

## Porphyrin's ring current as a driving force for halogen bond interactions: a computational study

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**Abstract:** We demonstrate herein a computational study probing the influence of metalloporphyrin ring current directionality on intermolecular halogen bonding (XB) during supramolecular self-assembly. The results demonstrate that porphyrin ring current can activate or deactivate halogen bonding interactions, an essential superamolecular driving force.

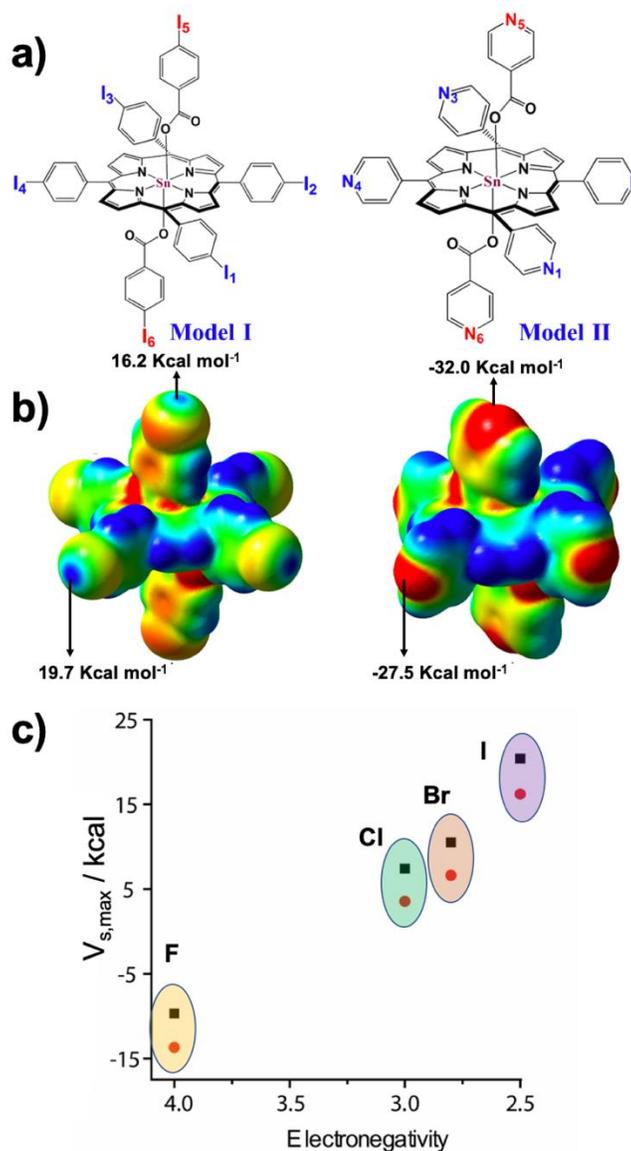
Noncovalent interactions play a pivotal role in different chemistry fields chemistry, and are particularly important for the various processes governing supramolecular chemistry and chemical biology.<sup>1-3</sup> Recognisance of the importance that non-covalent bonds have in chemistry has been growing steadily in the past few decades, as emphasized by Schneider's words: "*with courageous simplification one might assert that the chemistry of the last century was largely the chemistry of the covalent bonding, whereas that of the present century is more likely to be the chemistry of noncovalent bonding*".<sup>4</sup>

Hydrogen bonding (HB)<sup>5</sup> has been the subject of many investigations and is the most commonly characterized noncovalent interaction, largely due to its high importance in areas such as pharmaceutical co-crystals, supramolecular design, and protein chemistry. Recently however, other classes of non-covalent interactions e.g.  $\pi$ - $\pi$ , n- $\pi$ , lone pair- $\pi$ , and halogen bonding are capturing more attention.<sup>6-8</sup> Among those, we found that halogen bonding (XB) has been capturing wider attention in recent years, while being the subject of many theoretical<sup>9-12</sup> and experimental<sup>13-15</sup> investigations, with particular interest within biochemistry and materials science.<sup>16-22</sup> Analogous to HB, XB involves a halogen bond donor (D, consisting of a halogen atom) and a halogen bond acceptor (A, typically an electron rich atom). Thus, the interaction can be designated as XB: D-X...A. The halogen bond attraction originates due to the anisotropic charge distribution around the halogen atom (forming a ' $\sigma$ -hole')<sup>9-12</sup>, that can interact favourably with the partial negative charge on the electron-dense halogen bond acceptor.<sup>9-12</sup> Moreover, there are many other aspects that can affect the XB interactions including the size of the halogen bond donor, electronegativity of the acceptor (rarely P-, As and Sb have also served as XB acceptors), and hybridization of the carbon atom

bonded to D. <sup>23-28</sup> However, to the best of our knowledge, there have been very few studies attempting to establish how the electronic effect generated by metalloporphyrins can influence or guide the formation of XB interactions.

In our previous work on six coordinated tin-porphyrin complexes,<sup>29-31</sup> we observed an interesting phenomenon in the solid phase. The location of the halogen bond donor or acceptor on the porphyrin plays a critical role in the self-assembly process. In cases where the halogen atom is located at the equatorial position (outer ring), the porphyrin has a higher tendency to participate in XB interaction. Interestingly, placing the halogen atom at the axial position either results in weak XB interactions or inhibits them altogether. On the other hand, if any electronegative atoms such as N- or O-atoms are located on the axial positions, these atoms can become stronger XB acceptors.

We therefore hypothesized that the aromaticity of the porphyrin molecule can generate a ring current strong enough to enable changes in the potential of the  $\sigma$ -hole of the halogen atom and drive the supramolecular architecture to favour or disfavour the formation of halogen bonds. The porphyrin ring current effect has been previously studied by <sup>1</sup>H NMR (Nuclear Magnetic Resonance),<sup>32-35</sup> and Fukazawa *et al.* have shown that tin(IV)-porphyrins containing carboxylate linkers falling directly under the influence of the ring current in modulated systems are shifted upfield in the <sup>1</sup>H-NMR.<sup>35</sup> Motivated by Fukazawa's study and based on our solid state observations, we systematically investigated the relationship between the ring current and  $\sigma$ -hole potential and its directional influence on XB interaction during the self-assembly of the porphyrins.



**Fig. 1.** (a) Schematic representation two model; **Model I**, Sn(IV)-5,10,15,20-meso-tetrakis(4-halophenyl)porphyrin [Sn(L)<sub>2</sub>-TXPP](L= 4-halo- benzoate moiety and X= F, Cl, Br and I atoms), **Model-II**, Sn(IV)-5,10,15,20-meso-tetrakis(4-pyridyl)porphyrin [Sn(L)<sub>2</sub>-TPyP] (L= isonicotinate). (b) Computed electrostatic potential on the 0.01 au molecular surface of **model I** (shows V<sub>S,max</sub> of relative donors) and **model II** (shows V<sub>S,min</sub> of relative acceptors). Computational level: B3LYP/6-31G\*(d,p) and (c) the average σ-hole potential (V<sub>S,max</sub>) of equatorial halogen (square black) and axial halogen (circle, red) as a function of electronegativity in **model I**.

To begin our study we chose two complementary models where the donors and acceptors are observed in the presence and absence of the ring current environment. To force the donors and acceptors to be influenced directly by the ring current effect, we proposed a substituted Sn(IV)-based porphyrin with two axial linkers. **Model I** consists of Sn(L)<sub>2</sub>-5,10,15,20-meso-tetrakis(4-halophenyl)porphyrin (L= 4-F-,Cl-,Br-, or I-benzoate moiety and X= F, Cl, Br and I) and **model II** consists of a Sn(L)<sub>2</sub>-5,10,15,20-meso-tetrakis(4-pyridyl)porphyrin (L= isonicotinate) (**Fig. 1a**).

All of the compounds were subject to full energy minimization using a hybrid of B3LYP functional and 6-31G\* basis set for all atoms except for I- and Sn-atoms for which a LANL2DZ basis with a pseudopotential for the inner-core electrons was used. The electrostatic potential  $V(r)$  created by the nuclei and electrons in a molecule or charged molecular species is given rigorously by eq. (1):

$$V(r) = \sum_A \frac{Z_A}{|R_A - r|} - \int \frac{\rho(r') dr'}{|r' - r|}$$

In which  $Z_A$  is the charge on nucleus A, positioned at  $R_A$ , and  $\rho(r)$  is the electronic density function. Electrostatic potential can provide us physical values for each individual atom. It can also be determined experimentally by high-resolution diffraction methods.<sup>36–37</sup> In order to analyze and interpret intermolecular interactions,  $V(r)$  is computed to obtain the electrostatic surface; following the suggestion of Bader *et al.*,<sup>38</sup> this is frequently taken to be an outer contour of the molecule's electronic density, usually at 0.001 au. It has been demonstrated that the 0.001 au contour typically lies beyond the van der Waals radii of the atoms in the molecule,<sup>39</sup> so that  $V(r)$  on this surface is relevant to the onset of non-covalent interactions.<sup>40–42</sup>  $V(r)$  calculated on the molecular surface is labelled  $V_{S(r)}$ ; its local maxima and minima, of which there may be several, are designated as the  $V_{S,max}$  and  $V_{S,min}$ , respectively. Thus, positive  $\sigma$ -holes are typically characterized by  $V_{S,max}$ .  $V_{S,max}$  and  $V_{S,min}$  were calculated using the Multiwfn 3.3 program<sup>43</sup> from the optimized geometry of the model complexes. **Fig. 1b** illustrates the computed electrostatic potential as mapped in 0.01 au for clear visualization. We also mapped the electrostatic potentials in 0.001 au in which can be found in the ESI.

To test our hypothesis and we calculated based on model I the electrostatic potential (ESP) of the Sn-porphyrin containing I-atoms occupying the axial and the equatorial positions. The ESP clearly indicates the existence of a  $\sigma$ -hole along the C-I bond. Interestingly, the  $V_{S,max}$  values of  $\sigma$ -hole potentials vary based on the position of the I-atoms on the porphyrin ring. For example, all the equatorial I-atoms at the periphery of the porphyrin ring have  $V_{S,max}$  values close to 20 Kcal mol<sup>-1</sup> (Table 1), whereas lower  $V_{S,max}$  values around 16 Kcal mol<sup>-1</sup> were observed for I-atoms located on the axial position, which fall directly under the effect of ring current (Table 1). The change in the magnitude of the  $\sigma$ -hole  $V_{S,max}$  values shows how ring current can largely effect the affinity of the  $\sigma$ -hole towards electronegative elements. Furthermore, the  $V_{S,max}$  values dictate whether or not the halogen atoms at specific position can be involved directly in the formation of supramolecular architectures.

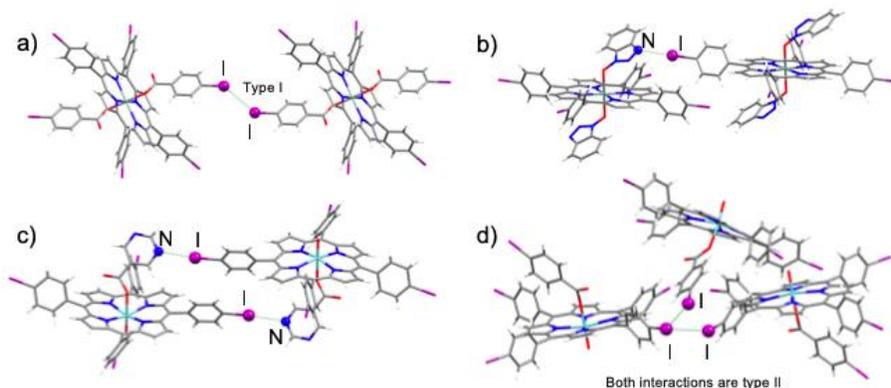
Next, we conducted calculations to determine the ESP of I-atoms by changing different hybrid functionals, the results of which are summarized in **Table 1**. These results show a trend that is consistent with the previous calculations, suggesting that the magnitude of  $\sigma$ -hole potential can be affected by the ring current. The ESP values of I-atoms on the axial positions are lower than those located at the equatorial position by  $\sim 4$  Kcal mol<sup>-1</sup>. To investigate whether this effect is also relevant to other halogens, we replaced the I-atoms with Br-, Cl- and F-atoms at both axial and equatorial position in [Sn(L)<sub>2</sub>-TXPP] system. Fig. 1c plots the electronegativity of the halogen atoms verses the  $V_{S,max}$  values

for both axial (red circles) and equatorial (black squares) halogen atoms. All porphyrin-halogen systems showed a similar trend to that obtained with I-based [Sn(L)<sub>2</sub>-TXPP]. As expected, the  $\sigma$ -hole potential increases according to the trend F<Cl<Br<I. Interestingly, in all cases halogen atoms at the axial position have  $V_{S,max}$  values nearly 4 Kcal mol<sup>-1</sup> than those in equatorial positions.

**Table 1.**  $\sigma$ -hole potential ( $V_{S,max}$ , Kcal mol<sup>-1</sup>) of iodine atom in **Model I** in different functional with 6-31G\*(d,p) basis set.

atom	B3LYP	B3PW91	B3P86	OPBE	PBE0
I1	19.6	19.9	20.1	20.1	20.1
I2	20.8	21	21.2	21.1	21.1
I3	19.7	20	20.2	20.1	20.1
I4	20.8	21	21.2	21.1	21.1
I5	16.2	16.3	16.4	15.9	15.9
I6	16.2	16.2	16.4	15.9	15.9

The influence of the ring current in directing halogen bonding interactions is evidenced by the preferred formation of Type II XB interactions in porphyrin-based crystal structures. For example, an analysis of the crystal structure of Sn(L)<sub>2</sub>-TIPP (Cambridge Structure Database (CSD) ref. code KIWTIW), in which the axial ligands consist of 4-iodobenzoate moieties (**Fig. 2a**),<sup>30</sup> revealed that the equatorial I-atoms participate in type II interactions with I...I contacts while the axial I-atoms form type I interactions.<sup>44,45</sup> Similarly, replacing I-atoms with Br-atoms at the axial linkers led for the formation of type I XB interactions.<sup>30</sup> From these two examples it is clear that axial halogen atoms are either reluctant to participate in XB interactions altogether or participate in type I XB interactions due to a decrease in the potential of the  $\sigma$ -hole. Type I XB interactions are not truly considered an attractive contact (two electropositive regions of halogens ( $\delta+$ ) are in short contact and can form due to crystal packing), whereas type II is more attractive in nature (the electropositive region ( $\delta+$ ) of one halogen is in direct contact with electronegative region ( $\delta-$ ) of the other which provides a stabilizing electrostatic interaction).<sup>44,45</sup>



**Fig. 2.** Selected crystal structures with attractive major interactions of (a) Sn(4-iodo-benzoate)<sub>2</sub>-TIPP (ref. code of KIWTIW), (b) Sn(1-hydroxybenzotriazole)<sub>2</sub>-TIPP (CSD ref. code HIRWAI), (c) Mo(O)-

(TIPP)(pyrimidine-5-carboxylate) (CSD ref. code VONGIQ) and (d) Mo(O)-(TIPP)(4-iodobenzoate) (CSD ref. code VONGOW).

Next, we explored what happens to XB donors. **Model II** contains [Sn(isonicotinate)<sub>2</sub>-TPyP] where the electronegative atom (nitrogen atom) is present at both axial and equatorial positions. The calculated  $V_{S,\min}$  values for nitrogen atoms demonstrate a reverse trend compared to the halogen-based system. The  $V_{S,\min}$  values for axial N-atoms are at nearly  $-32 \text{ Kcal mol}^{-1}$ , while N-atoms at the equatorial position of the porphyrin ring are at approximately  $-28 \text{ Kcal mol}^{-1}$ . This indicates that shielding effect of ring current enhances the negativity of the axial heteroatoms.

In fact, axial ligands containing nitrogen atoms (or oxygen atoms) were attractive, as was reported previously regarding Sn(L)<sub>2</sub>-tetrahalophenyl porphyrins with various pyridyl axial substituents.<sup>29</sup> The results have shown strong X $\cdots$ N interactions. For example, the crystal structure of Sn(1-hydroxybenzotriazolate)<sub>2</sub>-TIPP (CSD ref. code HIRWAI) showed the formation of 2D halogen-bonded networks with short intermolecular I $\cdots$ N interactions of  $2.99 \text{ \AA}$  supplemented by I $\cdots$ I interactions (**Fig. 2b**). The crystal structures of Sn-(isonicotinate)<sub>2</sub>-TIPP and Sn(isonicotinate)<sub>2</sub>-TBrPP (CSD ref. codes HIRVOV and HIRWIQ, respectively) show halogen bond-assisted aggregation into open *sql*-type networks, with distinct intermolecular I $\cdots$ N and Br $\cdots$ N contacts of  $3.15 \text{ \AA}$  and  $3.16 \text{ \AA}$  respectively.<sup>29</sup> Exchanging the roles of donor and acceptors in the above system as in the case of Sn(I/Br-carboxylate)-TPyP (CSD ref. codes HIRXAJ and HIRXEN, respectively) did not exhibit to date effective XB between the porphyrin scaffolds.<sup>29</sup>

The above described theoretical model is not only valid for six-coordinate Sn-porphyrins but also applicable to other five or six-coordinated metalloporphyrins. For example, the crystal structure of Mo(O)-(TIPP)(pyrimidine-5-carboxylate) (CSD ref. code VONGIQ, **Fig. 2c**), exhibits strong intermolecular interactions with I $\cdots$ N contact of  $2.995 \text{ \AA}$  and  $3.12 \text{ \AA}$  to form a 1D ladder type supramolecular self-assembly.<sup>46</sup> Interestingly, using another donor at the axial position as in the case of Mo(O)-(TIPP)(4-iodobenzoate) (CSD ref. code VONGOW, **Fig. 2d**) shows that axial halogen-atoms can participate in type II XB interactions.<sup>46</sup> In these molecules, the 4-iodophenyl ligand is inclined in an acute angle away from the ring current force which slightly minimizes its influence on  $\sigma$ -hole potential. Based on our calculations and solid-state observations it can be concluded that systems with donors located at periphery of the porphyrin and acceptors on the axial positions have a priori higher odds to form directional XB networks.

To summarize, the analysis of the results presented in this work offers some interesting observations: (i) the ring current influence both donors and acceptors by a magnitude of  $4 \text{ Kcal mol}^{-1}$  for both  $V_{S,\max}$  and  $V_{S,\min}$ ; (ii) the orientation of the axial ligand can play a very crucial role in terms of forming desired XB networks, will be subject to future investigation. (iii) minor fluctuations of the  $\sigma$ -hole potential on the interacting partners may cause in favour or against the formation of directional XB in the self-assembly process. Overall, the computed electrostatic potentials do offer some encouragement concerning the feasibility of preparing porphyrin-based halogen bonded supramolecular materials and framework solids, as well as a deeper insight on how to control the strength and type of XB interactions.

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## Conflicts of interest

There are no conflicts to declare

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