charge transfer interactions. HOMO-LUMO analysis was carried out to explore charge delocalization on the (2E)-IPPMP molecule. A molecular docking study has supported the anticonvulsant activity of the title molecule.

1. Introduction

Epilepsy is a rather neurobiological group of disorders. It has multiple origins and aspects depending upon the affected brain areas. It affects nearly 50 million people of the world's population [1–3]. The hydrazinecarboxamide derivatives have a wide spectrum of biological activities. Among these activities are anticancer and antioxidant [4], antifertility [5], antimicrobial [6, 7], anticonvulsant [8, 9], and anti-inflammatory [10] activities. The title molecule (2E)-2-[3-(1H-imidazol-1-yl)-1-phenyl-propylidene]-N-(4-methylphenyl)hydrazinecarboxamide ((2E)-IPPMP) was synthesized in our

laboratory and its crystal structure was previously reported [11]. (2E)-IPPMP exhibited anticonvulsant activity with 83% and 50% seizure protection at a dose level of 718 $\mu\text{mol/kg}$ in subcutaneous pentylenetetrazole (scPTZ) and maximal electroshock seizure (MES) screens, respectively, without any neurotoxicity [9].

Literature screening indicated that computational studies on the (2E)-IPPMP molecule have not yet been reported. Therefore, detailed investigations of structural properties and vibrational spectral analysis of the (2E)-IPPMP molecule were carried out in the present study using density functional theory (DFT) computations. Moreover, the biological

SCHEME 1: Synthesis of the title molecule (2E)-IPPMP. Reagents and conditions: (i) $\text{HN}(\text{CH}_3)_2 \cdot \text{HCl}$, $(\text{CH}_2\text{O})_n$, conc. HCl , ethanol, reflux, 2 h; (ii) imidazole, water, reflux, 5 h; (iii) *N*-(4-methylphenyl)hydrazinecarboxamide, few drops of acetic acid, ethanol, RT, 18 h.

activity of the title molecule has been predicted by molecular docking analysis. It is expected that the current investigations might support the development of new potent anticonvulsant agents.

2. Experimental

2.1. General. Melting point was recorded on a Gallenkamp melting point instrument and it is uncorrected. The Fourier transform infrared spectrum of MMIMI was recorded on a Perkin Elmer RXL spectrometer (Waltham, Massachusetts, USA) in the region $4000\text{--}400\text{ cm}^{-1}$, with samples in the KBr pellet method. The resolution of the spectrum was 2 cm^{-1} . The FT-Raman spectrum was measured in the range $3500\text{--}50\text{ cm}^{-1}$ using a Bruker RFS 100/S FT-Raman spectrophotometer (Ettlingen, Germany) with a 1064 nm Nd:YAG laser source of 100 mW power (Göttingen, Germany).

2.2. Synthesis. A solution containing *N*-(4-methylphenyl)hydrazinecarboxamide [12] (1.65 g, 10 mmol), 3-(1*H*-imidazol-1-yl)-1-phenylpropan-1-one (2.00 g, 10 mmol) [13], and a few drops of glacial acetic acid in ethanol (15 mL) was stirred at room temperature for 18 h. The reaction mixture was evaporated under reduced pressure and the residue was crystallized from ethanol to give 1.67 g (48%) of the title compound as colorless crystals (m.p. 476–478 K) which were suitable for single crystal X-ray analysis. ^1H and ^{13}C NMR as well as the mass spectral data of the title compound 2 are in accordance with the previously reported ones [9].

2.3. Theoretical Calculations. All DFT calculations of the (2E)-IPPMP molecule were performed using the Gaussian 09 program package [14] at the Becke3-Lee-Yang-Parr (B3LYP) level with a 6-311++G(d,p) basis set [15–17]. The structural parameters were computed in the gas phase as well as in the liquid phase using a polarizable continuum model (PCM) method. In order to correct the overestimations arising from some negative factors such as basis set truncation effect, neglecting electron correlations, and anharmonicity characters of the vibrational modes, the calculated wavenumbers were scaled using a uniform scaling factor of 0.9673 [18, 19]. Theoretical NMR calculation was performed on the basis of the GIAO (gauge-independent atomic orbitals) theory method using a Gaussian program.

FIGURE 1: Optimized structure of (2E)-IPPMP.

3. Results and Discussion

3.1. Synthesis. The target compound (2E)-IPPMP was obtained in a three-step reaction sequence as given in Scheme 1.

3.2. Structural Geometry Analysis. The structure of the (2E)-IPPMP molecule was optimized using the B3LYP method with a 6-311++G(d,p) basis set. The optimized molecular structure of the isolated molecule is shown in Figure 1. The optimized geometrical parameters of the isolated (2E)-IPPMP molecule in the gas and water phases are given in Table 1. The calculated values were compared with the X-ray diffraction results. In the (2E)-IPPMP molecule the two phenyl rings are bridged by a hydrazinecarboxamide skeleton containing an imidazole ring. The C-N bond lengths $\text{C}_{17}\text{--}\text{N}_{16}$ (1.4179 Å) and $\text{C}_{17}\text{--}\text{N}_{19}$ (1.3792 Å) are shorter than the normal single C-N bond length 1.480 Å [20]. This discrepancy is due to the conjugation of p-type electrons of the carbonyl group and nitrogen atom, allowing the electrons to smear out along the C-N bond. In the *para*-disubstituted phenyl ring, the calculated $\text{C}_{25}\text{--}\text{H}_{44}$ (1.0789 Å) bond length is shorter than that of the other C-C bonds; also, $\text{O}_{18} \cdots \text{H}_{44}$ distance is 2.25 Å, which is significantly shorter than the van der Waals radius (2.72 Å) [21] between O and H atoms, which indicates the possibility of C-H $\cdots$ O hydrogen bonding. The elongation of the $\text{C}_{20}\text{--}\text{C}_{21}$ (1.4004 Å) bond is due to the transfer of a lone pair of electrons from the amide nitrogen to the carbon atom. In the other phenyl ring, the $\text{C}_5\text{--}\text{H}_{31}$

TABLE 1: Structural geometry parameters of (2E)-IPMP compared with their experimental X-ray diffraction results.

Parameter	Bond length (Å)		Bond angle (°)		Solution phase		Parameter	Dihedral angle (°)		Solution phase
	Calc.	Exp. ^a	Calc.	Exp.	Calc.	Exp.		Calc.	Exp.	
C ₄ -C ₅	1.4012	1.386	120.31	120.52	120.25		C ₆ -C ₁ -C ₂ -C ₃	0.16	0.21	0.3706
C ₅ -C ₆	1.4024	1.382	120.00	119.72	120.05		C ₆ -C ₁ -C ₂ -H ₂₈	-179.76	179.84	-179.83
C ₁ -C ₆	1.3903	1.384	119.69	119.77	119.70		H ₂₇ -C ₁ -C ₂ -C ₃	-179.89	179.84	-179.44
C ₁ -C ₂	1.3956	1.361	119.62	119.51	119.65		H ₂₇ -C ₁ -C ₂ -H ₂₈	0.19	-0.13	0.36
C ₂ -C ₃	1.3928	1.363	120.20	120.24	120.17		C ₂ -C ₁ -C ₆ -C ₅	-0.63	0.23	-0.50
C ₃ -C ₄	1.3934	1.388	120.18	120.26	120.18		C ₂ -C ₁ -C ₆ -H ₃₁	179.22	179.80	179.97
C ₅ -C ₇	1.4919	1.487	120.13	120.76	120.19		H ₂₇ -C ₁ -C ₆ -C ₅	179.42	179.79	179.31
C ₈ -C ₇	1.5135	1.508	120.15	119.63	120.18		H ₂₇ -C ₁ -C ₆ -C ₃₁	-0.73	0.18	-0.21
C ₈ -C ₉	1.5434	1.525	119.71	119.63	119.64		C ₁ -C ₂ -C ₃ -C ₄	0.48	0.42	0.25
C ₈ -H ₃₂	1.0883	0.958	120.69	120.32	120.59		C ₁ -C ₂ -C ₃ -C ₄	-179.3	179.61	-179.76
C ₉ -H ₃₃	1.0932	0.948	119.24	119.89	119.12		H ₂₈ -C ₂ -C ₃ -C ₄	-179.6	-179.60	-179.54
C ₉ -H ₃₅	1.0907	0.970	120.05	119.79	120.28		H ₂₈ -C ₂ -C ₃ -H ₂₉	0.61	0.36	0.44
N ₁₀ -C ₉	1.0923	0.971	118.67	117.99	118.75		C ₂ -C ₃ -C ₄ -C ₅	-0.65	-0.72	-0.76
N ₁₀ -C ₁₄	1.4584	1.452	120.71	120.05	120.75		C ₂ -C ₃ -C ₄ -H ₃₀	-178.94	179.25	-179.59
N ₁₀ -C ₁₁	1.3677	1.348	120.61	121.06	120.49		H ₂₉ -C ₃ -C ₄ -C ₅	179.13	179.31	179.26
N ₁₃ -C ₁₂	1.3749	1.366	120.57	120.95	120.57		H ₂₉ -C ₃ -C ₄ -H ₃₀	0.84	0.71	0.42
N ₁₃ -C ₁₄	1.3677	1.304	118.99	119.58	120.27		C ₃ -C ₄ -C ₅ -C ₆	0.18	0.75	0.62
C ₁₁ -C ₁₂	1.3718	1.345	118.92	118.08	119.15		C ₃ -C ₄ -C ₅ -C ₇	-178.58	179.34	-178.67
C ₁₂ -H ₃₇	1.0790	0.930	115.01	115.92	115.26		H ₃₀ -C ₄ -C ₅ -C ₆	178.46	179.22	179.44
C ₁₁ -H ₃₆	1.0776	0.931	125.99	125.96	125.92		C ₄ -C ₅ -C ₆ -C ₁	-0.31	0.68	0.15
C ₁₄ -H ₃₈	1.0803	0.930	112.37	112.66	112.28		C ₄ -C ₅ -C ₆ -H ₃₁	0.46	0.51	0.002
C ₇ -N ₁₅	1.2849	1.287	109.46	109.95	109.63		C ₇ -C ₅ -C ₆ -C ₁	-179.4	179.51	179.53
N ₁₅ -N ₁₆	1.4036	1.367	110.05	111.01	109.68		C ₇ -C ₅ -C ₆ -C ₃₁	179.22	179.58	179.30
N ₁₆ -H ₃₉	1.0123	0.899	108.19	106.60	108.53		C ₇ -C ₅ -C ₆ -C ₃₁	-0.63	-0.39	-1.17
C ₁₇ -N ₁₆	1.4179	1.362	110.37	110.76	109.71		C ₄ -C ₅ -C ₇ -C ₈	-36.92	-29.26	-37.14
C ₁₇ -N ₁₉	1.3792	1.350	106.18	105.53	106.85		C ₄ -C ₅ -C ₇ -N ₁₅	146.04	152.80	145.29
N ₁₉ -H ₄₀	1.0093	0.889	111.95	113.52	111.52		C ₆ -C ₅ -C ₇ -C ₈	144.33	150.64	143.58
N ₁₉ -C ₂₀	1.4143	1.381	109.97	108.87	111.63		C ₆ -C ₅ -C ₇ -N ₁₅	-32.7	27.30	-33.99
C ₂₀ -C ₂₁	1.4005	1.384	107.08	108.87	111.63		C ₅ -C ₇ -C ₈ -C ₉	-52.66	-68.80	-55.35
C ₂₁ -C ₂₂	1.3895	1.381	109.97	108.87	111.63		C ₅ -C ₇ -C ₈ -H ₃₂	-172.89	49.95	-176.06
C ₂₂ -C ₂₃	1.3984	1.380	107.24	108.83	107.44		C ₃ -C ₇ -C ₈ -H ₃₂	70.77	166.33	66.90
C ₂₃ -C ₂₄	1.3972	1.376	127.03	126.90	126.69		C ₁₅ -C ₇ -C ₈ -C ₉	124.02	108.92	121.94
C ₂₄ -C ₂₅	1.3931	1.384	126.64	126.29	126.56		N ₁₅ -C ₇ -C ₈ -H ₃₂	3.79	-15.96	1.23
C ₂₀ -C ₂₅	1.3987	1.384	106.28	106.52	106.69		C ₅ -C ₇ -N ₁₅ -N ₁₆	-112.55	-132.34	-115.80
C ₂₁ -H ₄₁	1.0864	0.929	105.73	105.44	105.79		C ₈ -C ₇ -N ₁₅ -N ₁₆	-177.68	179.43	-178.97
C ₂₂ -H ₄₂	1.0853	0.930	132.17	124.35	132.18		C ₇ -C ₈ -C ₉ -N ₁₀	5.53	1.67	3.66
C ₂₄ -H ₄₃	1.0855	0.930	110.47	111.35	110.26		C ₇ -C ₈ -C ₉ -H ₃₄	-174.09	-26.97	-178.38
C ₂₅ -H ₄₄	1.0790	0.929	127.96	124.35	127.94		C ₇ -C ₈ -C ₉ -H ₃₅	63.7	66.15	60.44
C ₂₃ -C ₂₆	1.5095	1.608	121.56	124.35	121.80		H ₃₂ -C ₈ -C ₉ -N ₁₀	-54.99	-176.68	-59.11
C ₂₆ -H ₄₅	1.0928	0.960	121.90	124.30	121.80		H ₃₂ -C ₈ -C ₉ -H ₃₄	-53.12	175.97	-57.03
C ₂₆ -H ₄₆	1.0926	0.960	105.20	104.06	105.21		H ₃₂ -C ₈ -C ₉ -H ₃₅	-175.33	62.64	-178.21
C ₂₆ -H ₄₇	1.0957	0.960	112.32	112.62	112.05		H ₃₃ -C ₈ -C ₉ -N ₁₀	65.98	54.53	62.24
							H ₃₃ -C ₈ -C ₉ -H ₃₄	62.66	-54.53	59.38
								-59.55	-54.53	-61.80

^aTaken from [11].

TABLE 2: Second-order perturbation theory analysis of Fock matrix in natural bond orbital (NBO) basis for (2E)-IPPMP.

Donor (<i>i</i>)	Occupancy (<i>e</i>)	Acceptor (<i>j</i>)	Occupancy (<i>e</i>)	$E(2)^a$ kcal/mol	$E(j) - E(i)^b$ (a.u)	$E(i, j)^c$ (a.u)
$n_1(N_{10})$	1.55554	$\pi^*(C_{11}-C_{12})$	1.85684	30.62	0.29	0.087
$n_1(N_{10})$	1.55554	$\pi^*(N_{13}-C_{14})$	1.86721	46.48	0.28	0.103
$n_1(N_{13})$	1.9234	$\sigma^*(C_{11}-C_{12})$	1.98419	5.1	0.95	0.063
$n_1(N_{15})$	1.92552	$\sigma^*(C_7-C_8)$	1.97792	11.4	0.79	0.086
$n_1(N_{15})$	1.92552	$\sigma^*(N_{16}-H_{39})$	1.97686	2.02	0.77	0.036
$n_1(N_{16})$	1.79578	$\pi^*(C_7-N_{15})$	1.94162	9.06	0.36	0.052
$n_2(O_{18})$	1.83834	$\sigma^*(N_{16}-C_{17})$	1.98245	26.84	0.63	0.118
$n_2(O_{18})$	1.83834	$\sigma^*(C_{17}-N_{19})$	1.98641	24.58	0.69	0.119
$n_2(O_{18})$	1.83834	$\sigma^*(C_{25}-H_{44})$	1.97725	0.78	0.73	0.022
$n_1(N_{19})$	1.70657	$\pi^*(C_{20}-C_{25})$	1.64309	30.72	0.31	0.089
$\pi(C_2-C_3)$	1.6583	$\pi^*(C_4-C_5)$	1.64969	20.62	0.28	0.069
$\pi(C_4-C_5)$	1.64969	$\pi^*(C_1-C_6)$	1.66001	19.97	0.29	0.067
$\pi(C_{11}-C_{12})$	1.85684	$\pi^*(N_{13}-C_{14})$	1.86721	15.01	0.28	0.061
$\pi(N_{13}-C_{14})$	1.86721	$\pi^*(C_{11}-C_{12})$	1.85684	21.59	0.33	0.078
$\pi(C_{20}-C_{25})$	1.64309	$\pi^*(C_{21}-C_{22})$	1.70752	19.29	0.28	0.066
$\pi(C_{20}-C_{25})$	1.64309	$\pi^*(C_{23}-C_{24})$	1.64872	20.41	0.3	0.069
$\pi(C_{23}-C_{24})$	1.64872	$\pi^*(C_{20}-C_{25})$	1.64309	20.68	0.27	0.068
$\pi(C_{23}-C_{24})$	1.64872	$\pi^*(C_{21}-C_{22})$	1.70752	22.11	0.27	0.069
$\pi(N_{13}-C_{14})$	1.86721	$\pi^*(C_{11}-C_{12})$	1.85684	107.4	0.01	0.06
$\sigma(C_{26}-H_{46})$	1.98674	$\sigma^*(C_{23}-C_{24})$	1.64872	0.84	0.54	0.021
$\sigma(C_{26}-H_{47})$	1.97658	$\sigma^*(C_{23}-C_{24})$	1.64872	4.34	0.54	0.047
$\pi(C_{20}-C_{25})$	1.64309	$\pi^*(C_{23}-C_{24})$	1.64872	254.22	0.01	0.082
$\pi(C_{21}-C_{22})$	1.70752	$\pi^*(C_{23}-C_{24})$	1.64872	230.93	0.01	0.084

^a $E(2)$ means energy of hyperconjugative interactions. ^bEnergy difference between donor and acceptor *i* and *j* NBO. ^c $F(i, j)$ is the Fock matrix element between *i* and *j* NBO.

(1.0825 Å) bond is shorter than that of the other C-C bonds; also, $N_{15} \cdots H_{31}$ distance is 2.56 Å, which is significantly shorter than the van der Waals radius (2.75 Å) between N and H atoms, which indicates the possibility of C-H $\cdots$ O hydrogen bonding. In addition, C_5-C_6 (1.4024 Å) and C_4-C_5 (1.4012 Å) bond distances on either side of the cyanide group are appreciably greater than the other C-C bonds due to the resonance effect between the cyanide group and phenyl ring. In the imidazole ring, $C_{14}-N_{10}$ (1.3676 Å) and $C_{14}-N_{13}$ (1.3139 Å) bonds are relatively shorter due to the lone pair interaction from the nitrogen atom. The deviation of bond lengths of $N_{15}-H_{39}$ (1.0123 Å) and $N_{19}-H_{40}$ (1.0092 Å) is due to the different environment of the nitrogen atom. Conjugation of the carbonyl group with the hydrazine moiety would favor planarity, but the van der Waals repulsion between H_{39} and H_{40} hinders the achievement of coplanarity. A small deviation was obtained within the calculated structural parameters in the gas and liquid phases, which were due to the solvent interactions over the solution phase calculations.

3.3. Natural Bond Orbital Analysis. Natural bond orbital (NBO) analysis was performed using the NBO 3.1 program [22] as implemented in the Gaussian 09 program package for

the DFT method. The corresponding results are presented in Table 2. NBO analysis has proved to be an effective tool for chemical interpretation of hyperconjugative interaction and electron density transfer (EDT) from a filled lone pair to an unfilled antibonding orbital in the hydrogen bonding system [23–25]. The intramolecular C-H $\cdots$ O hydrogen bonding is formed due to the orbital overlap between $n(O)$ and $\sigma^*(C-H)$ which results in intramolecular charge transfer (ICT) causing stabilization of H-bonded systems. This interaction results in increased electron density (ED) of the C-H antibonding orbital, which strengthens the C-H bond. NBO analysis confirms C-H $\cdots$ O intramolecular hydrogen bonding formed by the orbital overlap between a lone pair $n_2(O_{18})$ and $\sigma^*(C_{25}-H_{44})$ antibonding orbital with stabilization energy of 0.78 kcal/mol. The most important interaction ($n-\pi^*$) and ($n-\sigma^*$) energies of $n_1(N_{10}) \rightarrow \pi^*(N_{13}-C_{14})$ and $n_2(O_{18}) \rightarrow \sigma^*(N_{16}-C_{17})$ are 46.48 and 26.84 kcal/mol, respectively. This larger $E(2)$ value shows ICT interactions of the molecule.

3.4. Vibrational Spectral Analysis. Computed vibrational wavenumbers and atomic displacements corresponding to the different normal modes are used to identify vibrational modes. The vibrational modes are assigned on the basis of

FIGURE 2: (a) Calculated (b) experiment infrared spectra of (2E)-IPPMP.

FIGURE 3: (a) Calculated (b) experiment Raman spectra of (2E)-IPPMP.

potential energy distribution analysis using the VEDA4 program [26]. The experimental infrared (IR) and Raman spectra are shown in Figures 2 and 3. The calculated vibrational wavenumbers, measured IR, and Raman band positions and their detailed assignments are given in Table 3.

3.4.1. Phenyl Ring Vibrations. Aromatic C-H stretching vibrations generally absorb in the region $3080\text{--}3010\text{ cm}^{-1}$ [27]. The observed weak IR band at 3119 cm^{-1} and Raman band at 3121 cm^{-1} correspond to aromatic C-H stretching mode. The blue shift of the C-H stretching wavenumber is due to weak intramolecular C-H $\cdots$ O hydrogen bonding. Aromatic C=C stretching vibrations occur in the region $1625\text{--}1430\text{ cm}^{-1}$ [28]. A medium IR band at 1539 cm^{-1} and a strong Raman band at 1591 cm^{-1} are observed, which correspond to aromatic C=C stretching mode. In-plane C-H deformation vibrations appear in the region $1290\text{--}1000\text{ cm}^{-1}$ [27]. Observed IR and Raman bands at 1288 and 1275 cm^{-1} are assigned to in-plane C-H deformation. In-plane ring deformation vibrations appear in the region $650\text{--}615\text{ cm}^{-1}$. Observed IR and Raman bands at 615 and 640 cm^{-1} are assigned to in-plane ring deformation.

3.4.2. Methylene Vibrations. Asymmetric and symmetric CH_2 stretching vibrations normally appear strongly at about 2926 and 2855 cm^{-1} [29]. The Raman band at 2941 cm^{-1} is assigned to CH_2 symmetric stretching vibration. Methylene scissoring vibrations normally appear in the region $1465\text{--}1445\text{ cm}^{-1}$ [29]. A medium band observed in IR at 1401 cm^{-1} is attributed to methylene scissoring mode. The twisting,

wagging vibrations appear in the region $1422\text{--}719\text{ cm}^{-1}$ [30]. The observed strong IR band at 1141 cm^{-1} and weak Raman band at 1177 cm^{-1} are assigned to CH_2 twisting modes for methylene. Wagging is observed in IR at 1352 cm^{-1} and Raman at 1361 cm^{-1} .

3.4.3. Methyl Vibrations. The asymmetric C-H stretching mode of CH_3 generally occurs at $2982\text{--}2962\text{ cm}^{-1}$ and CH_3 symmetric stretching at $2882\text{--}2862\text{ cm}^{-1}$ [29]. A weak Raman band at 2977 cm^{-1} is attributed to CH_3 symmetric stretching. Asymmetric bending vibrations of methyl groups occur in the region $1470\text{--}1450\text{ cm}^{-1}$ [28]. The observed weak Raman band at 1447 cm^{-1} is assigned to methyl scissoring vibration.

3.4.4. Secondary Amide Vibrations. Carbonyl stretching vibration in a secondary amide is expected in the region $1680\text{--}1630\text{ cm}^{-1}$ [28]. A very strong band at 1654 cm^{-1} is assigned to C=O stretching. N-H stretching vibrations generally appear in the region $3370\text{--}3170\text{ cm}^{-1}$. Observed IR and Raman bands at 3141 and 3140 cm^{-1} are attributed to N-H stretching. The in-plane N-H bending vibration usually appears from 1570 to 1515 cm^{-1} [28]. The observed very strong IR band at 1523 cm^{-1} and weak Raman band at 1527 cm^{-1} are assigned to in-plane N-H bending vibration.

3.4.5. Imidazole Vibrations. Imidazole C-H stretching vibrations are expected in the region $3145\text{--}3115\text{ cm}^{-1}$ [31, 32]. Observed Raman bands at 3121 and 3138 cm^{-1} and IR bands at 3119 and 3138 cm^{-1} are assigned to C-H stretching mode.

TABLE 3: Vibrational assignment of (2E)-IPPMP based on potential energy distribution method.

Calculated wavenumber (cm ⁻¹)		Experimental wavenumber (cm ⁻¹)		Assignment with PED%
Unscaled	Scaled	FT-IR	FT-Raman	
3610	3497	3207w	—	ν N-H (92)
3565	3453	3141vw	3140vw	ν N-H (99)
3265	3163	3138vw	3138w	ν C-H imd (83)
3241	3140	3119w	3121w	ν C-H ph (99)
3202	3102	—	3118w	ν C-H ph (86)
3182	3082	3083vw	—	ν C-H ph (67)
3164	3066	—	3065m	ν C-H ph (27)
3105	3008	—	3018w	ν_{as} C-H (55)
3073	2977	—	2977w	ν_{sy} C-H (36)
3059	2964	—	2941w	ν_{sy} C-H (48)
3019	2925	—	2917w	ν_{sy} C-H (18)
1776	1720	1654vs	—	ν C=O (78)
1639	1588	1589m	1593vs	ν C..C ph (42)
1614	1564	—	1569m	ν C..C ph (36)
1553	1504	1523vs	1527vw	β N-H (32)
1496	1449	1449m	—	ω N-H (33)
1492	1445	—	1447vw	δ_{sci} C-H (19)
1468	1422	1401m	—	δ_{sci} C-H (79)
1399	1355	1352w	1361vw	ω C-H (51)
1382	1339	—	1338vw	ν C-C imd (20)
1327	1286	1288w	—	β C-H ph (22)
1307	1267	—	1275w	β C-H ph (12)
1263	1223	—	1222w	β C-H ph (46)
1258	1219	1218m	—	β C-H ph (56)
1209	1171	1174vw	—	β C-H ph (28)
1177	1140	1141s	1177w	t C-H (18)
1118	1084	1089m	1088vw	ν N-N (23), β C-H ph (12)
1101	1067	—	1069vw	β C-H ph (10)
1075	1041	1039vw	—	ν N-N (19)
1061	1028	1020vw	1027vw	τ CHCH (70)
1043	1011	1011w	—	β C-H imd (32)
1023	991	—	998w	ν N-C (14)
985	954	947vw	—	τ HCCH (81)
947	918	931vw	—	τ CCCH (49)
940	911	911w	—	τ HCCC (47)
917	888	876vw	875vw	β CC imd (72)
820	794	797vw	796vw	τ HCCN (55)
785	761	769w	—	ν C..C (14)
673	652	660s	663vw	τ CNCN (63),
652	632	—	640w	β CC ph (24)
636	617	615m	—	τ CCNC (34), β CC ph (21)
614	595	590vw	586vw	τ CCNN (17)
414	401	—	401vw	τ CCCC (29)
370	359	—	354vw	τ CCNN (14)
199	193	—	204vw	τ CCCC (23)
71	69	—	71m	τ CNCN (14), τ NNCN (19)

ν , stretching; ν_{as} , asymmetric; ν_{sy} , symmetric stretching; ph, phenyl ring; imd, imidazole ring; δ_{sci} , scissoring; t , twisting; ω , wagging; β , in-plane bending; τ , Torsion; vs, very strong; s, strong; m, medium; w, weak; vw, very weak.

FIGURE 4: (a) HOMO and (b) LUMO plots of (2E)-IPPMP.

FIGURE 5: Natural charge distribution chart of the (2E)-IPPMP molecule.

The observed Raman band at 1338 cm^{-1} is attributed to C-C stretching mode [33].

3.4.6. Hydrazine Vibrations. In accordance with earlier reports and in agreement with the calculation, a weak band observed at 3207 cm^{-1} is assigned to hydrazine N-H stretching [27, 34]. Observed bands in IR and Raman at 1089 and 1088 cm^{-1} are assigned to N-N stretching vibration.

3.4.7. Skeletal Mode Vibrations. C-N and C-C stretching vibrations generally occur in the region $1150\text{--}850\text{ cm}^{-1}$ [34]. The weak IR and Raman bands observed at 1011 and 998 cm^{-1} are attributed to C-C stretching.

3.5. Frontier Molecular Orbital Energy Analysis. HOMO (highest occupied molecular orbital) and LUMO (lowest unoccupied molecular orbital) are important in defining the

reactivity of a chemical species. The energy of HOMO indicates nucleophilicity and LUMO indicates electrophilicity [35]. HOMO is spread over the methyl phenyl, hydrazinecarboxamide fragment and LUMO is located on ph 2. This shows the charge transfer between the two rings through the hydrazinecarboxamide path. The HOMO (-6.61 eV) and LUMO (-1.61 eV) energies reflect the charge transfer within the molecule. The HOMO-LUMO energy gap is 4.46 eV . The frontier molecular orbital diagrams are shown in Figure 4.

3.6. Natural Population Analysis. Natural population analysis provides an effective method to calculate atomic charges and electron distribution within a molecule [36]. The net atomic charges of the (2E)-IPPMP molecule obtained by natural population analysis are plotted in Figure 5. All hydrogen atoms have a net positive charge. The atoms H_{40} ($0.3852e$) and H_{39} ($0.3788e$) show more positive charge than other hydrogen atoms due to their attachment with a nitrogen atom. Among the hydrogen atoms ($\sim 0.2023e$) of the phenyl ring, H_{44}

TABLE 4: NMR chemicals shift values of ^{13}C and ^1H .

^{13}C			^1H		
Atom	$\delta_{\text{exp.}}$	$\delta_{\text{calc.}}$	Atom	$\delta_{\text{exp.}}$	$\delta_{\text{calc.}}$
C ₁	128.3	128.01	H ₂₇	7.39	7.16
C ₂	128.9	129.41	H ₂₈	7.43	7.19
C ₃	128.3	127.48	H ₂₉	7.39	7.16
C ₄	128.4	128.13	H ₃₀	7.84	7.50
C ₅	136.8	138.17	H ₃₁	7.84	7.63
C ₆	128.4	126.71	H ₃₂	3.33	2.61
C ₇	153.6	168.87	H ₃₃	3.33	2.89
C ₈	28.3	33.31	H ₃₄	4.14	3.77
C ₉	42.1	44.26	H ₃₅	4.14	3.19
C ₁₁	119.4	119.36	H ₃₆	6.87	6.87
C ₁₂	126.4	128.75	H ₃₇	7.29	6.56
C ₁₄	137.3	140.01	H ₃₈	7.65	6.82
C ₁₇	144.9	150.09	H ₃₉	10.24	6.70
C ₂₀	131.5	137.03	H ₄₀	8.79	5.70
C ₂₁	120.0	115.12	H ₄₁	7.13	6.27
C ₂₂	128.8	128.43	H ₄₂	7.53	6.80
C ₂₃	136.3	132.85	H ₄₃	7.53	6.85
C ₂₄	128.8	128.53	H ₄₄	7.13	7.90
C ₂₅	120.0	114.58	H ₄₅	2.28	1.78
C ₂₆	20.4	18.25	H ₄₆	2.28	1.80
			H ₄₇	2.28	2.08

($\sim 0.2452e$) shows the highest positive charge, being involved in C-H $\cdots$ O intramolecular hydrogen bonding. All carbon atoms are negatively charged except C₇, C₁₄, C₁₇, and C₂₀ due to their attachment with electronegative nitrogen or oxygen atoms. The atom C₁₇ (0.7991e) shows more positive charge and N₁₉ ($-0.6181e$) shows more negative charge, indicating charge delocalization in the molecule.

3.7. NMR Analysis. The scaled and experimental NMR (^1H and ^{13}C) chemical shift values for the (2E)-IPPMP molecule are presented in Table 4. The phenyl and imidazole ring carbon signals usually appear in the region 115–150 ppm. In this molecule, imidazole ring carbon signals are obtained at 119.4, 126.4, and 137.3 ppm, which are predicted at 119.36, 128.75, and 140.01 ppm, respectively.

Phenyl carbon signals were observed at 120.0, 128.4, 128.8, 128.9, 131.5, 136.3, 136.8, and 137.3 ppm, while their respective calculated ones were obtained at 115.12, 128.13, 128.53, 129.41, 137.03, 132.85, 138.17, and 140.01 ppm. A carbonyl carbon signal was seen at 144.9 ppm and its computed one was obtained at 150.09 ppm. This deviation may occur due to the presence of amide $\cdots$ amide interactions in the crystalline state. On the other hand, the computed ^1H chemical shift values for the title molecule showed good agreement with the experimental ones (Table 4).

3.8. Molecular Docking Analysis. The title molecule (2E)-IPPMP was energy minimized based on the DFT method. Molecular docking was performed using AutoDock 4.2. A target protein (PDB ID: IEOU) for antiepileptic agents was selected for the present docking analysis [37, 38]. The protein

FIGURE 6: Binding pose diagrams of the (2E)-IPPMP molecule with its target protein.

data bank file of the target protein was downloaded from the Research Collaboratory for Structural Bioinformatics (RCSB) database, with a resolution of 2.1 Å. Protein preparation was carried out by the following steps: (i) all water molecules were removed, (ii) hydrogen atoms were added to the crystal structure, (iii) Kollman charge was added, and (iv) a previously docked inhibitor (fructose-based sugar sulfamate RWJ-37497) was removed from the protein. Rigid protein and flexible ligand dockings were carried out using the AutoDock 4.2 program package [39] with the Lamarckian genetic algorithm, applying the following protocol: trials of 100 dockings, energy evaluations of 25000000, population size of 200, mutation rate of 0.02, crossover rate of 0.8, and elitism value of 1. The docking results were evaluated by sorting the docked conformations according to their predicted binding free energy. The protein-ligand interaction complex is given in Figure 6, displaying the conformer with the best predicted binding free energy (-7.94 kcal/mol).

The amino acids ASN11, TYR7, and LYS169 in the active sites of the target protein bind with the (2*E*)-IPMP ligand by N-H...O and N-H...N hydrogen bonds. These preliminary results support the exhibited anticonvulsant activity of the title molecule.

4. Conclusions

The geometry optimization and harmonic wavenumbers of the (2*E*)-IPMP molecule have been performed at ground state calculations using the DFT method. FT-IR and FT-Raman measurements helped functional group identification of the title molecule. The fundamental wavenumbers are in good agreement with the theoretical results. Shifting of vibrational wavenumbers and hyperconjugative results confirmed the presence of intermolecular/intramolecular interactions in the molecule. The molecular docking results predicted the anticonvulsant activity of the (2*E*)-IPMP molecule due to its ability to interact with a target protein (1E0U) for anticonvulsants. The results of the current study will support the development of new drug-like candidates in the anticonvulsant research area.

Competing Interests

The authors have declared that there are no competing interests.

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