Erciyes Üniversitesi
Fen Bilimleri Enstitüsü Dergisi
Cilt 36, Sayı 3 , 2020

Erciyes University
Journal of Institue Of Science and Technology
Volume 36, Issue 2, 2020

Molecular Structure and Electronic Properties of Diatrizoate, Ioxaglate Contrast Compounds

Keywords
Contrast agents 1,
HOMO, LUMO 2,
Electro-negativity 3,
Chemical hardness 4,
Chemical softness 5

Abstract: The optimization of 2,4,6 tri-iodobenzene, diatrizoate and, ioxaglate contrast agent was done in order to calculate the energetic behavior and dipole moment of the title compounds in the gas phase and in solution phases. The total energy for different orbital transitions, the energy gap between HOMO and LUMO, electro-negativity, chemical hardness, softness, electrophilicity index and dipole moment has been calculated with B3LYP/cep-4g, B3LYP/cep- B3LYP/31g, B3LYP/cep- B3LYP/121g and B3LYP/lanl2dz levels. The four important molecular orbitals (MO) for the title molecule: the second-highest and highest occupied MOs and the lowest and the second-lowest unoccupied MOs which were denoted as HOMO-1, HOMO, LUMO, and LUMO+1, respectively reflect measure of electron transition and are the critical parameters in determining molecular electrical transport properties.

Diatrizoat, Ioxaglate Kontrast Bileşiklerinin Moleküler Yapıları ve Elektronik Özellikleri

Anahtar Kelimeler
Kontrast maddeleri 1,
HOMO, LUMO 2,
Elektro-negatiflik 3,
Kimyasal sertlik 4,
Kimyasal yumuşaklık 5

Öz: 3.5 tri-iyodobenzen, diatrizoat, ioksaglat kontrast maddesinin optimizasyonu, gaz fazında ve çözelti fazlarında bileşiklerin enerjik davranışını ve dipol momentini hesaplamak için yapılmıştır. Farklı yörünge geçişleri için toplam enerji, enerji açığı HOMO ve LUMO oritalleri arasındai eneri aralığı, kimyasal sertlik, yumuşaklık, elektrofiliklik indeksi ve dipol momenti B3LYP / cep-4g, B3LYP / cep- B3LYP / 31g, B3LYP / cep- B3LYP / 121g ve B3LYP / lanl2dz seviyeleri ile hesaplandı. Çalışılan bileşilerin HOMO ve LOMO arasındaki enerji boşluklarının değerleri triiyodobenzen halkasına bağlı sustituentlerden etkilenmektedir. Bu değişim enerji aralığına bağlı olarak hesaplanan diğer değerlerinde değişime neden olmuştur. İkinci mertebeden bir pertürbasyon işleminden, etkileşim enerjisinin substitüsyona göre değiştiği bulunmuştur. DTZ bileşiğinin IR teorik spectrum değerlerinin deney sonuçları ile mükemmel bir uyum içinde olduğu gösterilmiştir.

*İlgili Yazar, email: noraldibashi@gmail.com

1. Introduction

The concept of contrast agents was introduced from 30 years ago as radiocontrast agents and their development initiated slowly by technical limitations [1].

During the past decade, they have become more dynamic. They used to intensify the vascular structures and organs visibility in x-ray based imaging techniques such as ultrasound, fluoroscopy and computed tomography (CT) [1]. Radiocontrast agents are commonly iodine-based compounds. The basis structure is a benzene ring. Iodinated contrasts consist of 2,4,6-triiodinated substituted benzene ring where iodine atoms arranged symmetrically at 2nd, 4th and 6th positions [2,3] Figure 1.

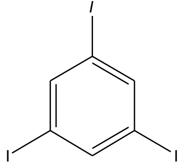


Figure 1. Triiodobenzene structure.

Different derivatives of iodinated contrast can be obtained by replacement of other hydrogen atoms on the benzene ring [2].

2,4,6-triiodobenzene (TIB) is the basis molecule of radicals (R) available for OH substituents. Of three OH atoms attach to benzene ring to make the molecule more soluble [2,3]. Iodine-based contrast media are usually classified as ionic or non-ionic[2]. Both types can be used in clinical radiology due to their solubility.

In 1956 Hoppe used a second acetylamino group and added it to the triiodobenzene ring to generate diatrizoate contrast agent [3,4] **Figure 2.** It is an ionic agent, water-soluble as it dissociates into negative and positive ions. This agent had minimized toxicity as animal studies showed [3].

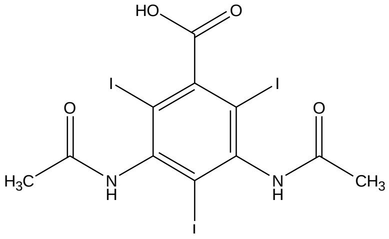


Figure 2. Diatrizoate structure.

It was commercialized as Hypaque and its derivatives were the standard contrast agents used until the 1970s when British company Baker and French company Guerbet together introduced new contrast agent named as ioxaglate [3] **Figure 3.** Ioxaglate contains two triiodinated benzene rings which have a carboxylic acid group. When these two rings are combined, the carboxylic acid group of one of them converted to a nonionizing radical and the carboxylic acid group of the other ring converted to an ionizing salt such as meglumine or sodium ioxaglate, It contains an iodine atom to practical ratio 6:2 which equivalent to the ratio of the low-osmole media 3:1 that making it more suitable for clinical use [5].

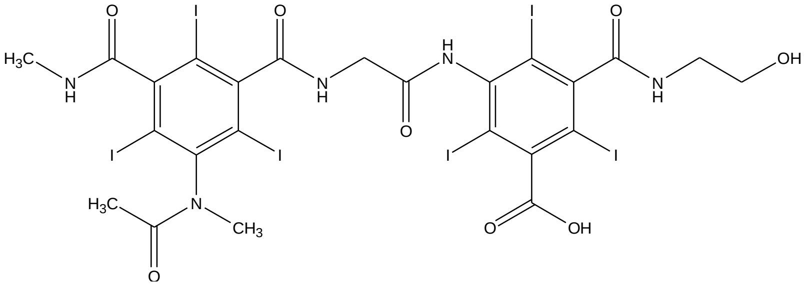


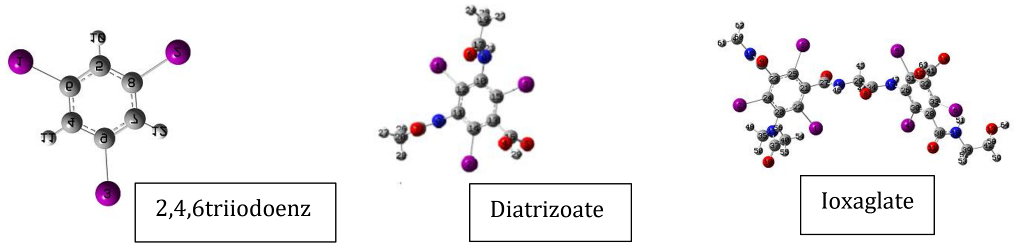
Figure 3.ioxaglate structure.

The optimization of 2,4,6-triiodobenzene, diatrizoate, and ioxaglate will be further considered in this study. The aim of our study is to calculate the energetic behaviour, dipole moment, chemical potential, hardness, softness electronegativity and electron excitation energy of the title compounds in gas phase and in water, ethanol, acetic acid, N,N-dimethyl formamide (DMF), dimethyl sulphoxide (DMSO) and chloroform as solvents using density functional theory.

Orbital energies based on the natural bond orbital (NBO) analysis illustrate the rule of intermolecular orbital interaction in the compound, especially charge transfer from filled donor to empty acceptor NBOs [6]. Estimation of NBOs energetic importance was performed by second-order perturbation theory for each donor NBO (i) and acceptor NBO (j). The stabilization energy related to electron delocalization between donor and acceptor was calculated as:

$$E = qi\frac{(Fi,j)^2}{\varepsilon j - \mathrm{\varepsilon i}} \qquad (1)$$

where q_i is the orbital occupancy ε_i, ε^j are diagonal elements, Fi, j is off-diagonal NBO Fuck matrix element [6]. The optimized molecular structure of the 2,4,6-triiodobenzene and its derivatives diatrizoate and ioxaglate were calculated at B3LYP/ lanl2dz level and illustrated in **Figure 4** with numbering of atoms.



2,4,6triiodoenz

Diatrizoate

Ioxaglate

Figure 4. Structure of triiodoezene and its derevatives diatrizoate and ioxaglat.

2. Material and Method

In this work, the three-dimensional analysis was carried out for evaluating the effect of substituting the groups in 2,4,6-triiodobenzene ring in positions 1, 3 and 5 to produce diatrizoate and ioxaglate compounds which are ionic monomeric and dimeric contrast agents, respectively.

Geometries of all these molecules were fully optimized in the gas phase and solution phases by using Lee-Yang-Parr correlation functional (B3LYP) and gradient corrected DFT with Beck's three-parameter hybrid exchange functional and with the (B3lyp/cep-4g, B3lyp/cep-31g, B3lyp/cep-121g, and B3lyp/lanl2dz) basis set with the Gaussian Program to examine the basis set dependence of the DFT HOMO and LUMO energies. We also performed single point energy calculations on the neutral systems using a basis set (B3lyp/cep-4g, B3lyp/cep-31g, B3lyp/cep-121g, and B3lyp/lanl2dz).

Based on the same theory, the vibrational frequency of diatrizoate was recorded to obtain the vibrational analysis and compared to the experimental results. A scale factor 0.96 was used as a correlation factor for computing results [7]. Molecular properties related to highest occupied molecular orbital energy (E_{HOMO}), and lowest unoccupied molecular orbital energy (E_{LUMO}) such as the hardness (η), softness (s), electronegativity (χ), chemical potential (μ), electrophilicity index (ω), nucleofugality (ΔE_n), and electrofugality (ΔE_e) were calculated by using the following formulation:

The hardness is half of the energy gap between HOMO and LUMO represented as

$$\eta = \frac{1}{2}(\mathrm{E}_{LUMO} - E_{HOMO}) = \frac{1}{2}(1 - A) \tag{2}$$

The softness can be calculated from hardness that:

$$S = \frac{1}{2\eta} \tag{3}$$

(Hard Soft Acid Bas (HSAB) principle.

Electronegativity can be calculated from E_{HOMO} and E_{LUMO} using the following equation:

$$\chi = -\frac{1}{2}\ (E_{HOMO}\ + E_{LUMO}) \tag{4}$$

From electronegativity, chemical potential, chemical potential can be estimated that

$$\mu = -\chi \tag{5}$$

$$\mu = \frac{1}{2}\ (E_{HOMO}\ + E_{LUMO}) \tag{6}$$

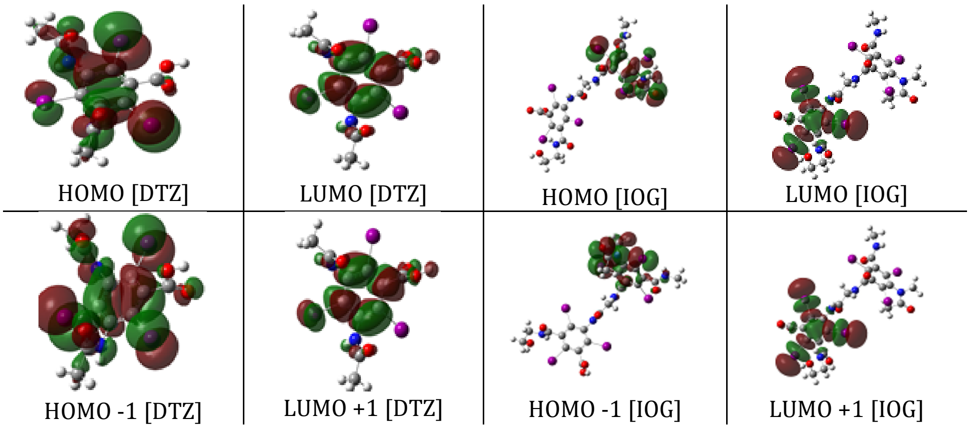
Electrophilicity index (ω), nucleofugality ΔEn and electrofugalityΔEe can be calculated from chemical potential μ and the hardness η by the following equations respectively [8]:

$$\omega = \frac{\mu^2}{2\eta} \tag{7}$$

$$\Delta E_n = \frac{(\mu + \eta)^2}{2\eta} \tag{8}$$

$$\Delta E_e = \frac{(\mu - \eta)^2}{2\eta} \tag{9}$$

3. Results



HOMO [DTZ] LUMO [DTZ] HOMO [IOG] LUMO [IOG]

HOMO -1 [DTZ] LUMO +1 [DTZ] HOMO -1 [IOG] LUMO +1 [IOG]

Figure 5 The surfaces of HOMO-1, HOMO, LUMO and LUMO+1were drawn by using B3LYP.

The surfaces of HOMO-1, HOMO, LUMO, and LUMO+1 were drawn and given in **Figure 5** to understand the bonding scheme of present compounds.

The energies of HOMO and LUMO of title compounds using different basis sets (B3LYP/cep-4g, B3LYP/cep-31g, B3LYP/cep-121g, and B3LYP/lanl2dz) in are given in **Table 1** as a sample of results which were performed in the gas phase.

Table 1. The energy of HOMO and LUMO and the energy of Orbitals near HOMO and LUMO in the gas phase.

Basis set(eV)	Cep-4g			Cep-31g			Cep-121g			Lanl2dz		
	TIB	DTZ	IOG	TIB	DTZ	IOG	TIB	DTZ	IOG	TIB	DTZ	IOG
LUMO+2	-1.12	-2.57	-2.76	-1.35	-1.66	-1.91	-1.34	-1.67	-1.91	-1.31	-1.65	-1.88
LUMO+1	-2.25	-2.61	-2.89	-1.35	-1.68	-2.46	-1.34	-1.69	-2.49	-1.31	-1.66	-2.28
LUMO)	-2.25	-2.69	-3.47	-2.36	-2.48	-2.65	-2.39	-2.50	-2.68	-2.16	-2.29	-2.47
HOMO	-7.29	-7.00	-6.98	-6.99	-7.03	-6.83	-7.04	-7.08	-6.89	-6.98	-7.00	-6.77
HOMO-1	-7.29	-7.17	-7.18	-7.00	-7.14	-6.91	-7.04	-7.18	-6.96	-6.98	-7.12	-6.86
HOMO-2	-7.79	-7.44	-7.25	-7.56	-7.23	-7.05	-7.58	-7.27	-7.10	-7.50	-7.17	-7.02

HOMO-LUMO energy-dependent calculation: electronegativity χ, hardness η, softness S, chemical potential μ, electrophilicity index ω, nucleofugality ΔE_n, and electrofugality ΔE_e were calculated from HOMO – LUMO energy gap in gas phase and in solution phases and the results are presented in **Tables 2**, **3**. **Table 2** illustrates the results in the gas phase and **Table 3** illustrates the results in water as a solution phase.

Table 2. Chemical calculation in the gas phase.

M	C	HOMO (eV)	LUMO (eV)	ΔE (eV)	X (eV)	η (eV)	S $(eV)^{-1}$	μ (eV)	ω (eV)	ΔE_e (eV)	ΔE_n (eV)
Cep-4g	TIB	-7.29	-2.25	5.04	4.77	2.52	0.20	-4.77	4.52	10.56	1.01
	DTZ	-7.00	-2.69	4.30	4.85	2.15	0.23	-4.85	5.45	11.38	1.68

	IOG	-6.98	-3.47	3.51	5.22	1.75	0.28	-5.22	7.78	13.88	3.43
Cep-31g	TIB	-6.99	-2.36	4.63	4.68	2.31	0.22	-4.68	4.73	10.57	1.21
	DTZ	-7.03	-2.48	4.55	4.75	2.28	0.22	-4.75	4.96	10.85	1.35
	IOG	-6.83	-2.65	4.18	4.74	2.09	0.24	-4.74	5.39	11.17	1.69
Cep-121g	TIB	-7.04	-2.39	4.64	4.72	2.32	0.22	-4.72	4.79	10.67	1.23
	DTZ	-7.08	-2.50	4.58	4.79	2.29	0.22	-4.79	5.02	10.96	1.37
	IOG	-6.89	-2.68	4.21	4.79	2.11	0.24	-4.79	5.44	11.28	1.71
Lanl2dz	TIB	-6.98	-2.16	4.81	4.57	2.41	0.21	-4.57	4.34	10.12	0.97
	DTZ	-7.00	-2.29	4.71	4.65	2.36	0.21	-4.65	4.58	10.41	1.11
	IOG	-6.77	-2.47	4.30	4.62	2.15	0.23	-4.62	4.97	10.67	1.42

Method M, Compounds C

Table 3. Chemical calculation in the water as a solution phase.

M	C	HOMO (eV)	LUMO (eV)	ΔE (eV)	X (eV)	η (eV)	S $(eV)^{-1}$	μ (eV)	ω (eV)	ΔE_e (eV)	ΔE_n (eV)
	TIB	-7.29	-2.27	5.02	4.78	2.51	0.20	-4.78	4.55	10.59	1.03
	DTZ	-7.29	-2.97	4.33	5.13	2.16	0.23	-5.13	6.08	12.29	2.03
Cep-4g	IOG	-7.19	-3.45	3.74	5.32	1.87	0.27	-5.32	7.57	13.82	3.18
	TIB	-6.93	-2.25	4.68	4.59	2.34	0.21	-4.59	4.50	10.26	1.08
	DTZ	-7.22	-2.46	4.76	4.84	2.38	0.21	-4.84	4.92	10.95	1.27
Cep-31g	IOG	-7.07	-2.53	4.53	4.80	2.27	0.22	-4.80	5.08	11.02	1.42
	TIB	-6.98	-2.28	4.70	4.63	2.35	0.21	-4.63	4.55	10.36	1.10
	DTZ	-7.25	-2.48	4.77	4.87	2.39	0.21	-4.87	4.96	11.02	1.29
Cep-121g	IOG	-7.11	-2.56	4.55	4.83	2.27	0.22	-4.83	5.13	11.10	1.44
	TIB	-6.94	-2.07	4.87	4.51	2.43	0.21	-4.51	4.17	9.89	0.88
	DTZ	-7.19	-2.29	4.90	4.74	2.45	0.20	-4.74	4.59	10.55	1.07
Lanl2dz	IOG	-7.19	-2.29	4.90	4.74	2.45	0.20	-4.74	4.59	10.55	1.07

Method M, Compounds C

The dipole moment values of the title compounds were investigated in the gas phase and in solution phase by using different solvents, and the results are presented in **Table 4.**

Table 4. Dipole moment of the of TIB, DTZ and IOG DTZ at B3LYP/6-311G(d, p) method.

M	C	Gas	water	Acetic acid	Chloroform	DMF	DMSO
		Dipole Moment(Debye)					
Cep -4g	TIB	0.36	0.45	0.43	0.42	0.45	0.45
	DTZ	7.28	8.47	8.34	8.05	8.46	8.45
	IOG	6.45	8.78	8.12	7.88	8.74	8.72
Cep -31g	TIB	0.45	0.59	0.56	0.55	0.59	0.59
	DTZ	6.55	9.23	8.70	9.15	9.19	9.17
	IOG	8.59	11.8	11.07	10.85	11.7	11.7
Cep -121g	TIB	0.45	0.59	0.57	0.56	0.59	0.59
	DTZ	6.32	8.52	8.52	8.34	9.04	9.00
	TIB	0.36	0.45	0.43	0.42	0.45	0.45
Lanal2dz	TIB	0.44	0.59	0.56	0.55	0.59	0.59
	DTZ	6.08	8.33	7.86	7.27	8.07	7.85
	IOG	8.65	11.6	11.00	10.81	11.5	11.9
Method M, Compounds C							

The perturbation energies of donor-acceptor interaction of Natural Bonding Orbitals [NBOs] of TIB, DTZ, and IOG are given in **Table 5.**

Table 5. Second order perturbation theory analysis of the Fuck matrix in NBO basis in TIB, DTZ and IOG.

Gas	Donor (i)	ED(i)I	Acceptor (j)	Type	ED(j)I	E(2) kcal/mol	ε(j)-ε(i) (a.u.)	F(i,j) (a.u.)
TIB	LP3I1	1.93	C_5-C_6	π *	0.39	9.73	0.20	0.04

	LP3I2	1.93	C_7-C_8	π *	0.39	9.38	0.21	0.04
	LP3I3	1.93	C_4-C_9	π *	0.39	9.26	0.21	0.04
DTZ	LP3I1	1.93	C_{11} - C_{12}	π *	0.45	9.63	0.20	0.04
	LP3I2	1.90	C_{13} - C_{14}	π *	0.42	12.43	0.19	0.05
	LP3I3	1.90	C_{10} - C_{15}	π *	0.45	12.49	0.18	0.05
IOG	LP3I1	1.91	C_{21}-C_{22}	π *	0.42	11.52	0.20	0.05
	LP3I2	1.91	C_{20}-C_{24}	π *	0.43	11.77	0.19	0.05
	LP3I3	1.91	C_{23}-C_{25}	π *	0.41	11.92	0.19	0.05

The assignments of vibration spectra have been performed by reported FT-IR spectra based on the theoretical predicted wavenumber by density functional B3LYP method, and used the scale factor of 0.96 [7]. **Table 6** represents the optimization output of IR for DTZ compound and compared to the experimental results by Fawaz et al., 2015 [9].

Table 6. FT-IR spectra of diatrizoate DTZ at B3LYP/6-31G(d, p) method.

Excrement frequency (cm^{-1})	Frequency Unscaled (cm^{-1})	Frequency Scaled (cm^{-1})	intensity	description
3523.95	3638	3529	62	ν (OH) stretch
	3623	3515	60	ν (NH) stretch
	3142	3047	30	ν (CH_3) stretch
1645	1695	1644	310	ν (CO) stretch β (CH) bend β (NH) bend
1522	1568	1521	40	N (CC)Ring stretch ν (CH)bend β (NH)bend
1474	1514	1468	34	β (CH_3)bend
	1501	1456	103	β (CH_3)bend β (NH) bend
	1483	1438	295	ν (CN) stretch β (CH_3)bend β (NH) bend
	1478	1434	158	ν (CN) stretch β (CH_3)bend β (NH) bend
	1435	1391	118	β (CH_3)bend
1371	1397	1355	231	N (CC)Ring stretch β(CH)bend
	1261	1224	135	ν (CC)Ring stretch ν (CO) stretch β (OH) bend. β (NH) bend
1221	1258	1220	85	ν (CC)Ring stretch β (NH) bend ν (CN) stretch β (CH_3)bend
	1101	1068	284	ν (CC)Ring stretch β (OH)bend β (CH_3)bend
970	1006	976	35	ν (CC)Ring stretch β (CH_3)bend
723	733	711	30	ν (CC)Ring stretch β (CN)bend

608	634	615	56	ν (CC) stretch ν (CC)Ring stretch β(OH)bend
502	523	508	169	β (NH) bend β (CH_3)bend β (NH) bend

4. Discussion and Conclusion

As seen in **Table 1**, the energies of HOMO have negative values and they became more negative by substitution. For example, in B3LYP/cep-121g basis set energies were -7.04 eV for 2,4.6-triiodobenzene [TIB], -7.08 eV for diatrizoate [DTZ]. However, it was - 6.98 eV for ioxaglate [IOG], as an effect of two 2,4.6-triiodobenzen rings. Likewise, the energies of LUMO had negative values and they became more negative by substitution. For example, in the same basis set cep–121g the energy of 2,4.6-triiodobenzene was -2.39 eV; -2.50 and -2.68 eV for diatrizoate and ioxaglate, respectively. The same results were obtained when the title compounds were optimized in solution phases by using different solvents.

On **Table 2** change in energy gap values in the gas phase indicates that energy gaps decrease by substitution. For example, when title compounds in the gas phase were optimized by using B3LYP/cep -121g basis set, the energy gap of TIB was 4.64 eV and that value decreased to 4.58 and 4.21 eV for DTZ and IOG, respectively due to 1, 3 and 5 substitution. The same results were obtained when the title compounds were optimized in solution phases by using different solvents **Table 3**. For example, when the title compounds were optimized using B3LYP/cep-121g basis set, the energy gap decreased from 4.70 eV for TIB to 4.55 eV for IOG.

Table 2 (in gas phase) and **Table 3** (in water as a solvent) show that the electronegativity increased with substitution. For instance, when the title compounds were optimized using B3LYP/ cep-121g, the electronegativity of TIB was about 4.72 eV. This value increased to about 4.79 eV for DTZ and for IOG the value was not affected by the presence of two 2,4.6-triiodobenzene rings and it was 4.79 eV. Likewise, in case of solution phases, the electronegativity increased by substitution. For example, based on Table 3 (in water as a solvent), when the title compounds were optimized using B3LYP/ cep-121g, the electronegativity increased from 4.63 eV for TIB to 4.87 eV for DTZ and 4,83 eV for IOG which was affected by the presence of two 2,4.6-triiodobenzene rings.

We can note from **Table 2 and 3**, that the softness values were not affected so much by the substitution and the three title compounds had nearly similar values. For example, when the title compounds were optimized using B3LYP/cep-121g, TIB and DTZ had the same value of 0.22 eV^{-1} and IOG had 0.23 eV^{-1}.

Based on **Table 2** (in gas phase) and **Table 3** (in water as a solvent), the chemical potential μ electrophilicity index ω**,** nucleofugality ΔE_n and electrofugality ΔE_e of the title compounds increased with substitution. For example, the optimization of title compounds using B3LYP/cep-121g indicated that the chemical potential μ of TIB was -4.72 eV and it was recorded as -4.79 eV for both DTZ and IOG. The electrophilicity index ω was 4.79 eV for TIB and it was recorded as 5.02 and 5.4 eV for DTZ and IOG, respectively. Electrofugality ΔE_e was 10.67 for TIB and it was recorded 10.96 and 11.28 for DTZ and IOG, respectively. Nucleofugality ΔE_n showed increase from 1.23 eV for TIB to 1.71 for IOG.

Dipole moments as presented in **Table 4** show that dipole moment is directly proportional to the increasing of substitution units both in gas and solution phases. For example, in the gas phase, the dipole moment for TIB was 0.45 Debye when it was optimized by using B3LYP/cep-121g, and this value increased remarkably by substitution and became 6.32 Debye and 8.69 Debye for DTZ and IOG, respectively. The same results were obtained in all solution phases. For instance, in case of using the water as a solvent, when the title compounds were optimized by using the same basis set B3LYP/cep -121g, the dipole moment for TIB was 0.59 Debye and this value increased by substitution and became 8.52 Debye and 10.9 Debye for DTZ and IOG, respectively. We noted that the results values were similar for each compound by using different basis sets except cep-4g which gave different values.

Natural Bonding Orbitals [NBOs] calculation from **Table 5** shows that interaction energy linked to the resonance in the molecule electron-donating from lone pair LP 3I2 to π*(**C7-C8**) recorded stabilization energy 9.38 Kcal/mole and LP 3I3 to π*(**C4-C9**) recorded stabilization energy 9.26 Kcal/mole in TIB compound. This values increased by substitution, as in DTZ compound, LP 3I2 to π*(**C13-C14**) recorded stabilization energy of 12.43 Kcal/mole and LP 3I3 to π*(**C10-C15**) recorded stabilization energy of 12.9 Kcal/mole. In IOG compounds, LP 3I2 to π*(**C13-C14**) recorded stabilization energy of 11.77 Kcal/mole and LP 3I3 to π*(**C10-C15**) recorded stabilization energy of 11.92 Kcal/mole, indicating that these values are affected by the presence of two 2,4.6-triiodobenzene in this dimeric contrast compound.

Finally, the optimization output of IR considered for DTZ compound was presented in **Table 6** and the characteristic vibrations were affected by the effects of induction and resonance of the aromatic structural fragment in these molecules. For example, The O-H stretching vibrations lie in the 3200-3500 cm^{-1} regions [7]. In the title compound, it appeared at 3529 cm^{-1} and it was in agreement with the experimental results recorded at 3524 cm^{-1}[9]. The carbonyl stretching vibrations of C=O lie in 1740–1810 cm^{-1} region and It is well known that if carboxyl groups form hydrogen bonds with water molecules or other polar groups then the vibrational frequency of the C=O bond can decrease considerably [10]. In the title compounds, the carbonyl stretching vibrations of C=O was observed in 1644 cm^{-1}, and it was in agreement with the experimental results recorded at 1645 cm^{-1}[9]. The C-C ring stretching vibrations lie in the 1430-1625 cm^{-1} region [7]. In the title compound, it appeared at 1521 cm^{-1}, and it was in agreement with the experimental results recorded at 1522 cm^{-1} [9]. The C-N stretching vibrations lie in the 1020-1250 cm^{-1} and 1266-1342 cm^{-1} region [11]. In the title compound, it appeared at 1220 cm^{-1}, and it was in agreement with the experimental results recorded at 1221 cm^{-1}[9].

Through the optimization of 2,4.6-triiodobenzene, diatrizoate, ioxaglate contrast agents by using Lee-Yang-Parr correlation functional (B3LYP), gradient corrected DFT with Beck's three-parameter hybrid exchange function, and with the B3LYP metho, our calculations show that the values of energy gaps between HOMO and LUMO in the title compounds increased by substitution and were affected by presence of two 2,4.6-triiodobenzene rings in case of IOG compound.

These changes led to alteration of other energy gap dependent values such as chemical potential, electronegativity, chemical hardness, electrophilicity index and dipole moment.

Based on a second-order perturbation treatment of the Fuck matrix in the NBO basis, the interaction energies linked to the resonance in the molecules showed that the electron-donating from lone pairs in title compounds increased by substitution.

Finally, from IR spectra of DTZ compound, the results were in excellent agreement with experiment results. Quantum chemical calculations have long-established great interest in finding ways to reliably and accurately predict the molecular and electronic properties of the compounds especially drug compounds to investigate any side effect or drug-drug interactions and additionally to predict potential new drugs.

References

[1] Correas, J. M., Bridal, L., Lesavre, A., Méjean, A., Claudon, M., & Hélénon, O. 2001. Ultrasound contrast agents: properties, principles of action, tolerance, and artefacts. European radiology, 11(8), 1316-1328.

[2] Spampinato M. V., Abid A., Matheus M. G. 2017. Current Radiographic Iodinated Contrast Agents magnetic resonance imaging. Clinics of North America, 25(4), 697-704.

[3] Buschur, M., & Aspelin, P. 2014. Contrast media: history and chemical properties. Interventional Cardiology Clinics, 3(3), 333-339

[4] Gurm, H. S. 2014.Renal Complications in the Catheterization Laboratory, An Issue of Interventional Cardiology Clinics, E-Book l. 3, No. 3. Elsevier Health Sciences.

[5] Singh, J., & Daftary, A. 2008. Iodinated contrast media and their adverse reactions. Journal of nuclear medicine technology, 36(2), 69-74.

[6] Gangadharan, R. P., & Krishnan, S., S. 2014. Natural Bond Orbital (NBO) Population Analysis of 1-Azanapthalene-8-ol. Acta Physica Polonica, A., 125(1).

[7] Sebastian, S., Sylvestre, S., Sundaraganesan, N., Amalanathan, M., Ayyapan, S., Oudayakumar, K., &

Karthikeyan, B. 2013. Vibrational spectra, molecular structure, natural bond orbital, first order hyperpolarizability, TD-DFT and thermodynamic analysis of 4-amino-3-hydroxy-1-naphthalenesulfonic acid by DFT approach. Spectrochimica Acta Part A: Molecular and Biomolecular Spectroscopy, 107, 167-178

[8] Sharma, P., Kumar, A., Singh, J., & Sahu, V. 2009. Theoretical evaluation of the global and local electrophilicity patterns to characterize hetero diels-alder cycloaddition in the synthesis of isoxazolo [4, 5-e](1, 2, 3, 4-tetrazine). Chinese Journal of Chemistry, 27(5), 868-876.

[9] El-Rahman, M. K. A., Riad, S. M., Gawad, S. A. A., Fawaz, E. M., & Shehata, M. A. 2015. Stability indicating spectrophotometric and spectrodensitometric methods for the determination of diatrizoate sodium in presence of its degradation product. Spectrochimica Acta Part A: Molecular and Biomolecular Spectroscopy, (136), 1167-1174.

[10] Fuente, E., Menéndez, J. A., Diez, M. A., Suarez, D., & Montes-Morán, M., A. 2003. Infrared spectroscopy of carbon materials: a quantum chemical study of model compounds. The Journal of Physical Chemistry B, 107(26), 6350-6359.

[11] Wei, L., Yang, X., Gao, Z. Q., Wang, D. Q., Xue, J. Q., Yang, W. J., .& Liu, Y. 2015. Oxovanadium (IV) schiff base complex derived from phenylalanine analogue containing 2, 3-diaminopropionic acid (DAP): synthesis, computational study, and biological evaluation. Synthesis and Reactivity in Inorganic, Metal-Organic, and Nano-Metal Chemistry, 45(3), 455-467.