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Spectroscopic (FT-IR, FT-Raman, UV, ¹H and ¹³C NMR) profiling and computational studies on methyl 5-methoxy-1*H*-indole-2-carboxylate: A potential precursor to biologically active molecules

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Abstract

Methyl 5-methoxy-1*H*-indole-2-carboxylate (MMIC) was prepared *via* esterification of commercially available 5-methoxyindole-2-carboxylic acid. The title molecule MMIC was characterised using FT-IR and FT-Raman in the ranges of 4000–500 and 4000–50 cm⁻¹, respectively. The fundamental modes of the vibrations were assigned and the UV-visible spectrum of the MMIC molecule was recorded in the range of 200–400 nm to explore its electronic nature. The HOMO-LUMO energy distribution was calculated and the bonding and anti-bonding structures of the title molecule were studied and analysed using the natural bond orbital (NBO) approach. The reactivity of the MMIC molecule was also investigated and both the positive and negative centres of the molecule were identified using chemical descriptors and molecular electrostatic potential (MEP) analysis. The chemical shifts of the ¹H and ¹³C NMR spectra were noted and the magnetic field environment of the MMIC molecule are discussed. The non-linear optical (NLO) properties of the title molecule were studied based on its calculated values of polarisability and hyperpolarisability. All computations were obtained by DFT methods using the 6-311++G (d,p) basis set.

Keywords: 5-Methoxyindole; FT-IR; FT-Raman; HOMO-LUMO; NLO

1. Introduction

The pineal gland synthesises and releases the pineal hormone *N*-acetyl-5-methoxytryptamine (melatonin, MLT) in a circadian rhythm, with high peripheral blood levels at night. It has been reported that MLT has sleep-inducing properties, as well as pain modulatory, antitumour, anti-inflammatory, and antioxidant effects [1-4]. Melatonin affects MT₁ and MT₂ receptors, which are G-protein-coupled receptors, as well as a low-affinity putative MLT binding site called MT₃[5,6].

Nonlinear optical (NLO) materials are attracting a great deal of attention due to their great impact on information technology and industrial applications [7,8]. NLO materials are characterised by their nonlinear response to the electric field associated with the light of a laser beam. Organic nonlinear optical materials have attracted growing interest due to their large optical susceptibilities, inherent ultrafast response times, and high optical thresholds for laser power compared with inorganic NLO materials [9]. Nevertheless, the burgeoning field of NLO research and applications is still in need of new NLO materials for a wide variety of processes.

The indole nucleus constitutes the core structure of a large number of melatoninergic ligands that can modulate melatonin receptors [10-12]. According to the literature, the molecular structure of methyl 5-methoxy-1*H*-indole-2-carboxylate (MMIC) has not been previously investigated using computational methods and hence its molecular characterisation will support the development of new bioactive compounds. Therefore, the present work involves vibrational profiling, as well as spectroscopic (FT-IR, FT-Raman, ¹H and ¹³C NMR) characterisation and investigation of the NLO properties, of the MMIC molecule using DFT computational approaches. Molecular electrostatic potential (MEP) and HOMO-LUMO analyses were also performed. It is believed that the results of the current investigation will give insight into the possible intermolecular interactions of the MMIC molecule, which could help with the rationalisation of intermolecular drug-receptor interactions with the purpose of designing new biologically active indole-bearing molecules.

2. Experimental details

2.1. General

The melting point was measured using a Gallenkamp melting point device and is uncorrected. The FT-IR spectrum of the MMIC molecule was recorded using KBr pellets on a Perkin Elmer RXL spectrometer (Waltham, Massachusetts, USA) with a spectral resolution of 2 cm⁻¹. The FT-Raman spectrum was obtained using a Bruker RFS 100/s spectrophotometer (Ettlingen, Germany) with an excitation wavelength of 1064 nm and using the emission of an Nd:YAG laser source (Goettingen, Germany). The NMR sample was dissolved in DMSO- d_6 and the NMR spectra were recorded using Bruker NMR spectrometer at 500 MHz for ¹H and 125.76 MHz for ¹³C at the Research Center, College of Pharmacy, King Saud University, Saudi Arabia.

2.2. Synthesis

A few drops of concentrated sulphuric acid were added to a suspension containing 5methoxyindole-2-carboxylic acid (1, 2.00 g, 0.01 mol) in absolute methanol (30 mL). The reaction mixture was heated to reflux for four hours, cooled to room temperature, and the precipitated solid filtered off to give 2.1 g (96%) of MMIC (2) as yellow crystals, m.p. 450–451 K [13].

2.3. Crystal structure determination

The methanolic solution of the MMIC molecule was subjected to slow evaporation to give single crystals suitable for X-ray analysis. Bruker SMART APEXII CCD diffractometer equipped with graphite monochromatic Mo K α radiation at 100 (2) K was used to collect the data. Cell refinement and data reduction were carried out by Bruker SAINT [14]. The title structure was solved using SHELXS-97 [15,16]. Full-matrix least-squares techniques with anisotropic thermal data for non-hydrogen atoms on F^2 were used to finalize the refinement. All the hydrogen atoms were placed in calculated positions (Tables T1-T3). Crystallographic data of the MMIC molecule have been deposited with the Cambridge Crystallographic Data Center (supplementary publication number CCDC-1052719). Copies of the data may be obtained free of charge from the Director, CCDC, 12 Union Road, Cambridge, CB2 1EZ, UK (deposit@ccdc.cam.ac.uk).

2.4. Quantum chemical calculations

Density functional theory (DFT) is an effective tool for calculating the electronic structures of molecules. The basis set, 6-311++G (d,p), was augmented by a 'd' polarisation function for heavy atoms and a 'p' polarisation for hydrogen atoms, in order to achieve a better representation of the polar bonds in the molecule [17,18]. All calculations in the present work were performed using the Gaussian 09W [19] program package on a personal computer. Geometrical parameters and vibrational wavenumbers were computed by optimising the geometry of the molecule using the B3LYP, M06-2X and B3PW91 methods with 6-311++G (d,p) as the basis set. The vibrational frequency assignments were calculated by the total energy distribution (TED) method using the vibrational energy distribution analysis (VEDA) program [20]. The optimised geometry of the MMIC compound was further used to complete a natural bond orbital (NBO) analysis using NBO version 3.1 [21], which is implemented in the Gaussian 09W package. The NMR chemical shifts of the title compound were also calculated using the gauge independent atomic orbitals (GIAO) method [22,23] with the B3LYP/6-311++G (d,p) functional method. ¹H and ¹³C isotropic magnetic shielding (IMS) of any X atom (carbon or hydrogen) was applied according to the value of TMS, $CS_X = IMS_{TMS} - IMS_x$. The energy distribution from HOMO to LUMO was calculated using the Gaussum 2.2.1 software program.

3. Results and discussion

3.1. Synthesis

The target molecule, MMIC (2), was prepared *via* esterification of the commercially available 5-methoxyindole-2-carboxylic acid (1) in methanol and a catalytic amount of sulphuric acid, as illustrated in Scheme 1 according to the published procedure [13].



Reagents and conditions: i) methanol, H_2SO_4 , reflux, 4h, 96%.

Scheme 1: Synthesis of the MMIC (2) molecule.

3.2. Structural geometry analysis

MMIC crystallizes in the monoclinic crystal system with space group P2_{1/n} with four molecules per unit cell (Z = 4) and cell dimensions of a = 7.8956(6), b = 5.8304(4) and c = 22.0407(16) Å. The crystal packing of the molecule with Z = 4 units is shown in Figure 1. The molecule consists of one methyl ester group and one methoxy group attached to the indole ring, as illustrated in Figure 2. The geometrical parameters of the title compound were computed by B3LYP, M06-2X and B3PW91 functionals with the basis set 6-311++G (d, p) and the results, along with the XRD values, are presented in Table 1. The geometrically optimized title molecule exhibited energy value of -442924.7202 Kcal.mol⁻¹. The calculated structural geometry parameters are well correlated with the experimental values as indicated, with their correlation coefficient (R²) values calculated as 0.9878, 0.9867 and 0.9876 (for bond lengths) and 0.9004, 0.9018 and 0.8990 (for bond angles) using B3LYP, M06-2X and B3PW91 functionals, respectively.







Figure 2. Optimized structure of the MMIC molecule.

Table 1. Geometrical parameters [bond length (Å), bond angle (°) and dihedral angle (°)] of the MMIC molecule.

Parameters	B3LYP/6	-311G++			
	(d ,	,p)	M06-2X/6-	B3PW91/6-	VDD
			311G++ (d,p)	311G++ (d , p)	AND
	Gas	Ethanol			
	Phase	Phase			<u></u>
Bond length (Å)					
C1-C2	1.426	1.4229	1.4177	1.4228	1.414
C1-C6	1.403	1.4029	1.4007	1.4007	1.413
C1-C7	1.429	1.4251	1.4308	1.4256	1.421
C2-C3	1.395	1.3946	1.3943	1.3929	1.396
C2-N14	1.375	1.3694	1.3723	1.37	1.371
C3-C4	1.389	1.3858	1.3835	1.386	1.372
С3-Н9	1.084	1.0844	1.0833	1.0848	0.949
C4-C5	1.415	1.4142	1.4129	1.4123	1.416
C4-H10	1.081	1.0826	1.0813	1.0827	0.950
C5-C6	1.388	1.3862	1.3826	1.3855	1.369
C5-O22	1.373	1.3664	1.3659	1.3659	1.374
C6-H11	1.083	1.0845	1.083	1.084	0.950
C7-C8	1.378	1.3791	1.3703	1.3767	1.369
C7-H12	1.078	1.0791	1.0779	1.0788	0.950
C8-N14	1.381	1.3751	1.3737	1.3755	1.377
C8-C15	1.464	1.4619	1.4681	1.4613	1.455
H13-N14	1.008	1.0083	1.0081	1.0074	0.891
C15-O16	1.215	1.2166	1.2069	1.2133	1.211
C15-O17	1.347	1.3365	1.3354	1.3412	1.239
C18-O17	1.439	1.4357	1.4292	1.4308	1.448
C18-H19	1.091	1.091	1.0903	1.0917	0.980
C18-H20	1.088	1.0876	1.0864	1.0884	0.980
C18-H21	1.091	1.091	1.0903	1.0917	0.980
C23-O22	1.419	1.4191	1.4097	1.4111	1.416
С23-Н24	1.089	1.0893	1.088	1.0899	0.979
С23-Н25	1.096	1.0952	1.0951	1.0969	0.980
C23-H26	1.096	1.0952	1.0951	1.0969	0.980
Bond angle (°)					
C2-C1-C6	119.55	119.6074	119.5603	119.5737	120.03
C2-C1-C7	106.84	106.8039	106.8566	106.829	106.59
C6-C1-C7	133.61	133.5887	133.5832	133.5973	133.39
C1-C2-C3	121.37	121.4031	121.4677	121.3741	121.46
C1-C2-N14	107.54	107.6847	107.6798	107.5716	108.06

C3-C2-N14	131.09	AC130.9122D	M130.8524RI	PT 131.0543	130.48
C2-C3-C4	118.17	118.0923	118.1029	118.1228	117.48
С2-С3-Н9	121.54	121.4706	121.4342	121.5811	121.39
С4-С3-Н9	120.29	120.4371	120.463	120.2962	121.29
C3-C4-C5	121.10	121.1861	121.0232	121.1636	121.78
C3-C4-H10	118.68	118.6405	118.6365	118.665	119.08
C5-C4-H10	120.22	120.1734	120.3403	120.1713	119.15
C4-C5-C6	120.85	120.8611	120.9388	120.824	121.33
C4-C5-O22	123.31	123.0891	123.1238	123.2498	113.67
C6-C5-O22	115.84	116.0498	115.9374	115.9262	125.08
C1-C6-C5	118.96	118.85	118.9071	118.9418	117.92
C1-C6-H11	121.74	121.4815	121.9535	121.7665	121.08
C5-C6-H11	119.29	119.6685	119.1394	119.2918	121.00
C1-C7-C8	106.97	106.784	106.5256	106.8286	107.19
C1-C7-H12	127.66	127.5635	128.0832	127.7802	126.41
C8-C7-H12	125.37	125.6526	125.3912	125.3911	126.41
C7-C8-N14	109.58	109.6743	110.182	109.668	109.70
C7-C8-C15	132.08	131.3485	131.6959	132.1618	130.54
N14-C8-C15	118.33	118.9772	118.1221	118.1702	119.70
C2-N14-C8	109.07	109.0531	108.756	109.1028	108.44
C2-N14-H13	127.87	127.04	127.9913	127.9496	126.39
C8-N14-H13	123.06	123.9069	123.2528	122.9476	123.99
C8-C15-O16	123.50	123.5079	123.3043	123.4144	124.91
C8-C15-O17	112.56	112.3885	112.5556	112.5613	112.04
O16-C15-O17	123.94	124.1036	124.1402	124.0244	123.05
C15-O17-C18	115.84	116.1871	115.2102	115.4832	116.78
O17-C18-H19	110.49	110.4329	110.2575	110.5861	109.54
O17-C18-C20	105.35	105.4598	105.6595	105.5124	109.45
O17-C18-O21	110.48	110.4327	110.2576	110.5858	109.40
H19-C18-H20	110.63	110.3967	110.7369	110.525	109.46
H19-C18-H21	109.22	109.6599	109.1585	109.0773	109.46
H20-C18-H21	110.64	110.3966	110.7368	110.5249	109.52
C5-O22-C23	118.94	118.6221	118.1587	118.6156	117.19
O22-C23-H24	105.81	105.8793	106.0639	105.9413	109.50
O22-C23-H25	111.65	111.5247	111.3917	111.7444	109.46
O22-C23-H26	111.65	111.5246	111.3912	111.7442	109.48
O24-C23-H25	109.12	109.1371	109.2342	108.9868	109.47
O24-C23-H26	109.12	109.1372	109.2347	108.987	109.44
H25-C23-H26	109.38	109.5328	109.4387	109.3243	109.48

The geometrical parameters for the title compound are presented in Table 1. Morzyk-Ociepa and Rozycka-Sokolowska [24] reported that the carboxylic acid bond lengths (C=O and C–O) are

1.265 Å and 1.270 Å, respectively. The computed values among different methods for the 15C–16O bond of the title compound are 1.215, 1.206 and 1.213 Å using B3LYP, M06-2X and B3PW9, respectively. The theoretical values are in good agreement with the XRD value (1.211 Å). In the case of the methoxy group connected to the left side of the indole ring, the bond lengths of 23C–22O computed with B3LYP, M06-2X and B3PW9 are 1.419, 1.410 and 1.411Å, respectively, and they are in good agreement with that of experimental value (1.416 Å). Whereas the C–O bond (15C–17O) on the right side of the ring is not as same as that of the computed values which has difference nearly ~1.1 Å. In the case of the N–H bond (H13-N14), the computed values are found to be higher than the experimental one (0.891 Å). It is also found that all of the C–C, C–N, and C–H bond lengths of the indole group are close to the experimental X-ray diffraction (XRD) values. In addition, the calculated geometrical parameters for the title molecule in the liquid state (ethanol) using the B3LYP method showed good agreement with the experimental XRD values, with correlation coefficients (\mathbb{R}^2) = 0.9892 and 0.9083 for bond lengths and angles, respectively.

The C–C bond lengths of the indole ring were found to be different from those of the benzene ring, where the difference between the lengths of the double and single bonds is not clearly observed in the benzene ring. Thus, the indole C–C single bond lengths (Å) were found to be 1.421 (C1-C7), 1.413 (C1-C6), and 1.416 (C4-C5) and the C=C double bond lengths (Å) were 1.369 (C5-C6), 1.372 (C3-C4), and 1.396 (C2-C3). In contrast to the benzene ring, the differentiation of double and single bond lengths is clearly observed. In the case of the C–N bond length (Å), the values were found to be 1.371 (C2-N14) and 1.377(C8-N14). The calculated values were found to be in good agreement with the XRD experimental values. There is a slight distortion of the indole bond lengths due to the attachment of the carboxylic acid methyl ester on the right side of the indole ring and the methoxy group on the left side of the indole ring. Upon comparing the optimised geometrical parameters with the XRD values. This might be because the theoretical calculations were performed in the gas phase, while the solid state was used in the experimental XRD measurements.

The angle for C8-C15-O16 is around 123° for the three computed methods, which is close to the experimental value (124.91°). The angle between the methoxy and carbonyl groups is around 115° and similarly the angle between indole and methoxy groups is around 118° , both are close to the experimental values (116.78 and 117.19, respectively). The C7-C8-N14 angle was observed at around 110° , which is very close to the XRD value at 109.70° . The angle of the 160-15C-170 functional group was found to be around 124° and it is close to the experimental value (123.05°). The angle where the carboxylic methyl ester group is connected with the indole ring (C8-C15-O17) was observed to be around 112° , which is also close to the XRD value (112.04°).

3.3. Crystal structure of the MMIC molecule

The asymmetric unit of the MMIC molecule, $C_{11}H_{11}NO_3$, has one independent molecule with a nearly planar indole residue. The crystal structure packing of the target molecule is stabilized by one intermolecular hydrogen bond with N1 works as hydrogen bond donor while O1 works as hydrogen bond acceptor. The distance of the interactions between N1—H1…O1 is 2.03 (1) Å and the angle is 160°. Symmetry code: -x, -y+1, -z. The atomic displacement parameters, fractional atomic coordinates and selected data collection for the crystal are displayed in Tables T1, T2 and T3, respectively.

3.4. Vibrational analysis

The vibrational spectral assignments were completed by recording the FT-IR and FT-Raman spectra and the theoretically predicted wavenumbers using the density functional B3LYP/6-311++G (d,p) method, as illustrated in Table 2. A scale factor was adopted for the computed infrared and Raman wavenumbers of the title molecule according to Scott and Radon [26]. The RMS value between the experimental and the predicted vibrational wavnumbers of the title molecule was calculated to be 26.4098. Figure S1 illustrates the correlation between the computed and experimental wavenumbers with a coefficient (R^2) value = 0.997. None of the predicted vibrational wavenumbers have any imaginary frequencies, which proves that the optimised structure is located at the local lowest point on the potential energy surface (PES). The title molecule possesses C₁ point group symmetry and it is distributed as:

$$\Gamma_{3N-6} = 49A^{(in-plane)} + 23 A^{(out-of-plane)}$$
(1)

Here "A`" represents the symmetric planar and "A``" represents the asymmetric non-planar vibrations. Figures S2 and S3 illustrate the IR and Raman active vibrations of the title molecule, respectively.

	Experimental		Theor	etical Waver	number	TED-100/
Mode Nos.	FT-IR	Raman	Scaled	IR _{Int}	Raman _{Act}	TED≥10%
1	3482b		3532	109.21	77.55	υNH (100)
2	3126w		3149	0.18	72.81	υCH (99)
3			3102	6.09	125.85	υCH (93)
4	3086vw		3087	3.76	105.44	υCH (99)
5			3072	6.72	78.07	υCH (93)
6	3048vw		3053	13.69	82.45	asyuCH (81)
7		3031vw	3026	26.59	160.66	asyuCH (92)
8	2992vw	2997w	3020	18.82	68.40	аsyvCH (98)
9	2934w	2944w	2953	42.75	73.32	asyuCH (100)
10			2949	44.86	243.52	symuCH (100)
11	1784s	1782m	2899	72.39	192.40	symuCH (92)
12	1746s	1760ms	1687	470.40	447.43	υOC (83)
13	1713vs	1745vs	1614	39.67	28.10	υCC (62)
14	1611s	1615w	1558	12.56	11.95	$\nu CC (32) + \beta CCC (10)$
15	1587s	1597ms	1520	224.35	430.43	υCCC (47)
16			1468	0.07	62.25	υCC (42)
17	1456vs		1453	44.84	6.27	βНСН (70)
18			1449	11.25	16.75	βHCH (89)
19			1442	8.68	16.63	βHCH (81) + γCHOH (11)
20		1434w	1434	15.07	17.79	βHCH (82) + γCHOH (16)
21			1434	9.23	15.55	γСННН (48)
22			1422	38.61	2.96	β HCO (41) + ν CHOH (40)
23			1415	48.94	85.54	β HCC (14) + ν CHHH (34)
24	1381vs	1380vw	1398	43.64	218.04	$\gamma CCCC(12) + \upsilon NC(25) + \beta CCC(12)$

Table 2. Vibrational wavenumbers obtained for the MMIC molecule at B3LYP/6-311++G(d,p) method [harmonic frequency (cm⁻¹), IR_{int}(Km/mol), Raman Activity (Å⁴/amu units)].

						$+\beta$ HNC(11)
25	1332vs		1352	44.55	17.25	υCC (11)
26	1307m	1309vw	1295	130.73	48.07	υCC (48) + υNC (17)
27	1264m	1268vw	1275	12.76	126.93	$\upsilon OC (10) + \beta HCC (22) + \beta CCC (14)$
28	1220m	1220m	1217	1047.21	179.23	υOC (31) + βHNC (11)
29			1206	12.16	15.44	β CCC (12) + β HCC (35)
						$vNC(10) + vOC (12) + \beta HNC (19)$
30			1200	50.24	8.18	+ βHCC (24)
						vOC (10) + βHCO (27) +
31		1174m	1174	66.61	38.80	γCHOH(36)
32	1161m		1162	70.64	23.67	βHCO (15) + γCHOH (16)
33		1153s	1143	38.95	7.84	υOC (10) + γCHOH (12)
34			1131	0.71	3.33	β HCH (17) + γ CHOH (82)
35			1128	0.71	3.04	β HCO (5O) + γ CHOH (44)
36	1096m		1121	24.49	8.93	$\nu CC (13) + \beta HCC (64)$
37	1039m	1044w	1084	33.31	11.22	βHCC (40)
38	1010m	1021s	1024	36.38	3.74	υOC (53) + βHCC (14)
39	978m	980vw	988	48.09	6.31	vNC(18) + vOC (47)
40			924	6.42	110.32	$vOC(20) + \beta CNC(19)$
41	905m		914	0.33	0.79	βCCC (57)
42	878w	884vw	891	1.75	0.61	τHCCH (89)
43			849	33.25	0.24	γCCCH (80)
44			812	6.76	4.05	$\nu NC (11) + \beta CCC (21)$
45	815m	808w	804	2.83	2.16	γCCCH (79) + γOCOC (13)
46	770vs	Y '	770	16.71	0.30	τHCCN (75)
						$\upsilon OC (10) + \beta OCO (28) + \beta COC$
47		765w	764	0.23	25.26	(11)
48			753	48.83	0.17	γ CCCH (11) + γ OCOC (54)

49		723m	729	14.70	18.06	$vCC(23) + vOC(19) + \beta CNC(14)$
50	707m	709s	718	10.83	0.05	τCCCC (57)
						$\beta CCC (10) + \beta CCN (11) + \beta CCO$
51	682m		621	3.89	6.12	(20)
52		604w	607	0.07	1.21	$\tau CCCN (51) + \tau CCCC (10)$
						τ HNCC (11) + τ CCCN (31) +
53	594s		587	13.09	0.01	τCCCC (37)
54	552m	552m	557	16.44	3.21	β CCC (36) + β COC (10)
						β CCO (26) + β CCC (19) + β COC
55		495ms	511	1.86	1.46	(13)
						β HCC (14) + τ HNCC(77) + γ CHHH
56	464vs		448	71.37	0.34	(34)
						$vCC(13) + \beta OCO (10) + \beta CCC (11)$
57			436	0.32	3.56	$+\beta COC (14)$
58			422	0.21	0.80	τCCCC (75)
59		351w	360	0.11	0.35	τCCCO (29) + τCCCN (38)
						$\beta CCN (18) + \beta CCO (15) + \beta COC$
60			357	15.29	0.76	(37)
61		298w	289	14.06	2.23	β OCO (10) + β COC (55)
62		277vw	280	2.11	7.13	υ CC(24) + β CCC (12) + β OCO (11)
			\geq			$\tau CCCC$ (10) + $\tau CCNC$ (35) +
63		261vw	261	3.01	0.18	τCNCC (11)
64			235	0.24	0.09	τHCOC (75)
65			209	0.31	0.42	β CCO (51) + β COC (23)
		ý.				$vOC(10) + \tau HCOC$ (12) +
						$\tau CCNC(12) + \tau CCOC(20) +$
66		165s	176	0.13	1.74	$\tau CCCO(21) + \tau CNCC(13)$
67		140m	145	1.53	0.81	$\tau HCOC$ (39) + $\tau CCOC$ (22) +

		ACCEPTED	MANUSCRIPT		
					τCCCO (13)
68	103vs	119	1.54	0.83	τHCOC (54) + τCCOC (27)
69		91	2.27	0.35	β CCO (22) + β CCC(47)
					$\tau NCCO$ (23) + $\tau CCOC$ (20) +
70		72	2.27	0.04	tCNCC (30)
71		69	0.88	1.23	τΝCCO (55) + τCCOC (26)
72		43	3.82	0.23	τCCOC (50) +τCNCC(21)

IR int-IR intensity; Ram_{Act} - Raman Activity; w-weak; vw- very weak; s-strong; vs-very strong; m-medium; br, sh- broad, shoulder, υ - stretching; υ_{sym} - symmetric stretching; υ_{asy} - asymmetric stretching; δ - in plane bending; γ - out-of –plane bending; τ - torsion.

ig, ,- out-of -plan,

3.4.1. C–H vibrations

The heteroaromatic structure shows the presence of C–H stretching vibrations in the region of 3100–3000 cm⁻¹, which is characteristic of such vibrations [27]. In this region, the bands are not affected appreciably by the nature of the substituents. The C–H stretching modes usually appear with strong Raman intensity and are highly polarised. This high polarisation might be the reason for the absence of Raman bands in the experimental spectra. In the indole ring of the MMIC molecule, there are four C–H bonds (C3-H9, C4-H10, C6-H11, and C7-H12), so we expected to observe four C–H stretching, C–H in-plane and C–H out-of-plane bending vibrations. In the FT-IR spectrum of the MMIC molecule, the weak bands at 3126 and 3086 cm⁻¹were assigned to C–H stretching vibrations. The theoretically computed wavenumbers for the title compound fall at 3149, 3102, 3087, and 3072 cm⁻¹ (mode nos.2-5, respectively) with a TED contribution of about 95%, as shown in Table 2.

The C–H in-plane bending vibration is usually expected to occur in the region of 1300–1000 cm⁻¹ and these vibrations are very useful for characterisation [27]. In the title MMIC molecule, the medium bands at 1264 and 1220 cm⁻¹ in the FT-IR spectrum and medium to weak bands at 1268 and 1220 cm⁻¹ in the FT-Raman spectrum were assigned to the C–H in-plane bending modes of the C3-H9, C4-H10, C6-H11, and C7-H12 units with a TED contribution of about 20%. The wavenumbers for this mode at 1275, 1217, 1206, and 1200 cm⁻¹ were assigned to C–H in-plane bending vibrations.

The C–H out-of-plane bending vibrations are normally observed as strongly coupled vibrations and occur in the region of 1000–750 cm⁻¹ [28]. The aromatic C–H out-of-plane bending vibrations fall at 849, 804, 764, and 753 cm⁻¹ (mode nos. 43, 45, 47, and 48, respectively) by the B3LYP/6-311++G (d,p) method and they showed good agreement with the recorded FT-IR band at 815 cm⁻¹ and the FT-Raman bands at 808 and 765 cm⁻¹. The computed, as well as the recorded spectral data, were found to be very consistent with reported values [29,30]. The TED contribution is about 70% as a mixed mode with other vibrations, as shown in Table 2.

3.4.2. $O-CH_3$ vibrations

The vibrational wavenumbers of the methoxy groups in the MMIC molecule include a large number of interesting interactions, such as electronic effects, intermolecular hydrogen bonding and Fermi resonance [31]. The electronic effects, such as back donation and induction, are mainly caused by the oxygen atom attached to the CH₃ group, which alters the position of the C–H stretching and bending modes [32,33]. The methoxy group vibrations were observed in both the IR and Raman spectra as intense bands, with a large variation from the normal values of the methyl groups. This is due to the electronic effect, which led to deviations from the expected values [34]. In the MMIC molecule, the two methoxy carbon atoms lie in the same plane, which is evident from the optimised structure, as shown in Figure 2. In the present study, the very weak bands observed in the FT-IR spectrum at 3048,

2944 cm⁻¹ were assigned to C18-H19, H20, and H21 (asymmetric stretching vibrations) and C23-H24, H25, and H26 (symmetric stretching vibrations), respectively. The theoretically computed wavenumbers for the asymmetric and symmetric stretching vibrations were at 3035, 3053, 2620, 3020, 2953 and 2949 cm⁻¹ (mode nos.6-11) with a TED contribution of about 90%. The O-CH₃ stretching vibrational mode has been assigned at around 1040 cm⁻¹ for anisole [35] and at 1000–100 cm⁻¹ for anisole and its derivatives [36]. In the MMIC molecule, the O-CH₃ stretching mode appeared as a medium strength band in the FT-IR spectrum at 1010 and 978 cm⁻¹ and as a strong band to a very weak band at 1021 and 980 cm⁻¹ in the FT-Raman spectrum, showing good agreement with the computed wavenumbers at 1028 and 988 cm⁻¹ (mode nos. 38 and 39) and coinciding with the experimental results, with a TED contribution of about 45%. Arslan and Algül [37] assigned the C–O–CH₃ angle bending mode to be around at 300 cm⁻¹ for anisole, and a bending mode at 421 cm⁻¹ for 4-methoxy benzaldehyde was found by Campaqnaro and Wood [38]. Others [39] have assigned the C-O-CH₃ bending mode in the region of 670–300 cm⁻¹ for anisole and its derivatives, mixed with C–C–C angle bending modes. We have assigned the predicted wavenumber at 360 cm⁻¹ (mode no. 59) to be the C-O-CH₃ angle bending mode, which showed good agreement with the recorded FT-Raman band at 351 cm⁻¹ with a TED contribution of 29%. The torsional mode of the O–CH₃ group vibrations for anisole has been predicted at around 100 cm⁻¹ by some researchers [37-39]. Balafour [36] assigned this mode at 82 cm⁻¹, and Lakshmaiah and Rao [40] calculated these vibrations as 58 cm⁻¹ for anisole and its derivatives. In the MMIC molecule, these modes were calculated at 145 and 119 cm⁻¹ and were assigned to the O–CH₃ torsional mode, showing good agreement with the observed FT-Raman spectral data, as presented in Table 2.

3.4.3. C=O vibrations

The C=O stretching vibration typically appears to be free from other vibrations. In many carbonyl-containing compounds, the C=O double bond has a force constant which is different from the structural units, such as C=C, C-C, and C-H. Only the structural C=C units have force constants of similar magnitudes to the C=O group. Carbonyl compounds show a very intense and narrow band in the region of 1800–1600 cm⁻¹ [41,42]. In the present study, the C15=O16 stretching vibrations were recorded in the FT-IR and FT-Raman spectra at 1746 and 1760 cm⁻¹, respectively, as strong bands. The computed wavenumber for this mode of vibration was at 1687 cm⁻¹ (mode no. 12) with a TED contribution of 83%, showing moderate agreement with experimental and literature data [41,42]. *3.4.4. Ring vibrations*

The identification of C=N and C–N vibrations is a difficult task, since the mixing of several bands is possible in the region. Silverstein *et al.* [41] assigned C=N stretching absorption in the region of 1382–1266 cm⁻¹ for aromatic amines. In benzamide, a band was observed at 1368 cm⁻¹ and it was assigned as C–N stretching [41]. In the present work, the FT-IR and FT-Raman bands observed at

1307 and 978 cm⁻¹, and 1309 and 980 cm⁻¹, respectively, have been assigned as the C–N stretching vibrations of the MMIC molecule. The predicted values of the C–N stretching vibrations were at 1295, 1200, and 988 cm⁻¹ (mode nos. 26, 30, and 39). The benzene ring carbon–carbon stretching vibrations occur in the region of 1430–1625 cm⁻¹. In general, the bands are of variable intensities and are observed at 1625–1590, 1575–1590, 1470–1540, 1430–1465, and 1280–1380 cm⁻¹ from the frequency ranges given by Varsanyi [43]. In this work, the wavenumbers computed by the B3LYP/6-311++G (d,p) method for the MMIC molecule at 1614, 1558, 1468, 1352, 1295, 1275, 1217, 1174, 1143, 1121, 988, and 812 cm⁻¹ (mode nos. 13, 14, 16, 25-28, 31, 33, 36, 39 and 44, respectively) were designated as the C–C stretching vibrations. The TED corresponding to all C–C vibrations lies between 30 and 70%, as shown in Table 2, in combination with C–H in-plane bending in this region. The in-plane deformation vibrationsare found at higher wavenumbers than the out-of-plane vibrations. Shimanouchi *et al.* [39] gave the frequency data for these vibrations for different benzene derivatives as a result of normal coordinate analysis. The other vibrations computed by the B3LYP/6-311++G (d,p) method showed good agreement with the recorded spectral data.

3.5. ¹H and ¹³C NMR spectral analysis

Application of the gauge independent atomic orbitals (GIAO) [44] approach to molecular systems is considerably more efficient when compared with *ab initio* self-consistent field (SCF) calculations. The GIAO calculation procedure is superior since it exhibits faster convergence of the calculated properties upon extension of the chosen basis set. Taking into consideration the computational cost and the effectiveness of the calculations, the GIAO method seems to be preferable in many aspects. Figure S4 illustrates the correlation between the computed and experimental chemical shift values of the title molecule having correlation coefficients (R^2) values = 0.865 and 0.990 for ¹H and ¹³C, respectively.

GIAO ¹H and ¹³C chemical shift calculations for the MMIC molecule were computed using the B3LYP/6-311++G (d,p) method for the gas and solution phases and the results are presented in Table 3. The signals of the aromatic protons were observed at 7.37–11.79 ppm. The hydrogen atom is the smallest atom and it is typically localised at the periphery of the molecules. Therefore, its chemical shift is more susceptible to intermolecular interactions in aqueous solution, compared with other heavier atoms. Attached hydrogen atoms or nearby electron-withdrawing atoms or groups will be subjected to reductions in shielding and their resonance will move towards a higher frequency. In contrast, electron donating atoms or groups increase the shielding and move the resonance towards a lower frequency. In the MMIC molecule, the observed and calculated chemical shifts for the hydrogen atoms of methyl groups are quite low due to their attachment to electron-withdrawing oxygen atoms. Thus, the methyl protons at C18 and C23 appeared as singlets, with three proton integrals at 3.87 and

3.77 ppm, respectively. The observed chemical shift values for the other protons are in good agreement with the computed ones (Table 3).

The range of ¹³C NMR chemical shifts for a typical organic molecule are usually expected to be above 10-200 ppm [45,46]. This accuracy ensures reliable interpretation of spectroscopic parameters. In the present study, the signals observed at 52.14 and 55.67 ppm in the ¹³C NMR spectrum of the MMIC molecule were assigned to methoxy carbons (C18 and C23). The signals for the aromatic carbons were observed at 102.43, 113.94, 116.77, 127.70, 133.23, and 154.44 ppm in the ¹³C NMR spectrum for the title molecule, since those carbon atoms belong to the benzene ring. The indole carbons (C7 and C8) were observed at 107.82 and 127.51 ppm, respectively. In general, the observed chemical shift values of the carbons in the MMIC molecule are in good agreement with the calculated values (Table 3).

Table 3. The experimental and theoretical ¹³C and ¹H NMR chemical shift values of the MMIC molecule.

		¹³ C				$^{1}\mathrm{H}$	
	$\delta_{exp.}$	δ_{c}	alc.		δ _{exp.}	δ _{ca}	ılc.
Atom	DMSO	Coorthoos	Solution	Atom	DMSO	Casahaaa	Solution
		Gas phase	phase			Gas phase	phase
C1	127.70	135.71	135.16	H9	7.37	7.43	7.64
C2	133.23	137.84	138.03	H10	6.94	7.15	7.34
C3	116.77	114.16	115.49	H11	7.11	7.42	7.44
C4	113.94	111.85	112.35	H12	7.07	7.17	7.25
C5	154.44	161.84	161.97	H13	11.79	8.31	8.57
C6	102.43	113.35	113.00	H19	3.87	3.95	3.98
C7	107.82	111.58	111.23	H20	3.87	3.62	3.78
C8	127.51	133.82	133.82	H21	3.87	3.95	3.98
C15	162.17	168.98	169.82	H24	3.77	4.01	4.08
C18	52.14	53.50	53.93	H25	3.77	3.71	3.81
C23	55.67	55.15	55.49	H26	3.77	3.71	3.81

3.6. UV-visible frontier molecular orbital analysis

The most common types of electronic transitions that occur in organic molecules are $\pi \to \pi^*$, $n \to \pi^*$ and $\pi^*(acceptor) \to \pi$ (donor) [47]. The Gausssum 3.0 program [48] was used to calculate group contributions to the molecular orbitals (HOMO and LUMO) and prepare the density of the state (DOS) spectrum, as shown in Figures 3 and S5, respectively. The DOS spectrum was calculated by convoluting the molecular orbital information with a GAUSSIAN curve of the unit cell. The recorded UV-vis absorption spectrum of the MMIC molecule was recorded in acetonitrile, along with the theoretical simulated spectrum as shown in Figure S6. In order to understand the nature of the electronic transitions, the positions of the experimental absorption peaks, the calculated absorption

peak (λ_{max}), the vertical excitation energies, and the oscillator strength (f) were calculated and are presented in Table 4.



Figure 3. HOMO-LUMO representation of the MMIC molecule.

Table 4. Calculated and experimental absorption wavelengths, energies and oscillator strengths of theMMIC using TD-DFT method at the B3LYP/6-311++G (d,p).

Excitation		Gas Phase		А	cetonitrile Phase	e	Experimental	Assignments	In solvent
	CI	Wavelength	Oscillator	CI	Wavelength	Oscillator	-		major
	expansion	(nm)	Strength	expansion	(nm)	Strength			contribution
	coefficient			coefficient					(≥10%)
Excited state 1	0.69760	344.68	0.0445	0.69961	349.77	0.0594	296	$n { ightarrow} \pi^*$	H→L (97%)
Excited state 2	0.68266 0.15527	288.05	0.4696	0.69072 0.12666	295.24	0.5926	247	$n { ightarrow} \pi^*$	H-1→L (93%)
Excited state 3	0.69274	248.79	0.0002	-0.10932 0.67908	246.33	0.0253	228	n→π*	H→L+2 (96%)

The first transition was from the $O(22)CH_3$ to the carboxylate group $C(O)OCH_3$ and the other two transitions took place in the indole ring N14 to 8C–7C and 2C–1C. Table 4 shows the oscillator strengths, which indicate the intensity of these transitions. The transitions in the gas phase are 0.0445, 0.4696, and 0.0002for $O(22)CH_3$ – $C(O)OCH_3$, 8C–7C and 2C–1C, respectively. In the acetonitrile phase, the same transitions are 0.0594, 0.592, and 0.025, respectively. These oscillator strength values showed that only the first two transitions will be present in the experimental and theoretical UV-vis

spectra. This is exactly what was observed in both the experimental and theoretical spectra in acetonitrile, at wavelengths 295 and 246 nm in the experimental spectrum and at 349 and 295 nm in the theoretical spectrum of the MMIC molecule. The corresponding values in the gas phase are at 344 and 288 nm, respectively. The surface of the frontier molecular orbital was described in order to understand the bonding scheme of the MMIC molecule. Four important molecular orbitals were examined i.e. the highest (HOMO) and the second highest occupied (HOMO-1) MOs, as well as the lowest (LUMO) and the second lowest unoccupied (LUMO +1) MOs. The predicted HOMO-LUMO molecular orbitals for the MMIC molecule are shown in Figure 3. The HOMO is located over the ether group, the HOMO \rightarrow LUMO transitions denote that the electron density will transfer from the ether group to the ring system. The energy gap between the HOMO and LUMO of the title molecule in the gas phase is 4.083 eV. The HOMO–LUMO contribution for the first transition is 93%, which is the reason for the very high stabilisation energy and oscillator value for this transition. The absorption wavelength values are almost equal in the gas phase and in acetonitrile, which indicates that the influence of the solvent in the optical activity of the molecule is negligible.

Chemical hardness is a good indicator of the chemical stability. The chemical hardness of the title molecule was found to be around 2.0 eV and this value is slightly decreased going from the gas phase to the solvent phase using either the B3LYPor theB3PW9 method. The chemical softness was around 0.5 eV, indicating that the chemical hardness is very high and hence, the compound is chemically stable. Similarly, the calculated electronegativity using the B3LYP method was observed to be 3.7 eV in the gas phase and 3.8 eV in ethanol phase. Electronegativity is a measure of the attraction of an atom for electrons in a covalent bond. When two different atoms are covalently bonded, the shared electrons will be more strongly attracted to the atom with greater electronegativity.

The electrophilicity index is a measure of the energy lowering due to the maximal electron flow between the donor (HOMO) and the acceptor (LUMO). Table 5 shows that the electrophilicity index of the MMIC molecule using the B3LYP method was 3.32 eV in the gas phase and 3.62 eV in ethanol. These are moderate values, and ensure strong energy transformation between the HOMO and LUMO [49]. The dipole moment in a molecule is another important electronic property. When a molecule has a large dipole moment, intermolecular interactions are very strong. The calculated dipole moment value for the title compound is 0.93 D in the gas phase and 1.39 D (using B3LYP) in the solvent phase. These are comparatively high, indicating that the MMIC molecule has strong intermolecular interactions.

Table 5. HOMO, LUMO, Kubo gap, global electronegativity, global hardness and softness, global electrophilicity index, and dipole moment of the MMIC molecule.

Parameters	Gas	Ethanol		
	B3LYP/ 6-	B3LYP/ 6-	B3PW91/ 6-	M06-2X/ 6-
	311G++ (d,p)	311G++ (d,p)	311G++(d,p)	311G++(d,p)
E _{HOMO} (eV)	5.722	5.858	5.7692	6.9956
E _{LUMO} (eV)	1.639	1.804	1.8285	0.6576
ΔE_{HOMO} - $E_{LUMO gap}$ (eV)	4.083	4.054	3.9406	6.3379
Chemical hardness (η)	2.041	2.0271	1.9703	3.1689
Global softness(σ)	0.489	0.493	0.5075	0.6311
Electronegativity(χ)	3.680	3.831	3.7989	3.8266
Electrophilicity index(ω)	3.318	3.621	3.6622	2.3105
Dipole moment (µ)	0.9333	1.3852	0.9277	0.7434

3.7. Molecular electrostatic potential (MEP) analysis

The MEP is used to analyse the reactivity of molecules. In most MEP diagrams, electrophilic attack is indicated as red and nucleophilic attack is represented in blue. The MEP diagram also displays the molecular shape, size, and negative, positive and neutral electrostatic potential *via* colour grading and helps researchers to analyse the physicochemical properties of molecules [50]. The different colours in Figure S7 represent different values of electrostatic potential at the surface of the MMIC compound. The electrostatic potential increases in the order red<orange<yellow<green
blue. The colour code of the maps was found to be in the range of -0.454 a.u (deepest red) to 0.454 a.u (deepest blue), where the red colour indicates the strongest repulsion and the blue colour indicates the strongest attraction. Regions of negative V(r) are usually associated with the lone pair of an electronegative atom. As seen in Figure S7, negative electrostatic potential is present over the oxygen atoms of the C=O and OCH₃ groups and a region with positive electrostatic potential is present over the hydrogen atoms and ring system. The high proportion of the light green colour probably represents the halfway point between the two extremes, red and blue. This analysis provides information about regions where the compound can be subject to intermolecular interactions.

3.8. Hyperpolarisabilities

Properties such as polarisability and hyperpolarisability were calculated for the title molecule in the gas phase. An isolated molecule of MMIC was taken and the NLO properties were studied using the DFT technique in order to show any indication of NLO character according to its calculated polarisability, hyperpolarisability and dipole moment. The hyperpolarisability and dipole moment values of urea as studied by Cassidy *et al.* [51] were considered as a reference.

Hyperpolarisabilities are very sensitive to the employed basis sets and levels of theoretical approach [52-54]. Thus, the electron correlation can change the value of hyperpolarisability. It is already established that the molecular hyperpolarisability and mechanical stabilities are enhanced in organic molecules containing O-H and N-H groups, which are involved in the hydrogen bond interactions [55]. Urea is one of the prototypical molecules used in the study of the nonlinear optical (NLO) properties of molecular systems. Therefore, it has frequently been used as a threshold value for comparative purposes. The highest values of the dipole moment were found to be 0.8352 and 0.8064 D along μ_x computed from B3LYP and B3PW91 methods, respectively, at 6-311++G (d,p) basis set. For the Y and Z directions, the values are equal to 0.4382 and 0.4586 D, and 0.0017 and 0.0005 D using the B3LYP and B3PW91 methods, respectively. However, the dipole moment calculated by the M06-2X/6-311++G (d,p) method is much lower than that obtained from the other two methods, as shown in Table 6. The first order hyperpolarisability total value for the MMIC molecule calculated using the B3LYP and B3PW91 methods with the 6-311++G (d,p) basis set are 11.146×10^{-30} and 11.124×10^{-30} esu, respectively, whereas the value obtained with M06-2X/6-311++G (d,p) is 9.443×10^{-30} esu, as illustrated in Table 7. The first order hyperpolarisability of the MMIC molecule is about 30 (using B3LYP and B3PW91) and 25 (using M06-2X) times greater than that of urea $(0.3728 \times 10^{-30} \text{ esu})$. This large hyperpolarisability value of the title molecule indicates that it has considerable NLO optical properties. Therefore, the title molecule can be subjected to future studies to investigate its NLO properties.

Table	6.	The	calculated	electric	dipole	moment	(Debye	components	for the	ne MMIC	molecule)	by
	E	B3LY	P, B3PW9	1 and M)6-2X 1	nethods a	t 6-311+	+G (d,p) basi	is set.			

Parameter	B3LYP/6-311++G (d,p)	B3PW91/6-311++G (d,p)	M06-2X/6-311++G (d,p)
μ_{x}	0.8352	0.8064	0.4942
μ_y	0.4382	0.4586	0.5553
μ_z	0.0017	0.0005	0.0006
μ	0.9432	0.9277	0.7434

B3PW91 and M06-2X methods at 6-311++G (d,p) basis set.

β components	B3LYP/6-311++G (d,p)	B3PW91/6-311++G (d,p)	M06-2X/6-311++G (d,p)
	a.u	a.u	a.u
β_{xxx}	-1356.6407	-1345.1045	-1133.9397
β_{xxy}	97.7461932	92.7165419	90.4670
β_{xyy}	20.7961061	17.6896171	10.1928
$oldsymbol{eta}_{yyy}$	25.8027336	27.0419735	25.1735
β_{xxz}	0.0367924	0.0341322	0.03341
eta_{xyz}	0.0162696	0.0155299	0.01567
eta_{yyz}	-0.015457	-0.0148109	-0.0129
eta_{xzz}	56.2656156	49.625379	40.1164
eta_{yzz}	41.5670401	39.0049653	27.4046
eta_{zzz}	0.0917631	0.082628 5	0.07404
β_{tot}	11.146×10^{-30} esu	11.124×10 ⁻³⁰ esu	9.443×10^{-30} esu

3.9. Natural bond orbital (NBO) analysis

NBO analysis is an effective tool for the chemical interpretation of hyperconjugative interactions and electron density transfer from the filled lone pair orbital of one subsystem to the vacant orbital of another subsystem. DFT calculations are used to analyse the various second order interactions between the filled orbitals and vacant orbitals of a system, giving a measure of the delocalisation and hyperconjugation [56,57]. The hyperconjugative interaction energy can be obtained from the second order perturbation method as:

$$E(2) = -n_{\sigma} \frac{\langle \sigma | F | \sigma \rangle^2}{\varepsilon_{\sigma*} - \varepsilon_{\sigma}} = -n_{\sigma} \frac{F_{ij}^2}{\Delta E}$$
(2)

where $\langle \sigma | F | \sigma \rangle^2$ or F_{ij}^2 is the Fock matrix element between the i and j NBO orbitals, ε_{σ} and ε_{σ^*} are the energies of σ and σ^* NBOs, and n_σ is the population of the donor σ orbital [58].The NBO analysis shows the various possible donors and acceptors in the molecule with their occupancy value in each position. Similarly, the various possible transitions among these donors and acceptors are provided. The intramolecular interaction is formed by orbital overlap between bonding C-C, C-O and C-H to anti-bonding C–C, C–O and C–H, which leads to intramolecular charge transfer (ICT) to stabilise the molecule. The $E^{(2)}$ value in Table 8 shows that the larger the $E^{(2)}$ values, the more intense the interactions between the electron donors and acceptor groups i.e. the greater the electron donating tendency from electron donors to electron acceptors, the greater the extent of conjugation in the whole system.

The electron density of the conjugated systems and of the double bond of the MMIC molecule is (~1.6 to 1.9 e), which denotes the strong delocalisation in the molecule. For example, the intramolecular hyperconjugation interaction of π (C3-C4) distributed to π^* (C1-C2), (C1-C6) has stabilisation energies of 17.11 and 18.30 KJ/mol; and the C5-C6 distributed to the π^* (C1-C2 and C3-C4) has stabilisation energies of 18.77 and 18.54 KJ/mol. In the same way, for the $\pi \rightarrow \pi^*$ transition observed in the indole ring C7-C8, energy is distributed to C1-C2 and C15-O16 with stabilisation energies of 22.24 and 19.08 KJ/mol. The other transitions are shown in Table 8.

The magnitudes of the charge transfer from the lone pair of the nitrogen atom LPN14 to various C–C bonds are as follows: C7-C18 and C1-C2 ($n \rightarrow \pi^*$, 37.03 and 35.94 KJ/mol, respectively), LPO16 to C15-O17 and C8-C15 ($n \rightarrow \pi^*$, 31.49 and 16.33 KJ/mol, respectively), LPO17 to C13-O14 ($n \rightarrow \pi^*$ 46.17 kJ/mol) and O22 to C5-C6 ($n \rightarrow \pi^*$ 25.65 KJ/mol). Transitions with higher stabilisation energies are correlated with the UV-visible transitions.

Donor (i)	Туре	ED/e	Acceptor (j)	Туре	ED/e	E(2) (Kj/Mol)	E(j)-E(i) (a.u)	F(i,j) (a.u)
C1-C2	σ	1.95891	C1-C6	σ^*	0.01948	3.01	1.24	0.055
C1-C2	σ	1.95891	C2-C3	σ^*	0.02138	4.26	1.23	0.065
C1-C2	σ	1.95891	C7-H12	σ^*	0.01123	3.44	1.11	0.055
C1-C2	σ	1.95891	H13-N14	σ^*	0.01806	4.15	1.05	0.059
C1-C2	π	1.56457	C3-C4	π^*	0.35245	20.40	0.27	0.067
C1-C2	π	1.56457	C5-C6	π^*	0.34778	18.34	0.28	0.065
C1-C2	π	1.56457	C7-C8	π^*	0.33971	19.24	0.27	0.066
C1-C6	σ	1.97339	C1-C2	σ^*	0.02864	3.38	1.23	0.058
C1-C6	σ	1.97339	C1-C7	σ^*	0.01815	3.81	1.23	0.061
C1-C6	σ	1.97339	C5-O22	σ^*	0.02944	3.43	1.05	0.054
C1-C7	σ	1.97033	C1-C6	σ*	0.01948	3.93	1.24	0.063
C1-C7	σ	1.97339	C2-C3	σ*	0.02138	3.70	1.23	0.060
C2-C3	σ	1.97613	C1-C2	σ*	0.02864	4.35	1.24	0.066
C2-C3	σ	1.97613	C2-N14	σ*	0.02381	2.33	1.17	0.047
C2-C3	σ	1.97613	C3-C4	σ*	0.01164	2.81	1.30	0.054
C2-N14	σ	1.98535	C1-C6	σ*	0.01948	2.26	1.39	0.050
C2-N14	σ	1.98535	C2-C3	σ*	0.02138	2.23	1.38	0.050
C2-N14	σ	1.98535	C8-C15	σ^*	0.05994	2.52	1.25	0.051
C3-C4	σ	1.97245	C2-N14	σ^*	0.02381	5.96	1.16	0.074
C3-C4	π	1.75388	C1-C2	π^*	0.51136	17.11	0.29	0.067
C3-C4	π	1.75388	C5-C6	π^*	0.34778	18.30	0.29	0.067
С3-Н9	σ	1.97908	C1-C2	σ^*	0.02864	4.13	1.06	0.059
C3-H9	σ	1.97908	C4-C5	σ^*	0.02927	3.77	1.07	0.057
C4-C5	σ	1.97779	C3-C4	σ^*	0.01164	2.85	1.29	0.054

Table 8. Second order perturbation theory of the Fock matrix NBO analysis of the MMIC molecule.

C4-C5	σ	1.97779	C5-C6	σ^*	0.01949	4.07	1.28	0.065
C4-H10	σ	1.97650	C2-C3	σ^*	0.02138	3.47	1.10	0.055
C4-H10	σ	1.97650	C5-C6	σ^*	0.01949	3.85	1.11	0.058
C5-C6	σ	1.97197	C4-C5	σ^*	0.02927	3.84	1.24	0.062
C5-C6	σ	1.97197	C4-C5	σ^*	0.02927	4.41	1.24	0.066
C5-C6	π	1.69983	C1-C2	π^*	0.02864	18.77	0.28	0.069
C5-C6	π	1.69983	C3-C4	π^*	0.35245	18.54	0.28	0.065
C5-O22	σ	1.99133	C3-C4	σ^*	0.01164	1.02	1.47	0.035
C5-O22	σ	1.99133	C1-C6	σ^*	0.01948	1.42	1.47	0.041
C6-H11	σ	1.97661	C4-C5	σ^*	0.02927	4.65	1.05	0.065
C7-C8	σ	1.97355	C1-C6	σ^*	0.01948	5.39	1.29	0.075
C7-C8	σ	1.97355	H13-N14	σ^*	0.01806	3.32	1.10	0.054
C7-C8	π	1.79173	C15-O16	π^*	0.29065	22.24	0.27	0.070
C7-C8	π	1.79173	C1-C2	π^*	0.51136	16.08	0.29	0.066
C7-H12	σ	1.98149	C8-N14	σ*	0.02103	3.17	0.98	0.050
C7-H12	σ	1.98149	C1-C2	σ*	0.02864	2.07	1.07	0.042
C8-N14	σ	1.98248	C2-C3	σ*	0.02138	4.40	1.37	0.069
C8-C15	σ	1.97570	C17-C18	σ*	0.01535	3.77	0.96	0.054
C8-C15	σ	1.97570	C7-C8	σ*	0.01494	3.47	1.29	0.060
H13-N14	σ	1.98902	C7-C8	σ*	0.01494	1.79	1.27	0.043
C15-O16	σ	1.99522	C8-C15	σ*	0.05994	2.09	1.52	0.051
C15-O16	π	1.98245	C7-C8	π*	0.33971	4.76	0.42	0.043
C15-O17	σ	1.99277	C8-N14	σ^*	0.02103	1.92	1.37	0.046
O17-C18	σ	1.99162	C8-C15	σ^*	0.05994	2.32	1.27	0.049
C18-H19	σ	1.99462	O17-C18	σ^*	0.01535	0.54	0.79	0.019
C18-H20	σ	1.99218	C15-O17	σ^*	0.09692	2.80	0.89	0.046
C18-H21	σ	1.99462	O17-C18	σ^*	0.01535	0.54	0.79	0.019

O22-C23	σ	1.99335	C5-C6	σ^*	0.01949	2.40	1.41	0.052
C23-H24	σ	1.99083	C5-O22	σ^*	0.02944	3.53	0.89	0.050
N14	LP(1)	1.62108	C7-C8	σ^*	0.01494	37.03	0.29	0.093
N14	LP(1)	1.62108	C1-C2	σ^*	0.02864	35.94	0.29	0.094
O16	LP(1)	1.98023	C8-C15	σ^*	0.05994	2.09	1.15	0.044
O16	LP(2)	1.85113	C15-O17	π^*	0.09692	31.49	0.63	0.128
O16	LP(2)	1.85113	C8-C15	π^*	0.05994	16.33	0.72	0.099
O17	LP(1)	1.96296	C15-O16	σ^*	0.01911	7.62	1.17	0.085
O17	LP(2)	1.79555	C15-O16	π^*	0.29065	46.17	0.33	0.113
O22	LP(1)	1.96303	C4-C5	σ^*	0.02927	6.75	1.08	1.08
O22	LP(2)	1.85531	C5-C6	π^*	0.34778	25.65	0.34	0.089

σ* <u>π*</u> 0.54.

4. Conclusions

A complete vibrational analysis of methyl 5-methoxy-1*H*-indole-2-carboxylate (MMIC) was carried out using various DFT methods with the 6-311G++(d,p) basis set. The computed geometrical parameters produced a good approximation and they were used as a foundation to calculate the other parameters in the current investigation. The FT-IR and FT-Raman spectra of the MMIC molecule were recorded and the observed wavenumbers were found to be well consistent with the computed ones. The TED contribution was about 70% as a mixed mode with other vibrations.

The absorption wavelength values in the UV study of the title molecule are almost equal in the gas and liquid phases, indicating that the influence of the solvent in the optical activity of the molecule is negligible. The calculated hyperpolarisability values of the MMIC molecule are higher than those of the reference NLO compound (urea) and hence MMIC can be considered as a new NLO organic material. The results of the current investigation might support the development of new bioactive indole-bearing molecules.

Supplementary Information

Figures S1-S7 as well as the X-ray data Tables (T1-T3) are given in the supporting information.

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References

- M. Ambriz-Tututi, H.I. Rocha-González, S.L. Cruz, V. Granados-Soto, Melatonin: a hormone that modulates pain, Life Sci. 84 (15) (2009) 489–498.
- [2] J.J. Lu, L. Fu, Z. Tang, C. Zhang, L. Qin, J. Wang, Z. Yu, D. Shi, X. Xiao, F. Xie, W. Huang, W. Deng, Melatonin inhibits AP-2β/hTERT, NF-κB/COX-2 and Akt/ERK and activates caspase/Cyto C signaling to enhance the antitumor activity of berberine in lung cancer cells, Oncotarget 7 (3) (2016) 2985–3001.
- [3] G. Tahan, R. Gramignoli, F. Marongiu, S. Aktolga, A. Cetinkaya, V. Tahan, K. Dorko, Melatonin expresses powerful anti-inflammatory and antioxidant activities resulting in complete improvement of acetic acid-induced colitis in rats, Dig. Dis. Sci. 56 (3) (2011): 715– 720.
- [4] R.J. Reiter, D.X. Tan, J.C. Mayo, R.M. Sainz, J. Leon, Z. Czarnocki, Melatonin as an antioxidant: biochemical mechanisms and pathophysiological implications in humans, Acta Biochim. Pol. 50 (4) (2003) 1129–1146.
- [5] V. Csernus, B. Mess, Biorhythms and pineal gland, Neuroendocrinol. Lett. 24 (6) (2003) 404–411.

- [6] O. Nosjean, M. Ferro, F. Coge, P. Beauverger, J.-M. Henlin, F. Lefoulon, J.-L. Fauchere, P. Delagrange, E. Canet, J.A. Boutin, Identification of the melatonin binding site MT₃ as the quinine reductase 2, J. Biol. Chem. 275.(40) (2000) 31311–31317.
- [7] D.S. Chemla, J. Zyss, Nonlinear optical properties of organic molecules and crystals, Academic Press, New York, NY, USA, 1987.
- [8] B.B. Ivanova, M. Spiteller, Possible application of the organic barbiturates as NLO materials, Crys. Growth Des. 10 (6) (2010) 2470–2474.
- [9] T. Pal, T. Kar, G.L. Bocelli, G. Rigi, Synthesis, growth, and characterization of L-arginine acetate crystal: a potential NLO material, Crys. Growth Des. 3 (1) (2003) 13–16.
- [10] M.I. Attia, P.A. Witt-Enderby, J. Julius, Synthesis and pharmacological evaluation of pentacyclic 6a,7-dihydrodiindole and 2,3-dihydrodiindole derivatives as novel melatoninergic ligands, Bioorg. Med. Chem. 16 (16) (2008) 7654–7661.
- [11] C. Markl, M.I. Attia, J. Julius, S. Sethi, P.A. Witt-Enderby, D.P. Zlotos, Synthesis and pharmacological evaluation of 1,2,3,4-tetrahydropyrazino [1,2-a]indole and 2-[(phenylmethylamino)methyl]-1*H*-indole analogues as novel melatoninergic ligands, Bioorg. Med. Chem. 17 (13) (2009) 4583–4594.
- [12] C. Markl, W.P. Clafshenkel, M.I. Attia, S. Sethi, P.A. Witt-Enderby, D.P. Zlotos, *N*-Acetyl-5-arylalkoxytryptamine analogs: Probing the melatonin receptors for MT₁-selectivity, Arch. Pharm. Chem. Life Sci. 344 (10) (2011) 666–674.
- [13] D. Coowar, J. Bouissac, M. Hanbali, M. Paschaki, E. Mohier, B. Luu, Effects of indole fatty alcohols on the differentiation of neural stem cell derived neurospheres, J. Med. Chem. 47 (25) (2004) 6270–6282.
- [14] Bruker. APEX2, SAINT and SADABS. Bruker AXS Inc., Madison, WI, USA, 2009.
- [15] G.M. Sheldrick, A short history of SHELX, Acta Cryst. A 64 (1) (2008) 112–122.
- [16] A.L. Spek, Structure validation in chemical crystallography, Acta Cryst. D: Biol. Cryst. 65 (2) (2009) 148–155.
- [17] G.A. Petersson, M.A. Al-Laham, A complete basis set model chemistry. II. Open-shell systems and the total energies of the first-row atoms, J. Chem. Phys. 94 (9) (1991) 6081–6090.
- [18] G.A. Petersson, A. Bennet, T.G. Tensfeld, M.A. Al-Laham, W.A. Shirley, J. Mantzaris, A complete basis set model chemistry. I. The total energies of closed-shell atoms and hydrides of the first-row elements, J. Chem. Phys. 89 (4) (1988) 2193–2218.
- [19] M.J. Frisch, G.W. Trucks, H.B. Schlegel, G.E. Scuseria, M.A. Robb, J.R. Cheeseman, G. Scalmani, V. Barone, B. Mennucci, G.A. Petersson, H. Nakatsuji, M. Caricato, X. Li, H.P. Hratchian, A.F. Izmaylov, J. Bloino, G. Zheng, J.L. Sonnenberg, M. Hada, M. Ehara, K. Toyota, R. Fukuda, J. Hasegawa, M. Ishida, T. Nakajima, Y. Honda, O. Kitao, H. Nakai, T. Vreven, J.A. Montgomery, Jr., J.E. Peralta, F. Ogliaro, M. Bearpark, J.J. Heyd, E. Brothers, K.N. Kudin, V.N. Staroverov, R. Kobayashi, J. Normand, K. Raghavachari, A. Rendell, J.C. Burant, S.S. Iyengar, J. Tomasi, M. Cossi, N. Rega, J.M. Millam, M. Klene, J.E. Knox, J.B. Cross, V. Bakken, C. Adamo, J. Jaramillo, R. Gomperts, R.E. Stratmann, O. Yazyev, A.J. Austin, R. Cammi, C. Pomelli, J.W. Ochterski, R.L. Martin, K. Morokuma, V.G. Zakrzewski, G.A. Voth, P. Salvador, J.J. Dannenberg, S. Dapprich, A.D. Daniels, Ö. Farkas, J.B. Foresman, J.V. Ortiz, J. Cioslowski, D.J. Fox, Gaussian-09, Revision A.02, Gaussian, Inc., Wallingford CT, 2009.
- [20] M.H. Jamroz, Vibrational energy distribution analysis VEDA 4, Warsaw, 2004.

- [21] E.D. Glendening, A.E. Reed, J.E. Carpenter, F. Weinhold, NBO version 3.1 Program manual, TCI, University of Wisconsin, Madison, 1998.
- [22] S.N. Azizi, A.A. Rostami, A. Godarzian, 29Si NMR chemical shift calculation for silicate species by Gaussian software, J. Phys. Soc. Jpn. 74 (5) (2005) 1609–1620.
- [23] C.M. Rohlfing, L.C. Allen, R. Ditchfield, Proton and carbon-13 chemical shifts: comparison between theory and experiment Chem. Phys. 87 (1) (1984) 9–15.
- [24] B. Morzyk-Ociepa, E. Rozycka-Sokolowska, Structures and spectroscopic studies of indolecarboxylic acids. Part III. Diamminetetrakis-μ-(O,O'-indole-3-carboxylate) dicopper (II), J. Mol. Struct. 784 (1) (2006) 69–77.
- [25] M.I. Attia, H.A. Ghabbour, H.-K. Fun, Crystal structure of methyl 5-methoxy-1*H*-indole-2-carboxylate, C₁₁H₁₁NO₃, Z. Kristallogr. New Crys. Struct. 231 (1) (2016) 313–314.
- [26] A.P. Scott, L. Radom, Harmonic vibrational frequencies: an evaluation of Hartree-Fock, Møller-Plesset, quadratic configuration interaction, density functional theory, and semiempirical scale factors, J. Phys. Chem. 100 (41)(1996) 16502–16513.
- [27] G. Varsanyi, Assignments for Vibrational spectra of Seven Hundred Benzene Derivatives, Vol. 1-2, Academic Kiacio, Budapet, 1973.
- [28] G. Thilagavathi, M. Arivazhagan, Density functional theory calculation and vibrational spectroscopy study of 2-amino-4, 6-dimethyl pyrimidine (ADMP), Spectrochim. Acta A: Mol. Biomol. Spectrosc. 79 (3) (2011) 389–395.
- [29] M. Karabacak, E. Postalcilar, M. Cinar, Determination of structural and vibrational spectroscopic properties of 2-, 3-, 4-nitrobenzenesulfonamide using FT-IR and FT-Raman experimental techniques and DFT quantum chemical calculations, Spectrochim. Acta A: Mol. Biomol. Spectrosc. 85 (1) (2012) 261–270.
- [30] M. Arivazhagan, S. Prabhakaran, R. Gayathri, Molecular structure, vibrational spectroscopic, first hyperpolarizability, NBO and HOMO, LUMO studies of *p*-iodobenzenesulfonyl chloride, Spectrochim. Acta A: Mol. Biomol. Spectrosc. 82 (1): (2011) 332–339.
- [31] P.S. Patil, S.M. Dharmaprakash, Synthesis, growth and characterization of second-order nonlinear optical crystal: 5-Br-2-thienyl-4'-methoxychalcone, J. Crys. Growth 305 (1): (2007) 218–221.
- [32] M.R. Delgado, V. Hernandez, J. Casado, J.L. Navarrete, J.M. Raimundo, P. Blanchard, J. Roncali, Vibrational study of push–pull chromophores for second-order non-linear optics derived from rigidified thiophene π-conjugating spacers, J. Mol. Struct. 651 (2003) 151–158.
- [33] M. Rumi, G. Zerbi, Conformational dependence of vibrational and molecular nonlinear optical properties in substituted benzenes: the role of π -electron conjugation and back-donation, J. Mol. Struct. 509 (1) (1999) 11–28.
- [34] J. Binoy, J.P. Abraham, I.H. Joe, V.S. Jayakumar, G.R. Pettit, O.F. Nielsen, NIR-FT Raman and FT-IR spectral studies and *ab initio* calculations of the anticancer drug combretastatin-A4, J. Raman Spectrosc. 35 (11) (2004) 939–946.
- [35] D. Sajan, J. Binoy, I.H. Joe, V.S. Jayakumar, J. Zaleski, Vibrational spectral studies of methyl 3-(4-methoxyphenyl)prop-2-enoate, a new organic non-linear optic crystal, J. Raman Spectrosc. 36 (3) (2005) 221–236.
- [36] W.J. Balfour, The vibrational spectrum of anisole, Spectrochim. Acta A: Mol. Biomol. Spectrosc. 39 (9) (1983) 795–800.

- [37] H. Arslan, Ö. Algül, Synthesis and *ab initio*/DFT studies on 2-(4methoxyphenyl)benzo[d] thiazole, Int. J. Mol. Sci. 8 (8) (2007) 760–776.
- [38] G.E. Campagnaro, J.L. Wood, The vibrational spectra and origin of torsional barriers in some aromatic systems, J. Mol. Struct. 6 (2) (1970) 117–132.
- [39] T. Shimanouchi, Y. Kakiuti, I. Gamo, Out-of-plane CH vibrations of benzene derivatives, J. Chem. Phys. 25 (6) (1956) 1245–1251.
- [40] B. Lakshmaiah, G. Ramana Rao, Vibrational analysis of substituted anisoles. I– Vibrational spectra and normal coordinate analysis of some fluoro and chloro compounds, J. Raman Spectrosc. 20 (7) (1989) 439–448.
- [41] R.M. Silverstein, C. Bassler, T.C. Morill, Spectrometric identification of organic compounds, 5thEd., John Wiley and Sons, 1991.
- [42] G. Socrates, Infrared and Raman characteristic group frequencies, Tables and Charts, 3th Ed., Wiley, Chichester, 2001.
- [43] G. Varsanyi, Assignments for vibrational spectra of seven hundred benzene Derivatives, Vol, 1-2, Academic Kiaclo, Budapest, 1973.
- [44] R. Ditchfield, Molecular orbital theory of magnetic shielding and magnetic susceptibility, J. Chem. Phys. 56 (11) (1972) 5688–5691.
- [45] H.O. Kalinowski, S. Berger, S. Brawn, Carbon-13 NMR spectroscopy, John Wiley and Sons, Chichester, 1988.
- [46] K. Pihlajer, E. Kleinpeter, (Eds), Carbon 13 Chemical shifts in structure and spectrochemical analysis, VCH publishers, Deerfield Beach, 1994.
- [47] W. Leng, J. Grunden, G.P. Bartholomew, G.C. Bazan, A.M. Kelley, Vibrational and electronic spectroscopy of a donor-acceptor substituted distyrylbenzene and its covalent dimmers, J. Chem. Phys. A 108 (46) (2004) 10050–10059.
- [48] N.M. O'Boyle, A.L. Tenderholt, K.M. Langer, cclib: a library for package-independent computational chemistry algorithms, J. Comput. Chem. 29 (5) (2008): 839–845.
- [49] S. Xavier, S. Periandy, Spectroscopic (FT-IR, FT-Raman, UV and NMR) investigation on 1-phenyl-2-nitropropene by quantum computational calculations, Spectrochim. Acta. A: Mol. Biomol. Spectrosc. 149 (2015) 216–230.
- [50] J.S. Murry, K. Sen, Molecular electrostatic potential concepts and applications, Elsevier, Amesterdam, 1996.
- [51] C. Cassidy, J.M. Halbout, W. Donaldson, C.L. Tang, Nonlinear optical properties of urea. Opt. Commun. 29 (2) (1979) 243-247.
- [52] H. Sekino, R.J. Bartlett, Hyperpolarizabilities of the hydrogen fluoride molecule: A discrepancy between theory and experiment?, J. Chem. Phys. 84 (5) (1986) 2726–2733.
- [53] J. Henriksson, T. Saue, P. Norman, Quadratic response functions in the relativistic fourcomponent Kohn-Sham approximation, J. Chem. Phys. 128 (2) (2008): 024105.
- [54] J.P. Hermann, D. Ricard, J. Ducuing, Optical nonlinearities in conjugated systems: β-carotene. Appl. Phys. Lett. 23 (4) (1973) 178–180.
- [55] S. Debrus, H. Ratajczak, J. Venturini, N. Pincon, J. Baran, J. Barycki, T. Glowiak, A. Pietraszko, Novel nonlinear optical crystals of noncentrosymmetric structure based on hydrogen bonds interactions between organic and inorganic molecules, Syn. Metals 127 (1) (2002), 99–104.

- [56] C. James, A.A. Raj, R. Reghunathan, V.S. Jayakumar, I.H. Joe, Structural conformation and vibrational spectroscopic studies of 2, 6-bis (*p-N*,*N*-dimethyl- benzylidene)cyclohexanone using density functional theory, J. Raman Spectrosc. 37 (12) (2006) 1381–1392.
- [57] R.W.A. Havenith, J.H. Van Lenthe, Delocalization in valence bond-hyperconjugation, Int. J. Quantum Chem. 109 (11) (2009) 2426–2429.
- [58] G. Varsanyi, Vibrational spectra of benzene derivatives. Academic Press: New York, NY, USA, 1969.

Figures Legends

- Scheme 1: Synthesis of the MMIC (2) molecule.
- Fig. 1: Crystal packing of the MMIC molecule.
- Fig. 2: Optimized structure of the MMIC molecule.
- Fig. 3: HOMO-LUMO representation of the MMIC molecule.

• DFT investigations on C_{11} $H_{11}NO_3$, a potential precursor to bioactive compounds

- FT-IR, FT-Raman, ¹H and ¹³C NMR spectral analyses were recorded.
- The geometrical parameters confirm the XRD data.
- The HOMO-LUMO and NLO properties of the title molecule were calculated