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Development of Novel Fluorescent Dye Molecules Based on BODIPY

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Degree of Doctor of Philosophy

Hawazen Hassanain, MSc (by Research)

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Declaration

Except where specific reference is made to other sources, the work presented in this thesis is the original work of the author. It has not been submitted, in whole or in part, for any other degrees.

Signed: Hawazen Hassanain

Date:

Abstract

This thesis details the synthesis, optical, fluorescence, electronic properties, solid state arrangement and intermolecular interaction of functionalized 4,4-difluoro-4-bora-3a,4a-diaza-s-indacene (BODIPY) chromophores. **Chapter 1** is a concise overview of the structure, synthesis routes, properties, applications, and fundamental concepts of BODIPY fluorophores.

The target of **Chapter 2** is to functionalize BODIPY chromophores at the 2,6-positions halogen substituents to afford molecules with strong absorbance in the visible spectrum and new electronic properties due to the presence of the heavy atoms on the BODIPY framework. We have investigated the halogenation and subsequent reactions of BODIPY species which are methylated in the 3,5-positions. The use of an excess of the halogenating reagent (N-iodosuccinimide) leads to selective halogenation of the α -methyl groups, which can be post-functionalized *via* nucleophilic substitution with morpholine, allowing the investigation of the effect of the combination of halogen atoms and non-conjugated tertiary amine substitution. The effect of such substitution on the solid-state arrangements, absorption, fluorescence and electronic properties of these dye molecules is reported.

Chapter 3 focuses on halogen bonding interactions in the solid-state structure of halogenated BODIPY compounds. The presence of halogen atoms, BF₂ moiety and/or other electron acceptor groups on BODIPY core can lead to interesting halogen bonding interactions in the solid-state structures of such compounds. Therefore, a search of the Cambridge Structural Database (CSD) was performed in order to find experimental evidence for halogen bonding interactions in the solid-state structures of halogenated BODIPY compounds. Hirshfeld surface analyses and fingerprint plots were used to

investigate the effect of different substituents on the intermolecular interactions and provide evidence for the occurrence of halogen bonding interactions which exist in crystal structures of BODIPY compounds.

The target of **Chapter 4** is to functionalize the BODIPY chromophores at the 2,6-positions by pyridyl and pyrimidyl substituents to afford molecules with strong absorbance in the visible spectrum and remarkable fluorescence in solution, thin film, powder and as single crystals. When CuI and 2,6-dipyridyl-1,3,5,7-tetramethyl,8-phenyl-4,4-difluoroboradiazaindacene (pyr-Bodipy) are reacted, a two-dimensional coordination polymer is formed. However, analogous reactions with 2,6-dipyrimidyl-1,3,5,7-tetramethyl,8-phenyl-4,4-difluoroboradiazaindacene (pyrm-Bodipy) afford a three-dimensional, metal-organic framework. The effect of such substitution on the solid-state arrangements, reflectance, fluorescence, infrared spectroscopy (IR), powder X-ray diffraction (XRD), and single crystal X-ray diffraction is reported.

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List of Symbols and Abbreviations

The following abbreviations appear in this dissertation:

δ	Chemical shift
$\text{\AA}$	Ångstrom(s)
BODIPY	4,4-difluoro-4-bora-3a,4a-diaza-s-indacene
^{13}C NMR	Carbon-13 Nuclear Magnetic Resonance
d	Doublet
dd	Doublet of doublets
DFT	Density functional theory
ϵ	Epsilon; molar extinction coefficient
E	Electrochemical potential, voltage
$E_{1/2}$	Half-wave potential
ESI-MS	Electrospray Ionisation Mass Spectrometry
^1H NMR	Proton Nuclear Magnetic Resonance
h	Hour
λ	Lambda ;wavelength
λ_{max}	Wavelength of maximum absorption or emission
HOMO	Highest occupied molecular orbital
Hz	Hertz
HRMS-ESI	High Resolution (Mass Spectrometry) Electrospray Ionization
I	electrical current
IR	Infrared spectroscopy
IUPAC	International Union of Pure and Applied Chemistry
J	Coupling constant

LUMO	lowest unoccupied molecular orbital
MALDI-TOF	Matrix Assisted Laser Desorption Ionization
MHz	Megahertz
Min	Minute
Mmol	Millimoles
MS	Mass Spectrometry
NEt ₃	Triethylamine
m/z	Mass to charge ratio
Φ	Quantum yield
Φ_F	Quantum yield of fluorescence
s	Singlet
Fc	Ferrocene [$(\eta^5\text{-C}_5\text{H}_5)_2\text{Fe(II)}$]
Fc ⁺	Ferrocenium [$(\eta^5\text{-C}_5\text{H}_5)_2\text{Fe(III)}]^+$]
T	Triplet
TLC	Thin Layer Chromatography

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Chapter 1

Introduction to BODIPY

1.1 Introduction

Bright colours and a wide range of applications make fluorescent dyes of interest in many fields of study including medical, biological, technological, industrial and environmental applications.¹⁻⁴ There are numerous examples of nonradioactive fluorescent organic dyes, which have been used for the fluorescence imaging of biomolecules in living cells and industrial applications, such as coumarin (**1-1**), fluorescein (**1-2**), rhodamine (**1-3**), 4,4-difluoro-4-bora-3a,4a-diaza-*s*-indacene, abbreviated as BODIPY (**1-4**), and cyanine dye (**1-5**) as shown in **Fig 1.1**.^{3, 5-7}

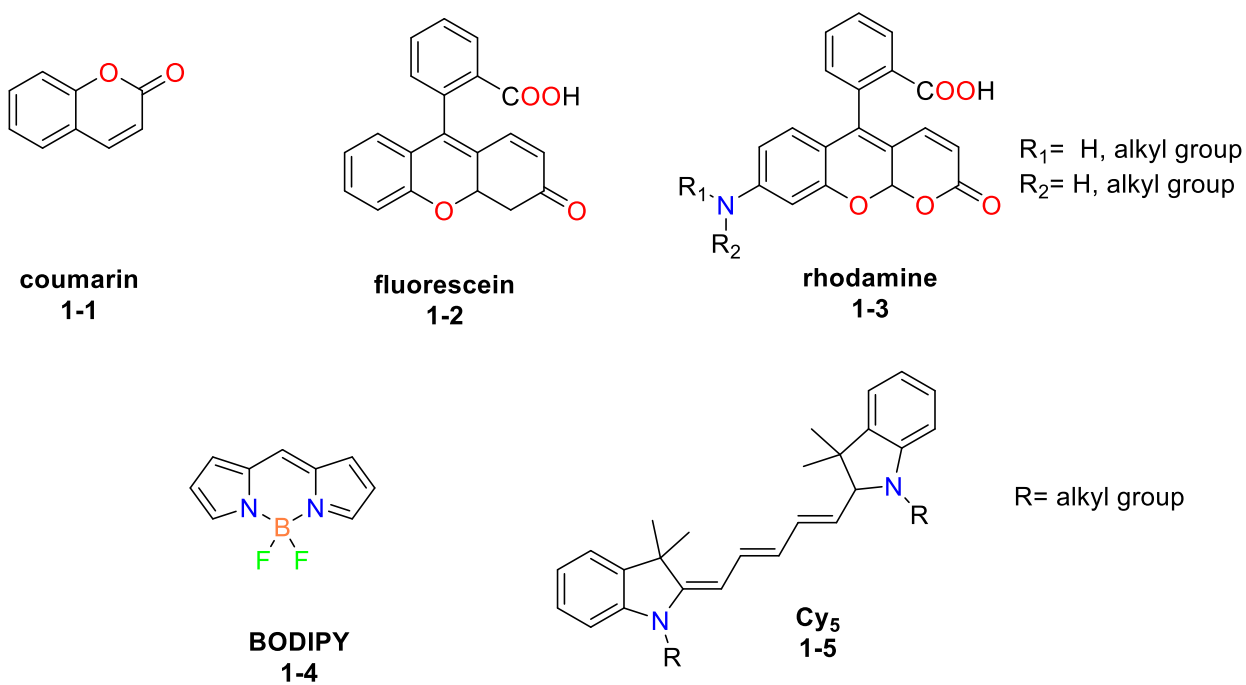


Fig 1.1. Commonly used fluorescent dyes.^{3, 5-7}

1.1.1 Introduction to BODIPY

BODIPYs were first reported by Treibs and Kreuze in 1968.⁸ The importance of BODIPYs in the field of biological imaging were recognized between the 1980s and 1990s, when Haugland and Kang applied for a series of patents on the use of BODIPY as a biomolecule label.⁹ Since then the interest in the application of BODIPY complexes has led to an increase in the number of patents and publications^{1, 9-12} in order to investigate other technological and environmental applications^{9, 13} such as in light-harvesting devices,¹⁴ solar cell technology,^{15, 16} chemical sensors,¹⁷ nanocrystals,⁹ biological marking, photodynamic therapy and drug delivery.¹⁸⁻²² This thesis details the synthesis and optical, electrochemical, photophysical, solid state analysis of different substituted BODIPY species. Therefore, this introduction will concentrate only on the BODIPY in general with a more detailed introduction, including more specific information, given at the start of each chapter.

1.1.2 Structure of BODIPY

BODIPY is formed from the complexation of a bidentate monoanionic dipyrromethene ligand with a disubstituted boron moiety, typically in the form of a BF₂ group, which is achieved by using boron trifluoride diethyl etherate as shown in **Fig 1.2**.²³ The dipyrromethene ligand is formed from the linking of the α -position of two pyrroles *via* a methine bridge.²⁴ BODIPY is an analogue of *s*-indacene (**1-6**), therefore, it is known as boradiazaindacene and the IUPAC numbering system (depicted in **Fig 1.2**)²³ follows the same rules as those used for (**1.7**).²³ Moreover, the BODIPY structure could be considered as an example of “rigidified” mono-methine cyanine as shown in **Fig 1.2**.²⁵ The BODIPY fluorophore is isoelectronic with heptamine cyanine possessing 12 π electrons equally delocalized over eleven atoms, rather than

the monomethine cyanine dye with 6π electrons equally distributed over five atoms because the boron centre does not take part in the electronic delocalization^{26, 27}

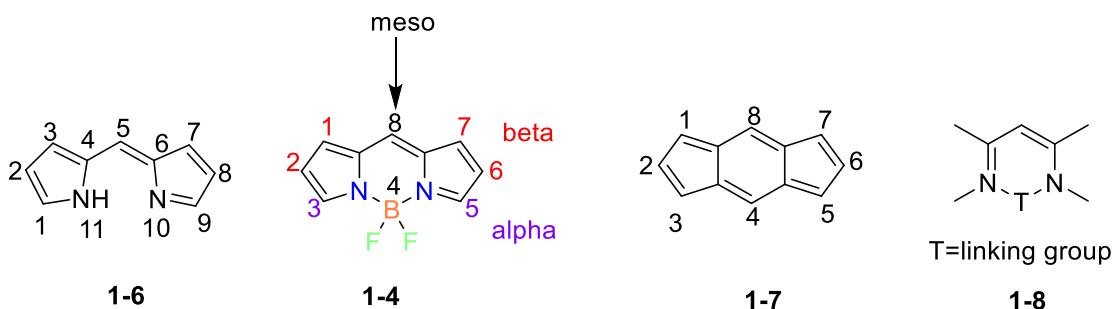


Fig 1.2. Structure of a basic dipyrin structure, basic BODIPY core structure (**1-4**) and its numbering system (the 8-position is often specified as *meso*, 3,5-positions are referred to as α , and 1,2,7,8-positions are referred to as β). *s*-Indacene (**1-7**) and its numbering system.²³ Structure of "rigidified" mono-methine cyanine (**1-8**).²⁵

The presence of a (BF₂) group restricts the flexibility of these compounds (*i.e.* prevents cis/trans isomerization of the dipyrromethene), which leads to unusually high fluorescence quantum yields.⁹ The π -electrons delocalize along the BODIPY framework which can be further extended by substitution or fusion of aromatic units to one or both pyrrole rings leading to further increasing the fluorescence.^{9, 25} The presence of an extended delocalization pathway by functionalizing the *meso*, α , and β positions of the BODIPY core can extend π conjugation and to generate a "push-pull" structure leading to red-shifted BODIPY dyes.²⁵

Furthermore, the BODIPY structure has an overall neutral charge, as shown in **Fig 1.3**, due to resonance stabilisation of the BODIPY framework.^{23, 24} The molecular dipole moment is oriented along the transversal axis and the negative charge is located around the fluorine atoms, and the positive charge around the *meso* position (**Fig 1.3b**).²⁸

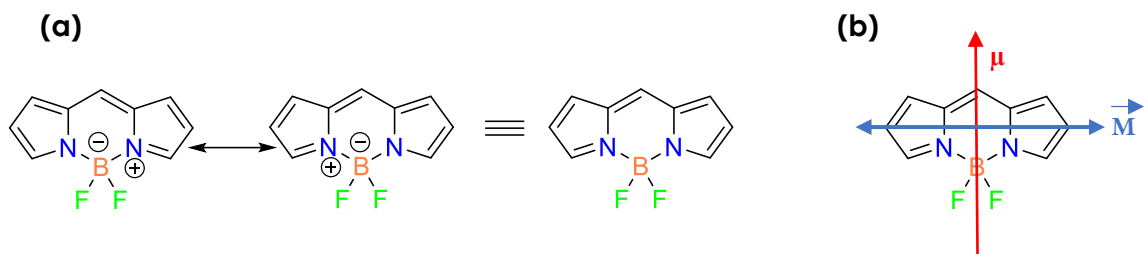
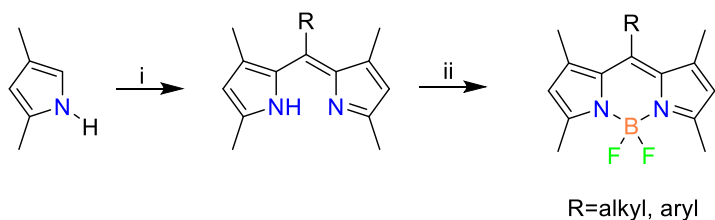


Fig 1.3 (a) The two equivalent resonance form of a BODIPY.^{23, 24} (b) Frontier molecular orbitals and charge distribution by means of the electrostatic potential mapped onto the electronic distribution. (b) The direction of the molecular dipole moment (μ) as well as the transition dipole moment (M) is also depicted, (b) Adapted from reference 28.

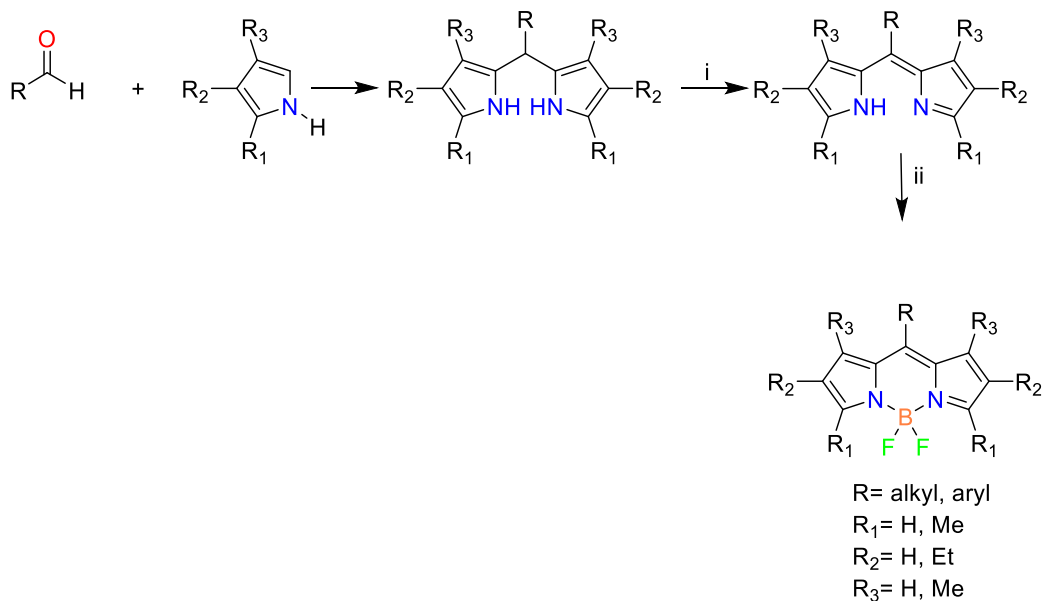
1.1.3 General BODIPY Synthesis

The general routes for preparing *symmetrical* BODIPYs is *via* the condensation of pyrrole with a highly electrophilic carbonyl compound (*e.g.* an acid anhydride or acyl chloride)⁹ to form a methene bridge, linking two pyrrole rings. The α and β positions in the pyrrole unit are commonly substituted to avoid polymerisation.⁹ After the preparation of dipyrin, the addition of boron trifluoride diethyl etherate in the presence of a base leads to the formation of the BODIPY compound (**Scheme 1.1**).⁹ The first method used to synthesise a BODIPY derivative, reported by Treibs and Kreuzer, followed such a strategy.²⁹



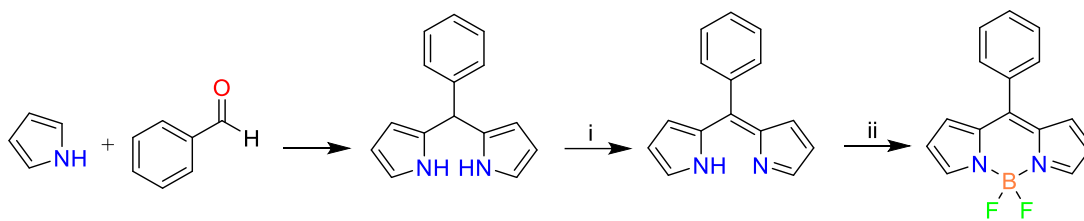
Scheme 1.1 The first synthesis of a boron dipyrin dye by Treibs and Kreuzer.²⁹ (i) acid anhydride or acyl chloride, (ii) Base, $\text{BF}_3 \cdot \text{Et}_2\text{O}$.

Condensation of aromatic aldehydes with pyrroles affords the dipyrromethane rather than the dipyrromethene and must be subsequently oxidized to generate the desired conjugated bipyrrolic system (**Scheme 1.2**). In order to avoid forming pyrrolic chains longer than two units, the starting pyrrole must have only one α -position available for reaction.



Scheme 1.2. The general route for BODIPY syntheses by using aldehyde. (i) oxidizing agent, (ii) base, $\text{BF}_3 \cdot \text{Et}_2\text{O}$.

In 2008, Wu *et al.* reported a new route with higher yield by using only an aldehyde such as benzaldehyde in a solvent-free condensation by using fully unsubstituted pyrrole. In this route, pyrrole is used as reactant and solvent. An acid catalyst is also used to initiate the reaction. The dipyrrolmethane is then oxidised using 2,3-dichloro5,6-dicyano-p-benzoquinone (DDQ) and converted to the BODIPY through reaction with boron trifluoride diethyl etherate.¹⁰



Scheme 1.3. Syntheses of BODIPY by Wu and co-workers.¹⁰ (i) oxidizing agent, (ii) base, $\text{BF}_3 \cdot \text{Et}_2\text{O}$.

1.1.4 Photophysical Properties of BODIPY

1.1.4.1 General

For a better understanding of the detection mechanisms of BODIPY-based molecular devices, presented in the next sections, herein the main photophysical processes and basic principles that are involved in the fluorescence sensing will be briefly discussed. In general, when considering the power of a fluorescent compound in sole respect to its optical properties, the three most commonly referenced data points are that of the absorption and emission maxima and the corresponding quantum yield and Stokes shift. During the photon absorption process an electron is excited from a lower energy level (ground state S_0) to a higher energy level (singlet excited state S_1). Upon the fast relaxation of the excited electron to the ground state (S_0) an emission of a photon is observed; this process is known as fluorescence and is shown in **Fig 1.4**. Other characteristic parameters of fluorophore are the absorption (λ_{abs}) and emission (λ_{emiss}) maxima. Fluorescence usually occurs at lower energies and longer wavelength than excitation. As shown in **Fig 1.4**, the energy difference between the S_0 and S_1 levels or the difference in energy between λ_{abs} and λ_{emiss} is known as the Stokes shift. The common reason for the Stokes shift is the loss of energy through the non-radiative vibrational relaxations, but

additional energy loss can take place through the solvent stabilization of excited state, complex formation, energy transfer, etc.^{30,31}

Fluorescence can be quantified through two major features: quantum yield and lifetime. The fluorescence quantum yield (Φ) is possibly the main characteristic of the efficiency of the fluorophore to emit light through fluorescence. The fluorescence quantum yield (Φ) is defined as the ratio between the number of emitted photons and the number of photons absorbed by the sample. Fluorophores with Φ value close to 1 are the best emitters, for nonfluorescent compounds Φ is approaching 0. Many conditions could control the fluorescence quantum yield such as temperature, solvent polarity, type of substituents in the fluorophore, etc.^{30,31}

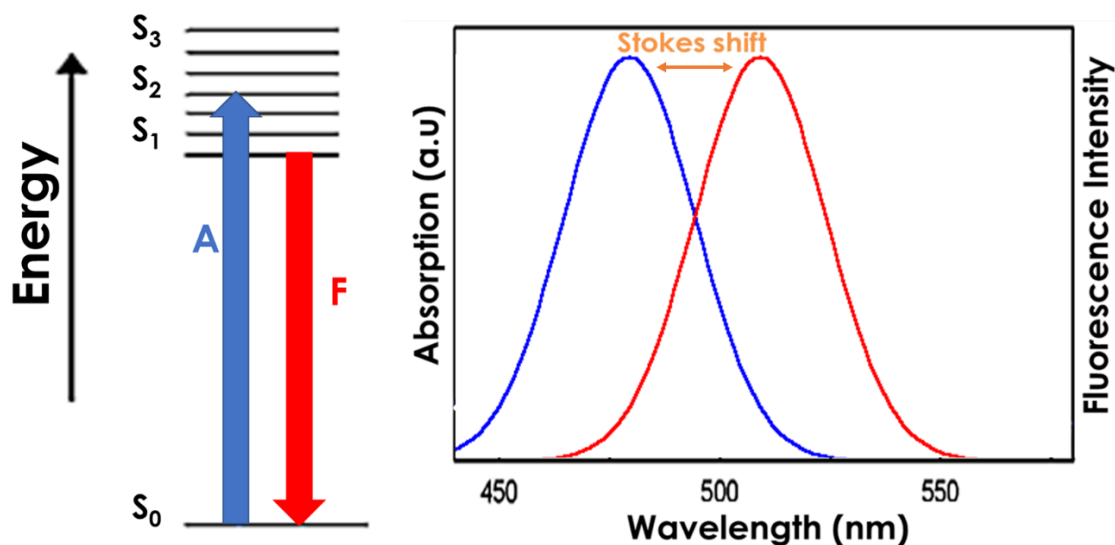


Fig 1.4 Jablonski diagram representing fluorescence energy levels and Stokes shift where A = absorption and F = fluorescence . Adapted from references 30-31.

Finally, another important parameter of fluorophores is fluorescence lifetime. The fluorescence lifetime (τ) refers to the average time the electron stays in the excited state before emitting a photon and returning to the ground state, as detected by fluorescence spectroscopy.

Fluorescence lifetime includes both relaxation pathways, radiative and radiationless (without emission of light quanta). Different compounds have different lifetimes and numerous compounds often display sub-nanosecond lifetimes ³⁰ (e.g. the fluorescence lifetime (τ) for BODIPYs in general is around 4-6 ns, which can be useful for a variety of applications).⁹

1.1.4.2 BODIPY Fluorescent Properties Quenching mechanisms

As previously mentioned, the fluorescence of BODIPY has gained importance due to use of BODIPY for biological, technological and environmental applications. Moreover, the BODIPY core holds an overwhelming potential for structural modification to tune the photophysical and chemical properties. The fluorescent properties of BODIPY are controlled by several mechanisms depending on the structural modifications in the BODIPY core : photo-induced electron transfer (PET),^{3, 25, 32, 33} intramolecular (internal) charge transfer (ICT), and resonance energy transfer (RET), more often referred to as fluorescence or Förster energy transfer (FRET),^{3, 25, 34} Dexter exchange,³⁵ and intersystem crossing (ISC).^{25, 36, 37}

The first of these mechanisms is PET, which involves the intramolecular electron transfer between an electron donor and acceptor in the excited state of BODIPY as result of oxidation or reduction which leads to quenching of the fluorescence.³ Depending on whether the fluorophore acts as a donor or acceptor, there are two types of PET– reductive and oxidative, and the direction of electron donation is determined by the redox potentials of the fluorophore and quencher. The PET mechanism can be described pictorially in terms of simplified

molecular orbital scheme (**Fig 1.5**). The fluorescence intensity of the molecule is altered as a result of the electron transfer process.³

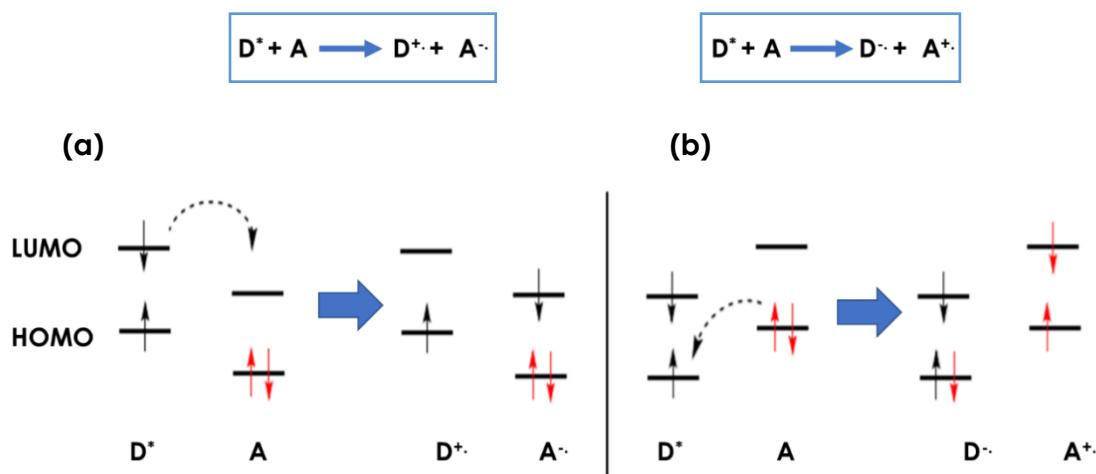


Fig 1.5. Schematic representation of the oxidative and reductive quenching mechanism. Adapted from fromBoens *et al.*³⁸

The second mechanism is the ICT mechanism. In this mechanism, the fluorophore has an electron-donating (EDG) group which is conjugated to an electron-withdrawing group (EWG). Upon excitation, the electron density distribution of the molecule is changed and changes in the dipole moment can be considered.²⁵ The solvent-dependent shift in the absorption and emission spectra would appear as a result of the increase in the dipole moment of the solvent.^{25, 38} In non-polar solvents, the excited molecule has a higher dipole moment and fluorescence from a local excited state (LE) is observed. In a polar solvent, during the lifetime of the excited state (or Franck–Condon state), the solvent shell around the dipole is equilibrated, resulting in the fluorescence from the lower energy state (ICT) with stabilized charge separation (**Fig 1.6**).³⁸ Therefore, these dyes are characterized by “normal” emission in

non-polar solvents from LE state, but due to the solvent stabilization in the polar media, a bathochromic shift and decrease in quantum yield in the emission of the ICT state are observed.³⁸ However, the ground state rarely has the bigger dipole moment than the excited state which leads to a shift in the emission spectrum to the shorter wavelength in polar solvents. The emission spectrum is shifted to the shorter wavelength.³⁸ **Fig 1.6** shows the mechanism of ICT based fluorescent probes.

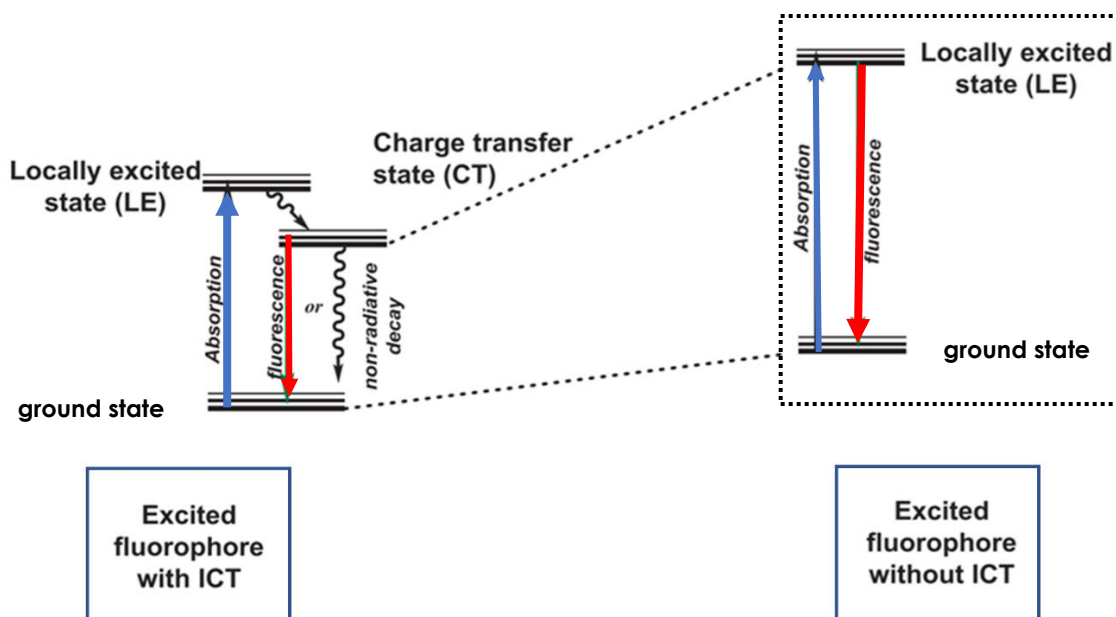


Fig 1.6. Illustration of mechanism of ICT based fluorescent probes.

However, the largest difference between PET and ICT sensors is the fluorescence response upon analyte recognition. PET probes show fluorescence quenching without pronounced spectral shifts which rules out ratiometric measurements at two wavelengths. Therefore, the terms “off–on” and “on–off” fluorescent sensors are often used with PET probes. In contrast, indicators based on ICT compounds display clear fluorescence band shifts upon analyte binding which make ratiometric measurements possible.^{25, 38} ICT-based probes not only

generate fluorescence intensity changes, but more importantly lead to shifts for both absorption and emission spectra due to the change of energy gap before and after binding events. This character makes it possible to measure the change simultaneously at two different wavelengths, which known as ratiometric measurement. There are numerous BODIPY-based probes for metal cations and pH sensing are in this category.³⁹⁻⁴²

The third mechanism is FRET. FRET is a non-radiative excitation energy transfer, which occurs between excited donor and acceptor in the ground state through the dipole-dipole interaction (also known as the Coulombic mechanism).⁴³ Usually, in FRET mechanism both the donor and the acceptor chromophores are joined in the same molecule, one of them acts as electron donor and the other chromophore acts as the electron acceptor.³ FRET can occur if the emission spectrum of the donor overlaps with the absorption spectrum of the acceptor, so that several vibronic transitions in the donor are in resonance with the corresponding transitions in the acceptor, and they have nearly the same energy (**Fig 1.7**). While the donor is always a fluorescent dye, the acceptor can also be a non-fluorescent compound. In this case, FRET is a quenching mechanism. If the acceptor is another fluorescent dye, a decrease in the donor's quantum yield and an increase in acceptor's fluorescence is observed. FRET efficiency is strongly dependent on the distance between the donor and acceptor with the optimal distances for different pairs being in a range of 1.5-6 nm.⁴⁴ FRET is often used for distance measurements in biological objects (for example, determination of protein conformation), for the investigation of supramolecular interactions, or mechanisms of chemical reactions.⁴⁴ Another application of FRET is the artificial enhancement of the Stokes shift. This phenomenon has also been widely used for the design of materials for photovoltaic devices, which contain a cascade of FRET pairs to cover a broad range of absorbed light wavelength.

For far-red and NIR BODIPY the FRET mechanism is usually coupled with ICT or PET mechanisms in order to achieve ratiometric signals.²⁵

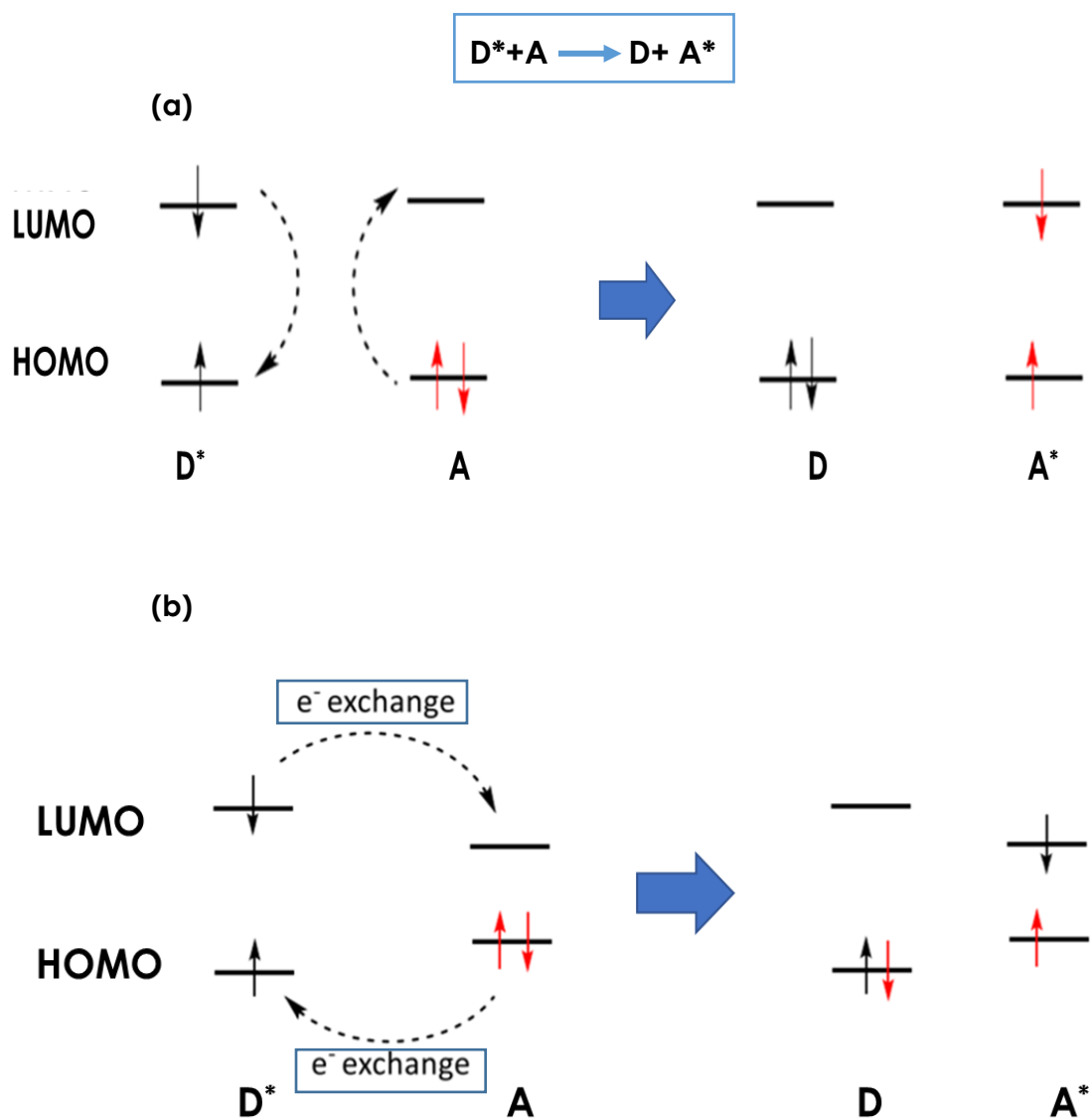


Fig 1.7. Schematic representation of (a) (FRET) mechanism. (b) Electron exchange of Dexter quenching mechanism.

Dexter exchange or Dexter quenching is an electron-exchange interaction, similar to FRET quenching. This kind of interaction occurs through the energy transfer from the excited donor to the acceptor in the ground state, but in this case, energy is transferred through electron exchange **Fig 1.7**. The electron from the LUMO orbital of the excited fluorophore is moved to the acceptor with simultaneous or consecutive transfer of an electron from the HOMO of the acceptor to the HOMO of the donor. Dexter quenching requires much shorter distances (wavefunctions overlap) of the interacting species for transfer of the excitation energy, in comparison to those in FRET. Also, Dexter exchange can be observed only at high concentrations of donor and acceptor.⁴³

Another, possible mechanism of the fluorescence quenching is the heavy atom effect (HAE) (**Fig 1.8**). Usually, fluorescence processes occur through the excitation of an electron from the singlet ground state to the singlet excited state, and then a subsequent radiative emission back to the ground state. When the electron is present in the singlet excited state, it by nature has its spin still paired with the ground state. If, this spin is reversed (*i.e.* the spins are parallel rather than anti-parallel a coupling between orbital and spin magnetic moments of the excited dye and a heavy atom is formed) the probability of the intersystem crossing (*e.g.* $S_1 \rightarrow T_1$) is increased. When this transformation of excited states occurs non radiatively and a singlet turns to a triplet or the reverse, this process is called intersystem crossing (ISC).^{37, 45-47} The ISC process results in a non-radiative loss of excited states. Moreover, the relaxation $T_1 \rightarrow S_0$ through the emission is symmetry forbidden and the formed triplet state is relatively long lived. Therefore, the triplet state can be quenched to the ground state by either internal conversion or energy loss by generating singlet oxygen.

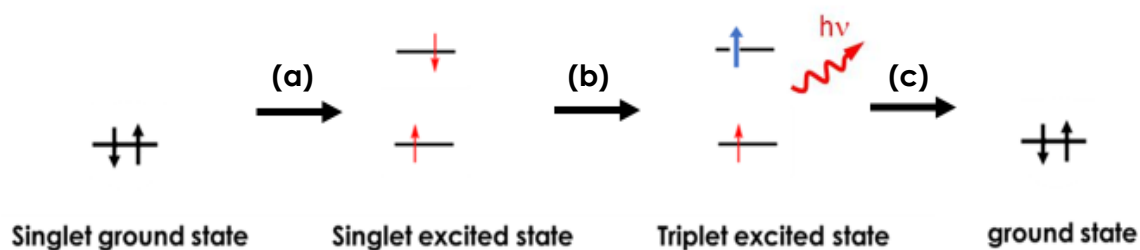


Fig 1.8. Schematic representation of intersystem crossing (ISC) mechanism. (a) excitation, (b) intersystem crossing, and (c) emission.

1.1.4.3 BODIPY Functionality and Fluorescence Mechanisms

A $\pi \rightarrow \pi^*$ transition occurs when the BODIPY framework absorbs a photon of UV light and the emission of a photon occurs when the electron relaxes back to the HOMO.^{24, 48} BODIPY compounds have high fluorescence quantum yields and they can absorb and emit light over a range 500-800 nm by modifying the BODIPY core.²⁴ **Fig 1.9** shows an example of the effect of modifying the BODIPY core,²⁴ which leads to a large Stokes shift.¹⁹

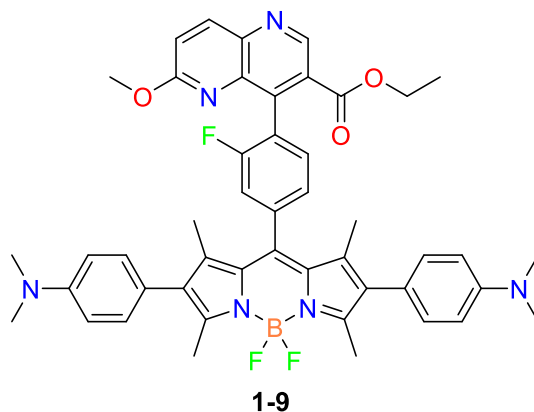


Fig 1.9 BODIPY analogue displaying a Stokes shift of 186 nm.¹⁹

Therefore, in order to understand the mechanisms which control the fluorescent properties of BODIPYs, we need to describe the effect of small structural modifications in the BODIPY framework on their optical and fluorescence properties. In general, there are two key functionalizations which create the most significant effects on fluorescence quantum yield. Firstly, the absence or presence of a group in the *meso* position of the dipyrin, its steric freedom and electronic nature will be discussed.

The second factor to be considered is the level and type of substitution around the BODIPY core at positions 1-3 and, or 5-7. For example, the only difference between **1-10** and **1-14** is the presence of a phenyl group in the *meso* position for **1-14**. The presence of this phenyl group leads to a lower quantum yield of 0.05 for **1-14** as opposed to 0.95 for **1-10** (**Fig 1.10**). This difference occurs because of the ability of the phenyl ring to quench the fluorescence by rotating (*i.e.* there is no steric restriction around rotation of this *meso* phenyl group). This rotation allows non-radiative emission to occur in the form of photo-induced electron transfer (PET) side reactions. In the case of electron transfer from the non-fluorescent component to the BODIPY core, the effect we see is the result of reductive PET or a-PET (wherein the “a” stands for acceptor in regard to the electronic state of the fluorophore itself). Consistent with this analysis the introduction of ortho-substituents on the *meso* phenyl ring has been observed to increase quantum yields. Moreover, the 1,7-substituents on the BODIPY core (*e.g.* compound **1-16**, **Fig 1.10**) showed intense fluorescent maxima the substitution in those positions inhibits free rotation of the phenyl group, creating a sterically hindered environment for the phenyl substituent and thus preventing energy loss from the excited states through non-irradiative processes.⁴⁹ It is also possible to control this effect through modification to the *meso* substituent rather than the dipyrin core itself. The presence of any groups which limit the ability for free-rotation of the *meso* functionality will generate a similar result.

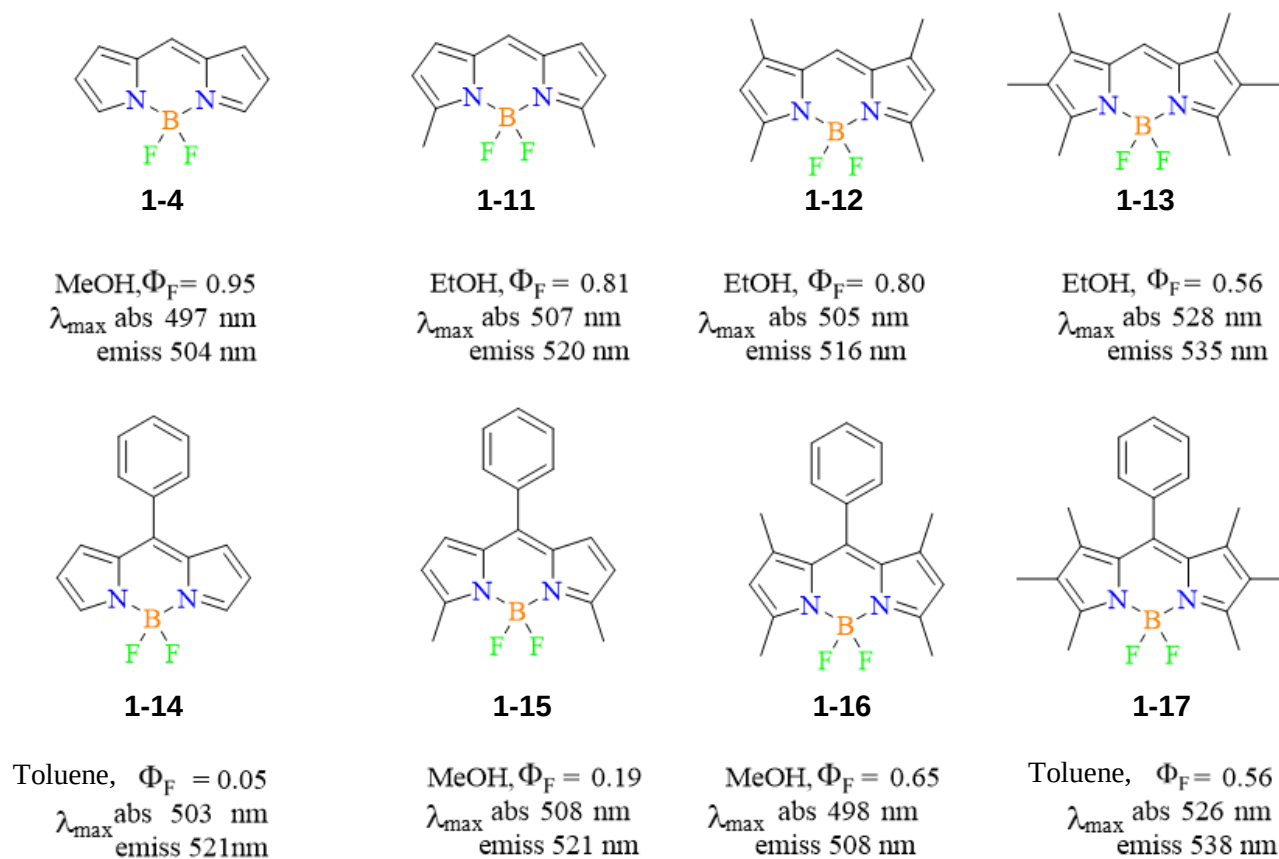
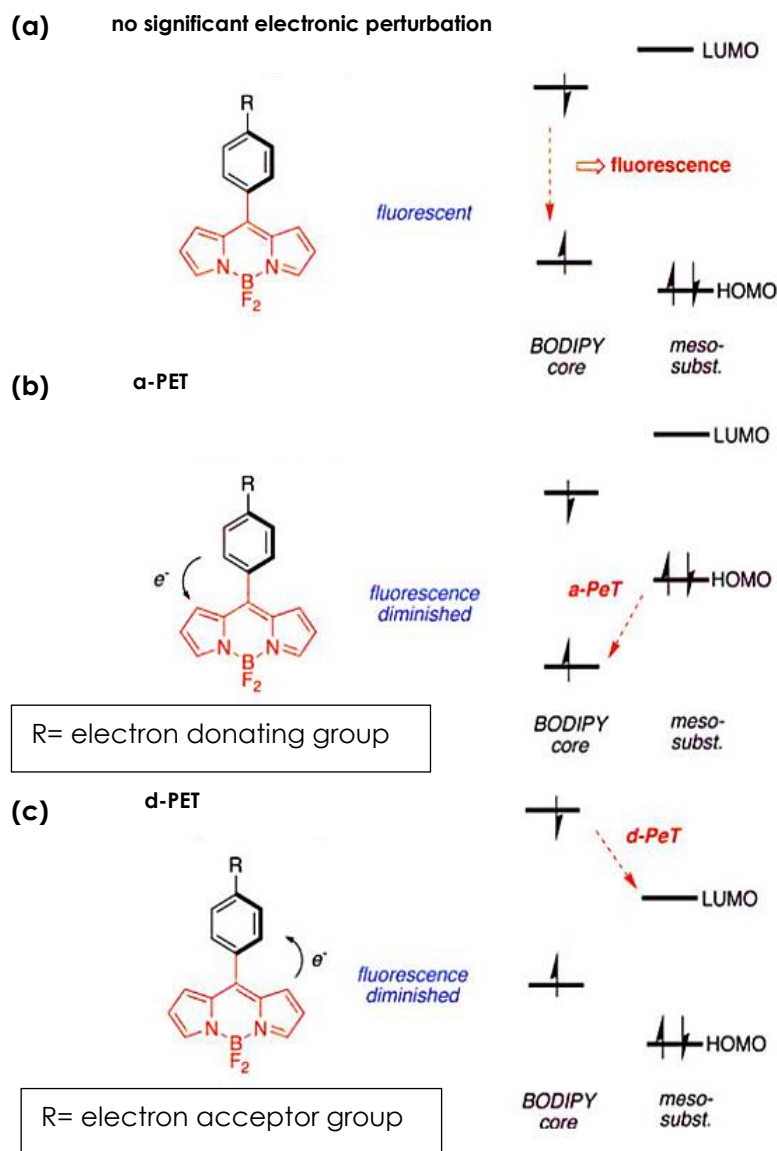


Fig 1.10. A selection of methylated “BODIPY core” derivatives, the equivalent *meso*-phenyl BODIPY’s and selected optical properties. (The optical data in the figure are from the previous publications).⁵⁰⁻⁵²

However, the choice of substituents is critical, as shown in **Scheme 1.4**, owing to the effect of electron donating or electron accepting groups at the *meso*-position upon the photo-electronics of the BODIPY framework. In the first case (**a**), the BODIPY frameworks fluoresce because there is no electron transfer within the framework. In the case of (**b**), the BODIPY compounds do not fluoresce in the presence of an electron donating group in the *meso*-position due to the PET mechanism. The donating group donates electrons to the BODIPY core in the excited state, and a reduction process is occurring. The electron transfer process in case of (**b**) is known as a-PET (where 'a' denotes acceptor). In third case (**c**), the presence of the electron acceptor group in the *meso*-position leads to electron transfer from the BODIPY core to the substituents in the excited state, and an oxidative process is occurring. The electron transfer process in case of (**c**) is known as d-PET (where 'd' denotes donor).²³ The level of substitution of the BODIPY core is another important factor, for example the quantum yield decreases from molecules **1-10** to **1-14** (**Fig 1.10**) due to the effect of increasing the level of substitution around the periphery. Similar to the effects observed for *meso* substitution, electron transfer can lead to a subsequent quenching of fluorescence.

Increasing the size of the substituent and elongation the of the length of conjugated from the core has a more drastic quenching effect. If the conjugation is broken the influence upon the electronic system is removed and the effect observed is minor in comparison. Anomalies in this trend are evident when the BODIPY targeted is *meso* substituted. This is clear when comparing **1-14** to **1-17** as the quantum yield actually increases by 0.60 for **1-16** when the framework is substituted at the 2 and 6 positions. The quantum yield also increases by 0.51 for **1-17** in comparison to the parent BODIPY **1-14**. Whilst these methyl substitutions do allow for further delocalization around the core, they also reduce the ability for PET side reactions

via the *meso* substituent through the reduction of the HOMO energy level and as this is the dominant effect, increased substitution in the presence of a PET active *meso* group actually leads to a stabilising effect on the compound's quantum yield. Comparing compound **1-16** with compound **1-17**, shows that alkylation at the 2,6-position generally leads to lower quantum yield but with higher absorption and emission wavelengths.



Scheme 1.4. Effects of *meso*-substituents on photoelectronics: (a) no significant perturbation, (b) reductive PeT and (c) oxidative PeT fluorescence quenching mechanisms. Adapted with permission from reference 23.

Another strategy to extend the π -electrons along the BODIPY core is to fuse aromatic units or to employ π -extended pyrrole units instead of simple pyrrole. This strategy can be used in order to extend the π -conjugation along the [a] bond, [b] bond and the “zig-zag” edge of the BODIPY. The absorption/emission spectra of the resulting BODIPYs are red shifted. **Fig 1.11.** shows bond [a] and bond [b] to which aromatic units could be fused and specific examples of aromatically fused BODIPY.

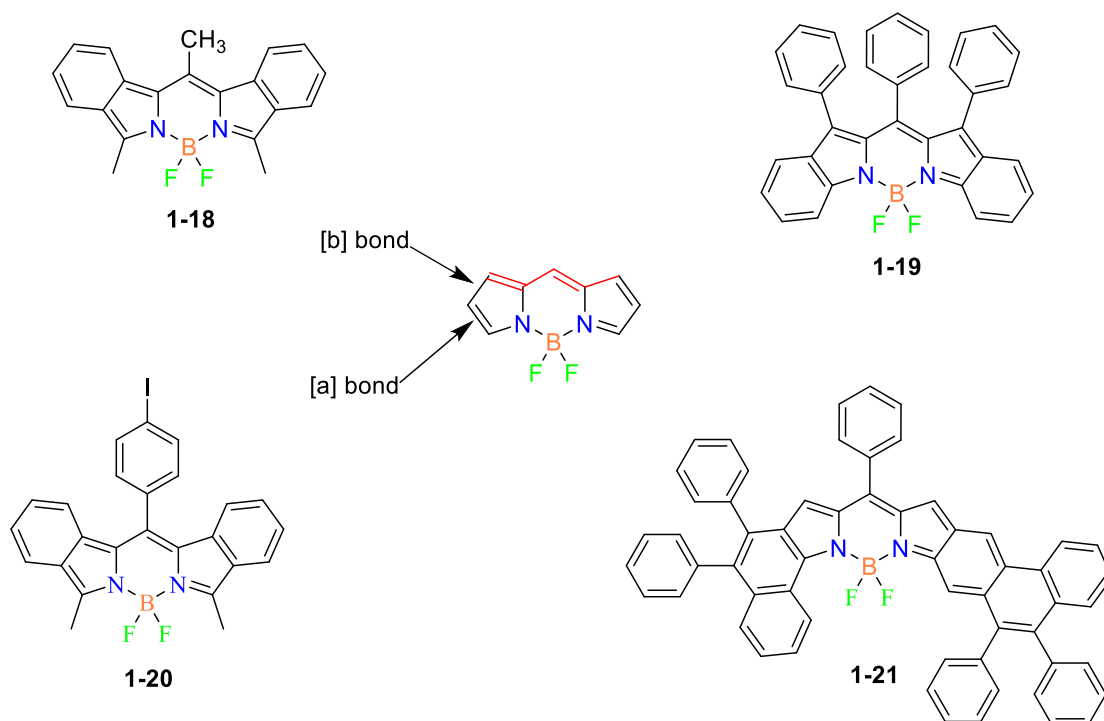
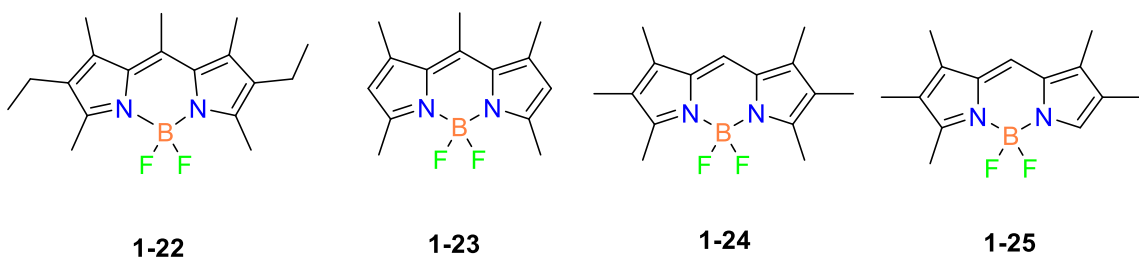


Fig 1.11. Structure of basic BODIPY core showing bond [a] and bond [b] to which aromatic units could be fused, “zig-zag” edge of the BODIPY is highlighted in red. Examples of aromatically fused BODIPY on bond [b] (compounds **1-18**, and **1-20**) or bond [a] (compound **1-19**, and **1-21**).⁸⁶⁻⁸⁹

1.1.5 BODIPY Electrochemistry

There have been many studies about the electrochemical properties of BODIPY.⁵³⁻⁵⁶ The nature of the substitution in the *meso*, α , and β position of the BODIPY core play a great role on the electrochemical properties of such dyes (**Scheme 1.5**, **Fig 1.12**).⁵⁶



Scheme 1.5. A selection of methylated “BODIPY core” derivatives.^{56, 57}

The fully substituted BODIPY (**1-22**, **Scheme 1.5**) shows a reversible one-electron oxidation and reduction, associated with the formation of stable radical ions as shown in **Fig 1.12**.^{6, 57} However, the absence of substitution in positions 2, 3, 5, or 6 causes instability of the radical cation produced on oxidation (compound **1-23** and **1-24**, **Scheme 1.5**, **Fig 1.12**). Moreover, the lack of *meso*-substitution in BODIPY framework (**1-24**, and **1-25**) leads to a more reactive radical anion produced from the reduction process. This result corresponds to the distribution of the electron density in the BODIPY core.^{56, 57}

More recently the electrochemical properties of a BODIPY (**1-26**) and a catechol-BODIPY adduct (**1-27**) were reported by using cyclic voltammetry (CV) and a coupled electrolysis/spectroscopic (UV-vis/EPR) method.¹ BODIPY (**1-26**) and (**1-27**) show similar reductive processes between (-1.15 and -2.17 V *vs.* Fc⁺/Fc) and an irreversible single oxidation processes between +0.80 and +1.19 V for both compounds (see **Fig 1.14**).

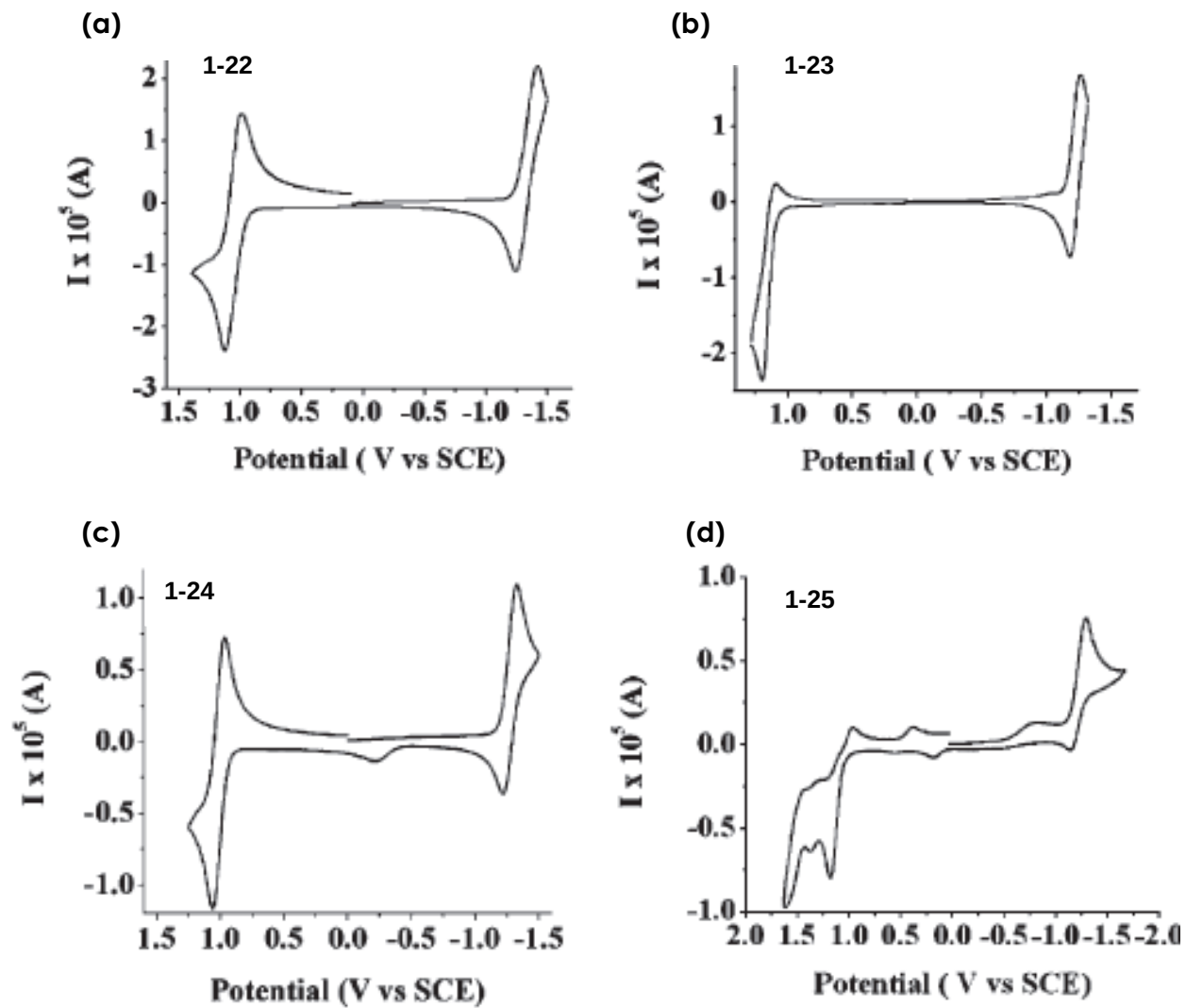
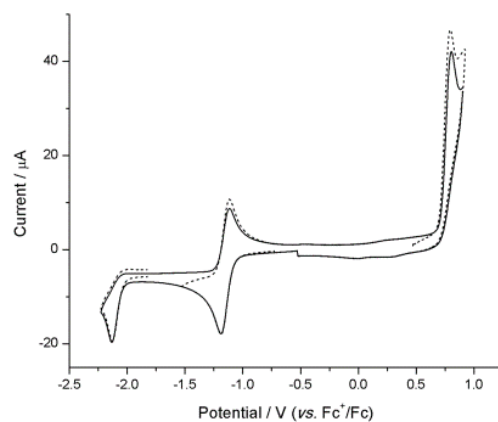


Fig 1.12. Cyclic voltammogram of dyes: (a) 1-22; (b) 1-23; (c) 1-24; (d) 1-25. Scan rate = 0.1 V/s; solvent = CH_2Cl_2 , supporting electrolyte = 0.1 M TBAPF₆. TBAPF₆ = Tetrabutylammonium hexafluorophosphate. Cyclic voltammogram in the figure are reproduced with permission from references 56-57.

(a)



(b)

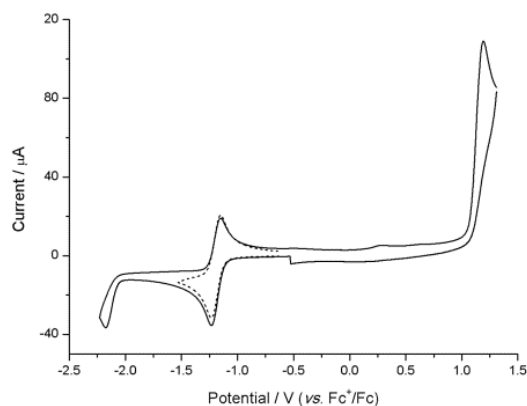


Fig 1.13 Cyclic voltammetry (CV) study of (a) **1-26** and (b) **127**.¹ Full range scan in solid line, individual redox process region scans overlaid in dotted lines. Cyclic voltammograms in the figure are reproduced with permission from reference 1.

DFT calculations show that in both cases the LUMOs are situated on the dipyrin unit. Additional electron density from B or F atoms is linked to the dipyrin unit in (**1-26**), and catecholate group linked to dipyrin unit in (**1-27**) (see **Fig 1.13**).

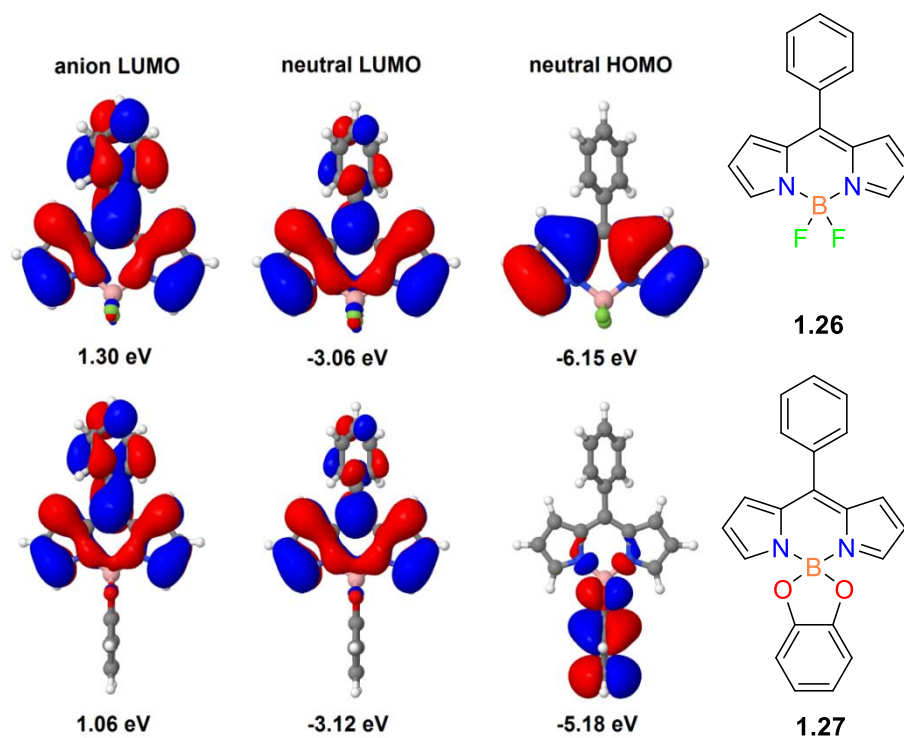


Fig 1.14 DFT calculated HOMO and LUMO diagrams and energies for (1-26) and (1-27), and LUMO diagrams and energies for (1-26 and 1-27).¹ Reproduced with permission from reference 1, 4.

Meso-substitution of the BODIPY framework can lead to reversible reduction processes. However, alkylation at α - and β -positions increases the electron density on the dipyrin core which makes the oxidation potential less positive.⁵⁸ Moreover, functionalizing BODIPY can minimize the oxidative instability observed for unsubstituted BODIPY by reducing the possibility of dimerization or polymerization processes, similar to those observed for pyrrole and thiophene compounds.^{59, 60}

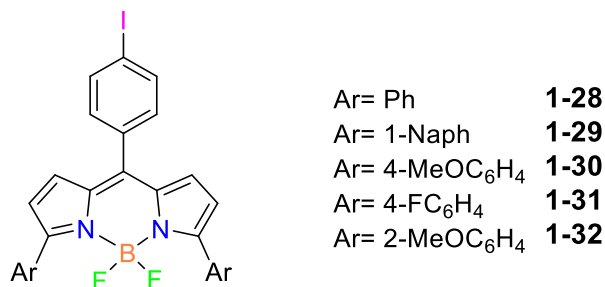


Fig 1.15 Examples of BODIPY compounds studied electrochemically by Burgess *et al.*, possessing varying aryl substituents at the α -position.⁵²

1.1.6 BODIPY Applications

The BODIPY family has many features, including their high quantum yields, sharp fluorescence, chemical and photochemical stability, tuneable absorption/emission and solubility in common solvents.^{3, 9, 23, 61} In addition to these properties, there are analogues of BODIPY which can be bound to different biological systems such as proteins,^{62, 63} viruses,⁶⁴ peptide hormones,⁶⁵ and nucleotides.⁶⁶ Therefore, BODIPYs have been used to probe hormone binding,⁶⁷ track intracellular processes,⁶⁸ chemical sensors,^{69, 70} provide *in vivo* biological imaging applications and scanning enzymes.²¹ Furthermore, BODIPYs have thermal and photochemical stability (*i.e.* insensitivity to polar solvents and pH) and low toxicities,^{9, 20, 71} which make them useful as fluorescent indicators, biological markers and drug delivery agents.¹⁸⁻²⁰ **Fig 1.16** demonstrates example of BODIPY analogues with their biological application.

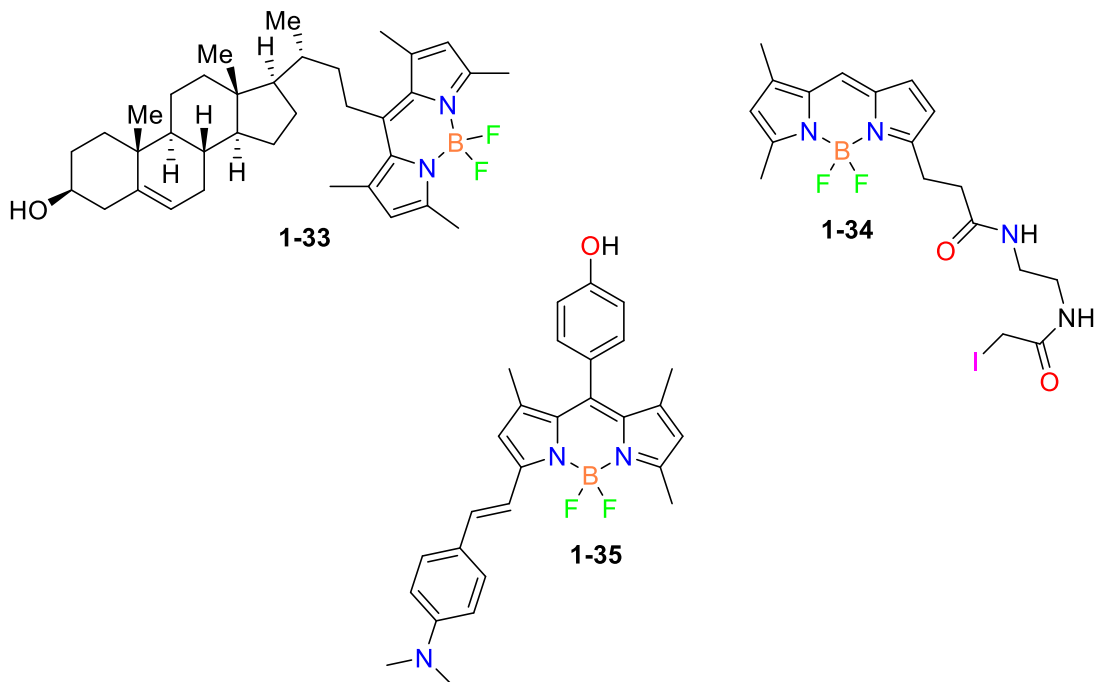


Fig 1.16 Structures of BODIPY-cholesterol (**1-33**),⁷² example of a BODIPY analogue used as a biological marker (**1-34**)²⁰ and the structure of 1,3,5,7-tetramethyl-8-(4-dimethylamino)-4-difluorobora-3a,4a-diaza-*s*-indacene used as a pH- sensors (**1-35**).¹⁷

In addition, halogenated BODIPYs have found applications as probes for photodynamic therapy (PDT), which is a non-invasive methodology for the treatment of malignant tumours,⁷³ age-related macular degeneration,⁷⁴ and the treatment of multidrug-resistant tumors.⁷⁵ The presences of heavy halogens on the BODIPY framework increases the rate of intersystem crossing resulting in the population of an excited triplet state. This process is required for the generation of reactive oxygen species.⁷³ **Fig 1.17** shows an example of BODIPY analogue which has been used as singlet oxygen generator. Upon illumination and under anaerobic conditions, $^1\text{O}_2$ is generated which leads to cell death.

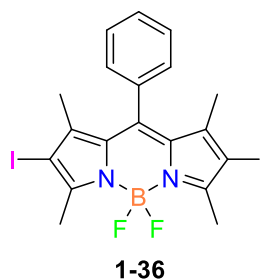


Fig 1.17 An efficient singlet oxygen generator based on an BODIPY.⁷⁶

However, for biological applications there are three main obstacles: the first one is the need for near-infrared absorption/emission (NIR-BODIPY) (*i.e.* emits light between 650–900 nm) as tissues and cells absorb light in the visible region, the emission wavelength of common BODIPYs.⁶⁶ The self-quenching of fluorescence due to the small Stokes shift of BODIPYs is the second obstacle.^{9, 23, 48, 66} The third obstacle is the solubility (or lack of solubility) of BODIPY in water. Therefore, water-miscible solvents, such as DMSO, are used to dissolve the sample before their use in biological applications. This protocol is not ideal for *in vivo* studies.³⁴ Therefore, there is intense interest in modifying BODIPY through the development of analogues and derivatives which could expand the use of BODIPY in the imaging of living cells.^{18, 34}

BODIPY compounds are excellent candidates for use as chemical sensors for monitoring toxic heavy metals such as the mercury(II),^{69, 70} lead (II),⁷⁷ silver (I)^{70, 78} zinc(II),⁷⁹ and copper(II),⁸⁰ in biological cells due to the need for highly sensitive and selective heavy metal ion fluorescent probes. Thus, BODIPY can be useful for environmental, biological, and industrial applications.⁸¹⁻⁸³ Fluorescent sensors involve a signalling moiety, the fluorophore, and an ionophore. The fluorophore produces photophysical changes which can be monitored.

The ionophore is preferentially coordinated to the ion of interest leading to PET quenching and switching on a fluorescence response.⁵⁹ **Fig 1.18** displays the structures of some BODIPY heavy metal ion sensors.

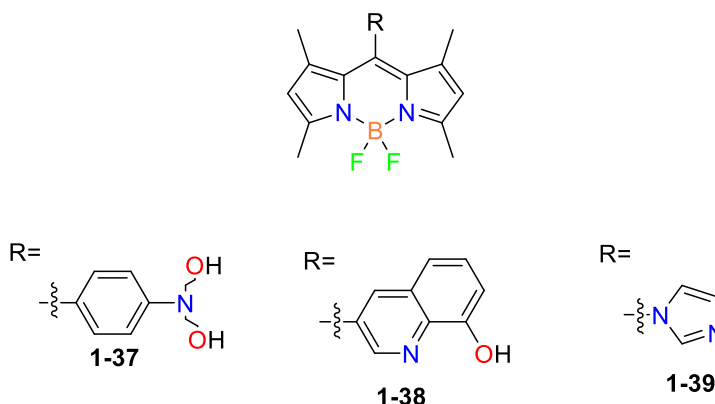


Fig 1.18. Structures of some BODIPY heavy metal ion sensors: BODIPY sensors for lead(II) (**1-37**),⁷⁷ for mercury(II) (**1-38**),^{69, 70} and mercury(II)/copper(II) (**1-39**).⁸⁴

Xie *et al.*⁸⁴ reported the use of (**1-39**) as a fluorescent sensor for copper(II) and mercury(II) cations.⁸⁴ This system preferentially coordinates with Cu^{2+} and Hg^{2+} cations, and the response can be observed by the naked eye, with the addition of copper causing a colour change from yellow to brown immediately. After 30 min, the colour of mixture changed from brown to colourless, indicating decomposition of the probe. The addition of mercury caused a colour change from yellow to pink immediately and the pink colour was retained after 30 min.⁸⁴

BODIPYs can act as electron donors which make them very important in industrial applications such as light-harvesting systems,¹⁴ solar cell technology^{15, 16} and nanocrystals.⁹ In 2008, Zhang *et al.* reported the first BODIPY-based light-harvesting system which consisted

of three types of BODIPY complexes possessing absorbance maxima at 501, 568, and 647nm. Compound **1-40** demonstrated strong absorption in the 300-700 nm region and highly efficient Forster-type energy transfer towards the central BODIPY component (see **Fig 1.19**).⁸⁵

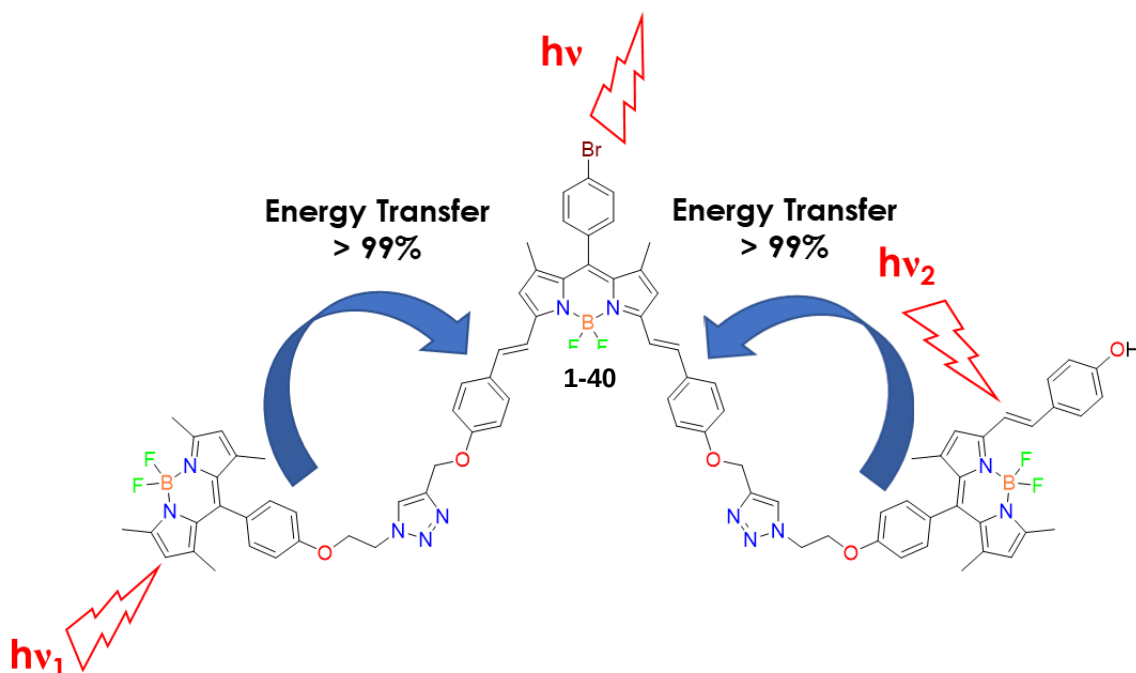


Fig 1.19. Structure of a light-harvesting systems containing three types of BODIPY fluorophores which exhibited very strong absorption in the region 300 to 700 nm. Reproduced from Xiaolin Zhang *et al.* Reproduced with permission from reference 85.

Finally, due to the wide range of applications for BODIPY this introduction has concentrated only on general applications of BODIPY. More specific applications will be given at the introduction of each chapter.

1.2 Thesis Outline

The amenability of BODIPY to substitution means that it is possible to develop compounds with specific targeting for imaging, biological and electronic applications.^{2,4,9} This thesis aims to introduce novel functionality to the BODIPY core and to investigate the effects of such substitution on the solid-state arrangements, intermolecular interactions, absorption, fluorescence, and electronic properties of the resulting BODIPY compounds.

The target of **Chapter 2** is to functionalize BODIPY chromophores using halogen substituents to afford molecules with strong absorbance in the visible spectrum and new electronic properties due to the presence of heavy atoms on the BODIPY framework. In particular, the halogenation of the α -methyl groups of the BODIPY will be pursued to enable further functionalization of the BODIPY. Post-functionalization *via* nucleophilic substitution introduces new substituents in a non-conjugated manner in contrast to other oxidation or Knoevenagel-type transformations on these positions. The effect of such substitution on the solid-state arrangements, absorption, fluorescence, and electronic properties of these dye molecules is reported.

Chapter 3 investigates the role of halogen bonding in the assembly of a series of halogenated BODIPY compounds bearing different substitution at the *meso* position, based on the solid-state structures of our compounds, and through CDC searches. The current understanding of halogen bonding in BODIPY structure and evidence of the presence of such interactions by measuring experimental distances and angles will be presented. Moreover, using Hirshfeld surface analysis and their associate fingerprints will provide evidence for such contacts and any other intermolecular contact present in the crystal structures. Finally, through the

amalgamation of this knowledge we will endeavour to understand how halogen bonds may become a powerful tool for molecular design and add to the knowledge for the metrics of these interactions.

Chapter 4 investigates the development of pyridyl and pyrimidyl functionalized BODIPYs in order to use them as a ligand in coordination polymer construction using copper iodide. Moreover, the investigation of the solid-state structure, photophysical and electrochemical properties of the ligand and the effect of the copper iodide on the solid-state structure, optical, and fluorescence properties of these dye molecules will be studied.

Chapter 5 summarises the results presented in this Thesis, evaluating the outcomes and revealing the scope for future work. The Appendix at the end of the thesis details the supporting data for all the **Chapter 3**.

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Chapter 2

**Morpholino-substituted BODIPY Species:
Synthesis, Structure and Electrochemical Studies**

2.1 Introduction

BODIPY compounds are a class of dye molecules that have been investigated extensively because of their applications in biology, materials and supramolecular chemistry.¹⁻⁵ The robust nature of the compounds and their attractive photochemical properties have led to their use in various applications^{1, 2, 4, 5} including light-harvesting devices,^{4, 6} solar cell technology,^{4, 7, 8} chemical sensors,⁹ nanocrystals,² biological marking, photodynamic therapy and drug delivery.^{4, 10-15} In order to develop BODIPY compounds with specific targeting such as imaging, biological and electronic applications, the modification of the dipyrin core is required. Several pre- or post-modifications can be done easily. As mentioned in **Chapter 1**, there are three main positions which are typically available for modification on a BODIPY core: the dipyrromethene core, boron centre, and *meso* substituent. Substitution at these positions cause very different effects, even if similar groups are introduced.

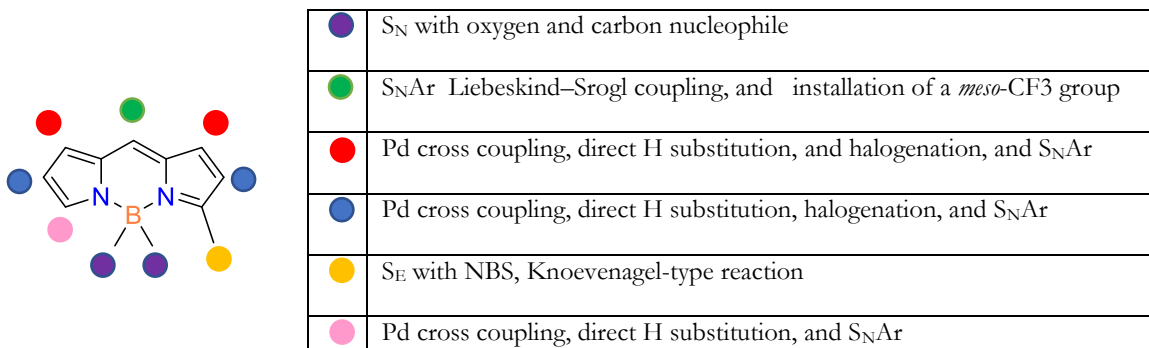
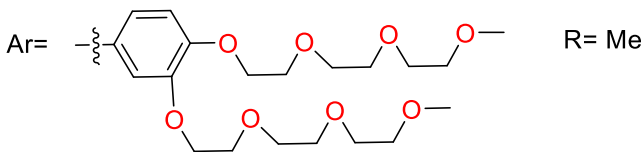


Fig 2.1. Possible post-functionalization sites of BODIPY structure and their preferential site(s) of attack.^{16, 17}

Fig 2.1. summarises the possible post-functionalization sites of a BODIPY core and the most popular reactions of these sites.^{16, 17} Perhaps the most widely known strategy to post-functionalize BODIPY is halogenation which could be followed by either nucleophilic substitution reactions,¹⁸⁻²¹ or through metal-catalyzed cross-coupling reactions (Stille, Heck, Suzuki, and Sonogashira).²²⁻²⁴

2.1.1 Functionalization of the BODIPY Core from the Boron Centre

Functionalization of BODIPY core from the boron centre by replacing the fluorine atoms with oxygen or carbon nucleophiles *via* nucleophilic substitutions reactions (S_N) have been previously reported in the literature.²⁵⁻³⁰ Aryl,²⁸ alkyl,²⁹ alkynyl, alkoxylates³⁰ and carboxylate groups have been used to replace the fluorine atoms by using strong nucleophiles of these compounds such as aryl lithium, Grignard, alkynyl lithium, or alkoxide reagents under very basic conditions to produce B-C bonded species.²⁵⁻³⁰ BODIPY structures with improved features (*e.g.*, quantum yield) and modified absorption/emission wavelengths are the result of this approach.²⁵⁻²⁷ **Scheme 2.1.** shows an example of BODIPY dyes, which are functionalized at the boron centre with morpholine *via* a Grignard reaction.³¹ Compound **2-2** displays absorption and emission peaks in ethanol at 498 nm and 508 nm, respectively. The fluorescence quantum yield of **2-2** in ethanol is 56%, which is attributed to the attached morpholine groups being out of the conjugation pattern.³¹



Scheme 2.1. Example of morpholine functionalized BODIPY by using Grignard reaction (i) 4-prop-2-ynyl-morpholine EtMgBr, THF, 60°C.³¹

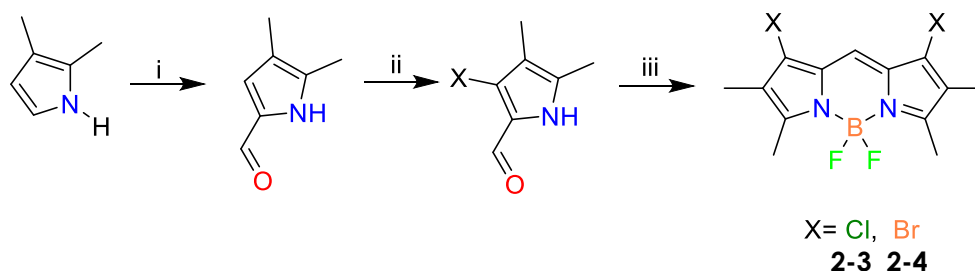
2.1.2 Functionalization of the BODIPY Core from the *Meso* Position

The *meso* position can be modified using different aldehydes and acid chloride derivatives during the synthesis of the dipyrromethene.³² The *meso* position can also be modified post synthesis of a *meso*-halogenated BODIPY. The S_NAr, Liebeskind cross-coupling and the installation of a CF₃ group at the *meso* position are also possible.³³⁻³⁵ This position on the BODIPY core remains the most utilized for its versatility in incorporating functional groups for ion capture ligands,³⁶⁻³⁸ donor-acceptor groups,^{39, 40} chiral auxiliaries,⁴¹ water solubilizing groups,^{42, 43} and biomolecules⁴⁴ for a variety of applications such as chemosensors, pH probes, light-harvesting devices and biological labels.

2.1.3 Functionalization of the BODIPY core from Dipyrrromethene Core

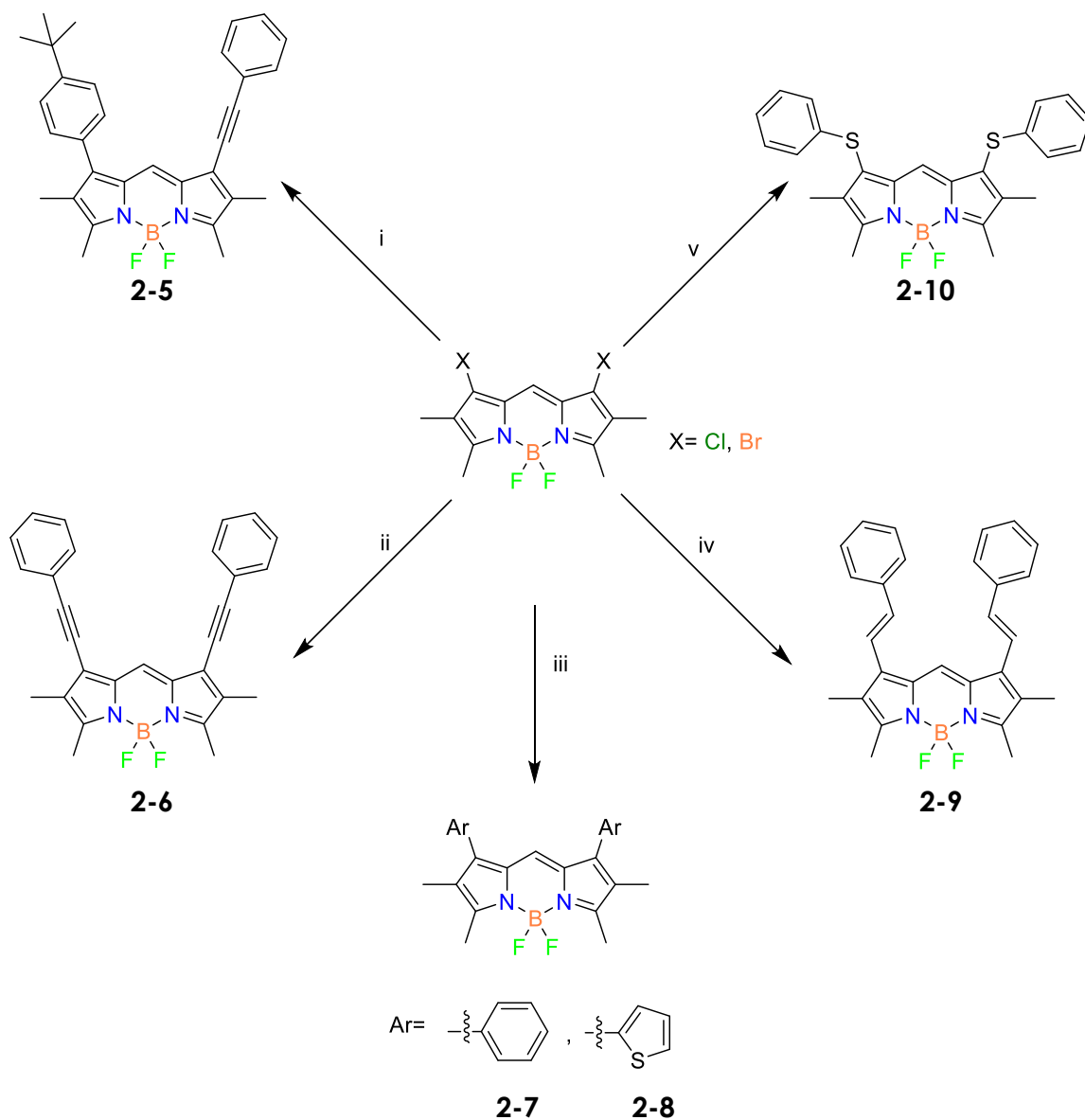
2.1.3.1 1,7- positions

The 1,7-positions can be halogenated and further substituted by S_NAr or Pd-catalyzed cross-coupling reactions.⁴⁵ Functionalization of the BODIPY core at the 1,7- positions is possible with pre-modifications of the starting pyrrole. **Scheme 2.2.** shows the conversion of halogenated pyrrole carbaldehyde to BODIPY *via* the Burgess method.¹⁶ Direct halogenation of the 1,7-positions of BODIPY is not possible because the 1,7- positions are electron poor, as are the 3,5-positions.⁴⁵ Therefore, in order for halogenation of these positions other reactive sites must be blocked.



Scheme 2.2. Synthesis route of 1,7-bis-halogenated BODIPY.¹⁶ (i) POCl_3 and DMF, (ii) $\text{NXS} = \text{N-halo succinimide}$, (iii) POCl_3 , base, $\text{BF}_3 \cdot \text{Et}_2\text{O}$. POCl_3 = Phosphorus oxide trichloride.

As described above, the halogenated BODIPYs are very important precursors to post-modification reactions because of their high reactivity towards palladium-catalyzed reactions (examples of this approach are shown in **Scheme 2.3**). Nevertheless, the 1,7-bis-halogenated BODIPY have a lower tendency toward nucleophilic substitution reactions than the 3,5-bis-halogenated analogues. Thus, these BODIPYs undergo nucleophilic substitution reactions only with thiolate anions, which have strong nucleophilic character.²¹



Scheme 2.3. Reactions of BODIPY when halogenated at the 1,7- positions (i)Suzuki/Sonogashira coupling, (ii) Sonogashira coupling, (iii)Suzuki/Stille coupling, (iv) Heck coupling, (v) Nucleophilic substitution.²¹

2.1.3.1 2,6- positions

The resonance structures of BODIPYs reveal that the 2- and 6-positions of the BODIPY core bear the least positive charges positions (**Fig 2.2**). This electron rich character makes the 2- and 6-positions susceptible to electrophilic substitution reactions.

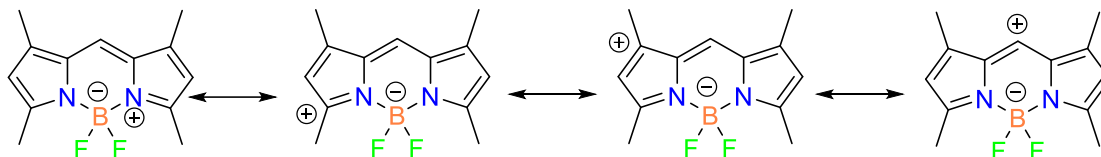
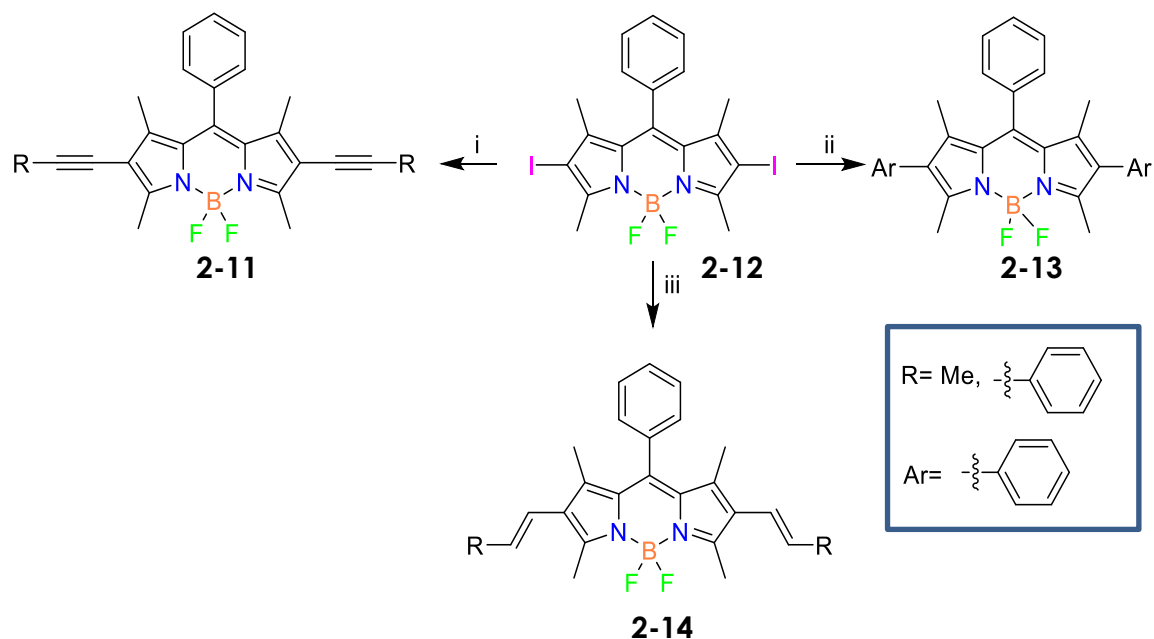


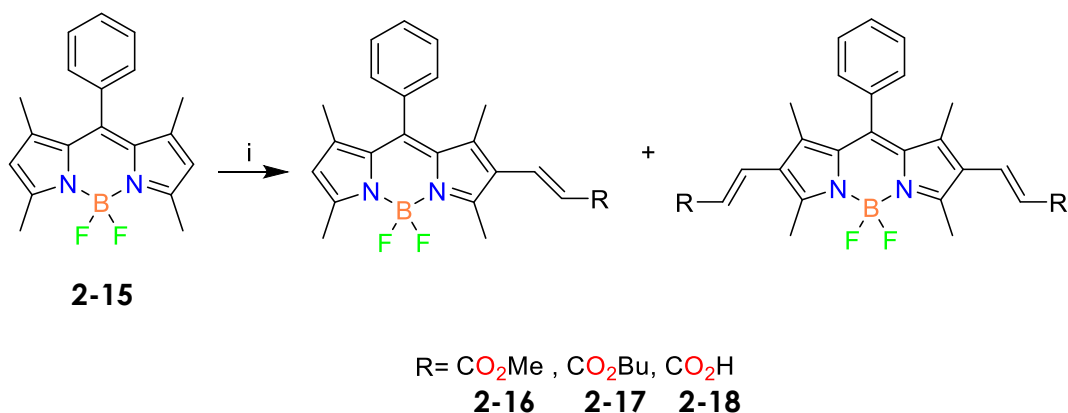
Fig 2.2. Illustration the resonance structures of 1,3,5,7-tetramethyl BODIPY showing the electrophilic positions.

There are several approaches to functionalize the 2,6 positions such as halogenation,⁴⁶ formylation,³² sulfonation,⁴⁷⁻⁵⁰ and nitration.⁵¹ Usually, the functionalization of the 2,6-positions by sulfonation and nitration reactions do not offer many advantages for subsequent post-modification. The only advantage of sulfonation is high water solubility⁵² without impacting the BODIPY's optical properties. Among these approaches, halogenation is the most important method. Mono- and di-halogenated products can be generated depending on reaction conditions. In most of these approaches, other positions of the pyrrole were blocked by methyl or ethyl substituents. The halogenated BODIPYs are versatile precursors facilitating post-modifications to construct systems that can be used as molecular sensors. Halogenated BODIPYs are highly reactive towards metal-catalyzed aryl cross-coupling reactions to achieve red-shifted dye structures because of the increased conjugation.²¹



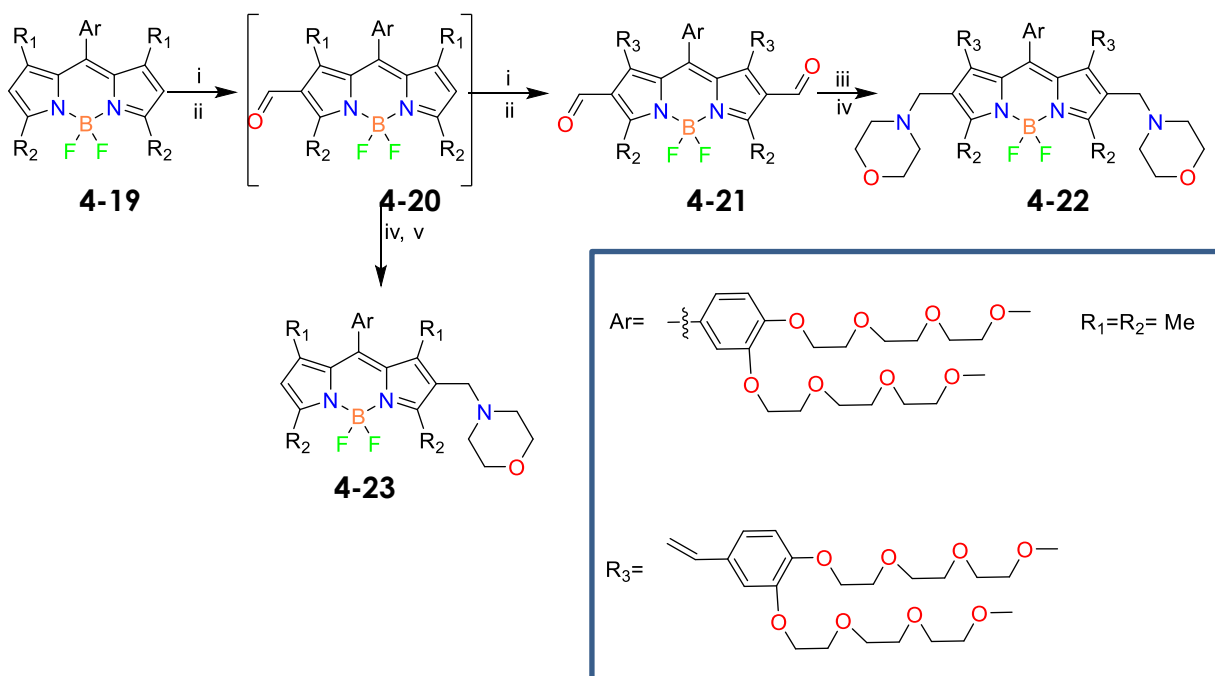
Scheme 2.4. Examples of palladium mediated cross-coupling reactions of 2,6-diiodoBODIPY dyes. (i) Sonogashira coupling, (ii) Suzuki coupling, (iii) Heck coupling.²¹

Moreover, metal-catalyzed reactions can be performed at the 2- and 6-positions of BODIPYs without the requirement for halogenation. Reaction at the 2- and 6-positions can occur by reacting a terminal alkene adjacent to an electron withdrawing group with the BODIPY in the presence of palladium(II) acetate (20 mol%) and either an oxidant, heat or in a microwave.⁴³ However, the problem with this reaction is the formation of a mixture of products. All the compounds synthesised had their absorption and emission maxima red-shifted to varying degrees. The majority of them also had reduced fluorescence quantum yields (Φ_F values ranging 0.25-0.73) relative to the starting BODIPY ($\Phi_F = 0.80$), presumably due to the electron withdrawing nature of the R groups.⁴³



Scheme 2.5. Example of oxidative functionalization of BODIPY.(i) Method A: 20 mol % of $\text{Pd}(\text{OAc})_2$, *t*-BuOOBz, AcOH/dioxane/DMSO, $\text{CH}_2=\text{R}$, 35 °C, 5 days.⁴³

Another important electrophilic substitution reaction ($\text{S}_{\text{E}}\text{Ar}$) that can be performed at the 2,6 positions is the Vilsmeier-Haack formylation to introduce aldehydes (**Scheme 2.6**) and subsequent functionalization of those aldehydes using a myriad of reactions (such as Grignard reaction, Knoevenagel condensation and oxidation of the aldehydes, Schiff bases).⁵³ **Scheme 2.6** shows an example of this methodology. Compounds **2-22** and **2-23** represent pH sensitive morpholine-functionalized BODIPY. A high fluorescence response is observed in aqueous solutions in basic conditions while their fluorescence is quenched in acidic conditions due to the d-PET effect from protonated morpholine moieties to the BODIPY cores.³¹



Scheme 2.6. Vilsmeier-Haack formylation at 2- and 6-positions of the BODIPY core and further post functionalization of these positions. (i) POCl₃, DMF, CH₂Cl₂, K₂CO₃, 0-50 °C, 2 h for **4-20** and 6h for **4-21**. (ii) NaHCO₃ .aq. (iii) morpholine, 40 °C, 4h (iv) NaBH(OAc)₃, AcOH, r.t, 18h. (v) morpholine, 40°C, 4h (iv) morpholine, NaBH(OAc)₃, CH₂Cl₂, r.t., 3 days.³¹

2.1.3.2 3,5 - positions

The 3- and 5- positions of the BODIPY core are often used for the construction of molecular sensors. This strategy is mainly based on halogenation of the 3, and 5-positions of the BODIPY core by using halogenation agents such as using an *N*-halosuccinimide reagent with an appropriate solvent at very low reaction temperatures (-78°C).²¹ In order to obtain mono-halogenated products, the di-halogenated BODIPY is further reacted with one equivalent of sodium methoxide in methanol at room temperature.

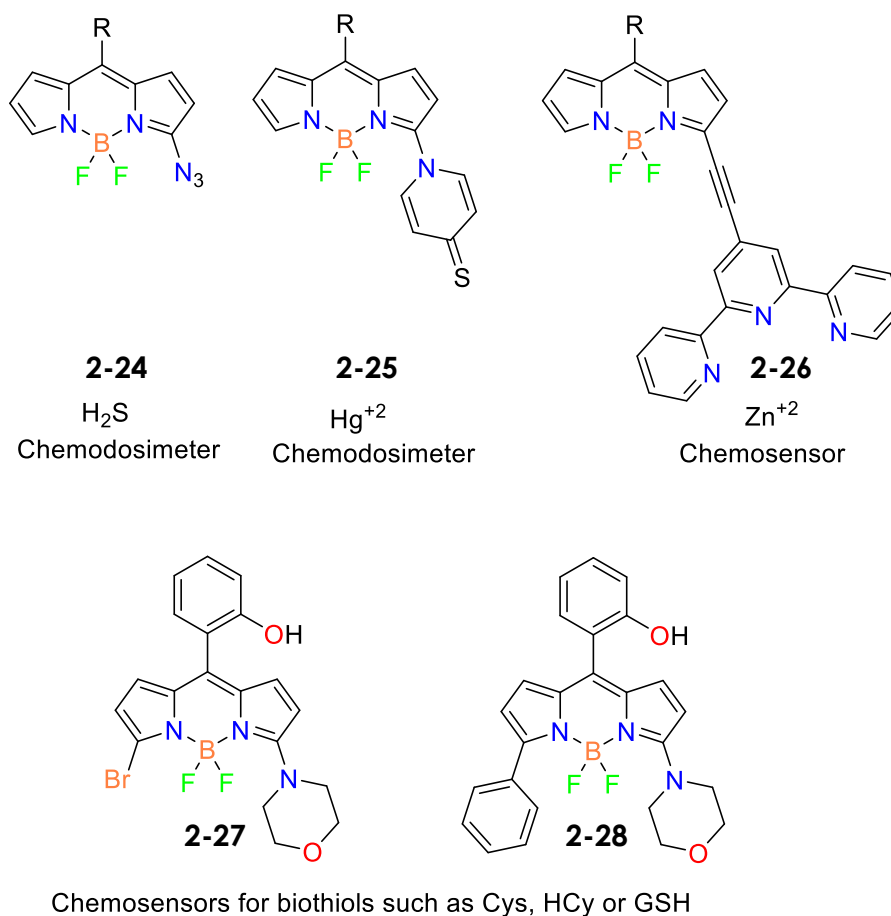


Fig 2.3. BODIPY based sensors functionalized from 3- position.^{21, 54} Cysteine (Cys), homocysteine (Hcy) and glutathione (GSH).⁵⁴

Both mono- and di-halo-BODIPYs are highly reactive towards many reagents in well-known reactions such as nucleophilic aromatic substitution ($\text{S}_{\text{N}}\text{Ar}$) (*e.g.*, R-SH , R-NH_2 , R-C^- , or R-OH) and Pd-catalyzed cross-coupling reactions. Some examples of molecular fluorescent sensors that were synthesized *via* the halogenation of 3- and 3,5- positions of the BODIPY core are given in **Fig 2.3**.^{21, 54}

2.1.3.3 Methyl Groups at 3- and ,5- Positions

The protons attached to methyl groups at 3- and 5- positions of the BODIPY core are considered acidic enough to participate in some condensation reactions. In particular, the well-known Knoevenagel condensation reaction, which allows the synthesis of styryl-BODIPYs to be carried out under relatively mild conditions. This has been achieved by reacting a 3,5-dimethyl BODIPY with appropriate aromatic aldehydes^{5, 55-57} under basic conditions and removal of water from the mixture. This can be achieved *via* the azeotropic removal of the water by a Dean-Stark apparatus, or by using 10Å molecular sieves.⁵⁸ In 1988, Haugland and Kang attempted the application of the Knoevenagel reaction of 1,3,5,7-tetramethyl-substituted BODIPY for the first time using 4-(dimethylamino)benzaldehyde, in the presence of a piperidine catalyst and in an alcoholic solvent at reflux temperature.⁵⁹ They successfully produced the 3-monostyryl derivative as a major product (**Fig 2.4**).⁵⁹ Methyl substituents at 1,7-positions of BODIPY are also considered as acidic but not as acidic as 3,5-methyl substituents so Knoevenagel condensation primarily occurs at 3,5-position rather than 1,7-positions and 3,5-mono- and/or distyryl compounds usually dominate the reaction products. However, extending the reaction time and elevated temperatures can activate 1,7-positions (for further Knoevenagel reaction with aldehyde derivatives) to afford 1,3,5-tristyryl- and 1,3,5,7- tetrastyryl-BODIPY dyes.⁶⁰

Another important factor is the effect of the functionality at the 2,6-positions. Liu and co-workers^{31, 61} reported that the presence of formyl groups at the BODIPY 2,6-positions initiated the formation of distyryl bonds at the 1,7-positions instead of the 3,5-positions. This is due to

the 1,7-methyl groups being activated by the introduction of formyl groups at the 2,6-positions (compound **2-21**, **Scheme 2.6**). Therefore, it is possible to form mono-, di-, tri- and tetra-styrene substituted BODIPYs, which exhibit large red shifts in absorption and emission spectra.⁵ A variety of functional groups can be attached to BODIPY *via* this methodology which lead to a variety of applications. For instance, the use of 4- dialkylaminobenzaldehydes introduce the ability of the BODIPY to behave as a pH sensor.

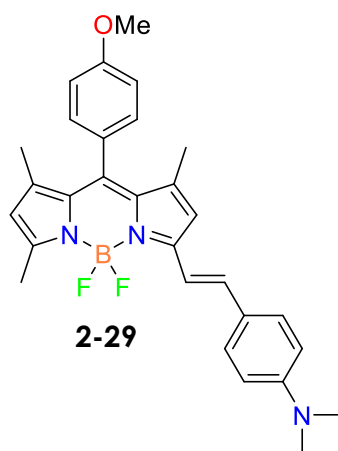
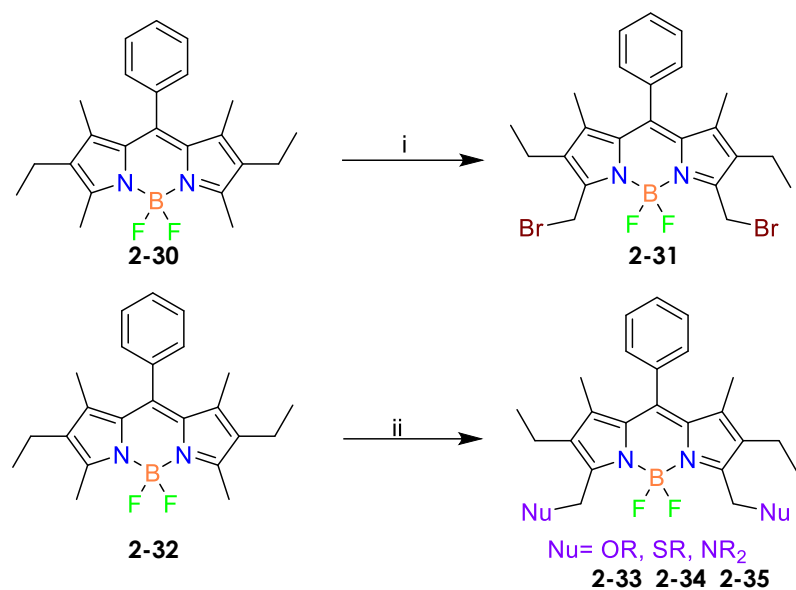


Fig 2.4. Monostyryl derivative of BODIPY reported by Haugland and Kang.⁵⁹

Moreover, the Knoevenagel reaction of BODIPY has obvious applications in the synthesis of BODIPY containing energy transfer systems and for other optoelectronic applications (*e.g.* solar cells).⁶²⁻⁶⁵ Another methodology to functionalize the methyl groups at 3- and 5- positions in BODIPY is nucleophilic substitution as shown in **Scheme 2.7**.



Scheme 2.7. A general synthetic route to 3,5-substituted BODIPY (i) Br₂ (ii) NBS, Nu, CH₂Cl₂, r.t.

These methodologies developed by Ulrich *et al.*⁶⁶ based on selective bromination of methyl groups in the α -position of pyrroles reported by Hayes and Kleinspehn,⁶⁶ and follow the selective preparation of mono- or dibromo intermediates by *in situ* nucleophilic substitution.⁶⁶ Compounds in this chapter are prepared based on this methodology.

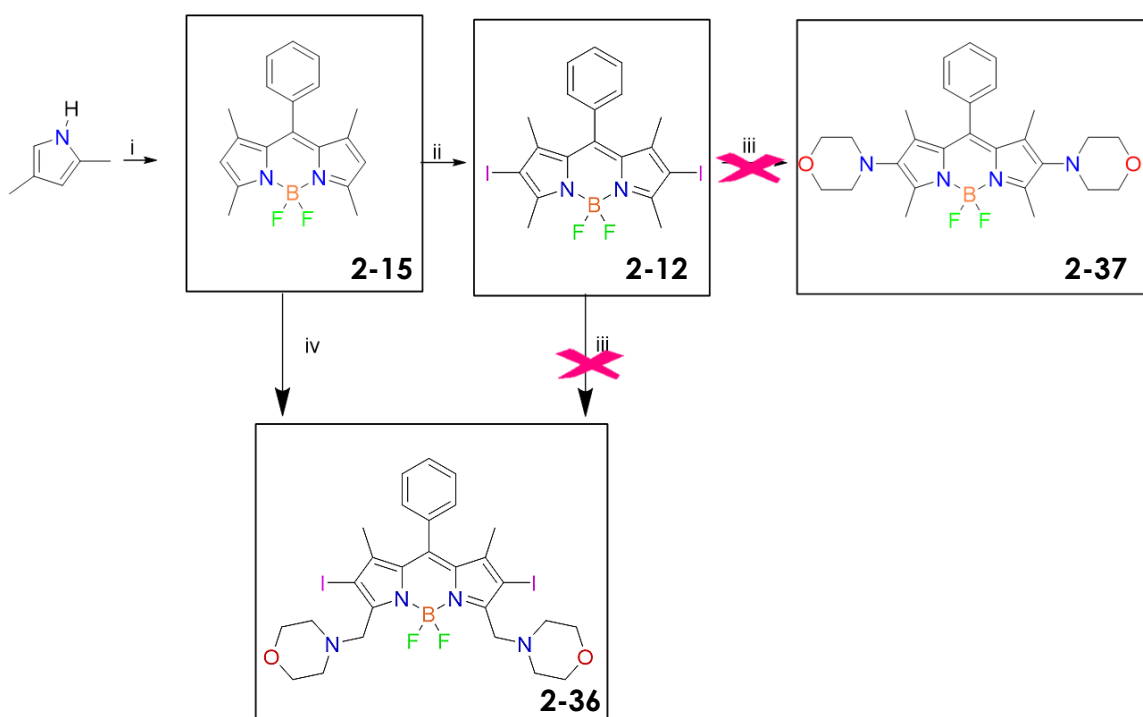
2.2 Aims and Objectives

The amenability of BODIPY to substitution means that it is possible to develop compounds with specific targeting for imaging, biological and electronic applications. Recently, the development of efficient synthetic methods for the regioselective electrophilic halogenation of BODIPYs has attracted intense research interest. Firstly, there are many studies focussed on the use of bromo- and iodo-functionalized BODIPYs as photosensitizers for solar hydrogen production^{67, 68} and as probes for PDT. Incorporation of iodine or bromine onto the BODIPY core enhances intersystem crossing to the triplet excited state upon irradiation, as required for efficient singlet oxygen generation in PDT.^{67,69,70} Secondly, halogenated BODIPYs are particularly attractive because they can be used as starting materials for the preparation of functionalized BODIPYs *via* both nucleophilic substitutions reactions,¹⁸⁻²¹ and metal-catalyzed cross-coupling reactions such as Pd(0)-catalyzed cross-coupling reactions.²²⁻²⁴ In particular, we are interested in the halogenation of the α -methyl groups of the BODIPY so that we can further functionalize the BODIPY. Post-functionalization *via* nucleophilic substitution introduces new substituents in a non-conjugated manner in contrast to other oxidation or Knoevenagel-type transformations at these positions. These methodologies developed by Ulrich *et al.*⁶⁶, based on selective bromination of methyl groups in the α -position of pyrroles,⁶⁶ follow the selective preparation of mono- or di-bromo intermediates by *in situ* nucleophilic substitution.⁶⁶ Extension of these methodologies using BODIPY analogues bearing unsubstituted β -positions can be made in order to combine the well-recognised direct electrophilic halogenation of 2,6-position⁴ and non-conjugated substituents at the α -carbon. We are particularly interested to use morpholine as a nucleophile to probe the effect of the

competition of an amine at the α -carbon with a halogen in the β -position on the properties and the solid-state structure of such species.

2.3 Results and discussion

2.3.1 Synthesis of BODIPY compounds 2-15, 2-12, 2-36, 2-37



Scheme 2.8. Synthesis of the substituted BODIPY compounds **2-15**, **2-12**, **2-36**, and **2-37**. (i) Benzoyl chloride, CH_2Cl_2 , r.t., 16 h, Et_3N , $\text{BF}_3 \cdot \text{Et}_2\text{O}$, r.t., 1 h. (ii) NIS, CH_2Cl_2 , r.t., 30 min. (iii) Morpholine, CH_2Cl_2 , reflux, 3 h or morpholine, Et_3N , reflux, 3 d. (iv) NIS, CH_2Cl_2 , r.t., 30 min, Morpholine, reflux, 3 h.

BODIPY **2-15** was prepared according to literature procedures⁷¹ *via* the condensation of 2,4-dimethylpyrrole with benzoyl chloride to form a methene bridge linking two pyrrole rings. After the preparation of the dipyrin, the addition of boron trifluoride diethyl etherate in the

presence of a base leads to the formation of the BODIPY compound **2-15** (Scheme 2.8). The direct electrophilic halogenation of **2-15** by N-iodosuccinimide affords **2-12**.^{71, 72} It should be noted that halogenation of the α -carbon (*i.e.* 3-, and 3,5- positions) was also observed by mass spectrometry and by NMR spectroscopy in solution. Unfortunately, the α -carbon-halogenated derivatives were not stable enough to be isolated but could be observed in solution, in an analogous manner to that reported by Ulrich *et al.*⁶⁶ Therefore, ¹H NMR and ¹⁹F NMR were used as important tools to investigate the selectivity behavior of halogenation of the BODIPY and the structural change during the iodination using NIS in deuterated chloroform.

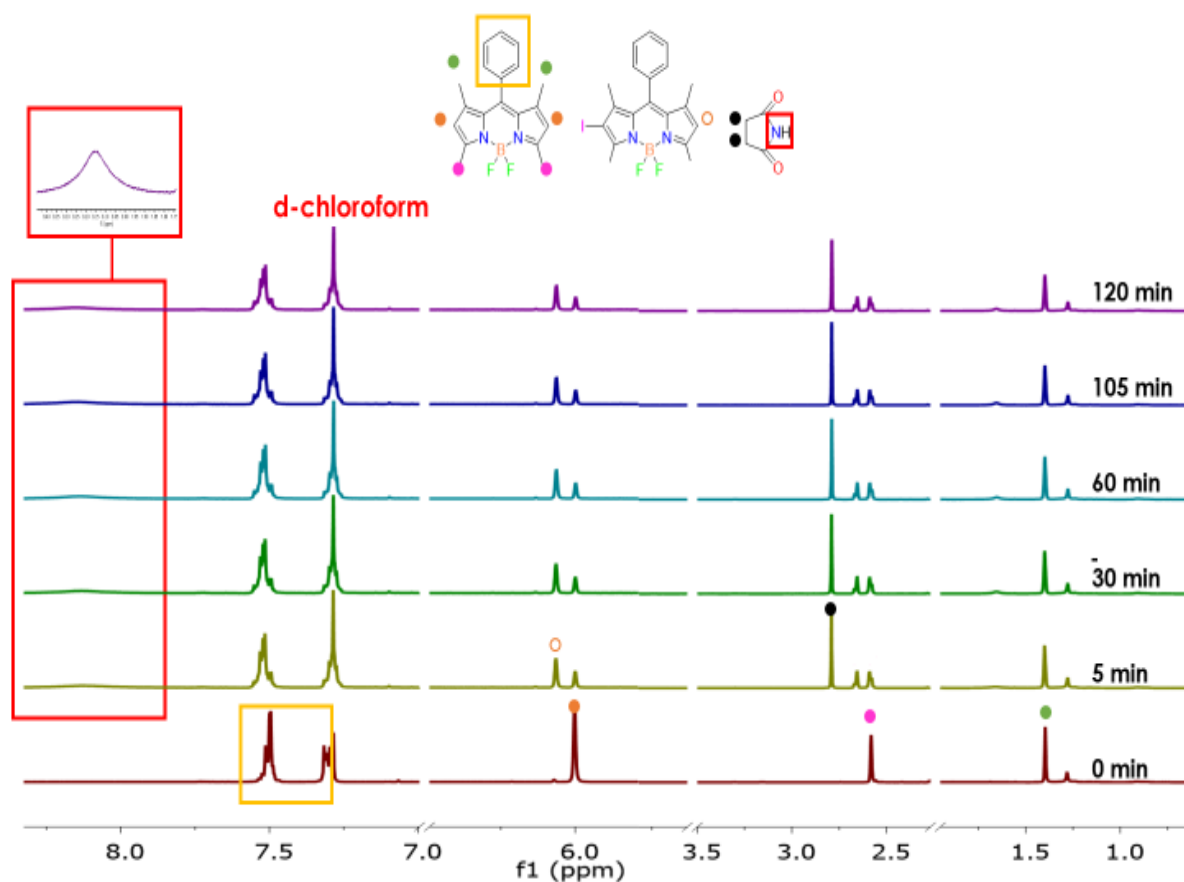


Fig 2.5. ¹H NMR experiment over time (r.t., CD₂Cl₃, 400 MHz), after the addition of 2 eq of NIS to **2-12**.

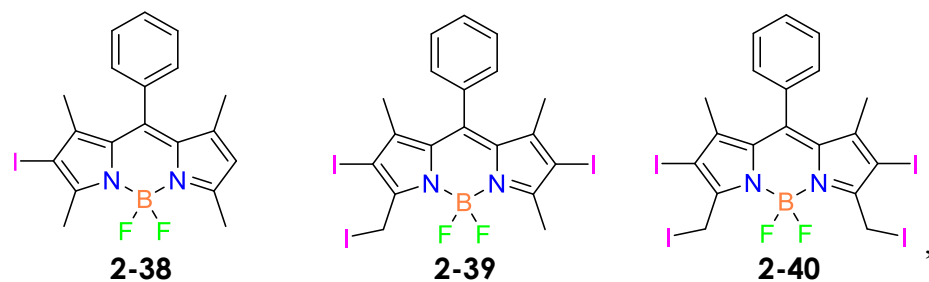


Fig 2.6. Halogenated BODIPY compounds **2-38**, **2-39**, and **2-40**.

BODIPYs monosubstituted at the 2-position (**2-38**) were obtained directly after the addition of 2eq of N-iodosuccinimide as shown in **Fig 2.5**. This was confirmed by monitoring the singlet assigned to the α -methyl group, methyl at 3,6-position, protons at the 2-position and the peak assigned to succinimide. After 5 min, a new singlet at 6.06 ppm started to appear, which was assigned to a proton at the 2-position in a mono-iodinated product **2-38**. Broad peaks were observed in the spectra at 8.40 ppm which were assigned to N-H proton in succinimide and a singlet at 2.79 ppm, which was assigned to the other protons from the succinimide (*i.e.* in the 3- and 4-position).

After 15 min, a mixture of mono- and di-iodination (*i.e.* 2,6-substituted) compounds were obtained. From the ^1H NMR data presented in **Fig 2.7**, it is apparent that the peak at 2.58 ppm, assigned to the α -methyl group (*i.e.* methyl at 3,5 positions of the parent BODIPY **2-15**) start to decline and three peaks grow at 2.59, 2.66, 2.65 ppm. The peak at 2.65 ppm is assigned to **2-12**, the downfield shift accounted for as an effect of the presence of iodine atom at 2- and 6- positions. The peaks at 2.59, and 2.66 corresponded to methyl at (3,5 position) resulting from mono-iodination.

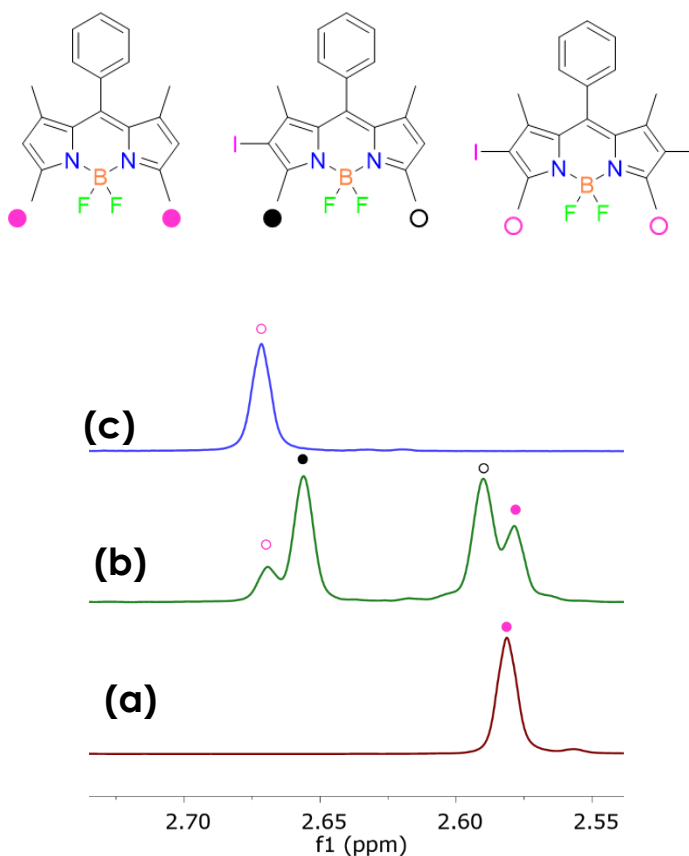


Fig 2.7. ^1H NMR experiment of (a) pure **2-15**, (b) 15 min after the addition of 2 eq of NIS. (c) pure **2-12**, recorded on a spectrometer operating at 400MHz.

The ^{19}F NMR spectrum after 15 min of iodination (**b** in **Fig 2.8**) is consistent with the ^1H NMR spectrum; ^{19}F NMR spectrum clearly shows three sets of quartets which are assigned to the parent BODIPY **2-15**, BODIPYs monosubstituted in the 2-position, and BODIPYs monosubstituted in the 2- and 6- positions (**2-12**). The major product at this stage was the monosubstituted BODIPY. After 2h, no change was observed in the ^1H NMR or ^{19}F NMR spectra. Also, there is no evidence of iodination of other positions of the BODIPY which is attributed to the blocking effects of 1,3,5,7-tetramethyl substituents. Therefore, halogenation of 2,6 positions is favourable in this case.

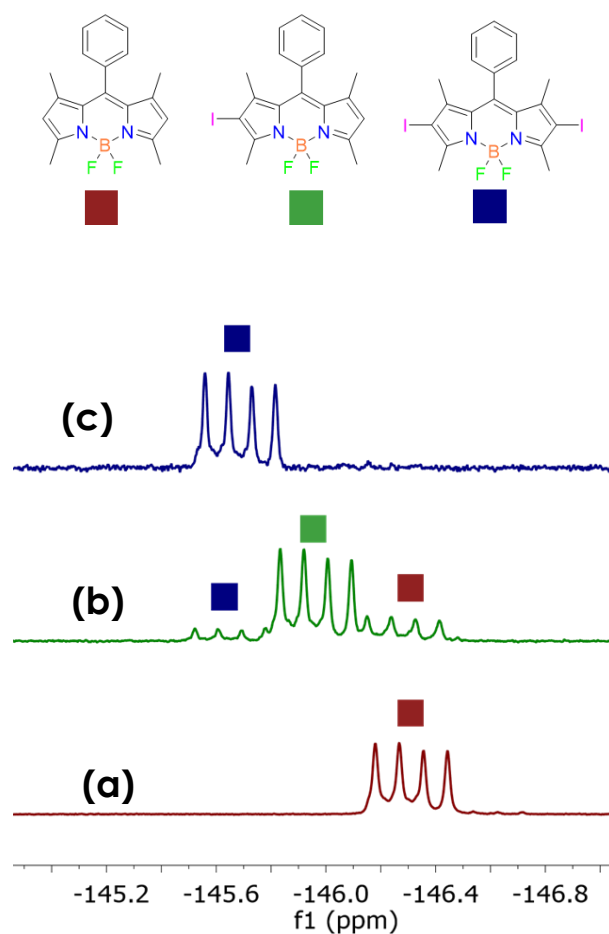


Fig 2.8. ^{19}F NMR of (a) pure **2-15**, (b) 15 min after the addition of 2 eq of NIS. (c) pure **2-12**, recorded on a spectrometer operating at 376MHz.

However, the introduction of iodo- atoms at the 6- and 2,6-positions of BODIPY may activate the methyl groups at the 3- and 3,5- positions towards halogenation which results in selective halogenation of these positions. Therefore, another 2 eq of NIS were added to the reaction mixture to examine this hypothesis. After 5 min, the first observation is the disappearance of the two singlet peaks assigned to both **2-15**, and **2-38**. (*i.e.* singlets at 6.00 and 6.06 ppm, respectively) (**Fig 2.9**). The second observation is the disappearance of the peaks at 2.58, 2.59 and 2.66 ppm as shown in **Fig 2.10**. This suggests that the major product at this stage is **2-12**.

Also, a new singlet peaks grows at 3.02 ppm which might be assigned to tri-iodinated compound (**2-39**).

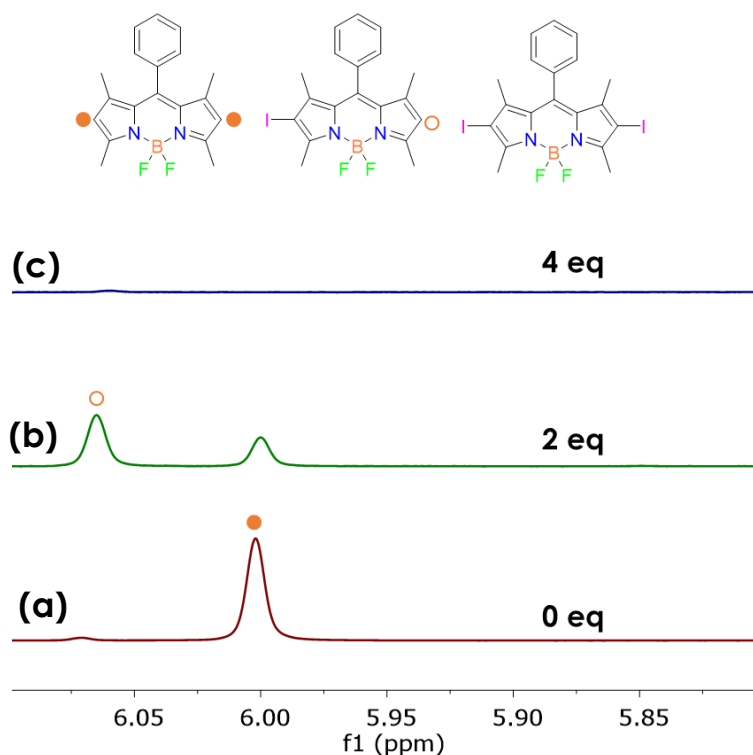


Fig 2.9. ¹H NMR experiment of (a) pure **2-15**, (b) After 5 min of the addition of 2 eq of NIS. (c) After 5 min of the addition of another 2 eq of NIS, recorded on a spectrometer operating at 400MHz.

After 24h, a singlet is observed at 3.75 ppm which corresponds to halogenation of the methyl at 3,5 positions. The direct electrophilic halogenation of **2-15** using an excess of NIS (*i.e.* 6 to 10 eq) leads to the formation of **2-40** directly. There is no evidence of the formation of penta- or hexa-substituted products within a week at room temperature.

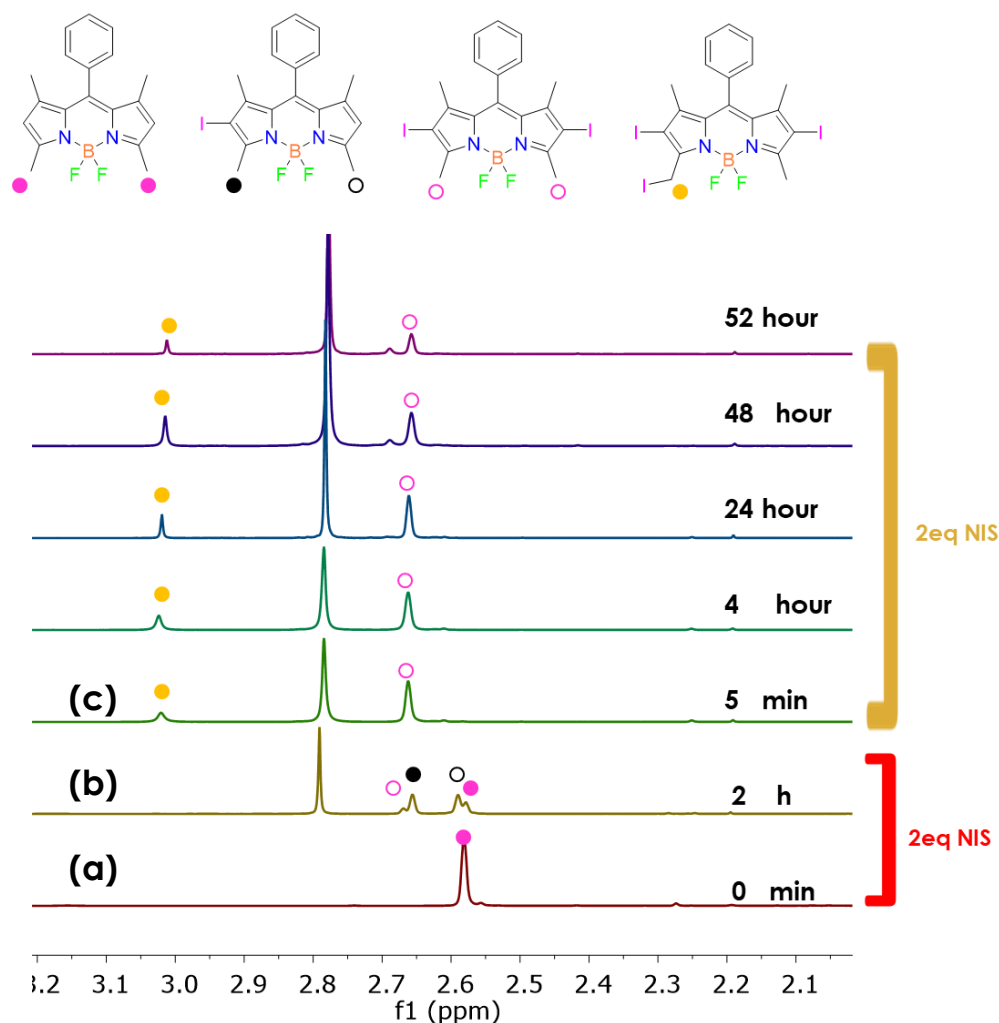


Fig 2.10. ^1H NMR spectra recorded over time (a) pure **2-15**, (b) after 5 min of the addition of 2 eq of NIS. (c) after 5 min of the addition of another 2 eq of NIS. Recorded on a spectrometer operating at 400 MHz, at r.t., in CH_2Cl_2 .

The previous detailed monitoring of the solution reactions enabled us to develop a methodology for selective preparation of tri- and/or tetra- iodinated intermediates, which could be substituted *in situ* after addition of a nucleophile in one-pot experiment. Therefore, the one-pot nucleophilic substitutions were achieved by adding a large excess of morpholine to the halogenated derivatives, in dichloromethane under reflux conditions. ^1H and ^{19}F NMR spectroscopy were used as important tools for investigating the structural change between **2-**

12 and **2-36**. Thus, samples of pure **2-12** and **2-36** were recorded in deuterated chloroform solution at room temperature (**Fig 2.11**, and **2.12**). The ^{19}F NMR spectrum of the isolated product (**2-36**, **Fig 2.11**), clearly shows a downfield shift (*ca.*10 ppm) of the quartet assigned to **2-36** indicating the possible effect of morpholine as an electron donating group.

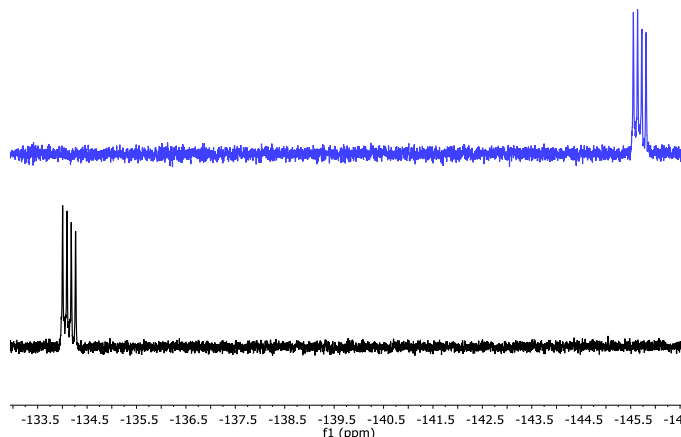


Fig 2.11. ^{19}F NMR spectra of **2-12** (blue) and **2-36** (black), recorded on a spectrometer operating at 376MHz. at r.t., in CD_2Cl_2 .

The first observation from ^1H NMR is the loss of the peak at 2.57 ppm in **2-12** and the presence of a new singlet at 3.84 ppm in the spectra recorded for **2-36**. This could be explained by the conversion of the methyl groups at 3 and 7 positions in **2-12** to CH_2 groups in **2-36**. The second observation in **2-36** is the presence of two signals (triplet at 3.73 ppm and 2.65 ppm), which corresponded to the morpholine moiety attached to BODIPY at the 3,5-positions. Increasing the reaction time to 3 days to examine the possibility of nucleophilic substitution of 2,6-positions does not show any evidence of substitution of 2 and/or 6-iodo substituents with morpholine. ^1H NMR spectra confirm that the nucleophilic substitution occurs just on the carbon at the 3,6 positions with no evidence of substituent of carbon at the 1,7 or 2,6 positions, confirming the selective preparation of tri- and tetra- iodinated

intermediates and their reactivity toward nucleophilic substitution. Also, the direct nucleophilic substitution of beta-halogenated BODIPY (**2-12**) using morpholine to afford **2-37** was unsuccessful. This might be explained by the low electron density in the LUMO at the 2,6-positions of the BODIPY.^{73, 74}

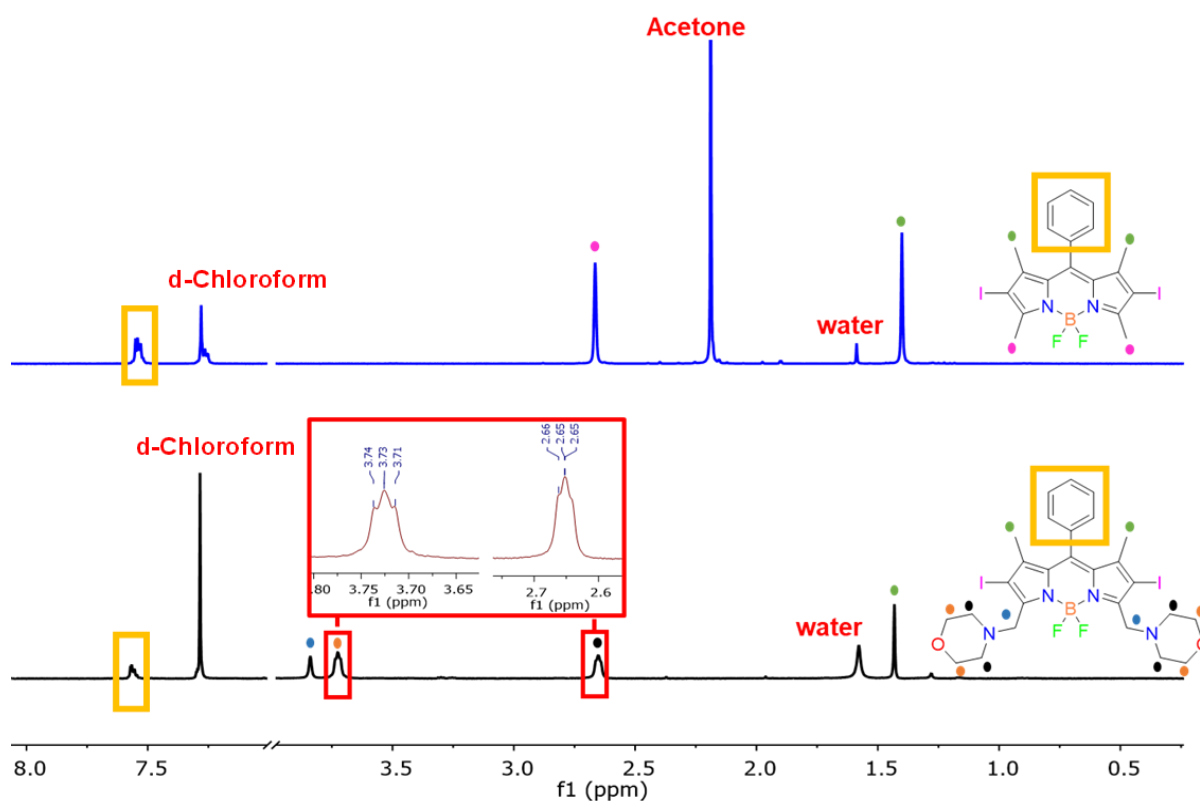


Fig 2.12. ¹H NMR spectra of **2-12** and **2-36** recorded on a spectrometer operating at 400 MHz.

2.3.2 Structural Studies

Single crystals of **2-12** and **2-36** were grown by vapour diffusion of diethyl ether into hexane solutions of the target compound and their molecular structures are shown in **Fig 2.13**. Structural determination by single-crystal X-ray diffraction revealed the BODIPY to crystallise in the triclinic space group $P2_1$ for **2-12** and the orthorhombic space group $P2_12_12_1$ for **2-36**. The X-ray crystal structures confirmed the chemical composition of both compounds as determined by spectroscopy. The crystal structure of **2-12** has been reported previously.^{15, 75-77}

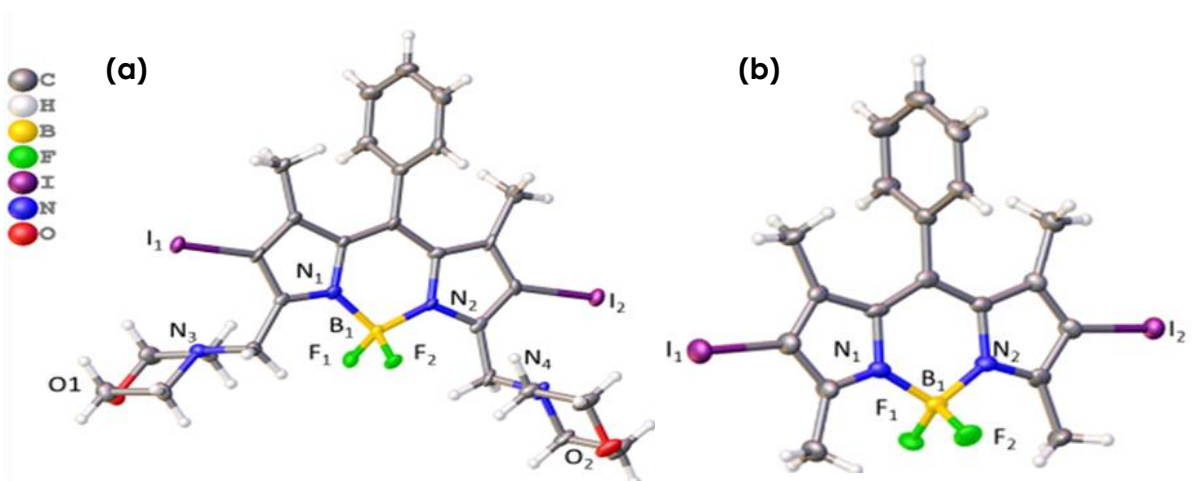


Fig 2.13. Crystal structure of (a) **2-36** , and (b) **2-12**. Carbon = grey, nitrogen= blue, boron=yellow , fluorine = green, iodine = purple, boron = orange, oxygen = red.

In comparison to previously reported boron-dipyrromethene compounds, the X-ray crystal structures of **2-12** and **2-36** revealed the expected planarity of the BODIPY core that extended through the 2,6-diiodo groups. The *meso* phenyl ring on the BODIPY cores (**2-12**, and **2-36**) is almost orthogonal to the indacene plane, which is expected to minimize unfavourable steric

clashes between the ortho-hydrogen atoms and the vicinal methyl groups on the pyrrole, forming dihedral angles of nearly 90° with respect to the plane of the BODIPY core (88° for **2-12** and 75° for **2-36**). The boron atom possesses nearly tetrahedral geometry with the two fluorine atoms also lying in a plane perpendicular to the BODIPY core. The B-N bond lengths in **2-12** [1.557(4) Å, 1.551(5) Å, Table 2.1] are similar to **2-36** [1.563(11) Å, and 1.560(10), Table 2.1] and similar to those of other 2,6 di-iodo analogues reported in literature.^{15, 75-77} Also, the average B-F distance for **2-12** and **2-36** is 1.55 Å, while the N-B-N and F-B-F angles are 106.70(3)°, 109.20(3)° for **2-12**, 106.60(6)°, 109.30(7)° for **2-36**, respectively, in good agreement with those of other reported analogues.^{15, 75-77}

Table 2.1. Bond lengths (Å) and angles (°) for **2-12**, and **2-36**.

	2-12	2-36
F₁-B₁	1.380(4)	1.383(11)
F₁-B₂	1.399(4)	1.391(9)
N₁-B₁	1.551(5)	1.563(10)
N₂-B₁	1.557(4)	1.560(10)
F₁-B₁-F₂	109.20(3)	109.30(7)
N₁-B₁-N₂	106.70(3)	106.60(6)

The intermolecular interactions in the crystal structure of **2-12**, and **2-36**, will be discussed in detail in **Chapter3**

2.3.3 Optical and Fluorescence Measurements

The optical properties of **2-15**, **2-12**, and **2-36** were measured showing UV-vis absorption peaks characteristic of those of BODIPY, corresponding to the ($S_0 \rightarrow S_1$, $\pi-\pi^*$) transition of the dipyrin ligands (**Fig 2.14**). The maxima of the bands of **2-12** and **2-36** in CH_2Cl_2 were observed at 533 and 539 nm, respectively, which show that iodination at the 2- and 6-positions of **2-15** leads to bathochromic shifts of about a 30 nm in absorption maximum for **2-12** ($\epsilon \approx 60\,000\text{ mol}^{-1}\text{dm}^3\text{cm}^{-1}$) in comparison with **2-1** and 18 nm bathochromic shift in comparison to the mono-iodinated derivatives reported in the literature.¹⁵ This is accounted by the strong $p-\pi$ conjugation of the iodine atoms at the 2,6- positions with the BODIPY core.

Table 2.2. UV-vis absorption and fluorescence data for compounds **2-15**, **2-12**⁵² and **2-36**. Literature data: for **2-15**, and **2-12** where recorded in methanol.^{52,78} Data for **2-36** were recorded in both CH_2Cl_2 and MeOH.

	$\lambda_{\text{max}} / \text{nm}$	$\lambda_{\text{em}} / \text{nm}$	Quantum yield	$\epsilon / \text{mol}^{-1}\text{dm}^3\text{cm}^{-1}$	Solvent
2-15	498	509	0.65	44 000	MeOH
2-12	529	556	0.02	69 000	MeOH
2-36	535	-	-	-	MeOH
2-36	539	556	0.0006	305 000	CH_2Cl_2

The low fluorescence quantum yield ($\Phi_F = 0.02$ in MeOH, **Table.2.2**)⁷⁸ was previously reported for such complexes as a prerequisite to efficient ISC (higher population of T1 state).^{15, 78} These spin-orbit perturbations can be achieved by the attachment of heavy atoms directly onto the BODIPY core.^{15, 28} Although halogen atoms are an electron withdrawing group (EWG), they possess lone pairs of electrons and thus act as resonance donors. Therefore, when halogens atoms are added at the 2,6-positions of BODIPY, they cause

destabilization of the highest occupied molecular orbital (HOMO) with respect to the lowest occupied molecular orbital (LUMO). This results in narrowing of the HOMO–LUMO band gap and a red shift in the absorption maxima, consistent with the experimental results.⁷⁸ It should be noted that the morpholine substituted species **2-36** displays intense absorptions ($\epsilon \approx 305,000 \text{ mol}^{-1}\text{dm}^3\text{cm}^{-1}$) and ($\approx 8 \text{ nm}$) bathochromic shift in comparison with **2-12**. The red shifts of peaks of **2-36** and fluorescence quenching with very low quantum yield could be due to the improved electron donating effect of the morpholine-substituted methylene groups at the 3,5-positions of the BODIPY core, compared with hydrogen atoms in **2-15**. In other words, the tertiary amines from morpholine act as electron donors which quench the BODIPY fluorescence *via* a-PET mechanism. Such behaviour has been described previously for BODIPY derivatives.^{28, 66, 79, 80} It should be noted that, the fluorescence quenching of **2-36** was observed in both methanol and dichloromethane with quantum yield ($\Phi_F = 0.0006$ in CH_2Cl_2 ,

Table 2.2)

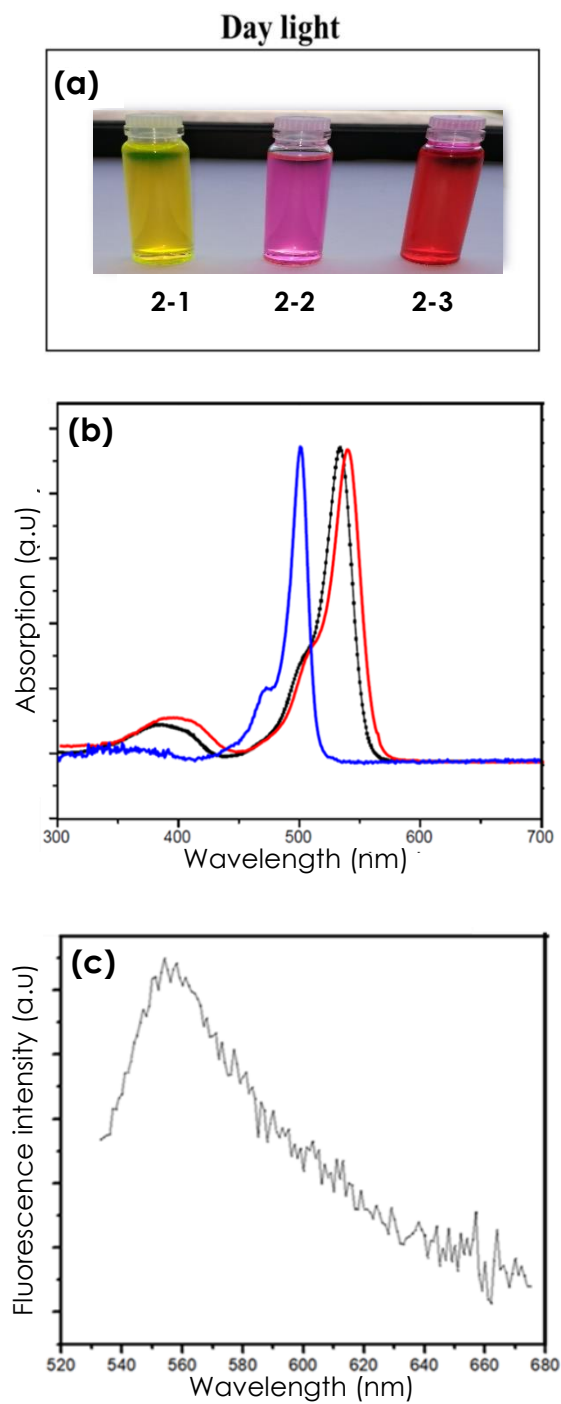


Fig 2.14. (a) Photographs showing the different colours of compounds **2-15**, **2-12** and **2-36** in CH_2Cl_2 . (b) Normalized UV-vis absorption spectra of **2-15** (blue lines), **2-12** (black lines) and **2-36** (red lines) in CH_2Cl_2 . (c) Fluorescence intensity spectrum of the **2-36**.

2.3.4

Electrochemistry Measurement

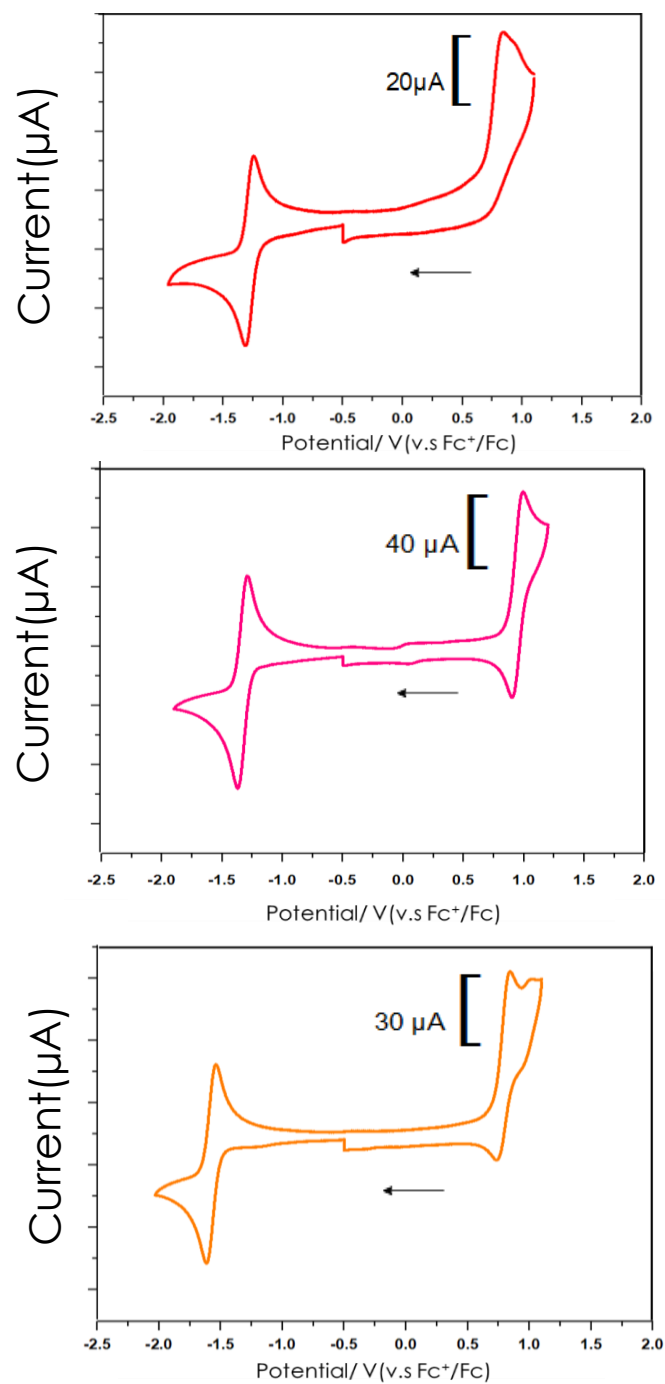


Fig 2.15. Cyclic voltammograms of 2-15 (orange), and 2-12 (pink), and 2-36 (red,) recorded in CH_2Cl_2 containing $[\text{nBu}_4\text{N}][\text{BF}_4]$ (0.4M).

The electrochemical behaviour of **2-15**, **2-12** and **2-36** in CH₂Cl₂ solution was investigated by cyclic voltammetry, and UV/vis spectroelectrochemistry in order to establish the comparative behaviour of the complexes. Cyclic voltammetry was conducted to further investigate the influence of iodine atoms and morpholine substitution upon the electronic properties of **2-36**. An electrochemically reversible one electron reduction process is observed at $E_{1/2}$ -1.29 (vs. Fc⁺/Fc).

The presence of heavy atoms such as iodine at the 2,6-positions of BODIPY leads to a shift in both the potential for the reduction and the oxidation processes to more positive values for **2-12** and **2-36** in comparison with the parent BODIPY, **2-15**, indicating that **2-12**, **2-36** are more difficult to oxidize (E_{ox} =+1.13, +0.89 vs. Fc⁺/Fc) (see **Fig 2.15**). Studies have focused on the use of **2-15** as an efficient photosensitizer which can be useful in photodynamic therapy.⁴⁶ Such behaviour is consistent with literature reports, where other analogues of **2-12** show more positive oxidation potentials than the Rose Bengal moiety, a commonly used photosensitizer for photodynamic therapy.⁴⁶ Thus, a suitable design strategy for developing photosensitizers with greater photostability could be to appropriately control the oxidation potential

Table 2.4. CV data for **2-15**, **2-12** and **2-36**. Potentials ($E_{1/2} = (E_p^c + E_p^a)/2$) in V vs. Fc⁺/Fc quoted to the nearest 0.01V. The anodic/cathodic peak separation ($\Delta E = E_p^c - E_p^a$) is given in brackets where applicable.

	$E_{1/2}$	E_p^c	E_p^a
2-15	-1.57 (0.07)	-1.60	-1.53
2-12	-1.33 (0.08)	-1.37	-1.28
2-36	-1.29 (0.07)	-1.30	-1.28

On the other hand, both BODIPY **2-12**, **2-36** are easier to reduce due to the positive shift in redox potentials in comparison with the parent BODIPY $E_{1/2}$ -1.33 V, -1.29 V and -1.57 V, (*vs.* Fc^+ / Fc), respectively. The positive shift indicates that the presence of non-conjugated tertiary amine substituents in the methylenes at the α -position have an overall greater electron donation effect on the Ph-dipyrrin moiety. Electrochemical data for **2-15**, **2-12**, and **2-36** are summarized in **Table 2.3**. Cyclic voltammograms of the couples for compounds (**2-12**, **2-2-15**, **2-36**) were recorded at a series of scan rates in the range from 20 to 300 mVs^{-1} in order to explore the nature of those processes. Analysis of the data presented show that E_p^a and E_p^c values were, in each case, found to be independent of the scan rate and the peak currents were approximately equal and varied linearly with the square root of scan rate as presented in **Fig 2.17**.

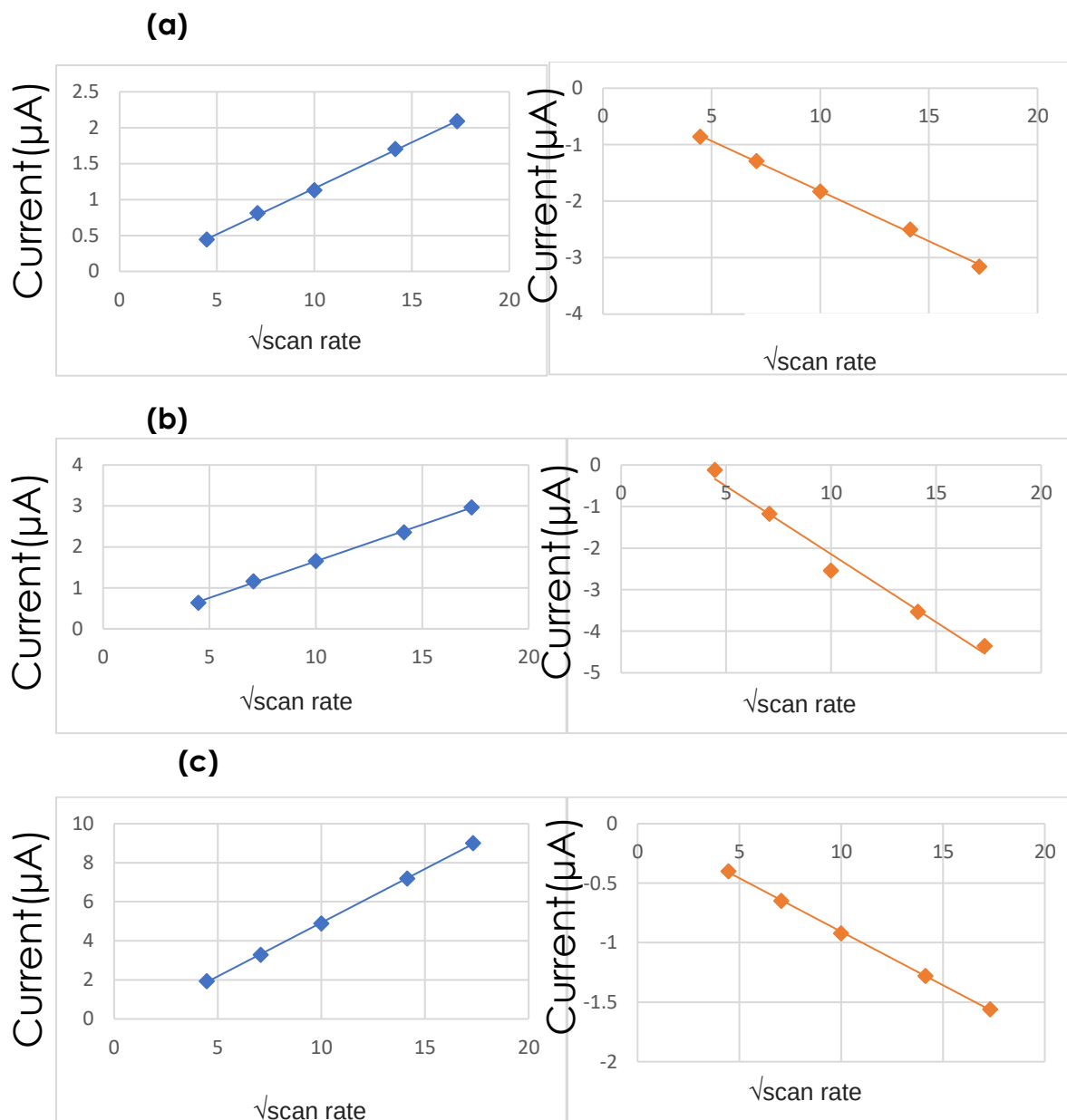


Fig 2.17. A plot of the anodic (blue, left) and cathodic (orange, right) peak current of (a) 2-15, (b) 2-12, (c) 2-36 as a function of scan rate.

In situ spectroelectrochemical methods were employed to probe the UV/Vis spectroscopic changes that accompany the one-electron reduction processes of **2-12**, and **2-36** (see **Fig 2.18**, **Table 2.5**). The *in situ* one-electron reduction of each compound was followed by UV-vis spectroelectrochemistry at an optically transparent electrode, and this similarity was found to extend to the UV-Vis spectra of the electrochemically generated anions (**Fig 2.18**, **Fig 2.19**, and **Table 2.5**).

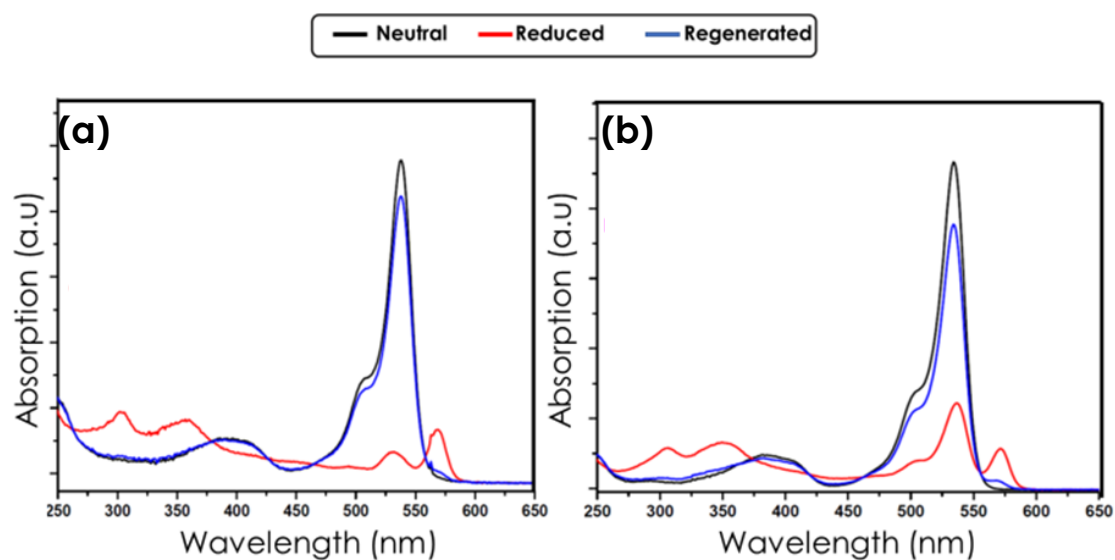


Fig 2.18. UV/Vis spectra for (a) **2-36**, and (b) **2-12**; spectra of neutral, reduced ($[\mathbf{2-12}]^{-1}$, and $[\mathbf{2-36}]^{-1}$) and regenerated species. Spectra were recorded in CH_2Cl_2 containing $[\text{tBu}_4\text{N}][\text{BF}_4]$ (0.4M) at 243 K. The data suggests a chemically non-reversible one-electron reduction.

Generation of the one-electron reduced radical anion shows depletion of the major bands for the neutral species (*ca.* 534 nm for **2-12**, and 538 nm for **2-36**) the corresponding development of a series of bands in the range 510–570 nm for **2-12** and **2-36**, all with significantly smaller absorption coefficients. In the range 290–450 nm, reduction leads to the development of new bands at *ca.* 303 and 353 nm for **2-36** and *ca.* 300 and 350 nm. for **2-12**. Applying a potential sufficient to reverse the reduction process did not regenerate the spectral

profile of **2-12**, and **2-36** fully, as would be seen if the process was chemically reversible. This is indicative of a chemical reaction of the radical anion, $([\mathbf{2-12}]^{-1})$, and $[\mathbf{2-36}]^{-1}$, having occurred to produce the an unknown species.

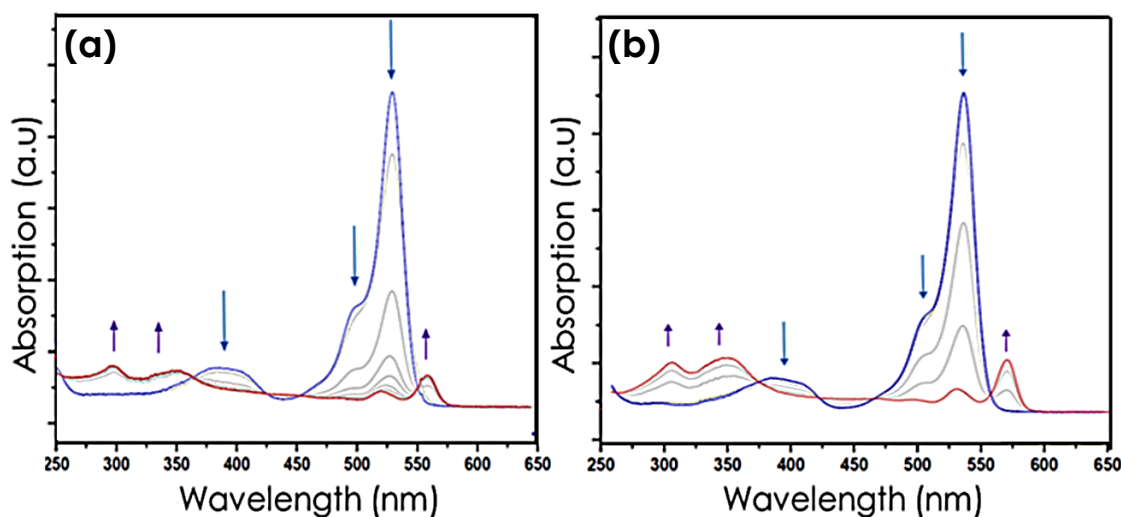


Fig 2.19. UV-vis absorption spectra recorded in CH_2Cl_2 containing $[\text{Bu}_4\text{N}][\text{BF}_4]$ (0.4 M) using spectroelectrochemical methods for **2-12**, and **2-36** at 273 K showing interconversion of (a) **2-36** (blue) to $[\mathbf{2-36}]^{-1}$ (red). (b) **2-12** (blue) to $[\mathbf{2-36}]^{-1}$. Arrows indicate the progress of the reduction.

Table 2.5 UV-vis spectroscopic data for **2-15**, **2-12** and **2-36** measured at 243 K in CH_2Cl_2 from spectroelectrochemistry. All values $\lambda_{\text{max}}/\text{nm}$ (for **2-12** $\epsilon \times 10^{-4}/\text{mol}^{-1}\text{dm}^3\text{cm}^{-1}$, for **2-36** $\epsilon \times 10^{-5}/\text{mol}^{-1}\text{dm}^3\text{cm}^{-1}$)

	Neutral $\lambda_{\text{max}} / \text{nm}$	Anion $\lambda_{\text{max}} / \text{nm}$
2-12	396(0.9), 503(2.4), 534(7.6)	301(1.5), 350(0.6), 568(1.4)
2-36	398(0.05), 506(0.16), 538(0.40)	304(0.06), 360(0.05), 570(0.04)

2.4 Conclusions

In summary, ^1H NMR and ^{19}F NMR spectra were used as a tool to investigate the selective behaviour of the halogenation of the BODIPY core and the structural change during the iodination. The intermediate tri- and tetra-iodo derivatives could not be isolated due to their high reactivity but were unambiguously identified by ^1H NMR and ^{19}F NMR spectroscopy. Also, we have demonstrated that it is possible to functionalize BODIPY with non-conjugated aminoalkyl substitution at the α -positions and halogen atoms at the β -positions, which give rise to highly coloured dye molecules with intense absorptions, ($\epsilon \approx 305,000 \text{ mol}^{-1}\text{dm}^3\text{cm}^{-1}$) and a positive shift in redox potentials. The more positive potential values might be due improved electron donation to the BODIPY core from the methylene and morpholino groups, and fluorescence quenching due to the presence of the amine functionality.

2.5 Experimental Section

2.5.1 Materials and General Methods

All reagents and solvents were purchased from Aldrich Chemicals, Alfa Aesar or Fisher Scientific UK, and used without further purification unless otherwise stated. Thin layer chromatography (TLC) was used to monitor the reactions. Column chromatography was used for purification (unless otherwise stated) by using silica gel (Merck silica gel 60, 0.2-0.5 mm, 50-130 mesh) as appropriate. ^1H and $^{13}\text{C}\{^1\text{H}\}$ NMR spectra were recorded at room temperature with either a Bruker AV400 or a Bruker AV3400, operating at 400 and 100 MHz respectively. ^{11}B and ^{19}F NMR spectra were recorded at room temperature with Bruker AV3400, operating at 128 and 376 MHz, respectively. Chemical shifts are quoted in ppm

relative to TMS (^1H and $^{13}\text{C}\{^1\text{H}\}$). $\text{BF}_3\cdot\text{OEt}_2$ was used as an external reference for ^{11}B NMR measurements and CFCl_3 as an external reference for ^{19}F NMR. Elemental microanalyses were performed by Tong Liu from University of Nottingham, School of Chemistry analytical services. Mass spectrometry was performed at the University of Nottingham, School of Chemistry.

2.5.2 Electrochemical Measurements

Cyclic Voltammetry (CV) experiments were performed using an Autolab PGSTAT20 potentiostat with a three-electrode arrangement in a single-compartment cell under an atmosphere of argon. A glassy carbon working electrode, a Pt wire secondary electrode and a saturated calomel reference electrode were chemically isolated from the test solution by a bridge tube containing electrolyte solution and fitted with a porous vycor frit, were used in the cell. The solutions were 10^{-3} M in test compounds and 0.4 M in tetra *n*-butylammonium tetrafluoroborate in dichloromethane as supporting electrolyte which was prepared using literature methods.⁸¹ The redox potentials are quoted versus the ferrocenium-ferrocene couple (Fc^+/Fc) which was used as an internal reference.⁸¹ Compensation for internal resistance was not applied. Dichloromethane was dried over calcium hydride under dinitrogen gas, ferrocene (Aldrich) was used as received and $[\text{Bu}_4\text{N}][\text{BF}_4]$ was prepared by a literature method.⁸²

2.5.3 Photophysical Measurement

Absorption UV/Vis, and fluorescence measurements were carried out at the University of Nottingham. Absorption UV/Vis spectra of solutions were measured with a Perkin Elmer Lambda 25 UV/Vis spectrometer in 1 cm pathlength quartz cuvettes. Excitation and emission photoluminescence spectra of solution samples were performed using an Edinburgh Instruments FLS920 Fluorometer. The fluorescence samples were run in standard quartz

fluorescence cuvettes, $l = 1 \times 1$ cm. All spectroscopy experiments were performed using spectrophotometric grade solvent and solutions never exceeded $A = 0.10$ at the excitation wavelength, or any longer wavelength, to minimize inner filter effects.

2.5.4 Synthetic Procedures

Synthesis of 1, 3, 5, 7-tetramethyl-8-phenyl-4,4-difluoroboradiazaindacene (2-15)

Under a dinitrogen atmosphere, benzoyl chloride (500 mg, 3.6 mmol) and 2,4-dimethylpyrrole (1 mL, 9.8 mmol) were added to CH_2Cl_2 (50 mL), the mixture was stirred at room temperature 18h, then Et_3N (4 mL) and $\text{BF}_3 \cdot \text{Et}_2\text{O}$ (4 mL) were added under ice-cold conditions, and the reaction mixture was stirred until the reaction completed as monitored by thin-layer chromatography (TLC). After the reaction, the mixture was poured into water (200 mL), the organic layer was collected and dried over anhydrous MgSO_4 and evaporated under reduced pressure. The crude product was further purified using column chromatography (CH_2Cl_2 :hexane = 2:1) to give **2.1** as an orange powder. 540 mg, Yield: 42.4 %. Data below was found to be consistent with the literature.⁷¹

^1H NMR (400 MHz, CDCl_3) δ 7.50-7.45 (m, 3H), 7.29-7.26 (m, 2H), 5.98 (s, 2H), 2.56 (s, 6H), 1.37 (s, 6H); ^{13}C NMR (100 MHz, CDCl_3) δ 155.4, 143.2, 141.7, 135.0, 129.2, 129.0, 127.9, 77.2, 14.6, 14.4; ^{11}B NMR (128 MHz, CDCl_3) δ 0.79 (t, $J = 33.1$ Hz); ^{19}F NMR: (376 MHz, CDCl_3) δ -146.32 (q, $J = 65.8$ Hz). MS (ESI) calcd for $[\text{M}]^+$: 324.16, found 324.17. Elemental Analysis: Calcd for $\text{C}_{19}\text{H}_{19}\text{BF}_2\text{N}_2$: C, 70.40; H, 5.91; N, 8.64. Found: C, 70.34; H, 6.07; N, 7.93%.

Synthesis of 2,6-diiodo, 1, 3, 5, 7-tetramethyl-8-phenyl-4,4 difluoroboradiazaindacene (2-12)

To a solution of **2-15** in CH₂Cl₂ (25 mL) was added excess NIS (459 mg, 2.04 mmol). The mixture was stirred at room temperature until total consumption of the starting material (1 h, as monitored by TLC). The crude product was then concentrated under vacuum and purified by silica gel column chromatography (hexane/CH₂Cl₂, 1:2). The red coloured fraction was collected, and the solvent was removed under reduced pressure to yield the desired compound. Data below was found to be consistent with the literature.⁷¹

¹H NMR (400 MHz, CDCl₃) δ 7.56-7.53 (m, 3H), 7.27-7.25 (m, 2H), 2.57 (s, 6H), 1.25 (s, 6H); ¹³C NMR (100 MHz, CDCl₃) δ 156.78, 145.37, 141.38, 134.74, 131.30, 129.54, 129.47, 127.79, 85.65, 16.95, 16.04. ¹¹B NMR (128 MHz, CDCl₃) δ 0.50 (t, *J* = 33.40 Hz); ¹⁹F NMR: (376 MHz, CDCl₃, δ -146.04 (q, *J* = 66.0 Hz). FD-MS: *m/z* calculated 575.97, observed 575.95([M]⁺, 100%) Elemental Analysis: Calcd for C₂₁H₂₁BF₂I₂N₂O: C, 40.68; H, 3.41; N, 4.52; Found: C, 40.96; H, 3.05; N, 4.79.

2,6-diiodo-5,7-dimethyl-1,3-bis(methylene) dimorpholine,8-phenyl-4,4 difluoroboradiazaindacene (2-36)

To a solution of **2-15** (170 mg, 0.51 mmol) in CH₂Cl₂ (25ml) was added 4 equivalents of NIS (459 mg, 2.04 mmol). The resulting mixture was stirred at room temperature in the absence of light for 1h. Morpholine was then added and the reaction mixture refluxed for 1h. The crude product was concentrated under vacuum and purified by silica gel column chromatography (hexane/CH₂Cl₂, 1:2). The deep red-coloured fraction was collected, and the solvent was removed under reduced pressure to yield the desired compound as a red solid. 90 mg, Yield: 26.4 %.

^1H NMR (400 MHz, CDCl_3) δ 7.57-7.55 (m, 3H), 7.29-7.30 (m, 2H), 3.84 (s, 4H) 3.36-3.76 (t, $J = 4.6$ Hz, 8H) , 2.65 (t, $J = 4.6$ Hz, 8H), 1.43 (s, 6H); ^{13}C NMR (500 MHz, CDCl_3) δ 155.96, 146.46, 143.37, 134.58, 131.20, 129.74, 127.60, 67.11, 53.63. 29.72 16.98; ^{11}B NMR (128 MHz, CDCl_3) δ 0.55 (t, $J = 33.1$ Hz); ^{19}F NMR: (376 MHz, CDCl_3) δ -134.13 (q, $J = 65.8$ Hz). (MALDI-TOF, DCTB/MeCN): m/z calculated 746.06, observed 746.1 ($[\text{M}]^+$, 100%). Elemental Analysis: Calcd for $\text{C}_{32}\text{H}_{43}\text{BF}_2\text{I}_2\text{N}_4\text{O}_2$: C, 46.97; H, 5.30; N, 6.85. Found: C, 46.45; H, 5.11; N, 6.35.

Attempted Synthesis of 2,6-dimorpholino 1,3,5,7-tetramethyl-8-phenyl-4,4-difluoroboradiazaindacene (2-37)

To a solution of **2-12** (170 mg, 0.51 mmol) in CH_2Cl_2 (25ml), morpholine (2 ml, 2.04 mmol) was added and the reaction mixture refluxed for 3h. The crude product was concentrated under vacuum and purified by silica gel column chromatography (hexane/ CH_2Cl_2 , 1:2). The deep red-coloured fraction was collected, and the solvent was removed under reduced pressure to yield a red solid. Analysis by ^1H NMR, ^{13}C NMR, ^{11}B NMR and ^{19}F NMR spectroscopy and mass spectrometry gave no evidence of the formation of **2-37**, indicating the presence of starting material **2-12**.

^1H NMR (400 MHz, CDCl_3) δ 7.56-7.53 (m, 3H), 7.27-7.25 (m, 2H), 2.57 (s, 6H), 1.25 (s, 6H); ^{13}C NMR (100 MHz, CDCl_3) δ 156.78, 145.37, 141.38, 134.74, 131.30, 129.54, 129.47, 127.79, 85.65, 16.95, 16.04. ^{11}B NMR (128 MHz, CDCl_3) δ 0.50 (t, $J = 33.40$ Hz); ^{19}F NMR: (376 MHz, CDCl_3 , δ -146.04 (q, $J = 66.0$ Hz).

Attempted Synthesis of 2,6-dimorpholino 1,3,5,7-tetramethyl-8-phenyl-4,4-difluoroboradiazaindacene (2-37)

To a solution of **2-12** (170 mg, 0.51 mmol) in CH₂Cl₂ (25ml) morpholine (2 ml, 2.04 mmol) and triethylamine (1ml) were added and the reaction mixture refluxed for 3 days. The crude product was concentrated under vacuum and purified by silica gel column chromatography (hexane/CH₂Cl₂, 1:2). The deep red-coloured fraction was collected, and the solvent was removed under reduced pressure to yield a red solid. Analysis by ¹H NMR, ¹³C NMR, ¹¹B NMR, and ¹⁹F NMR spectroscopy and mass spectrometry gave no evidence of the formation of **2-37**, indicating the presence of starting material **2-12**.

¹H NMR (400 MHz, CDCl₃) δ 7.56-7.53 (m, 3H), 7.27-7.25 (m, 2H), 2.57 (s, 6H), 1.25 (s, 6H); ¹³C NMR (100 MHz, CDCl₃) δ 156.78, 145.37, 141.38, 134.74, 131.30, 129.54, 129.47, 127.79, 85.65, 16.95, 16.04. ¹¹B NMR (128 MHz, CDCl₃) δ 0.50 (t, *J* = 33.40 Hz); ¹⁹F NMR: (376 MHz, CDCl₃, δ -146.04 (q, *J* = 66.0 Hz).

2.5.5 X-ray Crystallography

Single crystal diffraction data were collected for **2-12**, and **2-36**, at 120(2) K on a Rigaku Oxford Diffraction SuperNova, Atlas GV1000 diffractometer using mirror monochromated Cu K_α radiation. Using Olex2,⁸³ the structure was solved with the ShelXT⁸⁴ structure solution program using intrinsic phasing and refined with the ShelXL⁸⁵ refinement package using least squares minimisation.

Crystal data for **2-12** C₁₉H₁₇BF₂I₂N₂: space group *P*2₁/*n* (no. 14), *a* = 11.4551(3) Å, *b* = 12.9407(4) Å, *c* = 13.2532(4) Å, β = 90.788(2)°, *V* = 1964.43(10), *Z* = 4, *D*_{calc} = 1.947 g cm⁻³

³, $\mu = 25.351 \text{ mm}^{-1}$, $F(000) = 1096.0$ A. total of 7967 reflections were collected, of which 3866 were unique, with $R_{\text{int}} = 0.0275$. Final R_1 (wR_2) = 0.0272 (0.0702) with GOF = 1.076.

Crystal data for **2-36**: $\text{C}_{27}\text{H}_{33}\text{BF}_2\text{I}_2\text{N}_4\text{O}$. orthorhombic, space group $P2_12_12_1$ (no. 19) $a = 6.5790(1) \text{ \AA}$, $b = 18.7712(4) \text{ \AA}$, $c = 23.3004(4)$, $\alpha = 90^\circ$, $\beta = 90^\circ$, $\gamma = 90^\circ$, $V = 2877.50(9) \text{ \AA}^3$, $Z = 4$, $D_{\text{calc}} = 1.727 \text{ g cm}^{-3}$, $\mu = 17.541 \text{ mm}^{-1}$, $F(000) = 1472.0$. A total of 27321 reflections were collected, of which 5705 were unique, with $R_{\text{int}} = 0.092$. Final R_1 (wR_2) = 0.0350 (0.0744) with GOF = 1.003.

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Chapter 3

The role of Halogen Bonding Interactions in the Solid-State Structure of Halogenated BODIPY species.

3.1 Introduction

The study of intermolecular interactions is a topic of intense research activity in the fields of supramolecular chemistry, crystal engineering, and materials science.^{1, 2} The use of intermolecular interactions provides a modular approach to control the relative organisation of molecules and to create well-defined molecular arrangements. Intermolecular interactions that have been successfully used to prepare self-assembled structures include coordination bonds,^{3, 4} hydrogen bonding (HB),^{2, 5-8} halogen bonding (XB)^{9-13, 69-70} π - π stacking,^{14, 1} hydrophobic interactions, electrostatic interactions,¹⁵ and *van der Waals* interactions.¹⁶⁻¹⁸ This introduction is a brief review of current understanding of XB interaction.

3.1.1 Halogen Bond Story

The beginning of the halogen bond story can be traced back to 1814, when J. J. Colin and J. L. Gay-Lussac reported the formation of a dark blue coloured liquid upon combination of iodine and amylose.^{19, 20} After that in early of the 19th century,²¹ chemists had observed the formation of stable complexes between halogens and electron-rich compounds (the stable complexes between I₂, Br₂, or Cl₂ and ammonia and methylamines).²⁰⁻²² In the 1970's, the Nobel prize winning Odd Hassel provided for the first time a clear characterisation of halogen bonds where the covalent bonded halogens form stable interactions with other electron rich atoms as charge-transfer interactions.²¹ The “charge-transfer bonds”, referring to a bonding model wherein the charge from the lone pairs of an electron-rich atom (for instance an oxygen or nitrogen) is transferred to a Lewis acid, in this case the halogen, is similar to what is commonly observed with transition metal complexes.²⁰ The new term (halogen bond) started to appear in the chemical literature in mid-1990s to define the short-range interactions of

organic molecules in crystals and in solution.^{23, 24} However, in recent years dispersion and electrostatic forces have come to the forefront as the primary forces involved in halogen-bonds. Therefore, the halogen bond term reflects the electrostatic character of the interaction, similar to classic hydrogen bonding, rather than their charge-transfer nature. The unified definition of XB was given by the IUPAC Task Group in 2009: “Halogen bonding (XB) occurs when there is evidence of a net attractive interaction between an electrophilic region associated with a halogen atom in a molecular entity and a nucleophilic region in another, or the same, molecular entity”.²⁵⁻²⁷ The IUPAC definition could be summarized in one sentence, an XB is where there is evidence of bond formation between an electrophilic halogen atom X and a nucleophilic species Y. A typical XB is shown in **Fig 3.1**, where R-X is the XB donor that contains the electrophilic halogen atom X, and an R group which is usually covalently bonded to halogen X. The XB acceptor is represented as Y. Usually, the Y species contains at least one nucleophilic region. Therefore, it acts as a Lewis base that donates the electron density to the electrophilic XB donor in an XB interaction.²⁰

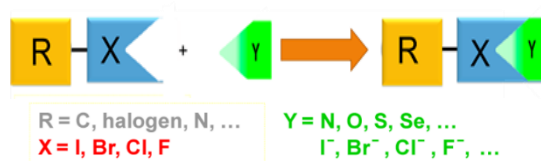


Fig 3.1 Schematic representation of halogen bonding. Reproduced from reference 20.

Occasionally, the terms iodine bond,^{20, 28, 29} bromine bond,^{20, 28} chlorine bond,^{20, 30, 31} and fluorine bond^{20, 32-34} have appeared in the literature to address the specific interactions involving one of the four halogen atoms as an electrophilic site.²⁰ Clearly, these terms could

be under the broader picture set of interactions named as halogen bonds. An advantage of the term XB is the possibility to make a direct and meaningful comparison among the behaviours of the four halogens.²⁰ Over the years, halogen bonds have been well-developed in the field of crystal engineering,^{1, 12, 35, 36} leading to the design of functional materials,^{37, 38} and finding applications in the areas of reactivity and catalysis,^{39, 40} self-assembly,⁴¹ and medicinal chemistry.⁴² Moreover, construction of porous materials based on halogen bonding could lead to the formation of flexible, dynamic voids⁴³⁻⁴⁶ opening up an opportunity to develop new and adaptable materials.^{46, 47}

3.1.2 Nature of the Halogen Bond

The obvious question that comes to mind when we try to describe the concept of halogen bonding is: How can halogens, which are considered electron rich, form short-range, stabilizing interactions with electron-rich Lewis bases?⁴⁸ In order to answer this question and rationalizing the XB in greater detail, a few theories and concepts have been proposed. The most popular one is the σ hole theory, which will be deduced below.⁸⁴

3.1.2.1 σ -hole theory

Until recently XB interactions were commonly considered to be predominantly electrostatic.⁴⁹⁵⁰ Indeed, the current widespread view in the literature is that the bonds are an electrostatic interaction in which an electron-rich species is attracted to the positively charged σ -hole formed in a covalently bonded halogen.^{49, 51, 52} The σ -hole defined as a region of positive electrostatic potential (ESP) that is generated on a polarized halogen atom which attached to

ⁱ Sigma holes are electron-deficient regions that arise from the anisotropic distribution of electron density on the atom of group 14 (tetrels), 15 (pnictogens), 16 (chalcogens), and 17 (halogens) elements when covalently bonded to electron-withdrawing Group.¹⁴⁶

electron-withdrawing groups as shown in **Fig 3.2**.^{38, 53} The positive ESP is labelled as the σ -hole due to spatial overlap with the σ^* orbital associated with the covalent bond adjoining the polarized halogen atom to the electron-withdrawing substituent.⁵⁴ This theory was developed by Politzer *et. al.*⁵⁵ To understand this theory, we need to take a close look at the atomic orbitals of group VII atoms. They have five electrons residing in the p -atomic orbitals of the valence shell and that, according to molecular orbital theory, it is the single valence electron of the p_x orbital that participates in forming a covalent σ -bond to a carbon atom. Thus, the depopulation of this orbital opposite the σ -bond (C-X, where C is carbon and X is a halogen) creates an electropositive crown (the σ -hole) at the halogen surface diametrically opposed to the σ -bond. The σ -hole acts as the halogen-bond donor to an electron-rich acceptor such as oxygen, nitrogen, sulfur, π -systems or other halogen atoms. Such interaction constitutes an X-bond.^{38, 55-59} The extent of polarization, and resultant σ -hole formation, increases with the size of the of the halogen donor atom, (i.e., $F < Cl < Br < I$).^{20, 38, 84} Thus, fluorine is not usually considered a halogen bond donor^{20, 60-63} This is explained as a result of the lack of a discernible σ -hole when a fluorine atom is covalently bonded. However, if the fluorine atom is attached to a particularly strong electron-withdrawing group it could act as an XB donor.^{20, 60, 62-64}

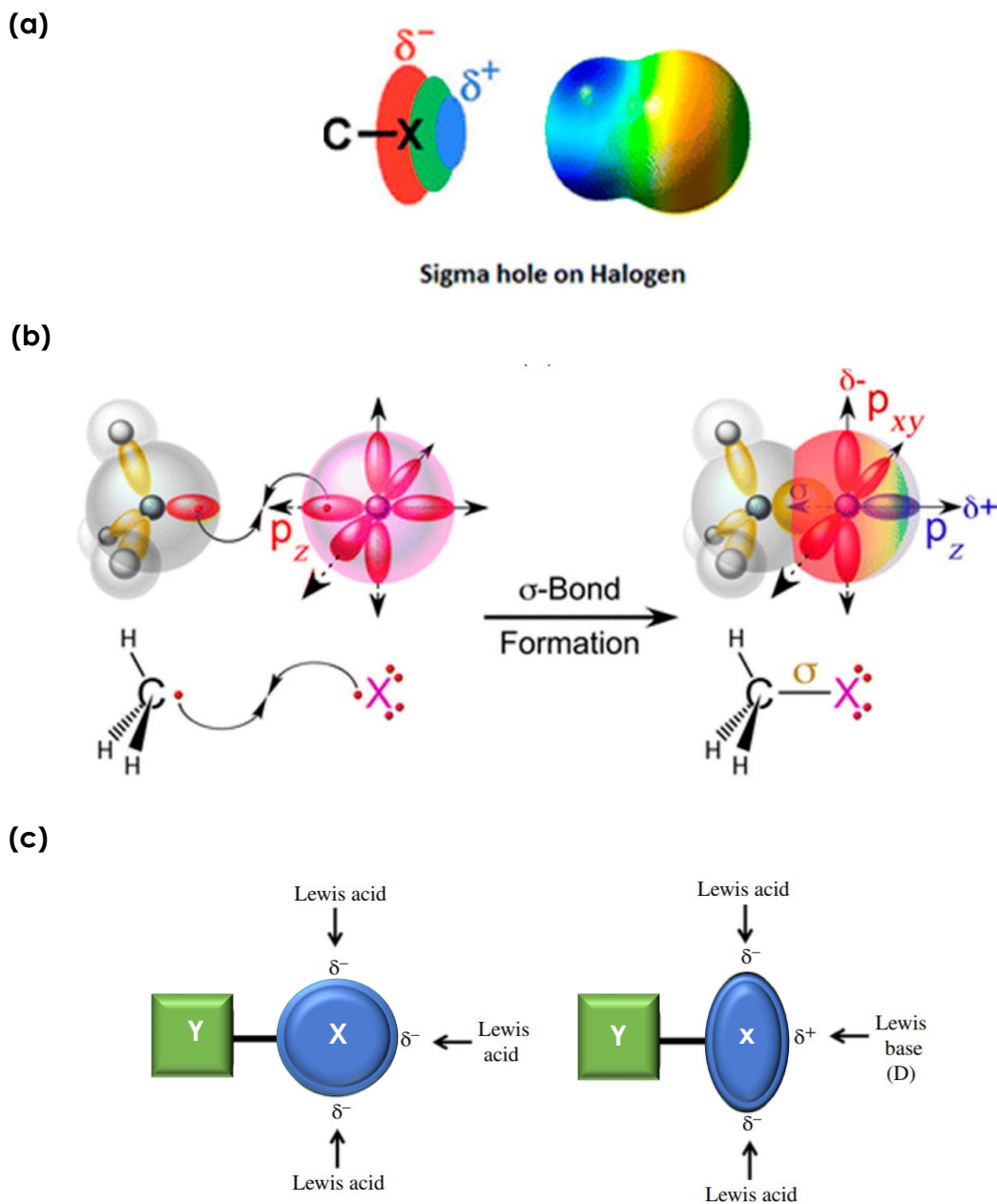


Fig. 3.2. The halogen bond (XB). (a) The σ -hole model for X-bonding.^{56, 65} The electropositive σ -hole (δ^+) that can interact with a region of electron density residing on a different atom. Here, the halogen atom (or R-X) is an “electron-poor” species and acts a halogen-bond donor (D). The acceptor (Y) possesses rich electron density and acts as a nucleophile, thereby completing the halogen bond between the donor sigma-hole and the acceptor lone pair.^{56, 65} (b) Another view detailing the formation of the σ -hole: The covalent bond (C-X) between the carbon atom and the halogen (σ -bond, yellow) pairs an electron from the carbon with one from the valence p_z -orbital of the halogen. The electron withdrawing nature of the R-C moiety results in the depopulation of the p_z -orbital of the halogen atom. As a result, it creates an electropositive crown (blue) and flattening of the atomic radius opposite the σ -bond, while the p_{xy} -orbital remains fully occupied, resulting in an electronegative annulus perpendicular to the covalent bond.^{56, 66} (c) Schematic representation of the electron density distribution of covalently bound halogen atoms (X) and the resulting attractive interactions with Lewis acids and bases.^{67, 68} (d) description based on the anisotropic distribution of the electron density.^{61, 67, 68} (a) and (b) reproduced from references 56 (c) adopted from ref 67, 68.

Moreover, the group attached to the halogen atom also influences the magnitude of the σ -hole. More electronegative groups give a greater magnitude of the partial positive charge of the σ -hole by removing electron density from the area of the σ -hole. For example, a σ -hole is observed on the chlorine atom of CF_3Cl , but not in CH_3Cl as the CF_3 group is more electron withdrawing than the CH_3 group. As a further consequence, the order of halogen bond acceptor strength is correlated to the type of atom attached to the halogen. In general, the order of acceptor strength follows the trend $\text{X-X} > \text{X-C(sp)} > \text{X-C(sp}^2\text{)} > \text{X-C(sp}^3\text{)}$.^{20, 25}

3.1.3 Halogen bonds vs hydrogen bonds

Intermolecular forces can be either isotropic, such as *van der Waals* interactions or directional, such as hydrogen bonds⁷¹ and halogen bonds.²⁷ The comparison between HB, and XB is interesting not only because this is a common comparison in the literature,⁷²⁻⁷⁵ but also because these two bonds have analogous structures, directionality and are comparable in strength.^{24, 76-78} Both contacts are electrostatic intermolecular interactions involving an electron donor and an electron acceptor. The use of a dotted line in the literature to illustrate XB and HB serves to emphasise both relatively weak bond energy and the limited charge transfer from the halogen or hydrogen, respectively to electron-poor species upon formation of the bond.

In the case of hydrogen bonds, the D-H acts as a hydrogen bond donor (*i.e.* the electropositive atoms), while hydrogen bond acceptors are electronegative atoms such as oxygen or nitrogen atoms (**Fig 3.2** and **3.3**).^{26, 79, 80, 84} The same terminology has also been adapted in halogen bonds, where the halogen in D-X acts as the halogen bond donor, while electronegative atoms such as nitrogen, oxygen, sulfur act as the halogen bond acceptors (**Fig 3.3**).^{26, 79, 80, 84} However,

halogens have the ability to act not only as XB donors in the direction of the σ -hole, but also as acceptors to H- or X-bond donors (**Fig 3.3**).⁸⁴ Halogen and hydrogen bonding are similar because both of them are directional interactions whose strength depends on the distance between bonded atoms and on the $D\cdots X-Y$ angle, where X is the electrophilic halogen atom (Lewis acid, XB donor), D is a donor of electron density (Lewis base, XB acceptor), and Y is a carbon, nitrogen, or halogen atom (**Fig 3.3, Fig 3.3**).^{25,84} The interatomic distances in hydrogen and halogen bonding is mostly closer than the sum of the interacting atoms' *van der Waals radii* (ΣR_{vdw}).

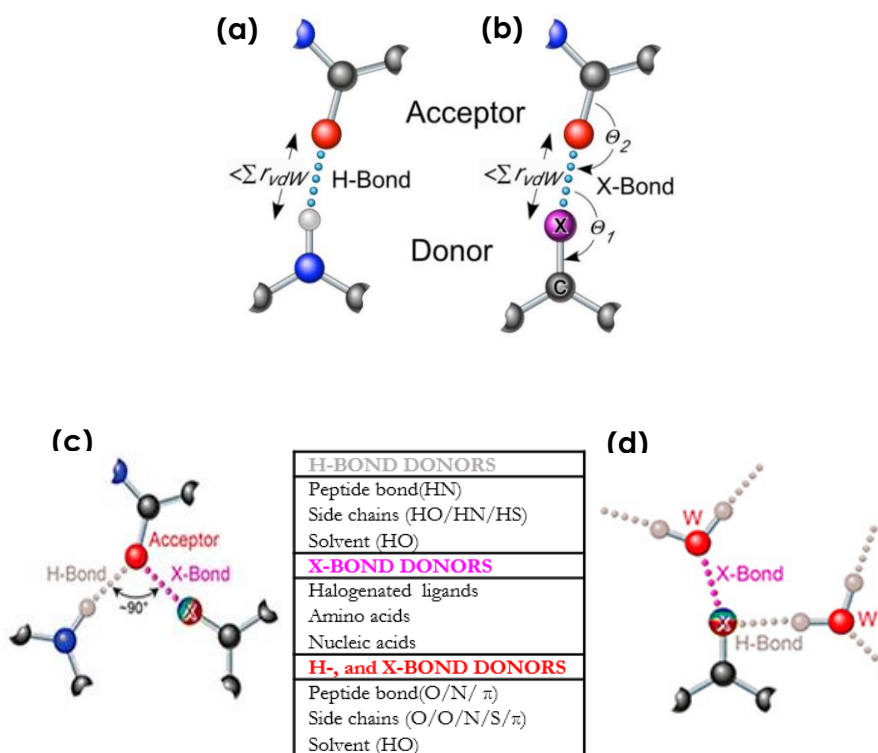


Figure 3.3 (a) Hydrogen bonds, (b) halogen-bonds, (c) Diagram of observed perpendicular interactions between hydrogen and halogen bonds, (d) halogen bonds (X-bonds) seen in biomolecular systems. The acceptor (A) (red, Oxygen) and donor (D), where the A-D distance could be shorter than the sum of their R_{vdw} .^{26, 79, 80} The terms “donor” and “acceptor” refer to the now accepted definitions, in which the donor is the electropositive atom while the acceptor is the electronegative atom in the two interactions.^{25, 80} The approach of the acceptor to the halogen and halogen to the acceptor are labelled as θ_1 and θ_2 , respectively. In (c) and (d) The halogen of the X-bond is shown with the electropotential polarized from positive (blue) to neutral (green) to negative (red). (a) and (b) reproduced from ref 48 (c) and (d) adopted from reference 56.

However, the most significant difference between XB and HB is the directionality inherent to halogen bonds due to the limited area of positive electrostatic potential of the polarized halogen available for interaction.^{81, 82} Therefore, XB bonds have a strong directional tendency toward a θ_1 angle (the angle of the acceptor approach toward the halogen with respect to the sigma bond). XB usually exhibit bond angles of 170 -180° (**Fig 3.3**).^{56, 83} Nevertheless, hydrogen bonds are more likely to have non-linear θ_1 angles. This discrepancy in geometries can be explained by analysis of σ -hole formation and electrostatic surface potentials of covalently bonded halogen and hydrogen atoms. In the case of XB, polarized halogens have a negative charge ring formed by remaining p_x and p_y valence electrons and surrounding the electropositive σ -hole. As result, a linear approach of the acceptor to the σ -hole of the halogen is found. In the case of HB, a covalently bonded hydrogen atom has only one electron, which is participating in the covalent bond. Thus, the electropositive potential on a covalently bonded hydrogen atom approaches a hemispherical shape by increasing electron-withdrawing ability of the substituent. The narrow focus area of the halogen σ -hole imparts directional preference to XB over the HB (**Fig 3.3**).

It should be noted that, pnictogen, and chalcogen bonds are also structurally similar to XB. However, this comparison is not as illuminating simply because properties of these bonds are not as well understood.^{21, 89} Indeed, most research on these bonds is crystallographic or computational.^{21, 89} Other delocalised secondary bonds such as dipole-dipole and *van der Waals* interactions are structurally dissimilar to XB and a comparison with these bonds is less informative as a result.

3.1.4 Types of Halogen Bond

Over the last decade, systematic studies have revealed that halogen related interactions, such as halogen...halogen, halogen...chalcogen, and halogen...pnictogens, are ubiquitous, noncovalent interactions in crystal engineering.⁸⁵ This section highlighted the halogen interaction in depth to demonstrate the generality of the interactions.

3.1.4.1 Halogen...Halogen interactions

In 1963, Sakurai *et al.*⁸⁶ observed that (CX₁...X₂C) contacts are found in two geometries. These geometries were classified into type I and type II by Desiraju and R. Parthasarathy.^{87, 88} Type I are symmetrical interactions where $\theta_1 = \theta_2$, and type II are bent interactions where $\theta_1 \approx 180^\circ$ and $\theta_2 \approx 90^\circ$ (**Fig 3.4**).^{20, 85, 87, 88} Usually, the θ_2 angle occurs for the lighter halogen atoms, which might be due to the possibility of positive polarization on the heavier halogen and the negative polarization of the lighter halogen.⁸⁵ Desiraju suggested the following criteria for the classification of type I and type II: contacts with $0^\circ \leq |\theta_1 - \theta_2| \leq 15^\circ$ are type I; while contacts with $|\theta_1 - \theta_2| \geq 30^\circ$ are type II; and contacts with $15^\circ \leq |\theta_1 - \theta_2| \leq 30^\circ$ are quasi-type I/type II.³⁷ The angular attributes of the type II interaction become more sharply demarcated when the polarizability of the halogen increases ($|\theta_1 - \theta_2| \geq 30^\circ$). The pure type II interaction is mainly in the region of 45–50° for Cl...Cl, 55–60° for Br...Br, and 65–70° for I...I interactions as a result of the electrostatic nature of (X...X) contacts.⁸⁵ For the distances, Type I interactions were more frequently at distances shorter than the *van der Waals contacts*, while type II were more frequent closer to the *van der Waals limit*.^{85, 89} This behaviour has been explained as a direct effect of the electrostatic nature of the XB. For example, type II (I...I) contacts formed at longer distances,

while type I contacts, being dispersive forces, operated preferentially at shorter distances.⁸⁷ Additionally, organic fluorine compounds prefer type I (F $\cdots$ F) contacts, whereas Cl, Br, and I prefer type II contacts.⁸⁵ However, hetero halogen $\cdots$ halogen interactions are predominately of type II geometry because of the greater polarizability of the electron density associated with the heavier halogens.⁸⁵

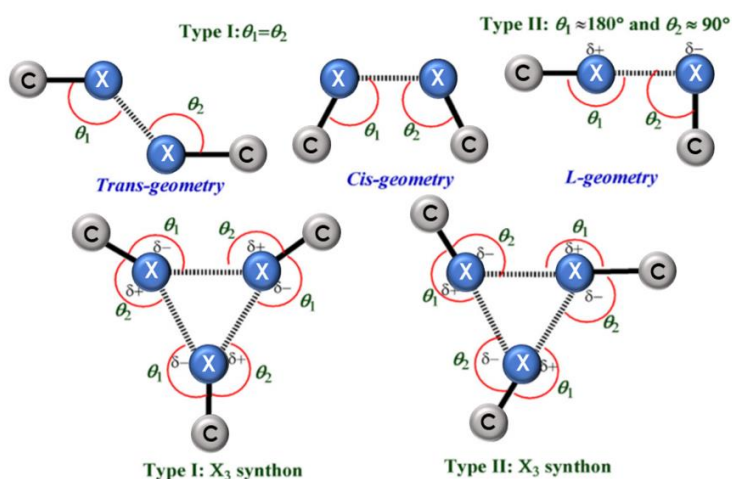


Fig 3.4. Geometrical classification of halogen $\cdots$ halogen interactions and X₃ synthons as type I and type II, respectively. Adopted from references 85, and 89.

Type I contacts have been further divided into trans and cis systems⁹⁰ (**Fig 3.4**) depending on the relative positions of the R groups covalently bound to X^{20, 90} and there is sufficiently evidence of X₃ (Cl₃, Br₃, I₃) supramolecular synthons in crystal engineering.^{85, 91, 92} Finally, type II contacts include an approach of the electrophilic region of one halogen atom to the nucleophilic region of the other, while in type I contacts the two halogen atoms minimize repulsion by interfacing the neutral regions of their electrostatic potential surfaces.⁹³

3.3.1.2 Halogen-Chalcogen, Halogen-Pnictogen interactions

Chalcogen (O, S, Se, Te), and pnictogens (N, P, As, Sb, Bi) are well known as strong XB-acceptor sites due to the electron-donating nature of those elements.⁸⁵ The chalcogen atom can be a multiple acceptor site toward XB formation.⁸⁹ The nitrogen atom organic tectons (such as pyridines⁹⁴ pyrimidines,⁹⁵ pyrazines,⁹⁶ and triazines^{97,98}) have been considered as amongst the best XB acceptors.^{85,89,99,100}

3.3.1.3 Halogen $\cdots$ other types interactions

Halogen $\cdots \pi$ contacts are another common weak interaction, which has often been overlooked because of the existence of other interactions.⁸⁵ Three types of halogen $\cdots \pi$ interactions have summarized by Shishkin and Schneider^{85,101} based on the location of the halogen atom relative to the aromatic plane: delocalized (D), semilocalized (SL) and localized (L), as shown in **Fig 3.5**.^{85,101} In the case of halogen $\cdots \pi$ delocalized contacts, the halogen atom is pointing towards the centre of the π cloud. In the case of halogen $\cdots \pi$ localized contacts, the halogen atoms are not bonded towards the centre of the aromatic ring but are interacting with a single carbon atom.

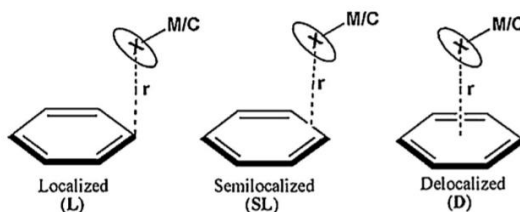


Fig 3.5. Schematic representations of the halogen $\cdots$ interactions. Taken from reference 85.

3.1.5 Polymorphism

Crystal polymorphism represents the ability of molecules to adopt varied packing arrangements, this includes conformational polymorphs, dynamic isomers or tautomerism. Crystal polymorphism has gained a considerable interest in different fields such as pharmacy, solid-state chemistry, and materials science.^{102, 103} Different polymorphs may display different physical and chemical properties as a result of different arrangements of the molecules in the crystal (having different solubilities, and melting points).¹⁰⁴ However, the different forms of a crystal structure will lead to identical liquid and vapour states. If there is a hydrate or solvent included in the crystal structure the pseudo polymorphism terminology is used. The relationships between polymorphs and their most stable forms are classified as mono-tropic or enantio-tropic. When the polymorphs are mono-tropically related, transformation from the metastable form to a stable form will happen and the process is irreversible. When the polymorphs are enantio-tropic related, the transformation process is reversible.

The polymorphism phenomenon is explained by Ostwald's law,¹⁰⁵ which indicates that when a system is departing from an unstable state, it does not necessarily form the most stable state, but rather arrives at the nearest metastable state.¹⁰⁵ Therefore, during the crystallization process the molecules will fall to the nearest minimum energy state as they assemble with a loss in free energy while still searching for the most stable form. Subsequently, an apparently stable structure which is first formed can be transformed in the end to another form. However, a material might not be polymorphic or it could be "trapped" in a kinetically accessed (metastable) state. In this case, the material will not be able to transform to the thermodynamically most stable state. This might happen, because of high activation barrier

to such a transformation from a metastable to the most stable state. Usually, polymorphs are obtained by varying experimental conditions used in the crystallization process (*i.e.* solvent, temperature and pressure).^{102, 103}

3.1.6 Hirshfeld surface analysis

Hirshfeld surface (HSs) represents a major advance in enabling supramolecular chemists and crystal engineers to gain insight into crystal packing behaviour (*i.e.* identifying and analysing intramolecular interactions between the molecules in the crystal packing).¹⁰⁶ A Hirshfeld surface is assembled by dividing space within the crystal into smooth, non-overlapping regions associated with electron density of the molecule, and the surface reflects the proximity of nearest neighbouring molecules.¹⁰⁷ The electron distribution of a sum of spherical of non-interacting atoms for the molecule of interest (the *promolecule*, $\rho_{int}(\mathbf{r})$) controls the corresponding sum over the crystal (the *procrystal*).^{108, 109} Following Hirshfeld, a molecular weight-function is defined $w(\mathbf{r}) = 0.5$ (see **equation 1**).^{108, 109}

$$w(\mathbf{r}) = \rho_{\text{promolecule}}(\mathbf{r}) / \rho_{\text{procrystal}}(\mathbf{r}) = \frac{\sum_{A \in \text{molecule}} \rho_A(\mathbf{r})}{\sum_{A \in \text{crystal}} \rho_A(\mathbf{r})} \quad (1)$$

$\rho_A(\mathbf{r})$ is defined as spherically-averaged atomic electron density centred at nucleus A, and the promolecule and procrystal are sums over the atoms belonging to the molecule and to the crystal respectively.¹⁰⁸

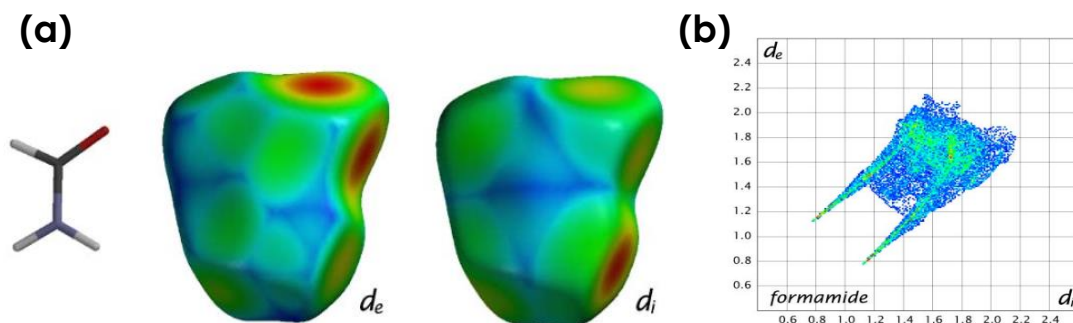


Fig 3.6 .(a) Hirshfeld surfaces for formamide with d_e (left) and d_i (right) mapped in colour (in both cases red represents the closest contacts, and blue the most distant contacts).¹⁰⁸ (b) The 2D fingerprint plot for formamide.¹⁰⁸

Calculations of the surfaces are defined by the molecule and the proximity of its nearest neighbouring atoms.¹⁰⁸ A Hirshfeld surface is represented by tens of thousands of surface points and is obtained by two parameters; (i) d_e which represents the distances between the surface and the nearest atoms outside the surface. (ii) d_i which represent the distances between the surface and the nearest atoms inside the surface. These parameters can be plotted as a three-dimensional surface and with the use of a red-green-blue colour scheme, properties and patterns for structural analysis are identified.^{108, 109} The blue colours represent longer contacts, white is used for contacts around the *van der Waals* separation, and red represents shorter contacts. **Fig 3.6** provides an example of Hirshfeld surfaces for formamide with d_e and d_i mapped in colour. Moreover, a three-dimensional picture of the intermolecular close contacts in a crystal is generated by measuring the distances d_e and d_i from the Hirshfeld surface and generating a fingerprint plot based on this value. A two-dimensional fingerprint of the intermolecular interactions in the crystal represents a unique full colour plot for every crystal, and it summarises the complex information contained in a molecular crystal. The colour of each point in the finger print plot corresponds to the relative area of the surface with

that (d_e , d_i) pair while the uncoloured points in the finger plot represents no contribution on the surface. The colours in the plot range from blue (relatively small contribution) through to red (the greatest contribution).^{108, 109} **Fig 3.6** presents an example of such a 2D fingerprint plot.¹⁰⁸ However, the only limitation of this method is the difficulty to highlight close contacts between large atoms because it does not take into account the relative sizes of atoms. Therefore, a normalised contact distance d_{norm} (**equation 2**) is used.¹⁰⁹ d_{norm} is an extension of d_e and d_i mapping, where the pairs, d_e and d_i , are normalised with respect to the *van der Waals radii* of their corresponding atoms. For each surface point d_{norm} requires, both the distance and identity of the nearest atoms internal and external to the surface.¹¹⁰ Therefore, less prominent interactions such as weak C-H $\cdots\pi$ interactions become evident¹¹⁰

$$d_{\text{norm}} = \frac{d_i - r_i^{\text{vdW}}}{r_i^{\text{vdW}}} + \frac{d_e - r_e^{\text{vdW}}}{r_e^{\text{vdW}}} \quad (2)$$

d_{norm} can be either negative or positive. If the contacts between the atoms (inside or outside) the Hirshfeld surface are shorter than *van der Waals* separations the d_{norm} value becomes negative. However, if it has a positive value, this means the contacts are longer than *van der Waals* separations. These d_{norm} values are represented by using a red–white–blue colour scheme. The blue colours represent longer contacts, white is used for contacts around the *van der Waals* separation, and red represents shorter contacts. Close intermolecular contacts are characterised by two identical red regions in normalised contact distance depending on the value of d_e and d_i .^{108, 109} Visualizing interactions in molecular crystals using Hirshfeld surface tools and 2D fingerprint plot (FPs) were analysed using Crystal Explorer (Version 3.1, and 17.1).^{110, 146}

3.2 Aims and Objectives

Halogen bonding (XB) is an attractive and valuable noncovalent interaction, which has recently been exploited as an important tool in the field of crystal engineering,^{1, 12, 21, 35} leading to the design of functional materials,³⁷ which find applications in the areas of reactivity, catalysis,³⁹ self-assembly,^{21, 41} and medicinal chemistry.^{21, 42} Halogen bonding (XB) usually refers to the attractive charge transfer interaction between the electron-deficient σ -hole (electrophilic region of a halogen such as bromine or iodine), and an electron-rich Lewis base of a neighbouring atom or molecule (a halogen bond acceptor).²⁵⁻²⁷ The presence of halogen atoms, (BF₂) group and other electron acceptor groups on a BODIPY *meso* position could lead to interesting halogen bonding interactions in the solid state arrangement of such compounds. Surprisingly, to the best of our knowledge, no detailed report has been found about halogen bonding investigations of BODIPY compounds. We are particularly interested to investigate the role of XB in the assembly halogenated BODIPY species bearing different substituents in the BODIPY *meso* position, including our own structures and those retrieved from the CDC). We have used Hirshfeld surfaces and their associated fingerprints to provide evidence for the occurrence contacts and any other intermolecular interactions which are present in the crystal structures. We combine this knowledge to try to understand how XBs could potentially become a powerful tool for molecular design.

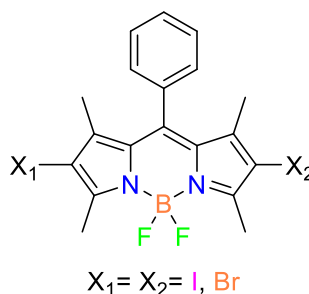
3.3 Results and discussion

Despite reports of XB, and other halogen... halogen interactions in the literature several decades ago, the ability to identify and characterise these interactions is mostly, though not entirely, limited to X-ray crystallography.^{21, 111-114} X-ray crystallography has been used to

identify when the distance between a halogen and its neighbour is shorter than the sum of the *van der Waals radii*, and if this is true for two or more atoms near a particular halogen, the halogen is involved in one or more XB/ halogen... halogen interactions. Another important factor for XB/ halogen... halogen interactions is the geometry (angles) between the halogen and its neighbour. Usually, type I interactions are shorter than type II interactions. Therefore, the approach adopted in this chapter consists of investigating the experimental distances and angles of XB intermolecular contacts observed in a series of halogenated BODIPY compounds bearing different substituents in the *meso* position. Hirshfeld surfaces (HSs), and their associated finger print plots were calculated to provide evidence for the occurrence of contacts and any other intermolecular interactions present in the crystal structures studied. Firstly, a comprehensive data set was developed by searching for halogenated BODIPY compounds in the CDC by using the Con Quest program, (the last update of the CDC used in searches was 2nd December 2018). The searches were limited to structures bearing either iodine, bromine, or chlorine atoms at 2,6-positions, and tetramethyl at 1, 3,5,7- positions which shows evidence of halogen bonding interactions. The assessment of structure where based on R-factor, data quality. Structures with errors or disorders where removed from the search. Additionally, distance and geometrical classification of halogen... halogen interactions (**Fig 3.4**) were used to determine the halogen contact. The resulting BODIPY structures were split in eight general groups based on the substituents in the *meso* position.

3.3.1 Group 1

Group 1 consists of BODIPY derivatives which are functionalized at the *meso* position with phenyl rings and at the 2,6-positions with either iodine, or bromine (**Scheme 3.1**). A search of the CDC finds four structures bearing iodine atoms at the 2,6-positions **CIMMOI**,¹⁴⁵ **CIMMOI01**,¹¹⁵ **CIMMOI03**,¹¹⁶ **CIMMOI02**,¹¹⁷ and a crystal structure on bromo derivative **OYULIF**.¹¹⁷ We also report the crystal structure of the iodo versions **BHASNR**, and the bromo versions **BHASNF**, and **BHASNM** from this thesis.



Scheme 3.1. Group 1 BODIPY complexes investigated in this study.

Structural determinations by single-crystal X-ray diffraction revealed that the iodo-functionalised species, **BHASNR**, **CIMMOI03**, **CIMMOI**, are iso-structures, therefore, the analyses will be just for **BHASNR**. Similarly, the bromo compounds **BHASNM**, and **OYULIF** are iso-structures, therefore, the analyses will be just for **BHASNM**. The asymmetric units of **CIMMOI01**, **CIMMOI03**, **CIMMOI02**, **BHASNR** contain one molecule. **CIMMOI** contains two molecules per asymmetric unit and, therefore, each separate molecule will be called **CIMMOI.a*** and **CIMMOI.b*** as shown in **Fig 3.6**. **Table 3.1** provides a summary of XB interactions observed for compounds in group.

3.3.1.1 Structures Demonstrating (C-I...F) Interactions

The packing motif observed for **BHASNR**, revealed the formation of a zig-zag linear pattern due to the formation of type I (trans geometry) halogen...halogen interaction between an iodine-atom on one BODIPY and the fluorine atoms from the neighbouring BODIPY (**a**, **Fig 3.7**). However, the packing motif of **CIMMOI02** along c- axis revealed the formation of different packing due to the formation of type II halogen bonding between iodine-atoms from one BODIPY and the fluorine atoms from the neighbouring BODIPY (**b**, **Fig 3.7**).

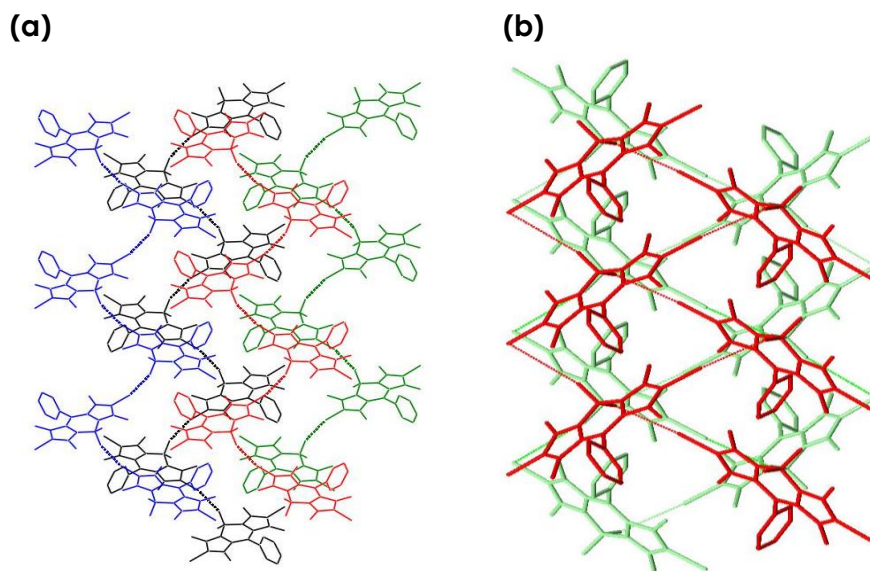


Fig 3.7. (a) View of **BHASNR** along the c-axis which revealed the formation of a wavy linear pattern, (b) orientation of **CIMMOI02** along c-axis. Hydrogen atoms, and hydrogen bonding interactions have been removed for clarity

Table 3.1. Summary of halogen-halogen interaction of **group1** compounds

Group 1									
	X ₁	X ₂	Meso	D	A	Types of halogen-halogen interaction	θ_1	θ_2	Distance
BHASNR	I	I	Phenyl	I	F	Type I	163.88 (11)°	152.65 (11)°	3.1165(19) Å
CIMMOI02	I	I	Phenyl	I	F	Type II	173.25 (3)	108.18 (6)°	3.2465(8) Å
CIMMOI.a*	I	I	Phenyl	I	I	Type II	163.30 (2)°	114.30 (2)°	3.7820(8) Å
CIMMOI.b*	I	I	Phenyl	I	I	Type II	160.20 (3)°	112.50 (2)°	3.8123(8) Å
BHASNF	Br	Br	Phenyl	Br	F	Type II	177.73(5)°	105.86 (10)°	3.2022(13) Å
BHASNM	Br	Br	Phenyl	Br	F	Type I	163.64(18)°	153.60 (3)°	2.970(3) Å
CIMMOI contains two molecules per asymmetric unit and, therefore, each separate molecule will be called CIMMOI.a* and CIMMOI.b*									

The (C–I $\cdots$ F) halogen $\cdots$ halogen interaction within the solid state structure of **BHASNR** ([I $\cdots$ F = 3.1165(19) Å; C–I $\cdots$ F = 163.89 (11) $^\circ$, B–F $\cdots$ I = 152.64 (19) $^\circ$, **Table 3.1**], as expected for type I halogen interaction.^{1, 12, 35} The large θ_2 angle could be due to the small σ -hole on the fluorine.¹⁴⁷ However, **CIMMOI02** shows type II (C–I $\cdots$ F) XB interactions, [I $\cdots$ F = 3.2465(8) Å; C–I $\cdots$ F = 173.25 (3) $^\circ$, B–F $\cdots$ I = 108.18 (6) $^\circ$, **Table 3.1**]. **Fig 3.8.** provides an example of single crystal X-ray structures of type I, and type II (C–I $\cdots$ F) XB interactions. It should be stated that, the I $\cdots$ F distance in all structures discussed are shorter than the sum of mean *van der Waals radii* of the two atoms (3.45Å). Comparison of the geometry classification of type I and type II halogen $\cdots$ halogen interaction reported by Desiraju⁸⁵ and the geometries observed in **BHASNR**, and **CIMMOI03** indicate that type I (C–I $\cdots$ F) halogen $\cdots$ halogen interactions are purely type I ($|\theta_1 - \theta_2| \leq 15^\circ$) and type II interactions show $|\theta_1 - \theta_2| \geq 30^\circ$, indicating purely type II interactions.

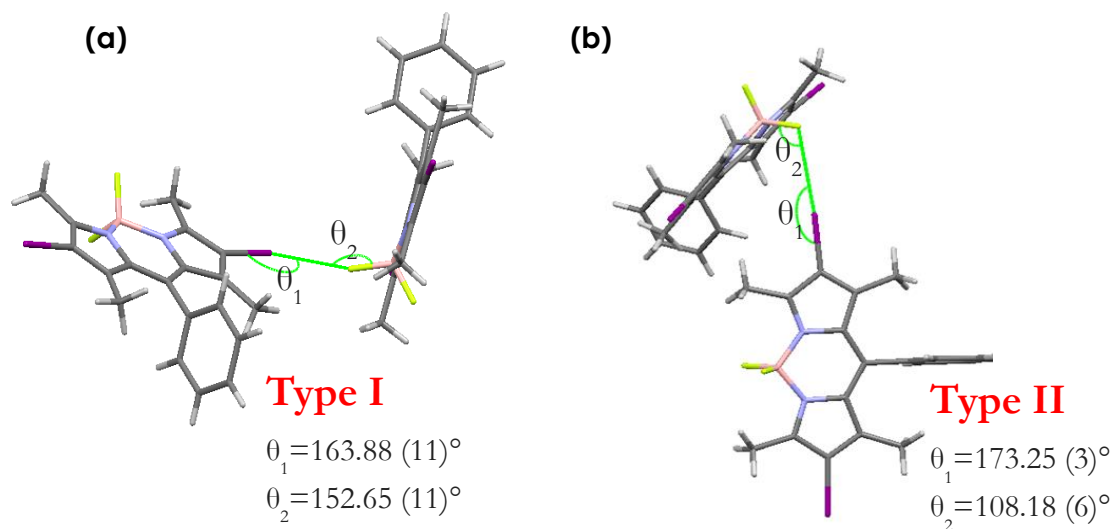


Fig 3.8. (a) Single crystal X-ray representation of (a) type I halogen bonding interaction in **BHASNR**, (b) type II halogen bonding interaction in **CIMMOI02**. Carbon = grey, nitrogen = blue, boron = pink, fluorine = green, iodine = purple.

In order to provide further evidence for the occurrence of (C–I $\cdots$ F) XB halogen bonds in the crystal structures of **BHASNR**, and **CIMMOI02**. Hirshfeld Surfaces were calculated for all the structures in this group. Inspection of the Hirshfeld surfaces of **BHASNR** and **CIMMOI02** (**Fig 3.9**) indicates that the most significant intermolecular interactions involve the iodine-atom from one side of the BODIPY as a halogen-bond donor and the fluorine atoms from the neighbouring BODIPY moiety as a halogen-bond acceptor. The fluorine atoms behave as acceptors due to the existence of the negative lateral sides of the atom caused by the aspherical charge density distribution.¹¹⁸ Therefore, HSs represented in **Fig 3.9** present intense red spots near both the iodine and fluorine atoms on the BODIPY core for both **BHASNR** and **CIMMOI02** corresponding to (C–I $\cdots$ F) XB interactions.

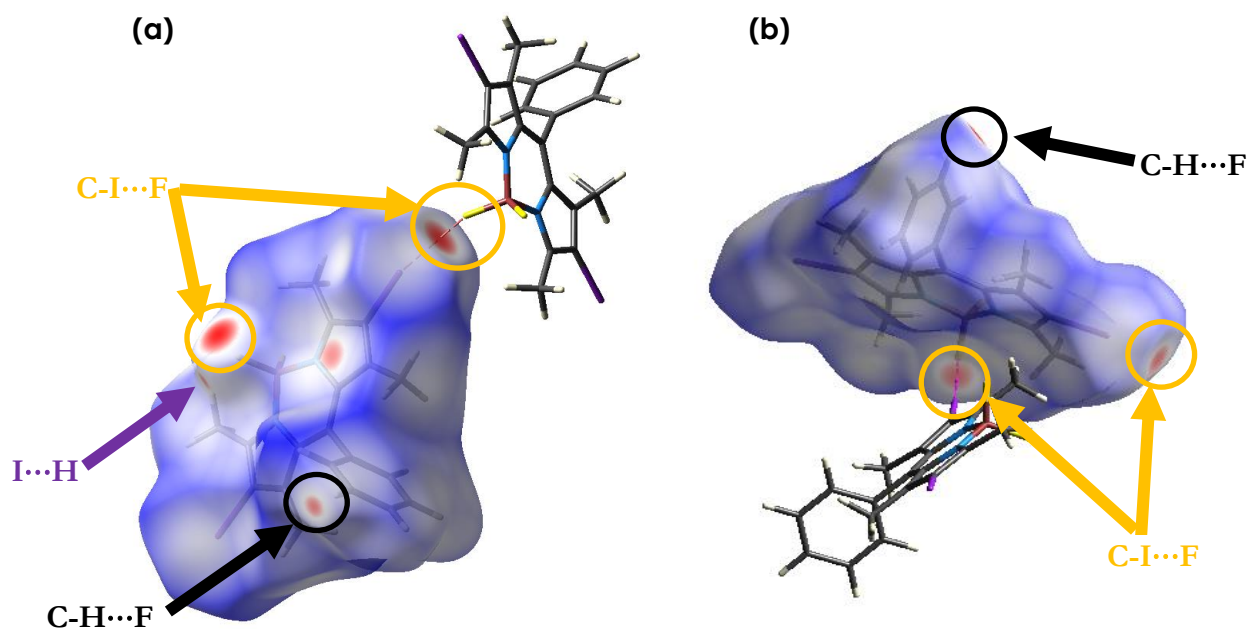


Fig 3.9 HSs representation (a) type I halogen interaction **BHASNR** , (b) type II halogen bonding **CIMMOI02**. The close (C–I $\cdots$ F) contact is highlighted in yellow, (C–H $\cdots$ F) hydrogen bonding contacts are highlighted in black. Carbon = grey, nitrogen = blue, boron = red, fluorine = green, , iodine = purple.

In case of **BHASNR**, the other iodine atom does not engage in halogen bonding, but rather acts as an acceptor in a short (C-H $\cdots$ I) contact involving a methyl group of α -carbon from the neighboring BODIPY. Both compounds shows close C-H $\cdots$ F contacts, highlighted in black in **Fig 3.9**, between the fluorine atom from BODIPY core and a neighbouring hydrogen from a phenyl ring (*meta*, or *para*-hydrogen), with distances ranging between 2.52-2.60 Å, within the range sum of the *van der Waals radii* for H and F, 2.56 Å.^{119, 120} It should be noted that, in all hydrogen bonding measurement in this chapter, the H-atoms position was not normalized.

3.3.1.2 Structures Demonstrating (C-I $\cdots$ Br) Interactions

Similarly to **BHASNR**, the bromo analogue, **BHASNF**, exhibits type II (C-Br $\cdots$ F) halogen bonds, [Br $\cdots$ F = 3.2022 (13) Å; C-Br $\cdots$ F = 177.73 (5)°, B-F $\cdots$ Br = 105.86 (10)°, **Table 3.1**]. However, **BHASNM** show type I halogen interaction (trans geometry) [Br $\cdots$ F = 2.970 (3) Å; C-Br $\cdots$ F = 163.64 (18)°, B-F $\cdots$ Br = 153.60 (3)° for **BHASNM**. The Br $\cdots$ F distance in all of these structures are shorter than the sum of mean *van der Waals radii* of the two atoms (3.30 Å).

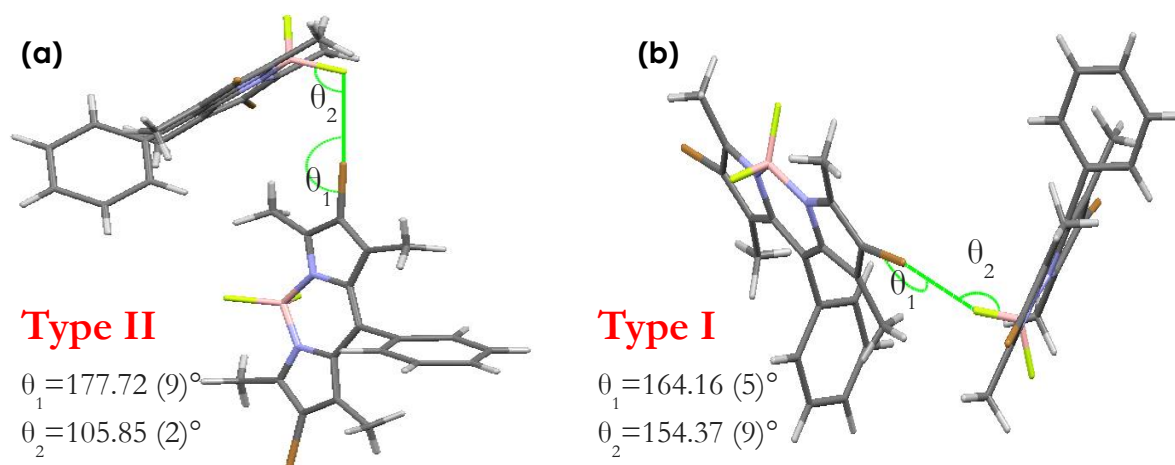


Fig 3.10. Views of single crystal X-ray structures showing (a) type I halogen bonding interaction for **BHASNM**, (b) type II halogen bonding interactions for **BHASNF**. Carbon = grey, nitrogen = blue, boron = pink, fluorine = green, bromine = orange.

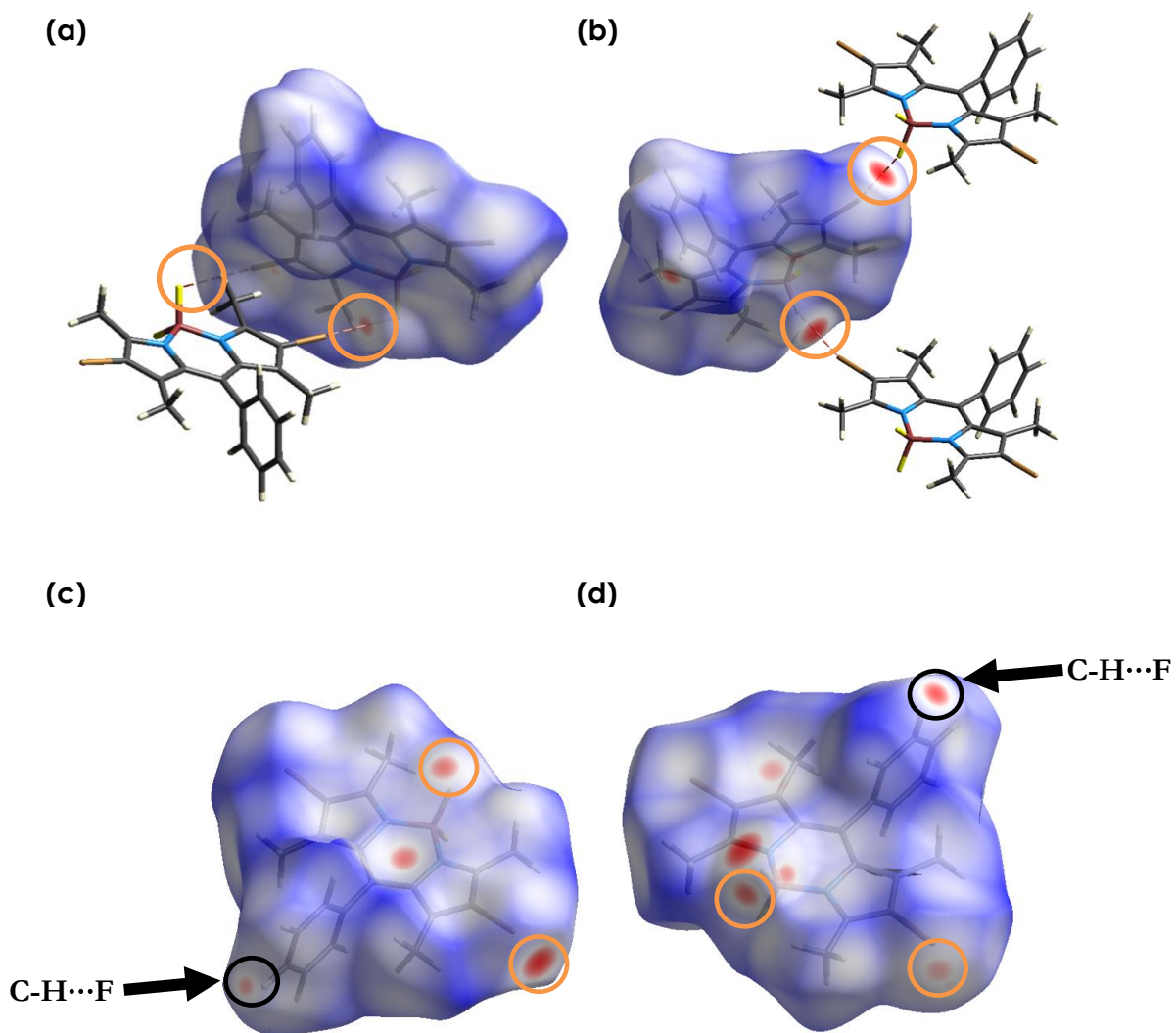


Fig 3.11. HSs calculated for (a) type II (C-I...Br) halogen bonds, (b) type I (C-I...Br) halogen bonds and HSs calculated for (c) **BHASNM**, (d) **OYULIF** viewed along the b axis. The close (C-I...F) contact is highlighted in orange, (C-H...F) hydrogen bonding contact highlighted in black. Carbon = grey, nitrogen = blue, boron = red, fluorine = green, bromine = orange.

Inspection of the Hirshfeld surfaces of **BHASNM** and **BHASNF** indicates that the most significant intermolecular interactions involve bromine atoms from one side of the BODIPY acting as a halogen-bond donor and the fluorine atoms from the neighbouring BODIPY moiety as a halogen-bond acceptor, in a similar manner to the iodo version. The second

observation from the HSs shown in (**Fig 3.11, a, b, c, and d**) is the red spot near the fluorine atoms on the BODIPY core for **BHASNM**. The close (CH $\cdots$ F) halogen bonding between the fluorine atom from BODIPY core and a neighbouring hydrogen from phenyl ring (para-hydrogen in case of **BHASNM**), with a distance of approximately 2.48 Å, shorter than the sum of the *van der Waals radii* for H and F (2.56 Å).^{119, 120}

3.3.1.3 Structures Demonstrating (C-I $\cdots$ I) Interactions

The packing motif of **CIMMOI.a***, and **CIMMOI.B***, reveals the formation of a zig-zag pattern as result of I $\cdots$ I close contacts. In these examples, each iodine acts as a donor and an acceptor.

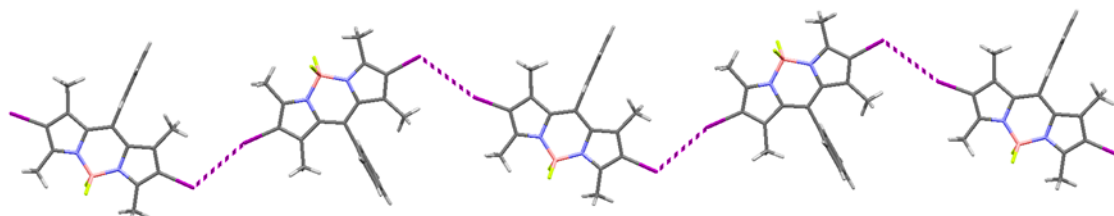
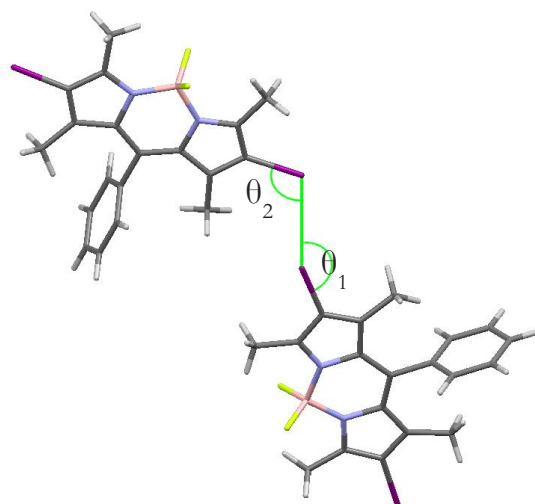


Fig 3.12. Orientation of **CIMMOI.a***, which revealed the formation of a 1D zig-zag pattern as result of type II (I $\cdots$ I) XB interactions. Hydrogen atoms have been removed for clarity.

The I...I distances range from 3.77 Å to 3.80 Å (**Table 3.1**), less than the sum of the *van der Waals radii* of two I atoms (3.96 Å).¹²¹ The angles that describe the halogen bond in **CIMMOI.a*** [$\theta_1 = 163.3(2)^\circ$, $\theta_2 = 114.3(2)^\circ$], **Fig 3.13, Table 3.1**] are slightly longer than those in **CIMMOI.b*** [$\theta_1 = 160.0(2)^\circ$, $\theta_2 = 112.5(2)^\circ$], **Fig 3.13, Table 3.1**]. The $|\theta_1 - \theta_2|$ value in **CIMMOI** range from 47-49°, within the range of pure type II interactions reported previously in the literature.⁸⁵ Surprisingly, the close (I...F) interaction is between **CIMMOI.a*** and **b*** with a distance of 3.578(5)Å, and 3.617(6)Å, which is longer than the sum of mean *van der Waals radii* of the two atoms (3.45Å). Therefore, in the calculated HSs this feature appears as a white spot rather than red, suggesting negligible interaction. However, the angles of this interaction are [C–I...F = 101.50 (6)°, B –F...I = 97.90(3)°], which are consistent with the geometry of symmetrical type I interactions (the $|\theta_1 - \theta_2| \leq 15^\circ$). This might be because the same iodine atom is involved in another strong XB interaction with the other iodine from the neighbouring BODIPY molecules, or may simply be due to close packing. It is useful to remember that the final solid-state structure is a consequence of several competing interactions and conclusions based only on distances are often an oversimplification and may be misleading. Therefore, computer modelling could be useful to give a wider picture of the nature of this interaction.

(a)



Type II

$\theta_1 = 163.3 (2)^\circ$, $\theta_2 = 114.3 (2)^\circ$, **CIMMOI.a***

$\theta_1 = 160.2 (3)^\circ$, $\theta_2 = 112.5 (2)^\circ$, **CIMMOI.b***

(b)

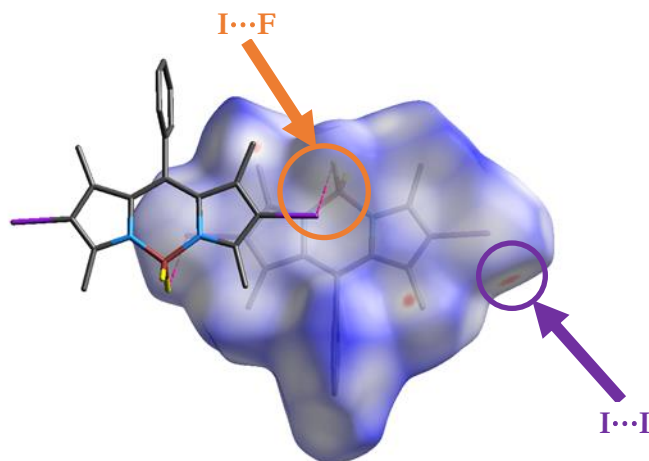


Fig 3.13. (a) Type II ($I \cdots I$)XB interaction observed in the single crystal X-ray structure of **CIMMOI.a*** and **b***. (b) HSS representation of (C-I $\cdots$ F) interaction, highlighted in orange , and type II ($I \cdots I$)XB highlighted in purple. Hydrogen in (b) were omitted for clarity. Carbon = grey, nitrogen = blue, boron = red, fluorine = green, iodine = purple.

3.3.1.4 Fingerprint and summary

In order to provide additional evidence for the occurrence of halogen...halogen interactions in **group 1** crystal structures the intermolecular contacts were plotted with 2D-fingerprint plots (**Fig 3.14** and **Fig 3.15**) giving a visual representation for all intermolecular non-covalent interactions. The percentage contribution of all the interactions present in the crystal structures were estimated through a 2D fingerprint (**Table 3.2**, **Fig 3.16**). From simple analysis, it immediately emerges that the H...H contacts have the highest contribution in comparison to all other interactions in the crystal structures. The I...I contact in **CIMMOI.a***, **b*** have a higher contribution to the HS in comparison to the other iodo-containing molecules, which is expected as both **a*** and **b*** forms show (I...I) XBs. The final observation is the presence of ‘wings’, which are a typical representation of C-H... π contacts in the fingerprint plot: 10.9% C...H area for **BHASNR**, **CIMMOI01** and **CIMMOI03**, smaller than **CIMMOI02** (17%) and larger than **CIMMOI.a***, **b*** (6.9 and 7.2 % C...H area respectively). However, the C-H... π contact in the bromo versions is larger than all the iodo versions (14.7% C...H area for **BHASNF**, 12 % for **BHASNM** and 11 % for **OYULIF**).

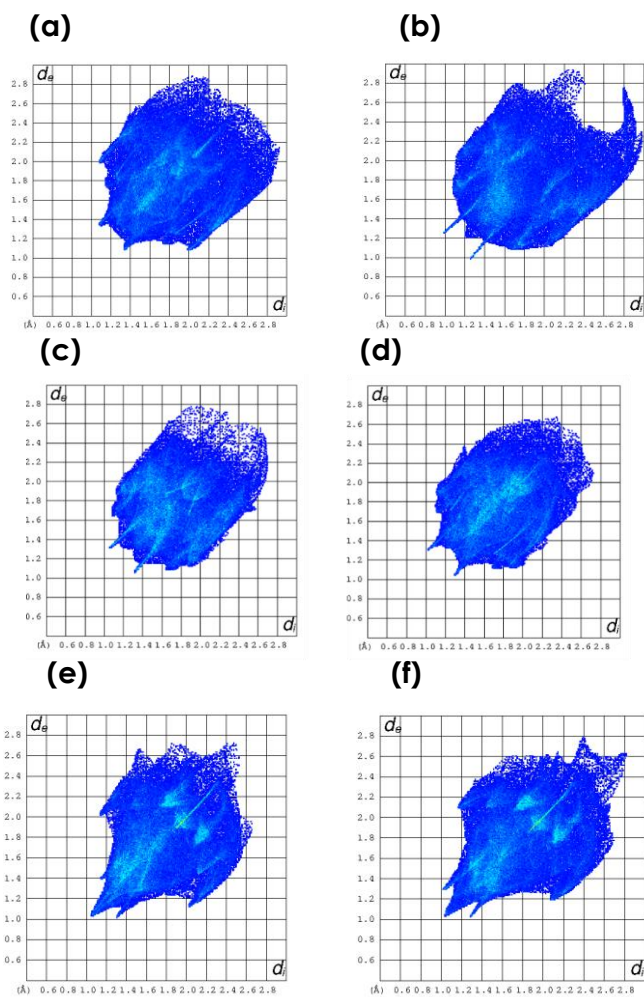


Fig 3.14 2D fingerprint plots of compounds (a) **BHASNR**, (b) **CIMMOI02**, (c) **BHASNF**, (D) **BHASNM**, (e) **CIMMOI.a*** and (f) **CIMMOI.b***.

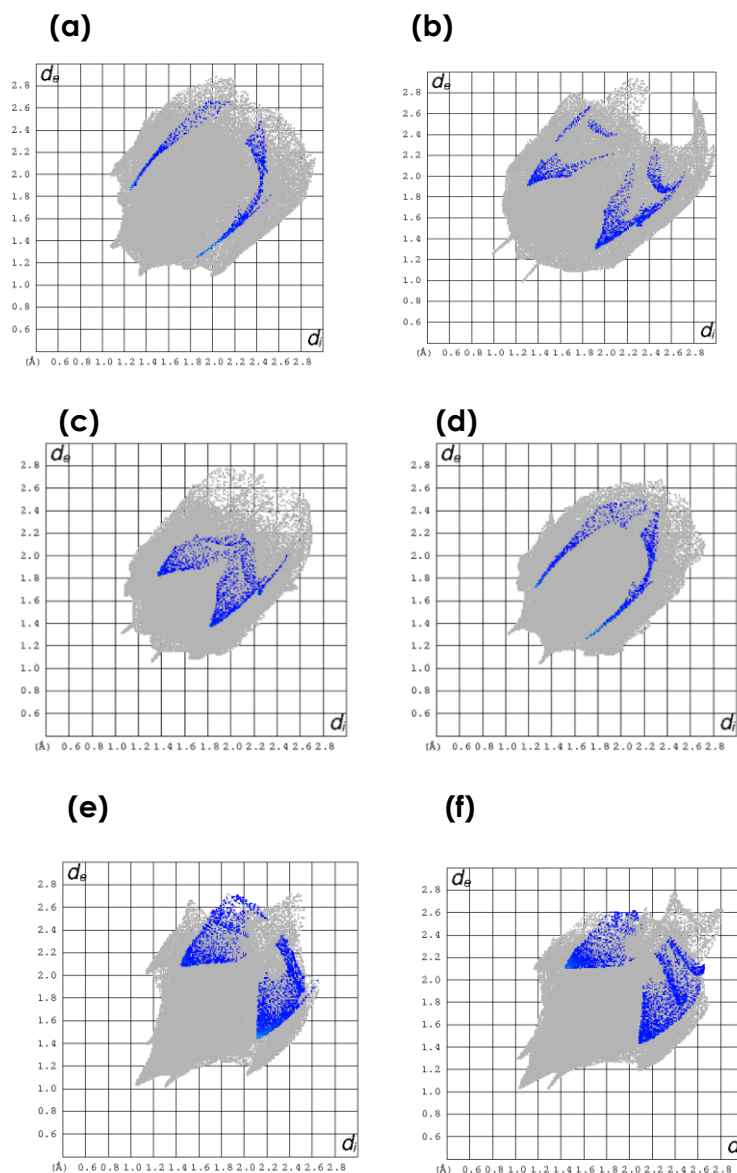
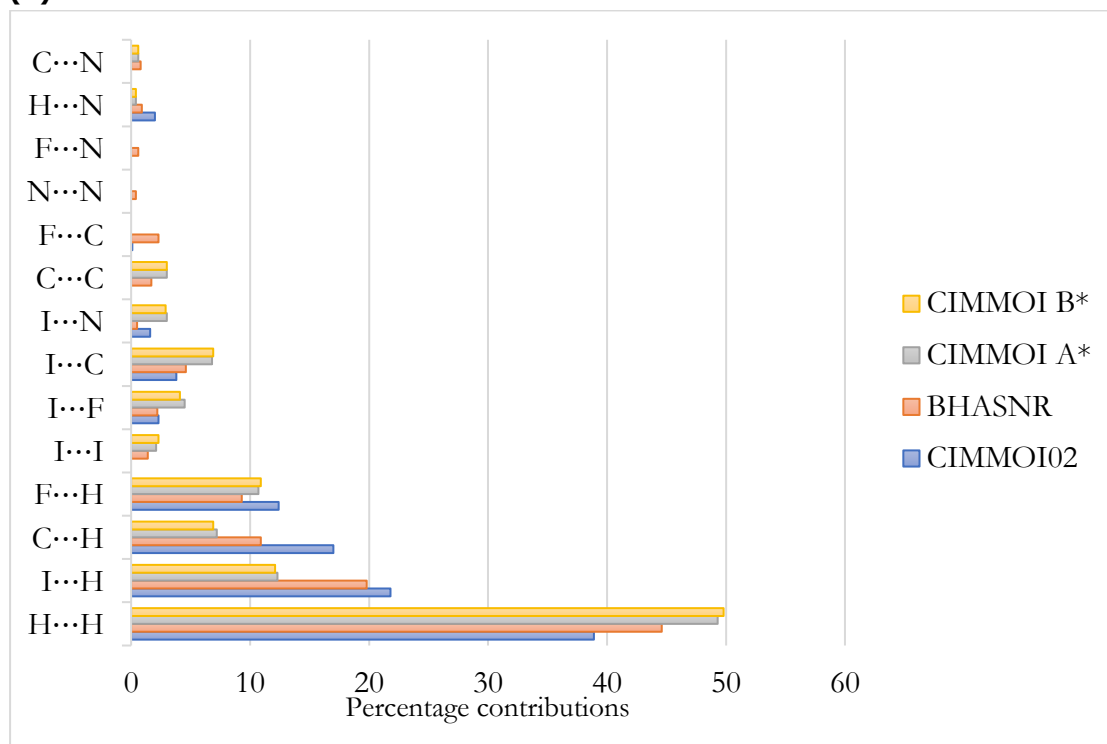


Fig 3.15. 2D fingerprint plots of compounds (a) **BHASNR**, and (b) **CIMMOI02**, highlighting the (C-I...F) intermolecular contacts. (c) **BHASNF**, (d) **BHASNM**, highlighting the (Br...F) intermolecular contacts. (e) **CIMMOI.a***, (f) **CIMMOI.b***, highlighting the (C-I...I) intermolecular contacts. To provide context, the outline of the fingerprint is shown in grey.

Table 3.2. Percentage contributions of individual intermolecular interactions to the Hirshfeld surfaces of **group 1** compounds

Iodo analogues					Bromo analogues		
Interaction	CIMMOI02	BHASNR	CIMMOI.a*	CIMMOI.b*	Interaction	BHASNF	BHASNM
H...H	38.9	44.6	49.3	49.8	H...H	40.8	45.9
I...H	21.8	19.8	12.3	12.1	Br...H	20.3	17.7
C...H	17	10.9	7.2	6.9	C...H	14.7	12
F...H	12.4	9.3	10.7	10.9	F...H	13.1	9.2
I...I	0	1.4	4.5	4.1	Br...Br	0	1.4
I...F	2.3	2.2	2.1	2.3	Br...F	2.1	2.4
I...C	3.8	4.6	6.8	6.9	Br...C	3.5	3.8
I...N	1.6	0.5	3	2.9	Br...N	1.6	0.5
C...C	0	1.7	3	3	C...C	1.5	1.9
F...C	0.1	2.3	0	0	F...C	0	2.3
N...N	0	0.4	0	0	N...N	0	0.3
F...N	0	0.6	0	0	F...N	0	0.8
H...N	2	0.9	0.4	0.4	H...N	2.1	1
C...N	0	0.8	0.6	0.6	C...N	0.1	0.7

(a)



(b)

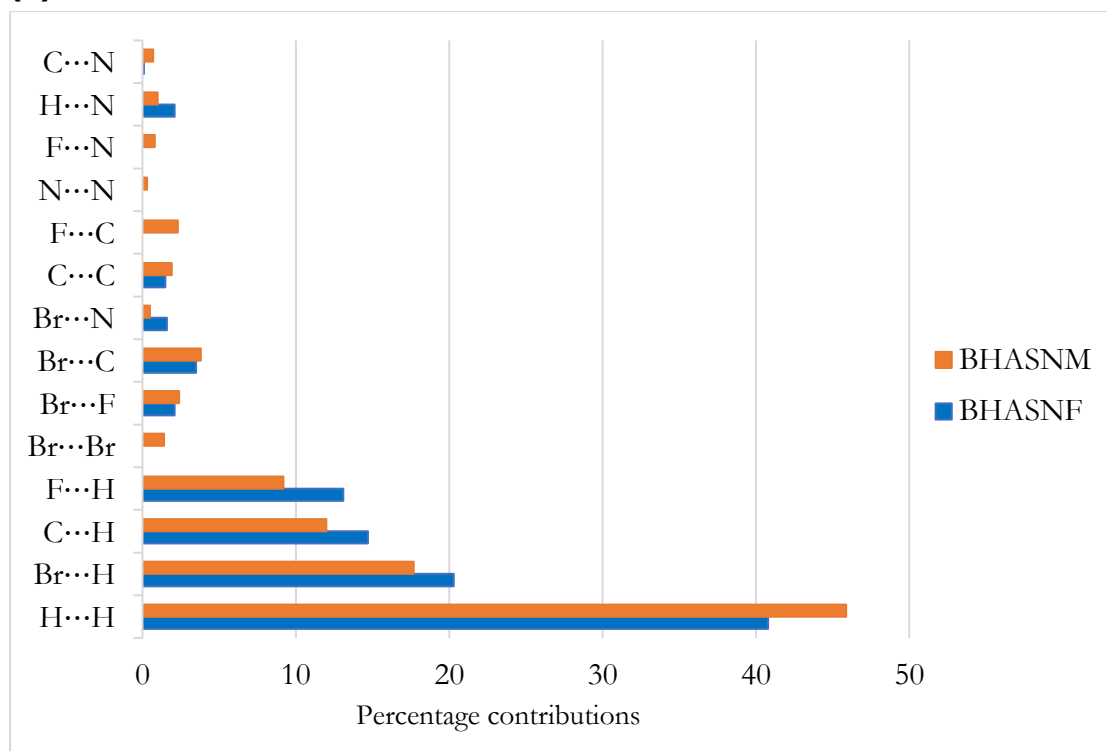
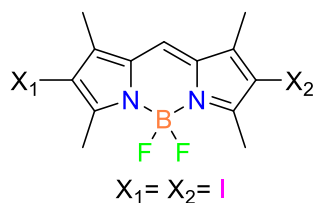


Fig 3.16. Percentage contributions of individual intermolecular interactions to the Hirshfeld surfaces of **group 1** compounds. (a) iodo directives. (b) bromo derivatives.

3.3.2 Group 2

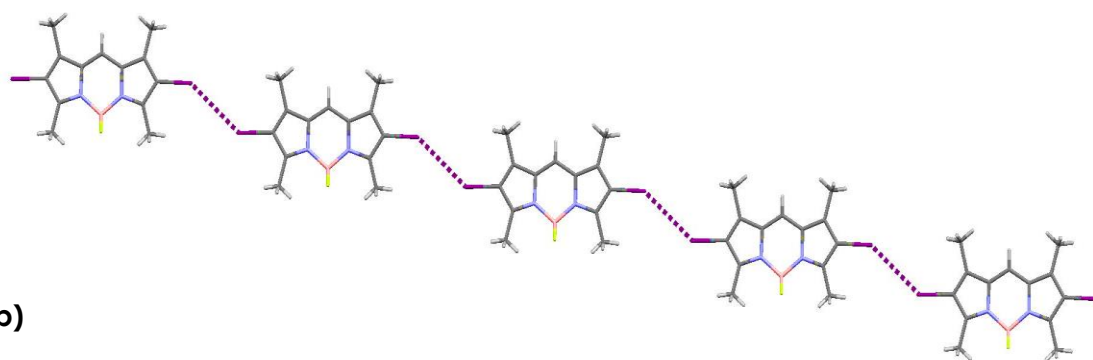
Group 2 consists only of the BODIPY derivative functionalized at the *meso* position with a hydrogen atom and the 2,6-positions bearing iodine atoms (**Scheme 3.2**). The synthesis of this compound was reported previously in the literature.¹²² However, to our knowledge, there are no reports of the crystal structure of this compound in the literature.



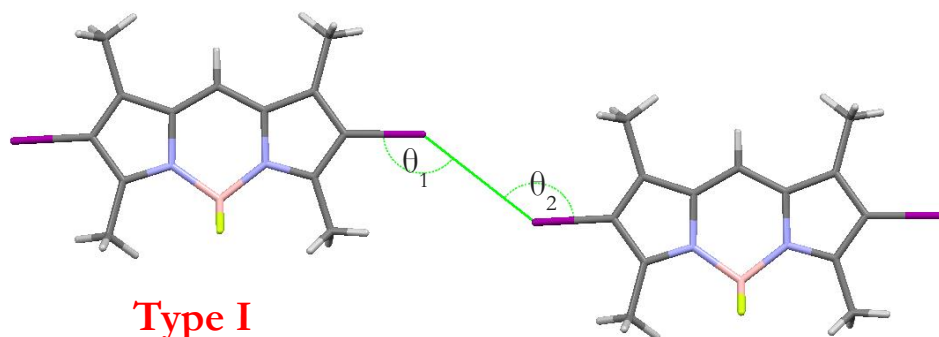
Scheme 3.2. Group 2 BODIPY complex investigated in this study.

In this thesis we report the crystal structure of the iodo derivative **BHASOT**, which displays the formation of a zig-zag pattern (**Fig 3.17**) as result of type I ($\text{I}\cdots\text{I}$) interaction [$\text{I}\cdots\text{I} = 3.7895(14) \text{ \AA}$, $\text{C}-\text{I}\cdots\text{I} = 142.30(4)^\circ$, $\text{C}-\text{I}\cdots\text{I} = 139.20(3)^\circ$]. The $\text{I}\cdots\text{I}$ distances is within the sum of the *van der Waals radii* (the sum of *van der Waals radii* of two I atoms is $3.96 \text{ \AA}$). The $|\theta_1 - \theta_2|$ value in **BHASOT** is less than 15° , indicating a purely type I interaction according to Desiraju's classification.⁸⁵ There is no evidence for any $\text{I}\cdots\text{F}$ (XB) interactions in this crystal structure. This could be because both iodine atoms are involved in just one interaction with another iodine atom. It should be noted that, due to technical problems with the CIF of this crystal structure and Crystal Explorer software, it was not possible to create Hirshfeld surfaces and 2D-fingerprint plots for **BHASOT**.

(a)



(b)



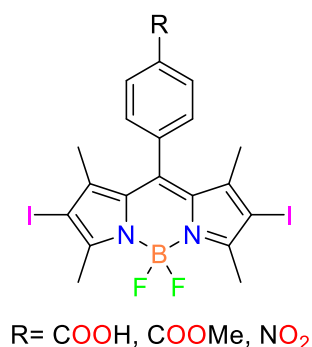
Type I

$$\theta_1 = 142.30 (4)^\circ, \theta_2 = 139.20 (3)^\circ$$

Fig 3.17. (a) Type I (I...I) halogen bonding of **BHASOT** which shows the formation of zig-zag pattern. (b) Type I (I...I) XB interactions for **BHASOT**. Carbon = grey, nitrogen = blue, boron = pink, fluorine = green, iodine = purple.

3.3.3 Group 3

This group consists of three BODIPY derivatives functionalized at the 2,6-positions with iodine, and in the *meso* position of the BODIPY core with a phenyl moiety which is in turn substituted with *para*-COOH, *para*-COOCH₃¹²³ or *para*-NO₂¹²⁴ (**JUCBAM**, **JUCBAJ**¹²³ **IDIHUB**,¹²⁴ respectively).



Scheme 3.3. Group 3 BODIPY complexes investigated in this study.

Table 3.3. Summary of halogen bonding of **group 3** compounds.

Group 3					
	D	A	θ_1	θ_2	Distance
JUCBAM	I	C=O	167.83 (4)°	90.61 (6)°	3.365 (4) Å
JUCBEQ	I	OCH3	162.06 (4)°	114.34 (9)°	2.9832(13) Å
IDIHUB	I	N=O	167.09(3)°	98.21(7)°	3.284(10) Å

The interaction of soft donor halogens such as I, with electronegative heteroatoms (such as O, N) it can be an example of halogen bonding.^{125, 126} In particular, there is a wide interest in halogen bonds involving oxygen as the halogen bond acceptor as this is the most common type of halogen bond involved in protein-ligand interactions.^{127, 128} Also, the interaction of iodine atoms and carbonyl oxygen atoms have been reported in literature.^{129,}

¹³⁰ The crystal structure of **JUCBAM**, is a good example of this approach where the carbonyl or carbonyl ester act as halogen bond acceptors and iodine atoms act as halogen bond donors.

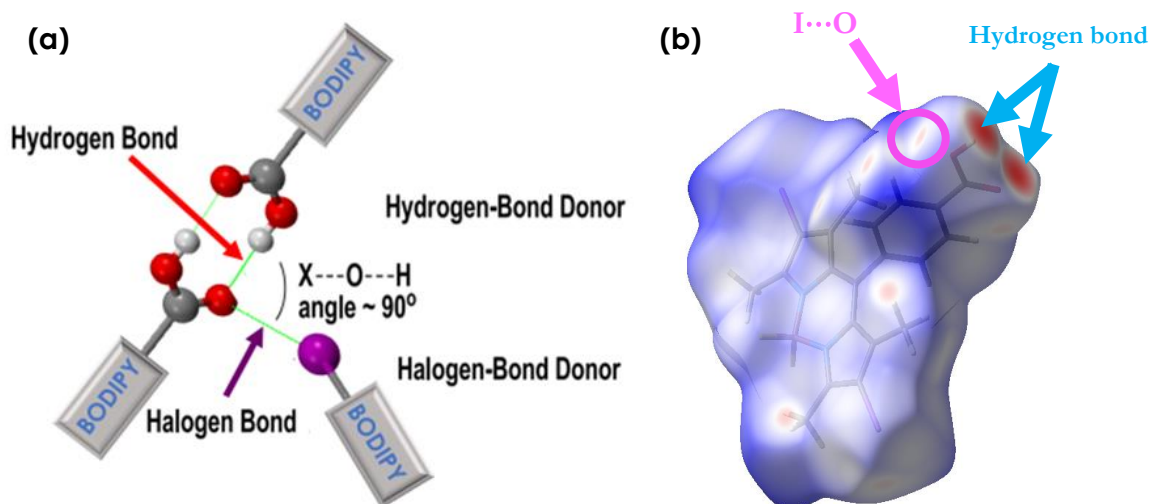


Fig 3.18. (a) Diagram of observed perpendicular interactions between hydrogen and halogen bonds involving the same carbonyl oxygen of **JUCBAM**. (b) Hirshfeld surface for **JUCBAM**. Carbon = grey, iodine = purple, oxygen = red.

In addition to this XB interaction a HB interaction is observed to the oxygen atom which is simultaneously participating in XB interactions. The HB interactions were observed to be perpendicular to the XB interactions, a phenomenon which was proposed to arise from the distribution of electrostatic potential on the oxygen atom (**Fig 3.18**). This phenomenon has been observed in amino acids and protein ligand in the Protein Databank.^{22, 48, 56, 131} Usually, in strong XB interactions with carbonyl oxygen atoms a $C=O\cdots X$ angle of approximately 125° is favoured, corresponding to an interaction with the sp^2 orbitals on the oxygen atom. As the XB interaction becomes weaker this angle changes due to additional interactions present in the structure and interaction with the π electron density of the carbonyl bond.^{22, 48, 56, 131} This suggests that both XB and HB share the carbonyl oxygen as the common acceptor.

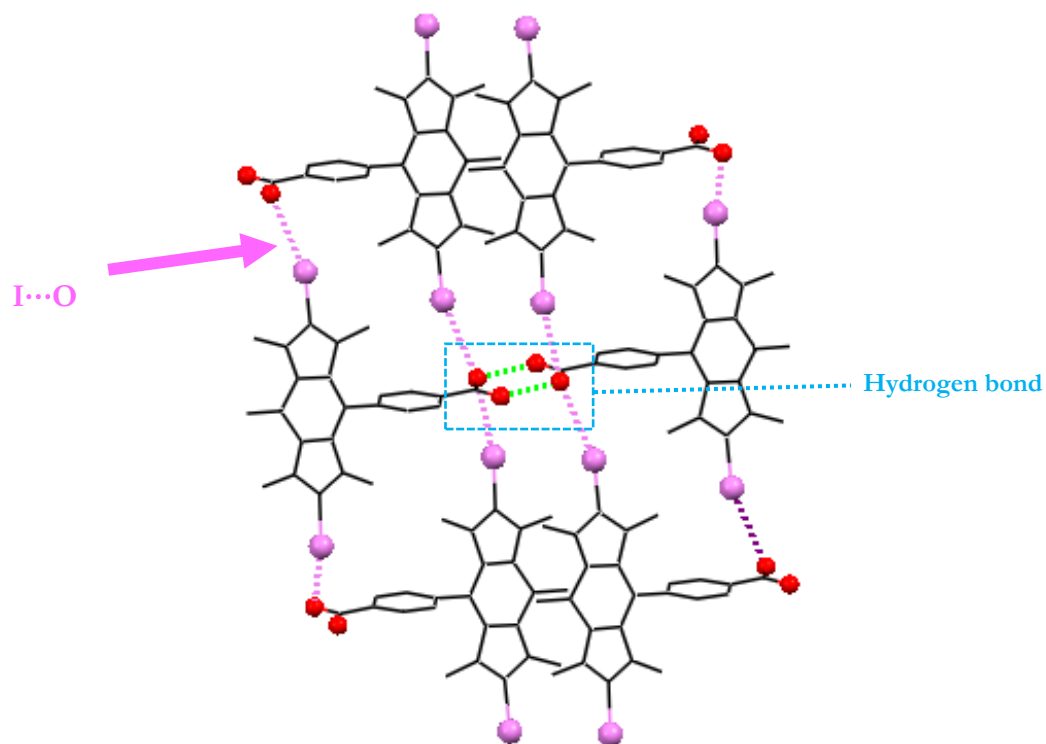


Fig 3.19. Orientation of **JUCBAM** which shows the formation of $(C=O \cdots I)$ XB (pink), and a arboxylic dimer HB, highlighted in green. Carbon, boron, nitrogen, and fluorine = black, oxygen = red, iodine = violet.

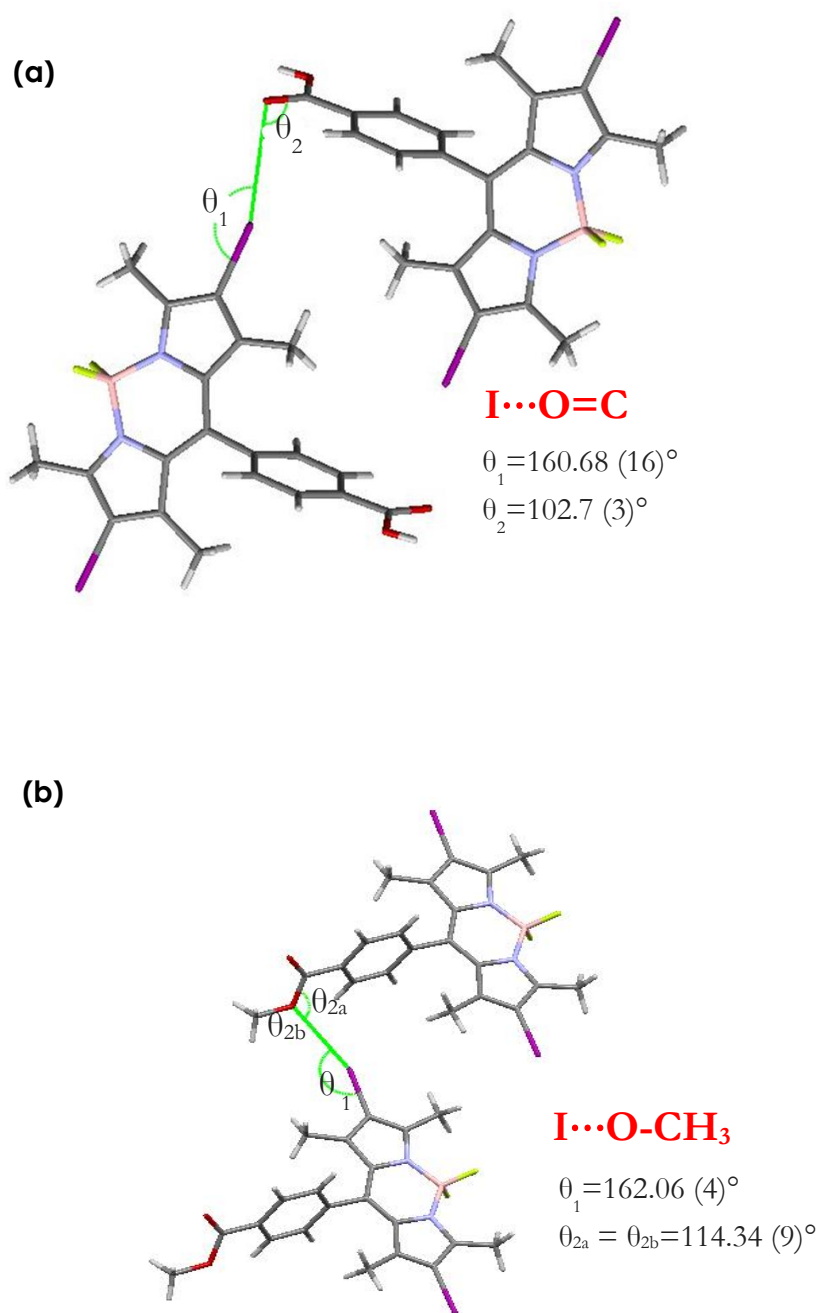


Fig 3.19. View of the single crystal X-ray structure showing (I...O=C) XB interactions of (a) **JUCBAM**, (b) **JUCBEQ**. Carbon = grey, nitrogen = blue, boron = pink, fluorine = green, , iodine = purple.

In **JUCBAM**, the I...O interaction could be considered as a weak interaction with a separation of 3.365 (4) Å and a C-I...O angle of 160.68 (17)°; the I...O=C angle was 102.70 (3)° (Fig 3.19, and Table 3.3), which is a significant deviation from alignment with the sp² orbitals on oxygen due to a secondary C=O...H hydrogen bond with a neighbouring

carboxyl group from the benzoic acid dimer. The distance of this interaction is shorter than the *van der Waals radii* of I $\cdots$ O (3.50 Å).¹²⁸ However, introducing a carbonyl ester on the para-position in **JUCBEQ** leads to slightly different packing where both of the iodine atoms in the 2,6-positions are involved in XB with either an oxygen from the methoxy group or from the carbonyl group, as shown in **Fig 3.19** and **Fig 3.20**. In the case of the carbonyl oxygen, the I $\cdots$ O separation is 2.9832(13)Å, C-I $\cdots$ O angle = 172.31(4)°; the I $\cdots$ O=C angle is 116.31(12)°. The difference in (I $\cdots$ O=C) angle in **JUCBEQ** in comparison with **JUCBAM** is expected as mentioned above. In **JUCBEQ** the iodine atom interacts with the sp² orbitals on the oxygen from carbonyl group and therefore the angle might be expected to be higher than that observed for **JUCBAM**. However, in **JUCBAM** the carbonyl oxygen is involved in both XB, and HB, therefore, the angle in this case is smaller. This could confirm the previous hypotheses of the ability, and the effect of halogen bonding halogen atoms to be involved in hydrogen bonds that are orthogonal. In the case of the methoxy oxygen in **JUCBEQ**, the I $\cdots$ O separation is 3.3068(12)Å, the C-I $\cdots$ O angle is 162.06(4)° and the I $\cdots$ O-C angle was 102.13(12)°. The (I $\cdots$ O-C) XB interaction (b in **Fig 3.19**, **Fig 3.20**) and appears as red spot in HSs (**Fig 3.20**).

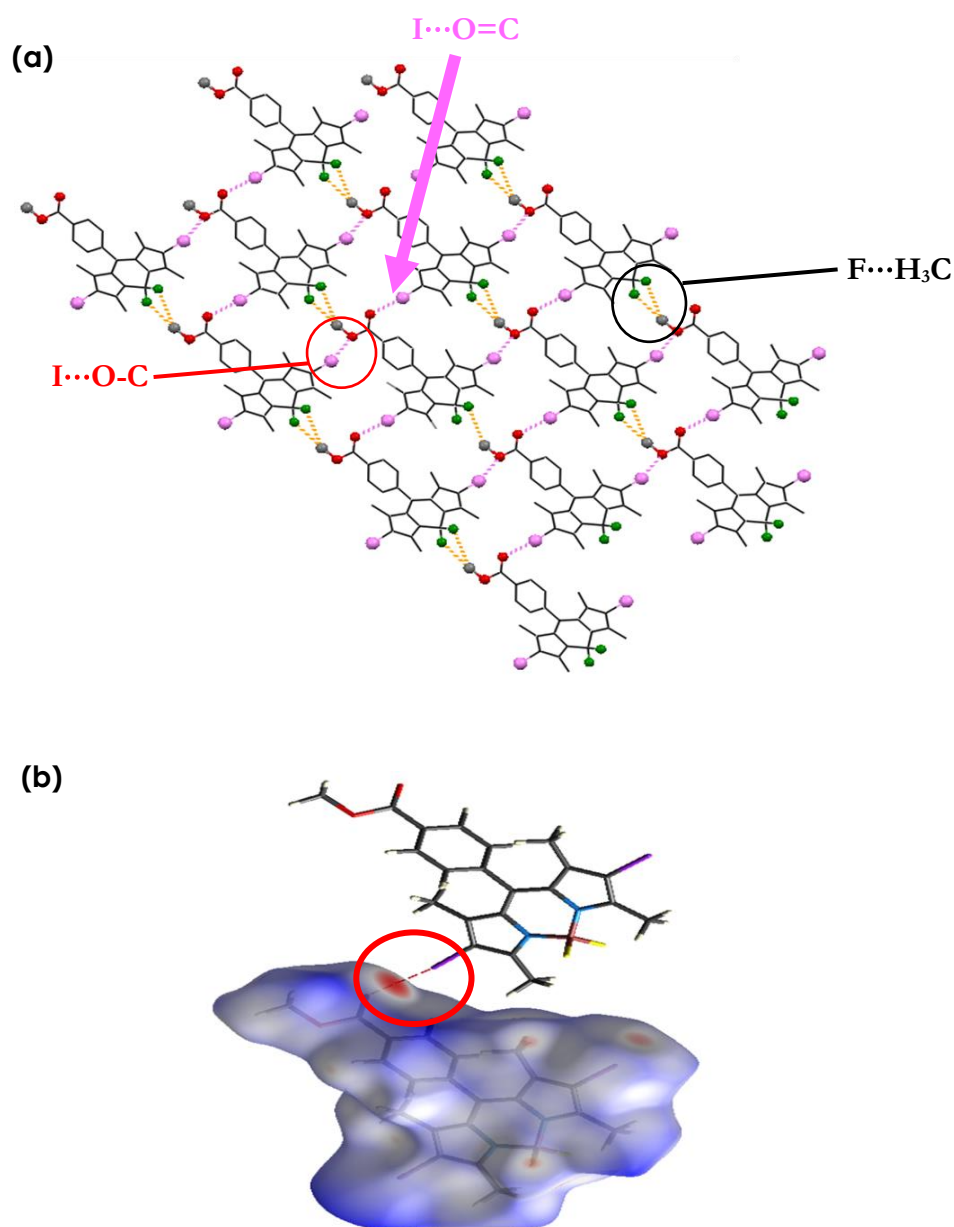


Fig 3.20. (a) Orientation of **JUCBAJ** which reveals the formation of $(C-I \cdots O=C)$ XB, $(C-I \cdots O-Me)$ XB and of $(CH_3 \cdots F)$ HB. Carbon, boron, and nitrogen = black, oxygen = red, iodine = violet, fluorine = green. Hydrogen atoms were removed for clarity. (b) HSS representation of close $(C-I \cdots O)$ contact of **JUCBAJ**, highlighted in red. (Carbon = grey, nitrogen = blue, boron = red, fluorine = green, iodine = purple).

The iodo $\cdots$ nitro interaction is an important example of halogen bonding,^{125, 126} where the strength and specificity of such interactions is necessary to gain structural control.^{125, 132}

This approach has been reported in crystal structures that contain aromatic COOH, iodo and nitro functional groups.^{125, 132} The crystal structure of **IDIHUB** shows the expected

iodo $\cdots$ nitro recognition to form linked dimers which allow the formation of stair-step chains (**Fig 3.21**). In this example every iodine atom forms a side-on approach with one O atoms of the nitro group in the neighbouring BODIPY (**Fig 3.21**, **Fig 3.22**).

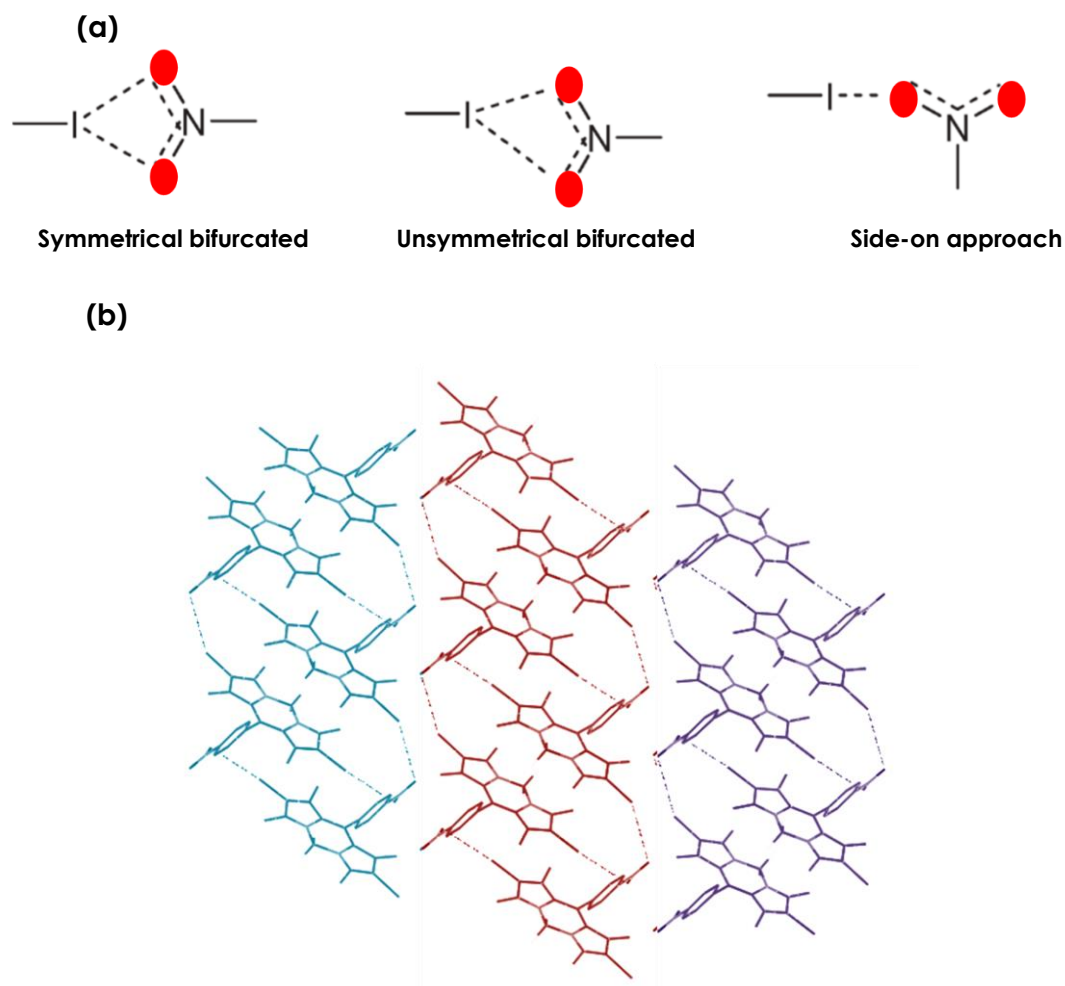


Fig. 3.21. (a) three variations of iodo nitro interactions,¹²⁵ oxygen atoms are presented as red circles. (b) Orientation of **IDIHUB** along the a-axis which reveals the formation of a stair-step chain pattern.

The distance of this interaction is 3.284(10) Å, shorter than the *van der Waals radii* of I/O (3.50 Å)¹²⁸, and shorter than other I $\cdots$ O-C, I $\cdots$ O=C XB interactions reported in this group. The I $\cdots$ O-N angle is 98.20(7)°, smaller than the corresponding angles reported in this group.

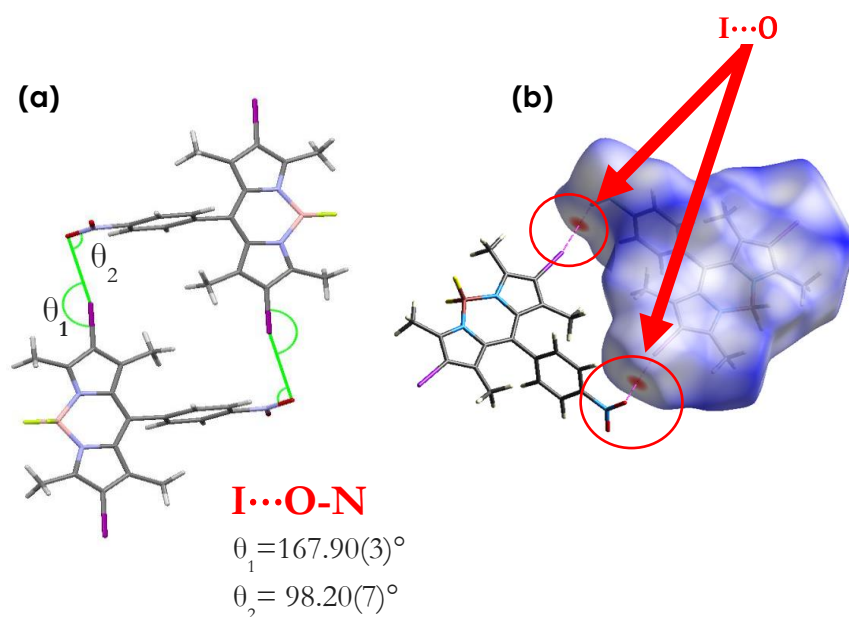


Fig 3.22. (a) View of the single crystal X-ray structure of **IDIHUB**, showing the close (C-I...O-N) XB halogen interaction. (b) HSs representation for **IDIHUB**. The close (C-I...O) contact is highlighted in red. Carbon = grey, nitrogen = blue, boron = pink, fluorine = green, iodine = purple.

3.3.3.1 Fingerprint Analysis and Summary

In order to provide additional evidence for the occurrence of XB interactions in **group 3**, the intermolecular contacts were plotted using 2D-fingerprint plots (**Fig 3.23**). The percentage contribution of all the interactions in the crystal structures were estimated through a 2D fingerprint (**Table 3.4**, **Fig 3.24**). In this group the most obvious thing to look to it is the percentage of I...O and O...H contacts. From simple analysis, it immediately emerges that the O...H contacts appear as strong spike in **JUCBAM** (a in **Fig 3.24**). O...H contacts also have a high contribution in comparison to both **IDIHUB**. This finding is expected as result of HB between the carboxylic acid groups in **JUCBAM**. The I...O contact in **IDIHUB** has a higher contribution to the surface in comparison with all other compounds in this group (5.9% I...O area).

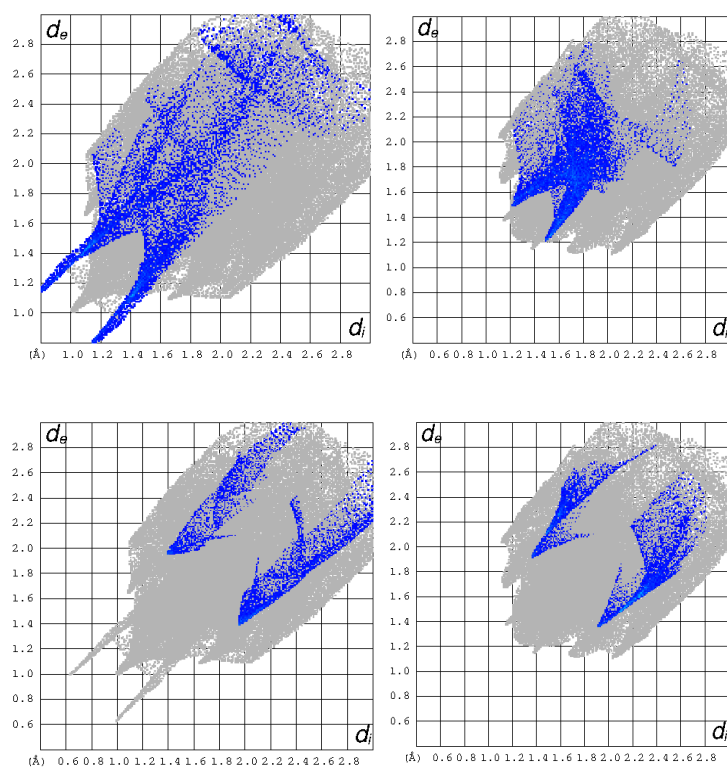
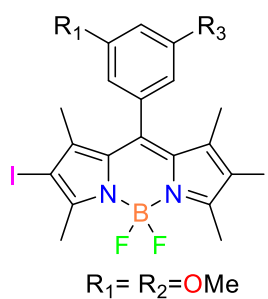


Fig 3.23. 2D fingerprint plots of compounds (a) **JUCBAM**, and (b) **IDIHUB**, which highlight the (O $\cdots$ H) intermolecular contacts. (c) **JUCBAM**, and (d) **IDIHUB**, which highlight the (I $\cdots$ O) intermolecular contacts.

3.3.4 Group 4

Vicente and co-workers¹³³ report the crystal structure of **DUBPIB**, a BODIPY functionalised in the 2,6-positions with iodine atoms, and with a phenyl in the *meso* position substituted with OMe groups in the *meta* position.



Scheme 1.4. Group 4 BODIPY complexes investigated in this study.

The packing motif of **DUBPIB** (**Fig 3.25**) revealed the formation of XB ($\text{C-I}\cdots\text{O}$) interactions between an oxygen from one methoxy group in the meso position and one iodine atom at the 2-position [$\text{I}\cdots\text{O} = 3.2171(10) \text{ \AA}$, $\angle \text{C-I}\cdots\text{O} = 166.61(4)^\circ$, $\angle \text{C-O}\cdots\text{I} = 98.80(7)^\circ$]. The distance of this interaction is shorter than the sum of the *van der Waals radii* of I/O ($3.50 \text{ \AA}$).¹²⁸ Also, the angles between the iodine sigma hole and the lone pair electrons of oxygen is within the range of a type II interaction ($160\text{--}180^\circ$ for θ_1 and $\approx 90^\circ$ for θ_2) (**Fig 3.26**).¹³⁴ These distances and angles are consistent with the data observed in **group 3**. It is noted that the other methoxy group is not involved in any XB and rather is involved in HB with another methoxy group. The other iodine atom is involved in type I ($\text{I}\cdots\text{I}$) halogen interaction between two neighbouring BODIPY molecules (**Fig 3.25**, and **Fig 3.26**).

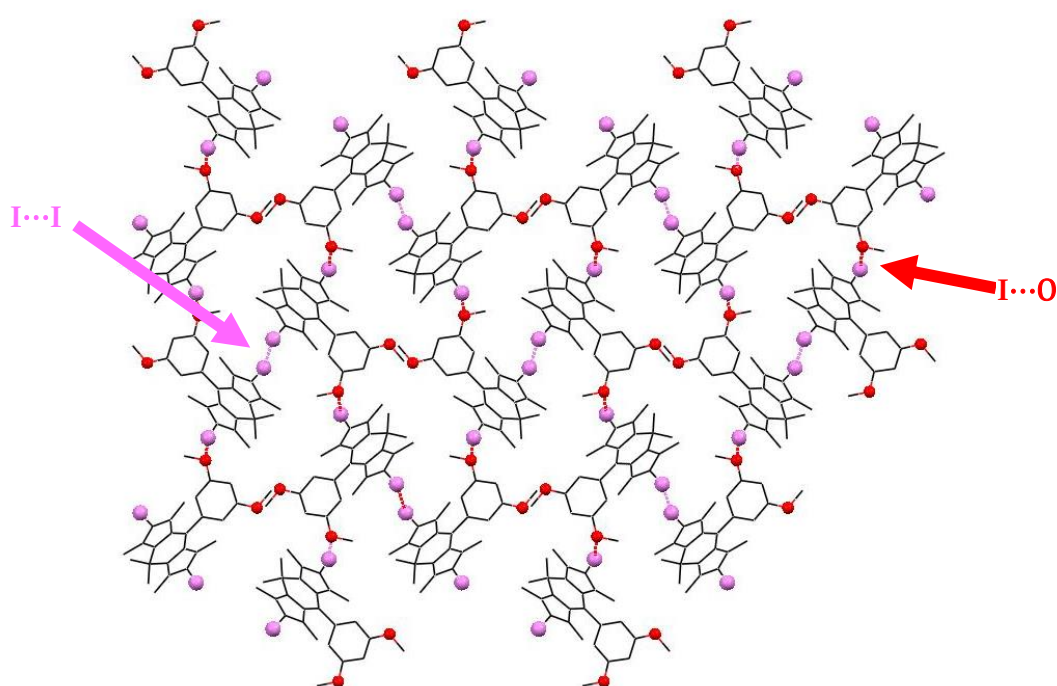
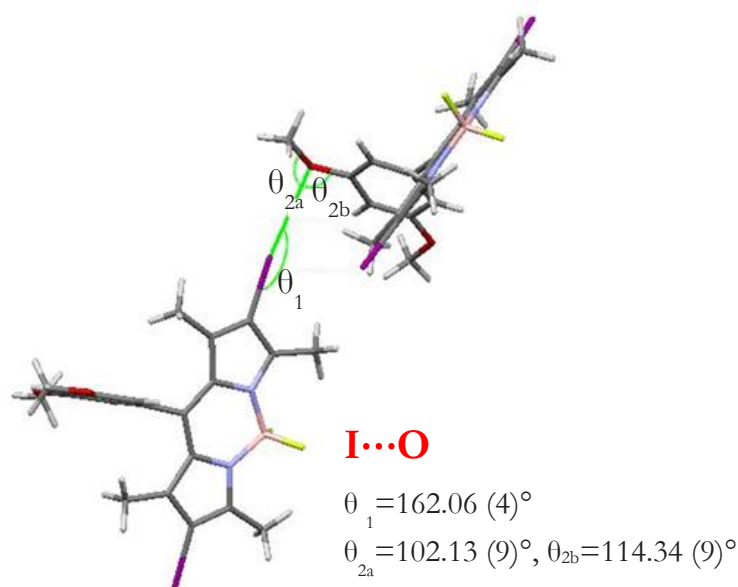


Fig 3.25. View of **DUBPIB** along the *a*-axis, showing the formation of sheet-like packing. Hydrogen atom, and HB have been removed for clarity.

The I $\cdots$ I distances are relatively short (3.56 Å) in comparison with the sum of the *van der Waals radii* for two iodine atoms (3.96 Å)¹²¹, which might indicate a strong interaction [I $\cdots$ I = 3.5664 (2) Å, C–I $\cdots$ I = 166.31 (3)°, C–I $\cdots$ I = 166.31 (3)°]. The more linear geometry in this case in comparison with **CIMMOI** in **group 1**, may be explained as an effect of the addition of two methoxy substituents on the *meso*-phenyl group, modifying solid-state packing. It should be noted, that both of XB are presented as intense red spots in HSs (**Fig 3.27**).

(a)



(b)

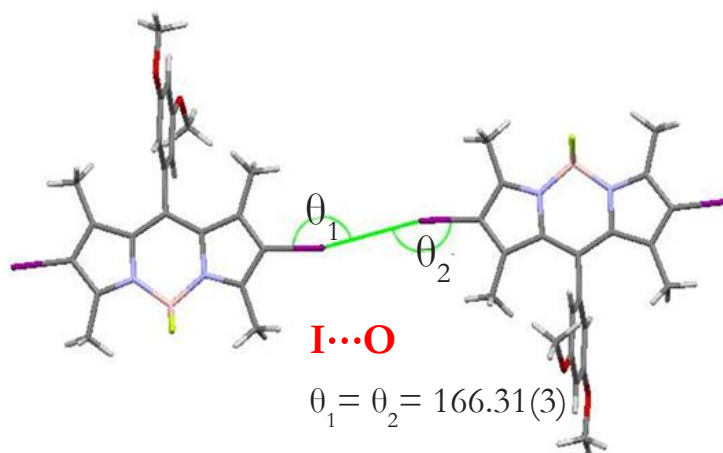


Fig 3.26. Single crystal X-ray representation of (a) (C–I $\cdots$ O) XB interaction. (b) (C–I $\cdots$ I) HB interaction of **DUBPIB**. Carbon = grey, nitrogen = blue, boron = pink, fluorine = green, iodine = purple, oxygen = red.

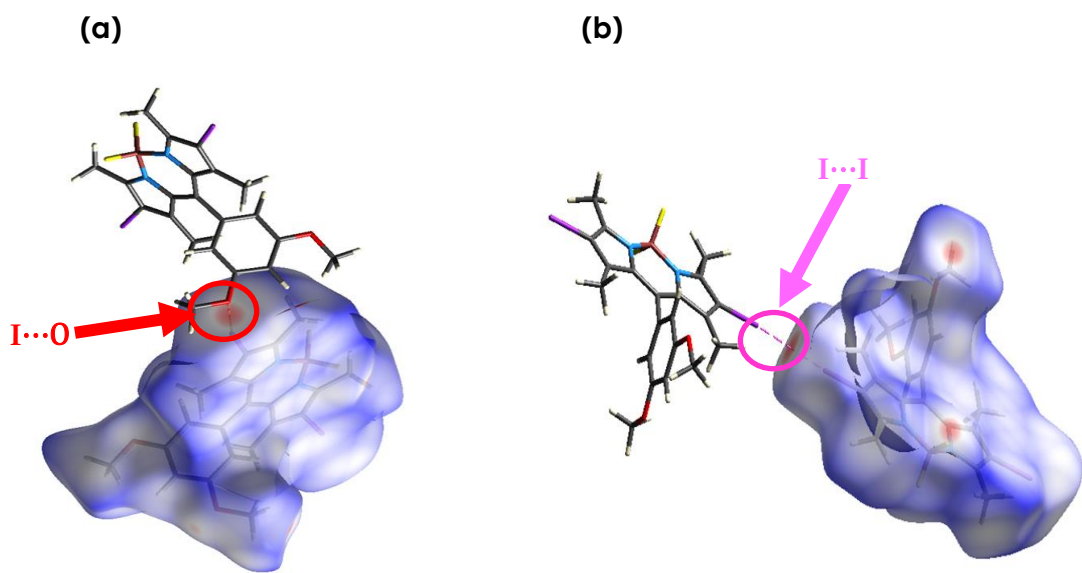


Fig 3.27. (a) HS representation of close (C-I...O) contact observed for **DUBPIB**, highlighted in red. (b) HS representation of close (C-I...I) XB highlighted in pink..Carbon = grey, nitrogen = blue, boron = red, fluorine = green, iodine = purple.

3.3.4.1 Fingerprint Plots and Summary

The percentage contribution of all the interactions present in each crystal structure was estimated using 2D fingerprint plots (Table 3.2, and a in Fig 3.17).

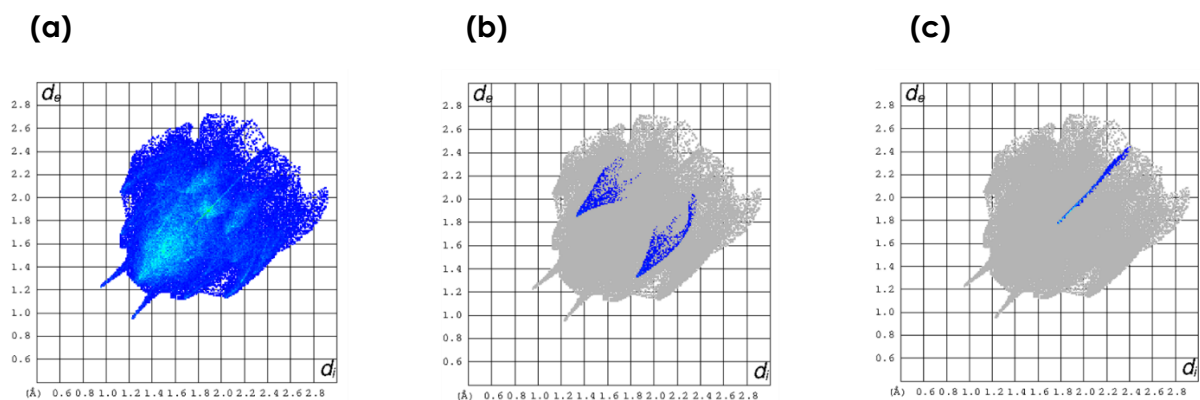


Fig 3.28 2D fingerprint plots of **DUBPIB** which highlight (a) all interaction, (b) I...O intermolecular contacts, (c) I...I intermolecular contacts; to provide context, the outline of the fingerprint is shown in grey.

The percentage contribution of interactions are represented (**Fig 3.32, Table 3.6.**) summarising the H...H, I...H, C...H, F...H, I...F, I...C, I...N, C...C, I...O, N...H, C...N, O...H intermolecular contacts for **DUBPIB**. The XB (C-I...O) contacts represent 1.7% of the Hirshfeld surface area in the 2D fingerprint plots and (I...I) just 1.1% of the surface area.

Table 3.7. Percentage contributions of individual intermolecular interactions to the Hirshfeld surfaces of **DUBPIB**

DUBPIB			
Interaction	Percentage	Interaction	Percentage
H...H	47.3	C...C	2.5
H...I	12.4	I...O	1.7
C...H	6.3	O...N	0.7
F...H	10.6	O...C	0.9
I...I	1.1	F...O	0.1
I...F	1.9	O...H	5.9
I...C	5.9	N...H	0.2
I...N	2.2	C...N	0.3

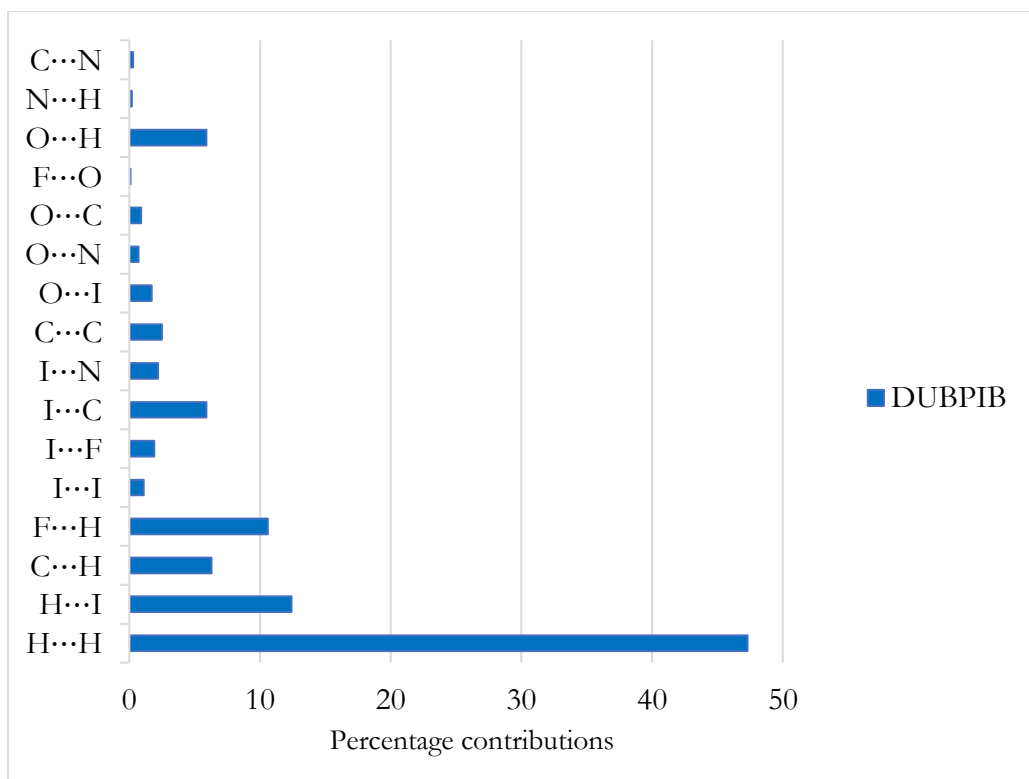


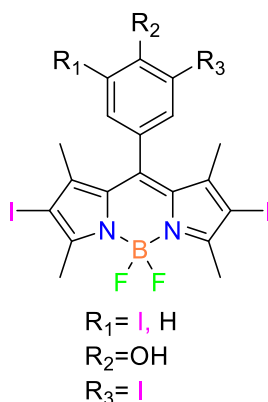
Fig 3.30. Percentage contributions of individual intermolecular interactions to the Hirshfeld surfaces of **DUBPIB**.

3.3.5 Group 5

A series of novel iodinated-BODIPY derivatives functionalised at the 2,6-positions with iodine atoms have been reported by Durmus and co-workers in 2017.¹³⁵ In this series, the BODIPY is functionalised with a *para*-OH substituted phenyl ring at the *meso*-position, and either one or two iodine atoms at the *meta*-position (**BELYOJ** and **BELYID**).¹¹⁵ From the point of view of halogen bonds, these complex systems provide a useful illustration of the effects of both electron withdrawing groups and the presence of the phenol oxygen on the halogen bonding patterns. **BELYOJ** and **BELYID** display complex intermolecular interactions. These interactions will be discussed in turn depending on the group involved in each interaction (*i.e.* -OH group, and I, F atoms).

3.3.5.1 Interactions Involving the Hydroxy Group

In general, the presence of XB interactions which involve hydroxyl oxygen atoms are common in the literature.^{127, 128} The electrostatic interaction between the halogen σ -hole and the oxygen lone pair played a great role in determining the geometry of these complexes.¹²⁷



Scheme 1.5. Group 5 BODIPY complexes investigated in this study.¹¹⁵

In **BELYID**, it was found that an interaction occurs between the halogen σ -hole (iodo atoms at 2,6-positions), and the lone pair on the oxygen (*para*-OH), leading to dimeric structures (**Fig. 3.31**). In this interaction, the halogen bond angle $105.17(18)^\circ$ is within the angle range of such interactions reported in the literature (95° to 115°)¹³⁶ and the $\text{I}\cdots\text{O}$ distances is $3.4010(2)$ is shorter than the sum of mean *van der Waals radii* of the two atoms ($3.49 \text{ \AA}$).¹²⁸ Red spots near both the hydroxy oxygen and the iodine atoms are observed in HSS calculated for this structure as result of the $\text{I}\cdots\text{O}$ close contact.

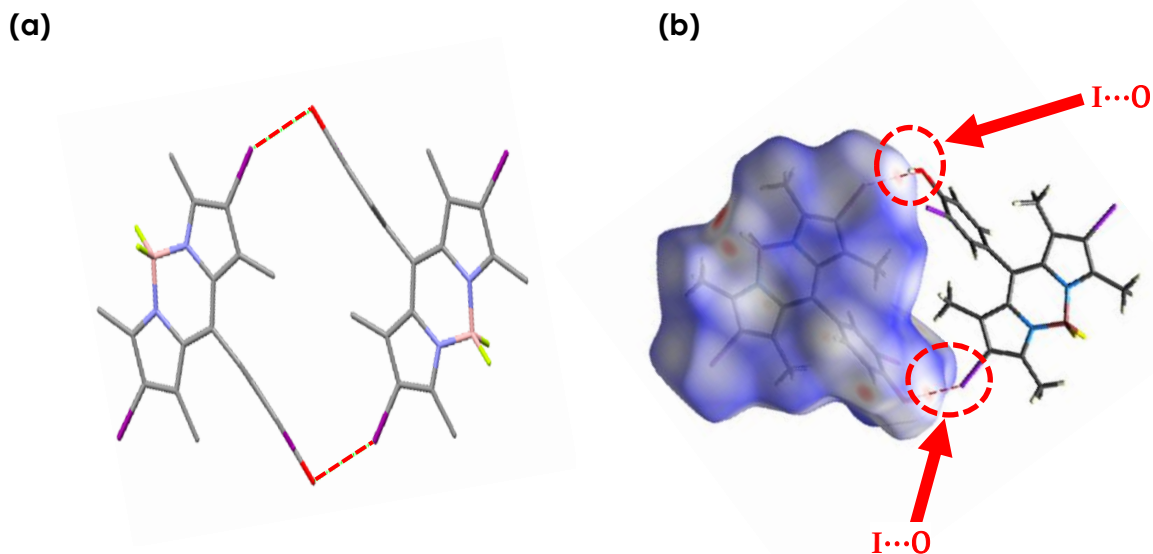


Fig 3.31. (a) Single crystal X-ray representation of **BELYOD** which shows the close (C-I...O) XB interaction, which leads to a dimeric structure. (b) HS representation for **BELYOD**. The close (C-I...O) contact is highlighted in red. Carbon = grey, nitrogen = blue, boron = red or pink, fluorine = green, iodine = purple.

However, **BELYOJ** does not show this type of interaction the closest (I...O) distances is 3.7220(4) Å, longer than the sum of *van der Waals radii* of the two atoms. Therefore, this interaction is best considered a close contact rather than XB.

Both compounds are involved in similar hydrogen bonding interactions between fluorine atoms on the BODIPY and the OH group located on the *meso*-aryl ring. HSs provide further evidence of such interactions by showing an intense red spot next to both the OH group, and fluorine atoms (**Figure 3.30, 3.31**). As described above there is another red spot next to the oxygen which indicates the presence of XB (I...OH) interactions.

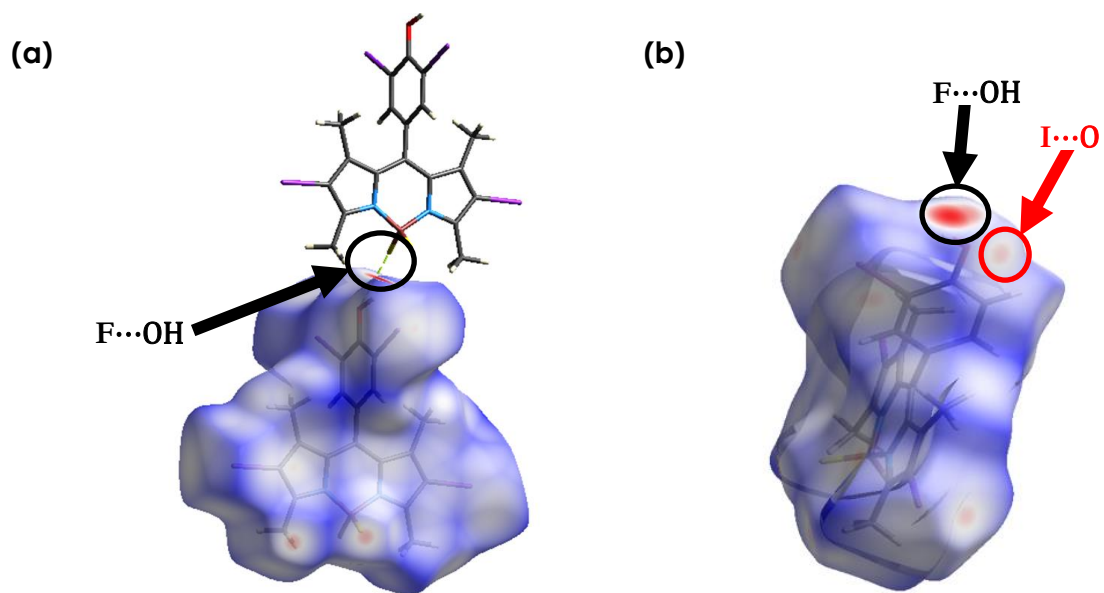
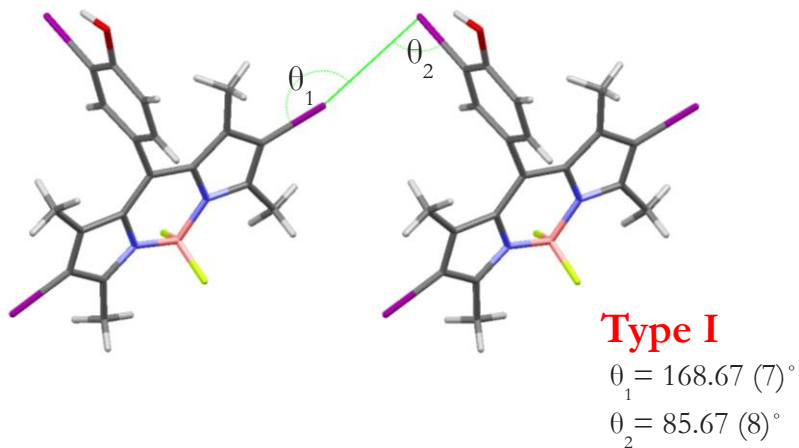


Fig 3.32. HSs representation of (a) **BELYOJ**, (b) **BELYID** , close (C-I...O) XB contact highlighted in red , close (F...OH) XB highlighted in black. Carbon = grey, nitrogen = blue, boron = red, fluorine = green, iodine = purple.

3.3.5.2 Interactions Involving Iodine Atoms

Both compounds show type II ($I\cdots I$) distances which range from 3.84 Å to 3.96 Å. In both cases the distances are less than the sum of the *van der Waals radii* of two I atoms (3.96 Å).¹²¹

(a)



(b)

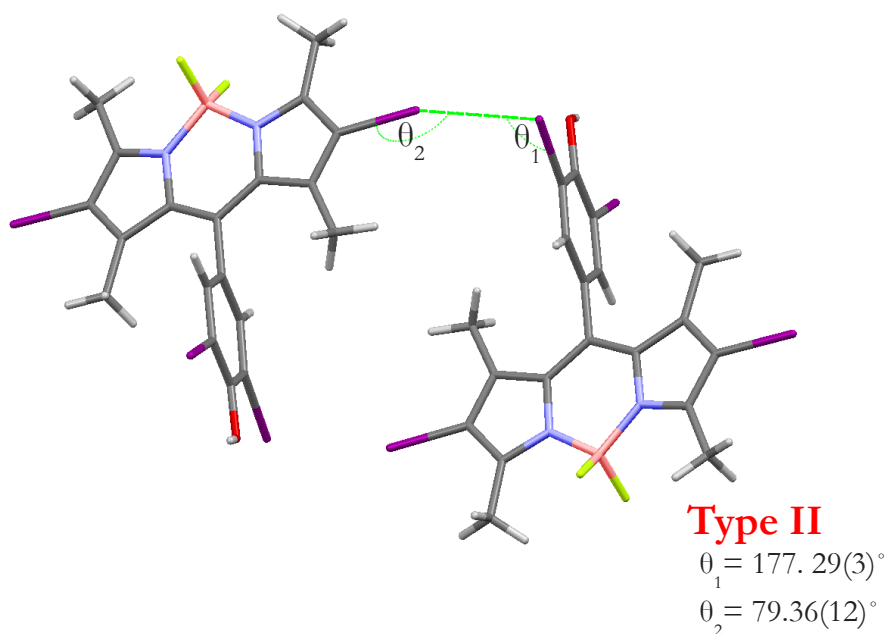
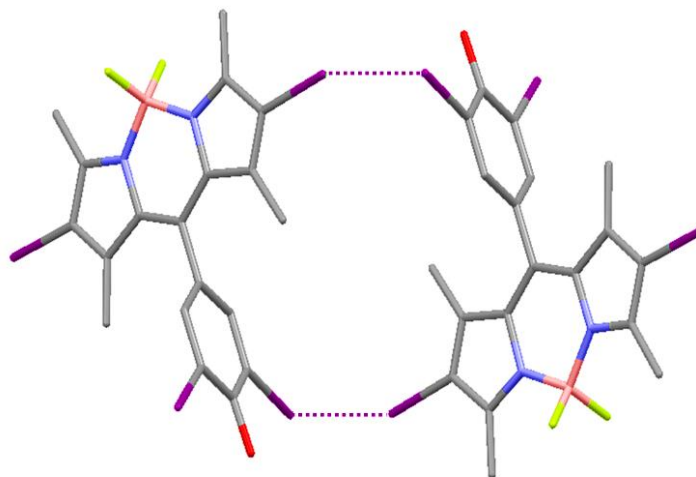


Fig 3.33. Single crystal X-ray structure showing (C-I $\cdots$ I) XB interactions. (a) **BELYOD** (b) **BELYOJ**. Carbon = grey, nitrogen = blue, boron = pink, fluorine = green, iodine = purple, oxygen=red

The angles that describe the halogen bond in **BELYOD** [$\theta_1 = 85.67(8)^\circ$, $\theta_2 = 168.67(7)^\circ$] and **BELYOJ** [$\theta_1 = 79.36(12)^\circ$, $\theta_2 = 177.29(3)^\circ$] lead to values of $|\theta_1 - \theta_2|$ which is in the range from $83\text{--}97^\circ$ for both compounds, typical of type II interactions reported in the literature.⁸⁵

(a)



(b)

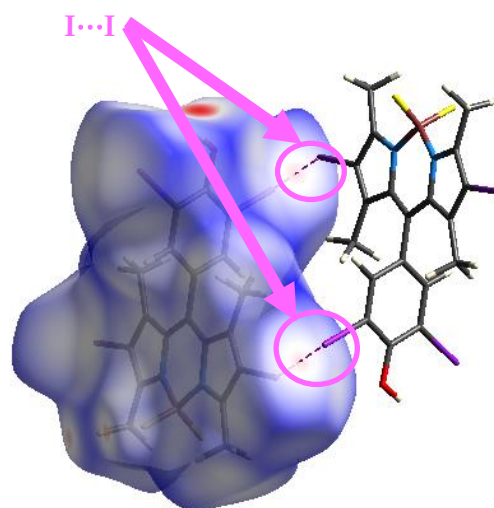


Fig 3.34.. (a) View of the crystal structure of **BELYOD** showing the (C-I...I) contact and (b) HS representation of the close (C-I...I) contact observed for **BELYOJ**, highlighted in pink. Carbon = grey, nitrogen = blue, boron = red, fluorine = green, iodine = purple.

It should be noted that in **BELYOJ** just one of the iodine atoms attached to the *meso* phenyl is involved in I...I halogen bonding resulting in a dimeric structure as demonstrated in **Fig 3.34**.

3.3.5.3 Fingerprint Analysis and Summary

Fig 3.35 shows the relative contributions calculated from 2D-fingerprint plots and highlights close contacts for **BELYOD** and **BELYOJ**. It is clear from **Fig 3.35**, **Fig 3.36** and **Table 3.8** that both **BELYID** and **BELYOJ** are calculated to have a 25.4% contribution of (I...H) interactions. However, the (F...H) contribution for **BELYID** is greater than that for **BELYOJ** (8.9% and 11.3% respectively). The halogen- halogen contact (I...I) for **BELYID** is approximately half of that for **BELYOJ** (6.4% for **BELYOJ** and 3 % for **BELYID**). This may be a result of the (I...I) XB interactions between the two adjacent BODIPY molecules (the BODIPY-2,6-position iodines and iodine atoms from the *meta*-position of the *meso*-phenyl) which leads to BODIPY dimers in **BELYOJ**.

Table. 3.8. Percentage contributions of individual intermolecular interactions to the Hirshfeld surfaces of **group 5** compounds.

	BELYOJ	BELYID		BELYOJ	BELYID
Interaction	Percentage	Percentage	Interaction	Percentage	Percentage
H...H	29.8	31.4	C...C	2.5	1.4
I...H	25.4	25.4	O...I	1.8	2.7
C...H	1.6	9.7	O...N	0	0
F...H	8.9	11.3	O...C	0	0
I...I	6.4	3	F...O	0.1	0
I...F	3.9	2.4	O...H	3.9	2.3
I...C	12.3	6.7	N...H	0.3	2.1
I...N	2.4	1	C...N	0.5	0.1

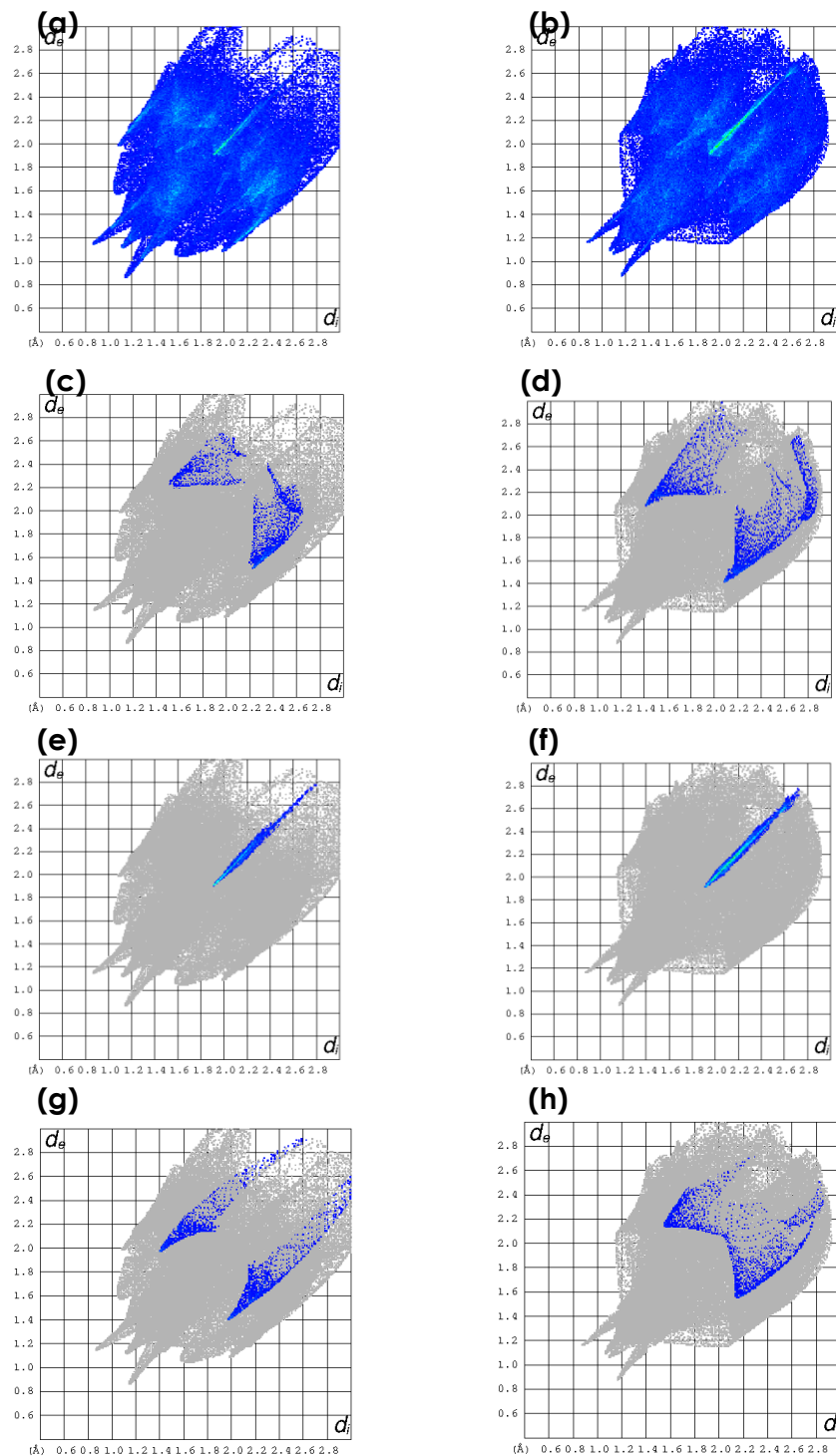


Fig 3.35.. 2D fingerprint plots for (a)**BELYOD**, (b) **BELYOJ**, and highlighting the I...F (c, d), I...I (e, f) I...O (g, h) intermolecular contacts; to provide context, the outline of the fingerprint is shown in grey

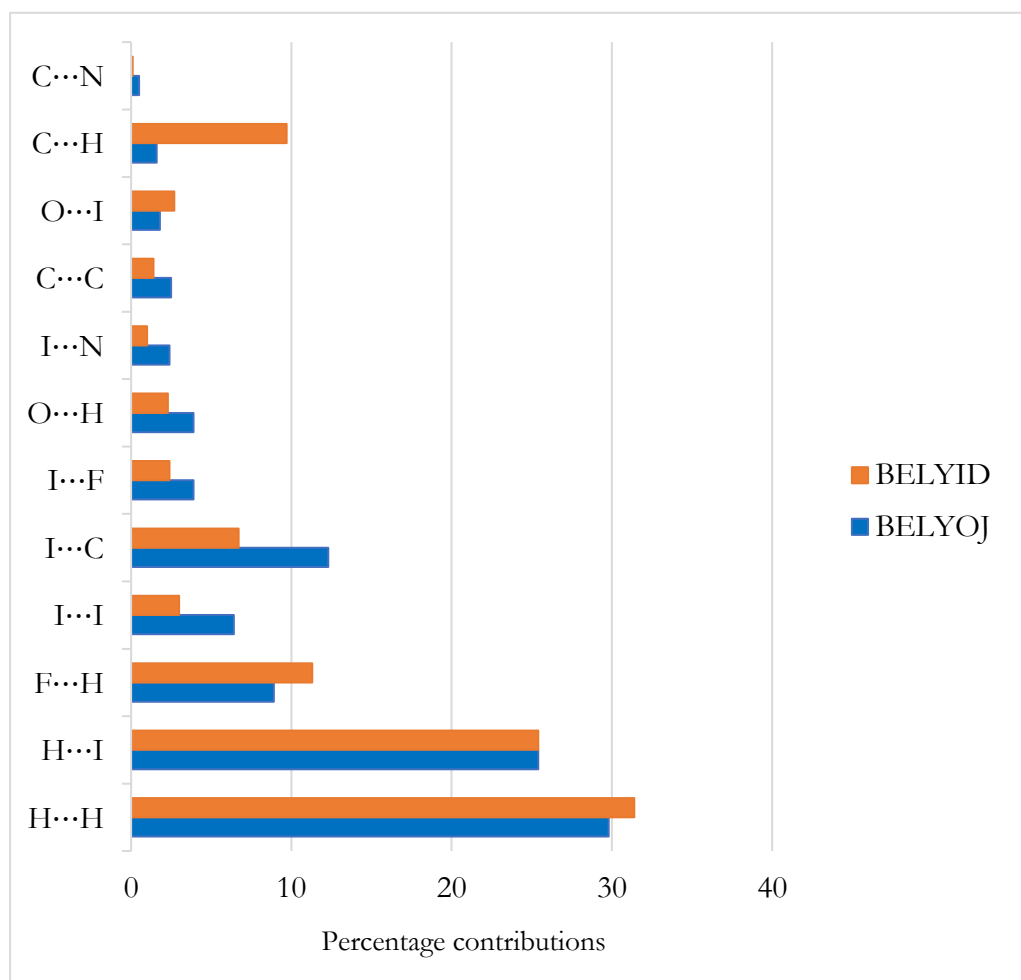
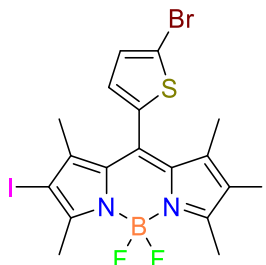


Fig. 3.36. Percentage contributions of individual intermolecular interactions to the Hirshfeld surfaces of compounds in **group 5**.

3.3.6 Group 6

In 2013, the crystal structure of **VIPCII**, a BODIPY functionalised at the 2,6-positions with iodine and a 2-bromo-thiophene group attached at the *meso*-position (**Scheme 3.6**) was reported by Vicente and co-workers.¹¹⁵ The presence of intermolecular halogen-halogen contact ($\text{I}\cdots\text{Br}$, $\text{Br}\cdots\text{F}$) in the crystal structure of **VIPCII** were reported without details on the type or the role of halogen bonding in the crystal structure. The presence of fluorine, iodine, bromine, and sulfur atoms in the same structure make this a fascinating

example of the competition between halogen and sulfur atoms in both halogen and hydrogen bonding.



Scheme 3.6. Group 6 BODIPY complex, **VIPCII**, investigated in this study.

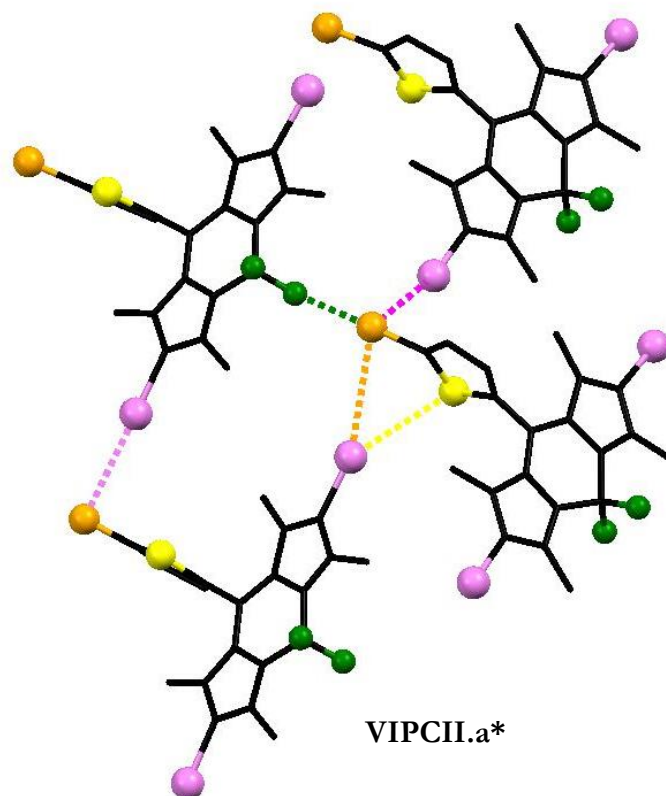
The asymmetric unit of **VIPCII** contains two molecules and will subsequently be called **VIPCII.a***, and **VIPCII.b***. **Fig 3.37** shows the d_{norm} surface of **VIPCII.a*** and **VIPCII.b***.

There are several observations from the structures shown in **Fig 3.37, 3.38, 3.39**: the first observation is the formation of short contacts by **VIPCII.a***, which are attributed to the transfer of negative charge from the sulfur atom (*i.e.* a Lewis base) to a polarizable bromo atom (*i.e.* a Lewis acid), which could be referred to as halogen bonds.¹²⁸ Reports in the literature suggest that any hydrogen bond acceptor can potentially act as an X-bond acceptor.^{137, 138} Thus, sulfur is shown to be a favourable acceptor for bromine halogen bonds.¹³⁸ The angle of approach of the sulfur acceptor to the halogen in **VIPCII.a*** (ca. 90° and the other one is about 120°) is less linear than the results from previous reports on sulfur acceptors in small-molecule assemblies, where the approach angles typically fall between 160 and 170°.¹³⁸ This could be due to the different hybridization of the sulfur atom in **VIPCII.a***, or a combination of other crystal packing effects. On the other hand, there is no evidence of the formation of Br...S interaction in **VIPCII.b***.

Table 3.9 Group 6 BODIPY complexes investigated in this study.

Group 6					
	D	A	θ_1	θ_2	Distance
VIPCII.a*	I	Br	167.83 (4)°	90.61 (5)°	3.5976(3) Å
	Br	F	158.39(5)°	130.16 (8)°	2.9713(8) Å
	I	S	145.12(3)°	90.56(5)°	3.9292(5) Å
VIPCII.b*	I	Br	162.41(4)°	89.12(5)°	3.7172(3) Å
	Br	F	168.07(5)°	134.03(8) °	2.9033(8) Å
	I	S	148.30(4)	86.89(5)	3.6263(5) Å

(a)



(b)

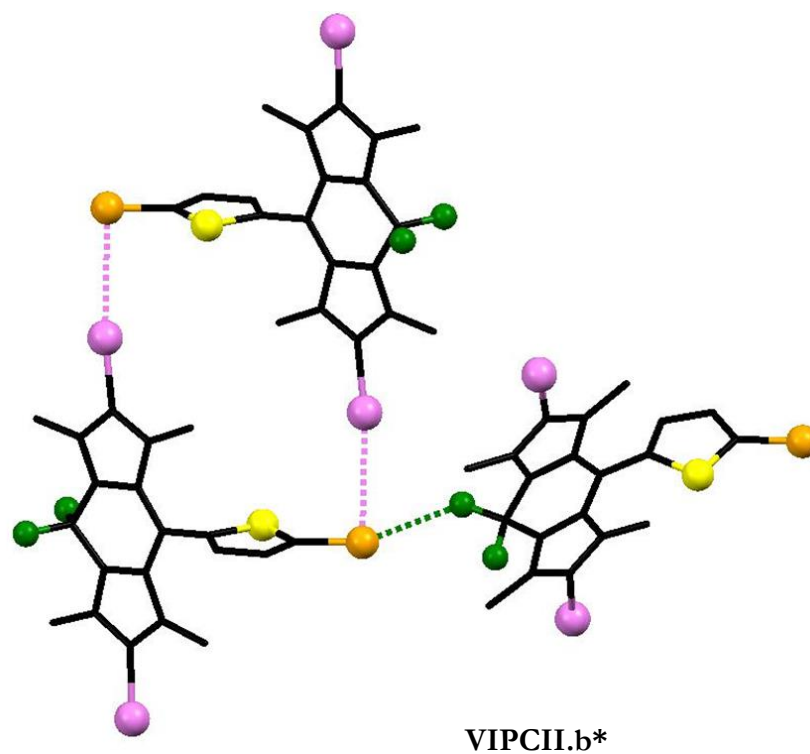


Fig 3.37. Arrangement of (a) **VIPCII.a*** and (b) **VIPCII.b***. Hydrogen atom have been removed for clarity. Carbon, boron, nitrogen = black, sulfur = yellow, iodine = violet, fluorine = green, bromo = orange.

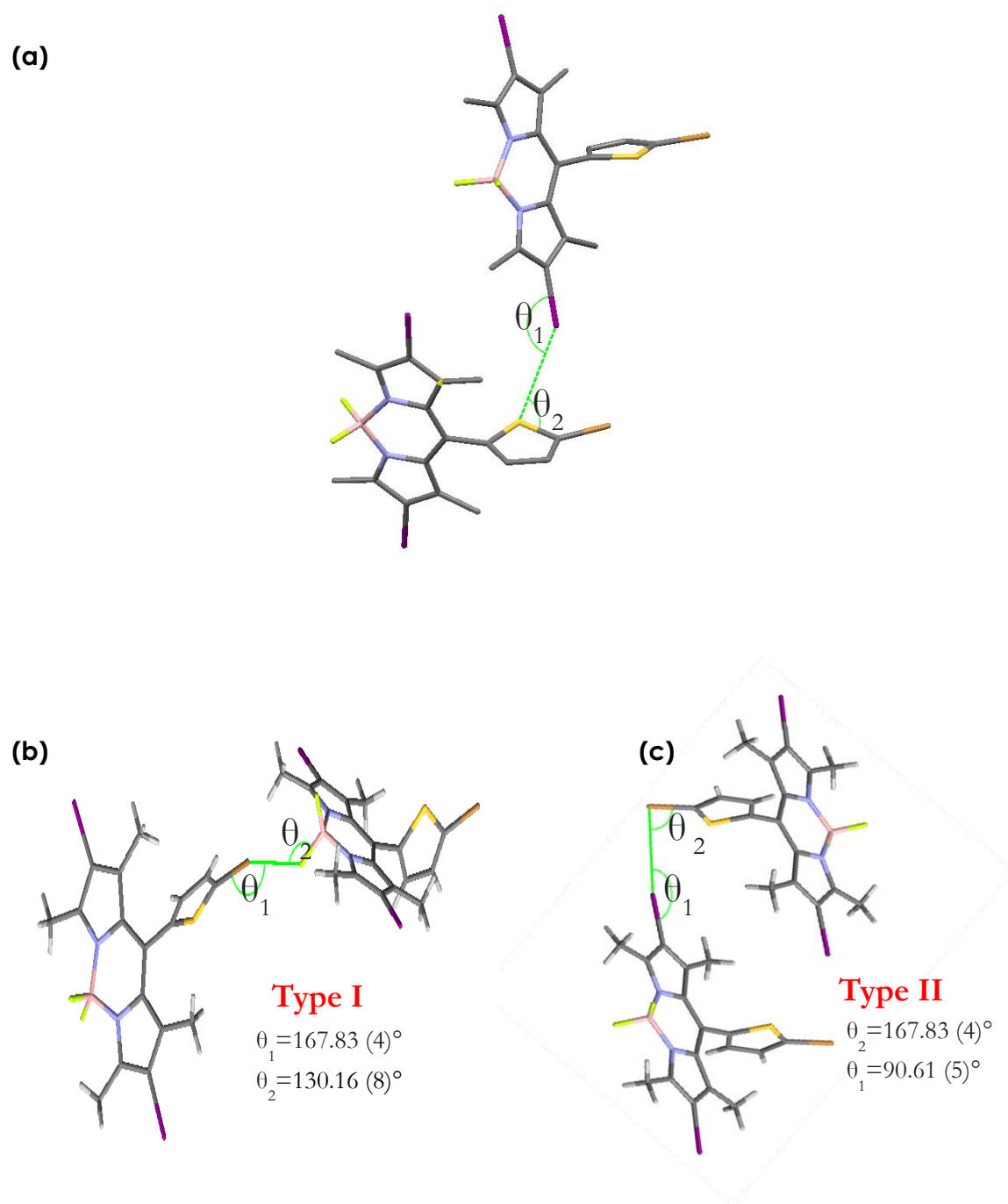


Figure 3.38. Views of the single crystal X-ray structures of **VIPCII.a*** and **VIPCII.b*** showing (a) (C-I $\cdots$ S) XB interaction, (b) (C-Br $\cdots$ F) XB interaction, (c) (C-Br $\cdots$ I) XB interaction. Carbon = grey, nitrogen = blue, boron = pink, fluorine = green, bromine = orange, sulfur =yellow, iodine = purple.

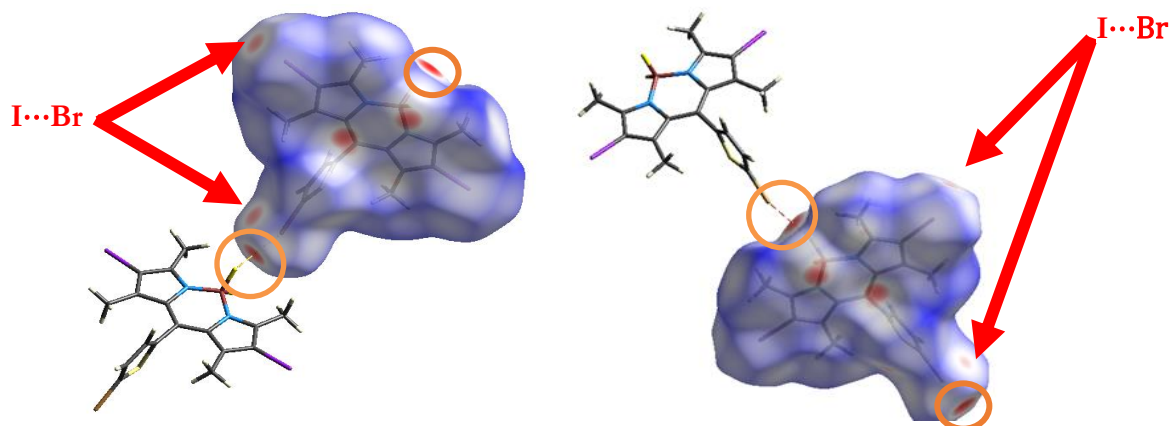


Figure 3.39. Calculated HSs for **VIPCII.a*** and **VIPCII.b*** showing the d_{norm} surface of (a) **VIPCII.a*** and **VIPCII.b*** viewed along the b-axis. The close (C-Br...F) contact is highlighted in orange, red arrows indicate (C-I...Br) XB interactions. Carbon = grey, nitrogen = blue, boron = red, fluorine = green, iodine = purple.

The second observation is the formation of type I (Br...F) interactions in both forms

VIPCII.a* and **VIPCII.b***: [Br...F = 2.9713(8) Å; C-Br...F = 158.39(5)°, B-F...Br =

130.16 (8)°, for **VIPCII.a***, Table 3.9] and [Br...F = 2.9033(8) Å, and C-Br...F = 168.07

(5)°, B-F...Br = 134.03(8)°, for **VIPCII.b***, Table 3.9]. The third observation is the

formation of type II (I...Br) XB interactions [I...Br = 3.5976(3) Å, C-I...Br = 167.83 (4)°,

C-Br...I=90.61 (5)°, for **VIPCII.a***, Table 3.9] and [C-I...Br = 3.7172(3) Å, and C-

Br...F = 162.41 (4)°, B-F...Br = 89.12 (5)°, for **VIPCII.b***, Table 3.9].

3.3.6.1 Fingerprint Analysis and Summary

Figure 3.40 shows the relative contributions of 2D-fingerprint plots, highlighting I⋯Br, and Br⋯F halogen bonding for **VIPCII.a***, and **VIPCII.b***. The I⋯Br contact in the fingerprint plot (5.4% I⋯Br area for form a*) is slightly larger than for form b* (4.4% I⋯Br area). The Br⋯F area in both forms are the same (2.7%). The numbers of interactions in terms of percentages are represented as a bar chart (**Fig 3.41**, **Table 3.16**) which summarises the intermolecular contacts in **VIPCII.a*** and **VIPCII.b***. It should be noted that the hydrogen bonding close contacts (I⋯H, F⋯H) in form **VIPCII.b*** are more significant than for form **VIPCII.a***, while the hydrogen bonding close contacts (Br⋯H,) in form **VIPCII.a*** are more significant than for form **VIPCII.b***.

Table 3.16. Percentage contributions of individual intermolecular interactions to the Hirshfeld surfaces of compounds **VIPCII.a*** and **VIPCII.b***.

Group 6					
	VIPCII.a*	VIPCII.b*		VIPCII.a*	VIPCII.b*
H⋯H	28.1	26.3	F⋯N	1.1	1.1
I⋯H	16.6	19.8	H⋯N	2.1	2.2
C⋯H	14.3	15.5	Br⋯H	8.2	7.3
F⋯H	5.2	5.3	Br⋯S	1.8	1.7
I⋯I	0.6	0.5	Br⋯I	5.4	4.4
I⋯F	1.2	0.3	S⋯H	2.4	2.3
I⋯C	3.3	2.2	S⋯F	1.6	1.6
C⋯C	0.6	0.6	I⋯S	1.7	3
F⋯C	2.6	2.7	C⋯N	0.4	0.4
N⋯N	0.1	0.1	Br⋯F	2.7	2.7

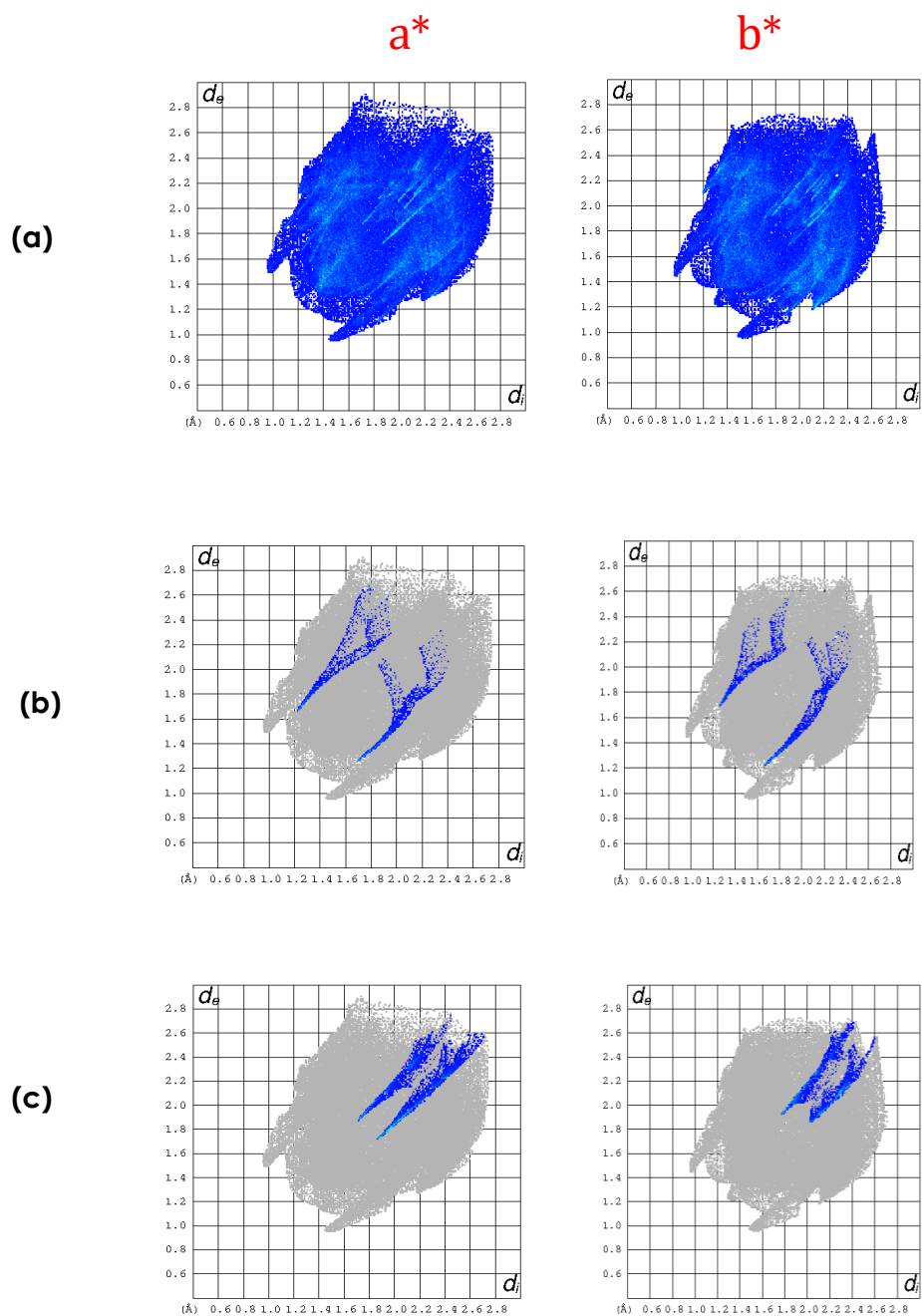


Fig 3.40. 2D fingerprint plots of (a) **VIPCII.a*** and **VIPCII.b***. (b) 2D fingerprint plots of compound **VIPCII.a*** and **VIPCII.b*** highlighting the (Br...F) intermolecular contacts. (c) 2D fingerprint plots of compound **VIPCII.a*** and **VIPCII.b*** highlighting the (Br...I) intermolecular contacts. To provide context, the outline of the fingerprint is shown in grey.

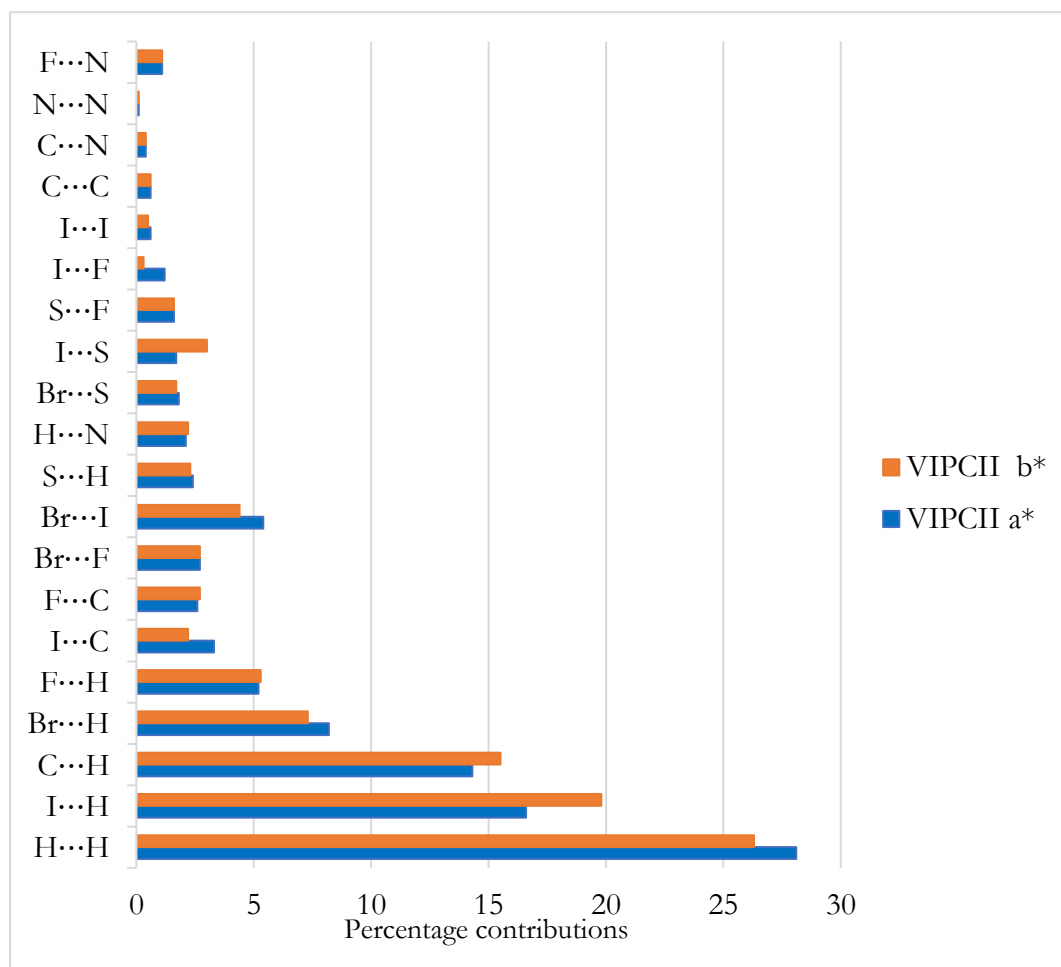
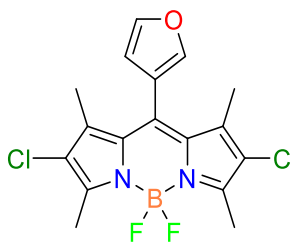


Fig 3.41. Percentage contributions of individual intermolecular interactions to the Hirshfeld surfaces of compounds **VIPCII.a*** and **VIPCII.b***.

3.3.7 Group 7

The crystal structure of **XELCEY**, which contains a BODIPY functionalized at the 2,6-positions with chlorine, and a furan ring at the *meso*-position has been reported¹³⁹ (**Scheme 3.7**).

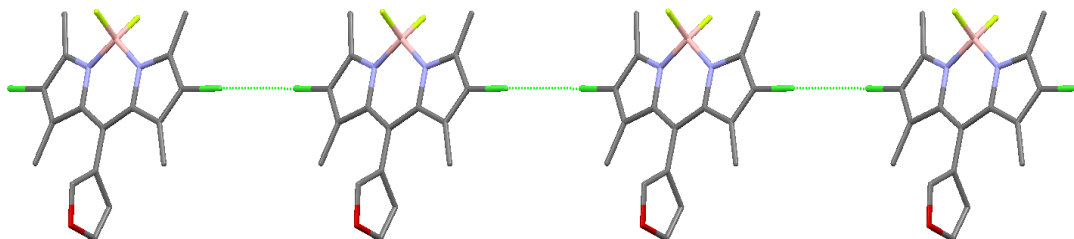


Scheme 3.7. Group 7 BODIPY complexes investigated in this study.

The evidence for XB in this system can be seen from the X-ray crystal structures of this molecule, where the distance between the halogen-bond donor atom and the halogen-bond acceptor atom (chlorine atoms) was less than the sum of their *van der Waals radii*. The significant observation from the crystal packing is the formation of almost linear (C–Cl $\cdots$ Cl) XB interaction, [C–Cl $\cdots$ Cl = 178.73(11)Å, C–Cl $\cdots$ Cl = 171.42(9)°, C –Cl $\cdots$ Cl = 3.4194(12)°] as shown in **Fig. 3.41**. The linear XB interaction suggests that there is a specific attractive intermolecular force between the chlorine atoms as a consequence of the non-spherical atomic charge distribution. This type of interhalogen bond (Cl $\cdots$ Cl bond) has been explained systematically by Price *et al.*¹⁴⁰

A close CH $\cdots$ F hydrogen bond between the fluorine atom from the BODIPY core and a neighbouring hydrogen from the furan ring, with a distance approximately equal to the sum of the *van der Waals radii* for H and F, 2.56 Å.^{119, 120} It should be noted that due to a technical problem with the cif of this crystal structure and Crystal Explorer software, it was not possible to calculate a Hirshfeld surface or 2D-fingerprint plots for **XELCEY**.

(a)



(b)

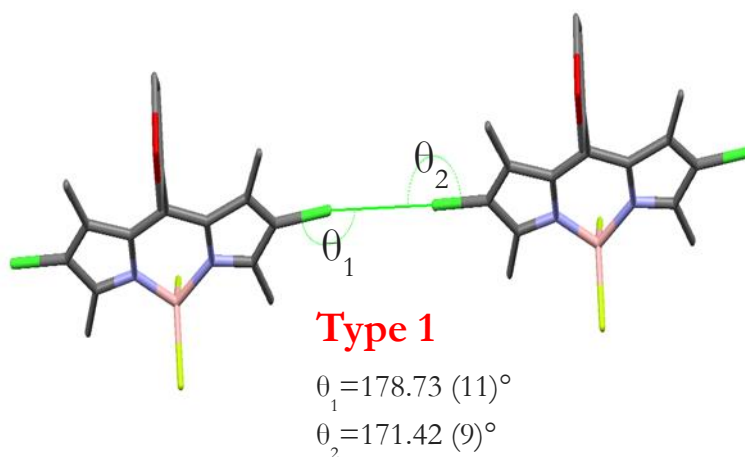
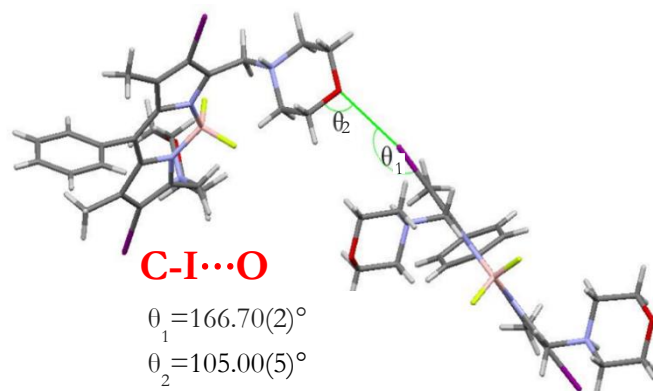


Fig 3.42. (a) Type II (Cl...Cl) halogen bonding of **BHASOT** which reveals the formation of a linear pattern (b) Single crystal X-ray structure of **XELCEY** showing type II (I...I) XB. Carbon = grey, nitrogen = blue, boron = pink, fluorine = green, chlorine = dark green.

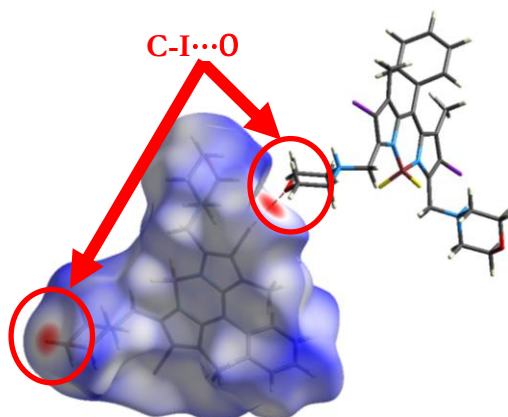
3.3.8 Group 8

The crystal structure of **BHASMQ** was reported in **chapter 2**. The crystallographic characterization of **BHASMQ** shows the presence of iodine atoms at the 2,6 positions of the BODIPY core and non-conjugated morpholine moieties attached to α -carbons, which gives unusual halogen-oxygen bonding.

(a)



(b)



(c)

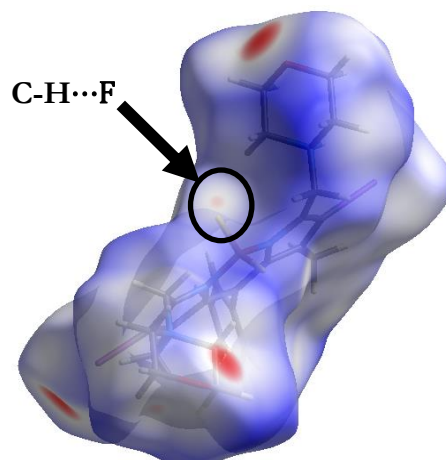
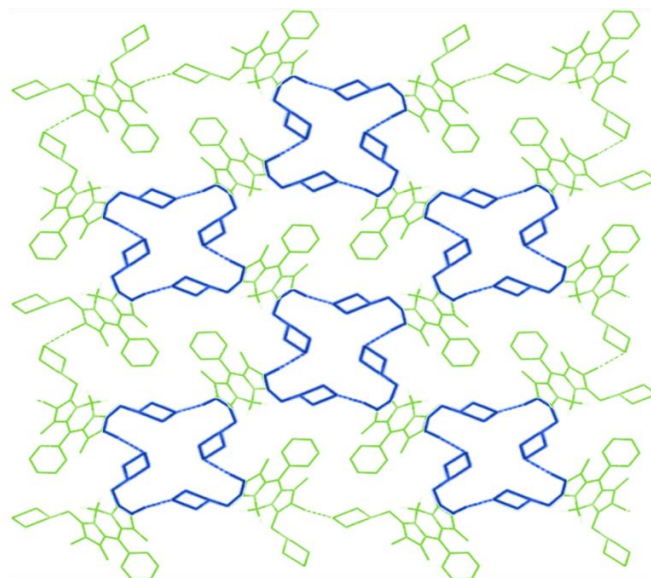


Fig 3.43. (a) Single crystal X-ray representation of (C-I...O) halogen bonding interaction observed in **BHASMQ**. (b) HSs calculated for **BHASMQ** showing close (C-I...O) contact, highlighted in red. (c) HSs representation of close (C-H...F) hydrogen bonding contact highlighted with a black circle. Carbon = grey, nitrogen = blue, boron = pink, fluorine = green, iodine = purple, oxygen=red.

The first observation from the HSs calculated for **BHASMQ**, shown in **Fig 3.43**, is the intense red spot near both the iodine and oxygen atoms on the BODIPY core, which corresponds to unusual (C–I $\cdots$ O) XB interaction, [C–I $\cdots$ O = 2.972(6) Å, C–I $\cdots$ O = 166.70(2)°, C–O $\cdots$ I = 105.00(5)°]. The I $\cdots$ O distance is shorter, over 20% shorter, than the sum of mean *van der Waals radii* of the two atoms (3.49 Å),¹²⁸ indicating a strong XB. The packing diagram of **BHASMQ** confirms the presence of XB bonds leading to the formation of sheets running parallel to the a-axis, **Fig 3.44**. The main observation of the packing is the presence of an X-type arrangement between every four BODIPYs. This happens due to presence of non-conjugated morpholino substituents at the α -carbon which leads to formation of angle of [C_{pyrrole}–C _{α carbon}–N_{Morph} = 109°] and the angle between α -carbon of the pyrrole ring and the iodine atom on the β -position is approximately 125°. However, viewing the packing along the a-axis shows a herringbone pattern. The second observation from the HSs (**Fig 3.43 c**) is the faint red spot near the fluorine atoms on the BODIPY core. Close CH $\cdots$ F hydrogen bonding is observed between the fluorine atom from one BODIPY and a neighbouring hydrogen from phenyl ring (*meta*-hydrogen), [CH $\cdots$ F = 2.615(5) Å; C $\cdots$ F = 3.538 (11) Å, C–H $\cdots$ F = 164.40 (6)°, B–F $\cdots$ C = 129.60 (5)°, B–F $\cdots$ H = 129.20(5)°]. The distance of approximately 2.61 Å which slightly longer than the sum of the *van der Waals radii* for H and F (2.56 Å)^{119, 120} suggesting a weak interaction. No close(C–I $\cdots$ F) interactions are observed in **BHASMQ**, possibly due to presence of the morpholine moieties, resulting in a more favourable I $\cdots$ O interaction being adopted.

(a)



(b)

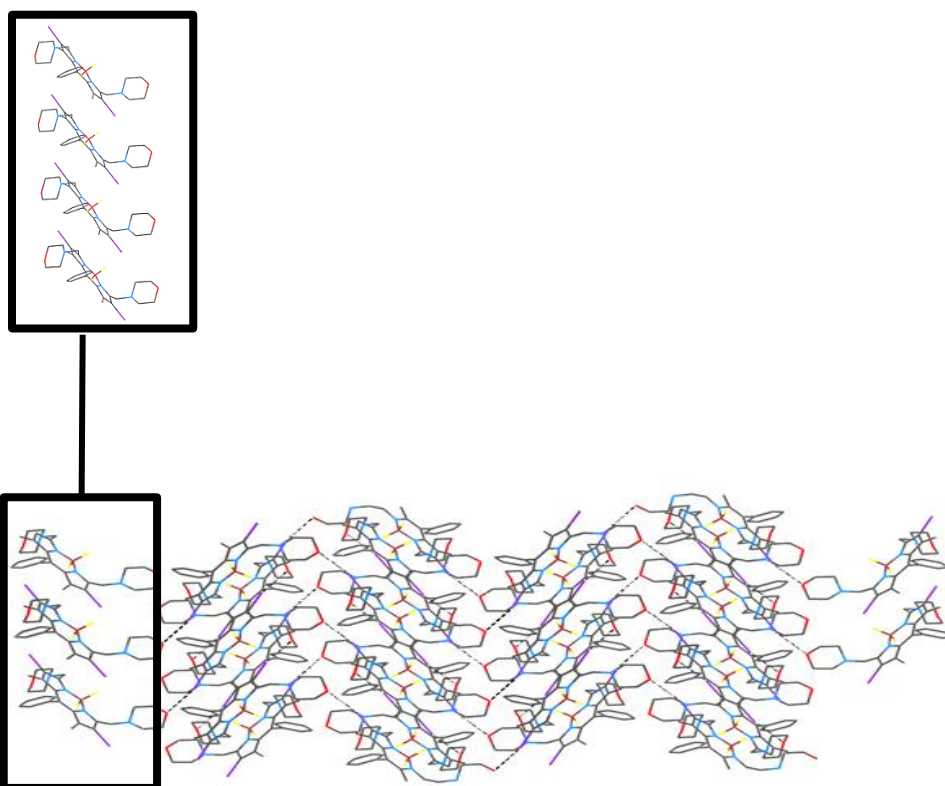


Fig 3.44. (a) Orientation of **BHASMQ** along the a-axis showing the formation of sheets. (b) View of the packing of **BHASMQ** perpendicular to the a-axis. Hydrogen atoms have been removed for clarity. Carbon = grey, nitrogen = blue, boron = red, fluorine = green, iodine = purple.

3.3.8.1 Fingerprint Analysis and Summary

Figure 3.45 shows the 2D fingerprint plots representing the contributions to the Hirshfeld surface. C-I...O contacts represent 3.3% of the surface area of the interactions. Further details of the contributions of different interactions for **BHASMQ** are shown in **Figure 3.46** , in **Table 3.17**).

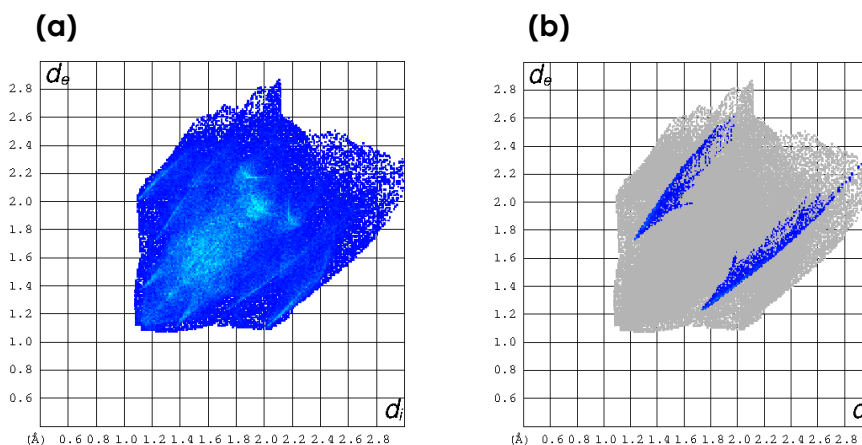


Fig 3.45. 2D fingerprint plots calculated for **BHASMQ** (a) full intermolecular interactions (b) I...O intermolecular contacts. To provide context, the outline of the fingerprint is shown in grey.

Table 3.17 Percentage contributions of individual intermolecular interactions to the Hirshfeld surfaces of BHASMQ.

BHASMQ			
Interaction	Percentage	Interaction	Percentage
H...H	61.8	I...N	1.2
I...H	10.7	C...C	2.1
C...H	5.4	I...O	3.3
F...H	6.8	N...H	1.2
I...F	1.2	C...N	0.7
I...C	2.1	O...H	4.5

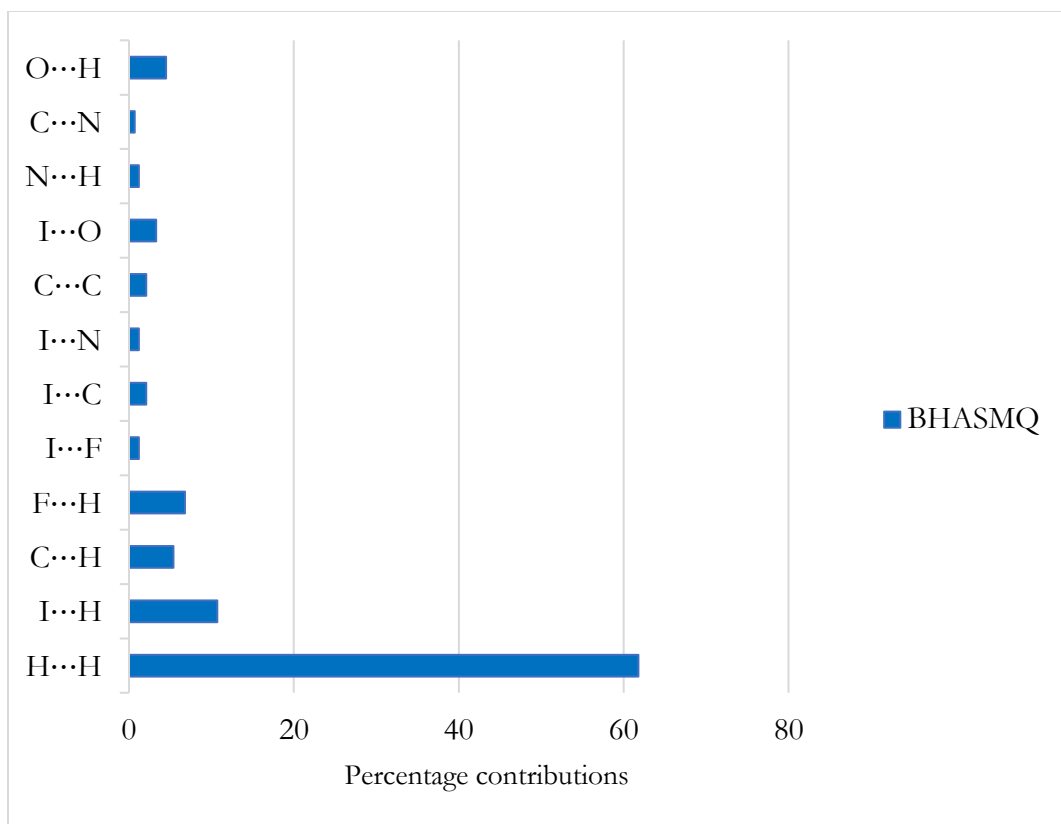


Fig 3.46 Percentage contributions of individual intermolecular interactions to the Hirshfeld surfaces of BHASMQ.

3.4 Conclusions

Halogen bonding can be attributed to the favourable interaction that exists between a halogen's electropositive σ -hole and an electronegative atom, such as oxygen, or other halogen atoms. We have investigated the solid-state structure of a series of halogenated BODIPY, where halogen...halogen, halogen...oxygen, halogen...sulfur, and hydrogen bonding interactions present in the resulting structures. These interactions were identified and analysed through distance, angles, Hirshfeld surface maps, two-dimensional (2D)-fingerprint analysis, and the percentage contribution for different kinds of non-covalent interaction. In all cases presented in this chapter, the halogen bond turned out to have a number of characteristic properties reminiscent of hydrogen bonding.

Firstly, analysing type I and type II interactions as a function of the distance afforded a further outcome. At distances shorter than the van der Waals contacts, type I interactions were more frequent. However, at the shortest distances type II were more frequent. It should be stated that, a comparison with data from a systematic CSD analysis shows that the halogen-bond distances and angles in all structures presented herein are consistent with commonly observed parameters.

Secondly, changes in the *meso*-position results in dramatic changes to the types of halogen bonding. For example, changes from type II (I...I) XB interactions to type I, by changing the *meso* substituent from phenyl to hydrogen. Moreover, **group 1** and 6 were the only examples where the BODIPY fluorine atoms are involved in halogen bonding with either iodine or bromine.

Thirdly, introducing electron-rich sites such as the carbonyl, the methoxy or the hydroxy oxygen or sulfur atoms have a direct effect on the type of interaction and change the packing of the crystal, indicating more control of the interaction by choosing the right substituent. For example, groups 2, 3 and 4, display small changes on the phenyl at the *meso*-position of BODIPY can have a dramatic effect and introduce more complex systems of HB and XB interactions.

The results described above in all the group above demonstrate that halogen bonding plays a major role in the control of intermolecular recognition and self-assembly processes of BODIPY compounds. Beyond the formation of exclusively halogen-bonded complexes, the potential cooperation with other weak noncovalent bonds such as hydrogen bonding opens new possibilities in materials science. It is clear that much work needs to be done to fully exploit the arsenal of interactions that are possible *via* logical introductions of σ -holes in halogenated BODIPY compounds.

3.5 Experimental Section

3.5.1 Synthetic Procedures

*Synthesis of 2,6-dibromo, 1, 3, 5, 7-tetramethyl-8-phenyl-4,4 difluoroboradiazaindacene (**BHASNF**, and **BHASNM**)*

To a solution of **2-15** in CH₂Cl₂ (25 mL) was added excess NBS (459 mg, 2.04 mmol). The mixture was stirred at room temperature until total consumption of the starting material (1 h, as monitored by TLC). The crude product was then concentrated under vacuum and purified by silica gel column chromatography (hexane/CH₂Cl₂, 1:2). The red coloured fraction was collected, and the solvent was removed under reduced pressure to yield the desired compound. Data below was found to be consistent with the literature.¹¹⁷

¹H NMR (400 MHz, CDCl₃) δ 7.57-7.52 (m, 3H), 7.28-7.26 (m, 2H), 2.64 (s, 6H), 1.39 (s, 6H); ¹¹B NMR (128 MHz, CDCl₃) δ 0.50 (t, *J* = 33.40 Hz); ¹⁹F NMR: (376 MHz, CDCl₃, δ -146.01. MS (ESI) calcd for [M]⁺ : 481.98, found 481.92.

*Synthesis of 2,6-diiodo, 1, 3, 5, 7-tetramethyl-4,4 difluoroboradiazaindacene (**BHASOT**)*

To a solution of , 1, 3, 5, 7-tetramethyl-4,4 difluoroboradiazaindacene in CH₂Cl₂ (25 mL) was added excess NIS (459 mg, 2.04 mmol). The mixture was stirred at room temperature until total consumption of the starting material (1 h, as monitored by TLC). The crude product was then concentrated under vacuum and purified by silica gel column chromatography (hexane/CH₂Cl₂, 1:2). The red coloured fraction was collected, and the solvent was removed

under reduced pressure to yield the desired compound. MS (ESI) calcd for $[M - H]^-$: 498.92, found 498.90.

3.5.2 X-ray crystallography

Single crystal diffraction data for **BHASNR**, **BHASOT**, **BHASNF**, and **BHASNM** were collected at 120(2) K on a SuperNova, Atlas or Bruker GV1000 diffractometer using mirror monochromated Cu K α radiation. Using Olex2,¹⁴¹ the structure was solved with the ShelXT¹⁴² structure solution program using Intrinsic Phasing and refined with the ShelXL¹⁴³ refinement package using Least Squares minimization. Visualizing interactions in molecular crystals using Hirshfeld surface tools and 2D fingerprint plot (FPs) were analysed using Crystal Explorer (Version 3.1, and 17.1).^{110, 144} Figures for all compounds were created using either with Crystal Explorer (Version 3.1, and 17)^{110, 146}, and/or Mercury (Version, 3.10.3).

The approach adopted in this chapter consists of investigating the experimental distances and angles of XB intermolecular contacts observed in a series of halogenated BODIPY compounds bearing different substituents in the *meso* position. Hirshfeld surfaces (HSs), and their associated fingerprint plots were calculated to provide evidence for the occurrence of contacts and any other intermolecular interactions present in the crystal structures studied. Firstly, a comprehensive data set was developed by searching for halogenated BODIPY compounds in the CDC by using Con Quest program, (the last update of the CDC used in searches was 2nd December 2018). The searches were limited to structures bearing either iodine, bromine, or chlorine atoms at 2,6-positions, and tetramethyl at 1, 3,5,7- positions which shows evidence of halogen bonding interactions. The assessment of structure where based on R-factor, data quality. Structures with errors or disorders where removed from the search. Additionally, distance and geometrical

classification of halogen... halogen interactions (**Fig 3.4**) were used to determine the halogen contact. The resulting BODIPY structures were split in eight general groups based on the substituents in the *meso* position.

Crystal Data for **BHASOT**: $C_{11}H_{10}BN_2F_2I_2$. Monoclinic, space group $P2_1/m$ (no. 11), $a = 8.7496(14)$ Å, $b = 7.2495(9)$ Å, $c = 12.2619(13)$ Å, $\alpha = 90^\circ$, $\beta = 98.447(13)^\circ$, $\gamma = 90^\circ$, $V = 769.34(18)$ Å³, $Z = 2$, $D_{\text{calc}} = 1.021$ g cm⁻³, $\mu = 32.225$ mm⁻¹, $F(000) = 468.0$, A total of 2939 reflections were collected, of which 1616, were unique, with $R_{\text{int}} = 0.0497$. Final R_1 (wR_2) = 0.0478 (0.1220) with GOF = 1.043.

Crystal Data for **BHASNF**: $C_{19}H_{17}BBr_2F_2N_2$ Monoclinic, space group $P2_1/n$, $a = 15.9185(4)$ Å, $b = 7.98870(10)$ Å, $c = 16.1471(3)$ Å, $\alpha = 90^\circ$, $\beta = 117.002(3)^\circ$, $\gamma = 90^\circ$, $V = 1829.56(8)$ Å³, $Z = 4$, $D_{\text{calc}} = 1.750$ g cm⁻³, $\mu = 5.838$ mm⁻¹, $F(000) = 952.0$, A total of 40851 reflections were collected, of which 3717 were unique, with $R_{\text{int}} = 0.0343$. Final R_1 (wR_2) = 0.0210 (0.0555) with GOF = 1.054.

Crystal Data for **BHASNM**: $C_{19}H_{17}BBr_2F_2N_2$. Monoclinic, space group $P2_1/n$, $a = 11.3799(9)$ Å, $b = 12.7378(9)$ Å, $c = 93.502(6)$ Å, $\alpha = 90^\circ$, $\beta = 117.002(3)^\circ$, $\gamma = 90^\circ$, $V = 1870.2(2)$ Å³, $Z = 4$, $D_{\text{calc}} = 1.712$ g cm⁻³, $\mu = 5.711$ mm⁻¹, $F(000) = 952$. A total of 7585 reflections were collected, of which 3694 were unique, with $R_{\text{int}} = 0.0414$,. Final R_1 (wR_2) = 0.0600 (0.1650) with GOF = 1.10.

3.6 References

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Chapter 4

**Structural Characterization, and Optical Properties
of Two Copper(I)-iodide BODIPY Compounds**

4.1 Introduction

The discovery of new materials has always been one of the essential steps in the development of the science to perform specific functions for a range of different applications. Coordination polymers are one of the results of this extensive research¹⁻⁴ with studies ranging from classical coordination chemistry to the developing field of bioinorganic chemistry.^{2, 5-9} The key features of coordination networks that make them so attractive are their intriguing topological features and the positioning of components in one, two or three-dimensional space,^{2, 5-8} which has given rise to advances in several fundamental and applied research aspects such as gas storage,^{10, 11} catalysis,¹² ion exchange, liquid crystals and ionic liquids.⁷

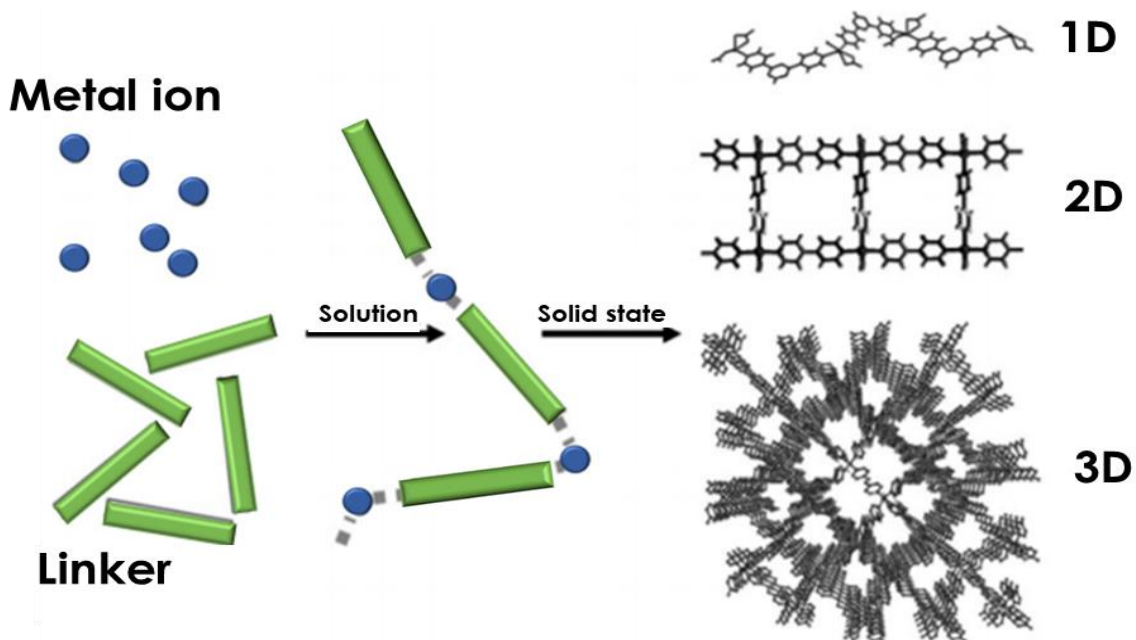


Fig 4.1. Formation of 1D, 2D, and 3D coordination polymers. Reproduced from references 17, and 21.

The synthesis of coordination polymers is performed by mixing an inorganic node (metal ion) and spacer (organic linker) in the desired ratio in solid state, or one or more solvents. The reaction temperature is variable, from room temperature using solvent diffusion methods or higher temperatures ($T = 120\text{--}260\text{ }^{\circ}\text{C}$) under solvothermal conditions^{13, 14, 15} The pressure, solvent or solvent ratio also plays an important role in the synthetic process.^{13, 14} The construction of the components in coordination polymers classically only exists in the solid state,¹⁶ as the products are generally insoluble or degrade upon dissolution.¹⁷ Therefore, structures of coordination polymers can only be determined by X-ray crystallographic methods and characterization in solution only proves the existence of oligomeric fragments.¹⁷ In the structures of coordination polymers, the building blocks interact through coordination interactions and weaker forces such as hydrogen bonds, π -stacking or *van der Waals* interactions in solution to form small molecular units which follow by self-assembly processes to grow the coordination polymer as presented in **Fig 4.1**.¹⁷

4.1.1 Overview of the Diversity of Coordination Polymers

There are four different kinds of building blocks used for the formation of infinite metal-organic frameworks: organic ligands, metal ions,¹⁷⁻¹⁹ counter ions and solvent molecules.¹⁷

4.1.1.1 Organic Ligands

An important aspect during the construction of coordination polymers is the coordination preferences of the metal centre toward the organic ligands. The organic ligands act as bridging organic groups between the metal ions.¹⁷ Therefore, the organic ligand molecules must be multidentate with at least two donor atoms, typically N-, O-, S or cyano donors. Another determining point is the feature of the “body” of the organic ligands such as rigidity, lengths,

functionalities symmetry, chirality.¹⁷ Organic linker may differ in their charges: most used ligands are neutral and anionic.¹⁷ Examples of organic ligand molecules are given on **Fig 4.2**.

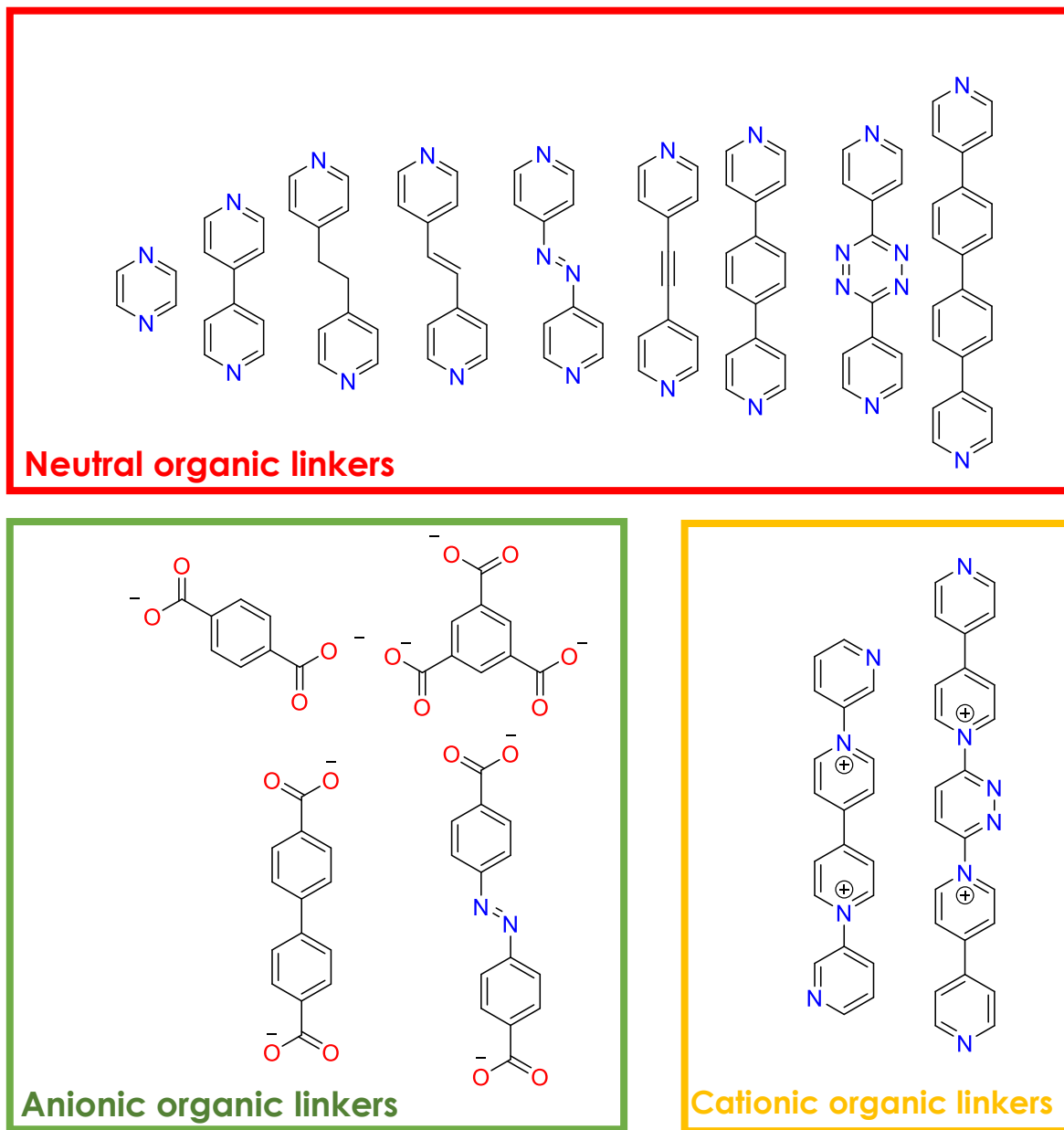


Fig 4.2. Organic linkers typically used in coordination polymers.²⁰

4.1.1.2 Metal Ion

The metal ions have a direct effect on the properties of the future materials depending on the coordination geometry of the metal. The metal ion will be involved in the structure depending on their size, hardness/softness, ligand-field stabilization energy and coordination geometries.^{17, 20}

4.1.1.3 Counter ions and Solvent Molecules

The use of neutral ligands leads to the presence of counter ions in the coordination polymer (*i.e.* counterbalance the positive charges obtained by ligation of neutral ligands to metal ions). Moreover, there may be the presence of solvent molecules co-crystallized in the solid-state structure of the coordination polymer.¹⁷ The counter ions and/or solvent molecules may act as guest molecules in the void spaces in the solid state, increasing the number of possible weak interactions in the final packing structure.¹⁷

4.1.2 Copper(I) in Coordination Polymer Construction

A variety of transition^{8, 21-29} and lanthanide³⁰⁻³⁴ metals have been used in coordination polymer syntheses. In general, there is an intense research interest in the use of Ag^I, Cu^I and Zn^{II} metal ions in the coordination polymer engineering because they have a d¹⁰ electronic configuration and thus are more “flexible” in their coordination behaviour. In particular, researchers have shown an increased interest of copper(I) complexes containing polydentate nitrogen ligands (soft-soft bonding preference).^{27, 35-40} The d¹⁰ electronic configuration of copper(I) lead to rich structural chemistry, which gives rise to a variety of attractive coordination framework architectures and remarkable photochemical and photophysical characteristics.^{3, 8, 18, 41-43}

Numerous coordination structures are reported by combination of conjugated ligands (polydentate nitrogen ligand) and CuX (X = Cl, Br, I)^{21-23, 27, 38, 44-48} to produce soft-soft bonding between the metal centres and the ligands. The use of copper halide allows the formation of neutral networks because halide counter anions are generally strongly coordinated to the Cu(I). These frameworks are quite stable, as there are no counter anions between the coordination polymer building block. Furthermore, combinations of Cu(I) halide with bidentate bridging ligands result in one-dimensional or two-dimensional networks, usually through the linking of Cu₂X₂ rings or (CuX)_n chains by the ligand.^{22, 27} See **Fig 4.3.** for examples of copper(I) halide structural motifs.

The most common motifs seen in copper(I) halide coordination polymers are the CuX monomer and the Cu₂X₂ rhomboid dimer. The coordination number of the Cu(I) centre can vary,^{23, 49, 50} for example the coordination number of the Cu(I) in CuX monomer is most commonly four. The rhomboid dimer can be thought of two as two monomers connected in a head to tail fashion. Both Cu(I) centres usually coordinate to the ligands to create two tetrahedral four coordinate Cu(I) centres. It also possible to have a mixed three/four coordinated Cu(I) centre in the rhombid dimer. The other relatively common CuX motifs are cubane tetramers, square Cu₂X₂ dimers, stepped cubane Cu₄X₄ chains and ladders (or stair-step), tetramers, zigzag [CuX]_n chains, and double stranded [Cu₂X₂]_n ladders, and banded ribbons or hexagon prism [Cu₆X₆]_n grid chains.^{23, 49, 50}

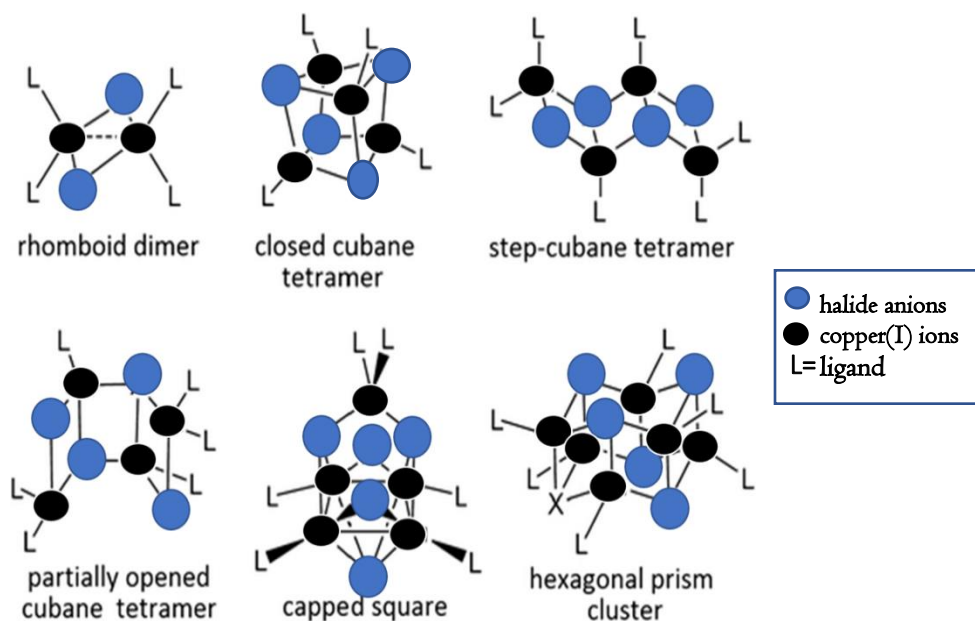


Fig 4.3. Structural motifs observed for copper(I) halides ● = copper(I) ions; ● = halide anions. Reproduced from reference 51.

Besides the variety of coordination framework architectures of copper(I) complexes, remarkable photochemical and photophysical characteristics are observed of such complexes. Therefore, a considerable amount of literature has been focused on exploring the photophysical behaviour of copper(I) complexes.⁵²⁻⁵⁵ Specifically, when halides coordinate to copper(I) many potential transitions become available, such as ligand to metal charge transfer (LMCT), metal to ligand charge transfer (MLCT), halide to ligand charge transfer (XLCT), and halide to metal charge transfer (XMCT).^{24, 56, 57} Additionally, for tetrameric copper(I) iodide compounds cluster-centred (CC) excited states are common.^{24, 57} The term cluster-centred emphasizes the localization of the excited state on the inorganic cluster significantly independent of the ligand.⁵⁷ Generally, copper(I) iodide compounds display both a lower energy (LE) emission and a higher energy (HE) emission. An example of this approach is

presented in **Fig 4.3**. In this example the LE emission involves orbitals delocalized over the inorganic cluster, and the HE emission involves the ligands π^* orbitals.^{108,55, 58} This compound shows temperature-sensitive luminescence, which is a feature of some copper (I) compounds. The temperature-sensitive luminescence known as luminescence thermochromism.²⁴⁻²⁶ Measurements of luminescent thermochromism are typically performed at liquid nitrogen temperatures, which can result in significant and measurable shifts in emission.⁵⁹ Moreover, luminescent thermochromism affects the relative intensities of the HE and LE emission. Copper(I) compounds can also undergo a π back-bonding, as the electron rich metal is in a low oxidation state. The metal donates electron density back to the ligand into a π^* orbital affording stronger bonds.⁴²

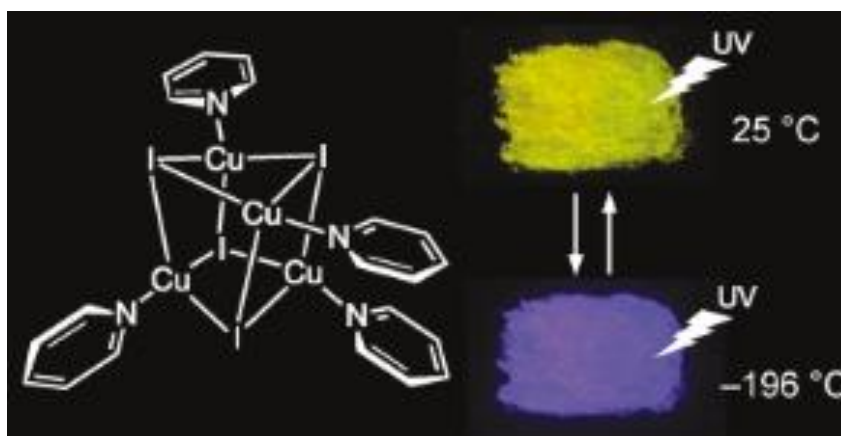


Fig 4.3. An example of luminescence thermochromism of Cu(I) compound. Reproduced from Reference 108.

On the other hand, the poor solubility and oxidative instability are the most common problems associated with the use of copper(I) halides in coordination polymer construction.⁴² Copper(I) halides are moderately soluble in acetonitrile^{42, 60} and sparingly soluble in other

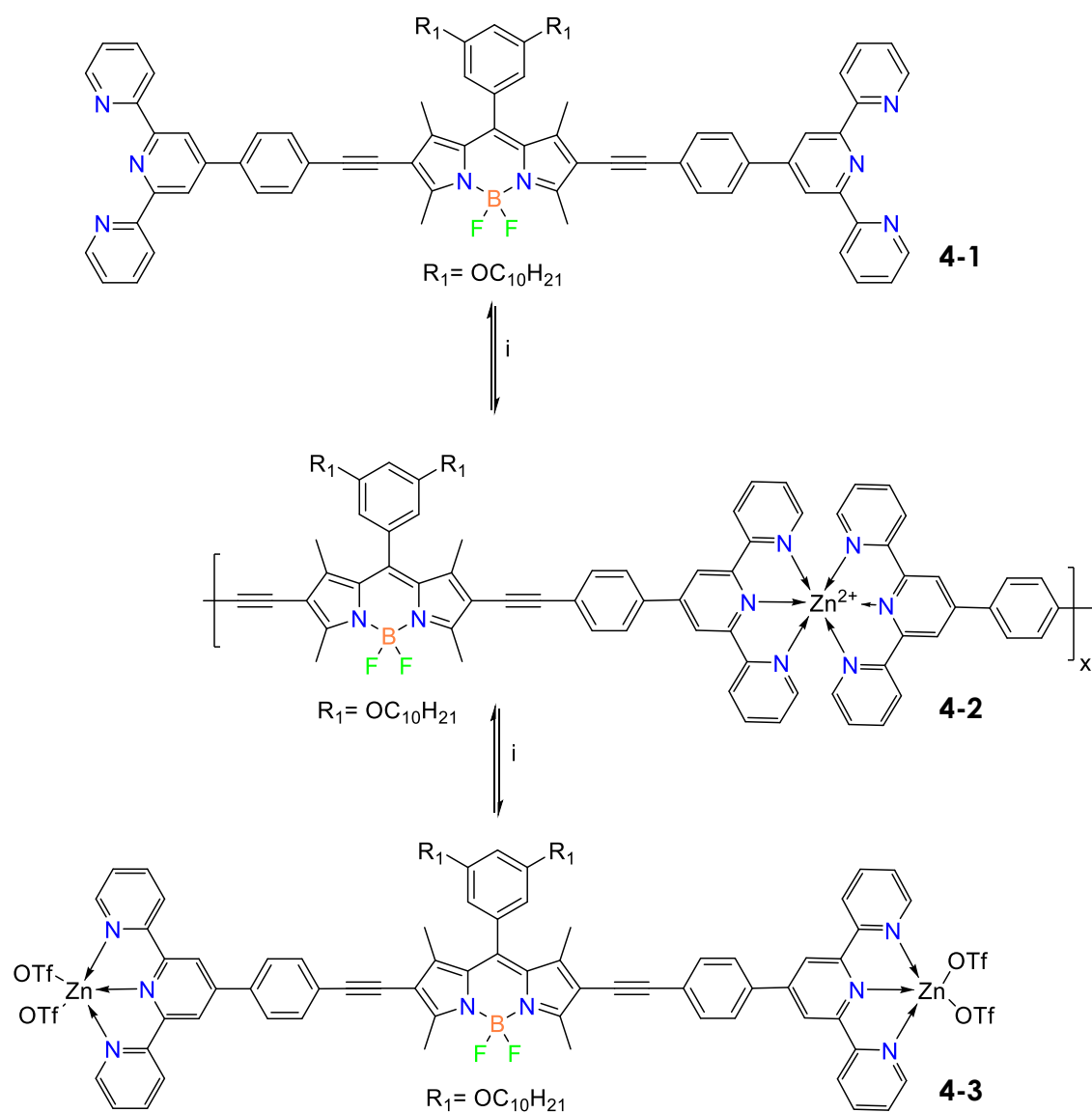
common organic solvents.⁴² Additionally, they have moderate solubility in mineralized aqueous solutions *via* using the corresponding alkali metal halide salt (*e.g.* saturated potassium iodide for copper(I) iodide).^{42, 61} This lack of the solubility of copper(I) species hinders the implementation of conventional solution synthetic crystal-growth techniques.⁴² It should be stated that, the experiments presented in this chapter rely on the solubility of copper(I) halides in acetonitrile. Secondly, molecular oxygen from the air could lead to oxidation of the copper by forming mixed valence copper(I/II) halides or potentially pure copper(II) halide complexes.^{42, 62} Copper(I) iodide is more stable to oxidation than copper(I) bromide, and chloride because iodide is a larger, softer, more polarizable species, the covalent interaction between copper(I) and iodide is more significant, and thus copper(I) iodide is more stable than copper(I) bromide, and chloride.

4.1.2 BODIPY Based Coordination Polymers

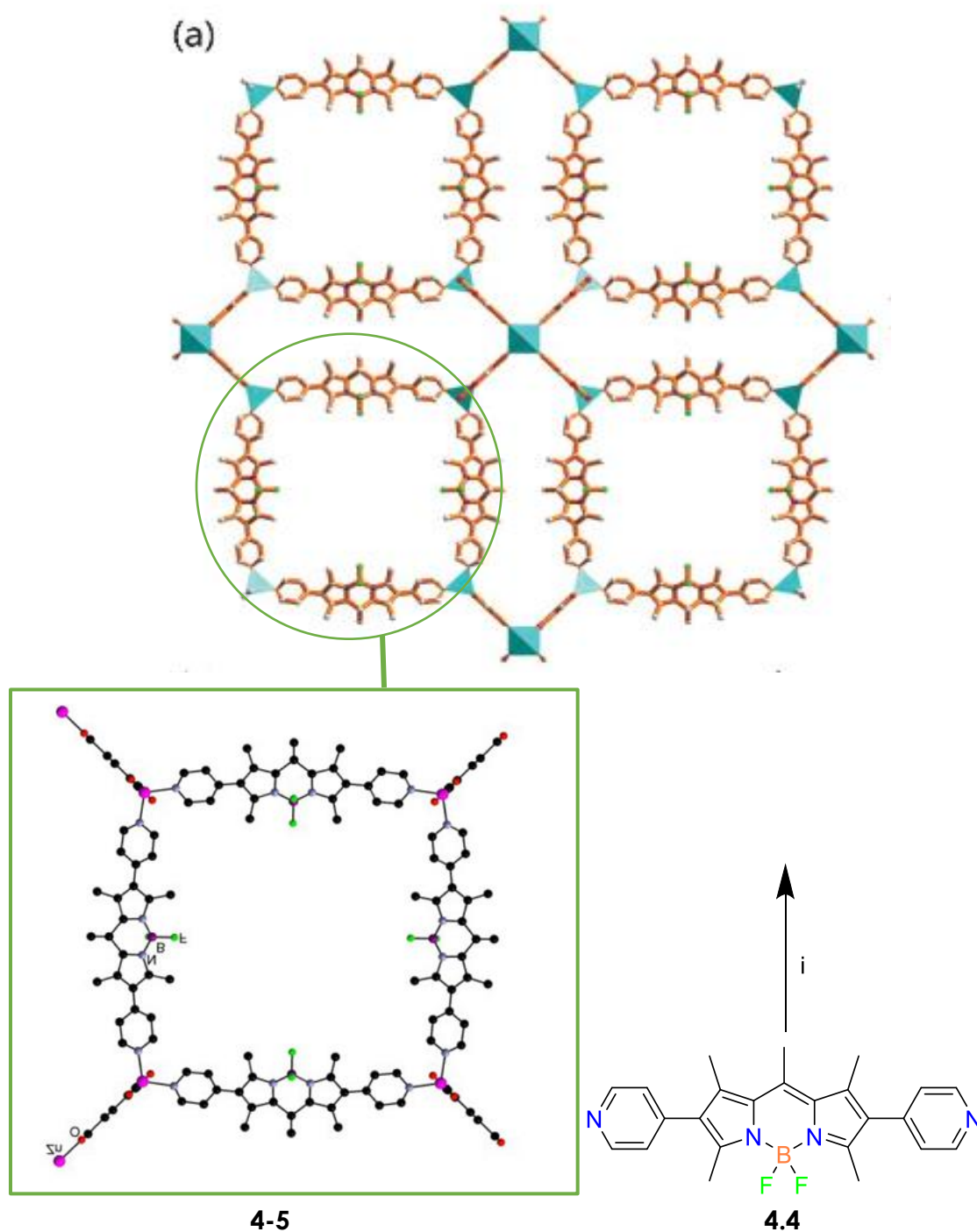
As a result of the modular, building-block approach it is possible to incorporate specific components into the coordination polymer framework that impart specific properties on the resulting material.²¹ Thus, ligands that possess such properties can be attractive to target designed CPs. An example of a family of interesting ligands is the BODIPY core. BODIPYs are highly functionalized, π -conjugated molecules that can be tailored to various applications.⁶³⁻⁶⁵ The BODIPY family has many excellent features, including their high quantum yields, tunable absorption/emission,⁶⁶⁻⁶⁹ and highly stability.^{66, 70, 71} Due to their excellent performance as dyes, flexibility in functionality and their optical reactivity, it could be advantageous to use peripheral coordinating functionalised BODIPY as linkers in coordination polymers and metal organic framework.⁷² The early attempts of using BODIPY for coordination polymer construction yielded non-crystalline systems.⁷² In 2009, Akkaya and his co-workers⁷³ prepared

BODIPY **4-1** (**Scheme 4.1**), where the (2, and 6) positions in the BODIPY core is functionalized by two ethynyl-terpyridyl groups.⁷³ Upon the addition of up to one equivalent of Zn(OTf)₂ the polymer (compound **4-2**) is formed, which confirmed by absorption, fluorescence and NMR spectroscopies. The absorption band in CHCl₃/MeOH mixture, shows an intense absorption peak as well as a blue shift in the emission band (from 608 to 602 nm). However, it was not possible to precipitate or crystallise the polymer (**4-3**) which was probably due to the presence of long alkyl chains on the dipyrromethene. Further addition of Zn(OTf)₂ afforded dinuclear Zn(II). The use of bipyridyl analogues of BODIPY **4-1** led to a more complicated behaviour as a result of the octahedral coordination of the metal ions.^{72, 73}

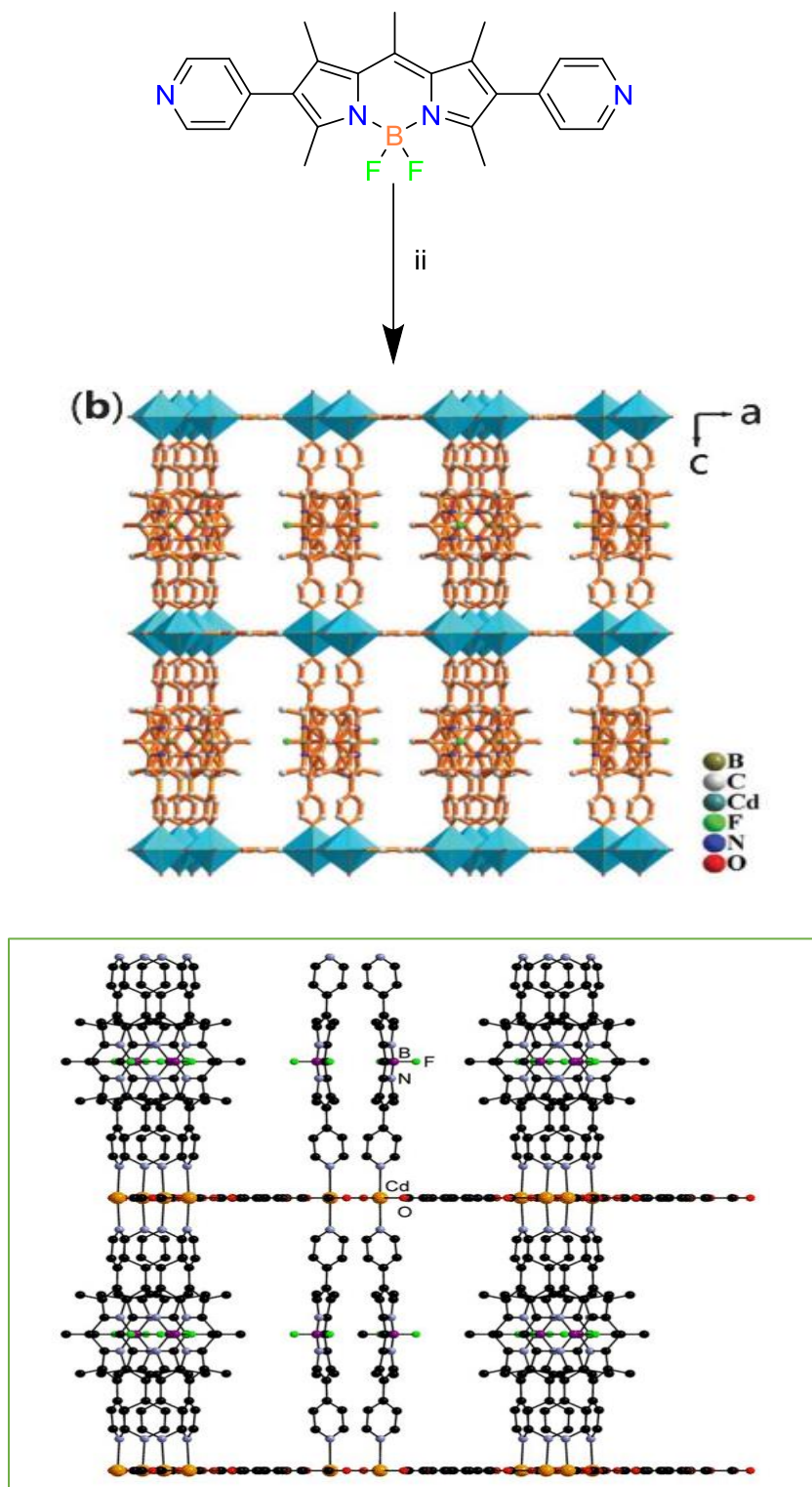
Two years later, Lan, You and coworkers explored the formation of luminescent gels by assembling Ag(I) salt with *meso* imidazolyl functionalized BODIPY.^{73, 74} In 2013, a pyridine-functionalized BODIPY ligand bearing two pyridyl moieties at (2, and 6) positions (compound **4-4** in **Scheme 4.2**, where R = CH₃), was employed in the construction of two MOF material. The first MOF was formed by combining BODIPY **4-4** with 1,3,5-benzenetricarboxylate (H₃btc) and the Zn(II) cation. In this case, two-fold layers formed by coordination of the BODIPY and H₃btc to Zn(II) mononuclear nodes to form a paddlewheel type Zn(II) nodes, which formed by binding of the carboxylate to Zn(II) nodes as MOF **4-5** in **Scheme 4.4**. The second MOF **4-6** was formed by combining BODIPY with 1,4-benzenedicarboxylate (H₂bdc) and Cd(II) centers.⁷⁵ In this case, binuclear Cd(II) nodes are bridged by H₂bdc ligands to form 3D framework with a Kagome sheets pillared by BODIPY. MOF **4-7** has the ability to retain its crystallinity upon solvent evacuation and to exhibit permanent porosity. Both materials (compound **4-3**, and **4-5**) show an emission at 542 nm upon excitation at 512 nm in the solid state, subsequently, from luminescence of the BODIPY struts.^{73, 74}



Scheme 4.1. Dynamic equilibrium between BODIPY (**4-1**), a polymer (**4-2**) and a dinuclear complex (**4-3**). (i) Zn(OTf)₂ in a CHCl₃/MeOH mixture.⁷³

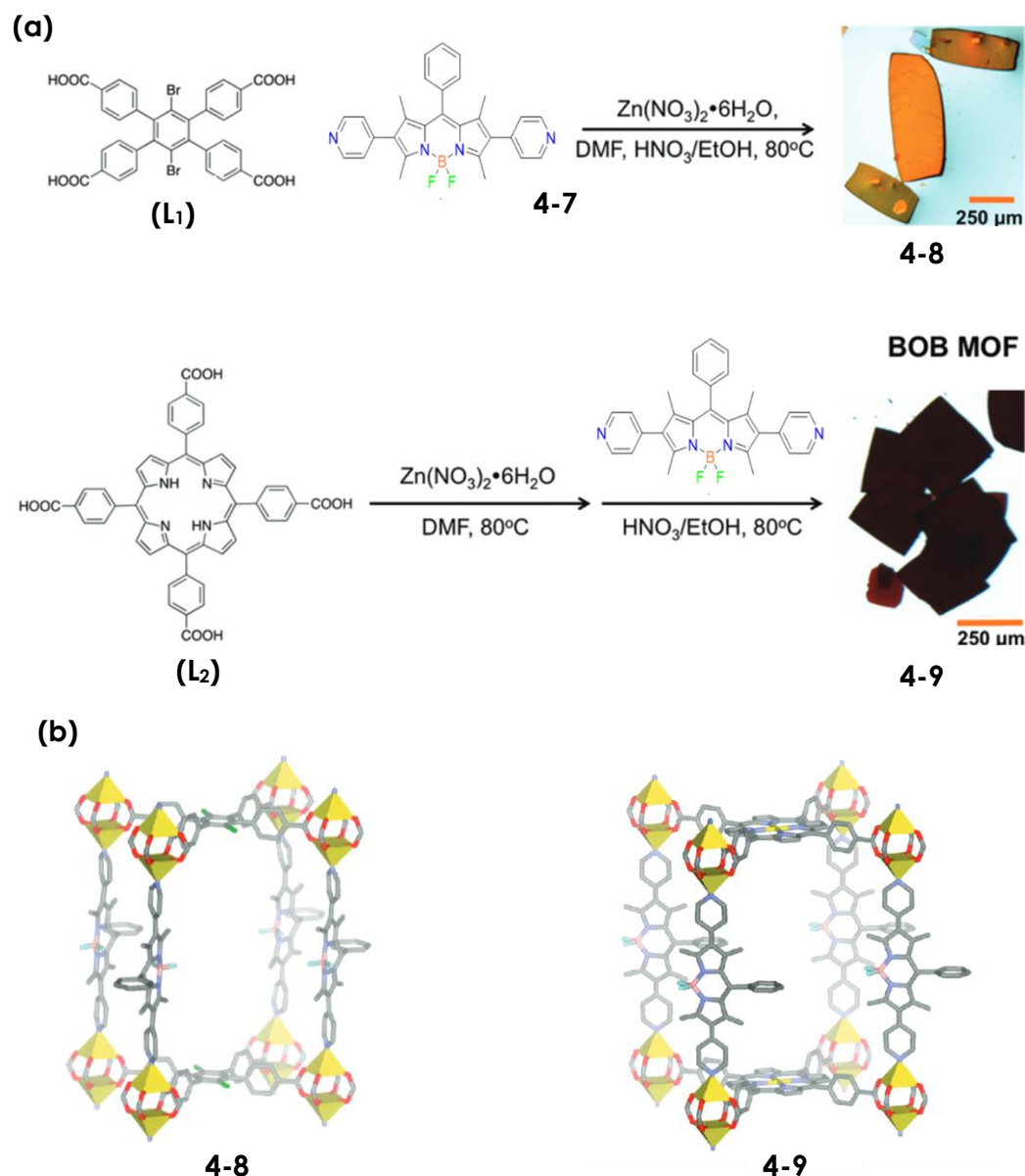


Scheme 4.2. Synthesis of the BODIPY compounds and crystal structures of the corresponding MOFs **4-5** $[\text{Cd}(\text{4.4})(\text{bdc})]$, (i) $\text{H}_3\text{btc}, \text{Cd}(\text{NO}_3)_2 \cdot 4\text{H}_2\text{O}$, DMF, and an aliquot of HNO_3 , EtOH 80 °C for 2 days. Hydrogen atoms have been omitted for clarity. Reproduced from references 72, and 74.



Scheme 4.3. Synthesis of the BODIPY compounds and crystal structures of the corresponding MOFs **4-6** ($[\text{Zn}_3(4-4)_2(\text{btc})_2(\text{H}_2\text{O})]$), (ii) $\text{H}_3\text{btc}, \text{Zn}(\text{NO}_3)_2 \cdot 6\text{H}_2\text{O}$, DMF, and an aliquot of HNO_3 , EtOH 85 °C for 2 days. (ii) Hydrogen atoms have been omitted for clarity. Reproduced from references 73, and 74.

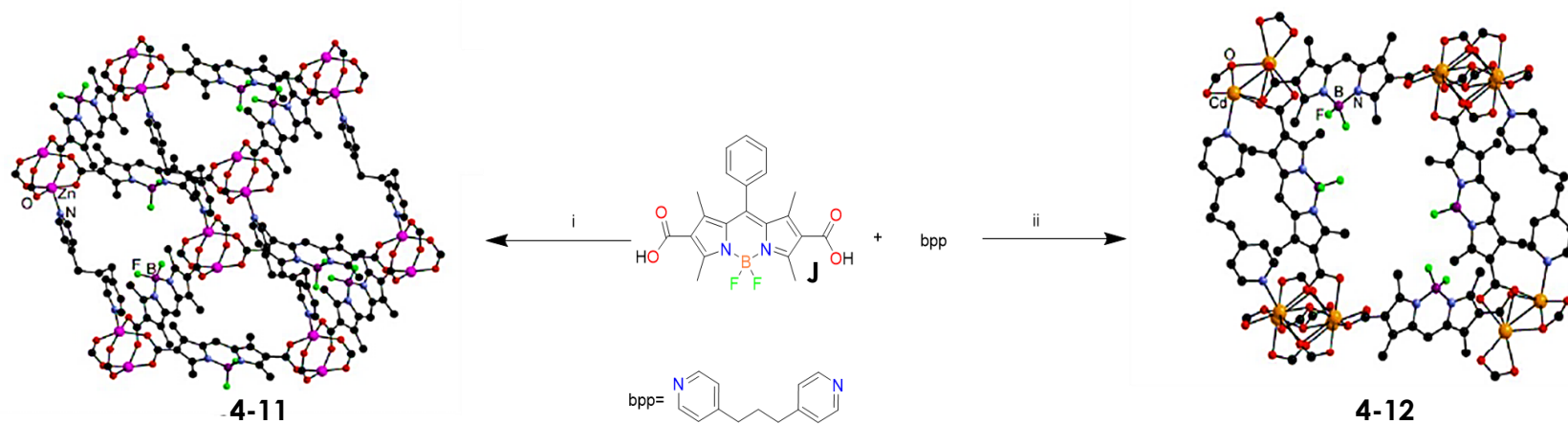
In the same year, Hupp and co-workers⁷⁶ reported an examples of luminescent MOFs where the BODIPY struts can perform either as source of emission or antenna for the sensitization of another emitter present in the construction.⁷⁶



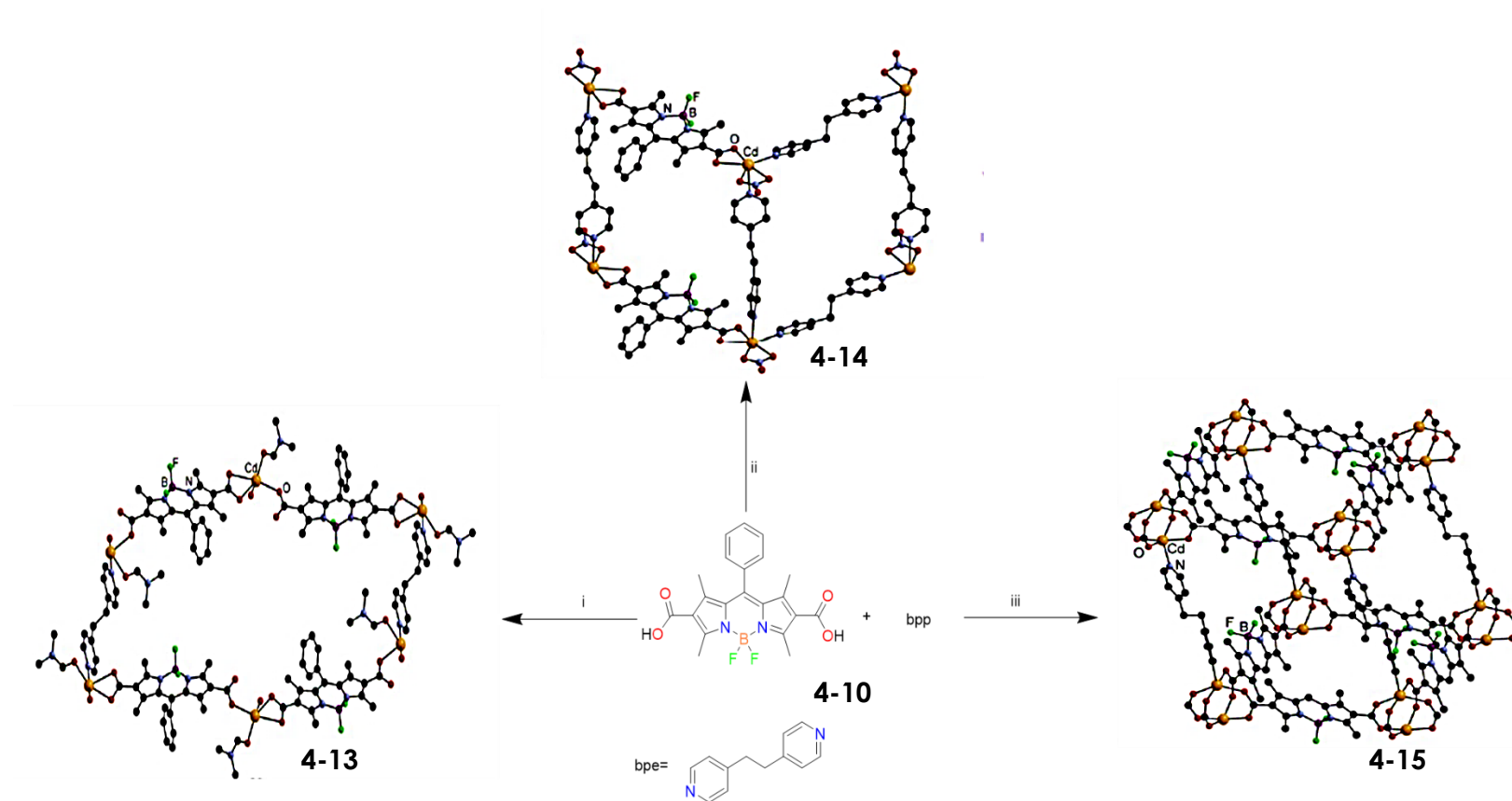
Scheme 4.3. (a) Synthesis of the BODIPY compounds **4-8** (**BOP MOF**, with the formula $\text{Zn}_2(\text{Zn-L}_1)(\text{4-7})$, and **4-9** (**BOB MOF** with the formula $\text{Zn}_2(\text{L}_2)(\text{4-7})$) and images to the right of the equations are digital photographs of the respective MOF crystals.⁷⁶ (b) Crystal structures of the corresponding MOFs **4-8**, and **4-9**. Hydrogen atoms have been omitted for clarity.^{72, 76} Atoms are coloured as follows: yellow polyhedral = Zn, red = O, green = Br, blue = N, pink = B, sky blue = F, grey = C. Reproduced from reference 76, and 72.

BODIPY **4-7** has been reacted with $\text{Zn}(\text{NO}_3)_2$, and tetracarboxylic acids based on an aromatic or a porphyrin core to yield MOFs **4-8** and **4-9**, respectively (**Scheme 4.3**). The coordination of the tetracarboxylates with binuclear $\text{Zn}(\text{II})$ paddlewheel nodes, which pillared by the BODIPY ligand formed 2D sheets. Upon excitation at 520 nm, the emission centers were detected at 596 nm, and 667 nm for **4-8** and **4-9**, respectively. The red shift in the emission of **4-9** could be explained by energy transfer from the BODIPY to the $\text{Zn}(\text{porphyrin})$ unit, which known to emit in this range. This is confirmed in the excitation spectrum collected for a fixed emission at 667 nm showing contribution from both struts. Combining emitters is an interesting approach for the preparation of light-harvesting materials.⁷⁷⁻⁷⁹

Ding, Zhao, Hou and coworkers⁸⁰ have explored the formation of pillared-layer structures, by using BODIPY **4-10** as the bridging ligand to form five MOFs (**4-11**, **4-12**, **4-13**, **4-14**, **4-15**) under different solvothermal conditions (**Scheme 4.4**, and **Scheme 4.5**).⁸⁰ In these examples, the BODIPY linker **4-10** functionalized by carboxylic acid moieties at the (2,6) positions which assemble with $\text{Zn}(\text{II})$ and $\text{Cd}(\text{II})$ cations. The bpe and bpp are used as pillars (*i.e.* bpe = 1,2-bis(4-pyridyl)ethane; bpp = 1,3-bis(4-pyridyl)propane). In case of **4-11**, two-dimensional sheets are formed, the $\text{Zn}(\text{II})$ cations are organized in a paddlewheel fashion and the bpp co-ligand acting as a pillar coordinated at the axial positions. However, changing the $\text{Zn}(\text{II})$ cation to $\text{Cd}(\text{II})$ cation formed more complex structure **4-12**. The construction of **4-13** is a three-dimensional structure but based on tetranuclear nodes bridged by both bpp and the conjugate base of **4-10**; no interpenetration is observed. An ethylene bridge has been used to limit the flexibility of the co-ligand (bpe). MOFs **4-13** and **4-14** are both two-dimensional networks based on mononuclear nodes bridged by bpe and **4-10** and capped by either DMF or water molecules or nitrate anions

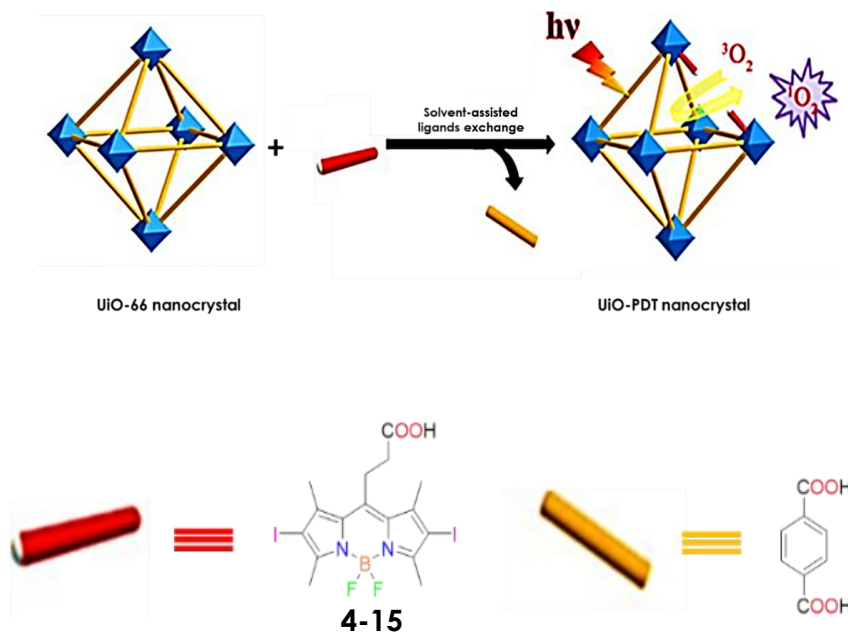


Scheme 4.4. Synthesis of the BODIPY compounds and crystal structures of the corresponding MOFs **4-11**, and **4-12**. (i) bpp, $\text{Cd}(\text{NO}_3)_2 \cdot 4\text{H}_2\text{O}$, DMF, and an aliquot of HNO_3 , EtOH (1/2), 80 °C. (ii) bpp, $\text{Zn}(\text{NO}_3)_2 \cdot 6\text{H}_2\text{O}$, DMF, and an aliquot of HNO_3 , EtOH (1/2), 80 °C. Hydrogen atoms have been omitted for clarity. Reproduced from reference 72.



Scheme 4.5. Synthesis of the BODIPY compounds and crystal structures of the corresponding MOFs **4-13**, **4-14** and **4-15** (i) bpe, $\text{Cd}(\text{NO}_3)_2 \cdot 4\text{H}_2\text{O}$, DMF, and an aliquot of HNO_3 , EtOH (1/2), 80°C . (ii) bpe, $\text{Cd}(\text{NO}_3)_2 \cdot 4\text{H}_2\text{O}$, DMF, and an aliquot of HNO_3 , EtOH (1/1), 80°C . (iii) bpe, $\text{Cd}(\text{NO}_3)_2 \cdot 4\text{H}_2\text{O}$, DMF, and an aliquot of HNO_3 , EtOH (1/2), 100°C . Hydrogen atoms have been omitted for clarity.⁷²

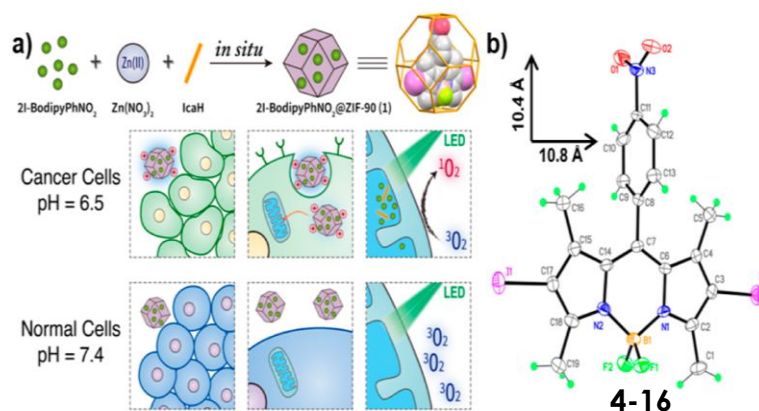
Furthermore, a pillared-layer architecture with a two-fold interpenetration, MOF **4-15**, has been obtained, as an analogue of **4-11** but incorporating the bpe ligand and Cd(II) cations.^{72, 80} The photophysical properties of the MOFs have been investigated considering the crystal structures and particularly the relative arrangement of the BODIPY cores. These five MOF's all demonstrated very low fluorescence intensities with minimally shifted spectra but there is a seemingly infinite number of framework combinations that can be pursued and thus these BODIPY-MOF's are of high interest. Compound **4-14** displayed a relatively higher quantum yield (0.017) which is explained by the absence of dimers formed by BODIPY cores within the crystal, unlike in the other MOFs where packing or interpenetration yields to aggregates.



Scheme 4.6. Schematic presentation of UiO-PDT nanocrystal synthesis and its application in PDT. Reproduced from reference 81.

In 2016, Xie *et al.*⁸¹ reported the synthesis of a nano-sized MOF (NMOF) based on BODIPY and zirconium metal. The BODIPY which has been used in this paper is the carboxyl-

functionalized diiodo-substituted BODIPY **4-16** which was incorporated into the nanoscale UiOMOFs (UiO-66) in order to exert the PDT into final product of UiO-PDT by solvent-assisted ligands exchange (SALE) (**Scheme 4.5.**). The great feature of SALE lies in its versatility and efficiency to introduce pre-designed linkers with new functions into frameworks without losing the topology of the parent crystal. The resulting MOF has low cytotoxicity in the dark, improved photophysical properties and cellular uptake. Additionally, it has highly efficiency to generate singlet oxygen which can be further applied as potential PDT agent in cancer treatment.⁸¹



Scheme 4.7. (a) Schematic illustration of the fabrication of 1 and artistic representation of its pH-driven selective uptake toward cancer and normal cells and mitochondria targeting under PDT conditions. (b) Perspective view of 2I-BODIPY PhNO₂. Reduced with permission from reference 82.

In 2018, Guan *et al.*⁸² reported for the first time an NMOF-based host–guest photosensitive system; 2I-BODIPY Ph-NO₂@ZIF-90 (**BODIPY 4-17**). The compound synthesized *via* a one-pot “ship-in-a-bottle” synthetic approach and the resulting NMOF has good features such as low cytotoxicity, high cell permeability, pH-driven charge reversion and selective intracellular uptake, mitochondria targeting, and strong ¹O₂ generating features by the “heavy

atom effect” (i.e. *via* PDT treatment mechanism). Therefore, it could selectively and effectively kill cancer cells.⁸²

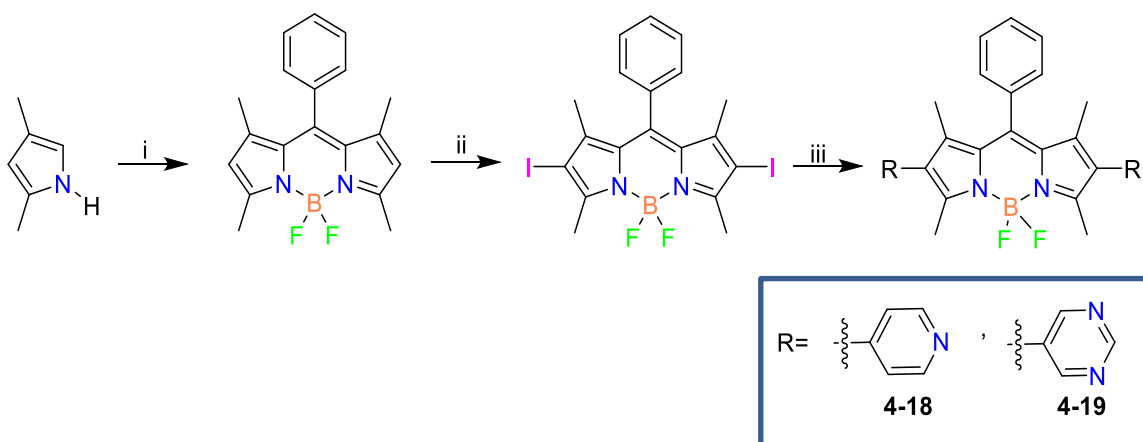
4.2 Aims and Objectives

This project focuses on the synthesis of novel coordination polymers based on BODIPY molecules and copper iodide moieties. In general, BODIPYs are highly functionalized, π -conjugated molecules that can be tailored to various applications⁶³⁻⁶⁵. Due to the flexibility in functionality and their optical and photophysical reactivity, it could be advantageous to use functionalized BODIPY as linkers in coordination polymers to afford materials with interesting photophysical properties.⁷² However, the coordination polymers based on BODIPY linkers have remained relatively unexplored⁸⁰ by several studies of using metal ions such as Zn(II),^{15, 72, 73, 75, 76} Ag(I)⁷⁴ and Cd(II).^{15, 75, 83} On the other hand, there is intense research interest of copper(I) complexes containing polydentate nitrogen ligands due to their rich structural chemistry as a result of the d^{10} electronic configuration of Cu(I), which gives rise to a variety of attractive coordination framework architectures and remarkable photochemical and photophysical characteristics,^{8, 41, 84} and various applications, such as stimuli-responsive luminescence,^{85, 86} solid-state lighting,^{87, 88} and antibiotic sensor.⁸⁴ Considering the strong coordination affinity of Cu(I) to pyridine and pyrimidine, we are thus interested in developing a pyridyl, and pyrimidyl functionalized BODIPY in order to use them as ligand in coordination polymer construction. We are particularly interested in the investigation of the solid-state structure, photophysical and electrochemical properties of the ligand and the effect of the copper iodide on the solid-state structure, optical, and fluorescence properties of these dye molecules.

4.3 Results and discussion

4.3.1 Synthesis and Structural Studies of the Ligands

A functionalized BODIPY ligand comprising two pyridyl donors in the 2- and 6-positions, 2,6-dipyridyl-1,3,5,7-tetramethyl-8-phenyl-4,4-difluoroboradiazaindacene (**4-18**; Pyr-BODIPY), was synthesized according to a literature procedure.⁸⁹ The synthetic procedures are summarized in **Scheme 4.8**. Briefly, the BODIPY ligand **4-18** was synthesised *via* Suzuki coupling reaction of 2,6-diiodo-1,3,5,7-tetramethyl-8-phenyl-4,4-difluoroboradiazaindacene and pyridinyl boronic acid.⁸⁹ Adapting the same strategy, a novel ligand (**4-19**; Pyrm-BODIPY) was prepared.



Scheme 4.8. Synthesis of the BODIPY compounds **4-18**, and **4-19**. (i) Benzoyl chloride, CH₂Cl₂, r.t., 16 h, Et₃N, BF₃·Et₂O, r.t., 1h. (ii) NIS, CH₂Cl₂, r.t., 30 min. (iii) 1,4-dioxane, water, 4-pyridinylboronic acid for (**4-18**)⁸⁹ or pyrimidine-5-boronic acid for (**4-19**), Cs₂CO₃ Pd(PPh₃)₄, N₂, reflux, 24h.

Single crystals suitable for X-ray diffraction were grown for compounds **4-18** and **4-19**. Two single crystal structures for compound (**4-18**) were successfully determined exhibiting polymorphism (**4-18.a***, **4-18.b***)

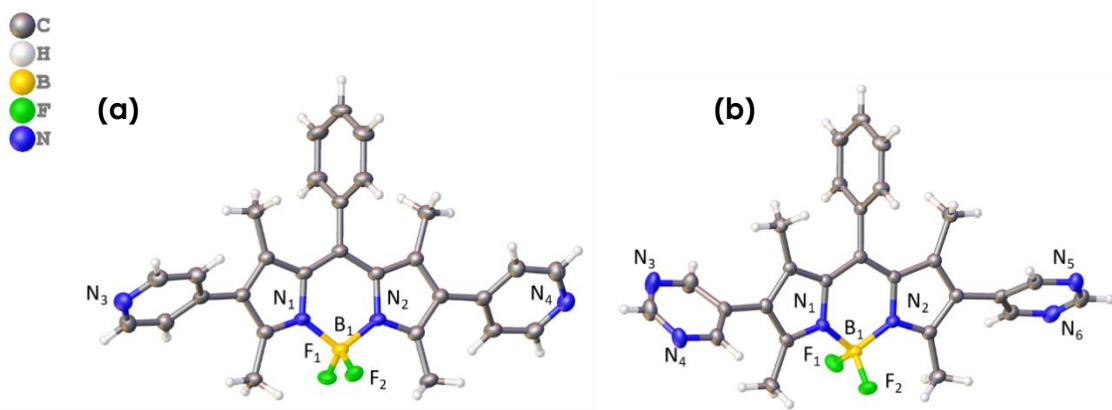
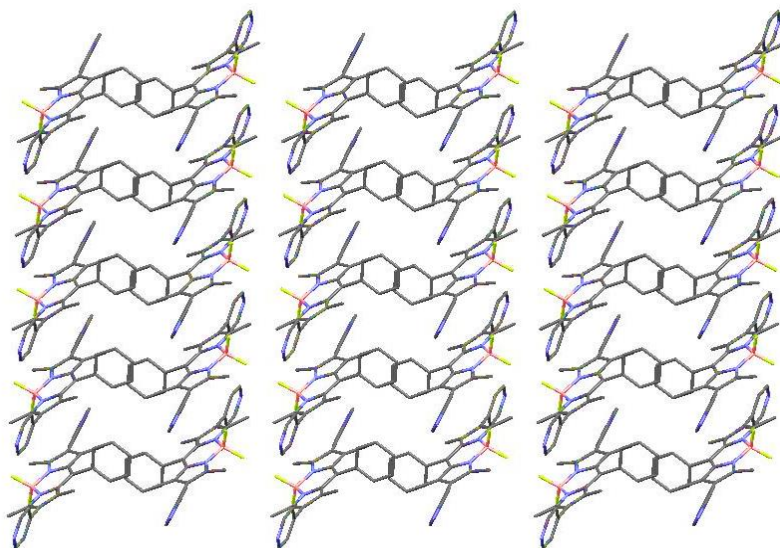


Fig 4.5. Crystal structure of the uncoordinated (a) Pyr-Bodipy, and (b) Pym-Bodipy ligand. Carbon = grey, nitrogen = blue, boron = yellow, fluorine = green.

In both compounds the solid-state structure confirms the identity of the product and the relative arrangement of the pyridine and pyrimidine moiety with respect to the BODIPY core (**Figure 4.5**). The Pyr-Bodipy and Pym-Bodipy compounds crystallise by slow evaporation of the compound, from CH_2Cl_2 (**4-18.a***, **4-18.b***) or acetonitrile (**4-19**) solution. Crystal **4-18.a*** crystallises in the triclinic space group $P-1$, while **4-18.b*** crystallise in monoclinic space group $I2/a$, and **4-19** crystallise in monoclinic space group $P2_1/c$. The asymmetric unit of (**4-18.a***, and **4-19**) contains one molecule while the asymmetric unit of (**4-18.b***) contains half a molecule of **4-18**. The *meso* phenyl ring on the BODIPY core (**4-18.a***, **b***, and **4-19**) is almost orthogonal to the indacene plane, which is expected to minimize unfavourable steric clashes between the ortho-hydrogen atoms and the vicinal methyl groups on the pyrrole. Interestingly, the relative orientation of nearest- neighbour molecules for these polymorphs are different, edge-to-face, tail -to-tail for **4-18.a***, and edge-to-face and face-to-tail for **4-18.b***, and edge-to-face, edge-to-tail and face -to-tail for **4-19**. The crystal lattices of the three forms have different symmetries with molecular polarity assumed as an ordering parameter. The packing motif of **4-18.a***, along b-axis is similar to **4-19** while along c-axis is different (**Fig 4.6, 4.7, 4.8**).

(a)



(b)

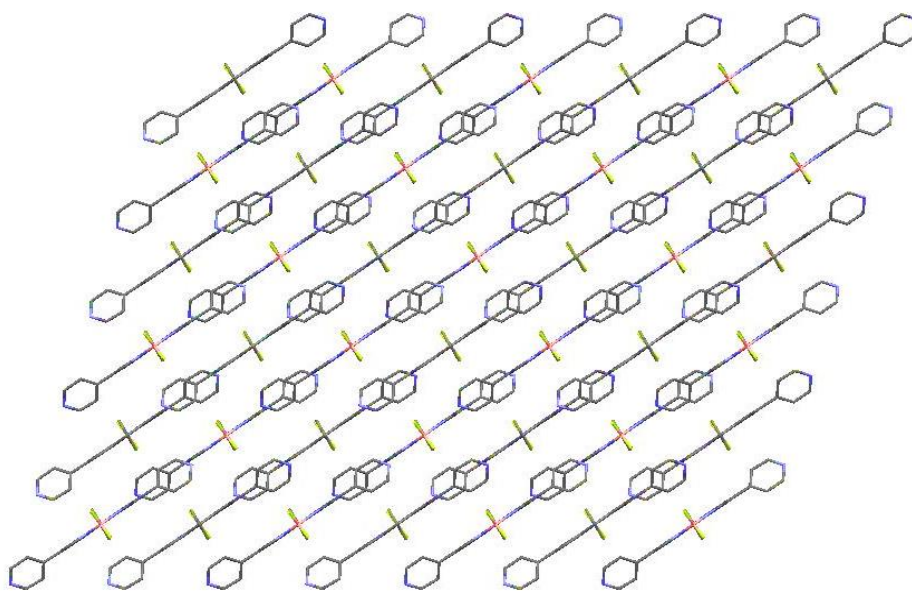
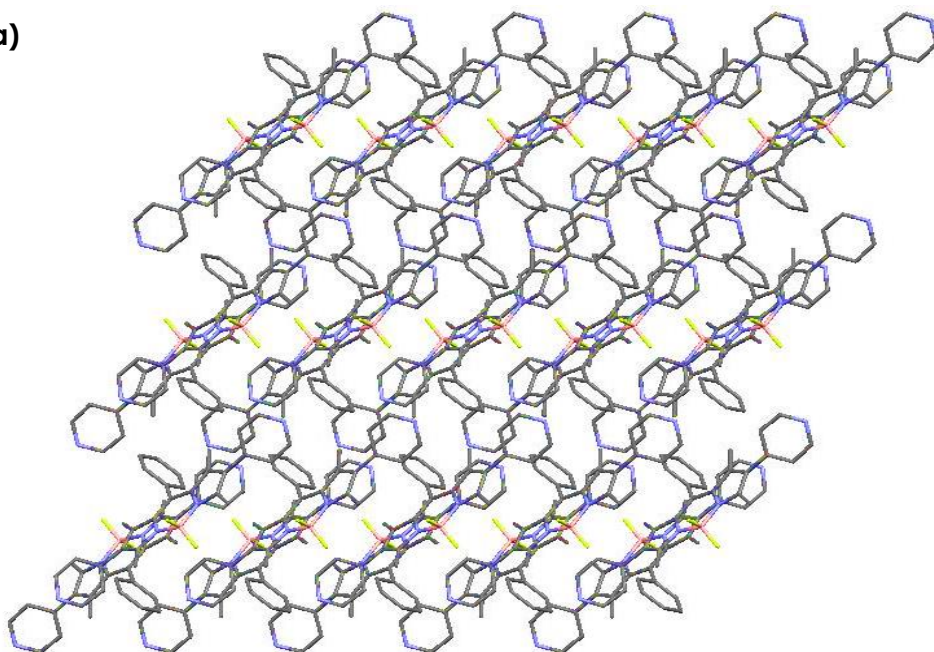


Fig 4.6. Orientation of (a) **4-18.a***, and (b) **4-18.b*** along the b-axis. All hydrogen atoms have been removed for clarity. Carbon = grey, nitrogen = blue, boron = pink, fluorine = green.

(a)



(b)

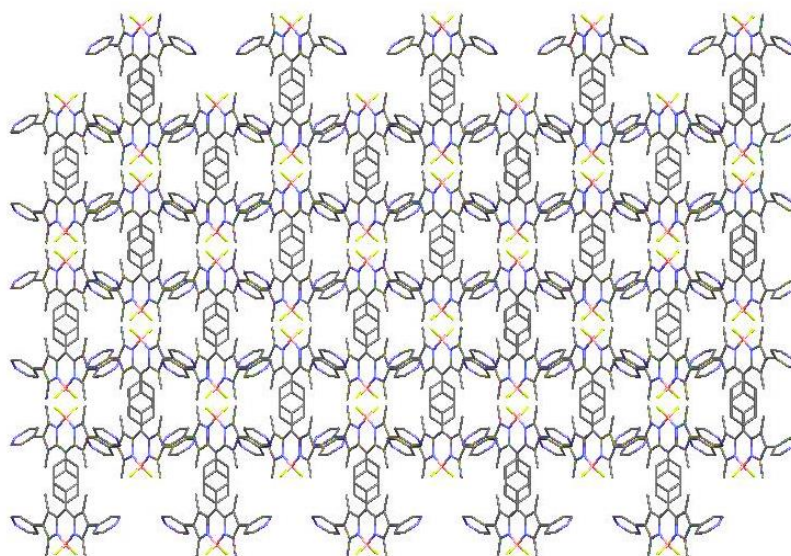
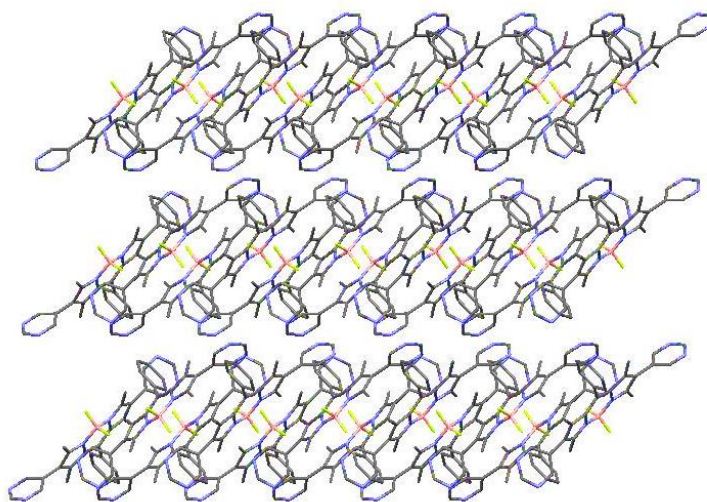


Fig 4.7. Orientation of (a) **4-18.a***, and (b) **4-18.b*** along the c-axis. All hydrogen atoms have been removed for clarity. Carbon = grey, nitrogen = blue, boron = pink, fluorine = green.

(a)



(b)

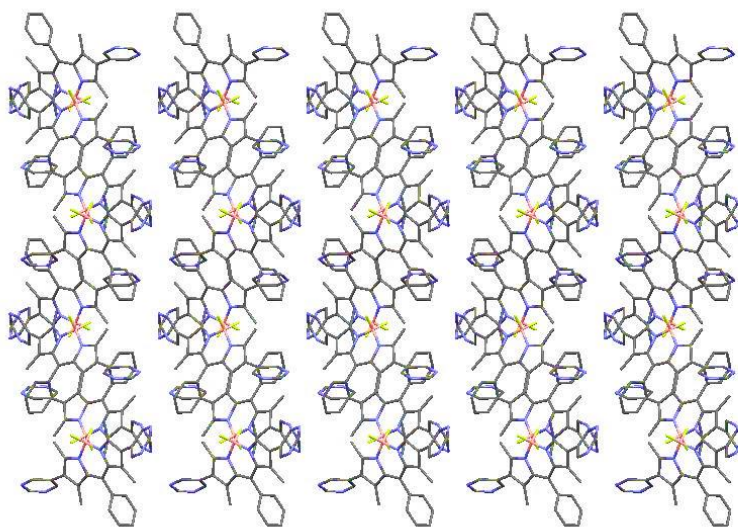


Fig 4.8. Orientation of **4-19** along the (a) b-axis (b) c-axis. All hydrogen atoms have been removed for clarity. Carbon = grey, nitrogen = blue, boron = pink, fluorine= green.

These compounds comprising pyridyl and, or pyrimidyl functionalities possess statistically comparable bond lengths and angles about the boron centre, with no deviations observed as a result of different β -substitution as showed in **Table 4.1**.

Table 4.1. Bond lengths (Å) and angles (°) for **4-18.a***, **4-18.b***, **4-19**.

	4-18.a*	4-19		4-18.b*
F₁-B₁	1.384(4)	1.389(2)	F₁-B₁	1.384(4)
F₂-B₁	1.389(4)	1.386(2)	F₁-B₁	1.389(4)
N₃-B₁	1.549(4)	1.552(2)	N₂-B₁	1.5484(18)
N₄-B₁	1.561(4)	1.551(2)	N₂-B₁	1.5484(18)
F₁-B₁-F₂	110.40(3)	109.71(15)	F₁-B₁-F₁	109.34(17)
N₄-B₁-N₄	106.40(2)	106.35(14)	N₂-B₁-N₂	106.93(16)

Crystallographic analysis of **4-18.a***, **4-18.b*** and **4-19** revealed the boron to be coordinated to one bidentate dipyrin ligand and two fluorine atoms in a distorted tetrahedral environment. The B-N bond lengths in **4-18.a*** [1.549(4) Å, 1.561(4) Å, Table 4.1] are similar to **4-18.b*** [1.5484(18) Å, Table 4.1] and [1.552(2) Å, for **4-19**]. The B-N bond lengths in (**4-18.a***, **4-18.b*** and **4-19**) are similar to those of other pyridyl analogues reported in literature^{69, 90} Also, the average B-F distance for **4-18.a***, **B** and **4-19** is 1.55 Å, while the average N-B-N and F-B-F angles are 106.40(2)°, 110.4(3)° for **4-18.a***, 106.93(14)°, 109.34(17)° for **4-18.a***, and 106.35(14)°, 109.71(15)° for **4-19**, respectively, in good agreement with those of other reported analogues.^{69,90}

In order to investigate and identify the various intermolecular interactions in **4-18.a***, **4-18.b*** and **4-19** as well understanding the effect of different crystal packing in **4-18.a***, and **4-18.b***, Hirshfeld surface analyses and their associated fingerprint plots were used.

Fig 4.9 shows the d_{norm} surface of **4-18.a*,b*** and **4-19**. Both d_i and d_e were measured for **4-18.a*, b** and **4-19**.

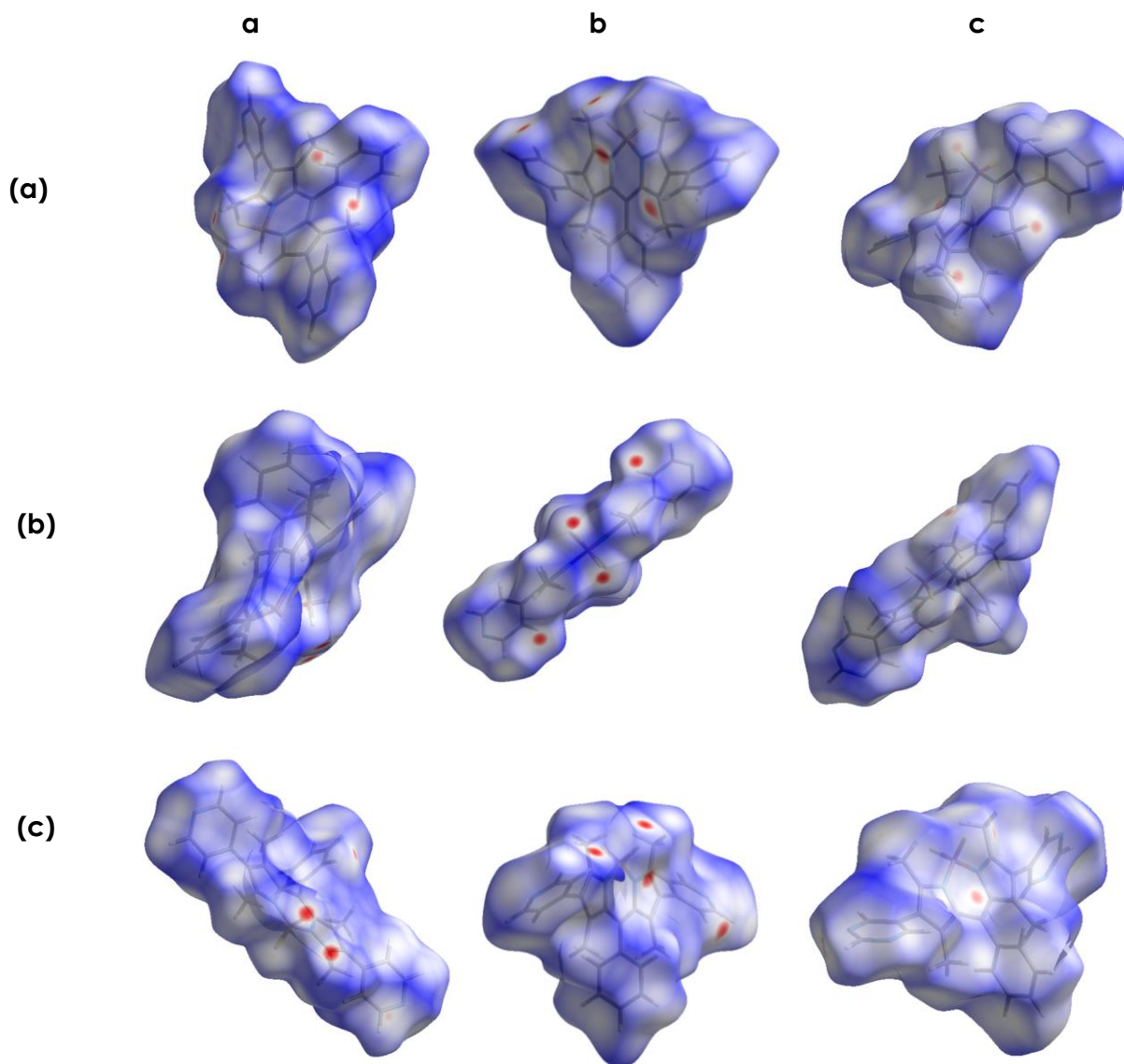


Fig 4.9 The d_{norm} surface of (a) **4-1.a***, (b) **4-1.b***, and (c) **4-19** , along a, b and c axis.

The first observation from the HSs represented in **Fig 4.9** is the intense red spot near the fluorine atoms on the BODIPY core for **4-18.a***, **4-18.b*** and **4-19**. In case of **4-18.a***, the

close CH $\cdots$ F contacts is between the hydrogen from methyl groups at the 3,5-positions of the pyrrole ring and a fluorine atom from a neighbouring BODIPY moiety, with a distance of approximately 2.44 Å which is shorter than the sum of the *van der Waals radii* for H and F, 2.56 Å, according to literature data.^{91, 92}

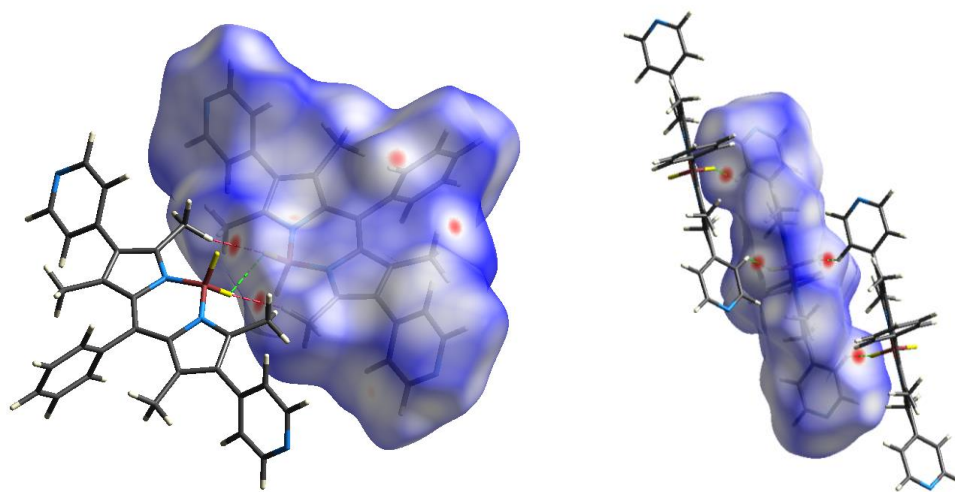


Fig 4.10 HSs of representation a close CH $\cdots$ F contact of **4-18.a*** (left) and **4-18.b*** (right).

The second case (**Fig 4.10**) is the close CH $\cdots$ F contacts in **4-18.b*** between fluorine atom from BODIPY core and a neighbouring hydrogen from pyridyl ring (β -hydrogen) which is approximately 2.44 Å.

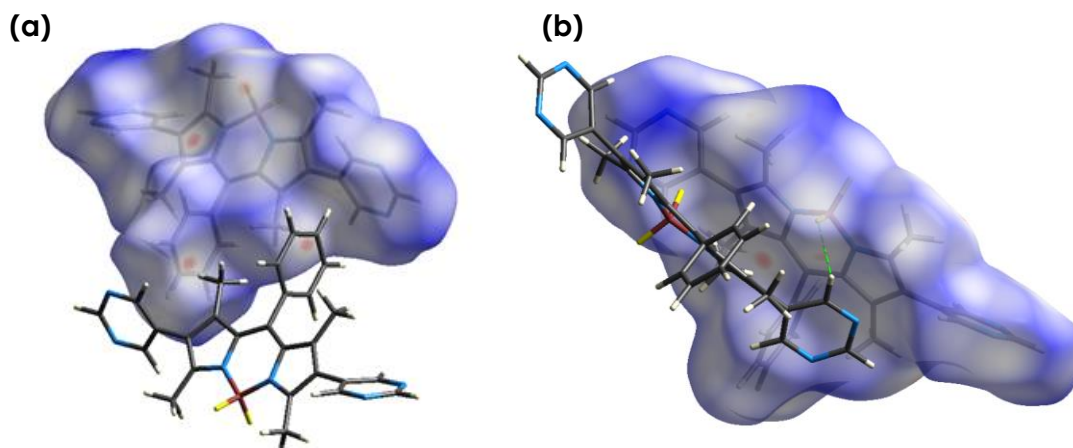


Fig 4.11 HSs of representation a close CH $\cdots$ F contact of **4-19**.

In the case of **4-19** (**Fig. 4.11**), there are two CH $\cdots$ F contacts. The first example (a, **Fig.4.11**) is the interaction between one hydrogen from methyl groups in the 3,5-positions of the pyrrole ring and a fluorine atom from a neighbouring BODIPY moiety, with a distance of 2.63 Å which is longer than **4-18a***. Another long CH $\cdots$ F contact is observed (b, **Fig.4.11**), between fluorine atom from BODIPY core and a neighbouring hydrogen from pyrimidyl ring with a distance of approximately 2.89 Å. In all the previous examples, fluorine atoms act as hydrogen-bond acceptors. **Fig 4.12** shows the 2D fingerprint plot contributions to the Hirshfeld surface area for CH $\cdots$ F contacts present in 2D fingerprint plots with 9.5% of the surface area in form **a***, 9.6% of the surface in **4.2**, and 11.5% of the surface in form **b***, respectively.

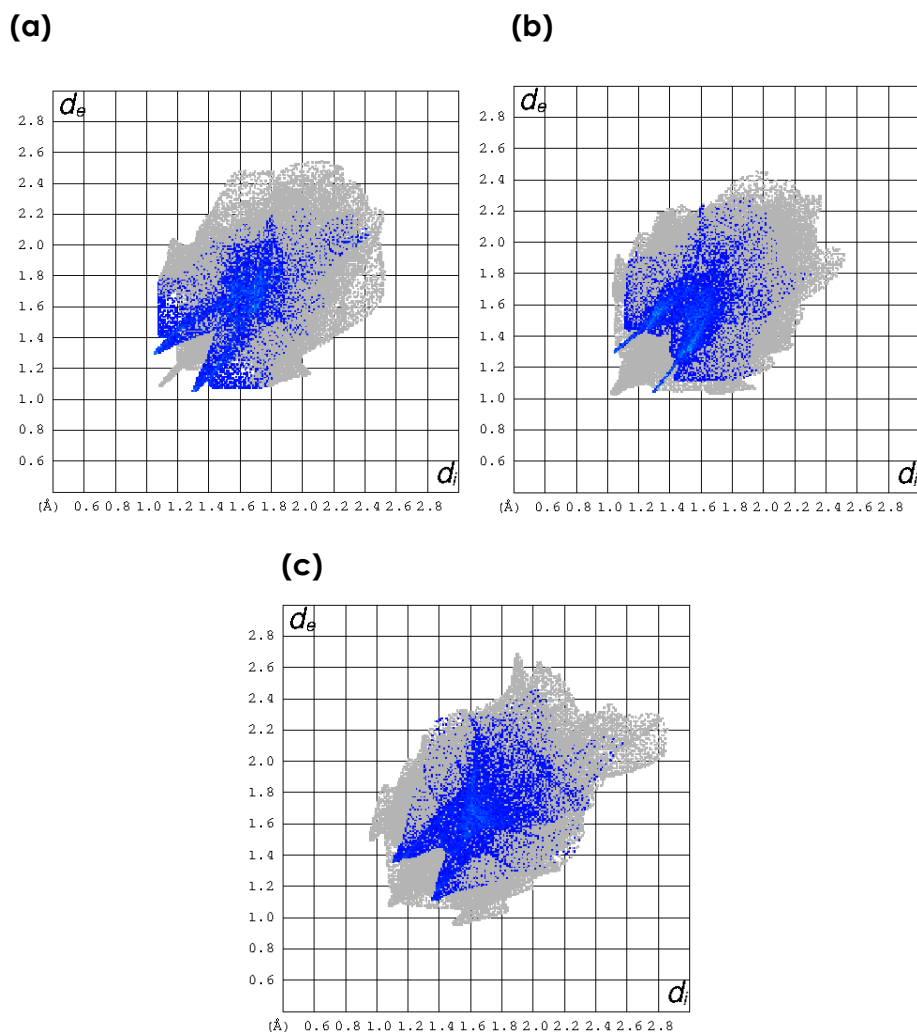
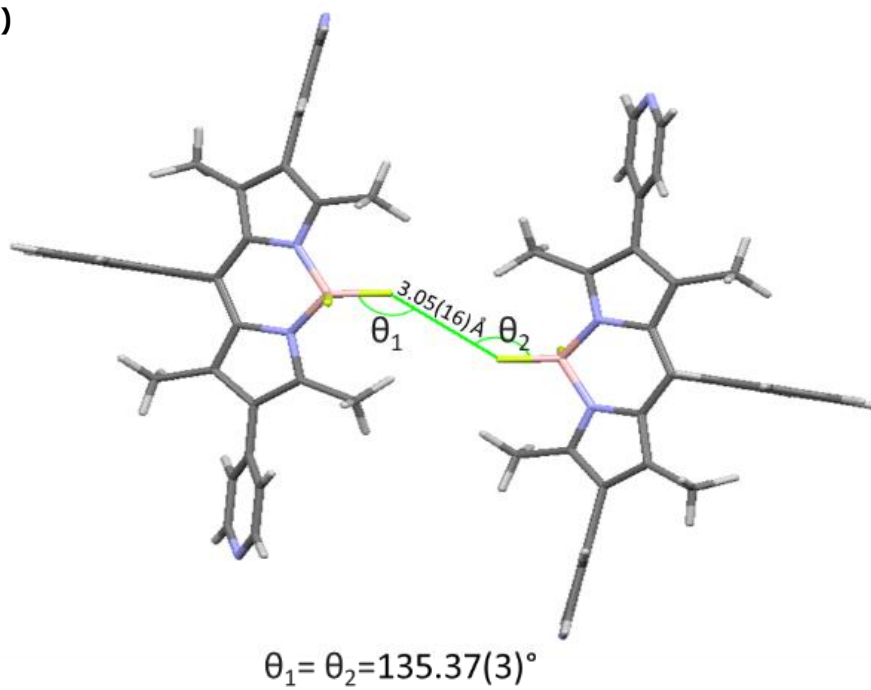


Fig 4.12. 2D fingerprint plots of compounds (a) **4-18.a***, (b) **4-18.b***, and (c) **4-19**, which highlight the F...H intermolecular contacts; to provide context, the outline of the fingerprint is shown in grey.

It should also be noted that in **4-18.a***, the distance between the fluorine atoms in the two neighbouring BODIPY is 3.053(2) Å, and the angles between B-F...F are identical, calculated as 135.37(11)°, within the range of type I halogen bonding interaction as discussed in **Chapter 3**. The B-F...F angle is in the range of type I (F...F) halogen bonding 137.51-135.41°, reported in CSD.⁹³

(a)



(b)

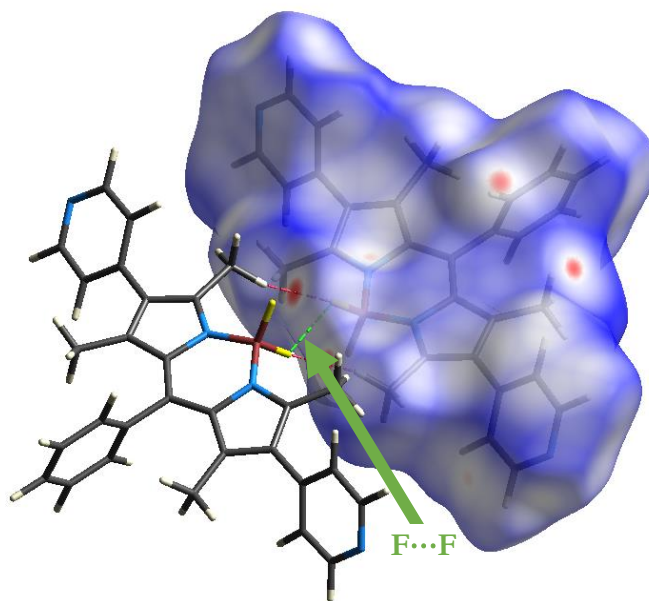


Fig 4.13. (a) Single crystal X-ray representation of type (I) halogen bonding interaction of **4-19.a***. (b) HSS representation a close F...F contact of **4-19.a**, which is highlighted in green.

However, the HSs does not show any red spot associated with F...F short contact (**Fig 4.13**), which might be because the distance between both the fluorine are longer than the range reported previously of such interaction 2.688(4) Å to 2.856(4) Å.⁹² Moreover, the F...F distance in **4-19** is longer than the doubled *van der Waals radius* of F (2.94 Å).^{92,94} As described in **Chapter 3**, the role of F...F nonvalent contacts in crystal packing is still ill-defined. According to Pauling's principle, fluorine atoms have the smallest radius and low polarization ability; therefore, fluorine's ability to act as a donor has been questioned repeatedly. However, theoretical and experimental charge density studies suggest the possibility of polarization of the electron cloud in fluorine.^{92,95}

The packing diagram of **4-18.a*** reveals that the molecules are connected by π - π interactions involving a pyridyl rings from one side of a BODIPY and a pyridyl from another BODIPY, where the plane [C₂₀ C₂₄ C₂₃ N₄ C₂₂ C₂₁] to plane [C₃ C₇ C₆ N₁ C₅ C₄] centroid distance is 2.92 Å, with 3.7115(3) Å as shift, 1.165(3)° as twist angle and fold angle of 17.3182(16)°. This interaction displays as intense red spot on HSs of **4-18.a*** (**Fig 4.14**). The pyridyl rings from the other side of the BODIPY are involved in (C-H... π) interactions with a proton from phenyl ring on the neighbouring BODIPY moiety. This interaction displays as intense red spot on HSs of **4-18.a*** as presented in **Fig 4.13**.

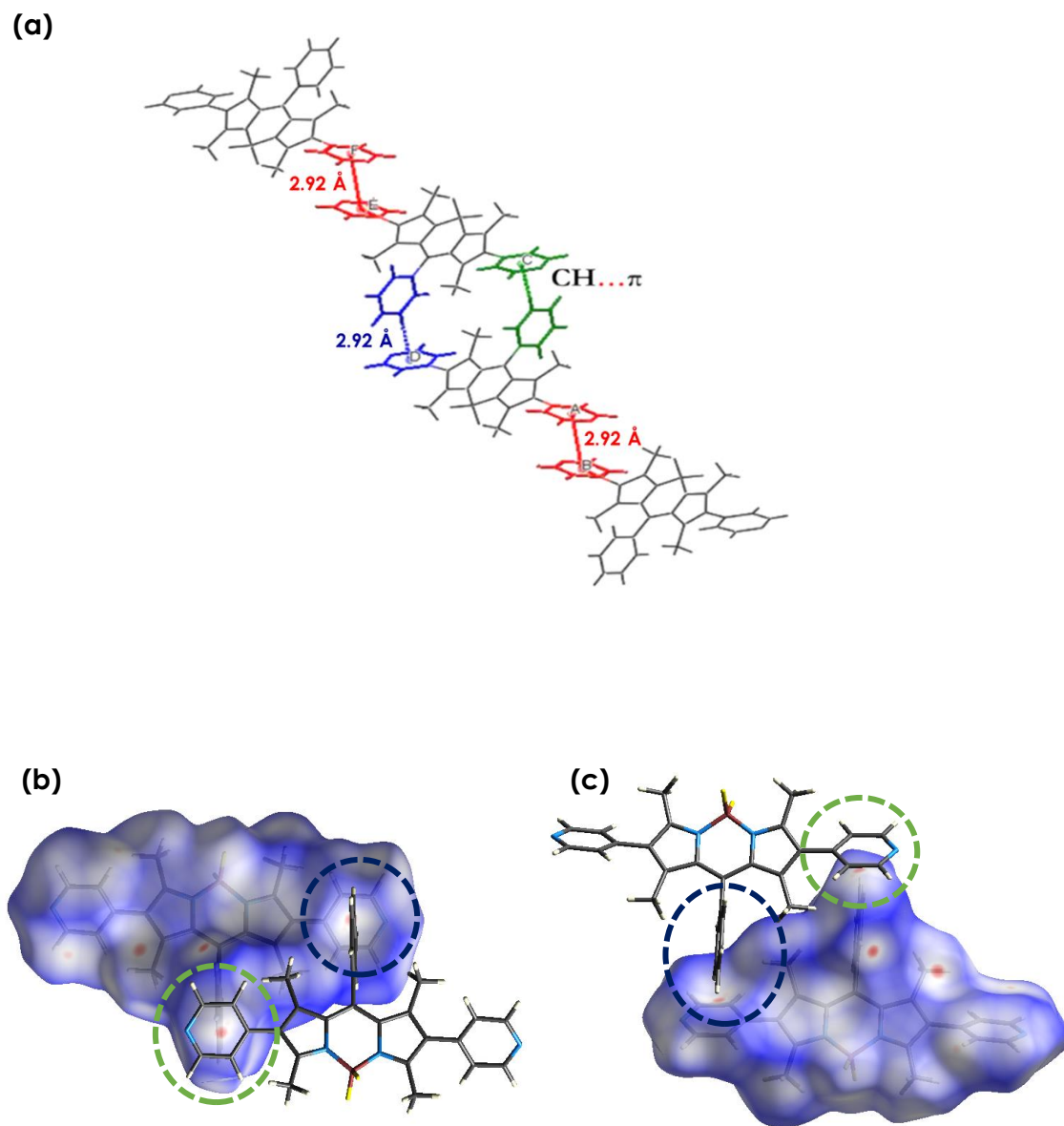


Fig 4.14. View of the single crystal X-ray structure of (a) Pyr-BODIPY (**4-18.a***) illustrating the formation of π - π interactions from one side of the BODIPY and CH... π interactions from the other side along the a-axis. (b), and (c) HSs representation of CH... π interactions in **4-18.a***, which is highlighted in blue and green.

However, the packing diagram of **4-18.b*** (**Fig 4.6**, and **a** in **Fig 4.6**) does not show any π - π interactions between the pyridyl rings. Moreover, the centroid-centroid distance between the phenyl in the *meso* positions is too long for π - π interactions with a distance of about 6.96Å (**b**

in Fig 4.14). CH $\cdots\pi$ interactions were also observed in **4-18.a*** and **4-18.b*** where H to centroid distance of **4-18.a*** is 2.65 Å, which is shorter than **4-18.b*** 2.85 Å. Therefore, the HSs of **4-18.b*** displays as white spot rather than red.

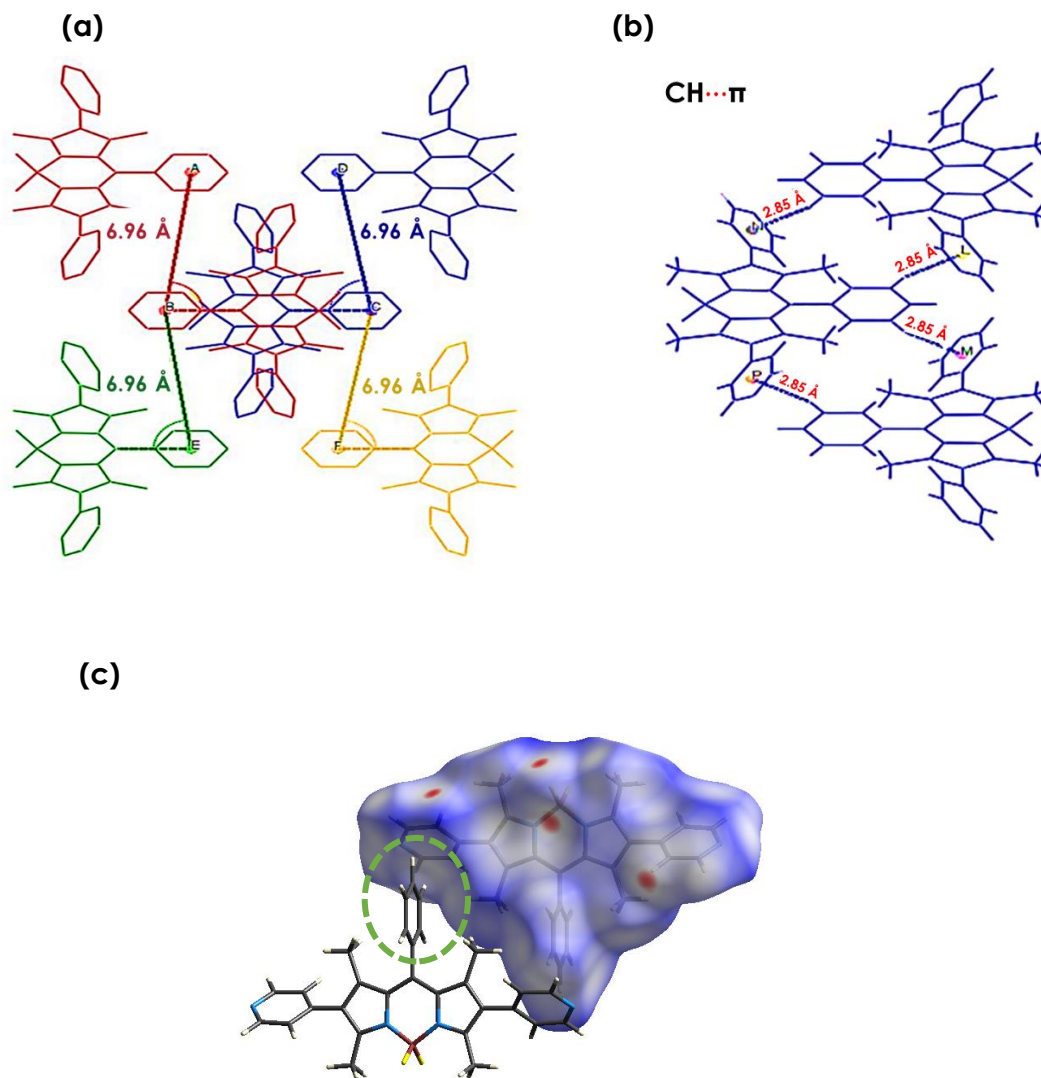


Fig 4.14 View of the single crystal X-ray structure of (a) Pyr-BODIPY (**4-18.b***) illustrating the long distance between the phenyl rings and no presence of π - π interactions. (b) CH $\cdots\pi$ interactions along the a-axis for **4-18.b***. (c) HS representation of CH $\cdots\pi$ interactions in **4-18.b***, which is highlighted in green.

Compound **4-19** illustrates the formation of hydrogen bonding between the pyrimidine ring from one side of a BODIPY (where the carbon atoms act as proton donors) and a nitrogen from the neighbourhood pyrimidine on another BODIPY that acts as hydrogen bonding acceptor. Also, $\text{CH}\cdots\pi$ interactions with a distance of 2.61 Å as presented in the crystal structure as showed in **Fig 4.14**

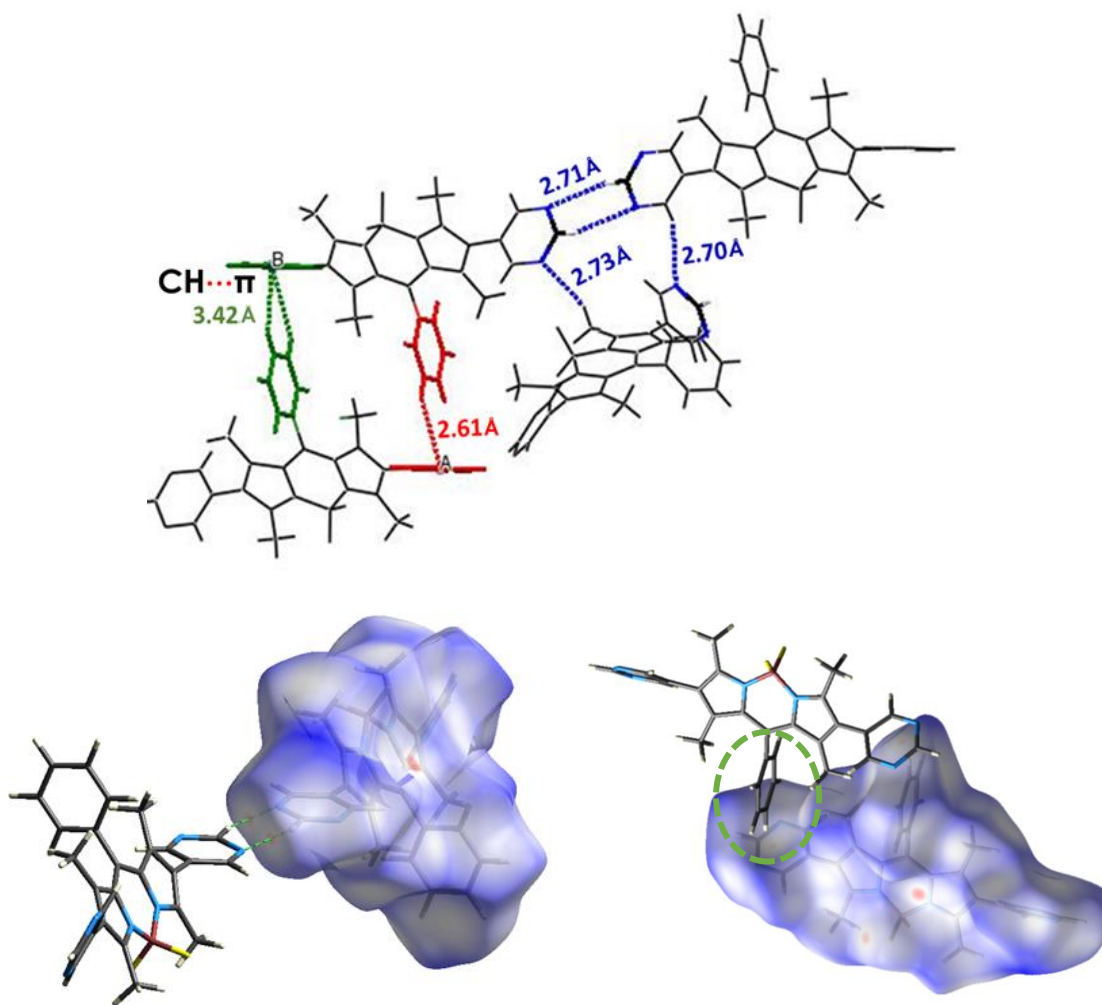


Fig 4.14 View of the single crystal X-ray structure of (a) Pym-BODIPY **4-19** illustrating the formation of hydrogen bonding between pyrimidine ring from one side of a BODIPY and a nitrogen from the neighbourhood pyrimidine on another BODIPY and $\text{CH}\cdots\pi$ interactions (b) HSs representation of the hydrogen bonding of **4-19**. (c) HSs representation of $\text{CH}\cdots\pi$ interactions in **4-19**, which are highlighted in green.

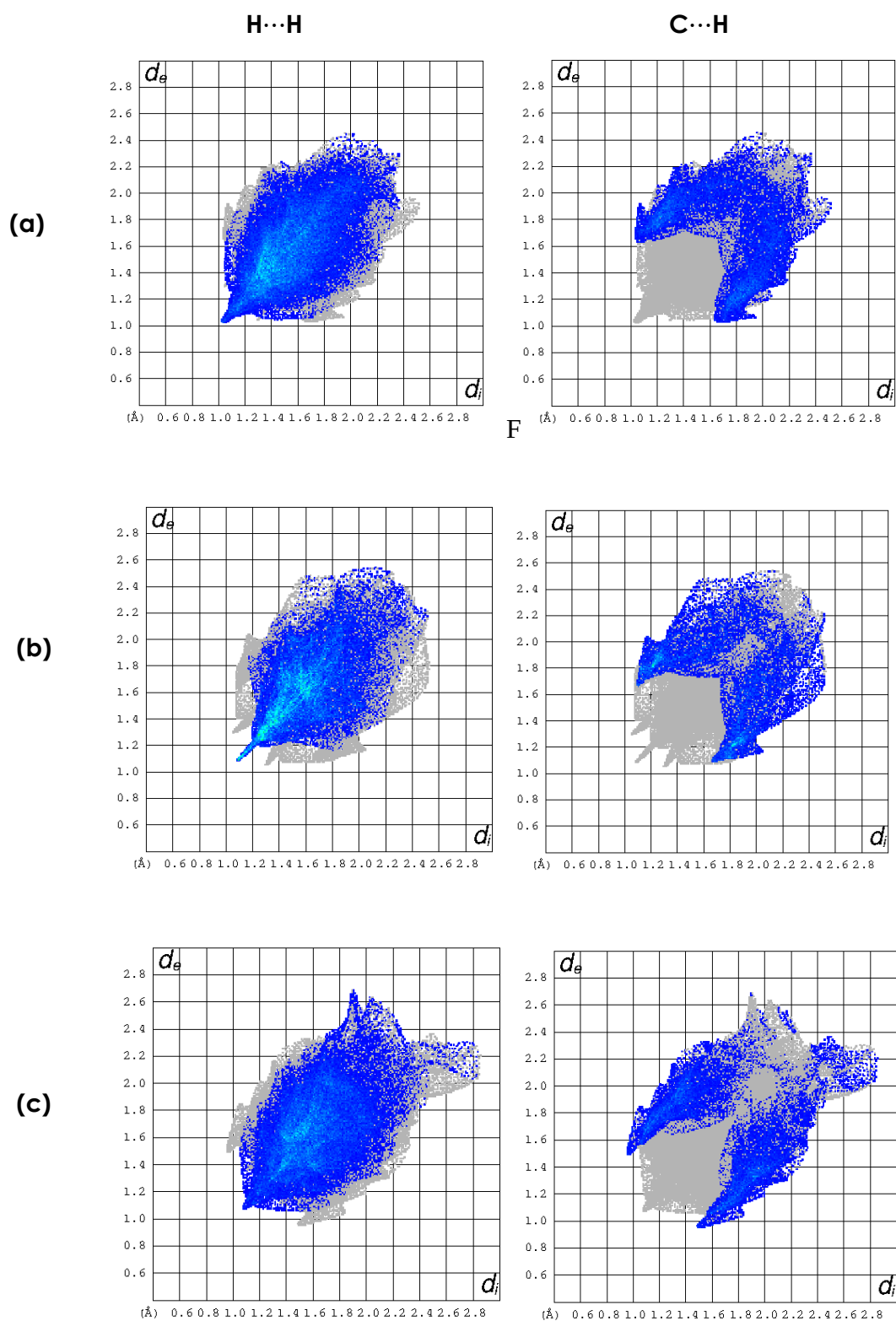


Fig 4.15. 2D fingerprint plots of compounds (a) **4-18.a***, (b) **4-18.b***, and (c) **4-19**, which highlight the C···H, H···H intermolecular contacts; to provide context, the outline of the fingerprint is shown in grey.

Fig 4.15 shows the relative contributions of 2D-fingerprint plots, which highlight C $\cdots$ H, H $\cdots$ H close contacts for **4-18.a***, **4-18.b*** and **4-19**. From this simple analysis, it immediately emerges that the ‘wings’ are a typical representation of a C-H $\cdots$ π contact in the fingerprint plot (22.7% C $\cdots$ H area of **4-18.b***) which is larger than **4-18.a*** (20.7%), and **4-19** (17.2% C $\cdots$ H area). The H $\cdots$ H contacts comprise about half of the surface area with 49.9% of in form a, 49.9% of the surface in form b, and 50.7% in **4-19**, respectively (see **Fig 4.15**).

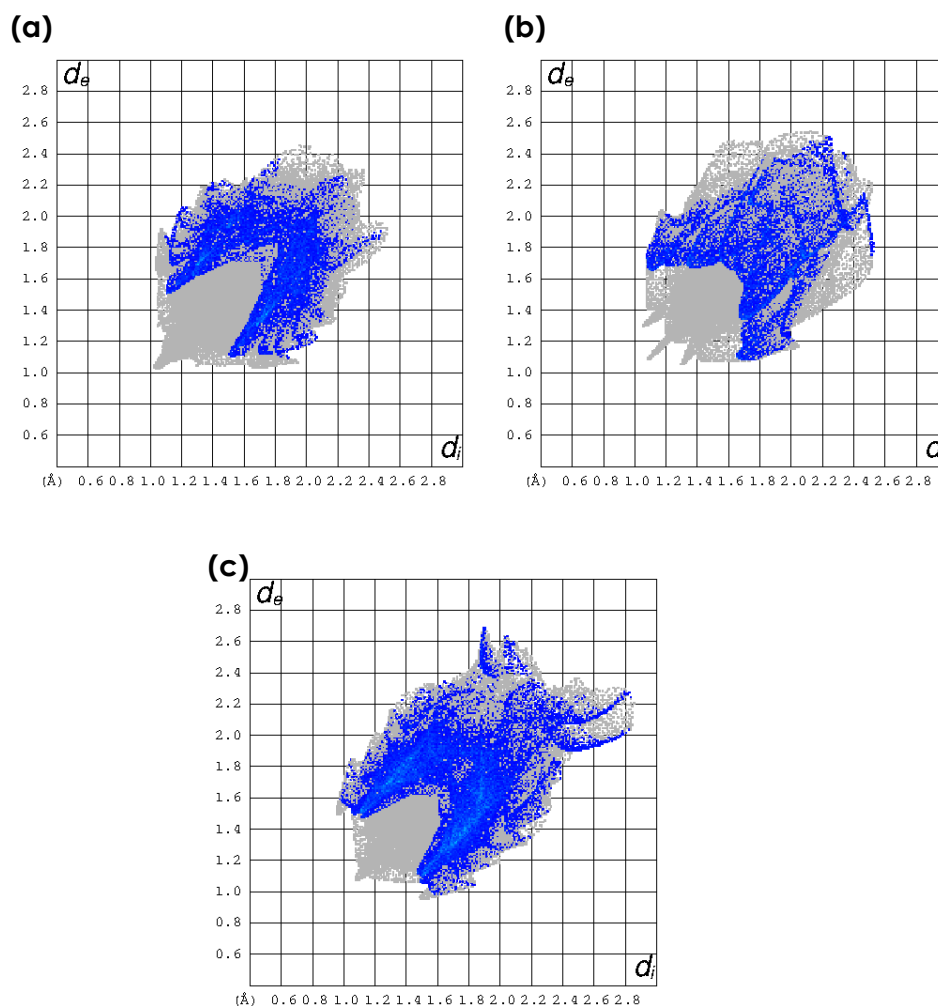


Fig 4.16. 2D fingerprint plots of compounds (a) **4-18.a***, (b) **4-18.b***, and (c) **4-19**, which highlight the N $\cdots$ H intermolecular contacts; to provide context, the outline of the fingerprint is shown in grey.

Forms **4-18.a*** and **4-18.b*** have close N...H surface areas (12.5 % in form **a***, and 13 % of form **b***), while **4-19** have about double the surface area with 23.3 % as presented in **Fig 4.16**. This could be explained by the ability of the pyrimidyl to form halogen bonding. The numbers of interactions in terms of percentages are represented as a bar chart (**Fig 4.17**), which summarizes the various intermolecular contacts in **4-18.a***, **4-18.b*** and **4-19**.

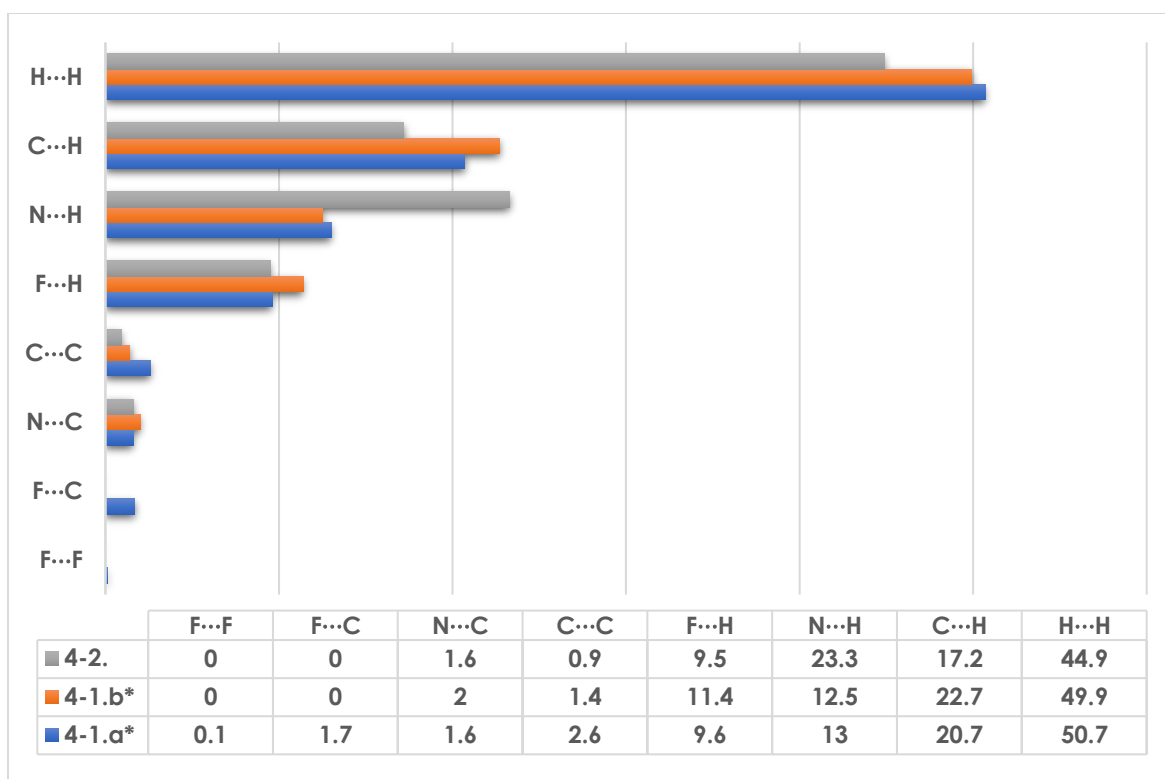


Fig 4.17 Percentage contributions of individual intermolecular interactions to the Hirshfeld surfaces of compounds **4-18.a***, **4-18.b*** and **4-19**.

4.3.2 Synthesis and Structural Studies of Coordination Polymers Based on BODIPY

The synthesis of the coordination polymer (**4-20**) was attempted by the slow solvent diffusion between an upper layer of CuI in acetonitrile and a lower layer of Pym-BODIPY in chloroform to afford a reddish-brown powder. However, storage of the powder for four weeks at room temperature or 4°C led to the formation of single crystals of copper iodide, which would suggest that the formation of infinite CuI single crystal is more favourable under these conditions.

However, brown single crystals of compound **4-20** were grown under solvothermal conditions, by reacting copper(I) iodide with **4-18** in acetonitrile. A structural determination by single-crystal X-ray diffraction revealed the coordination polymer to crystallise in the triclinic space group *P*-1 (**Fig 4.18**).

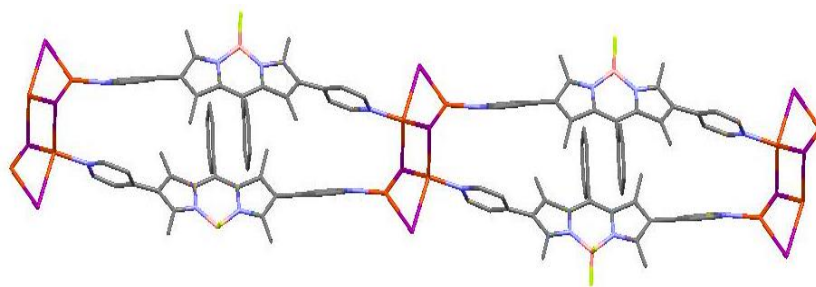
Table 4.2. Bond lengths (Å), and angles(°) for **4-20**.

4-20			
I1-Cu2 ¹	2.698(2)	I1 ¹ -Cu2-I1 ³	118.45(7)
I1-Cu2 ²	2.661(2)	I1 ¹ -Cu2-I2 ³	108.72(7)
I1-Cu1	2.614(2)	I1 ³ -Cu2-I2 ³	105.76(7)
I2-Cu2 ¹	2.716(2)	N4-Cu2-I1 ³	109.70(3)
I2-Cu1	2.502(2)	N4-Cu2-I1 ¹	108.70(3)
Cu2-N4	2.029(10)	N4-Cu2-I2 ³	104.60(3)
Cu1-N1	1.974(9)	I2-Cu1-I1	115.10(7)
Cu2 ¹ -I1-Cu2 ²	61.55(7)	I2-Cu1-Cu2 ²	65.30(7)
Cu1-I1-Cu2 ²	56.94(6)	N1-Cu1-I1	116.30(3)
Cu1-I1Cu2 ¹	72.97(7)	N1-Cu1-I2	125.10(3)
Cu1-I2-Cu2 ²	57.91(6)	C25-N4-Cu2	122.40(8)
C26-N4-Cu2	119.30(8)		

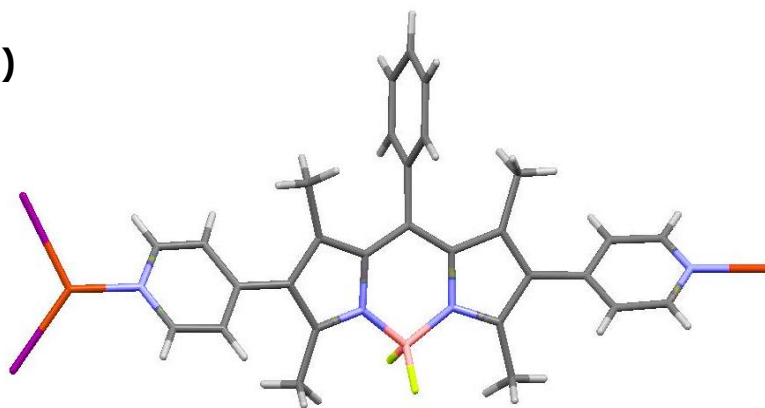
Structural refinement revealed that [Cu₄I₄(Pyr-BODIPY)₄]_∞ (**4-20**) adopts a 1 : 1 ligand: metal ratio (**Fig 4.18** and , **Table 4.2**) in which an unusual copper(I) iodide open cubane

configuration is formed. The open cubane configuration is also called the chair (or step) configuration.^{25, 96}

(a)



(b)



(c)

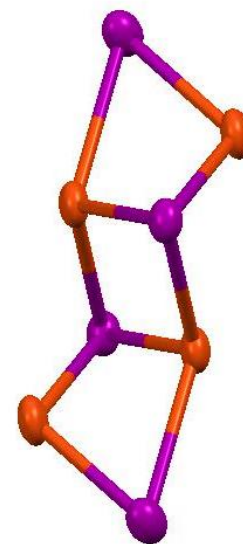


Fig 4.18. (a) Coordination of **4-18** around the Cu(I) centre to make one-dimensional polymer **4-20** (b) The asymmetric unit of **4-20**. (c) Copper(I) iodide open cubane configuration is formed. The open cubane configuration is also called the chair (or step) configuration. structures.^{25, 96} All hydrogen atoms have been removed for clarity. Carbon = grey, nitrogen = blue, copper = orange, iodine = purple, boron = pink, fluorine = green.

The Cu–I bond lengths observed for Cu(I) in **4-20** are 2.698(2), 2.661(2), 2.614(2), 2.716(2), 2.502(2) Å, which are comparable with those reported for various copper(I) iodide open cubane structures.^{25, 96} The iodide bridging arrangement results in a copper–copper separation of 2.533(2) Å, and 2.742(4) Å, which is shorter than the internuclear distance in metallic copper and consistent with Cu–Cu separations observed in other open cubane (CuI)₄^{25, 96} Copper(I) iodide open cubane cores can be defined as two binuclear [Cu₂I₂] subunits in

relatively weak interaction but within significant cuprophilic ($d^{10}-d^{10}$) bonding interaction^{83, 96-100} by considering the *van der Waals radii* of copper(I) (1.40 Å).

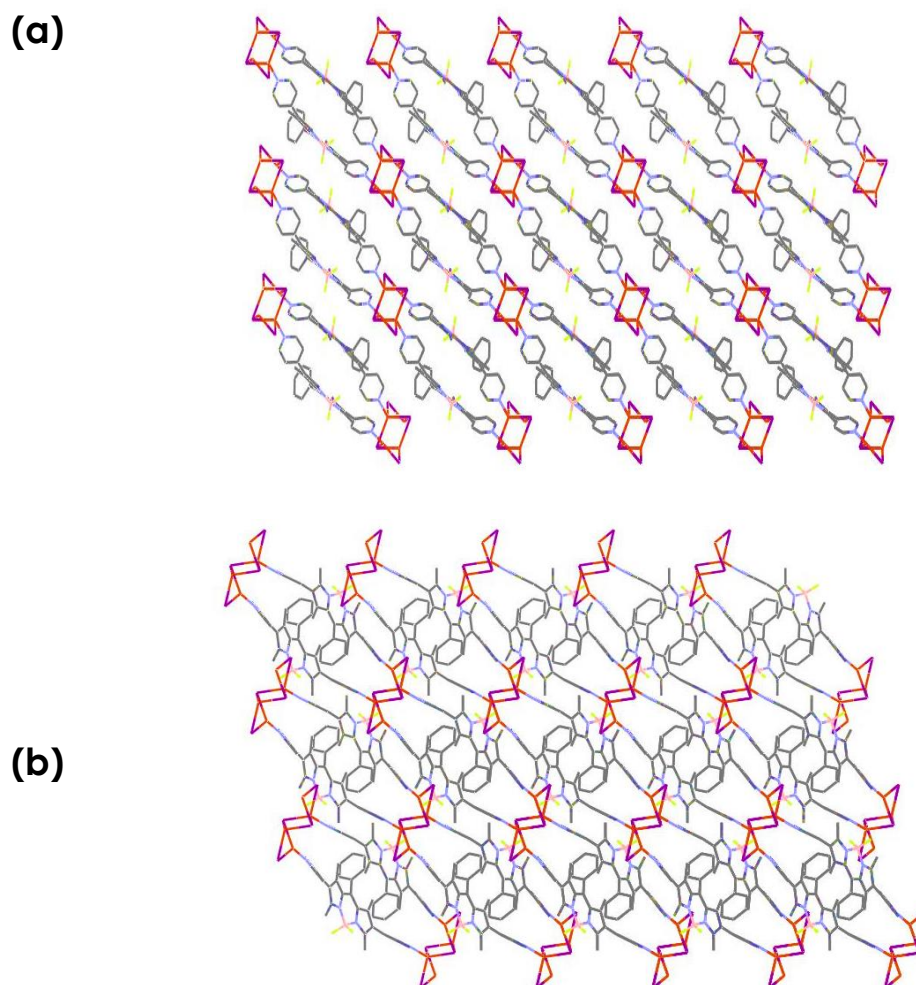


Fig 4.19. Orientation of **4-20** along (a) b-axis (b) c-axis. All hydrogen atoms have been removed for clarity. Carbon atoms = grey, nitrogen= blue, copper = orange, iodine = purple, boron = pink, fluorine = green.

The two pyridyl ring planes of **4-20** cross over each other at a dihedral angle of *ca.* 25.59° which is higher than **4-18.a*** (*ca.* 17.33°) and smaller than **4-18.b*** (*ca.* 73.5°). One of the pyridyl ring planes of **4-20** is tilted *ca.* 40.02° away from the indacene plane, which is smaller than **4-**

18.a* (*ca.* 54.02°) and lower than **4-18.b*** (*ca.* 53.53°). However, the other pyridine ring plane of **4-20** tilted *ca.* 58.69° away from the indacene plane.

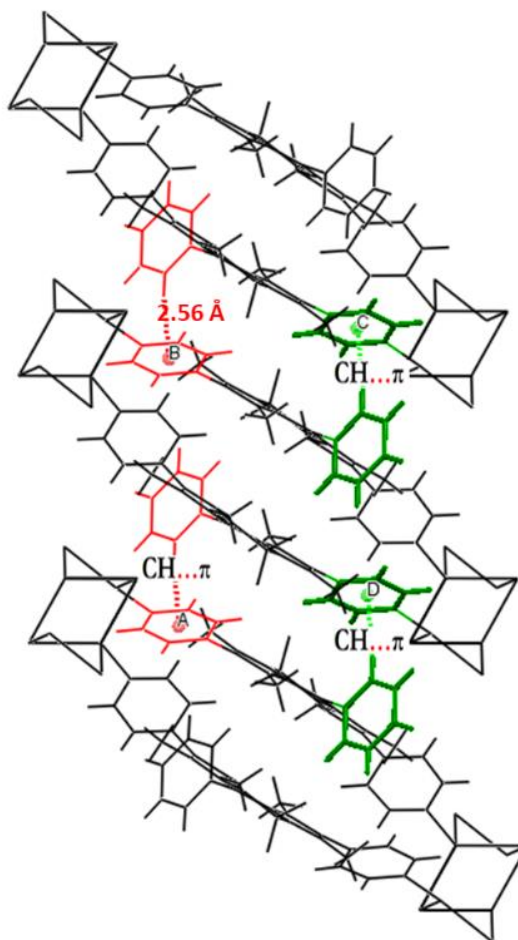


Fig 4.20 View of the single crystal X-ray structure of **4-20** illustrating the formation of CH... π interaction along a-axis presented in green and red.

Moreover, the packing diagram of **4-20** reveals that a pyridyl rings from one side of the BODIPY (*i.e.* from one side of the 2D chain) involve in (CH... π) interactions with a proton from phenyl ring on the neighbouring BODIPY as presented in **Fig 4.20**. Another contact

occurs between the H atom from the (*i.e.* proton from the benzene ring at the *meta*-position from the neighbouring 2D chain).

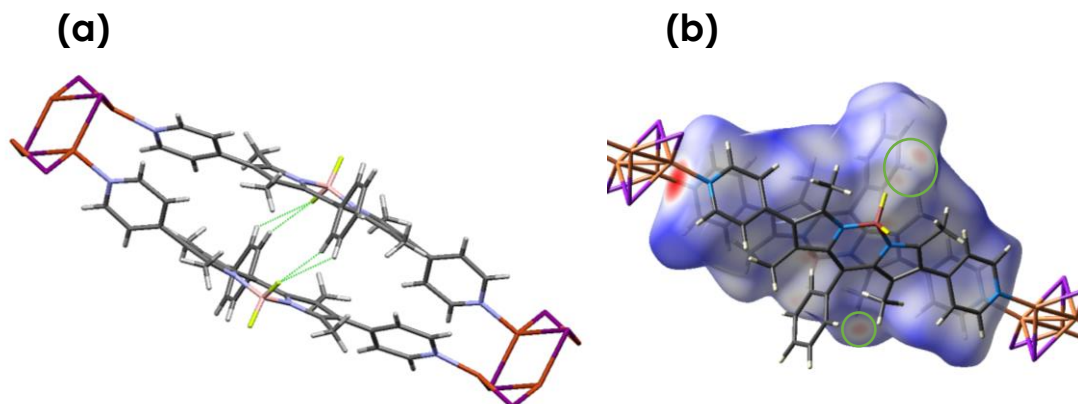


Fig 4.21. View of the single crystal X-ray structure of **4-20** illustrating the formation of $\text{CH}\cdots\text{F}$ with a distance of approximately 2.50 Å (b) HSs representation of $\text{CH}\cdots\text{F}$ contact, which highlight in green. Carbon = grey, nitrogen = blue, copper = orange, and iodine = purple, boron = pink, fluorine = green.

Furthermore, there is $\text{CH}\cdots\text{F}$ contacts between the hydrogen from phenyl rings (*i.e.* proton from the benzene ring at the *meta*-position) with and a fluorine atom from a neighbouring BODIPY with a distance of approximately 2.507(7) Å.

Yellow single crystals of compound **4-21** were grown by slow solvent diffusion between an upper layer of CuI in acetonitrile and a lower layer of Pym-BODIPY in chloroform. The X-ray structure determination of $[(\text{CuI})_2(\text{Pym-BODIPY})_2]_\infty$ reveals that the compound exists as a three-dimensional coordination network in which each approximately tetrahedral Cu(I) centre is bound by two iodide anions and two Pym-BODIPY ligands which results in a planar ribbon-type structure, where each Cu(I) centre is coordinated by two N-donors from the

pyrimidine N-donor (**Fig 4.22**, and **4.23**) (*i.e.* the rhomboid dimer can be thought of two as two monomers connected in a head tail fashion). The Cu–I bond lengths observed for CuI in **4-21** are 2.6132(11) and 2.6512(12) which are comparable with those reported for various copper(I) iodide ribbon-type.²¹

Table 4.3. Bond lengths (Å) and angles (°) for **4-21**.

4-21			
I1-Cu2 ¹	2.6132(11)	N27-Cu2-I1	108.85(18)
I1-Cu2 ²	2.6512(12)	N27-Cu2-I1 ¹	101.70(2)
Cu2-N27	2.059(7)	N27-Cu2-Cu2 ¹	122.77(19)
Cu1-N29 ²	2.057(6)	N29 ² -Cu2-I ¹	108.45(19)
N29 ² -Cu2Cu2 ¹	125.20(2)	N29 ² -Cu2-I1 ¹	104.13(18)
I1-Cu2 ¹ -I1 ¹	60.20(4)	C26-N27-Cu2	123.70(5)
Cu2-I ¹ -Cu2 ¹	58.11(4)	C28-N27-Cu2	119.00(5)
Cu2 ¹ Cu2I ¹	61.69(4)	C28-N29-Cu2 ³	119.30(5)

(a)

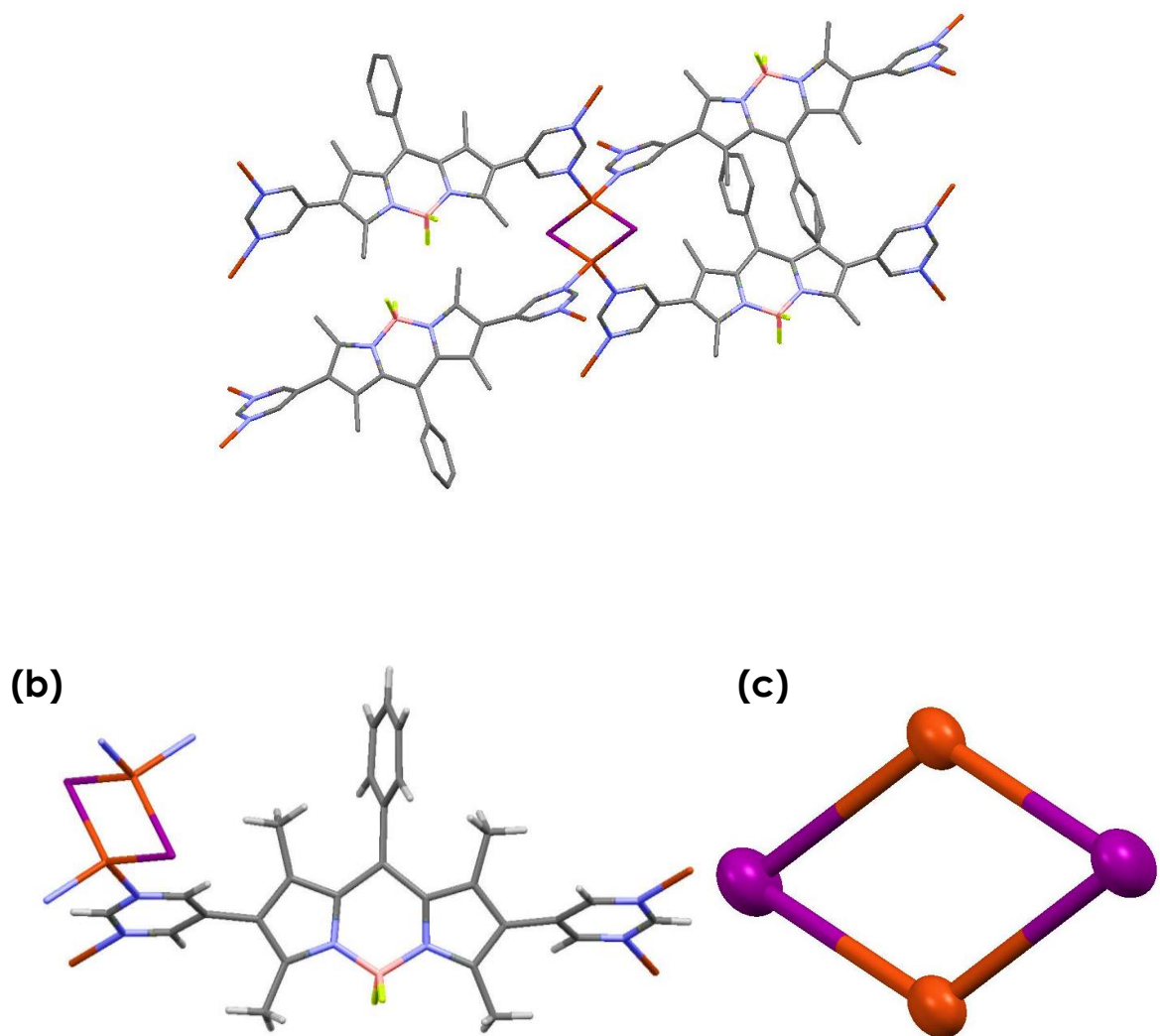
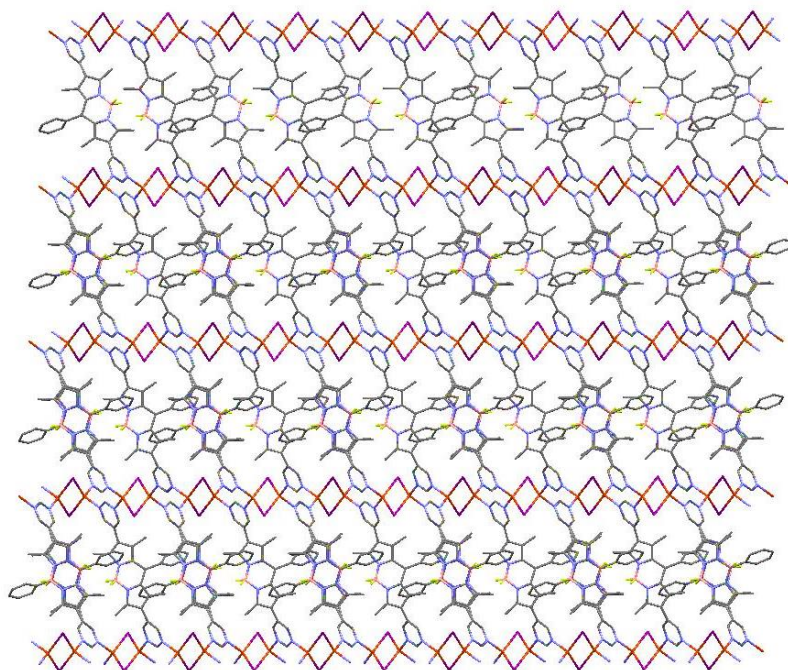


Fig 4.22. (a) Coordination of **4-19** around the Cu(I) centre to make three-dimensional coordination polymer (b) The asymmetric unit of **4-21** (c) copper(I) iodide open planar ribbon-type structures formed. All hydrogen atoms have been removed for clarity. Carbon = grey, nitrogen = blue, Copper = orange, and iodine = purple, boron = pink, fluorine = green.

(a)



(b)

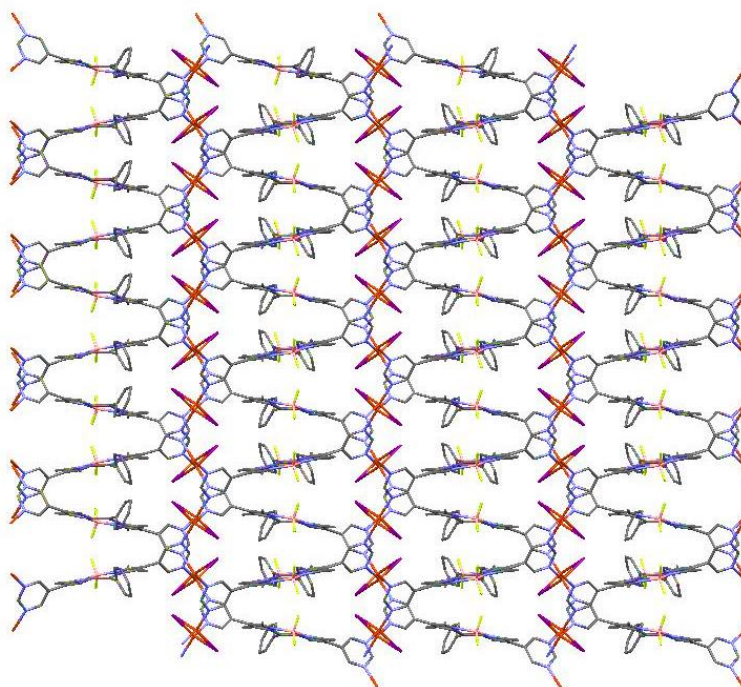


Fig 4.23. Orientation of **4-21** along the (a) b-axis (b) c-axis. All hydrogen atoms have been removed for clarity. Carbon = grey, nitrogen = blue, copper = orange, and iodine = purple, boron= pink, fluorine atoms = green.

Powder X-ray diffraction (PXRD) studies of **4-20**, and **4-21** were recorded, and compared to the patterns calculated from the single crystal data using Mercury. In the case of **4-20**, there is evidence of the presence of the compound, but amorphous material is also observed (*i.e.* broader peaks at about 14° and 30°), possibly due to loss of crystallinity under the conditions of the experiment as displayed in **Fig 4.24**.

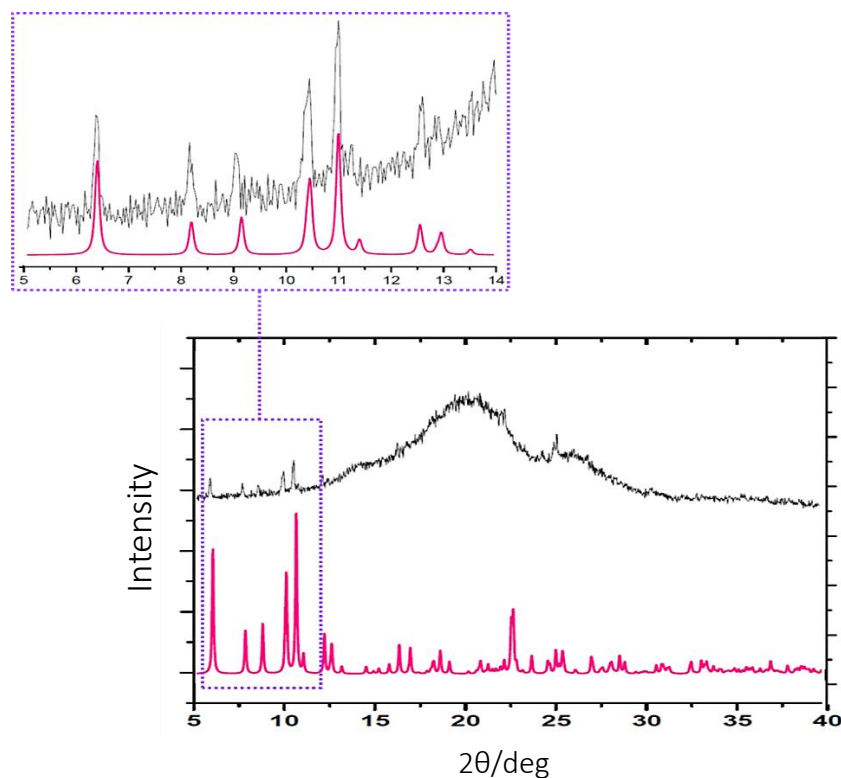


Fig 4.24. Calculated PXRD pattern for **4-20** calculated using Mercury (pink) and experimental pattern (Black).

Attempts to synthesize **4-20** by slow solvent diffusion between an upper layer of CuI in acetonitrile and a lower layer of pyr-BODIPY in chloroform formed a brownish red powder, which upon analysis showed an evidence of the present CuI (*i.e.* high angle region), and an amorphous material is also observed (*i.e.* broader peaks at about 14° and 30°), and no evidence

of the formation of the target compound **4-20** as presented in **Fig 4.25**. This might be due to the polymeric nature of CuX to form infinite CuX motive rather than complexation with bridging ligand to form the coordination polymer.

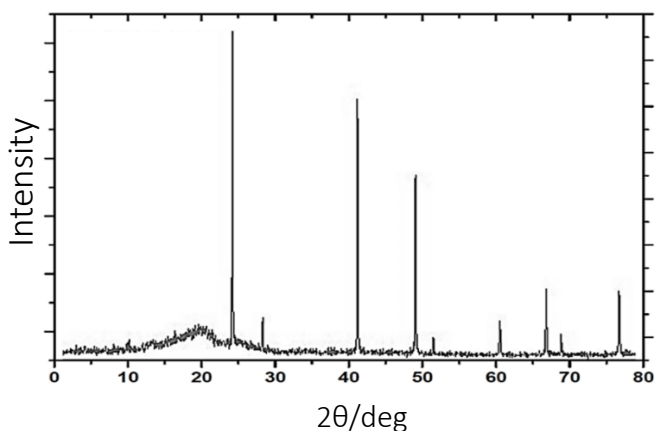


Fig 4.25. Experimental PXRD pattern for **4-21**. Pattern indicates losing of crystallinity upon drying.

In the case of solvothermal syntheses of **4-21** in acetonitrile, only an amorphous material is observed in the PXRD pattern. The broader peaks at *ca.* 14° and 30° are possibly due to loss of crystallinity under the conditions of the experiment as displayed in **Fig 4.26**.

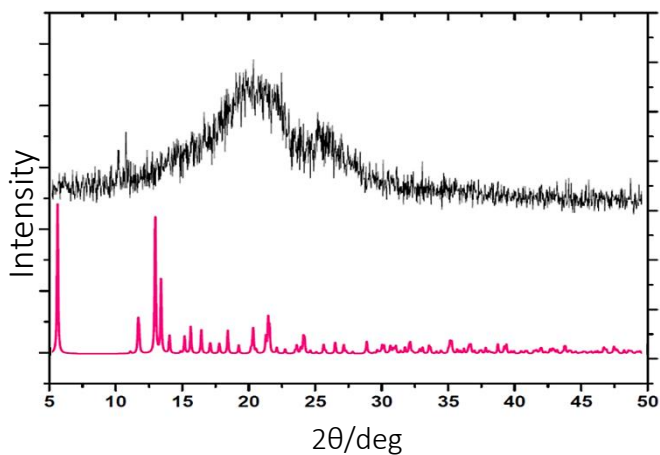


Fig 4.26. Calculated PXRD pattern for **4-21** calculated using Mercury (pink) and experimental pattern (Black). Pattern indicates losing of crystallinity upon drying.

4.2.3 Optical and Fluorescence Measurements

The absorption and fluorescence spectra of compounds **4-18** and **4-19** were recorded in CH₂Cl₂ solution, thin film, and as powder. As shown in **Fig 4.27**, the absorption spectra of a solution of **4-18** and **4-19** in dichloromethane shows sharp absorption bands around 518 nm for **4-18**, and 520 for **4-19**, which are attributed to the S₀ → S₁ transitions of the BODIPY group.

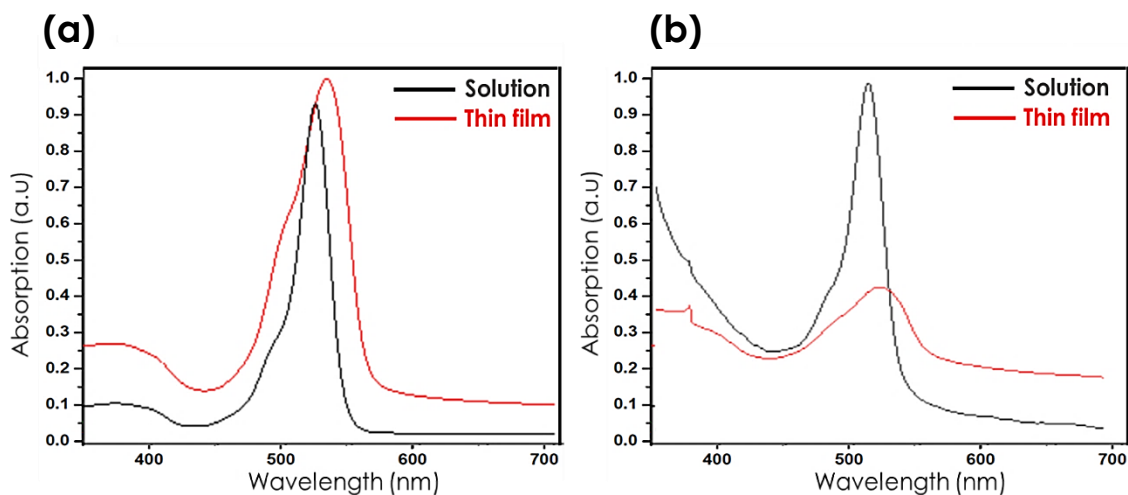


Fig 4.27. Absorption spectra of the (a) dyes **4-18**, (b) **4-19** in CH₂Cl₂ solution (black) and as thin films (red).

For further analyses, thin films of these two dyes were prepared for the determination of absorption and emission spectra in the solid state. Dye films were prepared by drop casting the solution with dichloromethane as the solvent, on to the quartz substrate and leaving it to dry. The absorption of the thin film shows (*ca.* 10 nm) red shift in the absorption of **4-18**, and **4-19**, also it shows a broader and structureless bands which may be attributed to strong intermolecular interactions in the solid-state (**Fig 4.27**). Photographs of compounds **4-18**, and

4-19, under visible light as crystals, amorphous, solid, powder, thin film and solution in CH_2Cl_2 are presented in **Fig 4.28**.

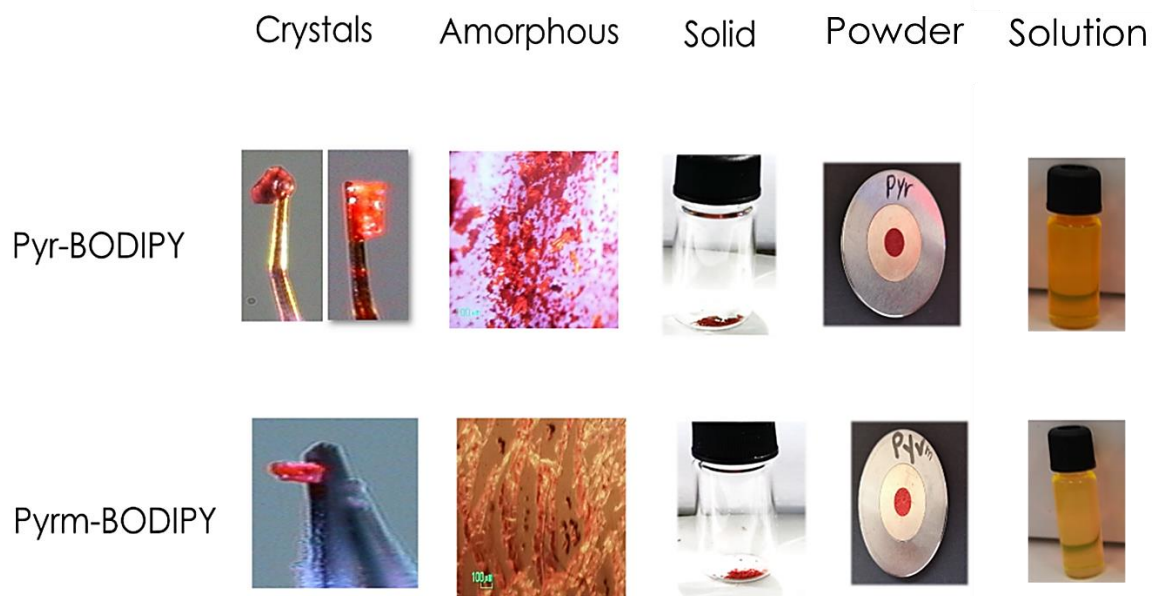


Fig 4.28. Photographs showing the different in colour of compounds **4-18**, and **4-19**, visible light. As crystals, amorphous, solid, powder, and solution in CH_2Cl_2 .

The fluorescence emission spectra of solutions of **4-18** and **4-19** in dichloromethane are mirror images of their respective absorption spectrum, showing strong and narrow peaks with maxima around 543 nm for **4-18** and 539 nm for **4-19** (**Fig 4.29**). Both dyes have high quantum yields (Φ_F) 0.86 and 0.90 respectively. The Stokes shifts of **4-18** is (*ca.* 25 nm) which is larger than **4-19** (*ca.* 19 nm). Exciting the solution of **4-18** and **4-19** by using different wavelength (320-520 nm) in order to explore the effect of that on the emission spectra does not show any effect on the emission spectra.

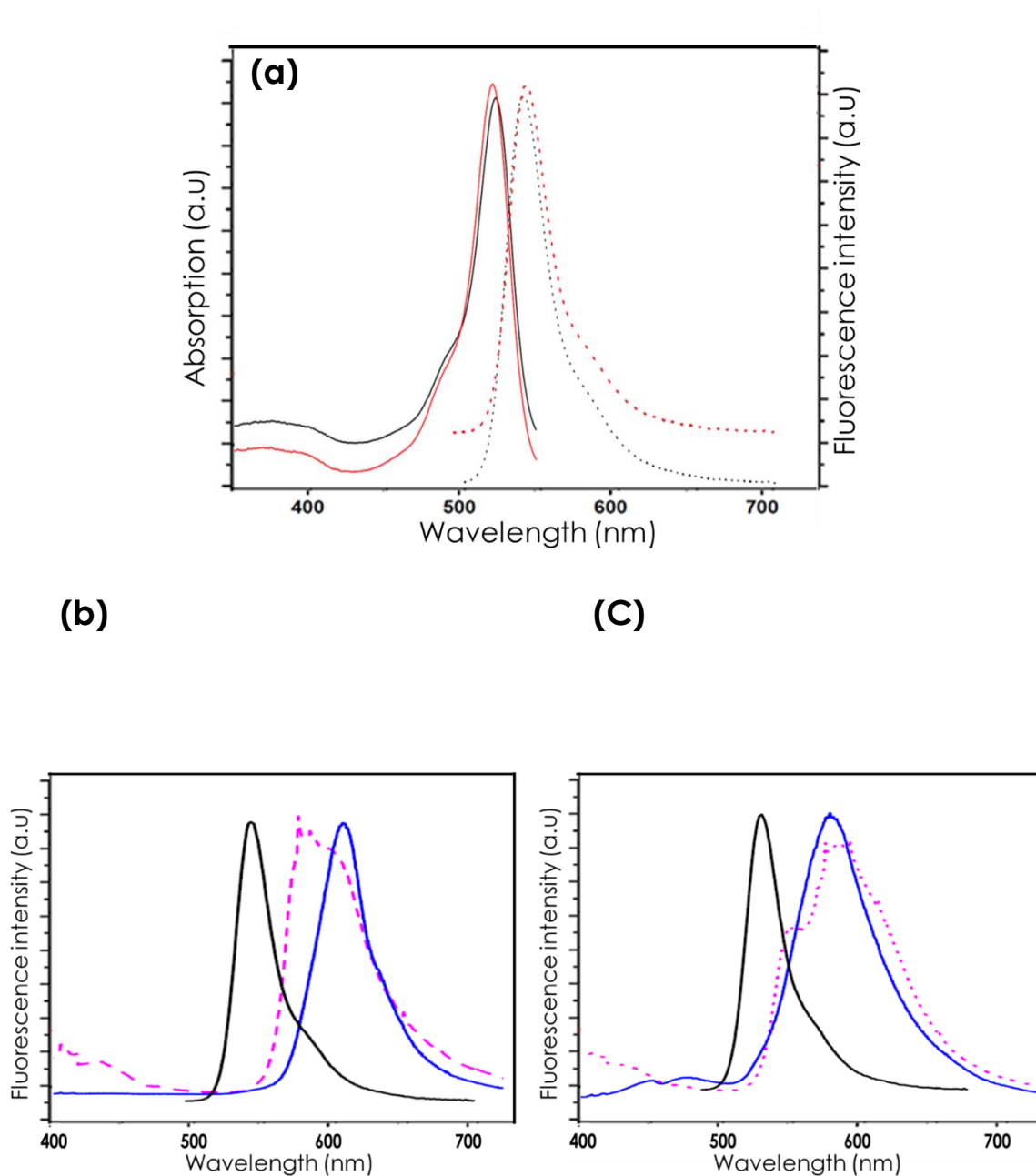


Fig 4.29. (a) Normalized UV-vis absorption (solid lines) and fluorescence (dashed lines) spectra of **4-1** (black lines) and **4.2** (red lines) in CH_2Cl_2 . Fluorescence (b) Pyr-BODIPY (c) Pym-BODIPY, spectra are coloured as follows: Solution in CH_2Cl_2 , = black solid lines, thin film pink dashed lines, powder = dark blue.

On the other hand, solid-state fluorescence is a rare characteristic of BODIPYs.¹⁰¹ Usually, the bright fluorescence of the BODIPY dyes is quenched in the solid state due to reabsorption and self-quenching¹⁰¹ (*i.e.* strong intermolecular staking in solid state, which obviously limits

the applications in optoelectronic devices)^{102, 103} However, introduction of pyridyl and pyrimidyl substituents on the 2,6 positions results in donor-acceptor-donor (D-A-D) BODIPY that shows high efficiency not just in solution but also in solid state, powder, and crystalline state. This could be explained by the effect of the substituents on the 2,6 positions on the packing of such dyes (*i.e.* more spaced packing in the crystal structure as described earlier in this chapter) due to the rigidity of the molecule in solid state which reduces the nonradiative decay that enhance fluorescent quantum yield in crystal compare to solution. This results in high luminescence of both powders and thin films in comparison to the solution.

The fluorescence maxima of **4-18** and **4-19** of the powder is redshifted to lower energy by ~ 66 nm for **4-18** and ~ 55 nm for **4-19**. Moreover, another smaller peak (shoulder) is clearly present in the spectrum of the dye film obtained using compound **4-18**, and **4-19**, which is indicative of the presence aggregate structures in this compound.

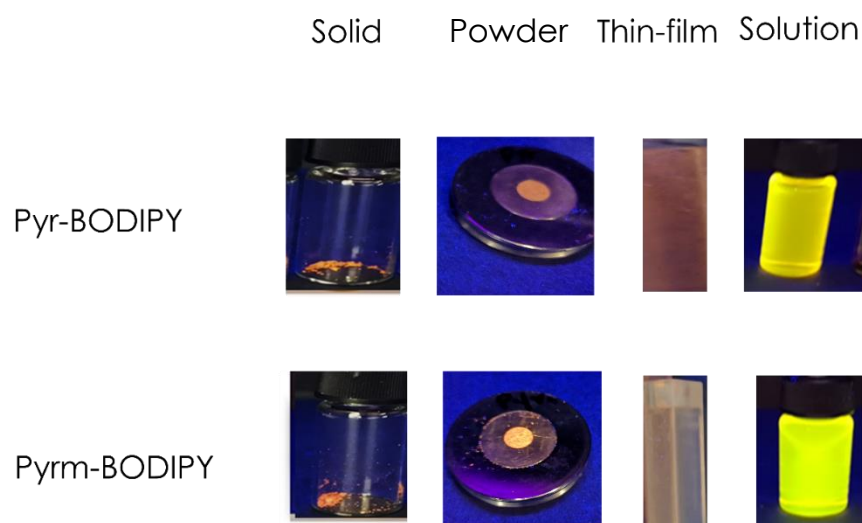


Fig 4.30. Photographs showing the differences in the colour of the florescence for compounds **4-18** and **4-19**, as a solid, powder, thin film and solution in CH_2Cl_2 .

Moreover, fluorescence micrographs images of single crystals of **4-18** and **4-19** were obtained by excitation of the crystals at 540-550 nm, which shows a red emission.

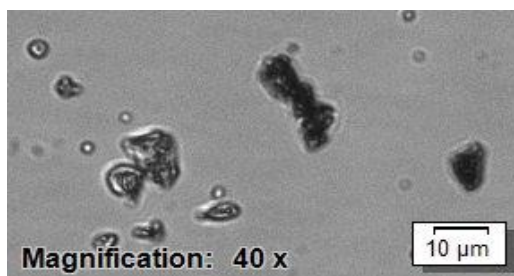
(a)



(b)



(c)



(d)



Fig 4.31. Micrographs images of single crystals of (a) **4-18**, (c) **4-19**. Fluorescence micrographs images of single crystals of (b) **4-18**, (d) **4-19**.

The reflectance spectra of compound **4-20** shows a narrow, more defined blue-shifted peak in comparison with **4-18**. The shift to higher energy might be due to the coordination to copper centre in open cubane conformation which stop the π – π interactions of the BODIPY. The reflectance spectra of compound **4-21** is broader than **4-19** which might be due to planar ribbon-type structures of the copper centre in case of **4-21**. On the other hand, compounds **4-20** and **4-21** shows fluorescence quenching response. The fluorescence quenching might be because the coordination between Cu^+ and the nitrogen atoms on the pyridine, and the pyrimidine rings, which induces ICTs and leads to concomitant quenching of the BODIPY fluorescence. This might occur because the metal donates electron density back to the BODIPY ligand into a π^* orbital. This phenomenon has been previously reported for pyridyl BODIPY which substituents on the 2,6 positions and Cu(I) .⁶⁹ Copper(I) compounds can undergo a phenomena known as π back-bonding.

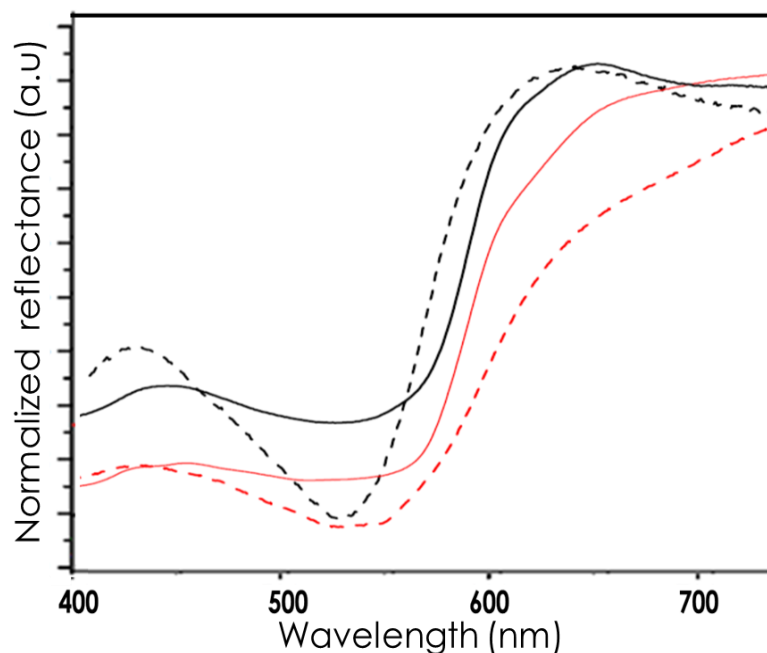


Fig 4.32. Normalized diffused reflectance spectrum of **4-18** (black lines), **4-19** (red lines), **4-20** (black dashed line), **4-21** (red dashed line).

4.3.4 Electrochemistry Measurement

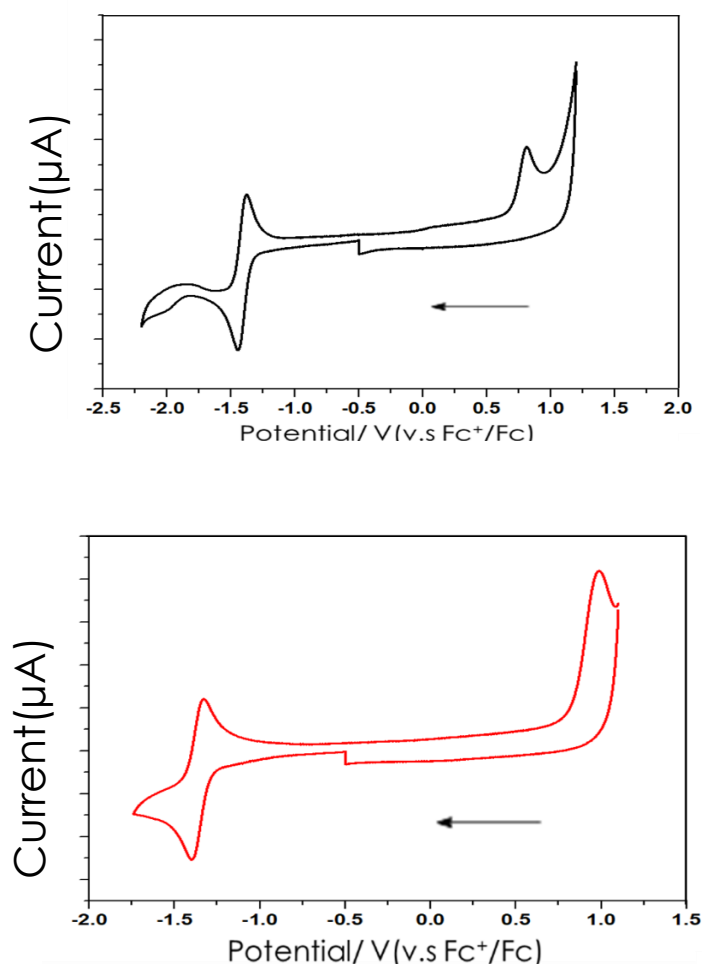


Fig 4.33. Cyclic voltammograms of **4-18** (black), and **4-19** (red) recorded in CH_2Cl_2 containing $[\text{nBu}_4\text{N}][\text{BF}_4](0.4\text{m})$.

Table 4.4. CV data for **4-18**, and **4-19**. Potentials ($E_{1/2} = (E_p^c + E_p^a)/2$) in V *vs.* Fc^+/Fc quoted to the nearest 0.01 V. The anodic/cathodic peak separation ($\Delta E = E_p^c - E_p^a$) is given in brackets where applicable

	$E_{1/2}$	E_p^c	E_p^a
4-18	-1.40 (0.07)	-1.37	-1.44
4-19	-1.35 (0.07)	-1.32	-1.39

The effect of the pyridyl and pyrimidyl substituent of the BODIPY on the electrochemical behaviour was measured by using cyclic voltammetry (see **Fig 4.33**). The CV experiments confirm that the two compounds exhibit similar behaviour upon reduction, with one reduction process with $E_{1/2}$ values of -1.40 V for **4-18** and -1.35 V for **4-19** (*vs.* Fc^+/Fc). The reduction processes for **4-18**, and **4-19** show a positive shift in redox potential in comparison with the parent BODIPY which have hydrogens at the 2,6 positions. This may occur because introducing pyridyl and pyrimidyl substituents on the 2,6 positions resulting in a push-pull BODIPY system. It is notable that **4-19** is considerably easier to reduce because the present of extra nitrogen in the pyrimidine moiety make it a stronger electron donor. Additionally, all the dyads were shown to exhibit a non-reversible oxidation process.

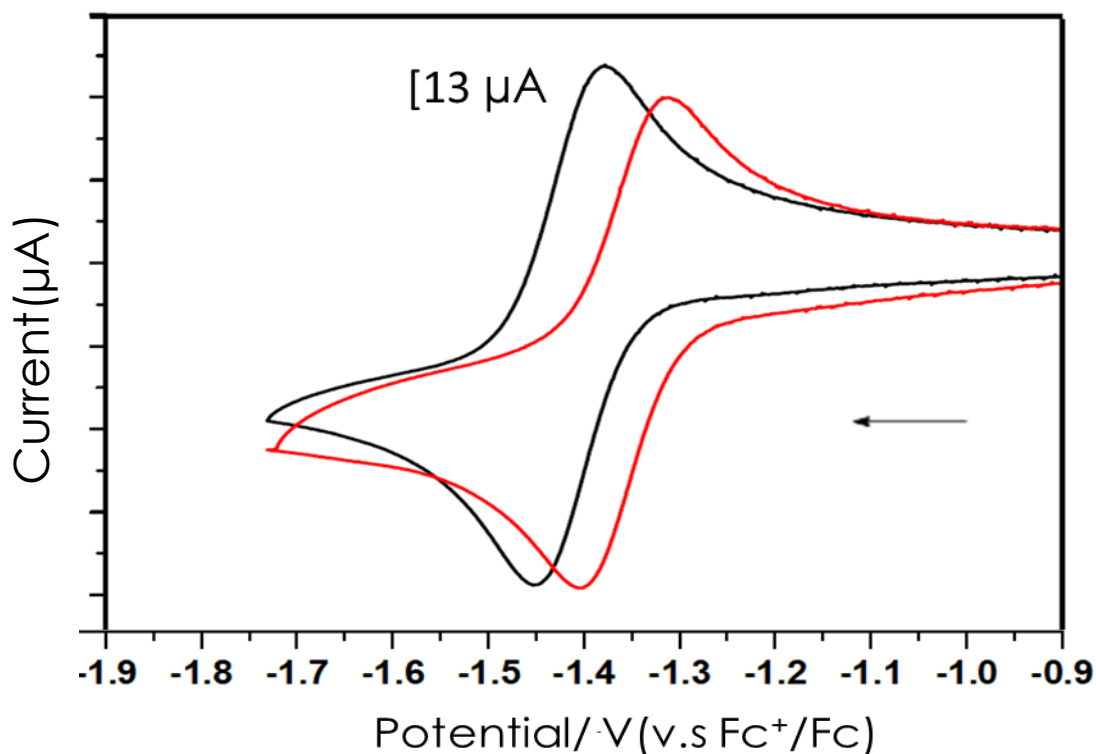


Fig 4.34. Cyclic voltammograms of **4-18** (black), and **4-19** (red) recorded in CH_2Cl_2 containing $[\text{Bu}_4\text{N}][\text{BF}_4]$ (0.4m)

Cyclic voltammograms of the couples were recorded at a series of scan rates in the range from 20 to 300 mVs^{-1} in order to explore the nature of those processes. Analysis of the data presented show that E_p^a and E_p^c values were, in each case, found to be independent of the scan rate and the peak currents were approximately equal and varied linearly with the square root of scan rate.

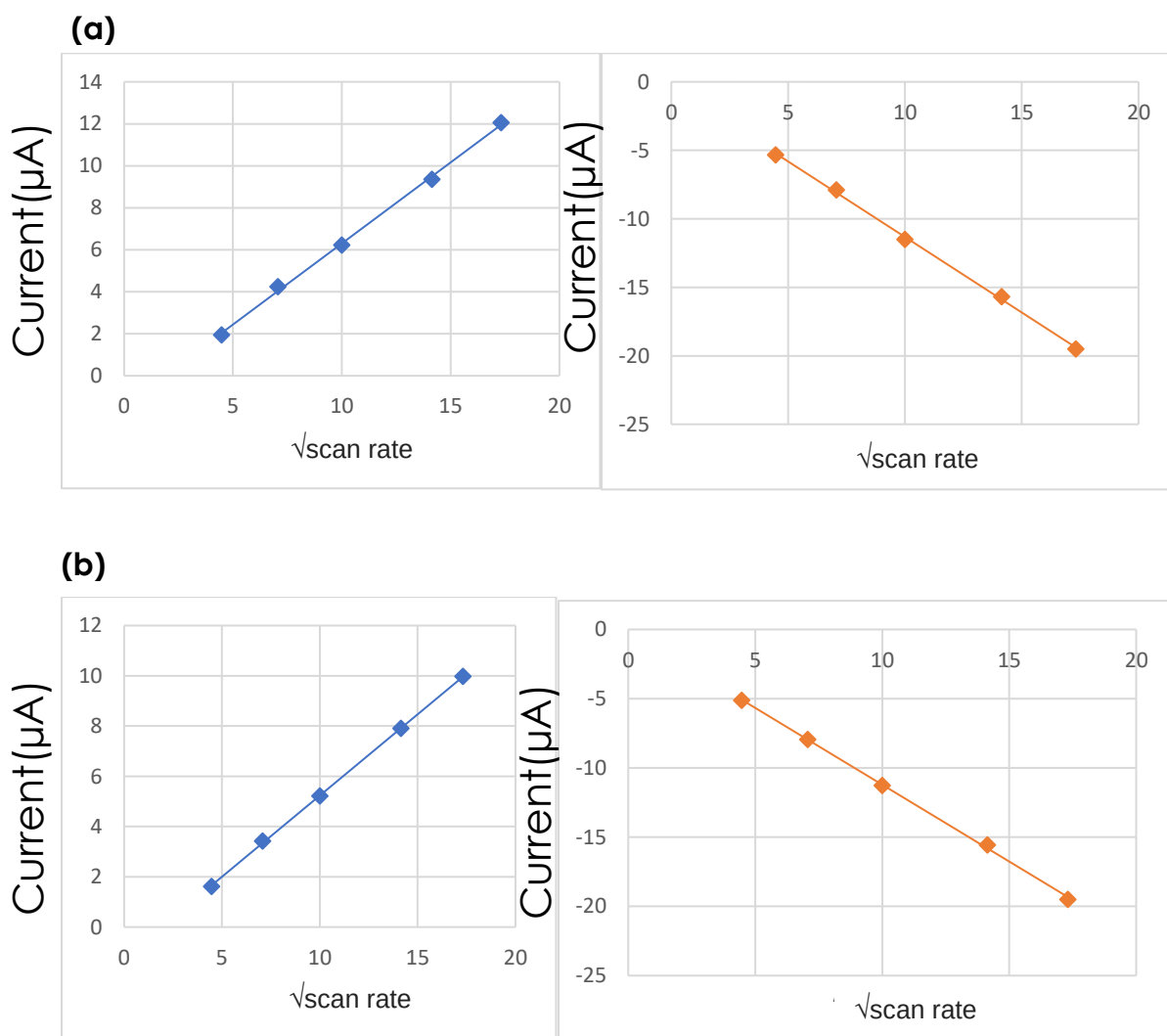


Fig 4.34. A plot of the anodic (blue, left)) and cathodic (orange, right) peak current of (a) **4-18**, (b) **4-19**.

4.4 Conclusions

We have demonstrated that simple structural modifications on the BODIPY core at the 2,6 positions with pyridine or pyrimidine can lead to bright emissive compounds in the solution, solid state, and thin film. Both dyes have high quantum yields (Φ_F) 0.86 and 0.90 respectively, in dichloromethane and a solid-state fluorescence which is rare characteristic of BODIPYs because of increasing the emission efficiency of BODIPY dyes as a result of (D–A–D) type molecule.

The crystal structure of compound **4-21** and polymorphs **4-18.a*** and **4-19.b*** show similar intermolecular interactions with different percentages due to different packing. Consequently, quantification of the intermolecular interactions present in compounds **4-18.a***, **b*** and **4-21** was realized by Hirshfeld surface analysis and 2D fingerprint plots. This analysis of intermolecular contacts present in the crystal packing of **4-18.a*** and **4-18.b*** leads us to conclude that these are different polymorphs.

Additionally, two coordination polymers-based copper(I) iodide and Pyr-BODIPY and Pyrm-BODIPY were syntheses. The first example presents the formation of a coordination polymer with a rare open cubane conformation for the CuI, the second example has demonstrated the formation of three-dimension coordination polymer with planar ribbon-type structures of the copper center. Compounds **4-20**, and **4-21** show fluorescence quenching responds result of inner structure increasing vibrational relaxation channel.

Cyclic voltammetric investigations on **4-18** and **4-19** displayed the expected one electron reduction processes. The modifications of the BODIPY core at (2,6) positions with pyridyl or

pyrimidyl substituents shift the BODIPY reduction to a more positive potential in comparison with the parent BODIPY. Additionally, the presence of extra nitrogen in the pyrimidyl-groups had the desired effect of pushing the BODIPY reduction of **4-19** to a more positive potential. However, at the same time this disrupted the communication.

4.5 Experimental Section

4.5.4 Materials and general methods

All reagents and solvents were purchased from Aldrich Chemicals, Alfa Aesar or Fisher Scientific UK, and used without further purification unless otherwise stated. Thin layer chromatography (TLC) was used to monitor the reactions. Column chromatography was used for purification (unless otherwise stated) by using silica gel (Merck silica gel 60, 0.2-0.5 mm, 50-130 mesh) as appropriate. ^1H and $^{13}\text{C}\{^1\text{H}\}$ NMR spectra were recorded at room temperature with either a Bruker AV400 or a Bruker AV3400, operating at 400 and 100 MHz respectively. ^{11}B and ^{19}F NMR spectra were recorded at room temperature with Bruker AV3400, operating at 128 and 376 MHz, respectively. Chemical shifts are quoted in ppm relative to TMS (^1H and $^{13}\text{C}\{^1\text{H}\}$). $\text{BF}_3\cdot\text{OEt}_2$ was used as an external reference for ^{11}B NMR measurements and CFCl_3 as an external reference for ^{19}F NMR.

Cyclic Voltammetry (CV) experiments were performed using an Autolab PGSTAT20 potationstat with a three-electrode arrangement in a single-compartment cell under an atmosphere of argon. A glassy carbon working electrode, a Pt wire secondary electrode and a saturated calomel reference electrode were chemically isolated from the test solution by a bridge tube containing electrolyte solution and fitted with a porous vycor frit, were used in the cell. The solutions were 10^{-3} M in test compounds and 0.4 M in tetra *n*-butylammonium tetrafluoroborate in dichloromethane as supporting electrolyte which was prepared using literature methods.¹⁰⁴ The redox potentials are quoted versus the ferrocenium-ferrocene couple (Fc^+/Fc) which used as an internal reference.¹⁰⁴ Compensation for internal resistance

was not applied. Dichloromethane was dried over calcium hydride under nitrogen gas, ferrocene (Aldrich) was used as received and $[\text{Bu}_4\text{N}][\text{BF}_4]$ was prepared by a literature method.

Absorption UV/Vis spectroscopy and fluorescence measurements were carried out at the University of Nottingham. Absorption UV/Vis spectra of both solutions and thin films were measured with a Perkin Elmer Lambda 25 UV/Vis spectrometer in 1 cm length quartz cuvettes. Excitation and emission photoluminescence spectra of solution samples were performed using an Edinburgh Instruments FLS920 Fluorometers. The fluorescence samples were run in standard quartz fluorescence cuvettes, $l = 1 \times 1$ cm. All spectroscopy experiments were performed using spectrophotometric grade solvent and solutions never exceeded $A = 0.10$ at the excitation wavelength, or any longer wavelength, to minimise inner filter effects. Excitation and emission photoluminescence spectra of the powder, and thin film samples were performed using an FLS980 Spectrometer. Dye films were prepared by drop casting the solution with dichloromethane as the solvent, on to the quartz substrate and leave it to dry. Diffuse UV-vis reflectance spectra were measured on a UV Vis NIR Agilent Cary Spectrometer equipped with an integrating sphere accessory.

Fluorescence micrographs images of Single crystals were carried out at the University of Nottingham. Excitation of the crystals at 540-550 nm were performed using Olympus IX73. Powder XRD is an analytical technique which was used to help identify the crystallinity of material and provide information about the atomic arrangement. Powdered samples were placed on circular kapton polyimide thin film to record the XRD pattern. The sample was bombarded with X-rays which were produced from a copper anode source ($K\alpha$ radiation is $1.54 \text{ \AA}$). The angle of diffraction, which is called theta angle, is measured in an angle twice that of the theta angle and this angle is called '2-theta'.

4.5.5 Synthetic Procedures

Synthesis of 2,6-dipyridyl-1, 3, 5,7-tetramethyl-8-phenyl-4,4 difluoroboradiazaindacene (4-18)

In order to synthesis **4-18**, a solution of 2,6-diiodo-1, 3, 5,7-dimethyl-8-phenyl-4,4 difluoroboradiazaindacene (100 mg, 0.19 mmol) in mixed solvent of 1,4-dioxane (60 mL) and water (6 mL), was added (90 mg, 0.78 mmol) of pyrimidine 4-boronic acid and Cs₂CO₃ (254 mg, 0.78mmol). The solution was bubbled with dry nitrogen gas for around 30 minutes. Then tetrakis(triphenylphosphine)palladium(0) (56 mg, 0.048mmol) was added under nitrogen atmosphere. The reaction mixture was refluxed in the absence of light until the reaction is complete which is monitored by thin layer chromatography. The crude product was purified using column chromatography (ethyl acetate: methanol = 10:1) to get **4-18** red solid 40 mg, yield: 47.77%.

¹H NMR (400 MHz, CDCl₃) δ 8.66 (d, 4H, J = 6 Hz), 7.53-7.57 (m, 3H), 7.37 (d, 2H, J = 9 Hz), 7.13 (d, 4H, J = 6 Hz), 2.60 (s, 6H), 1.36 (s, 6H).; ¹³C NMR (100 MHz, CDCl₃) 152.27, 150.65, 150.09, 143.07, 142.01, 137.80, 132.36, 131.19, 125.19, 121.40, 17.52, 15.52, 13.29; ¹¹B-NMR (128 MHz, CDCl₃) δ 0.92 (t, J = 31.82 Hz); ¹⁹F-NMR: (376 MHz, CDCl₃) δ -145.79 (q, J = 31 Hz). (HESI/MeOH): m/z calculated 478.21 observed 479.22, ([M+H]⁺, 100%). FT-IR (ATR, cm⁻¹): 441 w, 502m, 537s, 690s, 722s, 756w, 931w, 1070s, 1084s, 1121s, 1184s, 1180s, 1280w, 1312m, 1438m, 1486w, 1520w, 1589w, 1729mw, 2900w, 2923m, 2949w, 3059w.

Synthesis of 2,6-dipyridyl-1, 3, 5,7-tetramethyl-8-phenyl-4,4 difluoroboradiazaindacene (4.2)

A solution of 2,6-diiodo-1, 3, 5,7-dimethyl-8-phenyl-4,4 difluoroboradiazaindacene (100 mg, 0.19 mmol) in mixed solvent of 1,4-dioxane (60 mL) and water (6 mL), was added to (90 mg, 0.78 mmol) of pyrimidine 4-boronic acid and Cs_2CO_3 (254 mg, 0.78mmol). The solution was bubbled with dry nitrogen gas for around 30 minutes. Then tetrakis(triphenylphosphine)palladium(0) (56 mg, 0.048mmol) was added under nitrogen atmosphere. The reaction mixture was refluxed in the absence of light until the reaction is complete which is monitored by thin layer chromatography. The crude product was purified using column chromatography (ethyl acetate: methanol = 10:1) to get **4-19** as red solid 50 mg, yield 59.62%.

^1H NMR (400 MHz, CDCl_3) δ 9.21 (s, 1H); 8.68 (s, 2H); 7.72-7.49 (m, 7H), 7.27-7.39 (m, 1H), 2.60(s, 6H), 1.61 (s, 6H); 1.37 (s, 2H); 1.28 (s, 1H); ^{13}C NMR (100MHz, CDCl_3) 157.57, 157.42, 132.15, 132.05, 131.96, 131.94, 129.68, 128.57, 128.45, 127.86, 127.61, 77.33, 77.02, 76.70, 13.36, 12.78; ^{11}B -NMR (128 MHz, CDCl_3) δ 0.88 (t, $J = 32.14$ Hz); ^{19}F -NMR: (376 MHz, CDCl_3) δ -145.74 (q, $J = 32.11$ Hz). (HESI/MeOH): m/z calculated 479.1973 observed 479.1964, ($[\text{M}-\text{H}]^-$, 100%). FT-IR(ATR, cm^{-1}): 441 w, 502m, 537s 690s, 522s, 632w, 722s, 756w, 835w, 931w, 999 ms, 1070s, 1121s, 1284s, 1312ms, 1438ms, 1486w, 1520wm, 1589w, 1729m, 2850w, 2923m, 2949w, 3059w.

Attempted Synthesis of $[\text{Cu}_4\text{I}_4(\text{Pyr-BODIPY})_4]_\infty$ (4-20)

4-20 was synthesised by slow solvent diffusion between an upper layer of CuI (3mg, 0.1mmol) in acetonitrile (0.4 ml) and a lower layer of Pym-BODIPY (37mg, 0.07mmol) in

chloroform.(0.4ml) yielded brown crystals suitable for X-ray diffraction studies which upon analyses were confirmed as $(\text{CuI})_{\infty}$.

*Synthesis of $[\text{Cu}_4\text{I}_4(\text{Pyr-BODIPY})_4]_{\infty}$ (**4-20**)*

4-20 was synthesised by combining (3mg, 0.1mmol) CuI, and Pyr-BODIPY (35 mg, 0.07mmol) in 1ml of acetonitrile in a sealed scintillation vial. The mixture was heated in an oven at 55 °C for 3 days, which yielded brown shaped crystals, 30 mg.

FT-IR(ATR, cm^{-1}): 443w, 467w, 504m, 515m, 523m, 533s, 580s, 673ms, 691s, 718s, 753w, 796m, 837wm, 844wm, 864w, 995s, 1065s, 1085s, 1120s, 1176w, 1180s, 1241mw, 1290w, 1307ms, 1389ms, 1420m, 1440m, 1461m, 1604w, 1730mw, 1528s, 2850w, 2926w, 3059w.

*Synthesis of $[(\text{CuI})_2(\text{pyrm-BODIPY})_2]_{\infty}$ (**4-21**)*

4-21 was synthesised by slow solvent diffusion between an upper layer of CuI (3mg, 0.1mmol) in acetonitrile (0.4 ml) and a lower layer of Pyrm-BODIPY (37mg, 0.07mmol) in chloroform.(0.4ml). yielded brown crystals, 25 mg.

FT-IR(ATR, cm^{-1}): 439m, 457m, 506m, 515m, 523m, 535s, 582w, 617w, 693m, 720s, 751m, 844w, 864w, 926w, 955w, 993wm, 1071ms, 1120ms, 1182ms, 1253m, 1313mw, 1434m, 1471w, 1485w, 1537w, 1590w, 1730mw, 2848mw, 2920 mw, 3055w.

4.5.6 X-ray Crystallography

Single crystal diffraction data were collected for **4-18a**, **4-18b**, **4-19**, **4-20**, and **4-21**, at 120(2) K on a SuperNova, Atlas GV1000, or Rigauh XtaLab MM 007 diffractometer using mirror

monochromated CuK α radiation. Using Olex2,¹⁰⁵ the structure was solved with the ShelXT¹⁰⁶ structure solution program using intrinsic phasing and refined with the ShelXL¹⁰⁷ refinement package using least squares minimization.

Crystal data for **4-18.a***: C₂₉H₂₅B₁N₄F₂, triclinic, space group *P*-1, *a* = 6.2631(5) Å, *b* = 11.5815(7) Å, *c* = 16.4310(8) Å, α = 90.269(4)°, β = 91.458(5)°, γ = 105.041(6)°, *V* = 1150.56(13) Å³, *Z* = 2, *D*_{calc} = 1.381 g cm⁻³, μ = 0.757 mm⁻¹, *F*(000) = 500, a total of 7918 reflections were collected, of which 4495 were unique, with *R*_{int} = 0.0302. Final *R*₁ (*wR*₂) = 0.0828 (0.2386) with GOF = 1.023.

Crystal data for **4-18.b***: C₂₉H₂₅B₁N₄F₂, monoclinic, space group *I*2/*a*, *a* = 13.5686(4) Å, *b* = 13.2178(5) Å, *c* = 13.7790(5) Å, α = 90°, β = 105.947(4)°, γ = 90°, *V* = 2376.12(15) Å³, *Z* = 4, *D*_{calc} = 1.337 g cm⁻³, μ = 0.730 mm⁻¹, *F*(000) = 1000, a total of 4769 reflections were collected, of which 2358 were unique, with *R*_{int} = 0.0191. Final *R*₁ (*wR*₂) = 0.0405 (0.1102) with GOF = 1.040.

Crystal data for **4-19**: C₂₇H₂₃BN₆F₂, monoclinic, space group *P*2₁/*c*, *a* = 11.2952(3) Å, *b* = 17.0907(6) Å, *c* = 12.0417(3) Å, α = 90°, β = 94.541(3)°, γ = 90°, *V* = 2317.27(12) Å³, *Z* = 4, *D*_{calc} = 1.377 g cm⁻³, μ = 0.780 mm⁻¹, *F*(000) = 1000.0 A total of 11672 reflections were collected, of which 4529 were unique, with *R*_{int} = 0.0365. Final *R*₁ (*wR*₂) = 0.0414 (0.1011) with GOF = 1.039.

Crystal data for **4-20**: $C_{29}H_{25}BCu_2F_2I_2N_4$. triclinic, space group $P-1$ $a = 9.8116(11)$ Å, $b = 10.9371(10)$ Å, $c = 13.6945(12)$, $\alpha = 89.204(7)^\circ$, $\beta = 87.705(8)^\circ$, $\gamma = 78.296(8)^\circ$, $V = 1437.8(2)$ Å³, $Z = 2$, $D_{\text{calc}} = 1.974$ g cm⁻³, $\mu = 18.718$ mm⁻¹, $F(000) = 828$, a total of 9947 reflections were collected, of which 5588 were unique, with $R_{\text{int}} = 0.0791$. Final R_1 (wR_2) = 0.1144 (0.1982) with GOF = 1.047.

Crystal data for **4-21**: $C_{27}H_{23}BCu_2F_2I_2N_6$. Monoclinic, space group $P21/c$. $a = 14.6653(4)$ Å, $b = 9.0291(3)$ Å, $c = 12.2807(3)$, $\alpha = 90^\circ$, $\beta = 93.859(2)^\circ$, $\gamma = 90^\circ$, $V = 162247(8)$ Å³, $Z = 2$, $D_{\text{calc}} = 1.763$ g cm⁻³, $\mu = 16.870$ mm⁻¹, $F(000) = 828.0$, a total of 9721 reflections were collected, of which 3267 were unique, with $R_{\text{int}} = 0.0446$. Final R_1 (wR_2) = 0.0612 (0.2068) with GOF = 1.147.

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Chapter 5

Global Conclusions

5.1 Conclusions

BODIPYs are highly functionalized, π -conjugated molecules that can be tailored to various applications such as light-harvesting devices, solar cell technology, chemical sensors, nanocrystals, biological marking, photodynamic therapy and drug delivery. In order to develop BODIPY compounds with specific targeting such as imaging, biological and electronic applications, modification of the dipyrroin core is required. Several pre- or post-modifications can be done easily. There are three main positions which are typically available for modification on a BODIPY core: the dipyrromethene core, boron centre, and meso substituent. In this thesis we were mainly interested in functionalized dipyrromethene core and investigate the effect of such substitution on the optical, electrochemical, photophysical, solid state analysis of novel different substituted BODIPY species. In general, halogenated BODIPYs are attractive because they can be used as starting materials for the preparation of functionalized BODIPYs *via* both nucleophilic substitutions reactions, and metal-catalyzed cross-coupling reactions such as Pd(0)-catalyzed cross-coupling reactions.

The first part of this thesis explores the development of efficient synthetic methods for the regioselective electrophilic halogenation of BODIPYs. ^1H NMR and ^{19}F NMR spectra were used as a tool to investigate the selective behaviour of halogenation of the BODIPY core and the structural change during the iodination. The mono- and diiodo derivatives could be isolated from the reaction mixture. However, the intermediate tri- and tetra-iodo derivatives could not be isolated due to their high reactivity but were unambiguously identified by ^1H NMR and ^{19}F NMR spectroscopy. Halogenation of the α -methyl groups of the BODIPY (intermediate tri- and tetra-iodo) is also fascinating because it opens the possibility to further

functionalize the BODIPY. Post-functionalization *via* nucleophilic substitution introduces new substituents in a non-conjugated manner in contrast to other oxidation or Knoevenagel-type transformations on these positions. In particular, the functionalization of BODIPY with non-conjugated tertiary amine substitution at the β -positions and halogen atoms at the α -positions which give rise to highly coloured dye molecules with intense absorptions, ($\epsilon \approx 305,000 \text{ mol}^{-1}\text{dm}^3\text{cm}^{-1}$) and a positive shift in redox potentials. The more positive potential values could be due improved electron donation to the BODIPY core from the methylene and morpholino groups, and fluorescence quenching due to the presence of the amine functionality.

The second part of this thesis investigates the role of halogen bonding interactions in the assembly of a series of halogenated BODIPY bearing different substituents at the *meso*-position (based on our structures, and information from the CCSD). The presence of halogen atoms, BF_2 moieties and other electron acceptor groups on BODIPY *meso*-position leads to interesting halogen bonding interaction in the solid-state arrangements of such compounds. In general, halogen bonding can be attributed to the favourable interaction that exists between a halogen's electropositive σ -hole and an electronegative atom, such as oxygen, or other halogen atoms. Halogen $\cdots$ halogen, halogen $\cdots$ oxygen, halogen $\cdots$ sulfur, and hydrogen bonding interactions presented in BODIPY structures. Therefore, these interactions were identified and analysed through distance, angles, Hirshfeld surface map, 2D-fingerprint, and the percentage contribution for different kinds of non-covalent interactions. In all cases presented in **Chapter 3**, the halogen bond turned out to have several characteristic properties reminiscent of the well-known hydrogen bonding. Firstly, analysing type I and type II interactions as a function of the interaction distance afforded a valuable outcome: at distances shorter than the *van der Waals*

contacts, type I interactions were more common. Secondly, the *meso*-position plays a great role in the halogen bonding interactions, for example, the dramatic changes of the types of halogen interaction from type II (I $\cdots$ I) XB interaction to type I, through changing the *meso* substituent from phenyl to hydrogen. Thirdly, introducing electron-rich sites such as carbonyl, methoxy or hydroxy groups have a direct result on the packing of the crystal, which results in increased control of the resulting structure. Minor changes on the phenyl at *meso*-position of BODIPY could make a dramatic change and introduce a more complex system which include both HB, and XB interactions, making one of them more favourable than the other.

The third part of this thesis explores how simple structural modifications on the BODIPY can affect the solid-state structure, photophysical and electrochemical properties of the BODIPY core. In particular, we were interested in developing a pyridyl and pyrimidyl functionalized BODIPY and using them as ligands in coordination polymer construction with copper iodide. The crystal structure of the ligands Pym-BODIPY and Pyr-BODIPY compound **4-19** and polymorphs **4-18.a*** and **4-18.b*** show similar intermolecular interactions with different percentages due to different packing. Consequently, quantification of the intermolecular interactions presents in compounds **4-18.a***, **b*** and **4-19** was realized by Hirshfeld surface analysis and 2D fingerprint plots. This analysis of intermolecular contacts presents in the crystal packing of **4-18.a*** and **4-18.b*** leads us to conclude that these are different polymorphs. A rare example of (F $\cdots$ F) XB close contact is presenting in **4-18.b***.

On the other hand, the coordination polymer based on Pyr-BODIPY presents the formation of a rare open cubane configuration for CuI, the Pym-BODIPY has demonstrated the formation of a three-dimensional coordination polymer with planar ribbon-type structures of the copper centre. Powder X-ray diffraction studies of **4-20** and **4-21** were recorded, and comparison to patterns calculated from the single crystal diffraction data. In the case of **4-20**, there is evidence of the presence of the compound, but amorphous material is also observed, which is possibly due to loss of crystallinity under the conditions of the experiment. Similarly, the same broad peaks at *ca.* 14° and 30° are observed in **4-21**.

In term of photophysical properties, modifications on the BODIPY core at the 2,6 positions with pyridine or pyrimidine lead to bright emissive compounds in the solution, solid state, and thin film. Both dyes have high quantum yields (Φ_F) 0.86 and 0.90 respectively, in dichloromethane and a solid-state fluorescence which is rare characteristic of BODIPYs because of increasing the emission efficiency of BODIPY dyes as a result of (D–A–D) type molecule. However, coordination polymers (compounds **4-20** and **4-21**) displays fluorescence quenching response. The fluorescence quenching might be because the coordination between Cu⁺ and the nitrogen atoms on the pyridine, and the pyrimidine rings, which induces ICTs and leads to concomitant quenching of the BODIPY fluorescence. This might arise as an effect of phenomena known as π back-bonding effect, which has been previously reported for other pyridyl BODIPY which substituents on the 2,6 positions and Cu(I).²¹

Cyclic voltammetric investigations on **4-18** and **4-19** displayed the expected one electron reduction processes. The modifications of the BODIPY core at (2,6) positions with pyridyl or pyrimidyl substituents lead to moving the BODIPY reduction to a more positive potential in comparison with the parent BODIPY. Moreover, the presence of extra nitrogen in the

pyrimidyl-groups had the desired effect of moving the BODIPY reduction of **4-19** to a more positive potential. This was explained as an effect of the present of extra nitrogen in the pyrimidine moiety, which make it a stronger electron donor.