# Rational design of supramolecular chirality in porphyrin assemblies: the halogen bond case†‡

**Sankar Muniappan, Sophia Lipstman and Israel Goldberg***

**Asymmetric functionalization of the tetraarylporphyrin scaffold, combined with directional supramolecular halogen bonding, yields chiral architectures.**

The tailored induction of supramolecular chirality in non-covalent assemblies in solution, as well as in the solid state, without resorting to chiral reagents has been intensively studied in recent years, as such supramolecular materials may be useful in the processes of enantioselective synthesis, separation and catalysis, and the fabrication of polar devices.[1] While seeking protocols for the deliberate synthesis of homo-chiral supramolecular crystals from typically square planar tetraarylporphyrin components, our earlier studies revealed that introduction of a polar axis into the porphyrin unit (whether in a lateral or an axial direction) *via* asymmetric substitution of the molecular recognition groups (hydrogen bond donors and acceptors), in combination with specific directionality of the intermolecular interaction synthons that govern the self-assembly process, represents a useful strategy for the induction of non-centrosymmetric architectures.[2]

Exploring further the above guidelines, we report here the deliberate synthesis of non-centrosymmetric crystals based on the pre-designed compound 5-(4′-pyridyl)-10,15,20-tris(4′-iodophenyl)porphyrin (PyTIPP; Fig. 1) in different reaction environments and metalation states.§ PyTIPP bears a single pyridyl function and three diverging iodophenyl groups that can be involved in halogen bonds of the $N_{py}\cdots I$ type, as well as related $I\cdots I$ and $I\cdots\pi$ interactions,[3] and its molecular framework has a polar axis due to the asymmetric substitution. The resulting structures, involving the nitrobenzene solvate of PyTIPP (**1**), the DMF solvate of [Zn(py)-PyTIPP] (**2**) and the pyridine solvate of [Cu-PyTIPP] (**3**) were monitored by single crystal X-ray diffraction.‡ Together, they demonstrate a consistent assembly of the PyTIPP scaffolds into chiral architectures. This study provides a unique example of the induction of supramolecular chirality by halogen bonds (the tendency of halogen atoms to be involved in directional interactions with lone pair-possessing atoms) and confirms that such bonding can serve as an important tool in the patterning of supramolecular assemblies.[3] A unique example, showing that strong $I\cdots I$ halogen bonding can be used for

*School of Chemistry, Sackler Faculty of Exact Sciences, Tel Aviv University, Tel Aviv, Israel. E-mail: Goldberg@post.tau.ac.il; Fax: +972 3 6409293; Tel: +972 3 6409965*

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directing the construction of a chiral structure from a non-chiral module, has been reported recently.[3h]

All three crystal structures can best be described as being composed of flat supramolecular layers of porphyrin units (irrespective of their metalation state, molecular conformation and unit cell content), interconnected to one another by head-to-tail $N\cdots I$ bonds within 2.87–3.06 Å between adjacent molecules, perfectly aligned along straight lines (Fig. 2). The *trans*-related pyridyl and iodophenyl groups of the porphyrin moiety are involved in these interactions at distances that are considerably shorter than the sum of the corresponding van der Waals radii of N and I atoms (*ca.* 3.5–3.8 Å).[3a,4] Such neighboring chains further interact on both sides *via* secondary $I\cdots\pi$ interactions (at iodine-ring distances within 3.4–3.6 Å, with the sideways-directed C–I bonds of one chain being oriented nearly perpendicular to the iodophenyl and pyridyl aryl groups of adjacent $N\cdots I$-bonded chains).[5] In **2**, attractive inter-chain $I\cdots I$ contacts (within 3.68–3.73 Å) are also apparent.

In the three compounds, the halogen-bonded layers offset-stack along the normal direction at an interlayer distance of approximately 4.5 Å, as has been commonly observed in numerous porphyrin structures.[6] More interestingly, however, all the layers are aligned in the same direction, imparting chirality upon the entire 3D assembly. The latter is character-ized by space group symmetry $P1$ in **1** and **2**, and $C2$ in **3**. The chirality of the layered structure is preserved, even though there are four crystallographically-independent molecules (and layers) in **2** and two independent porphyrin moieties (and layers) in **3** (Fig. 3). The interlayer stacking is stabilized by dispersion forces between the porphyrin assemblies, as well as
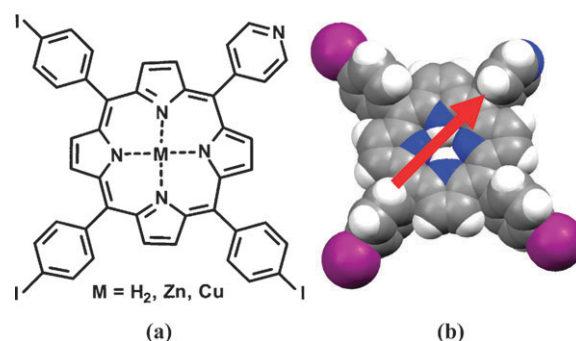


**Fig. 1** (a) Structural formula of the porphyrin building blocks [M-PyTIPP]. (b) Space-filling illustration of the free base PyTIPP derivative. The arrow indicates the main direction of the molecular asymmetry. Note the lack of inversion or strict mirror symmetry in the observed molecular conformation in the crystal (see text).
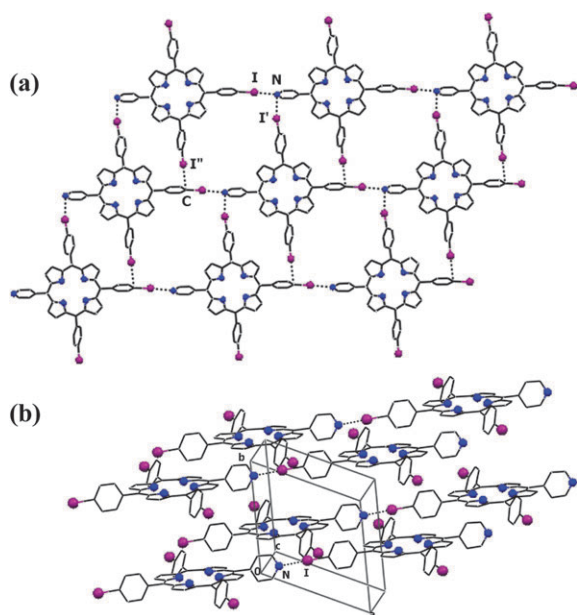
**Fig. 2** (a) The supramolecular layered assembly of PyTIPP in **1**. The dashed I···N contact indicates the directional halogen bond, while the I′···N and I″···C dashed lines represent the I···π interactions. (b) Uni-directional arrangement of two successive layers; only the N···I halogen bonds are indicated by dashed lines. (The crystal packing diagrams in all figures exclude the crystallization solvent.)

by cooperative dipolar attractions between iodophenyl groups (those not involved in the N···I bonds) of neighbouring layers, which are aligned in an anti-parallel fashion.

It is clearly apparent from the above examples that the consistent occurrence of supramolecular chirality in crystals of the [M-PyTIPP] scaffold (**1–3**) is associated with the asymmetric substitution of the pyridyl and iodophenyl functional groups on the porphyrin core. Moreover, the molecular structure cannot sustain a planar macrocyclic core, with the aryl substituents perfectly perpendicular to it, due to steric hindrance between the proxime protons on the peripheral C-atoms of the pyrrole groups and the *ortho* positions of the aryl rings (Fig. 1(b)). Thus, the [M-PyTIPP] unit, irrespective of its actual conformation (planar or distorted) and whether it is in its free base or metalated form, lacks inversion or mirror plane symmetry elements and is chiral (the chirality of the individual molecular units is particularly apparent in structure **3** due to their marked saddle-type deformation). This asymmetry, when combined with effective directional N···I halogen bonding between the porphyrin units (in spite of the low energy associated with the iodo···pyridine bonds),[3c,d] is transmitted to the layered supramolecular assemblies that form, and subsequently to the entire crystalline architecture of the stacked layers. In a recent publication, Miyata and co-workers proposed an elegant empirical explanation of the generation of chiral layered crystals from dynamically achiral (in solution) molecular units, which as a result of the supramolecular interactions, freeze in a chiral form.[1c] The observation of supramolecular chirality in the PyTIPP-based structures can be interpreted in similar terms. As in Miyata's case, the induced asymmetry of the porphyrin and the polarity of a

given N···I halogen-bonded chain preferentially effect the assembly of chains of similar chirality into layers of specific directionality, while optimising the inter-chain arrangement by I···I and I···π secondary interactions that involve the iodophenyl groups perpendicular to the chains. The observed 2.87–3.06 Å N···I contacts represent halogen bonds of medium strength. They are only slightly more extended that the shortest N···I bonds, of 2.69 Å, recorded thus far,[3h] yet they appear to be adequately effective in directing the multi-porphyrin self-assembly process in **1–3**.

Structures **1–3** reveal characteristic offset stacking of the supramolecular porphyrin layers, stabilized by dispersion forces[6] and supplemented by a minor coulombic contribution. For a quantitative estimate of the involved energies,[7] the atom–atom potential level[8] yields interactions of −45 to −53 kJ mol⁻¹ between pairs of closely-stacked porphyrin molecules, and PIXEL analysis[9,10] yields an interaction of −11 kJ mol⁻¹ between the model molecular pair iodobenzene–pyridine. Dispersive interactions are obviously orientation-insensitive, and the minor but quite effective halogen bond contribution could equally be well satisfied in a chiral or racemic arrangement. Thus, enthalpic contributions alone do not seem to be adequate for a discussion of crystal stereo-chemistry, which could be highly sensitive to entropic or even kinetic factors at the nucleation and growth stages. So how does nature account for the negative entropy associated with the chiral stacking in **1–3**? The answer to this question is provided by the crystallographic evaluations. As the structural models involved in this study incorporate heavy electron-rich iodine atoms, analyses of the anomalous dispersion effects in the crystallographic refinements indicate that all the examined crystals are twinned to a varying degree.‡ Thus, they represent conglomerates of solid domains of opposed chirality. The
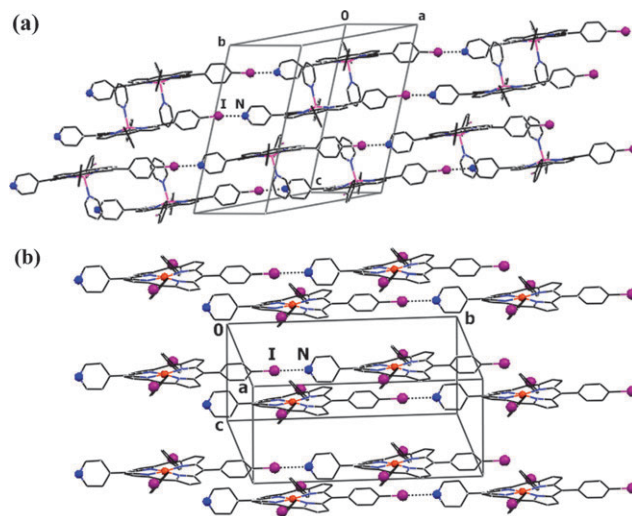


**Fig. 3** (a) Uni-directional arrangement of the four crystallographically-independent layers (viewed edge-on) of **2** in space group *P*1. (b) Supramolecular layered assembly of [Cu-PyTIPP] units and the uni-directional arrangement of three successive layers in **3**. The N···I halogen bonds are marked by dashed lines. Note that in **1**, the porphyrin core in flat, in **2** the Zn(py)-porphyrin core has a domed topology, while in **3** the Cu-porphyrin core reveals a saddle-type deformation into a chiral form.

occurrence of twinned (conglomerate), rather than racemic crystals, provides another indication of the high propensity of the [M-PyTIPP] system to exhibit, from a microscopic structural point of view, supramolecular chirality in the crystalline state.

However, this tendency cannot be harnessed at the present time in practical applications due to the conglomerate appearance of these materials. Yet, this study (along with our earlier results),[2] provides a useful concept and a reliable protocol for the supramolecular synthesis of polar porphyrin frameworks, which will be applied in future attempts to crystal-engineer chiral microporous solids.[11] A rigorous thermodynamic interpretation of the observed supramolecular chirality in crystals provides a considerable challenge for future investigations.

## Notes and references

‡ *Crystal data:*

**1**: $C_{43}H_{26}I_3N_5 \cdot 2C_6H_5NO_2$, $M_r$ = 1239.61, triclinic, space group $P1$, $a$ = 10.6814(3), $b$ = 11.1396(3), $c$ = 11.4818(4) Å, $\alpha$ = 103.635(1), $\beta$ = 93.441(1), $\gamma$ = 110.096(2)°, $V$ = 1231.87(6) Å³, $T$ = 110 K, $Z$ = 1, $\mu_{Mo\text{-}K\alpha}$ = 19.57 cm⁻¹, $\rho_{calc}$ = 1.671 g cm⁻³, prism 0.35 × 0.20 × 0.15 mm, 13 768 reflections measured, of which 9381 were unique ($R_{int}$ = 0.046) and 7890 with $I > 2\sigma(I)$. Final $R1$ = 0.042 and w$R2$ = 0.084 for the 7890 data above the intensity threshold. CCDC 662252.

**2**: $C_{48}H_{29}I_3N_6Zn \cdot C_3H_7NO$, $M_r$ = 1208.94, triclinic, space group $P1$, $a$ = 15.9721(4), $b$ = 17.4838(4), $c$ = 18.8968(5) Å, $\alpha$ = 66.985(1), $\beta$ = 86.963(1), $\gamma$ = 75.270(1)°, $V$ = 4690.9(2) Å³, $T$ = 110 K, $Z$ = 4, $\mu_{Mo\text{-}K\alpha}$ = 25.44 cm⁻¹, $\rho_{calc}$ = 1.712 g cm⁻³, needle 0.60 × 0.40 × 0.20 mm, 39 597 reflections measured, of which 29 624 were unique ($R_{int}$ = 0.066) and 20 744 with $I > 2\sigma(I)$. Final $R1$ = 0.067 and w$R2$ = 0.159 for the 20 744 data above the intensity threshold. CCDC 662254.

**3**: $C_{43}H_{24}CuI_3N_5$ (excluding disordered solvent), $M_r$ = 1054.91, monoclinic, space group $C2$, $a$ = 24.2489(13), $b$ = 20.5698(11), $c$ = 9.1014(5) Å, $\beta$ = 94.477(4)°, $V$ = 4525.9(4) Å³, $T$ = 110 K, $Z$ = 4, $\mu_{Mo\text{-}K\alpha}$ = 25.61 cm⁻¹, $\rho_{calc}$ = 1.548 g cm⁻³, plate 0.30 × 0.20 × 0.05 mm, 20 122 reflections measured, of which 10 024 were unique ($R_{int}$ = 0.066) and 7222 with $I > 2\sigma(I)$. Final $R1$ = 0.060 and w$R2$ = 0.148 for the 7222 data above the intensity threshold. CCDC 662255. In **3**, the contribution of the disordered solvent, which couldn't be modelled, was subtracted from the diffraction pattern.

The three chiral layered crystal structures (with all the layers oriented in the same direction) are pseudo-centrosymmetric, and the molecular frameworks within them arrange in a nearly centrosymmetric manner. It is the asymmetric disposition of the iodine atom between the halogen-bonded pyridyl and iodophenyl groups that makes the major difference; the iodine is 2.87–3.07 Å distant from the N-site it points at, but only ~2.1 Å from the $C_{phenyl}$ atom it covalently binds to. Alternative structural models, representing racemic intermolecular organization, were found to be highly inconsistent with the diffraction data, yielding high $R$-factors (the diffraction pattern is dominated by the strong I-scatterers, and the $R$-factors are very sensitive to their accurate positioning). All of the crystals were found to be twins of varying composition of inter-grown domains of opposing chirality: 1 : 1 (**1**), ~1 : 9 (**2**) and ~1 : 2.5 (**3**).

For crystallographic data in CIF or other electronic format see DOI: 10.1039/b719625c

§ *Synthesis of PyTIPP:* 1.25 g (5.4 mmol) of 4-iodobenzaldehyde and 0.34 ml (3.6 mmol) of 4-pyridinecarboxaldehyde were added to 35 ml of hot propionic acid at 120 °C. Then, 0.5 ml of distilled pyrrole (7.21 mmol) was added, and the resulting solution heated to reflux for 90 min. Next, the solvent was removed by vacuum distillation, and the crude product digested with hot water to remove traces of propionic acid, then filtered, washed with water and dried. The crude porphyrin mixture was dissolved in chloroform and loaded onto a silica column using chloroform. The desired porphyrin, PyTIPP, was eluted with 3% acetone in chloroform as the second fraction. The yield was found to be 0.165 g (9%) based on pyrrole. ¹H NMR (CDCl₃): 9.00 (dd, 2H,

$J$ = 5.9 Hz), 8.80 (m, 8H), 8.10 (asymmetric t, 8H, $J$ = 6 Hz, $J$ = 8.6 Hz), 7.89 (d, 6H, $J$ = 8.2 Hz), −2.93 (s, 2H). UV-vis in CH₂Cl₂: $\lambda_{max}$/nm (log $\varepsilon$) 419 (5.96), 515 (4.60), 549 (4.18), 589 (4.01), 645 (3.72). FAB mass spectrum ($m/z$) for $C_{43}H_{26}N_5I_3$: found 994, calc. 993.43.

*Preparation of metal derivatives:* The free base porphyrin (0.05 g, 5.03 mmol) was dissolved in 25 ml of CHCl₃. To this, M(OAc)₂ hydrate (where M = Cu(II) and Zn(II)) (0.09–0.125 g, 0.05 mol) in 2 ml of methanol was added, and the mixture heated for 10 min on a water bath at 75 °C and then evaporated to dryness. The crude porphyrin was next washed with water. The metal complexes were dried under vacuum and their yields were found to be almost quantitative. [Zn-PyTIPP]: ¹H NMR (DMSO-$d_6$): 8.98 (d, 2H, $J$ = 5.8 Hz), 8.79 (m, 8H), 8.16 (asymmetric t, 8H, $J$ = 5.76 Hz, $J$ = 8.2 Hz), 7.94 (d, 6H, $J$ = 8.2 Hz). UV-vis in a CH₂Cl₂/pyridine mixture: $\lambda_{max}$/nm (log $\varepsilon$) 429 (5.69), 562 (4.15), 602 (3.69). FAB mass spectrum ($m/z$) for $C_{43}H_{24}N_5I_3Zn$: found 1057, calc. 1056.8. [Cu-PyTIPP]: UV-vis in a CH₂Cl₂/pyridine mixture: $\lambda_{max}$/nm (log $\varepsilon$) 416 (5.82), 540 (4.37), 589 (4.18). FAB mass spectrum ($m/z$) for $C_{43}H_{24}N_5I_3Cu$: found 1055, calc. 1054.96.

*Supramolecular synthesis:* 4 mg (0.004 mmol) of PyTIPP was dissolved in 2 ml of chloroform, followed by a few drops of either nitrobenzene or ethyl benzoate, and allowed to evaporate slowly. X-Ray quality crystals of the nitrobenzene solvate (structure **1**) were obtained after 7 d. When ~4 mg (0.004 mmol) of [Zn-PyTIPP] and [Cu-PyTIPP] were dissolved in 1.5 ml of a 2 : 1 mixture of DMF/pyridine (v/v) and allowed to evaporate slowly, X-ray quality crystals of a DMF solvate of [Zn(py)-PyTIPP] (structure **2**) and a pyridine solvate of [Cu-PyTIPP] (structure **3**) were obtained after 10 d. The uniform identity of the crystal lattices formed from different reactions was confirmed in each case by repeated measurements of the unit cell dimensions of different single crystallites. All crystals were coloured red/purple.

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