The coordination chemistry of boron porphyrin complexes B_2OX_2 (TpYPP) (X = OH, F; Y = Cl, CH$_3$) and their chemical reactivities

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Abstract. The structure and coordination chemistry of boron porphyrin complexes B_2OX_2 (TpYPP) (X = OH, F; Y = Cl, CH$_3$) in connection with its chemical reactivity are analyzed at *ab initio* density functional theory B3LYP/6-31G* and restricted Hartree–Fock RHF/6-31G* levels of theory. Global reactivity and local selectivity descriptors are used as adequate tools to analyze the isomerism effect (Z or E isomer) and the substitution effect (X: in axial ligand; or Y: in porphyrin ligand). In all the cases, we find that the E conformation is the most stable one, in agreement with X-ray results, and that a principle of maximum hardness in the isomerism analysis is fullfilled. In the substitution analysis, we find that the three global reactivity indexes (h, w, c) and the two local reactivity indexes (f_k, electrostatic potential) used in this paper predict the same trend when an electron-withdrawing substituent is replaced by an electron donor. Finally, we show that substitution in the porphyrin ligand is slightly more significant than that in the axial ligand.

Keywords. Boron; porphyrin; reactivity; Fukui function.

1. Introduction

It has long been known that porphyrins, phthalocyanines and related heterocyclic molecules have a propensity to localize in solid tumors and persist there in the long term. This property of the porphyrins provides the basis of photodynamic therapy (PDT),[1] a binary therapeutic method that utilizes porphyrin derivatives localized in tumors, as *in situ* photosensitizers for the production of singlet oxygen on irradiation with red light.[2] Candidate porphyrin derivatives that contain boron for boron neutron capture therapy (BNCT) purposes are also of interest for potential PDT applications. Boronated porphyrins are a relatively new group of species of interest as potential boron carriers for BNCT.[3] These compounds are metal-chelating agents which for biochemically unknown reasons, exhibit a high propensity for tumor localization. BOPP, a water-soluble boronated porphyrin, was found to selectively localize in tumor cells to a much higher degree than borocaptate sodium (BSH) both *in vitro* and in small animal glioma models.[4,5] BNCT is a two-step

radiotherapy in which a selective radiation effect on tumor cells is achieved by first targeting the tumor with non-radioactive ^{10}B and then exposing it to low energy neutrons.[6] The stable ^{10}B isotope has a large cross-sectional area for the capture of thermal neutrons. The reaction yields intensively ionizing particles, ^{4}He^{2+} (***a***) particles and recoiling ^{7}Li^{3+} nuclei. The nuclear fragments thus produced are highly cytotoxic and move extremely short distances (5 ***m***m for Li particles and 9 ***m***m for ***a*** particles, approximately one cell diameter) within tissues. As a result, those cells that have bound or taken up a ^{10}B-containing agent are destroyed. Theoretically, BNCT is an ideal binary therapy in which each component is nonlethal. The neutron beam itself has a very low energy which does not cause appreciable damage to tissues. On the other hand, the boron agent selected should not have any toxicity.

The first synthesis of boron porphyrins was published by Carrano and Tsutsui in 1977.[7] Reaction of tetraphenylporphyrin (H$_2$TPP) with BCl$_3$ MeCN was reported to yield a porphyrin of the composition B$_2$(OH)$_4$TPP. However, the experimental data available did not allow a clear assignment of the coordination geometry. On the other hand, there is information

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on the synthesis of porphyrins containing boron functionalities in side chains appended to the porphyrin macrocycle. Typical examples include porphyrins with boronic acid groups, which have been utilized for receptor or coordination studies[8] and carboranyl porphyrins.[9] The latter are porphyrins that carry carboranyl units in side chains at either *meso*[9c] or *b* positions. Until here all these compounds do not contain boron atoms directly bounded in the macrocycle skeleton or in the core. The first structural characterization of a boron porphyrin of this kind was performed by Brothers *et al* in 1994.[10] The examination of the reaction described by Carrano and Tsutsui with 5,10,15,20-tetra-*p*-tolylporphyrin (H$_2$TPP) yielded a product with the composition B$_2$O(OH)$_2$(TPP). Similarly, the reaction of 5,10,15,20-tetra-*p*-chloroporphyrin with BF$_3$ OEt$_2$ in chlorobenzene containing a trace of water followed by chromatographic work gave a product with the formula B$_2$OF$_2$(T*p*ClPP). The latter compound was crystallized and characterized by X-ray diffraction, and shows an unusual coordination in porphyrin chemistry at the core with two inequivalent boron atoms.[10] Each boron atom is bound to two neighboring nitrogen atoms; one boron atom is located roughly in the plane of the nitrogen atoms, while the other is significantly displaced out of the plane (*E* isomer). Thus, the fluorine atoms are located on opposite sides of the macrocycle. This unusual geometry leads to a noplanar macrocycle conformation. A symmetric conformation (*Z* isomer) of this compound could not be obtained.

Since coordination of one boron atom to two porphyrin nitrogen atoms is not usual and constitutes a true challenge for experimentalists, the synthesis of complexes like B$_2$OX$_2$ (T*p*YPP) is a very attractive idea. These latter complexes are particularly interesting because the porphyrins present the great advantage that they are easily retained in the human body when are injected to patients suffering from some tumor.

The coordination chemistry of boron porphyrin complexes of the kind B$_2$OX$_2$ (T*p*YPP) (X = OH, F; Y = Cl, CH$_3$) has been studied at an experimental level,[11,12] but with the exception of a couple of calculations of total energies, nothing have been said about its chemical reactivity. Hence, our goal in the present work is to perform a quantum chemistry study of the molecular and electronic structure of several complexes B$_2$OX$_2$ (T*p*YPP) (X = OH, F; Y = Cl, CH$_3$) using several chemical reactivity descriptors. Figure 1 shows a scheme with the position of substituents X in *E* and *Z* isomers, and the position of substituents Y in one B$_2$OX$_2$ (T*p*YPP) complex. We will examine the isomerism effect of each complex (*Z* and *E* isomers) and the substitution effect generated in the axial ligand or in the porphyrin ligand.

2. Theoretical background

The chemical hardness (*h*) has been shown to be a useful global index of reactivity in atoms, molecules and clusters.[13,14] The theoretical definition of *h* has
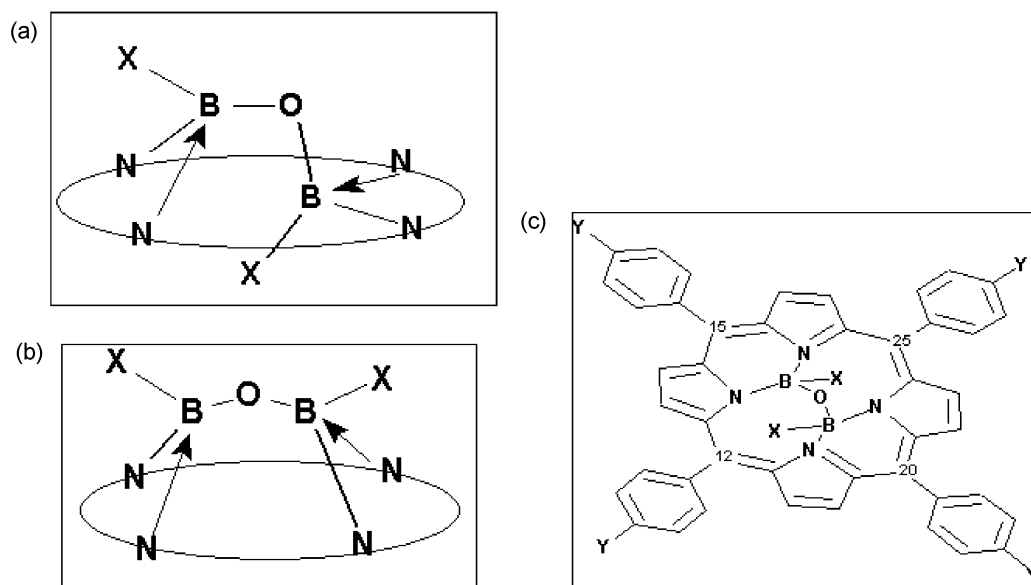

Figure 1. Scheme of: (**a**) the position of substituents X in *E* isomer; (**b**) the same in *Z* isomer; (**c**) the position of substituents Y in a B$_2$OX$_2$ (T*p*YPP) complex.

been given by the density functional as the second partial derivative of the electronic energy (E) with respect to the total number of electrons (N),[13,14] for a constant external potential $v(\vec{r})$,

$$h = \tfrac{1}{2}(\partial^2 E / \partial N^2)_{v(\vec{r})} = \tfrac{1}{2}(\partial m / \partial N)_{v(\vec{r})}. \tag{1}$$

The quantity m is the electronic chemical potential defined as,[13]

$$m = -c = (\partial E / \partial N)_{v(\vec{r})}. \tag{2}$$

The operational definition of h actually used considering the average frontier properties,[13] that is the variation in the energy when one electron is added or removed from the system is given by:

$$h = I - A, \tag{3}$$

which can be obtained using a finite difference approximation. I and A are the first vertical ionization potential and electron affinity, respectively. These energies are calculated using a ΔSCF procedure:

$$I = E(N-1) - E(N), \tag{4}$$

$$A = E(N) - E(N+1). \tag{5}$$

The terms $E(N)$, $E(N+1)$ and $E(N-1)$ correspond to the total energy of the ground state anion and cation, respectively. One additional form to obtain h and following Koopmans' theorem ($I = -e_{\text{HOMO}}$ and $A = -e_{\text{LUMO}}$) is:

$$h = e_{\text{LUMO}} - e_{\text{HOMO}}. \tag{6}$$

where HOMO is the highest occupied molecular orbital (MO) and LUMO is the lowest unoccupied MO. Analogously, the electronegativity defined in (2) can be quantified using the operational equation,

$$c = \tfrac{1}{2}(I + A) \approx \tfrac{1}{2}(e_{\text{HOMO}} + e_{\text{LUMO}}). \tag{7}$$

In previous studies of Fukui functions applied to macrocyclic such as porphyrin or tetra pyrrolic complexes, we have verified the reliability of the frontier molecular orbitals in the use of Fukui functions.[15–19] Based on this, we used (6) and (7) to evaluate the chemical hardness and electronegativity, respectively.

Parr *et al*[20] have introduced a global electrophilicity index w defined as,

$$w = m^2 / 2h. \tag{8}$$

This expression can be considered as a quantitative formulation of the model of Maynard *et al*[21] that have introduced the concept of "electrophilicity power" of a ligand as a measure of its electron saturation. According to the definition, ω measures the ability of a molecular species to soak up electrons. In this paper the electrophilicity values will be calculated using (6) and (7) to evaluate (8).

The local reactivity in a molecule along the space in a point $(\vec{r})$ can be obtained by means of the Fukui function, $f(\vec{r})$,[22,23]

$$f(\vec{r}) \equiv (\partial r(\vec{r}) / \partial N)_{v(\vec{r})}. \tag{9}$$

Equation (9) is a more useful tool for chemists when it is condensed to an atom (k) in a molecule. Since a molecule has always atoms or atomic regions with a trend to accept electrons, as well as atoms or atomic regions able to loose electrons, it is necessary to define how to calculate condensed Fukui functions in each of these cases. Thus, approximate condensed Fukui functions can be obtained by,[14,22,24]

$$f_k^+ \approx r_{k,\text{LUMO}}, \tag{10}$$

$$f_k^- \approx r_{k,\text{HOMO}}. \tag{11}$$

In this paper we have used (10) and (11) to determine the reactive sites in B_2OX_2 (TpYPP) complexes when they undergo an electrophilic attack (f^-) or a nucleophilic attack (f^+). Although these equations constitute approximate forms to calculate f^- and f^+, we have demonstrated in previous works on similar species that this methodology is valid and successful for macrocycles.[15–19]

3. Computational details

Full geometry optimization for the boron porphyrin complexes B_2OX_2 (TpYPP) (tetra para Y phenyl porphyrin) (X = OH, F; Y = Cl, CH$_3$) was performed using a DFT method with the 6-31G* basis set. We used Becke's three-parameter hybrid exchange functional (which includes the exact Hartree–Fock exchange based on Kohn–Sham orbitals[25]) with the LYP (Lee, Yang, Parr) correlation functional (B3LYP).[26] To see the effect of the electronic correlation, we also carried out restricted Hartree–Fock (RHF) cal-
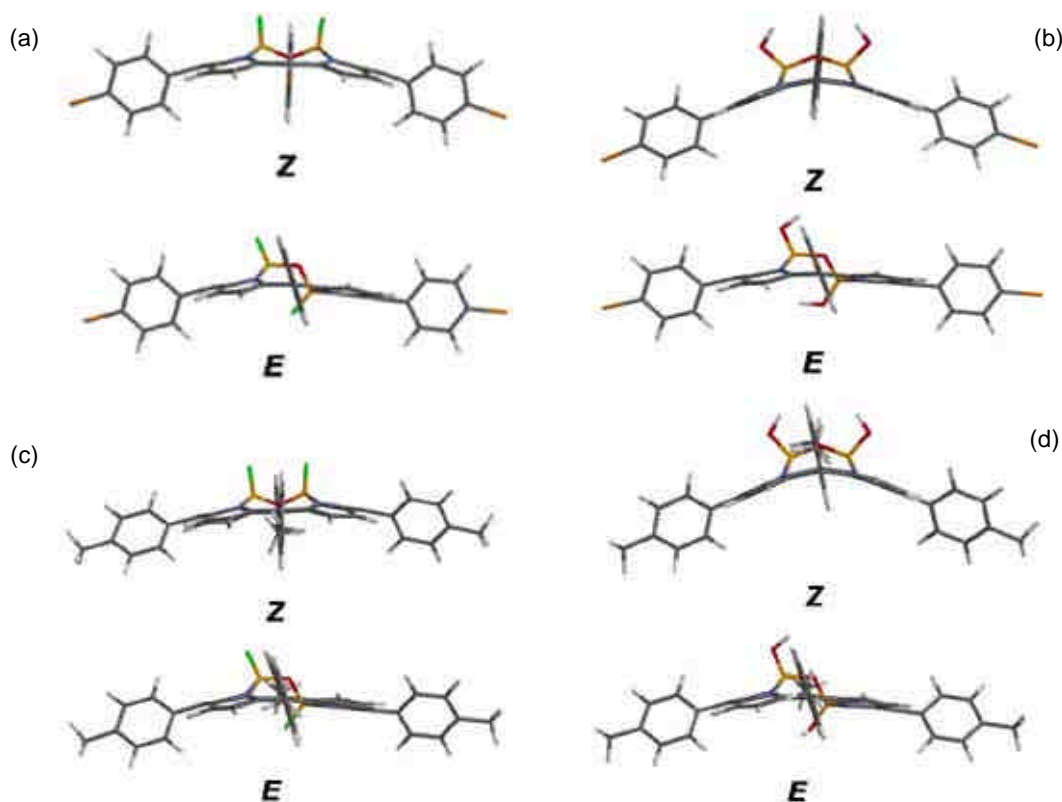
Figure 2. Optimized molecular geometries of B_2OX_2 (TpYPP) (X = OH, F; Y = Cl, CH$_3$) isomers at B3LYP/6-31G* level of theory: (**a**) X = F, Y = Cl; (**b**) X = OH, Y = Cl; (**c**) X = F, Y = CH$_3$; (**d**) X = OH, Y = CH$_3$.

culations with the same basis set, 6-31G*. All the theoretical calculations were carried out with the Titan 1·0·8 package.[27] Each optimized structure was verified to be an energy minimum having a positive value for all its vibrational frequencies.

4. Results and discussion

4.1 *Molecular structure*

A total of four types of B_2OX_2 (TpYPP) complexes were studied and their fully optimized geometries at B3LYP/6-31G* level of theory are shown in figure 2. We considered two substitutions in the axial ligand (X = OH, F) and two substitutions in the *para* positions of phenyl rings (Y = CH$_3$, Cl) corresponding to four previously synthetized complexes.[10–12] Each of these four complexes can exist in two isomeric forms: *E* and *Z*.[28] Only one of the complexes B_2OX_2 (TpYPP) has been characterized by X-ray analysis, that corresponding to X = F and Y = Cl.[10] It has been found that its structure is disordered such that the bridging oxygen and one fluorine atom could not be resolved

crystallographically. At variable temperature NMR experiments (218–323 K) confirm the existence of only one porphyrin isomer over this temperature range. The ^{11}B and ^{19}F NMR spectra have indicated that the two B and the two F atoms are chemically inequivalent. In agreement with these experiments, DFT calculations (Hedin–Lunqvist/Janak–Morruzi–Williams local correlation functional and a DN basis set) rendered the *E* isomer of B_2OF_2 (TpClPP) 15·9 kcal/mol more stable than the *Z* isomer.[10] On the other hand, the NMR analysis of $B_2O(OH)_2$ (TpCH$_3$PP) has indicated that this complex has low symmetry, giving a broad singlet signal corresponding to the two hydrogen atoms of the OH group.

According to our B3LYP/6-31G* calculations, the four complexes studied can exist in *E* and *Z* conformations. In all cases the phenyl rings are arranged in a practically perpendicular position with respect to the porphyrin plane to avoid the repulsion between their hydrogen atoms and those belonging to the pyrrol rings. In the case of the two complexes with X = F, we found for the *Z* isomer that the FBOBF moiety presents U-shape form strongly distorted by the repulsion between

Table 1. Relative[a] properties (*P*) between isomeric structures obtained at B3LYP/6-31G* and RHF/6-31G* levels of calculation. *E*: total energy (kcal/mol); ***h***: chemical hardness (eV); ***w***: electrophilicity (eV).

Structures	ΔE		*h*		*w*		*c*		*m*	
	B3LYP	RHF	B3LYP	RHF	B3LYP	RHF	B3LYP	RHF	B3LYP	RHF
$(OH, Cl)_E$	0·000	0·000	2·674	6·163	3·292	0·986	4·196	3·487	1·125	1·310
$(OH, Cl)_Z$	1·249	1·161	2·669	6·121	3·218	0·959	4·145	3·427	2·193	2·491
$(F, Cl)_E$	0·000	0·000	2·713	6·168	3·342	1·014	4·259	3·537	2·507	2·734
$(F, Cl)_Z$	28·332	32·756	2·696	6·059	3·521	1·082	4·357	3·621	3·836	4·401
$(OH, CH_3)_E$	0·000	0·000	2·543	6·173	2·643	0·737	3·667	3·017	2·486	2·724
$(OH, CH_3)_Z$	3·307	1·067	2·669	6·170	2·535	0·697	3·679	2·932	3·175	3·585
$(F, CH_3)_E$	0·000	0·000	2·564	6·145	2·783	0·791	3·778	3·118	3·158	3·444
$(F, CH_3)_Z$	26·035	29·775	2·495	6·059	3·001	0·867	3·870	3·241	5·669	6·370

[a]Referred to *E* isomer

the two F atoms as indicated by an BOB angle of about 131° and an FBO angle of about 121°. In contrast, in the *E* isomers the XBOBX moiety presents a less stressed asymmetric conformation in which one of the B atoms is practically in the porphyrin plane whereas the rest of the fragment is situated above this plane (see figure 2). As a consequence, these *Z* isomers (Y = Cl, CH$_3$) are 26–28 kcal/mol less stable than the corresponding *E* ones. Comparing these results with those at RHF level, we see that correlation energy tends to reduce by about 4 kcal/mol the difference in energy between these *Z* and *E* isomers (see table 1). These results are in good agreement with experimental studies previously reported.[10–12]

For the two isomers with X = OH, we found three possible *Z* conformations depending on the relative positions of the hydrogen atoms of the OH groups (both inward, both outward, one inward-one outward). It is interesting to note that in these three *Z* isomers the OBOBO moiety presents a W-shape form. These W-shape form causes two stabilizing effects: the repulsion between the two OH groups is decreased as they are more separated than in the U-chape conformation, and OH…O interactions with the bridging O atom are possible in two of the *Z* isomers (both inward and one inward–one outward). These W-shape conformations is accompanied by an important bending of the porphyrin plane, which is not costly energetically. We have only considered the most stable conformation of these three *Z* isomers which correspond to the two hydrogen atoms of the OH groups located inward. In this conformer, the two inward hydrogen atoms present a O–H…O interaction with the bridge oxygen atom. At B3LYP/6-31G* theory level, the two *Z* isomers (both inward) (Y = Cl, CH$_3$) are only about 1–3 kcal/mol less stable than the *E* ones. In this case

the difference in energy between *Z* and *E* isomers at RHF level is about 1 kcal/mol (see table 1). So, according to our results, both isomers *E* and *Z* could be present in a sample in accordance with the experimental observation.

4.2 *Isomerism analysis*

Table 1 contains the results of the total energy and the reactivity indexes obtained at DFT and RHF levels of theory for all the isomeric structures. In order to abbreviate, we will use in table 1 the nomenclature $(X, Y)_{E(Z)}$ to designate the isomers with the *X* substituent in the axial ligand, and the *Y* substituent in the porphyrin ligand. We found that with both DFT and RHF methods all the *Z* isomers, except for the (OH, CH$_3$)$_Z$ isomer, present a lower chemical hardness than the corresponding *E* isomers. This means that the latter present a higher resistance to deformation of electronic density under a given perturbation. These results for B$_2$OX$_2$ (TpYPP) complexes are in accordance with the principle of maximum hardness (PMH),[29] i.e. the *E* isomers present the lowest energy and the highest chemical hardness, and the *Z* isomers have the highest energy and the lowest chemical hardness. This fact indicates that the approximation used in (6) to obtain ***h*** is reasonable in these cases. We also observe that the absolute values of ***h*** calculated with the RHF method are overestimated with respect to the DFT values. This is a clear reflection of not taking into account electronic correlation in the RHF calculations.

The results for electrophilicity shown in table 1 indicate that the compounds with OH substituent present different behavior from those with F substituent. For the (OH, Y)$_{E(Z)}$ complexes, we found at the DFT level

Table 2. Differences of properties $(P)^a$ between structures presenting one substitution obtained at B3LYP/6-31G* and RHF/6-31G* levels of calculation. $\textbf{\textit{h}}$: chemical hardness (eV); $\textbf{\textit{w}}$: electrophilicity (eV); $\textbf{\textit{c}}$: electronegativity (eV); $\textbf{\textit{m}}$ dipole moment (debye).

Substitution	$\Delta\textbf{\textit{h}}$		$\Delta\textbf{\textit{w}}$		$\Delta\textbf{\textit{c}}$		$\Delta\textbf{\textit{m}}$	
	B3LYP	RHF	B3LYP	RHF	B3LYP	RHF	B3LYP	RHF
Axial ligand								
$(OH, Cl)_E/(F, Cl)_E$	0·039	0,005	0·050	0,028	0·063	0,051	1·382	1,424
$(OH, Cl)_Z/(F, Cl)_Z$	0·027	–0,062	0·303	0,123	0·213	0,194	1·643	1,910
$(OH, CH_3)_E/(F, CH_3)_E$	0·021	–0,028	0·140	0,054	0·112	0,101	0·672	0,720
$(OH, CH_3)_Z/(F, CH_3)_Z$	–0·174	0,111	0·466	0,170	0·191	0,309	2·494	2,785
Porphyrin ligand								
$(OH, Cl)_E/(OH, CH_3)_E$	–0·131	0,010	–0·649	–0,249	–0·530	–0,470	1·361	1,414
$(OH, Cl)_Z/(OH, CH_3)_Z$	0·000	0,049	–0·683	–0,262	–0·466	–0,495	0·982	1,094
$(F, Cl)_E/(F, CH_3)_E$	–0·149	–0,023	–0·559	–0,223	–0·481	–0,420	0·651	0,710
$(F, Cl)_Z/(F, CH_3)_Z$	–0·201	0,000	–0·520	–0,215	–0·488	–0,380	1·833	1,969

$^a\Delta P$ for (isomer A/isomer B) is calculated as $P_{\text{isomer B}} - P_{\text{isomer A}}$

that the *E* isomers are more electrophilic systems. A similar trend is obtained at RHF level of theory. An opposite behavior is found with the F substituent. For the $(F, Y)_{E(Z)}$ complexes we found at both DFT and RHF levels of theory that the *Z* isomers present higher electrophilicity than the *E* ones. The electronegativity calculated, also shown in table 1, gives as expected the same trend for the electrophilicity because the concept involved in both properties related to gain electrons is the same.

It is interesting to note that in general hardness, electrophilicity and electronegativity are not appreciably sensitive to conformational changes. At difference with the reactivity indexes, the numerical values of dipole moment calculated with DFT are very similar to those calculated with RHF. As expected, the *Z* structures present a higher value of $\textbf{\textit{m}}$ than the *E* ones, due to the fact that in the former the B–X bond dipole moments go in the same direction and add up producing an increase in the total dipole moment. It is interesting to remark that the complexes containing F atoms present larger dipole moments than the others with OH as substituent.

4.3 *Substitution analysis*

The properties studied to analyse the substitution effect of the axial ligand X and the porphyrin ligand Y are shown in table 2. In the case of the substitution occuring at the axial ligand, that is, an OH group or an F atom bonded to each of the boron atoms, we found that the chemical hardness increases when OH is substituted by F. This observed increase is about

≈ 0.02 eV (≈ 0.4 kcal/mol) to 0.04 eV (≈ 0.8 kcal/mol). Then an electron-withdrawing atom such as F produces a hardness increase in these systems. The only exception is when the substitution by F occurs in the (OH, $CH_3)_Z$ complex, where the latter results to be harder, with a value close to 0.2 eV (4 kcal/mol). An opposite trend is observed at RHF level. The substitution in the phenyl ring at the para position produces at DFT level a similar behavior with the exception of the pair (OH, Cl)$_Z$/(OH,CH$_3$)$_Z$. An exchange of a terminal atom as Cl, that is an electron-withdrawing atom, by a CH$_3$ group, that is an electron-donor group, produces a reduction of the chemical hardness. This fact occurs for the two axial ligands, OH and F. Our results indicate that the addition of electron-withdrawing substituents converts the complex in a harder system. On the contrary, the addition of electron-donor substituents leads to a softer system. An interesting issue here is that the values of $\Delta\textbf{\textit{h}}$ for substitution in the porphyrin ligand are about 0.1 eV (2 kcal/mol) to 0.2 eV (4 kcal/mol), higher than that obtained for substitution in the axial ligand, independent of the kind of axial ligand (OH or F). Therefore, we see that the substitution effect in the porphyrin ligand is of greater importance than that in the axial ligand. At this point, it is important to note that chemical hardness is an adequate property to analyse the effect of a substitution because it is independent of the number of electrons of the system. The substitution effect in the axial ligand on the electrophilicity shown in table 2 is clear: an increase of $\textbf{\textit{w}}$ occurs when the OH substituent is exchanged by an electron-withdrawing atom such as F. This is valid for the four pairs of complexes analysed by us.
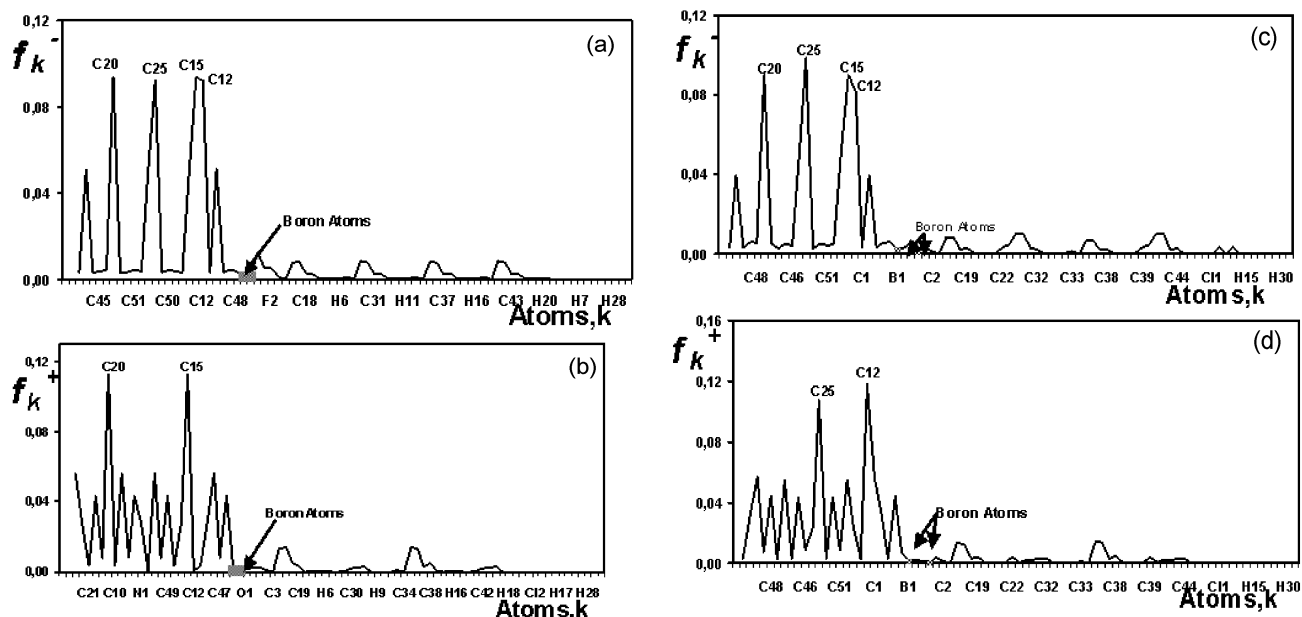
Figure 3. Values of condensed Fukui functions (f_k^+ and f_k^-) evaluated for each atom of the B_2OF_2 (TpClPP) complex. (a) f_k^-, Z isomer, (b) f_k^+, Z isomer, (c) f_k^-, E isomer, (d) f_k^+, E isomer.

The substitution effect in the porphyrin ligand on w indicates that the exchange of Cl by CH_3 generates a diminution in the electrophilicity leading to the same behavior obtained by substitution in the axial ligand. Our conclusion is then that the inclusion of an electron-withdrawing atom both in the axial ligand and in the porphyrin ligand produces a higher electrophilicity. However, the magnitude of this substitution effect depends on the ligand. In the case of the axial ligand, the effect on Δw goes from 0·1 eV (2 kcal/mol) to 0·5 eV (10 kcal/mol), whereas in the case of the porphyrin ligand it goes from 0·5 eV (10 kcal/mol) to 0·7 eV (14 kcal/mol). Thus, the substitution effect on electrophilicity is slightly more important when the substitution occurs in the porphyrin ligand. The same trend was observed for the chemical hardness. This fact may be explained in terms of the position that the substituent has in the porphyrin ligand. The substituent is bonded to the para position of phenyl rings which are linked to the porphyrin skeleton through the meso carbons. These meso carbon atoms have the largest weight in the construction of the frontier molecular orbitals of the system HOMO and LUMO. Then, the substituent can present an inductive and/or a resonant effect along the phenyl rings and gain or lose electronic density, depending on the kind on substituent, producing a larger effect on the porphyrin skeleton. In contrast, the substituents in the axial ligand are bonded to the boron atoms which do not participate in the construction of the frontier orbitals.

As shown in table 2 the electronegativity displays behavior similar to that of the electrophilicity: the substitution in the axial ligand of OH by F produces an increase in c, whereas substitution in the porphyrin ligand of Cl by CH_3 produces a decrease in c. Thus, the introduction of electron-withdrawing substituents (F, Cl) increases the electronegativity causing the complex to have a major capacity to gain electrons. The RHF method predict a similar quantitative trend.

Table 2 shows different behavior in the dipole moment when the substitution occurs in the axial ligand with respect to when it occurs in the porphyrin ligand. A substitution occurring in the axial ligand by a strong electron-withdrawing species, such as F provokes an increase in dipole moment in both isomers Z and E, due to the larger polarizability of the electronic density toward the F atom. However, the opposite trend is observed when the substitution occurs in the porphyrin ligand, when exchanging CH_3 by Cl.

4.4 *Fukui functions*

We also investigated the soft sites of higher reactivity in the B_2OX_2 (TpYPP) complexes by means of Fukui functions. Note that the Fukui functions only provide information about the soft sites of a species. To this end, we calculated only at DFT level of theory (to take into account correlation energy) the condensed
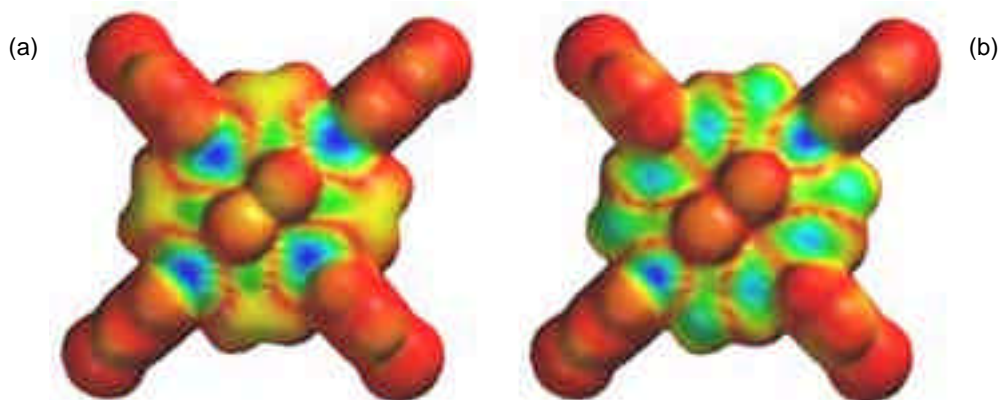
Figure 4. Graphical results of the Fukui functions of the Z B_2OF_2 (TpClPP) complex mapped into the electron density isosurface of 0.002 e/au^3: (**a**) f^-, (**b**) f^+. Blue color represents a region with large value of Fukui function and red color represents a region with a low value of Fukui function.
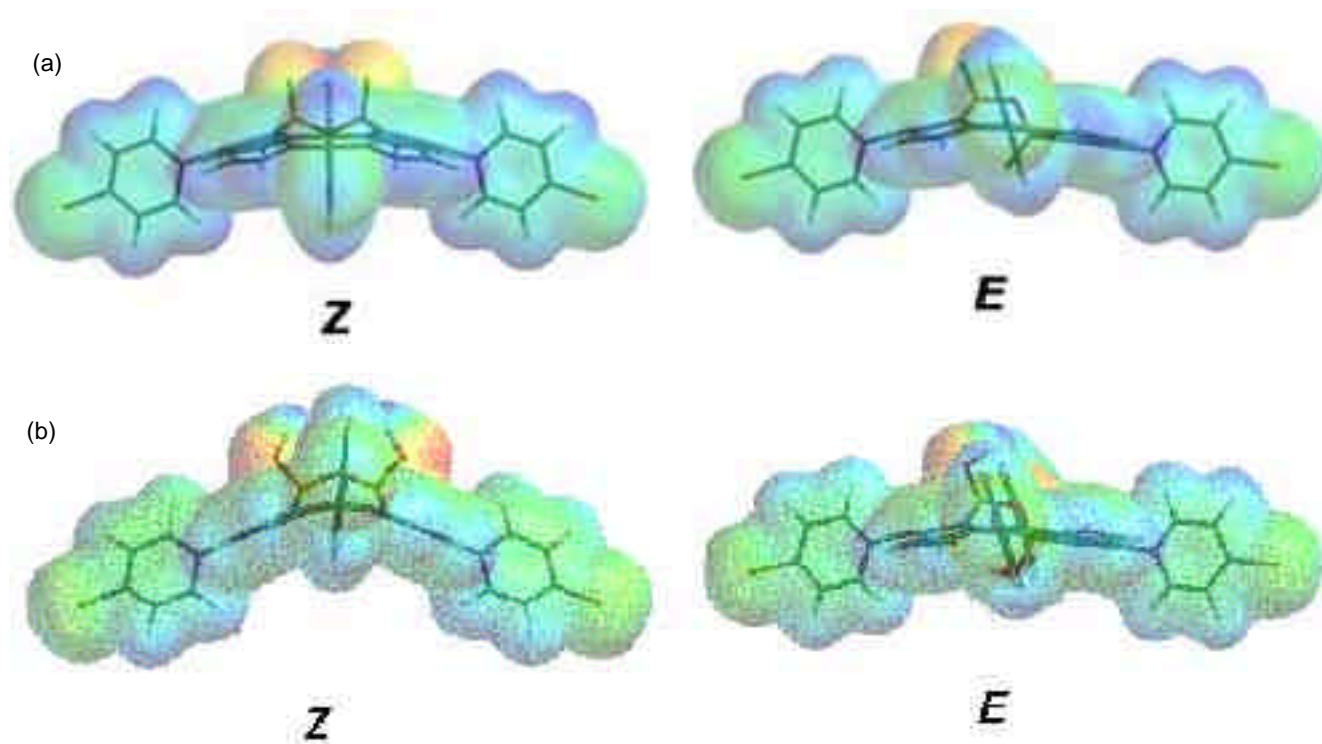

Figure 5. Electrostatic potential mapped into the electron density isosurface of 0.002 electrons/au^3. (**a**) B_2OF_2 (TpClPP); (**b**) $B_2O(OH)_2$ (TpClPP). Red color regions represent large negative values of the potential, blue color regions represent large positive values and orange, yellow and green regions represent intermediate values of the potential.

Fukui functions f_k^+ and f_k^- for both isomers Z and E for each of the complexes. We found similar results in all cases and as an illustration we only show in figure 3 the results obtained for the B_2OF_2 (TpClPP) complex. As may be seen in figures 3a and 3c, the reactive sites to an electrophilic attack (f_k^-) in both Z and E isomers correspond to the four meso carbons. This is in accordance with the experimental evidence

that in porphyrins the more reactive sites correspond to the meso carbons and not to the **b**-carbons belonging to the pyrrolic rings. It is interesting to note that the boron atoms present low values of the Fukui function and therefore are predicted to display low reactivity. Figures 3b and 3d show that the reactive sites to a nucleophilic attack are only two of the meso carbon atoms: C_{20} and C_{15} localizing along the BOB bridge

for Z isomers, and C_{25} and C_{12} placed perpendicularly to the BOB bridge for E isomers (see figure 1). Since the local electrophilicity is given by $w_k = w f_k^+$,[30] we may say that the more electrophilic sites in both Z and E isomers correspond to the meso carbons. We also included in figure 4 as an illustration, the graphical results for the Fukui functions of the Z B_2OF_2 (TpClPP) complex mapped onto the electron density isosurface of 0.002 e/au^3. As may be seen, Figure 4a shows the Fukui function for f^- clearly indicating that only four blue regions (largest Fukui function and consequently most reactive site) exist in the complex corresponding to the meso carbons. Figure 4b displays the Fukui function for f^+ indicating that there exist only two most reactive blue regions also corresponding to meso carbons.

4.5 *Electrostatic potential*

From the electrostatic point of view, we may identify the most reactive sites toward an electrophilic or nucleophilic attack, as hard sites that can react with hard substrates. Figure 5 displays the electrostatic potential[27] mapped onto an electron density isosurface of 0.002 electrons/au^3. As the results obtained at DFT level of theory are similar for all the complexes, we show in figure 5a the B_2OF_2 (TpClPP) complex (Z and E) and in figure 5b the $B_2O(OH)_2$ (TpClPP) complex (Z and E), as an illustration. In both figures we observe that the hard sites that are more reactive correspond to the substituent placed in the axial ligand, that is the F atom in figure 5a and the O(OH) atom in figure 5b. In the case of the E isomers, the oxygen atom in the BOB bridge appears also as a reactive site. Note that these reactive sites do not necessarily coincide with the soft reactive sites rendered by the Fukui functions. Finally, we found that the Cl positions do not constitute a hard reactive site.

5. **Conclusions**

In the present work, a theoretical investigation of the structure of the B_2OX_2 (TpYPP) (X = OH, F; Y = Cl, CH$_3$) complexes was performed at the PM3tm and B3LYP/6-31G* theory levels. In agreement with previous experimental investigations we found that when X = F the E isomers are much more stable (26–28 kcal/mol) than the Z ones. In the Z isomers, the FBOBF moiety present U-shape conformations strongly distorted by steric repulsions. On the contrary, when X = OH, the most stable Z isomer, which repre-sents the HOBOBOH moiety with a W-shape conformation with both hydrogen atoms inward, is only 1–3 kcal/mol less stable than the E isomer, so that both isomers could coexist in accordance with the results obtained in NMR studies.

A complete study of the chemical reactivity of the B_2OX_2 (TpYPP) (X = OH, F; Y = Cl, CH$_3$) complexes in their Z and E isomeric forms was also carried out at the B3LYP/6-31G* and RHF/6-31G* levels of theory. In all cases we found that the principle of maximum hardness is fulfilled. The effect of substitution in the axial ligands (F, OH) and in the porphyrin ligand (Cl, CH$_3$) was analyzed by means of three global reactivity indexes (*h*, *w*, *c*) and of two local reactivity indexes (f_k, electrostatic potential). Concerning the substitution, all the reactivity indexes follow the same trend, an increase in *h*, *w* and *c* being observed for electron-withdrawing substituents with respect to electron-donor substituents. The local reactivity indexes predict that the soft reactive sites are located in the meso carbons, in agreement with experimental evidence, while hard sites are located in the substituents F, O(OH) and in the O atom of the BOB bridge.

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