# Organic & Biomolecular Chemistry

Accepted Manuscript






ROYAL SOCIETY OF CHEMISTRY

www.rsc.org/obc

# Halogenated Boron-Dipyrromethenes: Synthesis, Properties and Applications

Vellanki Lakshmi, Malakalapalli Rajeswara Rao and Mangalampalli Ravikanth*

*Department of chemistry, Indian Institute of Technology Bombay, Mumbai 400076, India.*

E-mail: ravikanth@chem.iitb.ac.in

**Abstract**

Boron-dipyrromethene dyes (BODIPYs) containing halogens at pyrrole carbons are very useful synthons for the synthesis of variety of BOIDPYs for a wide range of applications. Among the functional groups, halogens are the functional groups which can be regiospecifically introduced at any desired pyrrole carbons of BODIPY framework by adopting appropriate synthetic strategies. The halogenated BODIPYs can undergo facile nucleophilic substitution reactions to prepare several interesting BODIPY based compounds. This review describes the synthesis, properties and potential applications of halogenated BODIPYs containing one to six halogens at the pyrrole carbons of BODIPY core as well as properties and applications of some of the substituted BODIPYs derived from halogenated BODIPYs.

## Introduction

The search for new organic/inorganic fluorescent dyes over the past decades with improved luminescence, electrochemical and charge-transport properties is a thriving subject which is undergoing rapid development. This widespread interest is motivated because of their use as light emitting films, electroluminescent materials, and molecular probes.[1,2] The applicability of organic/inorganic fluorescent dyes depends upon their photostability, solvatochromism, molar absorptivity, luminescence quantum yields, solubility and process ability. 4,4-Difluoro-4-bora-3a,4a-diaza-*s*-indacene (Chart 1) commonly named as BODIPYs are effective fluorescent probes/sensors. BODIPY derivatives have emerged as a fascinating class of dyes with excellent performance and stability with wide range of applications in biomolecular labels,[3,4] chromogenic probes and cation sensors,[5,6] drug delivery agents,[7,8] fluorescent switches,[9] electroluminescent films, laser dyes,[10-13] light-harvesters[14] and sensitizers for solar cells,[15] labelling[16] and photodynamic therapy.[17,18] These dyes have excellent features such as high molar extinction coefficients, high fluorescence quantum yields, strong chemical and photochemical stability in solution and in the solid state and remarkable electron/energy transfer properties.[19-21] Furthermore, their spectroscopic and photophysical properties are sensitive by attaching secondary units at the pyrrole core, the central pseudo *meso* position, and at the boron substituents.[22] The electronic properties of BODIPYs can be fine-tuned by using several different approaches such as introduction of functional substituents on the carbon framework, enlargement of the chromophore, substitution of the fluorine atoms by O- or C- donors or replacing the *meso*-CH position with a nitrogen bridge to name few such modifications.[19-22] These modifications on the BODIPY architecture provides new opportunities to tune the properties for various applications.

BODIPY dyes were first discovered in 1968 by Treibs and Kreuzer.[23] BODIPY dyes can be synthesized in two steps: In the first step, dipyrromethane unit **1** is prepared by

condensation of pyrrole and electrophilic carbonyl compound, such as acid anhydride, acyl chloride or aldehyde under catalytic amount of acid. In the second step, the dipyrromethane **1** is oxidized to dipyrromethene **2** followed by complexation with $BF_3 \cdot OEt_2$ in the presence of a base to afford BODIPY **3** (Scheme 1).[24,25] Using the standard synthetic approaches, several BODIPY dyes have been prepared from readily available pyrroles and the synthetic efforts were being focused on varying the nature of substituents located at 8-position.[26-28] BODIPY **3** exhibits good photophysical and electrochemical properties. BODIPY **3a** absorbs and emits in visible region at ~500 nm and 520 nm respectively (Figure 1a) with decent quantum yields and singlet state lifetimes.[29] The BODIPYs are electron deficient and generally show one reversible reduction (Figure 1b) along with one ill-defined oxidation. However, the spectral and electrochemical properties can be fine tuned by introducing suitable substituents at the various positions of BODIPY core.[19-21] In recent times, several excellent reviews on BODIPYs have been published because of their steadily increased popularity over last few decades. Loudet and Burgess in 2007 reviewed the complete synthetic aspects of various types of BODIPY dyes and their derivatives.[20] Ziessel and co-workers discussed photophysical properties and cation/anion sensing abilities of BODIPY dyes.[19,21] Awuah and You described the role of the BODIPYs as photosensitizers for photodynamic therapy of cancer.[17b] Boyle and co-workers discussed BODIPYs as components of novel light active materials.[30] Ni and Wu described the synthesis of NIR BODIPY dyes and their applications as fluorescent pH probes and bio imaging.[3a] Boens, Leen and Dehaen discussed synthesis and applications of BODIPY dyes as fluorescent indicators.[31] Shen and co-workers discussed spectral and photophysical properties of different types of long wavelength absorbing BODIPY dyes.[22a] Thus all these reviews have covered the synthesis and properties of BODIPYs as well as their applications as fluorescent indicators, photodynamic therapy, luminescent devices and energy transfer cassettes. While

working on BODIPYs, we realized that the functionalization at all the six pyrrole carbons of BODIPY core is one of the best strategies to prepare new types of BODIPYs for wide range of applications.[31] A perusal of literature reveals that the reports on functionalization of pyrrole carbons of BODIPY core is limited and only the functional groups such as halogens, formyl, cyano, azido, amido and ester were introduced at the pyrrole carbons of BODIPY frame work. Among the functional groups, only halogens have been introduced at all six pyrrole carbons of BODIPY core[32,] and the spectral and electrochemical properties were systematically studied by varying the number of halogen groups.[32,33] Furthermore, the halogenated BODIPYs were used as precursors to prepare several interesting BODIPY based systems.[34] The halogenated BODIPYs have tremendous potential to use them for the synthesis of several other novel BODIY based systems with properties suitable for variety of applications. In this review, we provide an overview of different synthetic strategies employed for the synthesis of halogenated BODIPYs containing one to six halogens at pyrrole carbons of BODIPY frame work; the systematic effect of increasing the number of halogens from one to six on spectral and electrochemical properties of BODIPY and the applications of halogenated BODIPYs towards the synthesis of novel BODIPYs along with discussion on their important properties.

**Halogenated BODIPYs**

The halogenated BODIPYs are the key building blocks to synthesize various substituted complex BODIPYs using palladium coupling reactions.[19-22] In addition, halogenated BODIPYs can find applications as probes for photodynamic therapy[18] (PDT), a noninvasive methodology for the treatment of malignant tumours. The presence of heavy halogens increases the rate of intersystem crossing resulting in the population of the triplet state which is required for the generation of reactive oxygen species.[35] A perusal of literature revealed that it is possible to introduce halogens at all pyrrole carbons of BODIPY

selectively[32] and regiospecifically[33] and most of these synthetic strategies were reported recently. There are three different strategies to synthesize halogenated BODIPYs: (1) using halogenated pyrroles for BODIPYs synthesis;[25] (2) halogenation of the dipyrromethane precursors[36,37] and use them for the synthesis of BODIPYs and (3) electrophilic substitution reactions on the BODIPYs.[38] These methods have been used to synthesize BODIPYs containing one to six halogens at the pyrrole carbons.

**Mono-halogenation**

The 2-halogenated **4a-4c** and 3-halogenated BODIPYs **5a** and **5b** were prepared by following different strategies shown in Scheme 2. The condensation of appropriate 4-halogenated-2-acylpyrrole with the desired substituted pyrrole in the presence of one equivalent of phosphorus oxychloride resulted in the formation of dipyrromethene which was complexed by adding excess triethylamine and $BF_3{\cdot}OEt_2$ to afford 2-halogenated BODIPYs[39] **4a-4c** (Scheme 2a). In this method, the halogen atom was varied from chlorine to bromine to iodine and prepared all three mono-halogenated BODIPYs **4a-4c** in 35-40% yields.[40-43] Alternately, 2-halogenated BODIPYs **4a-4c** were prepared by treating BODIPY **3b** with one or less than one equivalent of N-halo succinimide in $CH_2Cl_2$ in good yields[12,44] since 2-position of BODIPY is more prone for electrophilic substitution reactions (Scheme 2a). The halogenation at 2-position of BODIPY was also carried out by treating BODIPY **3** with brominating agent[33] such as $Br_2$ and iodinating agent[45] such as $I_2/HIO_3$ and afforded respective 2-halogenated BODIPYs **4a-4c** in high yields (Scheme 2a).

The 3-halogenated BODIPYs **5a** and **5b** were prepared by condensing 5-halogenated 2-acylpyrrole with substituted pyrrole in the presence of phosphorus oxychloride followed by treatment with excess $NEt_3/BF_3{\cdot}OEt_2$[39] (Scheme 2b). In this method, one can use any substituted pyrrole as second pyrrole to prepare range of 3-halogenated BODIPYs.

Alternately, treatment of *meso*-aryl dipyrromethane **1** with one equivalent of appropriate N-halo succinimide at -78 °C in THF followed by oxidation with DDQ and complexation with $NEt_3/BF_3{\cdot}OEt_2$ afforded 3-halogenated BODIPYs **5a** and **5b** in decent yields (Scheme 2b).[46]

**Di-halogenation**

**3,5-Dihalogenated BODIPYs**

The 3,5-dihalogenated BODIPYs **6a** and **6b** were prepared by starting with *meso*-aryl dipyrromethane **1** as shown in Scheme 2c. Treatment of *meso*-aryl dipyrromethane **1** with two equivalents of appropriate N-halo succinimide in THF at -78 °C followed by oxidation with DDQ and complexation with $NEt_3/BF_3{\cdot}OEt_2$ afforded the 3,5-dihalogenated BODIPYs **6a** and **6b**.[36,37] Although the other halogenated BODIPYs were also form in these reactions and chromatographic purification was required to separate the 3,5-dihalogenated BODIPY **6a/6b** from the mixture of halogenated BODIPYs. This is the only reliable method available to synthesize 3,5-dihalogenated BODIPYs **6a/6b**.

**2,6-Dihalogenated BODIPYs**

The 2,6-positions of BODIPY **3** bear the least positive charge and susceptible for electrophilic attack. The 2,6-dihalogenated BODIPYs[33,44,45] **7a-7c** were prepared by treating appropriate BODIPY **3** with N-halo succinimide (NXS) or $X_2$ ($Br_2$, $Cl_2$, $I_2$) in $CH_2Cl_2$ at room temperature or other slightly varied reaction conditions (Scheme 2d). Recently Wang et al.[47] showed that the regioselective dihalogenation at 2,6-positions can be much faster when reactions were carried out in hexafluoro-2-propanol using N-halosuccinimide as the halogen source (Scheme 2d).

**1,7-Dihalogenated BODIPYs**

The 1,7-positions of BODIPY **3** are electron poor like 3,5-positions and direct halogenation on BODIPY at these positions is not possible if other positions are not blocked with the substituents. Leen et al.[48] synthesized the first examples of 1,7-dihalogenated BODIPYs **8a** and **8b** by adopting two synthetic routes shown in Scheme 2e. In first strategy, the authors condensed the 2,3-dimethylpyrrole with acetyl chloride in $CH_2Cl_2$ followed by in situ complex formation to afford 2,3,5,6-tetrasubstituted BODIPY **3c** which was subjected to bromination by treating with $Br_2$ in $CH_2Cl_2$ and afforded 1,7-dibrominated BODIPY **8b** in excellent yield.[48] In the second strategy, the 2,3-dimethylpyrrole was first formylated at 5-position under standard Vilsmeier-Haack reaction conditions which was then halogenated at 4-position by treating with NXS and afforded 2,3-dimethyl-4-halo-5-formyl pyrrole. The substituted pyrrole was then treated with phosphorus oxychloride to afford dipyrromethene which was then complexed with $BF_3{\cdot}OEt_2$ and obtained 1,7-dihalogenated BODIPY **8a/8b** as sole product (Scheme 2e).[48] Thus, the 1,7-dihalogenated BODIPYs **8a** and **8b** can be prepared by only blocking all other pyrrolic positions of BODIPY. Oritz et al.[49b] reported synthesis of 1,2-diiodonenated **9a** and 2,3-diiodonenated BODIPYs **9b** by treating BODIPY **3e** (pyrrole carbons were blocked) with 2.5 equivalents of ICl in $CH_2Cl_2/CH_3OH$ and the resulted mixture of diiodonetaed BODIPYs **9a** and **9b** were separated by column chromatography (Scheme 2f). These kinds of dihalogenated BODIPYs **9a** and **9b** can be prepared only by blocking the second pyrrole ring carbons of BODIPY unit.

**Tri-halogenation**

2,3,5-Trichloro BODIPY **10a** was synthesized by treating BODIPY **3a** with four equivalents of N-chlorosuccinimide in THF (Scheme 2g) at room temperature.[12] Lakshmi and Ravikanth synthesized 2,3,5-tribromo BODIPY **10b** by treating *meso*-aryl dipyrromethane **1** with three equivalents of N-bromosuccinimide in $CH_2Cl_2$ at -78 °C followed by oxidation with DDQ and complexation with $BF_3{\cdot}OEt_2$.[32] In these bromination reactions, although the

other brominated BODIPYs also form, the major product is the desired compound **10b** which was separated by column chromatography (Scheme 2g). Jiao and co-workers[33] reported regiospecific bromination of BODIPYs by treating BODIPY with liquid bromine but they could not isolate tribromo BODIPY **10b**. Oritz et al.[49b] prepared the 1,2,3-triiodo BODIPY **11** by taking BODIPY **3e** in which one of the pyrrole ring carbons were blocked and treated with 4.5:4 ratio of $I_2/HIO_3$ in $CH_2Cl_2/CH_3OH$ at room temperature (Scheme 2h). The reaction resulted in the formation of mixture of two different types of 1,2,3-triiodo BODIPYs which were separated by column chromatography. The same research group also reported the synthesis of 2,3,6-triiodo BODIPY **12** by treating *meso*-aryl BODIPY with 3.5 equivalents of ICl and the resulted mixture of halogenated BODIPYs were separated by column chromatography to afford 2,3,6-triiodo BODIPY **12** (Scheme 2i).[49b]

**Tetra-halogenation**

The 2,3,5,6-tetrachloro BODIPY **13a** was synthesized by treating BODIPY **3a** with N-chlorosuccinimide.[12] The **13a** was also synthesized by treating the *meso*-thienyl BODIPY with sulfuryl chloride (Scheme 2j) at room temperature.[49a] Jiao et al.[33] reported the synthesis of 2,3,5,6-tetrabromo BODIPY **13b** by treating BODIPY **3a** with 6 equivalents of $Br_2$ in $CH_2Cl_2$. Lakshmi and Ravikanth[32] synthesized 2,3,5,6-tetrabromo BODIPY **13** by reacting *meso*-aryl dipyrromethane **1** with four equivalents of NBS in THF at -78 °C followed by oxidation with DDQ and complexation with $BF_3{\cdot}OEt_2$ (Scheme 2j). This method afforded the desired tetrabrominated BODIPY **13b** along with other brominated BODIPYs and the desired tetrabrominated BODIPY **13b** was separated from other brominated BODIPYs by column chromatography. Oritz et al.[49b] prepared tetraiodo BODIPY **14a** and mixed tetrahalogenated BODIPYs having two different types of halogens such as iodo and chloro groups **14b** and **14c** by treating BODIPY with 8 equivalents of ICl in $CH_2Cl_2/CH_3OH$ (Scheme 2k) and isolated tetrahalogenated BODIPYs **14a-14c** by column chromatography.

**Penta-halogenation**

The 1,2,3,5,6-pentabrominated BODIPY **15** was prepared either from *meso*-aryl dipyrromethane[32] **1** or *meso*-aryl BODIPY[33] **3a** (Scheme 2l). Jiao et al.[33] prepared by treating BODIPY **3a** with 40 equivalents of $Br_2$ in $CH_2Cl_2$ whereas Lakshmi and Ravikanth[32] prepared the same compound by treating *meso*-aryl dipyrromethane **1** with five equivalents of NBS in THF followed by oxidation with DDQ and complexation with $BF_3{\cdot}OEt_2$ (Scheme 2l). In both strategies, the pentabrominated BODIPY **15** forms as major product along with other minor brominated BODIPYs and column chromatography was used to isolate the 1,2,3,5,6-pentabrominated BODIPY **15** in decent yields.

**Hexa-halogenation**

Lakshmi and Ravikanth[32] and Ortiz et al.[12] used same synthetic strategy to prepare 1,2,3,5,6,7-hexahalogenated BODIPYs **16a** and **16b** by treating *meso*-aryl dipyrromethane **1** with excess equivalents of N-halosuccinimide in THF at room temperature followed by oxidation with DDQ and complexation with $BF_3{\cdot}OEt_2$ (Scheme 2m). Simple column chromatographic purification was required to afford pure hexahalogenated BODIPYs **16a** and **16b** in decent yield. Jiao et al.[33] also succeeded in synthesizing hexabrominated *meso*-aryl BODIPY **16b** by treating *meso*-aryl BODIPY **3a** with excess equivalents of $Br_2$ (Scheme 2m).

**Properties**

The introduction of halogens at the pyrrole carbons of BODIPY core, in general, alter the electronic properties of the BODIPY and there are several reports discussing the effect of halogen(s) on spectral and electrochemical properties of the BODIPY. Lakshmi and Ravikanth[32] carried out systematic study on alteration of electronic properties of the BODIPY

by sequential addition of of bromines from one to six at the pyrrole carbons of BODIPY. The crystal structures were solved for brominated BODIPYs[32,33] where the number of bromines were varied from two to six bromines. The crystal structures revealed that the dihedral angle between the BODIPY core (C6C5C10C15) and the *meso*-anisyl group was increased from 48° to 88° (Figure 2) with the increase of number of bromines. Thus, the *meso*-anisyl ring was almost in perpendicular orientation in pentabromo- **15** and hexabromo BODIPYs **16**. This observation indicates that only the bromine groups present at 1- and 7-positions causes steric hindrance and restricts the rotation of *meso*-anisyl group resulting in nearly perpendicular orientation of the *meso*-anisyl group with the BODIPY core.[32] The absorption properties of brominated BODIPYs (**5, 6, 10, 13, 15** and **16**) with a step wise increase in the number of bromines were studied and compared with unsubstituted *meso*-aryl BODIPY **3a** (Figure 3a). The studies indicated that each step wise increase in the number of bromine groups at the pyrrole carbons of BODIPY core resulted in a bathochromic shift compared to unsubstituted *meso*-aryl BODIPY **3a** and the magnitude of the red shift in absorption band depends on the number of bromines substituted at the BODIPY core. It was noted that each bromine substitution at the pyrrole carbon contributes 10 nm red shift compared to the absorption band of unsubstituted BODIPY **3a**. However, authors noted that the systematic red shift was possible only up to the introduction of four bromines and compounds with five and six bromines **15** and **16** did not show any further red shift. The plot of magnitude of red shifts versus the number of bromines substituted showed a clear non-linear curve which indicates that the magnitude of red shift with each bromine substitution is non-additive. The fluorescence spectral studies revealed that the brominated BODIPYs **(5, 6, 10, 13, 15** and **16)** show one single broad emission band which shifted gradually to higher wavelength with the increase of number of bromine groups up to four and no further red shifts were noted for penta **15** and hexabrominated BODIPYs **16**. The quantum yields were decent for mono to

tetrabrominated BODIPYs (**5, 6, 10, 13**) and significantly low for penta **15** and hexabrominated BODIPYs **16** due to heavy halogen effect which was more pronounced only for **15** and **16**.

The redox properties of brominated BODIPYs showed very interesting trend with the increase of number of bromines at the pyrrole carbons of BODIPY core. The BODIPYs are, in general, electron deficient and show one or two reductions but oxidation is either irreversible or absent. The brominated BODIPYs (**5, 6, 10, 13, 15** and **16**) showed one reversible reduction and one irreversible reduction and the comparison of first reduction wave of brominated BODIPYs along with unsubstituted *meso*-aryl BODIPY **3a** is presented in Figure 3b.[32] The addition of each bromine resulted in a successive anodic shift of reduction potential compared to unsubstituted *meso*-aryl BODIPY **3a** indicating that the BODIPY becomes easier to reduce with the increase of number of bromine groups. The linear relationship between $E_{1/2}$ for the first reduction and the number of Br groups (Figure 3c) indicates that the effect was additive and the slope of the straight line plot was 80 mV/Br group. Thus, the redox properties exhibited systematic trend with the increase of number of Br groups and first reduction potential of BODIPY was linearly related to the number of Br groups.[32]

**Applications**

The halogenated BODIPYs **4-16** are highly useful synthons to prepare several interesting BODIPY derivatives which have potential applications in various fields. The halogenated BODIPYs **4-16** were subjected to various transition metal-catalysed cross-coupling reactions as well as nucleophilic substitution reactions and the selective systems are described here.

**2-Substituted BODIPYs**

The 2-halogenated BODIPYs **4a-4c** were used to synthesize variety of 2-substituted BODIPYs **17-21** including BODIPY-chromophore conjugates (Scheme 3) under palladium catalyzed coupling conditions.[39-43] The *β–β* linked BODIPY dimer **18** was prepared by palladium catalyzed borylation with bis(pinacolato)diboron ($pin_2$ $B_2$) followed by in situ cross coupling sequence in the presence of $Cs_2CO_3$ as base.[50] When $CH_3COOK$ was used instead of $Cs_2CO_3$, authors obtained mono-boryl BODIPY **19a** (Scheme 3) which was used for the synthesis of *β–β* linked BODIPY trimer **19b** (vide infra). The *β–β* linked BODIPY dimer **18** showed significant bathochromic shifts in both absorption and emission spectra. However, the fluorescence quantum yield and lifetime of **18** were decreased compared to *meso*-aryl BODIPY monomer **3a** due to enhancement of non-radiative decay processes contributed by the decreased HOMO-LUMO gap as well as increased vibrational relaxation channels including the torsional motions around the *β–β* linkage of BODIPY dimer **18**.[50]

Ulrich et al.[51] carried out carbopalladium reaction by treating 2-iodo BODIPY **4c** with a palladium catalyst under stream of CO and in the presence of various nucleophiles, primary or secondary alcohols and afforded BODIPYs containing ester or amido substituents at 2-positions **17a-17c** (Scheme 3). The 2-halo BODIPYs **4b/4c** were reacted with various types of boronic acids under Suzuki coupling conditions and prepared several 2-substituted BODIPYs **20a-20f**. 2-Substituted BODIPYs[52-59] containing bulky substituents such as tetraphenylethene[52] **20d** and triphenylsilylphenyl[53] groups **20f** were found to be strongly fluorescent in the solid state because of inhibition of aggregation. The 2-halo BODIPYs **4b/4c** were also subjected to Sonagashira coupling by treating it with various aryls containing ethynyl functional groups and afforded ethynyl bridged BODIPY systems[41,44,60-62] **21a-21e** (Scheme 3). Some of these 2-substituted BODIPYs were used for various applications[44,45,60,61] (Scheme 4). Zhao and co-workers used 2-bipyridyl substituted BODIPY **21c** to prepare BODIPY-$Ir(bpy)_3$ complex **22** (Scheme 4a) by treating **21c** with $Ir(bpy)_2Cl_2$ in

$CH_2Cl_2/CH_3OH$.[61] This kind of complexes were used as triplet photosensitizers for singlet oxygen mediated photooxidation of 1,5-dihydronaphthalene to produce juglone.[61] Since these complexes were efficient for singlet oxygen production, the complexes were also used for photocytotoxicity in lung cancer cells upon irradiation. Thus, the complexes such as **22** also have potential applications in vivo photodynamic therapy of cancer.[61] Zhao and co-workers[59] also synthesized BODIPY-$C_{60}$ dyad **23** by reacting 2-thienyl substituted BODIPY **20b** with $C_{60}$ and sarcosine in toluene at reflux temperature (Scheme 4b) and used the dyad **23** as triplet photosensitizer for triplet-triplet annihilation upconversion. The authors claimed that this kind of heavy metal free BODIPY-$C_{60}$ dyad **23** can act as organic triplet photosensitizers which replace the conventional heavy transition metal based phosphorescent complexes such as **22**.[59] Akkaya and co-workers[45] used the 2-terpyridyl BODIPY **21e** as building block to prepare BODIPY-metal terpyridine complex **24** (Scheme 4c).

**3-Substituted BODIPYs**

The mono-3-halogenated BODIPYs **5a** and **5b** were used first to introduce aryl group at 3-position (Scheme 5) under transition metal catalyzed cross coupling reaction conditions.[39,41] The 3-halogenated BODIPYs **5a** and **5b** were subjected to Stille coupling reactions by treating with equimolar amount of $Sn(R)_4/RSn(Bu)_3$ (R = phenyl/furyl/thienyl) in the presence of catalytic amount of $Pd(PPh_3)_4$ in toluene at reflux temperature to afford 3-aryl BODIPYs **24a-24c** (Scheme 5).[39] Alternately, the 3-aryl BODIPYs **24a-24f** were prepared by subjecting 3-halogenated BODIPYs **5a**/**5b** to Suzuki coupling conditions by reacting with aryl/heteroarylboronic acids under Palladium catalyzed conditions.[39] The alkenylated BODIPYs **25a** and **25b** were prepared by treating 3-halogenated BODIPY **5a** with alkenes under Heck coupling reaction conditions (Scheme 5).[39] The 3-halogenated BODIPYs **5a**/**5b** were also subjected to palladium catalyzed Sonogashira reaction with aryl/alkyl ethynes to afford ethynylated BODIPYs **26a-26c**.[39,41] Recently, 3-ethyl substituted

BODIPY **27** was prepared by treating 3-bromo BODIPY **5b** with different organozinc reagents in the presence of $Pd(PPh_3)_2Cl_2$ under Negishi reaction conditions for the first time.[62] Thus, 3-halogenated BODIPYs **5a** and **5b** were used to prepare different types of substituted BODIPYs **24-27** under various types of palladium catalyzed coupling conditions.

The introduction of substituent at the 3-position of BODIPY by following any synthetic methods alter the electronic properties of the BODIPY dye which reflects in their spectral properties.[39,41,46] For example, the *meso*-aryl BODIPY **3a** absorbs and emits strongly at 500 and 520 nm respectively.[29] However, upon introduction of styryl group at 3-position of BODIPY by Heck coupling reaction,[39] the absorption and emission bands of **25a** experienced significant bathochromic shifts and absorbs at 559 nm and emits at 571 nm.[39] Similarly, the other properties such as extinction coefficients, quantum yield, singlet state lifetime, redox potentials etc. also alter significantly upon introduction of substituents at 3-position. In addition to simple substituents at 3-position, Ravikanth and co-workers[46,63,64] used 3-bromo BODIPY **5b** to synthesize covalently linked BODIPY-chromophore/redox active conjugates **28a-28g** under mild Pd(0) coupling conditions as shown in Scheme 6. The chromophores possessing very distinct features such as anthracene, terpyridine, porphyrin, Zn(II)porphyrin, 21,23-dithiaporphyrin, thiasapphyrin[46] **28a-28f** and redox active unit such as ferrocene[63-65] **28g** were connected at 3-position of boron-dipyrromethene dye (Scheme 6) by coupling of 3-bromo BODIPY **5b** with appropriate ethynyl functionalized chromophore/redox active in toluene/triethylamine in the presence of catalytic amount of $AsPh_3/Pd_2(dba)_3$ at 40 ºC. The spectral studies indicated that the interaction is stronger in ethynyl bridged BODIPY-anthracene conjugate **28a** compared to other ethynylphenyl bridged BODIPY-chromophore conjugates **28a-28f**.[46] The steady state fluorescence studies indicated that in ethynyl bridged BODIPY-anthracene conjugate **28a**, the BODIPY unit acts as energy acceptor (Figure 4a) and showed a possibility of energy transfer from donor

anthracene unit to acceptor BODIPY unit on selective excitation of anthracene unit at 350 nm.[46] However, in ethynylphenyl bridged BODIPY-porphyrin conjugates **28e** and **28f**, the BODIPY unit acts as energy donor and exhibited a possibility of singlet-singlet energy transfer from BODIPY unit to other chromophore unit. For example, in the BODIPY-porphyrin conjugate **28e**, on excitation of BODIPY unit at 488 nm, the emission was quenched from BODIPY unit significantly and the strong emission was observed from porphyrin unit (Figure 4b) because of singlet-singlet energy transfer from BODIPY unit to porphyrin unit.[46] Thus, the BODIPY can act as either energy donor or energy acceptor depends on the chromophore to which it is attached in the BODIPY-chromophore conjugates **28a-28f**.

The 3-mono-halogenated BODIPYs **5a** and **5b** were also subjected to nucleophilic substitution reactions by treating with O-, N- and S- based nucleophiles in the presence of base at reflux conditions (Scheme 7).[39,65] Ravikanth and co-workers[65] synthesized 3-oxypyridine BODIPY **35** by treating 3-bromo BODIPY **5b** with 3-hydroxypyridine and used compound **35** to prepare non-covalent BODIPY-Zn(II) porphyrin dyad **36a** and BODIPY-Ru(II) porphyrin dyad **36b** assembled via Zn(II)/Ru(II)-pyridine "N" interaction (Scheme 7). The 3-(pyridine-4-one)BODIPY **37** was prepared by treating 3-bromoBODIPY **5b** with 4-hydroxypyridine and converted to 3-(pyridine-4-thione)BODIPY **38** by treating it with Lawesson's reagent.[66] The 3-(pyridine-4-thione)BODIPY **38** was used as exclusive chemodosimetric sensor for Hg(II) ions as it shows significant enhancement in the fluorescent intensity and dramatic colour change from pink to fluorescent green in the presence of Hg(II) ions.[66]

The 3-amino BODIPY **41** was prepared by two different routes from 3-bromo BODIPY **5b**. Talukdar and co-workers[67] prepared the 3-amino BODIPY **41** by treating **5b** with 15%$NH_3$ in $H_2O/CH_3CN$ at room temperature (Scheme 7). Alternately, Ravikanth and

co-workers[68] prepared **41** by treating **5b** with sodium azide in acetonitrile followed by triphenylphosphine in tetrahydrofuran at reflux temperature. The 3-amino BODIPY **41** was used to prepare 2,4-dintrobenzenesulfoyl (DBS) appended BODIPY **42c** by treating **41** with DBS chloride in the presence of NaH (Scheme 7).[67] The BODIPY **42c** is non-fluorescent due to photo-induced electron transfer from BODIPY to DBS group. However, in the presence of thiophenols which cleaves the DBS group, the fluorescence was restored and thus **42c** can be used as turn-on fluorescent probe for selective detection of thiophenols.[67] Furthermore, the amino group of 3-amino BODIPY **41** was derivatized to prepare 3-phenylurea substituted BODIPY **42a** and 3-phenylthiourea substituted BODIPY **42b** under simple reaction conditions.[68] Authors demonstrated that **42a** can be used as colorimetric and ratiometric sensor for $F^-$ ion and **42b** can used as specific chemodosimetric sensor for $Hg^{2+}$ ion.[68]

The 3-azido BODIPY **39** was prepared by reacting **5b** with $NaN_3$ in acetone/water (1:1) at room temperature (Scheme 7).[69,70] The BODIPY **39** was found to be fluorescence turn-on probe for selective and sensitive detection of $H_2S$ and demonstrated in living cells.[69] The 3-azido BODIPY **39** was used as key precursor to prepare a series of trizole bridged BODIPY-chromophore conjugates **43a-43e** by treating 3-azido BODIPY **39** with ethynyl containing chromophore in the presence of CuI/DIPEA in THF/$CH_3CN$ at room temperature (Scheme 8).[70,71] The fluorescence studies indicated an efficient energy transfer from BODIPY to $BF_2$-smaragdyrin unit in conjugate **43e** but the energy transfer was not efficient from BODIPY to porphyrin macrocycles in conjugates **43b** and **43c**.[70]

**3,5-Disubstituted BODIPYs**

The 3,5-dihalo BODIPYs **6a** and **6b** were used to prepare symmetrically or asymmetrically aryl substituted BODIPY derivatives **44-47** by Stille, Suzuki, Heck, Sonagashira and Nagishi coupling reactions (Scheme 9).[62,72-75] Prior to this approach, the

3,5-diaryl substituted BODIPY derivatives were prepared from the aryl substituted pyrroles.[25] The accessibility of 3,5-dihalo BODIPYs **6a** and **6b** helped in the preparation of wide range of 3,5-diaryl substituted BODIPYs **44-47** under various Pd catalyzed coupling conditions in good yields.[72-75] Recently, Ziessel and co-workers[76] used 3,5-bis(thiophene-benzothiadiazole-thiophene) substituted BODIPY **44c** as bulk heterojunction solar cells by blending the dye **44c** with [6,6]phenyl$C_{61or71}$ butyricacid methylester which showed a power conversion efficiency of about 1.26% upon a mild thermal annealing. The presence of conjugated aryl groups at the 3,5-positions alter the electronic properties of the dye significantly which reflected in their spectral and electrochemical properties.[77] For example, the 3,5-distryl BODIPY **45** exhibit 50-70 nm shifts in its absorption and emission bands compared to the unsubstituted BODIPY **3a** which is due to the enhancement of conjugation.[77] Some of these 3,5-disubstituted BODIPYs were also used for wide range of applications since the substituents at the 3,5-positions significantly alter the electronic properties. Rajeswara Rao et al.[37] showed that the 3,5-bis(trimethylsilylethynyl)BODIPY [BODIPY$(CCTMS)_2$] **46b** can be used as selective colorimetric and fluorescent chemodosimeter for fluoride ion. The fluoride ion induced cleavage of trimethylsilyl group of **46b**, the protecting group of ethyne functionality, resulted in clear changes in UV-vis (Figure 5a) and fluorescence spectra as well as in solution colour. No such observations were made when compound **46b** was treated with other anions such as $Cl^-$, $Br^-$, $I^-$, $ClO_4^-$ and $HPO_4^{2-}$. Thus authors demonstrated that small alterations on the molecular structure of BODIPY dyes by using well-known reactions makes the BODIPYs to act as specific sensors for anions.[37] The 3,5-bis(ferrocenyl)BODIPY **46c** has been shown as fluorescent redox switch by absorption, electrochemical and fluorescent studies.[63] The compound **46c** showed strong charge transfer band at ~700 nm due to electron transfer from ferrocene to BODIPY unit along with absorption bands corresponding to BODIPY moiety and the compound was

weekly fluorescent. However, upon oxidation of ferrocene moiety of **46c** to ferrocenium ion resulted in decent fluorescence (Figure 5b) due to elimination of the possibility of electron transfer and thus **46c** acts as fluorescent redox switch.[63]

Furthermore, the 3,5-dihalo BODIPYs **6a** and **6b** were also used for nuclophilic substitution reactions by treating **6a/6b** with C-, O-, N-, S-, Se and Te- nucleophilic groups at reflux conditions and prepared wide variety of BODIPYs[78-89] **(48, 49)** substituted with different nucleophiles including BODIPYs substituted with crown ethers[78] **48k** (Scheme 10). These substituted BODIPYs **48, 49** were explored for wide range of applications as discussed here for some selected systems. The 3,5-bis(sulfosuccinimidyl diester) substituted BODIPY **50** synthesized from **48i**, was used for labelling proteins as the dye exhibits bright and stable fluorescence.[88] The crown ether substituted BODIPYs (Scheme 10b) such as **49c** was used as ratiometric fluorescent sensor for potassium ion.[78] Similarly, the 3-(ethynyl)phenylethynyl-5-(2-picolyl)amine substituted BODIPY **49e** exhibited selective fluorescent turn on chemosensor for $Cu^{2+}$ ion among various metal ions.[90,91] The di-2-picolyamine substituted BODIPY **49f** (Scheme 10a) was used as fluorometric sensor for heavy metal ions.[92]

Ravikanth and co-workers[65] used the BODIPY containing two oxypyridine substituents at 3,5-positions **48f** to prepare non-covalent BODIPY-metalloporphyrin triads **52** assembled using metal-pyridine "N" interaction (Scheme 10c). The BODIPY-metalloporphyrin triads **52a** and **52b** were prepared by treating BODIPY with two oxypyridine substituents at 3,5-positions **48f** with metalloporphyrin **51** (M= Zn(II), Ru(II), Scheme 10c).[65] The NMR studies on triads **52** indicated that triad based on oxypyridine-Ru(II) porphyrin **52b** is more stable than triad based on oxypyridine-Ru(II) pophyrin interaction is more stable than traid **52a** based on Zn(II) porphyrin interaction.[65] Four covalently linked trichromophore systems[93] **53a-53d** containing central BODIPY unit

connected to two different types of porphyrin units or one porphyrin and one expanded porphyrin units at 3,5-positions were synthesized by treating 3-bromo-5-porphyrinyl BODIPY **54a** or 3-bromo-5-rubyrinyl BODIPY **54b** with corresponding hydroxy porphyrin **55** or hydroxy expanded porphyrin **55c** in $CHCl_3$ at 60 °C as shown in Scheme 11. The absorption and electrochemical studies supported weak ground state interaction among the three chromophore units in trichromophore systems **53a-53d**. The fluorescence studies indicated that the BODIPY emission is quenched in all trichromophore systems **53a-53d** due to transfer of singlet-state energy of BODIPY to one or both macrocyclic units attached to BODIPY either radiatively or non-radiatively. However, the magnitude of BODIPY fluorescence quenching is varied among the trichromophore systems **53a-53d** and maximum quenching was observed for trichromophore system **53c**.[93]

**2,6-Disubstituted BODIPYs**

2,6-Dihalogen substituted BODIPYs **7a-7c** were also equally reactive like 3,5-dihalo substituted BODIPYs **6a** and **6b** and several 2,6-disubstituted BODIPY derivatives **56-59** were synthesized by coupling 2,6-dihalogenated BODIPYs **7a-7c** under transition metal catalysed reaction conditions (Scheme 12a). The groups such as terpyridyl, bipyridyl,[45] 2-(2-hydroxyphenyl)benzothiazole,[94] platinum(II) bis(aryleneethynylene) bis(trialkylphosphine),[95,96] at 2,6-positions of BODIPY **56a-56e** were prepared (Scheme 12a) by treating 2,6-dihalo BODIPY **7b**/**7c** with appropriate ethynyl containing chromophores under Sonagashira coupling conditions.[45,94-98] The terpyridyl containing BODIPY **56a** was used to prepare fluorescent metallosupramolecular coordination polymers **60** or BODIPY-metal terpyridyl complexes **61** (Scheme 12b).[45,97] The aromatic groups such as thienyl, phenyl,[99] biphenyl,[100] pyridyl,[101,102] triphenyl amine[103] were introduced at 2,6-positions of BODIPY by treating 2,6-dihalo BODIPY **7b**/**7c** with appropriate boronic acids under Suzuki coupling conditions.[99-104] The 2,6-dipyridyl BODIPY **57d** was used to prepare metal organic

frameworks by treating with Zn(II) porphyrin and these porphyrin-BODIPY based metal organic frameworks were used to study the light harvesting properties.[101] The 2,6-dipyridyl BODIPY **57d** was used for selectively sensing Cu(II) ions.[102] The triphenylamine substituted BODIPY **57a** was used in bulk heterojunction solar cells as electron donor which exhibited photovoltaic properties with a power conversion efficiency of 0.77%.[103] The BODIPY based polymers **58a-58c** were synthesized by treating 2,6-dihalo BODIPY **7b/7c** with distannyl arenes under Stille cross-coupling conditions.[104-106] Similarly, BODIPY homopolymer **59** was also synthesized from 2,6-dihalo BODIPY **7b/7c** in the presence of $Ni(COD)_2$/bipyridine (1:1) in DMF at 80 °C for three days (Scheme 12a).[104] These BODIPY based polymers **58a-58c, 59** were used for photovoltaic applications.

**1,7-Di substituted BODIPYs**

Similarly, the 1,7-dihalo substituted BODIPYs **8a** and **8b** were also subjected to various types of Pd coupling reactions as well as nucleophilic substitution reactions (Scheme 13).[48] The 1,7-positions of BODIPY **3** are rather electron poor like 3,5-positions and are susceptible to nucleophilic aromatic substitutions. However, among the nucleophiles based on nitrogen, oxygen, carbon and sulphur, only sulphur based nucleophiles were able to introduce at 1,7-positions of BODIPY.[48] Generally, the introduction of new substituents on BODIPY system make huge difference in its optical properties.[19-22] The studies showed that the introduction of new substituents by extending the conjugation at 1,7-positions of BODIPY (**63-66**) did not alter the optical properties significantly compared to 3,5-positions of BODIPY.[48]

**Tri, tetra and pentasubstituted BODIPYs**

The 2,3,5-tribromo BODIPY[32] **10b**, 2,3,5,6-tetrabromoBODIPY[32] **13b** and 1,2,3,5,6-pentabromo BODIPY[32] **15** were also used to prepare corresponding phenyl substituted BODIPYs **67-69** by reacting the respective halogen substituted BODIPYs **10/13/15** with

phenylboronic acid under Suzuki coupling conditions (Scheme 14a).[33] 2,6-Dichloro-3,5-dipyrrolyl BODIPY **68b** and 2,3,6-trichloro-5-pyrrolyl BODIPY **68c** were prepared by nucleophilic substitution of tetrachloro BODIPY **13a** with pyrrole under reflux conditions (Scheme 14b).[107] The sterically crowded hexaraylated BODIPYs **70a-70f** were prepared by treating 1,2,3,5,6,7-hexabromo BODIPY **16b** with various types of boronic acids such as phenyl, thienyl, *p*-tolyl, 4-fluorophenyl, *p*-anisyl, biphenyl and naphthylboronic acids under same Pd(0) mediated Suzuki cross coupling conditions (Scheme 15).[33,108-110]

The introduction of bulkier aryl group(s) at the pyrrole carbons of BODIPY alter the electronic properties of the BODIPY which reflects in their spectral and electrochemical properties. Lakshmi and Ravikanth studied the variations in spectral and electrochemical properties by systematically introducing one to six phenyl groups at the pyrrole carbons of BODIPY (**24a, 44a, 67-70**).[33] The absorption and fluorescence studies showed a bathocromic shift in absorption and emission bands, increase in quantum yield and singlet state lifetime up to the presence of four phenyl groups at the pyrrole carbons of BODIPY but the properties were reversed for five and six phenyl substituted BODIPYs **69** and **70.** The electrochemical studies indicated that the increase of number of phenyl groups at the pyrrole carbons of BODIPY frame work, the electron rich nature of BODIPY increases.[33]

Recently, Lakshmi and Ravikanth[111,112] also successfully synthesized mixed polyarylated BODIPYs containing two or three different types of aryl/alkyl groups **71-74** (Chart 2) using halogenated BODIPYs over sequence of steps. For example, the mixed BODIPYs containing two different types of aryl groups **71-73** such as BODIPY with three phenyl and three tolyls **72a** was prepared using 2,3,5-tribromo BODIPY **10b** as key precursor as shown in Scheme 16a.[111] The 2,3,5-tribromo BODIPY **10b** was first reacted with phenylboronic acid under Suzuki coupling conditions to afford 2,3,5-triphenyl BODIPY **67**.

The 2,3,5-triphenyl BODIPY **67** was treated with liquid $Br_2$ to obtain 1,6,7-tribromo-2,3,5-triphenyl BODIPY **75** which was further reacted with *p*-tolylboronic acid under Pd(0) coupling conditions (Scheme 16a) and afforded BODIPY containing two different types of aryl groups **72a**.[111] The BODIPY containing three different types of aryl groups **74a-74d** were also prepared over a sequence of steps of bromination followed by Suzuki coupling with aryl boronic acids as described here (Scheme 16b).[112] In the first step, the 3,5-dibromo BODIPY **6b** was converted to 3,5-diphenyl BODIPY **44a** under Suzuki coupling conditions which was then selectively brominated at 2,6-positions by treating 3,5-diphenyl BODIPY **44a** with 2.2 equivalents of liquid $Br_2$. The resulted 2,6-dibromo-3,5-diphenyl BODIPY **76** was reacted with *p*-tolylboronic acid under same Pd(0) coupling conditions to afford 2,3,5,6-tetrarayl BODIPY **77** which was then further subjected to bromination by treating it with liquid bromine and afforded 1,7-dibromo-3,5-diphenyl-2,6-ditolyl BODIPY **78**.[112] This 1,7-dibrominated 2,3,5,6-tetraaryl BODIPY **78** was then reacted with 4-fluorophenylboronic acid under Pd(0) coupling conditions to obtain polyarylated BODIPY containing three different types of aryl groups at the pyrrole carbons (**74a**). All these mixed polyaraylated sterically crowded BODIPYs **71-74** absorb and emit strongly in the region of 550–650 nm with decent quantum yields and singlet state lifetimes and are very stable under redox conditions.

**Conclusions**

Halogenated BODIPYs are versatile building blocks for the synthesis of wide range of BODIPYs with interesting applications. Halogens are the only functional groups which were placed at six pyrrole carbons of BODIPY framework. The synthetic strategies which were established would allow synthesizing any desired halogenated BODIPYs, and the halogenated BODIPYs gives an access to the variety of BODIPY compounds that can be made. Indeed, haxahalogenated BODIPYs are the only functionalized BODIPYs which

assists in the synthesis of hexasubstituted BODIPYs in one pot reaction. Thus, we hope that the halogenated BODIPYs would be exploited in the preparation of new BODIPY based compounds which can find applications in the various fields ranging from materials to medicine.

**Acknowledgement**

MR and VL thank DST and CSIR for financial support

**References**

**References**

(1) E. Terpetschnig, O. S. Wolfbeis, *Near-Infrared Dyes for High Technology Applications,* Ed., S. Dihne, U. Resch-Genger, O. S. Wolfbeis, K. Academic, Dordrecht, 1998, 161-182.

(2) T. Vo-Dinh, *Biomedical Photonics Handbook, Taylor & Francis, Inc.,* 2002, ISBN 0-8493-1116-0.

(3) (a) Y. Ni and J. Wu, *Org. Biomol. Chem.,* 2014, **12**, 3774-3791. (b) K. Umezawa, D. Citterio and K. Suzuki, *Anal. Sci.*, 2014, 327-349. (c) L. Yuan, W. Lin, K. Zheng, L. He and W. Huang, *Chem. Soc. Rev.,* 2013, **42**, 622-661.

(4) X. Qian, Y. Xiao, Y. Xu, X. Guo, J. Qian and W. Zhu, *Chem. Commun.,* 2010, **46**, 6418-6436.

(5) (a) M. J. Culzoni, A. M. de la Peña, A. Machuca, H. C. Goicoechea and R. Babiano, *Anal. Methods*, 2013, **5**, 30-49. (b) T. Ueno, Y. Urano, H. Kojima and T. Nagano, *J. Am. Chem. Soc.,* 2006, **128,** 10640-10641.

(6) Y. Mei, P. A. Bentley and W. Wang, *Tetrahedron Lett.,* 2006, **47**, 2447-2449.

(7) F. Rancan, A. Todorova, S. Hadam, D. Papakostas, E. Luciani, C. Graf, U. Gernert, E. Rühl, B. Verrier, W. Sterry, U. Blume-Peytavi and A. Vogt, *Eur. J. Pharm. Biopharm.,* 2012, **80**, 76-84

(8) A. Sharma, A. Khatchadourian, K. Khanna, R. Sharma, A. Kakkar and D. Maysinger, *Biomaterials,* 2011, **32**, 1419-1429.

(9) T. A. Golovkova, D. V. Kozlov and D. C. Neckers, *J. Org. Chem.,* 2005, **70,** 5545-5549.

(10) S. Mula, A. K. Ray, M. Banerjee, T. Chaudhuri, K. Dasgupta and S. Chattopadhyay, *J. Org. Chem.,* 2008, **73**, 2146-2154.

(11) D. Zhang, V. Martín, I. García-Moreno, A. Costela, M. E. Pérez-Ojeda and Y. Xiao, *Phys. Chem. Chem. Phys.,* 2011, **13***,* 13026-13033.

(12) G. Duran-Sampedro, A. R. Agarrabeitia, I. Garcia-Moreno, A. Costela, J. Bañuelos, T. Arbeloa, I. López Arbeloa, J. L. Chiara and M. J. Ortiz, *Eur. J. Org. Chem.,* 2012**,** 6335-6350.

(13) A. Costela, I. GarciÌa-Moreno, M. Pintado-Sierra, F. Amat-Guerri, R. Sastre, M. Liras, F. López Arbeloa, J. B. Prieto and I. López Arbeloa, *J. Phys. Chem. A,* 2009, **113**, 8118-8124.

(14) Z. Kostereli, T. Ozdemir, O. Buyukcakir and E. U. Akkaya, *Org. Lett.,* 2012*,* **14**, 3636-3639.

(15) (a) S. K. Singh and T. Gayathri, *Eur. J. Org. Chem.,* 2014, 4689-4707. (b) A. Bessette and G. S. Hanan, *Chem. Soc. Rev.,* 2014, **43**, 3342-3405.

(16) (a) Z. Li, M. Zheng, X. Guan, Z. Xie, Y. Huang and X. Jing, *Nanoscale,* 2014, **6**, 5662-5665. (b) D. Su, C. L. Teoh, S. Sahu, R. K. Das and Y.-Y. Chang, *Biomater.* 2014, **35**, 6078-6085. (c) I. Mikhalyov, N. Gretskaya and L. B.-Å. Johansson, *Chem. Phys. Lipids*, 2009, **159,** 38-44.

(17) S. G. Awuah and Y. You, *RSC Adv.*, 2012, **2**, 11169-11183.

(18) (a) I. S. Turan, F. P. Cakmak, D. C. Yildirim, R. Cetin-Atalay and E. U. Akkaya, *Chem. Eur. J.,* 2014, **20**, 16088-16092. (b) A. Kamkaew, S. H. Lim, H. B. Lee, L. V. Kiew, L. Y. Chung and K. Burgess, *Chem. Soc. Rev.,* 2013, **42**, 77-88.

(19) R. Ziessel, G. Ulrich and A. Harriman, *New J. Chem.,* 2007, **31**, 496-501.

(20) A. Loudet and K. Burgess, *Chem. Rev.*, 2007, **107***,* 4891-4932.

(21) G. Ulrich, R. Ziessel and A. Harriman, *Angew. Chem., Int. Ed.,* 2008, **47**, 1184-1201.

(22) (a) L. Luo, D. Wu, W. Li, S. Zhang, Y. Ma, S. Yan and J. You, *Org. Lett.,* 2014, **16**, 6080-6083. (b) H. Lu, J. Mack, Y. Yang and Z. Shen, *Chem. Soc. Rev.,* 2014, **43**, 4778-4823. (c) G. Ulrich, C. Goze, M. Guardigli, A. Roda and R. Ziessel, *Angew Chem., Int. Ed.*, 2005, **44**, 3694-3698.

(23) A. Treibs and F.-H. Kreuzer, *Justus Liebigs Ann. Chem.,* 1968, **718**, 208-223.

(24) H. J. Wories, J. H. Koek, G. Lodder, J. Lugtenburg, R. Fokkens, O. Driessen and G. R. Mohn, *Recl. Trav. Chim. Pays-Bas,* 1985, **104**, 288-291.

(25) A. Burghart, H. Kim, M. B. Welch, L. H. Thoresen, J. Reibenspies and K. Burgess, *J. Org. Chem.,* 1999, **64**, 7813-7819.

(26) H. C. Kang and Haughland, *US Patent,* 1993, 5187288.

(27) G. Ulrich and R. Ziessel, *J. Org. Chem.,* 2004, **69**, 2070-2083.

(28) H. Wang, F. R. Fronczek, M. G. H. Vicente and K. M. Smith, *J. Org. Chem*., 2014, **79**, 10342-10352.

(29) H. L. Kee, C. Kirmaier, L. Yu, P. Thamyongkit, W. J. Youngblood, M. E. Calder, L. Ramos, B. C. Noll, D. F. Bocian, W. R. Scheidt, R. R. Birge, J. S. Lindsey and D. Holten, *J. Phys. Chem. B,* 2005, **109**, 20433-20443.

(30) M. Benstead, G. H. Mehl and R. W. Boyle, *Tetrahedron*, 2011, **67**, 3573-3601.

(31) N. Boens, V. Leen and W. Dehaen, *Chem. Soc. Rev.,* 2012, **41**, 1130-1172.

(32) V. Lakshmi and M. Ravikanth, *Dalton Trans.,* 2012, **41,** 5903-5911.

(33) L. Jiao, W. Pang, J. Zhou, Y. Wei, X. Mu, G. Bai and E. Hao, *J. Org. Chem.,* 2011, **76**, 9988-9996.

(34) V. Lakshmi and M. Ravikanth, *Dyes Pigments,* 2013, **96**, 665-671.

(35) L. Huang, J. Zhao, S. Guo, C. Zhang, J. Ma. *J. Org. Chem.,* 2013, **78,** 5627-5637.

(36) M. Baruah, W. Qin, N. Basarić, W. M. De Borggraeve and N. Boens, *J. Org. Chem.,* 2005, **70**, 4152-4157.

(37) M. R. Rao, S. M. Mobin and M. Ravikanth, *Tetrahedron,* 2010, **66***,* 1728-1734.

(38) G. Meng, S. Velayudham, A. Smith, R. Luck and H. Liu, *Macromolecules,* 2009, **42,** 1995-2001.

(39) V. Leen, T. Leemans, N. Boens and W, Dehaen, *Eur. J. Org. Chem.,* 2011, 4386-4396.

(40) C.-W. Wan, A. Burghart, J. Chen, F. Bergström, L. B.-Å. Johansson, M. F. Wolford, T. Gyum Kim, M. R. Topp, R. M. Hochstrasser and K. Burgess, *Chem. Eur. J.,* 2003, **9**, 4430-4441.

(41) V. Leen, E. Braeken, K. Luckermans, C. Jackers, M. Van der Auweraer, N. Boens and W. Dehaen, *Chem. Commun*., 2009, 4515-4517.

(42) S. Niu, G. Ulrich, P. Retailleau and R. Ziessel, *Org. Lett.,* 2011, **13**, 4996-4999.

(43) W. Wu, J. Sun, X. Cui and J. Zhao, *J. Mater. Chem. C,* 2013, **1**, 4577-4589.

(44) W. Wu, H. Guo, W. Wu, S. Ji and J. Zhao, *J. Org. Chem.,* 2011, **76**, 7056-7064.

(45) Ö. A. Bozdemir, O. Büyükcakir and E. U. Akkaya, C*hem. Eur. J.,* 2009, **15**, 3830-3838.

(46) T. K. Khan and M. Ravikanth, *Tetrahedron,* 2011, **67**, 5816-5824.

(47) L. Wang, J.-W. Wang, A.-J. Cui, X.-X. Cai, Y. Wan, Q. Chen, M.-Y. He and W. Zhang, *RSC Adv.,* 2013, **3**, 9219-9222.

(48) V. Leen, D. Miscoria, S. Yin, A. Filarowski, J. M. Ngongo, M. Van der Auweraer, N. Boens and W. Dehaen, *J. Org. Chem.,* 2011, **76**, 8168-8176.

(49) (a) L. Wang, Y. Zhang and Y. Xiao, *RSC Adv.*, 2013, **3**, 2203-2206. (b) M. J. Ortiz, A. R. Agarrabeitia, G. Duran-Sampedro, J. B. Prieto, T. A. Lopez, W. A. Massad, H. A. Montejano, N. A. García and I. L. Arbeloa, *Tetrahedron,* 2012, **68**, 1153-1162.

(50) Y. Hayashi, S. Yamaguchi, W. Y. Cha, D. Kim and H. Shinokubo, *Org. Lett.,* 2011, **13**, 2992-2995.

(51) G. Ulrich, A. Haefele, P. Retaillau and R. Ziessel, *J. Org. Chem*., 2012, **77**, 5036-5048.

(52) Z. Li, Y. Chen, X. Lv and W.-F. Fu, *New J. Chem.,* 2013, **37***,* 3755-3761.

(53) L. Gai, H. Lu, B. Zou, G. Lai, Z. Shen and Z. Li, *RSC Adv.,* 2012, **2**, 8840-8846.

(54) N. J. Findlay, C. Orofino-Pena, J. Bruckbauer, S. E. T. Elmasly, S. Arumugam, A. R. Inigo, A. L. Kanibolotsky, R. W. Martin and P. J. Skabara, *J. Mater. Chem. C,* 2013, **1**, 2249-2256.

(55) (a) W. Wu, X. Cui and J. Zhao, *Chem. Commun.,* 2013, **49**, 9009-9011. (b) L. Huang, X. Cui, B. Therrien and J. Zhao, *Chem. Eur. J.,* 2013, **19,** 17472-17482.

(56) Y. Chen, J. Zhao, L. Xie, H. Guo and Q. Li, *RSC Adv.,* 2012, **2**, 3942-3953.

(57) S. Rihn, M. Erdem, A. De Nicola, P. Retailleau and R. Ziessel, *Org. Lett.,* 2011, **13**, 1916-1919.

(58) (a) G. Ulrixh, A. Barsella, A. Boeglin, S. Niu and R. Ziessel, *Chem. Phys. Chem*. 2014, **15**, 2693-2700. (b)C. Zhang, J. Zhao, S. Wu, Z. Wang, W. Wu, J. Ma, S. Guo and L. Huang, *J. Am. Chem. Soc.,* 2013, **135,** 10566-10578.

(59) W. Wu, J. Zhao, J. Sun and S. Guo, *J. Org. Chem*., 2012, **77**, 5305-5312.

(60) S. Niu, G. Ulrich, P. Retailleau and R. Ziessel, *Tetrahedron Lett.,* 2011, **52**, 4848-4853.

(61) P. Majumdar, X. Yuan, S. Li, B. Le Guennic, J. Ma, C. Zhang, D. Jacquemin and J. Zhao, *J. Mater. Chem. B,* 2014, **2**, 2838-2854.

(62) G. Duran-Sampedro, E. Palao, A. R. Agarrabeitia, S. de la Moya, N. Boens and M. J. Ortiz, *RSC Adv.,* 2014, **4**, 19210-19213.

(63) M. R. Rao, K. V. P. Kumar and M. Ravikanth, *J. Organomet. Chem*., 2010, **695**, 863-869.

(64) T. K. Khan, R. R. S. Pissurlenkar, M. S. Shaikh and M. Ravikanth, *J. Organomet. Chem.,* 2012, **697**, 65-73.

(65) T. K. Khan and M. Ravikanth, *Tetrahedron,* 2012, **68,** 830-840.

(66) T. K. Khan and M. Ravikanth, *Dyes Pigments*, 2012, **95**, 89-95.

(67) D. Kand, P. K. Mishra, T. Saha, M. Lahiri and P. Talukdar, *Analyst,* 2012, **137**, 3921-3924.

(68) E. Ganapathi, S. Madhu, T. Chatterjee, R. Gonnade and M. Ravikanth, *Dyes Pigments*, 2014, **102**, 218-227.

(69) T. Saha, D. Kand and P. Talukdar, *Org. Biomol. Chem*., 2013, **11**, 8166-8170.

(70) E. Ganapathi, S. Madhu and M. Ravikanth, *Tetrahedron*, 2014, **70**, 664-671.

(71) D. P. Chauhan, T. Saha, M. Lahiri and P. Talukdar, *Tetrahedron*, 2014, **55**, 244-247.

(72) T. Rohand, W. Qin, N. Boens and W. Dehaen, *Eur. J. Org. Chem.,* 2006, 4658-4663.

(73) S. Rihn, P. Retailleau, N. Bugsaliewicz, A. De Nicola and R. Ziessel, *Tetrahedron Lett.,* 2009, **50***,* 7008-7013.

(74) R. Ziessel, S. Rihn and A. Harriman, *Chem. Eur. J.,* 2010, **16,** 11942-11953.

(75) T. K. Khan, S. K. Jana, M. R. Rao, M. S. Shaikh and M. Ravikanth, *Inorg. Chim. Acta,* 2012, **383**, 257-266.

(76) A. Mirloup, N. Leclerc, S. Rihn, T. Bura, R. Bechara, A. Hébraud, P. Lévêque, T. Heiser and R. Ziessel, *New J. Chem.,* 2014, **38**, 3644-3653.

(77) W. Qin, T. Rohand, W. Dehaen, J. N. Clifford, K. Driesen, D. Beljonne, B. Van Averbeke, M. Van der Auweraer and N. Boens, *J. Phys. Chem. A,* 2007, **111***,* 8588-8597.

(78) M. Baruah, W. Qin, R. A. L. Valleé, D. Beljonne, T. Rohand, W. Dehaen and N. Boens, *Org. Lett.,* 2005, **7**, 4377-4380.

(79) T. Rohand, M. Baruah, W. Qin, N. Boens and W. Dehaen, *Chem. Commun.* 2006, 266-268.

(80) J. Han, O. Gonzalez, A. Aguilar-Aguilar, E. Peña-Cabrera and K. Burgess, *Org. Biomol. Chem.,* 2009, **7**, 34-36.

(81) E. Fron, E. Coutiño-Gonzalez, L. Pandey, M. Sliwa, M. Van der Auweraer, F. C. De Schryver, J. Thomas, Z. Dong, V. Leen, M. Smet, W. Dehaen and T. Vosch, *New J. Chem*., 2009, **33***,* 1490–1496.

(82) T. Rohand, J. Lycoops, S. Smout, E. Braeken, M. Sliwa, M. Van der Auweraer, W. Dehaen, W. M. De Borggraeve and N. Boens, *Photochem. Photobiol. Sci.,* 2007, **6**, 1061-1066.

(83) J. C. Er, M. K. Tang, C. G. Chia, H. Liew, M. Vandrell and Y.-T. Chang, *Chem. Sci.,* 2013, **4**, 2168-2176.

(84) W. Qin, V. Leen, W. Dehaen, J. Cui, C. Xu, X. Tang, W. Liu, T. Rohand, D. Beljonne, B. Van Avebeke, J. N. Clifford, K. Driesen, K. Binnemans, M. Van der Auweraer and N. Boens, *J. Phys. Chem. C*, 2009, **113**, 11731-11740.

(85) Y. A. Volkova, B. Brizet, P. D. Harvey, A. D. Averin, C. Goze and F. Denat, *Eur. J. Org. Chem.,* 2013, 4270-4279.

(86) L. Li, B. Nguyen and K. Burgess, *Bioorg. Med. Chem. Lett.,* 2008, **18**, 3112-3116.

(87) W. Qin, V. Leen, T. Rohand, W. Dehaen, P. Dedecker, M. Van der Auweraer, K. Robeyns, L. Van Meervelt, D. Beljonne, B. Van Averbeke, J. N. Clifford, K. Driesen, K. Binnemans and N. Boens, *J. Phys. Chem. A,* 2009, **113**, 439-447.

(88) (a) D. W. Domaille, L. Zeng and C. J. Chang, *J. Am. Chem. Soc.,* 2010, **132**, 1194-1195. (b) O. Dilek and S. L. Bane, *Bioorg. Med. Chem. Lett.*, 2009, **19**, 6911-6913.

(89) T. K. Khan, M. R. Rao and M. Ravikanth, *Eur. J. Org. Chem.*, 2010, 2314-2323.

(90) S. Yin, V. Leen, C. Jackers, D. Beljonne, B. Van Averbeke, M. Van der Auweraer, N. Boens and W. Dehaen, *Chem. Eur. J.,* 2011, **17**, 13247-13257.

(91) (a) J. Huang, X. Ma, B. Liu, L. Cai, Q. Li, Y. Zhang and K. Jiang, *J. Lumin.*, 2013, **141**, 130-136. (b) S. Yin, V. Leen, S. Van Snick, N. Boens and W. Dehaen, *Chem. Commun.*, 2010, **46**, 6329-6331.

(92) L.-Y. Niu, H. Li, L. Feng, Y.-S. Guan, Y.-Z. Chen, C.-F. Duan, L.-Z. Wu, Y.-F. Guan, C.-H. Tung, Q.-H. Tung and Q.-Z. Yang, *Anal. Chim. Acta,* 2013, **775**, 93-99.

(93) T. K. Khan and M. Ravikanth, *Eur. J. Org. Chem.*, 2012, 7011-7022.

(94) P. Yang, J. Zhao, W. Wu, X. Yu and Y. Liu, *J. Org. Chem.,* 2012, **77**, 6166-6178.

(95) W. Wu, J. Zhao, J. Sun, L. Huang and X. Yi, *J. Mater. Chem. C*, 2013, **1**, 705-716.

(96) W. Wu, J. Zhao, H. Guo, J. Sun, S. Ji and Z. Wang, *Chem. Eur. J.*, 2012, **18**, 1961-1968.

(97) F. Sozmen, B. S. Oksal, O. A. Bozdemir, O. Buyukcakir and E. U. Akkaya, *Org. Lett.,* 2012, **14**, 5286-5289.

(98) M. Vincent, E. Beabout, R. Bennett and P. Hewavitharanage, *Tetrahedron Lett.,* **2013**, *54,* 2050-2054.

(99) Y. Chen, J. Zhao, H. Guo and L. Xie, *J. Org. Chem*., 2012, **77**, 2192-2206.

(100) Y. hayashi, N. Obata, M. Tamaru, S. Yamaguchi, Y. Matsuo, A. Saeki, S. Seki, Y. Kureshi, S. Saito, S. Yamaguchi and H. Shinokubo, *Org. Lett*., 2012, **14**, 866-869.

(101) C. Y. Lee, O. K. Farha, B. J. Hong, A. A. Sarjeant, S. T. Nguyen and J. T. Hupp, *J. Am. Chem. Soc*., 2011, **133**, 15858-15861.

(102) L. Zhou, C.-C. Zhu, Y.-S. Xue, W.-J. He, H.-B. Du, J.-B. You and Y.-Z.; Li, *Inorg. Chem. Commun.,* 2013, **35**, 355-359.

(103) H. Zhao, B. Wang, J. Liao, H. Wang and G. Tan, *Tetrahedron Lett.,* 2013, **54***,* 6019-6022.

(104) S. P. Economopoulos, C. L. Chochos, H. A. Ioannidou, M. Neophytou, C. Charilaou, G. A. Zissimou, J. M. Frost, T. Sachetan, M. Shahid, J. Nelson, M. Heeney, D. D. C. Bradley, G. Itskos, P. A. Koutentis and S. A. Choulis, *RSC Adv.,* 2013, **3**, 10221-10229.

(105) E. Heyer, P. Retailleau and R. Ziessel, *Org. Lett.,* 2014, **16**, 2330-2333.

(106) M. Pamuk-Algi, S. Tirkes, S. Ertan, E. G. C. Ergun, A. Cihaner and F. Algi, *Electrochemica Acta*, 2013, **109**, 766-774.

(107) T. Jiang, P. Zhang, C. Yu, J. Yin, L. Jiao, E. Dai, J. Wang, Y. Wei, X. Mu and E. Hao, *Org. Lett.,* 2014, **16**, 1952-1955.

(108) A. Wakamiya, N. Sugita and S. Yamaguchi, *Chem. Lett*., 2008, **37**, 1094-1095.

(109) V. Lakshmi and M. Ravikanth, *J. Org. Chem*., 2011, **76**, 8466-8471.

(110) V. Lakshmi and M. Ravikanth, *Chem. Phys. Lett.*, 2013, **564**, 93-97.

(111) V. Lakshmi and M. Ravikanth*, Eur. J. Org. Chem*., 2014, 5757-5766.

(112) V. Lakshmi and M. Ravikanth, *RSC Adv.,* 2014, **4**, 44327-44336.

**Legends**

**Chart 1.** Representation of the 4-bora-3a,4a-diaza-*s*-indacene BODIPY framework with the numbering scheme derived from indacene

**Chart 2.** Sterically crowded polyarylated BODIPYs containing two/three different types of substituents

**Scheme 1.** General synthetic route for 4-bora-3a,4a-diaza-*s*-indacene BODIPY **3**

**Scheme 2.** Different synthetic routes for mono to hexahalogenated BODIPYs **4-16**

**Scheme 3.** Synthesis of BODIPY derivatives **17-21** from 2-halo BODIPYs under palladium coupling conditions

**Scheme 4**. BODIPY derivatives of 2-substituted BODIPYs **22-24**

**Scheme 5.** BODIPY derivatives **24-27** derived from 3-halo substituted BODIPY **5a** and **5b** under Palladium catalyzed coupling conditions

**Scheme 6.** Synthesis of BODIPY-chromophore conjugates **28a-28g** using 3-bromo BODIPY **5b.** Reaction conditions used were $Pd_2(dba)_3/AsPh_3$, toluene/TEA, 35-60 °C

**Scheme 7.** Nucleophilic substitution reactions on 3-halo BODIPY **5a** and **5b**

**Scheme 8.** Synthesis of BODIPY-chromophore conjugates **43a-43e** using 3-azido BODIPY **39.**

**Scheme 9.** Reactivity of 3,5-dihalogen BODIPYs **6a** and **6b** towards Pd coupling reactions

**Scheme 10.** Reactivity of 3,5-dihalogen BODIPYs **6a** and **6b** towards nucleophilic substitution reactions

**Scheme 11.** Synthetic scheme for bi and trichromophore systems **53a-53d.** [a]Reaction conditions used were $CH_3CN/CHCl_3$ (1:1), 60 °C

**Scheme 12.** Synthesis of the 2,6-disubstituted BODIPY derivatives **56-59** (a) from 2,6-dihalogenated BODIPY **7a-7c.** (b) Metal complex derivatives **60** and **61**

**Scheme 13.** Synthesis of 1,7-diaryl substituted BODIPYs **62-66** from 1,7-dibromo BODIPYs **8a/8b**

**Scheme 14.** Synthesis of phenylated BODIPY compounds **67-69**

**Scheme 15.** Synthesis of polyarylated BODIPY compounds **70a-70f**

**Scheme 16.** Synthesis of polyarylated BODIPYs containing (a) two different types **72a** (b) three different types of groups **74a** at pyrrole carbons.

**Figure 1.** (a) Absorption (solid line) and emission spectra (dotted line); (b) cyclic voltammogram (solid line) and differential pulse voltammogram (dotted line) of unsubstituted *meso*-tolyl BODIPY **3a**.

**Figure 2.** The crystal structures of brominated BODIPYs (a) **6b** (b) **10** (c) **13** (d) **15** and (e) **16**.

**Figure 3.** (a) Normalized absorption spectra (b) cyclic voltammograms ( ) differential pulse voltammetry (….) (c) linear plot between number of bromine atoms and reduction potential of brominated compounds **5, 6, 10, 13, 15** and **16** along with **3a**.

**Figure 4.** Normalized absorption (solid line) and emission (dotted line) spectra of compounds (a) **28a** and (b) **28e** recorded in toluene.

**Figure 5.** (a) The absorption spectra of **46b** in the presence of $F^-$ in $CH_2Cl_2$ (8 μM). (b) Fluorescence spectral changes ($\lambda_{ex}$ = 505 nm) of **46c** (10 μM) on the addition of $Fe(ClO_4)_3$ in toluene.

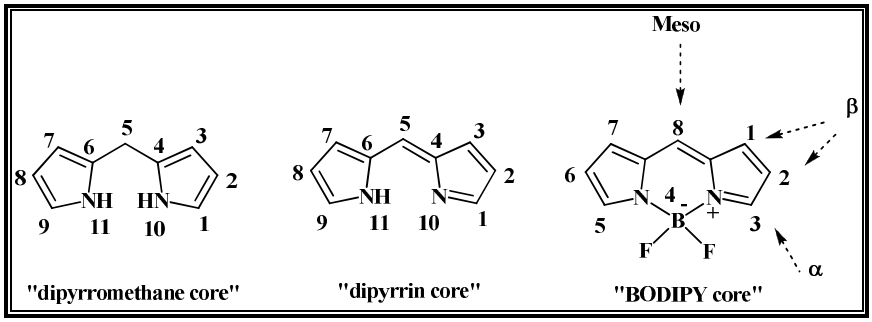



**Chart 1**

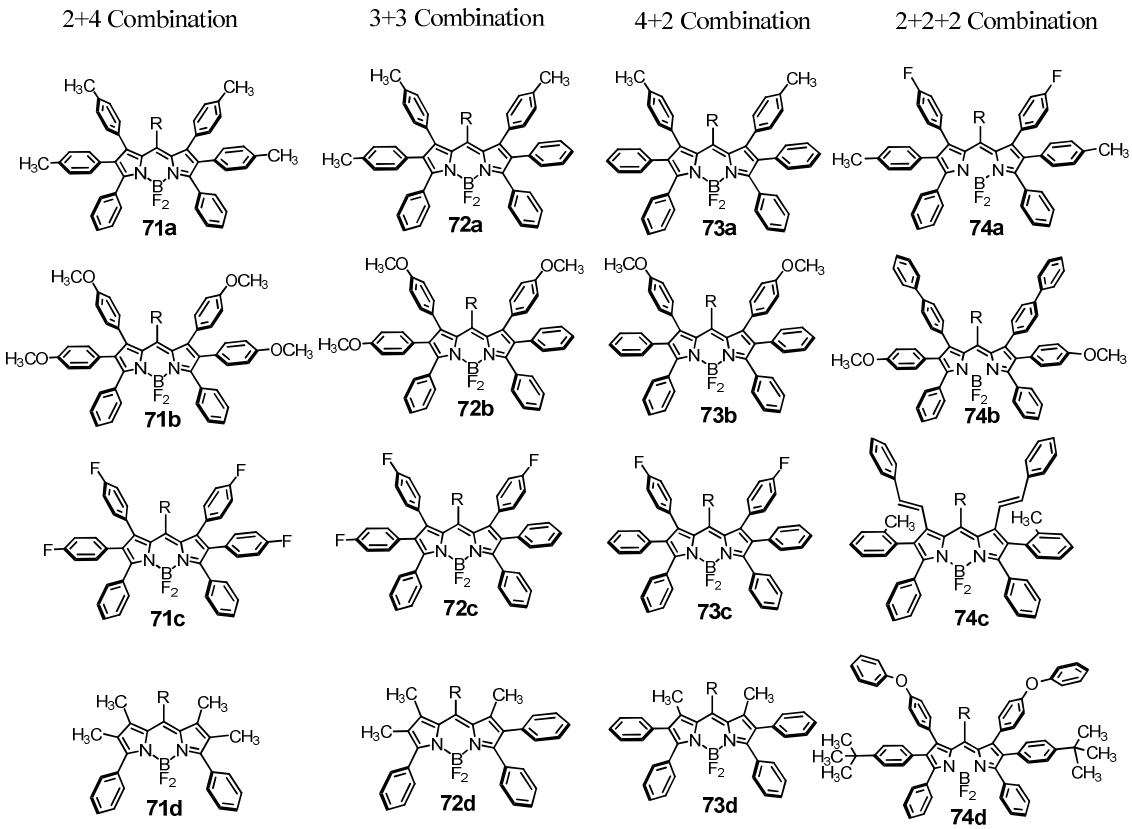
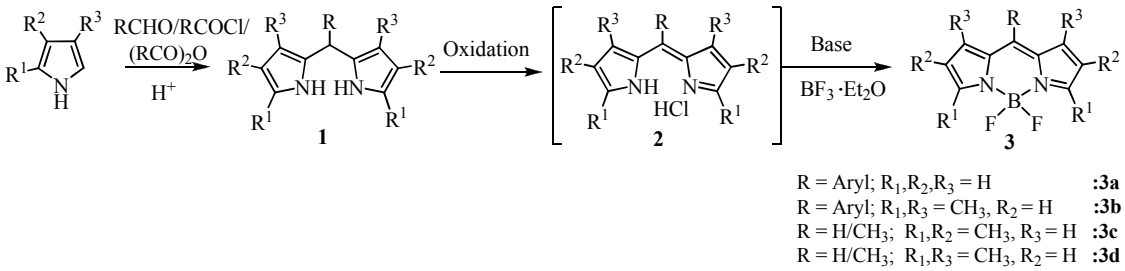


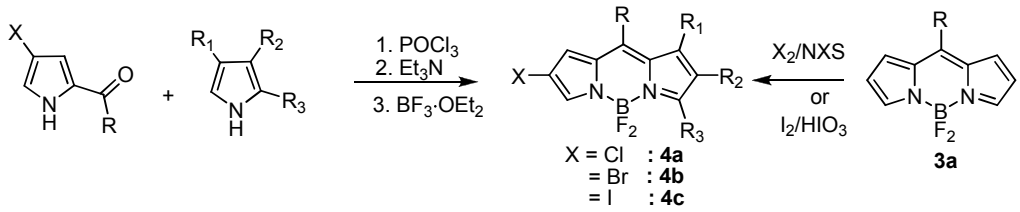

**Chart 2**



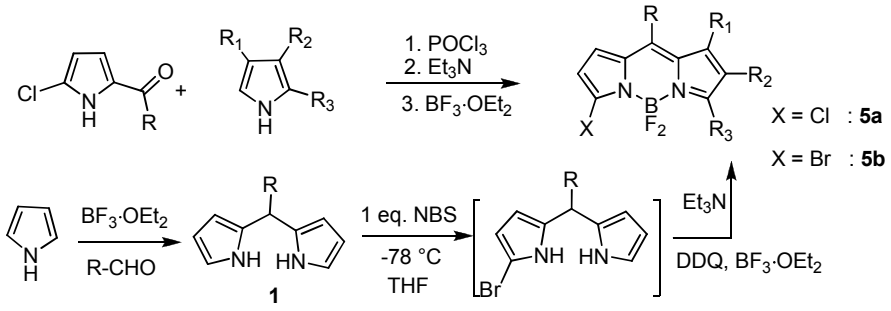

R = Aryl; $R_1$,$R_2$,$R_3$ = H **:3a**
R = Aryl; $R_1$,$R_3$ = $CH_3$, $R_2$ = H **:3b**
R = H/$CH_3$; $R_1$,$R_2$ = $CH_3$, $R_3$ = H **:3c**
R = H/$CH_3$; $R_1$,$R_3$ = $CH_3$, $R_2$ = H **:3d**

**Scheme 1**

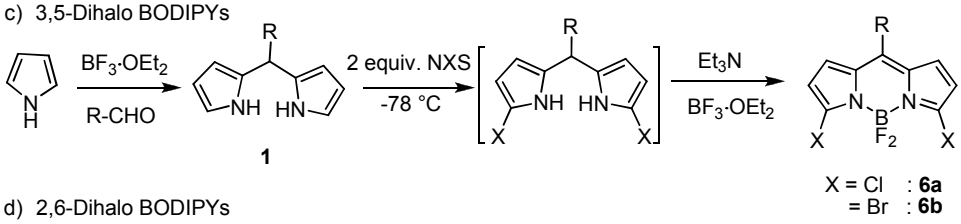
a) 2-Halo BODIPYs



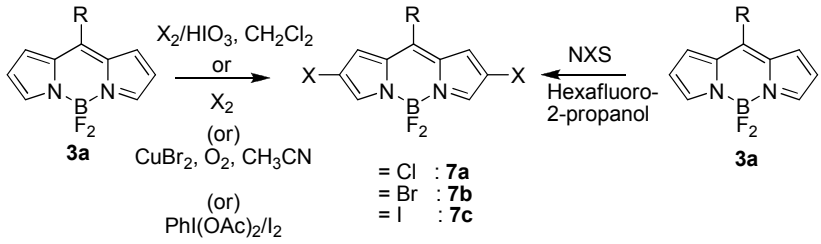

b) 3-Halo BODIPYs



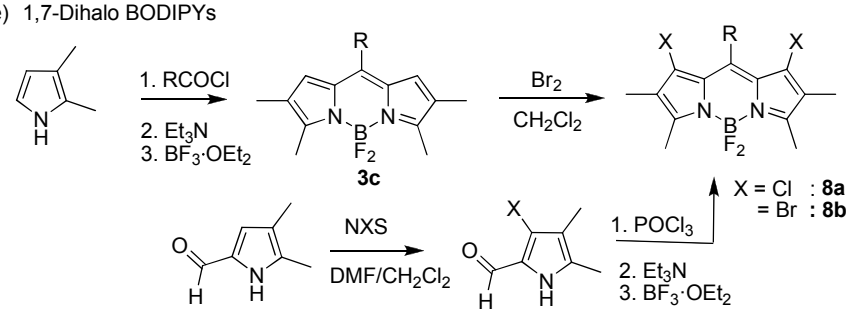

c) 3,5-Dihalo BODIPYs



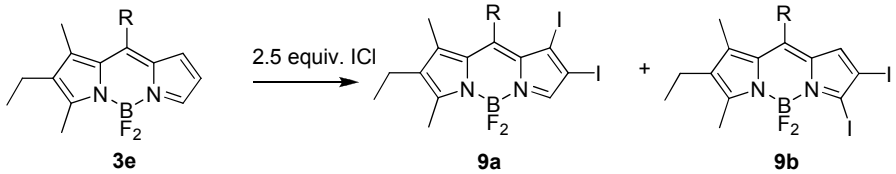

d) 2,6-Dihalo BODIPYs




e) 1,7-Dihalo BODIPYs

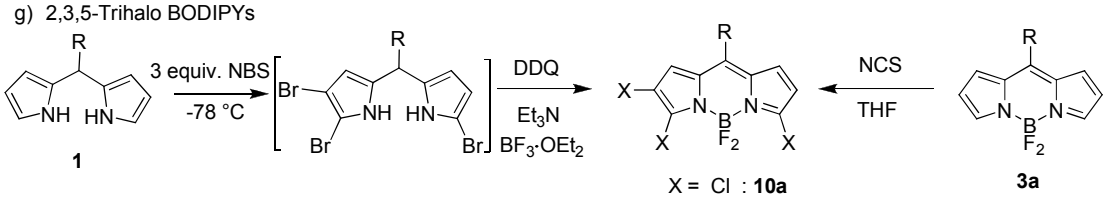



f) 1,2/2,3-Dihalo BODIPYs

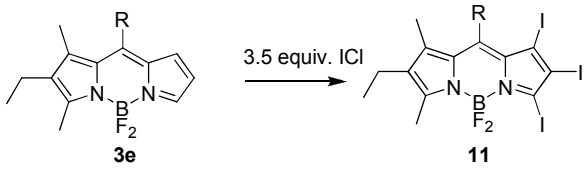



Contd..

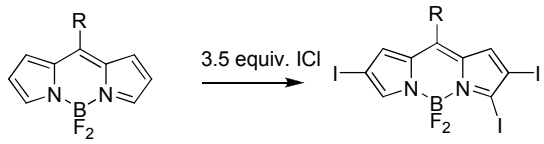
g) 2,3,5-Trihalo BODIPYs



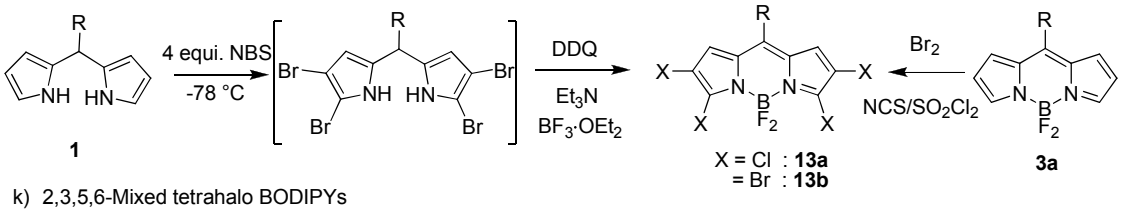

h) 1,2,3-Trihalo BODIPYs



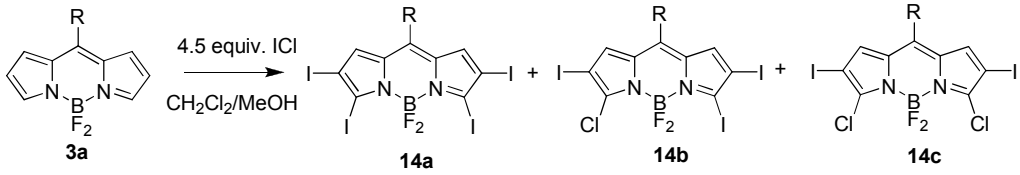

i) 2,3,6-Trihalo BODIPYs



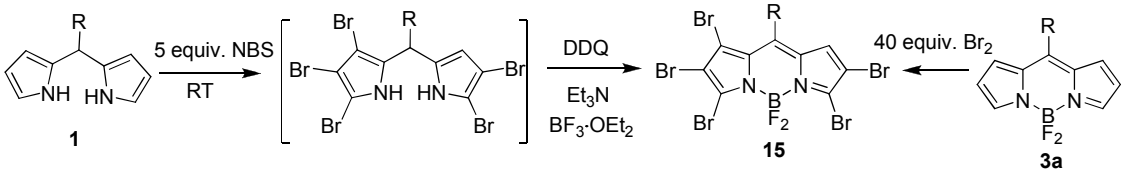

j) 2,3,5,6-Tetrahalo BODIPYS



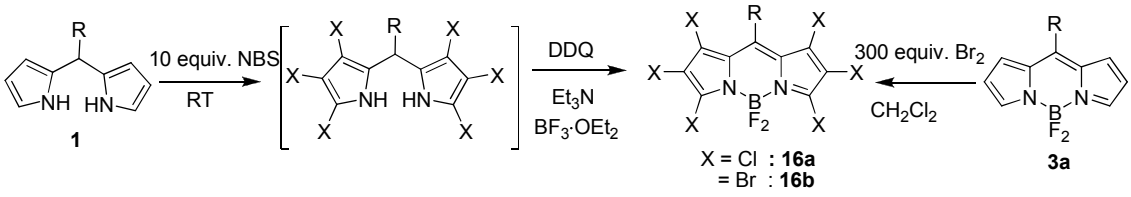

k) 2,3,5,6-Mixed tetrahalo BODIPYs



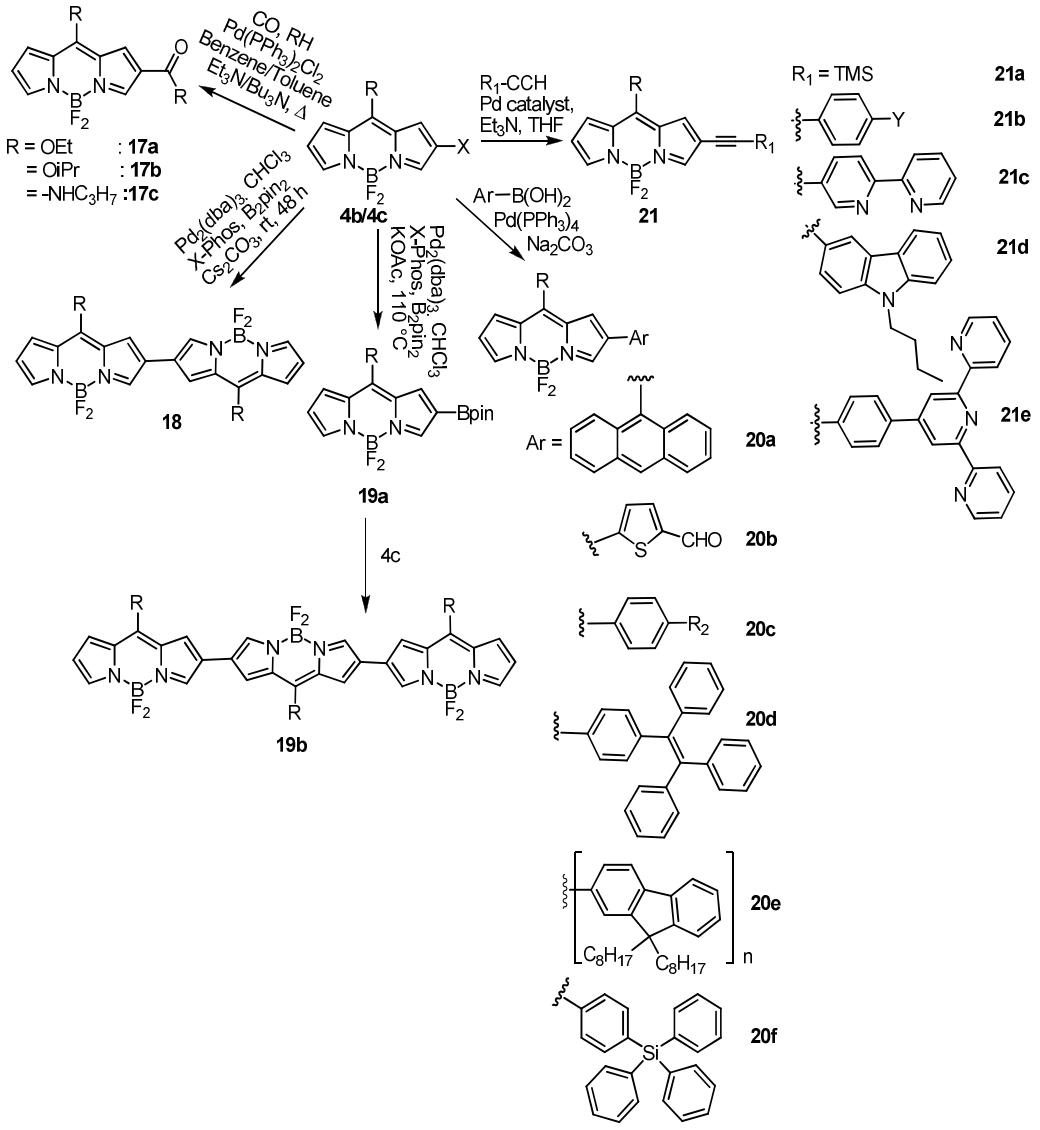

l) 1,2,3,5,6-Pentahalo BODIPYs



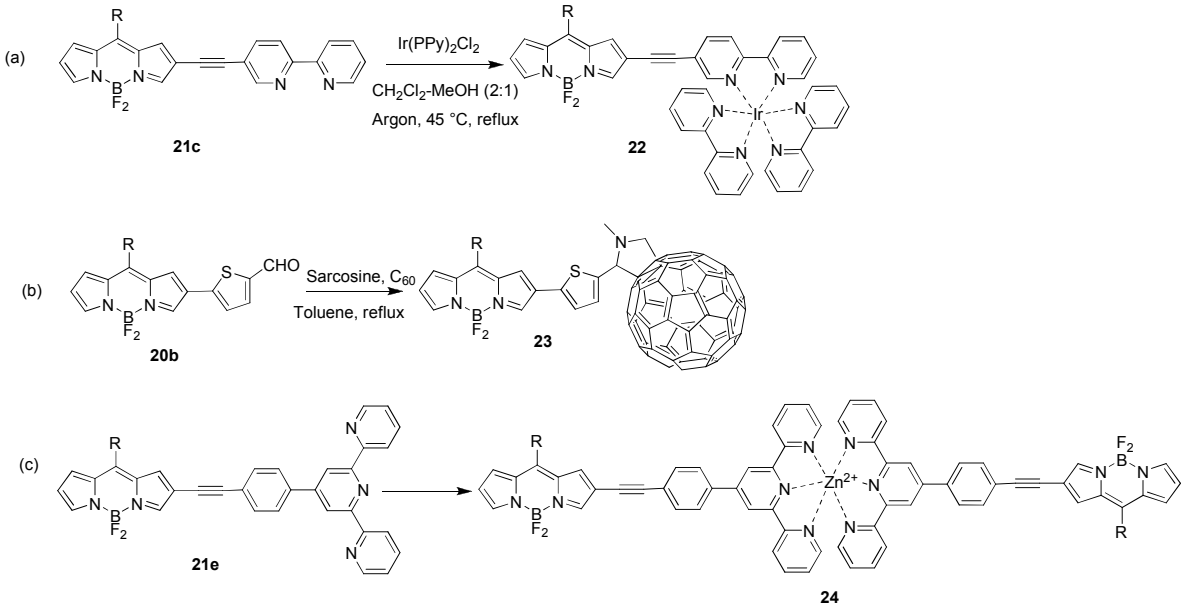

m) 1,2,3,5,6,7-Hexahalo BODIPYs



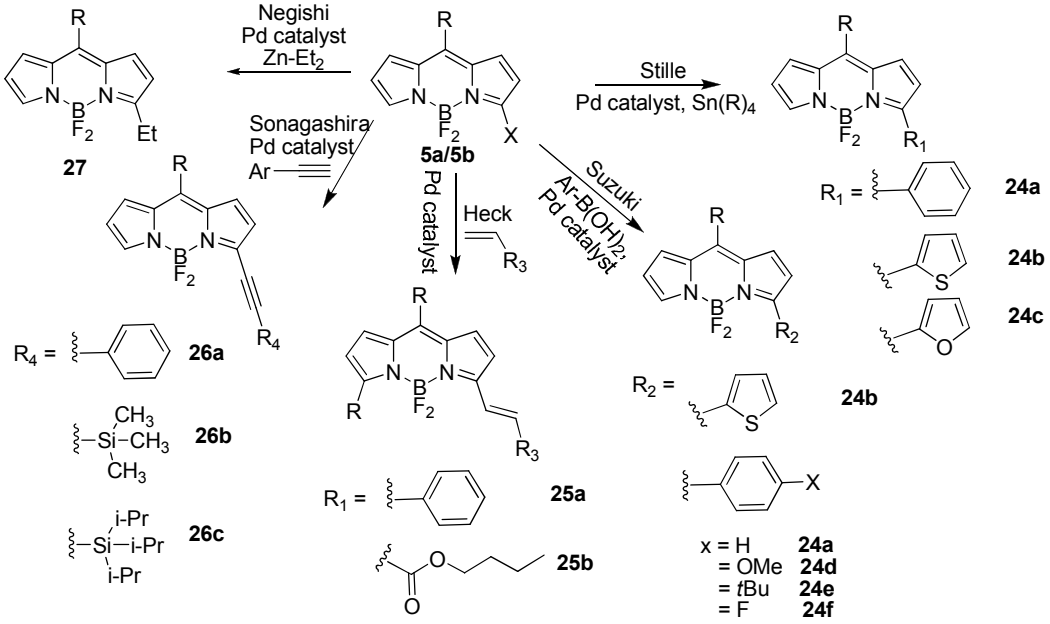

**Scheme 2**



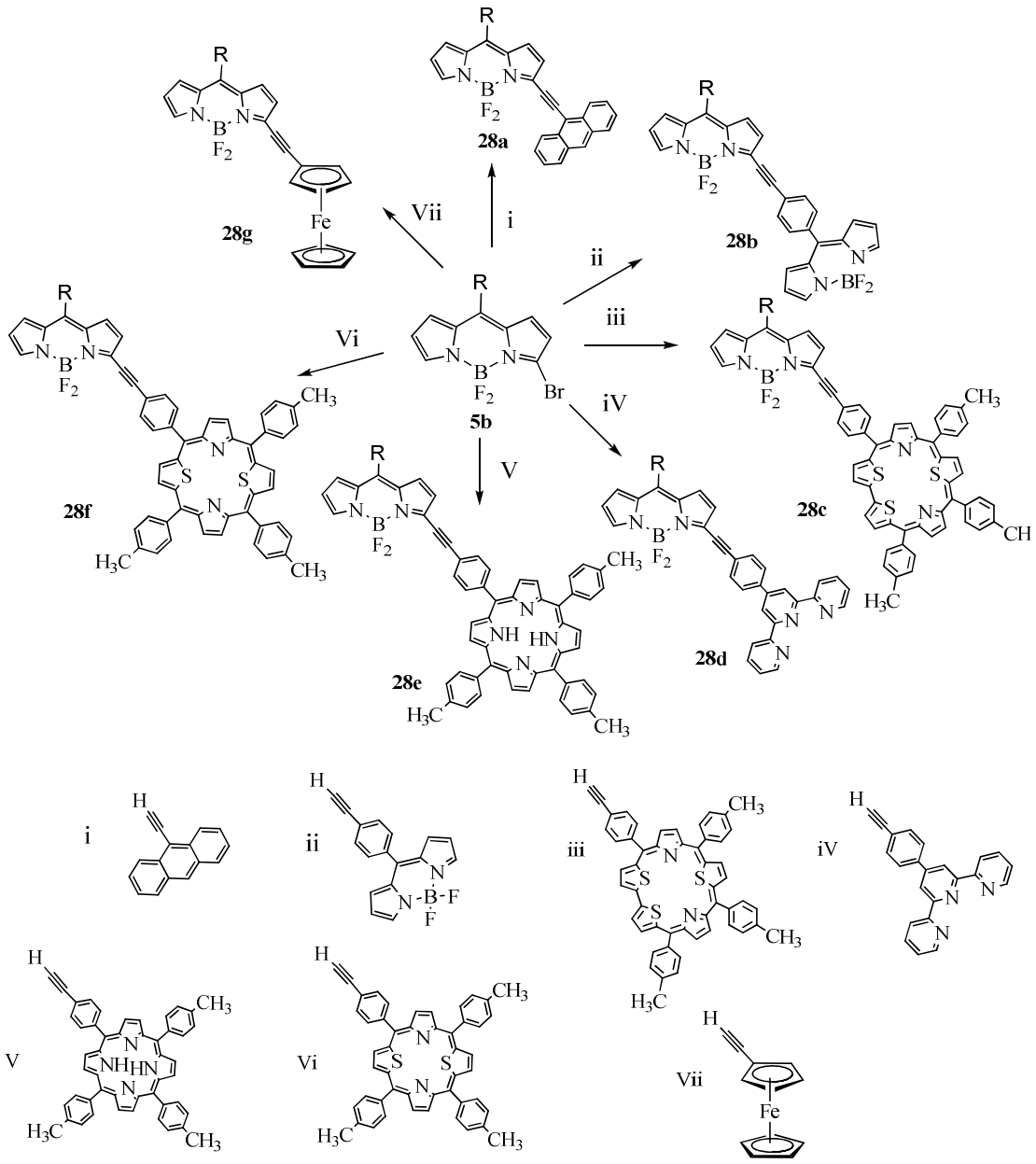

**Scheme 3**



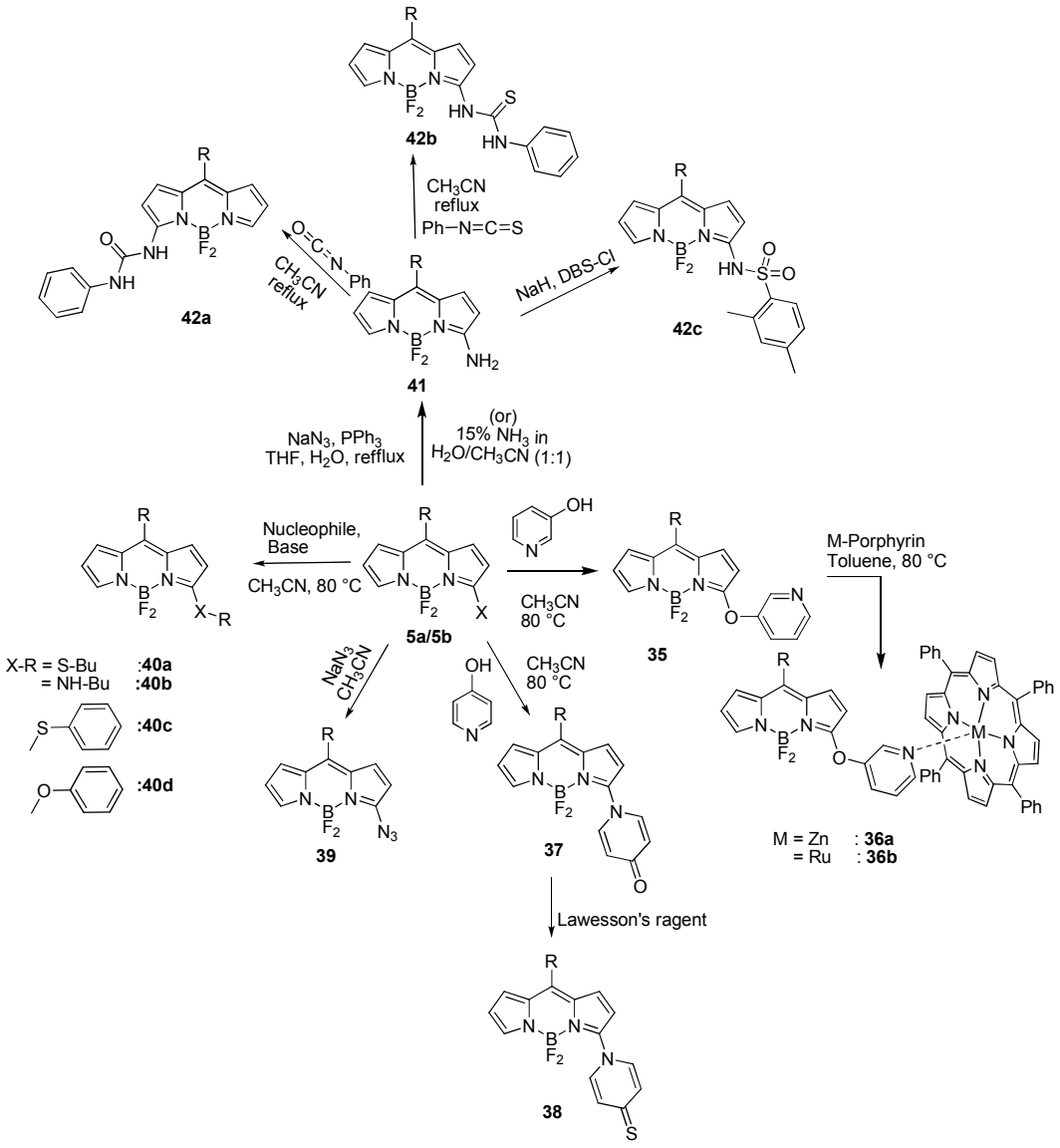

**Scheme 4**



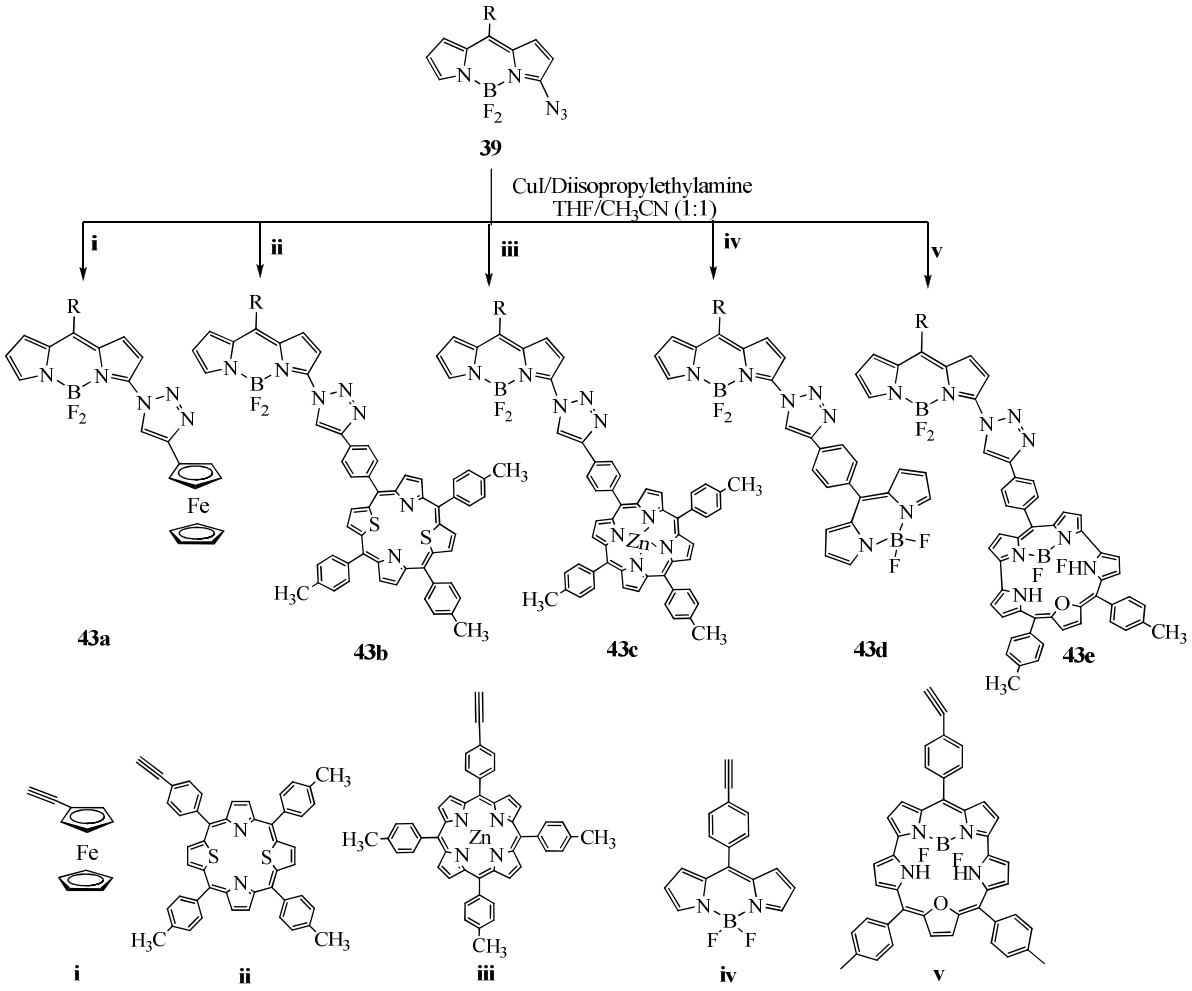

**Scheme 5**



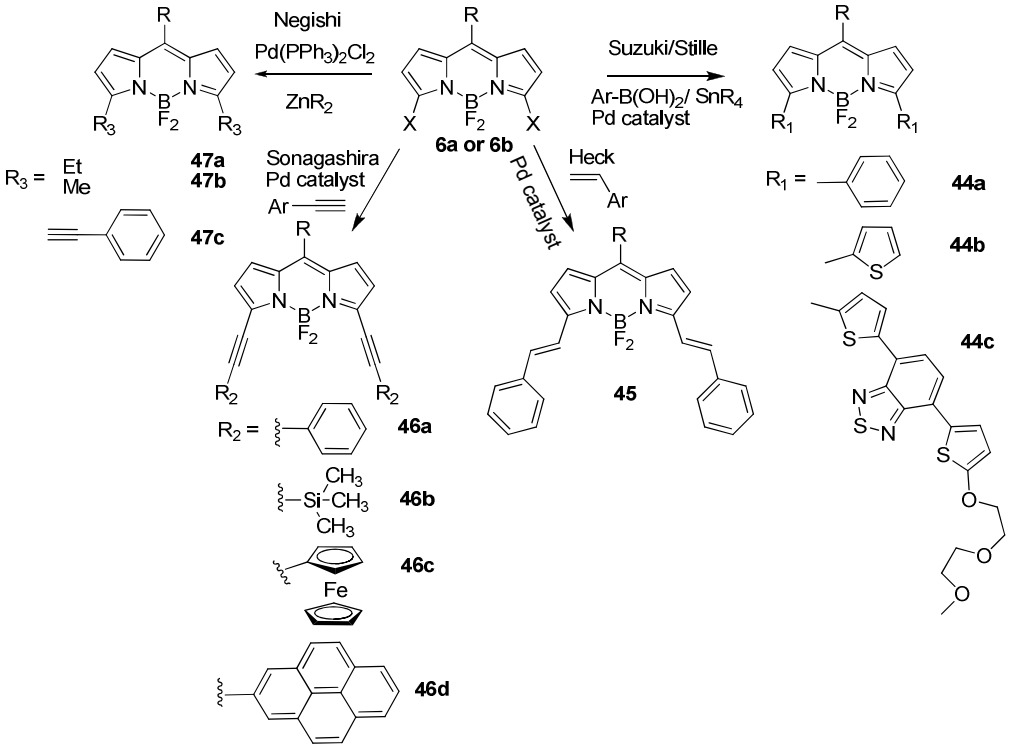

**Scheme 6**



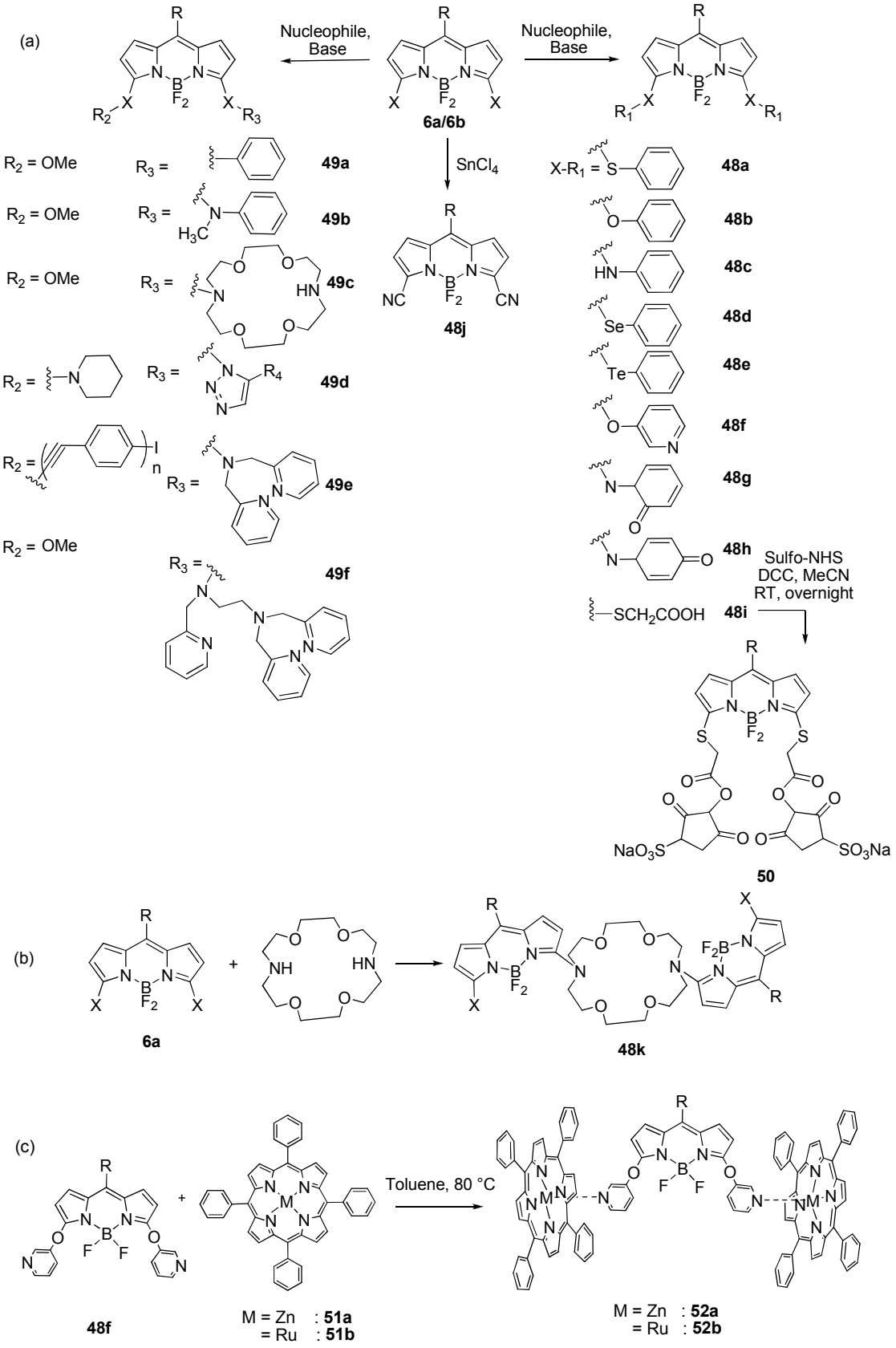

**Scheme 7**



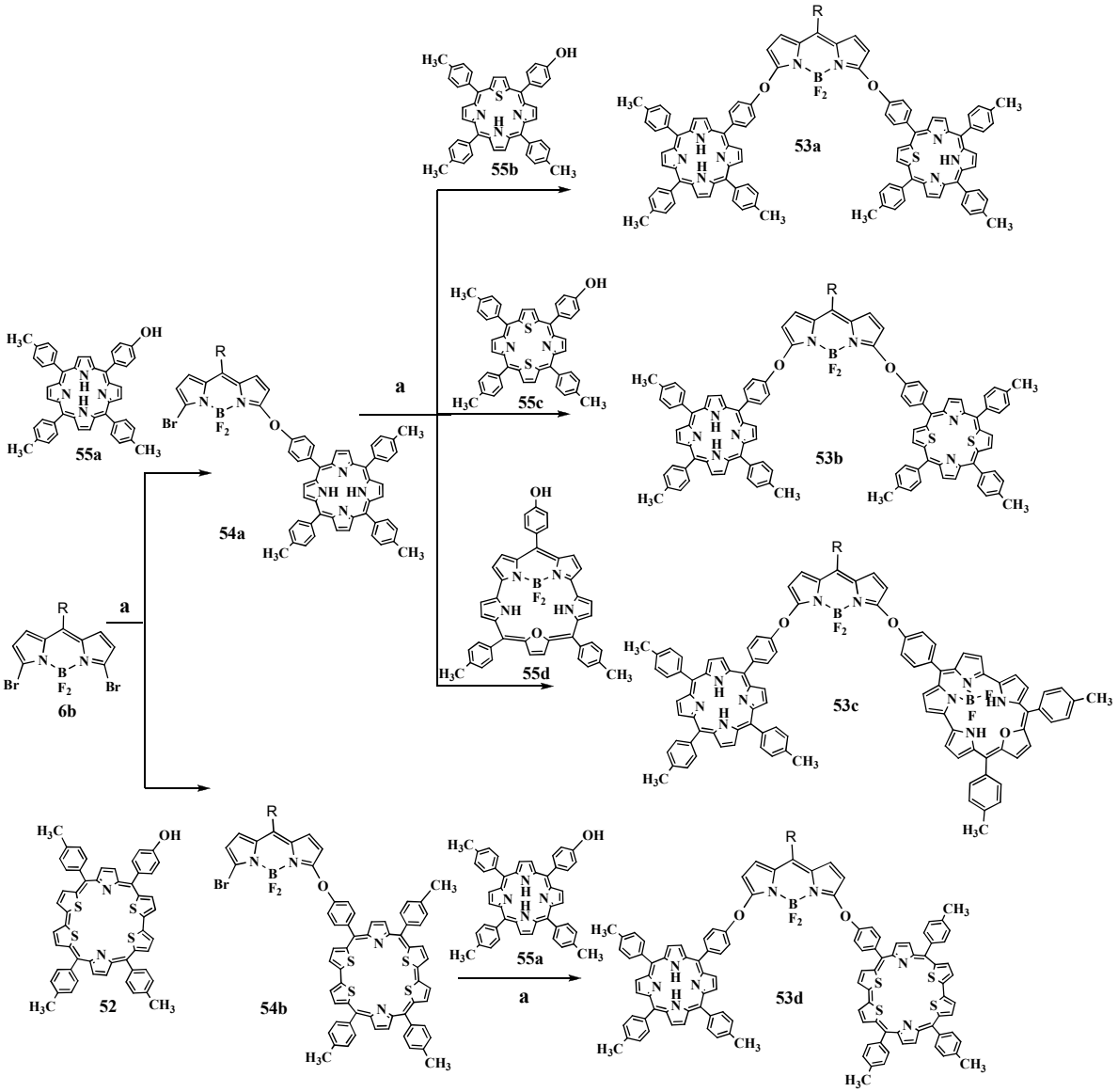

**Scheme 8**



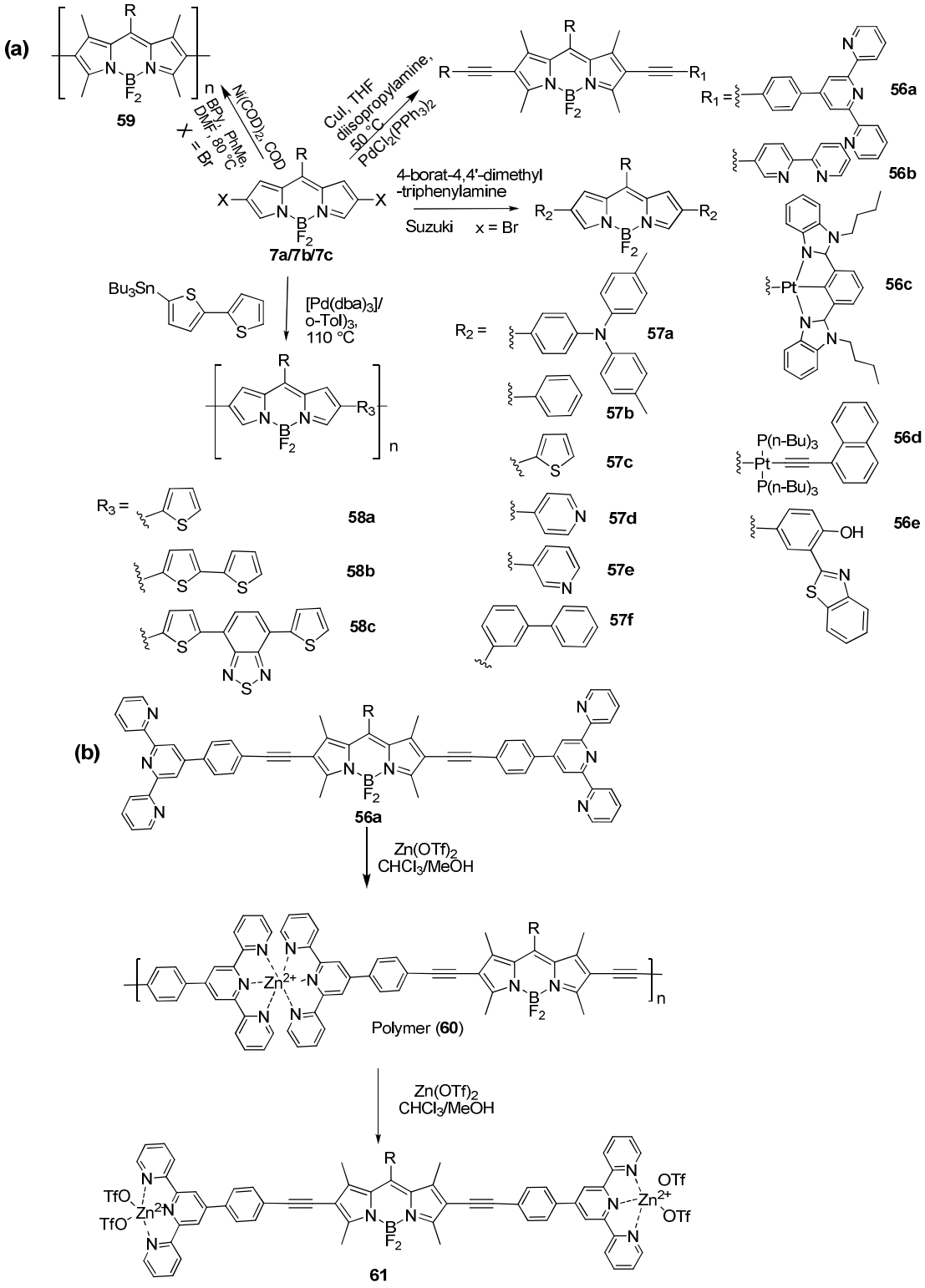

**Scheme 9**



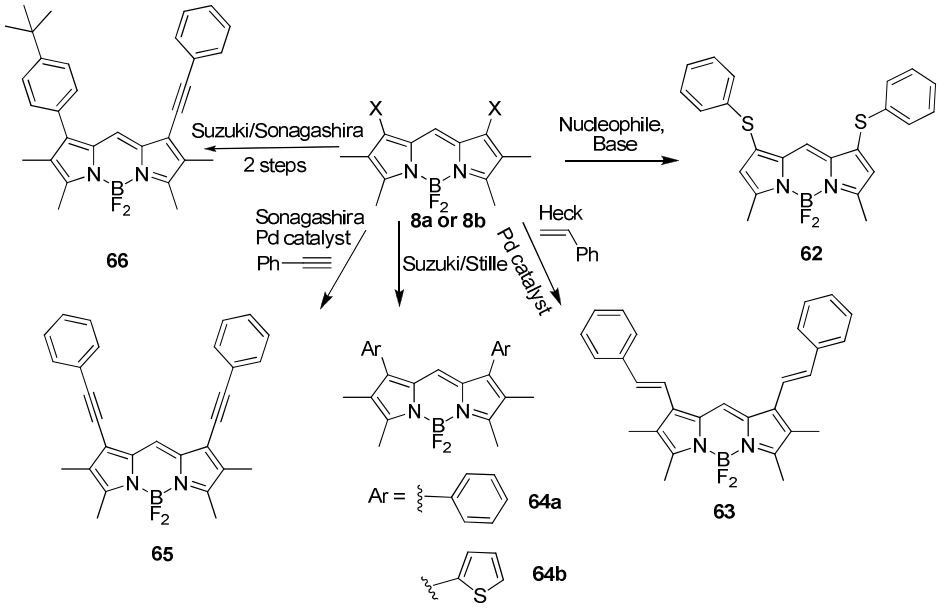

**Scheme 10**



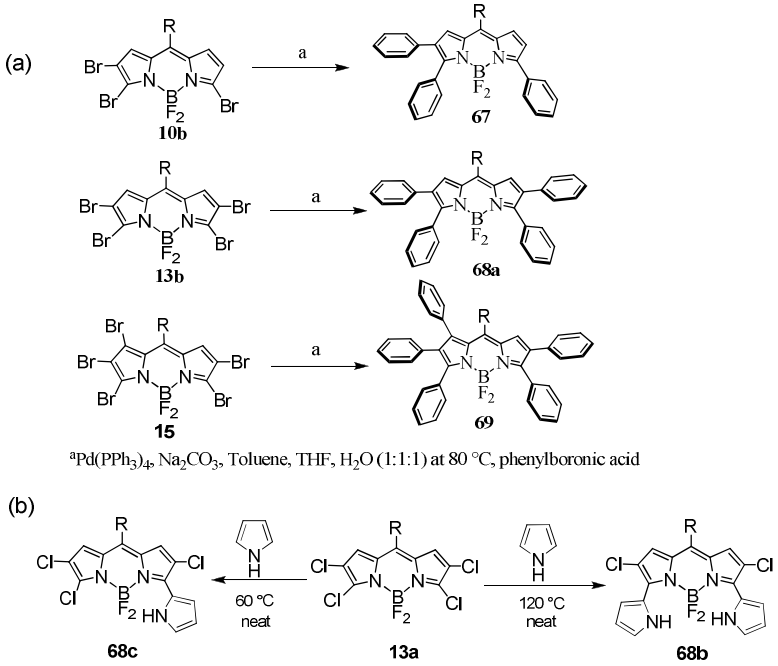

**Scheme 11**



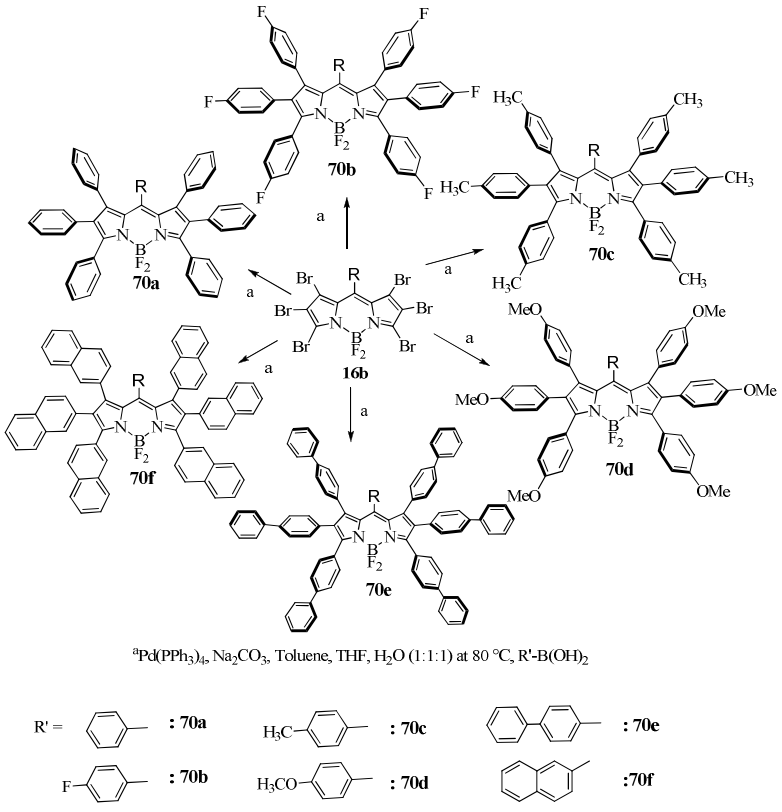

**Scheme 12**



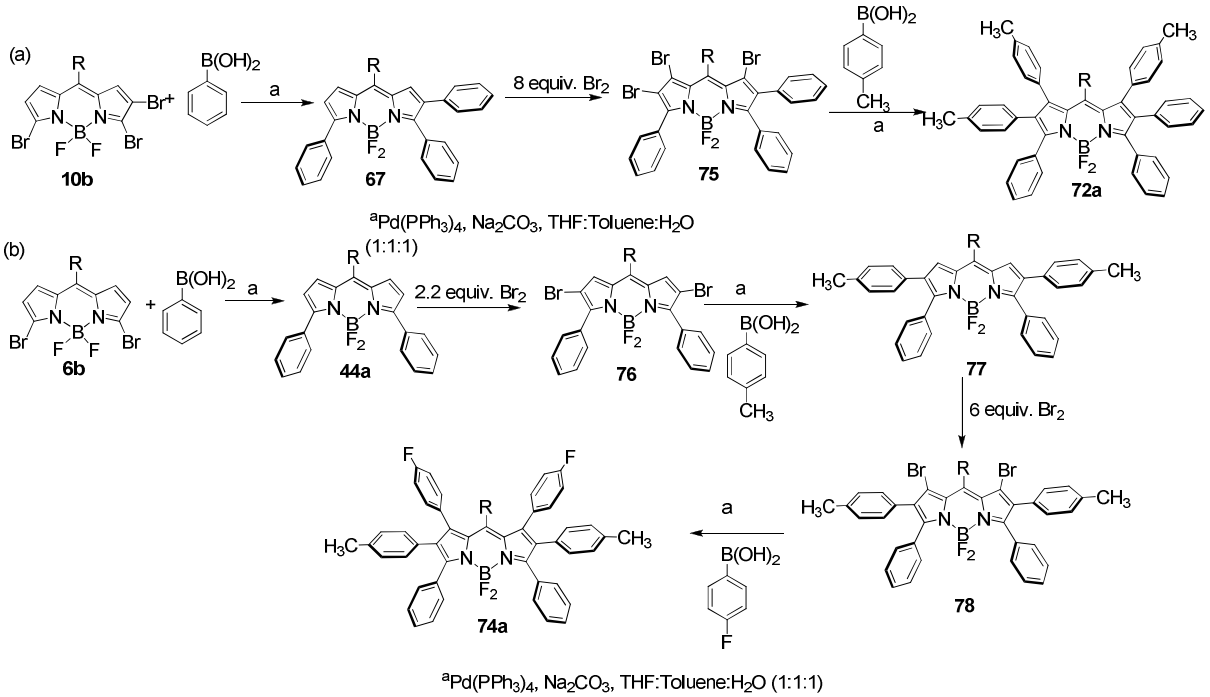

**Scheme 13**




**Scheme 14**




**Scheme 15**




**Scheme 16**

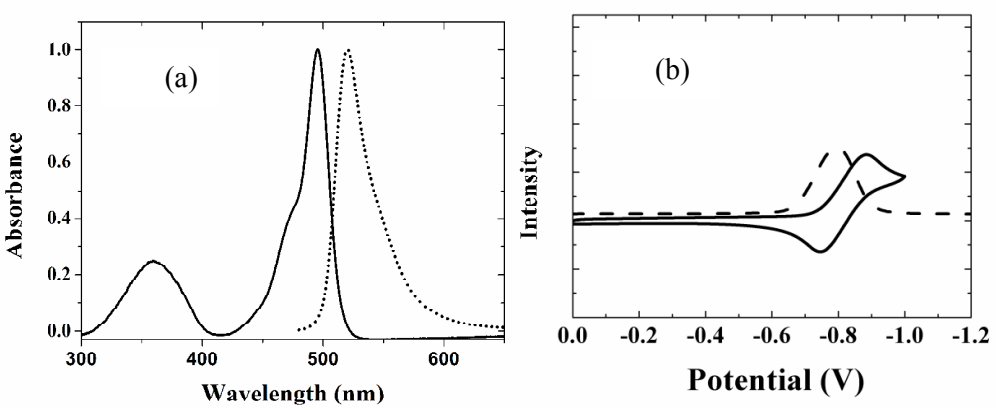



**Figure 1**

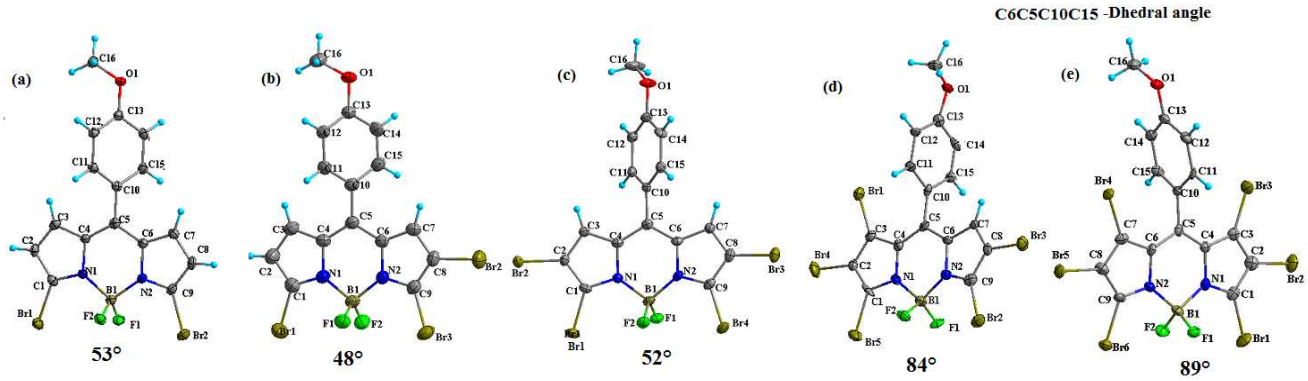



**Figure 2**

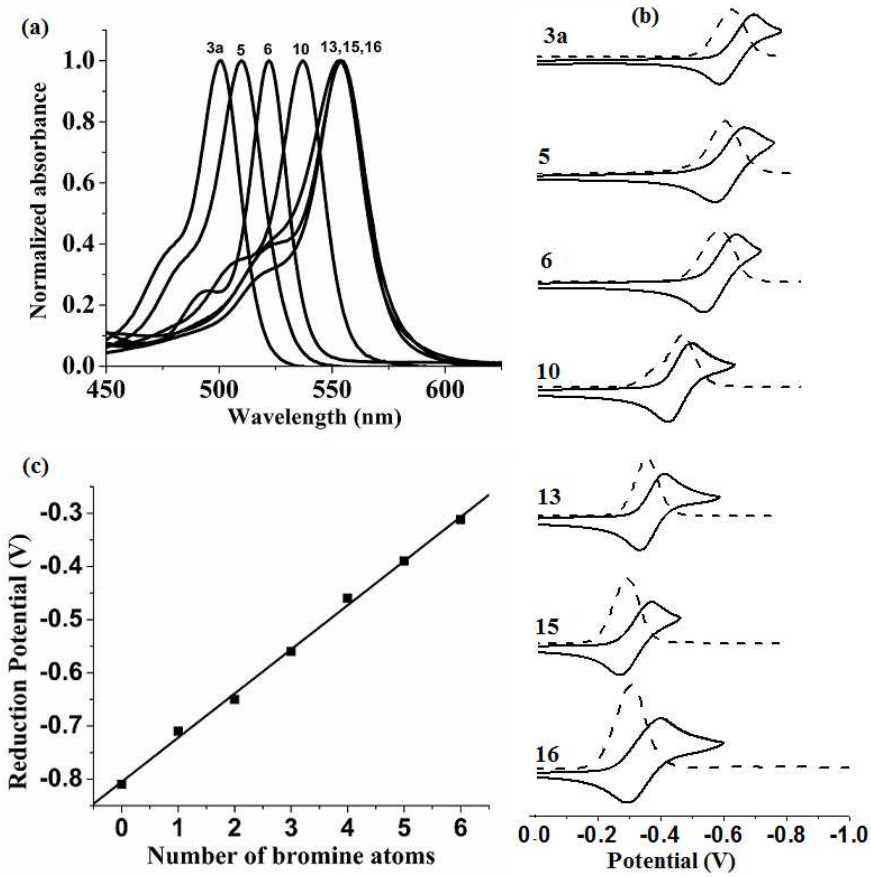



**Figure 3**

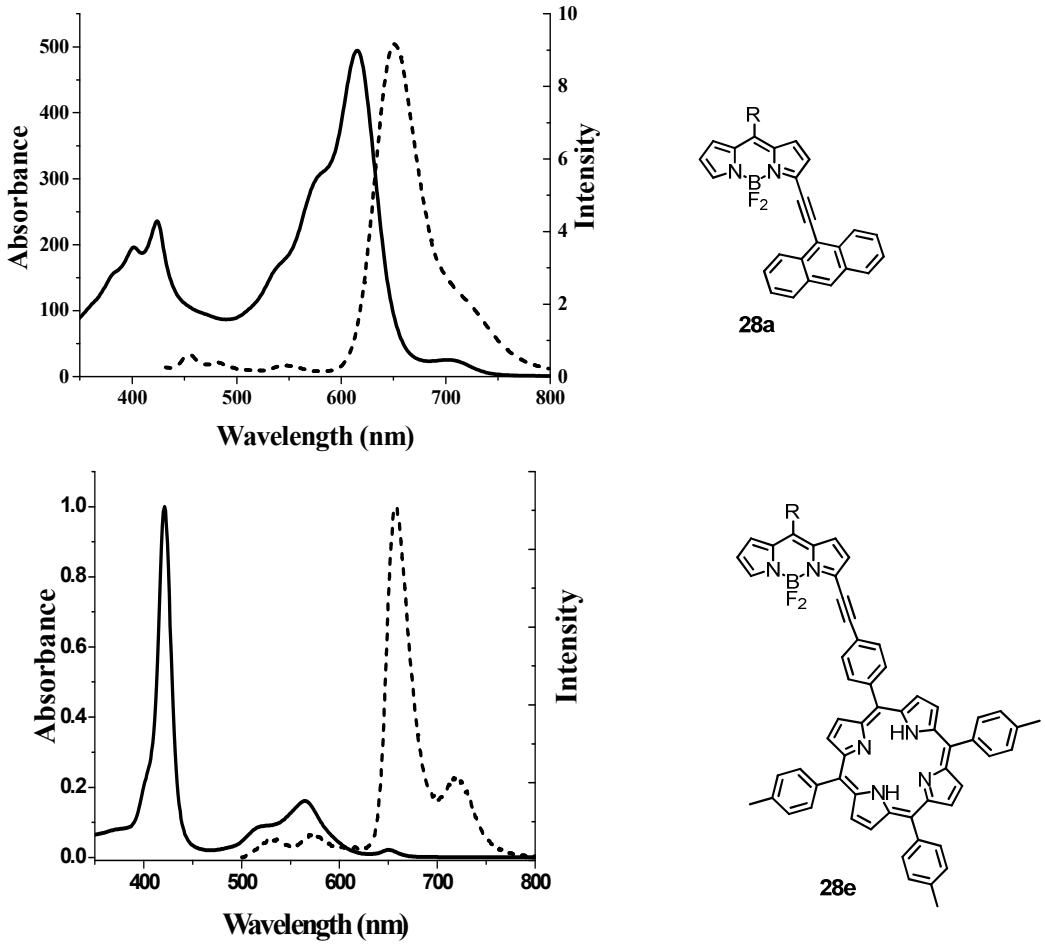



**Figure 4**

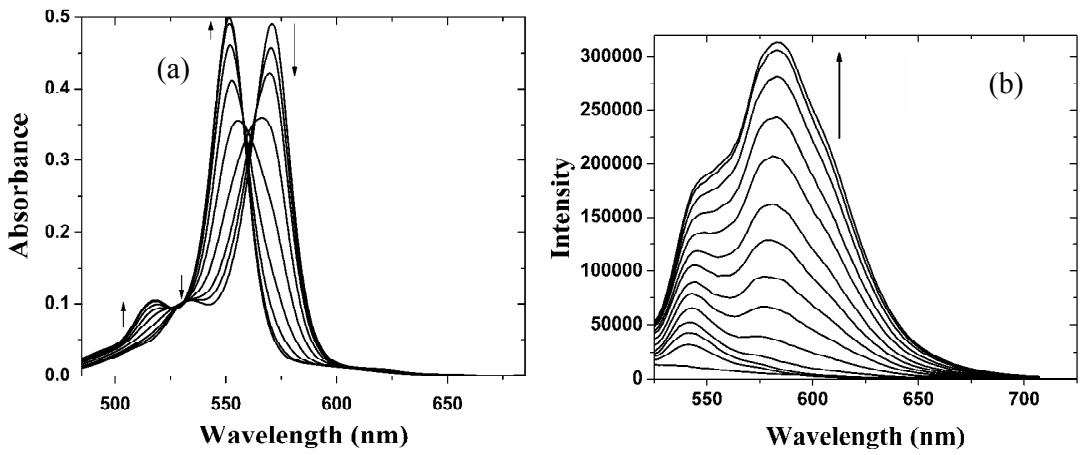



**Figure 5**