CHAPTER-1

INTRODUCTION TO BODIPY COMPOUNDS
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1.1. Preamble

Despite existing for almost a century, fluorescent dyes continue to attract the attention of scientists from an ever flourishing multidisciplinary arena. Recent developments in the field of personal diagnostics and in the area of organic electroluminescent devices have boosted interest in the development of next-generation emissive dyes. Countless classes of highly fluorescent organic compounds are now known, but the difluoro-boraindace family (4,4-difluoro-4-borata-
3a-azonia-4a-aza-s-indacene, abbreviated as Bodipy) has gained recognition as one of the more versatile fluorophores. Since the potential use of these dyes as biological labels was recognized,\textsuperscript{1,2} several new Bodipy dyes were designed and synthesized. Subsequently these dyes are considered as photostable substitutes of fluorescein. The use of Bodipy as effective biological labels has been complemented by their known propensity to function as tunable laser dyes.\textsuperscript{3} In parallel, more fundamental studies on the chemical reactivity and the photophysical properties of the new dyes emerged. Increasing versatile use of the Bodipys as organic photo-voltaic materials, and in emerging nanotechnological applications make the future extremely bright for the “porphyrin’s little sisters”.

1.2. Chemical Structures of Bodipy Dyes

The Bodipy framework consists of a dipyrromethene (PM) ligand complexed with a disubstituted boron atom, generally a BF\textsubscript{2} moiety. The PM ligand is formed by joining of two pyrrole units via an interpyrrolic methine bridge. Due to the complexation with BF\textsubscript{2}, the Bodipy fluorophore can be considered as an example of a “rigidified” monomethine cyanine dye (Figure 1.2.1) with fixed planarity of the chromophoric $\pi$-electron system.\textsuperscript{4} The rigidity, introduced by the boron complexation further prevents the cis-trans isomerization and interpyrrolic methine chain-twisting, eventually leading to unusual high fluorescence yields from the
dipyrrometheneboron framework, comparated to the flexible cyanine dyes. Conjugation of the π-electrons runs along the organic backbone, and can be extended further by attachment of suitable groups onto the periphery or to one or both the pyrrole fragments. The IUPAC numbering system for the Bodipy dyes (Figure 1.2.1) is different to that used for dipyrromethenes. However, the terms α-, β-, and meso-positions are used in just the same way for both systems.

Figure 1.2.1 (a) Chemical structure of the Bodipy core; (b) Molecular model of a representative Bodipy derivative functionalized on the Bodipy backbone and meso position.

The Bodipy derivatives are strongly UV-absorbing small neutral molecules with outstanding photophysical characteristics when compared to the classical fluorophores, such as fluorescein and rhodamines dyes, and show fluorescence emissions in the visible region. They have intense, nearly superimposable absorption and emission profiles (λ_{max} between 500-545 nm), large molar absorption coefficients (~40,000 to 80,000 M^{-1} cm^{-1}), high fluorescence quantum yields (Φ_f normally > 0.60), reasonably long fluorescence lifetimes (τ in ~ 1 to 10 ns range) and relatively small Stokes’ shift (~10 nm). The absorption spectra, recorded in solution or plastic films exhibit intense transitions that correspond to the S_0→S_1 process, together with clear vibrational fine structures, and a more modest set of transitions owing to the S_0→S_2 process. Both transitions usually show vibrational fine structures ranging from 1200 to 1400 cm^{-1}, typical of the molecular C=C framework of the Bodipy core. Owing to the strong
absorption transitions, the radiative rate constants of the Bodipys are usually quite high (ca. $10^8$ s$^{-1}$). Phosphorescence is generally a rare phenomenon with these dyes, due to negligible triplet energy state and a slow rate of intersystem crossing (ISC), except for some diiodo Bodipys where ISC is promoted due to the heavy-atom effect.\textsuperscript{6} In addition, a Bodipy with ancillary Ru(II)-polypyridine complex showed triplet emission.\textsuperscript{7} The Bodipy dyes have excellent thermal stability both in solution and in solid states, good solubility in many organic solvents; are resistant towards self-aggregation in polar solvents, and insensitive to changes in pH and solvent polarity.

The stability of Bodipy core is partially due to the first row elements (B, N, and F), which allow efficient orbital overlap to promote delocalisation of the π-system. Slightly polarized heteroatoms generate various electron-rich and electron-deficient reaction sites at different positions on the internally zwitterionic Bodipy framework that favour both nucleophilic and electrophilic substitution reactions on the Bodipy core, and have been used for their functionalization (\textit{vide infra}).

1.3. Synthetic Methodologies of Bodipys

Several methods for the synthesis of Bodipy have been developed since their accidental discovery in 1968 by Treibs and Kreuzer by reaction of 2,4-dimethylpyrrole with acetic anhydride in the presence of BF$_3$.OEt$_2$.\textsuperscript{8} The basic route of constructing the Bodipy core generally involves an acid-catalyzed condensation of two molecules of a 2-substituted pyrrole with an electrophilic carbonyl compound, \textit{e. g.} aldehyde, acid anhydride, and acyl chloride, followed by oxidation and complexation with BF$_3$.OEt$_2$. However, the oxidation step is not required when an acyl chloride is used as the electrophile. The synthyses using (i) pyrroles and
acid chlorides/ anhydrides or aldehydes, and (iii) from ketopyrroles are adequately discussed in an excellent review, and briefly described below.¹

### 1.3.1. Condensation of pyrroles with acid chlorides or anhydrides

In general, synthesis of the 8-substituted Bodipy dyes (i. e., those with substituents in the *meso* position) is relatively easy, and is accomplished via condensation of aromatic and aliphatic acyl chlorides with suitable pyrroles (Scheme 1.3.1).²e,³d,⁹a These conversions involve formation of unstable dipyrrmethene hydrochloride salt intermediates. Although, the intermediate salts are easier to handle and purify as the C-substitution increases, these are not generally isolated during the syntheses of the Bodipy dyes. In the particular case where the intermediate salt was isolated and purified by flash chromatography, the intermediate was treated with Et₃N in toluene before adding BF₃·OEt₂.⁹b

![Scheme 1.3.1](image)

**Scheme 1.3.1** Reagents and conditions: (i) (a) R⁴COCl/CH₂Cl₂/40 °C/1 h; (ii) (a) Et₃N or 'Pr₂EtN/toluene/25 °C/15 min; (b) BF₃·OEt₂/80 °C/15 min.

Besides acid chlorides, other activated carboxylic acid derivatives can also be used in this strategy. In particular, use of acid anhydrides produces a free carboxylic acid that may be used later to attach the probes to obtain various target molecules. One such approach using glutaric anhydride as the condensing agent helped in subsequent attachment of cholesterol to construct model fluorescent-labeled membranes (Scheme 1.3.2).⁹a
1.3.2. Condensation of pyrroles with aldehydes

This method, involving condensation of aromatic aldehydes with pyrroles requires an additional oxidation step to form the dipyrrromethene intermediates (Scheme 1.3.3). Generally DDQ and p-chloranil are used for the oxidation. However, the oxidizing reagents can introduce experimental complications, needing removal of the undesired byproducts. Also, use of aliphatic aldehydes has not been reported so far in this approach.

1.3.3. From ketopyrroles

The previous two synthetic strategies are extensively used to construct symmetrically substituted Bodipy dyes only. A slight modification of the method wherein a carbonyl-containing pyrrole is condensed with a C2-unsubstituted pyrrole molecule is useful in the syntheses of unsymmetrical Bodipy dyes, and has been used to prepare several Bodipy-based biological labels (Scheme 1.3.4). An active carboxylate group can be introduced at the 8-position by following a similar procedure. This route is useful for the preparation of reasonably large batches of dyestuffs, although it tends to be expensive in terms of solvent wastage. In general, these materials separate well on a chromatography column and can be purified to a high degree by
recrystallization. The main advantage of this method is its application to incorporate diverse substituents on the pyrrole rings.

\[
\begin{array}{c}
\text{Scheme 1.3.4} \text{ Reagents and conditions: (i) base/ BF}_3\text{OEt}_2.
\end{array}
\]

1.4. Derivatization of the Bodipy Framework

Usually the Bodipy dyes have certain problems, such as small Stokes’ shifts, poor solubility in aqueous media, and lack of functional groups for conjugation to biological materials.\textsuperscript{11} These restrict complete utilization of the Bodipy fluorophores for various biomedical and bioanalytical applications, and warrants efficient synthetic strategies for functionalization of the Bodipy core. To this end, the intrinsic electron-rich character of the Bodipy chromophore has been conveniently used for its derivatization at various positions to synthesize a range of new compounds covering the entire visible spectrum and beyond. In particular, the optoelectronic properties of the Bodipy molecules can be fine-tuned by functionalization of the core framework at the 8- (meso-), 2,6- and 3,5- positions, the B-center, as well as by rigidification of the Bodipy core. Some of these are demonstrated during the present investigation, as illustrated in the subsequent chapters.

1.4.1. Functionalization at the meso- or 8-position

Compared to the substitutions at the pyrrolic positions, the C-8 (meso)-functionalization is usually accomplished by direct acid-catalyzed condensation of suitable pyrroles with appropriately substituted aryl aldehydes or acyl chlorides.\textsuperscript{12} The meso-substitution does not change the spectral characteristics of the parent dye significantly due to the orthogonal geometry.
of the meso substituent and the Bodipy fluorophore, which results in poor electronic conjugation between the two moieties. Hence this strategy offers the most versatile method for introducing various “functionalities” on the Bodipy core for specific application such as selective sensors of redox active molecules,\textsuperscript{13,14} metal-chelators,\textsuperscript{15} and pH probes,\textsuperscript{16} light-harvesting arrays and biological labels\textsuperscript{17} (Figure 1.4.1).

![Chemical structures of some meso-substituted Bodipys.]

**Figure 1.4.1** Chemical structures of some meso-substituted Bodipys.

A sub-class of the Bodipy dyes commonly known as “aza-Bodipys” possesses a nitrogen atom at the meso-site in place of the carbon atom.\textsuperscript{18} These dyes exhibit intense absorption and emission profiles in the 650-850 range with high molar extinction coefficient, but moderate fluorescence quantum yields (0.23-0.36), and are insensitive to the solvent polarity. The lone pair of electrons on the meso-nitrogen reduce the HOMO-LUMO energy gap, resulting in red shifts in their absorption and emission maxima.\textsuperscript{19} Although the aza-Bodipy dyes are mostly important as photodynamic therapy (PDT) agents, several chemosensors have also been made using these compounds. For example, compound 4 show high selectivity in sensing Hg\textsuperscript{2+} ions.\textsuperscript{20} The spectra of these dyes can be easily pushed to the near-IR region by rigidifying the structure, or incorporation of electron-donating groups as shown with compound 10.
### 1.4.2. Functionalization at the 2,6-positions

The 2 and/or 6-positions of the Bodipy core are most susceptible to electrophilic attack since they bear the least positive charge. However, electrophilic substitution reactions at the designated positions of the Bodipys are limited only to sulfonation,\(^\text{21}\) halogenation,\(^\text{6}\) nitration,\(^\text{22}\) and formylation\(^\text{14}\) (Figure 1.4.2). Introduction of the sulfonate groups impart water-solubility to the hydrophobic Bodipy core without affecting the absorption and emission maxima significantly, while the introduction of electron withdrawing groups like nitro or halo groups drastically decrease the fluorescence quantum yields with respect to the parent dyes. The reduced fluorescence quantum yields of the bromo and iodo substituted Bodipy is attributed to the internal heavy-atom effect.\(^\text{6}\) Recently, the 2,6-diiodo Bodipys have been exploited to generate a myriad of diphenylethynyl-Bodipy oligomers as potential building blocks in the construction of several light-emitting conjugated polymers and functional supramolecular assemblies.\(^\text{23}\) It should be noted that this approach leaves the B-F bonds unscathed; the substitution reactions occur exclusively at the 2,6-positions, and is therefore a valuable route for selective substitution.

![Figure 1.4.2](image)

**Figure 1.4.2** Chemical structures of some 2- and/or 6-substituted Bodipys.

### 1.4.3. Functionalization at the 3,5-positions

The higher acidity of the methyl groups at the 3,5-positions of the Bodipys is utilized for functionalization by a base-catalyzed Knoevenagel-type condensations to generate a styryl group.\(^\text{2a,b,24}\)
A number of electron-donating, and recently even electron-withdrawing aromatic aldehydes have been used to introduce different styryl moieties at the 3- and/or 5-positions, in order to bring significant red-shifts in the absorption and emission spectra of the parent chromophore. This method offers a convenient route for generating highly functionalized Bodipy derivatives such as 1,3,5,7-tetrastyryl Bodipys in a single step by controlling the reaction conditions. Furthermore, the intermediate carbenium ion can be oxidized in situ to obtain the corresponding 3-formyl derivatives in respectable yields. The novel nucleophilic addition-elimination substitution reactions of the 3,5-dichloro-Bodipys with various O-, N-, S- and C-nucleophiles including heterocycles and even aza-18-crown-6 ethers have been carried out under forcing condition to obtain a variety of symmetrical and unsymmetrical Bodipys with substitution patterns that are...
difficult to realize otherwise. These synthetic strategies and the type of compounds synthesized by these are shown in Scheme 1.4.1 and Figure 1.4.3 respectively.

1.4.4. **Modification at the boron center**

Murase *et al.* reported first compound of this kind wherein the F atom was replaced with aryl groups using PhMgCl. The organometallic approach has been further developed by Ziesell’s group and used to introduce aryl, ethynylaryl, ethynyl and alkoxide subunits in place of the F atoms to generate a new family of highly luminescent, redox-active and photostable dyes called C-Bodipys, E-Bodipys and O-Bodipys, respectively (Scheme 1.4.2).

Scheme 1.4.2 Different methods for the substitution at the boron centre.

This strategy widens the area of Bodipy compounds as the limitations such as small Stokes’ shifts and fluorescence quenching can be overcome. Interestingly, unlike the BF₂-Bodipy dyes, where the substituent alteration can be used for tuning the absorption and fluorescence spectral profiles over a wide range, the substituents in the E-Bodipy dyes do not affect the photophysical
properties. The asymmetric derivative 15 (Figure 1.4.4) is an attractive dye, as it collects photons across most of the accessible spectral range. Several groups are currently exploring such Bodipy-based scaffolds to construct molecular dyads, photovoltaics, electroluminescent devices, energy transfer cassettes and supramolecular assemblies. 28e,29

![Chemical structures of some B-substituted Bodipys](image)

**Figure 1.4.4** Chemical structures of some B-substituted Bodipys.

1.5. **Variation of Properties by Structural Modifications**

1.5.1. **Spectral properties**

The photophysical characteristics of the synthetically modified Bodipys vary with respect to the number, nature, as well as the position of the attached substituents. 30 Additionally, the emission behaviour of the Bodipy fluorophore is greatly influenced by the steric interactions between their components and intramolecular rotations of their chromophoric units. 31 The changes in the absorption/emission characteristics of the Bodipy dyes vis-à-vis the substituent pattern is presented below.

**Meso-substitution**: Apart from the effect on quantum yield, substitution at the meso-site does not significantly change the absorption and emission wavelengths of the Bodipy core. In certain molecules, the reduction in the quantum yields results due to free rotation of the meso-substituents. For example, compared to compound 16, its 1,7-H-analogue, 17 shows a much
reduced quantum yield. In compound 16, the 1,7-substituents inhibit free rotation of the meso-phenyl group, and thus, prevents the non-radiative energy loss from the excited state (Figure 1.5.1).

![Figure 1.5.1 The effect meso- and B-substitutions on the emission of some Bodipy dyes.]

**F-substitution:** Substitution of F atoms with alkyl groups reduces the fluorescence quantum yield of the parent dye significantly, and the effect is more drastic with larger and bulkyl alkyl groups (Figure 1.5.1). On the other hand, substitution with an aryl or an ethynylaryl group augments fluorescence quantum yield. The commercially available BF₂-containing Bodipy 21 (Figure 1.5.2) is widely used for laser applications. Replacement of one or both of its F atoms with the phenyl or ethynylpyrenyl groups as in 22-24 make them highly fluorescent in solution. Further, while the absorption and fluorescence maxima of 21 are insensitive to the solvent polarity, the same for the B-Ar Bodips 22-24 show small red shifts in more polar solvents. This suggests minimum interactions of the B-aryl groups with more polar media. But most importantly, due to the presence of the UV-absorbing aryl substituents, these compounds can be regarded as energy transfer cassettes, especially when the B-Ar groups have good extinction coefficients. The Bodipy system 24 absorbs in the range 230-317 nm corresponding to the \( \pi \to \pi^* \) transition of the pyrene units, and emits exclusively from the Bodipy part, ascertaining total

**Figure 1.5.1** The effect meso- and B-substitutions on the emission of some Bodipy dyes.

16: \( R = \text{Me} (\phi = 0.65) \)
17: \( R = \text{H} (\phi = 0.19) \)
18: \( R = \text{Me} (\phi = 0.65) \)
19: \( R = n-\text{Bu} (\phi = 0.06) \)
20 (\( \phi = 0.014 \))
energy transfer. The cascade effect of these systems is very attractive for designing advanced optical materials because of the large virtual Stokes shifts (can also exceed 13000 cm$^{-1}$) of these dyes.

![Figure 1.5.2 Spectral changes in the F-containing and F-replaced Bodipys.](image)

**3,5-substitution:** There are opportunities to shift the emission wavelength of the Bodipy-based fluorophore towards lower energy using different synthetic methods. A relatively facile method involves extending the degree of π conjugation running through the central core. Thus, introduction of electron donating substituents at the 3,5-positions of BF$_2$-Bodipy can push the emission wavelengths to the red region by increasing the π-electron conjugation. Thus, compared to 25, the emission of the 3,5-diaryl substituted Bodipys 26-28 (Figure 1.5.3) are shifted to longer wavelengths (545-626 nm), with a gradual drop in their fluorescence quantum yields from 49% to 20%. However, in accord with the exponential energy-gap law, this is associated with a decrease in the fluorescence quantum yield. The distyrylboradiazaindacenes 30, synthesized from the corresponding 3,5-dimethyl derivative showed pronounced charge-transfer character, with much reduced fluorescence quantum yields in polar solvents. Water-soluble dyes were subsequently obtained by functionalization with oligo(ethyleneglycol) residues, which can be used for biological applications.
Modified Bodipy dyes showing different spectral properties.

Spectral changes of the Bodipy due to substitutions at different positions.

2,6-substitution. Using the facile electrophilic reaction at their 2,6-positions, heavy atoms, such as iodine are often attached to the Bodipy framework. Such a substitution favors intersystem crossing to increase triplet states yields, which are otherwise very poor in the Bodipy dyes. Although this reduced the fluorescence efficiency, the iodinated dyes such as 31 (Figure 1.5.4) are capable of generating significant amount of $^1O_2$ under aerobic conditions. This property is used in developing photodynamic agents for the treatment of cancers. Introduction of other
electron withdrawing groups such as NO$_2$ and SO$_3$H at 2,6-position(s) also decreases the fluorescence quantum yields of the Bodipys.$^{3a,3d}$

1.5.2. Redox Properties

The level of substitution of Bodipy core decides their redox chemistry.$^{34}$ Cyclic voltammograms (CVs) of derivatives lacking functionalities at the 2-, 6-, and meso-positions display irreversible oxidation and reduction, because of the high reactivity of the electrogenerated radical ions. The process of oxidative polymerization is a specific side reaction that leads to the irreversible redox behaviour. The redox process becomes more reversible with the addition of substituents, very often leading to the observation of clean looking cyclic voltammograms. In general, the removal of an electron from the Bodipy core to create the radical cation, i.e. oxidation of Bodipy takes place around 1.0 V vs saturated Calomel electrode (SCE). The reduction segments in the CV take place around -1.4 V vs SCE, corresponding to the radical anion generation. This difference $\Delta E$ of ~2.4 eV between the first oxidation and reduction waves is remarkably similar for most of the simple Bodipy derivatives. The well behaved electrochemical behavior of the Bodipy compounds has been exploited by Bard et al. to demonstrate electrochemically-generated chemiluminescence.$^{35}$ In general, the instability behavior of the oxidized Bodipys resembles that of pyrroles and thiophenes, but greater steric protection in these compounds prevents their fast dimerization and polymerization.$^{36}$

The electrochemical behavior can qualitatively and quantitatively explain phenomena like fluorescence quenching by photo-induced electron transfer (PET), aggregation-induced emission (AIE), and metal ion sensing behaviors of the Bodipys, attached to ligands, such as crown ethers. Of late, the azabodipys have aroused specific interest for biological applications.
for their efficient far-red and near-IR fluorescence. Like the cyanine framework, the nitrogen lone pair of electrons at the 8-position reduce the HOMO–LUMO energy gap.

1.6. Various applications of BODIPY dyes

1.6.1. Laser dyes

The Bodipys dyes are very useful for laser applications since they have low ISC rates and low triplet excitation coefficients over the entire laser spectral region,\(^ {3a,b,e,37}\) and often possess a triplet-triplet absorption coefficient about one-fifth that of the rhodamine dyes.\(^ {38}\) Some of the Bodipys dyes outperform the widely used laser dye, rhodamine 6G (Rh6G), considered as the benchmark in lasing efficiency and photochemical stability. Boyer and Pavlopoulos are the pioneers in exploring the lasing properties of the Bodipys dyes.\(^ {3}\) Various Bodipys dyes have been synthesized by changing the substituents in 2, 6 and 8-positions (Figure 1.6.1). Among these, the dyes 21 (PM567) and 32 (PM597) are commercially available, and extensively used for tunable dye laser applications. The reported\(^ {3d}\) efficiencies of some the dyes compared to the dye 34 are shown in Table 1.6.1. The popularity of the dye 32 is primarily due to its uncharacteristically high Stokes’ shift (30-38 nm) that drastically reduces self absorption to enhance the lasing efficiencies.\(^ {39}\)

Despite several advantages, there are two major limitations of the Bodipy dyes \(\text{viz.}\) small Stokes’ shifts and photochemical instability that need to be overcome for their wider application as laser dyes. The former reduces the lasing efficiency of the dyes due to the ground state absorption (GSA). The problem has been partially resolved by incorporating simple or bicyclic rigid aryl substituents at the C-3 center or the boron atom of the Bodipy moiety.\(^ {28b,9b,40}\) However, the photochemical degradation continues to be a hurdle in the long-term operation of the Bodipy-based liquid dye lasers, especially for high power and high-repetition rate operation.\(^ {41}\)
Figure 1.6.1 Various analogues of Bodipy dyes.

Table 1.6.1: Photophysical properties of the Bodipy Dyes\[^a\]

<table>
<thead>
<tr>
<th>No</th>
<th>(\lambda_{\text{max}}) (nm)</th>
<th>Log (\varepsilon)</th>
<th>(\lambda_{\text{fl}}) (nm)</th>
<th>(\Phi)</th>
<th>(\lambda_{\text{las}}) (nm)</th>
<th>RE (%)[^b]</th>
</tr>
</thead>
<tbody>
<tr>
<td>33</td>
<td>505</td>
<td>4.92</td>
<td>516</td>
<td>0.80</td>
<td>533</td>
<td>30</td>
</tr>
<tr>
<td>34</td>
<td>493</td>
<td>4.90</td>
<td>519</td>
<td>0.99</td>
<td>542</td>
<td>100</td>
</tr>
<tr>
<td>35</td>
<td>495</td>
<td>4.99</td>
<td>517</td>
<td>1.00</td>
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<td>90</td>
</tr>
<tr>
<td>36</td>
<td>518</td>
<td>4.67</td>
<td>543</td>
<td>0.70[^c]</td>
<td>570</td>
<td>75</td>
</tr>
<tr>
<td>21</td>
<td>517</td>
<td>4.81</td>
<td>546</td>
<td>0.83[^c]</td>
<td>570</td>
<td>100</td>
</tr>
<tr>
<td>37</td>
<td>493[^d]</td>
<td>4.97[^d]</td>
<td>531</td>
<td>0.38[^c]</td>
<td>556</td>
<td>50</td>
</tr>
<tr>
<td>38</td>
<td>493</td>
<td>4.62</td>
<td>533</td>
<td>[^g]</td>
<td>[^g]</td>
<td>[^g]</td>
</tr>
<tr>
<td>39</td>
<td>516[^e]</td>
<td>4.81</td>
<td>546[^e]</td>
<td>0.45[^f]</td>
<td>[^g]</td>
<td>[^g]</td>
</tr>
</tbody>
</table>

\[^a\] MeOH was used as the solvent unless mentioned otherwise. \[^b\] Relative Efficiency (RE) in laser power output, compared to that of 34 assigned as 100.\[^c\] In EtOH. \[^d\] \(\lambda_{\text{max}} = 495\) nm (log \(\varepsilon\) 5.26).\[^e\] In 10% CH\(_2\)Cl\(_2\) in MeOH. \[^f\] In CH\(_2\)Cl\(_2\). \[^g\] Unreproducible data due to photoinstability.

The photo-degradation of the Bodipys is believed to be due to their reaction at the C-8 olefin moiety with singlet oxygen \(^1\text{O}_2\), generated from their triplet states during photoexcitation (Scheme 1.6.1).\[^43\] Prevention of the dye decomposition with a triplet quencher like benzoquinone as well as trace amounts (1 wt% doping level) of \(^1\text{O}_2\) quenchers, such as 1,4-diazobicyclo[2.2.2]octane (DABCO), bis(3,3,5,5-tetramethylpiperidin-4-yl)decanedioate (Tin770), and N-tert-butyl-\(\alpha\)-phenylnitrone (TBP) supported the proposed mechanism.
Especially the highest efficacy of the $^1\text{O}_2$-quencher, DABCO, amongst the additives strongly suggested $^1\text{O}_2$ as the major causative agent for the dye decomposition. The modest effect of changing solvents (EtOH vs MeCN) can be attributed to the longer lifetime (30 µs) of $^1\text{O}_2$ in MeCN as opposed to that (10 µs) in EtOH. Some solid-state dye laser materials containing dispersed Bodipy dyes, developed with the primary aim of improving the laser energy output also showed better photostability compared to the liquid dye lasers. Possibly, polymerization of the suitable monomer containing the dispersed dyes provides the polymeric solid matrix free of oxygen to increase the photochemical half-lives of dyes.

$$\text{Dye (S}_0) + \text{hv} \rightarrow ^1\text{Dye (S}_1) \rightarrow ^3\text{Dye (T}_1)$$

$$^3\text{Dye (T}_1) + ^3\text{O}_2 \rightarrow \text{Dye (S}_0) + ^1\text{O}_2 (^1\Delta_g)$$

$$\text{O}_2 (\Delta_g) + Q \leftrightarrow \text{O}_2 (\Delta_g) - Q \rightarrow \text{Products}$$

$$[\text{O}_2 (3\text{E}_g) - Q] \rightarrow \text{O}_2 (3\text{E}_g) + Q]$$

1,2 addition of $^1\text{O}_2$

Scheme 1.6.1 Mechanism of photochemical decomposition of the Bodipy dyes.
1.6.2. *Energy cassette*

Optimum usage of the organic dyes, including the Bodipy molecules in flow cytometry and fluorescence microscopy is impeded due to their small Stokes’ shift. Covalent attachment of an ancillary light absorber to the Bodipy core to form a cassette provides an opportunity to overcome this problem. The aim is to channel all the photons absorbed by the secondary chromophore, usually an aromatic polycycle, to the Bodipy emitter. Thus, there is a large inequality in excitation and emission wavelengths, and the full benefits of the Bodipy emitter are retained. An important feature of these systems is that the two chromophores remain electronically isolated because of the orthogonal arrangement around the attaching sites. The structure of the dual-dye system is the determining factor for the rate of energy transfer, which decreases with increasing center-to-center separation, in line with a dipole–dipole transfer mechanism. The overall energy-transfer efficiency exceeds 90%, even in the most extended system. A number of BF₂-Bodips 40-43, bonded with secondary polycycle chromophore e. g., anthracene or pyrene as ancillary light absorbers has been developed (Figure 1.6.2). In another type of dual chromophore dyes such as compounds 14 and 15, or the aromatic polycycles (pyrene, perylene), or a mixture of both are attached to the B-atom. Although the absorption spectral profiles contain important contributions from each of the subunits, fluorescence occurs exclusively from the Bodipy fragment.
Figure 1.6.2 Examples of BF₂-Bodipys attached to some ancillary light absorbers.

1.6.3. Biological applications

Due to their excellent physicochemical properties and low dark toxicities,⁴⁶ the Bodipy dyes are among the most promising candidates as fluorescent labels and probes. Also, these dyes do not significantly influence the biological functions, on account of their small molecular size. Numerous Bodipy-based fluorescent labels are widely used to target important biological markers such as DNAs, RNAs, amino acids, lipids, dextran, and proteins.⁴⁷⁴⁸ In general, for effective bio-conjugation, the Bodipy-based probes are functionalized with reactive ligand/anchor groups (such as carboxylic acids, sulphonic acids, polyethylene glycol, polysaccharides and oligonucleotides) at the terminus.⁴⁹

More recently, some Bodipy derivatives have been evaluated as a totally new class of potent PDT agents, an application more commonly associated with porphyrins and phthalocyanines.⁶⁵⁰ To prove the possibility of spin–orbit perturbation, O’Shea and co-workers designed three aza-Bodipys according to the following modules relying on: i) the inherent spin–orbit coupling of the aza-Bodipy without heavy atoms; ii) intramolecular external heavy-atom effect⁵¹ in which bromine atoms are positioned on the aryl rings and not on the aza-Bodipy core,
giving rise to moderate $^1\text{O}_2$ generation; and iii) internal heavy atom effect$^{52}$ in the bromo-substituted aza-Bodipys, yielding the $^1\text{O}_2$ efficiently (Figure 1.6.3a). Introduction of functionalized styryl and distyryl groups with water-soluble moieties, such as PEG-ylated structures enhanced biocompatibility, hydrophilicity and cellular uptake. Based on these concepts, a few aza-Bodipy 44-46 and styryl/distyryl Bodipys 47-49 photosensitizers (PSs) (Figure 1.6.3b) have been developed, and some of the water-soluble and symmetrical distyryl Bodipys showed the in vitro localization and photocytotoxicity.$^{49,53}$ However, the hydrophobic nature of Bodipy core restricts their application in biological labelling. On the other hand, a high water-solubility, required for the biological applications often leads to the aggregation and self-quenching of these dyes. These warrant design of the Bodipys with proper balance in their hydrophobicity and hydrophilicity for their use as biolabel and as PDT agents.

**Figure 1.6.3** Some Bodipy photosensitizers (a) aza-Bodipys; (b) distyryl-Bodipys.

### 1.6.4. Use in microelectronics

The redox property of the Bodipys coupled with the unique combination of their facile synthesis, high absorption coefficient, and high photoluminescence efficiency make them attractive molecules for application in optoelectronics. The reversible (amphoteric) redox behavior of the Bodipy molecules makes them suitable as electron donors as well as acceptors. In
particular, due to the presence of a tetrahedral boron atom in the structure, the Bodipys can provide the platform for developing isotropic active materials for (opto)electronic devices and solar cells. Indeed, the Bodipy derivatives have been recently employed as p-type donor materials in conjunction with methanofullerene ~phenyl C61-butyric acid methyl ester (PCBM) as acceptors in bulk heterojunction (BHJ) solar cells. The introduction of one or two styryl units in the Bodipy structure permits modulation of the HOMO-LUMO gap, while the solubility and film-forming properties of the molecules are brought by the oligoxyethylene chains.

Thayumanavan et al. used the Sonogashira polymerization technique to synthesize novel \( \pi \)-conjugated copolymers incorporating Bodipy core as the “donor” and quinoxaline (Qx), 2,1,3-benzothiadiazole (BzT), \( N,N' \)-di(2’-ethyl)hexyl-3,4,7,8-naphthalenetetracarboxylic diimide (NDI), and \( N,N' \)-di(2’-ethyl)hexyl-3,4,9,10-perylene tetracarboxylic diimide (PDI) as the acceptors (Figure 1.6.4). The charge transport measurements of the polymers indicated that the Qx, and BzT-conjugated Bodipy polymers act as p-type semiconductors, while the PDI and NDI-conjugated Bodipy polymers function as n-type semiconductors, and the switch between p-type and n-type can be accomplished by a choice of suitable comonomers.

\[
\begin{align*}
\text{Bodipy-alt-Qx 52} & \quad \text{Bodipy-alt-NDI 53}
\end{align*}
\]

\[50 \quad R^1 = H, R^2 = CH=CC_6H_4-O(CH_2O)_{2}Me \]
\[51 \quad R^1 = R^2 = CH=CC_6H_4-O(CH_2O)_{2}Me \]

**Figure 1.6.4** Chemical structures of some Bodipy-based BHJ solar cells.

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1.7. **Conclusion and Rationale of the Present Work**

From the foregoing, the adaptability of the Bodipy molecules for various synthetic transformations in developing a diverse array of novel functional molecules is evident. It is now possible to produce derivatives having attachments placed at the *meso*, pyrrole, or boron sites of the Bodipy moiety, each providing distinct advantages for this purpose. The *meso*-site favors orthogonal geometries for the attached aromatic residues, which can minimize electronic coupling. Substitutions at the pyrrole sites allow coplanar geometries that maximize electronic communication between the subunits, while that at the boron center provides free rotation without any electronic coupling. Thus, the same appendage can exert different properties according to the site of its attachment.

Against the above backdrop, the objectives of the present work can be broadly classified as the following

(i) formulation of some Bodipy dyes with improved photo-stability, evaluation of their lasing performance as well as photo-stability under lasing conditions, and mechanistic rationalization of the results by theoretical calculations and triplet state studies;

(ii) development of red Bodipy dyes, preferably with good water solubility for their biological and other applications;

(iii) development of new Bodipy chemistry for regioselective functionalization, especially at the *meso*-position; and

(iv) exploration of their redox property for molecular electronics applications.

The results of these studies are discussed in Chapters-2-5, while the bibliography is listed in Chapter-6. Initially the work was focused on improving the photostability of the Bodipy dyes without compromising their lasing abilities. To this end, several new efficient Bodipy laser dyes
were rationally designed, synthesized, and their lasing property as well as photostability assessed. These, together with mechanistic rationalization of the results constitute the Chapter 2.

In the next part (Chapter-3), the study was extended towards development of new Bodipy chemistry for regioselective Knoevenagel condensation with aromatic aldehydes for introducing stryryl-moieties at the pyrrole rings and/or meso-position. The Knoevenagel condensation, carried out at the pyrrole rings was used for extending the π-conjugation of the Bodipy core for an easy access to some red Bodipy dyes. Most interestingly, a novel concept of steric strain release (SSR) was invoked to override the relative acidity factor of the C-3, C-7, and meso-methyl protons to direct the Knoevenagel condensation exclusively at the meso-methyl group. Further, fine tuning of the meso-functionalization protocol was achieved by increasing the electrophilicity of the aromatic aldehydes. The SSR hypothesis and the reaction mechanism were unequivocally proved by single crystal X-ray analyses of the parent and product Bodipys as well as the intermediate of the reaction.

Extending the studies towards biological applications some Bodipy-O-glycosides were developed by attaching glucose moiety to the Bodipy molecules. All the compounds showed in vitro toxicity to the human lung cancer A549 cells and the toxicity of few compounds could be attributed to their ability to cross cell surface and accumulate in the cytoplasm (Chapter-4). Finally, the study was extended towards development of new Bodipy based organic material for nanoelectronics (Chapter-5). The required novel materials were constructed by synthesizing a (σ–π) system comprising of an alkyl spacer (σ-moiety) and a suitable Bodipy molecule (π-moiety) followed by its grafting on Si wafers. Measurement of the charge transport properties of these materials showed current rectification behavior. The rectification characteristic was modulated to negative differential resistance (NDR) behavior by forming a supra-molecular
assembly of another Bodipy molecule. The bilayer formation allowed the supra-molecular assembly to undergo bias induced conformational changes, to exhibit the NDR behavior.