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## Molecular Structure Vibrational & Electronic Properties of Some Isatin Derivatives

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# Molecular Structure Vibrational & Electronic Properties of Some Isatin Derivatives

## Abstract

### Abstract

In this study, Natural Bonding Orbitals (NBOs) were applied to isatin, 5-fluoroisatin, 5-chloroisatin, 5-methylisatin and 5-methoxyisatin using the Lee-Yang-Parr correlation functional B3LYP with 6-311++G(2d,2p) basis set. Natural bonding analysis was performed to consider the transfer interactions of intra-molecular charge, pre-hybridization and electron density within the isatin, 5-fluoroisatin, 5-chloroisatin, 5-methylisatin and 5-methoxyisatin. In natural bonding orbital analysis, the wave functions of the electrons were explicated in sets of occupied Lewis type terms, (bonds or lone pairs) and sets of unoccupied non-Lewis (anti-bond and Rydberg) localized natural bonding orbitals. The electron density between these orbitals was correlated to stabilize the interaction of donor-acceptor orbitals. Second-order Perturbation Theory was employed to evaluate the stabilization energies of all possible interactions between donor and acceptor orbitals in natural bonding orbitals. The aim was to study the properties of these series and to produce a molecular geometry description, hyper-conjugative interactions, natural bond orbital (NBO) analysis and the HOMO-LUMO energy gap-dependent properties that are important for the stability of structures. From the results, it can be noted that for all forms, the HOMO-LUMO energy gap values decreased by substitution for the 5-fluoroisatin, 5-chloroisatin, 5-methylisatin and 5-methoxyisatin compounds and, with the exception of the deprotonated form in all the compounds, leading to less stable molecules. The anion form of the 5-methoxyisatin compound and the cation form of the 5-fluoroisatin, in which the HOMO-LUMO energy gap values increased, became more stable. It also appeared that the 5-CH<sub>3</sub>- and 5-Cl groups caused an increase in the linear polarizability and anisotropic polarizability values in all forms; however, the 5-OCH<sub>3</sub> and 5-F groups caused different effects in different forms. Furthermore, we concluded that the intramolecular hyper-conjugative interactions between bonded atoms changed by groups. These changes caused changes in the electron density values in the atoms, which in turn led to a change in the stabilization energy values of the isatin, 5-fluoroisatin, 5-chloroisatin, 5-methylisatin and 5-methoxyisatin.

## Keywords

Keywords: Isatin derivatives; hybridization; electron density; stabilization energies; pre hybridization

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## Cover Page Footnote

Thank you so much for informative reviews. It was very kind of them to spare the time. The manuscript has certainly benefitted from reviewers' input. We hope the paper meets the journal's formatting requirements. We ask an English native speaker to review it. He is an Australian person called Gorge

## 1. Introduction

The isatin ring system consists of a benzene ring fused to a five-membered pyrrole ring [1]. Isatin, or 1H-indole-2,3-dione, containing both the keto and amide groups [2] (Fig. 1), is a derivative of indole at the second and third positions of the ring [3]. In nature, isatin is found in plants such as the Caribbean tumorigenic plant that is used to obtain methoxy phenylpentyl isatins. Isatins also are found in humans as an adrenaline metabolic derivative [4].

In 1841 Erdman and Laurent obtained isatin (1H-indole-2,3-dione) from the oxidation of indigo with chromic and nitric acids [5]. Cane et al. (2000) identified isatin as a urinary compound produced in the body and excreted in urine [4]. Isatin is an important raw material in the synthesis of other heterocyclic compounds [6].

The presence of several centers of reaction in isatin has led to the production of many of its derivatives [7]. These have been evaluated as being valuable synthetic intermediates in the production of drugs and dyes [8]. Through the primary amine group, the isatin series is capable of entering N-acylation and N-alkylation [9]. The keto group at positions 2 and 3 can enter into condensation and addition reactions at the C–O bond [10].

Literature reviewers discovered that various derivatives of isatin have different activities, such as anti-cancer, anti-mycobacterial, anti-viral [11], anti-fungal, anti-bacterial, anti-HIV, anti-convulsion activities and anti-inflammatory properties [12]. In past decades, computer models played an important role in various fields, such as physical chemistry, physics, mechanical engineering and material science [13]. In the present time, computer models are important tools to explain the behavior of molecular systems displaying different external effects [14]. Molecular modeling is a complete computational technique and theoretical method used to investigate molecular behavior, especially interactions between molecules [15].

In this work, we performed quantum chemical calculations for isatin (Is), 5-fluoroisatin (5-F-Is) C<sub>8</sub>H<sub>4</sub>FNO<sub>2</sub>, 5-chloroisatin (5-Cl-Is) C<sub>8</sub>H<sub>4</sub>ClNO<sub>2</sub>, 5-methylisatin (5-CH<sub>3</sub>-Is) C<sub>9</sub>H<sub>7</sub>NO<sub>2</sub>, and 5-methoxyisatin (5-CH<sub>3</sub>O Is) C<sub>9</sub>H<sub>7</sub>NO<sub>3</sub> (Fig. 2).

The aim is to examine the hyper-conjugation interactions, natural bond orbital (NBO) analysis and

parameters related to HOMO–LUMO energy, such as chemical hardness, chemical softness and electronegativity for Is, 5-F-Is, 5-Cl-Is, 5-CH<sub>3</sub>-Is and 5-CH<sub>3</sub>O-Is [16]. Quantum chemical calculations were performed using the B3LYP/6-311G++(2d,2p) basis set.

## 2. Materials and methods

Is, 5-F-Is, 5-Cl-Is, 5-CH<sub>3</sub>-Is, and CH<sub>3</sub>O-Is were fully optimized using the DFT at the B3LYP level with the 6-311G++(2d,2p) basis set using the Gaussian 09 software [17]. The second-order Fock-matrix was applied to calculate the donor–acceptor interactions in the NBO basis. The interactions resulted in a loss of occupancy from the localized NBO of the idealized Lewis structure into an empty non-Lewis orbital. For each donor (*i*) and acceptor (*j*) interaction, the stabilization energy *E*(2) is evaluated with the following formula:

$$E(2) = \Delta E_{ij} = q_i \frac{F_{ij}^2}{(E_j - E_i)}$$

where *q<sub>i</sub>* is the donor orbital occupancy, *E<sub>i</sub>* and *E<sub>j</sub>* are the diagonal elements, and *F<sub>ij</sub>* is the off-diagonal NBO Fock-matrix element [18,19].

## 3. Results and discussion

The fully optimized isatin derivative molecules, using DFT with the B3LYP/6-311G++(2d,2p) basis set, the surfaces of HOMO–LUMO, and ESP, were drawn (see Fig. 3) to understand the bonding scheme of the present compounds.

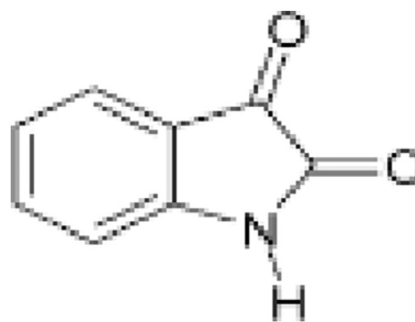
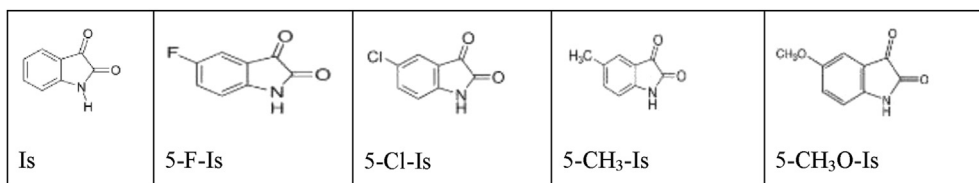


Fig. 1. Chemical structure of isatin (1H-indole-2,3-dione).

Fig. 2. Chemical structures of Is, 5-F-Is, 5-Cl-Is, 5-CH<sub>3</sub>-Is and 5-CH<sub>3</sub>O-Is.

### 3.1. HOMO–LUMO energy dependent calculation

Table 1 presents the energy values of Low Unoccupied Molecular Orbital (LUMO), High Occupied Molecular Orbital (HOMO) and energy gap values between HOMO and LUMO for the neutral, anion,

cation, protonated and deprotonated forms of Is, 5-F-Is, 5-Cl-Is, 5-CH<sub>3</sub>-Is, and 5-CH<sub>3</sub>O-Is molecules.

From the comparison results of the HOMO and LUMO energy values in Table 1, it can be noted that, with the exception of the anion form found to have positive values, the energy values for Is, 5-F-Is, 5-Cl-

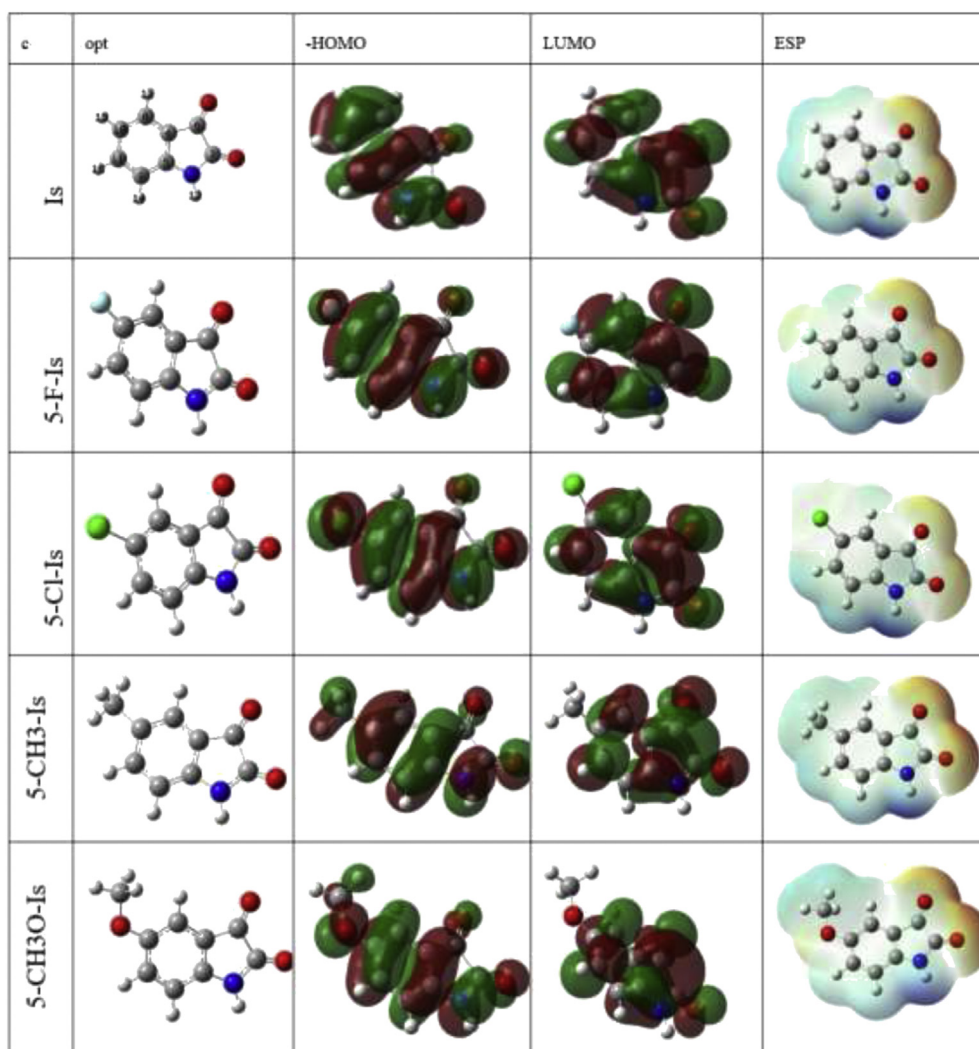


Fig. 3. The fully optimized, HOMO and LUMO and ESP shapes of Is, 5-F-Is, 5-Cl-Is, 5-CH<sub>3</sub>-Is and 5-CH<sub>3</sub>O-Is using the B3LYP/6-311G++(2d,2p) basis set.

Table 1

HOMO and LUMO energy of neutral, anion, cation, protonated and deprotonated form of the Is, 5-F-Is, 5-Cl-Is, 5-CH<sub>3</sub>-Is and 5-CH<sub>3</sub>O-Is using the B3LYP/6-311G++(2d,2p) level.

The form	compounds	HOMO (eV)	LUMO (eV)	ΔE (eV)
Neutral	Is	-6.78	-2.86	3.92
	5-F-Is	-6.80	-3.08	3.71
	5-Cl-Is	-6.85	-3.15	3.70
	5-CH <sub>3</sub> -Is	-6.56	-2.79	3.76
	5-CH <sub>3</sub> O-Is	-6.18	-2.80	3.38
Anion	Is	0.56	3.76	3.20
	5-F-Is	0.33	3.51	3.18
	5-Cl-Is	0.16	3.30	3.14
	5-CH <sub>3</sub> -Is	0.54	3.73	3.19
	5-CH <sub>3</sub> O-Is	0.49	3.71	3.22
Cation	Is	-12.04	-7.99	4.05
	5-F-Is	-11.93	-7.94	4.19
	5-Cl-Is	-12.13	-8.13	3.80
	5-CH <sub>3</sub> -Is	-11.77	-7.74	4.03
	5-CH <sub>3</sub> O-Is	-11.20	-7.57	3.63
Protonated	Is	-11.50	-8.61	2.88
	5-F-Is	-11.42	-8.83	2.59
	5-Cl-Is	-11.18	-8.79	2.40
	5-CH <sub>3</sub> -Is	-11.12	-8.45	2.67
	5-CH <sub>3</sub> O-Is	-10.50	-8.39	2.11
Deprotonated	Is	-11.96	-10.62	1.33
	5-F-Is	-12.00	-10.49	1.51
	5-Cl-Is	-11.77	-10.34	1.43
	5-CH <sub>3</sub> -Is	-11.59	-10.10	1.49
	5-CH <sub>3</sub> O-Is	-11.32	-9.49	1.83

Is, 5-CH<sub>3</sub>-Is and 5-CH<sub>3</sub>O-Is were found to have negative values in all forms.

The HOMO and LUMO energies and energy gap values between the HOMO and LUMO energy of Is, 5-F-Is, 5-Cl-Is, 5-CH<sub>3</sub>-Is and 5-CH<sub>3</sub>O-Is for the neutral, anion, protonated and deprotonated forms are given in Table 1. It can be concluded from the table that the HOMO and LUMO energy gap values for the neutral, anion and protonated forms decreased with the 5-substituted groups.

For example, the HOMO and LUMO energy gap values of Is was recorded as 3.92 eV and 2.88 eV for the neutral and protonated forms, respectively. The HOMO and LUMO energy gap values of 5-OCH<sub>3</sub>-Is are 3.38 eV and 2.11 eV in the neutral and protonated forms, respectively, which means that the HOMO and LUMO energy gap values depend on the substituent at position 5.

In the cation form, the HOMO–LUMO energy gap was recorded with the highest values, with these values decreasing in every 5-substitute group. The exception was the 5-fluoro-substituted group, which increased the HOMO–LUMO energy gap from 4.05 eV for the Is compound to 4.19 eV for 5-F-Is compound.

Table 2

Some quantum chemical parameters of neutral, anion, cation, protonated and deprotonated of Is, 5-Cl-Is, 5-F-Is, 5-CH<sub>3</sub>-Is and 5-CH<sub>3</sub>O-Is using the B3LYP/6-311G++(2d,2p) basis set.

Form	E.P	Is	5-Cl-Is	5-F-Is	5-CH <sub>3</sub> -Is	5-CH <sub>3</sub> O-Is	
Neutral	η (eV)	1.96	1.85	1.86	1.88	1.69	
	S (eV) <sup>-1</sup>	0.26	0.27	0.27	0.27	0.30	
	χ (eV)	4.82	5.00	4.94	4.68	4.49	
	μ (eV)	-4.82	-5.00	-4.94	-4.68	-4.49	
	ω (eV)	5.94	6.74	6.57	5.81	5.97	
	E <sub>n</sub> (eV)	2.09	2.67	2.56	2.07	2.32	
	E <sub>c</sub> (eV)	11.74	12.67	12.44	11.43	11.31	
	Anion	η (eV)	1.60	1.57	1.59	1.60	1.61
		S (eV) <sup>-1</sup>	0.31	0.32	0.31	0.31	0.31
		χ (eV)	-2.16	-1.73	-1.92	-2.14	-2.10
μ (eV)		2.16	1.73	1.92	2.14	2.10	
ω (eV)		1.46	0.95	1.16	1.43	1.37	
E <sub>n</sub> (eV)		4.41	3.47	3.87	4.36	4.27	
E <sub>c</sub> (eV)		0.10	0.01	0.03	0.09	0.07	
Cation		η (eV)	2.03	1.90	2.09	2.01	1.81
		S (eV) <sup>-1</sup>	0.25	0.26	0.24	0.25	0.28
		χ (eV)	10.02	10.03	10.03	9.75	9.38
	μ (eV)	-10.02	-10.03	-10.03	-9.75	-9.38	
	ω (eV)	24.75	26.48	24.04	23.63	24.28	
	E <sub>n</sub> (eV)	15.75	17.40	15.05	14.88	15.80	
	E <sub>c</sub> (eV)	35.78	37.46	35.12	34.39	34.57	
	Protonated	η (eV)	1.44	1.20	1.30	1.33	1.06
		S (eV) <sup>-1</sup>	0.35	0.42	0.39	0.37	0.47
		χ (eV)	10.06	9.98	10.12	9.78	9.44
μ (eV)		-10.06	-9.98	-10.12	-9.78	-9.44	
ω (eV)		35.09	41.61	39.52	35.87	42.18	
E <sub>n</sub> (eV)		25.75	32.23	30.04	26.75	33.27	
E <sub>c</sub> (eV)		45.86	52.19	50.29	46.32	52.15	
Deprotonated		η (eV)	0.67	0.71	0.76	0.75	0.92
		S (eV) <sup>-1</sup>	0.75	0.70	0.66	0.67	0.55
		χ (eV)	11.29	11.05	11.24	10.84	10.40
	μ (eV)	-11.29	-11.05	-11.24	-10.84	-10.40	
	ω (eV)	95.78	85.44	83.62	78.86	59.12	
	E <sub>n</sub> (eV)	84.82	74.75	72.76	68.39	49.17	
	E <sub>c</sub> (eV)	107.40	96.85	95.24	90.08	69.98	

E.P: Electronic property.

In the cation form, the HOMO–LUMO energy gap recorded the highest value. These values decreased in every 5-substitute group. In the deprotonated form, the HOMO–LUMO energy gap increased in the 5-substitute groups, with the highest value being recorded as 1.83 eV for the 5-OCH<sub>3</sub>-Is compound. Moreover, to assess the agreement of the present results, the electrochemical properties of hardness (η), softness (S), electronegativity (χ), chemical potential (μ), electrophilicity index (ω), electrofugality (E<sub>n</sub>) and nucleofugality (E<sub>c</sub>) of the neutral, anion, cation, protonated and deprotonated forms of the Is, 5-F-Is, 5-Cl-Is, 5-CH<sub>3</sub>-Is and 5-CH<sub>3</sub>O-Is were calculated using the B3LYP/6-311G++(2d,2p) level. These values are listed in Table 2.

It is known that the compound with the lowest HOMO–LUMO orbital energy gap is also the softest, and the compound with the highest HOMO–LUMO orbital energy gap is the hardest [20]. This is in good agreement with our results in Table 2, showing that the decrease in the HOMO–LUMO orbital energy gap values are in sequence with the increase in the hardness values.

For example, the highest energy gap was for the 5-F-Is compound in the cation form ( $\Delta E_{\text{gap}} = 4.196$  eV). This high gap value allowed it to be the hardest molecule with the highest recorded value of hardness ( $\eta = 2.09$  eV). The lowest energy gap was found in the Is compound in the deprotonated form ( $\Delta E_{\text{gap}} = 1.33$  eV). This lower gap value allowed it to be the softest molecule with the lowest recorded hardness value ( $\eta = 0.67$  eV).

As seen in Table 2, the electronic chemical potential was recorded as negative values for all the compounds in all forms, except for the anion form, which recorded positive values. The highest negative value of the chemical potential was recorded at  $\eta = -10.12$  eV for the 5-F-Is molecule in the protonated form.

On the other hand, the highest positive value of the electrochemical potential was found for the Is compound in the anion form at  $\mu = 2.16$  eV, decreasing to 1.73 eV, 1.92 eV, 2.14 eV, and 2.10 eV for the 5-Cl-Is, 5-F-Is, 5-CH<sub>3</sub>-Is and 5-CH<sub>3</sub>O-Is compounds, respectively.

Since the best electrophile will be the species displaying a high electronegativity value and a high softness value [21], the highest electrophilicity index values were for the compounds in the deprotonated form, having the highest electronegativity and softness values. For example, the Is compound in the deprotonated form compared with the other forms recorded the highest electronegativity and softness values as

11.29 eV and  $0.75 \text{ eV}^{-1}$ , respectively, and the highest electrophilicity index value of ( $\omega = 95.78$  eV). The values of the electrophilicity index decrease in the 5-substitution group in the deprotonated form. The lowest electrophilicity index value was recorded for the 5-OCH<sub>3</sub> compound ( $\omega = 59.12$  eV), which subsequently had the lowest electronegativity and softness values of 10.40 eV and  $0.55 \text{ eV}^{-1}$ , respectively.

### 3.2. The mean dipole polarizability and the anisotropic polarizability

The mean dipole polarizability values and anisotropic polarizability values of the neutral, anion, cation, protonated and deprotonated forms of Isatin and its derivatives for a potential candidate for NLO communication applications [22] were calculated using the B3LYP/6 311G++(2d,2p) level. These values were calculated in atomic units (a.u.), and converted into electrostatic units (esu) (for  $\alpha$ , 1 a.u. =  $0.1482 \times 10^{-24}$  esu) and are given in Table 3 [23].

In Table 3, it can be seen that in the 5-Cl-Is, 5-CH<sub>3</sub>-Is and 5-CH<sub>3</sub>O-Is compounds the linear and anisotropic polarizability increased in the 5-substitution in all forms. The highest value of linear polarizability was found for the 5-CH<sub>3</sub>O-Is compound in the anion form ( $\alpha = 18.97 \times 10^{-24}$  esu), whereas the highest value of the anisotropic polarizability was found for the 5-Cl-Is compound in the cation form ( $\Delta\alpha = 3.33 \times 10^{-24}$  esu) [22].

For the 5-F-Is compound, the linear polarizability and the anisotropic polarizability was not affected by the 5-F-substitution groups in any form.

From the linear polarizability and the anisotropic polarizability results in Table 3 and the quantum chemical properties in Table 2, one can note that the

Table 3

The mean dipole polarizability ( $\alpha$ ) and the anisotropic polarizability ( $\Delta\alpha$ ) of the Is, 5-Cl-Is, 5-F-Is, 5-CH<sub>3</sub>-Is and 5-CH<sub>3</sub>O-Is using the B3LYP/6-311G++(2d,2p) basis set.

The form	C	Is	5-Cl-Is	5-F-Is	5-CH <sub>3</sub> -Is	5-CH <sub>3</sub> O-Is
Neutral	$\alpha \times 10^{-24}$ esu	13.93	15.86	13.93	16.01	13.93
	$\Delta\alpha \times 10^{-24}$ esu	1.92	2.37	1.91	2.12	2.15
Anion	$\alpha \times 10^{-24}$ esu	16.15	18.23	16.15	18.53	18.97
	$\Delta\alpha \times 10^{-24}$ esu	2.48	3.00	2.49	2.77	2.71
Cation	$\alpha \times 10^{-24}$ esu	14.23	17.93	14.67	17.04	18.23
	$\Delta\alpha \times 10^{-24}$ esu	2.18	3.33	2.29	2.70	2.98
Deprotonated	$\alpha \times 10^{-24}$ esu	13.93	15.86	13.93	16.01	13.93
	$\Delta\alpha \times 10^{-24}$ esu	2.15	3.20	2.24	2.70	2.83
Protonated	$\alpha \times 10^{-24}$ esu	14.52	16.75	14.67	16.75	17.64
	$\Delta\alpha \times 10^{-24}$ esu	2.26	2.75	2.27	2.50	2.58

C (compounds), Is (isatin), 5-Cl (5-chloro), 5-F (5-fluoro), 5-CH<sub>3</sub> (5-methyl), 5-CH<sub>3</sub>O (5-methoxy).

Table 4

Second order perturbation theory analysis of Fock matrix in NBO basis of the Is, 5-Cl-Is, 5-F-Is, 5-CH<sub>3</sub>-Is and 5-CH<sub>3</sub>O-Is using the B3LYP/6-311G++(2d,2p) basis set.

Donor (i)	T	Acceptor (j)	T	Is		5-Cl-Is		5-F-Is		5-CH <sub>3</sub> -Is		5-CH <sub>3</sub> O-Is	
				ED(j)	E(2)	ED(j)	E(2)	ED(j)	E(2)	ED(j)	E(2)	ED(j)	E(2)
				( $\bar{e}$ )	Kcal mol <sup>-1</sup>	( $\bar{e}$ )	Kcal mol <sup>-1</sup>	( $\bar{e}$ )	Kcal mol <sup>-1</sup>	( $\bar{e}$ )	Kcal mol <sup>-1</sup>	( $\bar{e}$ )	Kcal mol <sup>-1</sup>
C <sub>4</sub> –C <sub>8</sub>	$\pi$	O <sub>1</sub> –C <sub>6</sub>	$\pi^*$	0.131	21.22	0.128	19.37	0.125	19.88	0.138	21.01	0.134	23.83
C <sub>4</sub> –C <sub>8</sub>	$\pi$	C <sub>5</sub> –C <sub>9</sub>	$\pi^*$	0.367	25.21	0.374	23.10	0.371	24.10	0.368	24.50	0.361	17.45
C <sub>4</sub> –C <sub>8</sub>	$\pi$	C <sub>10</sub> –C <sub>11</sub>	$\pi^*$	0.333	16.02	0.364	19.20	0.390	17.19	0.343	17.21	0.336	17.43
C <sub>5</sub> –C <sub>9</sub>	$\pi$	C <sub>4</sub> –C <sub>8</sub>	$\pi^*$	0.365	15.65	0.384	17.10	0.362	16.55	0.020	16.12	0.443	19.38
C <sub>5</sub> –C <sub>9</sub>	$\pi$	C <sub>10</sub> –C <sub>11</sub>	$\pi^*$	0.333	22.86	0.364	22.01	0.390	24.58	0.343	21.96	0.336	20.35
C <sub>10</sub> –C <sub>11</sub>	$\pi$	C <sub>4</sub> –C <sub>8</sub>	$\pi^*$	0.365	24.27	0.384	22.06	0.362	22.62	0.372	23.65	0.443	22.33
C <sub>10</sub> –C <sub>11</sub>	$\pi$	C <sub>5</sub> –C <sub>9</sub>	$\pi^*$	0.367	16.43	0.373	16.81	0.371	14.87	0.372	17.71	0.082	28.67
LP2O1		C <sub>4</sub> –C <sub>6</sub>	$\sigma^*$	0.068	20.20	0.069	20.68	0.069	20.73	0.068	20.16	0.147	26.08
LP2O1		C <sub>6</sub> –C <sub>7</sub>	$\sigma^*$	0.147	28.59	0.147	28.50	0.148	28.54	0.147	28.56	0.225	50.04
LP2O2		N <sub>3</sub> –C <sub>7</sub>	$\sigma^*$	0.084	28.92	0.083	28.95	0.084	29.17	0.083	28.82	0.443	32.93
LP2O2		C <sub>6</sub> –C <sub>7</sub>	$\sigma^*$	0.147	25.40	0.147	25.71	0.148	25.80	0.147	25.46	0.134	23.83
LP1N3		O <sub>2</sub> –C <sub>7</sub>	$\pi^*$	0.131	53.71	0.226	53.78	0.218	52.69	0.224	54.02	0.361	17.45
LP1N3		C <sub>5</sub> –C <sub>9</sub>	$\pi^*$	0.367	38.34	0.373	37.93	0.371	39.11	0.372	37.76	0.336	17.43

T: Type.

molecules with high electrochemical potential values have high linear polarizability values. This is in good agreement with the study by Sinha, L. et al., in 2011, who indicated that the species displaying low values of chemical hardness, high values of the electrochemical potential and high values of softness, had high values of linear polarizability [22]. The highest values of linear polarizability were in the anion form, which had the highest values of electrochemical potential. The lowest values of linear polarizability were recorded in the neutral form, which had the lowest values of electrochemical potential.

For example, the highest value of linear polarizability for the 5-OCH<sub>3</sub>-Is compound was in the anion form ( $\alpha = 18.97 \times 10^{-24}$  esu), which maintains a high value of electrochemical potential ( $\mu = 2.10$  eV).

### 3.3. Hyper-conjugative interactions results

Neutral bond orbital analysis is an efficient method to study the interactions between bonds and intra- and intermolecular bonding. It also provides a suitable basis for charge transfer or conjugative interactions in molecular systems. Table 4 lists some electron acceptors and electron-donors, in addition to the stabilization energy of interactions resulting from second-order perturbation theory analysis.

The larger stabilization energy value is the more condensed interaction between electron-donors and the greater extent of the whole system conjugation [24]. Table 4 presents the neutral bond orbital basis of the Is,

5-F-Is, 5-Cl-Is, 5-CH<sub>3</sub>-Is, and 5-CH<sub>3</sub>O compounds with stabilization energy values greater than 15 kcal.mol<sup>-1</sup>.

As seen in Table 4, the Is molecule,  $\pi(C_4-C_8) \rightarrow \pi^*(O_1-C_6)$ , having an electron density value of 0.131  $\bar{e}$ , leads to a stabilization energy of 21.22 kcal.mol<sup>-1</sup>. In the 5-F-Is, 5-Cl-Is, 5-CH<sub>3</sub>-Is and 5-OCH<sub>3</sub> molecules, the electron densities changed to 0.128  $\bar{e}$ , 0.125  $\bar{e}$ , 0.138  $\bar{e}$ , and 0.134  $\bar{e}$ , respectively. These changes lead to a decrease in the stabilization energy values to 19.37 kcal.mol<sup>-1</sup>, 19.88 kcal.mol<sup>-1</sup>, and 21.01 kcal.mol<sup>-1</sup> for the 5-F-Is, 5-Cl-Is, and 5-CH<sub>3</sub>-Is compounds, respectively, and an increase in the stabilization energy value of the 5-OCH<sub>3</sub>-Is compound to 23.83 kcal.mol<sup>-1</sup>.

In the  $\pi(C_4-C_8) \rightarrow \pi^*(C_5-C_9)$  Is molecule, the electron density is 0.367  $\bar{e}$ , which leads to a stabilization energy of 25.21 kcal.mol<sup>-1</sup>. This electron density value changed to 0.374  $\bar{e}$ , 0.371  $\bar{e}$ , 0.368  $\bar{e}$  and 0.361  $\bar{e}$ , for the 5-F-Is, 5-Cl-Is, 5-CH<sub>3</sub>-Is and 5-CH<sub>3</sub>O compounds, respectively. It also led to the respective decreases in stabilization energy values to 23.10 kcal.mol<sup>-1</sup>, 24.10 kcal.mol<sup>-1</sup>, 24.50 kcal.mol<sup>-1</sup> for the 5-F-Is, 5-Cl-Is, 5-CH<sub>3</sub>-Is compounds, with a remarkable decrease of 17.45 kcal.mol<sup>-1</sup> for the 5-OCH<sub>3</sub>-Is compound. On the other hand,  $\pi(C_4-C_8) \rightarrow \pi^*(C_{10}-C_{11})$  in the Is compound with an electron density of 0.333  $\bar{e}$  showed a stabilization energy of 16.02 kcal.mol<sup>-1</sup>. This electron density value changed to 0.364  $\bar{e}$ , 0.390  $\bar{e}$ , 0.343  $\bar{e}$  and 0.336  $\bar{e}$  for the 5-F-Is, 5-Cl-Is, 5-CH<sub>3</sub>-Is, and 5-CH<sub>3</sub>O-Is compounds, respectively, leading to increases in stabilization

Table 5

Occupancies of natural orbitals, and the polarization coefficient of atoms and calculated natural hybrids on atoms of the Is, 5-Cl-Is, 5-F-Is, 5-CH<sub>3</sub>-Is and 5-CH<sub>3</sub>O-Is using the B3LYP/6-311G++(2d,2p) basis set.

Bond (A-B)		$\pi\text{O}_2\text{-C}_7$	$\sigma\text{N}_3\text{-C}_5$	$\sigma\text{C}_5\text{-C}_9$	$\sigma\text{C}_8\text{-C}_{10}$	$\sigma\text{C}_9\text{-C}_{11}$	$\sigma\text{C}_{10}\text{-C}_{11}$	$\pi\text{C}_{10}\text{-C}_{11}$
Is	EDA% ED%	68.11	61.30	51.52	50.36	50.79	49.80	53.10
		31.89	38.70	48.48	49.64	49.21	50.20	46.90
	NBO	0.83(p <sup>1.00</sup> )O <sub>2</sub> + 0.57(p <sup>1.00</sup> )C <sub>7</sub>	0.78(sp <sup>1.79</sup> )N <sub>3</sub> + 0.62(sp <sup>2.76</sup> )C <sub>5</sub>	0.72(sp <sup>1.56</sup> )C <sub>5</sub> + 0.70(sp <sup>1.88</sup> )C <sub>9</sub>	0.71(sp <sup>2.76</sup> )C <sub>8</sub> + 0.71(sp <sup>2.76</sup> )C <sub>10</sub>	0.71(sp <sup>1.78</sup> )C <sub>9</sub> + 0.70(sp <sup>1.82</sup> )C <sub>11</sub>	0.71(sp <sup>1.82</sup> )C <sub>10</sub> + 0.71(sp <sup>1.76</sup> )C <sub>11</sub>	0.73(p <sup>1.00</sup> )C <sub>10</sub> + 0.69(p <sup>1.00</sup> )C <sub>11</sub>
	s%	0.00	35.77	39.03	35.96	35.98	35.41	0.00
		0.00	26.57	34.70	35.42	35.44	36.25	0.00
	p%	99.63	64.11	60.93	63.93	63.92	64.48	99.96
5-F-Is	ED%	67.89	61.11	51.40	50.32	50.22	49.82	51.44
	E%	32.11	38.89	48.60	49.68	49.78	50.18	48.56
	NBO	0.82(p <sup>1.00</sup> )O <sub>2</sub> + 0.57(p <sup>1.00</sup> )C <sub>7</sub>	0.78(sp <sup>1.81</sup> )N <sub>3</sub> + 0.62(sp <sup>2.73</sup> )C <sub>5</sub>	0.72(sp <sup>1.57</sup> )C <sub>5</sub> + 0.70(sp <sup>1.85</sup> )C <sub>9</sub>	0.71(sp <sup>1.92</sup> )C <sub>8</sub> + 0.71(sp <sup>1.57</sup> )C <sub>10</sub>	0.71(sp <sup>1.81</sup> )C <sub>9</sub> + 0.71(sp <sup>1.76</sup> )C <sub>11</sub>	0.71(sp <sup>1.59</sup> )C <sub>10</sub> + 0.71(sp <sup>1.90</sup> )C <sub>11</sub>	0.72(p <sup>1.00</sup> )C <sub>10</sub> + 0.70(p <sup>1.00</sup> )C <sub>11</sub>
	s%	00	35.56	38.78	34.19	35.51	38.66	00
		00	26.78	35.05	38.85	36.18	34.48	00
	p%	99.63	64.31	61.08	65.68	64.40	61.29	99.94
5-Cl-Is	ED%	67.66	61.07	51.41	49.80	50.21	50.38	55.54
	/E%	32.34	38.93	48.59	50.20	49.79	49.62	44.46
	NBO	0.82(p <sup>1.00</sup> )O <sub>2</sub> + 0.57(p <sup>1.00</sup> )C <sub>7</sub>	0.78(sp <sup>1.80</sup> )N <sub>3</sub> + 0.623(sp <sup>2.72</sup> )C <sub>5</sub>	0.72(sp <sup>1.57</sup> )C <sub>5</sub> + 0.70(sp <sup>1.86</sup> )C <sub>9</sub>	0.71(sp <sup>1.83</sup> )C <sub>8</sub> + 0.71(sp <sup>1.60</sup> )C <sub>10</sub>	0.71(sp <sup>1.80</sup> )C <sub>9</sub> + 0.71(sp <sup>1.80</sup> )C <sub>11</sub>	0.71(sp <sup>1.60</sup> )C <sub>10</sub> + 0.71(sp <sup>1.81</sup> )C <sub>11</sub>	0.75(p <sup>1.00</sup> )C <sub>10</sub> + 0.67(p <sup>1.00</sup> )C <sub>11</sub>
	s%	0.00	35.61	38.85	35.33	35.71	38.40	0.00
		0.00	26.86	34.92	38.5	35.69	35.58	0.00
	p%	99.63	64.26	61.1	64.56	64.2	61.51	99.97
5-CH <sub>3</sub> -Is	ED%	68.09	61.25	51.46	49.78	50.59	50.36	51.99
	E%	31.91	38.75	48.54	50.22	49.41	49.64	48.01
	NBO	0.83(p <sup>1.00</sup> )O <sub>2</sub> + 0.57(p <sup>1.00</sup> )C <sub>7</sub>	0.78(sp <sup>1.80</sup> )N <sub>3</sub> + 0.62(sp <sup>2.75</sup> )C <sub>5</sub>	0.72(sp <sup>1.56</sup> )C <sub>5</sub> + 0.70(sp <sup>1.87</sup> )C <sub>9</sub>	0.71(sp <sup>1.75</sup> )C <sub>8</sub> + 0.71(sp <sup>1.93</sup> )C <sub>10</sub>	0.71(sp <sup>1.77</sup> )C <sub>9</sub> + 0.70(sp <sup>1.81</sup> )C <sub>11</sub>	0.71(sp <sup>1.94</sup> )C <sub>10</sub> + 0.71(sp <sup>1.73</sup> )C <sub>11</sub>	0.72(p <sup>1.00</sup> )C <sub>10</sub> + 0.69(p <sup>1.00</sup> )C <sub>11</sub>
	s%	0.00	35.55	38.98	36.30	36.04	33.94	0.00
		0.00	26.64	34.77	34.12	35.54	36.56	0.00
	p%	99.63	64.21	60.97	63.60	63.86	65.98	99.96
5-CH <sub>3</sub> O-Is	ED%	67.94	61.12	51.37	49.88	50.36	50.50	51.99
	E%	32.06	38.88	48.63	50.12	49.64	49.50	48.01
	NBO	0.82(p <sup>1.00</sup> )O <sub>2</sub> + 0.57(p <sup>1.00</sup> )C <sub>7</sub>	0.78(sp <sup>1.82</sup> )N <sub>3</sub> + 0.62(sp <sup>2.74</sup> )C <sub>5</sub>	0.72(sp <sup>1.58</sup> )C <sub>5</sub> + 0.70(sp <sup>1.86</sup> )C <sub>9</sub>	0.71(sp <sup>1.86</sup> )C <sub>8</sub> + 0.71(sp <sup>1.61</sup> )C <sub>10</sub>	0.71(sp <sup>1.97</sup> )C <sub>9</sub> + 0.70(sp <sup>1.74</sup> )C <sub>11</sub>	0.71(sp <sup>1.74</sup> )C <sub>10</sub> + 0.70(sp <sup>1.86</sup> )C <sub>11</sub>	0.72(p <sup>1.00</sup> )C <sub>10</sub> + 0.69(p <sup>1.00</sup> )C <sub>11</sub>
	s%	0.00	35.38	38.73	34.96	35.82	34.88	0.00
		0.00	26.73	34.87	38.31	36.45	26.37	0.00
	p%	99.63	64.49	61.22	64.87	64.07	63.45	99.96
	99.88	73.19	65.01	61.63	63.45	64.99		



energy values to 19.20 kcal.mol<sup>-1</sup>, 17.19 kcal.mol<sup>-1</sup>, 17.21 kcal.mol<sup>-1</sup> and 17.43 kcal.mol<sup>-1</sup>, respectively.

The  $\pi(C_5-C_9) \rightarrow \pi^*(C_4-C_8)$  in the Is compound has an electron density value of 0.365  $\bar{e}$ , which leads to a stabilization energy of 15.65 kcal.mol<sup>-1</sup>. This electron density value changed to 0.384  $\bar{e}$ , 0.362  $\bar{e}$ , 0.020  $\bar{e}$ , and 0.443  $\bar{e}$  for the 5-F-Is, 5-Cl-Is, 5-CH<sub>3</sub>-Is and 5-OCH<sub>3</sub>-Is compounds, respectively, leading to respective increases in stabilization energy values to 17.10 kcal.mol<sup>-1</sup>, 16.55 kcal.mol<sup>-1</sup>, 16.12 kcal.mol<sup>-1</sup> and 19.38 kcal.mol<sup>-1</sup>. The same type of interaction is provided in the molecule linked to the resonance, which is electron-donating from LP1N<sub>3</sub> to  $\pi^*(C_5-C_9)$  in the Is compound, and shows an electron density value of 0.367  $\bar{e}$ , leading to a stabilization energy of 38.34 kcal.mol<sup>-1</sup>.

This electron density value, increased by substitution to 0.373  $\bar{e}$ , 0.371  $\bar{e}$ , 0.372  $\bar{e}$ , and 0.336  $\bar{e}$  for the 5-F-Is, 5-Cl-Is, 5-CH<sub>3</sub>-Is and 5-OCH<sub>3</sub>-Is compounds, respectively, leading to decreases in the stabilization energy values of the 5-F-Is, 5-CH<sub>3</sub>-Is and 5-OCH<sub>3</sub>-Is compounds to 37.93 kcal.mol<sup>-1</sup>, 37.76 kcal.mol<sup>-1</sup> and 17.43 kcal.mol<sup>-1</sup>, respectively, and an increase for the 5-Cl-Is compound to 39.11 kcal.mol<sup>-1</sup>. Furthermore, LP1N<sub>3</sub> to  $\pi^*(O_2-C_7)$  in the isatin compound, resulting from an electron density of 0.131  $\bar{e}$ , led to an enormous stabilization energy value of 53.71 kcal.mol<sup>-1</sup>. This value varied among the 5-substitution groups and were recorded as 0.226  $\bar{e}$ , 0.218  $\bar{e}$ , 0.224  $\bar{e}$  and 0.361  $\bar{e}$  for the 5-F-Is, 5-Cl-Is, 5-CH<sub>3</sub>-Is and 5-OCH<sub>3</sub>-Is compounds, respectively. This led to an increase in the stabilization energy values of the 5-F-Is and 5-CH<sub>3</sub>-Is compounds to 53.78 kcal.mol<sup>-1</sup> and 54.02 kcal.mol<sup>-1</sup>, respectively, and decreased the stabilization energy values of the 5-Cl-Is and 5-OCH<sub>3</sub> compounds to 52.69 kcal.mol<sup>-1</sup> and 50.02 kcal.mol<sup>-1</sup>, respectively. The LP2O1 to  $\sigma^*(C_4-C_6)$  in the Is compound, having an electron density of 0.068  $\bar{e}$ , led to a lower stabilization energy of 20.20 kcal.mol<sup>-1</sup>. This electron density value increased by substitution in the 5-F-Is, 5-Cl-Is and 5-OCH<sub>3</sub>-Is compounds to 0.069  $\bar{e}$ , 0.069  $\bar{e}$ , and 0.147  $\bar{e}$ , respectively. This led to an increase in the stabilization energies to 20.68 kcal.mol<sup>-1</sup>, 20.73 kcal.mol<sup>-1</sup> and 26.08 kcal.mol<sup>-1</sup>, respectively.

In contrast, the electron density for the 5-CH<sub>3</sub>-Is compound was recorded at 0.068  $\bar{e}$ , which led to a decrease in the stabilization energy to 20.16 kcal.mol<sup>-1</sup>. Electron donations from LP2O1 to  $\sigma^*(C_6-C_7)$  in the Is compound led to the stabilization energy of 28.59 kcal.mol<sup>-1</sup>. The stabilization energy values were not affected by the 5-F and 5-CH<sub>3</sub> substituted groups. However, the 5-OCH<sub>3</sub> substitute

groups led to a remarkable increase of the stabilization energy values, recorded at 50.04 kcal.mmol<sup>-1</sup>. This may be due to methoxy groups having the ability to withdraw electrons from the ring.

### 3.4. HOMO–LUMO energy dependent calculation results of NBO analysis such as the occupation numbers with their energies interacting

Natural bonding orbital analysis was performed on the Is, 5-F-Is, 5-Cl-Is, 5-CH<sub>3</sub>-Is and 5-CH<sub>3</sub>O-Is compounds to illustrate the delocalization of the electron density, the intramolecular hybridization within the isatin molecule, and the effect of the 5-substitute groups.

As seen in Table 5, there were negligible changes in the hybridization of the bonds between the atoms located far from the substituted position. For example, the  $\pi(O_2-C_7)$  bonds of the Is, 5-Cl-Is, 5-F-Is, 5-CH<sub>3</sub>-Is and 5-CH<sub>3</sub>O-Is compounds were formed from a p orbital in oxygen (a mixture of 0.00% s, and 99.63% p atomic orbitals) and a p orbital in C<sub>7</sub> (a mixture of 0.00% s and 99.88% p atomic orbitals).

On the other hand, notable changes can be observed for the hybridization of the bonds between the atoms located next to the substitution position, such as the  $\sigma(C_8-C_{10})$  in the Is molecule formed from the sp<sup>2.76</sup> hybrid in C<sub>8</sub>, which was a mixture of 35.96% s and 63.93% p. This value decreased to sp<sup>1.83</sup>, sp<sup>1.92</sup>, sp<sup>1.75</sup> and sp<sup>1.86</sup> hybrids in the C<sub>8</sub> for the 5-Cl-Is, 5-F-Is, 5-CH<sub>3</sub>-Is and 5-OCH<sub>3</sub>-Is molecules, respectively. These were mixtures of 35.33% s/64.56% p, 34.19% s/65.68% p, 36.30% s/63.60% p, and 34.96% s/64.87% p, respectively. These mixtures formed from the sp<sup>2.76</sup> hybrid in C<sub>10</sub>, which was a mixture of 35.42% s and 64.47% p in the Is molecule. This value decreased to sp<sup>1.60</sup>, sp<sup>1.57</sup>, sp<sup>1.93</sup>, and sp<sup>1.61</sup>, which were mixtures of 38.50% s/61.41% p, 38.85% s/61.10% p, 34.12% s/65.81% p, and 38.31% s/61.63% p for the 5-Cl-Is, 5-F-Is, 5-CH<sub>3</sub>-Is and 5-CH<sub>3</sub>O-Is molecules, respectively.

It is important to note that on the benzene ring, the hybrid changes only occurred in the  $\sigma$  bonds and there were no changes in the  $\pi$  bonds. There were, however, notable changes in the electron density for the  $\pi$  bonds and negligible changes for the  $\sigma$  bonds.

For example, there were no changes in the hybridization on  $\pi(C_{10}-C_{11})$  with 5-substitution such that the Is molecule and 5-substitute molecules recorded the same hybridization values on this bond (Table 5).

In contrast, the electron density value increased in the carbon (C<sub>10</sub>) from 53.10% for the Is molecules to

55.54% for the 5-Cl-Is molecules and respectively decreased to 51.44% and 51.99% for the 5-F-Is and 5-CH<sub>3</sub>-Is molecules.

The electron density value on C<sub>11</sub> decreased from 46.90% for the Is molecule to 44.49% for the 5-Cl-Is molecule and it increased to 48.56% and 48.01% for the 5-F-Is and 5-CH<sub>3</sub>-Is molecules, respectively.

#### 4. Conclusions

This theoretical study showed how 5-substituent groups affected polarity, hyper-conjugation, the hybridization of the studied molecules in calculations using the Lee–Yang–Parr correlation functionality, and the 6-311G++(2d,2p) basic set.

Through the optimization of the neutral, anion, cation, protonated and deprotonated title compounds, the HOMO–LUMO energy gap values of Is, 5-Cl-Is, 5-F-Is, 5-CH<sub>3</sub>-Is, and 5-OCH<sub>3</sub>-Is compounds in neutral and protonated forms were lower than the other forms and led to a decrease in the stability of all the molecules.

On the other hand, the HOMO–LUMO energy gap values in the deprotonated and anion forms increased for the 5-OCH<sub>3</sub>-Is compound, and in cation form, it increased for the 5-F-Is compound, which led to an increase in the stability of the formed molecules.

The linear polarizability and the anisotropic polarizability values had changed with various 5-substitute groups in the isatin molecule. They increased with the 5-CH<sub>3</sub>, 5-Cl substituted groups, and a remarkable increase having been recorded for 5-Cl-Is in an anion form.

In the 5-OCH<sub>3</sub>-Is compound, the values of the linear and anisotropic polarizability were very small in the neutral form, but there was a noticeable increase in the other forms.

From their quantum chemical properties, we concluded that the molecule with low values of chemical hardness and high values of electronic chemical potential had high polarizability values.

The highest values of the linear polarizability were in the anion form, which had the highest values of electronic chemical potential. Furthermore, we concluded that the intramolecular hyper-conjugative interactions between bonded atoms changed with substitution. These changes caused changes in the electron density values for the atoms, which in turn led to changes in the stabilization energy values of the title molecules.

It was found that there were negligible changes in hybridization values in the bonds between the atoms

located far from the 5-position. On the contrary, significant changes in hybridization values for bonds between adjacent atoms had been found. There were negligible changes in the electron density of the bonds between the atoms and  $\sigma$  bonds next to the substitution position, but notable changes for the  $\pi$  bonds.

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