Material Science Research India Vol. **10**(1), 37-50 (2013)

Natural Bond Orbital (NBO) Analysis of Certain Salicylanilide Derivatives

V.S. MADHAVAN[1], HEMA TRESA VARGHESE[2], C.YOHANNAN PANICKER[3]* and SAMUEL MATHEW[4]

[1]Deparatment of Physics, MES Ponnani College, Ponnani South, Malappuram, Kerala, India.
[2]Department of Physics, Fatima Mata National College, Kollam, Kerala, India.
[3]Department of Physics, TKM College of Arts and Science, Kollam, Kerala, India.
[4]Department of Physics, Mar Thoma College, Thiruvalla, Kerala, India.
*Corresponding author E-mail: cyphyp@rediffmail.com

(Received: January 25, 2013; Accepted: March 06, 2013)

ABSTRACT

Salicylanilides possess a wide range of biological activities and they act as inhibitors of the two component regulatory system in bacteria. A natural bond orbital analysis has been performed in order to study intra-molecular bonding, interactions among bonds and delocalization of unpaired electrons for certain salicylanilide derivatives. Stability of the molecules arising from hyper conjugative interactions, charge delocalization has been analyzed. The electron density (ED) is transferred from the n(O), n(Cl) n(N) to the anti-bonding π^*, σ^* orbital of the C–C ,C-O,C-N bonds. The results show that electron density in the anti-bonding orbitals and second order delocalization energies confirm the occurrence of intra-molecular charge transfer within the molecules.

Key words: NBO analysis, salicylanilides, DFT, hyper-conjugation.

INTRODUCTION

Natural Bond Orbitals (NBOs) are localized few-center orbitals that describe the Lewis-like molecular bonding pattern of electron pairs (or of individual electrons in the open-shell case) in optimally compact form. The natural bonding orbitals analysis has been performed in order to investigate intra-molecular charge transfer interactions, re-hybridization and delocalization of electron density within the molecules. In the NBO analysis[1, 2] the electronic wavefunctions are interpreted in terms of a set of occupied Lewis type (bond or lone pair) and a set of unoccupied non-Lewis (anti-bond or Rydberg) localized NBO orbitals. The delocalization of electron density (ED) between these orbitals corresponds to a stabilizing donor acceptor interaction. Second order perturbation theory has been employed to evaluate the stabilization energies of all possible interactions between donor and acceptor orbitals in the NBO basis. The interaction result in a loss of occupancy from the localized NBO of the idealized Lewis structure into an empty non-Lewis orbital. The delocalization effects (or donor acceptor charge transfers) can be estimated from the off diagonal elements of the Fock matrix in the NBO basis. Salicylanilides (2-hydroxy-N-phenylbenzamides) show manifold pharmacological activities[3-8]. The presence of amide (-NHCO-) groups in the structure of phenylcarbamoylphenyl-N-alkylcarbamates can cause interaction with various enzymes or enzymatic systems, for example, a carbamate moiety is characteristic for a number of herbicides acting as photosynthetic electron inhibitors[9,10]. Imramovsky *et al.*, [11] reported the photosynthesis inhibiting efficiency of a series of salicylanilide alkylcarbamates. Salicylanilides possess a wide range of biological activities and they act as inhibitors of the two component regulatory system in bacteria[12]. Salicylanilides have been shown to be active against many pathogens, including

Staphylococcus aureus[13], *Escherichia coli*, *Pseudomonas aeruginosa*[14], *Aspergillus fumigatus*[6], as well as being used as anthelminthics in veterinary practice[15]. Salicylanilides have shown activity against *M.tuberculosis*[16] although cytotoxicity in mammalian cells is a common problem. Salicylanilides have been suggested to target multiple specific targets in both prokaryotes and eukaryotes, including two component systems[7], transglycosylase[17], type III secretion systems[18], interleukin[19], and protein tyrosine kinase[20]. In the present work, the NBO analysis of a series of Salicylanilides derivatives, 4-Chloro-2-(3-chlorophenyl carbamoyl)phenyl acetate, 4-Chloro-2-(3,4-dichlorophenylcarbamoyl)phenyl acetate, 4-Chloro-2-(4-bromophenylcarbamoyl) phenyl acetate and 5-chloro-2-(3-chlorophenylcarbamoyl) phenylacetate are reported. Vibrational spectroscopic studies of these derivatives are reported by the authors previously[21-24].

Computational details

The natural bond orbitals (NBO) calculations were performed using NBO 3.1 program as implemented in the Gaussian 09 package[25, 26] at the DFT/B3LYP level in order to understand various second-order interactions between the filled orbitals of one subsystem and vacant orbitals of another subsystem, which is a measure of the intermolecular delocalization or hyper-conjugation. NBO analysis provides the most accurate possible 'natural Lewis structure' picture of 'j' because all orbital details are mathematically chosen to include the highest possible percentage of the electron density. A useful aspect of the NBO method is that it gives information about interactions of both filled and virtual orbital spaces that could enhance the analysis of intra and inter molecular interactions. The second-order Fock- matrix was carried out to evaluate the donor-acceptor interactions in the NBO basis. The interactions result 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) the stabilization energy (E2) associated with the delocalization i → j is determined as

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

q_i → donor orbital occupancy
E_i, E_j → diagonal elements
F_{ij} → the off diagonal NBO Fock matrix element

In NBO analysis large E(2) value shows the intensive interaction between electron-donors and electron-acceptors and greater the extent of conjugation of the whole system. The second-order perturbation theory analysis of Fock matrix in NBO basis shows strong intra-molecular hyper-conjugative interactions of π electrons are given in Tables 1, 3, 5, and 7 and the NBO results showing the formation of Lewis and non-Lewis orbitals are given in Tables 2,4,6 and 8.

RESULTS AND DISCUSSION

4-Chloro-2-(3-chlorophenyl carbamoyl)phenyl acetate

The intra-molecular hyper-conjugative interactions are formed by the orbital overlap between n(Cl) and π* (C–C) bond orbital which results in ICT causing stabilization of the system. The strong intra-molecular hyper-conjugative interaction of C_5-C_6 from of n3(Cl_{10}) → π* (C5-C6) which increases ED (0.3773e) that weakens the respective bonds leading to stabilization of 12.05 kcal mol^{-1}. Also another intra-molecular hyper-conjugative interactions are formed by the orbital overlap between n(Cl) and π*(C–C) bond orbital which results in ICT causing stabilization of the system. The strong intra-molecular hyper-conjugative interaction of C_{18}-C_{22} from of n3(Cl_{32}) → π* (C_{18}-C_{22}) which increases ED (0.395e) that weakens the respective bonds leading to stabilization of 12.23 kcal mol^{-1}. These interactions are observed as an increase in electron density (ED) in C-C anti-bonding orbitals that weakens the respective bonds. The strong intra-molecular hyper-conjugative interaction of C_{11}-N_{13} from of n2(O_{12})→ σ*(C_{11}-N_{13}) which increases ED (0.07808e) that weakens the respective bonds leading to stabilization of 25.38 kcalmol^{-1}. These interactions are observed as an increase in electron density (ED) in C-C anti-bonding orbitals that weakens the respective bonds. Again a strong intra-molecular hyper-conjugative interaction of O_{25}-C_{26} from of n2(O_{31}) → σ* (O_{25}-C_{26}) which increases ED (0.13015e) that weakens the respective bonds leading to stabilization of 40.21 kcalmol^{-1}. A strong

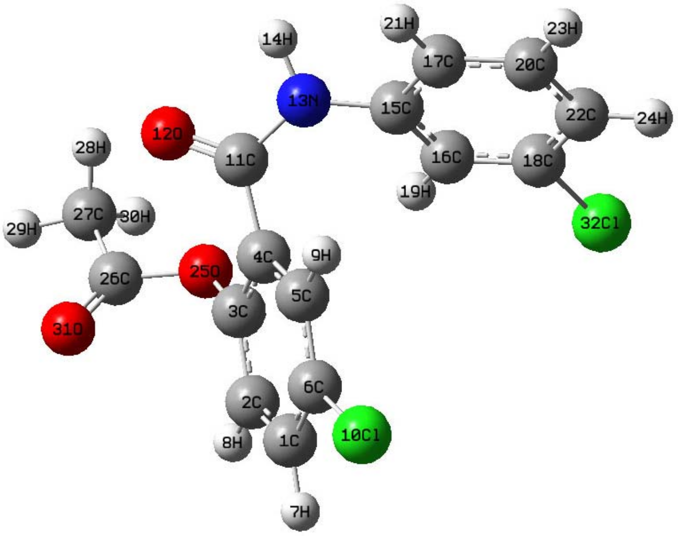

Fig. 1: 4-Chloro-2-(3-chlorophenyl carbamoyl) phenyl acetate

Table1. Second order perturbation theory analysis of Fock matrix in NBO basis corresponding to the intra-molecular bonds of the 4-Chloro-2-(3-chlorophenyl carbamoyl)phenyl acetate

Donor(i)	Type	ED/e	Acceptor(j)	Type	ED/e	E(2)	E(j)-E(i)	F(i,j)
C_1-C_2	σ	1.96920	C_6-Cl_{10}	σ^*	0.02945	4.73	0.85	0.057
C_3-C_4	π	1.64751	C_{11}-O_{12}	π^*	0.25055	11.54	0.32	0.056
C_4-C_5	σ	1.96236	C_6-Cl_{10}	σ^*	0.02945	4.47	0.85	0.055
C_6-Cl_{10}	σ	1.98900	C_4-C_5	σ^*	0.02139	2.49	1.27	0.050
N_{13}-H_{14}	σ	1.97755	C_{15}-C_{16}	σ^*	0.02621	2.60	1.20	0.050
C_{15}-C_{16}	σ	1.96807	C_{18}-Cl_{32}	σ^*	0.02950	4.35	0.85	0.054
C_{15}-C_{17}	σ	1.97529	C_{11}-N_{13}	σ^*	0.07808	2.59	1.15	0.049
C_{16}-C_{18}	σ	1.97862	N_{13}-C_{15}	π^*	0.03063	3.94	1.14	0.060
C_{17}-C_{20}	σ	1.97844	N_{13}-C_{15}	σ^*	0.03063	4.11	1.12	0.061
C_{18}-Cl_{32}	σ	1.98885	C_{15}-C_{16}	σ^*	0.02621	2.56	1.26	0.051
C_{20}-C_{22}	σ	1.97301	C_{18}-Cl_{32}	σ^*	0.02950	4.86	0.84	0.057
C_{10}-C_{15}	σ	1.98479	C_3-O_{25}	σ^*	0.03547	3.48	0.98	0.053
LP(1)Cl_{10}	n	1.99332	C_1-C_6	σ^*	0.02642	1.28	1.47	0.039
LP(2)Cl_{10}	n	1.97232	C_5-C_6	σ^*	0.02607	3.91	0.88	0.052
LP(3)Cl_{10}	n	1.93216	C_5-C_6	π^*	0.37733	12.05	0.33	0.061
LP(1)O_{12}	n	1.97597	C_{11}-N_{13}	σ^*	0.07808	1.78	1.12	0.040
LP(2)O_{12}	n	1.86183	C_{11}-N_{13}	π^*	0.07808	25.38	0.69	0.120
LP(1)N_{13}	n	1.69323	C_{11}-O_{12}	π^*	0.25055	39.49	0.32	0.102
LP(1)O_{25}	n	1.94112	C_{26}-O_{31}	σ^*	0.02086	7.22	1.17	0.083
LP(2)O_{25}	n	1.82270	C_{26}-O_{31}	π^*	0.18625	38.14	0.35	0.104
LP(1)O_{31}	n	1.97516	O_{25}-C_{26}	σ^*	0.13015	1.23	1.00	0.032
LP(2)O_{31}	n	1.83332	O_{25}-C_{26}	σ^*	0.13015	40.21	0.58	0.138
LP(1)Cl_{32}	n	1.99329	C_{18}-C_{22}	σ^*	0.02622	1.25	1.47	0.039
LP(2)Cl_{32}	n	1.97289	C_{16}-C_{18}	σ^*	0.02504	3.85	0.88	0.052
LP(3)Cl_{32}	n	1.93006	C_{18}-C_{22}	π^*	0.39507	12.23	0.33	0.062

Table 2: NBO results showing the formation of Lewis and non-Lewis orbtials of 4-Chloro-2-(3-chlorophenyl carbamoyl)phenyl acetate

Bond(A-B)	ED/energy	EDA%	EDB%	NBO	s%	p%
$\sigma C_1–C_2$	1.96920	50.10	49.90	$0.7078(sp^{1.83})C$	35.28	64.67
	-0.71182			$+0.7064(sp^{1.83})C$	35.37	64.59
πC_3-C_4	1.64751	47.78	52.22	$0.6912(sp^{1.00})C$	0.00	100.0
	-0.27331			$+0.7226(sp^{99.99})C$	0.03	99.94
σC_4-C_5	1.96236	50.99	49.01	$0.7140(sp^{1.84})C$	35.24	64.72
	-0.71430			$+0.7001(sp^{1.87})C$	34.79	65.17
σC_6-Cl_{10}	1.98900	45.68	54.32	$0.6759(sp^{3.39})C$	22.72	77.12
	-0.71904			$+0.7370(sp^{4.60})Cl$	17.79	81.75
$\sigma C_{15}-C_6$	1.96807	50.65	49.35	$0.7117(sp^{1.75})C$	36.36	63.61
	-0.71911			$+0.7025(sp^{1.89})C$	34.58	65.38
$\sigma C_{15}-C_{17}$	1.97529	51.15	48.85	$0.7152(sp^{1.75})C$	36.31	63.66
	-0.71732			$+0.6989(sp^{1.90})C$	34.41	65.55
$\sigma C_{16}-C_{18}$	1.97862	49.55	50.45	$0.7039(sp^{1.86})C$	34.99	64.97
	-0.73612			$+0.7103(sp^{1.59})C$	38.63	61.34
$\sigma C_{17}-C_{20}$	1.97844	50.31	49.69	$0.7093(sp^{1.80})C$	35.71	64.25
	-0.71172			$+0.7049(sp^{1.84})C$	35.25	64.71
$\sigma C_{18}-Cl_{32}$	1.98885	45.55	54.45	$0.6749(sp^{3.46})C$	22.39	77.44
	-0.71861			$+0.7379(sp^{4.60})Cl$	17.78	81.76
$\sigma C_{20}-C_{22}$	1.97301	49.74	50.26	$0.7053(sp^{1.86})C$	35.12	64.84
	-0.70865			$+0.7090(sp^{1.83})\ C$	35.26	64.70
$\sigma C_{26}-C_{27}$	1.98479	49.03	50.97	$0.7002(sp^{1.51})C$	39.80	60.15
	-0.65797			$+0.7139(sp^{3.60})C$	26.01	73.93
$n1Cl_{10}$	1.99332			$sp^{0.21}$	82.44	17.55
	-0.92204					
$n2Cl_{10}$	1.97232			$sp^{1.00}$	0.00	99.98
	-0.32380					
$n3Cl_{10}$	1.93216			$sp^{1.00}$	0.00	99.97
	-0.32232					
$n1O_{12}$	1.97597			$sp^{0.70}$	58.82	41.14
	-0.68723					
$n2O_{12}$	1.86183			$sp^{99.99}$	0.02	99.76
	-0.25643					
$n1N_{13}$	1.69323			$sp^{99.99}$	0.62	99.37
	-0.27386					
$n1O_{25}$	1.94112			$sp^{1.73}$	36.55	63.39
	-0.55618					
$n2O_{25}$	1.82270			$sp^{66.74}$	1.47	98.44
	-0.33868					
$n1O_{31}$	1.97516-			$sp^{0.76}$	56.89	43.05
	0.68145					
$n2O_{31}$	1.83332			$sp^{99.99}$	0.04	99.69
	-0.25878					
$n1Cl_{32}$	1.99329			$sp^{0.21}$	82.44	17.55
	-0.92336					
$n2Cl_{32}$	1.97289			$sp^{1.00}$	0.00	99.98
	-0.32450					
$n3Cl_{32}$	1.93006			$sp^{1.00}$	0.00	99.97
	-0.32323					

intra-molecular hyper-conjugative interaction of C_{26}-O_{31} from of $n2(O_{25})\rightarrow\pi^*$ (C_{26}-O_{31}) which increases ED (0.18625e) that weakens the respective bonds leading to stabilization of 38.14 kcal mol^{-1}. Also a very strong intra-molecular hyper-conjugative interaction of C_{11}-O_{12} from of $n1(N_{13})\rightarrow\pi^*$ (C_{11}–O_{12}) which increases ED (0.2505e) that weakens the respective bonds leading to stabilization of 39.49 kcalmol^{-1}.

The NBO analysis also describes the bonding in terms of the natural hybrid orbital $n2(Cl_{10})$, which occupy a higher energy orbital (-0.32380a.u.) with considerable p-character (99.98%) and low occupation number (1.97323a.u.) and the other $n1(Cl_{10})$ occupy a lower energy orbital (-0.92204) with p-character (17.55%) and high occupation number (1.99332a.u.).Also $n2(Cl_{32})$, which occupy a higher energy orbital (-0.32450a.u.) with considerable p-character (99.98%) and low occupation number (1.97289a.u.) and the other $n1(Cl_{32})$ occupy a lower energy orbital (-0.92336a.u.) with p-character (17.55%) and high occupation number (1.99329a.u.). Thus, a very close to pure p-type lone pair orbital participates in the electron donation to the σ^*(C–C) orbital for $n2(Cl_{10})\rightarrow\sigma^*$(C–C) and σ^*(C–C) orbital for $n1(Cl_{32})\rightarrow\sigma^*$(C–C) interactions in the compound.

4-Chloro-2-(3,4-dichlorophenylcarbamoyl) phenyl acetate

The strong intra-molecular hyper-conjugative interaction of C_4-C_5 from of $n3(Cl_{30})\rightarrow\pi^*$ (C_4-C_5) which increases ED (0.37305e) that weakens the respective bonds leading to stabilization of 10.16 kcal mol^{-1}. Also another intra-molecular hyper-conjugative interactions are formed by the orbital overlap between n(Cl) and π^*(C–C) bond orbital which results in ICT causing stabilization of the system. The strong intra-molecular hyper-conjugative interaction of C_{13}-C_{17} from of $n3(Cl_{31})\rightarrow\pi^*$ (C_{13}-C_{17}) which increases ED (0.45581e) that weakens the respective bonds leading to stabilization of 11.78 kcal mol^{-1}. Another is from n(Cl) and π^* (C–C) bond orbital which results in ICT causing stabilization of the system. The strong intra-molecular hyper-conjugative interaction of C_{13}-C_{17} from of $n3(Cl_{32})\rightarrow\pi^*$ (C_{13}-C_{17}) which increases ED (0.45581e) that weakens the respective bonds leading to stabilization of 11.74 kcal mol^{-1}.

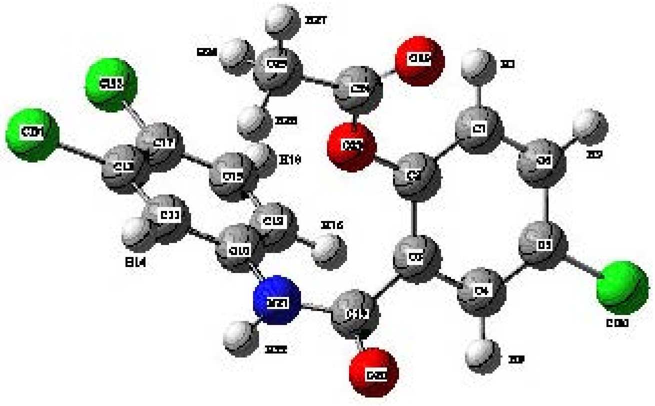

Fig. 2: 4-Chloro-2-(3,4-dichlorophenylcarbamoyl)phenyl acetate

Again a strong intra-molecular hyper-conjugative interaction of C_{19}-N_{21} from of $n2(O_{20})\rightarrow\sigma^*$ (C_{19}-N_{21}) which increases ED (0.07320e) that weakens the respective bonds leading to stabilization of 22.25 kcal mol$^{"1}$. A strong intra-molecular hyper-conjugative interaction of C_{24}-O_{29} from of $n2(O_{23})\rightarrow\pi^*$($C_{24}$-$O_{29}$) which increases ED (0.20995e) that weakens the respective bonds leading to stabilization of 41.56 kcalmol^{-1}. Also a very strong intra-molecular hyper-conjugative interaction of C_{19}-O_{20} from of $n1(N_{21})\rightarrow\pi^*$($C_{19}$–$O_{20}$) which increases ED (0.25931e) that weakens the respective bonds leading to stabilization of 43.65 kcal mol^{-1}. Again a strong intra-molecular hyper-conjugative interaction of O_{23}-C_{24} from of $n2(O_{29})\rightarrow\sigma^*$($O_{23}$-$C_{24}$) which increases ED

(0.12495e) that weakens the respective bonds leading to stabilization of 38.71 kcal mol^{-1}.

The NBO analysis also describes the bonding in terms of the natural hybrid orbital n2(Cl_{30}), which occupy a higher energy orbital (-0.32821a.u.) with considerable p-character (99.99%) and low occupation number (1.97714a.u.) and the other n1(Cl_{30}) occupy a lower energy orbital (-0.94737) with p-character (14.27%) and high occupation number (1.99419a.u.).Also n2(Cl_{31}), which occupy a higher energy orbital (-0.33722a.u.) with considerable p-character (99.84%) and low occupation number (1.97504a.u.) and the other n1(Cl31) occupy a lower energy orbital (-0.95640a.u.) with p-character (14.30%) and high occupation number (1.99395a.u.). Also n2(Cl_{32}), which occupy a higher energy orbital (-0.33356a.u.) with considerable p-character (99.82%) and low occupation number (1.97441a.u.) and the other n1(Cl_{32}) occupy a lower energy orbital (-0.95127a.u.) with p-character (14.42%) and high occupation number (1.99395a.u.). Thus, a very close to pure p-type lone pair orbital participates in the electron donation to the σ*(C–C) orbital for n2(Cl_{30}) →σ *(C–C) , σ *(C–C) orbital for n2(Cl_{31}) →σ *(C–C) and σ *(C–C) orbital for n2(Cl_{32}) →σ*(C–C) interactions in the compound.

4-Chloro-2-(4-bromophenylcarbamoyl)phenyl acetate

The strong intra-molecular hyper-conjugative interaction of C_4-C_5 from of n3(Cl_{20})→π* (C_4-C_5) which increases ED (0.39490e) that weakens the respective bonds leading to

Table 3: Second order perturbation theory analysis of Fock matrix in NBO basis corresponding to the intramolecular bonds of the 4-Chloro-2-(3,4-dichlorophenyl carbamoyl) phenyl acetate

Donor(i)	Type	ED/e	Acceptor(j)	Type	ED/e	E(2)	E(j)-E(i)	F(i,j)
C_1-C_6	σ	1.96577	C_2-O_{23}	σ*	0.03875	5.14	0.96	0.063
C_2-C_3	σ	1.65023	C_{19}-O_{20}	π*	0.25931	10.03	0.30	0.050
C_3–C_4	σ	1.95906	C_5-Cl_{30}	σ*	0.03499	4.87	0.78	0.055
C_5–Cl_{30}	σ	1.98833	C_1-C_6	σ*	0.01686	2.46	1.22	0.049
C_{10}-C_{11}	σ	1.96789	C_{13}-Cl_{31}	σ*	0.03100	4.29	0.79	0.052
C_{11}-C_{13}	σ	1.97284	C_{17}-Cl_{32}	σ*	0.03034	4.64	0.82	0.055
C_{12}-C_{15}	σ	1.96996	C_{17}–C_{32}	σ*	0.03034	4.56	0.79	0.053
C_{15}-C_{17}	σ	1.97453	C_{13}–C_{31}	σ*	0.03100	4.93	0.80	0.056
N_{21}-H_{22}	σ	1.98019	C_3-C_{19}	σ*	0.06271	4.30	1.05	0.061
C_{24}-C_{25}	σ	1.98459	C_2–O_{23}	σ*	0.03875	3.70	0.93	0.053
LP(1)O_{20}	σ	1.97766	C_{19}-N_{21}	σ*	0.07320	1.78	1.11	0.040
LP(2)O_{20}	n	1.87575	C_{19}-N_{21}	σ*	0.07320	22.25	0.66	0.110
LP(1)N_{21}	σ	1.67335	C_{19}-O_{20}	π*	0.25931	43.65	0.29	0.102
LP(1)O_{23}	σ	1.96057	C_{24}-O_{29}	σ*	0.02257	7.68	1.05	0.080
LP(2)O_{23}	n	1.76697	C_{24}-O_{29}	π*	0.20995	41.56	0.30	0.101
LP(1)O_{29}	n	1.97324	C_{24}-C_{25}	σ*	0.04321	2.66	1.08	0.048
LP(2)O_{29}	n	1.84656	O_{23}-C_{24}	σ*	0.12495	38.71	0.53	0.129
LP(1)Cl_{30}	n	1.99419	C_5-C_6	σ*	0.02502	1.01	1.47	0.035
LP(2)Cl_{30}	σ	1.97714	C_4-C_5	σ*	0.02388	3.26	0.85	0.047
LP(3)Cl_{30}	n	1.94118	C_4-C_5	π*	0.37305	10.16	0.31	0.054
LP(1)Cl_{31}	n	1.99395	C_{11}-C_{13}	σ*	0.02250	1.06	1.47	0.035
LP(2)Cl_{31}	n	1.97504	C_{13}-C_{17}	σ*	0.03878	3.96	0.83	0.051
LP(3)Cl_{31}	n	1.93595	C_{13}-C_{17}	π*	0.45581	11.78	0.29	0.058
LP(1)Cl_{32}	n	1.99395	C_{15}-C_{17}	σ*	0.02456	1.10	1.46	0.036
LP(2)Cl_{32}	n	1.97441	C_{13}-C_{17}	σ*	0.03878	4.13	0.83	0.052
LP(3)Cl_{32}	n	1.93681	C_{13}-C_{17}	π*	0.45581	11.74	0.29	0.058

Table 4: NBO results showing the formation of Lewis and non-Lewis orbtials of 4-Chloro-2-(3,4-dichlorophenylcarbamoyl)phenyl acetate

Bond(A-B)	ED/energy	EDA%	EDB%	NBO	s%	p%
$\sigma C_{1}-C_{6}$	1.96577	49.93	50.07	0.7066(sp$^{1.85}$)C	35.03	64.97
	-0.72037			+0.7076(sp$^{1.00}$)C	35.03	64.97
$\sigma C_{2}-C_{3}$	1.65023	48.44	51.56	0.6960(sp$^{99.99}$)C	0.03	99.97
	-0.29436			+0.7180(sp$^{99.99}$)C	0.02	99.98
$\sigma C_{3}-C_{4}$	1.95906	51.22	48.78	0.7157(sp$^{1.89}$)C	34.63	65.37
	-0.72540			+0.6915(sp$^{1.90}$)C	34.54	65.46
$\sigma C_{5}-Cl_{30}$	1.98833	45.17	54.83	0.6721(sp$^{3.63}$)C	21.62	78.38
	-0.68799			+0.7405(sp$^{5.92}$)Cl	14.45	85.55
$\sigma C_{10}-C_{11}$	1.96789	50.56	49.44	0.7110(sp$^{1.81}$)C	35.57	64.43
	-0.73695			+0.7032(sp$^{1.85}$)C	35.05	64.95
$\sigma C_{11}-C_{13}$	1.97284	49.15	50.85	0.7011(sp$^{1.87}$)C	34.80	65.20
	-0.75894			+0.7131(sp$^{1.55}$)C	39.25	60.75
$\sigma C_{12}-C_{15}$	1.96996	49.89	50.11	0.7063(sp$^{1.84}$)C	35.16	64.84
	-0.72839			+0.7079(sp$^{1.81}$)C	35.59	64.41
$\sigma C_{15}-C_{17}$	1.97453	48.85	51.15	0.6989(sp$^{1.93}$)C	34.17	65.83
	-0.75206			+0.7152(sp$^{1.55}$)C	39.17	60.83
$\sigma C_{24}-C_{25}$	1.98459	49.76	50.24	0.7054(sp$^{1.44}$)C	41.03	58.97
	-0.68976			+0.7088(sp$^{2.89}$)C	25.73	74.27
n1O_{20}	1.97766			sp$^{0.57}$	63.83	36.17
	-0.71073					
n2O_{20}	1.87575			sp$^{99.99}$	0.05	99.95
	-0.26649					
n1N_{21}	1.67335-			sp$^{1.00}$	0.01	99.99
	0.28463					
n1O_{23}	1.96057			sp$^{1.83}$	35.33	64.67
	-0.55677					
n2O_{23}	1.76697			sp$^{1.00}$	0.00	100.0
	-0.35561					
n1O_{29}	1.97324			sp$^{0.62}$	61.80	38.20
	-0.72760					
n2O_{29}	1.84656			sp$^{99.99}$	0.12	99.88
	-0.29499					
n1Cl_{30}	1.99419			sp$^{0.17}$	85.73	14.27
	-0.94737					
n2Cl_{30}	1.97714			sp$^{1.00}$	0.01	99.99
	-0.32821					
n3Cl_{30}	1.94118			sp$^{1.00}$	0.00	100.0
	-0.32628					
n1Cl_{31}	1.99395			sp$^{0.17}$	85.70	14.30
	-0.95640					
n2Cl_{31}	1.97504			sp$^{99.99}$	0.16	99.84
	-0.33722					
n3Cl_{31}	1.93595			sp$^{1.00}$	0.00	100.0
	-0.33479					
n1Cl_{32}	1.99395			sp$^{0.17}$	85.58	14.42
	-0.95127					
n2Cl_{32}	1.97441			sp$^{99.99}$	0.18	99.82
	-0.33356					
n3Cl_{32}	1.93681			sp$^{1.00}$	0.00	100.0
	-0.33080					

stabilization of 10.08 kcal mol^{-1}. Also another intra-molecular hyper-conjugative interactions are formed by the orbital overlap between n (O) and σ* (C–N) bond orbital which results in ICT causing stabilization of the system. The strong intra-molecular hyper-conjugative interaction of N_{22}-C_{23} from of n2(O_{25}) →σ* (N_{22}-C_{23}) which increases ED (0.07648 e) that weakens the respective bonds leading to stabilization of 26.06 kcal mol^{-1}. These interactions are observed as an increase in electron density (ED) in C-C anti-bonding orbitals that weakens the respective bonds. Another intra-molecular hyper-conjugative interactions are formed by the orbital overlap between n(Br) and σ*(C–C) bond orbital which results in ICT causing stabilization of the system. The strong intra-molecular hyper-conjugative interaction of C_{13}-C_{17} from of n3(Br_{21})→π*(C_{13}-C_{17}) which increases ED (0.38778e) that weakens the respective bonds leading to stabilization of 9.09 kcal mol^{-1}. Again a strong intra-molecular hyper-conjugative interaction of C_{27}-O_{29} from of n2(O_{26})→π*(C_{27}-O_{29}) which increases ED (0.20971e) that weakens the respective bonds leading to stabilization of 43.54 kcal mol^{-1}. A strong intra-molecular hyper-conjugative interaction of O_{26}-C_{27} from of n2(O_{29})→π* (O_{26}-C_{27}) which increases ED (0.12474 e) that weakens the respective bonds leading to stabilization of 41.46 kcal mol^{-1}. Also a very strong intra-molecular hyper-conjugative interaction of C_{23}-O_{25} from of n1(N_{22})→π*(C_{23}-O_{25}) which increases ED (0.28165e) that weakens the respective bonds leading to stabilization of 52.19 kcal mol^{-1}.

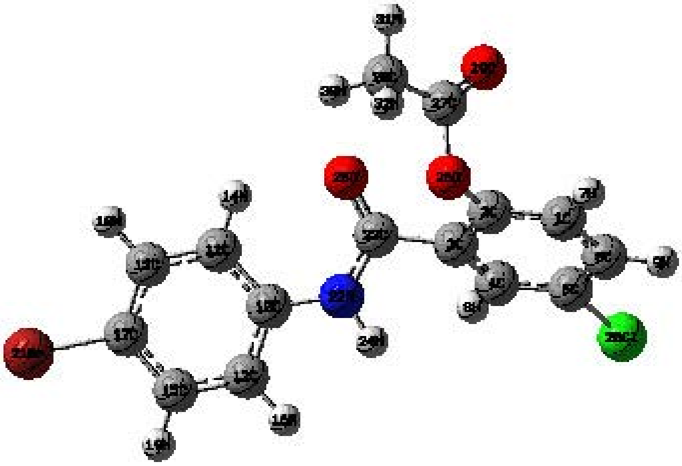

Fig. 3: 4-Chloro-2-(3,4-bromophenylcarbamoyl)phenyl acetate

The NBO analysis also describes the bonding in terms of the natural hybrid orbital n2(Cl_{20}), which occupy a higher energy orbital (-0.32870a.u.) with considerable p-character (100.0%) and low occupation number (1.97815a.u.) and the other n1(Cl_{20}) occupy a lower energy orbital (-0.94563) with p-character (14.46%) and high occupation number (1.99428a.u.).Also n2(Br_{21}), which occupy a higher energy orbital (-0.29450a.u.) with considerable p-character (100.00%) and low occupation number (1.97873a.u.) and the other n1(Br_{21}) occupy a lower energy orbital (-0.97568a.u.) with p-character (12.21%) and high occupation number (1.99530a.u.).Thus, a very close to pure p-type lone pair orbital participates in the electron donation to the →σ*(C–C) orbital for n2(Cl_{20})→σ *(C–C) and orbital for n2(Br21)→σ *(C–C) interactions in the compound.

5-chloro-2-(3-chlorophenylcarbamoyl) phenylacetate

The strong intra-molecular hyper-conjugative interaction of C_1-C_6 from of n3(Cl_{10})→π *(C_1-C_6) which increases ED (0.3871e) that weakens the respective bonds leading to stabilization of 10.74 kcal mol^{-1}.Also another intra-molecular hyper-conjugative interactions are formed by the orbital overlap between n(O) and π*(C–O) bond orbital which results in ICT causing stabilization of the system. The strong intra-molecular hyper-conjugative interaction of C_{12}-O_{13} from of n2(O_{11})$\rightarrow\pi^*$ (C_{12}-O_{13}) which increases ED (0.213e) that weakens the respective bonds leading to stabilization of 45.25 kcal mol$^{"1}$. These interactions are observed as an increase in electron density (ED) in C-C anti-bonding orbitals that weakens the respective bonds. Another intra-molecular hyper-conjugative interactions are formed by the orbital overlap between n(Cl) and π*(C–C) bond orbital which results in ICT causing stabilization of the system. The strong intra-molecular hyper-conjugative interaction of C_{23}-C_{25} from of n3(Cl_{32})$\rightarrow\pi^*$(C_{23}-C_{25}) which increases ED (0.3906 e) that weakens the respective bonds leading to stabilization of 10.53 kcal mol^{-1}.Again a strong intra-molecular hyper-conjugative interaction of O_{11}-C_{12} from of n2(O_{13})$\rightarrow\sigma^*$ (O_{11}-C_{12}) which increases ED (0.11944 e) that weakens the respective bonds leading to stabilization of 39.73 kcal mol^{-1}. A strong intra-molecular hyper-conjugative interaction of C_{18}-N_{20} from of n2(O_{19})$\rightarrow\sigma$ *(C_{18}-N_{20}) which increases ED (0.07389e) that weakens the respective bonds leading to stabilization of 23.51 kcal mol$^{"1}$. Also a very strong intra-molecular hyper-conjugative interaction of C_{18}-O_{19} from of n1(N_{20})$\rightarrow\pi^*$(C_{18}–O_{19}) which increases ED (0.26075e) that weakens the respective bonds leading to stabilization of 47.65 kcal mol^{-1}.

The NBO analysis also describes the bonding in terms of the natural hybrid orbital n2(Cl_{10}), which occupy a higher energy orbital (-0.32467a.u.) with considerable p-character (99.98%) and low occupation number (1.97760a.u.) and the other n1(Cl_{10}) occupy a lower

Table 5: Second order perturbation theory analysis of Fock matrix in NBO basis corresponding to the intramolecular bonds of the 4-Chloro-2-(4-bromophenylcarbamoyl) phenyl acetate

Donor(i)	Type	ED/e	Acceptor(j)	Type	ED/e	E(2)	E(j)-E(i)	F(i,j)
C_1-C_6	σ	1.96333	C_5-Cl_{20}	σ^*	0.03833	5.68	0.79	0.060
C_1-C_6	π	1.65046	C_2-C_3	π^*	0.41809	23.22	0.27	0.072
C_2-C_3	π	1.63502	C_{23}-O_{25}	π^*	0.28165	10.80	0.30	0.052
C_3-C_4	σ	1.95875	C_5-Cl_{20}	σ^*	0.03833	50.25	0.80	0.058
C_3-C_{23}	σ	1.96919	C_{10}-N_{22}	σ^*	0.03172	4.38	1.07	0.061
C_5–Cl_{20}	σ	1.98769	C_3-C_4	σ^*	0.02298	2.87	1.25	0.054
C_{11}–C_{13}	σ	1.96568	C_{17}-Br_{21}	σ^*	0.03601	5.30	0.77	0.057
C_{12}-C_5	σ	1.96689	C_{17}-Br_{21}	σ^*	0.03601	5.18	0.78	0.057
C_{17}-Br_{21}	σ	1.98579	C_{12}-C_{15}	σ^*	0.01737	3.12	1.23	0.055
N_{22}-H_{24}	σ	1.98380	C_{23}-O_{25}	σ^*	0.02695	4.31	1.23	0.065
C_{27}-C_{28}	σ	1.98315	C_2-O_{26}	σ^*	0.03841	4.24	0.97	0.058
LP(1)Cl_{20}	n	1.99428	C_5-C_6	σ^*	0.02629	1.01	1.51	0.035
LP(2)Cl_{20}	n	1.97815	C_4-C_5	σ^*	0.02686	3.12	0.89	0.047
LP(3)Cl_{20}	n	1.94380	C_4-C_5	π^*	0.39490	10.08	0.31	0.055
LP(1)Br_{21}	n	1.99530	C_{13}-C_{17}	σ^*	0.0.2654	1.10	1.56	0.037
LP(2)Br_{21}	n	1.97873	C_{15}-C_{17}	σ^*	0.0.2642	2.82	0.87	0.044
LP(3)Br_{21}	n	1.94519	C_{13}-C_{17}	π^*	0.0.38778	9.09	0.30	0.051
LP(1)N_{22}	n	1.66148	C_{23}-O_{25}	π^*	0.0.28165	52.19	0.29	0.112
LP(1)O_{25}	n	1.97371	N_{22}-C_{23}	σ^*	0.07648	2.49	1.11	0.048
LP(2)O_{25}	n	1.86177	N_{22}-C_{23}	σ^*	0.07648	26.06	0.70	0.122
LP(1)O_{26}	n	1.95825	C_{27}-O_{29}	σ^*	0.0.2255	8.32	1.08	0.085
LP(2)O_{26}	n	1.76193	C_{27}-O_{29}	π^*	0.0.20971	43.54	0.32	0.107
LP(1)O_{29}	n	1.97318	C_{27}-C_{28}	σ^*	0.0.04812	2.69	1.07	0.048
LP(2)O_{29}	n	1.84084	O_{26}-C_{27}	σ^*	0.0.12474	41.46	0.58	0.139

Table 6: NBO results showing the formation of Lewis and non-Lewis orbtials of 4-Chloro-2-(4-bromophenylcarbamoyl)phenyl acetate

Bond(A-B)	ED/energy	EDA%	EDB%	NBO	s%	p%
$\sigma C_1\text{-}C_6$	1.96333 -0.72785	49.84	50.16	0.7060(sp$^{1.84}$)C +0.7083(sp$^{1.85}$)C	35.21 35.12	64.79 64.88
$\pi C_1\text{-}C_6$	1.65046 -0.27907	50.74	49.26	0.7123(sp$^{1.00}$)C +0.7018(sp$^{1.00}$)C	0.00 0.00	100.0 100.0
$\pi C_2\text{-}C_3$	1.63502 -0.29232	48.37	51.63	0.6955(sp$^{1.00}$)C +0.6324(sp$^{99.99}$)C	0.00 0.00	100.0 100.0
$\sigma C_3\text{-}C_4$	1.95875 -0.73977	50.73	49.27	0.7123(sp$^{1.83}$)C +0.7019(sp$^{1.86}$)C	35.37 34.91	64.63 65.09
$\sigma C_3\text{-}C_{23}$	1.96919 -0.67810	52.37	47.63	0.7237(sp$^{2.33}$)C +0.6901(sp$^{1.79}$)C	29.90 35.87	70.01 64.13
$\sigma C_5\text{-}Cl_{20}$	1.98769 -0.68838	44.93	55.07	0.6703(sp$^{3.73}$)C +0.7421(sp$^{1.00}$)C	21.12 14.65	78.88 85.35
$\sigma C_{11}\text{-}C_{13}$	1.96568 -0.70889	49.77	50.23	0.7055(sp$^{1.84}$)C +0.7087(sp$^{1.81}$)C	35.22 35.53	64.78 64.47
$\sigma C_{12}\text{-}C_{15}$	1.96689 -0.71926	50.06	49.94	0.7076(sp$^{1.78}$)C +0.7067(sp$^{1.82}$)C	35.93 35.41	64.07 64.59
$\sigma C_{17}\text{-}Br_{21}$	1.98579 -0.64043	49.38	50.62	0.7027(sp$^{3.63}$)C +0.7115(sp$^{7.06}$)O	21.60 12.41	78.40 87.59
$\sigma C_{27}\text{-}C_{28}$	1.98315 -0.68075	49.73	50.27	0. 7052(sp$^{1.44}$)C +0.7090(sp$^{2.92}$)C	40.92 25.53	59.08 74.47
$n1Cl_{20}$	1.99428 -0.94563			sp$^{0.17}$	85.54	14.46
$n2Cl_{20}$	1.97815 -0.32870			sp$^{1.00}$	0.00	100.0
$n3Cl_{20}$	1.94380 -0.32665			sp$^{1.00}$	0.00	100.0
$n1Br_{21}$	1.99530 -0.97568			sp$^{0.14}$	87.79	12.21
$n2Br_{21}$	1.97873 -0.29450			sp$^{1.00}$	0.00	100.0
$n3Br_{21}$	1.94519 -0.29244			sp$^{1.00}$	0.00	100.0
$n1N_{22}$	1.66148 -0.28386			sp$^{99.99}$	0.10	99.90
$n1O_{25}$	1.97371 -0.68104			sp$^{0.69}$	59.23	40.77
$n2O_{25}$	1.86177 -0.26527			sp$^{99.99}$	0.10	99.90
$n1O_{26}$	1.95825 -0.51226			sp$^{2.32}$	30.14	69.86
$n2O_{26}$	1.76193 -0.35236			sp$^{99.99}$	0.78	99.22
$n1O_{29}$	1.97318 -0.69876			sp$^{0.72}$	58.15	4185
$n2O_{29}$	1.84084 -0.28834			sp$^{99.99}$	0.02	99.98

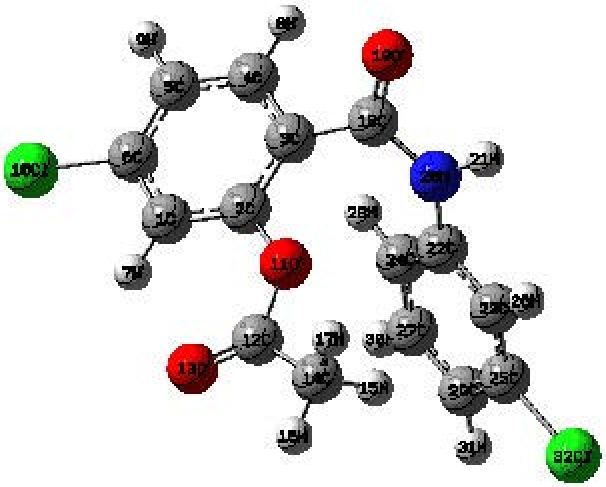

Fig. 4: 5-Chloro-2-(3-chlorophenylcarbamoyl)phenylacetate

Table 7: Second order perturbation theory analysis of Fock matrix in NBO basis corresponding to the intramolecular bonds of the 5-chloro-2-(3-chlorophenylcarbamoyl) phenylacetate

Donor(i)	Type	ED/e	Acceptor(j)	Type	ED/e	E(2)	E(j)-E(i)	F(i,j)
C_1-C_2	σ	1.96896	C_6-Cl_{10}	σ*	0.03654	4.82	0.82	0.05
C_1-C_6	σ	1.97514	C_2-O_{11}	σ*	0.04019	4.94	1.03	0.064
C_1-C_6	π	1.67644	C_2-C_3	π*	0.42225	20.86	0.29	0.071
C_2-C_3	π	1.64819	C_{18}-O_{19}	π*	0.26075	8.82	0.32	0.049
C_3-C_4	σ	1.96519	C_2-O_{11}	σ*	0.04019	4.11	1.00	0.057
C_4-C_5	σ	1.96784	C_6-Cl_{10}	σ*	0.03654	5.57	0.80	0.060
C_4- C_5	π	1.65305	C_1-C_6	π*	0.38714	23.59	0.27	0.072
N_{20}-H_{21}	σ	1.97834	C_3-C_{18}	σ*	0.06647	4.74	1.08	0.065
C_{22}-C_{24}	σ	1.65122	C_{27}-C_{29}	π*	0.01802	21.57	0.29	0.071
C_{23}-C_{25}	σ	1.97806	N_{20}-C_{22}	σ*	0.03284	3.63	1.15	0.058
C_{23}-C_{25}	π	1.70306	C_{22}-C_{24}	π*	0.37734	19.24	0.30	0.069
C_{24}-C_{27}	σ	1.97629	N_{20}-C_{22}	σ*	0.03284	4.65	1.11	0.064
C_{27}-C_{29}	σ	1.96897	C_{25}-Cl_{32}	σ*	0.03736	5.69	0.79	0.060
C_{27}-C_{29}	π	1.65888	C_{23}-C_{25}	π*	0.39068	23.52	0.26	0.071
LP(1)Cl_{10}	σ	1.99400	C_5-C_6	σ*	0.02632	1.03	1.50	0.035
LP(2)Cl_{10}	n	1.97760	C_1-C_6	σ*	0.02700	3.28	0.89	0.048
LP(3)Cl_{10}	σ	1.93692	C_1-C_6	π*	0.38714	10.74	0.32	0.057
LP(1)O_{11}	σ	1.95754	C_{12}-O_{13}	σ*	0.02288	8.52	1.08	0.086
LP(2)O_{11}	n	1.76189	C_{12}-O_{13}	π*	0.21315	45.25	0.32	0.108
LP(1)O_{13}	n	1.97334	C_{12}-C_{14}	σ*	0.04584	2.48	1.08	0.046
LP(2)O_{13}	n	1.84857	O_{11}-C_{12}	σ*	0.11944	39.73	0.58	0.137
LP(1)O_{19}	n	1.97680	C_{18}-N_{20}	σ*	0.07389	1.85	1.13	0.041
LP(2)O_{19}	σ	1.87256	C_{18}-N_{20}	σ*	0.07389	23.51	0.70	0.116
LP(1)N_{20}	n	1.68348	C_{18}-O_{19}	π*	0.26075	47.65	0.31	0.109
LP(1)Cl_{32}	n	1.99416	C_{23}-C_{25}	σ*	0.02489	0.98	1.51	0.035
LP(2)Cl_{32}	n	1.97808	C_{23}-C_{25}	σ*	0.02489	3.14	0.89	0.047
LP(3)Cl_{32}	n	1.94190	C_{23}-C_{25}	π*	0.39068	10.53	0.32	0.056

Table 6: NBO results showing the formation of Lewis and non-Lewis orbtials of 4-Chloro-2-(4-bromophenylcarbamoyl)phenyl acetate

Bond(A-B)	ED/energy	EDA%	EDB%	NBO	s%	p%
σC_1-C_2	1.96896 -0.74668	49.53	50.47	0.7038(sp$^{1.97}$)C +0.7104(sp$^{1.55}$)C	33.64 39.17	66.36 60.83
σC_1-C_6	1.97514 -0.75555	49.60	50.40	0.7043(sp$^{1.88}$)C +0.7099(sp$^{1.56}$)C	34.72 39.12	65.28 60.88
πC_1-C_6	1.67644 -0.29247	48.33	51.67	0.6952(sp$^{1.00}$)C +0.7188(sp$^{1.00}$)C	0.00 0.00	100.0 100.0
πC_2-C_3	1.64819 -0.29091	48.32	51.68	0.6951(sp$^{99.99}$)C +0.7189(sp$^{99.99}$)C	0.02 0.01	99.98 99.99
σC_3-C_4	1.96519 -0.72784	51.48	48.52	0.7175(sp$^{1.87}$)C +0.6965(sp$^{1.86}$)C	34.90 34.65	65.10 65.35
πC_4-C_5	1.96784 -0.72418	49.86	50.14	0.7061(sp$^{1.86}$)C +0.7081(sp$^{1.86}$)C	35.23 35.01	64.77 64.99
σC_4-C_5	1.65305 -0.27586	48.47	51.53	0.6962(sp$^{1.00}$)C +0.7178(sp$^{1.87}$)C	0.00 0.00	100.0 100.0
σC_{22}-C_{24}	1.65122 -0.28157	49.87	50.13	0.7062(sp$^{1.00}$)C +0.7080(sp$^{99.99}$)C	0.00 0.02	100.0 99.98
πC_{23}-C_{25}	1.97806 -0.76021	49.64	50.36	0.7046(sp$^{1.85}$)C +0.7096(sp$^{1.54}$)C	35.03 39.36	64.97 60.64
σC_{23}-C_{25}	1.70306 -0.29660	48.73	51.27	0.6981(sp$^{1.00}$)C +0.7160(sp$^{1.00}$)C	0.01 0.00	99.99 100.0
σC_{24}-C_{27}	1.97629 -0.72283	50.31	49.69	0.7093(sp$^{1.83}$)C +0.7049(sp$^{1.84}$)C	35.34 35.16	64.66 64.84
σC_{27}-C_{29}	1.96897 -0.72213	49.62	50.38	0.7044(sp$^{1.86}$)C +0.7098(sp$^{1.84}$)C	34.93 35.15	65.07 64.85
πC_{27}-C_{29}	1.65888 -0.27452	48.94	51.06	0.6996(sp$^{1.00}$)C +0.7145(sp$^{1.00}$)C	0.00 0.00	100.0 100.0
n1Cl_{10}	1.99400 -0.94295			sp$^{0.17}$	85.27	14.73
n2Cl_{10}	1.97760 -0.32467			sp$^{99.99}$	0.02	99.98
n3Cl_{10}	1.93692 -0.32298			sp$^{1.00}$	0.00	100.0
n1O_{11}	1.95754 -0.52212			sp$^{2.32}$	30.08	69.92
n2O_{11}	1.76189 -0.35564			sp$^{99.99}$	0.06	99.94
n1O_{13}	1.97334 -0.70367			sp$^{0.69}$	59.06	40.94
n2O_{13}	1.84857 -0.28842			sp$^{99.99}$	0.04	99.96
n1O_{19}	1.97680 -0.68397			sp$^{0.64}$	60.81	39.19
n2O_{19}	1.87256 -0.25927			sp$^{99.99}$	0.07	99.93
n1N_{20}	1.68348 -0.27670			sp$^{1.00}$	0.00	100.0
n1Cl_{32}	1.99416 -0.94692			sp$^{0.17}$	85.32	14.68
n2Cl_{32}	1.97808 -0.32921			sp$^{1.00}$	0.00	100.0
n3Cl_{32}	1.94190 -0.32746			sp$^{1.00}$	0.00	100.0

energy orbital (-0.94295) with p-character (14.73%) and high occupation number (1.99400a.u.). Also n2(Cl_{32}), which occupy a higher energy orbital (-0.32921 a.u.) with considerable p-character (100.00%) and low occupation number (1.97808a.u.) and the other n1(Cl_{32}) occupy a lower energy orbital (-0.94692a.u.) with p-character (14.68%) and high occupation number (1.99416a.u.). Thus, a very close to pure p-type lone pair orbital participates in the electron donation to the σ*(C–C) orbital for n2(Cl_{10})→σ *(C–C) and σ*(C–C) orbital for n2(Cl_{32})→σ *(C–C) interactions in the compound.

CONCLUSIONS

A natural bond orbital analysis has been performed in order to study intramolecular bonding, interactions among bonds and delocalization of unpaired electrons for certain salicylanilide derivatives. The electron density (ED) is transferred from the n(O), n(Cl) n(N) to the anti-bonding π*, σ* orbital of the C–C ,C-O,C-N. Stability of the molecules arising from hyper-conjugative interactions and charge delocalization has been analyzed using natural bond orbital analysis. The results show that electron density in the anti-bonding orbitals and second order delocalization energies confirm the occurrence of intra-molecular charge transfer within the molecule.

REFERENCES

1. Reed, A.E., Curtiss, L.A., Weinhold, F., *Chem. Rev*. **99**: 899 (1988).
2. Chocholousova, J., Spirko, V.V., Hobza, P., *Phys. Chem. Chem. Phys*. **6**: 22 (2004).
3. Vinsova, J., Imramovsky, A., *Ces. Slov. Farm*.**53**: 294 (2004).
4. Vinsova, J., Imramovsky, A., Buchta, V., Ceckova, M., Dolezal, M., Staud, F., Jampilek, J., Kaustova, J., *Molecules* **12**:1 (2007).
5. Imramovsky, A., Vinsova, J., Ferriz, J.M., Dolezal, M., Jampilek, J., Kaustova, J., Kunc, F., *Bioorg. Med. Chem*. **17**: 3572 (2009).
6. Imramovsky, A., Vinsova, J., Ferriz, J.M., Buchta, V., Jampilek, J., *Bioorg. Med. Chem. Lett*. **19**: 348 (2009).
7. Ferriz, J.M., Vavrova, K., Kunc, F., Imramovsky, A., Stolarikova, J., Vavrikova, E., Vinsova, J., *Bioorg. Med. Chem*. **18**: 1054 (2010).
8. Otevrel, J., Mandelova, Z., Pesko, M., Guo, J., Kralova, K., Sersen, F., Vejsova, M., Kalinowski, D., Kovacevic, Z., Coffey, A., Csollei, J., Richardson, D.R., Jampilek, J., *Molecules* **15**: 8122 (2010).
9. Abian, M.I.G., Panzera, F., Saez, J.L., Abian, J.F.G., Torre, C., Martin, G.G., *Protoplasma* **204**: 119 (1998).
10. Rao, V.S., Principles of Weed Science, ed. 2, Science: Enfield, New Hampshie, UK (2000).
11. Imramovsky, A., Pesko, M., Ferriz, J.M., Kralova, K., Vinsova, J., Jampilek, J., *Bioorg. Med. Chem. Lett*. **21**: 4564 (2011).
12. El-Sayed, A.A., Dorgham, S.M., Kantouch, A., Int. J. Biol. *Macromolecules* **50**: 273 (2012).
13. Macielag, M.J., Demers, J.P., Fraga-Spano, S.A., Hlasta, D.J., Johnson, S.G., Kanojia, R.M., Russell, R.K., Sui, Z., Weidner-Wells, M.A., Werblood, H., Foleno, B.D., Goldschmidt, R.M., Loeloff, M.J, Webb, G.C., Barrett, J.F., *J. Med. Chem*. **41**: 2939 (1998).
14. De La Fuente, R., Sonawane, N.D., Arumainayagam, D., Verkman, A.S., *Br. J. Pharmacol*. **149**: 551 (2006).
15. Chandrawathani, P., Yusoff, N., Wan, L.C., Ham, A., Waller, P.J., *J. Vet. Res. Commun*. **28**: 479 (2004).
16. Waisser, K., Matyk, J., Divisova, H., Husakova, P., Kunes, J., Klimesova, V., Kaustova, J., Mollmann, U., Dahse, H.M., Miko, M., *Arch. Pharm. (Weinheim)* **339**: 616 (2006).
17. Cheng, T.J., Wu, Y.T., Yang, S.T., Lo, K.H., Chen, S.K., Chen, Y.H., Huang, W.I., Yuan, C.H., Guo, C.W., Huang, L.Y., Chen, K.T., Shih, H.W., Cheng, Y.S., Cheng, W.C., Wong, C.H., *Bioorg. Med. Chem.* **18**: 8512 (2010).
18. Dahlgren, M.K, Kauppi, A.M., Olsson, I.M., Linusson, A., Elofsson, M., *J. Med. Chem*. **50**: 6177 (2007).
19. Brown, M.E., Fitzner, J.N., Stevens, T., Chin, W., Wright, C.D., Boyce, J.P., *Bioorg. Med.*

Chem. **16**: 8760 (2008).

20. Leichti, C., Sequin, U., Bold, G., Furet, P., Meyer, T., Traxler, P., *Eur. J. Med. Chem.* **39**: 11 (2004).
21. Madhavan, V.S., Mary, Y.S., Varghese, H.T., Panicker, C.Y., Mathew, S., Van Alsenoy, C., Vinsova, J., *Spectrochim. Acta* **89**: 308 (2012.
22. Madhavan, V.S., Varghese, H.T., Mathew, S., Vinsova, J., Panicker, C.Y., *Spectrochim. Acta* **72**: 547 (2009).
23. Varghese, H.T., Panicker, C.Y., Madhavan, V.S., Mathew, S., Vinsova, J., Van Alsenoy, C., *J. Raman Spectrosc*. **40**: 1211 (2009).
24. Panicker, C.Y., Varghese, H.T., Madhavan, V.S., Mathew, S., Vinsova, J., Van Alsenoy, C., Mary, Y.S., Mary, Y.S., *J. Raman Spectrosc*. **40**: 2176 (2009).
25. Frisch, M.J., et al, Gaussian09, Revision B.01., Gaussian Inc, Wallingford CT (2010).
26. Glendening, E.D., Reed, A.E., Carpenter, J.E., Weinhold, F., NBO Version 3.1, Gaussian Inc., Pittsburgh, PA.