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DFT CALCULATIONS AND SPECTROSCOPIC STUDY ON TRIGONELLINE, A BIOLOGICALLY ACTIVE COMPOUND OF FENUGREEK

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Abstract
Fenugreek (Trigonella foenum-graecum) is a medicinal plant which is widely used for its pharmacological properties. Fenugreek seeds have been extracted by soxhlet extraction method with the solvent ethanol for an alkaloid Trigonelline. In this present study extracts have been subjected to FT-Infrared and FT-Raman analysis for the structural determination of different functional groups present in spices. Quantum chemical computations such as the molecular geometry, vibrational frequencies, UV-Vis spectroscopic parameters, HOMO-LUMO energies, molecular electrostatic potential (MEP), natural bond orbitals (NBO), nonlinear optics (NLO) and thermodynamic properties of title molecule have been calculated by using DFT/B3LYP method with 6-311++G (d,p) basis set in ground state for the first time. The obtained results show that the calculated spectroscopic data are in a good agreement with experimental data.
The time dependent DFT (TD-DFT) method was employed to predict its electronic properties, such as electronic transitions by HOMO and LUMO energies, various global reactivity and selectivity descriptors (chemical hardness, chemical potential, softness, electrophilicity index) also calculated.
Key words : MEP - Molecular electrostatic potential, NBO - Natural bond orbitals, NLO - nonlinear optics,HOMO- Higher occupied molecular orbital, LUMO- Lower unoccupied molecular orbital, TD-DFT- Time dependent density functional theory.

1.Introduction

Natural products once served humankind as the source of all drugs and higher plants provided most of these therapeutic agents. Today, natural products (and their derivatives and analogs) still represent over 50% of all drugs in clinical use, with higher plant-derived natural products representing 25% of the total [1]. The World Health Organization estimates that 80% of the people in developing countries of the world rely on traditional medicine for their primary health

care and about 85% of traditional medicine involves the use of plant extracts [2]. Examples of important drugs obtained from plants are digoxin from Digitalis spp., quinine and quinidine from Cinchona spp., vincristrine and vinblastine from Catharanthus roseus, atropine from Atropa belladona and morphine and codeine from Papaver somniferum. It is estimated that 60% of anti-tumour and anti-infectious drugs already in the market or under clinical trial are of natural origin. Fenugreek (Trigonella Foenum Graecum), native to southern Europe and Asia, is an erect annual herb with white flowers and hard yellowish brown seeds and has been regarded as a treatment for just about every ailment known to man. The seeds of this plant are used by people in Asia, Africa and Mediterranean countries as one of the ingredients in daily diets. It is used in many domains including medicine, nutrition, beverages, fragrances, cosmetics and for other industrial purposes [3]. Fenugreek is known to have several pharmacological effects including hypoglycaemia [4], hypocholesterolemia, gastroprotective, chemopreventive [5], antioxidant, anti inflammatory, antipyretic and appetite stimulation. According to Croteau bioactive compounds of plants are divided into three main categories: (a) terpenes and terpenoids (approximately 25,000 types), (b) alkaloids (approximately 12,000 types) and (c) phenolic compounds (approximately 8000 types). Regarding its phytochemical composition, previously reported data on fenugreek highlighted the presence of alkaloids such as choline and trigonelline, flavonoids and phenolic acids, polysaccharides, triterpenoids, steroidal sapogenins and nicotinic acid. Trigonelline (1-Methylpyridinium-3-carboxylate) is an alkaloid with chemical formula C7H7NO2. It is readily soluble in water or warm alcohol, less so in cold alcohol and slightly so in chloroform or ether. Trigonelline is a major active constituent of fenugreek which is reported to have hypoglycemic, antitumor, mutagenic and osmoregular properties [6]. Trigonelline may also have several therapeutic properties, such as anti-migraine, anti-carcinogenic (cervix and liver), antiseptic, hypoglycemic and hypocholesterolemic, activities [7]. Trigonelline is an important bioactive marker with estrogenic, anti-diabetic, and anti-invasive properties.

The density functional theory (DFT) is a popular method for the calculation of molecular structures, vibrational frequencies and energies of molecules. The density functional theory studies on the vibrational and electronic spectra of 1-Methylpyridinium-3-carboxylate has not been reported so far. Thus, in the present investigation, owing to the biological importance of substituted pyridines, an extensive experimental and theoretical studies of 1-Methylpyridinium-3-carboxylate compound has been undertaken by recording their FT-IR, FT-Raman for the proper assignment of the vibrational frequencies. In this work, our aim is to investigate molecular structure, FT-IR and FT-Raman spectroscopic and electronic properties via the DFT method (detail quantum chemical computation), both experimentally and theoretically on 1-Methylpyridinium-3-carboxylate. Other conformational spectroscopic tools could be helpful for better understanding of molecular structures. Many authors apply molecular modeling as promising conformational tool for confirming their FT-IR experimental work. The present investigation was undertaken to study the optimized molecular structural parameters, vibrational frequencies, thermo-dynamical parameters, total dipole moment and hyper polarizability, HOMO–LUMO energy gap for 1-Methylpyridinium-3-carboxylate using DFT/B3LYP utilizing 6-311++G(d,p) basis set.

2.Experimental

Fenugreek are collected from the local markets of Chennai, Tamil Nadu, India. Dried fenugreek are ground and powdered with the help of mortar and pestle. 20 g of sample was mixed with 100 ml of ethanol. Extracts were made by using soxhlet apparatus for 6 hours at 70°C). The extracts were cooled and filtered through Whatman filter paper no. 1 and evaporated using hot air oven to near dryness at 65- 70°C. Extracts (Trigonelline) were placed in dark glass bottles and stored at 4°C until further analysis [8]. .The FT-IR spectrum of the freshly prepared Trigonelline (1-Methylpyridinium-3-carboxylate) belonging to C1 point group symmetry have been recorded in the region 4000–400 cm-1, using Bruker IFS 66V Spectrometer and FT-Raman spectrum has been recorded in the region 4000–100 cm-1, using Bruker : RFS 27 Spectrometer.

3.Vibrational Analysis

The maximum number of potentially active observable fundamentals of a non-linear molecule which contains N atoms is equal to (3N−6), apart from three translational and three rotational degrees of freedom. The detailed vibrational assignment of the experimental wavenumbers is based on normal mode analyses and a comparison with theoretically scaled wave numbers with PED. The calculated frequencies are usually higher than the corresponding experimental quantities, due to the combination of electron correlation effects and basis set deficiencies. After applying the scaling factors, the theoretical calculations reproduce the experimental data well in agreement. The observed and calculated infrared and Raman spectra of 1-Methylpyridinium-3-carboxylate have been shown in Figs 1.1 and 1.2 respectively. The observed and scaled theoretical frequencies, IR intensities, and Raman activities, PEDs and mode of description are listed in Table 1.1.

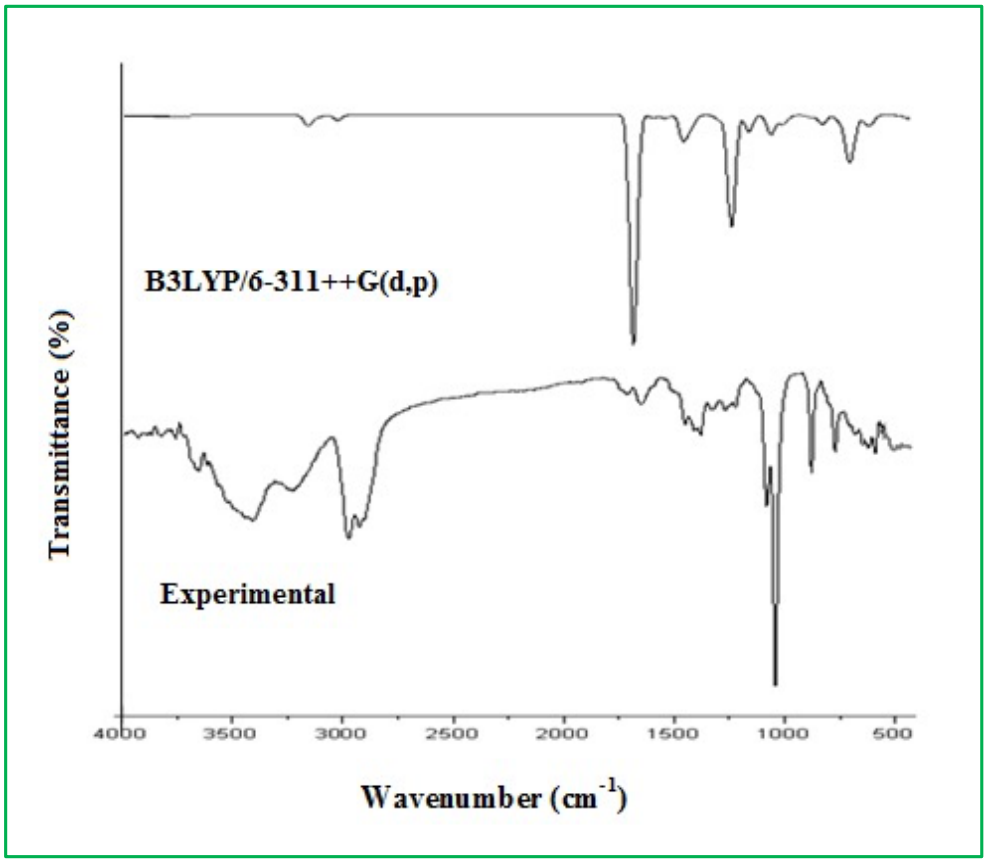

Fig 1.1 Experimental and theoretical FTIR spectra of 1-Methylpyridinium-3-carboxylate

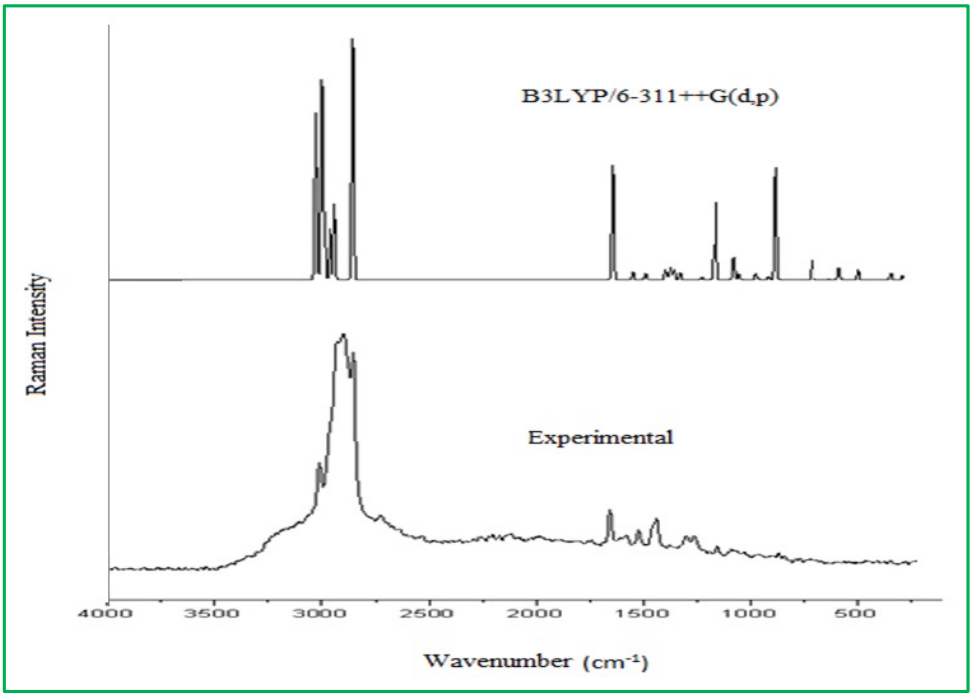

Fig 1.2 Experimental and theoretical FT-RAMAN spectra of 1-Methylpyridinium-3-carboxylate

Table 1.1 Experimental and calculated DFT-B3LYP/6-311++G(d,p) levels of vibrational frequencies (cm-1) of1-Methylpyridinium-3-carboxylate.

Experimental wave number $(cm)^{-1}$		Frequencies cm^{-1}	FT-IR		FT-Raman		Assignment of vibrational modes				
FT-IR	FT-Raman	scaled	Relative	Absolute	Relative	Absolute					
		3099	0	0	133	69	γCH(92)				
		3077	16	4	48	25	γCH(97)				
3011	3012	3075	3	1	116	61	γCH(93)				
2957	2899	3064	3	1	43	22	γCH(98)				
2926	2880	3040	4	1	41	21	γCH(99)				
2854	2726	3020	2	0	60	31	γCH(100)				
		2947	10	2	192	100	γCH(101)				
1745	1656	1671	455	100	91	48	γOC(95)				
1639	1580	1585	6	1	6	3	γCC(59)	γNC(10)	βHCC(10)		
1546	1523	1534	6	1	5	3	γCC(17)	γNC(22)	βCCN(10)	βCCC(15)	
		1457	44	10	8	4	βHCH(51)	γHCNC(20)			
	1440	1444	5	1	4	2	γCC(10)	βHCC(24)			
		1429	13	3	10	5	βHCH(76)	γHCNC(15)			
1402		1415	12	3	8	4	γCC(20)	βHCC(16)	βHCH(30)		
1379		1391	0	0	6	3	βHCC(16)	βHCH(62)			
Experimental wave number $(cm)^{-1}$		Frequencies cm^{-1}	FT-IR		FT-Raman		Assignment of vibrational modes				
FT-IR	FT-Raman	scaled	Relative	Absolute	Relative	Absolute					
	1301	1304	9	2	2	1	γCC(37)	γNC(23)			
		1257	51	11	25	13	βHCC(56)				
1240	1266	1246	180	40	61	32	γOC(71)				
		1173	32	7	18	9	γNC(37)	βCCN(10)	βHCC(13)	βCNC(10)	
1161	1157	1153	2	0	5	2	γCC(19)	βHCC(58)			

1111		1101	0	0	1	0	βHCH(32)	τHCNC(53)			
	1089	1085	17	4	5	3	βHCC(33)	τHCNC(28)			
1072		1072	25	5	1	1	βCCN(19)	βHCC(25)	βCCN(18)	βCCC(10)	
1043		1028	17	4	3	1	γCC(11)	γNC(10)	βHCC(16)	τHCNC(24)	
		1001	4	1	90	47	γCC(12)	γNC(12)	βCCN(14)	βCCC(20)	βCNC(23)
		981	0	0	0	0	τHCCC(63)	τHCCN(23)			
		919	1	0	0	0	τHCCC(50)	τHCCN(21)	τCCNC(12)		
	870	897	4	1	0	0	τHCCC(59)	τCCCN(10)			
879	843	854	18	4	16	8	γNC(41)	γCC(18)	βCCC(10)		
772	767	782	12	3	1	0	τHCCN(29)	τHCCC(29)	OUT OCOC(16)		
		744	68	15	9	5	βOCO(59)				
		723	46	10	0	0	τHCCC(13)	OUT OCOC(59)			

Experimental wave number $(cm)^{-1}$		**Frequencies cm^{-1}**	**FT-IR**		**FT-Raman**		**Assignment of vibrational modes**				
FT-IR	**FT-Raman**	**scaled**	**Relative**	**Absolute**	**Relative**	**Absolute**					
676		668	13	3	8	4	βCCN(31)	βOCO(22)	βCCN(12)		
623		645	14	3	0	0	τHCCC(11)	τCCNC(46)	τCCCN(24)		
		531	1	0	5	3	γNC(17)	βOCC(20)	βCCC(11)	βCNC(21)	
		485	7	1	3	2	βOCC(39)	βCNC(22)	βCCC(16)		
		432	4	1	0	0	τCCNC(43)	OUT CCCN(26)			
		391	0	0	0	0	τHCCC(12)	τCCNC(38)	τCCCN(11)	OUT CCCC(15)	
	375	366	2	0	1	1	γCC(11)	βOCC(17)	βCNC(54)		
	348	320	9	2	1	1	γCC(47)	βCNC(14)			
	198	198	2	1	2	1	τCCNC(22)	OUT CCCN(56)			
		162	4	1	0	0	βOCC(16)	βCCC(70)			

	68	121	3	1	1	0	τCCCN (21)	OUT CCCC(58)			
		47	0	0	0	0	τOCCC (81)				
		38	0	0	0	0	τHCNC (96)				

γ-stretching; β-bending;τ-Torsion,inp-plane bending,opb-out of plane bending.Absolute-absorption intensity.Relative -absorption

3.1 C-H stretching

C–H stretching frequencies appear in the range of 3100–3000 cm−1 [9]. The theoretically calculated scaled down vibrations corresponding to C–H stretch show good agreement with the experimentally observed vibrations at 3012 for asymmetric and 2899, 2880, 2726 cm−1 for symmetric stretching in FT-Raman and 3011, 2957, 2926 and 2854cm−1 in FT-IR. For our 1-Methylpyridinium-3-carboxylate molecule the band predicted by the B3LYP method ranges between 3099 and 3020 cm−1 for C-H stretching vibrations and the PED contribution of these modes is 100%. The bands appeared with medium and very strong intensities.

3.2 Methylene group vibrations

For the assignments of CH2 group frequencies, basically six fundamentals can be associated to each CH2 group namely, CH2 symmetric stretch; CH2 antisymmetric stretch; CH2 scissoring and CH2 rocking modes which belong to in-plane vibrations. In addition to that, CH2 wagging and twisting modes of CH2 group would be expected to be for out-of-plane symmetry species. The C–H stretching of the methylene groups are at lower frequencies than those of the aromatic C–H ring stretching. The CH2 antisymmetric stretching vibrations are generally observed in the region 3000–2900cm−1, while the CH2 symmetric stretch will appear between 2900 and 2800cm−1 [10].In the present assignment the CH2 bending modes follow,in decreasing frequency, the general order CH2 sciss > CH2wagg > CH2 twist > CH2 rock. Since the bending modes involving the hydrogen atom attached to the central carbon atom falls in the 1450–875cm−1 range, there is extensive vibrational coupling of these modes with CH2 deformations, particularly with the CH2 twist. It is notable that both CH2 scissoring and CH2 rocking are sensitive to molecular confirmation. In our 1-Methylpyridinium-3-carboxylate molecule the scaled vibrational frequencies computed by B3LYP/6-311++G(d,p) method at 1415 cm-1 have been assigned to CH2 scissoring modes [11] as they show good correlation with recorded FT-IR spectra at 1402 cm-1. The computed wave number at 1391 cm-1 has been assigned to CH2 rocking vibration and it shows good agreement with recorded FT-IR bands at 1379 cm-1 as shown in Table 1.1. The CH2 twisting vibrations [12] have been observed as a weak band in FT-IR spectrum at 1111 cm-1with a good PED.

3.3 Ring vibrations

There are six ring stretching vibrations in each compound readily assigned in the range, 1590–1000 cm-1. In the 1-Methylpyridinium-3-carboxylate compound the FT-IR bands of asymmetric and symmetric C–C stretching have been found at 1639 and 1546 cm-1 respectively. The Raman bands of C–C stretching of the pyridine ring appear at 1580,1523 and 1440 cm-1. The

identification of C–N vibration is a very difficult task since mixing of several vibrations have been possible in this region. Silverstein has [13] assigned C–N stretching absorption in the region 1382–1266 cm-1for aromatic amines. In our present work, the band observed at 1301 cm-1in FT-Raman is assigned to be C–N stretching vibration. The theoretically computed B3LYP/6-311++G(d,p) value at 1304 cm-1 shows good agreement with experimental data. The CCC bending vibrations exhibit the characteristic frequencies at 995 and 1010 cm-1respectively [14] . The bands occurring at 1072 cm-1in the FT IR spectrum and in FT-Raman 1089 cm-1 have been assigned to the CCC in-plane bending modes which are good agreement with the calculated frequencies at 1072 and 1001 cm-1.The wavenumber 676 cm-1is assigned to the CNC in-plane bending mode of 1-Methylpyridinium-3-carboxylate. The CCC and CNC out of plane bending modes are attributed to the Raman frequencies observed at 375 and 348 cm-, respectively. All these assignments agree well with the reported literatures [15]. The CCC in-plane bending and out of plane vibrations are described as mixed modes as there are about 10-54% PED contributions.

3.4 C-O and C=O vibrations

The carbonyl stretching frequency has been most extensively studied by infrared spectroscopy [16]. This multiple bonded group is highly polar and therefore gives rise to an intense infrared absorption band. In the present study the carbonyl-stretching vibrations are found in the region of 1780–1700 cm-1. i.e., medium band at 1745 cm-1 in FT-IR and 1656 cm-1as a medium strong band in FT-Raman spectrum have been assigned to C=O stretching vibration shows small deviation calculated by B3LYP/6-311+G(d,p) method at 1671 cm-1 with PED contribution of 95%. The absorption is sensitive for both the carbon and oxygen atoms of the carbonyl group. Normally, the C–O stretching vibrations occur in the region 1260–1000 cm-1. In the present study, the C–O stretching vibration have been assigned at 1246 cm-1 for the 1-Methylpyridinium-3-carboxylate molecule at B3LYP/6-311++G(d,p) level and it is also observed at 1240 cm-1 in FT-IR spectrum and the band at 1266 cm-1 in FT-Raman .The PED contribution of this mode is 71%.

4.Optimized Geometry

The first task for our computational work is to determine the Molecular structure of 1-Methylpyridinium-3-carboxylate (Trigonelline). This is calculated by B3LYP level with 6-311++G(d,p) basis set and data is presented in table 1.2, in accordance with the atom numbering scheme given in Fig 1.3. Since the exact crystal structure of 1-Methylpyridinium-3-carboxylate compound is also not available, the optimized structure can be only compared with other similar systems for which the crystal structures are solved.For a similar compound 1-(4-chloro-phenyl)-3-phenyl-succinimide (CPPS), since there is no exact X-ray crystal structure the theoretical values could not be compared with experimental data [17]. In Trigonelline, the C-C bond length is greater than C-H bond, however maximum bond length of 2.37A˚ is for O-H. This may be because the electron-rich O9 atom shares its electron with the electron deficient atoms in the vicinity like H11. In trigonelline, for carboxylate ion (formic acid), the C=O bond length and the C-O bond lengths are averaged to the same (1.25 A.U) because of resonance. The C-C-C bond angle has been found to be equal to 120˚ and the smallest bond angle between C7-O9-H11 has been observed at 91.7˚.

Delocalization occurs between the lone pair of electrons in O9 and O8 with the surrounding C and H atoms which are electron deficient. The O9 tries to conjugate with H11 and form a five membered ring to increase stability and decrease its bond angle to about 91.7˚. The change in the pyridine ring C-H bond length is attributed to change in charge distribution of the carbon atoms in the pyridine ring due to substitution. The carbon atoms in pyridine ring are sigma bonded to hydrogen atoms and substitution of carbonyl groups for hydrogen atoms reduces the electron density at ring carbon atoms. This change has been shown for C1-N6 (1.35 A.U) and C5-N6 (1.36 A.U) which have greater bond lengths than C-H (1.08 A.U). The ring carbon atoms exert a large attraction on the valence electron cloud of the H atoms resulting in the increase in C-H force constant and a decrease in corresponding bond length which results in substituted benzenes [18].

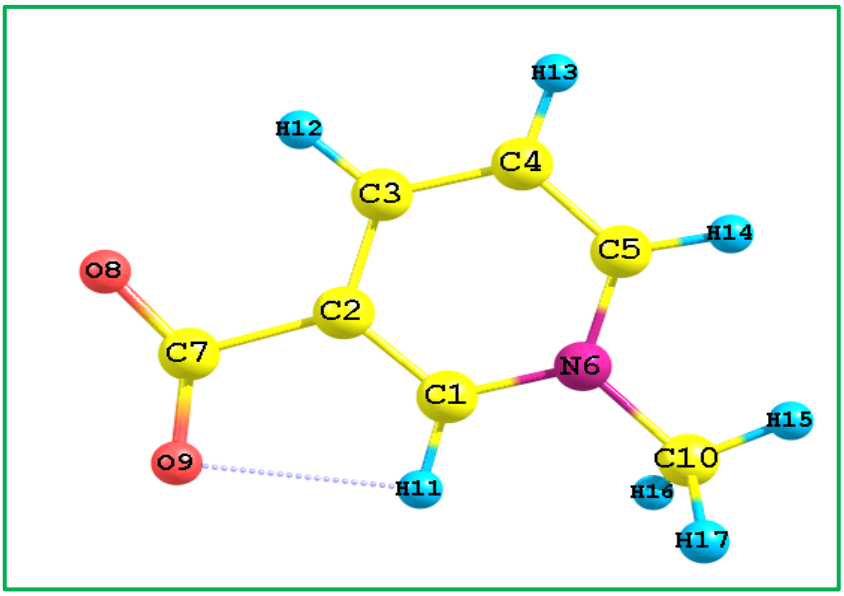

Fig. 1.3 The structure of 1-Methylpyridinium-3-carboxylate predicted by the B3LYP/6-311++G(d,p) level.

Table 1.2 Optimized geometrical parameters of 1-Methylpyridinium-3-carboxylate molecules, bond length (Å), bond angles (˚)

Bond length	B3LYP	Bond angle	B3LYP
C1-C2	1.38	C2-C1-N6	121.5
C1-N6	1.35	C2-C1-H17	119.7
C1-H11	1.08	C1-C2-C3	118.2
C2-C3	1.39	C1-C2-C7	118.9
C2-C7	1.57	N6-C1-H17	118.8
C3-C4	1.40	C1-N6-C5	120.7
C3-H12	1.09	C1-N6-C10	118.9
C4-C5	1.38	C1-H11-O9	96.8

C4-H13	1.08	C3-C2-C7	122.9
C5-N6	1.36	C2-C3-C4	119.9
C5-H14	1.08	C2-C3-H12	117.5
N6-C10	1.48	C2-C7-O8	113.4
Bond length	**B3LYP**	**Bond angle**	**B3LYP**
C7-O8	1.24	C2-C7-O9	113.0
C7-O9	1.25	C4-C3-H12	122.7
C10-H15	1.09	C3-C4-C5	119.4
C10-H16	1.09	C3-C4-H13	121.8
O9-H11	2.37	C5-C4-H13	118.8
C10 - H17	1.09	C4-C5-N6	120.3
		C4-C5-H14	123.2
		N6-C5-H14	116.6
		C5-N6-C10	120.4
		N6-C10-H15	109.3
		N6-C10-H16	109.4
		N6-C10-H17	109.4
		O8-C7-O9	133.6
		C7-O9-H11	91.7
		H15-C10-H16	109.6
		H15-C10-H17	109.6
		H16-C10-H17	109.6

5.NBO Analysis

The NBO analysis provides an efficient method for studying intra and inter-molecular bonding and interaction among bonds, and also provides a convenient basis for investigating charge transfer or conjugative interaction in molecular systems [19]. In order to investigate the intra and intermolecular interactions, the stabilization energies of the 1-Methylpyridinium-3-carboxylate compound were performed using second-order perturbation theory. For each donor (i) and acceptor (j), the stabilization energy E(2) associated with delocalization i → j is estimated.

In a literature it was revealed thatNBO analysis has been performed on the compound 3-(4-chlorophenyl)-2-[(5-thioxo-4,5-dihydro-1,3,4-oxadiazol-2yl) methylthio]quinazolin-4(3H)-one by using the DFT with Becke-3-Yang-Parr (B3LYP) combined with standard basis sets 6-31G(d,p) and 6-311++G(d,p) using GAUSSIAN 03W program package. For their compound, the delocalization of electrons due to LP(1)N9→ π*(N7–C8), LP(1)N9→ π*(C10–O17) and LP(1)N22→ σ*(C21–S24) have the highest intramolecular charge transfer interaction (ICT) energies E(2) of 53.25, 43.28 and 71.58 kJ/mol respectively. The results of second-order perturbation theory analysis of the Fock Matrix in NBO basis for (Trigonelline) 1-

Methylpyridinium-3-carboxylate at B3LYP/6-311++G(d,p) level of theory have been calculated and presented in Table 1.3.

Table 1.3 Second order perturbation theory analysis of Fock matrix in NBO basis for1-Methylpyridinium-3-carboxylate.

Donor (i)	Type	ED/e	Acceptor (j)	Type	ED/e	[a]E(j) – E(i) (a.u)	[b]F(i,j) (a.u)	[c]E(2) (kJ/mol)
C1-C2	σ	1.9664	C2-C3	σ*	0.0301	1.4000	0.0800	5.65
			C2-C7	σ*	0.0682	1.4100	0.0730	4.66
			C3-H12	σ*	0.0200	1.1900	0.0510	2.72
			N6-C10	σ*	0.0221	0.9800	0.0670	5.67
C1-N6	σ	1.9814	C5-N6	σ*	0.0380	1.4400	0.0720	4.47
	π	1.8175	C2-C3	π*	0.2772	0.4500	0.0530	7.53
			C4-C5	π*	0.2436	0.4400	0.0940	24.12
	π*	0.4815	C2-C3	π*	0.2772	0.0900	0.1010	52.93
			C4-C5	π*	0.2436	0.0800	0.0730	29.20
C1-H11	σ	1.9756	C2-C3	σ*	0.0301	1.1800	0.0670	4.71
			C5-N6	σ*	0.0380	1.0600	0.0690	5.65
C2-C3	σ	1.9653	C1-C2	σ*	0.0291	1.3700	0.0780	5.58
			C2-C7	σ*	0.0682	1.4000	0.0820	5.95
			C3-C4	σ*	0.0226	1.3900	0.0620	3.43
Donor (i)	**Type**	**ED/e**	**Acceptor (j)**	**Type**	**ED/e**	**[a]E(j) – E(i) (a.u)**	**[b]F(i,j) (a.u)**	**[c]E(2) (kJ/mol)**
			C4-H13	σ*	0.0215	1.1200	0.0550	3.31
			C7-O9	σ*	0.0824	1.1700	0.0550	3.17
	π	1.5414	C1-N6	π*	0.4815	0.2200	0.0960	51.18
			C4-C5	π*	0.2436	0.3100	0.0670	16.12
			C7-O8	π*	0.3614	0.3700	0.0820	21.99
	π*	0.2772	C7-O8	π*	0.3614	0.0500	0.0950	68.63
C2-C7	σ	1.9715	C1-C2	σ*	0.0291	1.3300	0.0790	5.94
			C1-N6	σ*	0.0297	1.2300	0.0560	3.16
			C2-C3	σ*	0.0301	1.3500	0.0800	5.90
C3-C4	σ	1.9714	C2-C3	σ*	0.0301	1.4000	0.0610	3.31
			C4-C5	σ*	0.0208	1.5200	0.0850	5.88
			C5-H14	σ*	0.0246	1.1100	0.0650	4.80

C3-H12	σ	1.9749	C1-C2	σ*	0.0291	1.1300	0.0690	5.28
			C4-C5	σ*	0.0208	1.2800	0.0550	2.95
C4-C5	σ	1.9685	C3-C4	σ*	0.0226	1.4900	0.0810	5.48
			C3-H12	σ*	0.0200	1.2800	0.0580	3.29
			C5-N6	σ*	0.0380	1.3600	0.0840	6.41
			N6-C10	σ*	0.0221	1.0700	0.0580	3.87
C4-C5	π	1.7097	C1-N6	π*	0.4815	0.2800	0.0540	11.55
			C2-C3	π*	0.2772	0.3700	0.0790	20.58
C4-H13	σ	1.9682	C2-C3	σ*	0.0301	1.1900	0.0540	3.04
			C4-C5	σ*	0.0208	1.3100	0.0620	3.66
			C5-N6	σ*	0.0380	1.0600	0.0840	8.25
C5-N6	σ	1.9792	C1-N6	σ*	0.0297	1.4500	0.0720	4.44
			C4-C5	σ*	0.0208	1.7000	0.0900	6.04
C5-H14	σ	1.9716	C1-N6	σ*	0.0297	1.0700	0.0700	5.74
			C3-C4	σ*	0.0226	1.1800	0.0710	5.34
C7-O9	σ	1.9911	C2-C3	σ*	0.0301	1.3300	0.0590	3.21
C10-H15	σ	1.9925	C1-N6	σ*	0.0297	1.0900	0.0530	3.21
O8	LP(1)	1.9793	C2-C7	σ*	0.0682	1.2600	0.0520	2.60
O8	LP(2)	1.8693	C2-C7	σ*	0.0682	0.8300	0.1050	16.08
O8	LP(2)		C7-O9	σ*	0.0824	0.6000	0.1190	28.61
O9	LP(1)	1.9865	C2-C7	σ*	0.0682	1.3200	0.0520	2.47
O9	LP(2)	1.9310	C2-C7	σ*	0.0682	0.8000	0.0680	7.28
Donor (i)	**Type**	**ED/e**	**Acceptor (j)**	**Type**	**ED/e**	**[a]E(j) – E(i) (a.u)**	**[b]F(i,j) (a.u)**	**[c]E(2) (kJ/mol)**
O9	LP(2)		C7-O8	σ*	0.0329	0.8600	0.0900	11.47
O9	LP(3)	1.5869	C7-O8	π*	0.3614	0.2300	0.1070	59.93

aE(j) – E(i)Energy difference between donor and acceptor i and j NBO orbitals,bF(i,j) is the Fock matrix element between i and j NBO orbital's. cE(2) means energy of hyper conjugative interaction (stabilization energy),

The strong intra molecular hyperconjugation interactions are found between σ and π bonding electrons of C-C, C-O, C-N, C-H and O-H and σ* and π* antibonding ones of C-C, C-H, C-O, C-N and O-H. Additionally, intramolecular charge transfers (ICT) from the lone pair electrons of O atoms to σ* and π* antibonding ones of C-C and C-O are also observed in molecules. The stabilization energy values greater than 2 kJ mol-1 are listed in Table 1.3. The strong intra molecular hyperconjugative interactions of π→π* transitions are in C1-N6→C2-C3, C4-C5 [E(2) = 7.53, 24.12 kJ/mol], C2-C3→C1-N6, C4-C5, C7-O8 [E(2) =51.8, 16.12, 21.99 kJ/mol] and C4-C5 →C1-N6, C2-C3 [E(2) =11.55, 20.58 kJ/mol] . The interaction energy is electron withdrawing from the ring through π*(C1-N6) of the NBO conjugated with π*(C2-C3)

resulting with large stabilisation of 52.93kJ/mol and π*(C2-C3) of the NBO conjugated with π*(C7-O8) resulting with large stabilisation of 68.63 kJ/mol. Delocalisation occurs only in pi bonds and lone pairs of electrons. Here, the maximum energy delocalization takes place in the π* – π* transition which quantity alters the intermolecular hydrogen bonding.

Other strong interactions are observed between lone pair electrons of O atoms and σ* antibonding ones of C7-O9 and C7-O8 bonds. These hyperconjugative interactions are in LP2 of Oxygen atom (O8) [ED=1.86933e]→ σ* (C7-O9)[ED=0.08236e] [E(2)=28.61 kJ mol-1], LP2 (O9)[ED=1.93097e]→ σ*(C7-O8)[ED=0.03294e] [E(2)= 11.47kJ mol-1] and LP3(O9) [ED=1.58692e]→π*(C7-O8)[ED=0.36143e] [E(2)= 59.93 kJ mol-1] stabilization energies, respectively.

6.NLO analysis

The polarizability α and the hyper polarizability β and the electric dipole moment μ of 1-Methylpyridinium-3-carboxylate compound are calculated by finite field method using B3LYP/6-311++G (d,p) basis set available in DFT package. The first order hyperpolarizability (β tot) of 1-Methylpyridinium-3-carboxylate molecule along with related properties (μ, αo and Δα) are calculated and it is based on the finite-field approach. In the presence of an applied electric field, the energy of a system is a function of the electric field. Polarizabilities and hyperpolarizabilities characterize the response of a system in an applied electric field [20]. They determine not only the strength of molecular interactions (long-range inter induction, dispersion force, etc.) as well as the cross sections of different scattering and collision process but also the nonlinear optical properties (NLO) of the system [21]. The total static dipole moments μ, the mean polarizability α 0, the anisotropy of the polarizabilities Δα and the mean first hyper-polarizability β tot, using the x, y and z components are determined.

The value of the polarizability (Δα) and hyperpolarizability (β tot) components of GAUSSIAN 03W output are reported in atomic units (a.u). The calculated values are converted into electrostatic units (esu) (α: 1a.u = 0.1482 X10-24 esu, β: 1a.u = 8.6393 x 10-30 esu).

Table 1.4 The electric dipole moments (Debye) μ, polarizability α (in esu), βhyperpolarizability and βtot (10−30 esu) value of1-Methylpyridinium-3-carboxylate

Parameters	B3LYP/6-311++G(d,p)	Parameters	B3LYP/6-311++G(d,p)
μ_x	-5.8306	β_{xxx}	-2025.7840
μ_y	0.6093	β_{xxy}	-177.6059
μ_z	-0.0001	β_{xyy}	-194.3541
μ (D)	5.8624	β_{yyy}	37.4205
Parameters	**B3LYP/6-311++G(d,p)**	**Parameters**	**B3LYP/6-311++G(d,p)**
α_{xx}	137.0785	β_{xxz}	0.2211
α_{xy}	1.2616	β_{xyz}	0.0648
α_{yy}	111.0370	β_{yyz}	-0.0213

α_{xz}	0.0006	β_{xzz}	-43.7792
α_{yz}	0.0002	β_{yzz}	41.4921
α_{zz}	53.2484	β_{zzz}	0.0246
$\alpha_{(a.u)}$	100.4546	β_{tot} (esu)	1.9577×10^{-29}
Δα (esu)	3.6870×10^{-23}		

For the compound Methylboronic acid the polarizabilities and hyperpolarizabilities have been calculated using the DFT-B3LYP method and 6-311++G(d,p) basis set, based on the finite-field approach. Total dipole moment of methylboronic acid molecule is approximately two times smaller than that of urea and first order hyperpolarizability of title molecule is approximately equal to that of urea (μ and β of urea are 1.3732 Debye and 0.3728 ×10−30 esu) [22]. In our present study, the total static dipole moment, polarizabilities and first order hyper-polarizabilities of 1-Methylpyridinium-3-carboxylate have been calculated and listed in Table 1.4. The calculated first hyperpolarizability of 1-Methylpyridinium-3-carboxylate molecule is 1.9577 x 10−29 esu and the values of μ, Δα are 5.8624 D, 3.6870 x10−23 esu. The values of μ , Δα and β for urea calculated by B3LYP/6-311++G(d,p) method are 0.9884 D, 3.8312 x10−24 esu and 0.37289 x10−30 esu respectively [23]. Urea is one of the essential molecules used for comparison to determine the NLO properties of molecular systems. Therefore, it is used as a reference molecule in NLO studies. The polarizability and first hyperpolarizability for 1-Methylpyridinium-3-carboxylate molecule is approximately 9.6 and 52 times more than that of urea. These results indicate that 1-Methylpyridinium-3-carboxylate compound is a good candidate for nonlinear optical material.

7.UV Visible Analysis

Ultraviolet spectral analysis of 1-Methylpyridinium-3-carboxylate compound has been investigated experimentally with ethanol as solvent in solution phase and theoretical calculation in gas phase. It has spectra in the 200–800 nm range and shown in Fig 1.4. The medicinal material, Trigonelline was extracted by petroleum ether-ethanol and detection wavelength was set at UV 265 nm [24]. The absorption maxima values for our compound have been found to be 270 nm. These transitions are due to the chromophores of the C=O and C=N. The substituents amides, acids, esters on carbonyl group show pronounced hypsochromic effect on the n → π* transitions. The hypsochromic effect is due to the inductive effect of nitrogen, oxygen or halogen atoms. The heteroatom withdraws electrons from carbonyl carbon and makes carbonyl oxygen lone pair of electrons more stabilized due to its involvement in increasing C=O bond order. As a result, the n → π* transition of these compounds is shifted to the 200-215 nm range relative to 270 nm in aldehydes and ketones. Conjugation of the carbonyl group with double bond shifts both n → π* and π → π* transitions to longer wavelengths. The effect on π → π* band is more pronounced. As the number of conjugated double bonds is increased, the gap between highest occupied molecular orbital (HOMO) and lowest unoccupied molecular orbital (LUMO) is progressively lowered. Therefore, the increase in size of the conjugated system gradually shifts the absorption maximum (λmax) to longer wavelength and also increases the absorption.

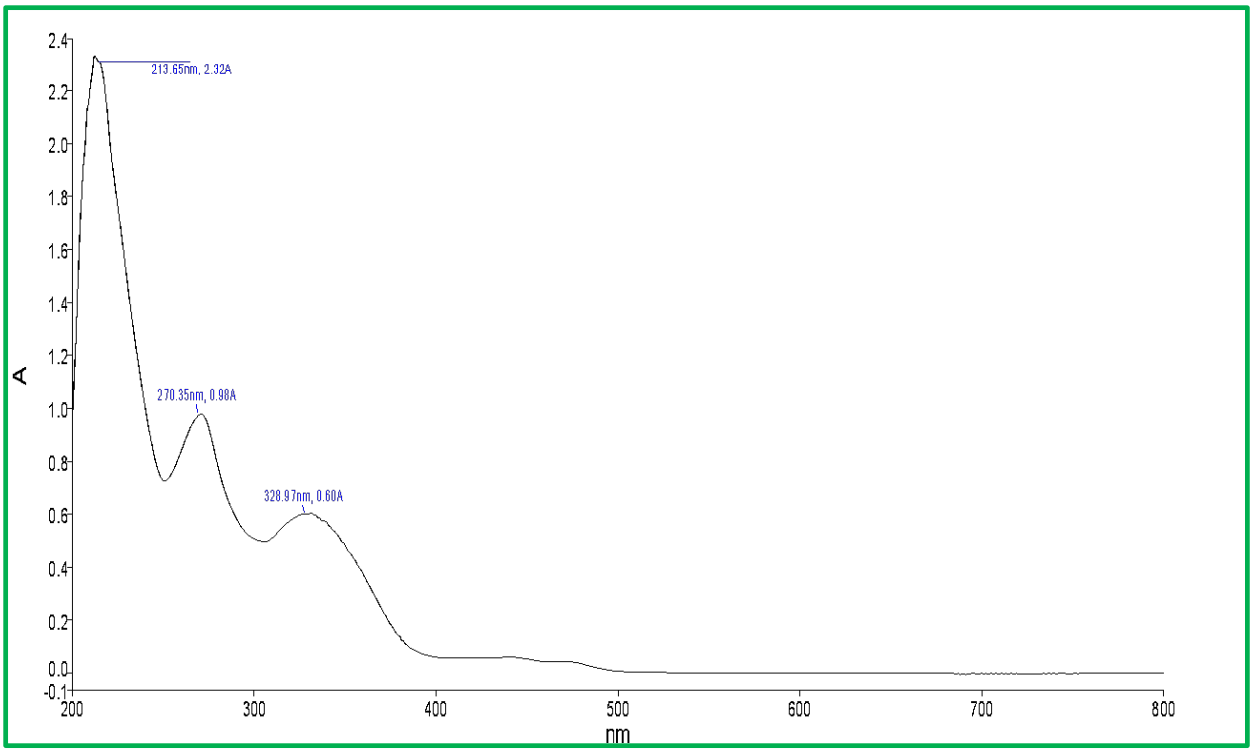

Fig 1.4 Experimental UV-VIS spectra of Chloramphenicol (CLP)

8.Frontier Molecular Orbitals

The highest occupied molecular orbital (HOMO) represents the outermost orbital filled by electrons and behaves as an electron donor, while the lowest unoccupied molecular orbital (LUMO) considers as the first empty innermost orbital unfilled by electron and behaves as an electron acceptor. These orbitals are also called frontier molecule orbitals (FMOs) [25]. The energy gap between HOMO and LUMO indicates molecular chemical stability and is a critical parameter to determine molecular electrical transport properties. In our study, HOMO - LUMO energies and their 3D plots of the 1-Methylpyridinium-3-carboxylate (Fig 1.5) compound have been investigated following the literature.

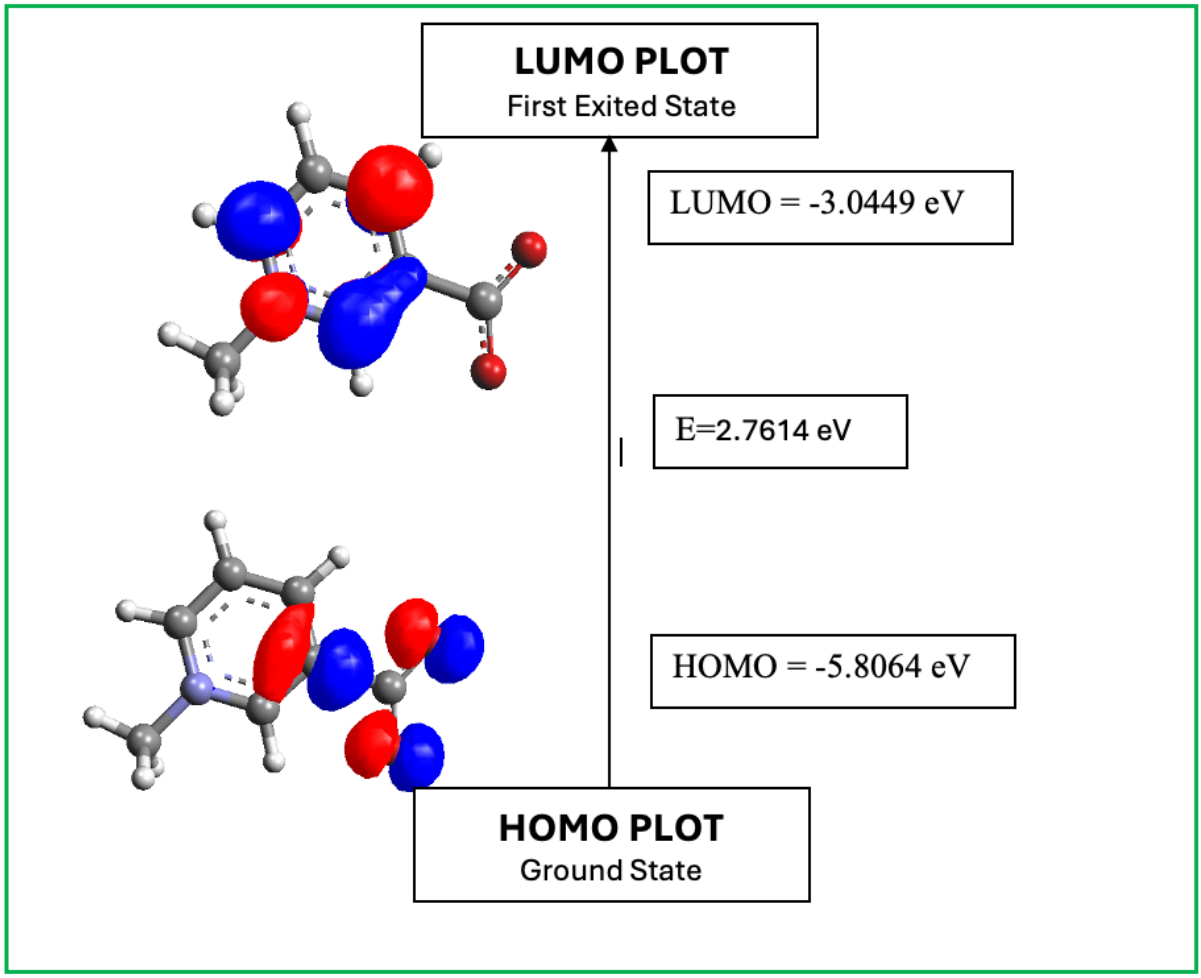

Fig 1.5 Highest occupied and Lowest unoccupied molecular orbitals of 1-Methylpyridinium-3-carboxylate

The narrow energy gap between HOMO and LUMO facilitates intramolecular charge transfer which makes the material NLO active. Trigonelline has a number of conjugated double bonds namely two C=O, C= N in its structure. As conjugated bonds increase in number the gap between highest occupied molecular orbital (HOMO) and lowest unoccupied molecular orbital (LUMO) is gradually lowered and it is as low as 2.7 eV for trigonelline compared to the other compounds we have investigated. Trigonelline molecule is relatively a more soft molecule (as HOMO-LUMO gap is less than 3 e V) in comparison with others studied in the present work.

9.Analysis of Molecular Electrostatic Potential (MEP)

The molecular electrostatic potential surface (MEPs) for 1-Methylpyridinium-3-carboxylatemolecule in 3D plots is illustrated in Fig 1.6.

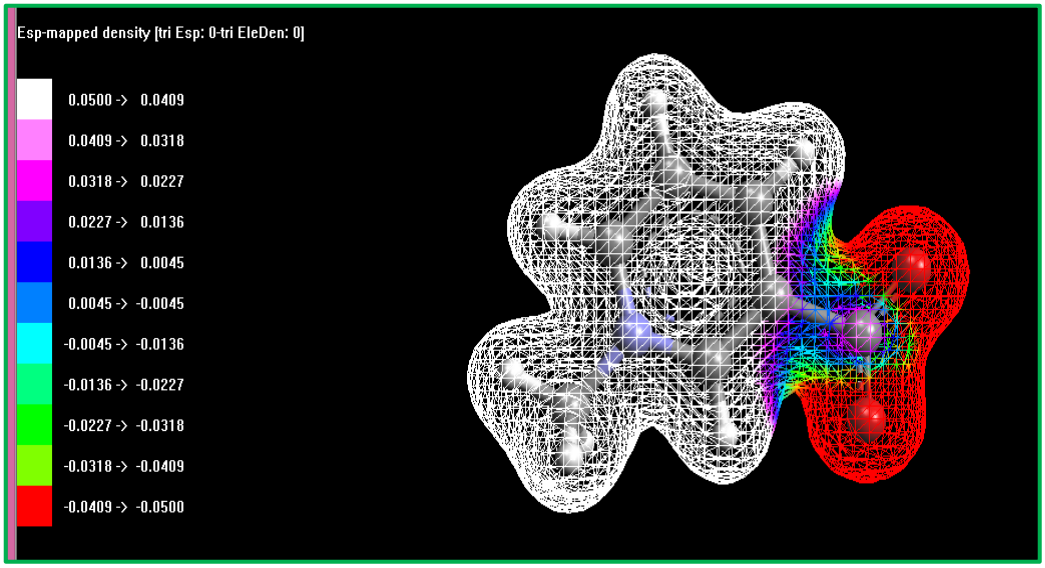

Fig 1.6 Molecular Electrostatic Potential(MEP) of 1-Methylpyridinium-3-carboxylate

The MEPs is a plot of electrostatic potential mapped onto the constant electron density surface. The MEPs superimposed on top of the total energy density as a shell. The different values of the electrostatic potential at the surface are represented by different colors. The color code of these maps in the range between -0.05 a.u. (deepest red) and 0.05 a.u. (white) in compound, where white indicates the strongest attraction (nucleophilic attack) and red indicates the strongest repulsion (electrophilic attack). The importance of MEPs lies in the fact that it simultaneously displays molecular size, shape as well as positive, negative and neutral electrostatic potential regions in terms of color grading and is very useful in research of molecular structure with its physicochemical property relationship [26]. As can be seen from the MEPs map of the 1-Methylpyridinium-3-carboxylate molecule, while regions having the positive potential are over H atoms of the Methylpyridiniumgroup and a bluish colour due to the presence of Nitrogen in the pyridine structure of our compound, the regions having the negative potential are over the oxygen atom (O8 and O9) present in carboxylate group of our compound. From these results, we can say that the H11, H12, H13, H14, H15, H16 and N6 atoms indicate the strongest attraction and the corresponding oxygen (O8 and O9) atoms indicates the strongest repulsion. For a similar compound 1-(4-chloro-phenyl)-3-phenyl-succinimide MEP was calculated by density functional theory (B3LYP) at 6-311++G(d,p) standard basis set.

10. Density of States (DOS)

DOS (density of states) which provides the molecular orbital contribution of different constituting elements to the total system for the 1-Methylpyridinium-3-carboxylate compound has been calculated using GaussSum software following the calculation methodology adopted for the compound thio semicarbazone [27] and the corresponding DOS are represented in Fig 1.7. In the boundary region, neighboring orbitals may show quasi degenerate energy levels. In such cases, consideration of only the HOMO and LUMO may not yield a realistic description of the frontier orbitals.For this reason, the total (TDOS), sum of α and β electron density of states [28], in terms of Mulliken population analysis have been calculated and created by convoluting the molecular

orbital information with Gaussian curves of unit height and fullwidth at half maximum (FWHM) of 0.3 eV by using the Gauss Sum 2.2 program [29]. The HOMO is at 5.8 eV indicated by the green line and the LUMO at 3 eV indicated by the blue line.

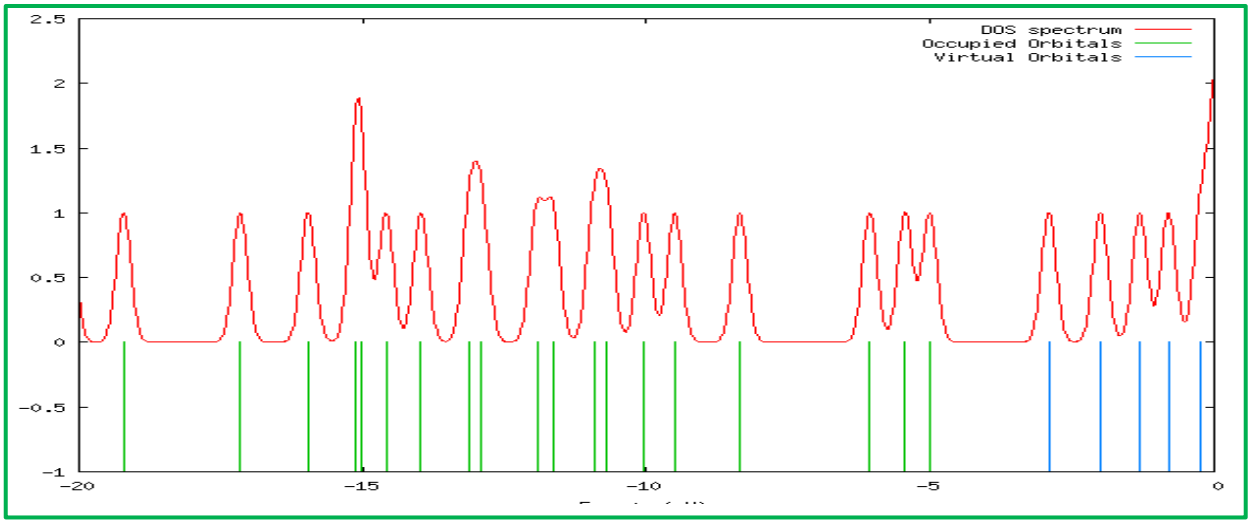

Fig 1.7 The DOS of the 1-Methylpyridinium-3-carboxylate using Guass Sum.

11. Thermodynamic Properties

On the basis of theoretical frequencies obtained from density functional calculations THERMO. PL [30] is used to calculate the statistical standard thermodynamic parameters like entropy (S), Heat capacity (C) and enthalpy (H) in gas phase and listed in table 1.5. These thermodynamic functions are increasing with temperature ranging from 100 to 1000 K , due to the fact that the molecular vibrational intensities increase with temperature. The correlation equations between heat capacity, entropy, enthalpy changes and temperatures are fitted by quadratic formulas and the corresponding fitting factors (R2) for these thermodynamic values are 0.9999, 1.0000 and 0.9997, respectively. For a similar compound 5-methyl-N-[4-(trifluoromethyl) phenyl]-isoxazole-4-carboxamide the thermodynamic properties have been studied. The corresponding fitting equations for trigonelline are as follows:

CP = 228.1792 +0.5333 T-1.18368 ×10-4 T2 (R2=0.99995)

S = 10.0597+0.4852 T-1.9076×10-4 T2 (R2=0.999895)

H = -4.4565 +0.0572 T+1.3937T×10-4 T2 (R2=0.99956)

All the thermodynamic data supplies helpful information for the further study on 1-Methylpyridinium-3-carboxylate. They can be used to compute the other thermodynamic energies according to relationships of thermodynamic functions and estimate directions of chemical reactions according to the second law of thermodynamics in the Thermo chemical field.

Table 1.5 Thermodynamic properties for 1-Methylpyridinium-3-carboxylate obtained by B3LYP/6-311++G (d,p) method.

T (K)	S (J/mol.K)	Cp (J/mol.K)	H (kJ/mol)
100	278.72	61.66	4.60
200	331.74	96.14	12.45
298.15	377.19	134.54	23.75
300	378.03	135.28	24.00
400	422.32	173.93	39.49
500	464.85	207.49	58.61
600	505.20	235.03	80.78
700	543.18	257.45	105.45
800	578.79	275.85	132.14
900	612.19	291.16	160.51
1000	643.56	304.02	190.29

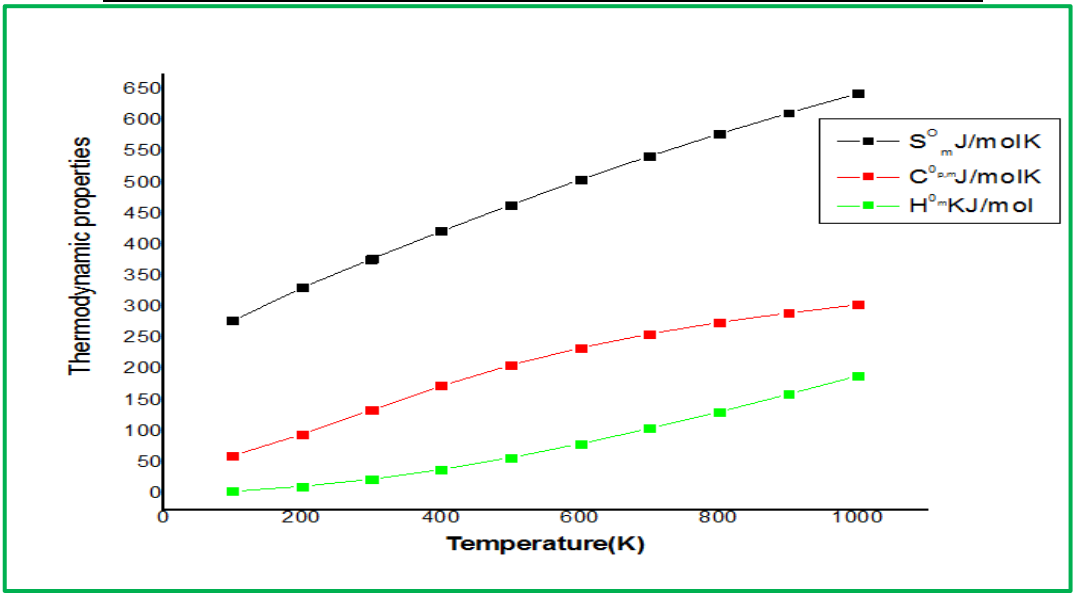

Fig 1.8 Correlation graphs of Thermodynamic properties at different temperature of the 1-Methylpyridinium-3-carboxylate

12. Conclusion

Spices and condiments are an integral part of the human diet, particularly in the Orient. Besides their use to impart flavor and color, for food preservation and to enhance palatability, they are extensively used for their beneficial effects on health. Fortunately, even long-term consumption of these substances is not known to produce any side effects. Scientific evidence in favor of some of these beneficial properties is now emerging, supporting their use for ameliorating certain disorders. Active compounds are chemical components present in spices which have therapeutic values. Trigonelline (1-Methylpyridinium-3-carboxylate), is an active compound extracted from Fenugreek and the structure has been elucidated by FT-IR and FT-Raman. In the present work the molecular structure, vibrational wavenumbers, the electronic absorption wavelengths, HOMOs, LUMOs, MEP, NBO analyses and NLO properties of the isolated

Trigonelline molecule have been calculated at the DFT/B3LYP/6-311++G(d,p) level. Fukui functions, local softness and electrophilicity indices for selected atomic sites in the 1-Methylpyridinium-3-carboxylate compound have been calculated. The results confirm the ability of the methodology (DFT) used in evaluating vibrational spectra of the 1-Methylpyridinium-3-carboxylate molecule precisely. The correlations between the thermodynamical parameters and temperature show the increase in the heat capacities, entropies and enthalpies with increasing temperature owing to the rise in intensities of the molecular vibrations.Lower values of hardness and Mulliken electronegativity, low HOMO- LUMO gap supports the fact that the compound is moderately stable, soft and has reasonably good chemical activity. Finally, it can be concluded that the results from the present study are very encouraging and indicate that further research needs to be done to explore their potential for future prospects.

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