

**OPTIMIZATION OF ORTHOGONAL REACTIONS ON
BODIPY DYES FOR ONE-POT SYNTHESIS OF LIGHT
HARVESTING DENDRIMERS**

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MASTER OF SCIENCE

By

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February, 2013

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ABSTRACT

OPTIMIZATION OF ORTHOGONAL REACTIONS ON BODIPY DYES FOR ONE-POT SYNTHESIS OF LIGHT HARVESTING DENDRIMERS

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For more than a decade, synthetic organic chemistry has dealt with focusing on highly selective and efficient reactions that can proceed under mild conditions which would then be categorized under the term “orthogonal click chemistry”. These types of reaction have served number of applications for years as in peptide synthesis, homogeneous catalysis and development of supramolecular systems. On the other side, after a partial understanding of how photosynthetic bacteria and plants harvest solar radiation in order to carry their necessary carbon dioxide reduction reaction by converting light to chemical energy, artificial light harvesting systems have captivated a lot attention of scientists. Because today’s one of the biggest and inevitable problems is to discover/invent alternative energy sources/devices for future demands, these artificial light harvesting and solar concentrator systems are highly open for further development and optimization. However, like most other macromolecular systems, synthesis of these kind of devices should be straightforward so as to decrease the cost and to increase the efficiency. At this point, orthogonal click reactions, being mild and efficient synthetic models, can undoubtedly be worthwhile to consider as proper tools for easy preparation of light harvesting molecules. Here we propose a synthesis of

thiol, Michael accepting groups, amine and isothiocyanate modified BODIPY dyes for light harvesting cascade preparation. Moreover, the optimization of Michael addition type thiol – ene reaction of these functionalized dyes has been discussed. Among methyl methacrylate, cyanoacetic acid and nitroolefin functionalizations, it was found that nitroolefin attached BODIPY dyes are the most reactive one. The achieved product has been investigated in terms of fluorescence and energy transfer.

Keywords: BODIPY, light harvesting dendrimer, orthogonal reactions, click chemistry, one-pot synthesis, thiol – ene reaction

ÖZET

IŞIK HASAT EDEN TEK AŞAMALI DENDRİMER SENTEZİ İÇİN BODIPY BOYAR MADDELERİ ÜZERİNDE ORTOGONAL REAKSİYONLARIN OPTİMİZASYONU

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Geçen on, yirmi yıl içinde sentetik organik kimya dalı daha sonralardan “ortogonal klik reaksiyonları” adı altında incelenecek olan, yüksek seçiciliğe ve etkiye sahip reaksiyonları incelemeye aldı. Bu tip reaksiyonlar yıllarca peptit sentezi, homojen katalizörler ve supramoleküler sistemlerin geliştirilmesi gibi bir çok alanda kullanım imkanı buldular. Diğer taraftan, fotosentetik bakterilerin ve bitkilerin ışık enerjisini kimyasal enerjiye çevirerek karbon dioksiti indirgemek için güneş ışığını nasıl hasat ettiğinin kısmen anlaşılmasının ardından ışık hasatı yapan yapay sistemlerin önemi daha da arttı. Günümüzün en önemli ve kaçınılmaz sorunlarından birinin gelecek için alternatif enerji kaynaklarını ve cihazlarını geliştirmek olması, bu ışık hasadı yapan ve güneş ışığını yoğunlaştıran yapay sistemlerin geliştirilmesi yolunu açtı. Ancak, diğer makromoleküler sistemler gibi, maliyeti düşürmek için bu çeşit araçların sentezlenmesinin kolay ve etkili olması gerekir. Bu noktada, ortogonal klik reaksiyonları, ılıman şartlarda ilerleyebilmesi ve etkili olması nedeniyle, ışık hasatlayan moleküllerin kolay hazırlanmasına ortam hazırlayabilir ve kuşkusuz incelenmeye değerdir. Bu yüzden bu tezde ışık hasadında kullanılmak üzere tiyol, Michael alıcı gruplar, amin ve izotiyosiyanatla fonksiyonlandırılmış BODIPY boyar maddelerinin sentezi

önerildi. Ayrıca, bu maddelerin üzerinde Michael tipi tiyol – alken reaksiyonunun optimizasyonu tartışıldı. Hazırlanan metil metakrilat, siyanoasetik asit ve nitroolefin gruplarının arasında nitroolefin takılmış BODIPY molekülü en etkili olarak bulundu. Bu reaksiyonun sonucunda oluşan molekülün floresans ve enerji transfer ölçümleri alındı.

Anahtar Kelimeler: BODIPY, ışık hasadı yapan dendrimerler, ortogonal reaksiyonlar, klik kimyası, tek-aşamalı sentezler, tiyol – alkene reaksiyonu.

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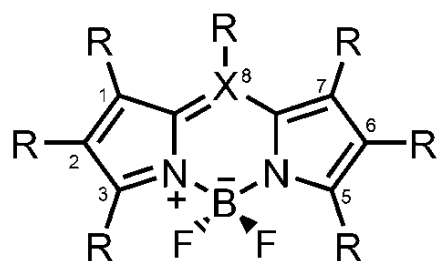
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LIST OF ABBREVIATIONS

BODIPY	Boradiazaindacene
DCM	Dichloromethane
TLC	Thin layer chromatography
NMR	Nuclear magnetic resonance
UV-VIS	Ultraviolet Visible
HOMO	Highest Occupied Molecular Orbital
LUMO	Lowest Unoccupied Molecular Orbital
TOF	Time of Flight
Et₃N	Triethylamine
MS	Mass Spectroscopy
MeOH	Methanol



R = H or any other group
X = C or N

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Chapter 1

Introduction

1.1 The “Orthogonality” Term and Click Chemistry

1.1.1 The Orthogonality Term

In multistep organic synthesis, chemoselectivity of protecting groups have gained vital importance in order to play easily with the functional groups in different chemical environments. The term “orthogonality” was first used for this chemoselectivity of a particular protecting group in the presence of other functionalities in 1977 by Merrifield[1]. Although it was limited to this definition at those times, the understanding from the term has dramatically broadened such that any mild and efficient covalent or non-covalent interactions that can proceed with no crosstalk was counted as orthogonal reactions. After recognizing the orthogonal protecting groups’ versatility, the orthogonal coupling reactions were to be pushed one step further in order to avoid protection and deprotection steps in multistep construction of complex molecules. For that purpose, Ogawa *et al* has proposed a new way of glycosylation that employs orthogonal strategy in 1994 using phenylthioglycosides and glycosyl fluorides as acceptor and donor molecules respectively[2]. They describe their new approach as following: “ The criteria for this concept to be practical are that X should be unaffected under condition b required to activate the other donor (i.e. Y), and *vice versa*, and both X and Y should remain compatible with subsequent manipulations of temporary protecting groups. For this orthogonal strategy, we selected the phenylthio group for X and fluoride for Y...” [2]. The same group has developed similar orthogonal systems for use in solid phase oligosaccharide synthesis on polymer supports[3], [4].

1.1.2 Orthogonal Reactions in Dendrimers

Fast preparations of polymers and dendrimers have also utilized this protection – deprotection free orthogonal strategy, reported first by Zimmerman[5]. He and coworkers demonstrated first orthogonal dendrimer synthesis of two AB₂ type monomers via employing Sonogashira coupling and Mitsunubi esterification reactions alternatively (Figure 1). They basically utilized the “orthogonality” of these two types of reactions in order to avoid protection and deprotection steps. After that, Fréchet extended this approach using AB₄ monomers for more rapid construction of a dendrimer and etherification reactions[6]. Another orthogonal dendrimer synthesis was proposed

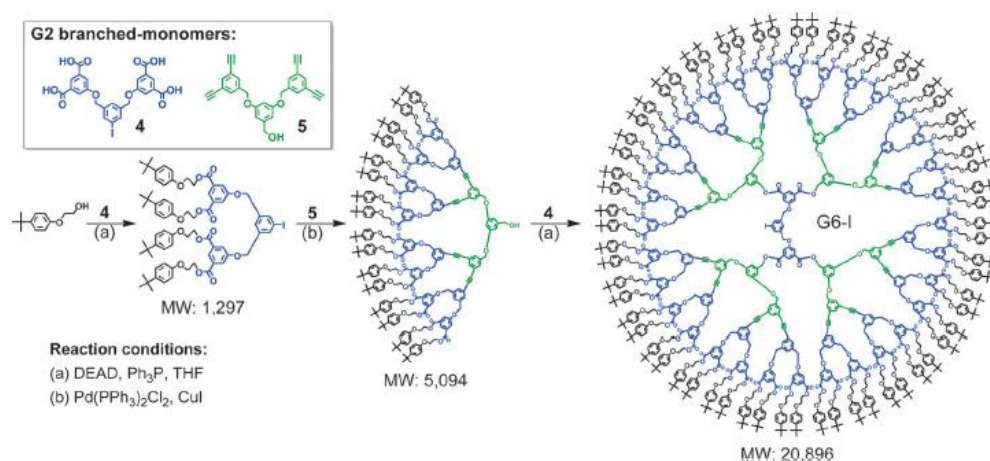


Figure 1. Rapid synthesis of G6 dendrimer by orthogonal Mitsunubi and Sonogashira reactions.

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by Majoral and coworkers in a manner of divergent approach[7]. In this strategy, the two orthogonal reactions were reported as condensation reaction of aldehyde and phosphorhydrazides, and Staudinger reaction of azide and phosphines. No need for activating agent, protecting group or deprotection steps makes this synthesis a suitable orthogonal system according to those days' terminology. As a

development over Zimmerman's heterogeneous linkage systems, Yu and co-workers have described a new set of reactions that utilizes same type of chemical constituents, in that case, vinylene-type functional groups[8]. In this sense, two AB₂ type monomers were alternatively to undergo Heck and Horner–Wadsworth–Emmons reactions with the same vinyl moiety ending up homogeneous dendrons with a single functionality.

Hawker group reported several dendrimer synthesis approach utilizing CuAAC[9]:[10] and thio-ene[11] reactions to accelerate the synthetic process. After that, Hawker tried to push the limits of the acceleration of dendrimer synthesis using thiol-ene and CuAAC click reactions on AB₂/CD₂ type so that G6 dendrimer has been prepared in a single day[12]. Another Hawker's work has demonstrated a new set of orthogonal reactions for the rapid growth of the dendritic scaffold by using epoxy – amine and thiol – ene reactions[13]. Recently, Monteiro has utilized a set of functional groups that can be used for two orthogonal reactions, namely, CuAAC and nitroxide radical coupling (NRC) to prepare dendrimers. The synthesis has been undergone by using convergent, divergent and simultaneous approach. Furthermore, this synthetic utility has been extended to linear telechelic polymer building block, such as polystyrenes, polyethylene glycols, PNIPAM.

Lowe *et. al.* reported another facile orthogonal synthesis of polyfunctional materials utilizing thiol – ene and thiol – yne reactions[14]. First thiol – ene reaction has been mediated by phosphine catalysts and undergone via anionic mechanism, whereas, thiol – yne reaction was conducted via radicalic mechanism, therefore, claims the orthogonality of two mechanistically different reactions.

Recently, Zhang *et.al.* have developed processable dendrimer with carbazoles as a transporting unit[15]. Synthetic approach of two alternating reactions that provides orthogonality was CuAAC and Williamson ether synthesis. Protection and activation could be avoided by this method.

More examples will be provided in Section 1.1.5.

1.1.3 Chemical Ligation of Peptides

Chemical synthesis of peptides and proteins is substantial among very broad research themes, such as biomedical materials, therapeutic drug discovery *etc.* Although, probably mostly used synthetic method is solid-phase approach which employs stepwise synthetic steps, it is thought not to be sufficiently versatile method for longer sequences since multiple purification steps may become problematic[16–18]. Therefore, new practical method with less purification steps for proteins greater than 200 amino acid residues was required. At the beginning of 90s, chemical ligation method was reported to attach multiple small peptide sequences covalently with specific reactions. In this method, chemoselective reactions of unprotected peptides have been utilized[19]. Later on, an extension of this method, native chemical ligation of peptides have been reported[20–22]. In these work, basically, peptide- α -thioester linkage between unprotected peptide segment and another unprotected amino-terminal Cys containing peptide segment have been formed and without any change in the reaction conditions, the intermediate entropically goes intramolecular reaction forming a native peptide bond. The orthogonality of this lies in the fact that intermediate thioester linkage is not reactive towards hydroxyl nucleophiles, rather it chooses to react with thiols(Figure 2).

1.1.4 Orthogonal Catalysis

In organic synthesis, transition metal catalyzed reactions have attracted much attention because of their unique chelating capabilities. However, their efficiency have been limited by multistep obstacles varying from workup to purification. Therefore, one-pot chemoselective catalytic processes have been utilized under different names but similar terminologies, such as tandem, domino, zipper, cascade, orthogonal or multifunctional catalysis *etc.* Buchwald and co-workers have improved Cu-catalyzed N1 arylation reaction with aryl iodides and bromides, and Pd-catalyzed C3 arylation reaction of oxindoles with aryl chlorides

and tosylates[23]. In this study, Pd-dialkylbiarylphosphine-based catalyst system arylated oxindole at 3 position, whereas, Cu-diamine-based catalyst system arylated only nitrogen site. Same group has revealed orthogonal N- and O- arylation of aminophenols based on Copper catalysts derived from CuI and picolinic acid for O-arylation of 3-aminophenols, and biarylmonophosphine-based palladium catalyst for N-arylation of 3- and 4- aminophenols[24].

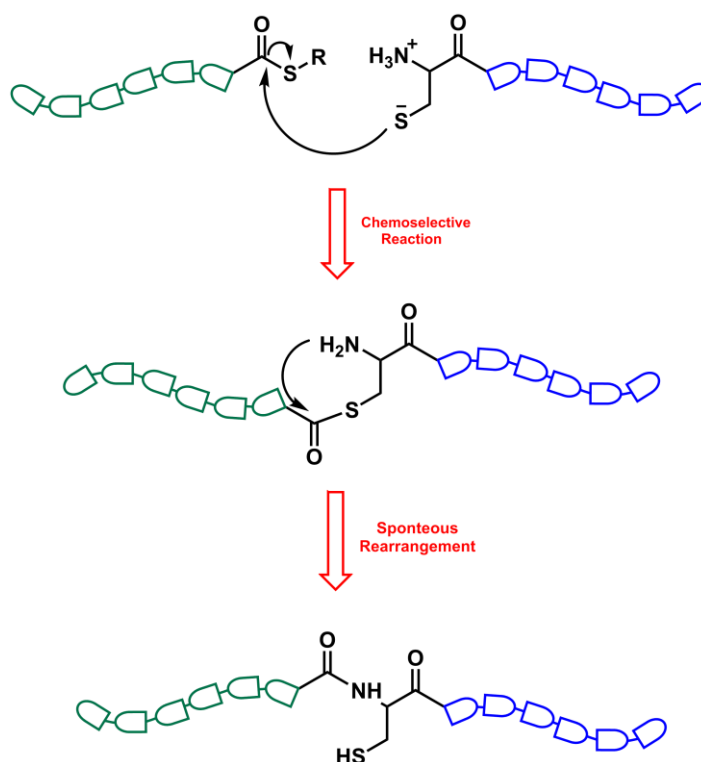


Figure 2. Native chemical ligation of peptides by [20]. The initial thioester ligation product undergoes rapid intramolecular reaction because of the favorable geometric arrangement.

In more complex orthogonal catalytic systems, the desired features should be two or more catalytic cycles that can operate simultaneously which in turn has to employ fully orthogonal sites. Chung and co-workers have developed a set of Pd(II) catalysts and Co nanoparticles that can catalyze the synthesis of fenestranes from an enyne and alkyne diesters in three steps at one pot[25]. The synthesis of fenestranes was occurred in three independent catalytic cycles where the first and the last steps were catalyzed by Co nanoparticles whereas the second step selectively employed allyl palladium chloride thereby allowing an orthogonal process.

With similar approach, Hidai, Uemaru and coworkers have reported sequential reaction system utilizing heterobimetallic catalysts such as $[\text{Cp}^*\text{RuCl}(\text{m-SMe})_2\text{RuCp}^*\text{Cl}]$ and PtCl_2 for the synthesis of tri- and tetra-substituted furans and pyrroles[26]. Selectivity achieved among the reaction of propargylic alcohols with ketones. Another tandem catalysis in a single medium has been exemplified by Komon *et. al*[27]. Three well-defined tandem catalysts have been developed for the synthesis of branched polyethylene from a single monomer. These orthogonal catalysts react with single ethylene molecule in such a unique manner that the branched polyethylene formed thereby could not be achieved in any single or two step catalytic cycle systems. Moreover, various properties could be assigned to these polyethylenes by just changing the ratio of these three homogeneous catalysts(Figure 3).

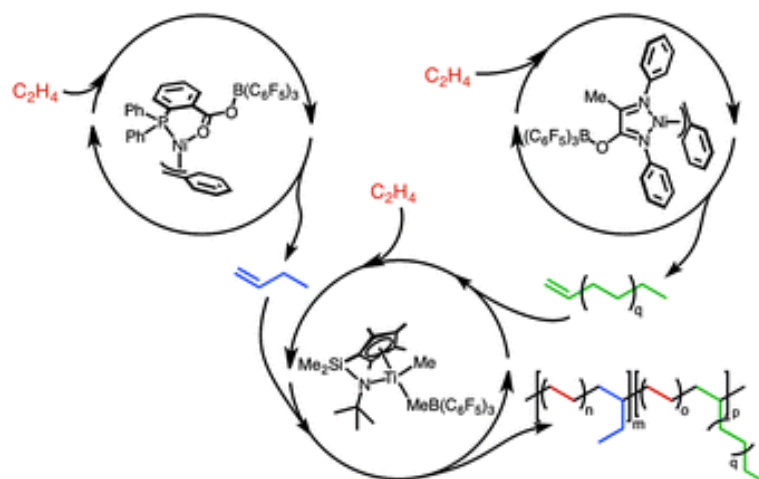


Figure 3. Three tandem catalytic cycles in a single medium. In these cycles, three orthogonal organometallic catalysts work.

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1.1.5 Orthogonal Click Reactions and Bioorthogonality

Leaving the adventurous world of click chemistry to numerous reviews published in literature[28–32], this section will mainly emphasize on the orthogonality aspect of click type reactions. The “click” term was first described

by Sharpless in 2001 as any reaction containing components that effectively react with each other, while they are blind to a broad range of reagents, solvents and other functional groups[33]. Thus, it can be comfortably deduced that any clickable groups bears a potential of being orthogonal reaction components. As a first example, copper catalyzed azide-alkyne cycloaddition (CuAAC) is one of the most widely used click reactions of today's research. It is a highly chemoselective reaction that goes under mild conditions and the functional groups (azides and alkynes) are relatively stable[33]. In this respect, Lin and Walsh have prepared carbohydrate – modified cyclic peptide antibiotics using chemoenzymatic approach[34]. The implicit orthogonality lies in the fact that the azide groups have been carried through several steps and stayed unreactive towards many functional groups. Similarly, Gin *et. al.* have demonstrated a stepwise functionalization of cyclodextrin macrocycles for the synthesis of cyclodextrins and cyclodextrin analogues from oligosaccharides[35]. This azide and alkyne functionalization on the same unit reacts with each other forming cyclodextrin macrocycles in an easy way.

1.1.6 Orthogonal Functionalization of Polymers

Post-functionalization of polymers have also utilized click chemistry in order to enable easy conversions under mild conditions[36]. Among these modifications, there are several functional groups including isocyanates[37], oxazolones[38], epoxides[39], thiols[40], alkynes[41], *etc.* Hawker group has synthesized a water soluble terpolymer with alkyne and hydroxyl ends that can be further functionalized by CuAAC and esterification reactions in both one pot orthogonal strategy or cascade type synthesis[42]. Lyon described a similar approach for the formation of multi-responsive gels[43]. The authors made use of azide/alkyne and amine/carboxylic acid functional groups for orthogonal coupling of CuAAC and EDC based amidation. Yang and Weck have used CuAAC and hydrazone formation for the functionalization of poly(norbornene) based random copolymers[44], while Tunca *et.al.* developed a similar process for the synthesis

of heterograft copolymers using CuAAC and Diels-Alder reaction[45]. Again, Tunca and co-workers have improved this orthogonal synthesis one step further, that is, they have synthesized linear tetrablock copolymers in one pot by using three orthogonal reactions, namely, CuAAC, Diels-Alder and nitroxide radical coupling(Figure 4)[46].

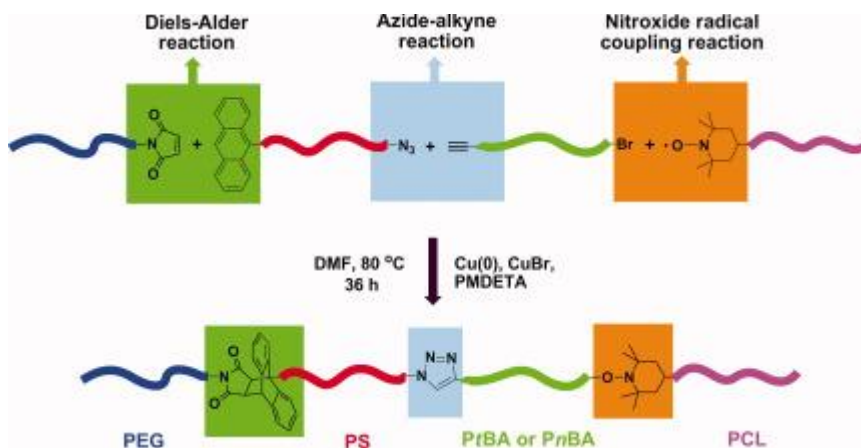


Figure 4. Synthesis of heterograft polymers using orthogonal CuAAC – Diels-Alder – Nitroxide Coupling reactions.

From[46]. Adapted with permission from John Wiley and Sons.

Although the high chemoselectivity of CuAAC makes it to be a good choice of orthogonal reaction in the presence of many other functional groups, the method is not merely perfect due to inconsistencies in some environments. For example, copper catalyst may be poisoned by nucleophilic thiol species and its removal can be problematic at workup, and oxime formation is not compatible with CuAAC[47].

Some specific imine formation reactions can also be accounted as click reaction and have been classified by Sharpless[33]. The difference of this from the conventional CuAAC click reaction is that it may be reversible at some conditions. With this knowledge, Elisev and Lehn have developed a dynamic combinatorial library based on orthogonal imine formation and metal – ligand exchange reactions[48]. Orthogonal exchange reactions are not limited by this

work however, there are also hydrazone formation – disulfide exchange[49] and imine formation – nitrene[50] formation have been reported.

1.1.7 Bioorthogonal Click Reactions

The growing importance of the development of orthogonal reactions in organic synthesis resulted questions about the reactions in biological systems. Since natural biological environment have lots of different proteins, peptides, carbohydrates and enzymes, the reaction expected to occur in this environment should of course be blind all those molecules in the presence of a number of functional groups. Therefore, a new research area started growing in terms of orthogonality, but this time, it was coupled to biological systems. Bertozzi put the term bioorthogonality first at 2003 and defined as any chemical reaction that can occur inside of the living system without interfering with the native biochemical process[51].

A potential bioorthogonal reaction should first occur in aqueous media and beyond that, it should go in living cells and organisms. With this respect, a modified Staudinger reaction reported by Bertozzi and Saxon can be counted as a bioorthogonal reaction[52]. The conventional Staudinger reaction occurs between azide and phosphines in aqueous environment and essentially unreactive towards biomolecules inside the cells or living organisms. However, it is initial adduct, the aza-ylide is not stable in water. At this point, Bertozzi and Saxon developed a new triarylphosphine molecules that can go under rearrangement and form a stable aza-ylide adduct.

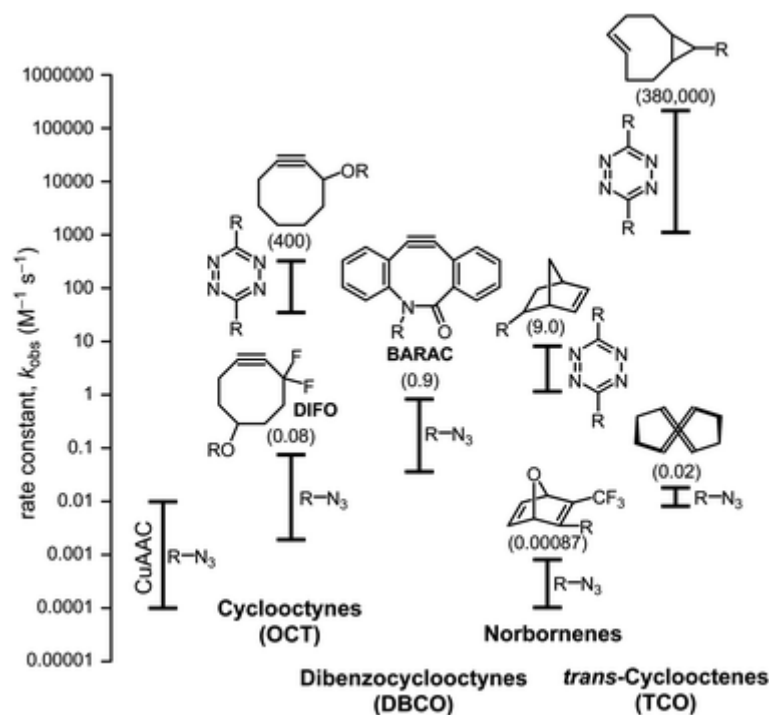


Figure 5. Comparison of rate constants of bioorthogonal reactions reported in literature. Numbers in paranthesis are the largest rate constants reported in those series.

From[53]. Adapted with permission from John Wiley and Sons.

The conventional CuAAC has been used as bioorthogonal reaction in different cell environments[54], however, the toxicity of copper has always been a problem. Although, polytriazole ligands have been used to protect the cells from reactive oxygen species formed by Cu-catalyzed reduction of oxygen[55], no considerable development has been achieved unless Bertozzi and co-workers presented strain promoted azide-alkyne cycloaddition (SPAAC)[51]. In this reaction, under the light of Wittig and Krebs study on cycloalkynes and phenyl azides[56], Bertozzi and co-workers have developed cyclooctyne ring molecules that can react with azides about 70 times slower than in CuAAC, but it occurs in the absence of any catalysts. The main driving force for this reaction is, as its name states, high ring strain of cyclooctyne ring which is also a smallest stable alkyne ring and has ring strain of 19.9 kcal/mol[57]. The rate has been accelerated by different cyclooctyne designs like dibenzocyclooctynes[58] and difluorosubstituted cyclooctynes[59]. One of the drawbacks of these systems was

their tedious synthesis and their low water solubility because of the aromatic rings. As a solution, Sletten and Bertozzi reported dimethoxyazacycloctyne (DIMAC) system showing higher hydrophilicity[60].

A tetrazine based inverse electron demand cycloaddition has also great importance among bioorthogonal reactions because of its high rates[61]. Lemke *et. al.* have developed norbornene and *trans*-cyclooctene units that can react with tetrazine units in an inverse-electron-demand Diels – Alder cycloaddition to label living cells[62]. A modification of this cycloaddition is called strain promoted inverse electron demand Diels – Alder cycloaddition (SPIEDAC) and showed accelerated reaction rate with irreversibility because of the loss of N₂[63].

1.2 Energy Transfer Mechanisms and Light Harvesting Phenomenon

Photosynthesis has become invaluable inspiration source of scientists for years in terms of especially energy harvesting from sunlight. In 1932, Emerson and Arnold have shown that multiple chlorophyll species have to be concentrated around one center that can reduce one carbon dioxide molecule[64]. This was concluded to a perfect design that can absorb sunlight (by donor molecule excitation), transfer it to a center and a specific reaction can undergo therein. Later, this energy funneling has proven to be a result of “resonance energy transfer”.

When a molecule is excited, there are number of pathways that this absorbed energy can follow such as fluorescence, phosphorescence, radiationless decay, intersystem crossing, *etc.*(Figure 6) Thus, if essential conditions have been fulfilled such as sufficient distance between chromophores or spectral overlap of them, donor molecule transfer its energy (when it is excited) to another acceptor molecule in a non-radiative way such that lifetime of the donor molecule’s excited state is shortened[65]. This process is called resonance energy transfer (RET) or

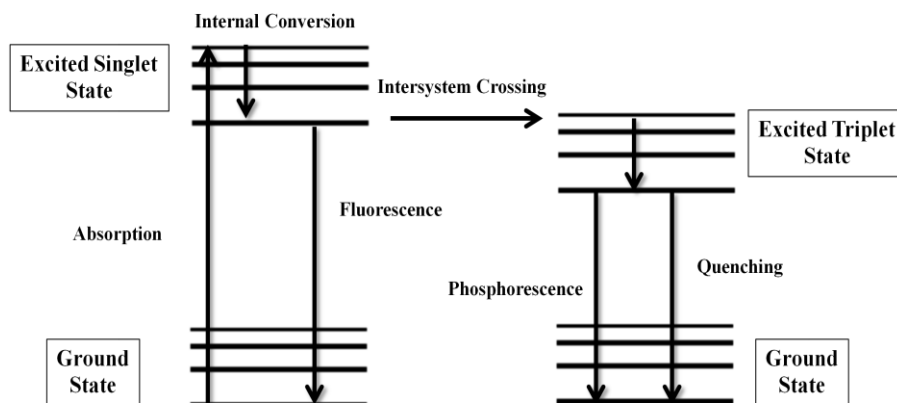


Figure 6. Jablonski Diagram

electronic energy transfer (EET). This phenomenon was proved with fluorescence quenching experiments. Therefore, it was sometimes called Fluorescent Resonance Energy Transfer or simply FRET. This however should not be confused with Förster Resonance Energy Transfer (due to same acronym) which is a different RET mechanism suggested by Förster[66].

For energy transfer, at least one donor molecule and one acceptor molecule are required. Between these two molecules, there has to be some interaction or coupling. Energy difference between HOMO and LUMO of donor and acceptor molecules are defined as ΔE_D and ΔE_A respectively, and V as interaction energy, the coupling will be strong if

$$V \gg \Delta, \quad (1.1)$$

$$\text{whenever } \Delta = \Delta E_d - \Delta E_a > 0. \quad (1.2)$$

In the case of Coulomb coupling, excitation oscillates between donor and acceptor with a frequency,

$$\Omega = \frac{\sqrt{\Delta^2 + |V|^2}}{h} \quad (1.3)$$

That means, energy of the electronic excitation is delocalized between donor and acceptor. However, for most applications, instead of oscillation, directional energy transfer is required. Therefore, Förster approximates weak coupling limit for this equation to make RET from donor to acceptor possible.

1.2.1 Förster Energy Transfer Mechanism

When the distance between the donor and acceptor molecules is large, the coupling is restricted to the electric dipole – dipole interactions between donor and acceptor. The coupling described here can be defined as coupling of the multipolar transition moments of the donor and acceptor molecules via electrostatic interaction, in other words coupled oscillators. This distance should vary from 30 Å - 100 Å.

The coulombic interactions between these two molecules result into a virtual photon exchange (rather than an electron transfer) from excited donor to ground state acceptor. The overlap of the donor's emission and acceptor's absorption is essential since RET rate is proportional to it. The distance between donor and acceptor molecules and relative orientation of the transition dipoles have also important parameters in RET rate. Considering all of these, RET rate can be defined as follows;

$$k^{Forster} = \frac{\phi_D R_0^6}{\tau_D} \frac{1}{R^6}, \quad (1.4)$$

ϕ_D := Quantum yield of the donor in the absence of acceptor,

τ_D := Lifetime of the excited donor in the absence of acceptor,

R := The distance between donor and acceptor.

where

$$R_0^6 = \frac{9000 \ln(10) \kappa^2 I}{128 \pi^5 N n^4}.$$

(1.5)

I := Förster overlap integral of the normalized donor emission and acceptor absorbance,

κ := Orientation factor associated with the dipole – dipole interaction,

n := Refractive index of the medium,

N := Avogadro's number.

The Förster formula described above converges to accuracy in the absence of perturbation of donor emission line shape or fluorescence lifetime, acceptor absorption line shape, oscillator strength, and static disorder. If energy transfer dynamics is incoherent which is attributed to weak donor acceptor interaction, this formula can also be accurate.

1.2.2 FRET Efficiency

By using time-resolved approach, one can easily calculate Förster energy transfer efficiency.

$$k_{\text{FRET}} = 1/\tau_{\text{DA}} - 1/\tau_{\text{D}} \quad (1.6)$$

$$E = \tau_{\text{D}} k_{\text{FRET}} / (1 + \tau_{\text{D}} k_{\text{FRET}}) \quad (1.7)$$

where k_{FRET} is the FRET rate and E is the energy transfer efficiency. τ_{D} and τ_{DA} represents the excited state lifetime of donor in the absence and presence of acceptor respectively. When combining equation (1.6) and (1.7) ;

$$E = 1 - \tau_{\text{DA}}/\tau_{\text{D}} \quad (1.8)$$

In addition to time-resolved approach, one can also use steady-state approach. The difference is that in steady-state approach, quantum yield of donor is used instead of excited state lifetime of that (eqn. 1.9).

$$E = 1 - \Phi_{\text{DA}}/\Phi_{\text{D}} \quad (1.9)$$

Enhancement in fluorescence emission of acceptor can also be used in steady state approach:

$$E = A_{\text{A}}(\lambda_{\text{D}}) / A_{\text{D}}(\lambda_{\text{D}}) * [I_{\text{AD}}(\lambda_{\text{A}}^{\text{em}}) / I_{\text{A}}(\lambda_{\text{A}}^{\text{em}}) - 1] \quad (1.10)$$

where A_{A} and A_{D} are defined as absorbance values of acceptor and donor respectively at the maximum absorbance of donor. I_{AD} and I_{A} are integrated area of emission of acceptor in the presence and absence of donor respectively.

1.2.3 Dexter Type Energy Transfer

Whenever the distance between chromophores gets smaller, the dipole – dipole approximation used in Förster type fails. At this point, high intermolecular interactions should be taken account. Also, molecular orbitals can overlap significantly, so that exchange interaction becomes important. This case is simply called Dexter type energy transfer when the distance is in range of 6-20 Å^o[67].

In this type of energy transfer, rather than photon transfer between donor and acceptor, electron is exchanged in a non-radiative process through orbitals of donor and acceptor molecules. This is mostly associated with quenching process. The process was utilized within many types of emitting materials, such as white organic light emitting diodes[68], energy up-conversion systems[69], [70].

Unlike Förster type in which rate constant is sixth power dependent on the distance between two chromophores, Dexter proposes energy rate constant that decays exponentially with the distance. Hence, this mechanism is also called short-range energy transfer.

Since electron is being exchanged from one to another party, besides spectral overlap of the chromophores used, orbital overlap is essential in this mechanism. Whenever this overlap established, excited electron placed on LUMO of the donor is transferred to LUMO of the acceptor, whereas ground state electron at HOMO of acceptor molecule is transferred to HOMO of the donor molecule. By this way, acceptor molecule is left in excited state which can then be emitting photons and fluoresce.

Energy transfer rate can be calculated as follows:

$$k_{Dexter} = K J \exp\left(\frac{-2R_{DA}}{L}\right) \quad (1.11)$$

where K is orbital interaction (experimental factor), J is the spectral overlap integral and R_{DA} is the distance between donor and acceptor molecules.

1.2.4 Light Harvesting Dendrimers

As discussed before, photosynthesis has become inspiration for all artificial light harvesting systems. These antennas was aimed to collect solar energy and redirect it to a particular center for further purposes. Dendrimers are usually used for this antenna systems which may be useful not only for energy

conversion, but also for sensitization of photovoltaics[71], signal amplification[72], molecular lenses[73].

In biosystems, the process occurs in specific region that includes light harvesting complexes (array of chromophores) which can absorb light and convert into chemical energy to the reaction center. In such systems of purple bacteria, high number of bacteriochlorophylls are wheel like organized and formed light harvesting antenna complexes 1 and 2 (LH1 and LH2)[74], [75].

Biomimicry of these complexes has been studied for years especially using dendrimers due to their tree-like structure which can enable the funnelling of the energy occurs effectively. First, Moore *et.al.* have reported unidirectional energy transfer using phenylacetylene dendrimers in which perylene dye is present at the focal core. Therefore, strong absorption in around 300 nm of the phenyl groups ends up showing emission in the range 350-450 nm which corresponds to the emission wavelength of perylene dyes[76], [77].

Furthermore, Mullen and coworkers have synthesized polyphenylene dendrimers which have naphthalene dicarboxymonoimide (NDI) at the periphery, perylene dicarboxymonoimide (PDI) in the interior, and terrylene tetracarboxydiimide (TDI) at the focal core.

As natural light harvesting chromophore, porphyrin have been used for dendritic design of antenna complexes. Lindsey *et al.* have reported star-shaped porphyrin dendrimer design in which the chromophores are connected via diphenylethyne units[78]. Similar design using metalloporphyrins has been reported by Sanders as well[79]. In addition, Aida and coworkers synthesized multi-porphyrin arrays to approach the light harvesting antenna complex of purple bacteria which has four Zn porphyrin heptamer units responsible for energy donation and a focal free porphyrin unit as an acceptor[80], [81].

Chapter 2

Experimental

2.1 General

All chemicals and solvents purchased from Aldrich and Merck were used without further purification. Column chromatography of all products was performed using Merck Silica Gel 60 (particle size: 0.040–0.063 mm, 230–400 mesh ASTM). Reactions were monitored by thin layer chromatography using Merck TLC Silica gel 60 F254. Anhydrous tetrahydrofuran was obtained by refluxing over sodium metal/benzophenone prior to use.

^1H NMR and ^{13}C NMR spectra were recorded on Bruker DPX-400 (operating at 400 MHz for ^1H NMR and 100 MHz for ^{13}C NMR) in CDCl_3 solvent with tetramethylsilane as internal standard. All spectra were recorded at 25 °C and coupling constants (J values) are given in Hz. Chemical shifts are given in parts per million (ppm) and splitting patterns are shown as s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet), and p (pentet).

Mass spectra were recorded with Agilent Technologies 6224 TOF LC/MS. Absorption spectra were performed by using a Varian Cary-100 and Varian Cary 5000 UV-VIS-NIR absorption spectrophotometer. Fluorescence measurements were conducted on a Varian Eclipse spectrofluorometer.

2.2 Synthesis of Compound 1

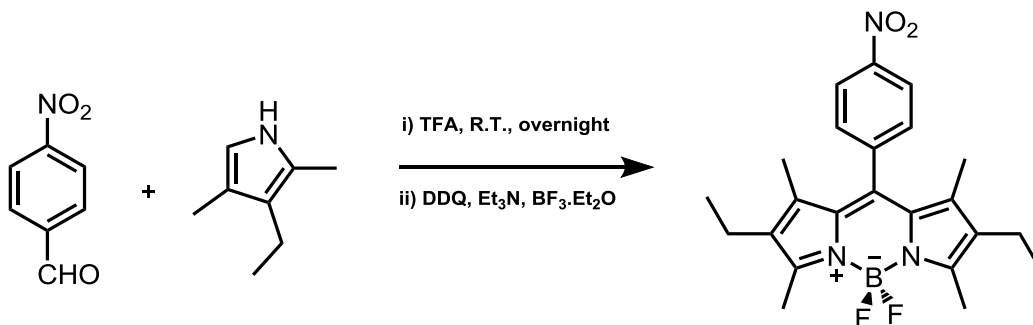


Figure 7. Synthesis of Compound 1

4-nitrobenzaldehyde (1 g, 6.66 mmol) and 2,4-dimethyl pyrrole (1.6 g, 13.2 mmol) were dissolved in 250 mL Ar degassed DCM. After addition of one drop of trifluoroacetic acid, the solution was left stirring at room temperature overnight. *P*-chloranil (1.55 g, 4.27 mmol) was added and further stirred for 30 min. 8 mL triethylamine and 8 mL BF₃.Et₂O were added consecutively. After further stirring at room temperature for 30 min., extraction has been done with brine solution. Organic layer is dried over Na₂SO₄ and evaporated in *vacuo*. The product was purified with DCM/Hex (1:2) using silica gel column chromatography (430 mg, 1.01 mmol, 15%).

¹H NMR (400 MHz, CDCl₃) δ 8.40 (d, *J* = 8.4 Hz, 1H), 7.56 (d, *J* = 8.4 Hz, 1H), 2.56 (s, 4H), 2.33 (q, *J* = 7.5 Hz, 2H), 1.28 (s, 4H), 1.01 (t, *J* = 7.5 Hz, 4H). ¹³C NMR (101 MHz, CDCl₃) δ 154.99, 148.24, 142.89, 137.68, 133.51, 129.93, 124.26, 17.06, 14.55, 12.60, 12.01.

MS HRMS (TOF-ESI): *m/z* calculated for [M]⁺ 405,21384 found 405,2199 Δ = -14,83 ppm

2.3 Synthesis of Compound 2

Compound 2 was synthesized according to the literature[82]. Compound 1 (230 mg, 0.54 mmol) was dissolved in DCM(2 mL), EtOH(10 mL), H₂O (2 mL) and Fe powder (300 mg, 5.4 mmol) were added to the reaction mixture followed by refluxing. After that, HCl solution in methanol (2 mL, 0.5 M) was added dropwise and refluxing continued for 4 hours more. After TLC analysis showed the complete consumption of starting material, the Fe powders were filtrated and the reaction was concentrated at reduced pressure. The product was purified by flash silica gel column chromatography with DCM/MeOH (95:5) (165 mg, 0.41 mmol, 77%)

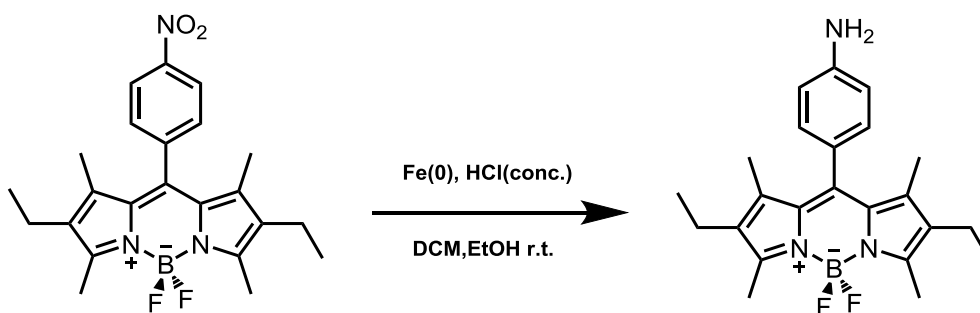


Figure 8. Synthesis of Compound 2

¹H NMR (400 MHz, CDCl₃) δ 7.03 (d, J = 8.3 Hz, 2H), 6.80 (d, J = 8.4 Hz, 2H), 2.54 (s, 6H), 2.33 (q, J = 7.6 Hz, 4H), 1.42 (s, 6H), 1.00 (t, J = 7.6 Hz, 7H).

2.4 Synthesis of Compound 3

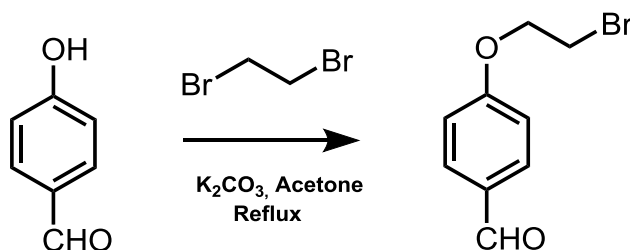


Figure 9. Synthesis of Compound 3

1,2-dibromoethane (8.5 mL, 98.28 mmol) was added to the mixture of 4-hydroxybenzaldehyde (3 g, 24.57 mmol) in acetone (30 mL). Catalytic amount of 18-crown-6 ether and potassium carbonate (3,6 g) were added and the reaction mixture was refluxed overnight. Organic layer is dried over Na₂SO₄ and evaporated in vacuo. The product was purified with DCM using silica gel column chromatography (4 g, 17.46 mmol, 71%).

¹H NMR (400 MHz, CDCl₃) δ 9.92 (s, 1H), 7.87 (d, *J* = 8.8 Hz, 2H), 7.04 (d, *J* = 8.7 Hz, 2H), 4.40 (t, *J* = 6.2 Hz, 2H), 3.69 (t, *J* = 6.2 Hz, 2H).

2.5 Synthesis of Compound 4

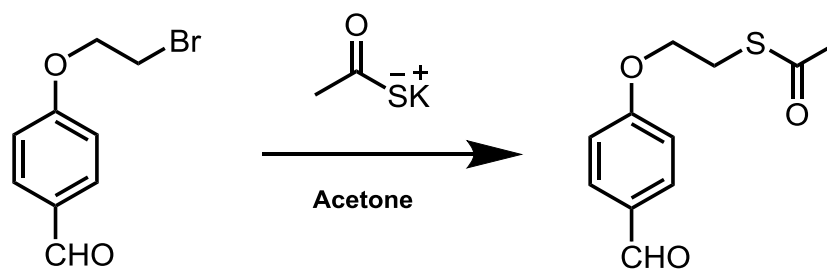


Figure 10. Synthesis of Compound 4

Compound **3** (2.4 g, 10.48 mmol) was dissolved in acetone (15 mL) and potassium thioacetate (2.28 g, 20 mmol) was added to the solution. The mixture was heated to 60 °C overnight. After that, acetone was evaporated under reduced pressure and extraction has been conducted with DCM and water. Organic layer is dried over Na₂SO₄ and evaporated in vacuo. The product was purified with DCM using silica gel column chromatography (1.95 g, 8.7 mmol, 83%).

¹H NMR (400 MHz, CDCl₃) δ 9.90 (s, 1H), 7.85 (d, *J* = 8.9 Hz, 2H), 7.03 (d, *J* = 8.8 Hz, 2H), 4.19 (t, *J* = 6.5 Hz, 2H), 3.31 (t, *J* = 6.5 Hz, 2H), 2.39 (s, 3H).

2.6 Synthesis of Compound 5

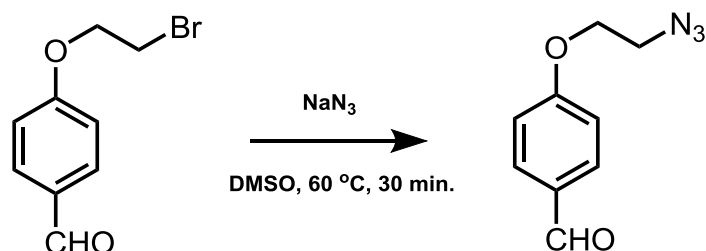


Figure 11. Synthesis of Compound 5

Compound 3 (2.4 g, 10.48 mmol) was dissolved in minimum DMSO and excess amount of sodium azide was added to the solution. The mixture was heated to 60 °C for about 30 min. Extraction has been conducted with DCM and water. Organic layer is dried over Na₂SO₄ and evaporated in *vacuo*. The product was purified with DCM using silica gel column chromatography (2 g, 10.46 mmol, 99.8%).

¹H NMR (400 MHz, CDCl₃) δ 9.90 (s, 1H), 7.85 (d, *J* = 8.8 Hz, 2H), 7.03 (d, *J* = 8.7 Hz, 2H), 4.23 (t, *J* = 6.2 Hz, 2H), 3.65 (t, *J* = 6.2 Hz, 2H).

2.7 Synthesis of Compound 6

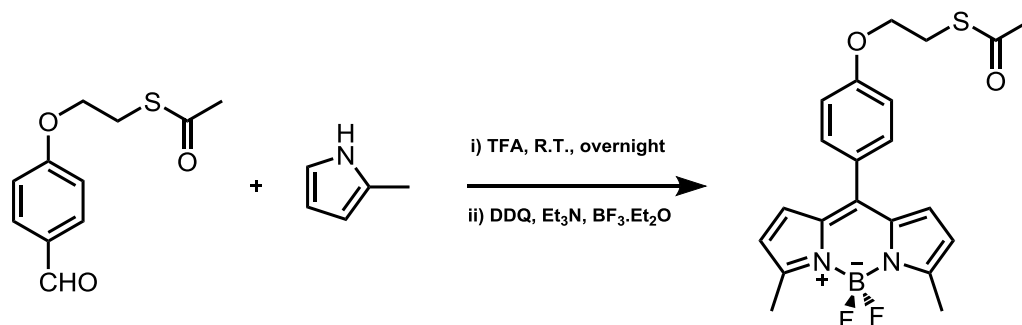


Figure 12. Synthesis of Compound 6

Compound **4** (1 g, 4.46 mmol) and 2-methyl pyrrole (0.76 g, 9.37 mmol) were dissolved in 250 mL Ar degassed DCM. After addition of one drop of trifluoroacetic acid, the solution was left stirring at room temperature overnight. *P*-chloranil (1.62 g, 4.46 mmol) was added and further stirred for 30 min. 8 mL triethylamine and 8 mL BF₃.Et₂O were added consecutively. After further stirring at room temperature for 30 min., extraction has been done with brine solution. Organic layer is dried over Na₂SO₄ and evaporated in *vacuo*. The product was purified with DCM/Hex (1:1) using silica gel column chromatography (475 mg, 1.14 mmol, 26%).

¹H NMR (400 MHz, CDCl₃) δ 7.47 (d, *J* = 8.6 Hz, 2H), 7.03 (d, *J* = 8.6 Hz, 2H), 6.76 (d, *J* = 4.1 Hz, 2H), 6.29 (d, *J* = 4.1 Hz, 2H), 4.19 (t, *J* = 6.5 Hz, 2H), 3.34 (t, *J* = 6.5 Hz, 2H), 2.67 (s, 6H), 2.41 (s, 3H).

2.8 Synthesis of Compound **7**

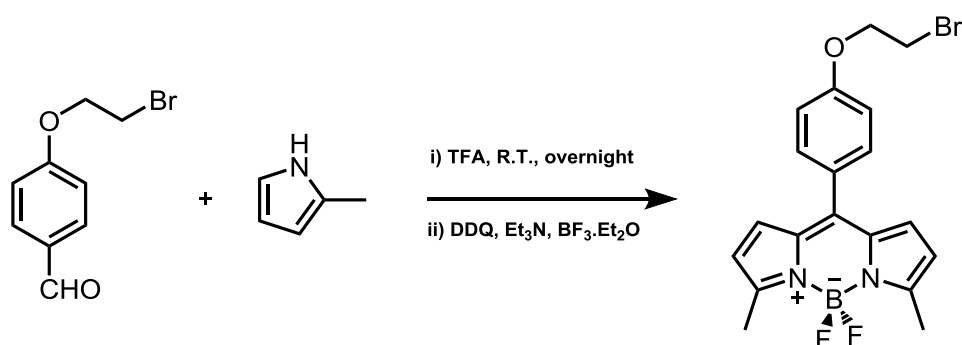


Figure 13. Synthesis of Compound **7**

Compound **3** (1 g, 4.46 mmol) and 2-methyl pyrrole (0.76 g, 9.37 mmol) were dissolved in 250 mL Ar degassed DCM. After addition of one drop of trifluoroacetic acid, the solution was left stirring at room temperature overnight. *P*-chloranil (1.62 g, 4.46 mmol) was added and further stirred for 30 min. 8 mL triethylamine and 8 mL BF₃.Et₂O were added consecutively. After further stirring at room temperature for 30 min., extraction has been done with brine solution. Organic layer is dried over Na₂SO₄ and evaporated in *vacuo*. The product was

purified with DCM/Hex (1:2) using silica gel column chromatography (435 mg, 1.04 mmol, 24%).

^1H NMR (400 MHz, CDCl_3) δ 7.46 (d, $J = 8.6$ Hz, 2H), 7.04 (d, $J = 8.6$ Hz, 2H), 6.74 (d, $J = 4.1$ Hz, 2H), 6.31 (d, $J = 4.1$ Hz, 2H), 4.4 (t, $J = 6.3$ Hz, 2H), 3.67 (t, $J = 6.3$ Hz, 2H), 2.67 (s, 6H).

2.9 Synthesis of Compound 8

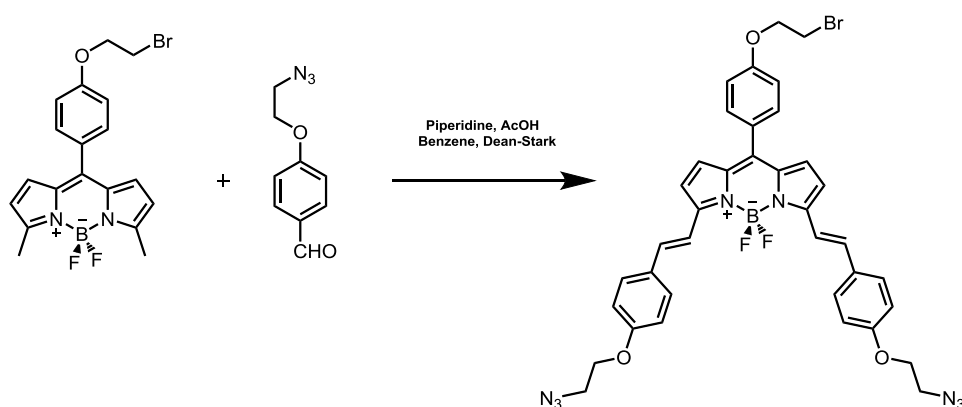


Figure 14. Synthesis of Compound 8

Compound **7** (150 mg, 0.36 mmol) and compound **5** (145 mg, 0.75 mmol) were dissolved in 25 mL benzene. Then, 0.4 mL piperidine and 0.4 mL glacial acetic acid were added consecutively to the solution. The reaction flask was left heating using Dean-Stark apparatus. After concentration of the solution, the reaction was followed by TLC till green colored spot dominated. Then, residual benzene was evaporated under nitrogen gas and product was directly purified without extraction using silica gel column chromatography, DCM (90 mg, 0.12 mmol, 30%).

^1H NMR (400 MHz, CDCl_3) δ 7.66 (d, $J = 16.2$ Hz, 2H), 7.59 (d, $J = 8.8$ Hz, 4H), 7.51 (d, $J = 8.8$ Hz, 2H), 7.25 (d, $J = 16.2$ Hz, 2H), 6.94 (d, $J = 8.8$ Hz, 4H), 6.87 (d, $J = 4.5$ Hz, 2H), 6.77 (d, $J = 4.4$ Hz, 2H), 4.31 (t, $J = 6.5$ Hz, 2H), 4.23 (t, $J = 6.2$ Hz, 4H), 3.65 (t, $J = 6.2$ Hz, 4H), 3.21 (t, $J = 6.5$ Hz, 2H).

2.10 Synthesis of Compound 9

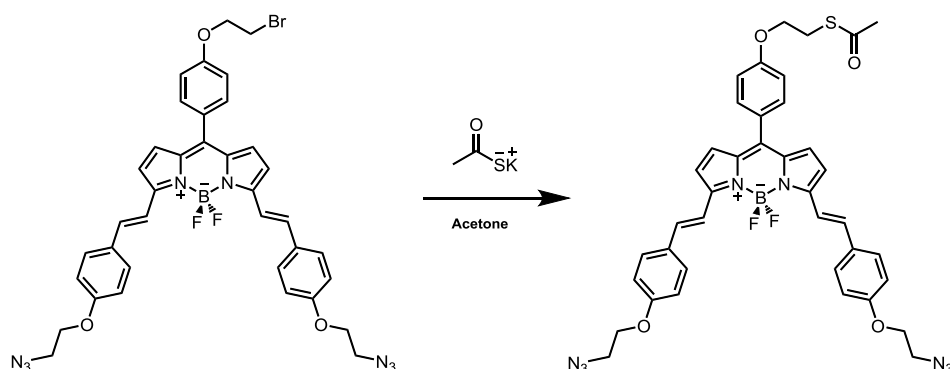


Figure 15. Synthesis of Compound 9

Compound **8** (74 mg, 0.098 mmol) was dissolved in acetone (15 mL) and potassium thioacetate (25 mg, 0.2 mmol) was added to the solution. The mixture was heated to 60 °C overnight. After that, acetone was evaporated under reduced pressure and extraction has been conducted with DCM and water. Organic layer is dried over Na₂SO₄ and evaporated in vacuo. The product was purified with DCM using silica gel column chromatography (60 mg, 0.08 mmol, 82%).

¹H NMR (400 MHz, CDCl₃) δ 7.66 (d, *J* = 16.2 Hz, 2H), 7.59 (d, *J* = 8.8 Hz, 4H), 7.51 (d, *J* = 8.8 Hz, 2H), 7.25 (d, *J* = 16.2 Hz, 2H), 6.94 (d, *J* = 8.8 Hz, 4H), 6.87 (d, *J* = 4.5 Hz, 2H), 6.77 (d, *J* = 4.4 Hz, 2H), 4.19 (t, *J* = 6.5 Hz, 2H), 4.23 (t, *J* = 6.2 Hz, 4H), 3.65 (t, *J* = 6.2 Hz, 4H), 3.23 (t, *J* = 6.5 Hz, 2H), 2.41 (s, 3H).

2.11 Synthesis of Compound 10

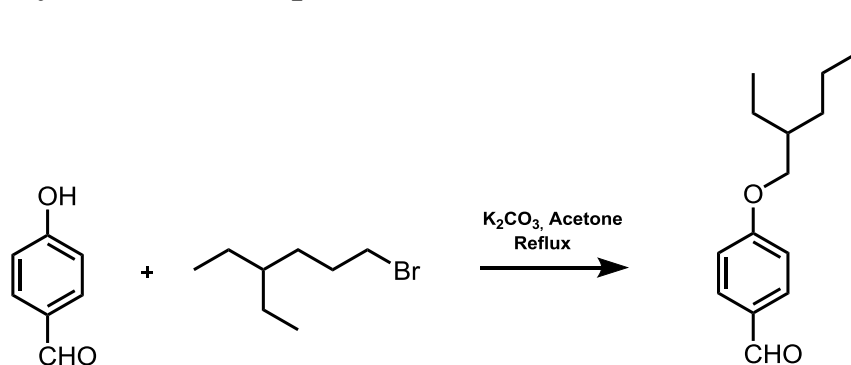


Figure 16. Synthesis of Compound 10

4-hydroxybenzaldehyde (2 g, 16.4 mmol) and 2-ethylhexylbromide (3.8 g, 19.6 mmol) were mixed in 30 mL acetone in the presence of potassium carbonate (6.79 g) and catalytic amount of 18-crown-6 ether. The mixture was refluxed overnight. After evaporation of the solvent, extraction was done using DCM. Organic layer is dried over Na_2SO_4 and evaporated in *vacuo*. The product was purified with DCM/Hex (1:4) using silica gel column chromatography (3 g, 12.8 mmol, 78%).

1H NMR (400 MHz, $CDCl_3$) δ 9.89 (s, 1H), 7.83 (d, $J = 8.8$ Hz, 2H), 7.01 (d, $J = 8.7$ Hz, 2H), 3.96 (d, $J = 3.6$ Hz, 2H), 1.77 (dt, $J = 12.2, 6.1$ Hz, 1H), 1.62 – 1.23 (m, 8H), 1.03 – 0.82 (m, 6H).

MS HRMS (TOF-ESI): m/z calculated for $[M+H]^+$ 235,16926 found 235,1755 $\Delta = -26.72$ ppm

2.12 Synthesis of Compound 11

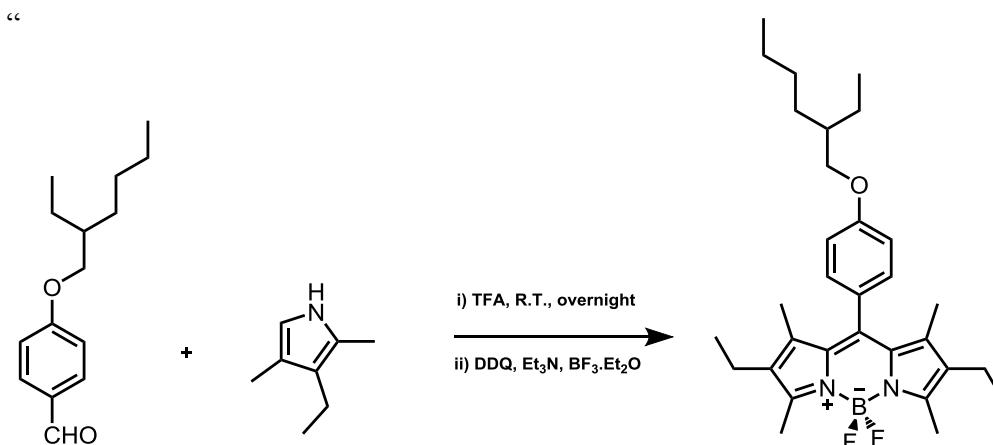


Figure 17. Synthesis of Compound 11

Compound **10** (1 g, 4.27 mmol) and 2,4-dimethyl-3-ethyl pyrrole (1.09 g, 8.9 mmol) were dissolved in 250 mL Ar degassed DCM. After addition of one drop of trifluoroacetic acid, the solution was left stirring at room temperature overnight. *P*-chloranil (1 g, 4.27 mmol) was added and further stirred for 30 min. 8 mL triethylamine and 8 mL BF₃.Et₂O were added consecutively. After further stirring at room temperature for 30 min., extraction has been done with brine solution. Organic layer is dried over Na₂SO₄ and evaporated in *vacuo*. The product was purified with DCM/Hex (1:5) using silica gel column chromatography (486 mg, 0.82 mmol, 19%).

¹H NMR (400 MHz, CDCl₃) δ 7.17 (d, *J* = 8.5 Hz, 2H), 7.01 (d, *J* = 8.5 Hz, 2H), 3.92 (d, *J* = 5.9 Hz, 2H), 2.55 (s, 6H), 2.33 (q, *J* = 7.5 Hz, 4H), 1.79-1.68 (m, 1H), 1.63 – 1.45 (m, 8H), 1.37 (s, 6H), 0.98-0.83 (m, 12H).

2.13 Synthesis of Compound 12

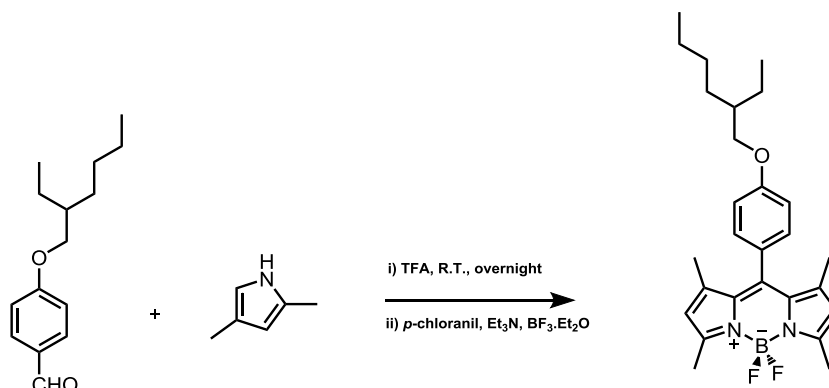


Figure 18. Synthesis of Compound 12

Compound **10** (1 g, 4.27 mmol) and 2,4-dimethyl pyrrole (0.85 g, 8.9 mmol) were dissolved in 250 mL Ar degassed DCM. After addition of one drop of trifluoroacetic acid, the solution was left stirring at room temperature overnight. *P*-chloranil (1 g, 4.27 mmol) was added and further stirred for 30 min. 8 mL triethylamine and 8 mL BF₃·Et₂O were added consecutively. After further stirring at room temperature for 30 min., extraction has been done with brine solution. Organic layer is dried over Na₂SO₄ and evaporated in *vacuo*. The product was purified with DCM/Hex (1:3) using silica gel column chromatography (415 mg, 0.92 mmol, 21%).

¹H NMR (400 MHz, CDCl₃) δ 7.17 (d, *J* = 8.7 Hz, 2H), 7.02 (d, *J* = 8.7 Hz, 2H), 6.00 (s, 2H), 3.91 (d, *J* = 5.9 Hz, 2H), 2.57 (s, 6H), 1.79-1.68 (m, 1H), 1.60 – 1.48 (m, 8H), 1.46 (s, 6H), 1.02 – 0.83 (m, 12H).

¹³C NMR (101 MHz, CDCl₃) δ 129.10, 115.15, 70.84, 39.41, 30.54, 29.15, 23.46, 14.35, 11.16.

2.14 Synthesis of Compound 13

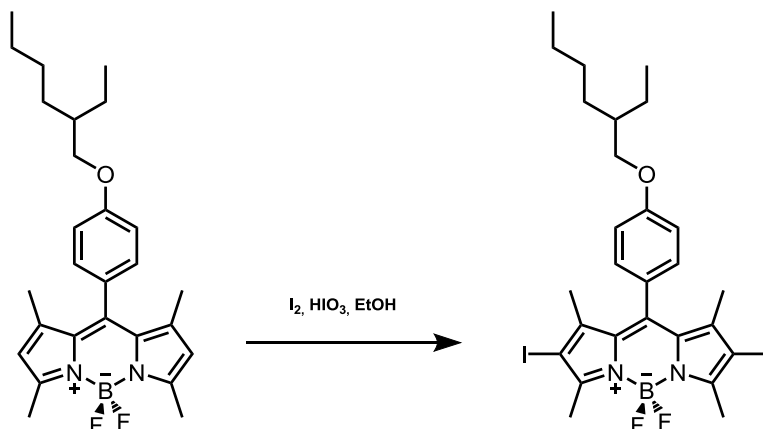


Figure 19. Synthesis of Compound 13

Compound **12** (800 mg, 1.82 mmol) and iodine (970 mg, 3.82 mmol) were dissolved in 100 mL ethanol. Iodic acid (800 mg, 4.55 mmol) was dissolved in 1 mL distilled water separately and introduced to the first solution dropwise at room temperature. The reaction was completed after about 30 min. Quenching was occurred by addition of saturated sodium thiosulfate solution and further stirring for 10 min. The reaction mixture was concentrated by evaporation of solvents and extracted with DCM. Organic layer is dried over Na₂SO₄ and evaporated in *vacuo*. The product was purified with DCM/Hex (1:3) using silica gel column chromatography (937 mg, 1.33 mmol, 73%).

¹H NMR (400 MHz, CDCl₃) δ 7.19 (d, *J* = 8.7 Hz, 2H), 7.04 (d, *J* = 8.7 Hz, 2H), 3.92 (d, *J* = 5.9 Hz, 2H), 2.57 (s, 6H), 1.79-1.68 (m, 1H), 1.60 – 1.48 (m, 8H), 1.46 (s, 6H), 1.02 – 0.83 (m, 12H).

¹³C NMR (101 MHz, CDCl₃) δ 129.01, 115.48, 70.96, 39.40, 30.54, 29.14, 23.87, 23.03, 17.19, 16.00, 14.09, 11.15.

MS HRMS (TOF-ESI): *m/z* calculated for [M+H]⁺ 702,07069 found 702,0879 Δ = -24.45 ppm

2.15 Synthesis of Compound 14

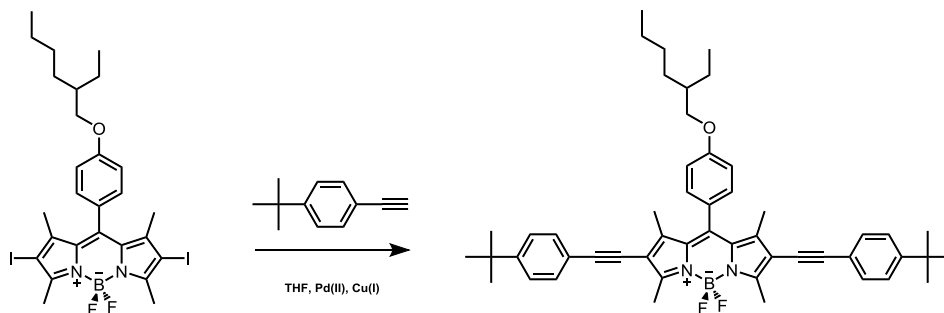


Figure 20. Synthesis of Compound 14

Compound **13** (800 mg, 1.13 mmol) was dissolved 30 mL distilled THF and 10 mL triethylamine. The flask was argon degassed for 30 min. and while degassing, PdCl₂(PPh₃)₂ (98 mg, 0.14 mmol) and CuI (58 mg, 0.23 mmol) were added at once. Finally, tert-butylphenyl acetylene (550 mg, 3.4 mmol) was introduced to the solution and the reaction was left for stirring for 30 min. After TLC analysis showed the consumption of starting material, 200 mL water was added. Extraction was done with DCM. Organic layer is dried over Na₂SO₄ and evaporated in *vacuo*. The product was purified with DCM/Hex (1:3) using silica gel column chromatography (735 mg, 0.98 mmol, 85%).

¹H NMR (400 MHz, CDCl₃) δ 7.42 (d, *J* = 8.6 Hz, 4H), 7.37 (d, *J* = 8.7 Hz, 4H), 7.18 (d, *J* = 8.7 Hz, 2H), 7.06 (d, *J* = 8.7 Hz, 2H), 3.94 (d, *J* = 5.9 Hz, 2H), 2.73 (s, 6H), 1.87 – 1.75 (m, 1H), 1.61 (s, 6H), 1.59 – 1.43 (m, 8H), 1.36 (s, 18H), 1.05 – 0.96 (m, 6H).

MS HRMS (TOF-ESI): *m/z* calculated for [M+H]⁺ 764,47976 found 764,4859 Δ = -8.05 ppm

2.16 Synthesis of Compound 15

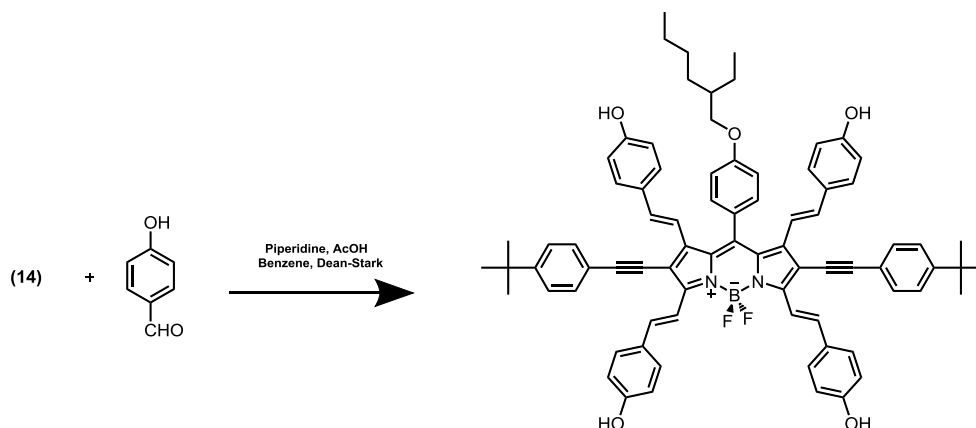


Figure 21. Synthesis of Compound 15

Compound **14** (150 mg, 0.2 mmol) and 4-hydroxybenzaldehyde (244 mg, 2 mmol) were dissolved in 25 mL benzene followed by addition of 0.6 mL piperidine and 0.6 mL glacial acetic acid. The solution was left stirring using Dean-Stark apparatus. The solvent has been evaporated using high temperatures and the reaction was followed by TLC until pale grey-green color was appeared and starting molecule was consumed. After that, any residual solvent was evaporated by N₂ degassing and the product was directly purified with silica gel column chromatography DCM/MeOH (95:5) (38 mg, 0.032 mmol, 16%).

¹H NMR (400 MHz, CDCl₃) δ 8.40 (d, *J* = 16.3 Hz, 2H), 7.58 (d, *J* = 16.2 Hz, 2H), 7.47 (d, *J* = 8.5 Hz, 2H), 7.29 (dd, *J* = 19.4, 8.8 Hz, 4H), 7.01 (d, *J* = 8.6 Hz, 1H), 6.78 (dd, *J* = 8.5, 4.3 Hz, 4H), 6.58 (d, *J* = 8.4 Hz, 2H), 5.73 (d, *J* = 16.2 Hz, 1H), 5.20 (s, 1H), 3.23 (s, 6H), 2.52 (s, 2H), 2.17 (dd, *J* = 15.5, 7.8 Hz, 1H), 2.07 (d, *J* = 4.9 Hz, 4H), 1.21 (s, 18H), 0.93 – 0.57 (m, 6H).

2.17 Synthesis of Compound 16

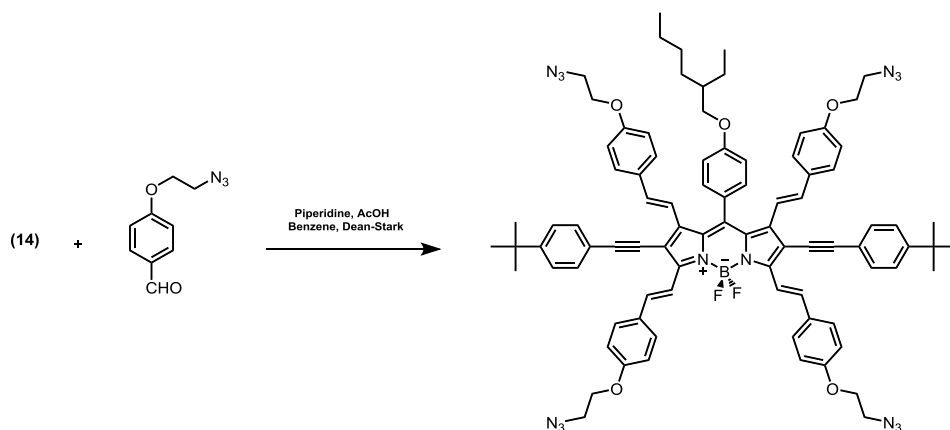


Figure 22. Synthesis of Compound 16

Compound **14** (150 mg, 0.2 mmol) and Compound **5** (381 mg, 2 mmol) were dissolved in 25 mL benzene followed by addition of 0.6 mL piperidine and 0.6 mL glacial acetic acid. The solution was left stirring using Dean-Stark apparatus. The solvent has been evaporated using high temperatures and the reaction was followed by TLC until pale grey-green color was appeared and starting molecule was consumed. After that, any residual solvent was evaporated by N₂ degassing and the product was directly purified with silica gel column chromatography DCM/MeOH (97:3) (79 mg, 0.05 mmol, 27%).

¹H NMR (400 MHz, CDCl₃) δ 8.49 (d, *J* = 16.3 Hz, 2H), 7.76 (d, *J* = 16.3 Hz, 2H), 7.70 (d, *J* = 8.6 Hz, 2H), 7.63 (d, *J* = 8.6 Hz, 4H), 7.44 – 7.35 (m, 8H), 7.27 (d, *J* = 8.4 Hz, 2H), 7.02 (d, *J* = 8.5 Hz, 2H), 6.98 (d, *J* = 8.6 Hz, 4H), 6.89 (d, *J* = 8.6 Hz, 4H), 6.74 (d, *J* = 8.6 Hz, 4H), 5.84 (d, *J* = 16.2 Hz, 2H), 4.21 (t, *J* = 4.9 Hz, 4H), 4.07 (t, *J* = 4.9 Hz, 4H), 3.86 (d, *J* = 5.5 Hz, 2H), 3.65 (t, *J* = 4.9 Hz, 4H), 3.56 (t, *J* = 4.9 Hz, 4H), 1.86 – 1.72 (m, 1H), 1.56 - 1.40 (m, 8H), 1.36 (s, 18H), 1.05 – 0.95 (m, 6H).

¹³C NMR (101 MHz, CDCl₃) δ 160.42, 159.18, 158.23, 153.08, 151.32, 141.74, 138.29, 137.81, 133.51, 133.62, 131.47, 130.87, 130.64, 130.48, 129.31, 128.07, 126.70, 125.64, 120.67, 119.32, 117.10, 115.26, 114.94, 114.50, 108.88,

98.82, 85.97, 70.88, 66.97, 50.15, 39.67, 34.87, 31.22, 30.71, 28.96, 23.90, 23.10, 14.20, 11.34.

2.18 Synthesis of Compound 18

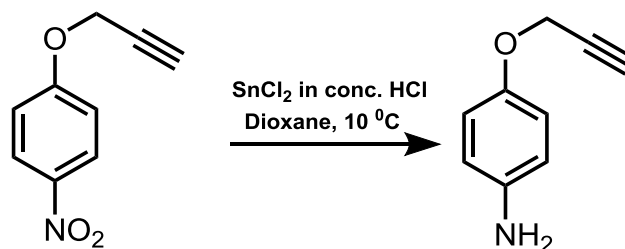


Figure 23. Synthesis of Compound 18

Compound **17**, 4-(prop-2-yn-1-yloxy)aniline was prepared according to the literature[83]. Ice-cooled solution of tin(II) chloride dihydrate (20 g, 91 mmol) in 30 mL HCl was added dropwise to a solution of p-nitropropargyl ether (6 g, 37 mmol) in dioxane at 10 °C. The reaction mixture was stirred for 48 h at room temperature and neutralized with aqueous NaOH solution at last. Extracted with dichloromethane (4 x 50 mL) and water. Organic layer is dried over Na₂SO₄ and evaporated in *vacuo*. The product was purified with EtOAc/Hexane/Et₃N (49:49:2) using silica gel column chromatography (2.84 g, 19 mmol, 57%).

¹H NMR (400 MHz, CDCl₃) δ 6.76 – 6.72 (m, 2H), 6.72 – 6.45 (m, 2H), 4.51 (t, *J* = 2.0 Hz, 2H), 3.37 (s, 2H), 2.49 – 2.32 (m, 1H).).

¹³C NMR (100 MHz, CDCl₃, δ ppm) 150.70, 140.97, 116.42, 116.23, 79.16, 75.17, 56.76

MS HRMS (TOF-APCI): *m/z* calculated for [M+H]⁺ 148.0762, found 148.0765, Δ = 0.01 ppm

2.19 Synthesis of Compound 19

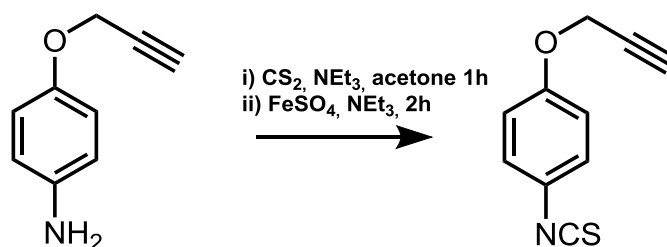


Figure 24. Synthesis of Compound 19

According to the literature[84]. Compound **18** was dissolved (600 mg, 4.08 mmol) in acetone (5 mL). Carbon disulfide (0.2 mL), triethylamine (2.3 mL) was added to the reaction mixture successively and mixed at room temperature for 1 h. Catalytic amount ferrous sulfate and triethylamine was added to the reaction mixture, and it was further stirred for 2 h. Upon consumption of the starting material, excess carbon disulfide was removed by distillation. The reaction mix was quenched by 25 mL ice-cooled water with constant stirring, the product was isolated by filtration and dried under *vacuo*. The product was purified by silica gel column chromatography using DCM/Hex (1:1). White pellet crystals (341 mg, 44%).

¹H NMR (400 MHz, CDCl₃) δ 7.31 – 7.14 (m, 2H), 7.01 – 6.89 (m, 2H), 4.70 (dd, *J* = 12.7, 2.4 Hz, 2H), 2.59 – 2.50 (m, 1H).

¹³C NMR (100 MHz, CDCl₃, δ ppm) 155.69, 134.29, 126.25, 123.87, 115.20, 77.18, 75.37, 55.38.

MS HRMS (TOF-APCI): *m/z* calculated for [M-NCS]⁻ 132.0575, found 132.0315, Δ = 196.88 ppm

2.21 Synthesis of Compound 21

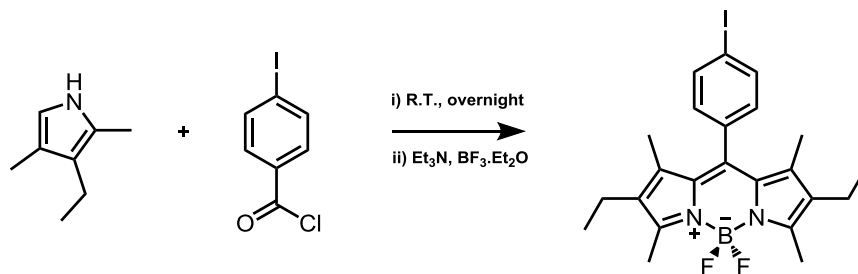


Figure 26. Synthesis of Compound 21

4-iodobenzoyl chloride (0.987 g, 3.7 mmol) and 2,4-dimethyl-3-ethyl pyrrole (1 mL, 7.4 mmol) were dissolved in 200 mL DCM which was previously Ar degassed for 30 min. The reaction flask was remained constant stirring at refluxing condition overnight. 8 mL Et₃N and 8 mL BF₃·Et₂O were added consecutively. After further stirring at room temperature for 30 min., extraction has been done with brine solution. Organic layer is dried over Na₂SO₄ and evaporated in *vacuo*. The product was purified with DCM/Hex (1:2) using silica gel column chromatography (300 mg, 0.59 mmol, 16%).

2.22 Synthesis of Compound 22

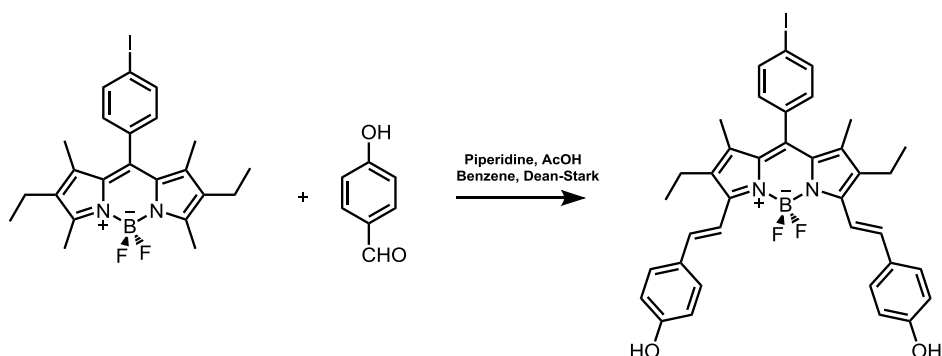


Figure 27. Synthesis of Compound 22

Compound **21** (150 mg, 0.29 mmol) and 4-hydroxybenzaldehyde (76 mg, 0.62 mmol) were dissolved in 25 mL benzene. Then, 0.2 mL piperidine and 0.2 mL glacial acetic acid were added consecutively to the solution. The reaction flask was left heating using Dean-Stark apparatus. After concentration of the solution, the reaction was followed by TLC till green colored spot dominated. Then, residual benzene was evaporated under nitrogen gas and product was directly purified without extraction using silica gel column chromatography, DCM (85 mg, 0.12 mmol, 41%).

^1H NMR (400 MHz, DMSO) δ 8.35 (d, $J = 8.3$ Hz, 2H), 7.88 (d, $J = 8.7$ Hz, 4H), 7.83 (d, $J = 16.9$ Hz, 2H), 7.65 (dd, $J = 12.4, 4.1$ Hz, 4H), 7.27 (d, $J = 8.6$ Hz, 4H), 3.00 (q, $J = 7.1$ Hz, 4H), 1.75 (s, 6H), 1.50 (t, $J = 7.5$ Hz, 6H).

^{13}C NMR (101 MHz, DMSO) δ 159.13, 149.69, 138.76, 138.45, 136.77, 136.57, 134.82, 133.70, 132.21, 131.06, 129.30, 128.14, 116.52, 96.02, 17.74, 14.38, 11.68.

2.23 Synthesis of Compound 23

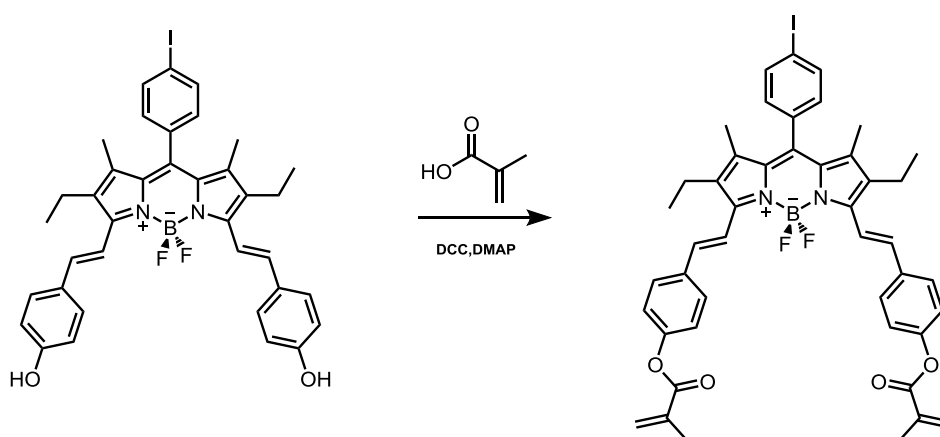


Figure 28. Synthesis of Compound 23

Compound **22** (75 mg, 0.11 mmol) and methacrylic acid (20 mg, 0.23 mmol) were dissolved in minimum amount of DCM. 2 equivalents of DCC (45,32 mg) and 0.2 equivalent of DMAP (2.6 mg) were introduced to the solution at room temperature. Following by TLC, the reaction was stopped after two hours. Extraction was done with DCM and organic layer is dried over Na₂SO₄ and evaporated in *vacuo*. The product was purified with DCM/Hex (1:1) using silica gel column chromatography (78 mg, 0.09 mmol, 83%).

¹H NMR (400 MHz, CDCl₃) δ 7.89 (d, *J* = 8.1 Hz, 2H), 7.75 (d, *J* = 16.8 Hz, 2H), 7.67 (d, *J* = 8.5 Hz, 4H), 7.29 (d, *J* = 16.8 Hz, 2H), 7.20 (d, *J* = 8.4 Hz, 4H), 7.11 (d, *J* = 8.1 Hz, 2H), 6.39 (s, 1H), 5.79 (s, 2H), 2.63 (q, *J* = 7.5 Hz, 4H), 2.10 (s, 6H), 1.40 (s, 6H), 1.19 (t, *J* = 7.4 Hz, 6H).

2.24 Synthesis of Compound 24

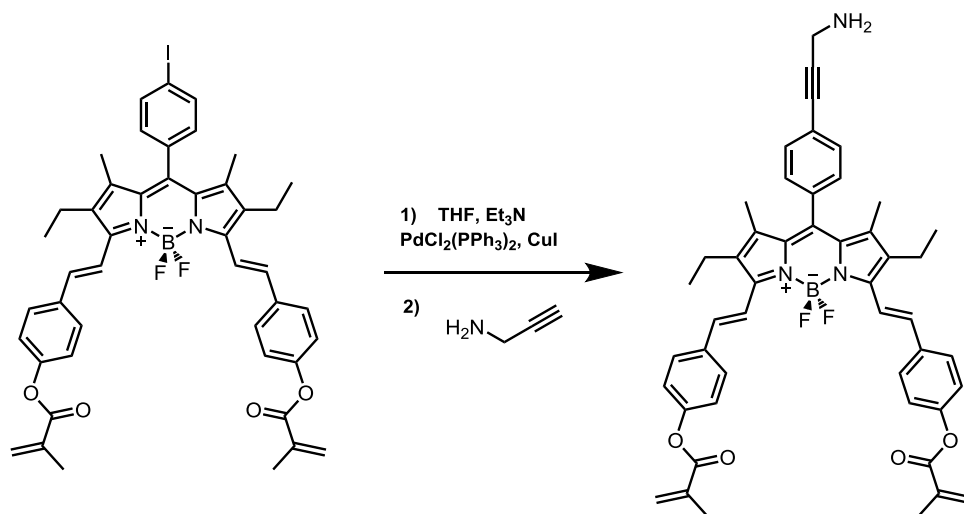


Figure 29. Synthesis of Compound 24

Compound **23** (50 mg, 0.064 mmol) was dissolved 10 mL distilled THF and 5 mL triethylamine. The flask was argon degassed for 30 min. and while degassing, PdCl₂(PPh₃)₂ (9,8 mg, 0.014 mmol) and CuI (5,8 mg, 0.023 mmol) were added at once. Finally, propargyl amine (5,5 mg, 0.1 mmol) was introduced to the solution and the reaction was left for stirring for 30 min. After TLC analysis showed the consumption of starting material, 200 mL water was added. Extraction was done with DCM. Organic layer is dried over Na₂SO₄ and evaporated in *vacuo*. The product was purified with DCM/Hex (1:3) using silica gel column chromatography (735 mg, 0.98 mmol, 85%).

¹H NMR (400 MHz, CDCl₃) δ 7.75 (d, *J* = 16.8 Hz, 2H), 7.67 (d, *J* = 8.6 Hz, 4H), 7.59 (d, *J* = 8.2 Hz, 2H), 7.30 (d, *J* = 8.3 Hz, 2H), 7.22 (d, *J* = 14.2 Hz, 2H), 7.19 (d, *J* = 8.6 Hz, 4H), 6.39 (s, 2H), 5.79 (s, 2H), 3.74 (s, 2H), 2.63 (q, *J* = 7.3 Hz, 4H), 2.10 (s, 6H), 1.60 (s, 2H), 1.38 (s, 6H), 1.18 (t, *J* = 7.5 Hz, 6H).

2.25 Synthesis of Compound 25

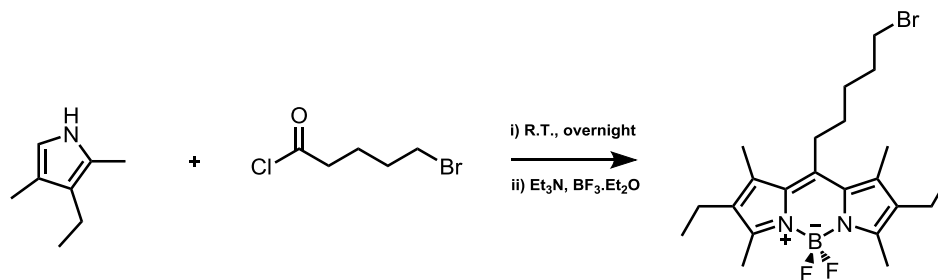


Figure 30. Synthesis of Compound 25

6-bromohexanoyl chloride (2.14 g, 10 mmol) and 2,4-dimethyl-3-ethyl pyrrole (1.23 g, 21 mmol) were dissolved in 200 mL DCM which was previously Ar degassed for 30 min. The reaction flask was remained constant stirring at refluxing condition overnight. 8 mL Et₃N and 8 mL BF₃.Et₂O were added consecutively. After further stirring at room temperature for 30 min., extraction has been done with brine solution. Organic layer is dried over Na₂SO₄ and evaporated in *vacuo*. The product was purified with DCM/Hex (1:3) using silica gel column chromatography (800 mg, 1.77 mmol, 21%).

¹H NMR (400 MHz, CDCl₃) δ 3.58 (t, *J* = 2.2 Hz, 2H), 3.01 (t, *J* = 2.2 Hz, 2H), 2.52 (s, 6H), 2.42 (q, *J* = 7.6, 2.1 Hz, 4H), 2.34 (s, 6H), 1.92 – 1.79 (m, *J* = 13.3, 7.0 Hz, 2H), 1.67 (m, 4H), 1.07 (t, , *J* = 7.5 Hz , 6H).

MS HRMS (TOF-ESI): *m/z* calculated for [M]⁺ 388,23619 found 388,2459 Δ = -25,1 ppm

2.26 Synthesis of Compound 26

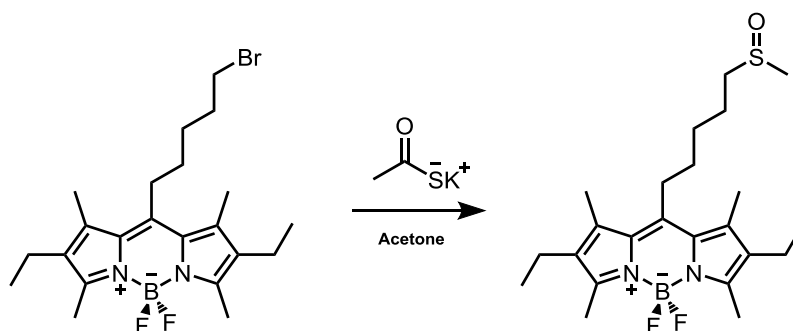


Figure 31. Synthesis of Compound 26

Compound **25** (500 mg, 1.1 mmol) was dissolved in 20 mL acetone and potassium thioacetate (252 mg, 2.2 mmol) was added to the reaction flask. The solution was stirred at 60 °C overnight. Extraction was done with DCM. Organic layer is dried over Na_2SO_4 and evaporated in *vacuo*. The product was purified with DCM/Hex (1:1) using silica gel column chromatography (460 mg, 1.06 mmol, 96%).

^1H NMR (400 MHz, CDCl_3) δ 2.97 (t, $J = 7.0$ Hz, 2H), 2.91 (t, $J = 7.0$ Hz, 2H), 2.51 (s, 6H), 2.41 (q, $J = 7.5$ Hz, 4H), 2.34 (s, 3H), 2.33 (s, 6H), 1.71-1.53 (m, 6H), 1.06 (t, $J = 7.5$ Hz, 6H).

2.27 Synthesis of Compound 27

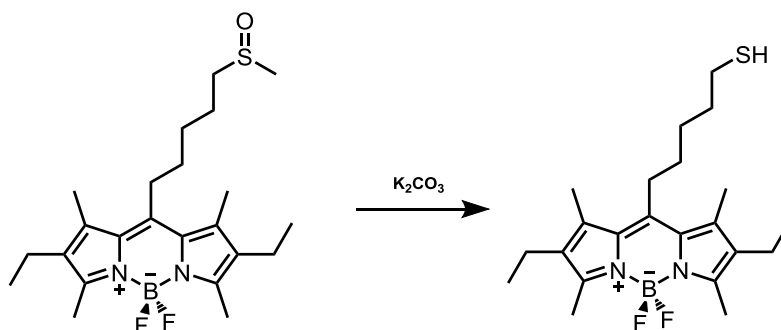


Figure 32. Synthesis of Compound 27

Compound **26** (200 mg, 0.46 mmol) was dissolved in 10 mL ethanol and the solution was Ar degassed for 30 min. Catalytic amount of potassium carbonate was added and the solution was further stirred for 2 h at room temperature while N₂ bubbling. Extraction was done with DCM. Organic layer is dried over Na₂SO₄ and evaporated in *vacuo*. The product was purified with DCM/Hex (1:1) using silica gel column chromatography (150 mg, 0.37 mmol, 78%).

¹H NMR (400 MHz, CDCl₃) δ 2.96 (t, , *J* = 7.0 Hz, 2H), 2.59 (dd, *J* = 14.4, 7.1 Hz, 2H), 2.52 (s, 6H), 2.41 (q, *J* = 7.5 Hz, 4H), 2.36 (s, 6H), 1.76 – 1.60 (m, 6H), 1.37 (t, *J* = 7.8 Hz, 1H), 1.07 (t, *J* = 7.6 Hz, 6H).

2.28 Synthesis of Compound 29

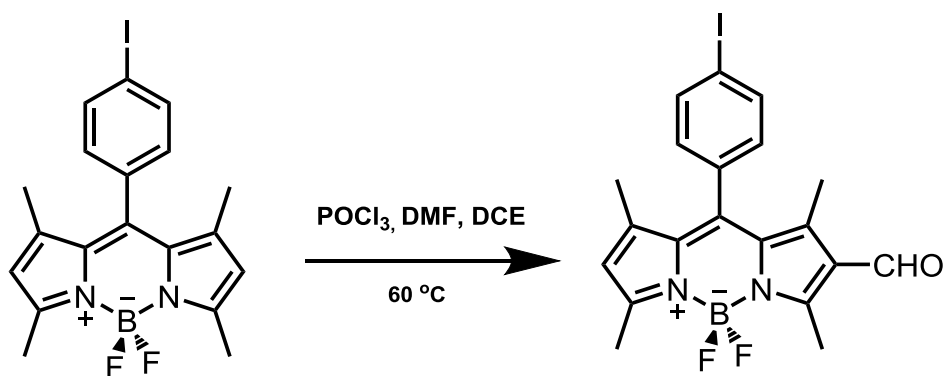


Figure 33. Synthesis of Compound **29**

According to the literature[85], ice-cooled anhydrous DMF(1 mL) was subjected to nitrogen gas for a while and POCl₃ (1 mL) was added to this solvent. Resulting yellow liquid was left stirring for 30 min. at room temperature. After that, a solution of Compound **28** (200 mg, 0.44 mmol) in dichloroethane (20 mL) was dropwise added to the previous solution followed by heating up to 60 °C. After 4 hours of stirring, reaction was cooled down to room temperature, and poured into ice-cooled saturated NaHCO₃ solution. Extraction was done with DCM and organic layer is dried over Na₂SO₄ and evaporated in *vacuo*. The

product was purified with DCM/Hex (1:1) using silica gel column chromatography (135 mg, 0.28 mmol, 64%).

^1H NMR (400 MHz, CDCl_3) δ 10.02 (s, 1H), 7.91 (d, $J = 8.0$ Hz, 2H), 7.07 (d, $J = 8.0$ Hz, 2H), 6.18 (s, 1H), 2.83 (s, 3H), 2.63 (s, 3H), 1.72 (s, 3H), 1.48 (s, 3H).

2.29 Synthesis of Compound 30

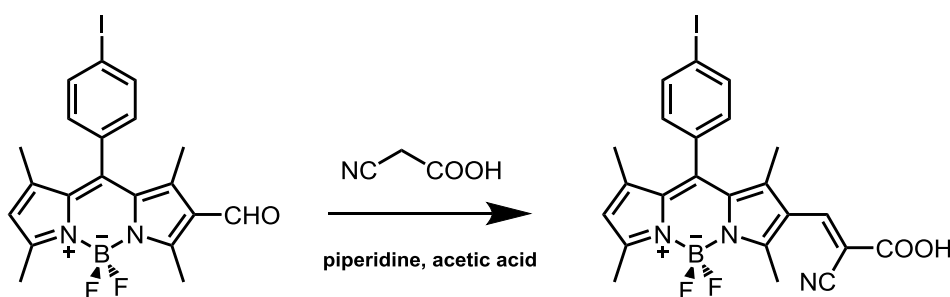


Figure 34. Synthesis of Compound 30

The synthesis has been conducted according to the literature[86]. Compound **29** (100 mg, 0.21 mmol) and cyanoacetic acid (82 mg, 0.9 mmol), were dissolved in benzene. A drop of piperidine and a drop of acetic acid were added to the reaction flask consecutively under argon atmosphere. The reaction mixture was refluxed for 4 h. and washed with water. Organic layer is dried over Na_2SO_4 and evaporated in *vacuo*. The product was purified with DCM/MeOH (98:2) using silica gel column chromatography (56 mg, 0.10 mmol, 49%).

^1H NMR (400 MHz, CDCl_3) δ 8.04 (s, 1H), 7.79 (d, $J = 6.7$ Hz, 2H), 6.96 (d, $J = 6.7$ Hz, 2H), 6.08 (s, 1H), 2.55 (s, 3H), 2.40 (s, 3H), 1.43 (s, 3H), 1.31 (s, 3H).

2.30 Synthesis of Compound 31

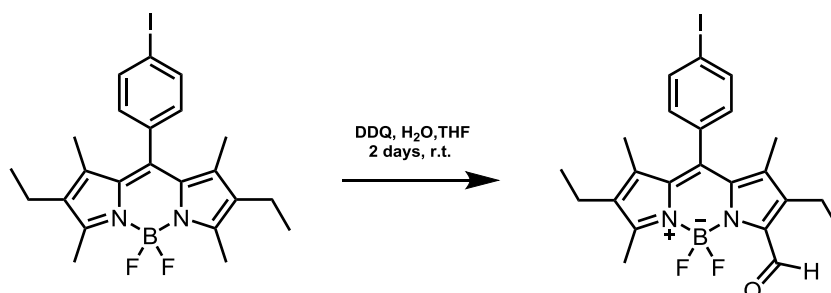


Figure 35. Synthesis of Compound 31

According to the literature[87], Compound **30** (80 mg, 0.16 mmol) was dissolved in THF/H₂O (10 mL/ 0.1 mL) mixture and Ar degassed for 10 min. To this solution, ice-cooled solution of DDQ (140 mg, 0.62 mmol) in THF (5 mL) was added dropwise. The reaction was stirred at room temperature overnight. The solvent was evaporated and the residue was extracted with DCM. Organic layer is dried over Na₂SO₄ and evaporated in *vacuo*. The product was purified with DCM/Hex (1:1) using silica gel column chromatography (60 mg, 0.12 mmol, 74%).

¹H NMR (400 MHz, CDCl₃) δ 10.41 (s, 1H), 7.92 (d, *J* = 8.0 Hz, 2H), 7.09 (d, *J* = 8.0 Hz, 2H), 2.72 (q, *J* = 7.4 Hz, 2H), 2.67 (s, 3H), 2.38 (q, *J* = 7.6 Hz, 2H), 1.43 (s, 3H), 1.34 (s, 3H), 1.05 (t, *J* = 7.5 Hz, 6H).

¹³C NMR (101 MHz, CDCl₃) δ 185.92, 143.42, 140.51, 138.57, 138.01, 137.15, 134.38, 134.23, 130.01, 95.29, 17.56, 17.12, 14.33, 14.01, 13.73, 12.61 10.83.

MS HRMS (TOF-ESI): *m/z* calculated for [M+Na]⁺ 542,0178 found 542,09683 Δ = 14,7 ppm

2.31 Synthesis of Compound 32

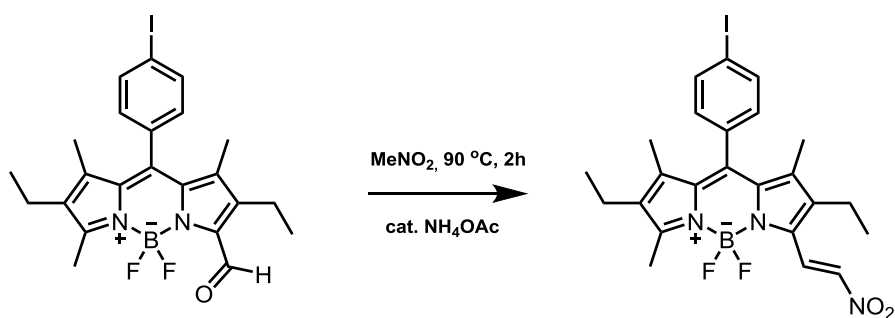


Figure 36. Synthesis of Compound 32

Compound **31** (55 mg, 0.10 mmol) and catalytic amount of NH₄OAc were dissolved in excess amount of nitromethane (3 mL). The reaction flask was heated to 90 °C for 4 h until purple color dominated the solution. After that, nitromethane was evaporated under reduced pressure, and the residue was directly purified by silica gel column chromatography with DCM. (46 mg, 0.081 mmol, 81%).

¹H NMR (400 MHz, CDCl₃) δ 8.37 (d, *J* = 13.8 Hz, 1H), 7.91 (d, *J* = 8.2 Hz, 2H), 7.84 (d, *J* = 13.8 Hz, 1H), 7.07 (d, *J* = 8.2 Hz, 2H), 3.76 (t, *J* = 6.4 Hz, 6H), 2.66 (s, 3H), 2.52 (q, *J* = 7.5 Hz, 2H), 2.37 (q, *J* = 7.6 Hz, 2H), 1.87 (t, *J* = 6.4 Hz, 6H), 1.40 (s, 3H), 1.06 (dt, *J* = 19.2, 7.6 Hz, 6H).

¹³C NMR (101 MHz, CDCl₃) δ 165.47, 142.73, 139.09, 137.75, 137.58, 136.68, 135.27, 135.05, 134.25, 133.64, 127.37, 95.25, 53.41, 31.57, 29.68, 22.63, 18.02, 17.12, 14.39, 14.04, 13.61, 12.48, 11.40.

2.32 Synthesis of Compound 33

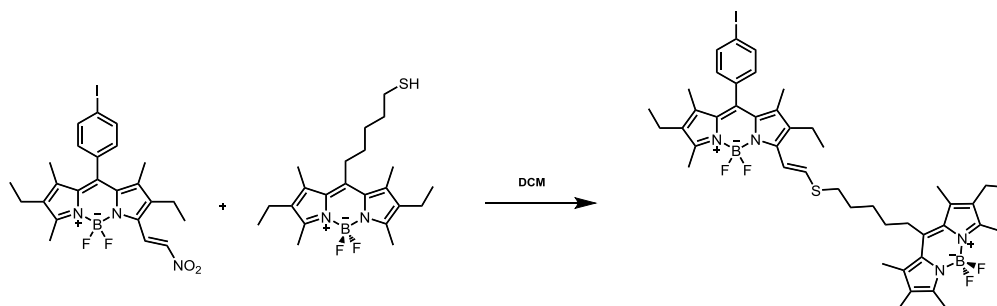


Figure 37. Synthesis of Compound 33

Compound **32** (20 mg, 0.035 mmol) was dissolved in 2 mL DCM and added to the solution of Compound **27** (15 mg, 0.035 mmol) in 2 mL DCM. The reaction was left for stirring for one hour at room temperature while following with TLC. After all starting material has been consumed, the product was directly purified with silica gel column chromatography DCM:Hex (1:1) (30 mg, 0.031 mmol, 88%)

^1H NMR (400 MHz, CDCl_3) δ 7.85 (d, $J = 8.2$ Hz, 2H), 7.12 (d, $J = 16.0$ Hz, 1H), 7.07 (d, $J = 8.3$ Hz, 2H), 6.98 (d, $J = 16.0$ Hz, 1H), 3.05 (t, $J = 7.1$ Hz, 2H), 2.98 (t, $J = 7.1$ Hz, 2H), 2.58 – 2.47 (m, 10H), 2.46 – 2.32 (m, 10H), 1.39 – 1.32 (m, 10H), 1.07 (t, $J = 6.4$ Hz, 6H), 1.00 (t, $J = 7.6$ Hz, 2H).

Chapter 3

Discussion

3.1 Aim of the Project

In the light of the background information presented in the introduction part of this thesis, it can be comfortably stated that, the motivation for this research was to broaden the concept of orthogonality within dendrimer field. Aside from common understanding from one-pot synthesis of dendrimers (which can generally be expanded as sequential couplings, protection /deprotection-free reactions), we thought that multiple “simultaneous” reactions that take place at the same time and same place could more fit in with the term orthogonal one-pot reactions. In that respect, our goal was to define a set of functional groups that would be insensitive to each other without any crosstalk, except their orthogonal counterparts, and the reactions would be as mild and efficient as possible at ambient conditions without any activating agents, catalysts and even acids or bases. Moreover, our another desire was to utilize this strategy for a specific application, namely, for a light harvesting dendrimer. Therefore, this project has ultimately aimed to develop a set of fluorescent molecular compartments that can covalently assemble (via orthogonal reactions) in ambient conditions, forming a unimolecular light harvesting dendrimers or cascades. In this discussion part of the thesis, the optimization process of these orthogonal couplings will be discussed, different functional groups attached to the BODIPY molecules will be exhibited, and finally, some of the synthesized light harvesting cascades will be examined.

3.2 Thiol – Methyl Methacrylate / Amine – Isothiocyanate Functional Groups on BODIPY Dyes

According to the recent work of Ma *et al.*, cysteamine efficiently reacts with 2-[(methacryloyl)oxy]ethyl acrylate (MAEA) in two kinetically chemoselective ways[88]. One is occurred between the thiol end of cysteamine and methyl methacrylate end of MAEA, whereas the other reaction is between amine end of cysteamine and acrylate end of MAEA. Therefore, orthogonal strategy has been claimed for these molecules in order to synthesize facile polyester dendrimers. The group clears the orthogonality concept for these reactions by indicating that these two reactions are “kinetically” differentiated. It was reported that amine end of cysteamine reacts with methacrylate end at inconsiderably slow rate, thus, can not compete with thiol groups. On the other side, isothiocyanate groups are well known with their reasonably stable structures and extended reactivity towards primary aromatic ends[89]. Also, thiol groups can not attack isothiocyanates in the presence of amine functionalizations[90]. Therefore, these two aforementioned reactions, namely, thiol – methyl methacrylate and amine – isothiocyanate, could be perfect candidates for orthogonal reaction strategies. After this accomplishment, the

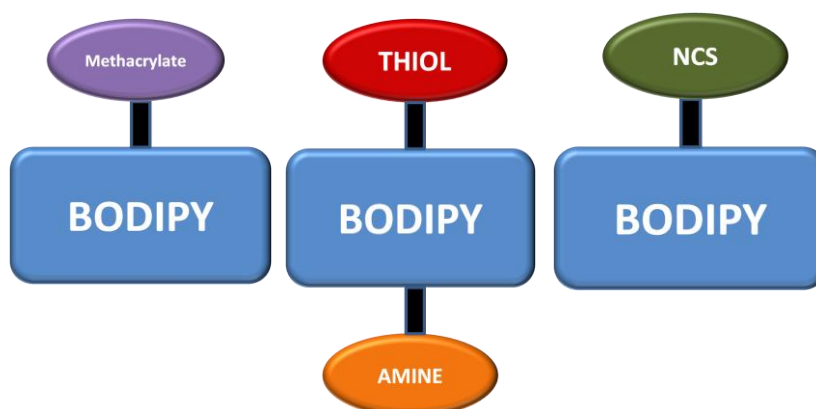


Figure 38. Schematic Representations of Orthogonal Compartments

second task was to conjugate these end groups in three main BODIPY cores in a way that they can easily react with each other when they come together, while they are stable in other conditions (Figure 38).

Synthesis has started with methyl methacrylate functionalized BODIPY (MMA-BOD) while thiol/amine functionalized BODIPY (TA-BOD) and isothiocyanate functionalized BODIPY (ITC-BOD) synthesis have been conducted in parallel of that.

Tetra-styryl conjugation for acceptor core molecule (MMA-BOD) has been aimed to prepare for three reasons: **i)** increasing the number of the donor molecules to raise extinction coefficient of the system, **ii)** obtaining dendrimers grow symmetrically in geometry and **iii)** redshifting the absorption/emission wavelength upon increasing conjugation[91]. In order to increase chemical yield, highly organic soluble 2-ethylhexyl-group has been attached to the aldehyde in the preparation of corresponding tetra-methyl BODIPY dye (Figure 16 and Figure 17). However, Knoevenagel condensation of 4-hydroxybenzaldehyde with **11** was not succeeded according to TLC analysis (Figure 39).

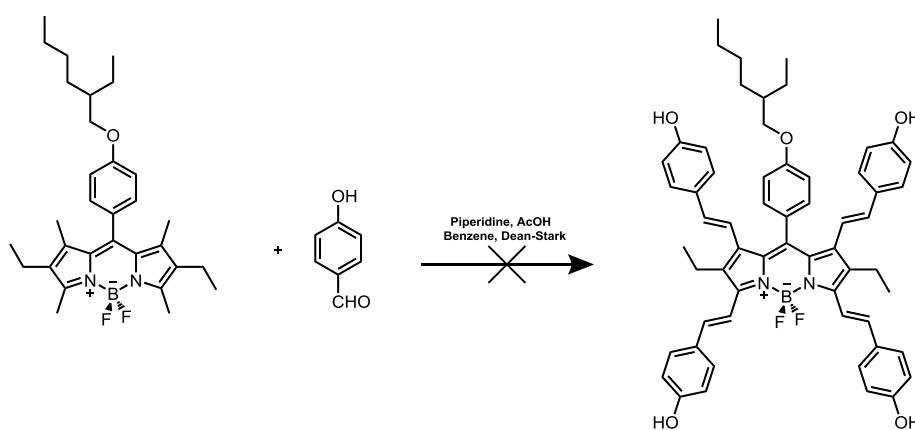


Figure 39. The reaction of **11** and 4-hydroxybenzaldehyde

The possible reason was attributed to insufficient solubility of compound **11** for the reaction. Therefore, as an alternative solution, tert-butyl phenylacetylene groups have been attached to compound **13** by Sonogashira

coupling to 2 and 6 positions of BODIPY core. Knoevenagel condensation with 4-hydroxybenzaldehyde with compound **14** has yielded desired tetra-styryl BODIPY dye (Figure 21). Another advantage of these tert-butyl phenylacetylene groups was to increase the absorption/emission wavelength of the core which is desirable for light harvesting systems.

At the beginning, TA-BOD was planned to be synthesized as di-styryl conjugation with thiol moiety at meso position of BODIPY core, whereas, two amine functionalizations are placed to the styryl ends. For this, Compound **6** has been successfully synthesized with thioacetate groups attached to the meso position. Considering the air sensitivity of thiol groups, hydrolysis of thioacetate was left to the last step.

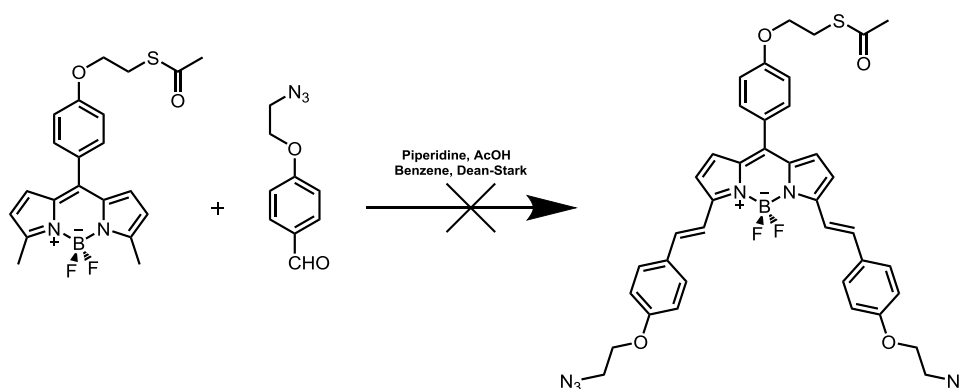


Figure 40. The reaction of Compound **5** and Compound **6**

TLC analysis during reaction process has revealed no reasonable amount of product formed, instead, almost all of the starting material was seemed to be decomposed or side-reactions dominated the environment (Figure 40). Deeper thinking on the condensation reaction conditions have resulted in suspect on the thioacetate moiety which might be hydrolyzed in the presence of piperidine and formed thiolate ion, ready to attack any electrophiles at this very high temperatures. Indeed, it was reported that thiol groups readily react with activated alkenes (styryl groups in our case) in the presence of piperidine base catalyst[92], [93].

With this experience, it has been concluded thiol/thioacetate groups should be attached to the distyryl BODIPY dye afterwards. First, bromo-BODIPY (Compound 7) was synthesized for this reason and Knoevenagel condensation reaction has been successfully achieved with Compound 5. After the substitution of bromide with thioacetate group, Staudinger reaction conditions were thought to be enough for reduction of azide ends to amines in a very mild manner. However, once again, the reaction has yielded a lot of side-products and desired molecule was not achieved (Figure 41). It has been concluded that thioacetate groups were most probably hydrolyzed in the presence of triphenyl phosphine[94] and newly formed thiol groups reacted with styryl bridges which was catalyzed by PPh₃[95].

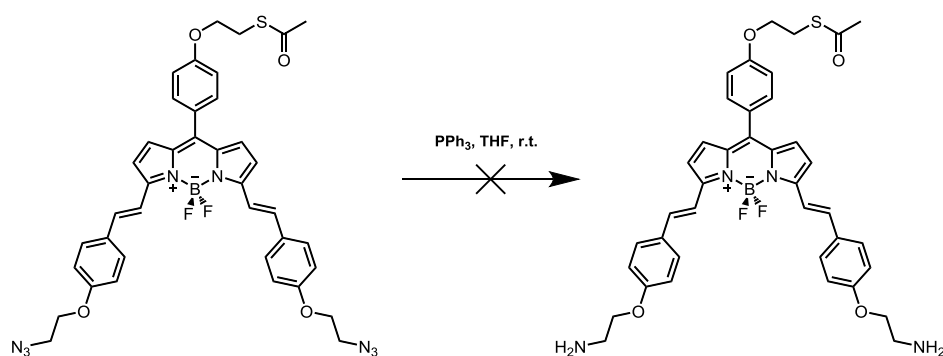


Figure 41. The reduction of Compound 9

Because the presence of styryl conjugation on BODIPY core becomes problematic in terms of thiol groups, the synthetic pathway was changed such that thiol groups would be placed on BODIPY core alone. That also resulted a total change in other compartments for the sake of conservation of orthogonality between functional groups. Therefore, a new set of compartments was defined as the following: **i)** tetra-styryl BODIPY molecule would bear isothiocyanate groups on themselves (NCS-BOD), **ii)** the double functional TA-BOD would be replaced by amine – methyl methacrylate conjugated BODIPY (AMM-BOD) and **iii)** thiol group would be attached to BODIPY dye alone as a donor molecule (SH-BOD) (Figure 42).

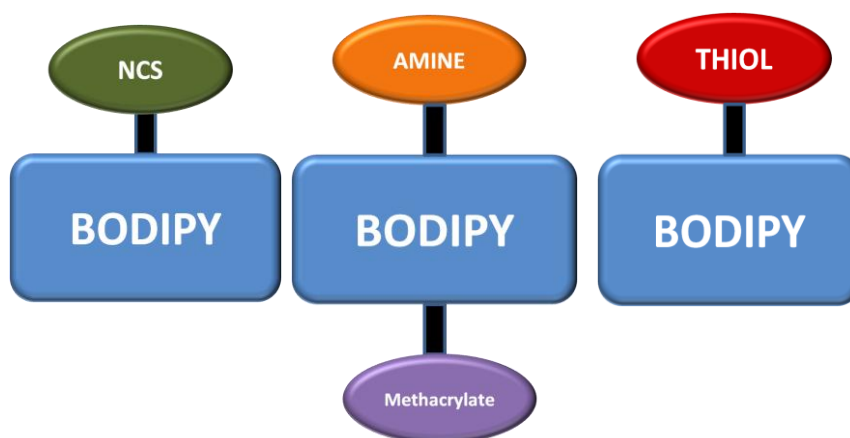


Figure 42. Schematic Representation of Orthogonal Compartments – Different Arrangement

For the first approach, tetra-styryl BODIPY core molecule has been synthesized with respect to new synthetic pathway (Compound **16**) and isothiocyanate molecule (Compound **19**) has been linked to that core via click reaction, giving a final molecule (Compound **20**). On the other side, the structure of thiol containing BODIPY molecule has been changed (from Compound **6** to Compound **27**) since new design would have higher quantum yield. Coming to the double-functional compartment, AMM-BOD, BODIPY with iodophenyl group at meso position has been synthesized and di-styryl functionalized under Knoevenagel conditions. Methyl methacrylate ends have been attached by neat Steglich (DCC-DMAP) esterification to the aromatic hydroxyl groups of styryl bridges. Finally, amine functionalization has been achieved by Sonogashira coupling of propargyl amine and iodide head of BODIPY, resulting a desired Compound **24**.

After all three compartments have been prepared successfully, two of them (SH-BOD and AMM-BOD) were mixed at room temperature without any other reagents for try out, and unlike the report on Ma's work (*vide supra*), there occurred no change for days in terms of reaction (Figure 43).

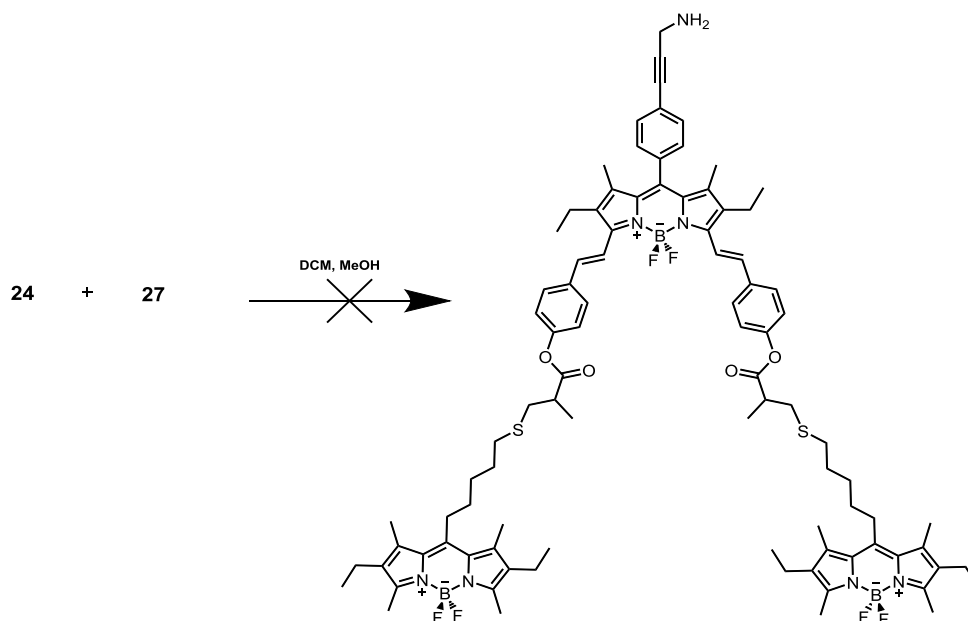


Figure 43. The reaction of **24** and **27**

The point that contrasts with Ma's work was the size of reactant molecules and concentration. In that study, thiol bearing molecule was cysteamine having very low molecular weight with respect to AMM-BOD and the reaction took place at gram scale in about 1 mL solvent which was very concentrated. Surprisingly, there are also some recent literature examples reporting that methacrylates are weak Michael acceptors and the reaction with thiols does not occur in the absence of some specific phosphine or amine type catalysts[95], [96].

3.3 Cyanoacetic acid Functional Group on BODIPY dyes

For the reason that AMM-BOD didn't work as expected, new strong Michael accepting functional groups have been investigated which can replace methyl methacrylate. One example could be cyanoacetic acid group. It was attached to the iodo-phenyl BODIPY core by first formylating it and then condensation reaction (Compound **30**). The reaction between SH-BOD and

Compound **30** did also failed although cyanoacetic acid is strong electron withdrawing group that could result sufficient electron deficiency on β -carbon for attack of thiolate ion (Figure 44). However, most probably, enolate formation upon deprotonation of carboxylic acid group might have quenched thiolate ion formation, thus, the desired Michael addition reaction.

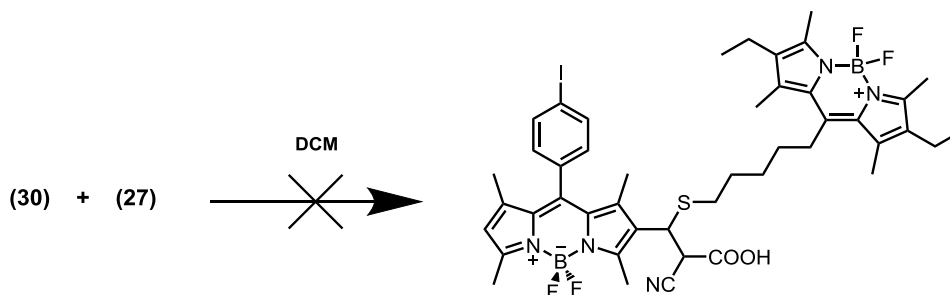


Figure 44. The reaction of Compound **30** and Compound **27**

3.4 Nitroethenyl – BODIPY Conjugates

Recently, in our group, nitroethenyl - BODIPY conjugates have been reported as potential fast biological thiol sensors by PeT On-Off mechanism as a result of Michael addition reaction between cysteine and BODIPY[85]. With similar thinking, formylation of BODIPY at position 3 has been done and nitroethenyl – BODIPY was synthesized in the presence of nitromethane (Compound **32**). This compound has been dissolved in DCM together with Compound **27**, and after 2 h stirring at room temperature, reasonable amount of molecules have reacted with each other resulting Compound **33** successfully. If this reaction has proceeded via Michael addition mechanism, the conjugation of nitro-bonded group would have broken, and thus, the absorption and emission wavelength of acceptor molecule (Compound **33**) would be very similar to the those of donor molecule (SH-BOD). However, bright pink emission of the molecule and fluorescence measurements have shown that acceptor molecule

emits at higher wavelength than donor molecule which proves the difference between them, namely, a conjugation(Figure 45). One of the best explanation for this would be that the reaction was not a Michael addition, instead, it was a substitution reaction (Figure 37). Indeed, Hao's work has already reported this mechanism for a similar nitroolefin functionalized BODIPY[97].

3.5 Amine - Isothiocyanate Reaction

In order to investigate the reaction between isothiocyanate modified tetra-styryl BODIPY and amine modified BODIPY, these two compounds, namely Compound **20** and Compound **2** were dissolved in 10 mL DCM under Ar atmosphere. Overnight stirring has showed that aromatic amine placed at meso position of BODIPY dye was very unstable and easily oxidized instead of reaction with isothiocyanates[98]. Therefore, it was concluded that a different amine (probably aliphatic) functionalized BODIPY dye can be used for this reaction.

3.6 Photophysical Results

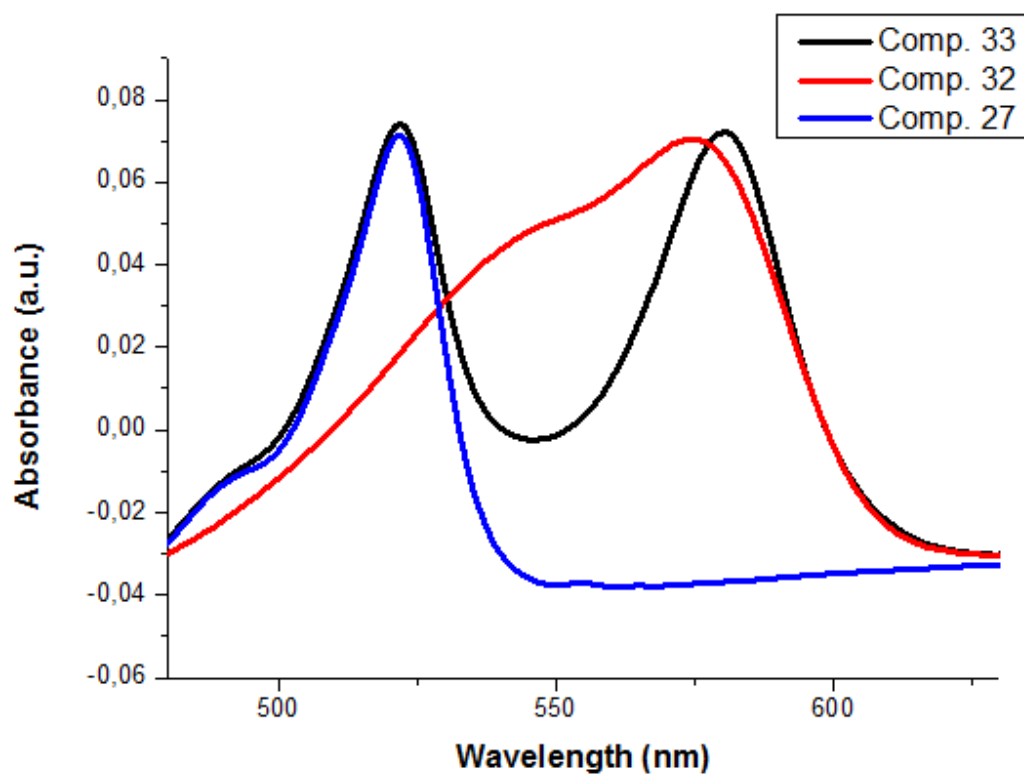


Figure 45. Absorption Spectrum of Compounds 27, 32, 33

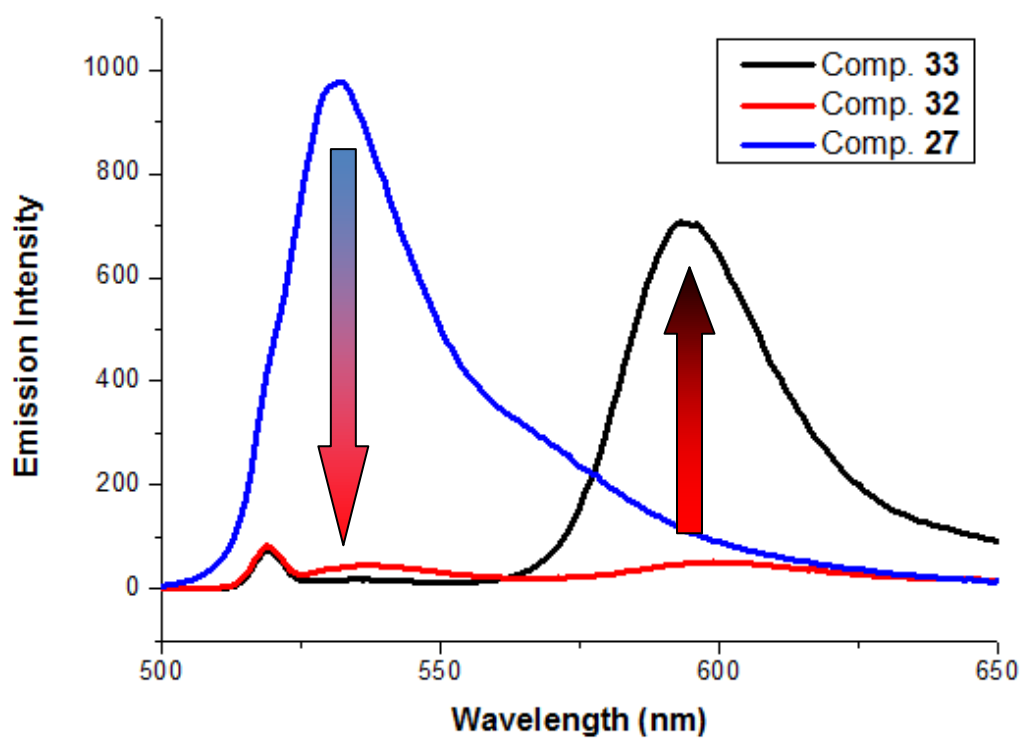


Figure 46. Emission Spectrum of Compounds 27, 32, 33. All dyes are excited at 520 nm

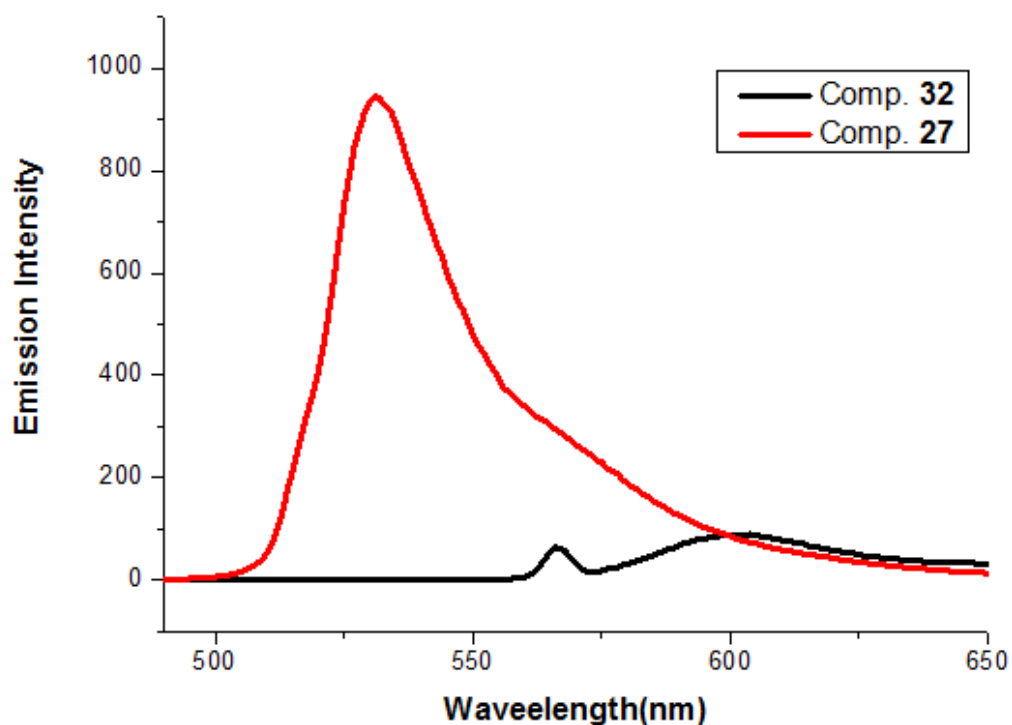


Figure 47. Emission Spectrum of compounds 27 (excited at 517 nm) and 32 (excited at 567 nm)

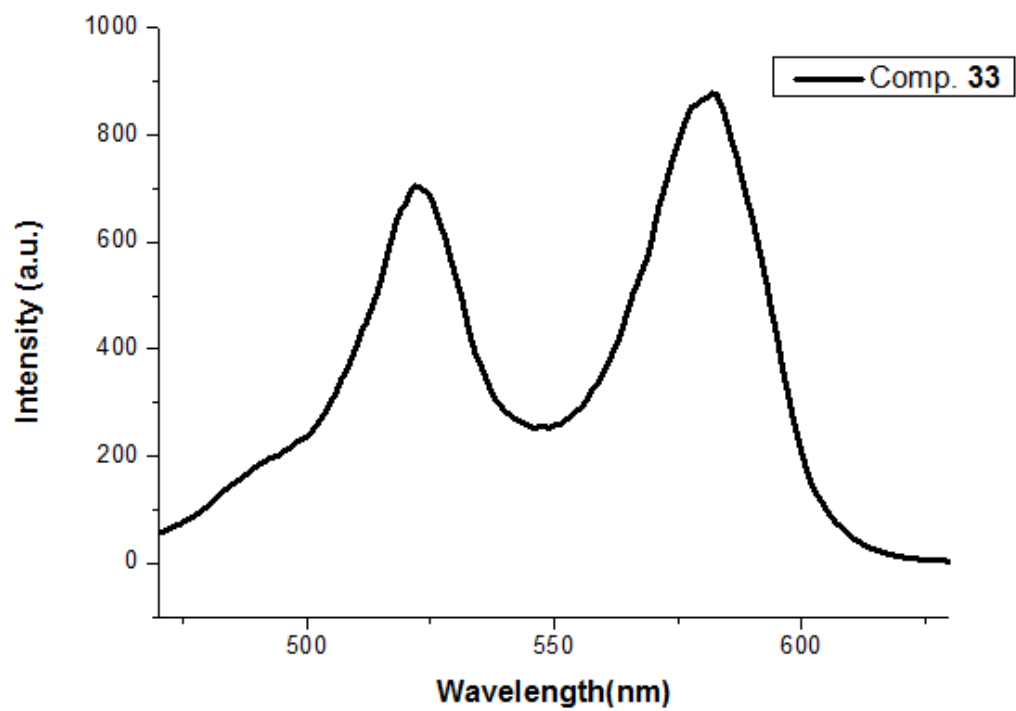


Figure 48. Excitation Spectrum of Compound 33

Chapter 4

Conclusion

Perception of the bright future of orthogonal click chemistry has led us to investigate some kind of potentially orthogonal functional groups on BODIPY dye molecules. In this regard, it was aimed to optimize the conditions, relative placement and reaction availability of these groups for one-pot, fast and mild synthesis of light harvesting cascades. Basically, two different types of reaction have been tried to accomplish: **i)** Michael addition type thiol – ene reaction, and **ii)** amine – isothiocyanate reaction. It was known that thiol – ene reactions undergo very efficiently by UV irradiation (radical mechanism) or specific base catalysis (anionic mechanism). However, in the presence of a proper Michael-accepting groups with sufficiently strong electron withdrawing groups, thiol's nucleophilicity will be enough for attack in the absence of these kinds of initiators/catalysts. Hence, among methyl methacrylate, cyanoacetic acid and nitroolefin functionalized BODIPY dyes, nitroolefin has been reported as the most reactive towards thiol-functionalized BODIPY through, instead, substitution reaction. Cyanoacetic acid functionalized dye was also expected as very reactive, however, it was observed that carboxylic acid moiety was destabilizing the thiolate ion. After the observation of the reaction availability of them, the initial product of nitroolefin modified dye and thiol functionalized dye reaction was investigated further for its light harvesting properties. Indeed, nice energy transfer ability from olefin BODIPY to thiol BODIPY has been monitored via fluorescence spectroscopy.

On the other hand, amine – isothiocyanate reaction is well known for its capability to undergo in very mild conditions, especially when –NCS group is bonded to aromatic environment. Nevertheless, successfully prepared isothiocyanate functionalized tetra – styryl BODIPY dyes didn't react with amine

– BODIPY and the reason was attributed to very fast oxidation of amine residue and hence deactivation towards –NCS groups.

For future aspects, it was planned to develop nitroolefin BODIPY such that amine functionalization would be attached via Sonagashira reaction and then would be mixed with SH-BOD. The orthogonality of amine groups will be observed. It is foreseen that the presence of amine functionalization will even fasten the reaction of thiol – nitroolefin in a manner of self-catalysis. Furthermore, different Michael accepting groups will be developed on BODIPY core, such as maleimide or maleate groups which are also well – known for their extreme reactivity towards thiol groups. Amine – NCS reaction will also be optimized in terms of synthesizing more stable amine functionalized BODIPY dyes.

For the final goal, successfully prepared three compartments that bear different orthogonal moieties will mixed simultaneously in the ambient conditions without catalysis and it is expected them to reorganize themselves such that perfect light harvesting dendrimer is formed very easily. In this way, a specific kind of covalent self-assembly would be established and the product of this assembly process will do accomplish work as light harvesting dendrimer or solar concentrator.

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Appendix Data

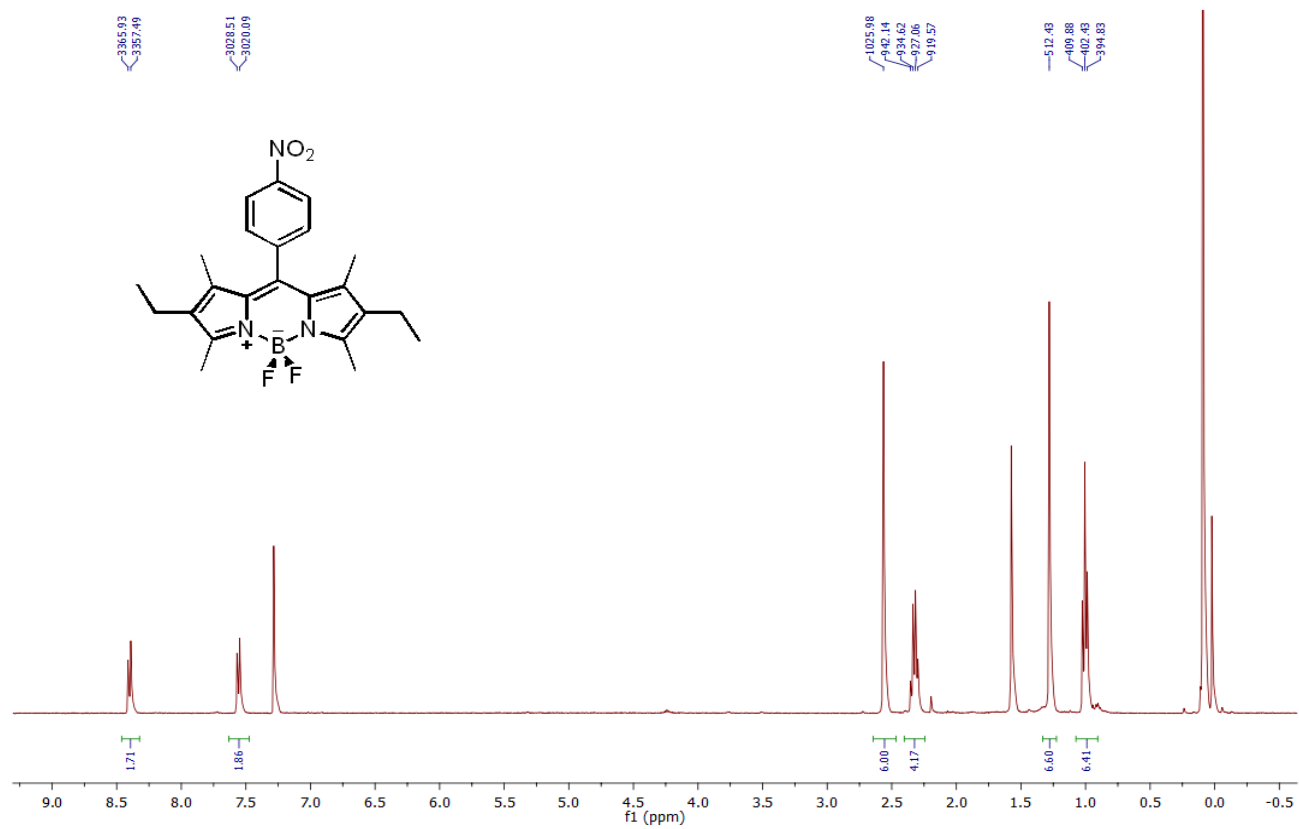


Figure 49. ¹H NMR Spectrum of Compound 1

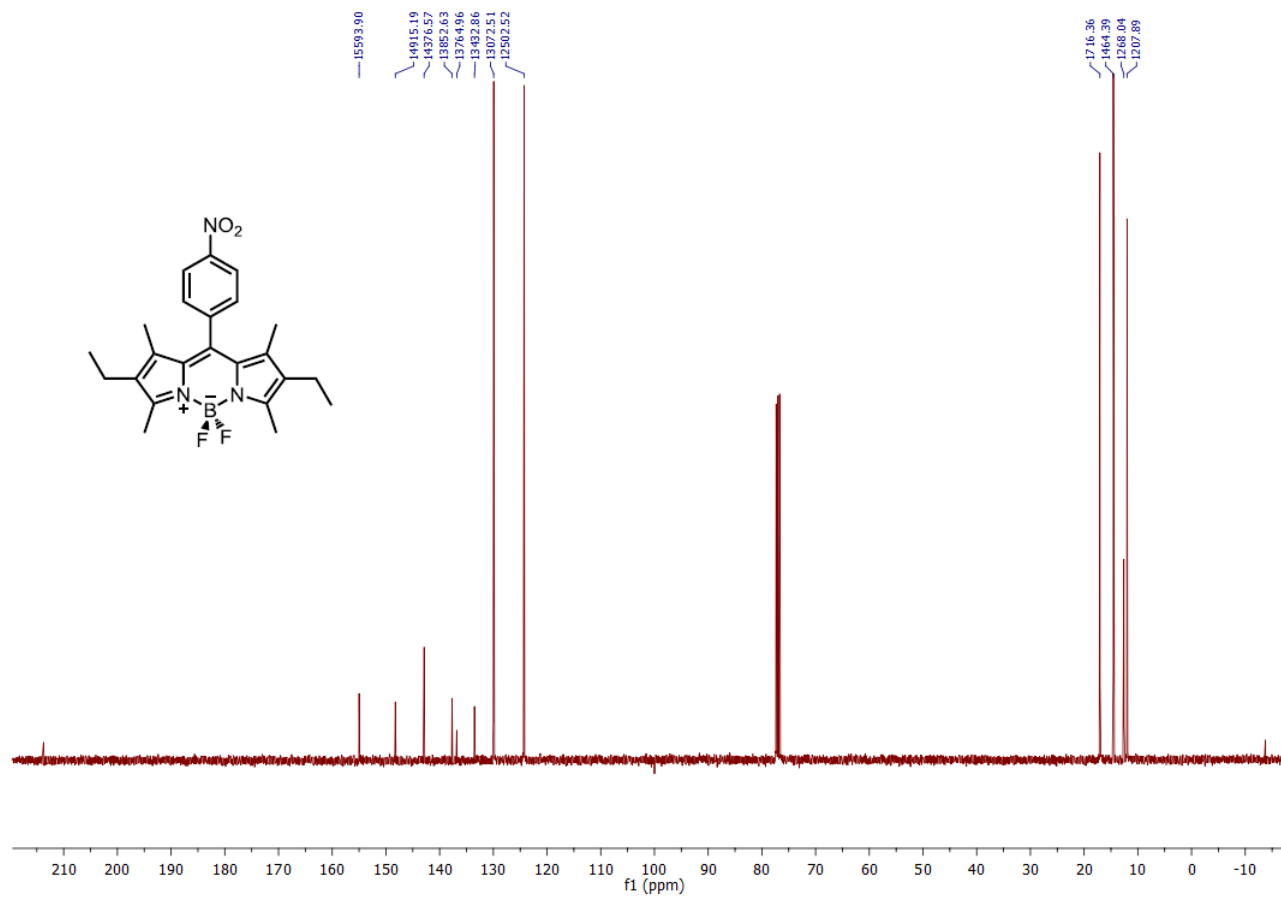


Figure 50. ¹³C NMR Spectrum of Compound 1

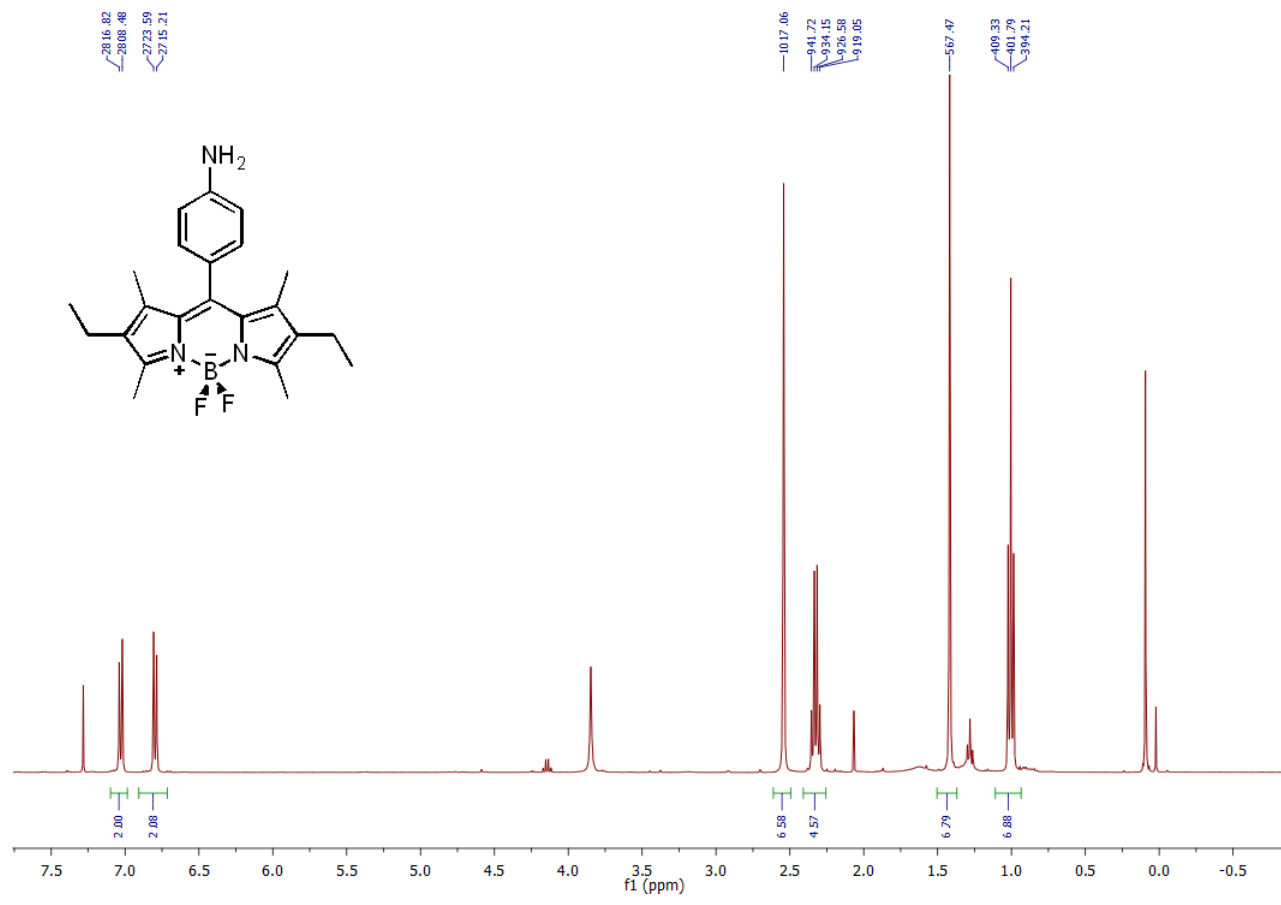


Figure 51. ¹H NMR Spectrum of Compound 2

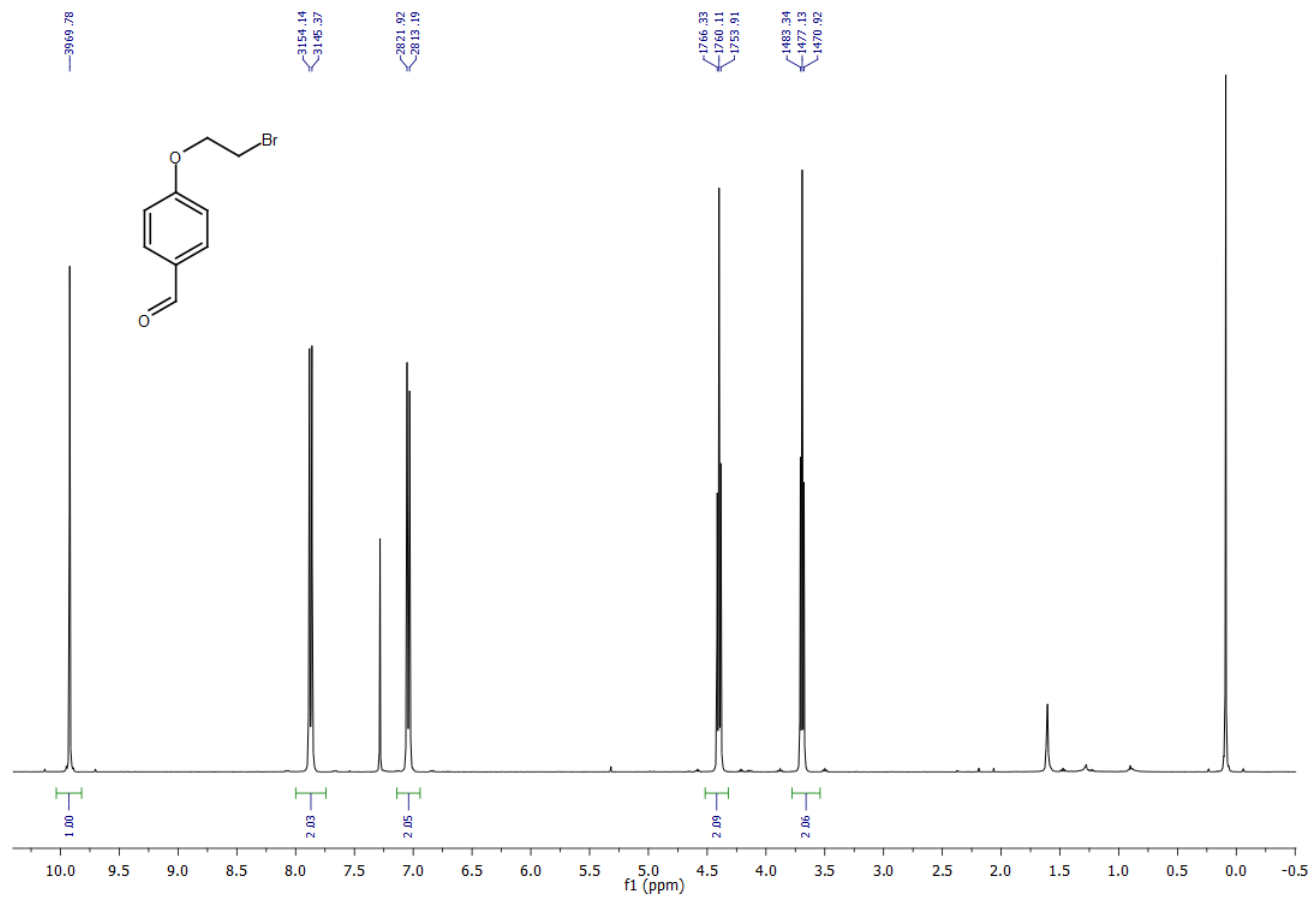


Figure 52. ¹H NMR Spectrum of Compound 3

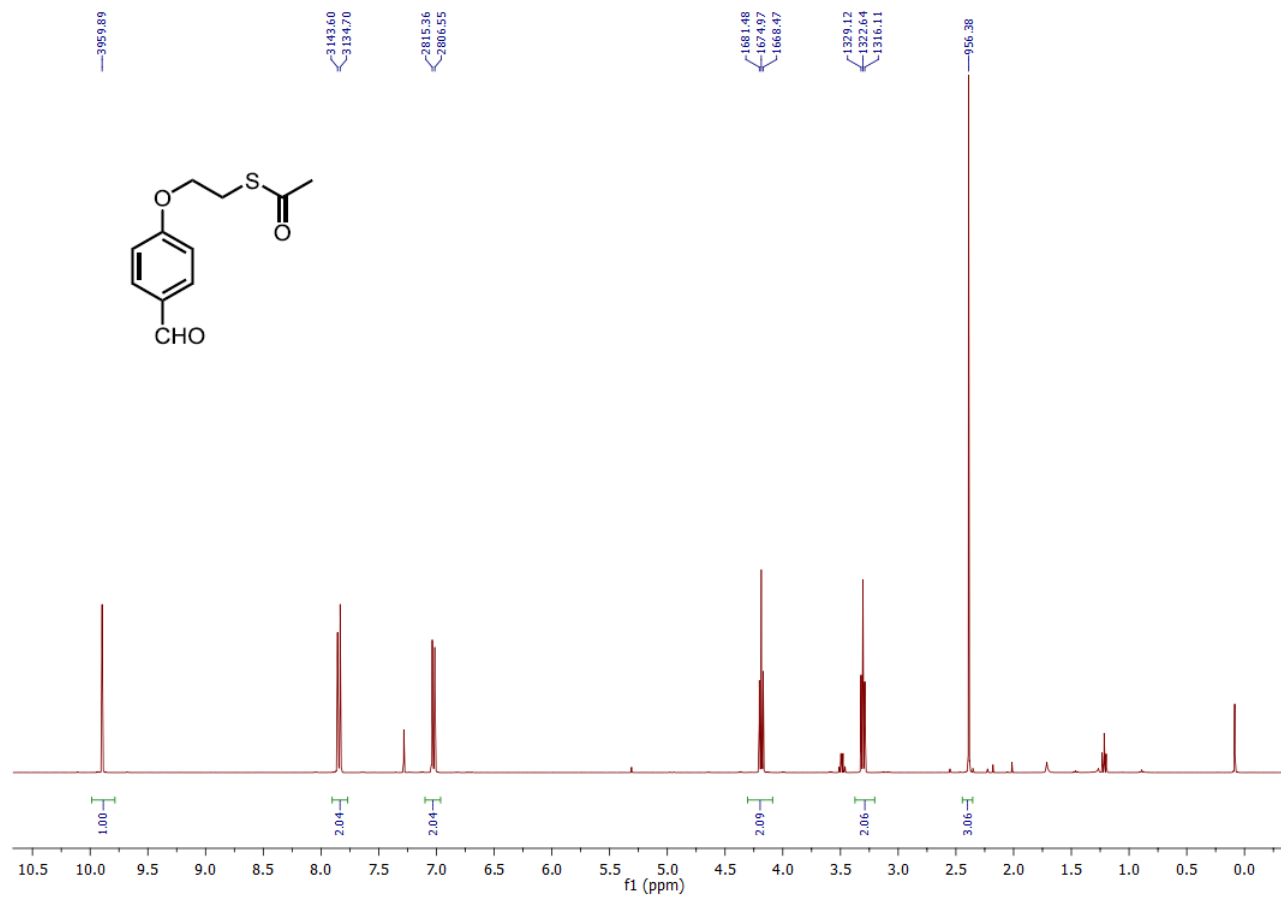


Figure 53. ¹H NMR Spectrum of Compound 4

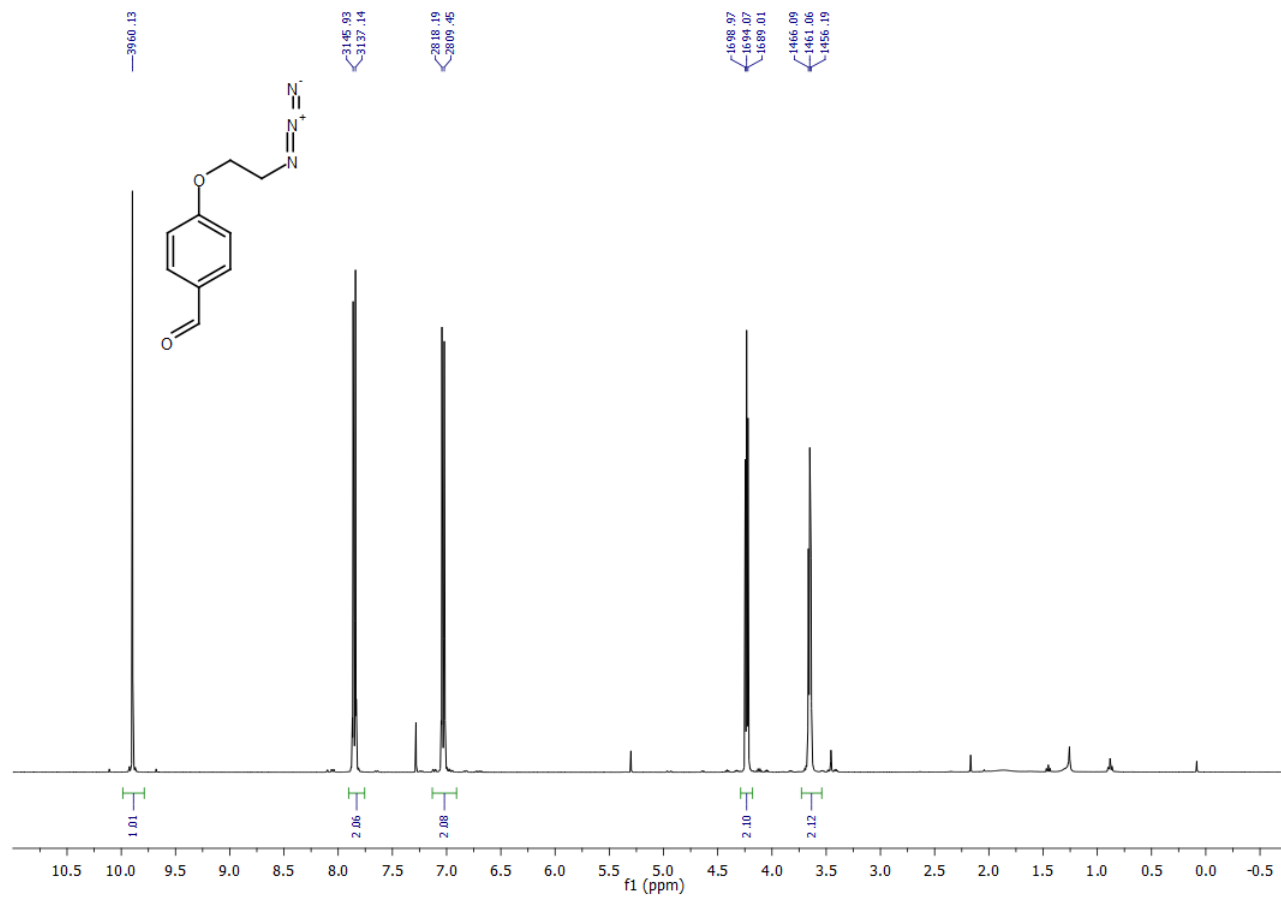


Figure 54. ¹H NMR Spectrum of Compound 5

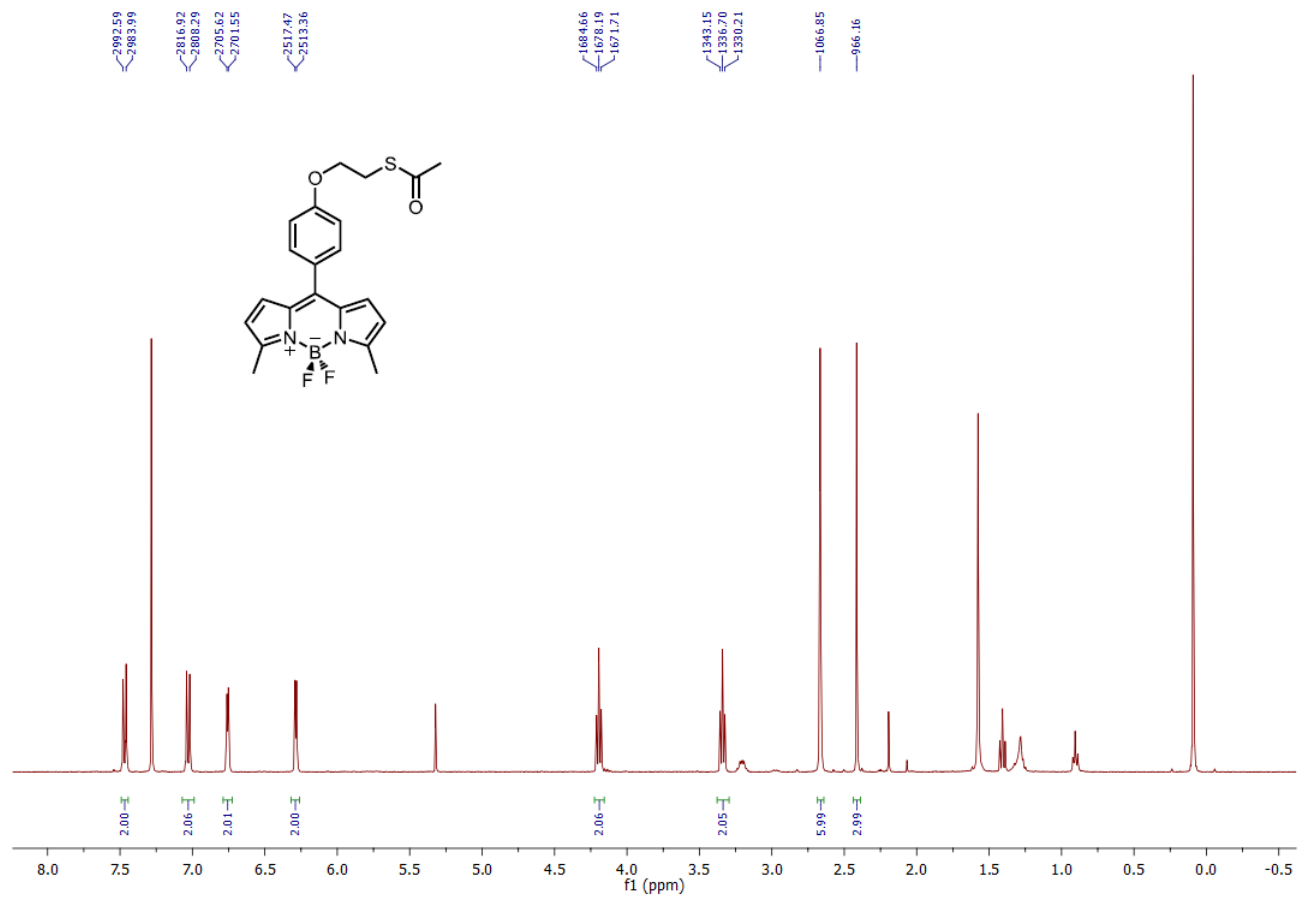


Figure 55. ¹H NMR Spectrum of Compound 6

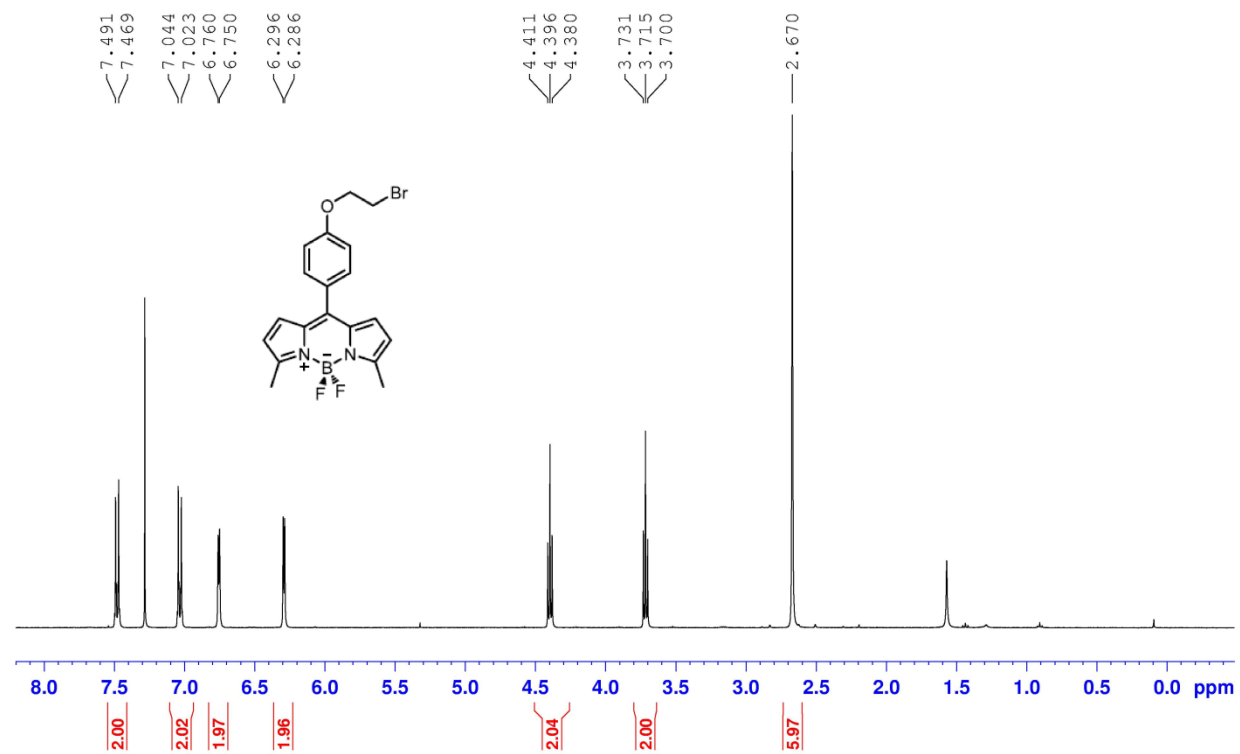


Figure 56. ¹H NMR Spectrum of Compound 7

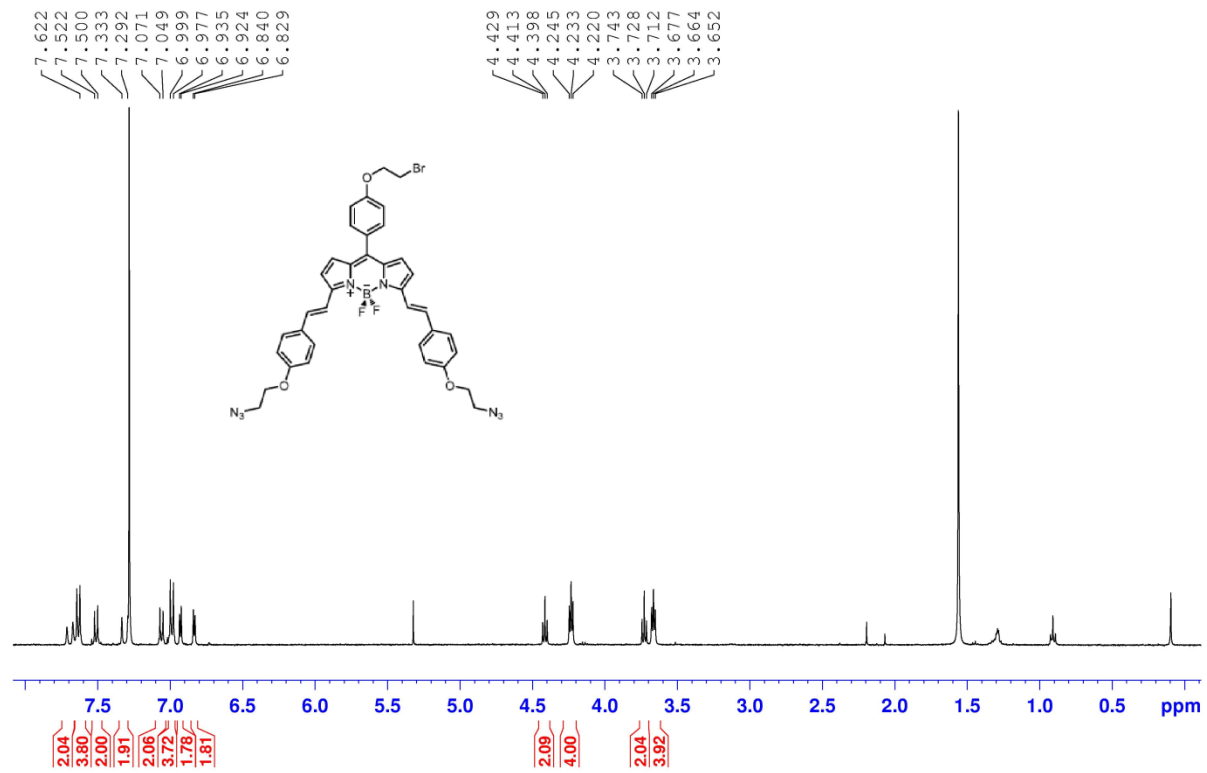


Figure 57. ¹H NMR Spectrum of Compound 8

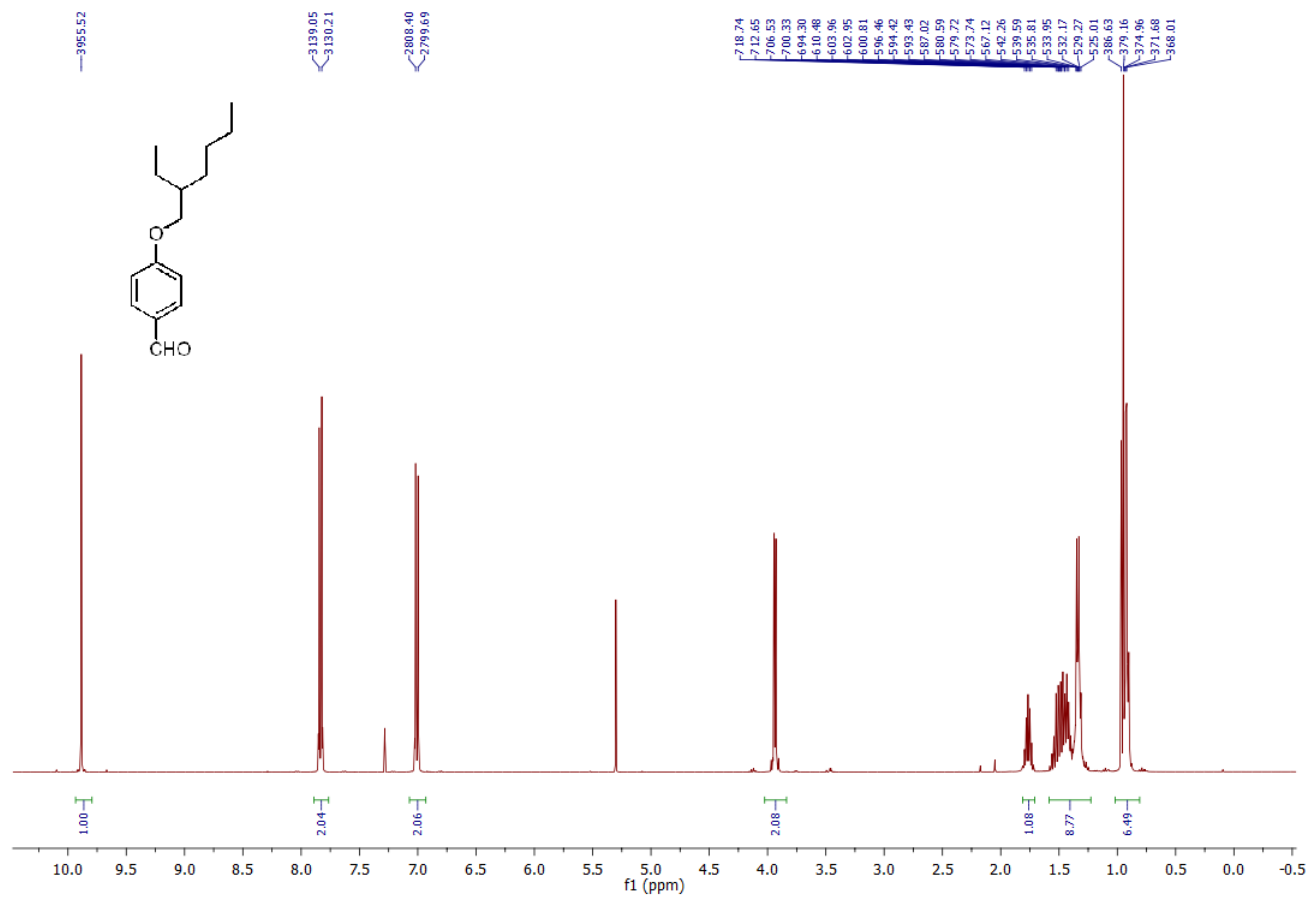


Figure 58. ^1H NMR Spectrum of Compound 10

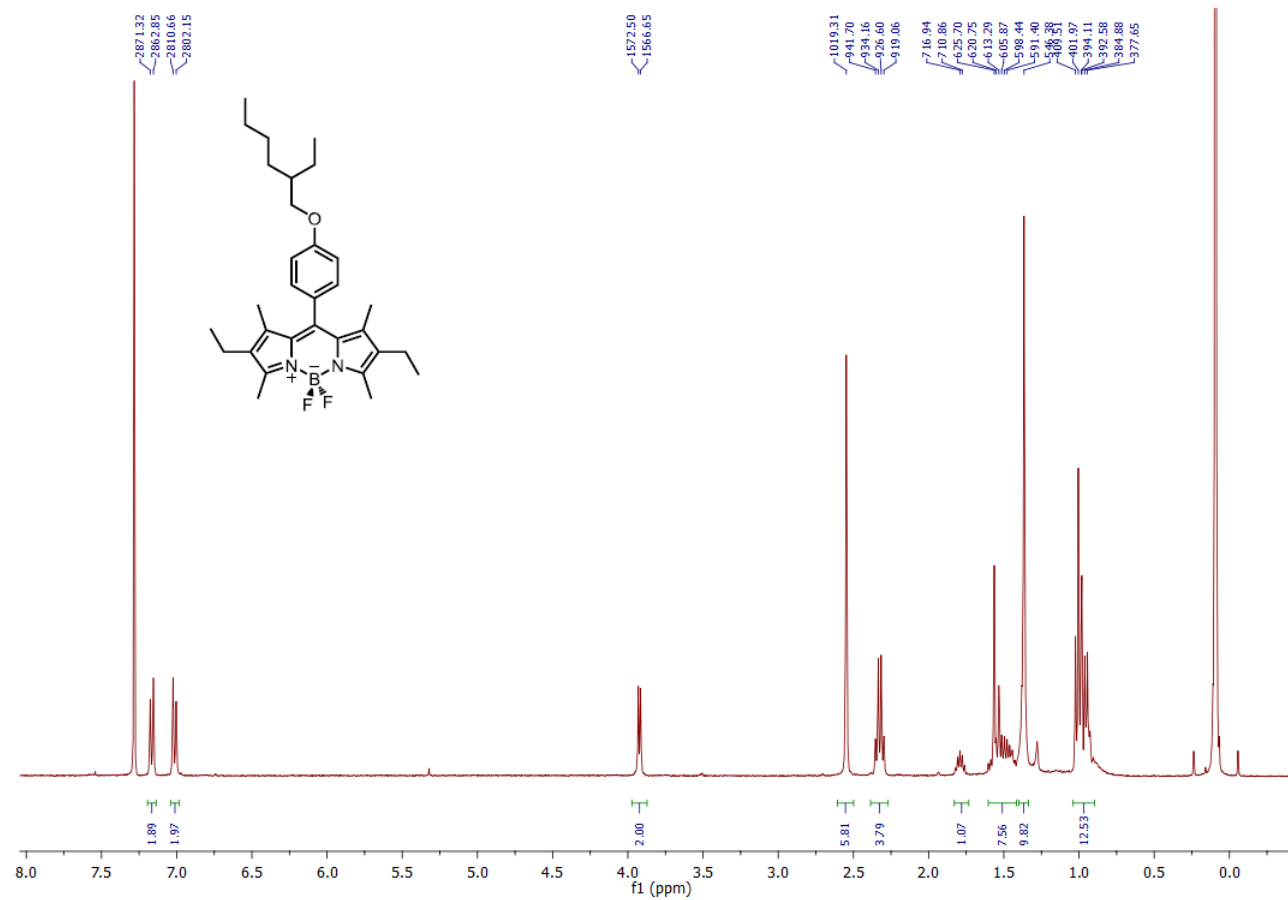


Figure 59. ¹H NMR Spectrum of Compound 11

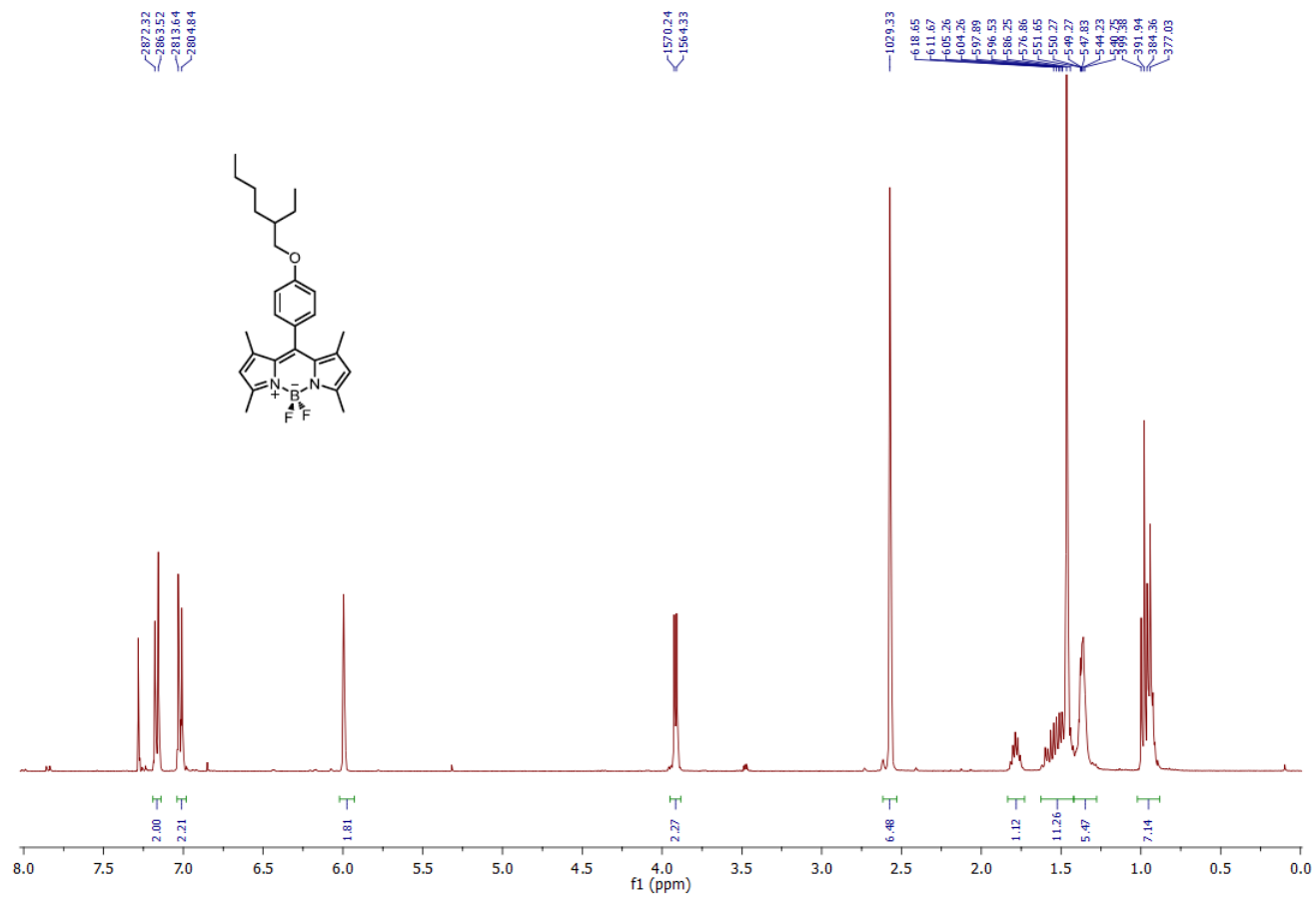


Figure 60. ¹H NMR Spectrum of Compound 12

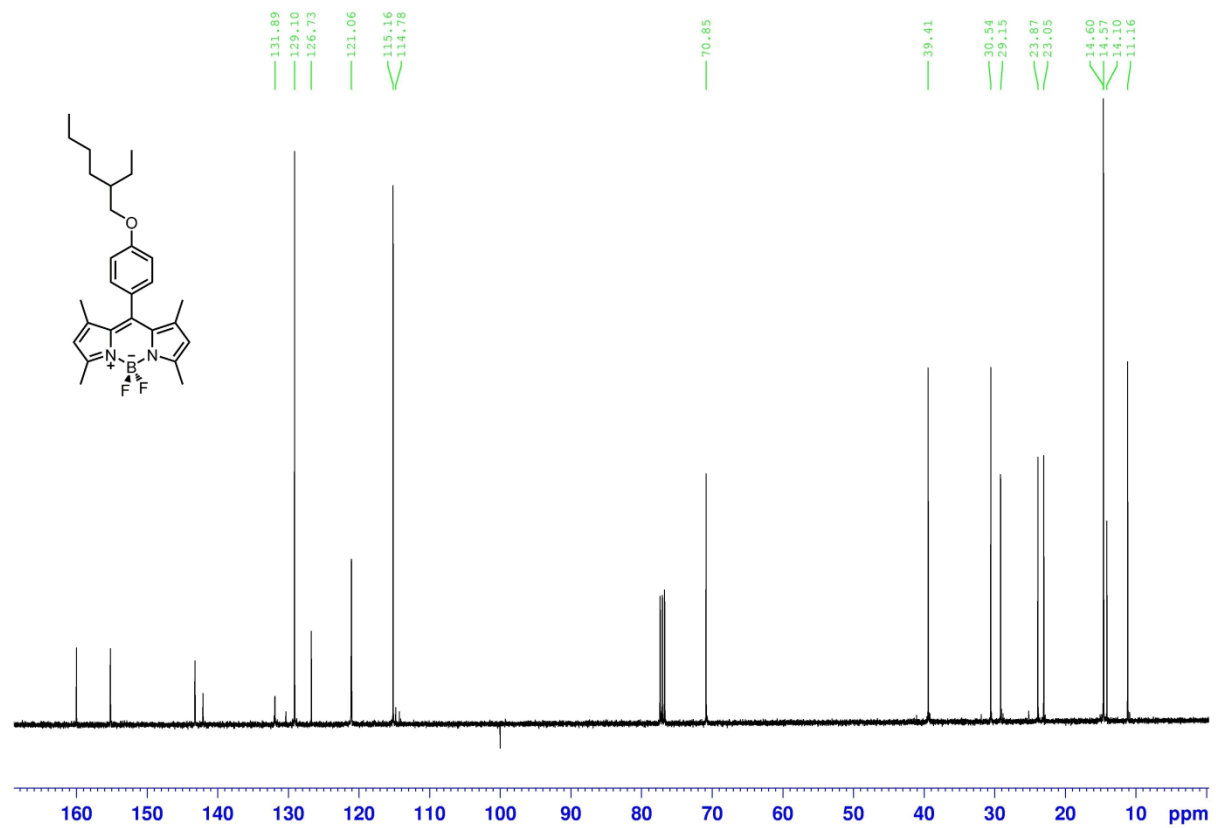


Figure 61. ^{13}C NMR Spectrum of Compound 12

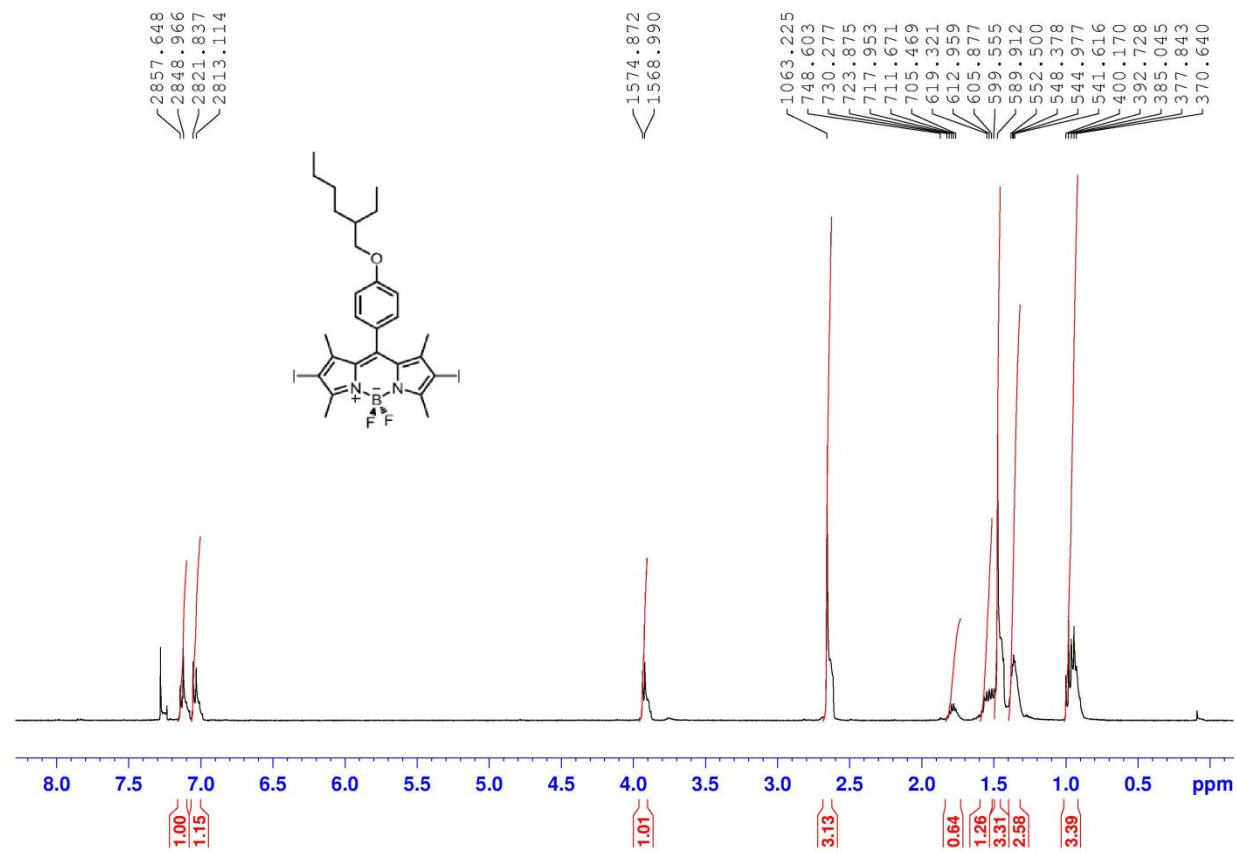


Figure 62. ¹H NMR Spectrum of Compound 12

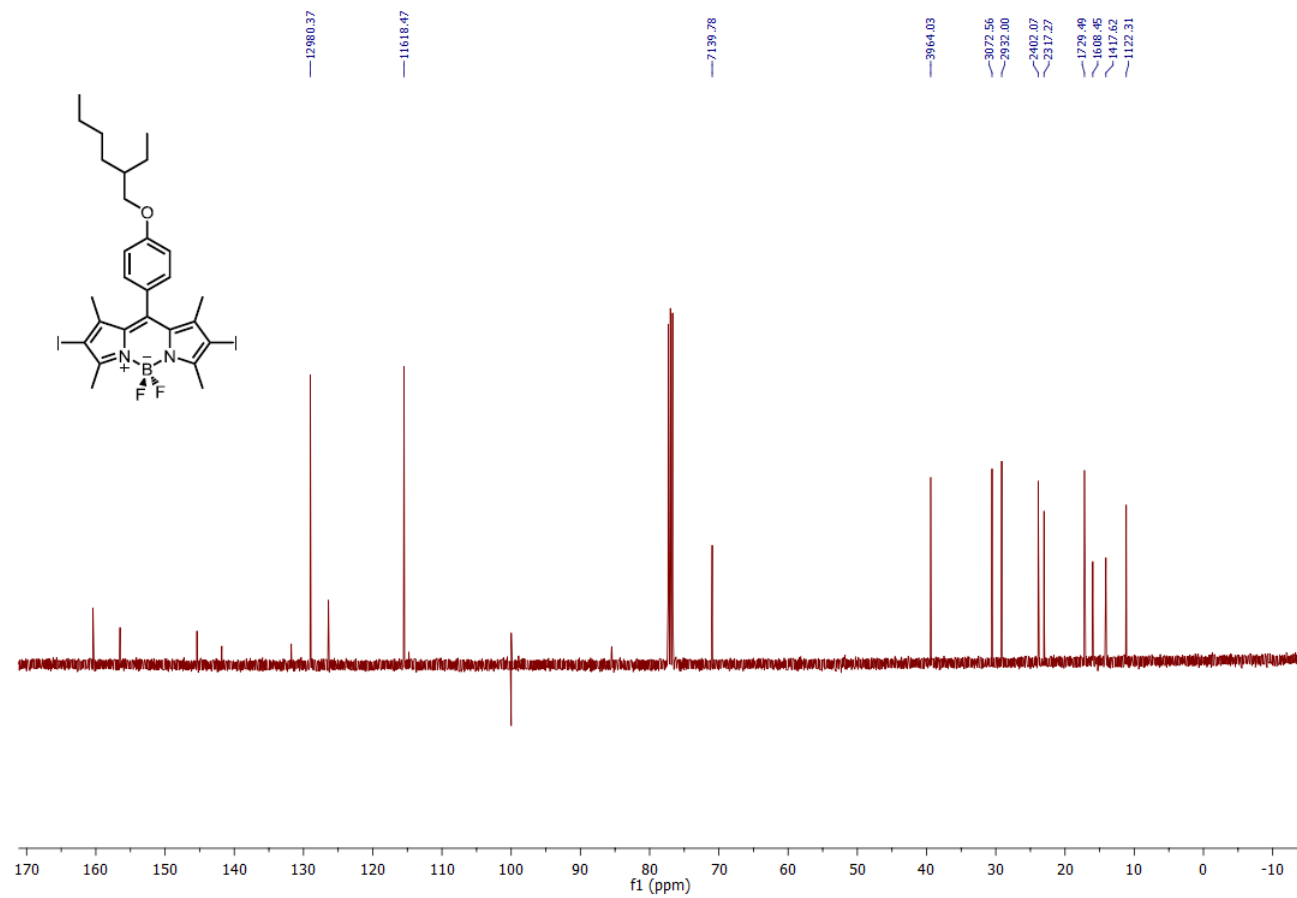


Figure 63. ^{13}C NMR Spectrum of Compound 13

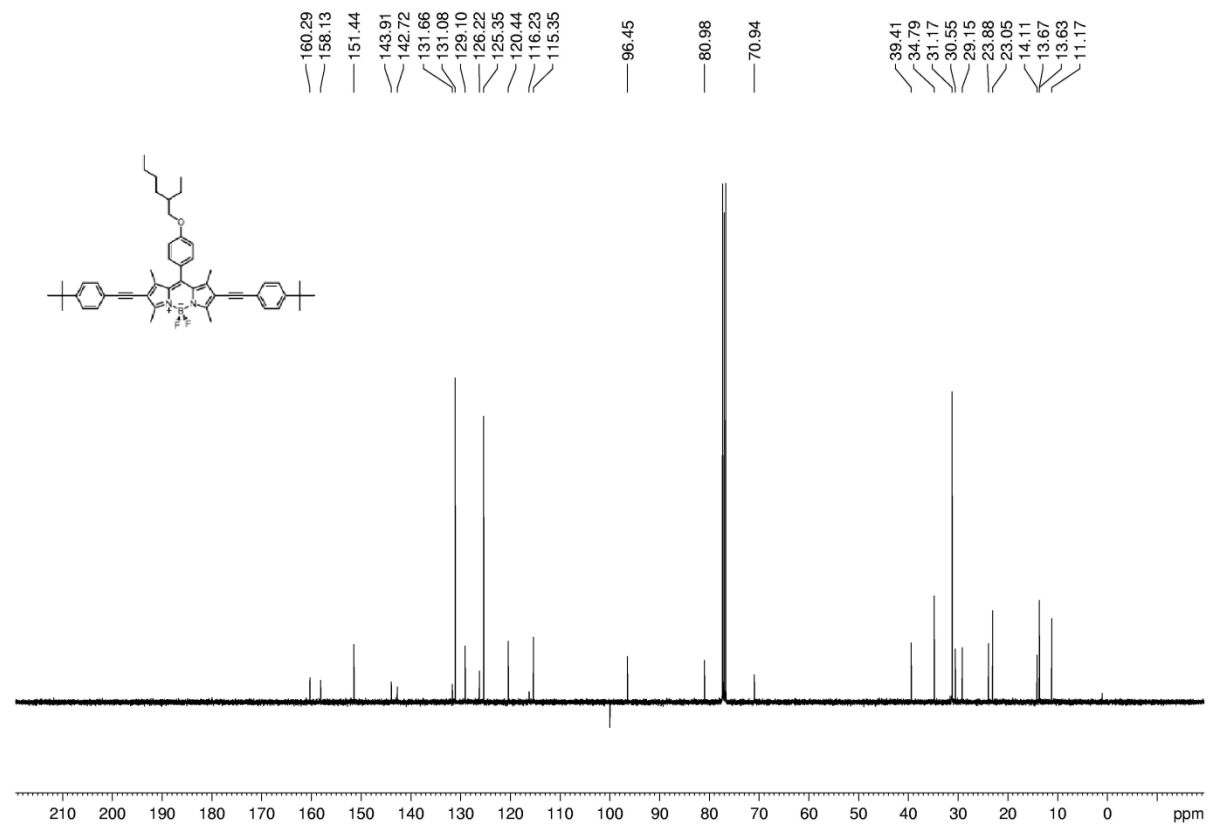


Figure 65. ^{13}C NMR Spectrum of Compound 14

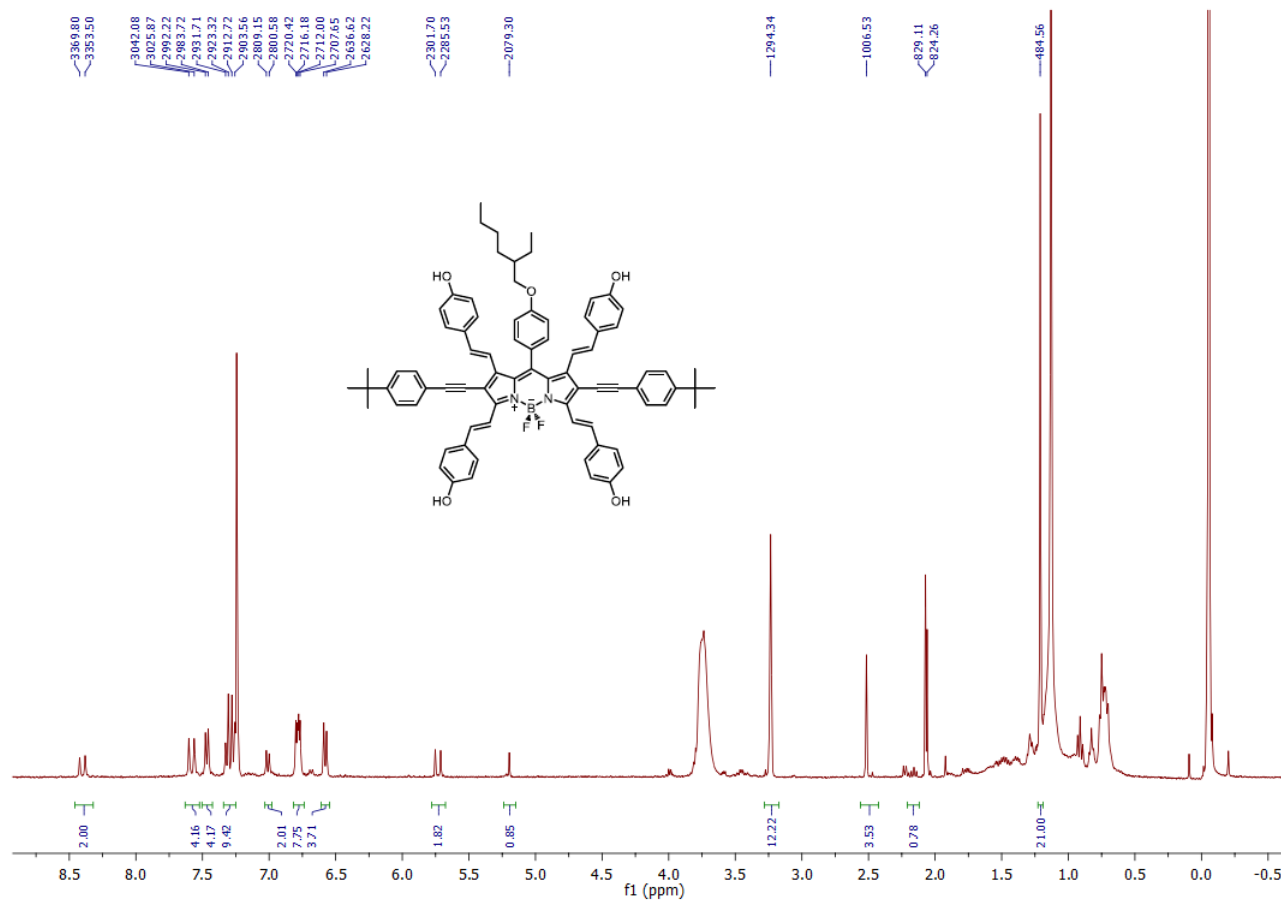
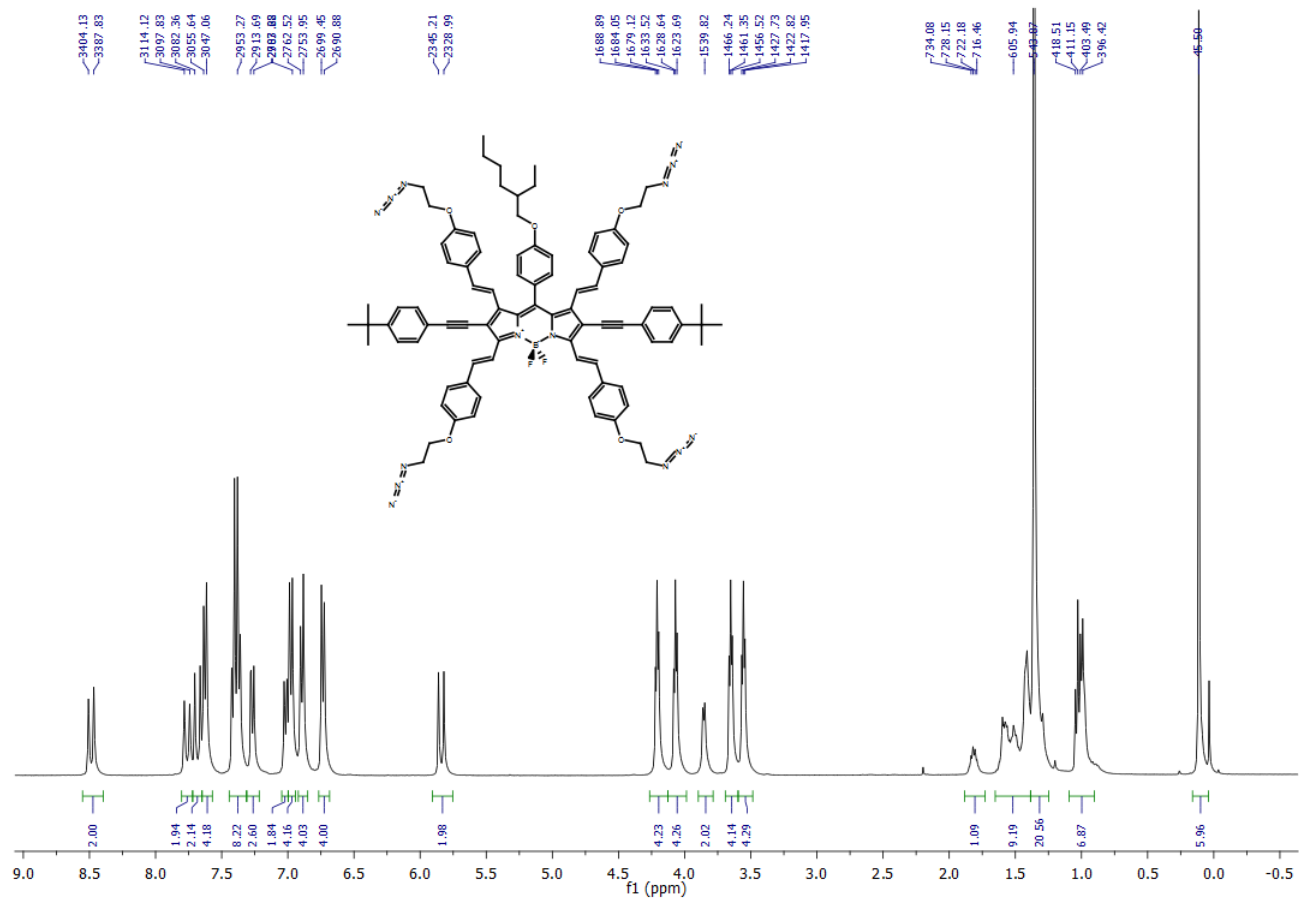


Figure 66. ¹H NMR Spectrum of Compound 15



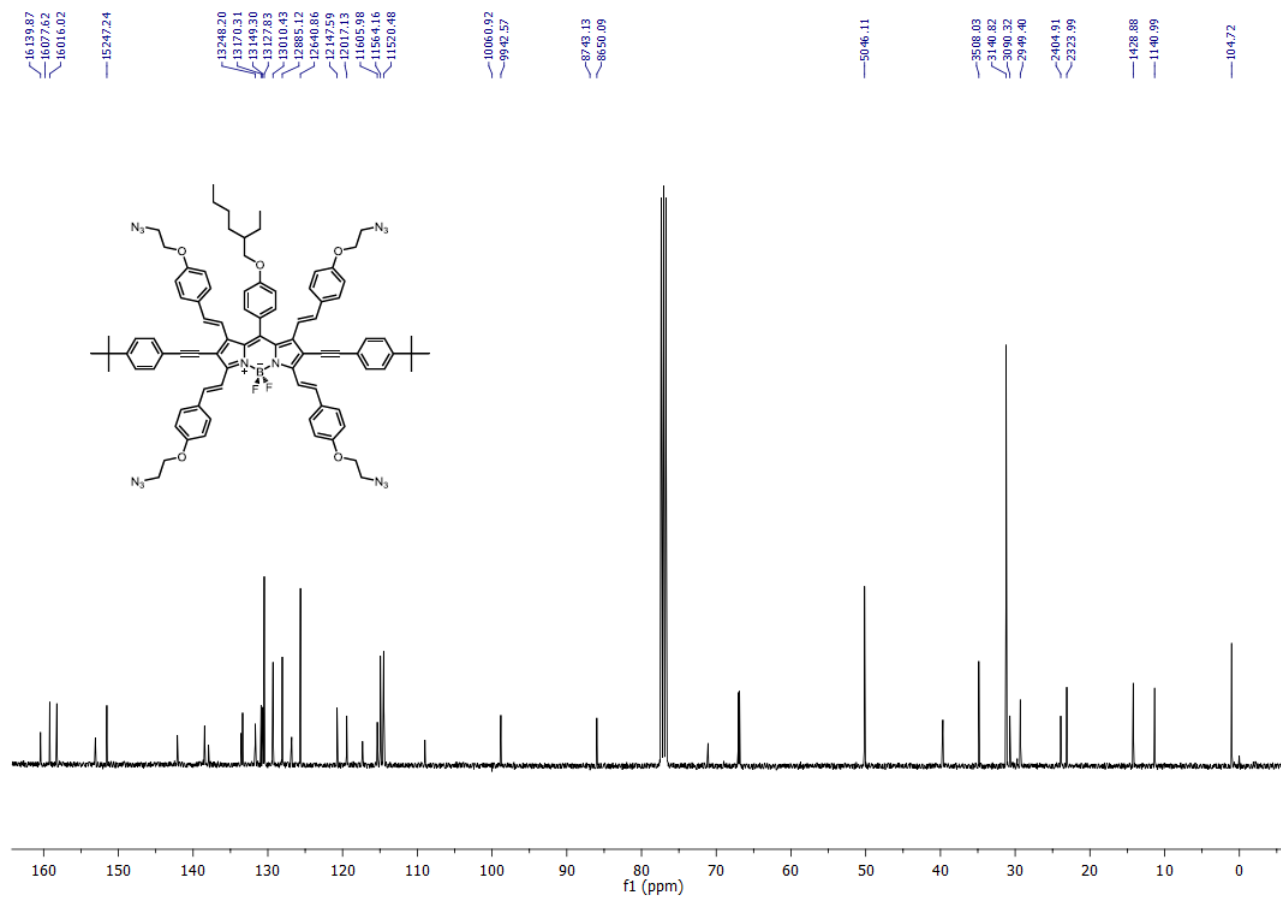


Figure 68. ¹³C NMR Spectrum of Compound 16

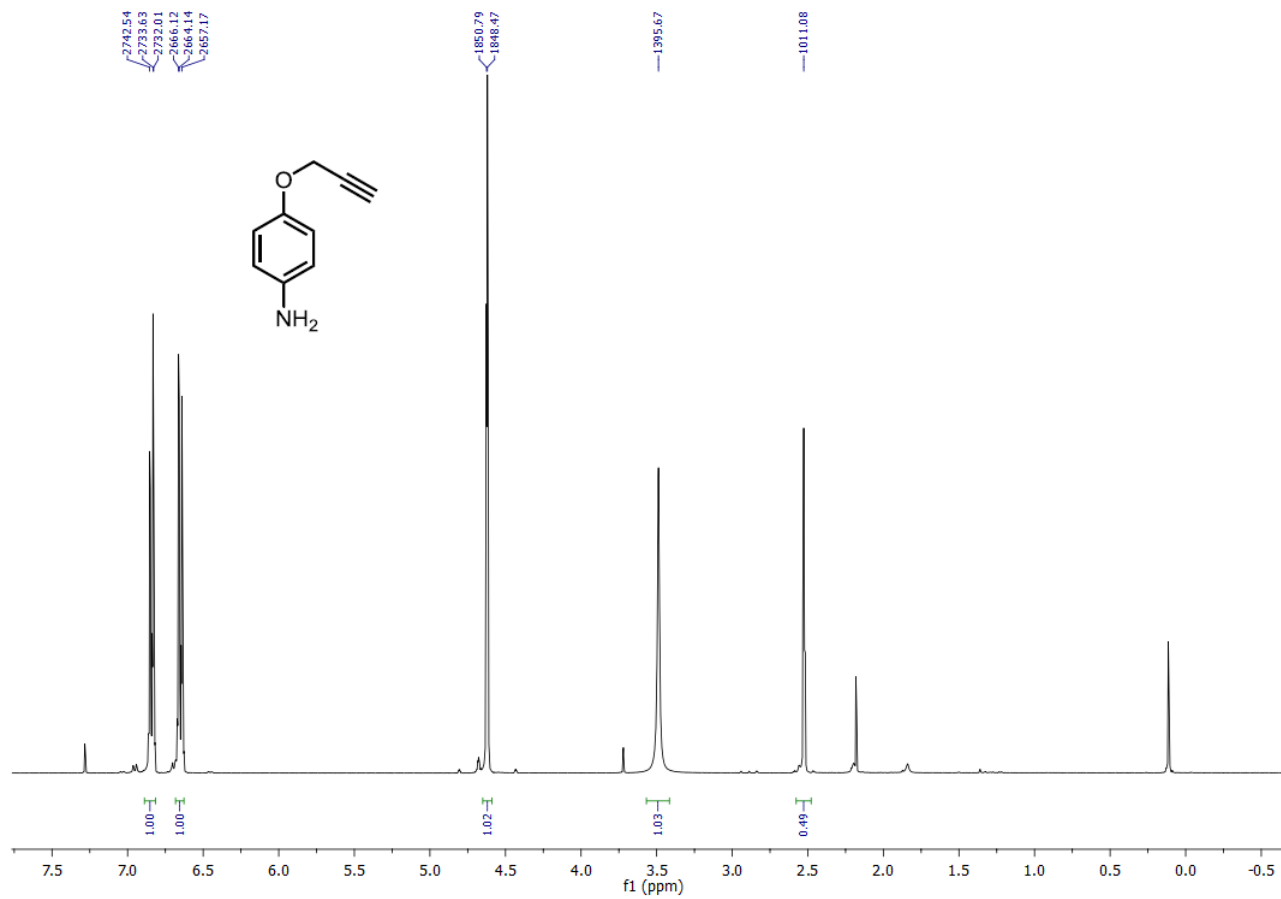


Figure 69. ¹H NMR Spectrum of Compound 18

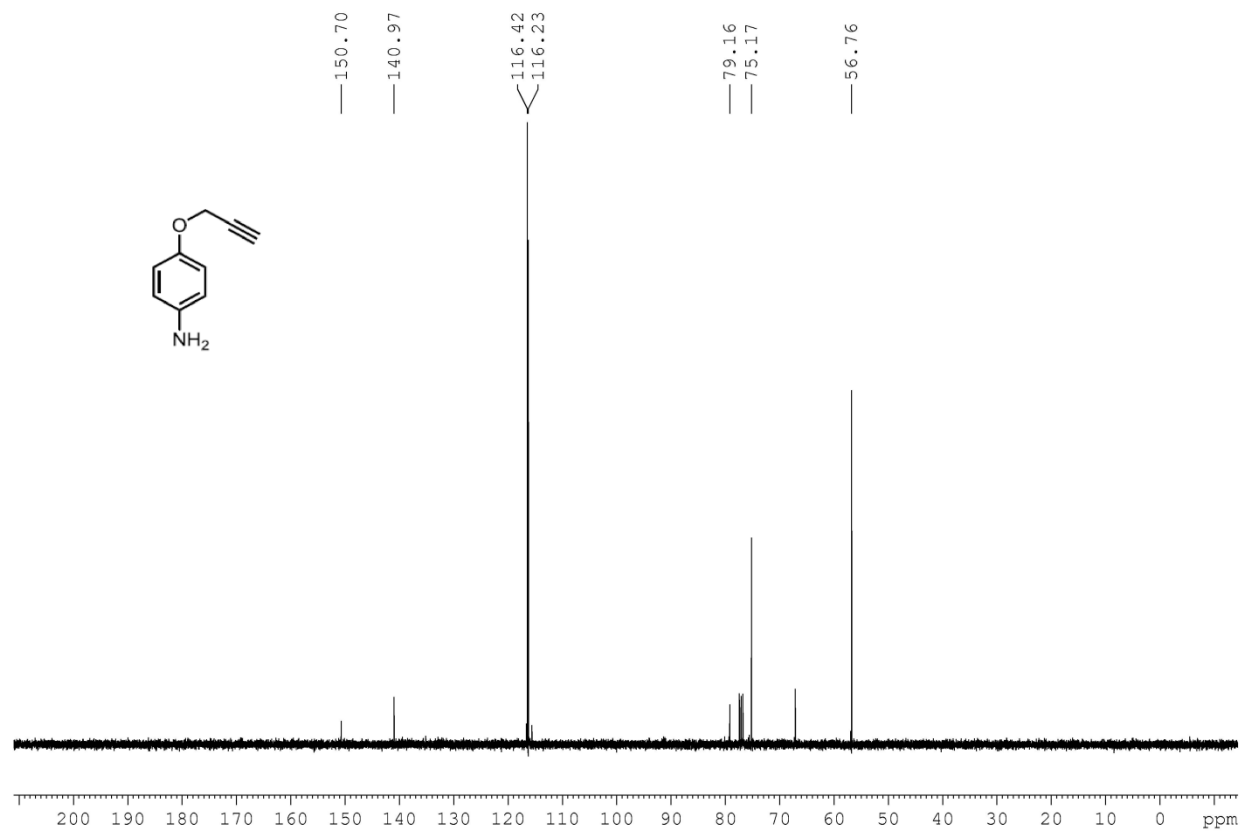


Figure 70. ^{13}C NMR Spectrum of Compound 18

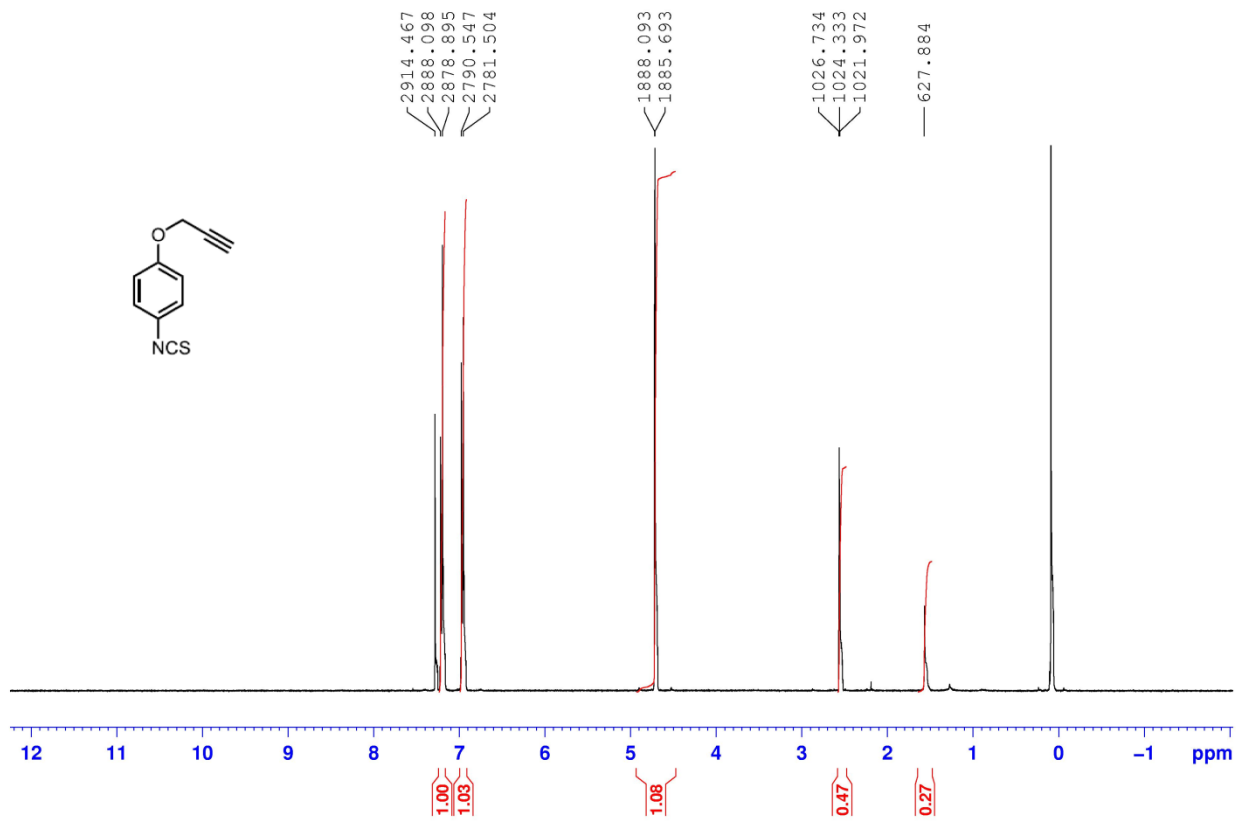


Figure 71. ¹H NMR Spectrum of Compound 19

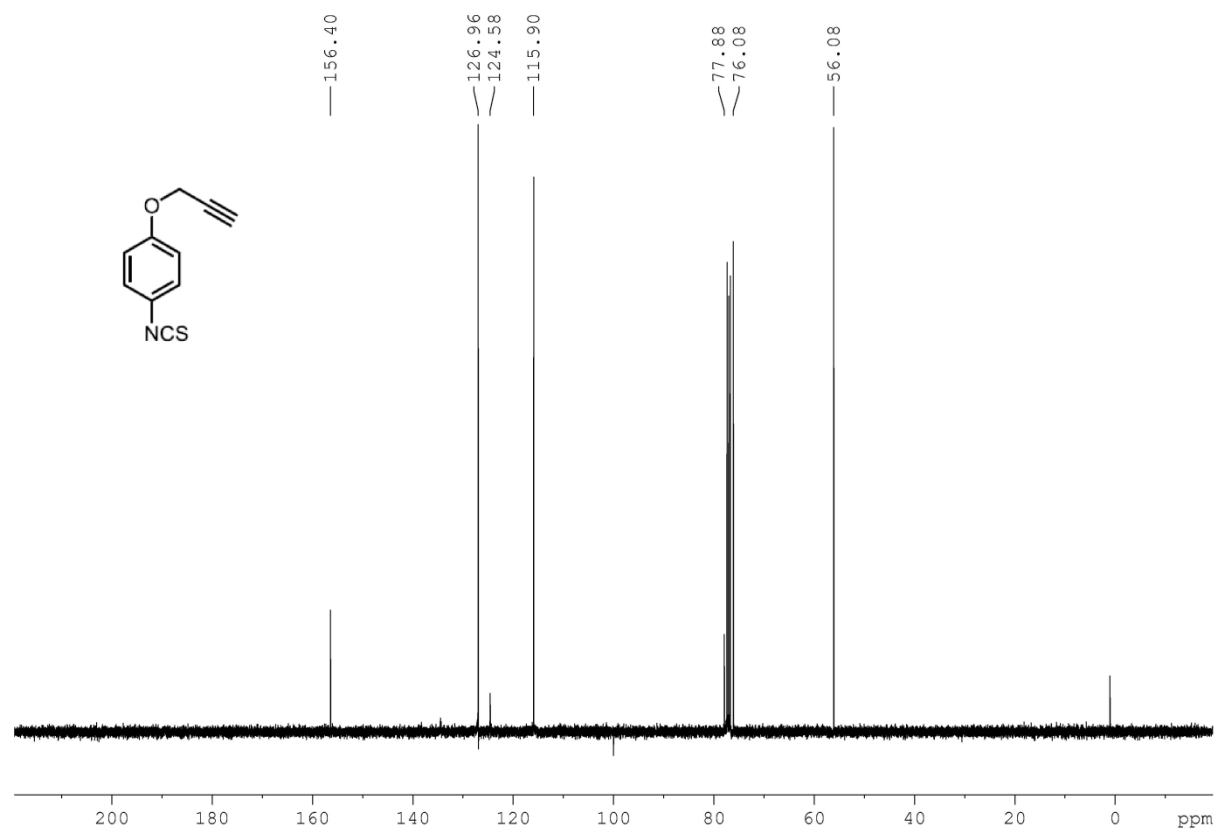
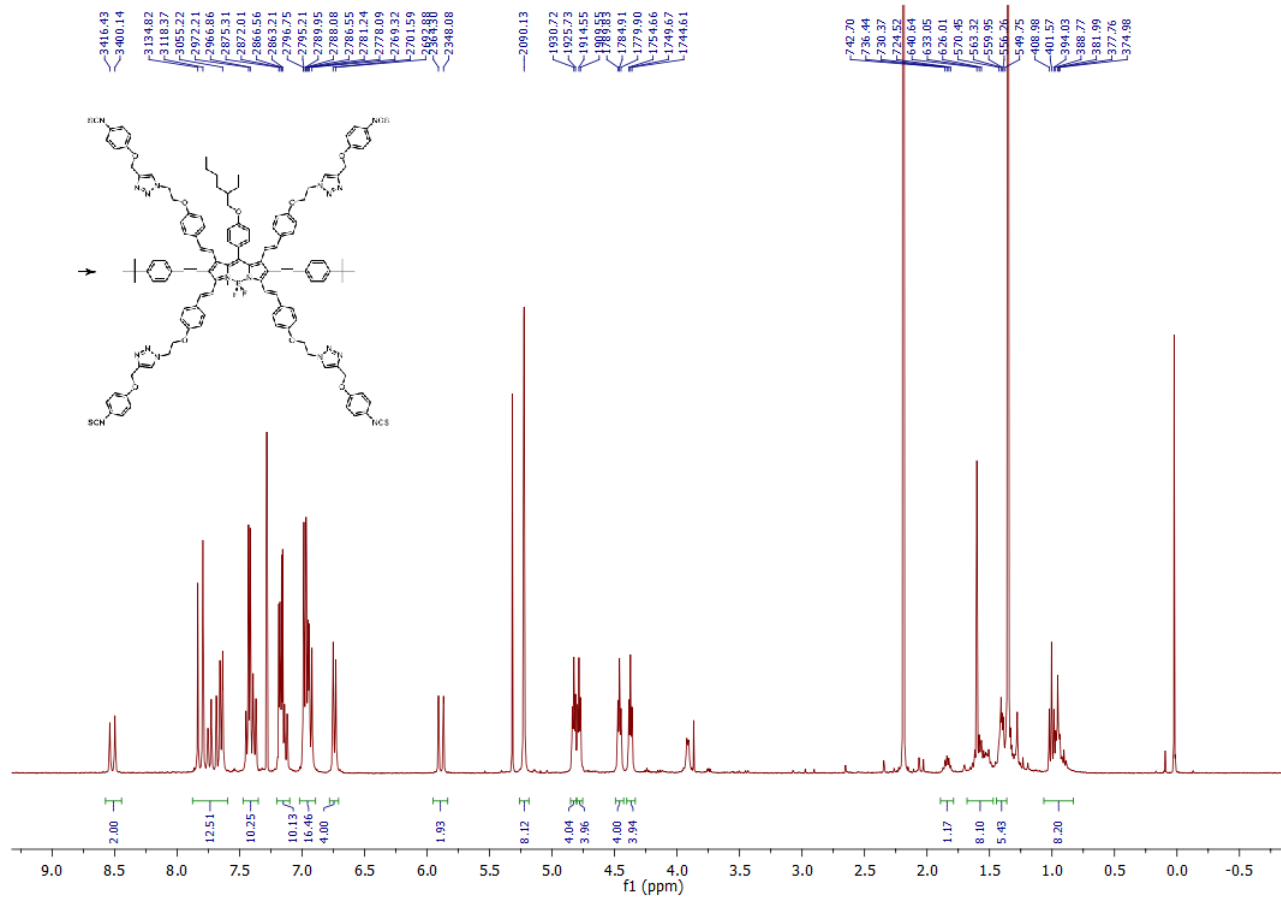


Figure 72. ¹³C NMR Spectrum of Compound 19



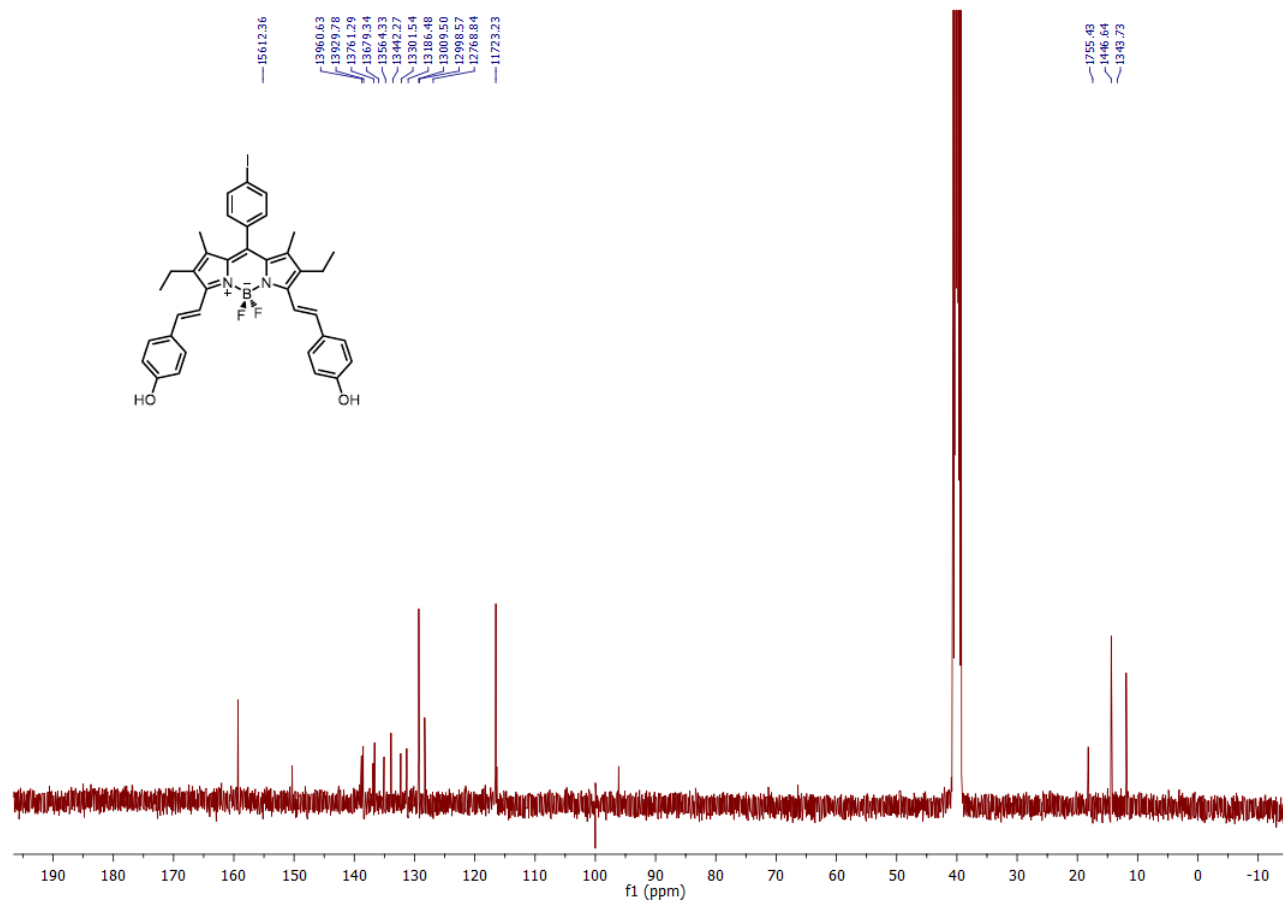


Figure 75. ¹³C NMR Spectrum of Compound 22

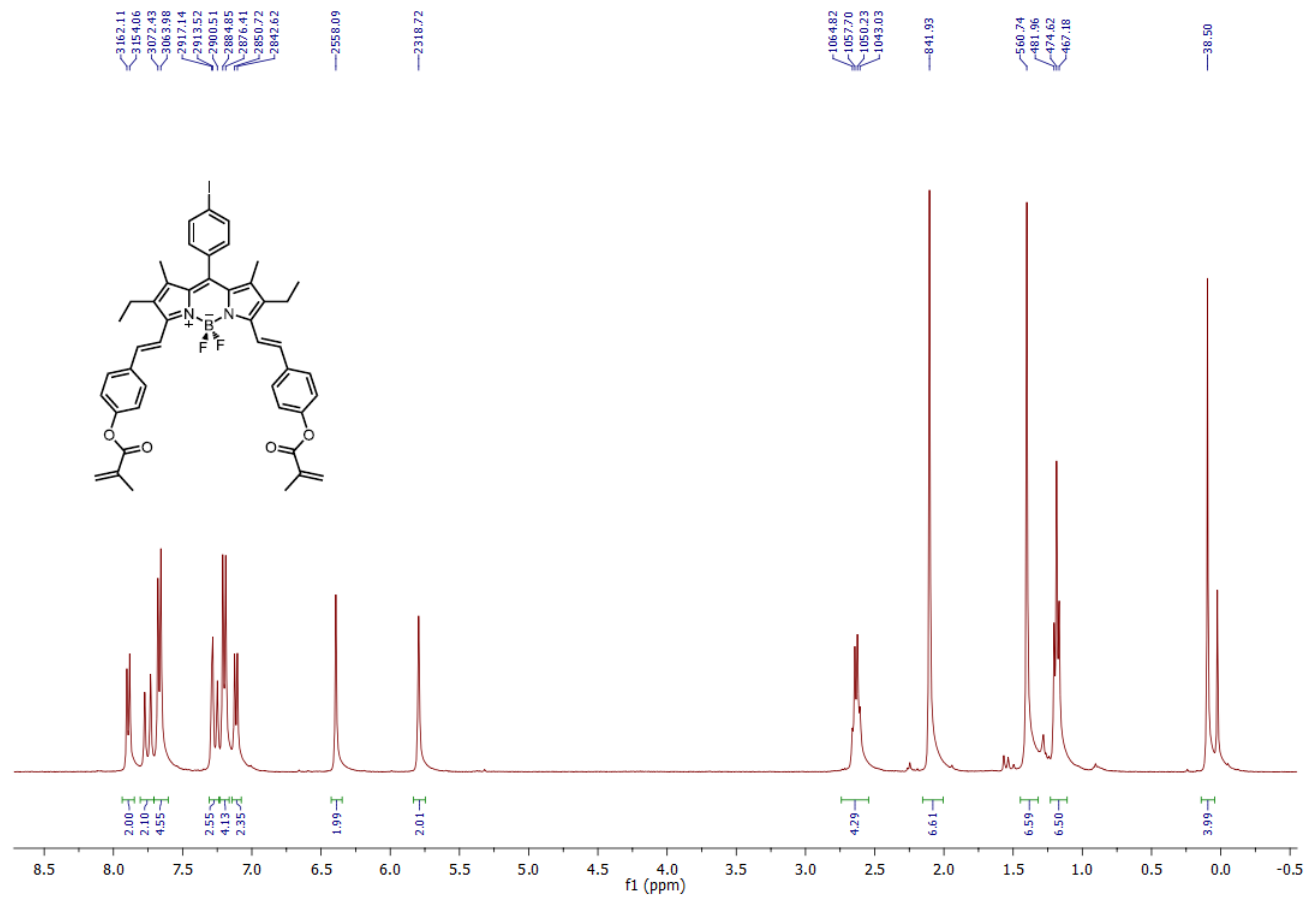


Figure 76. ¹H NMR Spectrum of Compound 23

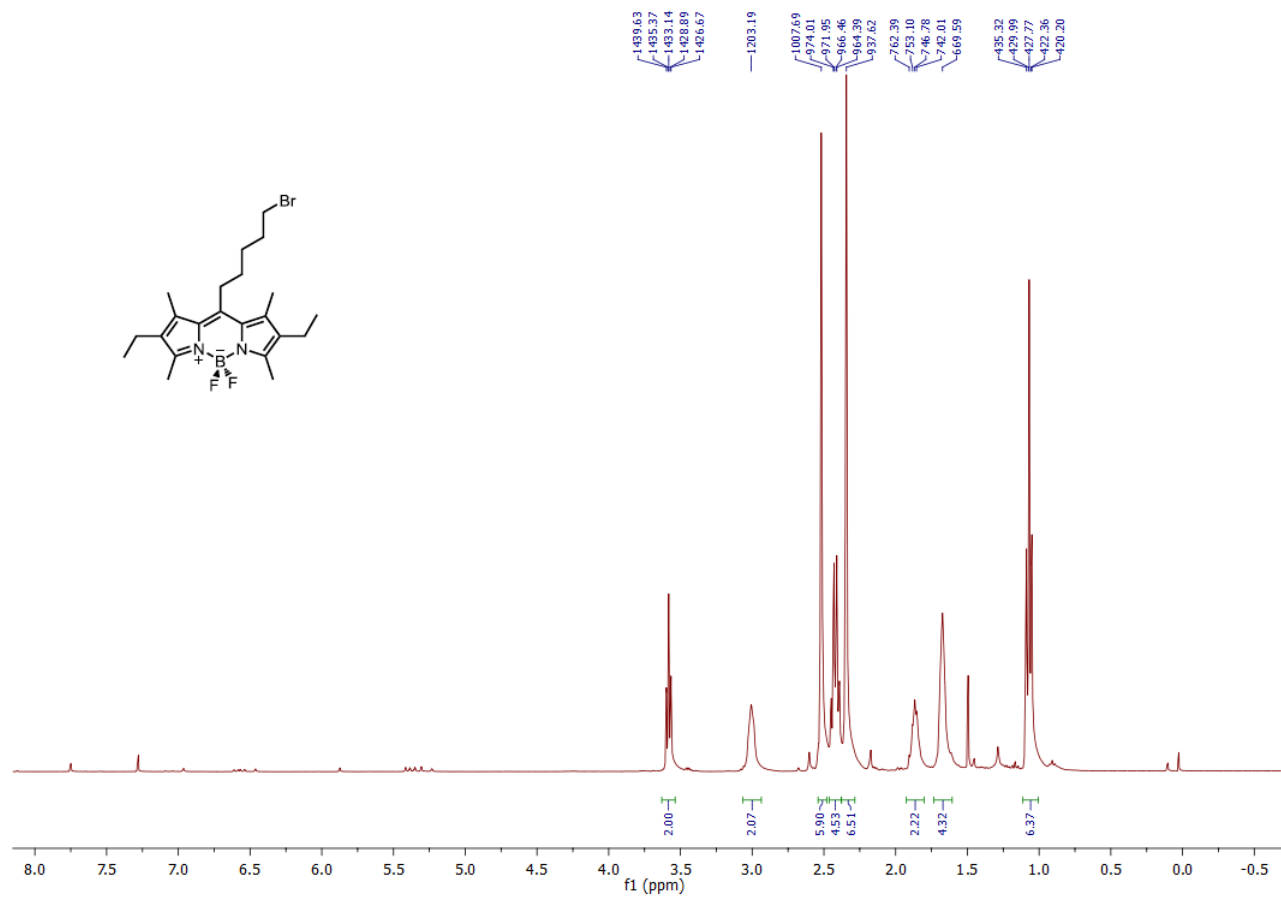


Figure 78. ¹H NMR Spectrum of Compound 25

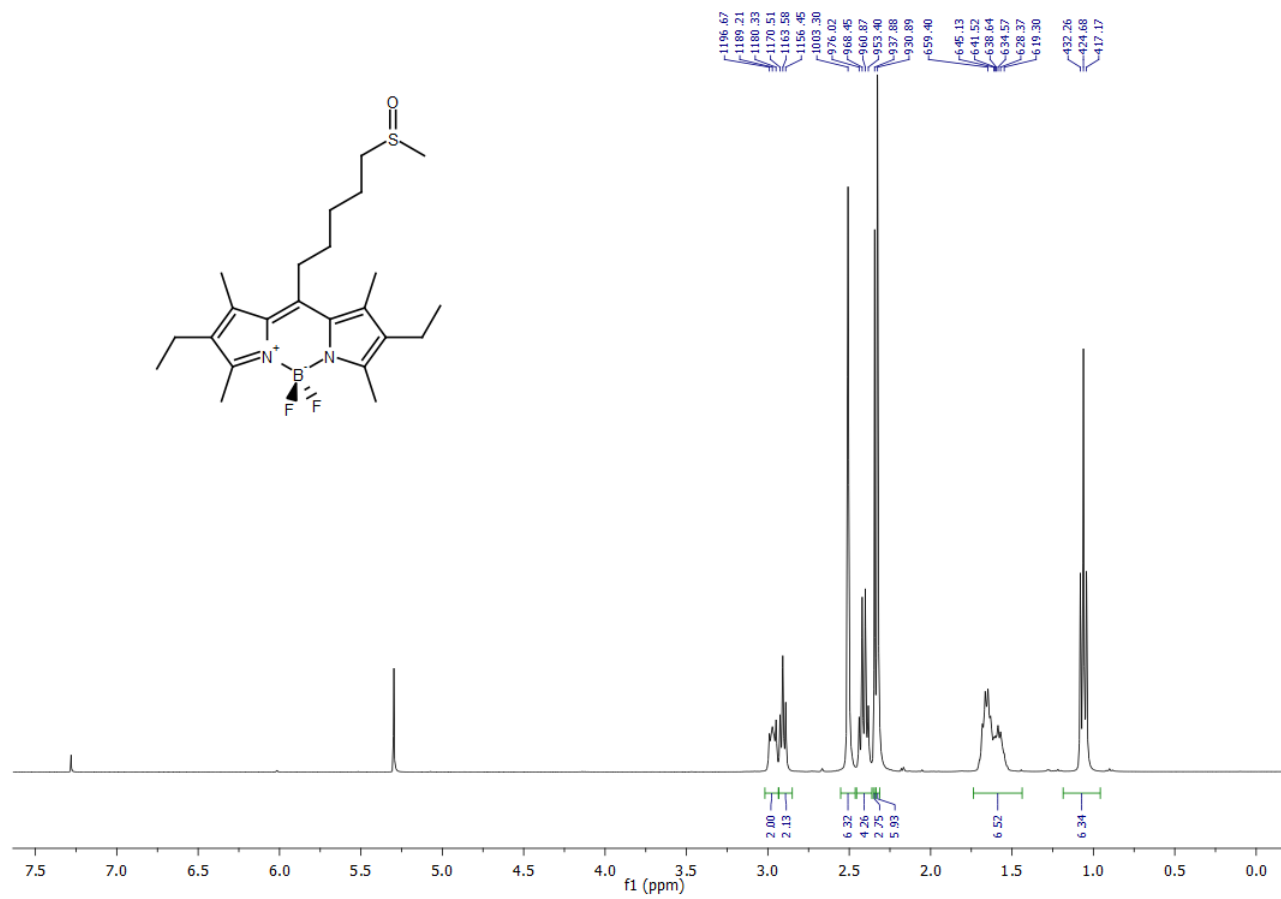


Figure 79. ¹H NMR Spectrum of Compound 26

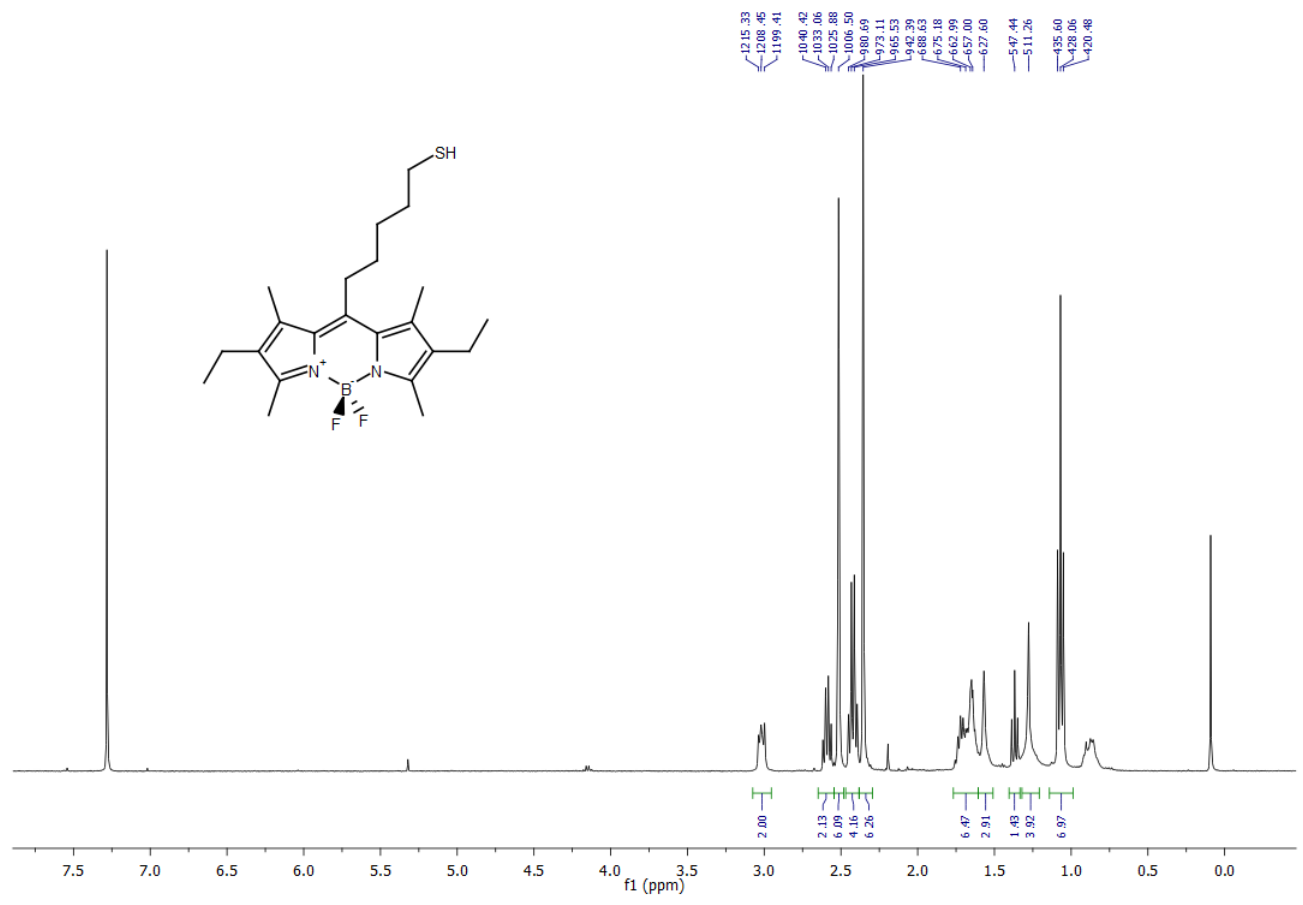


Figure 80. ¹H NMR Spectrum of Compound 27

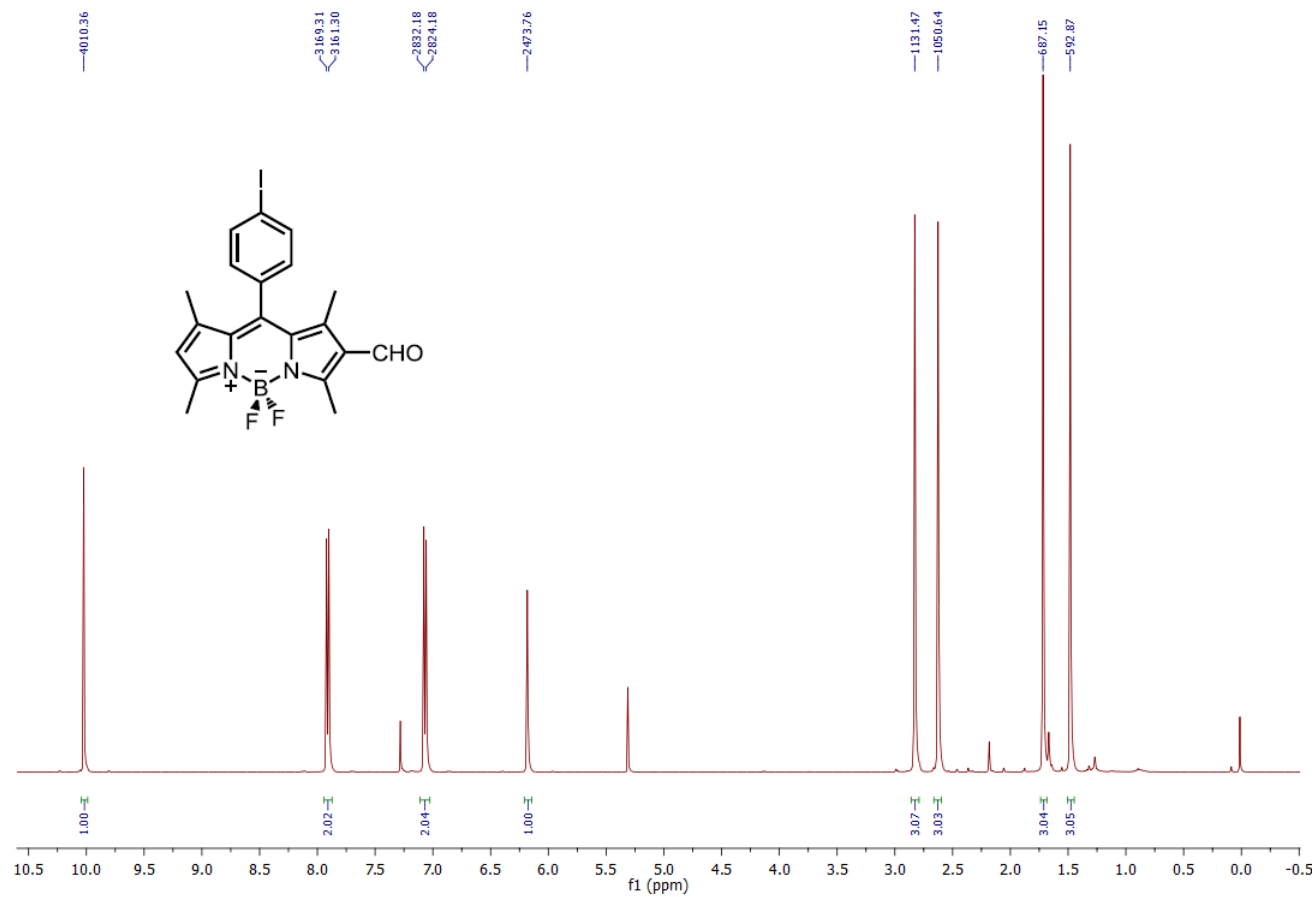


Figure 81. ¹H NMR Spectrum of Compound 29

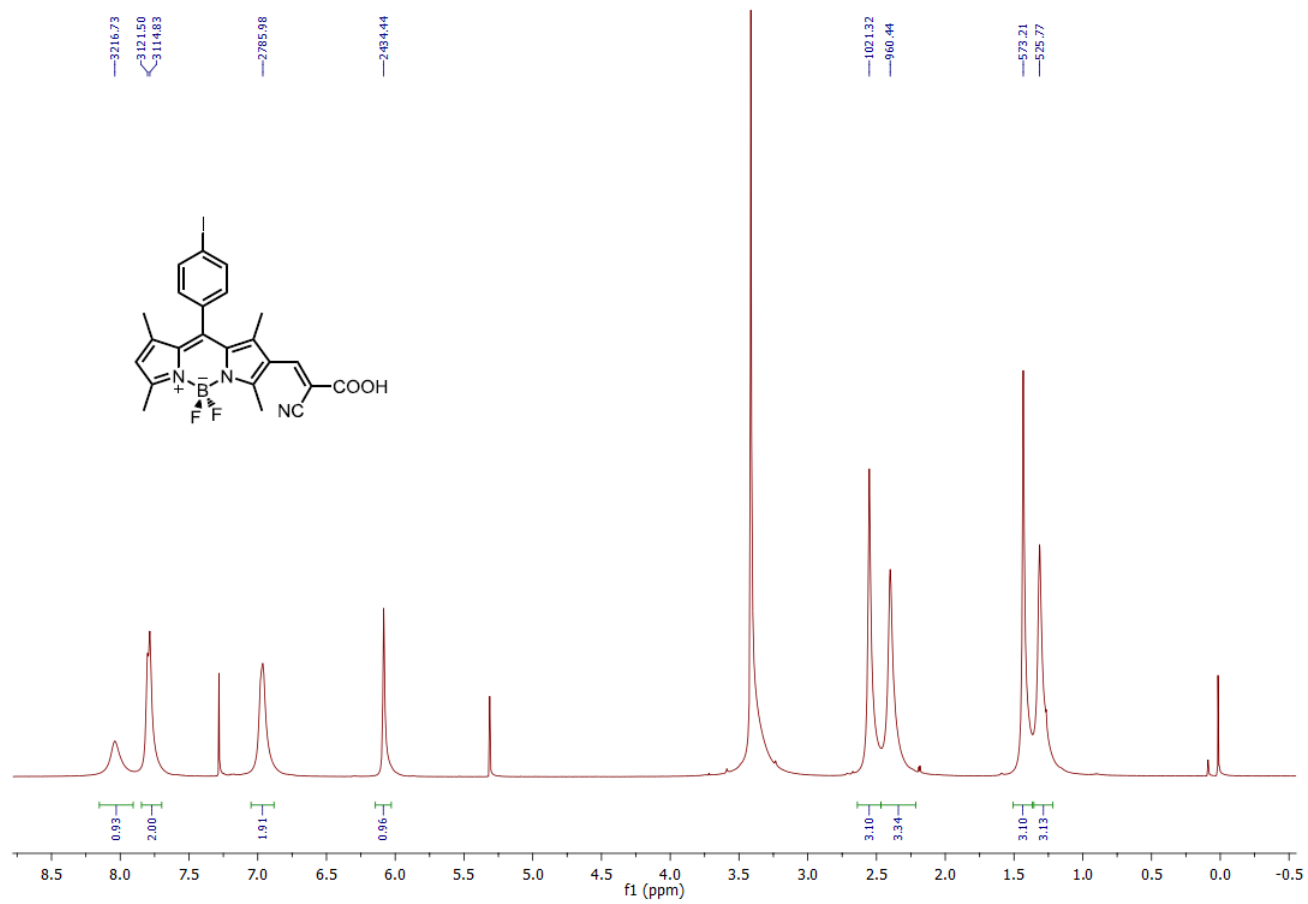


Figure 82. ¹H NMR Spectrum of Compound 30

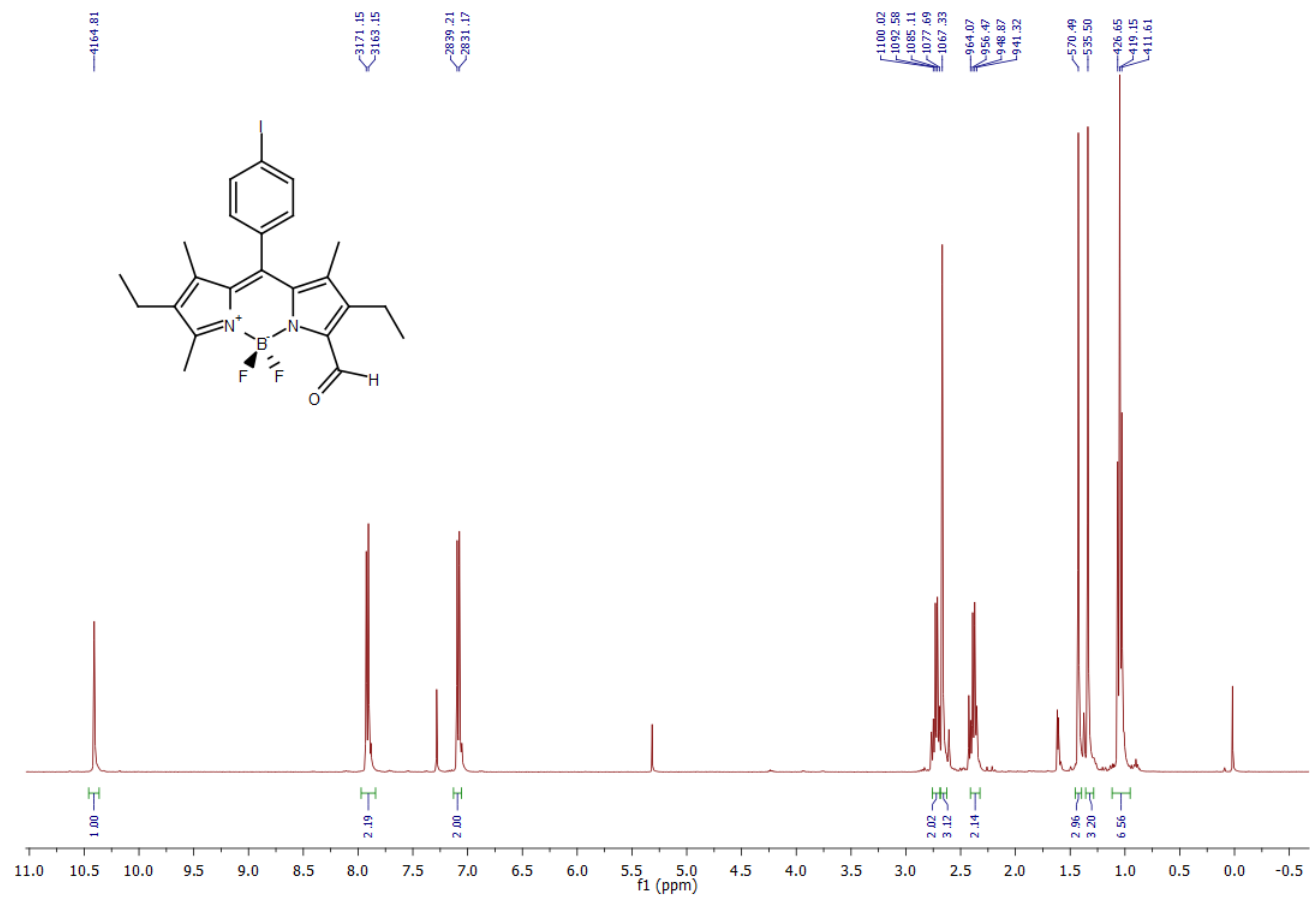


Figure 83. ¹H NMR Spectrum of Compound 31

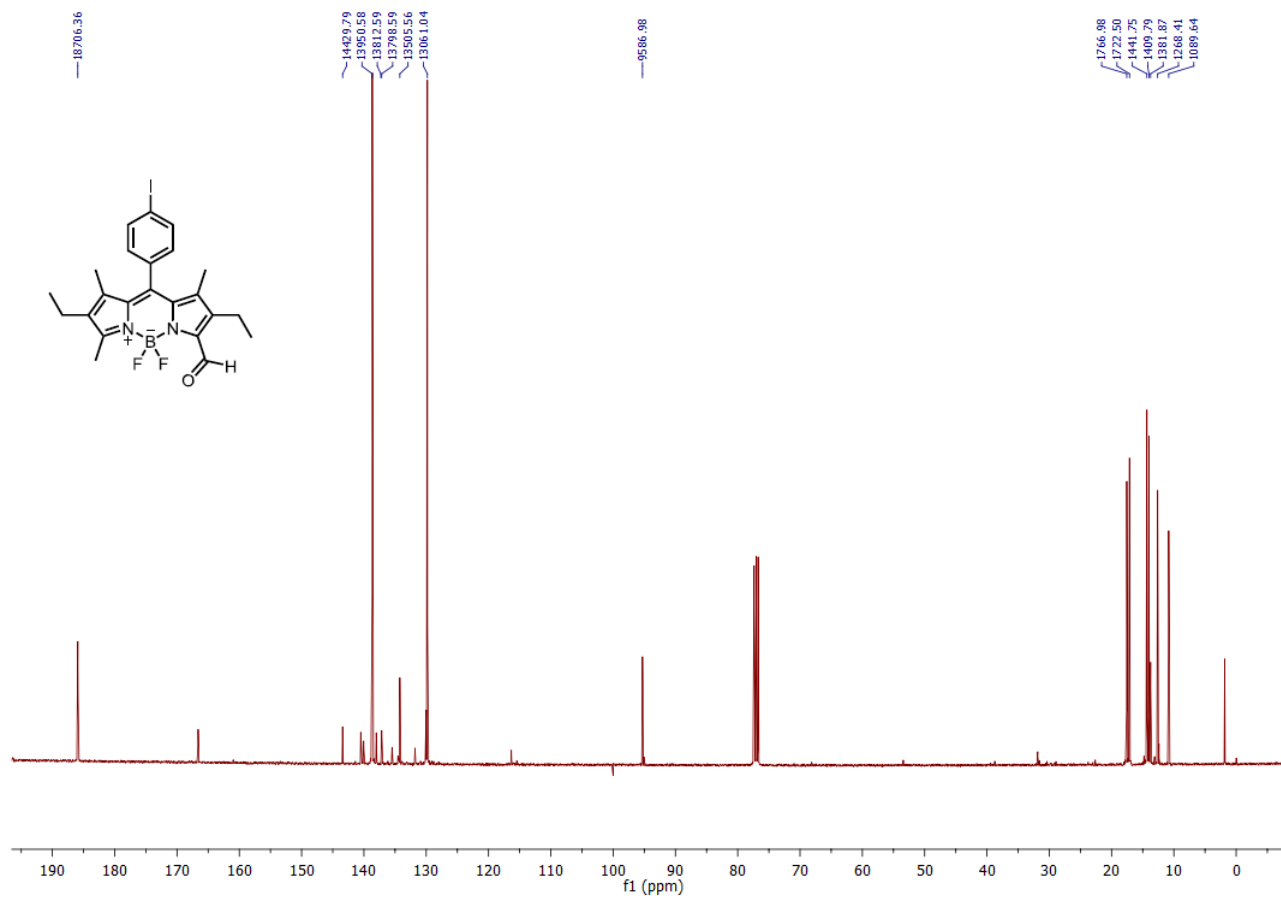


Figure 84. ¹³C NMR Spectrum of Compound 31

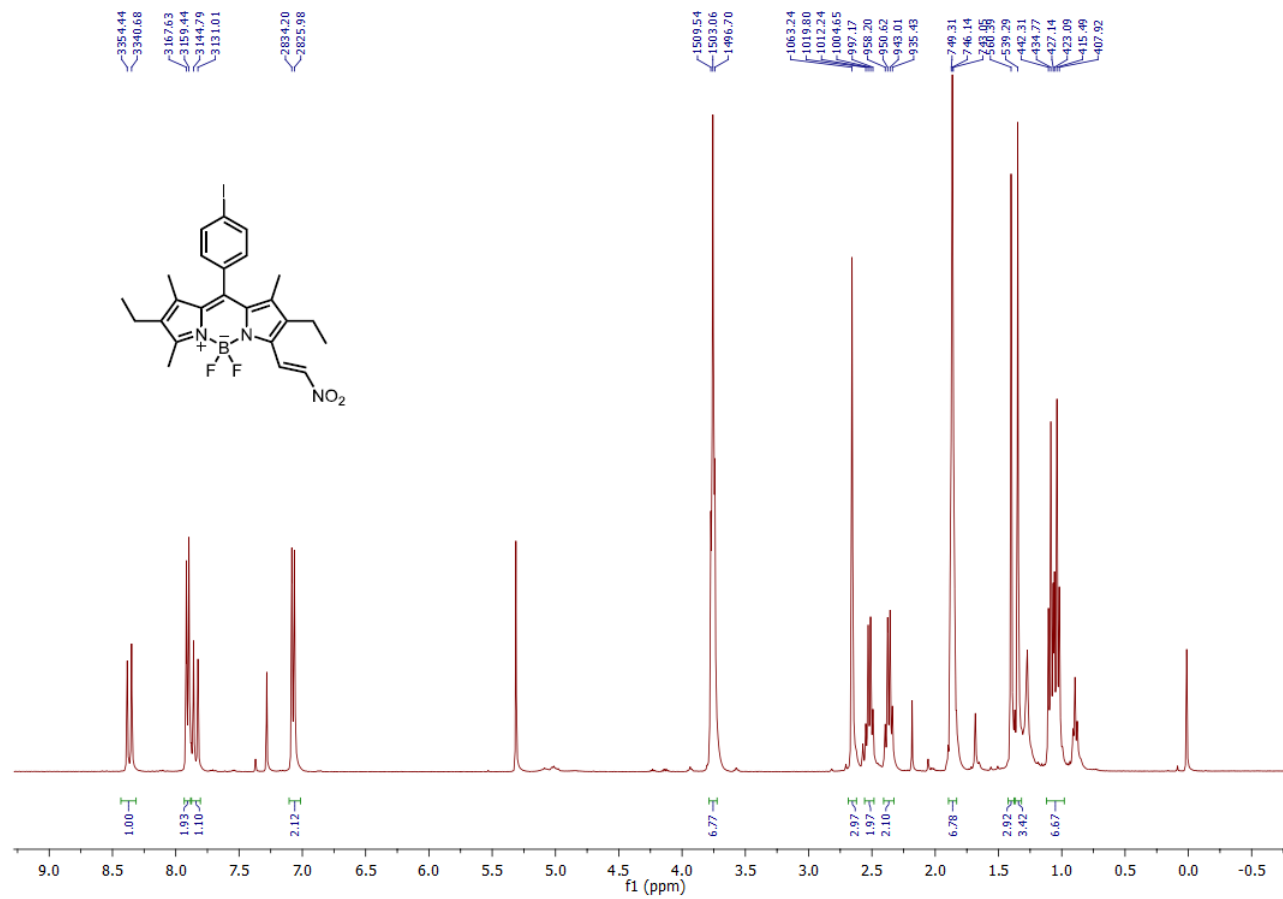


Figure 85. ¹H NMR Spectrum of Compound 32

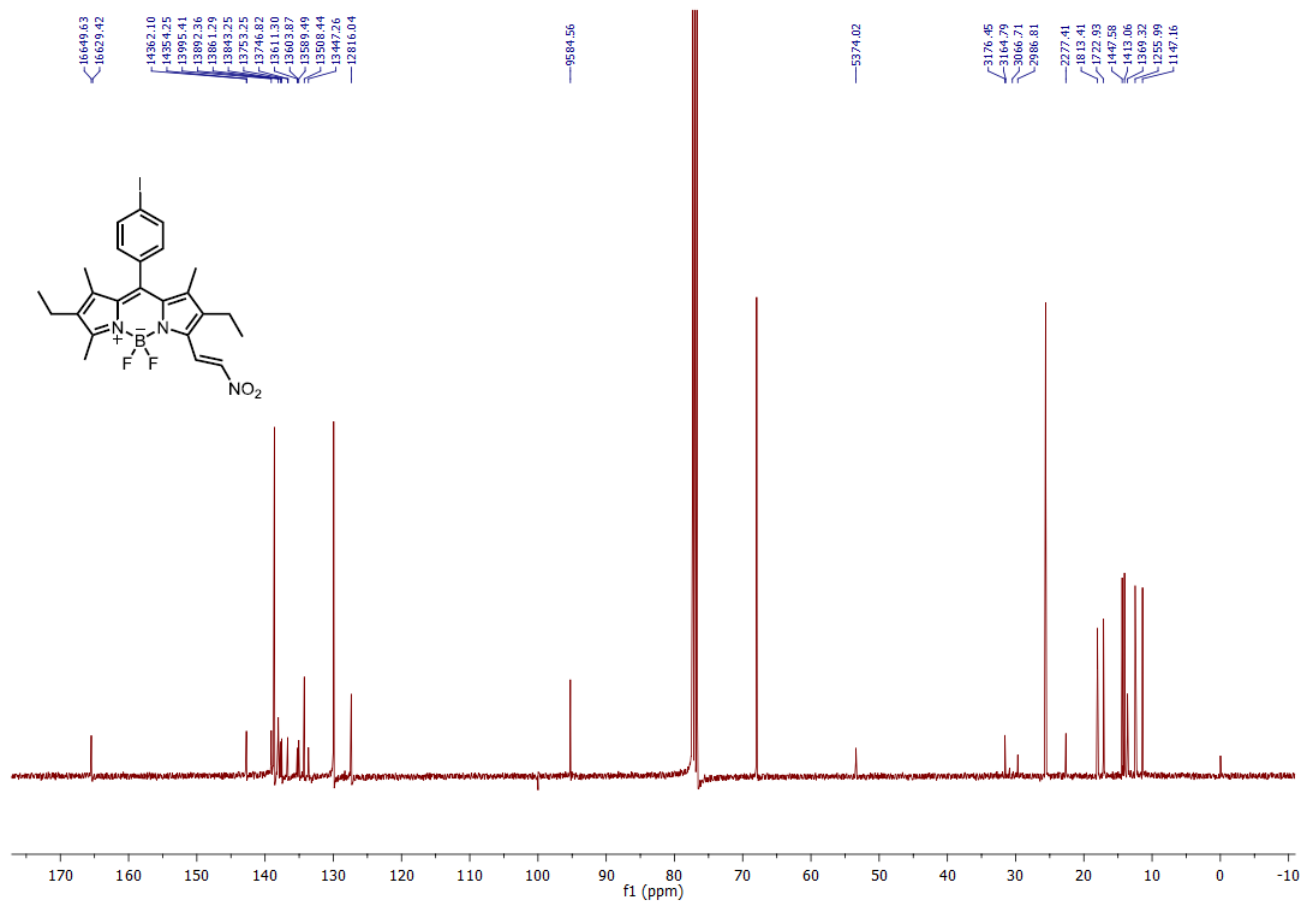


Figure 86. ¹³C NMR Spectrum of Compound 32

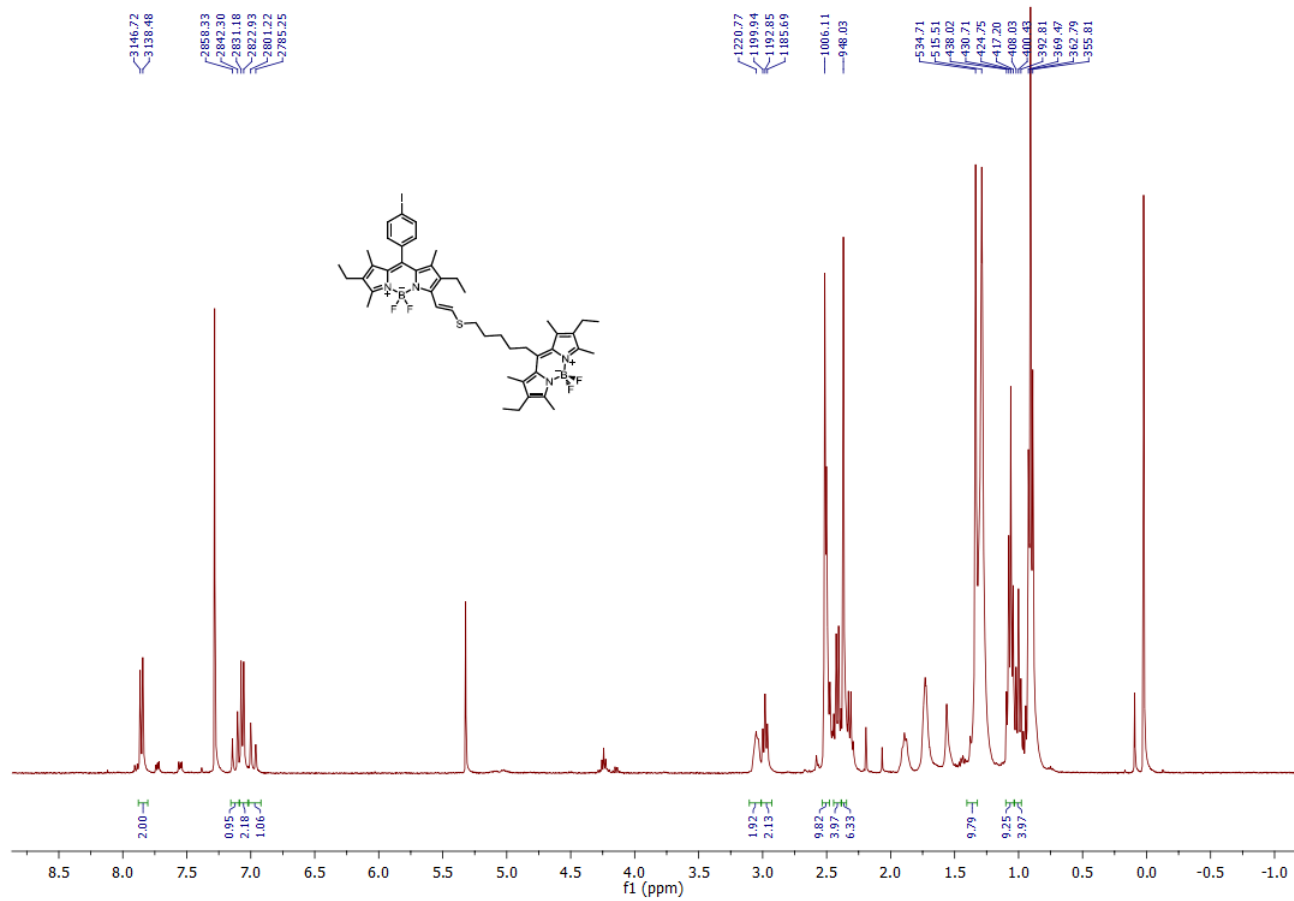


Figure 87. ^1H NMR Spectrum of Compound 33

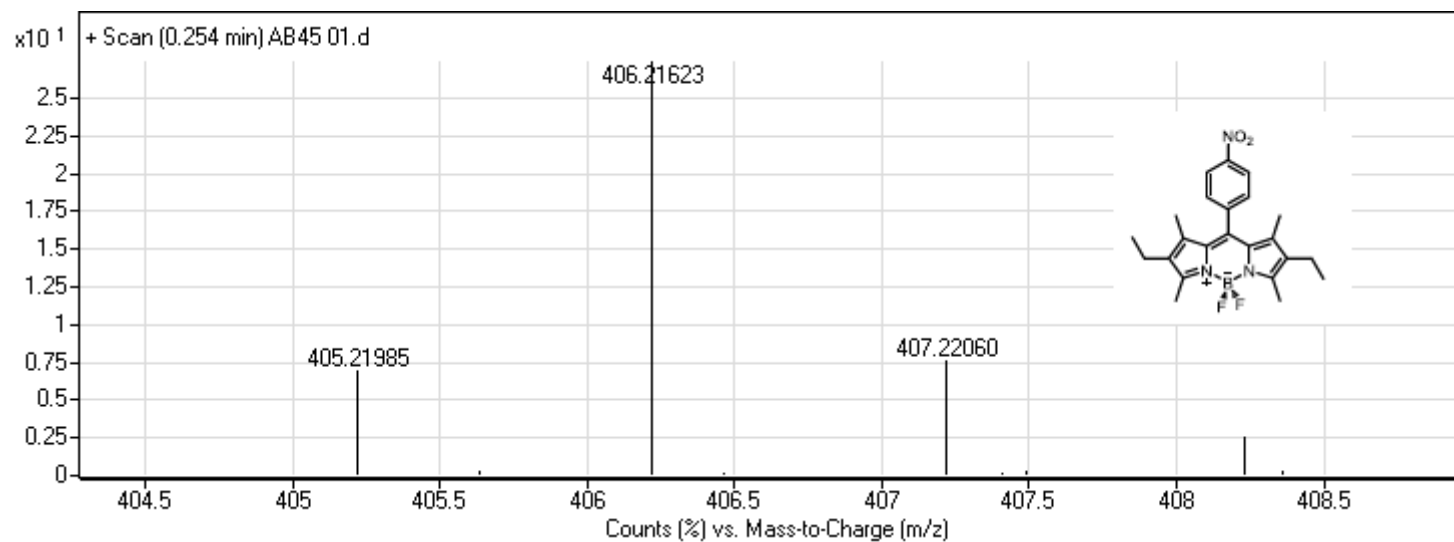


Figure 88. Mass Spectrum of Compound 1

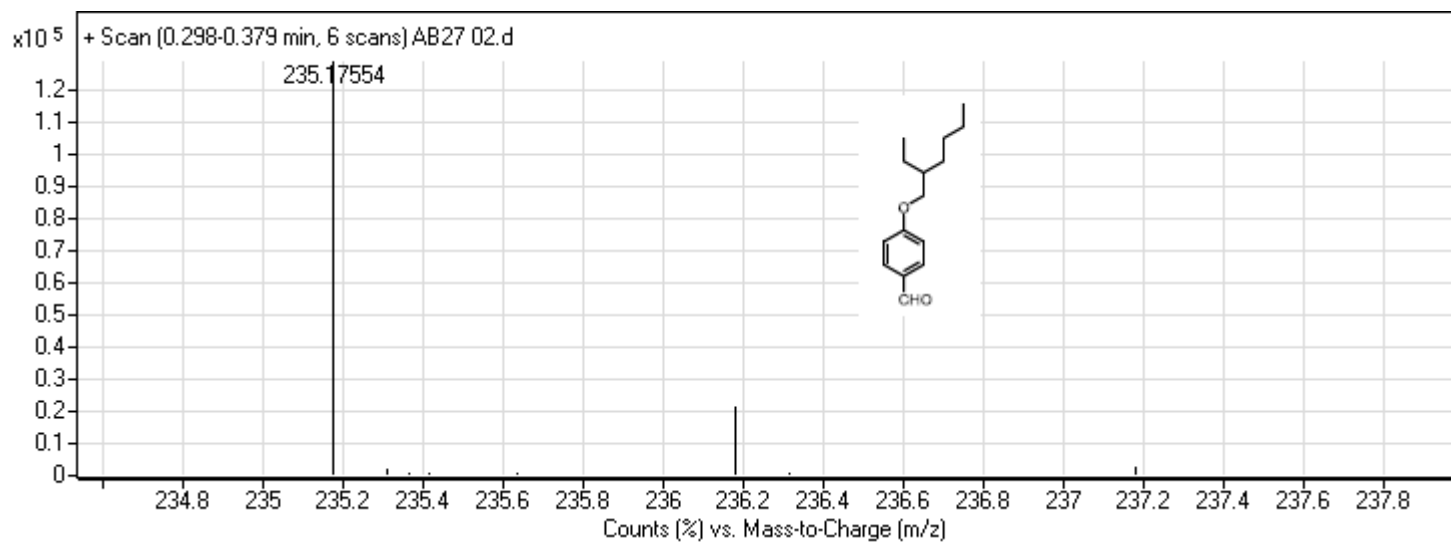


Figure 89. Mass Spectrum of Compound 10

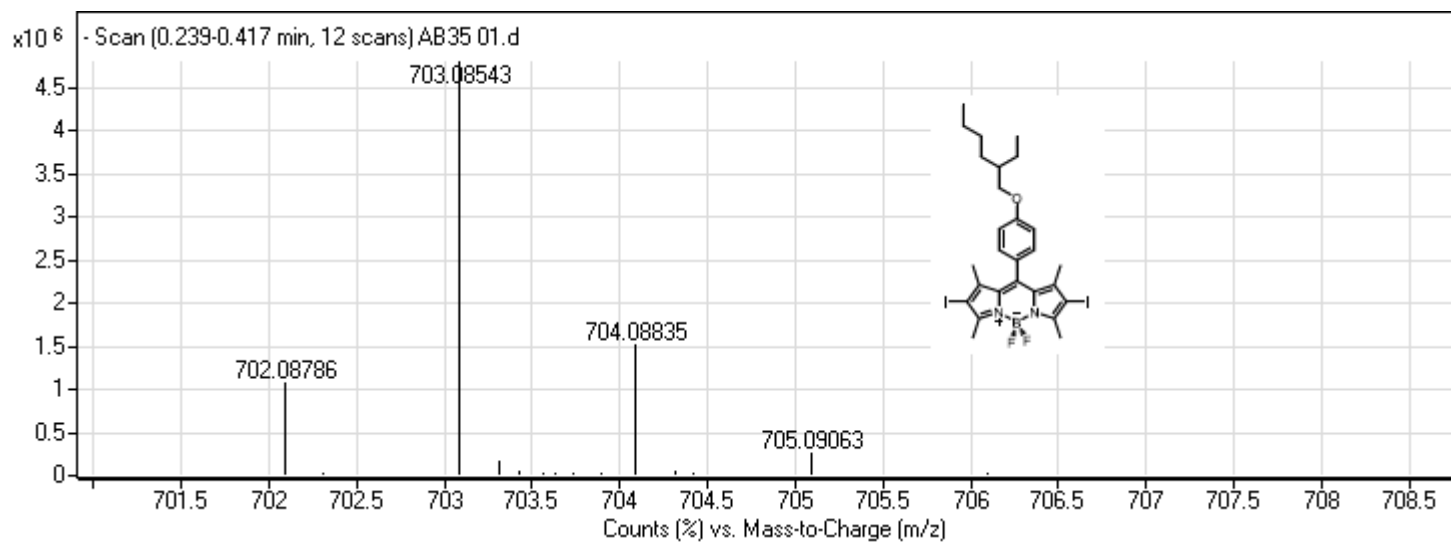


Figure 90. Mass Spectrum of Compound 13

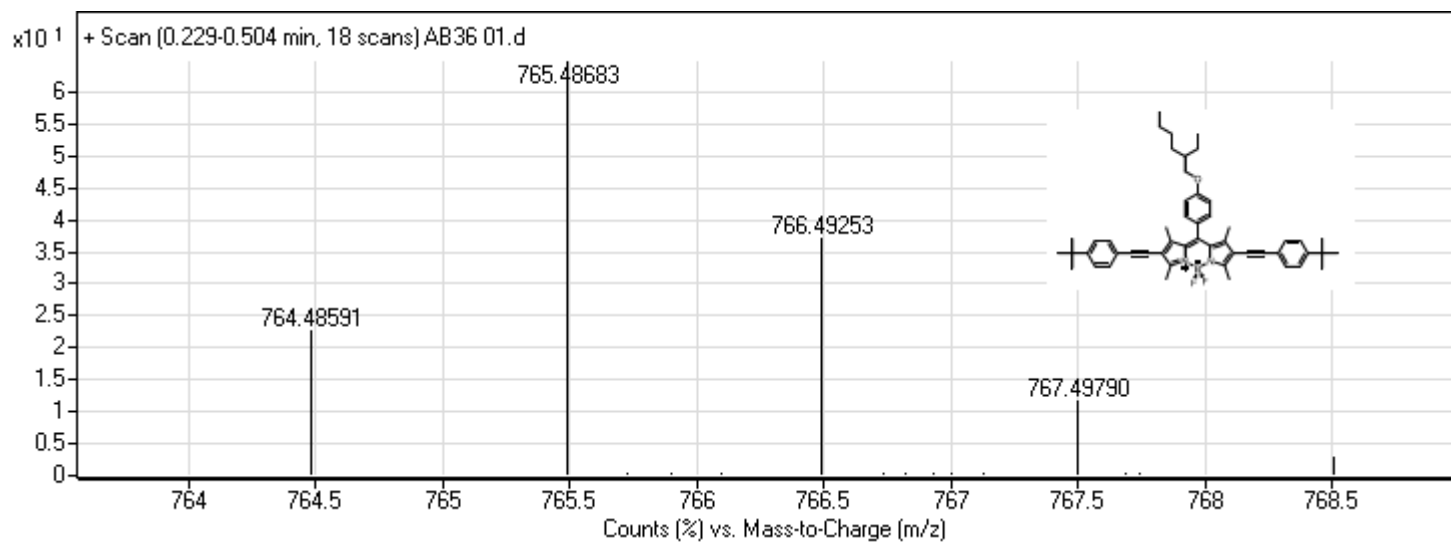


Figure 91. Mass Spectrum of Compound 14

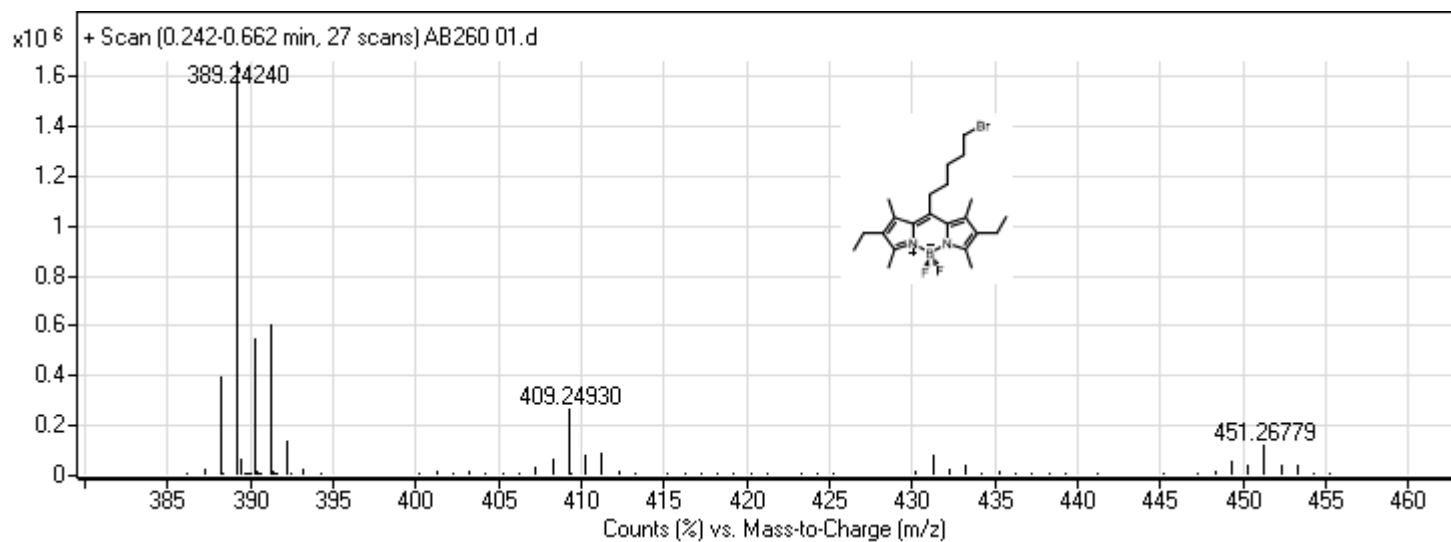


Figure 92. Mass Spectrum of Compound 25

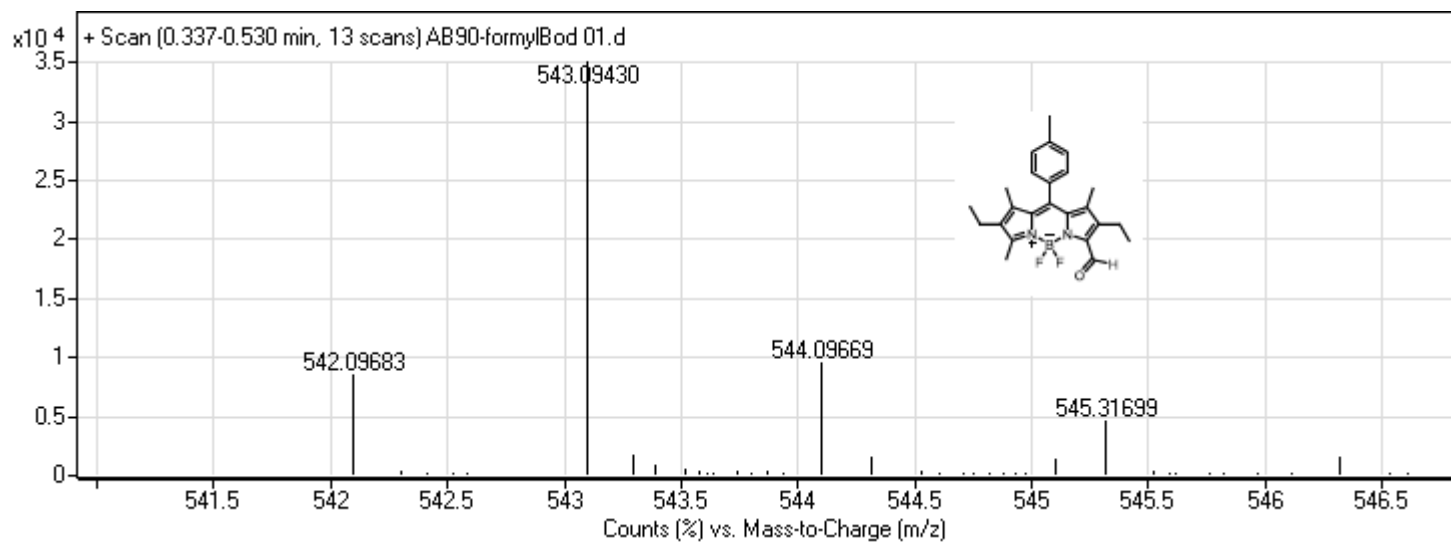


Figure 93. Mass Spectrum of Compound 31