



Natural Bond Orbital Analysis of 2-Chloro-7-Methylquinoline-3-Carbaldehyde

Nihal KUŞ* and Saliha ILICAN

Eskisehir Technical University, Science Faculty, Eskisehir, Turkey

Quinolines are aromatic compounds formed from benzene rings and fused to these rings with pyridine heterocyclic system. In this study, 2-Chloro-7-Methylquinoline-3-Carbaldehyde (CIMQC) molecule, which is a quinoline derivative, was selected and analyzed. Two minimum energies were found for the CIMQC at the theory level B3LYP/6-311++G(d,p). The energy difference ($\Delta E + ZPV$) between the two conformers (CIMQC-1 and CIMQC-2) was calculated as 13.4 kJ mol^{-1} . Considering both conformers, the relative stability of the conformers was explained using the natural bond orbital (NBO) method and performed. Donor and acceptor pairs and orbital energies for NBO pairs were calculated by the Fock matrix equation. Orbital interactions were examined, and $\pi-\pi^*$ orbital interactions were found in the rings of the both conformers. Dominant orbital interactions of selected NBOs for CIMQC-1 and 2 were calculated at the theory level B3LYP/6-311++G(d,p) and plotted. From the calculations, the total stabilization energy difference between the two conformers was found to be 22.2 kJ mol^{-1} . The molecular electrostatic potential (MEP) surfaces of the two conformers were calculated by the DFT/B3LYP/6-311++G(d,p) method and drawn.

Keywords: 2-Chloro-7-Methylquinoline-3-Carbaldehyde, NBO method, Stabilization energy.

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*Corresponding author: nkus@eskisehir.edu.tr

1. Introduction

Quinolines are bicyclic heteroaromatic organic compounds consisting of a benzene with pyridine ring. It is a colorless hygroscopic liquid with a pungent odor. It is very soluble in an organic solvents, but very slightly soluble in water. Quinoline ($\text{C}_9\text{H}_7\text{N}$) was first introduced in 1834 and was isolated by the chemist, German scientist Friedlieb F. Runge, who first described the caffeine composition [1]. Quinoline derivatives are widely used in various pharmacologically active synthetic and natural medicines [2-8]. In the past and still today, the quinoline derivative most commonly used as an antimalarial is quinine [(R)-(6-methoxyquinolin-4-yl)((2S,4S,8R)-8-vinylquinuclidin-2-yl)methanol] [9, 10]. Quinolines have also found applications in optics, pesticides, dyes and fungicide industries [11, 12]. In addition, quinolones have been used

as an antibacterial agent since 1963 and pharmacological quinolone derivatives have been synthesized. Fluoroquinolones, which are quinolone derivatives derived from quinoline, are also used as antibiotic drugs [13].

It is of great importance to investigate the molecular details of these structures, which are important in all these application areas. In our previous studies, molecular structure and chemical properties of the quinoline derivatives (5-hydroxyquinoline [14], 3-quinolinecarboxaldehyde [15], 4-chloro-7-iodoquinoline-3-carboxylate [16], 4-oxo-7-methylquinoline-3-carboxylate and ethyl 4-Hydroxy-5-methylquinoline-3-carboxylate [17]) were investigated and reported by computational method and experimentally using matrix isolation spectroscopy.

In this study, the molecular structure and orbital interactions of 2-chloro-7-methyl-quinoline-3-carbaldehyde (CIMQC), a quinoline derivative, were investigated. computationally with B3LYP/6-311++G(d,p) level. By scanning the

molecule, two stable conformations with minimum energy were found. Orbital interactions, stabilization energies with the most stabilized orbitals were calculated by the NBO method and discussed.

2. Theoretical backgrounds

The calculation of energies and minimization for the CIMQC were used with the Density Functional Theory (DFT) integrated in the Gaussian 09 [18] program. The three-parameter hybrid density functional was used and calculations were done using the 6-311++G(d,p) basis set. B3LYP which defines Becke's gradient exchange correction and the Lee, Yang and Parr, [19, 20] was used in all calculations. Orbital stabilization energies of the CIMQC were clarified using the NBO theory. The method was used considering Weinhold and co-workers, by NBO 3.1 [21] as integrated in Gaussian 09.

3. Results and Discussion

CIMQC consists of benzene and pyridine ring system, and chlorine atom and aldehyde group connected to the 2nd and 3rd carbons of pyridine respectively. The crystal structure of CIMQC was solved by Subashini and coworkers. [22], and the molecule has been shown to crystallize in the space group P21/n (monoclinic) with $a=15.458(3)$ Å, $b=3.9352(8)$ Å, $c=16.923(3)$ Å, $\beta=112.854(3)^\circ$, and $Z=4$. CIMQC has two conformers (Fig. 1). Both conformers are planar and have C1 symmetry. The conformers of the CIMQC (CIMQC-1 and CIMQC-2) were obtained by scanning the C4–C3–O–H dihedral angle in 15 degree steps, and it was optimized using DFT with B3LYP/6-311++G(d,p) basis set and the geometries of this molecule with minimum energy. The calculated energies, energy differences and dipole moments of both conformers are given in Table 1. According to the calculations, CIMQC-1 is more stable than the CIMQC-2 and $\Delta E(\text{ZPV})$ energy difference is about 13.4 kJ mol⁻¹. As a result of the calculation, the higher the dipole moment of the 2nd conformer (*ca.* 6.41 debye) indicates that the polarization is higher. In a previous study on 3-furaldehyde [23], two conformations were found and the energy difference was 4.40 kJ mol⁻¹. The aldehyde group was similarly planar structure, as in our current study. In the matrix isolation experiment performed, the phototransformation of conformers to each other was observed with the UV light with a wavelength of $\lambda > 234$ nm given to the molecule. This was experimental proof that it has two conformers at minimum energy.

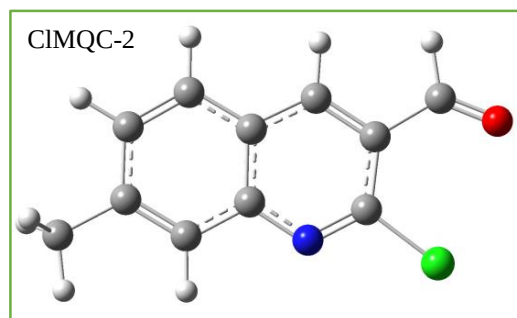
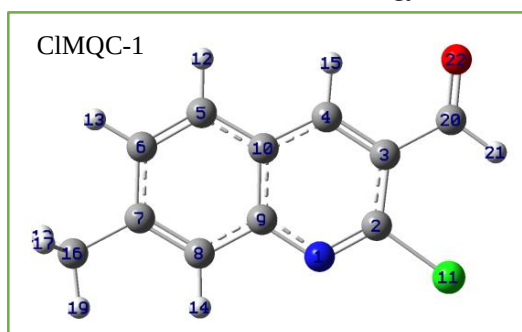


Fig.1. Two conformers of CIMQC molecule. Color codes for O, C, H, N, and Cl atoms are red, gray, white, blue, and green, respectively.

Table 1. Calculated electronic energies (with and without zero point vibrational energy) and their relative energies and dipole moments, obtained from B3LYP/6-311++G(d,p) level.

Energies	CIMQC-1	CIMQC-2
E(R3BLYP) (hartree)	-1014.339490	-1014.334196
E(ZPV) (hartree)	-1014.177950	-1014.172844
μ (debye)	4.5781	6.4067
ΔE (kJ mol⁻¹)	0	13.900
$\Delta E(\text{ZPV})$ (kJ mol⁻¹)	0	13.406

Stabilization energies were calculated based on the orbital interactions of the donor and acceptor pairs and it was found that the more stable conformation was the stable conformation in the 2nd state. The calculated stabilization energies were analyzed by considering the orbital interactions between the pyridine ring and the aldehyde group. The orbital interaction energies given in the Table 2 were calculated using the Fock matrix equation. $E(2)$ stabilization energies, between donor, lone pairs and acceptor, non Lewis, Rydberg orbitals (filled and empty orbitals) NBOs, were estimated by the second-order perturbation approach [24],

$$E(2) = \Delta E_{ij} = q_i \frac{F_{ij}^2}{\varepsilon_j - \varepsilon_i} \quad (1)$$

In above equation, q_i is the donor orbital occupancy, ε_i and ε_j are the diagonal elements and F_{ij} is NBO the off-diagonal NBO Fock matrix element.

Table 2. Donor and acceptor interactions and stabilization energies for NBO pairs results from calculated by the Fock matrix equation (Eq.1) for two conformers of ClMQC^a.

Conformer	Pair	Donor NBO (i)	Acceptor NBO (j)	$E(2)$ kJ mol ⁻¹	$s_i - s_j$ au	F_{ij} au
ClMQC-1	A1	π (N–C2)	π^* (C9–C10)	17.95	0.35	0.076
	B1	π (C3–C4)	π^* (N–C2)	26.96	0.27	0.076
	C1	π (C3–C4)	π^* (C9–C10)	13.67	0.29	0.058
	D1	π (C3–C4)	π^* (C20–O)	16.28	0.32	0.068
	E1	π (C5–C6)	π^* (C7–C8)	18.18	0.31	0.067
	F1	π (C5–C6)	π^* (C9–C10)	15.52	0.28	0.063
	G1	π (C7–C8)	π^* (C5–C6)	15.67	0.29	0.061
	H1	π (C7–C8)	π^* (C9–C10)	20.38	0.28	0.070
	J1	π (C9–C10)	π^* (N–C2)	14.72	0.25	0.056
	K1	π (C9–C10)	π^* (C3–C4)	22.47	0.27	0.074
	L1	π (C9–C10)	π^* (C5–C6)	16.32	0.29	0.065
	M1	π (C9–C10)	π^* (C7–C8)	13.22	0.29	0.059
	N1	LP1(N)	σ^* (C2–C3)	10.56	0.85	0.086
	P1	LP3(Cl)	π^* (N–C2)	15.26	0.31	0.066
	Q1	LP2(O)	σ^* (C3–C20)	18.32	0.69	0.101
	R1	LP2(O)	σ^* (C20–H21)	21.10	0.63	0.105
ClMQC-2	A2	π (N–C2)	π^* (C9–C10)	18.37	0.35	0.077
	B2	π (C3–C4)	π^* (N–C2)	23.78	0.28	0.073
	C2	π (C3–C4)	π^* (C9–C10)	13.39	0.30	0.058
	D2	π (C3–C4)	π^* (C20–O)	18.80	0.33	0.074
	E2	π (C5–C6)	π^* (C7–C8)	18.06	0.31	0.067
	F2	π (C5–C6)	π^* (C9–C10)	15.58	0.29	0.063
	G2	π (C7–C8)	π^* (C5–C6)	15.89	0.29	0.061
	H2	π (C7–C8)	π^* (C9–C10)	20.37	0.28	0.070
	J2	π (C9–C10)	π^* (N–C2)	14.63	0.25	0.056
	K2	π (C9–C10)	π^* (C3–C4)	22.05	0.27	0.073
	L2	π (C9–C10)	π^* (C5–C6)	16.60	0.28	0.066
	M2	π (C9–C10)	π^* (C7–C8)	13.24	0.29	0.059
	N2	LP1(N)	σ^* (C2–C3)	10.39	0.83	0.084
	P2	LP3(Cl)	π^* (N–C2)	17.40	0.30	0.068
	Q2	LP2(O)	σ^* (C3–C20)	19.74	0.68	0.105
	R2	LP2(O)	σ^* (C20–H21)	23.60	0.61	0.109

^a See atom numbering in Fig. 1. LP: lone-pair orbital.

According to the NBO results, the strongest polarization exhibited from C3–C4 to N–C2 bond. And they were hybridized pure p character. NBO interactions for both conformers are given in Table 2. Considering the total stabilization energies resulting from orbital interactions, it was calculated that the 1st conformer is more stabilized and energy difference is *ca.* 22.2 kJ mol⁻¹. While π bonds were observed in the rings, three sigma bonds were observed from the interaction of nitrogen and oxygen. the total σ -type energy (Q and R) is 39.42 and 43.34 kJ mol⁻¹ for ClMQC-1 and ClMQC-2, respectively. These interactions are known as the back donation effect, from aldehyde oxygen lone electron pairs (especially p -type lone pair; LP2) to C3–C20 and C20–H21 aldehyde bonds. Back

donation effect is defined as the most significant effect that causes a C–H bond attached to a carbonyl moiety to be longer than expected [25].

In Fig. 2 and 3, interactions of types A–M pairs show delocalization as a π -type of the molecule and N, Q, R pairs interacted as a σ -type interactions. These results agreed with the study of 3-furaldehyde[23].

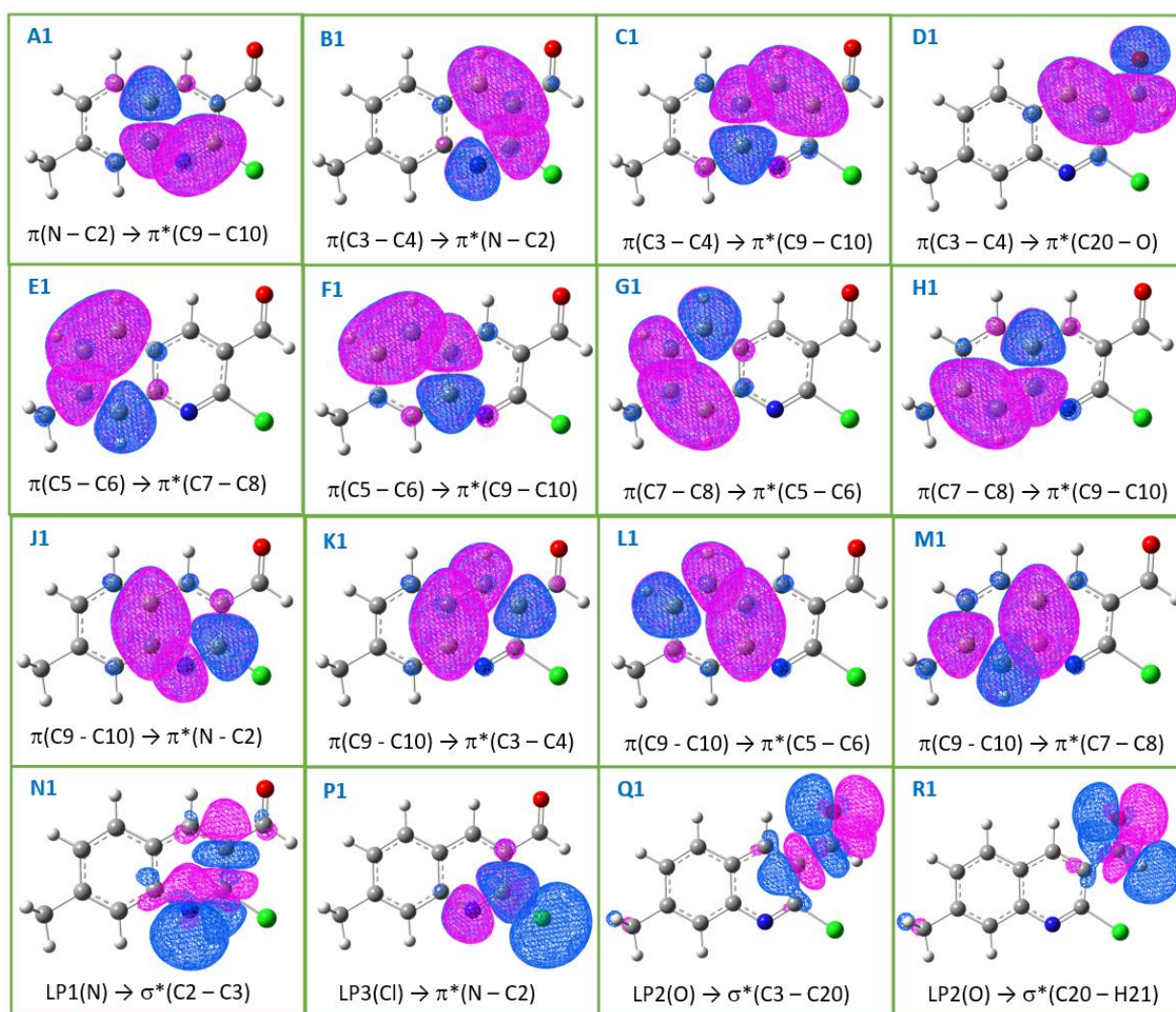


Fig.2. Dominant orbital interactions scheme for selected NBOs of ClQMC-1 related to electron density calculated at the B3LYP/6 311++G(d,p) level (given in Table 2). For isovalues of electron densities, 0.02 e is taken into account. Blue and magenta colors indicate the states of positive and negative wave function signs, respectively.

Table 3 summarizes percentage of the occupancies of the core, valence and Rydberg of orbitals due to Lewis and non-Lewis for ClQMC-1 and ClQMC-2. These results show delocalization of electron densities between donor and acceptor orbitals depend on Lewis and non-Lewis

NBO orbitals. Total Lewis and non-Lewis were calculated 97.696% and 2.304% (for ClQMC-1) and 97.683% and 2.317%, respectively.

Table 3. Total Lewis and non-Lewis occupancies (valence, core, and Rydberg shells).

	ClQMC-1	ClQMC-1
Core	35.98767 e (99.966%)	35.98768 e (99.966%)
Valence Lewis	67.57026 e(96.529%)	67.55620 e(96.509%)
Total Lewis	103.55793 e(97.696%)	103.54388 e(97.683%)
Valence non-Lewis	2.23711 e(2.110%)	2.24733 e(2.120%)
Rydberg non-Lewis	0.20496 e(0.193%)	0.20879 e(0.197%)
Total non-Lewis	2.44207 e(2.304%)	2.45612 e(2.317%)

($e=1.60217646 \times 10^{-19}$ C)

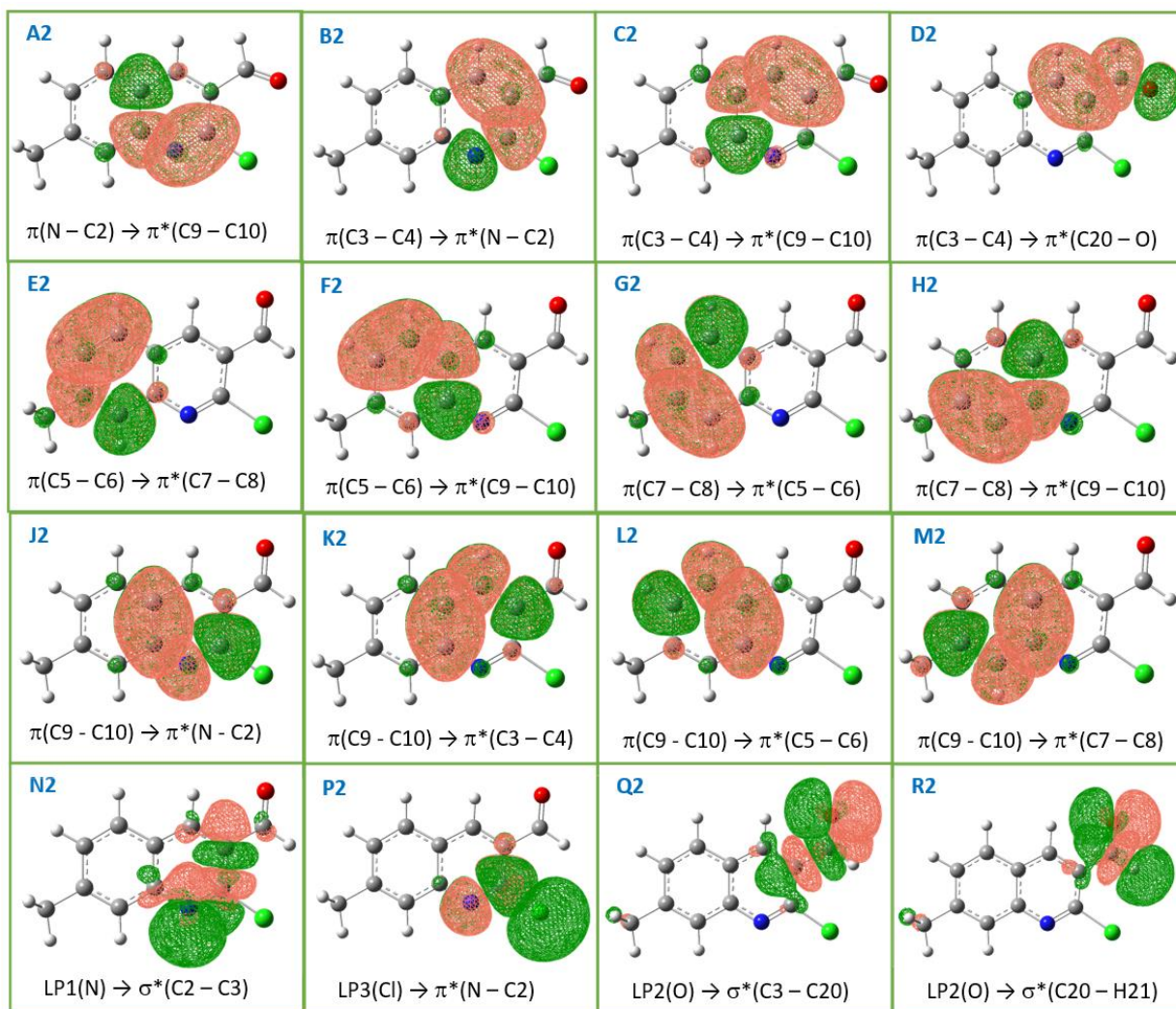


Fig.3 Dominant orbital interactions scheme for selected NBOs of CIMQC-2 related to electron density calculated at the B3LYP/6 311++G(d,p) level (given in Table 2). For isovalues of electron densities, 0.02 e is taken into account. Green and orange colors indicate the states of positive and negative wave function signs, respectively.

Table 4. Orbitals, occupancy, coefficients and hybridization for CIMQC-1, calculated using B3LYP/6-311++G(d,p) level.

Group	NBO	Occupancy ratio	Coefficients (%) ^a		Hybridization ^b
			A	B	
donor	$\pi(\text{N-C2})$	1.83286	57.58	42.42	$0.7588p + 0.6513p$
	$\pi(\text{C3-C4})$	1.67440	57.41	42.59	$0.7577p + 0.6526p$
	$\pi(\text{C5-C6})$	1.74513	49.18	50.82	$0.7013p + 0.7129p$
	$\pi(\text{C7-C8})$	1.69856	48.24	51.76	$0.6945p + 0.7195p$
	$\pi(\text{C9-C10})$	1.51200	46.33	53.67	$0.6806p + 0.7326p$
	LP(1)N	1.89356			$sp^{2.70}$
	LP(3)Cl	1.91491			p
	LP(2)O	1.88433			p
acceptor	$\sigma^*(\text{C2-C3})$	0.04606	50.94	49.09	$0.7137sp^{1.39} - 0.7004sp^{2.01}$
	$\sigma^*(\text{C3-C20})$	0.06316	46.29	53.71	$0.6803sp^{2.16} - 0.7329sp^{1.75}$
	$\sigma^*(\text{C20-H21})$	0.05961	41.67	58.33	$0.6455sp^{2.17} - 0.7637s$
	$\pi^*(\text{C3-C4})$	0.27389	42.59	57.41	$0.6526p - 0.7577p$
	$\pi^*(\text{C5-C6})$	0.22811	50.82	49.18	$0.7129p - 0.7013p$
	$\pi^*(\text{C7-C8})$	0.25080	51.76	48.24	$0.7195p - 0.6945p$
	$\pi^*(\text{C9-C10})$	0.45948	53.67	46.33	$0.7326p - 0.6806p$
	$\pi^*(\text{N-C2})$	0.34532	42.42	57.58	$0.6513p - 0.7588p$
	$\pi^*(\text{C20-O})$	0.10174	66.78	33.22	$0.8172p - 0.5763p$

^a The A and B values create a bond for the NBO orbitals of the atomic orbitals of the two atoms, corresponding to the contributions of the atoms that formed these pairs, and are obtained from the coefficients of the polarizations.

^b Definition of hybrid orbitals.

Table 5. Orbitals, occupancy, coefficients and hybridization for CIMQC-2, calculated using B3LYP/6-311++G(d,p) level.

Group	NBO	Occupancy ratio	Coefficients (%) ^a		Hybridization ^b
			A	B	
donor	$\pi(\text{N-C2})$	1.80898	57.71	42.29	$0.7597p + 0.6503p$
	$\pi(\text{C3-C4})$	1.69355	55.67	44.33	$0.7461p + 0.6658p$
	$\pi(\text{C5-C6})$	1.74495	49.34	50.66	$0.7024p + 0.7117p$
	$\pi(\text{C7-C8})$	1.69731	48.39	51.61	$0.6956p + 0.7184p$
	$\pi(\text{C9-C10})$	1.51750	46.20	53.80	$0.6797p + 0.7335p$
	LP(1)N	1.89595			$sp^{2.71}$
	LP(3)Cl	1.89568			p
acceptor	LP(2)O	1.86965			p
	$\sigma^*(\text{C2-C3})$	0.05019	51.12	48.88	$0.7150sp^{1.43} - 0.6992sp^{1.98}$
	$\sigma^*(\text{C3-C20})$	0.06572	46.26	53.74	$0.6802sp^{2.14} - 0.7331sp^{1.68}$
	$\sigma^*(\text{C20-H21})$	0.07038	43.07	56.93	$0.6563sp^{2.32} - 0.7545s$
	$\pi^*(\text{C3-C4})$	0.27479	44.33	55.67	$0.6658p - 0.7461p$
	$\pi^*(\text{C5-C6})$	0.23406	50.66	49.34	$0.7117p - 0.7024p$
	$\pi^*(\text{C7-C8})$	0.25100	51.61	48.39	$0.7184p - 0.6956p$
	$\pi^*(\text{C9-C10})$	0.45750	53.80	46.20	$0.7335p - 0.6797p$
	$\pi^*(\text{N-C2})$	0.33254	42.29	57.71	$0.6503p - 0.7597p$
	$\pi^*(\text{C20-O})$	0.11006	65.93	34.07	$0.8120p - 0.5837p$

^a The A and B values create a bond for the NBO orbitals of the atomic orbitals of the two atoms, corresponding to the contributions of the atoms that formed these pairs, and are obtained from the coefficients of the polarizations.

^b Definition of hybrid orbitals.

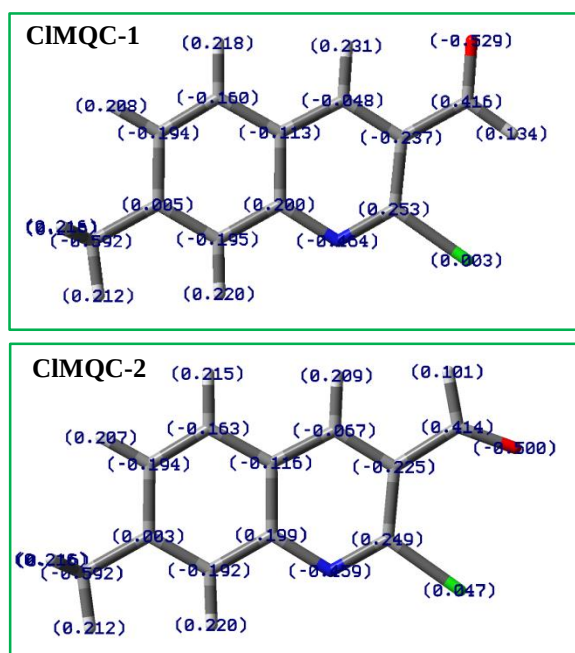
Taking into account the stabilization energies of CIMQC higher than 10%, the occupancy ratio of the bond orbitals, NBO coefficients of the atoms and their hybridizations are given in Table 4 and 5. This Table also presents the bonding percentage of atomic orbitals in each atom, subtracted from the NBO polarization coefficients for NBO orbitals. All anti-bonding orbitals cause weak delocalization and make no comparatively contribution to occupied NBOs. According to the NBO interactions, both rings of the molecule show strongest p hybridization. Hybridization is almost the same for acceptor for both conformers.

Table 6. NBO charges^a for CIMQC-1 and CIMQC-2, calculated using B3LYP/6-311++G(d,p) level^b.

Atom	CIMQC-1	CIMQC-2
N1	-0.46375	-0.45945
C2	0.25336	0.24914
C3	-0.23697	-0.22544
C4	-0.04847	-0.06654
C5	-0.15965	-0.16301
C6	-0.19410	-0.19376
C7	0.00461	0.00286
C8	-0.19453	-0.19170
C9	0.19995	0.19887
C10	-0.11280	-0.11587
Cl11	0.00264	0.04668
H12	0.21821	0.21532
H13	0.20762	0.20737
H14	0.21959	0.22028
H15	0.23129	0.20879
C16	-0.59244	-0.59226
H17	0.21638	0.21610
H18	0.21638	0.21610
H19	0.21190	0.21223
C20	0.41570	0.41418
H21	0.13438	0.10053
O22	-0.52926	-0.50043

^a Electron unit; $e = 1.60217646 \times 10^{-19}$ C.

^b Fig. 1 shows atom numbers.

**Fig.4.** Natural atomic charges for two conformers.

The natural charges for two conformers are given in Fig.4 and Table 6. The charges on atoms are identical. The dipole interactions can be related with the strongly polarized C-O bond in the molecule (for CIMQC-1, charges on C and O are of *ca.* +0.42 and *ca.* -0.53 e, respectively; for CIMQC-2, charges on C and O are of *ca.* +0.41 and *ca.* -0.50 e, respectively).

Surface maps of molecular electrostatic potential (MEP) is a color-coded map of the calculated electron density surface. The electron density surface of a molecule is the surface that represents the approximate maximum distance that the electron density in a molecule can reach (also called the Van der Waals surface). Molecular electrostatic potential gives important information about the determination of the regions where electrophilic and nucleophilic reactions can occur in the molecule. MEP of CIMQC conformers were drawn using GaussView5 visualization program, and these maps are given in Fig. 5. MEP surfaces visualize charge regions of the molecule. In scale bar, the red and blue colours indicate negative and positive values, respectively. These values are between $-4.656\text{e-}2$ (max. red region) and $+4.656\text{e-}2$ (max. blue region) for CIMQC-1, and between $-5.356\text{e-}2$ (max. red region) and $+5.356\text{e-}2$ (max. blue region) for CIMQC-2, respectively. The both maps showed that the negative electrostatic potentials (red region, electrophilic attack) were intensified around the O atom while the positive electrostatic potential (blue region, nucleophilic attack) were intensified around the H atoms. From Fig. 5, it can be seen that between O and C20 atoms attraction is more concentrated.

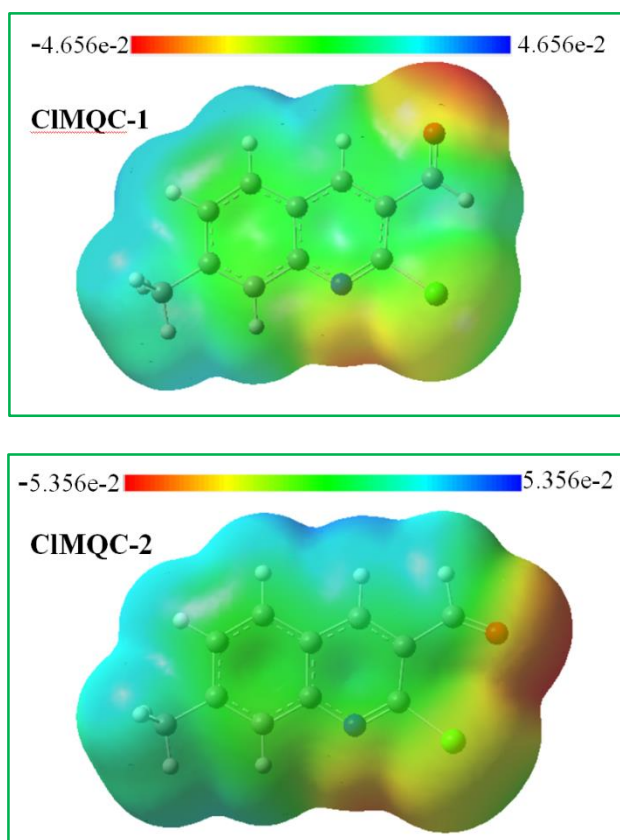


Fig.5. MEP surface for two conformers, calculated using B3LYP/6-311++G(d,p) level.

4. Conclusion

The conformers of CIMQC were calculated in the ground electronic state using B3LYP/6-311++G(d,p) level. CIMQC-1 was more stable than the other conformer *ca.* 13.4 kJ mol^{-1} . Orbital interaction energies, electron density surfaces and hybridizations of the CIMQC-1 and CIMQC-2 conformers were determined using B3LYP/6-311++G(d,p) level with NBO method. Strong orbital interactions of conformers were analyzed and discussed. It was seen that delocalization was over the two rings. Back donation effect was observed from $\text{LP2}(\text{O})$ to $\sigma^*(\text{C3-C20})$ and $\sigma^*(\text{C20-H21})$ aldehyde bonds. NBO charges were also determined. The both maps showed that the negative electrostatic potentials were intensified around the O atom while the maximum electrostatic potential were intensified around the H atoms.

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