

**TC.
GEBZE TECHNICAL UNIVERSITY
GRADUATE SCHOOL OF NATURAL AND APPLIED SCIENCES**

**SYNTHESIS OF BARBITURIC ACID-FUNCTIONALIZED
BODIPY DERIVATIVES AND INVESTIGATIONS OF THEIR
SELF-ASSEMBLY STRUCTURES**

BÜŞRA AKYOL

**A THESIS SUBMITTED FOR THE DEGREE OF
MASTER OF SCIENCE
DEPARTMENT OF CHEMISTRY**

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GEBZE

2022

T.C.
GEBZE TEKNİK ÜNİVERSİTESİ
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BARBİTÜRİK ASİT İLE
FONKSİYONLAŞTIRILMIŞ BODİPY
TÜREVLERİ SENTEZİ VE
KENDİLİĞİNDEN DÜZENLENMİŞ
YAPILARIN İNCELENMESİ

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SUMMARY

4,4-Difluoro-4-bora-3a,4a-diaza-s-indacene (BODIPY) dyes are immensely colored compounds which have been attracting attention owing to their important photophysical and optoelectronic properties, such as large absorption coefficient, small Stokes shift, high fluorescence quantum yield, high chemical stability. Another miraculous property is easy functionalization. BODIPYs have eight different positions to functionalize with different reactions like Knoevenagel, Sonogashira, Suzuki, Vilsmeier and cross-coupling. Through functionalization, it makes possible physicochemical and spectral properties adaptation. Thanks to their remarkable properties, they can be applied in different areas such as solar cell, sensing, medical treatment, photothermal and photodynamic therapies.

Self-assembly is important to construct supramolecular structures. Especially, hydrogen bonding is a well-known non-covalent interaction to design self-assembled structures. According to literature, barbituric acid and its derivatives demonstrating hydrogen bonding ability are beneficial to construct this type of architecture.

In this thesis, a BODIPY derivative was functionalized with barbituric acid which has multiple hydrogen bonding ability that are directional to have highly ordered hydrogen bonded mediated self-assembled structures to control over BODIPY's photophysical properties. Synthesis of barbituric acid functionalized BODIPY derivatives via Vilsmeier and Knoevenagel reactions were achieved and characterized with FT-IR, ^1H -NMR, ^{13}C -NMR spectroscopy and mass spectrometry. Hydrogen bonding mediated self-assembled structures were investigated through UV-Vis and fluorescence spectrophotometer, ^1H -NMR spectroscopy and dynamic light scattering method (DLS).

Key Words: BODIPY, Supramolecular, Self-assembly, Hydrogen bonding, Barbituric acid.

ÖZET

4,4-difluoro-4-bora-3a,4a-diaza-s-indasen (BODIPY) boya türleri, geniş absorpsiyon katsayısı, küçük Stoke kayması, yüksek floresans kuantum verimi, yüksek kimyasal stabilite gibi önemli fotofiziksel ve optoelektronik özelliklere sahip olmalarından dolayı dikkatleri üzerine çekmiştir. Mucizevi özelliklerinden biri de kolayca fonksiyonlandırılmasıdır. BODIPY, Knoevenegal, Sonagashira, Suzuki, çapraz bağlama gibi reaksiyonlar ile fonksiyonlandırılabilen sekiz farklı pozisyona sahiptir. Dikkat çeken bu özellikleri sayesinde güneş hücresi, sensör, tıbbi tedavi, fototermal ve fotodinamik terapi gibi alanlarda uygulanabilirler.

Kendiliğinden bir araya gelme supramoleküler yapılar inşaa etmekte önemlidir. Özellikle hidrojen bağı kendiliğinden biraraya gelen yapıları oluşturmak için en çok bilinen non-kovalent etkileşimdir. Literatürde hidrojen bağ yapma özelliği gösteren barbitürik asit ve türevlerinden bu tarz yapılar yapmada faydalandığı görülmektedir.

Bu tezde, BODIPY yapısı, fotofiziksel özelliklerinin kontrol altında tutulması amacı ile birden çok hidrojen bağı yapabilen barbitürik asit ile fonksiyonlandırılmış, hidrojen bağı ile kendiliğinden bir araya gelerek oluşabilecek düzenli supramoleküler yapılar literatürde yer alan çeşitli yöntemlerle elde edilerek incelenmiştir. Vielsmeier ve Knoevenegal reaksiyonları aracılığıyla barbitürik asit ile fonksiyonlandırılmış BODIPY türevleri sentezlenmiş, karakterizasyonları FT-IR, ¹H-NMR, ¹³C-NMR, kütle spektroskopisi ile gerçekleştirilmiştir. Non-kovalent hidrojen bağları sonucu kendiliğinden düzenlenme ile oluşturdukları supramoleküler yapılar UV-Vis, floresans spektrofotometre, ¹H-NMR spektroskopisi ve dinamik ışık saçılımı metodu (DLS) ile incelenmiştir.

Anahtar Kelimeler: BODIPY, Supramoleküler, Kendiliğinden bir araya gelme, Hidrojen bağı, Barbitürik asit.

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LIST OF ABBREVIATIONS AND ACRONYMS

<u>Abbreviations and Acronyms</u>	<u>Explanations</u>
°	: Degree
Φ_F	: Fluorescence Quantum Yield
$^1O_2$	: Singlet oxygen
AFM	: Atomic force microscopy
BODIPY	: Boron dipyrin, 4,4-difluoro-4-bora-3a,4a-diaza-s-indacene
$BF_3 \cdot Et_2O$	: Boron trifluoride diethyl etherate
$CHCl_3$	: Chloroform
$CDCl_3$	: Deuterated chloroform
DBU	: 1,8-diazabicyclo[5.4.0]undec-7-ene
DCE	: 1,2-dichloroethane
DCM	: Dichloromethane
DDQ	: 2,3-Dichloro-5,6-dicyano-1,4-benzoquinone
DLS	: Dynamic Light Scattering Method
DMF	: Dimethylformamide
DNA	: Deoxyribonucleic acid
Et_3N	: Triethylamine
EtOAc	: Ethyl acetate
FT-IR	: Fourier Transform Infrared Spectroscopy
H_2S	: Hydrogen sulfide
HOMO	: Highest Occupied Molecular Orbital
K_2CO_3	: Potassium carbonate
LUMO	: Lowest Unoccupied Molecular Orbital
MALDI-TOF-MS	: Matrix-Assisted Laser Desorption/Ionization Time-of-Flight Mass Spectrometry
MCH	: Methylcyclohexane
MeOH	: Methanol
$NaHCO_3$	: Sodium bicarbonate
Na_2SO_4	: Sodium sulfate
NIR	: Near-infrared

NMR	: Nuclear Magnetic Resonance
NPs	: Nanoparticles
PDT	: Photodynamic therapy
POCl ₃	: Phosphoryl chloride
RT	: Room temperature
STM	: Scanning tunneling microscopy
TCE	: 1,1,2,2-Tetrachloroethane
TFA	: Trifluoroacetic acid
THF- <i>d</i> ₈	: Deuterated tetrahydrofuran
THF	: Tetrahydrofuran
TLC	: Thin Layer Chromatography
UIPAC	: International Union of Pure and Applied Chemistry
UV-NIR	: Ultra-Violet Near Infrared
UV-Vis	: Ultraviolet–visible spectroscopy

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1. INTRODUCTION

BODIPYs and their derivatives are types of photosensitive organic dyes firstly reported by Treibs and Kreuzer [1]. BODIPY is composed of boron and dipyrromethene. According to IUPAC nomenclature of BODIPY is 4,4-difluoro-4-bora-3a,4a-diaza-s-indacene includes eight different positions which are; meso, two α positions, four β positions and two boron positions to functionalize [2]. BODIPY and its derivatives have important properties such as small Stokes shift, strong absorption, narrow absorption and emission, pH insensitive, stable chemical structure, high fluorescence quantum efficiency, low photobleaching and polarity, so researchers benefit from them because it is applicable in several areas such as light-harvesting system, medical treatment, solar cell, liquid crystals, sensing and photodynamic therapy [3]. One of the application areas of BODIPY structures is supramolecular chemistry providing magnificent structures.

Supramolecular chemistry is explained by Jean-Marie Lehn as ‘chemistry beyond the molecule’ can be explained as chemistry relies on noncovalent interactions between small molecules to self-assemble resulting in molecular assemblies. Self-assembly means two or more molecules or ions are coming together spontaneously to build larger aggregate species with reversible supramolecular interactions. The concept of self-assembly has been taken attention over the last decades to obtain different substances having various functions. Hydrogen bonding can be admitted as the most important non-covalent interaction for designing supramolecular structures owing to strength and high directionality degree [4]. There are many various types of molecular patterns that have been defined to assemble into supramolecular constructions with hydrogen bonds like cyanuric acid/barbituric acid and melamine. Melamine and cyanuric acid\barbituric acid derivatives are eager to make 6-membered self-assembly rosettes and also, they can make self-assembled structures as lamellar packing and helical twisting [5].

Despite the fact that barbituric acid has a reputation in medicinal chemistry, studies of its properties in organometallic, coordination and supramolecular chemistries are relatively new [6]. Accompanied with their metal binding abilities, they also have their own multiple sides to make non-covalent bonds to constitute supramolecular structures.

BODIPY self- assembled structures have also received great attention owing to the impressive properties which are discussed in following chapters.

The aim of this thesis is to synthesize barbituric acid functionalized BODIPYs and investigate their expected self-assembled structures.



2. BODIPY

2.1. History and Structure of BODIPY

Treibs and Kreuzer wanted to synthesize acylated pyrroles in 1968. When they tried to achieve this, they realized that 2,4-dimethylpyrrole was acylated with a member of Lewis acid, boron trifluoride and acetic anhydride (Figure 2.1) formed fluorescent compounds which were worthy of attention [1]. These products were composed of 4,4-difluoro-4-bora-3a,4a-diaza-s-indacene (generally abbreviated as BODIPY) skeleton is an organic luminophore having donor/acceptor frameworks [7], [8].

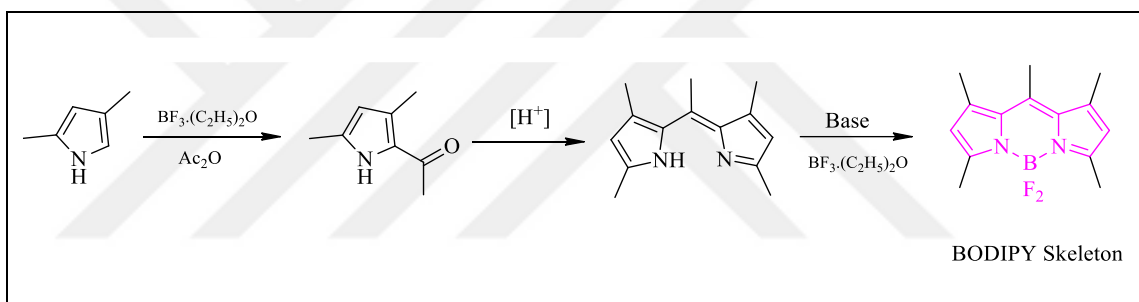


Figure 2.1: First synthesis of BODIPY in the literature by Treibs and Kreuzer.

BODIPY is composed of disubstituted boron and dipyrromethene. Generally, boron was disubstituted with two fluorine atoms. Owing to the BF_2 part, there is an N-B-N-bridge that causes a π -electrons planetary system in which resonance structures can be obtained by delocalization of a positive charge among nitrogen atoms in Figure 2.2.

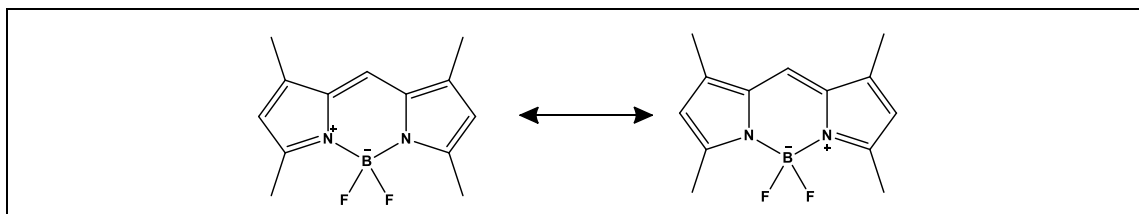


Figure 2.2: Resonance structures of BODIPY.

According to crystal structure of BODIPY main core, boron atom, instead of being coplanar with dipyrrole part, 4.3° angle departs from main plane (Figure 2.3). Moreover, there was a quietly difference between B-F bond distance leads to slight bending [9].

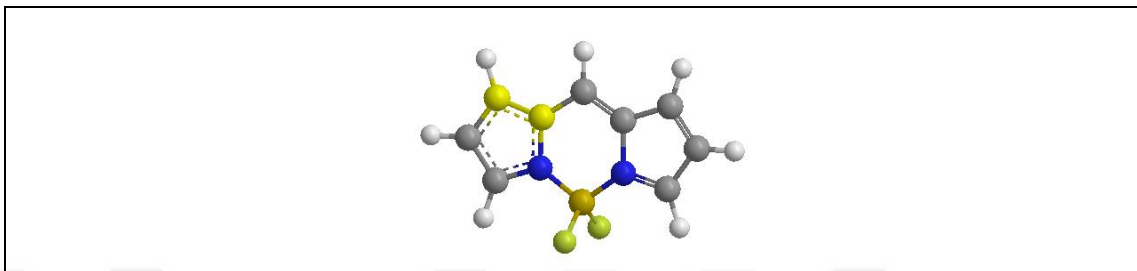


Figure 2.3: BODIPY structure.

2.2. Nomenclature of BODIPY

In accordance with IUPAC chemical nomenclature system, BODIPY compound has eight different reactive positions that can be functionalized easily. Besides, the conventional numbering system is used as meso (8-), two α positions (3- and 5-), four β positions (1-, 2-, 7- and 6-) and two boron positions (4', 4'') (Figure 2.4).

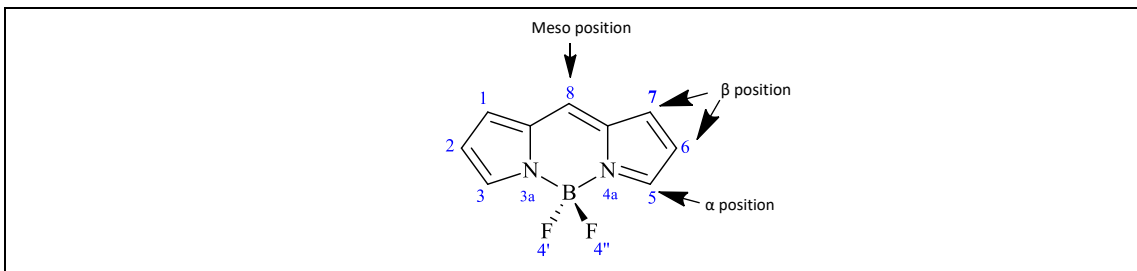


Figure 2.4: Nomenclature of BODIPY.

2.3. Synthesis of BODIPY

Basic synthesis method for BODIPY derivatives could be accepted as a condensation reaction with pyrrole and electrophilic carbonyl structures treated with boron trifluoride diethyl etherate in company with a tertiary amine like 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) and triethylamine. Oxidation of dipyrromethanes is achieved with p-chloranil or 2,3-dichloro-5,6-dicyno-1,4-benzoquinone (DDQ) used as

oxidant to have dipyrromethene. By using this method different kinds of BODIPY can be synthesized [10].

Before unsubstituted BODIPY core synthesized, dimethyl substituted structure (Figure 2.5) is obtained and could be used as a reference to other alkylated ones [11]. If substituted BODIPY is compared with unsubstituted one, it is more stable and easily synthesized.

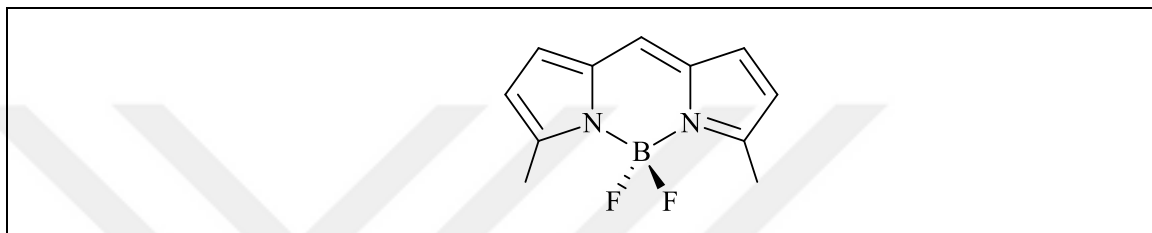


Figure 2.5: Substituted BODIPY.

Although first BODIPY was obtained in 1968, unsubstituted BODIPY (Figure 2.6 BODIPY dye **3**) core had not been reported since nucleophiles and electrophiles of BODIPY is very reactive in which carbon atoms' electron density is polarized because of nitrogens in the pyrrole rings [12], [13]. Dipyrromethene (Figure 2.6 BODIPY dye **2**) without any substituents was found as unstable in solution at above -40°C temperatures and noticed that it has been reacted with different nucleophiles [14]. Therefore, dipyrromethene was stabilized by oxidation of dipyrromethane (Figure 2.6 BODIPY dye **1**). Unsubstituted BODIPY was synthesized with 5-10 % yield as a pale red solid which is stable and shows cubic flakes crystal structure obtained from aqueous methanol [10].

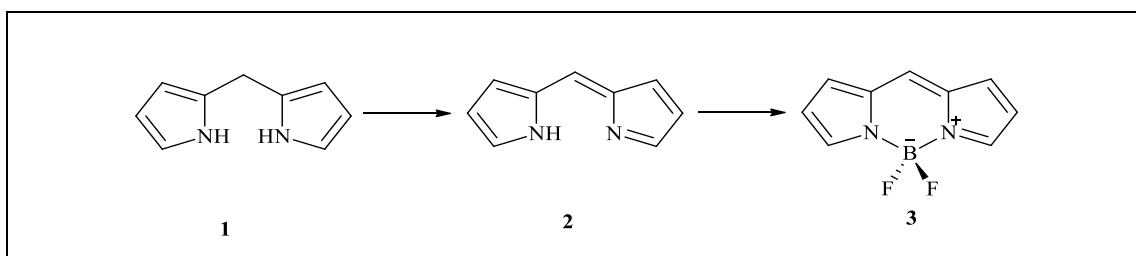


Figure 2.6: Synthesis steps of unsubstituted BODIPY core.

BODIPY skeleton enables researchers to create various fluorescent probes with post-modifications and functionalization. Applied modifications can be diversified with receptors, linkers, quenchers and organic-conjugates via several reaction types. Generally, boron and meso positions have an effect upon steric hindrance whereas other positions impact mostly electronic delocalization [15]. Possible reactions can be summarized according to Figure 2.7; for 2,6 positions experiences halogenation reactions then functionalize with Suzuki, Sonogashira, click, amidation coupling, Knoevenagel, etc. and for 1,7-positions' functionalization is limited because of low reactivity and steric hindrance [16].

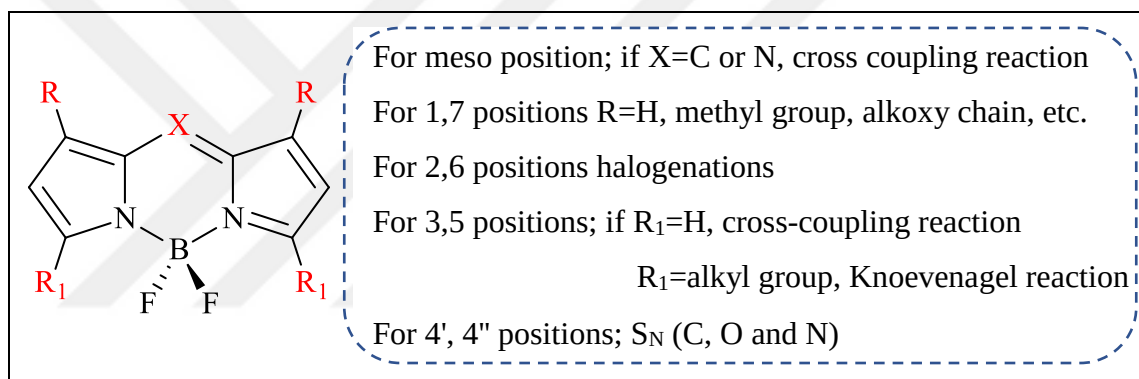


Figure 2.7: Positions of BODIPY and possible reactions.

2.3.1. Functionalized BODIPY via Meso Substituent

Dipyrrin type synthesis is a well known area from porphyrin chemistry. Most porphyrin synthesis methods can be used for BODIPY structures so it is called 'porphyrin's little sister' in the literature [17]. Most substitutions are done with phenyl or aromatic groups at 8-position for BODIPY core owing to both synthetic easiness and diverse functionality ensured by aromatic aldehydes with lack of explicit impacts on spectroscopic features because of inadequate conjugations with the core. But a BODIPY dye in Figure 2.8 (1) quantum yield is found more than 2 (Figure 2.8) since 1,7 substituents inhibit aryl groups rotations so non-radiative decay from molecular motions will be lowered [18].

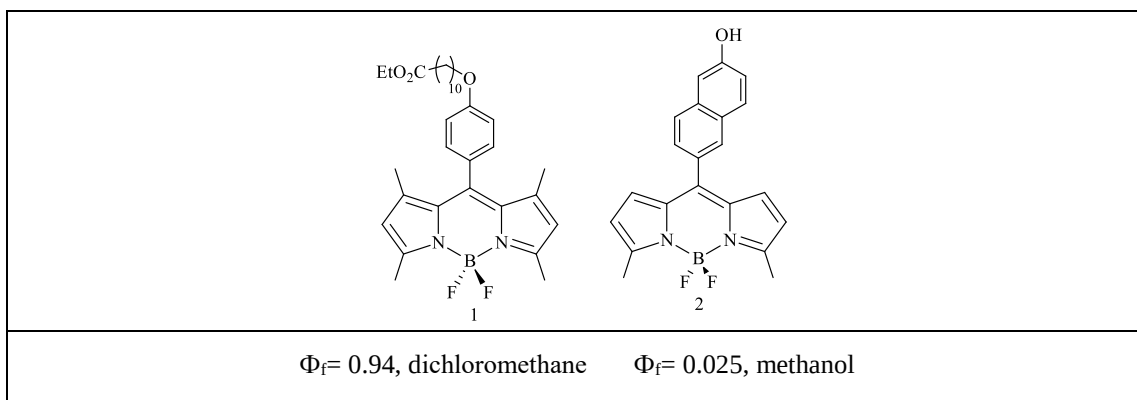


Figure 2.8: Alkyl and aryl substituted BODIPY structures.

When aliphatic aldehydes are used instead of aromatics, generally the oxidation step is not in the tendency to happen. Moreover, if aromatic aldehydes are used with substituted pyrrole, high yields are obtained in the dipyrromethane part since unsubstituted pyrroles, especially alpha positions, are eager to be polymerized.

One of the meso-substituted BODIPY derivatives can be obtained by reaction pyrroles with aldehydes. Reaction occurs condensation between aromatic aldehyde and pyrrole in the presence of acid catalyst (commonly trifluoroacetic acid). The product synthesized in this part is relatively unstable and sensitive to air, acid and light so purification is not applied. DDQ is used as an oxidant. Obtained dipyrryn reacts with boron trifluoride diethyl etherate ($\text{BF}_3 \cdot \text{Et}_2\text{O}$) in a basic environment (like triethylamine) to pull off acidic hydrogen bonded with nitrogen atoms (Figure 2.9) [19].

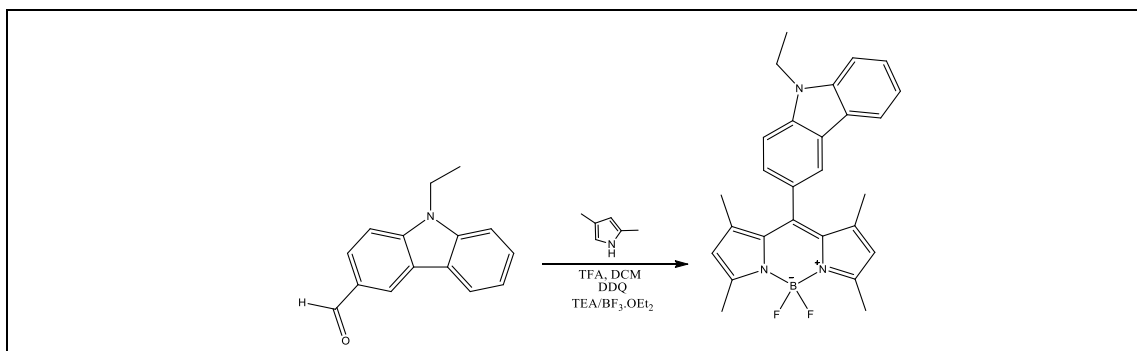


Figure 2.9: An example of substituted BODIPY synthesis.

If pyrrole is unsubstituted, reaction is applied with pyrrole as a solvent to avoid possible polymerization [20], [21].

2.3.2. Mono- and Diformyl BODIPYs Synthesis

Meso substituents and BODIPY core are relatively perpendicular as a consequence of this electronic conjugation between them is very poor. Therefore pyrrolic positions are much more desirable to functionalize.

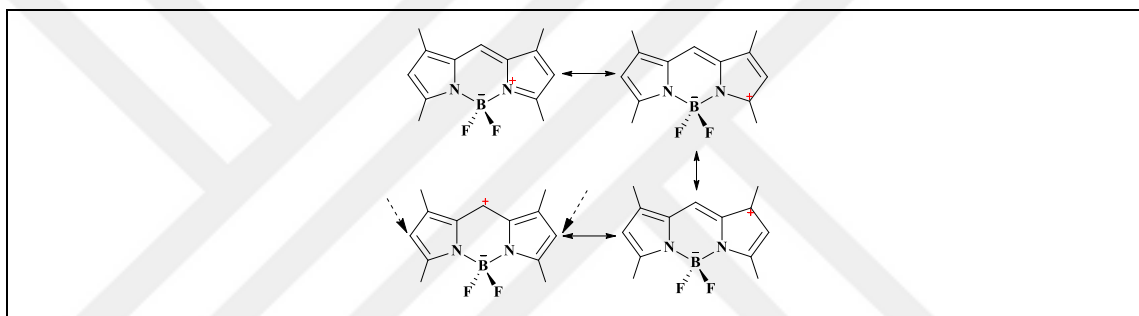


Figure 2.10: Susceptible positions on tetramethyl-BODIPY.

As shown in Figure 2.10, 2, 6-BODIPY positions are less positively charged than other positions so they are susceptible to electrophilic attack. For 2-position, high regioselectivity was recognized. Jiao et al., reported acylation of tetramethyl-BODIPY with Vilsmeier reagent (DMF+POCl₃) gives 2-formyl BODIPY with a high yield (Figure 2.11) [22] which enables further functionalization (Figure 2.12) [23]. Before this article, some electrophilic reactions are reported such as nitration, halogenation [24], sulfonation [25] and palladium-catalyzed functionalization.

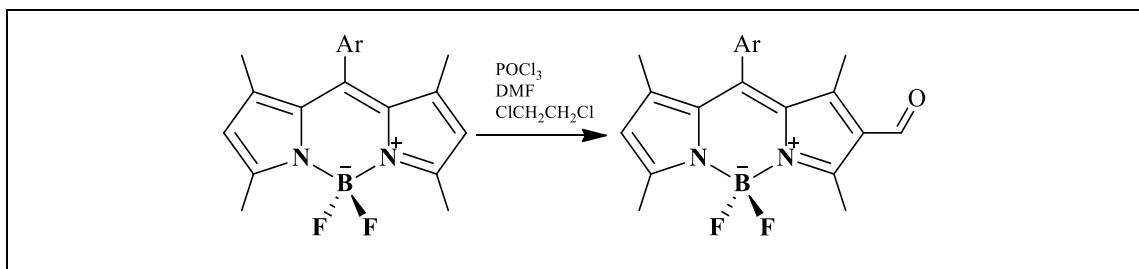


Figure 2.11: β -formyl-BODIPY via Vilsmeier-Haack reaction.

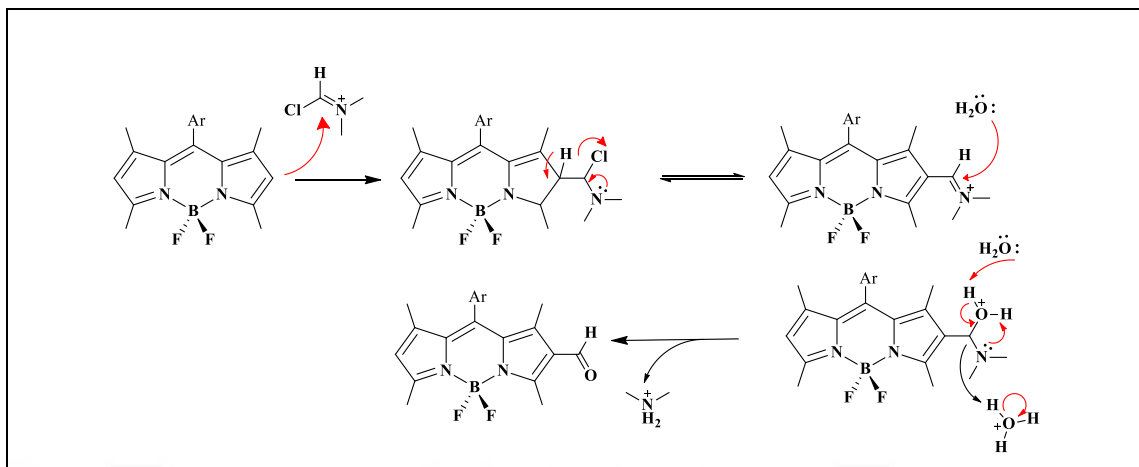


Figure 2.12: Reaction mechanism of formyl BODIPY via Vilsmeier Haack reaction.

2, 6-positions of BODIPY are functionalized with formyl groups (Figure 2.13) which were reported by using 6-formyl-BODIPY via Vilsmeier-Haack reaction [26].

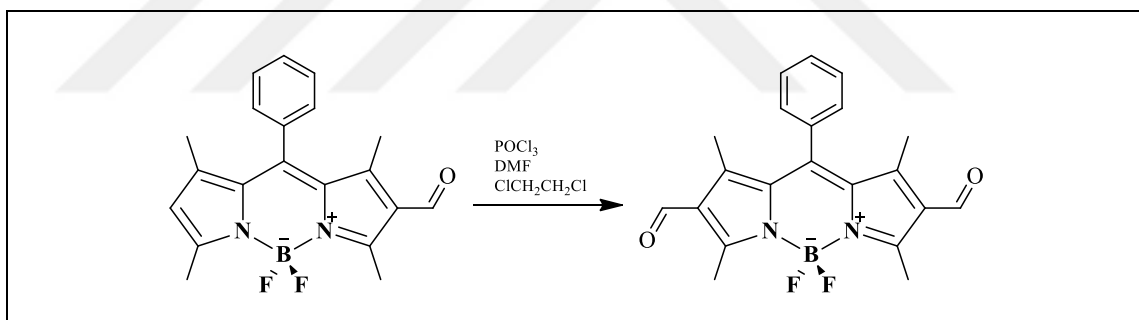


Figure 2.13: β -diformyl-BODIPY via Vilsmeier-Haack reaction.

Attachment of formyl groups to BODIPY dyes causes red- or blue shifts of emission and absorption maxima.

2.3.3. Knoevenagel Condensation Reaction

Knoevenagel condensation is a kind of nucleophilic addition reaction in the presence of active hydrogen and carbonyl groups under basic conditions and resulting water removal (Figure 2.14). The Dean-Stark apparatus can be used for discard water. BODIPY derivatives can be functionalized with this type of reactions (Figure 2.15). Especially, 3,5-methyl cites are very acidic and protons of this methyl group show great chemical shift in

the aliphatic area so they provide condensation between the BODIPY core and aromatic aldehydes [27].

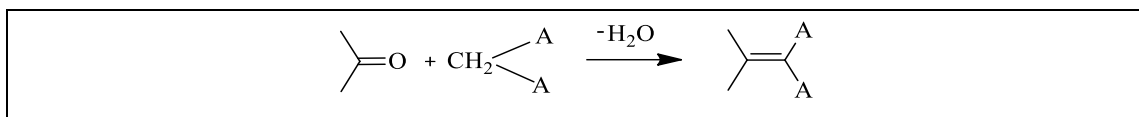


Figure 2.14: Knoevenagel condensation double bond formation.
(A=electron-withdrawing group).

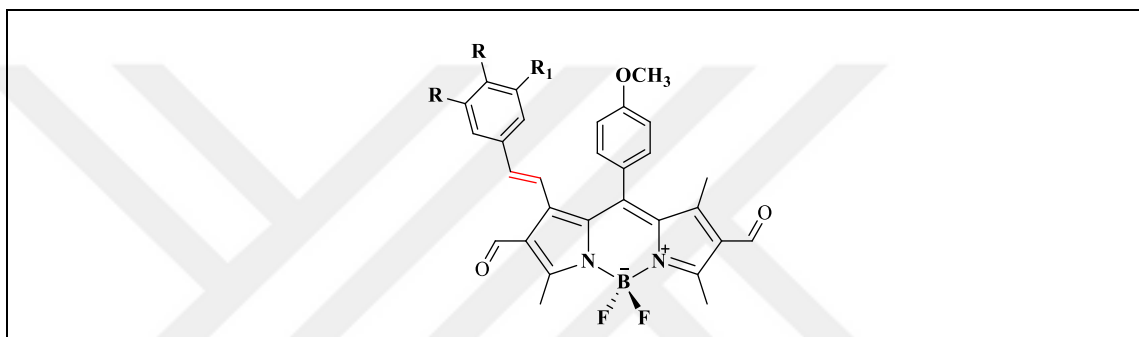


Figure 2.15: Functionalized BODIPY via Knoevenagel condensation.

2.4. Applications of BODIPY

Initially, interest in BODIPY was mostly observed in biological labeling. As time passed thanks to advancements in functionalization of BODIPY has led adjustments of its chromophore and it became applicable in different research fields (Figure 2.16) such as photodynamic therapy, solar cell, liquid crystals [28], drug delivery systems [29], molecular logic gates [30], sensing, bioimaging, photothermal therapy [31].

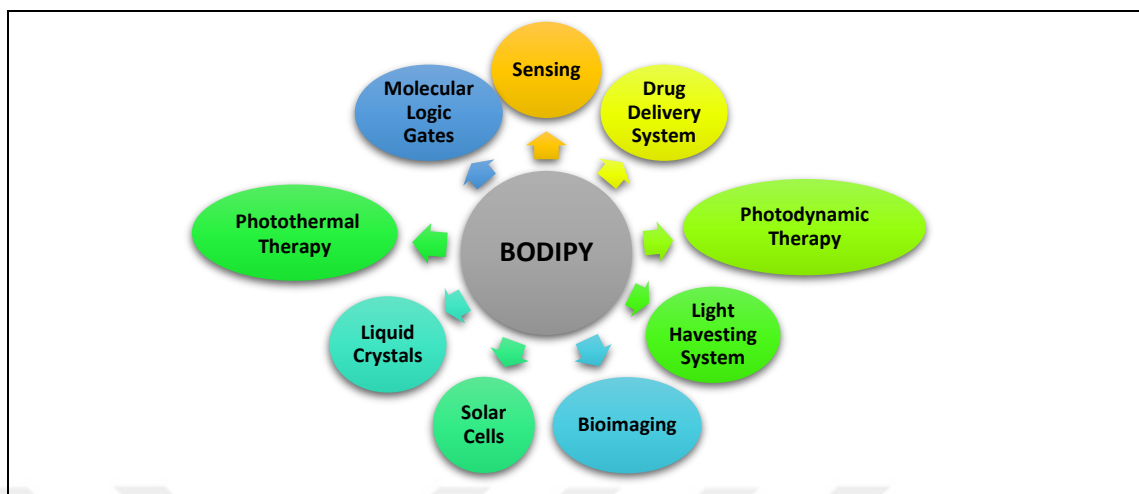


Figure 2.16: Application areas of BODIPY.

Alternative ways such as gene, photothermal and photodynamic therapy [32] have been developed for cancer treatment instead of chemotherapy to minimize its harmful side effects. For photodynamic therapy (PDT) [33], [34], a photosensitizer is activated with light having specific wavelength to generate reactive oxygen like singlet oxygen ($^1\text{O}_2$) then this kills tumor cells. Ruan et al. reported [35] BDP-Br (Figure 2.17) photosensitizer demonstrates singlet oxygen generation with high efficiency thanks to heavy atom effect.

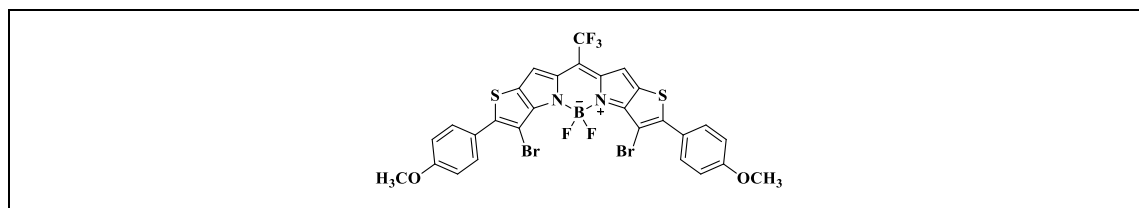


Figure 2.17: BDP-Br₂.

In photothermal therapy [36], near-infrared (NIR) laser photo absorbers are irradiated with NIR laser to create heat to damage cancer cells. Photodynamic therapy and photothermal therapy are applied not only separately but also together. Chen et al. combined both treatments. Self-assembled BODIPY-conjugated hyaluronic acid polymer synthesized and formed nanoparticles called BODIPY-HA NPs can be a promising nanomedicine for cancer treatment [37].

Solar cell [38], can be called also as photovoltaic cell is a device converts light energy of light into electrical energy by virtue of photovoltaic effect. According to an article reported in 2019 [39], two NIR BODIPY dyes were synthesized for dye-sensitized solar cell type. Co-sensitized structure was obtained by using them together as a result of high power conversion efficiency as 6.67 %.

Cells' intracellular environment is very complex due to various interactions of different biomolecules. Important information can be obtained from this dynamic medium to understand biological mechanisms [40]. BODIPY fluorescent molecules' derivatives can be utilized as probes for bio-imaging. Akkaya group synthesized azido-added 3,5-distyryl groups -modified BODIPY (Figure 2.18) to track intracellular H_2S which is detected with reduction of azide to amine [41].

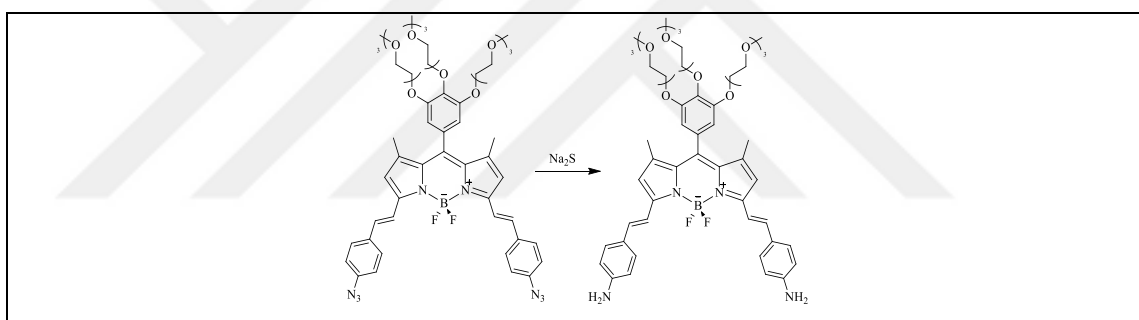


Figure 2.18: A red-shifted BODIPY probe.

2.5. Properties of BODIPY

Although the first BODIPY derivative was synthesized in 1968, it had not been taken inverse attention until the possible application in biological labeling was noticed [42]. As a result of this notification, curiosity about BODIPYs' fluorescence abilities has been rising among biochemists and biologists so an increase of papers was observed in the 1990s [42]. Since then, the interest in BODIPY has been risen day by day thanks to having high photoluminescence quantum yield and molar extinction coefficients ($\epsilon > 70\,000\text{ M}^{-1}\text{ cm}^{-1}$), high solubility in organic solvent, exquisite chemical stability, adjustable absorption-emission wavelengths, great photostability and facile functionalization [43].

BODIPY dyes generally have absorption and emission peaks between 480-550 nm. For unsubstituted BODIPY core (Figure 2.19 [10]), there is an acute absorption around 500 nm can be associated as S_0-S_1 ($\pi-\pi^*$) transition and another peak at about 480 nm is because of 0-1 vibrational transition. If BODIPY is substituted through pyrroles' electrophilic positions with double, triple bonds or aromatic rings, absorption and emission peaks shift to longer wavelengths which are between 50-300 nm according to the π -system. If it is functionalized with alkyl or amino electron donating groups, heavy atoms such as bromine and iodine, there will be 10-50 nm red shifted peaks owing to decrease in the HOMO-LUMO gaps. Various modifications on BODIPY allow tuning absorption and emission bands in a wide range.

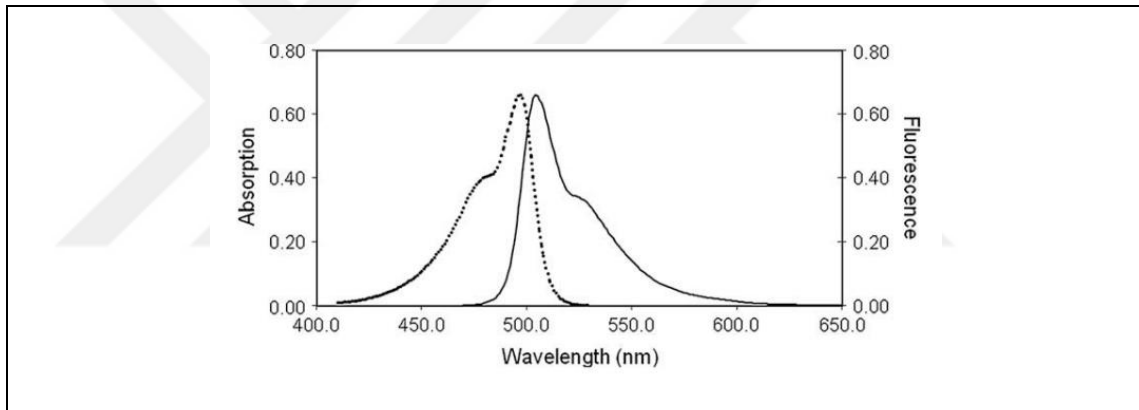


Figure 2.19: The absorption and emission spectra of unsubstituted BODIPY (.....excitation in methanol; --emission in methanol).

3. SUPRAMOLECULAR CHEMISTRY

3.1. History and Definitions

First definition can be accepted about supramolecular chemistry was explained by Jean-Marie Lehn, who won the first Nobel Prize in Chemistry for molecular recognition works in 1987 with Charles J. Pederson and Donald J. Cram, as ‘chemistry of molecular assemblies and of the intermolecular bond’. Steed J. and Atwood J.L express this definition as ‘chemistry beyond the molecule [44]. After the Nobel Prize was given for design of crown ethers, cavitands and cryptands, recognition of this area was succeeded. Again in 1996, Nobel Prize for Chemistry was given to Kroto, Smalley and Curl for their works about fullerene chemistry, in 2003. Peter Agre and Roderick MacKinnon deserved the prize for discovery of water channels and cation-anion channels characterization. Lastly Jean-Pierre Sauvage and Sir J. Fraser Stoddart won the prize for design and synthesis of molecular machines in 2016.

Supramolecular chemistry consists of host-guest structure (Figure 3.1) in which large molecules called hosts wrap the small molecules that are called as guests [44]. As an example, as mentioned before, Jean-Marie Lehn synthesized cryptand (Figure 3.2 blue color) as a host molecule shows activity in the presence of alkali metal, K^+ as a guest [45].

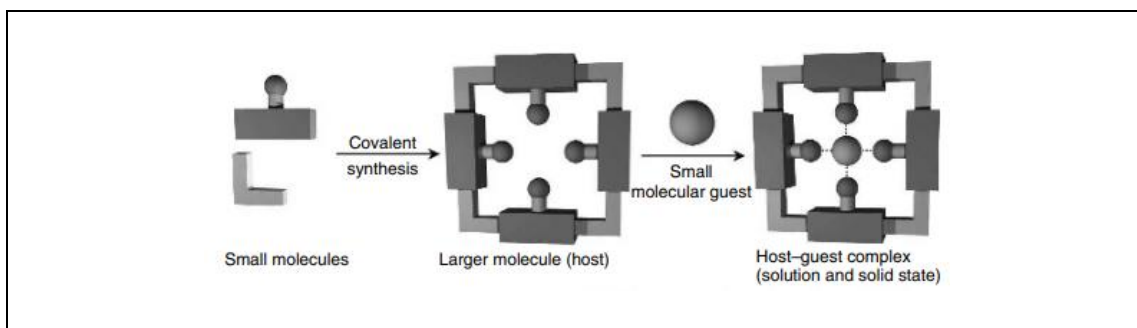


Figure 3.1: Host-guest complexation.

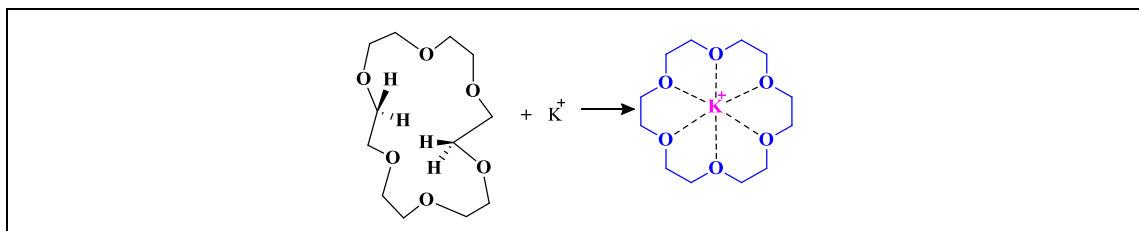


Figure 3.2: Lehn's synthesized molecule called cryptand.

After the area gained its reputation, Lehn explained as each units of multicomponent molecular structures are held together by non-covalent intermolecular interactions like ion-ion interactions, ion-dipole interactions, dipole-dipole interactions, hydrogen bonding, cation/anion/ $\pi-\pi$ interactions, van der Waals forces and close packing etc. [46]. Non-covalent interactions have energy smaller than those 200-400 kJ/mol commonly for covalent bonds. In these bonds, ion-ion electrostatic interactions are relatively strong having 4-40 kJ/mol energy and hydrogen bonding has strength between 4-120 kJ/mol [47].

Molecular design, which includes recognition, complementarity, preorganisation, self-assembly and self-replication, is a key point for supramolecular chemistry [48]. Unfortunately, sometimes building supramolecular structures displays challenges so it limits its usage [49]. Reversible non-covalent and covalent reactions are difficult to control since they are both sensitive to environmental situations. By virtue of this, byproducts that can be obtained [50]. Moreover, unexpected results can be faced owing to unpredictable solvent effects [51]. To cope with these kinds of challenges; templating strategies, use of highly diluted environments, longer reactions, complicated synthetic routes and gradual reagents addition can be useful [52]. Basically, supramolecules are kind of aggregates where components come together with design or spontaneously to give larger structures.

Supramolecular structures are widespread in nature such as enzymes, reactions in living cells and DNA double helix [53]. Moreover, mimicking biological constructions such as seeds and fruits by using molecules is very challenging. Peanut-shaped nanostructures consisting of two fullerene surrounded with a polyaromatic shell which has dumbbell-like shape is synthesized. Artificial peanuts are obtained via metal-ligand coordination and aromatic-aromatic π -stacking interactions [54].

Supramolecular chemistry is applied almost all areas [55] such as sensors [56]–[58], chromatography [59], organic electronics [60], crystal engineering [61], photodynamic therapy [62], soft nanotechnology, drug delivery systems [63], targeting, food and textile industries.

3.2. Self-assembly

Self-assembly needs molecular structures including at least two interaction sites to create numerous connections. Ascertaining repulsive or attractive interactions, each molecule in self-assembled structures are encoded with information like charge, shape or polarizability etc. [64].

Molecular self-assembly is generally constituted with supramolecular interactions, but also benefit from kinetically temporal covalent bonds. There will be a balance between non-aggregated and aggregated forms owing to inherent mobility in molecules so leads to various diverse properties like self-healing, error correction and sensitivity towards external stimuli [65]. Controlling over these self-assembled nanostructures are well known, thus they can be applied in various applications categorized as; biomedical sciences such as diagnostics and sensing [66], therapy and delivery [67], information technologies such as organic electronics [68], information processing and storage [69], environmental sciences such as chemical storage nanomaterials, separation/purification/transport, nanomaterials for catalysis [70].

According to Whitesides G.M and Grzybowski B., self-assembly can be separated into two main kinds: static and dynamic [71]. In static self-assembled ordered structure formation may need energy. When it is obtained, it will be stable. Most studies have concentrated on this type. Oil droplets in water are formed from lipid molecules or a functional ribosome is formed from RNA and ribosomal protein consolidation. Both can be examples from nature for static one. If a system is dissipating energy, dynamic self-assembly occurs.

3.2.1. Self-assembled Structures Examples from Nature

Molecular aggregates structures transportation through membrane and recognition phenomena are both subjects of biochemistry and biomimetic supramolecular chemistry. Living beings consist of highly organized assemblies and they can perform notably specific structures with high complexity [72].

There are many examples of self-assembled structures in nature. One of the best known examples can be DNA double helix formed from single-stranded oligonucleotides complementing each other. Recognition is achieved with very selective hydrogen bonding between adenine-thymine or guanine-cytosine base pairs shown in Figure 3.3. This structure was discovered by Watson and Crick in 1953 then approved with crystal structure observations [73].

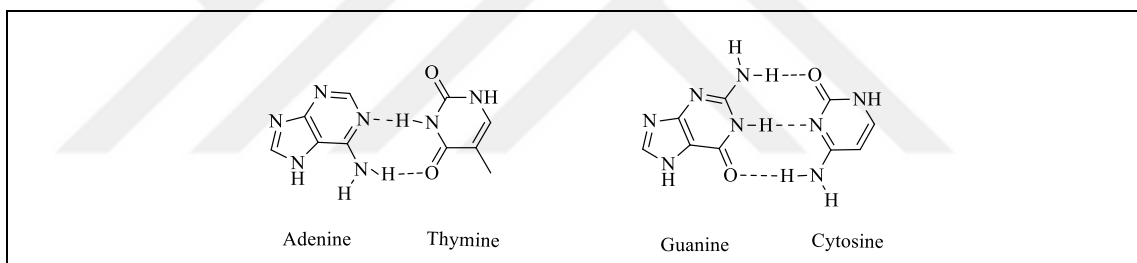


Figure 3.3: Hydrogen bonds in DNA structure.

Another example can be biomembranes include amphiphilic phospholipids bilayers that consist of a glycerol unit with hydrophilic phosphate ester called head group and two hydrophobic fatty acids called tails. Synthetic and natural amphiphiles may self-assemble into structures such as vesicles and micelles in water.

Tobacco mosaic virus can be another fascinating supramolecular example that comprises single strand ribonucleic acid surrounded by 2130 identical protein units sheath so the whole virus shows a supramolecular assembly. When it is exposed to change in physical or chemical, the assembly can be broken into building blocks. The impressive property of the structure is that, after it is broken into pieces, these components get together under a physiological environment resulting in an exact self-assembly and also regain its functionality [74]. This large structure is formed from only certain types of subunits. Some parts of the compound are very selective so they can fit as complementary

numerous weak interactions to take advantage to control process and response to the stimuli. The common point of all self-assembled structures in nature, they make use of weak noncovalent interactions between subunits so formation of structure can be obtained.

3.2.2. Hydrogen Bonding

Hydrogen bond can be accepted as the most important non-covalent interaction to design supramolecular structures due to its strength and high degree of directionality [4]. There is a dipole-dipole interaction occurring between a proton donor and an acceptor. Amino acids, nucleobases and carbohydrates are examples of natural hydrogen bond donors and acceptors sources. When a hydrogen atom is attached to an electronegative atom like nitrogen and oxygen they will become hydrogen bond donors so bonded hydrogen will be partially positively charged. Hydrogen bond acceptors are electron-withdrawing molecules interacting with this positively charged hydrogen. Its strength changes between 4-120 kJ/mol. Hydrogen bond geometry and acceptor-donor group types regulate length, strength and nature of interaction [75]. Briefly, hydrogen bonds are the most beneficial interactions to make self-assembly of organisms into well-defined aggregates [76]. DNA double helix is the most well-known hydrogen bonded supramolecular structure from nature.

In an example inspired from nature, grabbing mechanism of proteins for copper ions owing to polypeptidyl histidine imidazole chains, selective copper ion can be gathered from water because it is one of the most used heavy metals that is very toxic especially for human's health in huge quantities, although it is vital for individuals' physiology [77]. There are some challenges to extract this heavy ion like incomplete ion removal, high costs, and toxic generation [78]. Therefore, zinc imidazole salicylaldoxime (ZIOS) supramolecule that is water stable and administrates unexpected adsorption kinetics which is very fast up to 50 times compared to others is designed including pendant imidazole rings which are hovered to hunt copper ions [79]. Simulations of molecular dynamics demonstrate this supramolecular structure may flexibly breathe water with lattice contraction and expansion and the water can be carried into lattice with hopping between hydrogen bonds. Furthermore, suspension of copper ions can be selective with ZIOS under

pH<3, this is a very important result that has been never experienced before. Unlike other structures, this one is durable to water exposure for weeks.

A lot of molecular patterns have been defined to assemble into supramolecular architectures like cyanuric acid (Figure 3.4 (red))/barbituric acid and melamine (Figure 3.4 (blue)) or derivatives [80]. A single melamine structure can constitute three hydrogen bonds along cyanuric acid composing a highly stable network [81]. Given as an example, one of triazine derivatives, melamine, is accepted as a precursor for polymeric melon or graphitic carbon nitride that takes attention owing to photocatalytic properties.

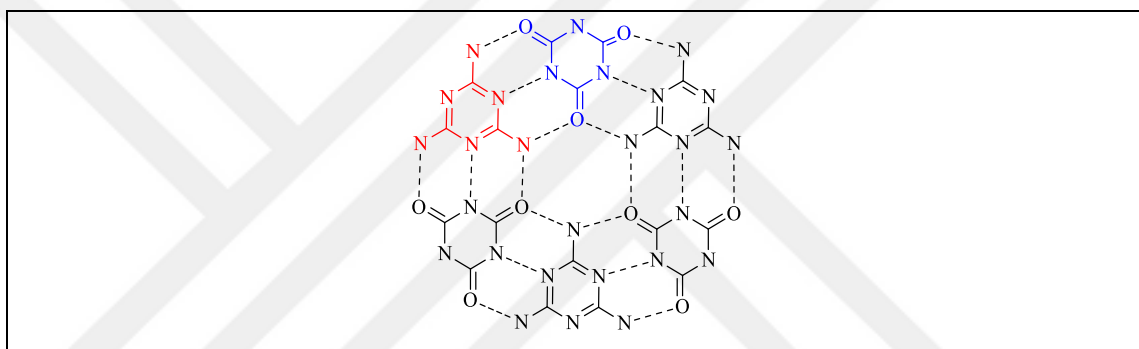


Figure 3.4: Melamine-cyanuric acid hydrogen bonds (---).

In Figure 3.4, flower-like spherical structure is incorporated into graphitic carbon nitride and obtained structure called as MCA-CN showed strong optical absorption, broadens band gap and increment in photoexcited charge carriers lifetime compared to dicyanide diamide (DCDA-CN). Therefore, molecular cooperative assemblies that depend on solvent type, temperature synthesis and precursor molecules have been attracting attention.

According to Yagai et al., a combination of N, N'-disubstituted melamine (Figure 3.5) and barbiturate (or isocyanurate) is a promising research area constructing supramolecular building blocks that coaggregate DAD·ADA (D: donor, A: acceptor) complementary triple hydrogen bonds which enable various supramolecular buildings such as cyclic hexamers called as rosettes and two polymeric tape-like called as linear and crinkled (Figure 3.6) [82], [83]. They have reported barbiturate-melamine self-assembly that is a pioneer presented with photoswitching properties. Melamine's azobenzene unit photoisomerisation enhances thermodynamic stability of rosette in a solution. If solvent

is removed, supramolecular structure in solid state can be retained. Thanks to hydrogen bonds formed with barbituric acids, magnificent self-assembled structures have been synthesized.

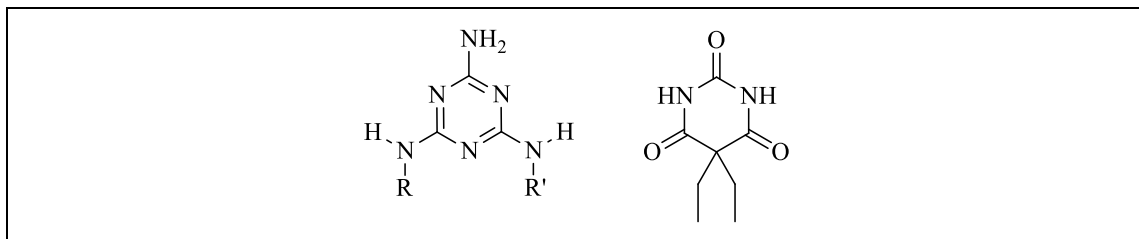


Figure 3.5: N, N'-disubstituted melamine and 5, 5-diethyl barbituric acid structures.

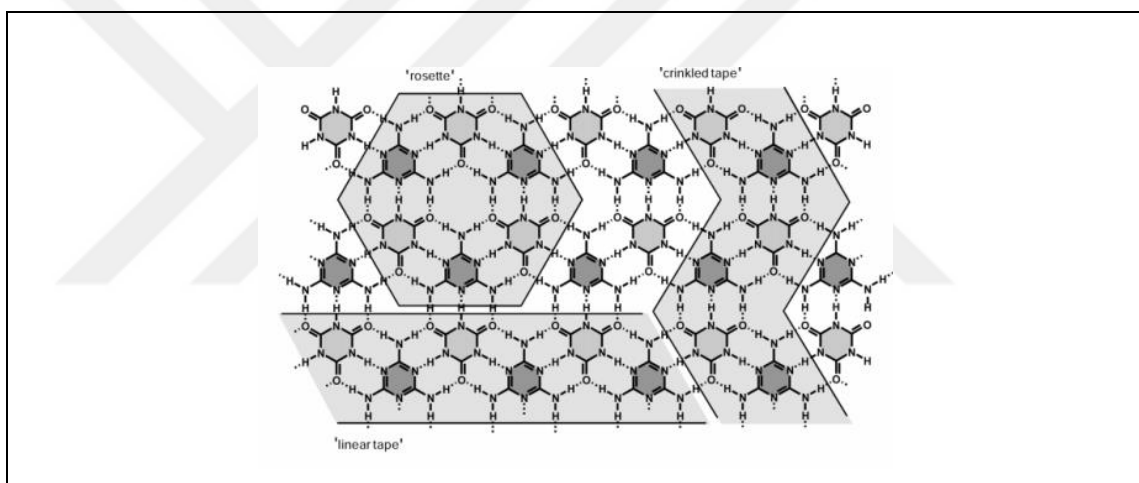


Figure 3.6: Melamine/cyanuric acid motifs.

3.2.3. Hydrogen Bonds with Barbituric Acid

Barbituric acid, namely 2, 4, 6-(1H, 3H, 5H)-pyrimidinetrione, was synthesized by condensation of urea in the presence of diethyl malonate in 1864 for the first time by Adolf von Baeyer. Grimaux synthesizes barbituric acid from malonyl chloride and urea and shows it as a derivative of pyrimidine [84]. Barbiturates are drugs derived from barbituric acid [85]. Actually, there is no therapeutic activity in barbituric acid, however its derivatives gain this role [86]. Barbital (Figure 3.7), is one of barbituric acid derivatives that was effective on dogs to sleep. At the beginning of the 1900s, barbiturates were consumed in medicine and they attracted massive attention in the 1960s for treatment of

insomnia, seizure and anxiety. Unfortunately, several side effects are observed on some individuals who are elders, babies and pregnant [87].

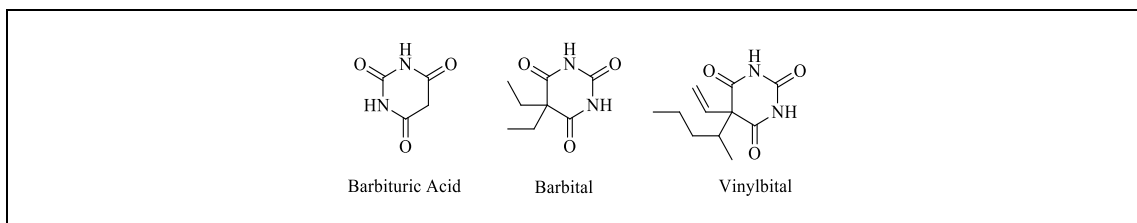


Figure 3.7: Barbituric acid and its derivatives as medicine.

Despite the fact that barbiturates have a reputation mainly for applications in medicinal chemistry, applications in the research areas like coordination and supramolecular chemistries have been increasing attention day by day [88]. It can be also applied to magnetic and non-linear optical materials, drug cocrystal design, molecular receptor construction, photochemistry and catalysis [89], [90]. Especially, molecular recognition of barbituric acids with hydrogen bonds, other non-covalent interactions and metal-ion coordination has been drawing attention.

Melamine and barbituric or cyanuric acid self-assembled examples are given in the previous part. More enormous supramolecular structure examples of them are encountered in the literature. According to Yagai [91], self-assembled functionalized dyes and related π -conjugated structures show astonishing electronic and photonic properties. Therefore, investigation of self-assembly pathways, stimuli-responsive peculiarities, π - π stacking adjustments, nano to microscale constructions of self-organized, long-short range control over chromophore-chromophore directions, diversity of materials' qualifications are getting importance to study on organic functional materials. Yagai administered supramolecular self-assemblies and their π -conjugated systems whose organizations are controlled by complementary multiple hydrogen bonding (CMHB) between melamine and cyanuric/barbituric acid units. To examine these structures, scientists use scanning tunneling microscopy (STM) and atomic force microscopy (AFM) [92].

Bassani et al., have combined barbituric acid with fullerene units (Figure 3.8) and obtain linear hydrogen-bonded alignment buckyballs by crystallographic examination [93].

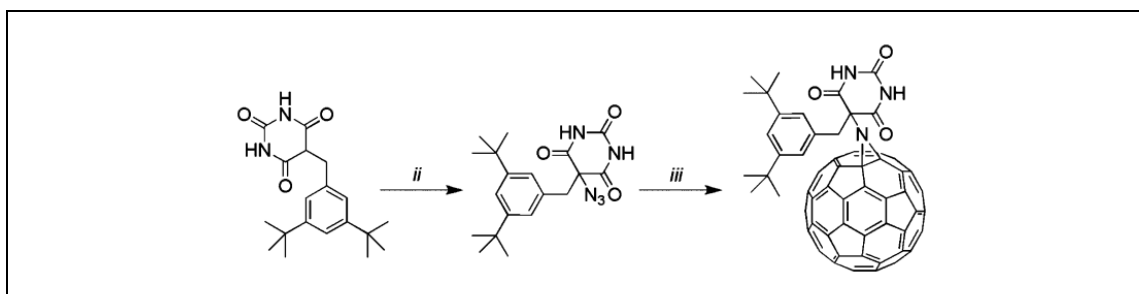


Figure 3.8: Barbituric acid functionalized fullerene.

Yagai et al., developed barbiturated π -conjugated molecules as CMHB for melamine receptors, results show that some barbiturated π structures self-assemble to create uniform nanorings (Figure 3.9) [94]. In a study [95], at low concentration barbiturate functionalized with dendric aliphatic group self-assembled (Figure 3.10 compound 1). Stilbene (Figure 3.10 compound 2) and phenylene (Figure 3.10 compound 3) derivative of barbiturate were synthesized to investigate π -conjugated core. According to the result, reduction of π -conjugated unit could decrease of supramolecular polymerization degree.

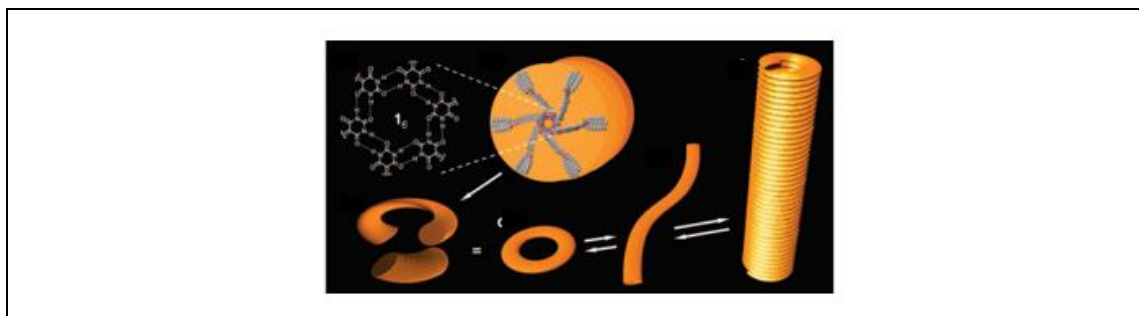


Figure 3.9: Illustration of proposed mechanism for 1 into nanorings, nanofibers and nanocoils as cyclic hexamer 1₆.

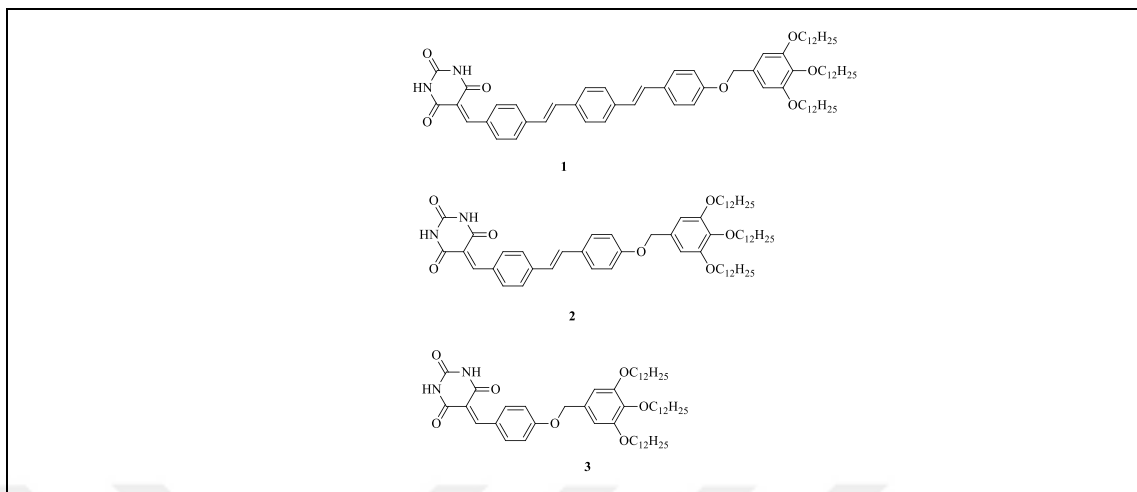


Figure 3.10: Barbituric acid functionalized molecules.

In their recent published article, Lehn et al., (Figure 3.11) [96] utilize barbituric acid functionalized structures and their self-assembly to establish two dynamic covalent libraries (DCLs) given name as DCL-1 and DCL-2 on the basis of dynamic covalent bonds as C=C/C=N organo-metathesis between two imines and two Knoevenagel derivatives. Each DCL includes a barbituric acid component which can undergo double self-construction process which is hexameric hydrogen bonded macrocycles formed then produce supramolecular polymer resulting in viscous gel state.

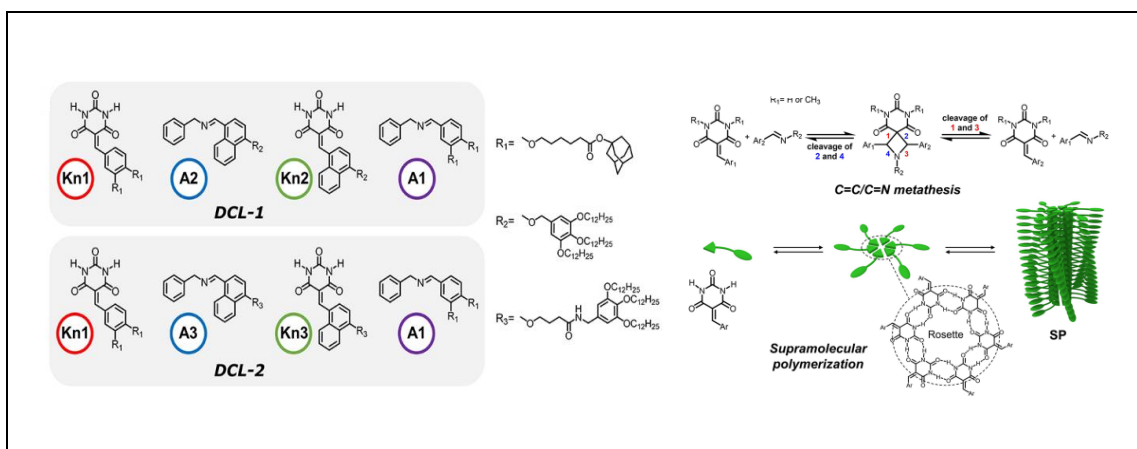


Figure 3.11: DCL-1 and DCL-2 and supramolecular polymerization.

4. SELF-ASSEMBLED BODIPY STRUCTURES VIA HYDROGEN BONDING

Squaraines, porphyrins and others are self-assembly of π -conjugated structures which generate functional elements both in solid and solution state. Furthermore, they can be applied in various areas [97]. In the last two decades, self-assembled BODIPY dyes have gained increasing attention because of their impressive electronic and photophysical characters as mentioned before. Interestingly, self-assembled BODIPY structures are explored fewer than others even if its derivative was reported in 1968.

Thanks to excitation coupling theory defined by Kasha et al., photophysical properties of self assembled BODIPY structures can be interpreted (Figure 4.1) [98], [99]. Because of molecular transition dipole interactions, dye aggregates showing exciton delocalization shifted absorption maxima compared to monomers. If two structures get close enough, their transition dipoles collaborate and excited state energy will split. There are two types of aggregates that are well-known as H- and J-aggregates called by E.E Jelley. If monomers build head-to-tail arrangement, the only transition lowest energy excited state (S_1) is allowed and named as J-aggregates, showing intense, narrow, red shifted (bathochromic) absorbance with approximately fluorescence. On the other hand monomers build face-to-face structures in only excited state, highest level electronic transition is allowed so H-aggregates demonstrate hypsochromic (blue) shift in absorption spectra and this type of aggregates can be characterized by displaying a fluorescence emission quenching. To have ideal J-aggregate, the slip angle (Θ) between conversion dipole moments is 90° besides for H-aggregate slip angle is zero. Dyes do not aggregate if the angle is 57.5° calles magic angle, for this situation exciton coupling will be canceled.

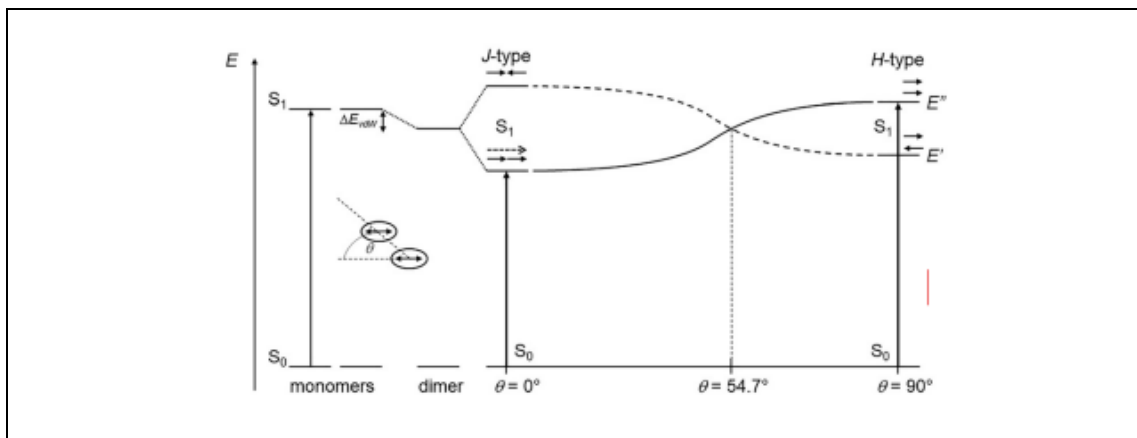


Figure 4.1: Exciton coupling theory by Kasha with excited state as a function of slip angle.

In solution and solid state, BODIPYs generally show face-to-face aromatic interactions with H-kind exciton coupling and obtaining aggregation caused quenching (Aggregation caused quenching-ACQ). To overcome this limitation and to gain emissive materials in solid-state are based on adjustment of non-covalent interactions administering highly directional self-assembled interactions. Hydrogen bonding interactions provide pre-organized supramolecular architectures. When BODIPY core is functionalized with bulky substituents, obtained structure avoids face-to-face π - π stacking so solid-state products are achieved with appreciated optical characters for material science applications.

Tang et al, published their works including a compound that was not able to show fluorescence ability in ethanol. When they added water into this solution, there were nanoparticles which gained fluorescence ability. This situation was called aggregation induced emission enhancement (AIEE). This research topic has been very popular for research areas like science and technology.

Halogen bonding has also been attracting attention owing to accomplishment of such desirable self-assembled systems. As an example which shows halogen and hydrogen bonding interactions [100], Özcan et al., synthesize mono and di-halogenated BODIPY dyes with p-nitrobenzene group which is a kind of powerful halogen bonding donor at meso position. According to Figure 4.2, structures 1a-c single crystals were observed from non-polar and polar solvents whereas for structure 1d there are two polymorphic crystals

that were observed depending on solvent kinds. As stated in the article, single-crystal XRD data affirmed 1a and 1b do not make halogen bonds even if they include I or Br in their structures. However, 1c and 1d are halogenated, showing iso-structural crystal packing with dimers formed by CH---F hydrogen bonds and F--- π interactions. Therefore 1D tubular structures were obtained and they are stabilized by halogen bonding as C-X---O (Br---O, I---O). For 1d-II crystal packing of polymorph displayed 1D chains again with halogen bonding (I---O), they linked further and showed a 3D supramolecular network owing to CH---F and CH---O hydrogen bonds. Thanks to strong halogen bonding, 1d-II exhibits fluorescence in solid state. Unfortunately, 1a-d administration is a weak emission because of the heavy-atom effect.

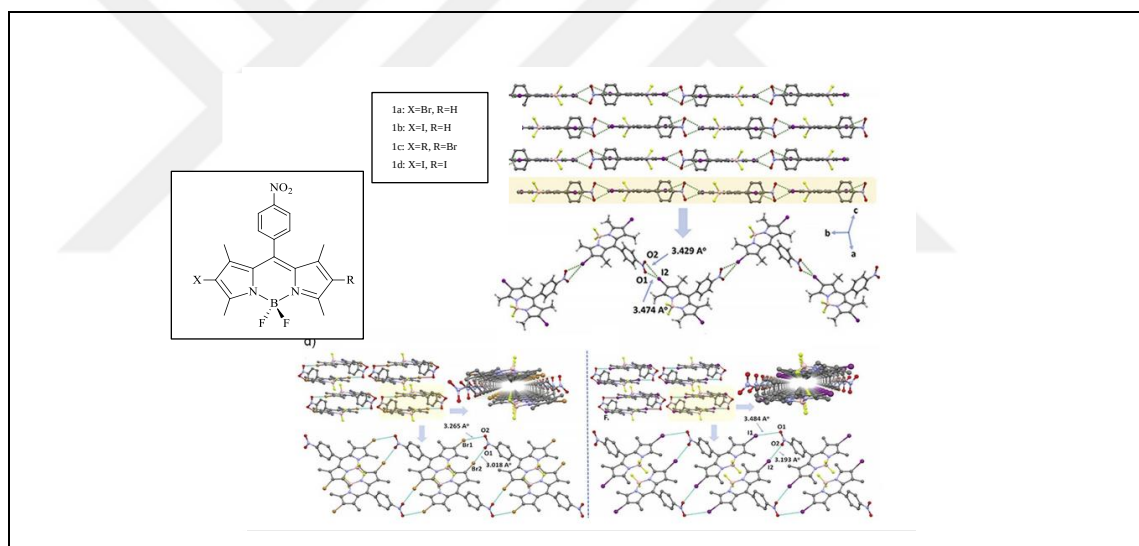


Figure 4.2 : (a) Structures of 1a-d, (b) 1d-II (in acetonitrile) crystal structure (c) representation of 1D zigzag of 1d-II (d) representation 1D nanotube for 1c (e) for 1d.

Zhang et al., observed self-assembly in polar solvents as nanowires for uracil-functionalized BODIPYs (Figure 4.3). Fluorescence quantum yields in CH_2Cl_2 or CHCl_3 are found as 48 %, 42 %, 39 % for 1a, 1b, 1c. Due to aggregation in methylcyclohexane (MCH), the structure of 1a showed a decrease in fluorescence quantum yields to 13 %, it can be because of large non-radiative decay constants for aggregate when it is compared to monomers. But 1b and 1c give an increase in emission intensity as 58 % and 48 % in methylcyclohexane. Different substituents presented in the boron center influenced molecular packing. For 1b and 1c, dimeric cores formed intramolecular hydrogen

bonding, 1D structures obtained by hydrogen bonds and lateral aromatic interactions [101].

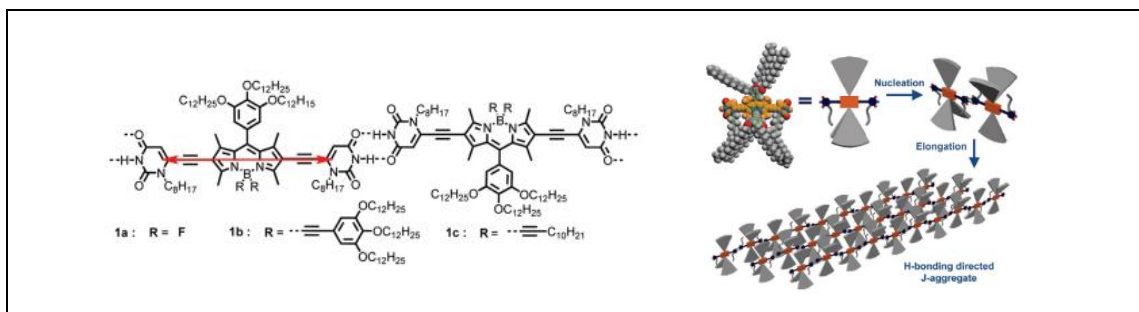


Figure 4.3: Synthesized compounds 1a, 1b, 1c and representation of 1D J-aggregates nucleation, elongation mechanism.

In this thesis, barbituric acid functionalized BODIPY derivatives were synthesized and their characterization was achieved through FT-IR, ¹H-NMR, ¹³C-NMR, mass spectrometry. Hydrogen bonded self-assembled structures were investigated via UV-Vis and fluorescence spectrophotometer, ¹H-NMR spectroscopy and dynamic light scattering method (DLS).

5. MATERIALS AND METHODS

5.1. Materials and Instruments

The list of chemicals used for synthesis, purification and analysis of obtained products is given in Table 5.1 and the devices that are benefited during the thesis study are given in Table 5.2.

Table 5.1: Chemicals used for synthesis, purification and analysis of obtained products.

Name	Manufacturer	Catalog No/ Cas No
3,4-Dihydroxybenzaldehyde	Sigma-Aldrich	139-85-5
DMF	Merck	68-12-2
Triethylamine	Merck	121-44-8
1-bromododecane	Acros Organics	143-15-7
2,4-dimethylpyrrole	Sigma-Aldrich	625-82-1
DDQ	Merck	84-58-2
Trifluoroacetic Acid	Merck	76-05-1
BF ₃ . OEt ₂	Merck	109-63-7
POCl ₃	Merck	10025-87-3
1,2-Dichloroethane	Merck	107-06-2
DMSO	Merck	67-68-5

Table 5.1: Continue.

Ethanol	Technical	64-17-5
NaHCO ₃	Fluka	144-55-8
Barbituric Acid	Alfa Aesar	67-52-7
Na ₂ SO ₄	Merck	7757-82-6
K ₂ CO ₃	Merck	584-08-7
n-hexane	Technical	110-54-3
THF	Merck	109-99-9
Dichloromethane	Technical	75-09-2
Ethyl acetate	Technical	141-78-6
Silica Gel 60	Merck	7631-86-9

Table 5.2: The devices were benefited from.

Name	Model	Location
FT-IR Spectroscopy (FT-IR)	Perkin Elmer	Gebze Technical University
Nuclear Magnetic Resonance Spectrometry (NMR)	Varian 500 MHz	Gebze Technical University
Mass Spectroscopy	Bruker Microflex LT MALDI-TOF MS	Gebze Technical University
UV-Vis Spectrophotometry	Schimadzu 2001 UVPc	Gebze Technical University
Fluorescence Spectrophotometer	Varian Cary Eclipse	Gebze Technical University
Dynamic Light Scattering (DLS)	Malvern Zetasizer Nano-ZS	Gebze Technical University

5.2. Experimental Studies

5.2.1. Synthesis of compound 1

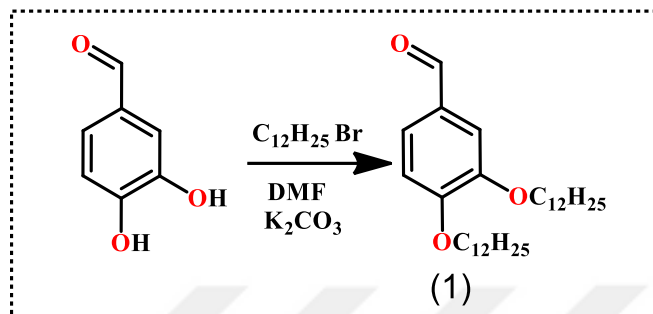


Figure 5.1: Synthesis of compound 1.

In a 100 mL flask, 3, 4-dihydroxybenzaldehyde (1.00 g, 7 mmol) in anhydrous DMF (32 mL) was stirred under argon atmosphere. 1-bromododecane (6.12 g, 25 mmol) and potassium carbonate (2.78 g, 20 mmol) were added then the temperature was set to 75 °C and it was stirred overnight. The reaction was over according to TLC. It was poured into ice water. Suction filtration was applied to gather precipitate. The obtained product was purified by silica gel column chromatography with hexane/ethyl acetate (v/v=85/15) as the eluent (white precipitate, 3.2 g, 92 %) (Figure 5.1) [102].

FT-IR [(ATR) $\nu_{\text{maks}}/\text{cm}^{-1}$]: 2920-2848 (aliphatic C-H), 2764 (aldehyde C-H), 1686 (C=O), 1681 (C=C) (Figure 5.2).

$^1\text{H-NMR}$ (500 MHz, CDCl_3 , ppm): δ 9.85 (s, 1H, CHO), 7.41-7.45 (m, 2H, Ar-CH), 6.97 (d, 1H, Ar-CH, $J=8.10$ Hz), 4.06-4.11 (m, 4H, OCH_2), 1.85-1.90 (m, 4H, CH_2), 1.48-1.51 (m, 4H, CH_2), 1.26-1.41 (m, 32H, CH_2), 0.90 (t, 6H, CH_3 , $J=6.90$ Hz) (Figure 5.3).

$^{13}\text{C-NMR}$ (125 MHz, CDCl_3 , ppm): δ 191.17, 154.83, 149.59, 130.01, 126.75, 111.90, 111.10, 69.27, 32.07, 29.84, 29.77, 29.53, 29.51, 29.21, 29.13, 26.14, 26.09, 22.84, 14.26 (Figure 5.4).

MALDI-TOF-MS (DHB): m/z Calcd: 474.77 g/mol, Found: 475.71 $[\text{M}+\text{H}]^+$ (Figure 5.5).

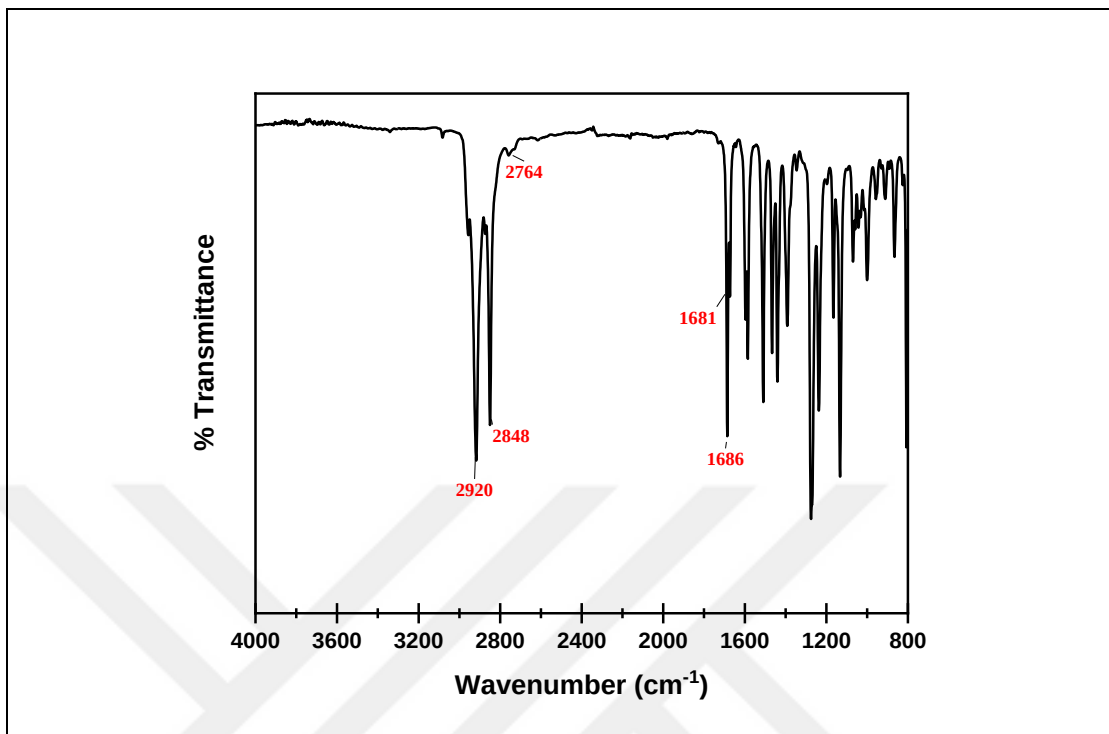


Figure 5.2: FT-IR spectrum of compound **1**.

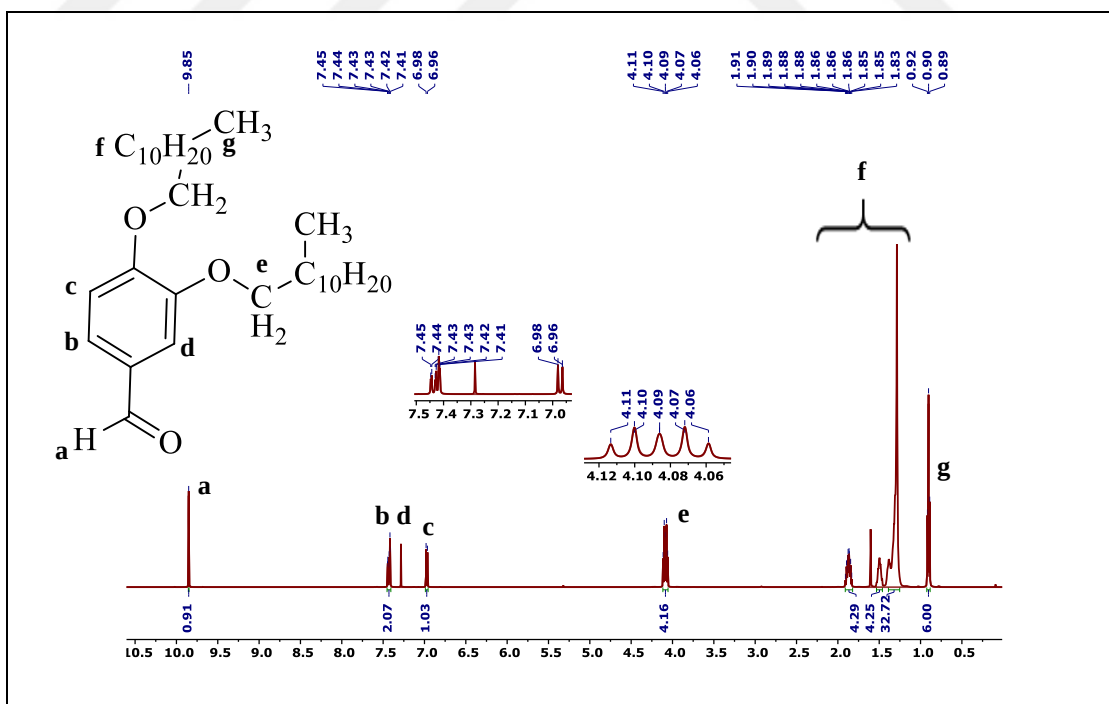


Figure 5.3: ¹H- NMR spectrum of compound **1**.

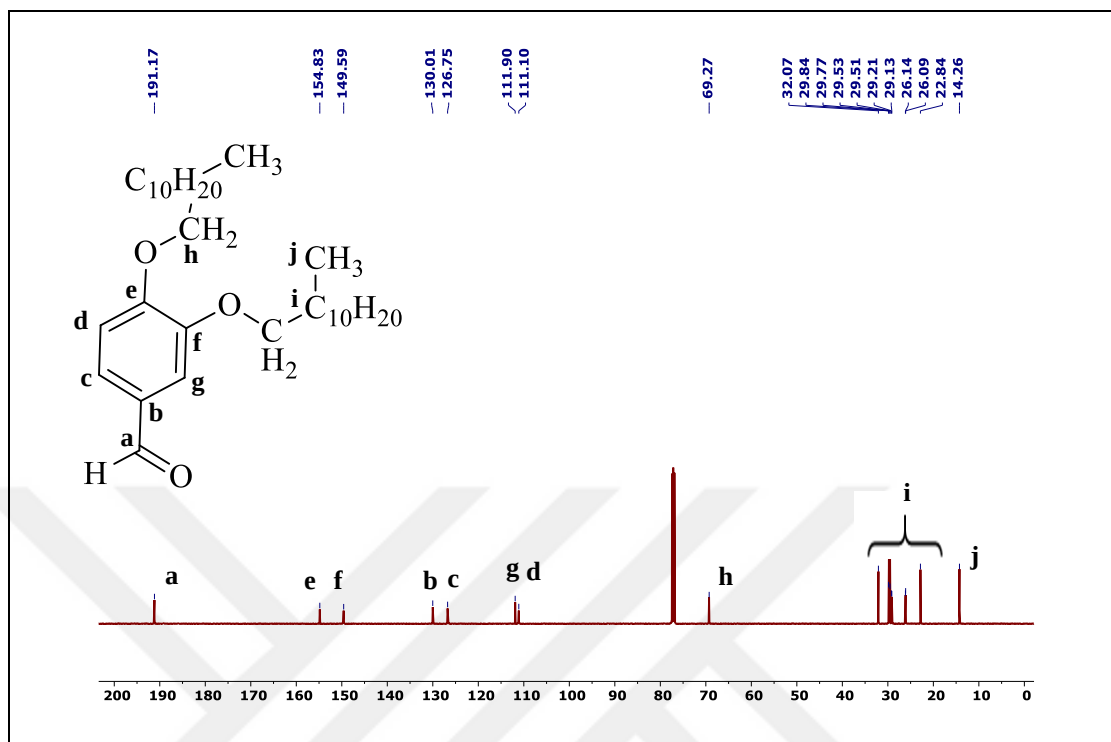


Figure 5.4: ^{13}C - NMR spectrum of compound 1.

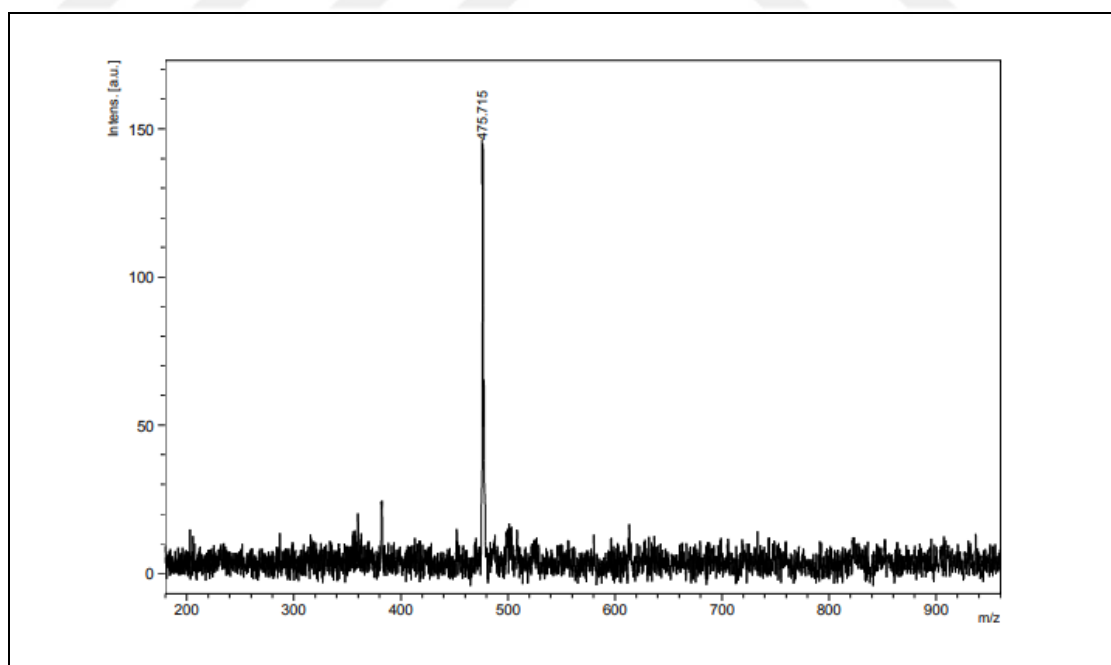


Figure 5.5: MALDI-TOF-MS spectrum of compound 1.

5.2.2. Synthesis of compound 2

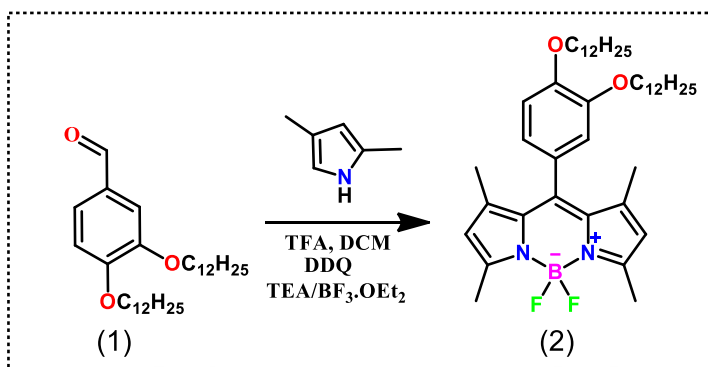


Figure 5.6: Synthesis of compound 2.

In a three-neck round bottom flask, 300 mL anhydrous dichloromethane was deaerated with argon for 15 minutes. Compound **1** (1000 mg, 2.1 mmol) was added and stirred for another 15 minutes. After adding **2**, 4-dimethylpyrrole (406.6 mg, 4.3 mmol) and trifluoroacetic acid (TFA; 10 drops), the resulting solution was observed as red. The reaction was stirred at room temperature in the dark overnight. DDQ (478 mg, 2.1 mmol) was added then the red-purple color solution was stirred for an additional hour. Et₃N (5.0 mL) was added dropwise over a period of 15 minutes. After 30 minutes, BF₃.OEt₂ (5 mL) was added dropwise in 15 minutes, it was stirred for 2 hours. When the reaction was over, it was washed with water (3 × 300 mL) then dried over anhydrous Na₂SO₄. The solvent was distilled. Silica gel column chromatography was applied to a synthesized compound in hexane: ethyl acetate (v/v=9/0.1) as the eluent (orange solid, 230 mg, 16 %) (Figure 5.6).

FT-IR [(ATR) $\nu_{\text{maks}}/\text{cm}^{-1}$]: 2925-2856 (aliphatic C-H) (Figure 5.7).

¹H-NMR (500 MHz, CDCl₃, ppm): δ 6.98 (d, 1H, Ar-CH, J= 8 Hz), 6.79-6.80 (m, 2H, Ar-CH), 6.00 (s, 2H, CH), 4.0 (t, 2H, OCH₂, J=6.70 Hz), 3.97 (t, 2H, OCH₂, J=6.70 Hz), 2.57 (s, 6H, CH₃), 1.80-1.91 (m, 4H, CH₂), 1.50 (s, 6H, CH₃), 1.28-1.36 (m, 36H, CH₂), 0.89-0.92 (m, 6H, CH₃) (Figure 5.8).

^{13}C -NMR (125 MHz, CDCl_3 , ppm): δ 155.26, 149.74, 149.61, 143.23, 141.90, 131.76, 127.11, 121.04, 120.41, 113.77, 113.32, 69.46, 69.23, 31.94, 29.72, 29.69, 29.65, 29.61, 29.50, 29.43, 29.38, 29.28, 29.22, 26.07, 25.97, 22.71, 14.58, 14.46, 14.13 (Figure 5.9).
MALDI-TOF-MS (DIT): m/z Calcd: 692.81 g/mol, Found: 692.80 $[\text{M}]^+$, 675.38 $[\text{M}+\text{H}-\text{F}]^+$, 647.47 $[\text{M}-\text{BF}_2]^+$ (Figure 5.10).

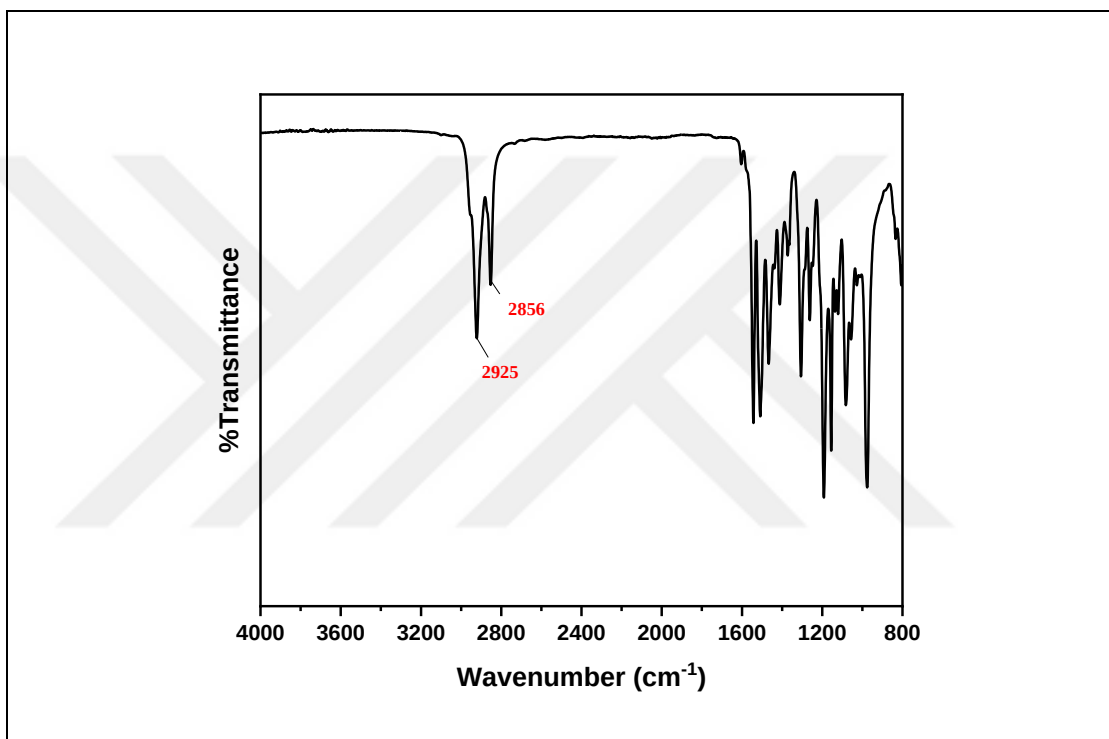


Figure 5.7: FT-IR spectrum of compound 2.

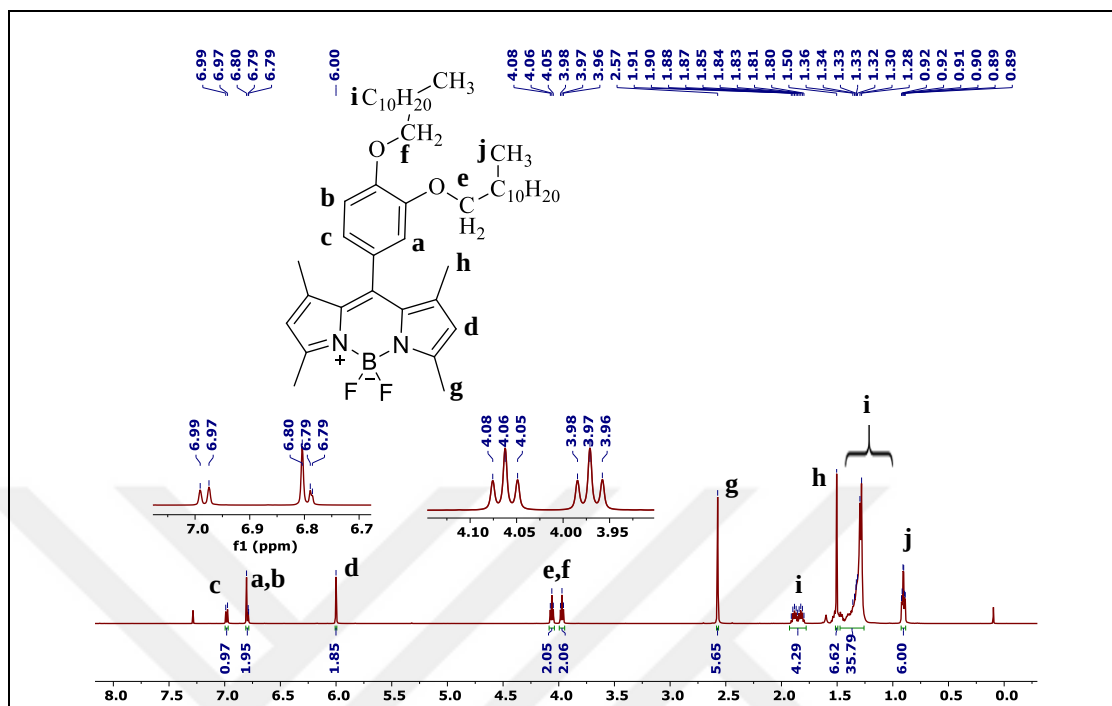


Figure 5.8: ^1H -NMR spectrum of compound 2.

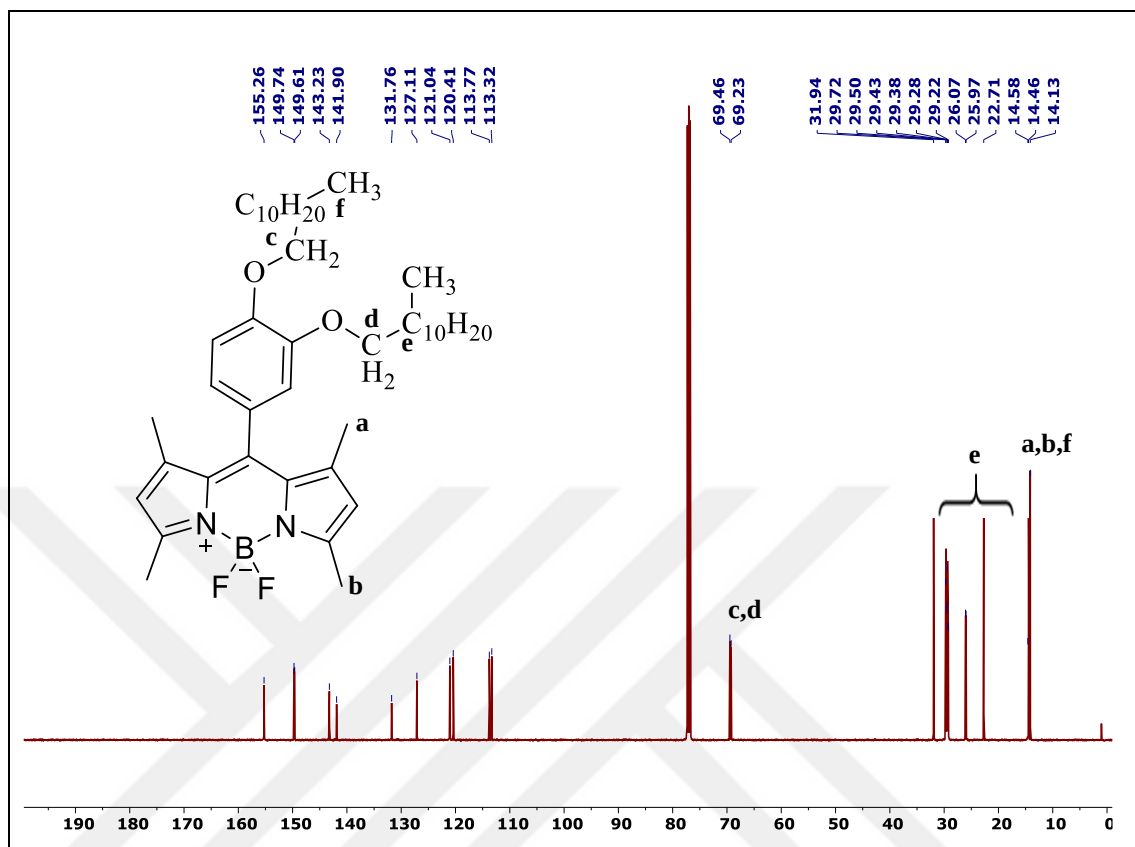


Figure 5.9: ¹³C-NMR spectrum of compound 2.

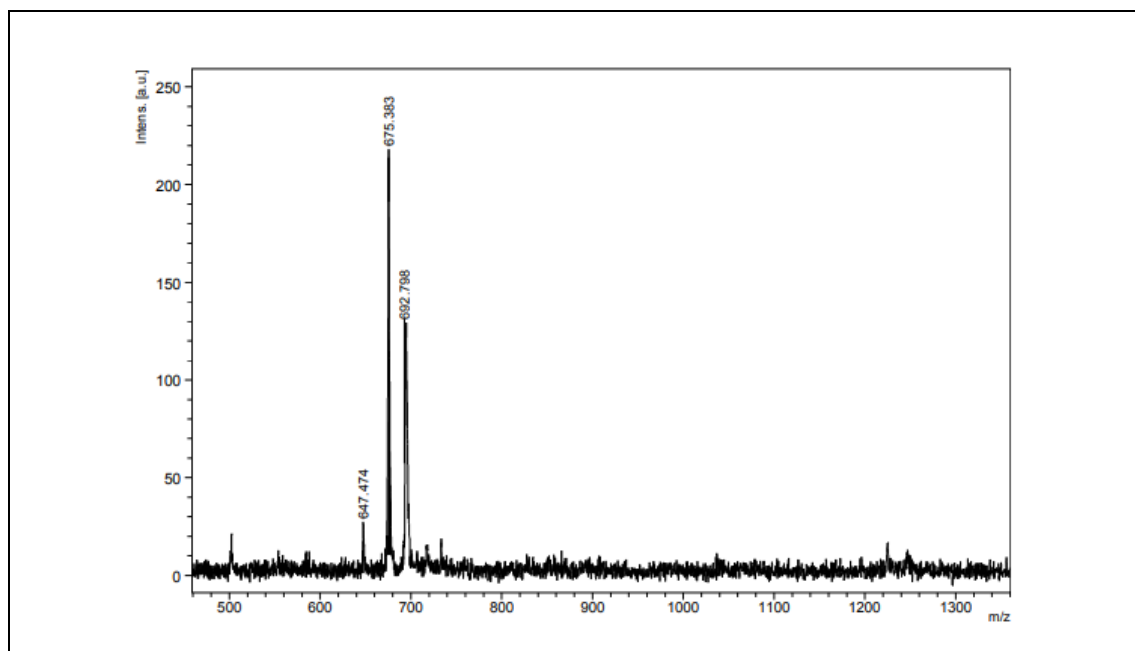


Figure 5.10: MALDI-TOF-MS spectrum of compound 2.

5.2.3 Synthesis of compound 3

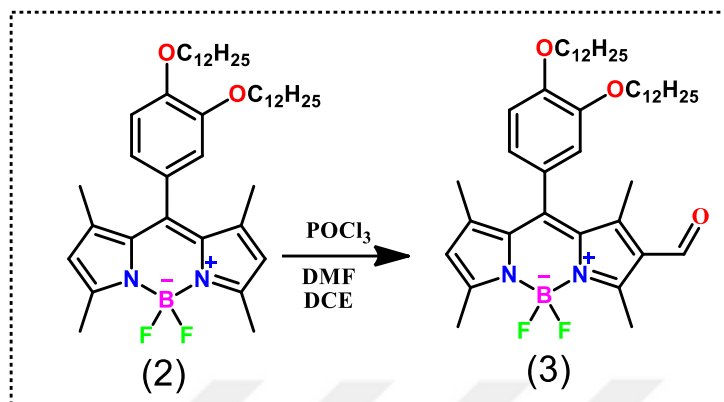


Figure 5.11: Synthesis of compound 3.

In a two neck-round bottom flask placed on an ice bath, anhydrous DMF (1 mL) was put under argon atmosphere. POCl₃ (1 mL) was added then it was allowed to stir for 30 minutes at room temperature. Pale yellow viscous solution was obtained. The compound 2 (100 mg, 0.15 mmol) was dissolved in 10 mL 1, 2-dichloroethane (DCE) then slowly added to the mixture with a dropping funnel. The mixture was set to 68 °C, stirred for an additional 2 hours then cooled to room temperature. It was poured into an ice-cold saturated NaHCO₃ solution. It was warmed up to room temperature then extracted twice with DCM and dried over anhydrous Na₂SO₄. Suction filtration was applied then evaporated. It was purified by silica gel column chromatography using ethanol/DCM (v/v=1/100) as the eluent. Orange color product was obtained (71 mg, 68 %) (Figure 5.11) [103].

FT-IR [(ATR) $\nu_{\text{maks}}/\text{cm}^{-1}$]: 2296-2856 (aromatic C-H), 2756 (aldehyde C-H), 1664 (C=O) (Figure 5.12).

¹H-NMR (500 MHz, CDCl₃, ppm): δ 10.02 (s, 1H, CHO), 6.99 (d, 1H, Ar-CH, J=7.99 Hz), 6.76-6.78 (m, 2H, Ar-CH), 6.14 (s, 1H, CH), 4.05 (t, 2H, OCH₂, J=6.7 Hz), 3.95 (t, 2H, OCH₂, J=6.7 Hz), 2.82 (s, 3H, CH₃), 2.61 (s, 3H, CH₃), 1.79-1.88 (m, 4H, CH₂), 1.76 (s, 3H, CH₃), 1.53 (s, 3H, CH₃) 1.25-1.33 (m, 36H, CH₂), 0.86-0.89 (m, 6H, CH₃) (Figure 5.13).

^{13}C -NMR (250 MHz, CDCl_3 , ppm): δ 185.97, 161.36, 156.39, 150.09, 150.02, 147.40, 143.79, 142.96, 134.42, 130.13, 126.26, 126.11, 123.81, 120.24, 113.85, 112.95, 69.58, 69.25, 31.94, 29.72, 29.70, 29.67, 29.63, 29.61, 29.49, 29.43, 29.37, 29.25, 29.21, 26.06, 25.97, 22.70, 15.08, 14.97, 14.13, 13.02, 11.73 (Figure 5.14).

MALDI-TOF-MS (DIT): m/z Calcd: 720.82, Found: 720.17 $[\text{M}]^+$, 701.05 $[\text{M-F}]^+$, (Figure 5.15).

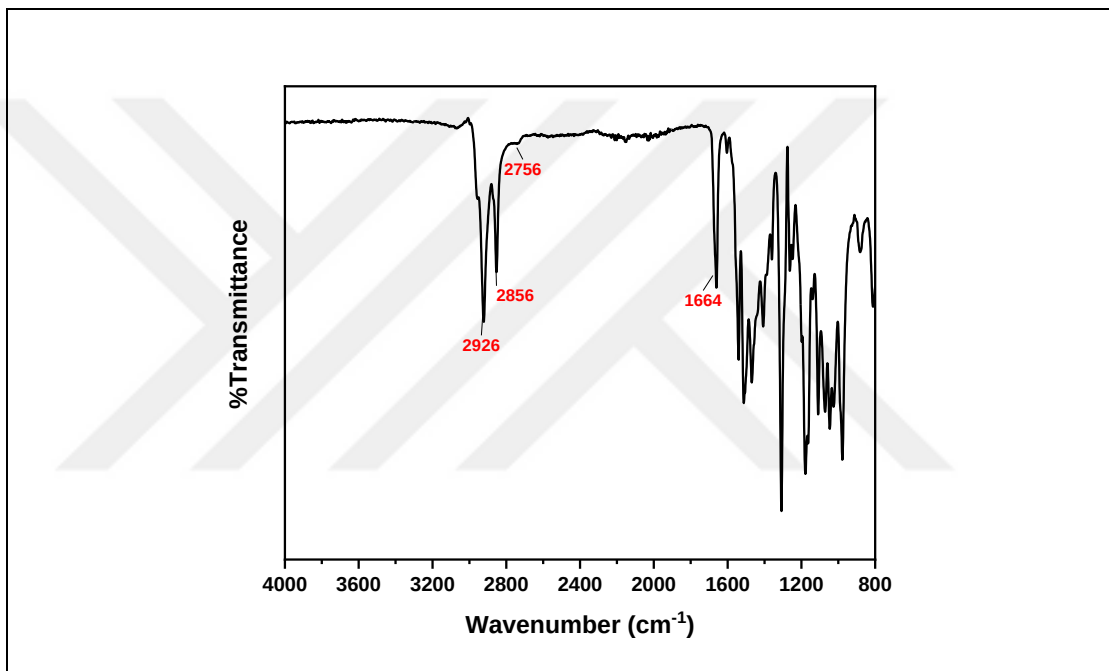


Figure 5.12: FT-IR spectrum of compound 3.

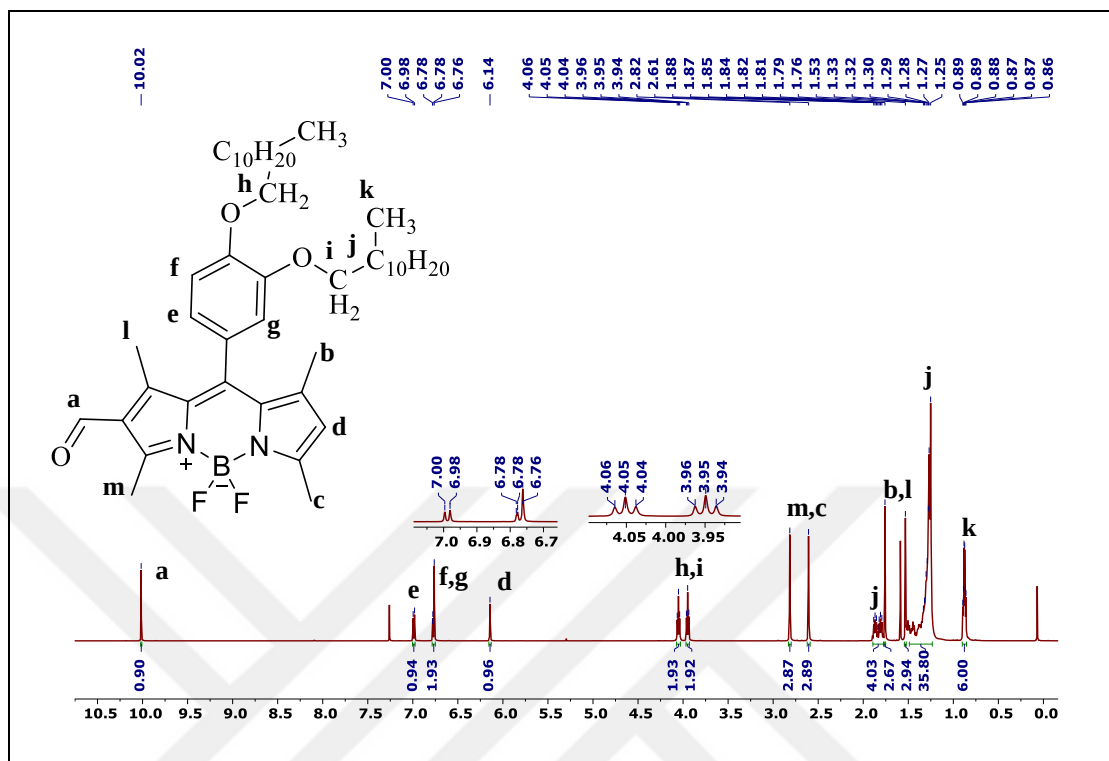


Figure 5.13: ^1H -NMR spectrum of compound 3.

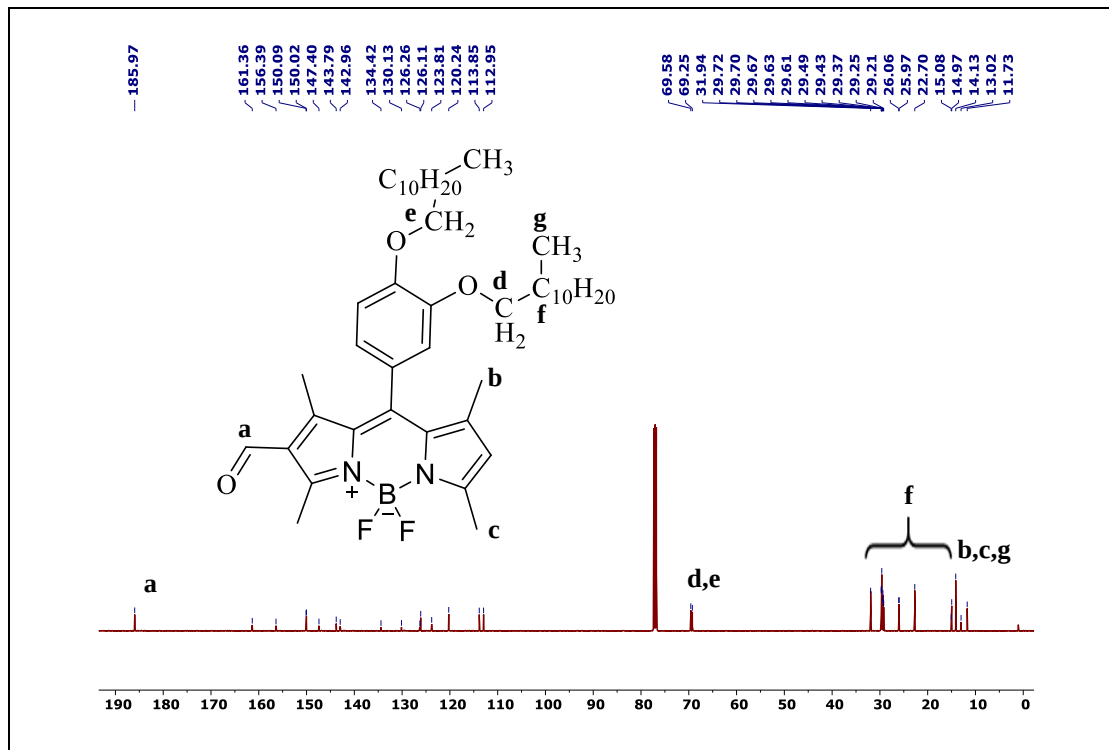


Figure 5.14: ^{13}C -NMR spectrum of compound 3.

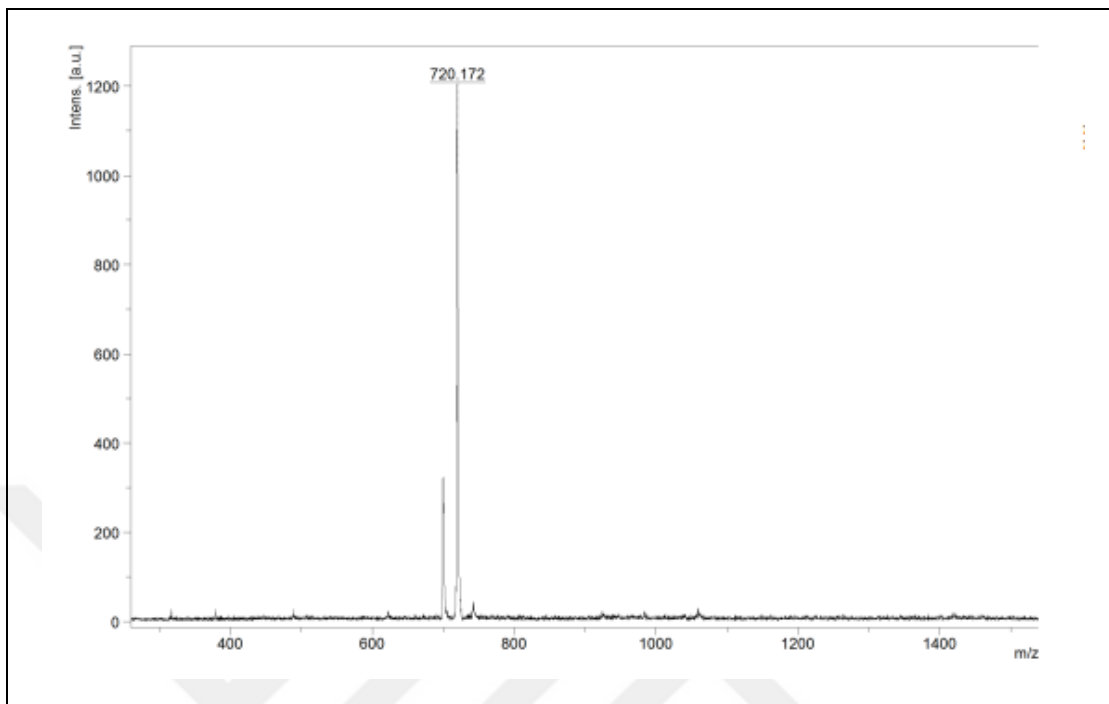


Figure 5.15: MALDI-TOF-MS spectrum of compound **3**.

5.2.4. Synthesis of compound **4**

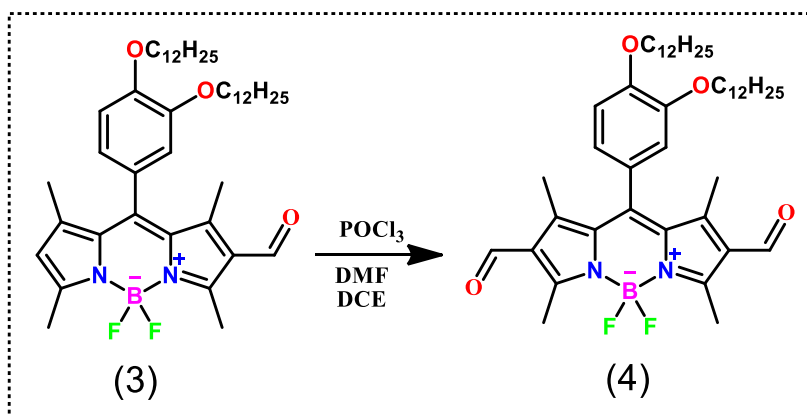


Figure 5.16: Synthesis of compound **4**.

In a two neck-round bottom flask placed on an ice bath, anhydrous DMF (0.5 mL) was added under argon. POCl_3 (0.5 mL) was added then it was allowed to stir for 30 minutes at room temperature. Pale yellow viscous solution was obtained. The compound **3** (60 mg, 0.08 mmol) was dissolved in 5 mL 1, 2-dichloroethane (DCE) then slowly added to the mixture with a dropping funnel. The mixture was set to 65 °C, stirred for an

additional 2 hours then cooled to room temperature. Brownish solution was poured into ice-cold saturated NaHCO₃ solution. It was warmed up to room temperature then extracted with water twice, dried over anhydrous Na₂SO₄. Suction filtration was applied then evaporated. It was purified by silica gel column chromatography using ethanol/DCM (v/v=1/100) as the eluent (orange solid, 30 mg, 62 %) (Figure 5.16).

FT-IR [(ATR) $\nu_{\text{maks}}/\text{cm}^{-1}$]: 2922-2854 (aliphatic C-H), 2720 (aldehyde C-H), 1673 (C=O) (Figure 5.17).

¹H-NMR (500 MHz, CDCl₃, ppm): δ 10.06 (s, 2H, CHO), 7.03 (d, 1H, Ar-CH, J=7.9 Hz), 6.76-6.79 (m, 2H, Ar-CH), 4.07 (t, 2H, OCH₂, J=6.7 Hz), 4.00 (t, 2H, OCH₂, J=6.7 Hz), 2.87 (s, 6H, CH₃), 1.85-1.91 (m, 2H, CH₂), 1.82 (s, 6H, CH₃), 1.25-1.53 (m, 38H, CH₂), 0.86-0.89 (m, 6H, CH₃) (Figure 5.18).

¹³C-NMR (125 MHz, CDCl₃, ppm): δ 185.69, 160.51, 150.58, 150.36, 148.43, 147.59, 132.23, 128.02, 127.99, 127.97, 125.31, 119.93, 113.97, 112.42, 69.66, 69.28, 31.94, 31.93, 29.72, 29.70, 29.64, 29.63, 29.60, 29.48, 29.42, 29.39, 29.37, 29.21, 29.19, 26.05, 25.96, 22.71, 22.70, 14.13, 13.75, 12.22. (Figure 5.19).

MALDI-TOF-MS (DHB): m/z Calcd: 748.83 g/mol, Found: 749.95 [M+H]⁺, 730.16 [M+H-F]⁺ (Figure 5.20).

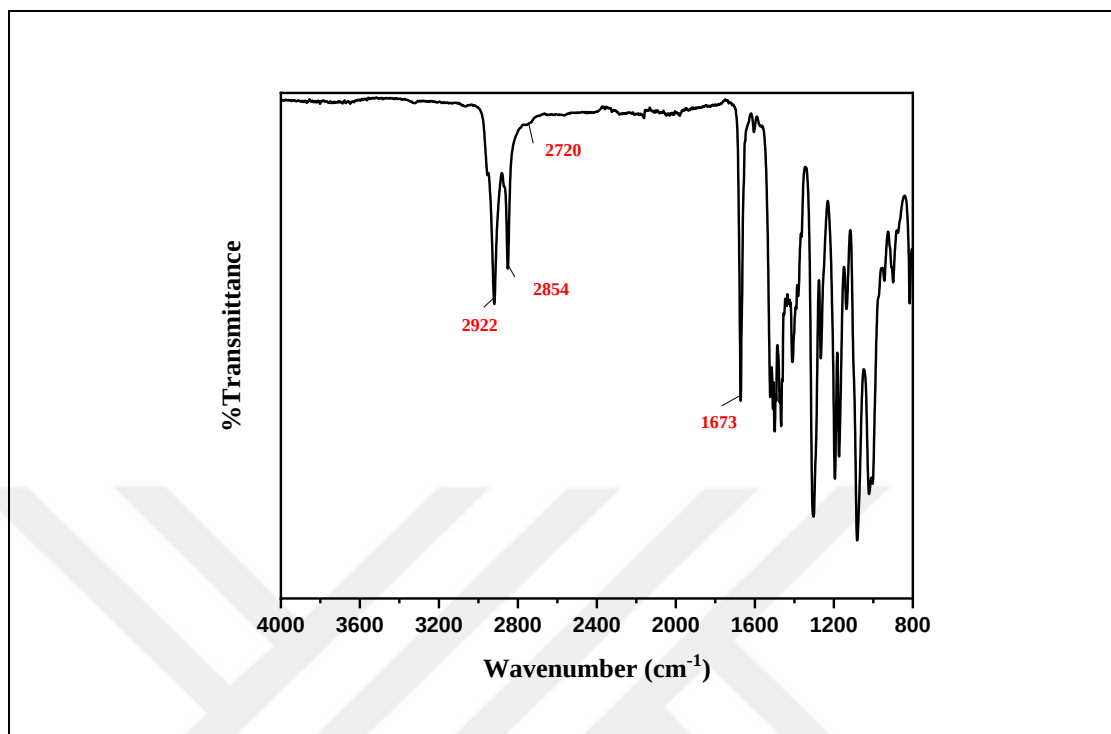


Figure 5.17: FT-IR spectrum of compound 4.

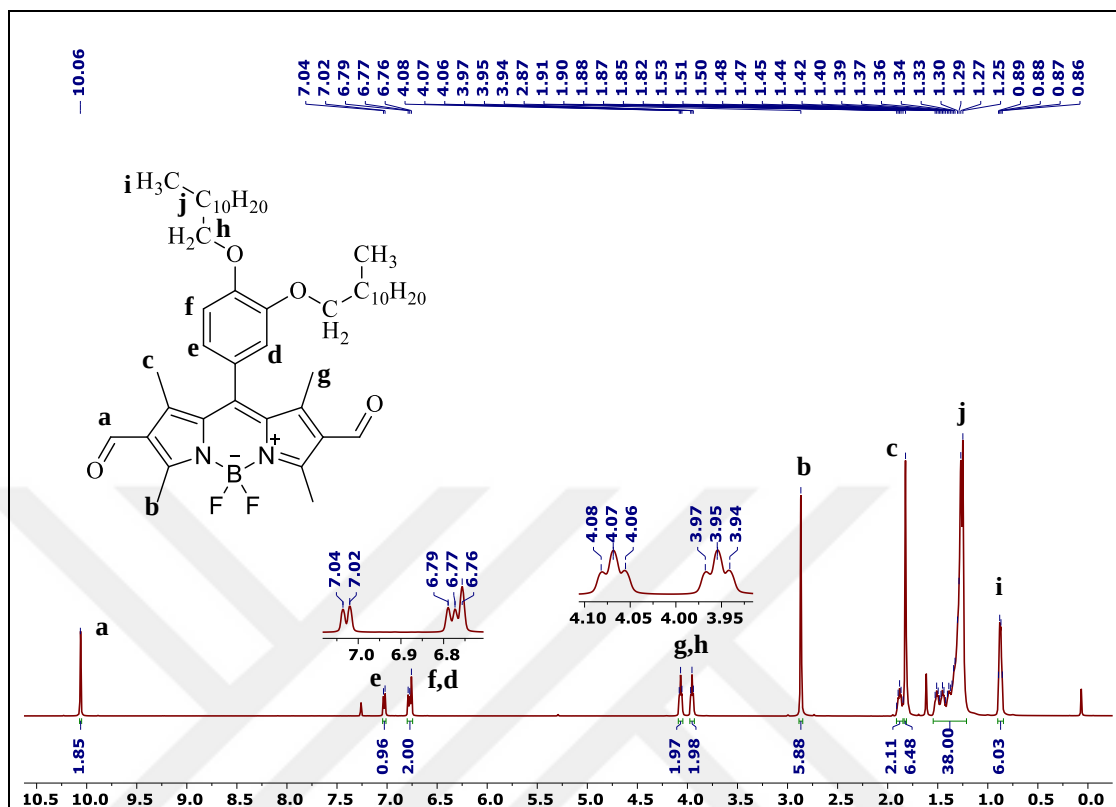


Figure 5.18: ^1H -NMR spectrum of compound 4.

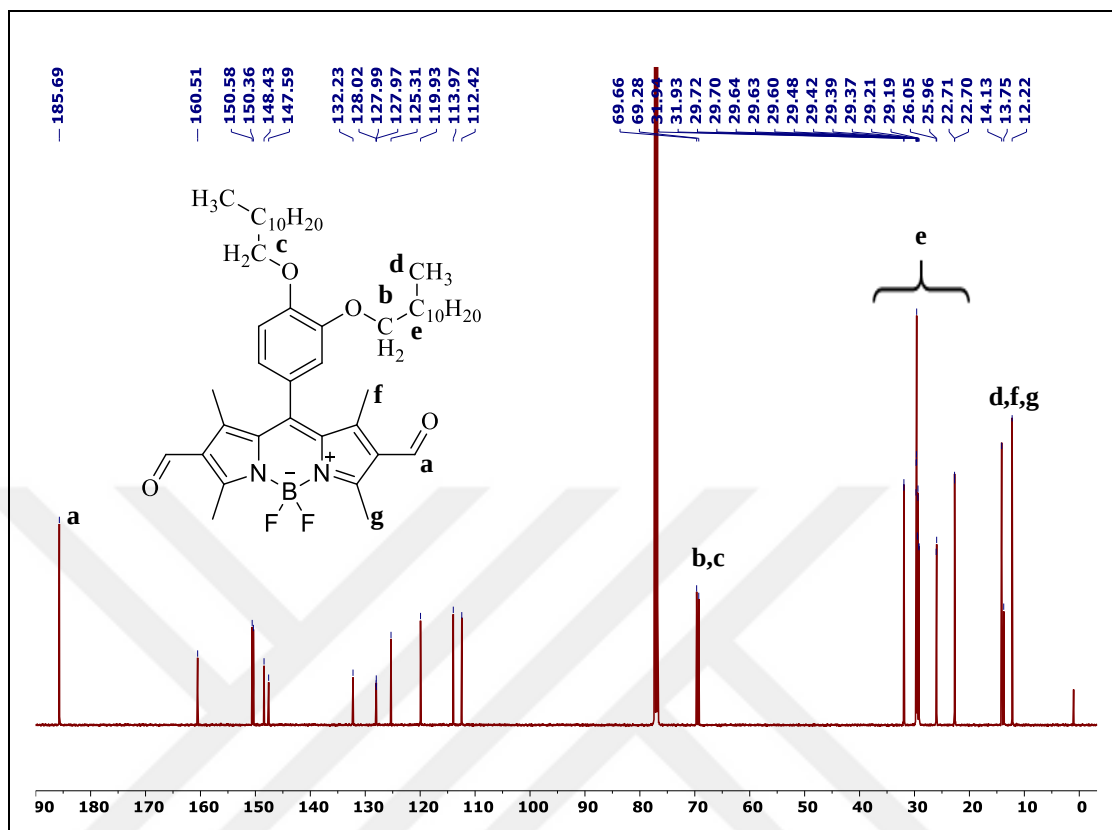


Figure 5.19: ^{13}C -NMR spectrum of compound 4.

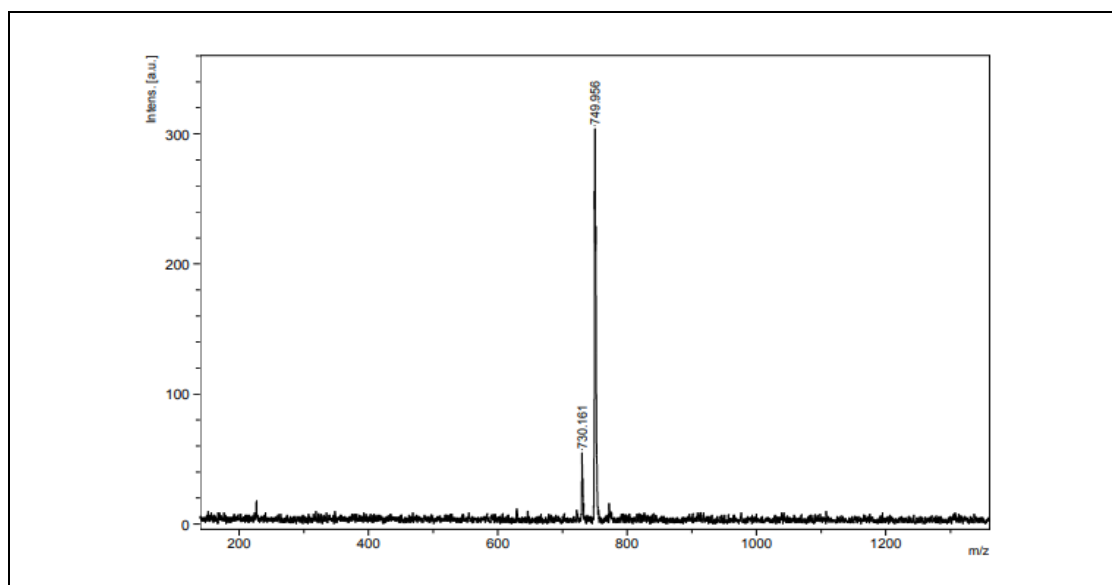


Figure 5.20: MALDI-TOF-MS spectrum of compound 4.

5.2.5. Synthesis of compound 5

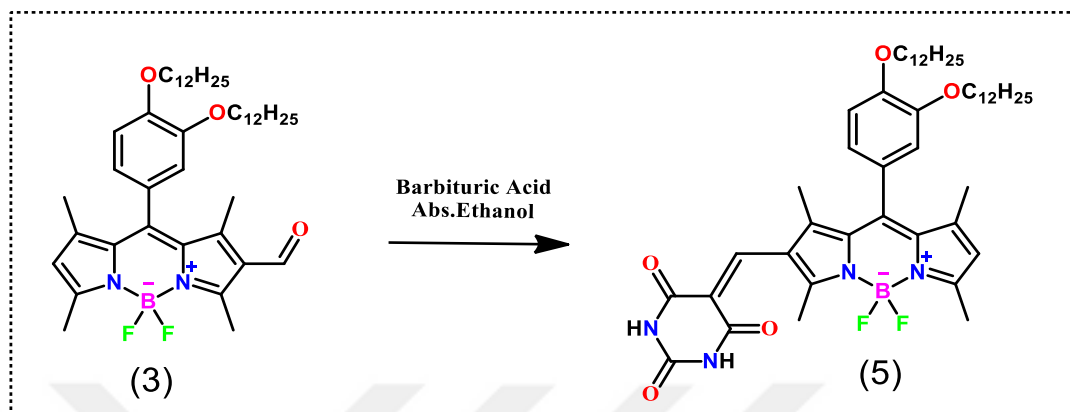


Figure 5.21: Synthesis of compound 5.

The compound **3** (73 mg, 0.1 mmol) and barbituric acid (132 mg, 1 mmol) were stirred in absolute ethanol (7 mL) under argon atmosphere. The reaction mixture was refluxed overnight. Obtained product was washed with water. Pink precipitate was gathered by filtration (39 mg, 46 %) (Figure 5.21).

FT-IR [(ATR) $\nu_{\text{maks}}/\text{cm}^{-1}$]: 3200-3054 (barbituric NH), 2917-2910 (aliphatic C-H) (Figure 5.22).

$^1\text{H-NMR}$ (500 MHz, CDCl_3 , ppm): δ 8.45 (s, 1H, CH), 8.35 (s, 1H, NH), 8.03 (s, 1H, NH), 7.01 (d, 1H, Ar-CH, $J=8.10$ Hz), 6.82 (m, 2H, Ar-CH), 6.17 (s 1H, CH), 4.07 (t, 2H, OCH_2 , $J=6.70$ Hz), 3.98 (t, 2H, OCH_2 , $J=6.70$ Hz), 2.63 (s, 3H, CH_3), 2.56 (s, 3H, CH_3), 1.81-1.92 (m, 4H, CH_2), 1.56 (s, 3H), 1.49 (s, 3H, CH_3), 1.28-1.33 (m, 36H, CH_2), 0.88-0.92 (m, 6H, CH_3) (Figure 5.23).

$^1\text{H-NMR}$ (500 MHz, $\text{CDCl}_3/\text{D}_2\text{O}$, ppm): δ 8.45 (s, 1H, CH), 7.01 (d, 1H, Ar-CH, $J=8.10$ Hz), 6.82 (m, 2H, Ar-CH), 6.17 (s 1H, CH), 4.07 (t, 2H, OCH_2 , $J=6.70$ Hz), 3.98 (t, 2H, OCH_2 , $J=6.70$ Hz), 2.63 (s, 3H, CH_3), 2.56 (s, 3H, CH_3), 1.81-1.92 (m, 4H, CH_2), 1.56 (s, 3H, CH_3), 1.49 (s, 3H, CH_3), 1.28-1.33 (m, 36H, CH_2), 0.88-0.92 (m, 6H, CH_3) (Figure 5.24).

^{13}C -NMR (125 MHz, CDCl_3 , ppm): δ 162.66, 161.33, 159.82, 156.49, 151.01, 150.08, 150.00, 148.80, 147.32, 143.07, 134.45, 131.42, 129.50, 126.05, 123.94, 120.34, 114.00, 113.83, 112.93, 69.55, 69.22, 31.94, 29.65, 29.62, 29.39, 29.26, 29.22, 29.00, 26.07, 25.98, 22.70, 18.44, 15.12, 14.98, 14.84, 14.21, 14.13, 14.08. (Figure 5.25).

MALDI-TOF-MS (DIT): m/z: Calcd: 830.89 g/mol, Found: 830.75 $[\text{M}]^+$, 812.58 $[\text{M}+\text{H}-\text{F}]^+$ (Figure 5.26).

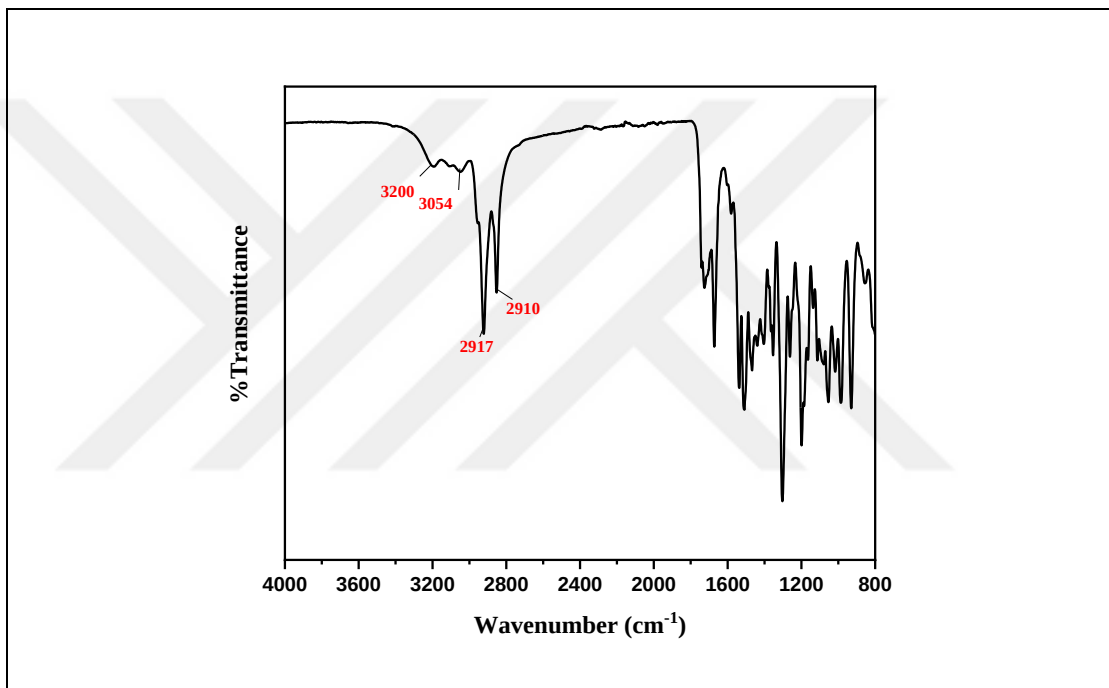


Figure 5.22: FT-IR spectrum of compound 5.

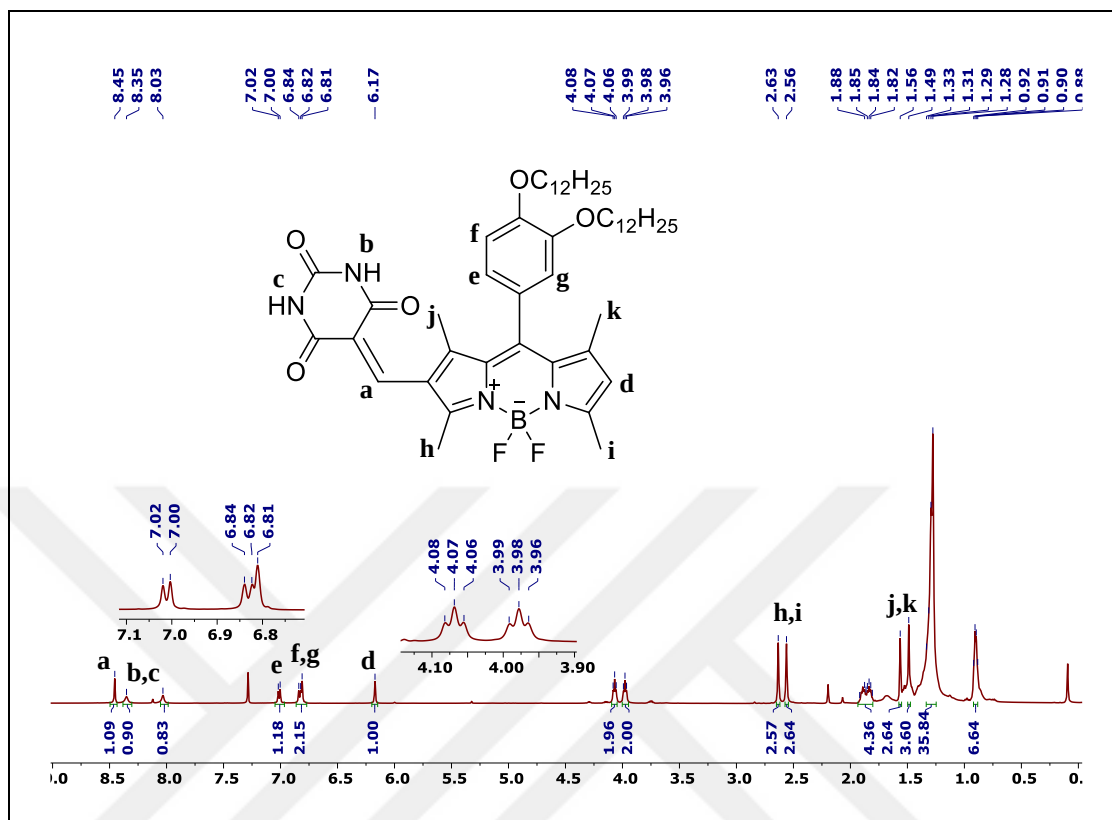


Figure 5.23: ¹H-NMR spectrum of compound 5.

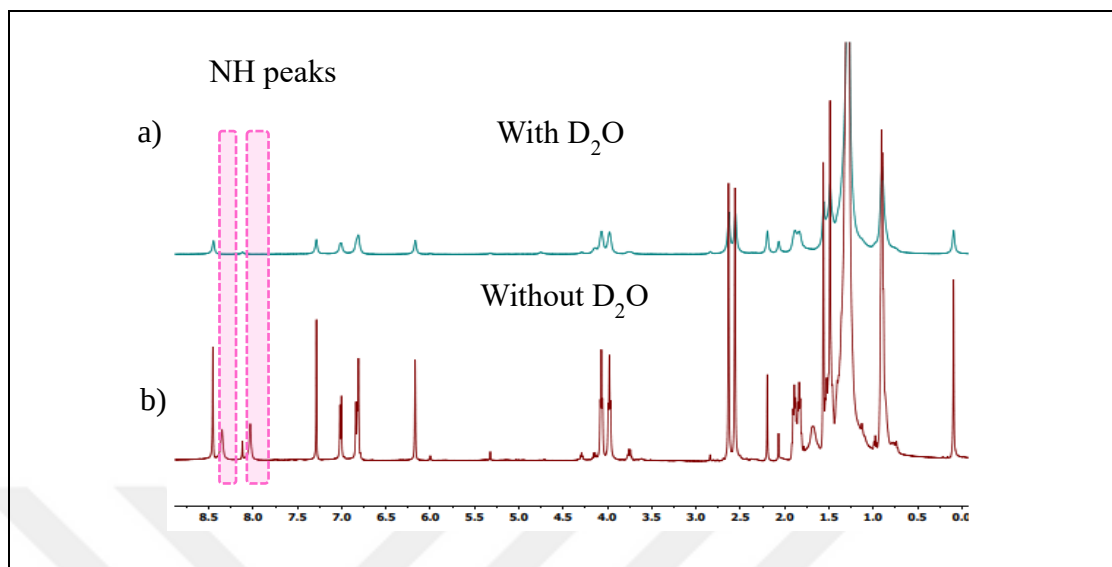


Figure 5.24: ^1H -NMR spectrum of compound 5 (a) in CDCl_3 and D_2O , (b) in CDCl_3 .

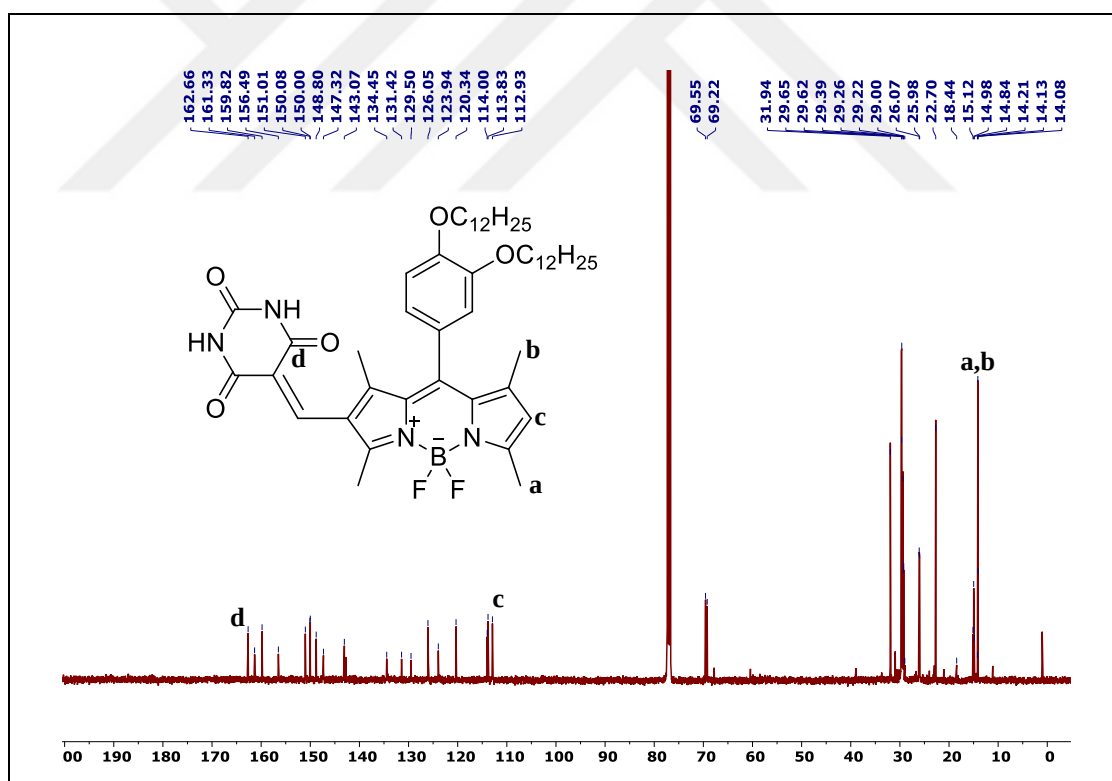


Figure 5.25: ^{13}C -NMR spectrum of compound 5.

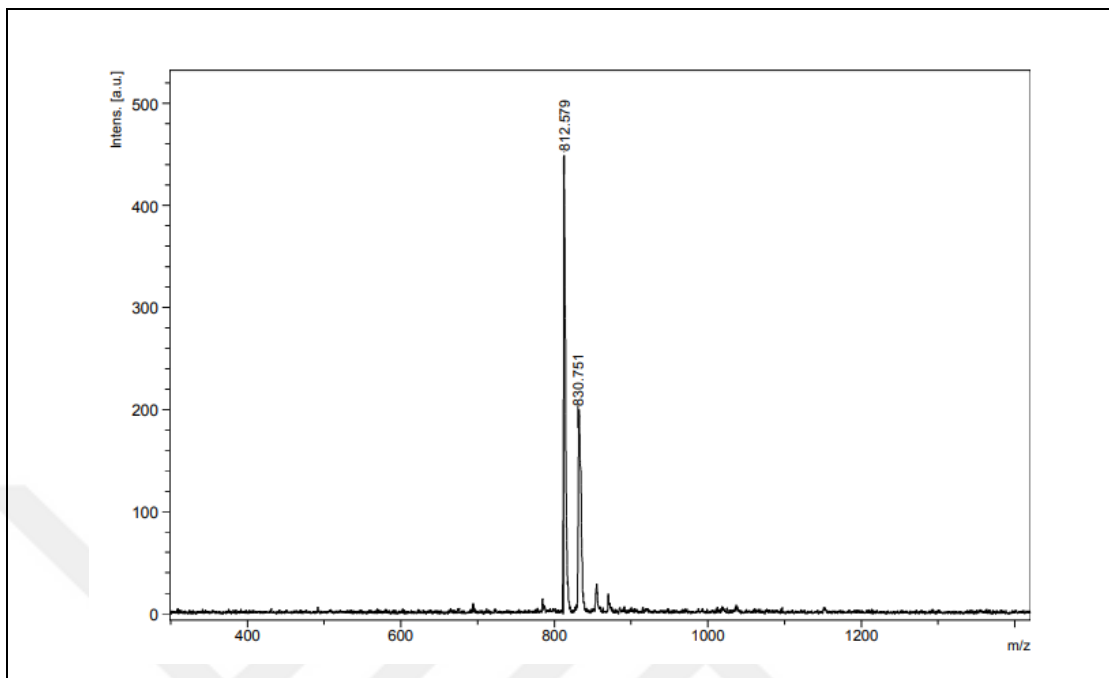


Figure 5.26: MALDI-TOF-MS spectrum of compound 5.

5.2.6. Synthesis of compound 6

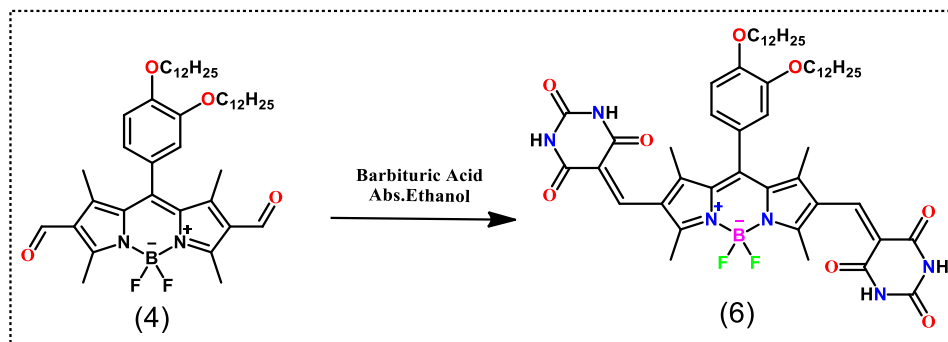


Figure 5.27: Synthesis of compound 6.

The compound 4 (30 mg, 0.04 mmol) and barbituric acid (56 mg, 0.4 mmol) were stirred in absolute ethanol (10 mL) under argon atmosphere. The reaction mixture was refluxed overnight. Obtained product was washed with water. Purple precipitate was gathered by filtration (31 mg, 79 %) (Figure 5.27).

FT-IR [(ATR) $\nu_{\text{maks}}/\text{cm}^{-1}$]: 3201-3027 (barbituric NH), 2923-1153 (aliphatic C-H) (Figure 5.28).

¹H-NMR (500 MHz, THF-*d*₈, ppm): δ 10.43 (s, 2H, NH), 10.29 (s, 2H, NH), 8.20 (s, 2H), 7.10 (d, 1H, Ar-CH, J = 8.3 Hz), 7.03 (s, 1H, Ar-CH), 6.90-6.92 (m 1H, Ar-CH), 4.04 (t, 2H, OCH₂, J = 6.5 Hz), 3.98 (t, 2H, Ar-CH, J = 6.5 Hz), 2.48 (s, 6H, CH₃), 1.77-1.83 (m, 4H, CH₂), 1.53 (s, 6H, CH₃), 1.29-1.34 (m, 36H, CH₂), 0.87-0.90 (m, 6H, CH₃) (Figure 5.29).

¹H-NMR (500 MHz, THF-*d*₈/D₂O, ppm): δ 8.20 (s, 2H), 7.10 (d, 1H, Ar-CH, J = 8.3 Hz), 7.03 (s, 1H, Ar-CH), 6.90-6.92 (m 1H, Ar-CH), 4.04 (t, 2H, OCH₂, J = 6.5 Hz), 3.98 (t, 2H, Ar-CH, J = 6.5 Hz), 2.48 (s, 6H, CH₃), 1.77-1.83 (m, 4H, CH₂), 1.53 (s, 6H, CH₃), 1.29-1.34 (m, 36H, CH₂), 0.87-0.90 (m, 6H, CH₃) (Figure 5.30).

¹³C-NMR (125 MHz, THF-*d*₈, ppm): δ 162.31, 160.62, 158.09, 150.57, 150.44, 149.68, 149.60, 145.36, 144.32, 143.99, 132.24, 127.63, 126.22, 120.19, 119.76, 113.80, 113.24, 68.93, 68.71, 31.91, 29.71, 29.68, 29.65, 29.36, 26.12, 26.07, 24.83, 22.59, 13.92, 13.46, 13.25. (Figure 5.31).

MALDI-TOF-MS (DIT): m/z Calcd. 968.97 g/mol, Found: 969.19 [M]⁺, 992.19 [M+Na]⁺, 950.26 [M-F]⁺ (Figure 5.32).

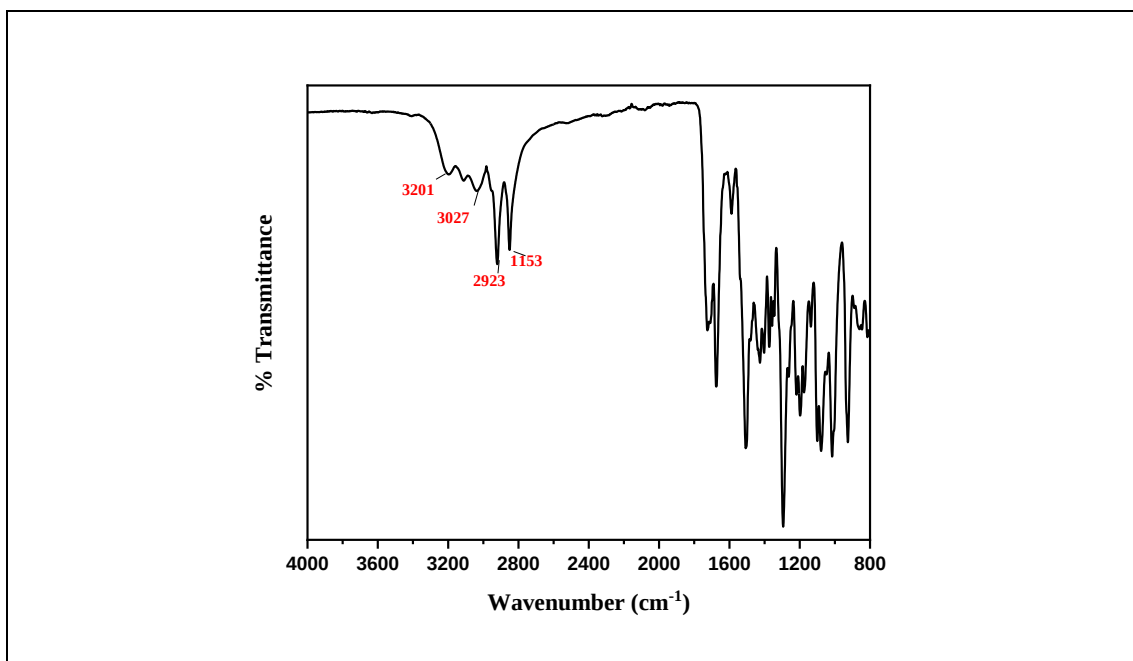


Figure 5.28: FT-IR spectrum of compound **6**.

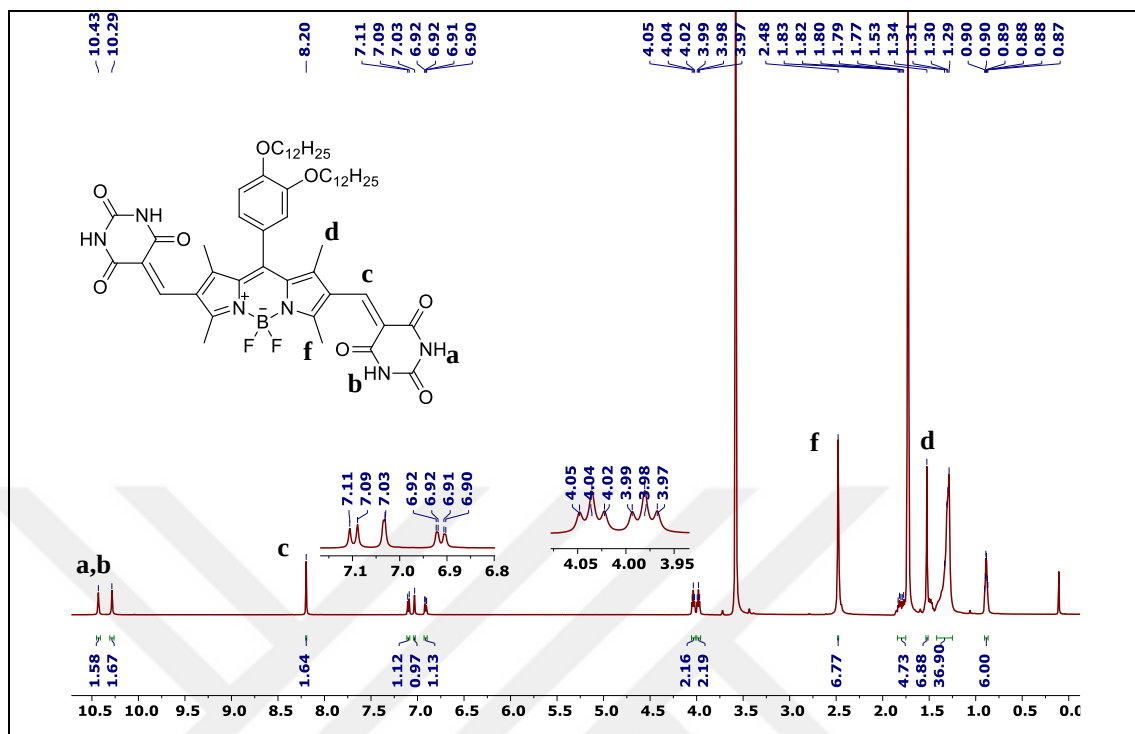


Figure 5.29: ^1H - NMR spectrum of compound **6**.

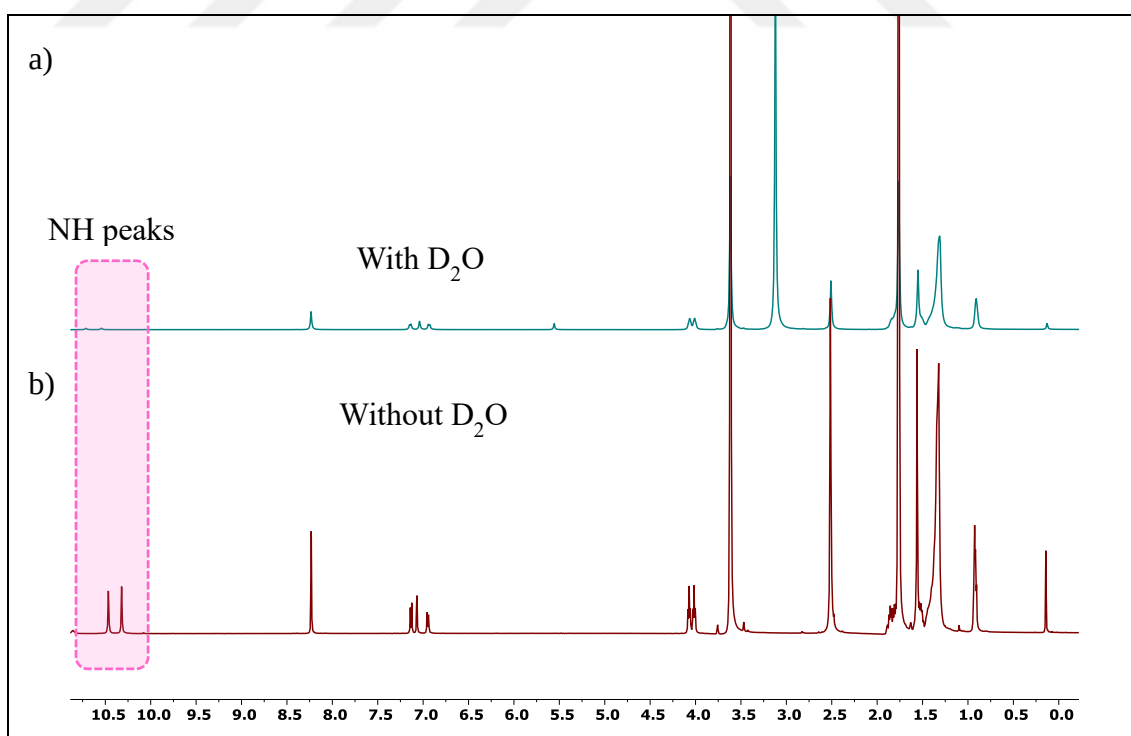


Figure 5.30: ^1H - NMR spectrum of compound **6** in (a) THF-d_8 and D_2O , (b) in THF-d_8 .

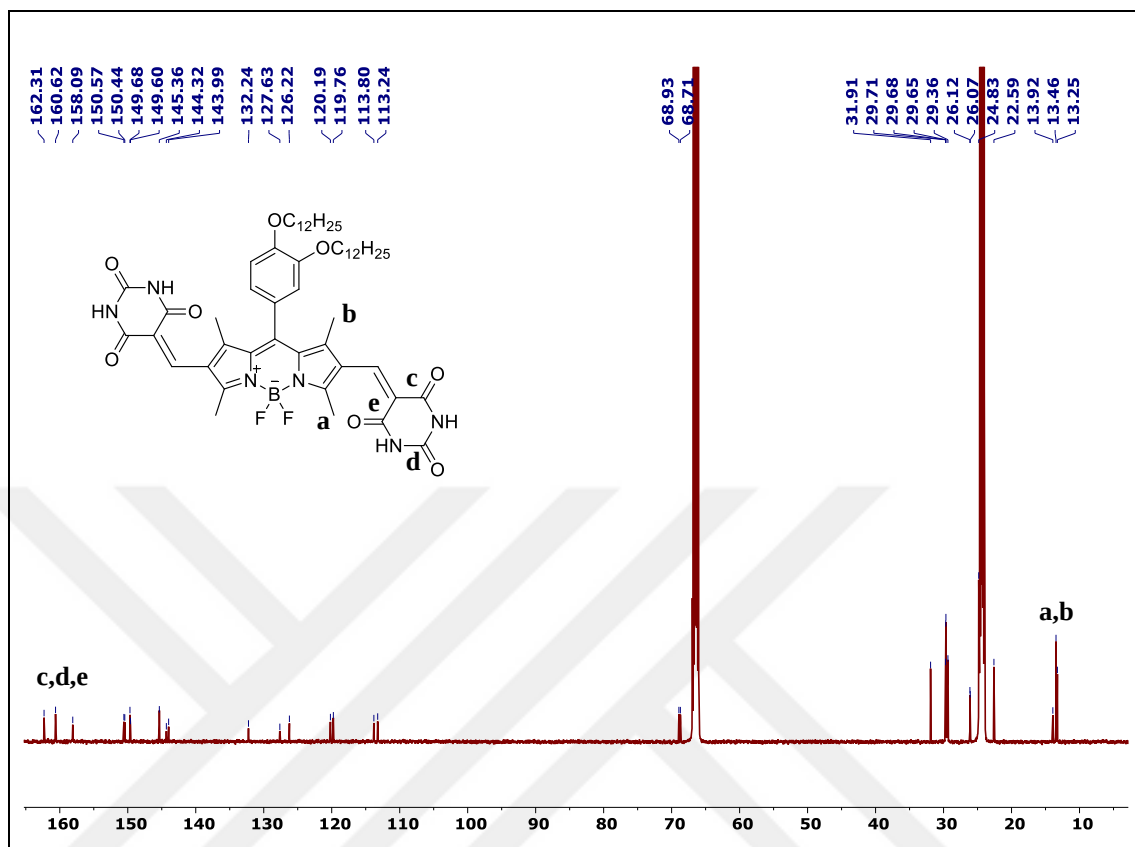


Figure 5.31: ^{13}C - NMR spectrum of compound 6.

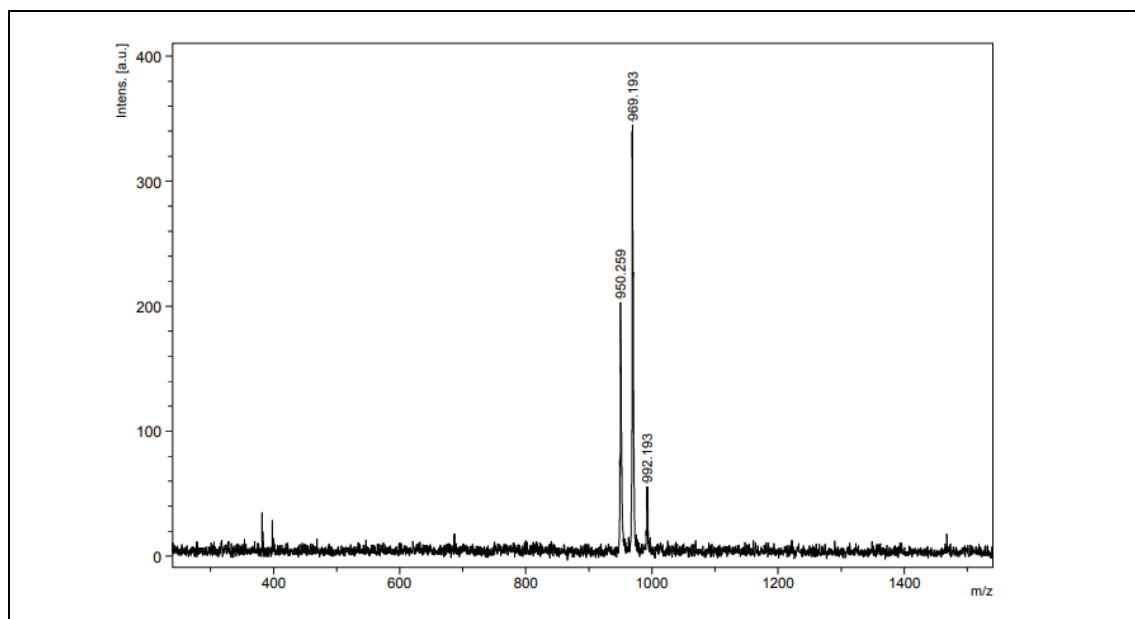


Figure 5.32: MALDI-TOF-MS spectrum of compound 6.

5.3. Absorption and Emission Spectroscopy of the Synthesized Compounds

All products were characterized with FT-IR spectroscopy, nuclear magnetic resonance spectrometry, mass spectroscopy and UV-Vis. According to UV-Vis data, compound **2**, **3**, **4**, **5**, **6** show narrow spectra with two maxima which are a shoulder and a sharp peak corresponding to allowed S_0-S_1 ($\pi-\pi^*$) transitions of π conjugated delocalized core and their vibrational outstanding structures at 500, 497, 504, 534, 564 nm as expected since BODIPY dyes are characterized by strong absorption bands between 500-580 nm. There are second absorption peaks between 330-470 nm that are attributed as transitions from ground state to higher excited state S_0-S_2 . Compound **5** and **6** are getting conjugated because of substitution of barbituric acid. The extension of the conjugation system causes shifts in the spectrum toward longer wavelengths (lower frequency, lower energy) absorptions as expected. Compound **5** bearing only one barbituric acid substituted at 2 position of a BODIPY chromophore showed 34 nm red-shifted absorption while compound **6** bearing two barbituric acids at 2-6 positions showed 64 nm red-shifted absorption in THF comparing compound **2** having only meso substituted BODIPY core. There were many reports that confirm that π -system extension contributes to increased delocalization in structures. Powerful π -delocalization was achieved within two five-membered rings, central six-membered ring and two barbituric six-membered ring structures displaying bathochromic shift (Figure 5.33).

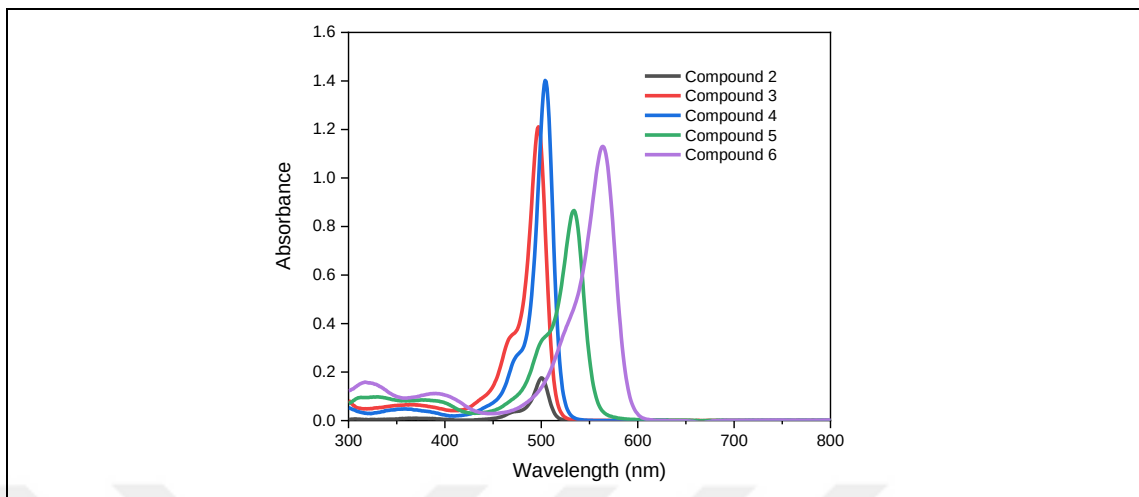


Figure 5.33: UV-Vis spectra of **2-6** compounds in THF (10 μ M).

Their molar absorptivities were calculated in THF as 17 900, 133 100, 132 242, 91 600 and 115 757 $\text{L}\cdot\text{mol}^{-1}\cdot\text{cm}^{-1}$, respectively because all products are highly soluble in THF. Generally, BODIPYs administrate small bandwidth and immense molar extinction coefficient between 76 600 and 117 300 $\text{M}^{-1}\text{cm}^{-1}$ is unique for planar aromatic structure of a rigid BODIPY core with a low degree of conformational freedom (Figure 5.34).

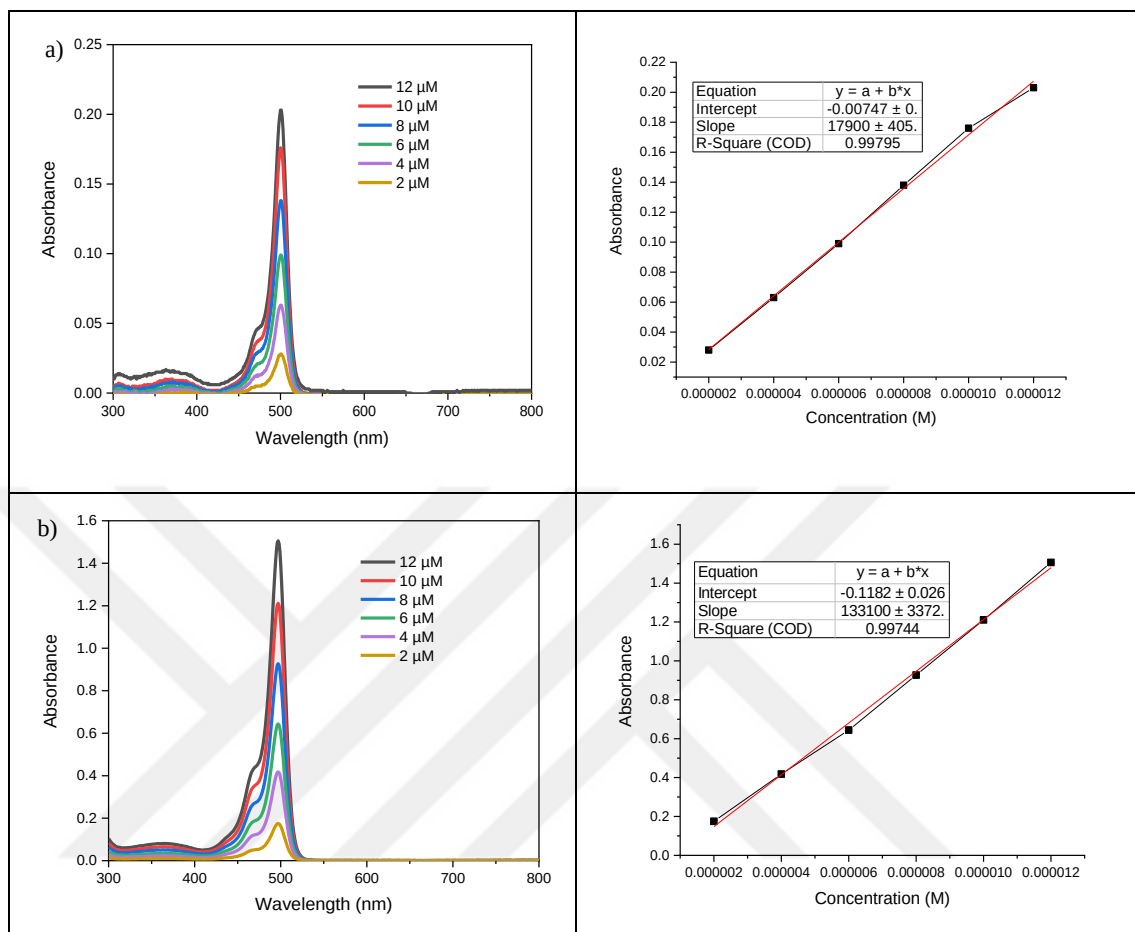


Figure 5.34: UV-Vis spectra of compounds (a) 2, (b) 3, (c) 4, (d) 5 and (e) 6 in THF at different concentrations.

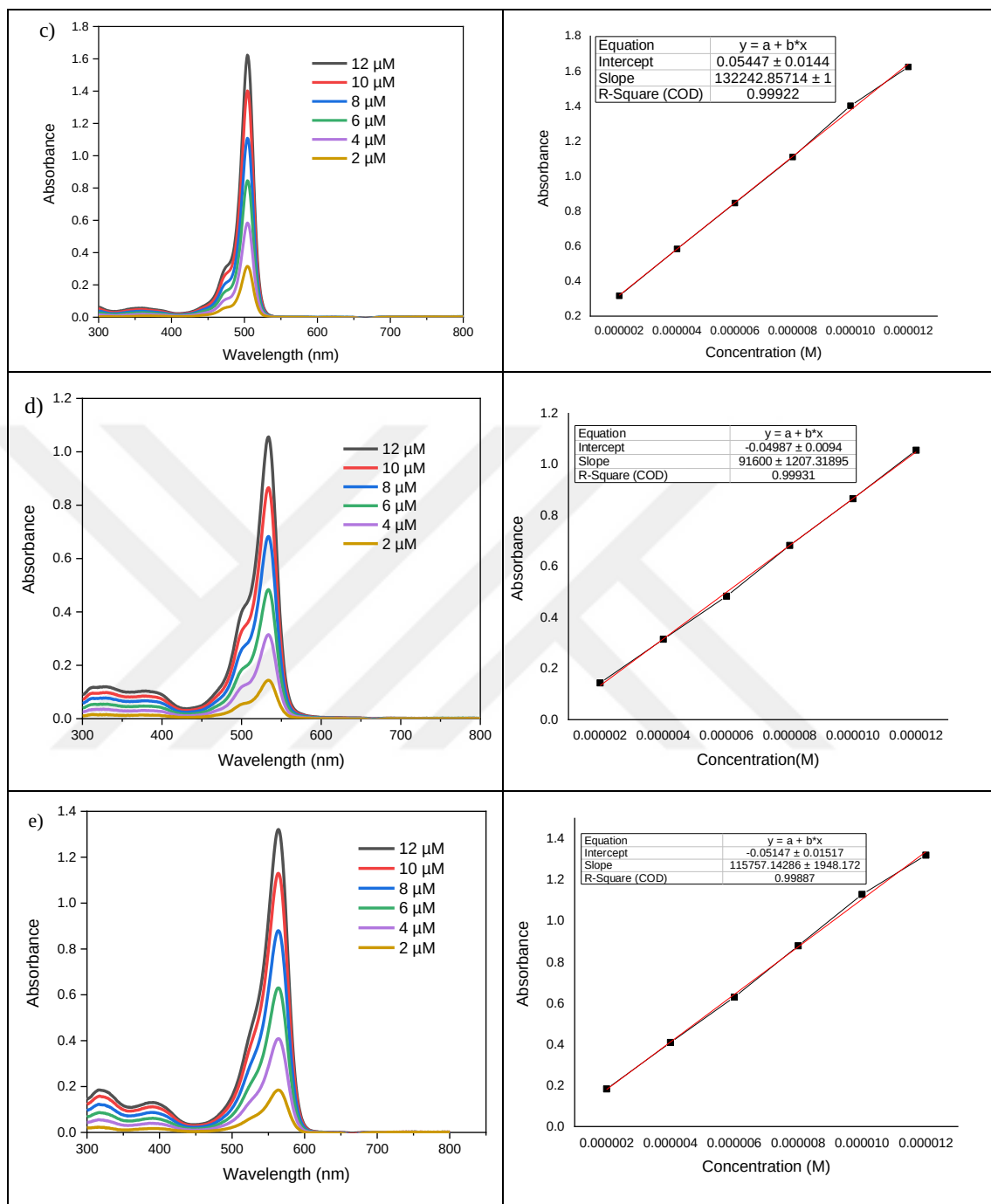


Figure 5.34: Continue.

As shown in Figure 5.35, absorption of compound **5** was obtained at 534 nm in THF which is in the green region of the spectrum so its complementary color was reddish. Absorption of compound **6** was seen at 564 nm in THF which is in the yellow region of the spectrum so its complementary color was pink.

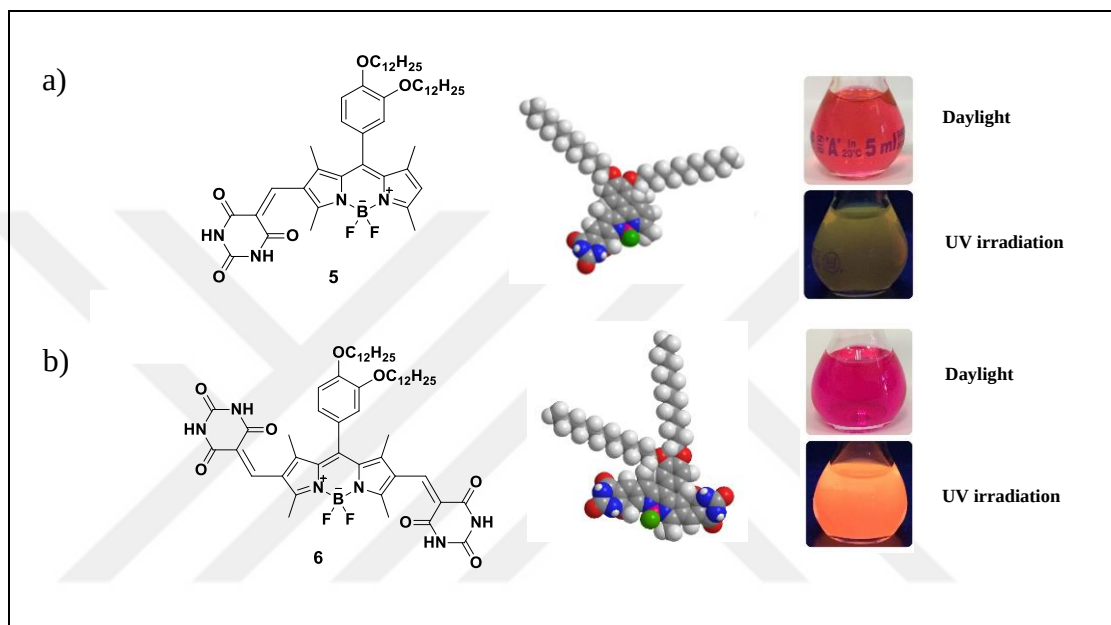


Figure 5.35: Schematic representation of (a) compound **5** (C₄₈H₆₉BF₂N₄O₅) and (b) compound **6** (C₅₃H₇₁BF₂N₆O₈) with the photos of THF solution (10⁻⁴ M) under daylight and UV lamp (λ_{ex}: 365 nm). Carbon, oxygen, nitrogen, boron, fluorine and hydrogen atoms are represented in gray, red, blue, green, pink and pale gray, respectively.

In Figure 5.36, UV-Vis and fluorescence spectra of solutions of compounds **3**, **4**, **5**, **6** were obtained. For compound **3**, fluorescence maximum intensity was found at 515 nm and Stokes shift as 18 nm, for compound **4**, at 505 nm with 15 nm Stokes shift. Compound **5** showed two maximum peaks at 510 and 554 nm in fluorescence spectra. For compound **6** gave maximum intensity at 590 nm with 26 nm Stokes shift.

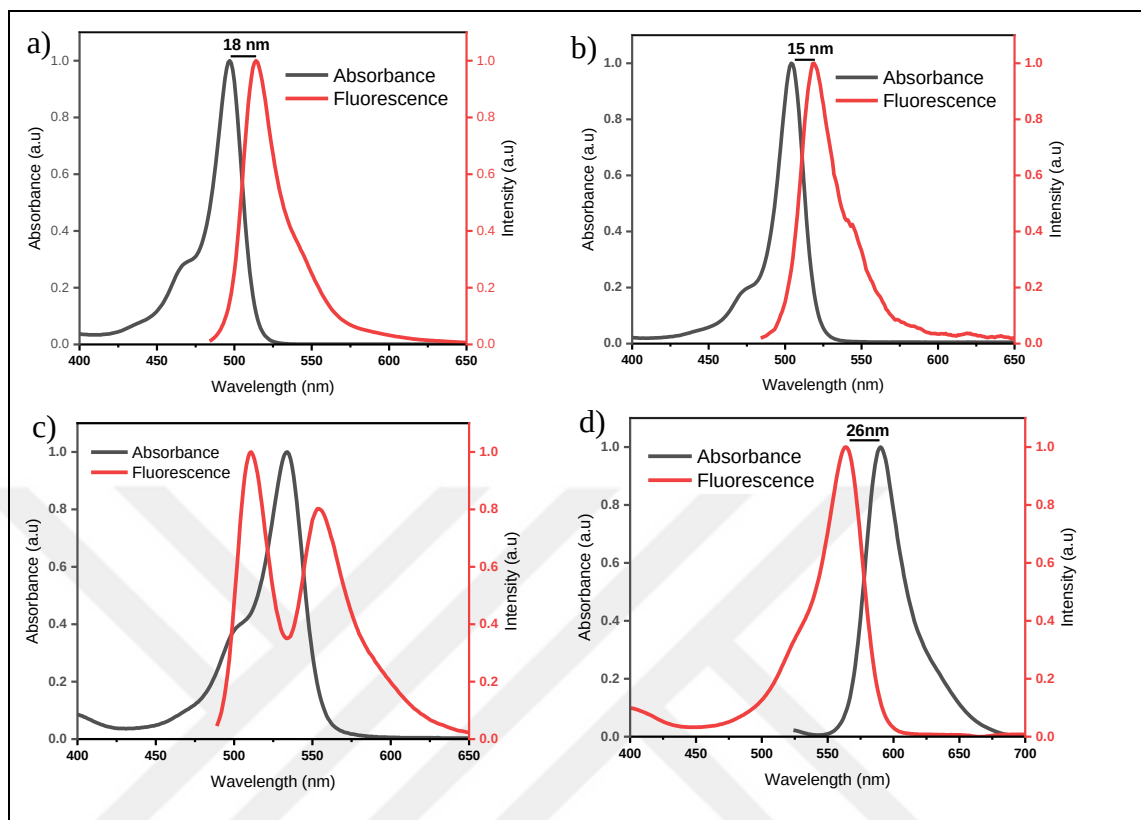


Figure 5.36: UV-Vis and fluorescence spectra of solutions of compound **3** ($\lambda_{\text{ex}}=470$ nm), **4** ($\lambda_{\text{ex}}=470$ nm), **5** ($\lambda_{\text{ex}}=475$ nm), **6** ($\lambda_{\text{ex}}=510$ nm), (10^{-5} M) in THF.

Photophysical properties of compound **5** and **6** were examined in different solvents to investigate if there was any change in solutions depending on polarities (Figure 5.37a and 5.38a). Main absorption bands of compounds **5** and **6** were slightly influenced by solvent polarities (Table 5.3 and 5.4). Absorption of compound **5** was hardly blue-shifted when solvent was used from carbon tetrachloride and chloroform ($\lambda=542$ nm) to acetonitrile ($\lambda=528$ nm). The data are coherent with behavior of BODIPY dyes. According to literature [104], BODIPY dyes administrate blue-shifted absorption from non-polar solvent to polar one. Carbon tetrachloride and chloroform are less polar than acetonitrile so blue-shifted absorption peak was observed in acetonitrile if the solution is compared with carbon tetrachloride and chloroform. Compound **6** dissolved in a few solvents, contrast to compound **5**, which were NMP, acetone, ethanol, ethyl acetate, THF and 1,4-dioxane and it showed blue-shifted absorption peaks from 1,4-dioxane ($\lambda=565$) to NMP ($\lambda=556$). 1,4-dioxane is less polar than NMP so a 9 nm hypsochromic shift was observed that is coherent with the literature. As explained before, extension of conjugation tends to produce longer wavelength shifts in the spectrum. Therefore, compound **6** demonstrates absorption peaks at higher wavelengths. These behaviors were observed in fluorescence emission photographs in various solvents, different tones of pink and fluorescent emission can be seen simply by naked eyes (Figure 5.37b and 5.38b). In polar solvents, fluorescence color of solutions was observed as green, in non-polar solvents displayed red color. The results are coherent to the absorption peaks in the UV-Vis spectrum.

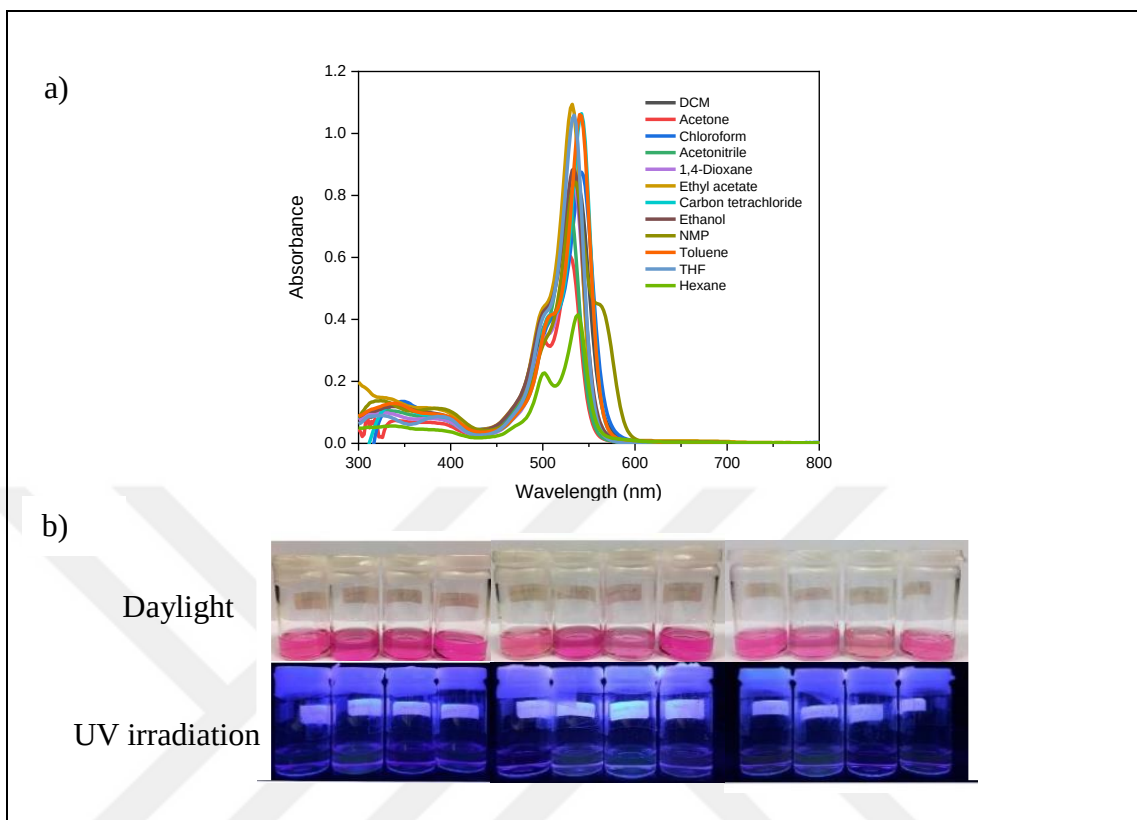


Figure 5.37: Solvent dependent UV-Vis studies of (a) compound **5** in different solvents ($c=1 \times 10^{-5}$ M). The photos of (b) solutions under daylight and UV lamp (λ_{ex} : 365 nm) in ethanol, toluene, DCM, chloroform, acetonitrile, carbon tetrachloride, hexane, NMP, THF, 1,4-dioxane, acetone and ethyl acetate, respectively.

Table 5.3: Absorption (λ_{max}) of compound **5** in different solvents.

Solvents	Absorbance	λ_{max}
Acetonitrile	0.791	528
Acetone	0.603	530
Ethyl Acetate	1.094	532
Ethanol	0.886	534
NMP	0.843	534
THF	1.059	534
1,4-dioxane	0.831	534
DCM	0.833	538
Hexane	0.415	538
Toluene	1.061	540
Chloroform	0.857	542
Carbon tetrachloride	1.064	542

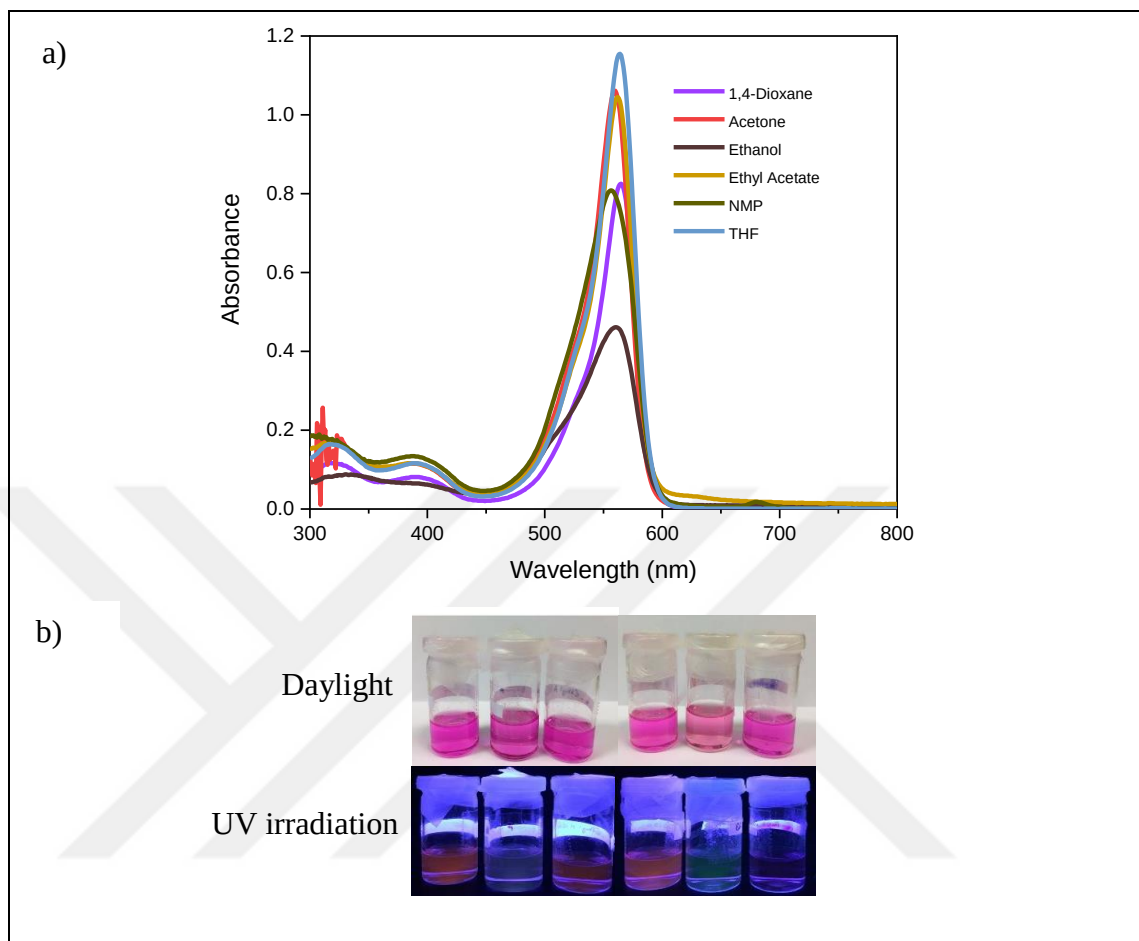


Figure 5.38: Solvent dependent UV-Vis studies of (a) compound **6** in different solvents ($c=1 \times 10^{-5}$ M). The photos of (b) solutions under daylight and UV lamp (λ_{ex} : 365 nm) in THF, NMP, ethyl acetate, 1,4-dioxane, ethanol and acetone, respectively.

Table 5.4: Absorption (λ_{max}) of compound **6** in different solvents.

Solvents	Absorbance	λ_{max}
NMP	0.808	556
Acetone	1.061	560
Ethanol	0.461	560
Ethyl Acetate	1.045	562
THF	1.155	564
1,4-dioxane	0.825	565

6. RESULTS AND DISCUSSION

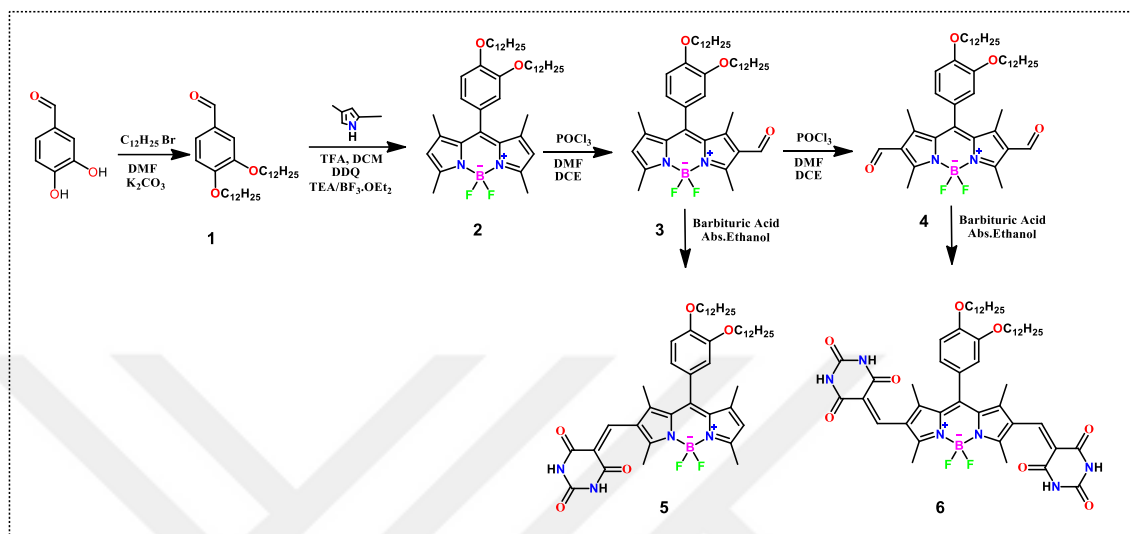


Figure 6.1: General synthesis procedures of the molecules (1-6).

Supramolecular structures have been gained attention because of their unique properties derived from their reversible and dynamic self-assembly, like stimuli responsiveness and self-healing. They are outstanding for various research areas such as biomedicine and optoelectronics thanks to their astonishing photophysical properties. However, controlling molecular interactions during self-assembly duration is a main source of problems causes unexpected photophysical characters. To obstacle this issue sterically bulky substituents can be introduced chromophore's core. Moreover alkyl groups at meso position of a BODIPY core provide good solubility in organic solvents for further modifications. And also to have hydrogen bonded mediated self-assembled structures, long alkyl rings are needed. Due to these reasons, bulky 3,4-dihydroxybenzaldehyde was alkylated with 1-bromododecane to obtain compound **1** according to the literature [102] (Figure 6.1). Meso-substituted BODIPY core (compound **2**) was obtained by condensation reaction between 2, 4-dimethylpyrrole and synthesized aromatic aldehyde derivative compound **1** in the presence of trifluoroacetic acid as an acid catalyst. In this step purification was not applied because obtained product was not stable. DDQ was used as an oxidant then dipyrin was obtained reacted with boron trifluoride

diethyl etherate in basic medium provided by trimethylamine to pull off acidic hydrogen from nitrogen atoms. Fluorescent orange compound was obtained.

To have a high-degree of internal order self-assembled structures, specific functional groups such as barbituric acid which has ability to engage in directional non-covalent forces like hydrogen bonding was preferred to add to our molecular design. Thanks to barbituric acid's intermolecular hydrogen bonding (N-H----O) ability demonstrates high aggregation capability is observed in many literatures. Formyl groups were substituted to BODIPY core so barbituric acid can get involved in Knoevenagel condensation reaction. 2-6 positions are less positively charged so they can be exposed to electrophilic attack. Firstly, tetramethyl BODIPY core was functionalized with Vilsmeier reagent to have 2-formyl BODIPY (compound **3**) [103]. Compound **4** having diformyl groups in 2-6 positions of BODIPY core was obtained using Vilsmeier reagent and compound **3**. By reason of Knoevenagel condensation which is a type of nucleophilic addition reaction mono (compound **5**) and dibarbituric acid (compound **6**) substituted products were obtained.

Over the last few years, a rising interest has been dedicated to the comprehensive analysis of thermodynamic vs kinetic pathways in self-assembled structures for a great range of compounds. To establish control over competing pathways can be succeeded through various approaches like external stimuli application and molecular design methods. For this reason, regulating molecular packing of chromophores' assembly suggests an encouraging strategy to adjust photochemical and photophysical properties of pigments. Because of this, supramolecular organizations with special functions and applications could be acquired. BODIPY chromophores enable the examination of the self-assembly process in both nonpolar and polar media. BODIPY core not only permits to tune electronic and optical properties but also initiates diverse non-covalent interactions and governs solubility in different solvents. It has been demonstrated that according to substituents of BODIPY core, structures tend to constitute either parallel J-aggregates with red-shifted absorption and blue-shifted absorption antiparallel H-aggregates [106]. As explained in the previous part, there is change observed in ethanol solutions as color, UV-Vis and fluorescence data depending on day. For both solutions, hypsochromic shift is

obtained in UV-Vis which indicates H-type of aggregation for a BODIPY derivative. To support this, bandgap and DLS data are used.

In the light of UV-Vis data, in ethanol solutions, color change was observed for both compounds' solutions depending on time as a day. Therefore, data were collected as the day passed. According to Figure 6.2 compounds **5** and **6** were dissolved in ethanol and there was a color change observed day by day from pink to orange for both of them (Figure 6.2 g-h). Their ability to self-assemble was investigated by common spectroscopic instruments such as UV-Vis and fluorescence. For compound **5**, UV-Vis absorption band was observed at 534 nm for the first day, after 15 days a gradual increase of aggregation band with $\lambda_{\text{max}}=505$ nm totally 29 nm blue-shifted was obtained. For compound **6**, first day absorption at 553 nm after 15 days, 45 nm blue-shift with $\lambda_{\text{max}}=508$ nm was observed absorption spectra. Fluorescence maximum was obtained for **5** as 514 nm for **6** as 518 nm and their narrow Stokes shifts 9 nm and 10 nm were observed respectively (Figure 6.2 e-f). According to fluorescent spectroscopy data, there were gradual increases fluorescence abilities about 170 times so it could be assumed that compounds **5** and **6** form antiparallel H-type aggregates causing emission enhancement that contrasts with quenched aggregation that is typical for BODIPY dyes.

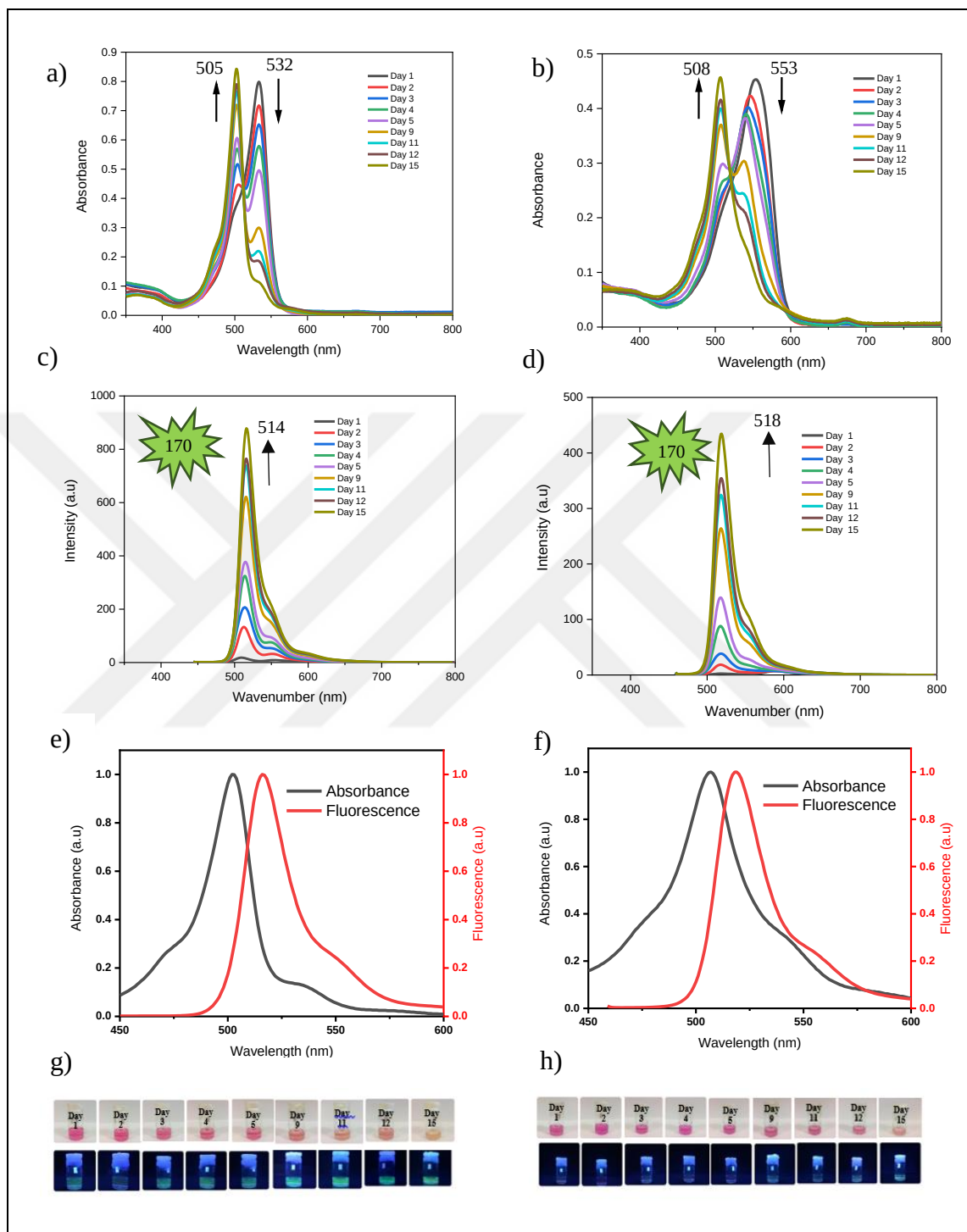


Figure 6.2: UV-Vis spectra of compounds (a) **5** and (b) **6** in ethanol (10^{-5} M) day by day.

Fluorescence spectra of (c) **5** ($\lambda_{\text{ex}}=435$ nm) and (d) **6** ($\lambda_{\text{ex}}=455$ nm) compounds in ethanol (10^{-5} M) day by day. Stokes shift of (e) **5** and (f) **6**. The photos of compounds (g) **5** and (h) **6** in ethanol solutions (10^{-5} M) on different days under daylight and UV lamps (λ_{ex} : 365 nm).

Band gaps were calculated for compound **5** and **6** via UV-Vis in ethanol, on the first day they are found as 2.13 eV and 2.05 eV (Figure 6.3 a,b), after a month, they are found as 2.33 eV and 2.22 eV (Figure 6.3 c,d) which implies band gaps are increasing as expected since there is a blue-shifted absorption peak is obtained for both solutions so the results are consistent with UV-Vis absorption spectrum.

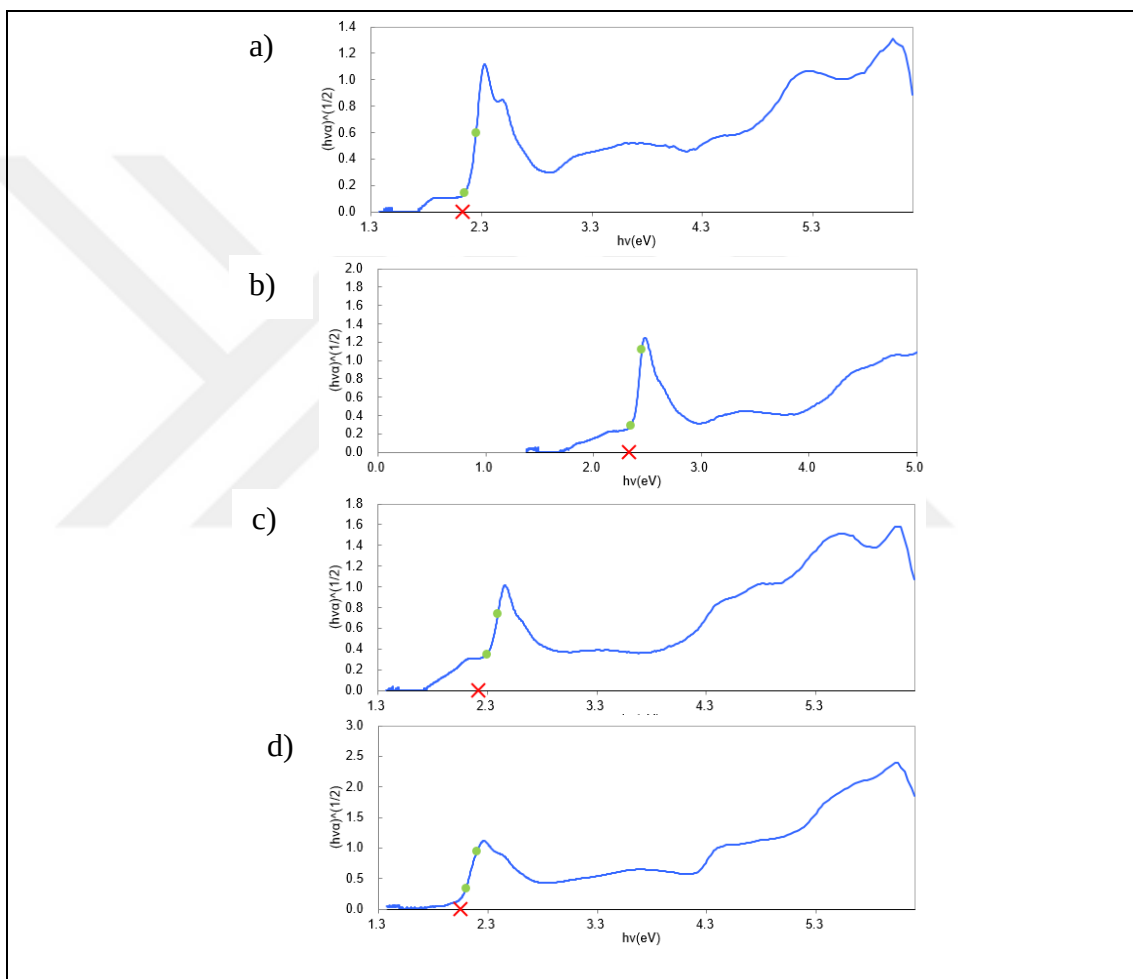


Figure 6.3: Bandgap data through UV-Vis on the first day (a) for compound **5** (b) for compound **6** and after a month (c) for **5** and (d) for **6** in ethanol (10^{-5} M).

DLS administered size distribution for compound **5** and **6** ($c=10^{-5}$ M) at RT (Figure 6.4). Compounds were measured in THF on the first day and after two weeks data were obtained in ethanol. There is absence of any huge aggregates in THF for both of them; on the other hand in ethanol, they reveal detectable large aggregates (diameter greater than 10 nm) confirming aggregation formation.

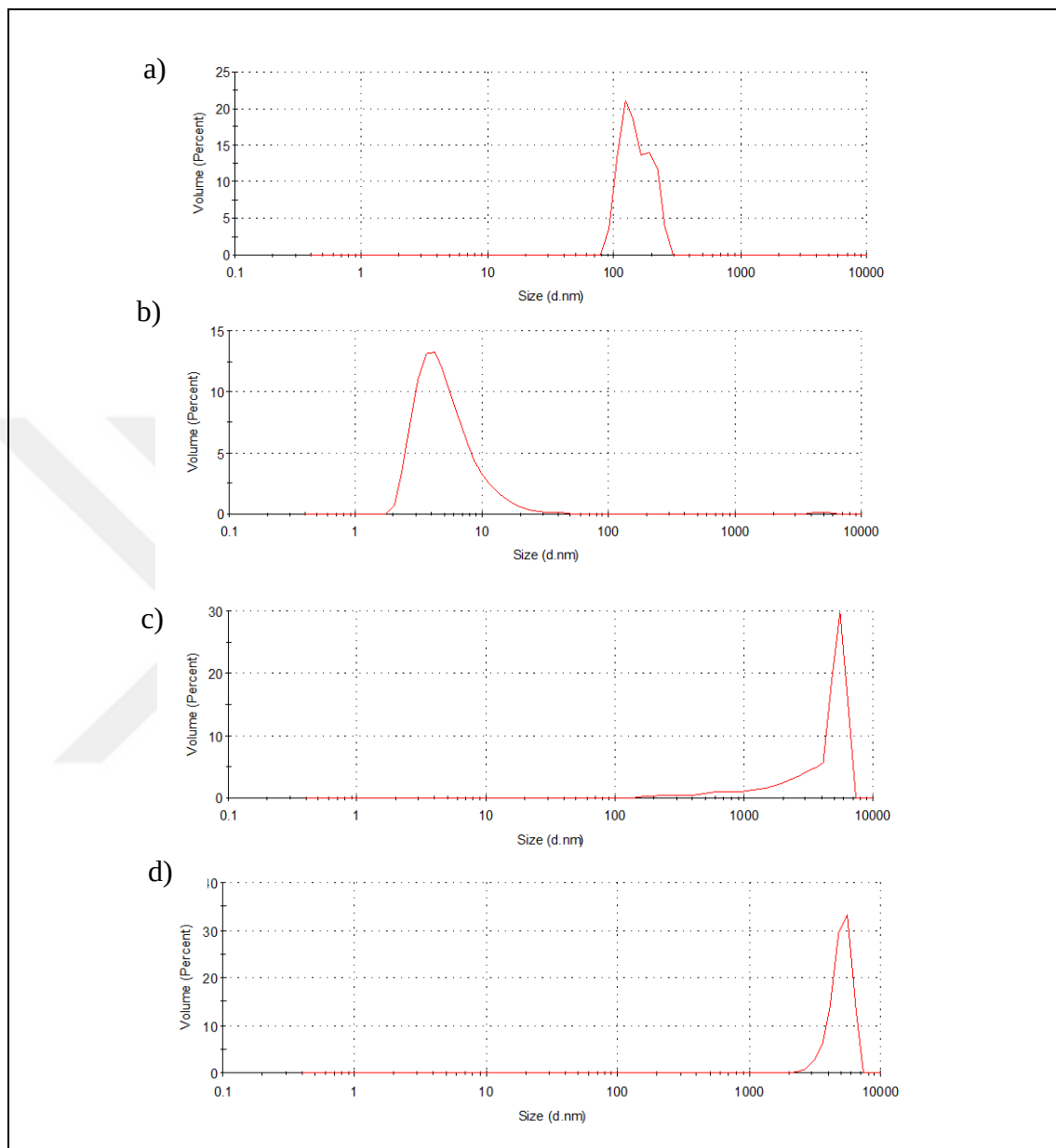


Figure 6.4: Typical DLS size distribution (by volume) of solution (a) **5** and (b) **6** in THF (10^{-5} M) on the first day and after 2 weeks (c) **5** and (d) **6** in ethanol (10^{-5} M).

According to studies of Yagai et al., different solvent systems were tried to observe change in photophysical properties of compounds through their self-assembled structures [105]. Compound **6** is highly soluble in THF but scarcely soluble in nonpolar solvents such as hexane, MCH and TCE. The effect of these nonpolar solvents on the self-assembly ($c=1 \times 10^{-5}$ M) in THF was investigated by UV-Vis, fluorescence and DLS to demonstrate

a solvent-induced effect of complexity in supramolecular systems based on various hydrogen bonds. Increasing the proportion of nonpolar solvents causes change in absorption peaks. Differences were observed when solvent ratios are 90:10 hexane/THF, 90:10 MCH/THF and 97:3 TCE/THF. Compound **6** showed maximum absorption at 564 nm in THF. When nonpolar solvents were added there was red-shifted absorption introducing parallel J-type aggregation. Solutions' color turned pink to pale pink or purple (Figure 6.5 (c)). Moreover, a decrease in emissions was observed. There is a fascinating fluorescence data observed for both solutions in high proportion of MCH and hexane as Anti-Stokes photoluminescence, which is also called as up-conversion in which photoemission energies will be higher than excitation energy. There is not enough information about the upconversion process but it could be one of them, more investigation should be done to confirm it. For a solution with 97:3 TCE/THF, there was a decrease in fluorescence and Stokes shift was obtained as 22 nm (Figure 6.5 (f)).

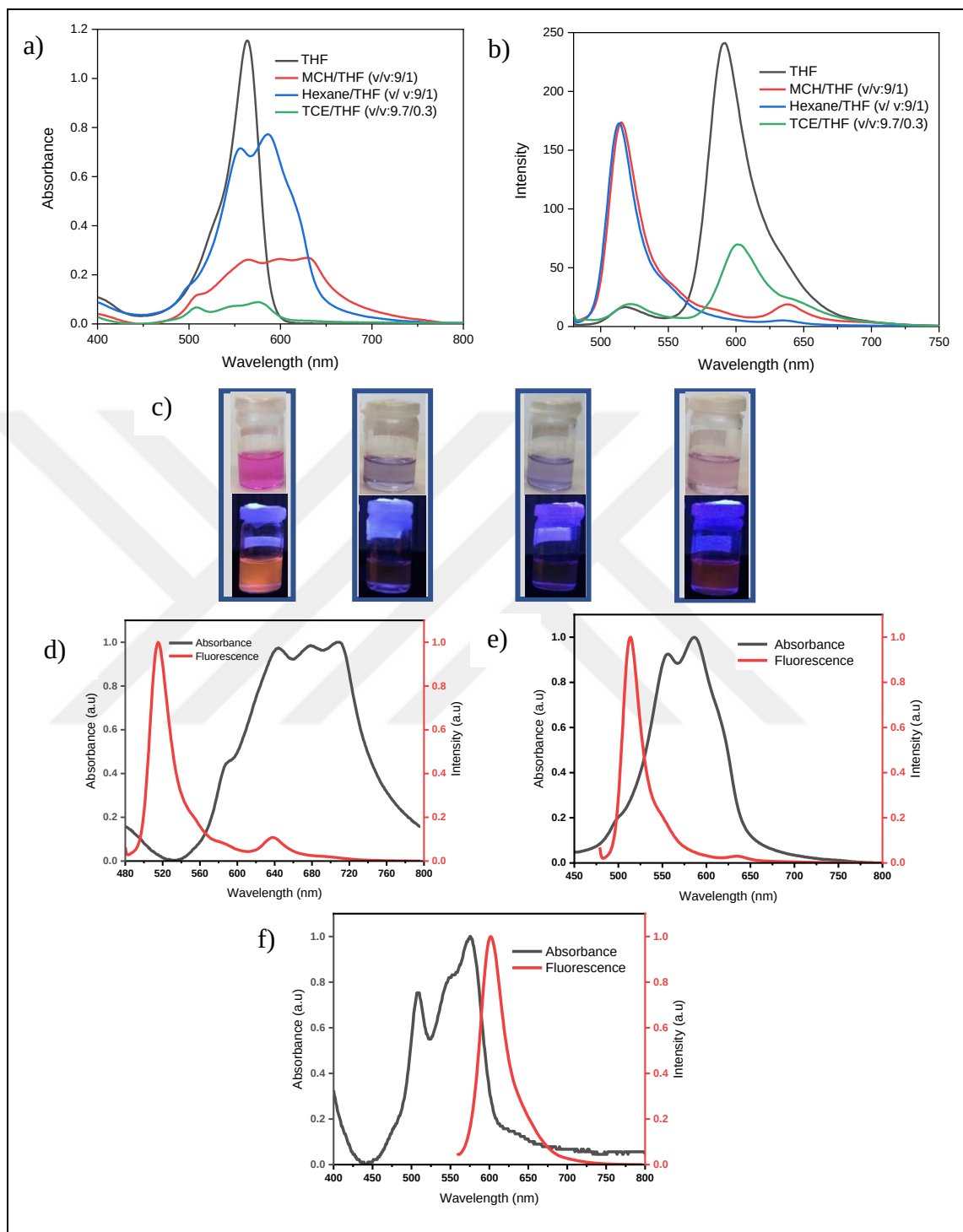


Figure 6.5: UV-Vis spectra (a) of solutions of compound **6** (10^{-5} M) in THF, MCH/THF (v/v:9/1), hexane/THF (v/v:9/1) and TCE/THF (v/v:9.7/0.3) and (b) their fluorescence spectra ($\lambda_{\text{ex}}=470$ nm). (c) The photos of solutions under daylight and UV lamp in THF, MCH/THF (v/v:9/1), hexane/THF (v/v:9/1), TCE/THF (v/v:9.7/0.3), respectively. Stokes shift for (d) MCH/THF (v/v:9/1), (e) hexane/THF (v/v:9/1) and (f) TCE/THF (v/v:9.7/0.3) solutions.

Band gap was also calculated for **6** solutions as THF, MCH/THF (v/v:9.0/1.0), hexane/THF (v/v:9.0/1.0) and TCE/THF (v/v:9.7/0.3) to boost formation of aggregation in these solvent systems as 2.05, 1.63, 1.82, 1.93 eV (Figure 6.6), respectively. Results imply that the band gap is decreasing as the bathochromic shift increases. MCH/THF solution shows more red-shifted absorption so its bandgap is lower than others.

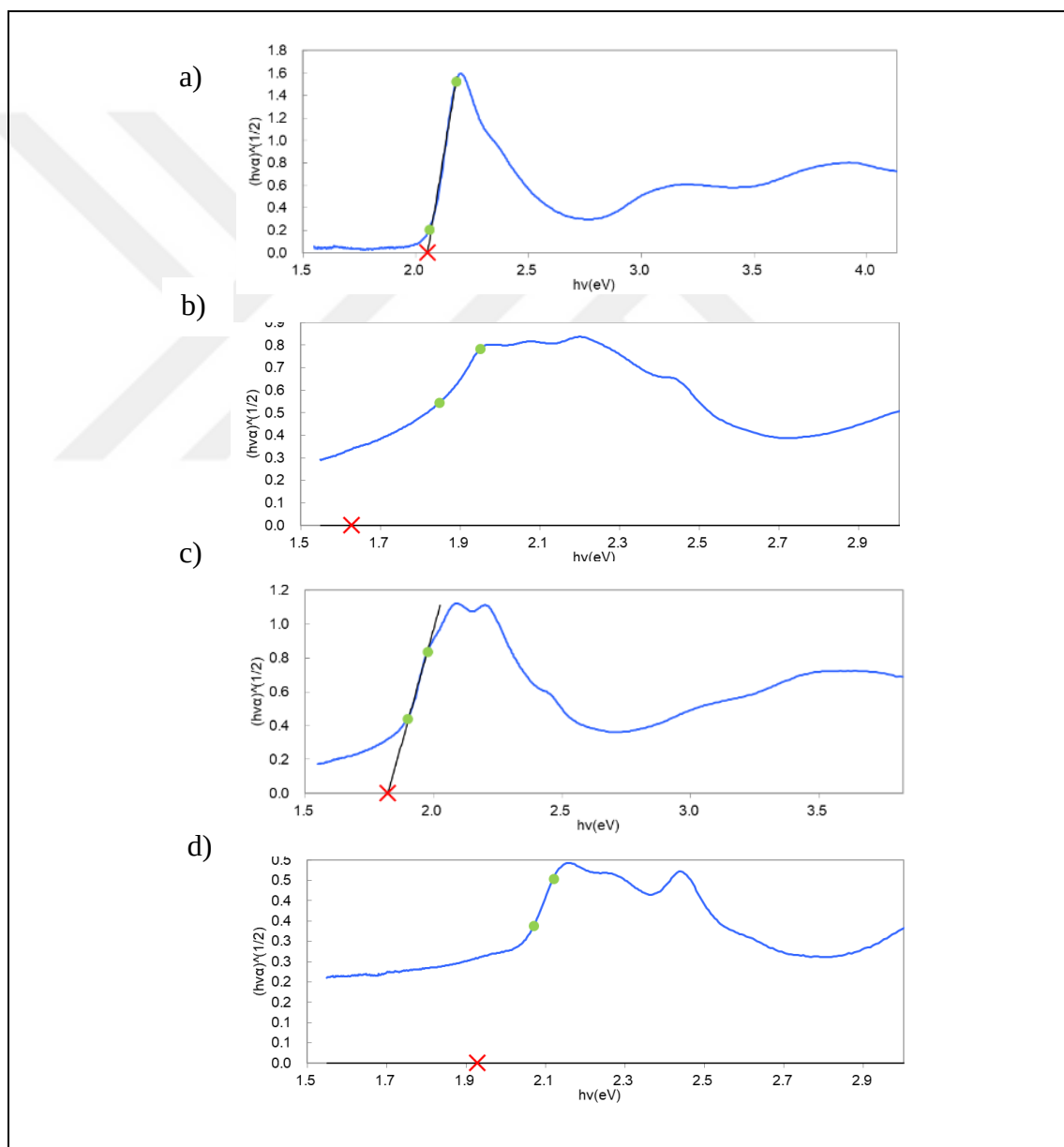


Figure 6.6: Bandgap data through UV-Vis for compound **6** (a) in THF, (b) MCH/THF, (c) hexane/THF and (d) TCE/THF.

According to DLS data, size distributed about 7 nm (Figure 6.7 (a)) in THF solution but it is increasing when MCH/THF (v/v:9.0/1.0) (934 nm), hexane/THF (v/v:9.0/1.0) (866 nm) and TCE/THF (v/v:9.7/0.3) (3696) are used as solvent conforming there could be aggregates (Figure 5.43 (b-d)).

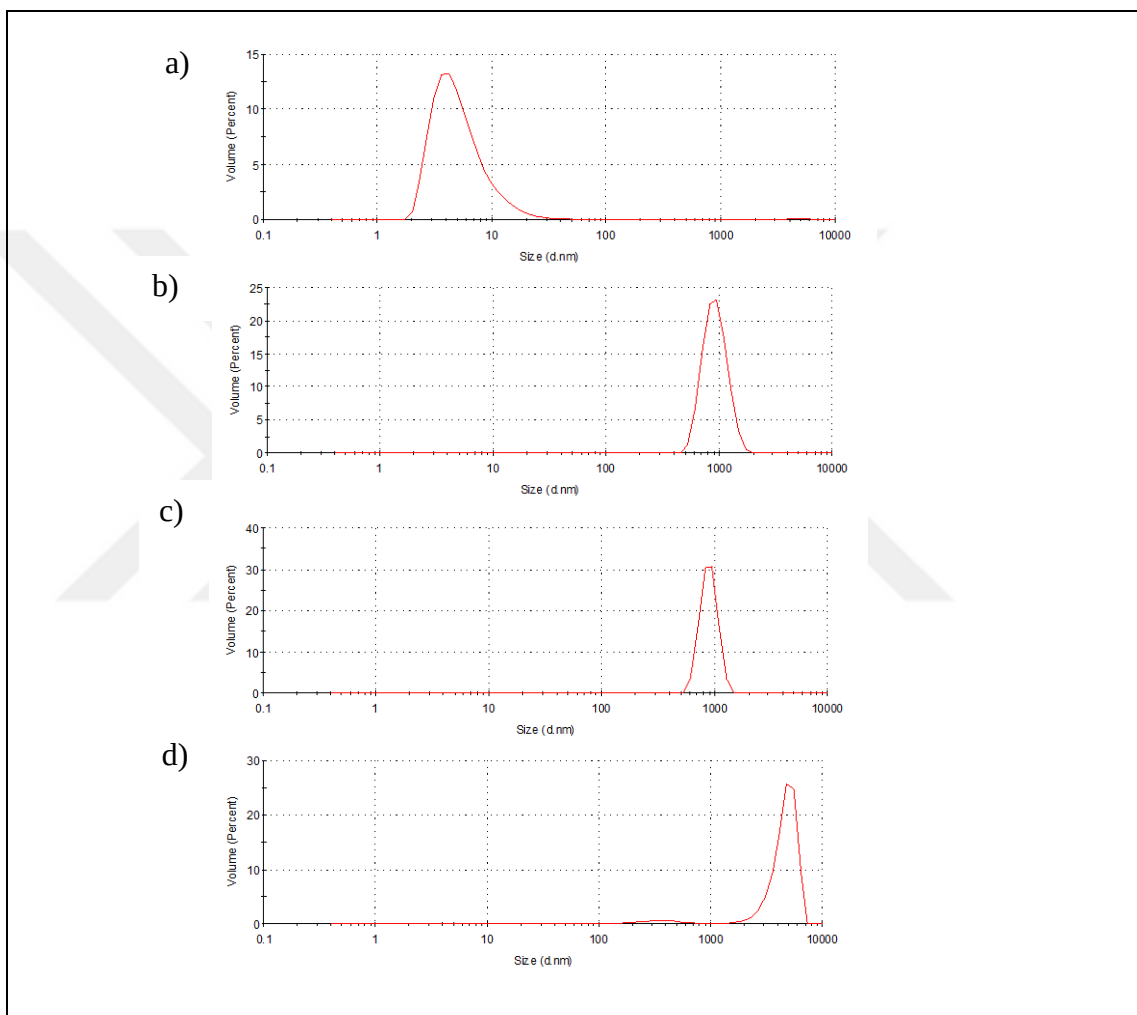


Figure 6.7: DLS size distribution of compound **6** solution (a) in THF, (b) MCH/THF, (c) hexane/THF and (d) TCE/THF.

As mentioned above, barbituric acid and derivatives have been shown to be able to construct sextuple hydrogen bonding rosettes as shown in Figure 6.8 (1b) and (3b) for compound **5** and **6**. Moreover barbituric acid and analogues can also form tape shown in Figure 6.8 for compound **5** (2b) and compound **6** (4b) are possible structures.

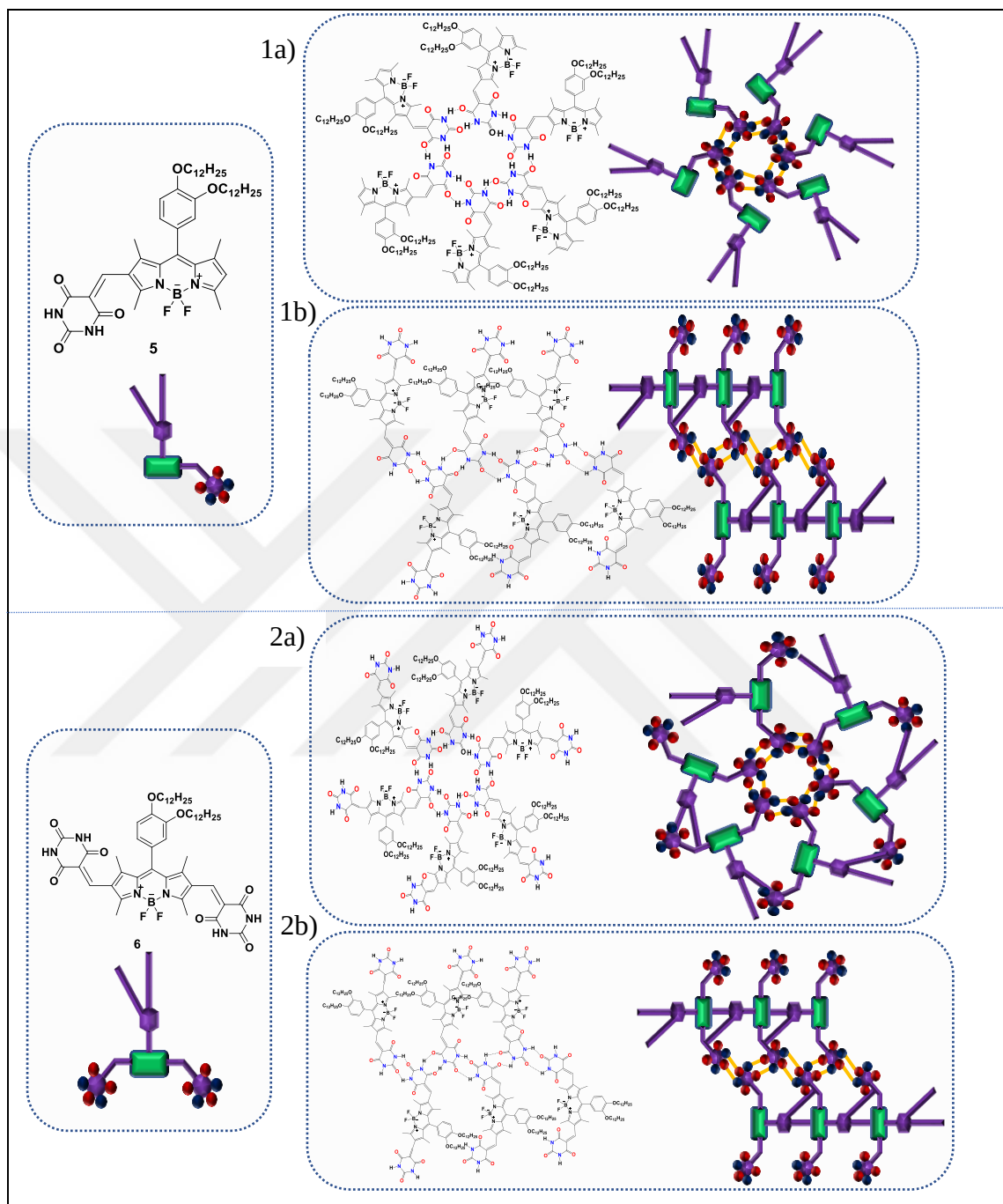


Figure 6.8: Schematic representation of compound 5 and compound 6 hydrogen-bonded rosette (1a, 2a) and tape-like (1b, 2b) structures.

In another study of Yagai et al., concentration-dependent ^1H -NMR measurements were applied to examine rosette or tape-like structures of barbituric functionalized self-assembly [107]. In our study, hydrogen-bonded self-assembly of compound 5 is interpreted with concentration-dependent ^1H -NMR in CDCl_3 . To specify NH signals in

^1H -NMR deuterium oxide was added to the solution. Peaks are 8.03 and 8.35 ppm indicating two NH signals (Figure 5.24). When the concentration is increased from $c=1 \times 10^{-3}$ to 2×10^{-1} , barbituric acid's two NH signals administrate a downfield shift, suggesting intermolecular hydrogen bonding (Figure 6.9). Chemical shifts' difference between two NH signals enhances with increasing concentration ($\Delta\delta_{\text{ppm}}=0.15$ ppm for $c=1 \times 10^{-3}$ M, $\Delta\delta_{\text{ppm}}=0.48$ ppm for $c=2 \times 10^{-1}$ M). This phenomenon is a characteristic of cyclic hydrogen-bonded rosette formation according to studies in the literature mentioned before.

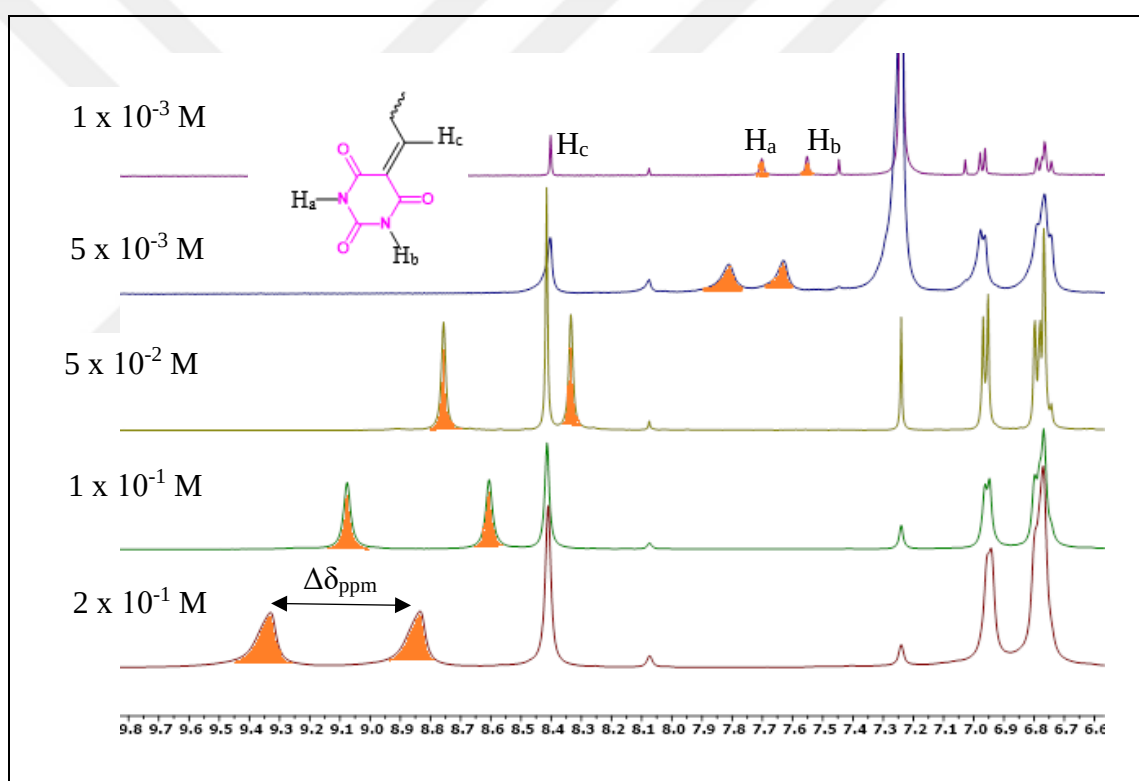


Figure 6.9: Concentration-dependent ^1H -NMR of compound **5** ($c= 1 \times 10^{-3}$ to 2×10^{-1} M) in CDCl_3 .

NH-signals were detected in compound **6** with addition of deuterium oxide. They were found at 10.43 and 10.29 ppm (Figure 5.30). However, compound **6** cannot be used to investigate concentration-dependent ^1H -NMR measurements due to its low solubility in CDCl_3 .

7. CONCLUSION

The aim of the thesis is to synthesize barbituric acid-functionalized BODIPY derivatives and investigate their self-assembled structures via common methods in the literature such as UV-Vis, fluorescence spectrometer, ^1H -NMR and DLS. Barbituric acid has the ability to have multiple hydrogen bonds which are very directional so we can have highly ordered self-assembled fascinating structures so photophysical properties of BODIPY could be controlled [107]. To achieve this, firstly an aldehyde derivative including long alkyl rings was synthesized to have ordered-structures [102]. Then, BODIPY core was synthesized with a condensation reaction between 2, 4-dimethylpyrrole and synthesized aromatic aldehyde. Mono-formyl and di-formyl BODIPY derivatives were obtained, lastly they were functionalized with barbituric acid through Knoevenagel condensation reaction. There are two types of aggregation that could be obtained for a BODIPY core that are H and J-types. Compounds **5** and **6** were dissolved in different solvents to examine if there was a change in solutions. There were fascinating photophysical properties observed in ethanol depending on days. Both solutions of compounds give blue-shifted absorption as 29 nm for compound **5** and 45 nm for compound **6** which is a sign of H-type aggregates of BODIPY. The data were supported as an increase in particle size in ethanol compared with THF solutions that showed no change in this solvent medium depending on time. Furthermore, there was increase in fluorescence ability about 170 times after 15 days was observed for both compounds. Moreover, compound **6** is scarcely soluble in MCH, TCE and hexane. Different solvent ratios were used to see if self-assembled structures are obtained. According to results, solutions administrate different photophysical results as red-shifted absorption and also there was an increment in particle size observed indicating J-type aggregation. To examine self-assembled structures via hydrogen-bonding ability of barbituric acid to observe whether there is rosette or tape-like structure formation is to conduct concentration-dependent ^1H -NMR where NH peaks were specified with NMR-data adding deuterium oxide. When concentration is increasing NH peaks show downfield shift and also chemical shift differences between NH protons are increasing which is a sign of intermolecular hydrogen bonded rosette formation [108].

REFERENCES

- [1] Treibs A., Kreuzer F.H., (1968), "Difluorboryl komplexe von di und tripyrrylmethenen", Justus Liebigs Annalen. Chemie, 718, 208-223.
- [2] Li F. Z., Yin J. F., Kuang G. C., (2021), "BODIPY-based supramolecules: Construction, properties and functions", Coordination Chemistry Reviews, 448.
- [3] Tao J., Sun D., Sun L., Li Z., Fu B., Liu J., Zhang L., Wang S., Fang Y., Xu H., (2019), "Tuning the photo-physical properties of BODIPY dyes: Effects of 1, 3, 5, 7- substitution on their optical and electrochemical behaviours", Dyes and Pigments, 168, 166–174.
- [4] Steed J. W., Turner D. R., Wallace K. J., (2007), "Core Concepts in Supramolecular Chemistry and Nanochemistry", John Wiley.
- [5] Jun Y. S., Lee E. Z., Wang X., Hong W. H., Stucky G. D., Thomas A., (2013), "From melamine-cyanuric acid supramolecular aggregates to carbon nitride hollow spheres", Advanced Functional Materials, 23 (29), 3661–3667.
- [6] Carter M. K., (1951), "The story of barbituric acid", Journal of Chemical Education, 28 (10), 524.
- [7] Singh P.K., Majumdar P., Singh S.P., (2021), "Advances in BODIPY photocleavable protecting groups", Coordination Chemistry Reviews, 449, 214193.
- [8] Bandi V., D'Souza F. P., Gobeze H. B., D'Souza F., (2015), "Multistep energy and electron transfer in a "V-configured" supramolecular BODIPY-azaBODIPY-fullerene triad: Mimicry of photosynthetic antenna reaction-center events", Chemistry - A European Journal, 21 (6), 2669–2679.
- [9] Arroyo I. J., Hu R., Merino G., Tang B. Z., Peña-Cabrera E., (2009), "The smallest and one of the brightest. Efficient preparation and optical description of the parent borondipyrromethene system", Journal of Organic Chemistry, 74 (15), 5719–5722.
- [10] Tram K., Yan H., Jenkins H. A., Vassiliev S., Bruce D., (2009), "The synthesis and crystal structure of unsubstituted 4,4-difluoro-4-bora-3a,4a-diaza-s-indacene (BODIPY)", Dyes and Pigments, 82 (3), 392–395.
- [11] Loudet A., Burgess K., (2007), "BODIPY dyes and their derivatives: Syntheses and spectroscopic properties", Chemical Reviews, 107 (11), 4891–4932.

- [12] Schmitt A., Hinkeldey B., Wild M., Jung G., (2009), "Synthesis of the core compound of the BODIPY dye class: 4,4'-difluoro-4-bora-(3a,4a)-diazas-indacene", *Journal of Fluorescence*, 19 (4), 755–758.
- [13] Arroyo I. J., Hu R., Merino G., Tang B. Z., Peña-Cabrera E., (2009), "The smallest and one of the brightest. Efficient preparation and optical description of the parent borondipyrromethene system", *Journal of Organic Chemistry*, 74 (15), 5719–5722.
- [14] Bamfield B. P., Johnson A. W., Leng J., Cook A. H., Majer J. R., Treibs A., Herrmann E., (1954), "The Reaction of Dipyrromethene Salts with Methyl Ketones and with Dicyanornethane", *Journal of Chemical Sciences*, 1292.
- [15] Squeo B. M., Ganzer L., Virgili T., Pasini M., (2020), "BODIPY-Based Molecules, a Platform for Photonic and Solar Cells", *Molecules (Basel, Switzerland)*, 26 (1).
- [16] Kubota Y., Yagi S., (2021), "Progress in the Science of Functional Dyes", Springer.
- [17] Krzemien W., Rohlickova M., Machacek M., Novakova V., Piskorz J., Zimcik P., (2021), "Tuning photodynamic properties of bodipy dyes, porphyrins' little sisters", *Molecules*, 26 (14).
- [18] Baruah M., Qin W., Basaric N., De Borggraeve Wim M., Boens N., (2005), "BODIPY-based hydroxyaryl derivatives as fluorescent pH probes", *The Journal of Organic Chemistry*, 70, 4152.
- [19] Sengul I. F., Okutan E., Kandemir H., Astarci E., Çoşut B., (2015), "Carbazole substituted BODIPY dyes: Synthesis, photophysical properties and antitumor activity", *Dyes and Pigments*, 123, 32–38.
- [20] Antonangelo A. R., Westrup K. C. M., Burt L. A., Bezzu C. G., Malewschik T., Machado G. S., Nunes F. S., McKeown N. B., Nakagaki S., (2017), "Synthesis, crystallographic characterization and homogeneous catalytic activity of novel unsymmetric porphyrins", *RSC Advances*, 7 (80), 50610–50618.
- [21] Lee' C.-H., Lindsey J. S., (1994), "One-Flask Synthesis of Meso-Substituted Dipyrromethanes and Their Application in the Synthesis of Trans-Substituted Porphyrin Building Blocks", *Tetrahedron*, 50, 11427-11440.
- [22] Jiao L., Yu C., Li J., Wang Z., Wu M., Hao E., (2009), " β -formyl-BODIPYs from the Vilsmeier-Haack reaction", *Journal of Organic Chemistry*, 74 (19), 7525–7528.
- [23] Wu L., Burgess K., (2008), "A new synthesis of symmetric borindacene (BODIPY) dyes", *Chemical Communications*, 4933-4935.

- [24] Yogo T., Urano Y., Ishitsuka Y., Maniwa F., Nagano T., (2005), "Highly efficient and photostable photosensitizer based on BODIPY chromophore", *Journal of the American Chemical Society*, 127 (35), 12162–12163.
- [25] Li L., Han J., Nguyen B., Burgess K., (2008), "Synthesis and spectral properties of functionalized, water-soluble BODIPY derivatives", *Journal of Organic Chemistry*, 73 (5), 1963–1970.
- [26] Kang Jin., Huo Fangjun., Yue Yongkang., Wen Ying., Chao Jianbin., Zhang Yongbin., Yin Caixia., (2017), "A solvent depend on ratiometric fluorescent probe for hypochlorous acid and its application in living cells", *Dyes and Pigments*, 136, 852-858.
- [27] Zhu S., Zhang J., Vegesna G., Tiwari A., Luo F.T., Zeller M., Luck R., Li H., Green S., Liu H., (2012), " Controlled Knoevenagel reactions of methyl groups of 1, 3, 5, 7-tetramethyl BODIPY for uique BODIPY dyes", *Royal Society of Chemistry*, 2, 404-407.
- [28] Frein S., Camerel F., Ziessel R., Barbera J., Deschenaux R., (2009), "Highly Fluorescent liquid-crystalline dendrimers based on borondipyrromethene dyes", *Chemistry of Materials*, 21 (17), 3950–3959.
- [29] Porubský M., Gurská S., Stanková J., Hajdúch M., Džubák P., Hlaváč J., (2019), "Amino-BODIPY as the ratiometric fluorescent sensor for monitoring drug release or “power supply” selector for molecular electronics", *RSC Advances*, 9 (43), 25075–25083.
- [30] Eördögh Á., Paganini C., Pinotsi D., Arosio P., Rivera-Fuentes P., (2020), "A Molecular Logic Gate Enables Single-Molecule Imaging and Tracking of Lipids in Intracellular Domains", *ACS Chemical Biology*, 15 (9), 2597–2604.
- [31] Li C., Lin W., Liu S., Zhang W., Xie Z., (2019), "Self-destructive PEG-BODIPY nanomaterials for photodynamic and photothermal therapy", *Journal of Materials Chemistry B*, 7 (30), 4655–4660.
- [32] Kessel D., (2019), "Photodynamic therapy: A brief history", *Journal of Clinical Medicine*, 8 (10).
- [33] Ruan Z., Zhao Y., Yuan P., Liu L., Wang Y., Yan L., (2018), "PEG conjugated BODIPY-Br₂ as macro-photosensitizer for efficient imaging-guided photodynamic therapy", *Journal of Materials Chemistry B*, 6 (5), 753–762.
- [34] Kamkaew A., Lim S. H., Lee H. B., Kiew L. V., Chung L. Y., Burgess K., (2013), "BODIPY dyes in photodynamic therapy", *Chemical Society Reviews*, 42 (1), 77–88.

- [35] Liu L., Fu L., Jing T., Ruan Z., Yan L., (2016), "PH-Triggered Polypeptides Nanoparticles for Efficient BODIPY Imaging-Guided Near Infrared Photodynamic Therapy", *ACS Applied Materials and Interfaces*, 8 (14), 8980–8990.
- [36] Zou L., Wang H., He B., Zeng L., Tan T., Cao H., He X., Zhang Z., Guo S., Li Y., (2016), "Current approaches of photothermal therapy in treating cancer metastasis with nanotherapeutics", *Theranostics*, 6 (6), 762–772.
- [37] Chen B., Cao J., Zhang K., Zhang Y. N., Lu J., Zubair Iqbal M., Zhang Q., Kong X., (2021), "Synergistic photodynamic and photothermal therapy of BODIPY-conjugated hyaluronic acid nanoparticles", *Journal of Biomaterials Science, Polymer Edition*, 32 (15), 2028–2045.
- [38] Dambhare M. v., Butey B., Moharil S. v., (2021), "Solar photovoltaic technology: A review of different types of solar cells and its future trends", *Journal of Physics: Conference Series*, IOP Publishing Ltd.
- [39] Shah M. F., Mirloup A., Chowdhury T. H., Alexandra S., Hanbazazah A. S., Ahmed A., Lee J. J., Leclerc N., Abdel-Shakour M., Islam A., (2019), "A near-infrared thienyl-BODIPY co-sensitizer for high-efficiency dye-sensitized solar cells", *Sustainable Energy and Fuels*, 3 (11), 2983–2989.
- [40] Kolemen S., Akkaya E. U., (2018), "Reaction-based BODIPY probes for selective bio-imaging", *Coordination Chemistry Reviews*, 354, 121–134.
- [41] Ozdemir T., Sozmen F., Mamur S., Tekinay T., Akkaya E. U., (2014), "Fast responding and selective near-IR Bodipy dye for hydrogen sulfide sensing", *Chemical Communications*, 50 (41), 5455–5457.
- [42] Ulrich G., Ziessel R., Harriman A., (2008), "The chemistry of fluorescent bodipy dyes: Versatility unsurpassed", *Angewandte Chemie - International Edition*, 47 (7), 1184–1201.
- [43] Nguyen V. N., Ha J., Cho M., Li H., Swamy K. M. K., Yoon J., (2021), "Recent developments of BODIPY-based colorimetric and fluorescent probes for the detection of reactive oxygen/nitrogen species and cancer diagnosis", *Coordination Chemistry Reviews*, 439.
- [44] Steed J. W., Atwood J. L., (2009), *Supramolecular Chemistry*, Wiley.
- [45] Lehn J. M., (1978), "Cryptates: the chemistry of macropolycyclic complexes", *Accounts of Chemical Research*, 11(2), 49-57.
- [46] Lindoy L.F., Atkinson I. M., (2007), "Self-Assembly in Supramolecular Systems", *Royal Society of Chemistry*.

- [47] Huang F., Anslyn E. V., (2015), "Introduction: Supramolecular Chemistry", *Chemical Reviews*, 115 (15), 6999-7000.
- [48] Lehn J. M., (2007), "From supramolecular chemistry towards constitutional dynamic chemistry and adaptive chemistry", *Chemical Society Reviews*, 36 (2), 151-160.
- [49] Ollerton K., Greenaway R. L., Slater A. G., (2021), "Enabling Technology for Supramolecular Chemistry", *Frontiers in Chemistry*, 9.
- [50] Wu A., Isaacs L., (2003), "Self-sorting: The exception or the rule?", *Journal of the American Chemical Society*, 125 (16), 4831-4835.
- [51] Würthner F., (2022), "Solvent Effects in Supramolecular Chemistry: Linear Free Energy Relationships for Common Intermolecular Interactions", *Journal of Organic Chemistry*, 87, 3, 1602-1615.
- [52] Martí-Centelles V., Pandey M. D., Burguete M. I., Luis S. v., (2015), "Macrocyclization reactions: The importance of conformational, configurational, and template-induced preorganization", *Chemical Reviews*, 115 (16), 8736-8834.
- [53] Chidchob P., Sleiman H., (2016), "Supramolecular Chemistry with DNA", Wiley.
- [54] Yazaki K., Akita M., Prusty S., Chand D. K., Kikuchi T., Sato H., Yoshizawa M., (2017), "Polyaromatic molecular peanuts", *Nature Communications*, 8.
- [55] Schneider H. J., (2012), "Applications of Supramolecular Chemistry", 1st Edition, CHC Press.
- [56] Bobacka J., Ivaska A., Lewenstam A., (2008), "Potentiometric ion sensors", *Chemical Reviews*, 108 (2), 329-351.
- [57] Malinowska E., Górski Ł., Wojciechowska D., Reinoso-García M. M., Verboom W., Reinhoudt D. N., (2003), "Potentiometric studies of complexation properties of tetrafunctionalized resorcinarene-based cavitands", *New Journal of Chemistry*, 27 (10), 1440-1445.
- [58] Pla L., Lozano-Torres B., Martínez-Máñez R., Sancenón F., Ros-Lis J. v., (2019), "Overview of the evolution of silica-based chromo-fluorogenic nanosensors", *Sensors (Switzerland)*, 19 (23).
- [59] Atwood J. L., Koutsantonis G. A., Raston C. L., (1994), "Purification of C₆₀ and C₇₀ by selective complexation with calixarenes", *Nature*, 368, 229-231.
- [60] Kreuer K. D., Paddison S. J., Spohr E., Schuster M., (2004), "Transport in proton conductors for fuel-cell applications: Simulations, elementary reactions, and phenomenology", *Chemical Reviews*, 104 (10), 4637-4678.

- [61] Schmaltz B., Jouaiti A., Hosseini M. W., de Cian A., (2001), "Double stranded interwound infinite linear silver coordination network", *Chemical Communications*, (14), 1242–1243.
- [62] Kwon N., Kim H., Li X., Yoon J., (2021), "Supramolecular agents for combination of photodynamic therapy and other treatments", *Chemical Science*, 12 (21), 7248–7268.
- [63] Webber M. J., Langer R., (2017), "Drug delivery by supramolecular design", *Chemical Society Reviews*, 46, 6600.
- [64] Lehn J. M., (1995), "Supramolecular Chemistry", Weinheim.
- [65] Busseron E., Ruff Y., Moulin E., Giuseppone N., (2013), "Supramolecular self-assemblies as functional nanomaterials", *Nanoscale*, 5 (16), 7098–7140.
- [66] Park S. Y., Lytton-Jean A. K. R., Lee B., Weigand S., Schatz G. C., Mirkin C. A., (2008), "DNA-programmable nanoparticle crystallization", *Nature*, 451 (7178), 553–556.
- [67] Yadav S., Sharma A. K., Kumar P., (2020), "Nanoscale Self-Assembly for Therapeutic Delivery", *Frontiers in Bioengineering and Biotechnology*, 8.
- [68] Casalini S., Bortolotti C. A., Leonardi F., Biscarini F., (2017), "Self-assembled monolayers in organic electronics", *Chemical Society Reviews*, 46 (1), 40–71.
- [69] Pei H., Liang L., Yao G., Li J., Huang Q., Fan C., (2012), "Reconfigurable three-dimensional DNA nanostructures for the construction of intracellular logic sensors", *Angewandte Chemie - International Edition*, 51 (36), 9020–9024.
- [70] Qi B., Wu C., Liu Y., Liu J., Zhang H., (2019), "Self-Assembled Magnetic Pt Nanocomposites for the Catalytic Reduction of Nitrophenol", *ACS Applied Nano Materials*, 2 (7), 4377–4385.
- [71] Whitesides G. M., Grzybowski B., (2002), "Self-Assembly at all scales", *Science*, 295, 2418–2421.
- [72] Barba-Bon A., Nilam M., Hennig A., (2020), "Supramolecular Chemistry in the Biomembrane", *ChemBioChem*, 21 (7), 886–910.
- [73] Watson J. D., Crick F. H. C., (1953), "Molecular structure of nucleic acids", *Nature*, 171, 737–738.
- [74] Butler P. J. G., (1999), "Self-Assembly of tobacco mosaic virus: The role of an intermediate aggregate in generating both specificity and speed", *Philosophical Transactions: Biological Sciences*, 354, 537–557.

- [75] Jeffrey G. A., (1996), "Hydrogen bonds and molecular recognition", *Food Chemistry*, 56, 241-246.
- [76] Prins L. J., Reinhoudt D. N., Timmerman P., (2001), "Noncovalent synthesis using hydrogen bonding", *Angewandte Chemie International Edition*, 40, 2382-2426.
- [77] Lee S., Barin G., Ackerman C. M., Muchenditsi A., Xu J., Reimer J. A., Lutsenko S., Long J. R., Chang C. J., (2016), "Copper Capture in a Thioether-Functionalized Porous Polymer Applied to the Detection of Wilson's Disease", *Journal of the American Chemical Society*, 138 (24), 7603–7609.
- [78] Fu F., Wang Q., (2011), "Removal of heavy metal ions from wastewaters: A review", *Journal of Environmental Management*, 92 (3), 407–418.
- [79] Bui N. T., Kang H., Teat S. J., Su G. M., Pao C. W., Liu Y. S., Zaia E. W., Guo J., Chen J. L., Meihaus K. R., Dun C., Mattox T. M., Long J. R., Fiske P., Kostecky R., Urban J. J., (2020), "A nature-inspired hydrogen-bonded supramolecular complex for selective copper ion removal from water", *Nature Communications*, 11 (1).
- [80] Seto C. T., Whitesides G. M., (1990), "Self-Assembly Based on the Cyanuric Acid-Melamine Lattice", *Journal of American Chemical Society*, 112, 6409-6411.
- [81] Ranganathan A., Pedireddi V. R., Rao C. N. R., (1999), "Hydrothermal synthesis of organic channel structures: 1:1 hydrogen- bonded adducts of melamine with cyanuric and trithiocyanuric acids [3]", *Journal of the American Chemical Society*, 121 (8), 1752–1753.
- [82] Yagai S., Karatsu T., Kitamura A., (2003), "Photoresponsive melamine·barbiturate hydrogen-bonded assembly", *Chemical Communications*, 3 (15), 1844–1845.
- [83] Timmerman P., Prins L. J., (2001), "Noncovalent synthesis of melamine-cyanuric/barbituric acid derived nanostructures: Regio- and stereoselection", *European Journal of Organic Chemistry*, 17, 3191-3205.
- [84] López-Muñoz F., Ucha-Udabe R., Alamo C., (2005), " The history of barbiturates a century after their clinical introduction", *Neuropsychiatric Disease and Treatment*, 1(4) 329-343.
- [85] Wesson D. R., Smith D. E., (1977), *Barbiturates: Their Use, Misuse and Abuse. Human Sciences.*
- [86] Rai S. K., Tewari A. K., (2018), "Dual role of drugs: beneficial and harmful aspects", *Synthesis of Medicinal Agents from Plants*, Elsevier, 305–332.
- [87] Schwab S., Spranger M., Schwarz S., Hacke W., (1997), "Barbiturate coma in severe hemispheric stroke", *Neurology Journal*, 48(6) 1608-1613.

- [88] Mahmudov K. T., Kopylovich M. N., Maharramov A. M., Kurbanova M. M., Gurbanov A. v., Pombeiro A. J. L., (2014), "Barbituric acids as a useful tool for the construction of coordination and supramolecular compounds", *Coordination Chemistry Reviews*, 265 (1), 1–37.
- [89] Chang S. K., Hamilton A. D., (1988), "Molecular recognition of biologically interesting substrates: synthesis of an artificial receptor for barbiturates employing six hydrogen bonds", *Journal of the American Chemical Society*, 110 (4) 1318-1319.
- [90] Chang T. M. S., Langer R., Sparks R. E., Reach G., (1988), "Drug delivery systmes in biotechnology", *Artificial Organs*, 12 (3) 248-251.
- [91] Yagai S., (2015), "Supramolecularly engineered functional π -assemblies based on complementary hydrogen-bonding interactions", *Bulletin of the Chemical Society of Japan*, 88 (1), 28–58.
- [92] Kawasaki T., Tokuhiko M., Kimizuka N., Kunitake T., (2001), "Hierarchical self-assembly of chiral complementary hydrogen-bond networks in water: Reconstitution of supramolecular membranes", *Journal of the American Chemical Society*, 123 (28), 6792–6800.
- [93] Chu C. C., Raffy G., Ray D., Guerzo A. del, Kauffmann B., Wantz G., Hirsch L., Bassani D. M., (2010), "Self-assembly of supramolecular fullerene ribbons via hydrogen-bonding interactions and their impact on fullerene electronic interactions and charge carrier mobility", *Journal of the American Chemical Society*, 132 (36), 12717–12723.
- [94] Yagai S., Kubota S., Saito H., Unoike K., Karatsu T., Kitamura A., Ajayaghosh A., Kanesato M., Kikkawa Y., (2009), "Reversible transformation between rings and coils in a dynamic hydrogen-bonded self-assembly", *Journal of the American Chemical Society*, 131 (15), 5408–5410.
- [95] Yagai S., (2015), "Supramolecularly engineered functional π -assemblies based on complementary hydrogen-bonding interactions", *Bulletin of the Chemical Society of Japan*, 88 (1), 28–58.
- [96] Gu R., Lehn J. M., (2021), "Constitutional Dynamic Selection at Low Reynolds Number in a Triple Dynamic System: Covalent Dynamic Adaptation Driven by Double Supramolecular Self-Assembly", *Journal of the American Chemical Society*, 143 (35), 14136–14146.
- [97] Ariga K., Nishikawa M., Mori T., Takeya J., Shrestha L. K., Hill J. P., (2019), "Self-assembly as a key player for materials nanoarchitectonics", *Science and Technology of Advanced Materials*, 20 (1), 51–95.

- [98] Fothergill J. W., Hernandez A. C., Knowlton W. B., Yurke B., Li L., (2018), "Ab Initio Studies of Exciton Interactions of Cy5 Dyes", *Journal of Physical Chemistry A*, 122 (46), 8989–8997.
- [99] Chuang C., Bennett D. I. G., Caram J. R., Aspuru-Guzik A., Bawendi M. G., Cao J., (2019), "Generalized Kasha's Model: T-Dependent Spectroscopy Reveals Short-Range Structures of 2D Excitonic Systems", *Chem*, 5 (12), 3135–3150.
- [100] Özcan E., Dedeoglu B., Chumakov Y., Gürek A. G., Zorlu Y., Çoşut B., Ayhan M. M., (2021), "Halogen-Bonded BODIPY Frameworks with Tunable Optical Features", *Chemistry - A European Journal*, 27 (5), 1603–1608.
- [101] Zhang Y., Liu P., Pan H., Dai H., Ren X. K., Chen Z., (2020), "Alignment of supramolecular J-aggregates based on uracil-functionalized BODIPY dye for polarized photoluminescence", *Chemical Communications*, 56 (80), 12069–12072.
- [102] Qu X., Bian Y., Chen Y., Wei X., (2020), "A sensitive BODIPY-based fluorescent probe for detecting endogenous hydroxyl radicals in living cells", *RSC Advances*, 10 (48), 28705–28710.
- [103] Işık M., Özdemir T., Şimşek Turan I., Kolemen S., Akkaya E.U., (2013), "Chromogenic and Fluorogenic Sensing of Biological Thiols in Aqueous Solutions using Bodipy Based Reagents", *Organic Letters*, 15, 1, 216-219.
- [104] Lopez Arbeloa T., Lopez Arbeloa F., Lopez Arbeloa I., Garcia-Moreno I., Costela A., Sastre R., Amat-Guerri F., Spain S., (1999), "Correlations between Photophysics and Lasing Properties of Dipyrrromethene-BF Dyes in Solution", *The Journal of Physical Chemistry A*, 24, 339-374.
- [105] Kawaura M., Aizawa T., Takahashi S., Miyasaka H., Sotome H., Yagai S., (2022), "Fluorescent supramolecular polymers of barbiturate dyes with thiophene-cored twisted p-systems", *Chemical Science*, 13, 1281.
- [106] Rybczynski P., Kaczmarek-Kędziera A., (2021), "BODIPY dimers: structure, interaction, and absorption spectrum", *Structural Chemistry*, 32 (3), 953–965.
- [107] Silly F., Kawaura, M., Aizawa T., Ouchi H., Yagai S., (2022), "Rod and Helical Organic Fiber Structures Revealing Lamellar and Rosette Ordering Pathways in Self-Assembly of Barbiturate Oligothiophene Derivatives", *The Journal of Physical Chemistry*, 126, 2780-2787.
- [108] Ouchi H., Lin X., Kizaki T., D.D Prabhu., Silly F., Kajitani T., Fukushima T., Nakayama K., Yagai S., (2016), "Hydrogen-bonded oligothiophene rosettes with a benzodithiophene terminal unit: self-assembly and application to bulk heterojunction solar cells", *Chemical Communications*, 52, 7874-7877.

BIOGRAPHY

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APPENDICES

Appendix A: Structures of synthesized compounds.

Table A1.1: Structures of synthesized compounds.

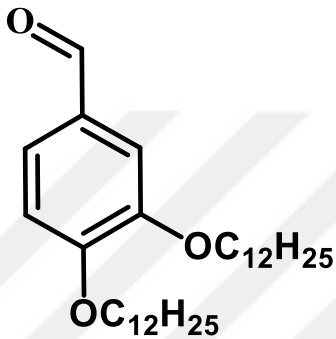
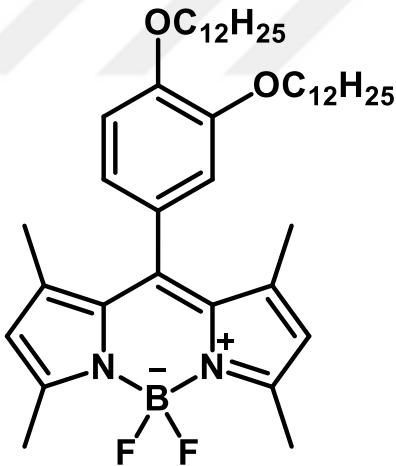
	Compound 1 White color M.w: 474.77 g/mol $C_{31}H_{54}O_3$
	Compound 2 Orange color M.w: 692.81 g/mol $C_{43}H_{67}BF_2N_2O_2$

Table A1.1: Continue.

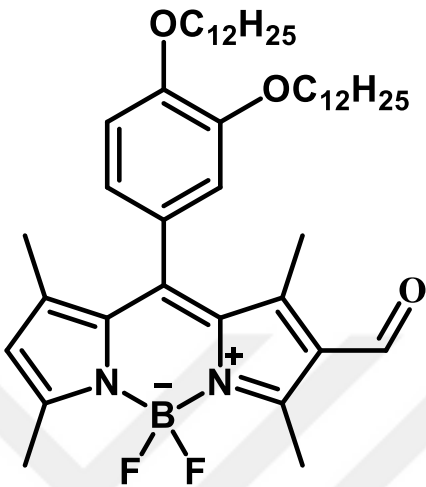
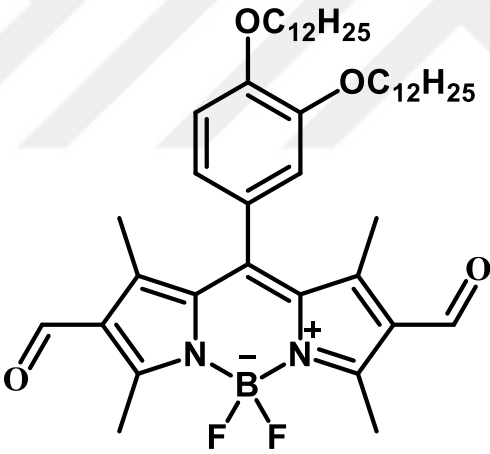
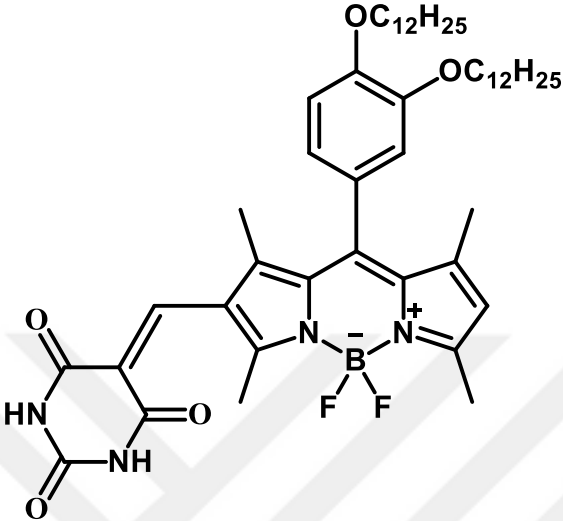
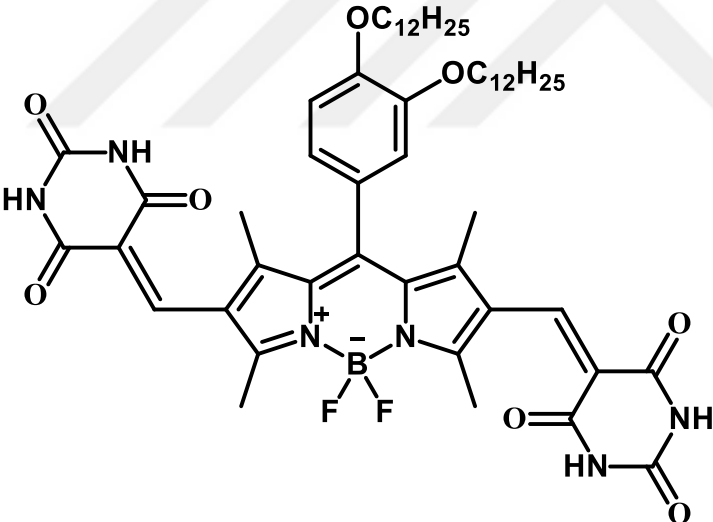
	Compound 3 Orange color M.w: 721.919 g/mol $C_{44}H_{67}BF_2N_2O_3$
	Compound 4 Orange color M.w: 748.83 g/mol $C_{45}H_{67}BF_2N_2O_4$

Table A1.1: Continue.

	Compound 5 Pink color M.w: 830.89 g/mol $C_{48}H_{69}BF_2N_2O_5$
	Compound 6 Purple color M.w: 968.97 g/mol $C_{53}H_{71}BF_2N_6O_8$