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Tautomerism in some dihalophenolindophenol dyes – A DFT study

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Abstract

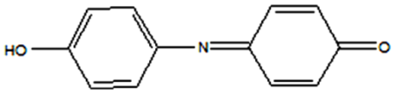
Indophenol is a deep blue dye (the group with various substituents). It is found in many dyes used in hair coloring and textile, and found applicability as lubricants, redox materials, liquid crystal displays, etc. A variant of it, dichlorophenol-indophenol, is often used to determine the presence of vitamin C. Indophenol and its derivatives may exhibit resonance-assisted proton tautomerism. In the present study some of those types of tautomers have been investigated within the constraints of density functional theory (DFT) at the level of B3LYP/6-311++G(d,p). All the species presently considered (in vacuum conditions) have not only exothermic heat of formation values but also possess favorable Gibbs free energy of formation values and they are electronically stable. Various structural and quantum chemical data have been collected and discussed including IR and UV-VIS spectra.

1. Introduction

Indophenol, (phenol-indophenol), $C_{12}H_9NO_2$ (4-(4-hydroxyphenyl)iminocyclohexa-2,5-dien-1-one), is a deep blue dye [1-3] that is the product of the Berthelot's reaction [4], a common test for ammonia [5]. The indophenol group of dyes, with various substituents in place of OH and various ring substitutions, are found in many dyes used in hair coloring and textiles, etc. [3,6,7].

Dichlorophenol-indophenol (DCPIP), a form of indophenol, is often used to determine the presence of vitamin C (ascorbic acid) [8]. Various articles exist in the literature about 2,6-dichloroindophenol [9-13].

Indophenol itself is used in hair dyes, lubricants, redox materials, liquid crystal displays, fuel cells and chemical-mechanical polishing. It is an environmental pollutant and is toxic to fish [14,15]. 2,6-dichlorophenolindophenol (DCPIP, DCIP or DPIP) is a chemical compound ($C_{12}H_7Cl_2NO_2$) used as a redox dye. DCPIP can be used to measure the rate of photosynthesis. It is part of the Hill reagents family. When exposed to light in a photosynthetic system, the dye is decolorized by chemical reduction. DCPIP has a higher affinity for electrons than ferredoxin and the photosynthetic electron transport chain can reduce DCPIP as a substitute for NADP+, that is normally the final electron carrier in photosynthesis. As DCPIP is reduced and becomes colorless, the resultant increase in light transmittance can be measured using a spectrophotometer. DCPIP can also be used as an indicator for vitamin C [16].



Indophenol

Pharmacological experiments suggest that DCPIP may serve as a pro-oxidant chemotherapeutic targeting human cancer cells in an animal model of human melanoma; DCPIP-induced cancer cell death occurs by depletion of intracellular glutathione and upregulation of oxidative stress [17].

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Keywords and phrases: indophenol, dichlorophenol-indophenol, DCPIP, tautomerism, DFT calculations.

In the present study, proton tautomerism in some dihalophenolindophenol dyes is considered within the constraints of density functional theory (DFT).

2. Method of Calculations

In the present study, all the initial optimizations of the structures leading to energy minima have been achieved first by using MM2 method which is then followed by semi empirical PM3 self consistent fields molecular orbital method [18-20]. Afterwards, the structure optimizations have been achieved within the framework of Hartree-Fock and finally by using density functional theory (DFT) at the level of B3LYP/6-311++G(d,p) [21,22]. Note that the exchange term of B3LYP consists of hybrid Hartree-Fock and local spin density (LSD) exchange functions with Becke's gradient correlation to LSD exchange [23]. The correlation term of B3LYP consists of the Vosko, Wilk, Nusair (VWN3) local correlation functional [24] and Lee, Yang, Parr (LYP) correlation correction functional [25]. In the present study, the normal mode analysis for each structure yielded no imaginary frequencies for the $3N-6$ vibrational degrees of freedom, where N is the number of atoms in the system. This search has indicated that the structure of each molecule considered corresponds to at least a local minimum on the potential energy surface. Furthermore, all the bond lengths have been thoroughly searched in order to find out whether any bond cleavage occurred or not during the geometry optimization process. All these computations were performed by using SPARTAN 06 program [26].

3. Results and Discussion

The main types of proton tautomerism in organic molecules with decreasing likeliness are 1,3; 1,5 and 1,7. However, the tautomerism in indophenols presently considered is the resonance assisted one which eventually induces proton tautomerism [27]. Figure 1 shows two of the resonance structures of phenol-indophenol.

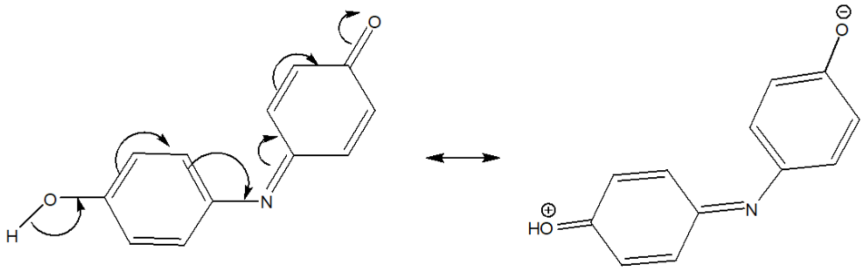


Figure 1. Two of resonance structures of indophenol.

Figure 2 shows the optimized structures of the species considered. Note that indophenol (structure-1 or 2) has equivalent tautomers due to symmetry (they possess equivalent valence bond structures). Moreover, dihaloindophenol tautomers considered are pair wise isomeric. Structures-3 and -4 possess fluorine, whereas -5 and -6 chlorine atoms at ortho/vicinal positions to the oxygen atom (either -OH or =O). In structures-7 and -8 the halogen atoms (fluorine, in 7 and chlorine in 8) are attached to different rings. Also note that the rings of tautomer-3 are coplanar but in its tautomer-4 they are not. Similarly, the coplanarity exists in structure-5 but not in its isomer/tautomer-6. In Figure 2, structures 1,3 and 5 fall into class of type-A tautomers whereas 2,4, and 6 are in type-B. Note that structure 7 and 8 are not tautomers of each other. Their tautomers are not considered presently.

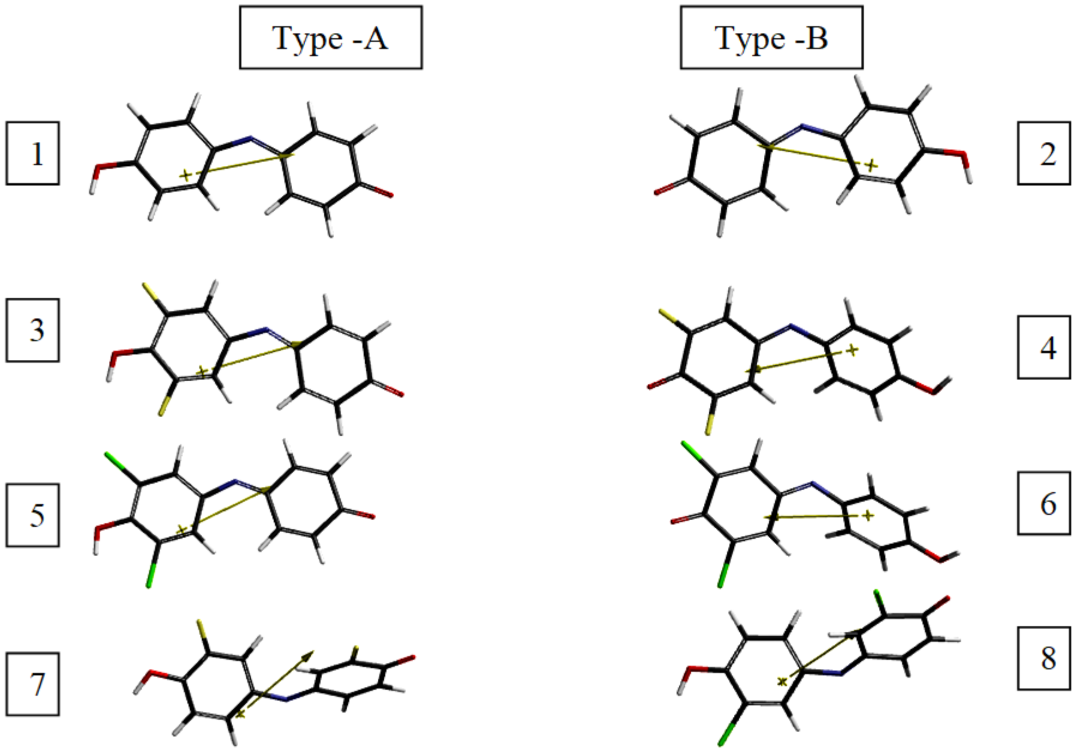


Figure 2. Optimized structures of the indophenols considered (fluorine ivory colored; chlorine is in green).

Table 1 shows some of the standard thermochemical formation data of the species considered. The data reveal that the standard heat of formation (H°) values of all the species are exothermic, and they are favored according to their G° (Gibbs free energy of formation) values. The algebraic order of H° and G° values for isomeric tautomers are the same as 4<3 and 6<5, respectively. So B-type tautomers are more exothermic and more favored than their A-type counter parts.

Table 1. Some thermo chemical properties of the species considered.

Species	H°	S° (J/mol°)	G°
1	-1753423.398	422.12	-1753549.255
2	-1753423.398	422.12	-1753549.255
3	-2274699.871	453.04	-2274834.946
4	-2274716.966	449.28	-2274850.920
5	-4166954.882	466.49	-4167093.956
6	-4166969.428	463.54	-4167107.635
7	-2274714.598	450.21	-2274848.830
8	-4166979.562	463.10	-4167117.639

Energies in kJ/mol.

Table 2 shows some energies of the species considered where E, ZPE and E_C stand for the total electronic energy, zero point vibrational energy and the corrected total electronic energy, respectively. According to the data, they are all electronically stable structures. The stability order for isomeric tautomers are 4>3 and 6>5.

Table 2. Some energies of the species considered.

Species	E	ZPE	E_C
1	-1753914.07	476.13	-1753437.94
2	-1753914.07	476.13	-1753437.94
3	-2275146.75	433.18	-2274713.57
4	-2275164.50	434.36	-2274730.14
5	-4167377.96	425.95	-4166952.01
6	-4167393.02	426.76	-4166966.26
7	-2275161.82	433.85	-2274727.97
8	-4167403.22	426.85	-4166976.37

Energies in kJ/mol.

Aqueous and solvation energy values (E_{aq} and E_{solv}, respectively) for the species considered are shown in Table 3. The algebraic order of aqueous and solvation energy values for isomeric tautomers are 4<3 and 6<5. Thus, B-type tautomers are hydrated better (see Figure 2 for the direction of dipole moment vectors). The solvation energies were calculated by adopting SM5.4/A model [26].

Table 3. Some energies of the species considered.

Species	E_{aq}	E_{solv}
1	-1753954.35	-40.280
2	-1753954.35	-40.280
3	-2275173.88	-27.131
4	-2275193.32	-28.816
5	-4167407.37	-29.410
6	-4167430.68	-37.663
7	-2275198.20	-36.387
8	-4167433.27	-30.054

Energies in kJ/mol. Solvation energy by SM5.4/A model.

Table 4 lists some calculated properties of the species considered. It is worth mentioning that the polar surface area (PSA) is defined as the amount of molecular surface area arising from polar atoms (N,O) together with their attached hydrogen atoms. Although these compounds are isomeric, their PSA values differ from each other, meaning that the same kind of atoms might be influenced by electronic factors differently at different positions.

The dipole moment and polarizability values for them are also tabulated in Table 4. The orders of dipole moment and polarizability values are the same for the tautomeric pairs which are 3<4; 5<6. Note that the resultant dipole moment is the vectorial sum of bond dipoles. Apparently, A-type tautomers have smaller values compared to the respective values of B-type tautomers (see Figure 2). Obviously, tautomers 1 and 2 are characterized with the same value of dipole moment or polarizability value. As for the structures 7 and 8 which are not tautomers, but have fluorine (7) or chlorine (8) atoms on both of the rings. The dipole moment and polarizability values are greater for the fluorine substituted one.

As for the log P values, all the species considered have log P values which are either positive or close to zero. Note that a negative value for log P means the compound has a higher affinity for the aqueous phase (it is more hydrophilic); when log P = 0 the compound is equally partitioned between the lipid and aqueous phases; whereas a positive value for log P denotes a higher concentration in the lipid phase (i.e., the compound is more lipophilic). The tautomeric species possess (pair wise, 3 and 4; 5 and 6) the same log P values [26].

Table 4. Some calculated properties of the species considered.

Species	Area (Å²)	Volume (Å³)	PSA (Å²)	Ovality	Log P	Dipole moment	Polarizability
1	221.23	204.84	40.310	1.32	1.46	5.85	57.27
2	221.23	204.84	40.310	1.32	1.46	5.85	57.27
3	231.77	213.97	39.638	1.34	0.39	3.24	58.00
4	231.80	213.53	41.029	1.34	0.39	7.12	58.05
5	250.34	231.85	38.597	1.37	1.19	3.38	59.45
6	251.31	231.63	40.698	1.38	1.19	6.98	59.52
7	231.96	213.60	41.046	1.34	0.39	6.19	58.03
8	221.23	204.84	40.310	1.32	1.46	5.85	57.27

Polarizabilities in 10^{-30} m^3 units. Dipole moments in debye units.

In general, the effect of the halogens on the properties considered presently is dependent on the type of the tautomer as well as the kind of the halogen. The rings of A- or B-type tautomers are not completely independent from each other, although in some tautomers they are not coplanar, thus have only partial conjugation.

Figure 3 displays the chemical function descriptor (CFD) patterns of the species which are the present focus of interest.

Figure 4 displays the calculated IR spectra of the tautomers (1-6) considered. It is worth mentioning that structures 1 and 2; 3 and 4; 5 and 6 are pair wise isomeric tautomers. In all the spectra, the peak at the far left stands for O-H stretching. The carbonyl stretching of tautomer-1 occurs at 1699 cm^{-1}. The skeletal stretching of the ring having carbonyl happens at 1562 cm^{-1}. In between 1668 cm^{-1} and 1609 cm^{-1} various bending vibrations and skeletal breathings take place. Note that tautomers-1 and -2 identical valence bond structures. The other spectra, in shape, resemble the spectrum of 1 or 2 having some minute shifts of the respective wave numbers. The sharp peak in spectrum of tautomer-3 at 1333 cm^{-1} is the overlap of various stretchings and bendings.

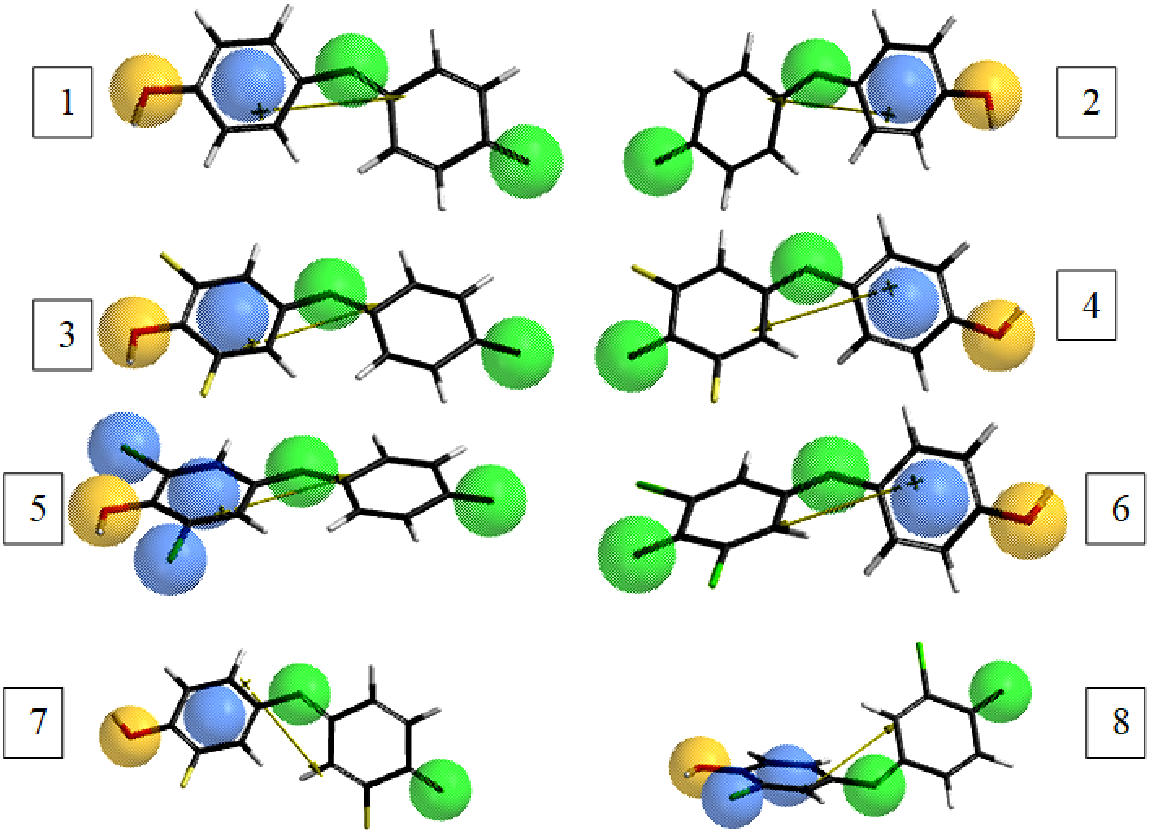
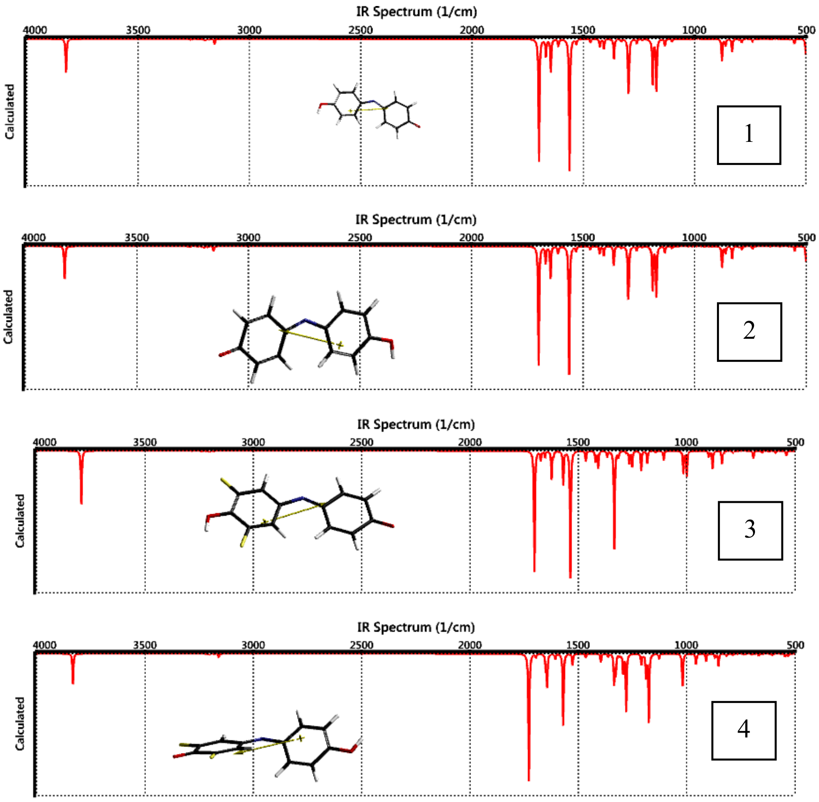


Figure 3. The CFD patterns of the species considered. (Yellow: HBD and HBA; Green: HBA; Blue: Hydropobe).



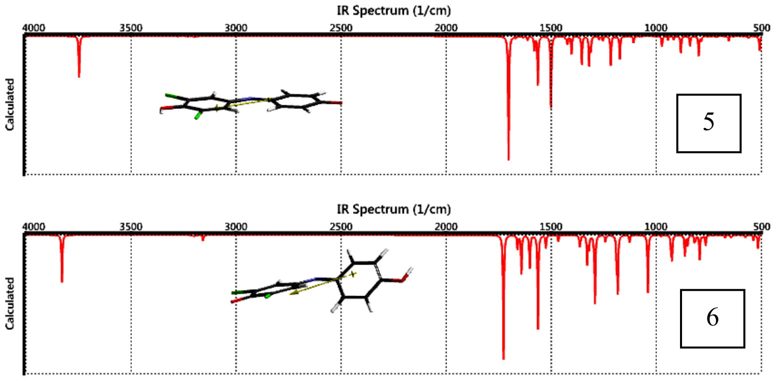


Figure 4. The calculated IR spectra of the tautomers considered.

Figure 5 shows some of the molecular orbital energy levels of the tautomers considered. As expected distribution of the energy levels differ between the tautomeric pairs having different valence bond structures e,g., 3 and 4; 5 and 6. It is to be mentioned that the inner lying molecular orbitals are assumed to be responsible for the thermal stability.

Table 5 lists the HOMO, LUMO energies and the interfrontier molecular orbital energy gap, $\Delta\varepsilon$, values ($\Delta\varepsilon = \varepsilon_{LUMO} - \varepsilon_{HOMO}$) of the species considered. The algebraic orders of the HOMO and LUMO energies for isomeric tautomers are 3<4; 5<6 and 4<3; 6<5, respectively. Thus, the interfrontier molecular orbital energy gap values, constitute the order of 4<3 and 6<5.

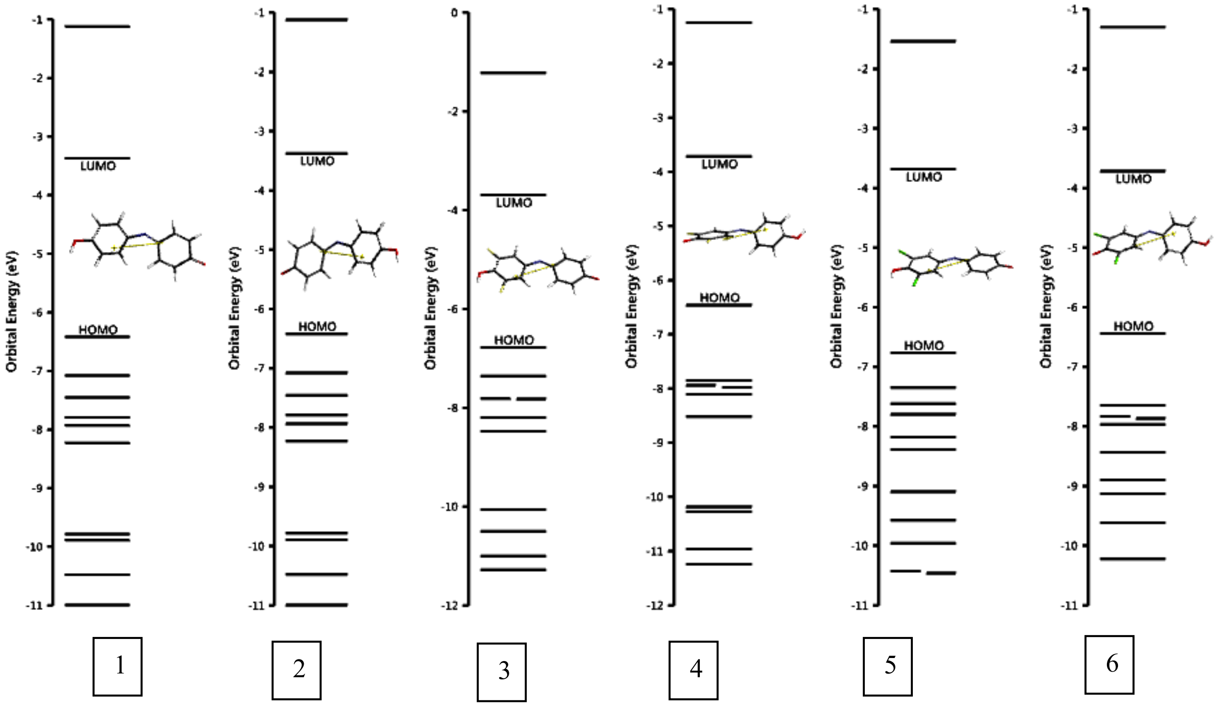


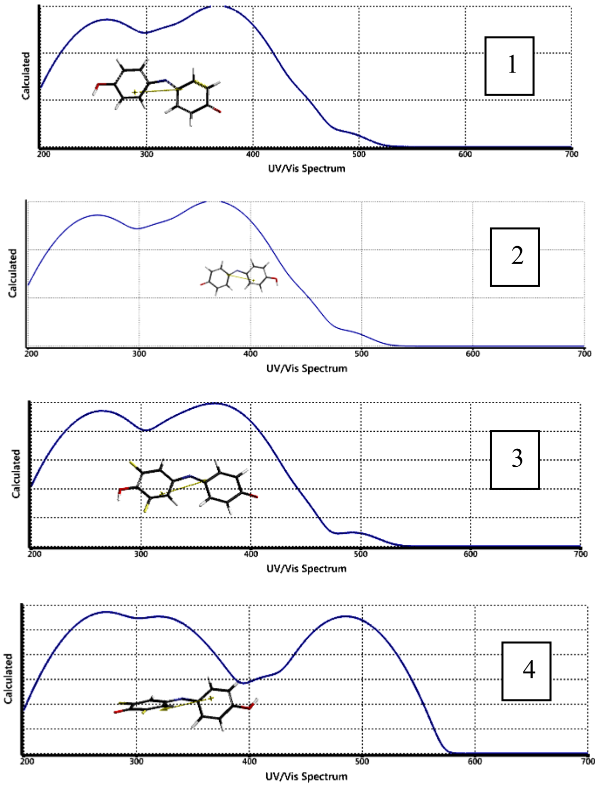
Figure 5. Some of the molecular orbital energy levels of the tautomers considered.

Table 5. The HOMO, LUMO energies and Δε values of the species considered.

Species	HOMO	LUMO	Δε
1	-619.47	-325.41	294.06
2	-619.47	-325.41	294.06
3	-653.89	-356.44	297.45
4	-623.24	-358.49	264.75
5	-652.95	-355.52	297.43
6	-621.62	-358.69	262.93
7	-628.29	-353.64	274.65
8	-630.15	-356.34	273.81

Energies in kJ/mol.

Figure 6 shows the calculated UV-VIS spectra (TDDFT) of the species considered. As seen in the figure, all the spectra are spread over UV and some part of the visible region having some not well-developed shoulders, thus main peaks are broadened which do not vary much in shape for the species, so do the intensities and positions. Generally, of the considered tautomers, the B-type ones somewhat exhibit a bathochromic shift to the visible region. The spectra and value of the transition moment which is responsible for the excitations of nonbonding or π-orbitals [28,29] seem to be rather sensitive to molecular stereochemistry, the extent of any π-conjugation between the rings (arising from the groups attached to the rings and the position of the substituents they possess).



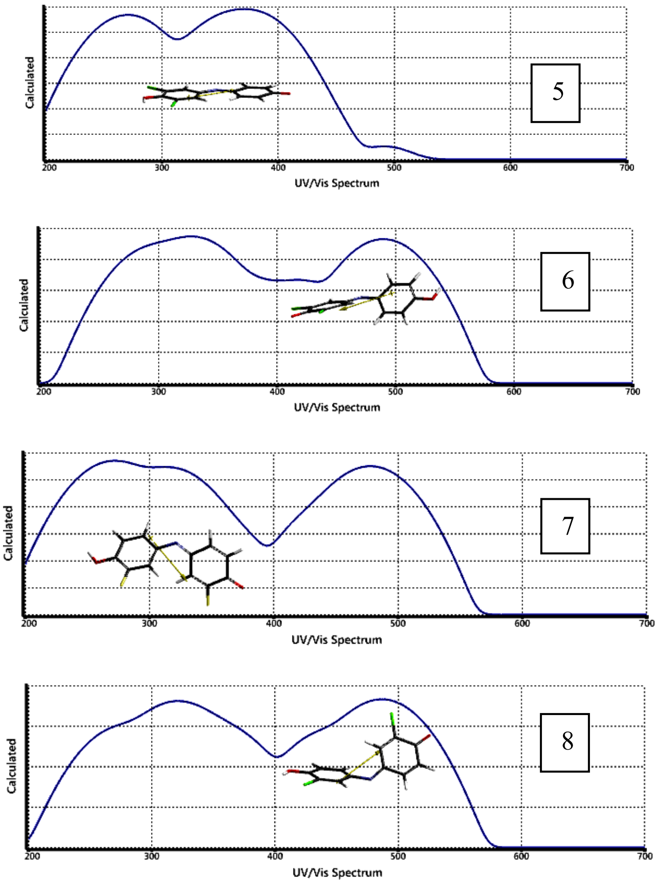


Figure 6. The calculated UV-VIS spectra (TDDFT) of the species considered.

4. Conclusion

The present density functional treatise has revealed that indophenol based dihalo structures may exhibit proton tautomerism induced by resonance. The tautomers other than indophenol itself have different valence bond structures, thus constitute isomeric pair with each other. Since the rings of these tautomeric pairs are not coplanar with each other in all the cases, different extents of π-conjugation occur. Also, different extent of n-π and π-π interaction between the substituent atoms and the rings result in ample conjugated paths which affect not only the UV-VIS spectra but also some physical properties of the tautomers. By varying the position of the halogen substituents and their kinds various color possibilities could be considered. Medical applications and toxicological aspects of substituted (halogen or others) indophenols might be worth investigating.

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