Research Paper

A comparison of Electronic Properties of Ionic versus Nonionic Contrast Media

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ABSTRACT: *The energetic behavior and dipole moment of diatrizoate (DTZ) as ionic contrast media and iohexol (IHX) as nonionic contrast media (IDX) were calculated based on the optimization of the both compounds in the gas phase and in solution phases using Lee-Yang-Parr correlation functional B3LYP/6+311G (d, p) and gradient corrected DFT the basis sets (cep 4g, cep121g). The energy gap between high occupied molecular orbital (HOMO) and the low unoccupied molecular orbital (LUMO), electrophilicity index, dipole moment, chemical softness and chemical hardness has been calculated in order to compare the molecular electrical transport properties of the two compounds as ionic and nonionic contrast media.*
KEYWORDS: *contrast agent, diatrizoate, iohexol, ionic, correlation functional*

I.   INTRODUCTION

The contrast agents that use today are all based on 2, 4, 6-tri-iodinated benzene ring Figure1 and were known as Iodinated contrast agents [1]
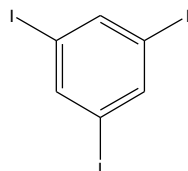

Figure. 1. 2,4,6-triiodobenzene(TIB) chemical structure.

Iodinated contrast agents can exist as monomers (single tri-iodinated benzene ring) or dimers (2 tri-iodinated benzene rings linked together by an organic functional group) [2]. In addition iodinated contrast agents can exist as ionic contrast agents which dissociates into negative and positive ions such as diatrizoate (DTZ) one of title compounds Figure 2. It is water .soluble molecule generated by used a second acetyl- amino group and added it to triiodide benzene ring) [3].
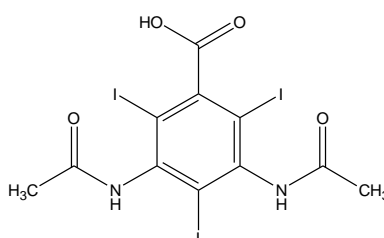

Figure 2. Diatrizoate structure.

It is a high-osmolar ionic monomer have an osmolality greater than that of blood and have been connected with high risk of adverse reactions) [4].

The second generation of contrast compounds were developed were non-ionic monomer compounds. These agents include iohexol (IHX) (omnipaque), one of our title compounds Figure 3 which are low molecular weight molecule, water-soluble that do not ionizate in a solution, resulting in low osmolality [5].
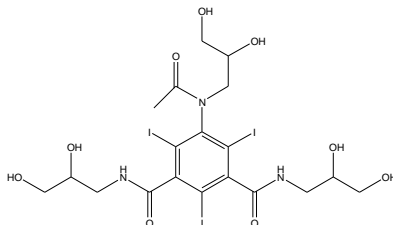

Figure 3. Iohexol chemical structure.

this study The optimization of diatrizoate and iohexol contrast agents were done in order to compare the energetic behavior and dipole moment of these two contrast compounds in the gas phase and in solution phases by using [water, ethanol, chloroform, acetic acid] as solvents. The energy gap between High Occupied Molecular Orbitals HOMO and Law Unoccupied Molecular Orbitals LUMO, chemical hardness, chemical softness, electro-negativity, electrophilicity index and dipole moment have been calculated for the two title compounds with B3LYP/cep-4g, B3LYP/121g. The values of energy gaps between HOMO and LOMO in the tittle compounds were effected by kind of compound ionic or nonionic. These changes in HOMO and LOMO led to change in the other values of energy gap dependent.

II.   METHOD AND COMPUTATION

The optimized molecular structure of the title compounds diatrizoate DTZ as ionic compound and iohxaol IHX as nonionic compound were calculated at B3LYP/6-311+G(d,p) level and were given in Fig 4,5 respectivly

Figure .4 the optimized molecular structure of diatrizoate molecule as ionic compound.
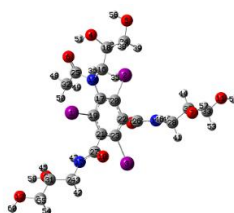

Figure .5. The optimized molecular structure of iohxaol molecule as nonionic compound.

Molecular properties, related to HOMO and LUMO including the chemical hardness (η), chemical softness (s), electronegativity (χ), chemical potential (μ), electrophilicity index (ω) and nucleofugality ΔE_n, electrofugality ΔE_e were calculated.

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

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

From electronegativity, chemical potential estimated that it is the negative value of electronegativity.

$$\mu = -\chi \tag{2}$$

$$\mu = \frac{1}{2}(E_{HOMO} + E_{LUMO}) \tag{3}$$

The finite difference approximation to chemical hardness gives,

$$\eta = \frac{1}{2}(E_{LUMO} - E_{HOMO}) = \frac{1}{2}(I - A) \tag{4}$$

Where hardness is a half of the energy gap between HOMO and LUMO. The softness then can be calculated from hardness that from Hard Soft Acid Base (HSAB) Principle:

$$S = \frac{1}{2\eta} \tag{5}$$

Electrophilicity index (ω) and nucleofugality ΔEn, electrofugalityΔEe can be calculated from chemical potential μ and the hardness η by the following relationships respectively [6].

$$\omega = \frac{\mu^2}{2\eta} \tag{6}$$

$$\Delta En = \frac{(\mu + \eta)^2}{2\eta} \tag{7}$$

$$\Delta Ee = \frac{(\mu - \eta)2}{2\eta} \tag{8}$$

III.   RESULTS AND DISCUSSION

3.1 HOMO-LUMO ENERGY CALCULATIONS energy calculations.

The surfaces of HOMO and LUMO the two title molecules were drawn and given in Figure 6 to understand the bonding scheme of contrast agents diatrizoate and iohexol.
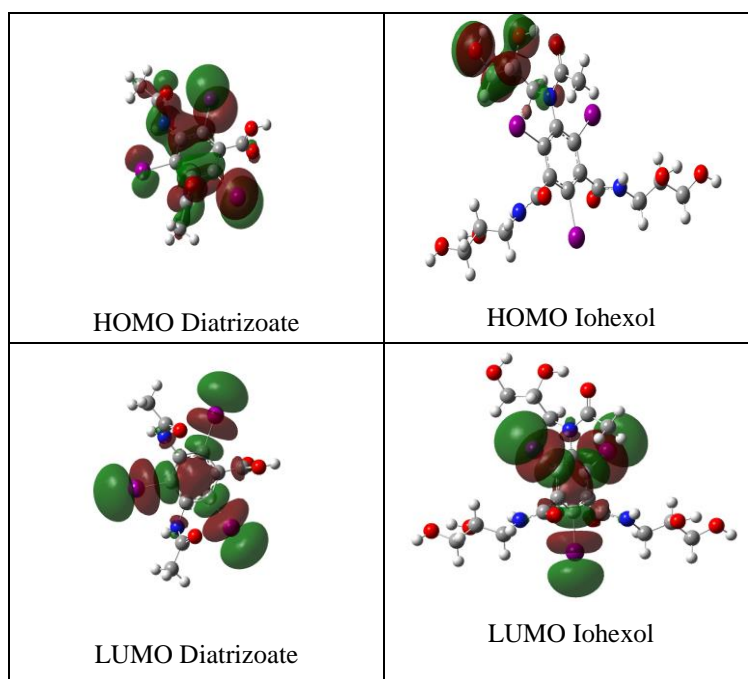

| HOMO Diatrizoate | HOMO Iohexol |
| LUMO Diatrizoate | LUMO Iohexol |

Figure 6. The surfaces of HOMO and LUMO the two title molecules

The energy of HOMO and LUMO of the two compounds, diatrizoate DTZ as ionic contrast agent and iohexol IHX as nonionic contrast agent were calculated using density function theory with cep-4g and cep-21g basis sets in gas phase and were listed in Table 1.

Table 1. The energies of HOMO, LUMO of diatrizoate (DTZ) and iohexol (IHX) in the gas phase using DFT method with basis set (B3LYP/cep-4g and B3LYP/cep-121g)

DFT Method	Gas phase	LUMO(eV)	HOMO(eV)
cep-4g	DTZ	-2.69	-7.00
	IHX	-2.83	-6.00
cep-121g	DTZ	-2.50	-7.08
	IHX	-2.59	-6.92

As seen in Table1, the energies of HOMO have negative values and they became more negative (decreased) by ionization. For example; in B3LYP/cep-121g method the energy of IHX as nonionic contrast agent was -6.00 eV, that value became more negative for DTZ, as ionic contrast agent, it recorded -7.00 eV. On the other hand the energies of LUMO had negative values and they became less negative by ionization. For example; in the same method B3LYP/cep-121g the energy of IHX as nonionic contrast agent was -2.83eV, that value became less negative for DTZ as ionic contrast agent, it recorded -2.69eV.

These changes in HOMO, LUMO energy by ionization effected on HOMO-LUMO energy gaps. Therefore, to assess the agreement of the present results, the HOMO-LUMO gaps were calculated directly as the difference in HOMO and LUMO values in gas phase and in different six solvents, water, ethanol, chloroform, acetic acid using the DFT method with cep-4g, and cep121g basis sets. The results were reported in Table 2.

Table2. The HOMO-LUMO gaps of diatrizoate (DTZ) as ionic contrast agent and iohexol (IHX) as nonionic contrast agent in gas phase and in   different solvents using the DFT functional theory with cep-4g and cep-21g basis sets

Basis sets	Solvents	DTZ $\Delta E(eV)$	IHX $\Delta E(eV)$
Cep-4g	gas	4.31	3.17
	water	4.33	3.64
	ethanol	4.33	3.63
	chloroform	4.35	3.54
	Acetic acid	4.34	3.56
	DMF	4.33	3.64
Cep-121g	gas	4.58	4.33
	water	4.77	4.63
	ethanol	4.77	4.62
	chloroform	4.75	4.60
	Acetic acid	4.76	4.61
	DMF	4.77	4.63

As it appeared in Table 2 the values of HOMO-LUMO energy gap in gas phase and in solution phases for ionic contrast agent DTZ were more than nonionic contrast agent IHX. For example, HOMO-LUMO energy gap values for ionic contrast agent DTZ in gas phase with cep-4g, recorded 4.31 eV but for nonionic contrast agent IHX, it recorded only 3.17 eV.

These results indicated that the ionic contrast agent DTZ was more stable than the nonionic compound IHX depending on the truth that indicates that the stability increasing by increasing the HOMO-LUMO energy gap values [7]. On the other hand, from the same Table 3, one can note that the nonionic contrast agent IHX recorded notable increasing in energy gap by solvation in the all solvents in compare to the ionic contrast agent DTZ. For example, HOMO-LUMO energy gap values for ionic contrast agent DTZ with cep-4g increased by only about 0.02 eV by solvation in water, but for nonionic contrast agent IHX, HOMO-LUMO energy gap values increased by about 0.47 eV by solvation in water.

3.2 Electrochemical properties calculation

The chemical calculations of electronic properties of diatrizoate (DTZ) as ionic contrast agent and iohexol (IHX) as nonionic contrast agent in the gas phase and in the different solvents using the DFT with cep-4g and cep-21g basis sets were calculated and listed in Table 3 and Table 4 respectively.

From Tables 3, 4 by using cep-4g and cep-121g basis sets with DFT method in gas phase and in solution phases, the electronegativity χ appeared more negative for ionic contrast agent DTZ than nonionic contrast agent IHX, For example when DFT /cep-4g was used in gas phase, the electronegativity values for DTZ recorded -4.65 eV where for IHX, it recorded -4.54 eV. In solution phases it can note that the electronegativity χ became more negative (decreased) by solvation for the both compounds.

These effects on the electronegativity values led to effect on the chemical potential which recorded more values for ionic contrast agent DTZ than nonionic contrast agent IHX.

Table 3. The chemical calculation of electronic properties of diatrizoate (DTZ) and iohexol (IHX) in the gas phase and in the different solvents using the DFT with cep-4g basis sets

Cep-4g		Electronic properties						
solvent	compound	χ (eV)	η(eV)	s(eV)$^{-1}$	μ(eV)	ω(eV)	E_n(eV)	E_e(eV)
Gas	DTZ	-4.65	2.36	0.21	4.65	4.58	10.41	1.11
	IHX	-4.54	2.17	0.23	4.54	4.74	10.36	1.29
Water	DTZ	-5.13	2.16	0.23	5.13	6.08	12.29	2.03
	IHX	-4.74	1.82	0.27	4.74	6.18	11.84	2.35
Ethanol	DTZ	-5.12	2.16	0.23	5.12	6.05	12.25	2.01
	IHX	-4.73	1.81	0.28	4.73	6.18	11.82	2.35
chloroform	DTZ	-5.05	2.17	0.23	5.05	5.87	12.00	1.90
	IHX	-4.67	1.77	0.28	4.67	6.16	11.71	2.38
Acetic acid	DTZ	-5.07	2.17	0.23	5.07	5.92	12.07	1.93
	IHX	-4.69	1.78	0.28	4.69	6.16	11.74	2.37

Table 4. The chemical calculation of diatrizoate (DTZ) and iohexol (IHX) in the gas phase and in the different solvents using the DFT with cep-121g basis set

Cep-121g		Electronic properties						
solvent	compound	χ (eV)	η(eV)	s(eV)$^{-1}$	μ(eV)	ω(eV)	E$_n$(eV)	E$_e$(eV)
Gas	DTZ	-4.79	2.29	0.22	4.79	5.02	10.96	1.37
	IHX	-4.75	2.17	0.23	4.75	5.21	11.05	1.54
Water	DTZ	-4.87	2.39	0.21	4.87	4.96	11.02	1.29
	IHX	-4.85	2.31	0.22	4.85	5.08	11.09	1.39
Ethanol	DTZ	-4.86	2.38	0.21	4.86	4.96	11.02	1.29
	IHX	-4.85	2.31	0.22	4.85	5.09	11.09	1.39
chloroform	DTZ	-4.86	2.38	0.21	4.86	4.96	11.01	1.30
	IHX	-4.85	2.30	0.22	4.85	5.11	11.11	1.41
Acetic acid	DTZ	-4.86	2.38	0.21	4.86	4.96	11.01	1.29
	IHX	-4.85	2.30	0.22	4.85	5.10	11.11	1.41
DMF	DTZ	-4.86	2.38	0.21	4.86	4.96	11.02	1.29
-4.85	IHX	-4.85	2.31	0.22	4.85	5.09	11.09	1.39

From Tables 3, 4 by using different basis sets (cep 4g, ep-121g) with DFT method in gas phase and solution phases, the chemical potential values for ionic contrast agent DTZ was greater than nonionic contrast agent IHX in both basis sets. For example when cep-4g was used in gas phase, the chemical potential value for ionic compound DTZ recorded 4.65 eV, this value of chemical potential decreased for nonionic compound IHX to recorded 4.54 eV.

From the same Tables 3, 4 it was clear that both compounds recorded increasing in the chemical potential values by solvation in all different solvents used and they did not effect by the type of solvent except in chloroform and acetic acid solvents.

The dipole moment of diatrizoate (DTZ) and iohexol (IHX) at B3LYP/6-31G (d, p) method with (Cep-4g, Cep-21g) basis sets in the gas phase and in the different solvents are recorded and listed in Table 5

Table 5. Dipole moment of diatrizoate (DTZ) and iohexol (IHX) at B3LYP/6-31G (d, p) method with (Cep-4g, Cep-21g) basis sets in the gas phase and in the different solvents.

DFT	Dipole moment (Debye)						
Basis sets	compound	Gas	water	Acetic acid	Ethanol	Chloroform	DMF
Cep-4g	DTZ	6.7982	9.0575	8.6180	8.9713	8.4738	9.0129
	IHX	9.8661	11.7428	11.4208	11.6959	11.3225	11.7203
Cep-21g	DTZ	6.2536	8.8016	8.3434	8.7280	8.1799	8.7673
	IHX	9.9534	11.8064	11.5208	11.7544	11.4165	11.7797

From Table 5, one can note that the dipole moment values of ionic compound DTZ is less than the dipole moment values of nonionic compound IHX in gas phase and in all different solution phases by using DFT methods with both basis sets (cep 4g and cep-121g). Fore instant when DFT/cep-4g was used in the gas phase the dipole moment value for DTZ as ionic compound was 6.7982 Debye this value increased for IHX as nonionic compound to recorded 9.8661 Debye. From the same Tables 5, it can note either that the dipole moment values increased by solvation for both title compounds and they recorded the highest values in water as a solvent with both used basis sets. For example, when DFT/cep-21g used in gas phase the dipole moment

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values of DTZ and IHX was 6.2536 Debye, 9.9534Debye respectively, these values were increased by solvation to record the highest values in water as a solvent 8.8016 Debye, 11.8064 Debye for DTZ and IHX respectively.

IV. CONCLUSION

Through The optimization of diatrizoate as ionic contrast agent and iohexol as nonionic contrast agent by using Lee-Yang-Parr correlation functional (B3LYP) and gradient corrected DFT with cep-4g, and cep-121g basis sets, our calculations indicate that the values of HOMO-LUMO energy gap in gas phase and in solution phases for contrast agents increase by ionization and became more stable that ionic contrast agent DTZ has more HOMO-LUMO energy gap than nonionic contrast agent IHX.

The HOMO-LUMO energy gap values of the derivatives recorded increasing by solvation in all solvents by using of all basis sets with both methods DFT and RHF and these increasing did not effect by the type of solvents except in case of acetic acid and chloroform and it was suggested that this is due to the low of dielectric constant of acetic acid and chloroform (6.2, 4.8) comparing to the other solvents which is (47, 38, 25) for DMSO, DMF and ethanol respectively [8]. This change in The HOMO-LUMO energy gap led to change in the other energy gap dependent values such as electronegativity values which by substitution and solvation, they became more negative led to increasing in chemical potential values for all compounds, Electrophilicity index, and nucleofugality ΔE_n values increased for all compounds in all the types of solvents by all used basis sets with both methods DFT, RHF and it did not effect by the type of solvent only in case of chloroform and acetic acid. In contrast electrofugality ΔE_e values recorded decreasing by sustitution and by solvation and there was no effect of type of a solvent in all solutions except chloroform and acetic acid.

Therefore, we can conclude that water ethanol DMF and DMSO are different on chloroform and the acetic acid solvent and this is in a good agreement with Smiatek1, Wohlfarth and Holm who concluded that the DMSO and water are good solvents whereas chloroform can be represent as a poor solvent [9].

We concluded either that the hardness values have direct relationship with the HOMO-LUMO energy gape values changes by substitution or by solvation and that is in a good agreement with the fact which indicate that the hardness values of the molecule increased if the HOMO-LUMO energy gape values increased. Theoretically calculated values of the dipole moment indicated that by substitution and by solvation the dipole moment values of substitution molecules form DTZ, IOG, IHX and IDX were appreciably higher than TIB molecule form

the perturbation energy of donor-acceptor interaction, the perturbation energy of donor-acceptor interaction of the bonds on TIB benzene ring and the comparable bonds on benzene ring of its derivatives in different solvents using DFT with cep- 121g basis sets show intensive effect on the stabilization energies of these bond by substitution and by solvation. Finally from IR spectra of DTZ compound, the results were in excellent agreement with experiment results [10].

So the quantum chemical calculation have long established great interest in finding ways to reliable and accurately predict the molecular and electronic properties of the compounds.

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