Chapter

DFT Study on Interaction of Estrone and Imidazolium-Based Hydrophobic Ionic Liquids

Sai Saravanan Ambi Venkataramanan and Ramalingam Anantharaj

Abstract

Affinity of estrone on imidazolium-based hydrophobic ionic liquids was computed at the B3LYP/6-31G(d) level. Columbian interactions and other closed-shell interactions, in general, were observed to be pivotal to the binding of the EDC species on visualizing the optimized structures as well as probing the proximity of electronegative and electropositive groups between estrone and ionic liquids. The interaction strength was also studied using calculation of binding energy values of each system. $[BMIM]^+[PF6]^-$ was found to be the most binding ionic liquid. Estrone was found to be highly bonded in the vicinity of $[PF6]^-$ species with a binding energy of −9.57 kcal/mol. The Ionic Liquids under study, $[BMIM]^+[NTF2]^-$ and $[BMIM]^+[BF4]^-$, also illustrated promising binding nature with binding energies of −7.63 and −8.61 kcal/mol. AIM analysis was carried out to validate the nature of intermolecular interactions by calculating the topological properties at (3,−1) bond critical points.

Keywords: DFT, endocrine disrupting compounds, computational quantum chemistry, molecular interaction

1. Introduction

Chemical substances that inhibit the reception sites in endocrine systems in our body are collectively termed as endocrine-disrupting compounds (EDCs). These carcinogens are proliferating in large quantities in all forms of water media, ranging from domestic water to ocean streams [1]. Although these contaminations are extremely minimal in quantity, such as in the order of ppm, these prove to be a significant competitive inhibitor and obstruct the transmission of endocrine hormones to certain parts of our bodies leading to a diverse array of problems, including development of cancerous tissues and abnormal change in sexual orientation of a person altogether. Recent research works in the domain of wastewater treatment have shed some light on this issue stating that most wastewater discharge plants and sewage treatment plants currently being operated in the industry are also affected by exposure to EDCs [2].

Ionic liquids have been reported as novel green solvents in various domains ranging from catalysis [3] to extraction [4], owing to its ease in screening of these solvents by subtle manipulation of thermodynamic variables. A review publication by Tomasi et al. [5] presents a theoretical study of quantum mechanical continuum solvation models which is developed to overcome computational costs which attribute via explicit introduction of solvent molecules over the solute phase. Multiple articles have been presented using hydrophobic ionic liquids and DES for extraction of potential endocrine descriptors such as diethylstilbestrol, bisphenol-A, and dichlorodiphenyltrichloroethane (DDT) [6]. However, less emphasis is shed toward compounds such as estrone and other estrogen-based endocrine-disrupting compounds, in general.

Ab initio-based quantum chemistry methods attempt to solve the Schrödinger equation to extract intricate details such as electron distribution, underlying molecular interaction, as well as reactivity in a proposed virtual environment. Recent advancements in computational facilities have paved way to run these simulations in a much faster means and have also enabled theoretical chemists to solve a range of problems in disciplines ranging from spectroscopy [7] to solvent extraction [8]. In this work, we use ab initio calculations using benchmarked computational procedures to study the interacting behavior of estrone and ionic liquids such as $[BMIM]^+[NTF2]^-$, $[BMIM]^+[PF6]^-$, and $[BMIM]^+[BF4]^-$. This study is meant to be a primer for understanding the affinity of estrone so as to theoretically validate if the solvent is a potential extractor when commercially employed in standard liquid-liquid extraction procedures.

2. Computational section

2.1 Overview of computational quantum chemistry

Density functional theory (DFT) is one of the most commonly employed methods to solve Schrödinger's equation by proposing a few justifiable approximations. In contradiction to the wave function methods used earlier, this method is the perfect adaptation for solving large systems involving a huge network of atoms and molecules. Since many rudimentary terms are overlapping in both the methods, the most primitive Hartree-Fock (HF) theory is used to explain the terms in a more elegant manner.

The energy computed from this method will take into account the potential energy of electrons and nuclei based on the relative positions with respect to each other as well as the average kinetic energy of electrons in every orbital. Assuming Born-Oppenheimer approximation, the relative velocity of nuclei is considered insignificant and so does its contribution in the kinetic energy of the system. The columbic interaction of electrons with respect to each other is brought about by assuming a mean field wherein each electron interacts with the averaged field of all the other electrons.

Kohn and Sham's work, in particular, attracted many researchers working in the field of DFT as they attempted to use the standard self-consistent field method to obtain the exchange-correlation energies as well apart from the basic Columbian energies obtained from HF theory [9]. Therefore, owing to their contribution, DFT is also colloquially referred to as Kohn-Sham (KS) formalism. Perdew et al. [10] proposed the advancements in the field of DFT functionals to that of a ladder, where every step leads to a better approximation and, hence, accuracy. The drawback of DFT method is that it can be used only for ground state computations as well as does not, by itself, reveal a detailed picture of electronic distribution owing to which, the optimized structure may not show any key resemblance when compared with other higher accurate methods. However, HF assumes linear combination of atomic orbital (LCAO) which helps to elucidate primitive picture of electrons in the molecule and, hence, can be used as an input for the method of higher accuracy, such as the configuration interaction method, which are collectively termed as post-HF methods.

DFT methods used in the present scenario describe the changes in total energy of the system, via exchange and correlation of electrons and electrons and nuclei using hybrid functionals. These sets of mathematical functions utilize a subset of exact exchange from HF, while the remaining uses predefined functions from each individual pure functional [11]. The most commonly used hybrid functional, obtained as a result of this implementation, is the B3LYP hybrid functional. As for the basis is concerned, standard 6-31G(d) basis set is invoked though higher accurate ECP sets are available [12] simply due to the fact that various literature studies in ionic liquids akin to that of ours have obtained better results using this model chemistry in conjunction with B3LYP.

2.2 Computational details and methodology

The interacting monomers, namely, estrone and each of the three ionic liquids $[BMIM]^+[NTF2]^-$, $[BMIM]^+[PF6]^-$, and $[BMIM]^+[BF4]^-$, were constructed using Gaussview6 [13] and were optimized separately at the B3LYP/6-31G(d) level using Gaussian16 program [14] to find the corresponding geometry and energy at the ground state. Since all the bonding parameters of the monomers are unknown, none of them were restricted under optimization.

The estrone is then introduced selectively to various regions in the vicinity of the ionic liquid such as near the electropositive and electronegative moieties, the imidazolium ring, and the cation and anion groups of ionic liquid to search for all possible interaction sites of the EDC. All these optimized systems can be visualized as various minima in the potential energy surface (PES), and only the properties and structure corresponding to the global minimum are presented for discussion.

The absence of imaginary frequencies at all optimized ground states justified that the proposed geometry is a minimum in the PES and not a transition state (TS) intermediate.

The keyword “output = wfn” is invoked along with the default settings to create. wfn extension file which is then used in multiwfn package to calculate topological properties at all bond critical points.

3. Results and discussion

3.1 Optimized structures of the complex at the B3LYP/6-31G(d) level

Optimized structures of estrone/ionic liquid complexes are depicted in **Figure 1**. Estrone was found closer to the anion species, especially just near the electronegative atoms having most negative partial charges in all the three cases. For instance, in the case of $[BMIM]^+[NTF2]^-$ and estrone, apart from O—H and F—H interactions which are visible from the proximity of the groups at the optimized structure, it can be seen that there is a substantial difference in the partial atomic charges of S(1.125e) and C(−0.394e) at one end followed by partial atomic charges 0.6e and −0.49e on the carbon-bearing fluoride and hydrogen atoms on $[NTF2]^-$ and estrone, respectively. While in the other case such as $[BMIM]^+[BF4]^-$ and estrone, the vicinity of the bromine and fluoride is not justified by oppositely polarized moieties in estrone, however, also not indicative of an open-shell or covalent interaction as well simply because all the outer shell electrons of the atoms involved

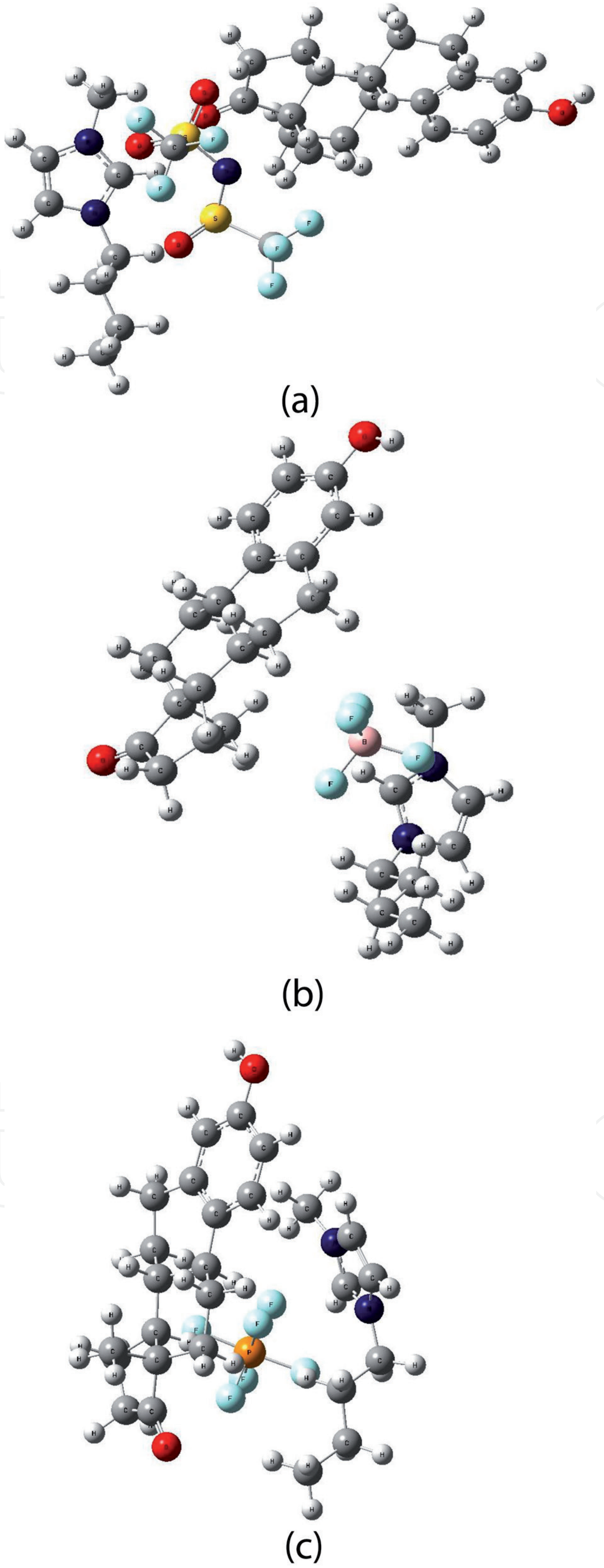

Figure 1.
Optimized structures of [BMIM]$^+$[NTF2]$^-$ and estrone (a), [BMIM]$^+$[BF4]$^-$ and estrone (b), and [BMIM]$^+$[PF6]$^-$ and estrone (c) complexes at the B3LYP/6-31G(d) level.

are already satisfied while, at the same time, not providing any window of opportunity for extending the coordination due to the absence of d-type orbitals in their individual atomic structure. These results suggest that electrostatic interactions and other closed-shell interactions between atoms of complimentary polarities are predominant when compared to the effects of covalent interactions and π cloud effects contributed via imidazolium ring.

3.2 Interaction energy calculations

The schematic representation for complex formation is given by Eq. (1):

$$A + B \rightarrow A \cdots B \tag{1}$$

in which A, B, and A···B represent the estrone, ionic liquid, and estrone/ionic liquid complex, respectively.

Interaction energy calculations give a numerical estimate of the ability of the EDC to interact with the ionic liquid by means of chemisorptions occurring at the molecular level. These values are determined by Eq. (2):

$$\Delta E_{\boldsymbol{int}} = E_{A \cdots B} - [E_A + E_B] \tag{2}$$

These interaction energy values are tabulated in **Table 1**. It is to be noted that the values presented here include the zero-point correction.

Negative values indicate good interaction behavior of estrone in the presence of the ionic liquid. In comparison, it can be seen that $[BMIM]^+[PF6]^-$ and estrone system bind the complex with stronger interaction strength contributing to the highest negative binding energy of −9.57 kcal/mol.

Model chemistry: B3LYP/6-31G*

Molecule/system	**Total electronic energy (Hartrees)**	**System**	**Interaction energy**	
			(Hartrees)	**(kcal/mol)**
$[BMIM]^+[NTF2]^-$	−2250.231194	$[BMIM]^+[NTF2]^-$ and estrone	−0.012152	−7.63
Estrone	−849.256955	$[BMIM]^+[PF6]^-$ and estrone	−0.015246	−9.57
$[BMIM]^+[PF6]^-$	−1363.714993	$[BMIM]^+[BF4]^-$ and estrone	−0.013718	−8.61
$[BMIM]^+[NTF2]^-$ and estrone	−3099.500301			
$[BMIM]^+[PF6]^-$ and estrone	−2212.987194			
$[BMIM]^+[BF4]^-$	−847.587891			
$[BMIM]^+[BF4]^-$ and estrone	−1696.858564			

Total electronic energy of various species in Hartrees is also provided for reference, all results obtained at the B3LYP/6-31G(d) level.
**Denotes addition of (d) polarizable function to the 6-31G Basis set.*

Table 1.
Interaction energy of various estrone/ionic liquid systems in Hartrees and kcal/mol.

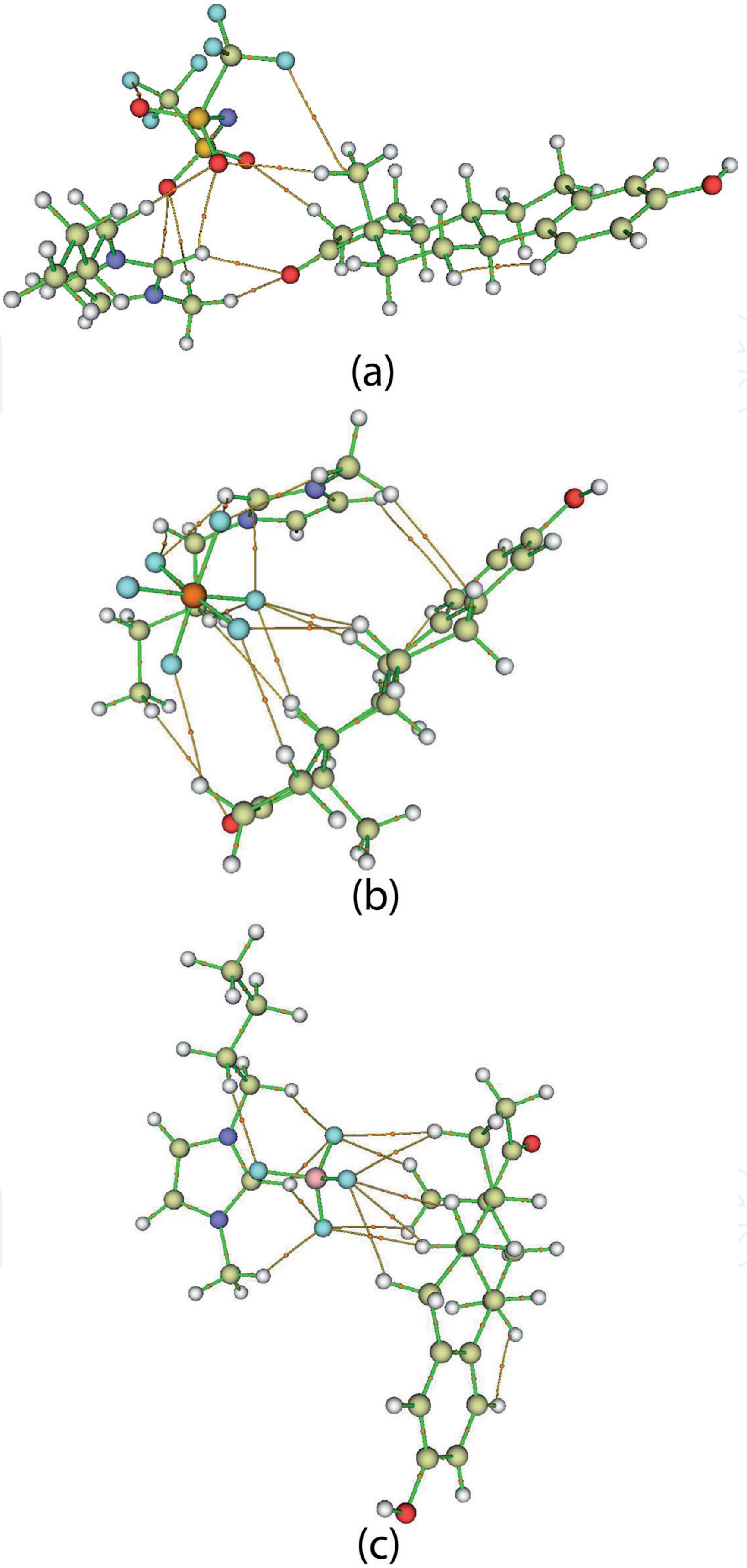

Figure 2.
Optimized structures of [BMIM]$^+$[NTF2]$^-$ and estrone (a), [BMIM]$^+$[PF6]$^-$ and estrone (b), and [BMIM]$^+$[BF4]$^-$ and estrone (c) complexes at the B3LYP/6-31G(d) level containing (3, −1) bond critical points (in orange). Color code: white, hydrogen; red, oxygen; yellow, carbon; royal blue, nitrogen; light blue, fluorine; pink, boron; brown, phosphorous; and dark yellow, sulfur; orange, (3, −1) bond critical point.

3.3 Atoms in molecule (AIM) analysis

(3,−1) Bond critical points (BCPs) obtained from atoms in molecule (AIM) analysis are presented as the representation index of the electronic interaction and distribution between a given bond pair in this study. Multiwfn software is used to calculate the topological properties of bond critical points and perform complete AIM analysis [9]. **Figure 2** gives a visual representation of (3,−1) BCPs of estrone/ionic liquid complexes. Previous literature studies proposed that the non-covalent interacting nature can alternatively be described by examining the ratio of Lagrangian kinetic energy ($G(r_c)$) and potential energy density ($V(r_c)$) given by [$-G(r_c)/V(r_c)$] [15]. The aforementioned ratio at (3,−1) bond critical points is used to determine the nature of interactions.

This topological study is used as a validation tool to justify the proximity of estrone in various cases. Firstly, on introduction of $[BMIM]^+[NTF2]^-$, we can see multiple hydrogen-bonded interactions with O and F atoms, evident with the discussion provided in the first section. Since these are hydrogen-bonded interactions and, hence, clearly non-covalent, other interactions such as the C—F interaction between estrone carbon and F atom on $[NTF2]^-$ are investigated. At this intermolecular critical point, we have $G(r_c)$ and $V(r_c)$ values of 0.003604 and −0.002431, respectively, clearly having a ratio greater than 1. In the second case, pertaining to $[BMIM]^+[PF6]^-$, akin to the first case, most interactions are hydrogen-bonded interactions apart from the C-H interactions between the cation of the ionic liquid and hydrogen of the EDC. The two critical points obtained bear $G(r_c)$ and $V(r_c)$ values of 0.002434, 0.002517 and −0.001707, −0.001741, respectively. In the case of $[BMIM]^+[BF4]^-$, all intermolecular interactions are F-bonded interactions which simply arise out of difference in electronegativities and, hence, are completely non-covalent interactions.

Moreover, all interactions were found to have positive Laplacian of electron density at the intermolecular critical points (in the range of $0.01 e\text{Å}^{-5}$), which suggests closed-shell interaction nature. All the three cases reveal that intermolecular interactions are completely non-covalent in nature in conjunction with the observation made on assessing the optimized structure.

4. Conclusions

The interaction behavior of (1:1) estrone and imidazolium-based hydrophobic ionic liquids such as $[BMIM]^+[NTF2]^-$, $[BMIM]^+[PF6]^-$, and $[BMIM]^+[BF4]^-$ was studied at the B3LYP/6-31G(d) level of theory. The optimized structures were presented to study the vicinity of EDC with respect to each ionic liquid. The ZPE-corrected binding energy values were found to be negative, indicating fruitful interaction of the EDC and ionic liquid species. Based on the interaction strength, the affinity of estrone on ionic liquids can be described as $[BMIM]^+[PF6]^- > [BMIM]^+[BF4]^- > [BMIM]^+[NTF2]^-$. AIM analysis was carried out to find the nature of interactions, so as to get the electronic distribution at the intermolecular region. It was found out that all interactions were characterized by positive Laplacian of electron density and $-G(r_c)/V(r_c) > 1$ at intermolecular critical points illuminating the non-covalent nature of interactions existing between EDC and ionic liquids.

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