การสังเคราะห์และสมบัติเชิงแสงของเอซา-โบดิพีที่มีหมู่แทนที่เป็นอนุพันธ์ไทโอฟีน

นางสาวพรพนา เทพวงษ์

วิทยานิพนธ์นี้เป็นส่วนหนึ่งของการศึกษาตามหลักสูตรปริญญาวิทยาศาสตรมหาบัณฑิต
สาขาวิชาเคมี ภาควิชาเคมี
คณะวิทยาศาสตร์ จุฬาลงกรณ์มหาวิทยาลัย
ปีการศึกษา 2558

SYNTHESIS AND OPTICAL PROPERTIES OF AZA-BODIPY SUBSTITUTED BY THIOPHENE DERIVATIVES

Miss Pornpana Tepwong

A Thesis Submitted in Partial Fulfillment of the Requirements
for the Degree of Master of Science Program in Chemistry
Department of Chemistry
Faculty of Science
Chulalongkorn University
Academic Year 2015

Thesis Title	SYNTHESIS AND OPTICAL PROPERTIES OF AZA-BODIPY SUBSTITUTED BY THIOPHENE DERIVATIVES
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พรพนา เทพวงษ์ : การสังเคราะห์และสมบัติเชิงแสงของเอซา-โบดิพีที่มีหมู่แทนที่เป็นอนุพันธ์ไทโอฟีน (SYNTHESIS AND OPTICAL PROPERTIES OF AZA-BODIPY SUBSTITUTED BY THIOPHENE DERIVATIVES) อ.ที่ปรึกษาวิทยานิพนธ์หลัก: ผศ. ดร. วรวรรณ พันธุมนาวิน, อ.ที่ปรึกษาวิทยานิพนธ์ร่วม: ผศ. ดร.ยงศักดิ์ ศรีธนาอนันต์, 94 หน้า.

การสังเคราะห์อนุพันธ์ไทอีนิล เอซา-โบดิพีชนิดใหม่สามารถทำได้ผ่านการควบแน่นไปเป็นโครงสร้างไดพิโรมีทีน ซึ่งได้ดำเนินการใน 4 ขั้นตอนคือ ปฏิกิริยาแทนที่ด้วยหมู่เอซิลแบบฟรีเดล-คราฟส์, ปฏิกิริยาการเติมของไมเคิล, ปฏิกิริยาการควบแน่นเป็นไดพิโรมีทีน และปฏิกิริยาการเกิดสารประกอบเชิงซ้อนกับโบรอนไตรฟลูออไรด์ไดเอทิลอีเทอเรท สารไทอีนิลฟีนิลเอซา-โบดิพี (TPAB) สามารถสังเคราะห์ได้จาก 4 ขั้นตอนนี้ในปริมาณ 5 เปอร์เซ็นต์รวมทุกขั้นตอน อนุพันธ์ 1,7-เฮกซิลอกซีฟีนิล ในกลุ่มของไทอีนิล แอลคอกซีฟีนิล เอซา-โบดิพี (TAAB) สามารถสังเคราะห์ได้ในปริมาณ 0.8 เปอร์เซ็นต์จากทุกขั้นตอน และ 1,7-ฟีนิล-3,5-(3’,4’-เอทิลีนไดออกซี-2’-ไทอีนิล) โบดีพี (EPB) สามารถสังเคราะห์ได้แทนอนุพันธ์ของเอซา-โบดิพีที่ต้องการในปริมาณ 0.4 เปอร์เซ็นต์ การพิสูจน์เอกลักษณ์ของสาร TAAB และ EPB โดยใช้เทคนิคทางยูวี-วิสิเบิลสเปกโตรสโกปี และ ฟลูออเรสเซนต์สเปกโตรสโกปีแสดงให้เห็นว่าอนุพันธ์เอซา-โบดิพีชนิดใหม่ที่สังเคราะห์ได้มีช่วงการดูดกลืนและการคายแสงที่ความยาวคลื่นที่เพิ่มขึ้น เมื่อเทียบกับสารต้นแบบ ซึ่งสนับสนุนสมมติฐานที่ว่า หมู่แอลคอกซีบนวงฟีนิลที่ตำแหน่งที่ 1,7 และหมู่ 3’,4’-เอทีลีนไดออกซีไทโอฟีนที่ตำแหน่งที่ 3,5 ของโครงหลักเอซา-โบดิพีมีผลทำให้เกิดการลดช่องว่างระหว่างระดับพลังงานโฮโม (HOMO) และ ลูโม (LUMO) โดยเพิ่มความเป็นระนาบและการเคลื่อนที่ของอิเล็กตรอนของระบบพายคอนจูเกต

ภาควิชา เคมี ลายมือชื่อนิสิต .....

สาขาวิชา เคมี ลายมือชื่อ อ.ที่ปรึกษาหลัก .....

ปีการศึกษา 2558 ลายมือชื่อ อ.ที่ปรึกษาร่วม .....

5672030623 : MAJOR CHEMISTRY
KEYWORDS: THIOPHENE / EDOT / AZA-BODIPY / BATHOCHROMIC SHIFT

PORNPANA TEPWONG: SYNTHESIS AND OPTICAL PROPERTIES OF AZA-BODIPY SUBSTITUTED BY THIOPHENE DERIVATIVES. ADVISOR: ASST. PROF. WORAWAN BHANTHUMNAVIN, Ph.D., CO-ADVISOR: ASST. PROF. YONGSAK SRITANA-ANANT, Ph.D., 94 pp.

Novel thienyl aza-BODIPY derivatives were successfully synthesized by means of aza-dipyrromethene core condensations. The syntheses were carried out via 4 steps: Friedel-Crafts acylation, Michael addition, condensation to yield aza-dipyrromethene, which was then complexed with boron trifluoride etherate. The thienyl phenyl aza-BODIPY (TPAB) parent was obtained from the 4-step procedure as black blue solid in 5 % overall yield. The novel 1,7-hexyloxy phenyl derivative of thienyl alkoxyphenyl aza-BODIPY (TAAB) was obtained in 0.8 %yield overall. The 1,7-phenyl-3,5-(3',4'-ethylenedioxy-2'-thienyl)-BODIPY (EDOT-phenyl BODIPY, EPB) was obtained instead of the desired aza-BODIPY analog in 0.4 yield overall. The characterizations of TAAB and EPB by UV-Vis spectra and Fluorescent spectra exhibited the relative bathochromic shift of absorption maxima and emission maxima compared to the corresponding thienyl phenyl parents. This shift supported the hypothesis that the presence of alkoxy groups on the phenyl rings at 1,7-positions and conjugated 3,4-ethylenedioxythiophene (EDOT) at 3,5-positions could decreases the HOMO–LUMO gap, which is attributed to an enhancement of the planarity and electron mobility of the **π**-conjugated system.

Department:	Chemistry	Student's Signature	.....
Field of Study:	Chemistry	Advisor's Signature	.....
Academic Year:	2015	Co-Advisor's Signature	.....

ACKNOWLEDGEMENTS

My utmost gratitude goes to my thesis advisor, Assist. Prof. Dr.Worawan Bhanthumnavin and co-advisor, Assist. Prof. Dr.Yongsak Sritana-anant, for their expertise, kindness, support, opportunity and most of all, for their patience during the course of research including completing this thesis.

I am sincerely grateful to the members of the thesis committee, Assoc. Prof. Dr.Vudhichai Parasuk, Assist. Prof. Dr. Anawat Ajavakom and Assoc. Prof. Dr.Siritron Samosorn for their valuable comments and suggestions.

I gratefully acknowledge the members of the YS and WB research group, Mahamakut building for their companionship and friendship.

Finally, I would like to take this opportunity to express my sincere appreciation and thanks to my parents and Chulalongkorn University.

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LIST OF ABBREVIATIONS

^{13}C NMR	: carbon-13 nuclear magnetic resonance spectroscopy
^{1}H NMR	: proton nuclear magnetic resonance spectroscopy
anh.	: anhydrous
$BF_3{\cdot}OEt_2$	: borontrifluoride etherate
CCA	: **α**-cyano-4-hydroxycinnamic acid
CH_2Cl_2	: dichloromethane
cm^{-1}	: unit of wavenumber (IR)
DIPEA	: *N*,*N*-diisopropylethylamine
d	: doublet (NMR)
dd	: double of doublet (NMR)
ddd	: double of double of doublets
equiv or eq	: equivalent
EtOAc	: ethyl acetate
EtOH	: ethanol
g	: gram
h	: hour
HCl	: hydrochloric acid
Hz	: hertz
HOMO	: highest occupied molecular orbital
IR	: infrared spectroscopy
J	: coupling constant
LUMO	: lowest unoccupied molecular orbital
m	: multiplet (NMR)
MeOH	: methanol
min	: minute
mg	: milligram
MHz	: megahertz

mL	: milliliter
mol	: mole
mmol	: millimole
m.p.	: melting point
m/z	: mass per charge ratio
M	: molar
MS	: mass spectrometry
NaOH	: sodium hydroxide
ppm	: parts per million (unit of chemical shift)
qd	: quadruple of doublet (NMR)
rt	: room temperature
s	: singlet (NMR)
sat.	: saturated
st	: stretching vibration (IR)
t	: triplet (NMR)
TLC	: thin layer chromatography
UV-Vis	: ultra-violet and visible spectroscopy
v	: volume (mL)
^{o}C	: degree celsius
δ	: chemical shift
λ_{max}	: maximum wavelength
π	: pi

CHAPTER I

INTRODUCTION

1.1 Borondipyrromethene (BODIPY)

BODIPY is an important compound which has been widesly used in numerous fields such as biological science [1-3], modern medicine [4], and physical sciences [5-8]. BODIPY was discovered in 1968 by Triebs and Kreuzer who noticed that the acylation of 2,4-dimethylpyrrole was acid catalyzed. Subsequent condensation with acetic anhydride save the first precursor. Complexing by boron trifluoride, resulted in the formation of a highly fluorescent compound. (**Figure 1.1**) [9]

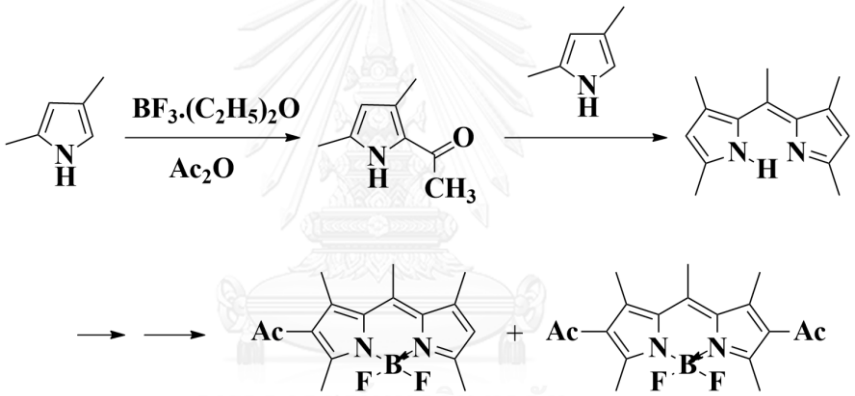


Figure 1.1 The first synthesis of boron dipyrrin dye

However, many researchers' interests in the BODIPY dyes and their potential applications in biological labeling started to appear in the 1980s, in which BODIPY labeled ligands as highly selective D1 and D2 dopaminergic probes were first synthesized. [10] In recent years, BODIPY derivatives were also studied and found applications in photodynamic systems and polymer or dye sensitized solar cell. [4, 11]

4,4-Difluoro-4-bora-3a,4a-diaza-s-indacene was the IUPAC name of BODIPY and the numbering systems of dipyrromethane and dipyrrin were described in **Figure 1.2**. The terms ***α***-, **β**- and *meso* positions are used in the same way. In all three structures, the central carbon atom between the 2 pyrrole rings is refered to as the meso position

and the positions adjacent to the nitrogen atoms of carbon are called the **α**-positions. [12]

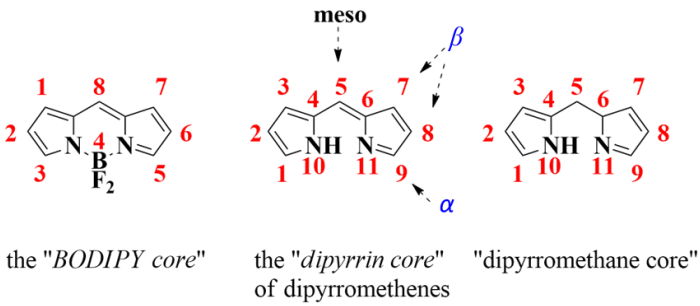


Figure 1.2 IUPAC numbering of BODIPY, dipyrrin, and dipyrromethane cores.

BODIPY dyes have increasingly attracted attention of researchers due to their distinctive properties, such as high photoluminescent quantum yields, sharp emission and absorption bands, large molar absorption coefficients, high environmental stability, and high solubility in many organic solvents. [5] Moreover, their spectroscopic and photophysical properties can be fine-tuned by structural modifications at appropriate positions of dipyrromethene core to extend the **π**-conjugation towards red-shifted or near-IR chromophores. The modifications of BODIPY structures may be divided into 2 cases: substitutions at proper positions with electron withdrawing or electron donating groups, or changing the carbon atom at 8 position (*meso*-) into a nitrogen atom. [13] The substitution of BODIPY dyes at 1,7 positions was not very popular because the dihedral angle effect between hydrogen atom at 8 position with substituents at 1,7 positions leads to decline of emission wavelengths. Connections via 2,6 positions were often carried out *via* cross-coupling reactions for polymer applications. [14] Especially, the 3,5 positions were the most likely place to extend **the π**-conjugated system for biological applications. [15] Furthermore, these positions can easily be functionalized and substituted, which are known to endow BODIPYs with spectral transitions that are significantly red-shifted. For the second strategy, the carbon atom at 8 position (*meso*-) is replaced with nitrogen atom called “aza-BODIPY”, (**Figure 1.3**) which will be described in detail below. [16]

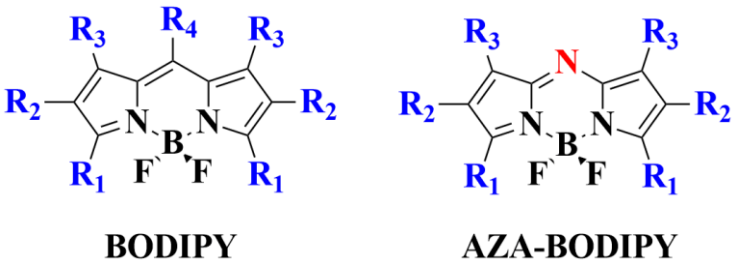


Figure 1.3 Structures of BODIPY and aza-BODIPY

1.2 Aza-BODIPY

At present, more researchers give more attention to photophysical properties and synthesis of aza-BODIPY. It can be seen that publications of aza-BODIPY have followed an upward trend over the recent period as shown in **Figure 1.4**.

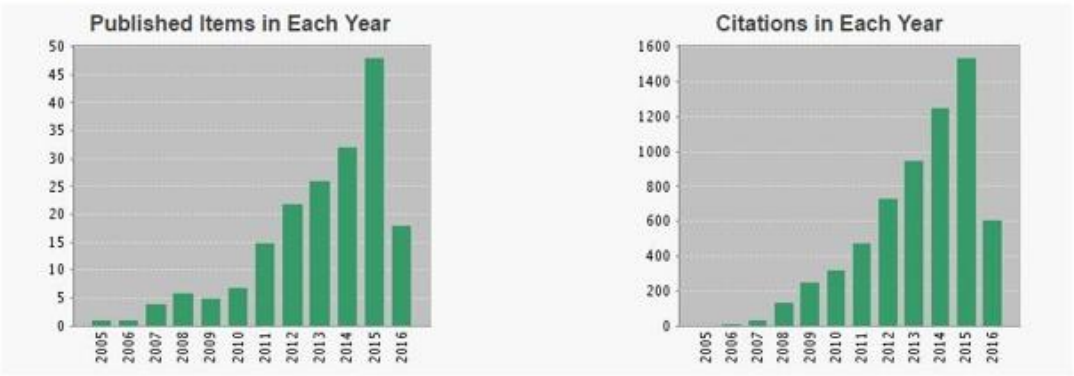


Figure 1.4 Publications and citation reports of aza-BODIPY (until April, 2016)

Aza-dipyrromethene boron difluoride (aza-BODIPY) dyes, or aza-analog of BODIPY, have attracted much attention due to their intense absorption and strong fluorescence at long wavelength region combined with their excellent photostability. Aza-BODIPY show UV absorption about 100 nm longer than those of BODIPY analogs. Their absorptions are mostly in the 600-800 nm region.

Aza-BODIPY has gained much interest among researchers and has created numerous research successes because of several advantages such as: high

photoluminescent quantum yields, strong absorption and emission in the near-IR (NIR) rigion, decrease HOMO-LUMO gap, narrow and sharp absorption and emission band and large molar absorption coefficient. [17, 18]

The high photophysical properties has led to many useful products for many applications such as: biomedical imaging, sensing of cations and anions, fluorescent tags for DNA sequencing, absorbing dyes, sensitizer for singlet O_2 generation,. photosensitizer in photodyanamic therapy (PDT agent), fluorescent probe, fluorescent sensor for polymer characterization, NIR-emitting chemosensors for heavy metal detection, photovoltaics, solar cell, and organic light-emitting devices.

There has been increased interests in the synthesis and optical property tuning of aza-BODIPY dyes to move the spectral bands into the NIR region. This can be modulated through extending conjugation with various substituents. Most of these derivatives are tetraphenyl aza-BODIPYs, having four phenyl groups directly substituted on the 1, 3, 5, and 7 positions of the aza-BODIPY core (**Figure 1.5**). The 3- and 5-substituents of aza-BODIPY are particularly important for their torsional steric between the phenyl rings and the plane of the central chromophore which is one of the important issues for developing longer wavelength aza-BODIPY. The NIR bathochromic shifts observed in these “constrained” molecules can be claimed to the better electron delocalization due to the enhancement of coplanarity of the 3- and 5-phenyl groups with the aza-BODIPY core. [18]

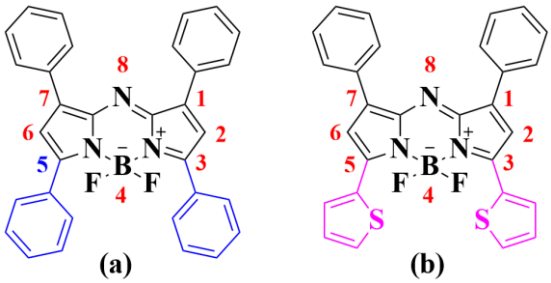


Figure 1.5 Tetraphenyl aza-BODIPY (**a**) and 3,5-dithienyl-1,7-diphenyl aza-BODIPY (**b**)

Zhang and co-worker proposed replacing the common phenyl groups by smaller five-membered rings for decrease of the steric clash between protons of phenyl rings, (**Figure 1.5**) which had achieved significant bathochromic shifts. Accordingly, thiophene was chosen because many materials containing thiophene in the structures often present a wide range of interesting optical properties. In fact, thiophene has been introduced into BODIPY dyes and showed clear red shift in both absorption and emission. [17]

1.3 Thiophene and thiophene derivatives

Thiophene, also commonly called “thiofuran”, is a heterocyclic compound that has many potential uses in various scientific and industrial fields. Thiophene-based materials are used in bioimaging applications and biomolecular diagnostics. [19] It is found that thiophene is the most efficient unit for increasing optical nonlinearity parameters due to the conjugation with different aromatic π-systems. [20-22] These systems illustrated electron donor properties, good stability, long wavelength of absorption and emission and decreased bandgap between HOMO-LUMO. Therefore, thiophene and derivatives are excellent building blocks to be used in the donor-acceptor type structures for design of new fluorophores with efficient photophysical properties for several applications.

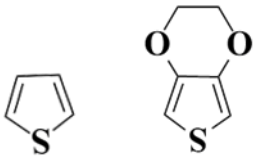
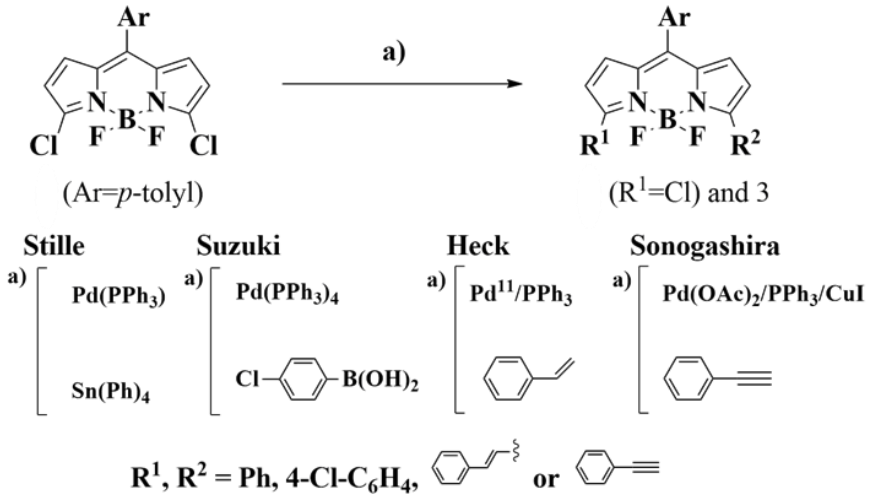


Figure 1.6 Thiophene and 3,4-ethylenedioxythiophene (EDOT)

3,4-Ethylenedioxythiophene (EDOT) (**Figure 1.6**) is a derivative of thiophene with strong electron-donor properties. Roquet and co-worker demonstrated that self-rigidification makes EDOT a particularly interesting building block for the molecular engineering of various classes of π-conjugated system such as push-pull chromophores, π-conjugated fluorophores, conjugated oligomers and small band gap and functional electrogenerated conjugated polymers.

1.4 Literature reviews

In 2006, Rohand *et al*. reported the synthesis of BODIPYs functionalized at the 3-, 5-positions with one or two aryl, ethenylaryl, and ethynylaryl moieties by palladium–catalyzed coupling reactions of the 3,5-dichloro BODIPY derivative using the Stille, Suzuki, Heck and Sonogashira reactions. [15] The reaction yielded products under mild conditions. Asymmetrical monosubstituted and symmetrical disubstituted products could be successfully prepared as shown in **Scheme 1.1**. The UV-Vis absorption and fluorescence data of such novel fluorophores indicated that the extended conjugation shifted their excitation and emission maxima to longer wavelengths than comparable alkyl-substituted materials and led to extremely bright fluorescent dyes.



Scheme 1.1 Palladium-catalyzed coupling reactions of BODIPY derivatives

The replacement of the chlorine atoms by aryl, ethenylaryl, and ethynylaryl residues yields dyes with absorption (excitation) maxima ranging from green to red and emission maxima stretching to the near-infrared spectral region with very high (nearly 1.0) fluorescence quantum yields.

Poirel and co-worker successfully synthesized the unsymmetrical 3,5-dioligothienyl-BODIPY derivatives and studied optical and redox properties of novel compounds (**Figure1.7**). [13] The key step is the monobromination of the 2,6-dimethyl-3,5-dithienyl-BODIPY at the α positions of the thiophene moiety. The additional thiophene modules are attached by Pd-catalyzed cross-coupling reactions. Increasing the number of modules on each side of the BODIPY core shifts the absorption to 677 nm and the emission to 769 nm.

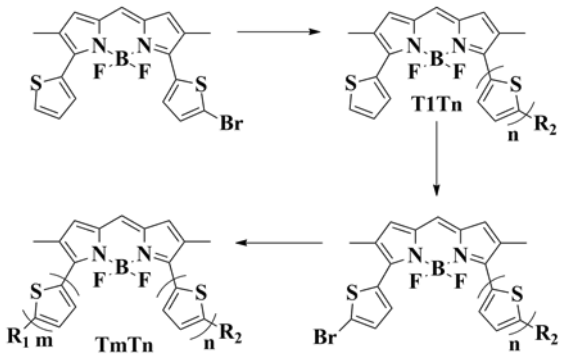


Figure 1.7 The synthesis of unsymmetrical 3,5-dioligothienyl-BODIPY

Zhang and co-worker accomplished the synthesis of 1,3,5,7-tetraphenyl aza-BODIPY, replacing the phenyl rings with thiophene which achieved significant bathochromic shifts (**Figure 1.8**). [17] They found that one of the target molecules, DDTAB, emitted strong NIR fluorescence and could be a very competitive NIR fluorophore.

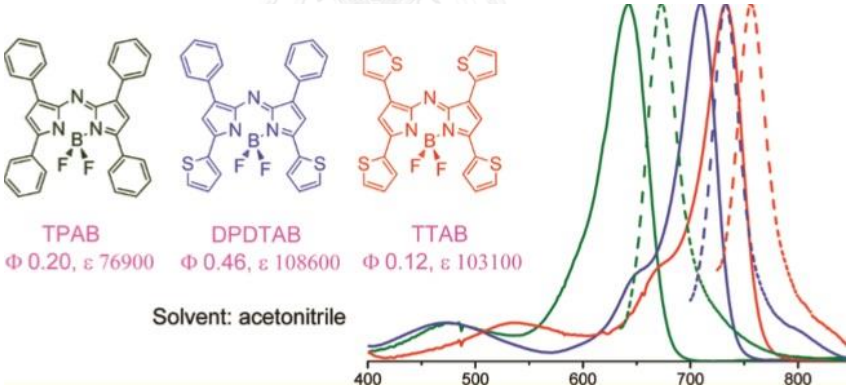


Figure 1.8 Synthesis of thienyl aza-BODIPY

In 2011, Gresser *et al*. reported the synthesis of a series of novel thiophene-substituted aza-BODIPY dyes by a general procedure and complemented by a Stille-coupling of a brominated species with 2-tributylstannylthiophene. [16] They investigated the optical as well as the electrochemical properties of the compounds and compared the results to those density functional theory (DFT) calculations. The influence of the thiophene substituents was discussed in term of dependence of the position at the aza-BODIPY core regarding the HOMO and LUMO frontier orbitals.

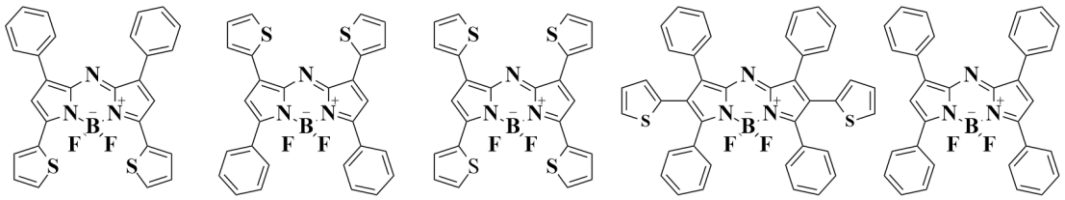


Figure 1.9 Thiophene-substituted aza-BODIPYs

It was found that the absorption maxima of the aza-BODIPY compounds prepared could be shifted into the red spectral region by replacing phenyl with thiophene moieties. This effect can be attributed to an increase of the HOMO energies while the LUMO energies remain nearly constant, resulting in an overall reduced gap. Moreover, analysis of the frontier orbitals revealed that the contribution to the HOMO coefficients and energies, influenced by the thiophene substituents, is stonger than on the LUMO energies. (**Figure 1.10**) The largest effect was found for the thiophene substituted at all 1,3,5,7 positions of the substituted aza-BODIPY.

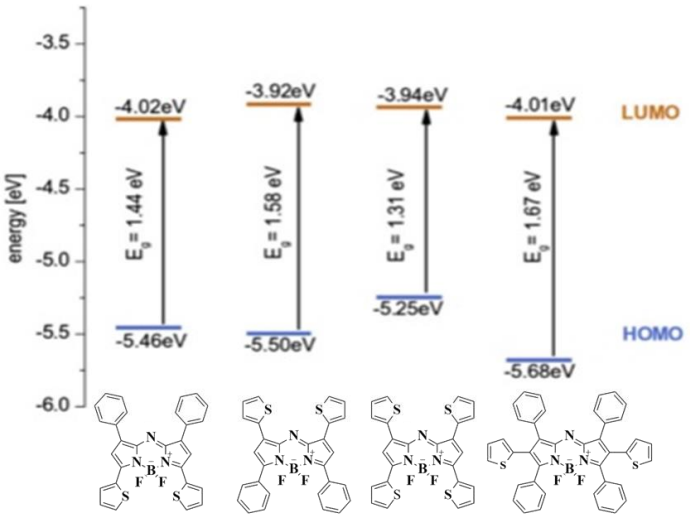


Figure 1.10 HOMO and LUMO energy values for the aza-BODIPY derivatives

Dai *et al*. reported the facile synthetic method to produce soluble 3,4-ethylenedioxythiohene (EDOT) oligomer by using iron(III) nitrate as the oxidizing agent. [23] Two EDOT oligomers such as octamers and octadecamers were obtained as the

major products. The results of UV-Vis absorption and fluorescence are shown in **Figure 1.11**. The UV-Vis absorption spectra of the EDOT oligomers have one prominent band in the visible region that can be attributed to the π,π^* transition, which made the absorption band maximum red-shift from 460 nm (for octamer) to 530 nm (for octadecamer). The decreased HOMO-LUMO band gap was because the conjugation length of the oligomer increases.

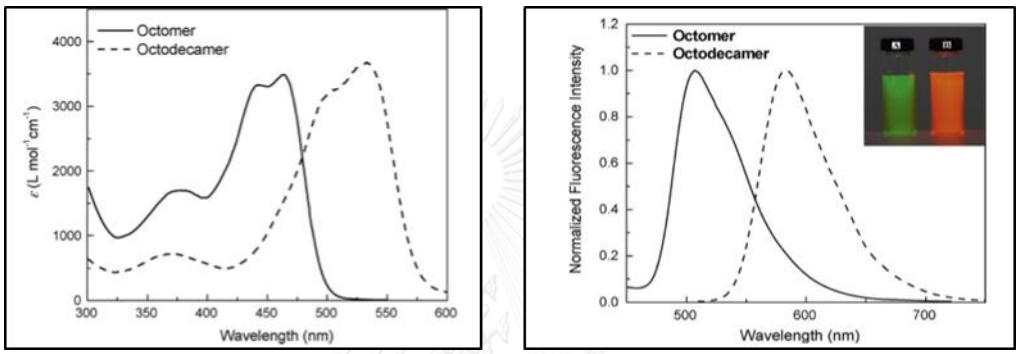


Figure 1.11 UV-Vis absorption spectra and normalized fluorescence spectra for EDOT octamer and octadecamer in dichloromethane

1.5 Objectives

In this research, we designed and attempted to synthesize three thienyl aza-BODIPY derivatives: **TPAB**(**4**), **TAAB**(**17**) and **EPAB**(**10**), (**Figure 1.12**) and studied photophysical properties of three compounds. The electron rich EDOT at 3,5-positions and higher electron donating ability of the alkoxyphenyl groups at 1,7-positions were expected to help decrease the HOMO-LUMO gap of the aza-BODIPY core and hence move the optical properties bathochromically towards near IR region.

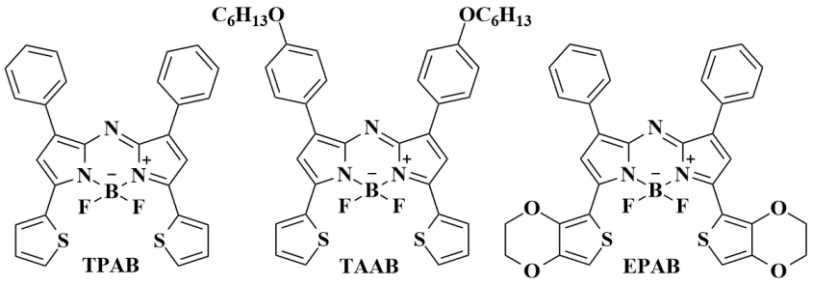


Figure 1.12 Structures of **TPAB**, **TAAB** and **EPAB**

CHAPTER II

EXPERIMENT

2.1 Chemicals

Thin layer chromatography (TLC) was performed on aluminium sheets precoated with silica gel (Merck Kieselgel 60 F254) (Merck KgaA, Darmstadt, Germany). Column chromatography was performed using silica gel 0.06-0.2 mm or 70-230 mesh ASTM (Merck Kieselgel 60 G, Merck KgaA, Darmstadt, Germany) and silica gel 0.04-0.06 mm or 230-400 mesh ASTM (Merck Kieselgel 60 G, Merck KgaA, Darmstadt, Germany). Analytical grade solvents were used in the synthesis. Solvents used in column chromatography were distilled from commercial grade prior to use. Other reagents were purchased as AR grade from the following venders:

- RCI Labscan (Bangkok, Thailand): chloroform ($CHCl_3$), ammomium acetate (NH_4OAc)
- Carlo Erba (Milan, Italy): potassium carbonate (K_2CO_3), dichloromethane (CH_2Cl_2), sodium chloride (NaCl), pyridine (C_5H_5N)
- Fluka Chemical (Buchs, Switzerland): *tert*-butyl alcohol ($C_4H_{10}O$), ammonium trifluoroacetate ($CF_3CO_2NH_4$), oxalyl chloride ($C_2O_2Cl_2$)
- Merck Co. (Darmstadt, Germany): ethanol absolute (C_2H_5OH), sodium hydroxide (NaOH), concentrated hydrochloric acid, methanol (MeOH), diethylether $(C_2H_5)_2O$, sodium sulfate (Na_2SO_4)
- Cambridge Isotope Laboratories, (USA): deuterated chloroform ($CDCl_3$), deuterated acetone (acetone-d_6)
- Sigma-Aldrich (USA): thiophene (C_4H_4S), Aluminium chloride anhydrous ($AlCl_3$), nitromethane (CH_3NO_2), ammonium chloride (NH_4Cl), 3,4-ethylenedioxythiophene ($C_6H_6O_2S$), cinnamoyl chloride (C_9H_8Cl), 4-(hexyloxy)benzaldehyde ($C_{13}H_{18}O_2$),
- Panreac (Spain): anhydrous magnesium sulfate ($MgSO_4$)

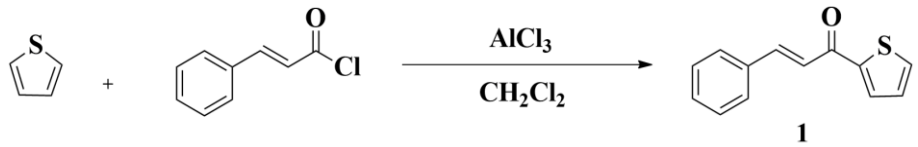
- Acros organic (USA): *N*,*N*-Diisopropylethylamine ($C_8H_{19}N$), Boron trifluoride etherate (BF_3•OEt_2)
- HiMedia Laboratories Pvt. Ltd. (India): malonic acid ($C_3H_4O_4$), AR grade

2.2 Instruments and equipments

Melting points were determined with a Stuart Scientific Melting Point SMP1 (Bibby Sterlin Ltd., Staffordshire, UK). The ^{1}H NMR spectra were recorded on a Varian Mercury NMR spectrometer operated at 400.00 MHz. ^{13}C NMR spectra were recorded on a Bruker NMR spectrometer operated at 100.00 MHz for ^{13}C nuclei (Varian Company, USA). IR spectra were recorded on a Nicolet 6700 FT-IR RXI spectrometer (Perkin Elmer Instruments, USA). Mass spectra were recorded on Waters Micromass Quatto micro API ESCi Spectrometer (Waters, USA) and MALDI-TOF-MS (Bruker DALTONICS Microflexs, USA). The UV-Vis absorption spectra were recorded on UV-VISIBLE Spectrophotometer: UV-2550 (Shimadzu Corporation, Kyoto, Japan). Fluorescence emission spectra were obtained from a Varian Cary Eclipse spectrofluorometer (Varian, USA).

2.3. Thienyl aza-BODIPY (TPAB) synthesis

2.3.1 Synthesis of thienyl-3-phenylprop-2-en-1-one (1)



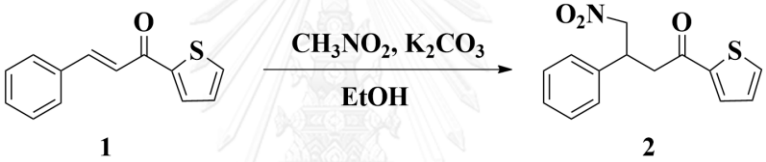
1

Friedel-Crafts acylation of thiophene was carried out as follow: Aluminium chloride (1.345 g, 10 mmol) was suspended in CH_2Cl_2 (8 mL) at 0 °C under N_2 atmosphere. Cinnamoyl chloride (1.689 g, 10 mmol) was added dropwise in 10 min. The stirred orange suspension was added thiophene (0.4 mL, 5 mmol) and stirred for 1 h. About 20 mL of H_2O was carefully added and the organic layer was washed with saturated NaOH (100%), 2 M NaOH, and saturated NaCl, dried

over Na_2SO_4 anhydrous and concentrated in vacuo to give the crude product as a yellow solid. Purification by column chromatography on silica gel using 20:80 mixture of EtOAc and hexane as the eluent yielded the product as a pale yellow solid (0.667 g, 65%). m.p.= 92-95 °C (lit. m.p.= 90 °C) [24]

^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.90 (d, *J*=2.7 Hz, 1H), 7.80 (d, *J*=11.9 Hz, 1H), 7.70 (d, *J*=2.7 Hz, 1H), 7.66 (m, 2H) 7.46 (d, *J*=7.5 Hz 1H), 7.45 (t, *J*=2.7 Hz, 1H), 7.43 (m, 2H), 7.21 (dd, *J*=4.9, 3.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 182.0, 145.6, 144.1, 134.8, 133.8, 131.8, 130.6, 129.0, 128.2, 121.7; ESI-MS (EtOAc) m/z: $[M+H]^+$= 215.12.

2.3.2 Synthesis of thienyl-4-nitro-3-phenylbutan-1-one (2)



1 2

Michael addition, Method 1 [16]:

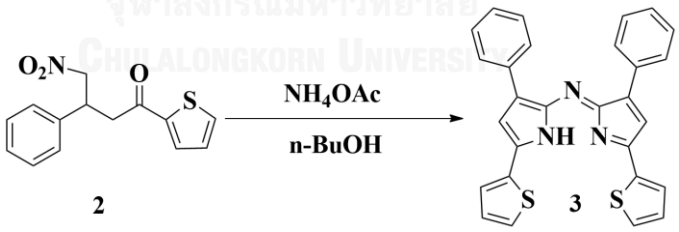
Compound **1** (0.650 g, 3 mmol), nitromethane (0.8 mL, 15 mmol) and potassium carbonate (0.8 mg, $6x10^{-3}$ mmol) were dissolved in ethanol (7 mL) and heated to reflux for 7 h. After cooling to rt, the solvent was removed in vacuo to yield a pale orange oil. It was redissolved in ethyl acetate and washed with water (3x20 mL). The organic layer was washed with sat. NaCl, dried over anh. Na_2SO_4 and concentrated in vacuum. The resulted orange-brown oil product was purified by column chromatography on silica gel using 20:80 mixture of EtOAc and hexane as the eluent to afford the product as pale orange oil (0.735 g, 88%).

Michael addition, Method 2:

Compound **1** (0.678 g, 3 mmol), nitromethane (0.8 mL, 15 mmol) and potassium carbonate (0.8 mg, $6x10^{-3}$ mmol) were dissolved in ethanol (5 mL) and heated under microwave at 120 °C for 30 min. After cooling to rt, the solvent was removed in vacuo to yield a pale orange oil. It was redissolved in ethyl acetate and washed with water (3x20 mL). The organic layer was washed with sat. NaCl, dried over anh. Na_2SO_4 and concentrated in vacuum. The resulted orange-brown oil product was purified by column chromatography on silica gel using 20:80 mixture of EtOAc and hexane as the eluent to afford the product as pale orange oil (0.56 g, 65%).

^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.57 (d, *J*=3.8 Hz, 1H), 7.45 (d, *J*=3.8 Hz, 1H), 7.20 (m, 1H), 7.15 (m, 2H), 7.11 (m, 2H), 6.98 (m, 1H), 4.63 (ddd, *J*=12.5, 12,6, 7.4 Hz, 2H), 4.08 (m, 1H), 3.25 (qd, *J*=11.6, 11.4, 7.7, 7.0 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 189.8, 143.6, 139.0, 134.3, 132.4, 129.1, 128.4, 127.9, 127.5, 79.5, 42.2, 39.6; ESI-MS (EtOAc) m/z: $[M+H]^+$= 276.04.

2.3.3 Synthesis of thienyl aza-dipyrromethene (3)



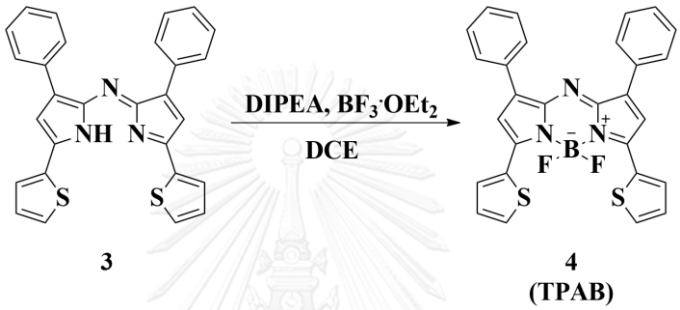
2 3

A solution of compound **2** (0.2753 g, 1 mmol) and ammonium acetate (1.54 g, 20 mmol) in *n*-butyl alcohol 4 mL was heated under microwave at 140 °C for 60 min. After cooling to rt, water was added to the reaction mixture, and then extracted with dichloromethane. The combined organic layers were washed with water and brine, dried with Na_2SO_4 anhydrous, and concentrated to give a dark blue solid. This crude mixture was purified by two steps column chromatography using 40:60

dichloromethane and then hexane and 20:80 EtOAc:hexane as the eluents to obtain the desired product as a black blue solid (0.021 g, 5.8 %). [25]

^{1}H NMR (400 MHz, acetone-d_6) **δ** (ppm): 8.48 (s, 1H), 7.55 (d, *J*=7.8 Hz, 4H), 7.35 (t, *J*= 7.6 Hz, 4H), 7.23-7.06 (m, 6H), 7.03 (d, *J*=3.7 Hz, 2H), 6.71 (s, 2H).

2.3.4 Synthesis of thienyl aza-BODIPY (4, TPAB)



Method 1

To a solution of compound **3** (0.099 g, 0.21 mmol) in dichloroethane (5 mL), *N,N*-diisopropylethylamine (DIPEA, 1.0 mL, 5.74 mmol, 29 eq) and $BF_3{\cdot}OEt_2$ (1.8 mL, 14.3 mmol, 68 eq) were added under nitrogen and stirred for 10 h. To the reaction mixture was added 10 mL of MeOH, and then this mixture was concentrated in vacuo. The crude product was purified by column chromatography on silica gel using 20:80 CH_2Cl_2 and hexane as the eluent to provide a black blue solid (0.05 g, 50%). [16]

Method 2

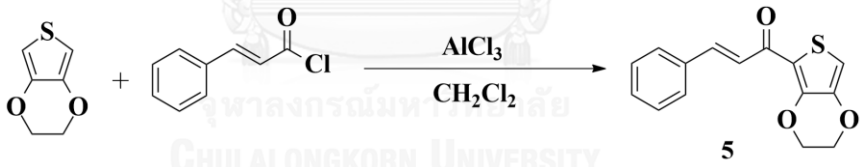
TPAB was prepared using dipyrromethene condensation from section 2.3.3 (compound **2** (0.2753 g, 1 mmol), ammonium acetate (1.54 g, 20 mmol) in *n*-butyl alcohol 4 mL) After cooling to rt, water was added to the reaction mixture, and then extracted with dichloromethane. The combined organic layers were washed with water and brine, dried with Na_2SO_4 anhydrous, and concentrated to give a dark blue solid which used without purification. Then the solution of intermediate (0.099 g, 0.2 mmol)

in dichloroethane (10 mL), *N,N*-diisopropylethylamine (DIPEA, 1 mL, 5.74 mmol, 29 eq) and $BF_3{\cdot}OEt_2$ (1.0 mL, 7.96 mmol, 39.8 eq) were added under nitrogen and stirred for 10 h. To the reaction mixture was added 10 mL of MeOH, and then this mixture was concentrated in vacuo. The crude product was purified by column chromatography on silica gel using 20:80 of CH_2Cl_2 and hexane as the eluent to provide black blue solid (0.045 g, 50%). [16, 25]

^{1}H NMR (400 MHz, acetone-d_6) **δ** (ppm): 8.15 (d, *J*=3.0 Hz, 2H), 7.70 (d, *J*=4.1 Hz, 2H), 7.56 (d, *J*=6.9 Hz, 4H), 7.41 (t, *J*=7.3 Hz, 4H), 7.36 (t, *J*=6.5 Hz, 2H), 7.18 (t, *J*=4.1 Hz, 2H), 7.04 (s, 2H); MALDI-TOF-MS (CCA) m/z: $[M+H]^+$= 507.08; UV-Vis (EtOAc): λ_{max} = 627 nm; Fluorescence (DCM): λ_{max} = 650 nm; IR (ATR, cm^{-1}): 2950 (C-H st), 1728, 1586 (C=C st), 1543 (C=N), 1190 (C-N).

2.4 EDOT phenyl BODIPY (EPB) synthesis

2.4.1 Synthesis of 3′,4′-ethylenedioxy thienyl-3-phenylprop-2-en-1-one (5)



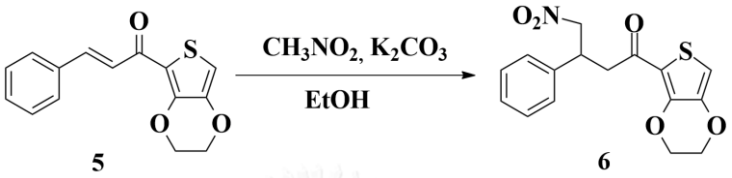
5

The synthesis of compound **5** followed the procedure of Friedel-Crafts acylation in section 2.3.1 (EDOT (0.53 mL, 5 mmol), cinnamoyl chloride (1.33 g, 10 mmol), aluminium chloride (1.67 g, 10 mmol)), except that this reaction mixture was stirred for 3 h to give the crude product as a black-orange solid. Purification by column chromatography on silica gel using 40:60 mixture of EtOAc and hexane as the eluent yielded the product as a pale yellow solid (0.72 g, 53%). m.p. = 120-123 °C. [24]

^{1}H NMR (400 MHz, $CDCl_3$) **δ** (ppm): 7.82 (d, *J*=15.6 Hz, 1H), 7.65 (d, *J*=13.1 Hz, 1H), 7.63 (t, 2H), 7.39 (m, 3H), 6.73 (s, 1H), 4.43 (m, 2H), 4.26 (m, 2H); ^{13}C NMR (100 MHz,

$CDCl_3$) **δ** (ppm): 181.1, 144.4, 143.0, 141.9, 135.3, 128.7, 123.9, 123.7, 109.1, 65.5, 64.0; ESI-MS (EtOAc) m/z: $[M+H]^+$= 273.19.

2.4.2 3′,4′-Ethylenedioxy thienyl-4-nitro-3-phenylbutan-1-one (6)



Method 1:

Compound **6** was prepared using Michael addition procedure from section 2.3.2 method 1 [16] (compound **5** (0.68 g, 2.5 mmol), nitromethane (0.67 mL, 12.5 mmol), potassium carbonate (0.8 mg, $6x10^{-3}$ mmol)), but heated to reflux for 4 h. After cooling to rt, the solvent was removed in vacuum to yield orange oil. It was redissolved in ethyl acetate and washed with water. The organic layer was washed with sat. NaCl, dried over anh. Na_2SO_4 and concentrated under vacuum. The resulted orange-brown oil product was purified by column chromatography on silica gel using 35:65 mixture of EtOAc and hexane as the eluent to afford the product as a yellow solid (0.506 g, 86%).

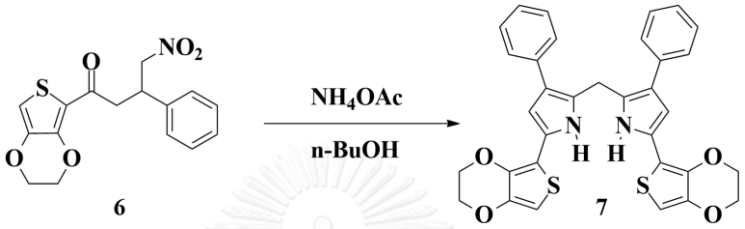
Method 2:

Compound **6** was prepared using Michael addition method 2 from section 2.3.2 (compound **5** (0.68 g, 2.5 mmol), nitromethane (0.67 mL, 12.5 mmol), potassium carbonate (0.8 mg, $6x10^{-3}$ mmol)) to yield brown oil of compound, which was purified by column chromatography on silica gel using 35:65 of EtOAc and hexane as eluent to afford the product as a yellow solid (0.64 g, 77%). m.p. = 121-124 °C.

^{1}H NMR (400 MHz, acetone-d_6) **δ** (ppm): 7.40 (d, *J* =7.3 Hz, 1H), 7.32 (t, *J*=7.5 Hz, 2H), 7.24 (t, *J* =7.3 Hz, 2H), 6.85 (s, 1H), 5.00 (dd, *J* =12.8, 5.8 Hz, 1H), 4.88 (dd, *J* =12.8,

9.6 Hz, 1H), 4.36 (m, 2H), 4.22 (m, 2H), 4.18 (dd, *J* =9.4, 6.5 Hz, 1H), 3.42 (dd, *J* =17.4, 6.6 Hz, 1H), 3.32 (dd, *J* =17.5, 7.5 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) **δ** (ppm): 188.7, 144.9, 141.7, 139.3, 128.9, 127.7, 127.5, 119.5, 109.4, 79.6, 65.5, 63.9, 44.2, 39.5; ESI-MS (EtOAc) m/z: $[M+H]^+$= 334.20**;** IR (ATR, cm^{-1}): 1210 (C-O), 1590 (C=C st), 1650 (C=O)

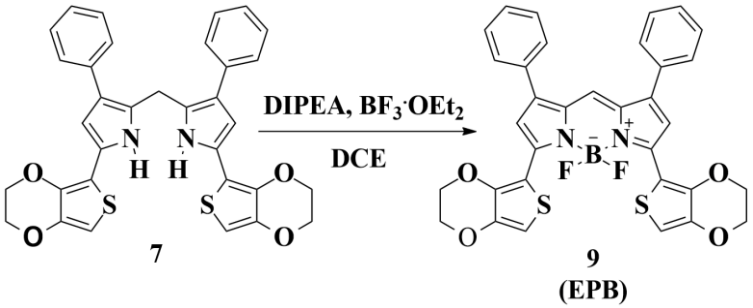
2.4.3 EDOT–dipyrromethene (**7**)



The microwave heating procedure in section 2.3.3 [25] (compound **6** (0.33 g, 1mmol), ammonium acetate (1.54 g, 20 mmol), *n*-butanol 4 mL) was used to make compound **7,** but lengthened to 80 min to give dark red-violet oil. This crude mixture was purified by flash column chromatography using 60:40 dichloromethane and hexane, followed by column chromatography using 40:60 EtOAc and hexane as the eluent to obtain the unintended dipyrromethene product **7** as a pale green solid (0.034 g, 6%).; m.p.=120-123 ℃.

^{1}H NMR (400 MHz, acetone-d_6) **δ** (ppm): 10.28 (s, 1H), 7.58 (d, *J* =7.8 Hz, 4H), 7.31 (t, *J* =7.8 Hz, 4H), 7.23 (m, 2H), 7.13 (t, *J* =7.4 Hz, 2H), 6.66 (s, 2H), 6.27 (s, 1H), 4.34 (m, 4H), 4.27 (m, 4H); ^{13}C NMR (100 MHz, acetone-d_6) **δ** (ppm): 143.0, 137.3, 136.9, 129.7, 129.4, 129.1, 127.0, 126.3, 126.0, 125.9, 125.6, 116.0, 115.9, 111.2, 65.8, 65.5; MALDI-TOF-MS (CCA) m/z: $[M+H]^+$= 578.36; UV-Vis (EtOAc): λ_{max} = 289 nm.

2.4.4 EDOT-BODIPY (9, EPB)

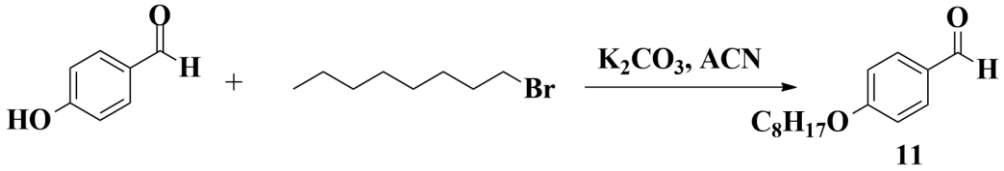


To a solution of compound **7** (0.21 g, 0.36 mmol) in dichloroethane (5 mL), *N,N*-diisopropylethylamine (DIPEA, 1.0 mL, 5.74 mmol, 15.9 eq) and $BF_3{\cdot}OEt_2$ (1.0 mL, 7.96 mmol, 22 eq) were added under nitrogen and stirred at 40 ºC in oil bath for 23 h. The reaction mixture was added 10 mL of MeOH, and then this mixture was concentrated in vacuo. The crude product was purified by flash column chromatography on silica gel using CH_2Cl_2 as the eluent to provide a green solid (0.006 g, 26%). [16]

^{1}H NMR (400 MHz, acetone-d_6) δ (ppm): 7.63 (m, 6H), 7.52 (m, 4H), 7.34 (s, 2H), 6.93 (s, 2H), 4.47 (m, 4H), 4.27 (m, 4H); ^{13}C NMR (100 MHz, acetone-d_6) δ (ppm): 143.0, 136.9, 130.6, 130.0, 129.9, 129.7, 129.5, 129.4, 126.5, 125.9, 116.0, 107.1, 103.6, 65.7, 65.5; MALDI-TOF-MS (CCA) m/z: $[M+H]^+$= 623.64; UV-Vis (EtOAc): λ_{max} = 660 nm; Fluorescence (DCM): λ_{max} = 680 nm.

2.5 Alkoxy-thienyl aza-BODIPY (Alkoxy-TPAB)

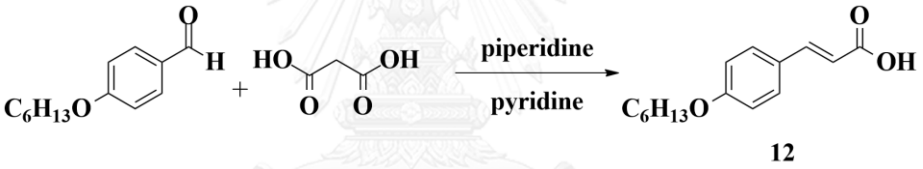
2.5.1 4-Octoxybenzaldehyde (11)



4-Hydroxybenzaldehyde (0.369 g, 3 mmol) was dissolved in acetonitrile 5 mL. Octylbromide (1.10 mL, 6 mmol) and K_2CO_3 (0.637 g, 4.5 mmol) were added under nitrogen and heated to reflux for 8 h. The reaction mixture was added 20 mL of water and then this mixture was extracted with EtOAc (3x20 mL) and concentrated in vacuo. The crude product was purified by column chromatography on silica gel using 20:80 EtOAc and hexane as the eluent to provide a white solid. (0.58 g, 80.8%).

^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 9.86 (s, 1H), 7.82 (d, *J*=8.8 Hz, 2H), 6.98 (d, *J*=8.7 Hz, 2H), 4.02 (t, *J*=6.6 Hz, 2H), 1.78 (m, 2H), 1.43 (m, 2H), 1.31 (m= 8H), 0.88 (t, *J*=6.5 Hz, 3H).

2.5.2 4-Hexyloxycinnamic acid (12)

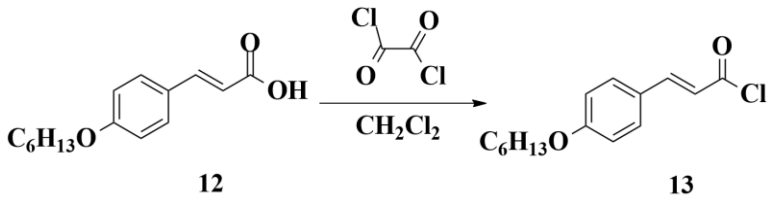


12

A mixture of 4-hexyloxybenzaldehyde (1.0 mL, 5 mmol), malonic acid (1.56 g, 15 mmol), piperidine (0.2 mL, 2 mmol) in 10 mL of pyridine was refluxed for 5.5 h on a sand bath. The reaction mixture was cooled, poured into water and acidified with conc. hydrochloric acid, and extracted with diethyl ether. The organic layer was washed with water and dried with sodium sulfate anhydrous. The solvent was removed on a rotary evaporation, and the residue was recrystallized from hexane-chloroform (5:1) to give the product **12** as white solid (0.70 g, 57%).; m.p.=157-159 °C. [26]

^{1}H NMR (400 MHz, acetone-d_6) δ (ppm): 7.74 (d, *J*=15.9 Hz, 1H), 7.49 (d, *J*=8.70 Hz, 2H), 6.90 (d, *J*=8.70 Hz, 2H), 6.31 (d, *J*=15.9 Hz, 1H), 3.99 (t, *J*=6.5 Hz, 2H), 1.79 (m, 2H) 1.42 (m, 2H), 1.34 (m, 4H), 0.90 (t, *J*=6.9 Hz, 3H); ^{13}C NMR (100 MHz, acetone-d_6) δ (ppm): 189.3 162.4, 147.2, 144.0, 134.8, 132.9, 131.4, 129.3, 128.3, 120.2, 115.8, 114.9, 68.9, 32.3, 26.4, 23.3, 14.3.; MALDI-TOF-MS (m/z): $[M+H]^+$= 247.38; IR (ATR, cm^{-1}): 3328 (OH st), 1700 (C=O st), 2950 (C-H st).

2.5.3 *trans*-4-Hexyloxycinnamoyl chloride (13)

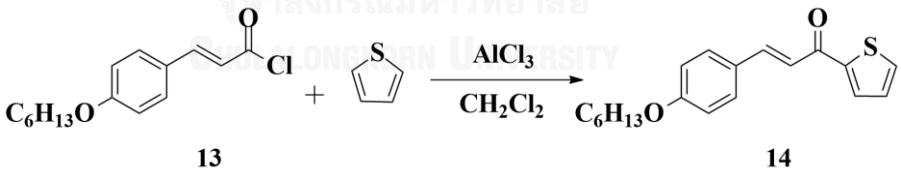


12 13

Compound **12** (0.25 g, 1 mmol) was dissolved in dichloromethane 20 mL and treated with oxalyl chloride (0.1 mL, 1.1 mmol). The reaction mixture was stirred for 15 h at room temperature to afford product **13** as yellow oil (0.2356 g, 87%), which was used directly without further purification. [27]

^{1}H NMR (400 MHz, $CDCl_3$) **δ** (ppm): 7.74 (d, *J*=15.9 Hz, 1H), 7.49 (d, *J*=8.7 Hz, 2H), 6.90 (d, *J*=8.70 Hz, 2H), 6.31 (d, *J*=15.9 Hz, 1H), 3.99 (t, *J*=6.5 Hz, 2H), 1.79 (m, 2H), 1.42 (m, 2H), 1.34 (m, 4H), 0.90 (t, *J*=6.9 Hz, 3H).

2.5.4 Thienyl-3-[4-hexyloxyphenyl]prop-2-en-1-one (14)



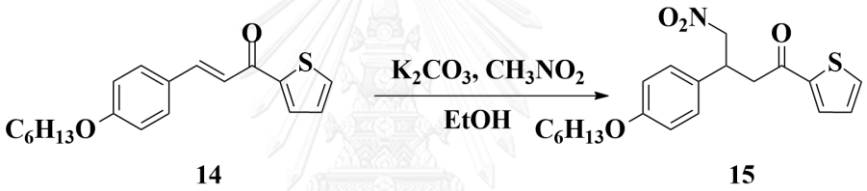
13 14

Compound **13** (0.97 g, 3.5 mmol) and thiophene (2.9 mL, 35 mmol) was dissolved in 15 mL of dichloromethane at 0 °C. Aluminium chloride (1.167 g, 8.75 mmol) was divided into 4 portions and added into the reaction at every hour. The reaction mixture was stirred under N_2 atmosphere for 6 h at 0 °C. About 15 mL of H_2O was added and the organic layer was washed with NaOH (100%), 2 M NaOH, and sat.NaCl, dried over anh. Na_2SO_4 and concentrated under vacuum to give the crude product as a yellow solid. Purification by series of column chromatography on silica gel using sequentially 10:90 mixture of EtOAc and hexane, 50:50 CH_2Cl_2 and hexane,

60:40 CH_2Cl_2 and hexane as the eluents yielded the product as a pale yellow solid (0.70 g, 29%).; m.p. = 103-106 °C. [24]

^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.84 (d, *J*=4.4 Hz, 1H), 7.79 (d, *J*=4.5 Hz, 1H), 7.64 (d, *J*=4.5 Hz, 1H), 7.58 (d, *J*=8.7 Hz, 2H), 7.30 (d, *J*=15.5Hz, 1H), 7.15 (t, *J*=7.9 Hz, 1H), 6.91 (d, *J*=8.7 Hz, 2H), 3.97 (m, 2H), 1.78 (m, 2H), 1.43 (m, 2H), 1.33 (m, 4H), 0.89 (m, 3H).; ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 189.7, 162.4, 147.2, 144.4, 134.8, 132.9, 131.4, 129.3, 128.3, 120.2, 115.8, 68.9, 32.3, 29.1, 26.4, 23.3, 14.3.; MALDI-TOF-MS (m/z): $[M+H]^+$= 313.33.

2.5.5 Thienyl-4-nitro-3-(4-hexyloxy-phenyl)butan-1-one (15)

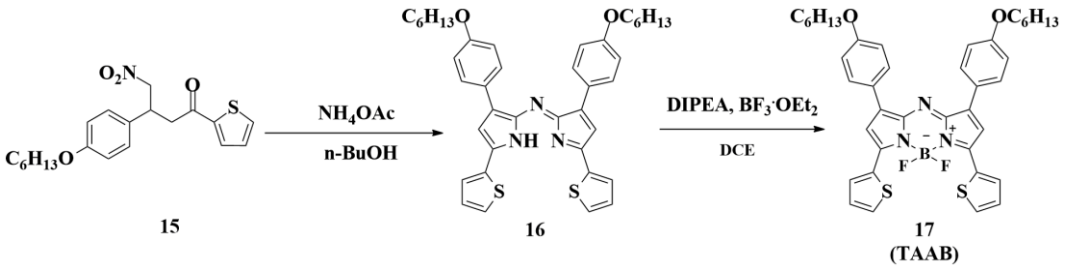


14 15

Compound **15** was prepared using Michael addition procedure from section 2.3.2 method 2 (compound **14** (0.37 g, 2.5 mmol), nitromethane (0.34 mL, 12.5 mmol), potassium carbonate (0.3 mg, $2.25x10^{-3}$ mmol)), to yield a red orange oil. It was redissolved in ethyl acetate and washed with water. The organic layer was washed with sat. NaCl, dried over anh. Na_2SO_4 and concentrated under vacuum. The resulted black orange oil product was purified by column chromatography on silica gel using 20:80 mixture of EtOAc and hexane as the eluent to afford the product as a pale orange solid (0.25 g, 56%).; m.p. = 75-78 °C.

^{1}H NMR (400 MHz, acetone-d_6) δ (ppm): 7.90 (d, *J* =3.5 Hz, 1H), 7.84 (d, *J* =4.8 Hz, 1H), 7.33 (d, *J*=8.4, 2H), 7.19 (t, *J*=4.3 Hz, 1H), 6.88 (d, *J* =8.4 Hz, 2H), 4.91 (ddd, *J* =12.6, 12.5, 7.7 Hz, 2H), 4.17 (m, 1H), 3.94 (t, *J*=6.4 Hz, 2H), 3.50 (ddd, *J*=12.5, 12.4, 7.1 Hz, 2H), 1.75 (m, 2H), 1.46 (m, 2H), 1.35 (m, 4H), 0.92 (t, *J* =6.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 206.4,.191.0, 159.5, 145.0, 135.1, 133.6, 129.7, 129.3, 115.5, 80.7, 68.6, .42.9, 40.0, 32.4, 26.5, 26.5, 23.3, 14.4.

2.5.6 4-(Hexyloxyphenyl)-Aza-BODIPY (17, TAAB)



15 16 17 (TAAB)

Compound **17** was prepared using microwave heating procedure in section 2.3.3. (compound **15** (0.39 g, 1 mmol), ammonium acetate (1.54 g, 20 mmol)) to gave a dark red oil (intermediate **16**) which was used without purification. Then the solution of compound **16** (0.46 g, 0.7 mmol) in dichloroethane (10 mL), *N,N*-diisopropylethylamine (DIPEA, 1 mL, 5.74 mmol, 8.2 eq) and $BF_3{\cdot}OEt_2$ (1.0 mL, 7.9 mmol, 11.3 eq) were added under nitrogen and stirred at rt for 24 h. The reaction mixture was added 10 mL of MeOH, and then this mixture was concentrated in vacuo. The crude product was purified by two steps column chromatography on silica gel using 40:60 of CH_2Cl_2 and hexane followed by 20:80 of EtOAc:hexane as the eluents to provide a green solid (0.05 g, 10%). [16, 25]

^{1}H NMR (400 MHz, acetone-d_6) **δ** (ppm): 8.13 (d, *J*=3.8 Hz, 1H), 7.66 (d, *J*=5.1 Hz, 1H), 7.49 (d, *J*=8.7 Hz, 2H), 7.33 (s, 1H), 7.16 (m, 1H), 6.97 (d, *J*=8.7 Hz, 2H), 3.94 (t, *J*= 6.5 Hz, 2H), 1.68 (m, 2H), 1.23 (m, 2H), 1.16 (m, 4H), 0.77 (m, 3H).; MALDI-TOF-MS (CCA) m/z: $[M+H]^+$= 708.11.; UV-Vis: λ_{max} = 633 nm; Fluorescence (DCM, nm): λ_{max} = 649 nm.

CHAPTER III

RESULTS AND DISSCUSION

3.1 Synthesis and characterization of derivatives of aza-BODIPY

Novel thienyl aza-BODIPYs were designed and synthesized by means of aza-dipyrromethene condensations with extended phenyl or alkoxy phenyl groups at 1, 7 positions and thienyl groups at 3, 5 positions (**Figure 3.1**). It is postulated that conjugations of electron rich thienyl and phenyl groups would decrease the HOMO–LUMO gap of the aza-BODIPY core, which is attributed to an enhancement of the planarity and electron mobility of the π-conjugated system.

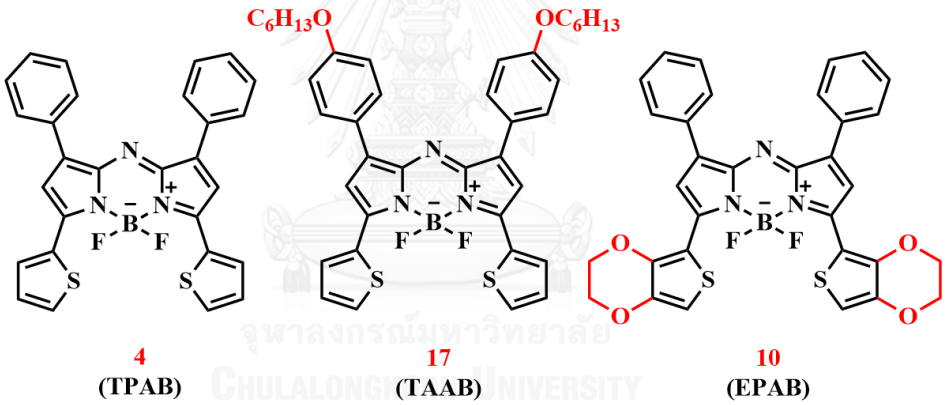
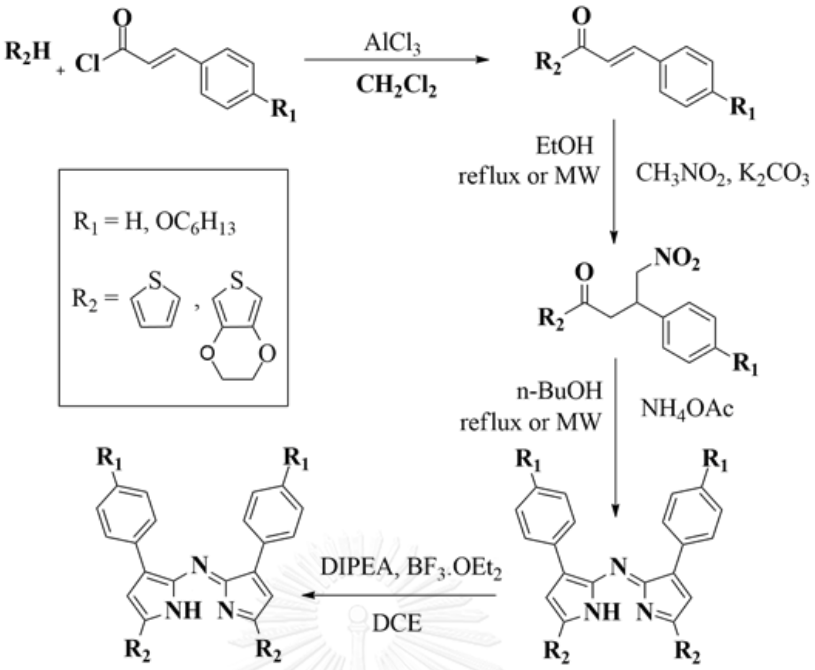


Figure 3.1 Targets of derivatives of thienyl aza-BODIPYs

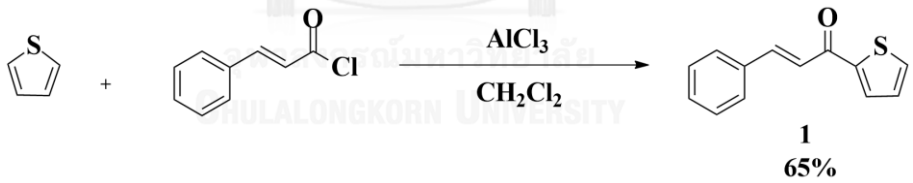
The derivatives of aza-BODIPY were synthesized in 4 steps as shown in **Scheme 3.1**. The synthesis started with Friedel-Crafts acylation, followed by Michael addition and condensation to yield a solid aza-dipyrromethene, which was then complexed with boron trifluoride diethyl etherate.



Scheme 3.1 Synthetic route of derivatives of aza-BODIPY

3.1.1 Synthesis and characterization of thienyl phenyl aza-BODIPY (TPAB)

3.1.1.1 Friedel-Crafts acylation



Scheme 3.2 Synthesis of thienyl-3-phenylprop-2-en-1-one (**1**)

The synthesis of thienyl-3-phenylprop-2-en-1-one (**1**) was carried out via electrophilic aromatic substitution using cinnamoyl chloride on thiophene in the presence of aluminium chloride as a catalyst to give the yellow solid product in 65 %yield. The ^{1}H NMR spectrum showed doublet peaks of alkene protons at 7.90 and 7.46 ppm and the signal of the thienyl rings protons at 7.80, 7.70 and 7.45 ppm (**Figure A.1**, **Appendix A**). ^{13}C NMR spectrum showed the signal of the carbonyl group, two signals of alkene and eight types of other carbons (**Figure A.2**, **Appendix A**). Moreover,

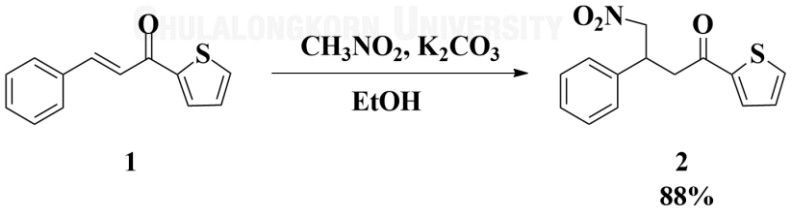
the molecular weight of **1** was confirmed by mass spectrometer ESI-MS: $[M+H]^+$ m/z = 215.12 (**Figure A.3**, **Appendix A**).

Table 3.1 The conditions for synthesis of compound **1**

Entry	Reaction temperature (°C)	Time (h)	%yield
1	0	2	35
2	0	1	41
3	rt	1	65

It was found that the best condition was addition of thiophene into reaction mixture at room temperature, which gave the product in 65 %yield. The reactions at 0 °C was probably too slow and induced many side reactions such as oversubstitution on the product. Moreover, it was found that at approximately 1 h was sufficient to give the product in good yield, whereas longer reaction time at 2 h may cause more side reactions and decrease the yield slightly.

3.1.1.2 Michael addition



1 **2** **88%**

Scheme 3.3 Synthesis of 3′,4′-ethylenedioxy thienyl-4-nitro-3-phenylbutan-1-one **(2)**

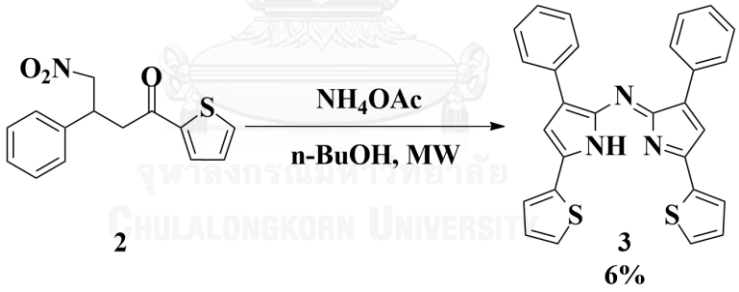
Compound **2** was efficiently obtained via compound **1** reacted with nitromethane in basic condition under microwave heating, but better with reflux EtOH condition (**Table 3.2**). The success was evidenced by the appearance in the ^{1}H NMR spectrum showing signals of thiophene and phenyl protons at 7.11-7.57 ppm, together with the complicate signals of protons at stereogenic center (3.25 ppm) and adjacent

diastereotopic centers at 4.08 and 4.63 ppm (**Figure A.4**, **Appendix A**). ^{13}C NMR spectrum showed the signals of the expected structure of compound **2** (**Figure A.5**, **Appendix A**). Moreover, the molecular weight of **2** was confirmed by mass spectrometer ESI-MS: $[M+H]^+$ m/z = 276.04 (**Figure A.6**, **Appendix A).** High temperature in microwave may have caused some decompositions of the product or side reactions and lowered the yield.

Table 3.2 The reaction conditions for the synthesis of **2**

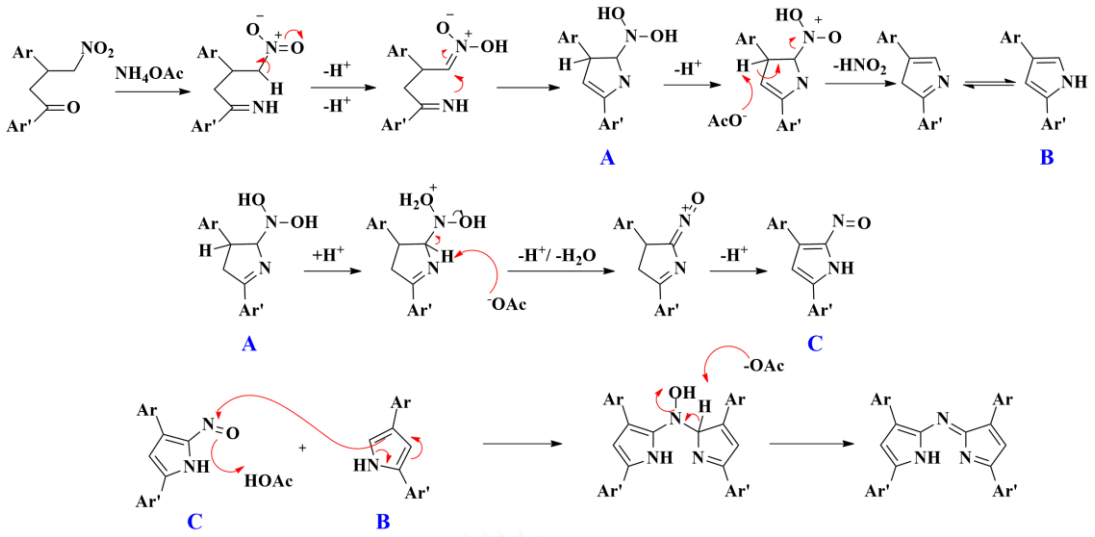
Entry	Reaction condition	Time	%yield
1	reflux	7 h	88
2	MW 120°C	20 min	65

3.1.1.3 Synthesis of aza-dipyrromethene 3



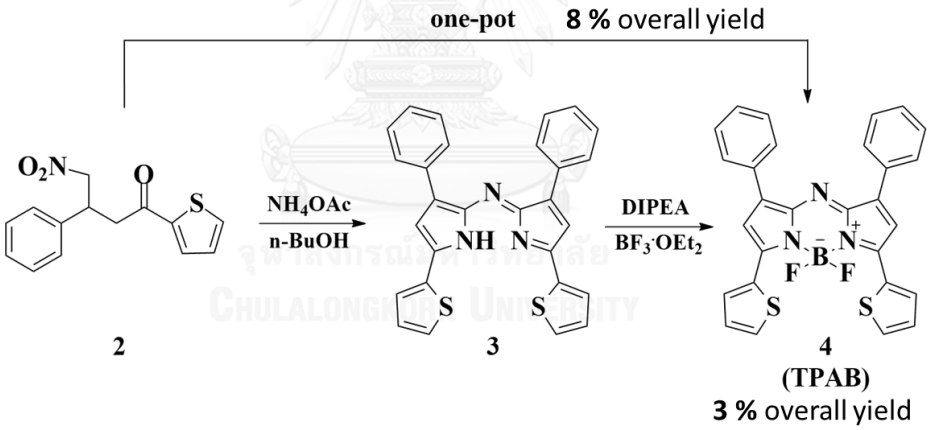
Scheme 3.4 Synthesis of aza-dipyrromethene **3**

Aza-dipyrromethene was obtained via multiple condensations of compound **2** and ammonium salt under microwave heating condition as the black blue solid in rather low 6% yield. The mechanism of its formation is presented in **Scheme 3.5**. [12] The ^1H NMR spectrum showed signals of N-H at 8.48 ppm, the pyrrole ring at 6.71 ppm, and all the other aromatic protons between 7.03-7.55 ppm (**Figure A.7**, **Appendix A**).



Scheme 3.5 Mechanism of the formation of Aza-dipyrromethene

3.1.1.4 Synthesis of thienyl phenyl aza-BODIPY (4, TPAB)



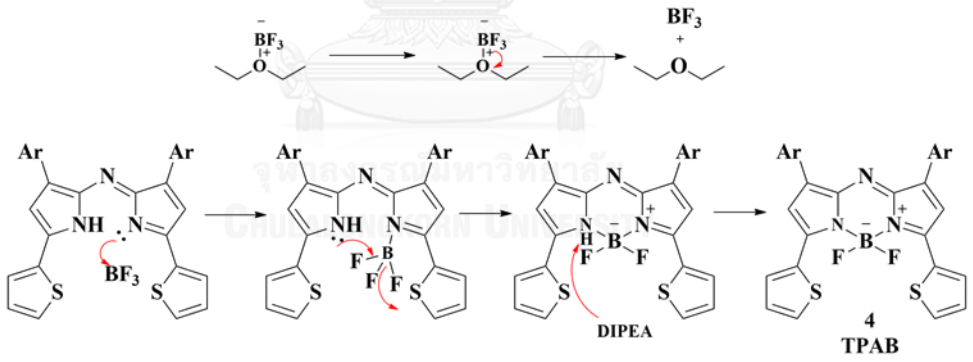
Scheme 3.6 Synthesis of thienyl phenyl aza-BODIPY (**4**, **TPAB**)

Two steps synthesis of thienyl phenyl aza-BODIPY (**4**, **TPAB**) from compound **2**, either as separated steps via **3** or combined one-pot condition, were both carried out to yield the black blue solid product **TPAB** (**Table 3.3**), whick followed by the mechanism in **Scheme 3.7**. The ^{1}H NMR spectrum showed relatively similar signals of dipyrromethene moiety with slightly shifted peaks. However, no signal of N-H appeared, which demonstrated the success in complexation to **TPAB** (**Figure A.8**,

Appendix A). Moreover, the molecular weight of **3** was confirmed mass spectrometer MALDI-TOF MS: $[M+H]^+$ m/z = 507.08 (**Figure A.9**, **Appendix A**). The UV-Vis spectrum showed the maximum absorption wavelength (λ_{max}) at 627 nm (**Figure A.10**, **Appendix A**), and the maximum emission wavelength (λ_{max}) at 650 nm from fluorescent spectrum. (**Figure A.11**, **Appendix A**).

Table 3.3 The two-step synthetic conditions towards **TPAB**

Entry	Condition	DCE (mL)	Time (h)	One step yield from 3 (%)	Overall yield from 2 (%)
1	Separated step via **3**	5	10	50	3
2	Separated step via **3**	10	10	45	2.7
3	Combined one pot	10	10	-	8

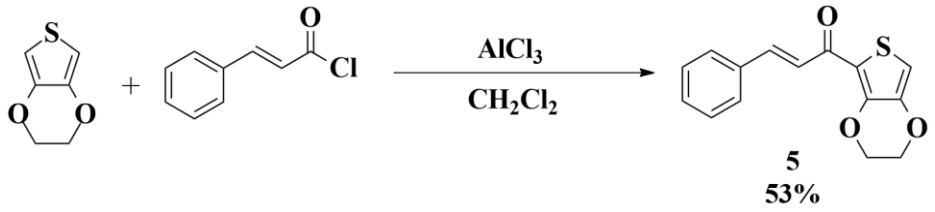


Scheme 3.7 The mechanism of **4** (**TPAB**) complexation

The volume of solvent had some effects on the reaction. In the reaction mixture with less solvent (Entry 1), compound **3** was converted to the product in 50 %yield, slightly higher than the more diluted condition (Entry 2). However, because of the very low yield of the first step, the combined two steps into one-pot reaction was preferred. It gave higher overall yield and also simplified the purification process by column chromatography (**Table 3.3**).

3.1.2 Synthesis and characterization of EDOT phenyl aza-BODIPY (EPAB)

3.1.2.1 Friedel-Crafts acylation



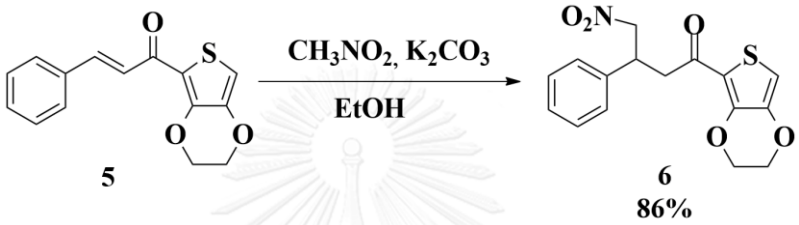
Scheme 3.8 Synthesis of compound **5**

The synthesis of **5** followed the same procedure of Friedel-Crafts acylation as shown earlier in **section 3.1.1.1** to give the product as pale yellow solid up to 53 %yield (**Table 3.4**). lower amount of reagent and reaction time would lead the reaction towards incompletion and probably more decomposition of the precursor, as observed in much lower yield of product. (Entry 1) The ^{1}H NMR spectrum showed the doublet signal of alkene protons at 7.82, 7.65 ppm, the thienyl ring protons at 6.73 ppm, and the ethylenedioxy moiety at 65.5, 64.0 ppm (**Figure A.12**, **Appendix A**). ^{13}C NMR spectrum showed one signal of carbonyl group at 181.1 and two signal of ethylene group of EDOT at 65.5, 64.0 ppm (**Figure A.13**, **Appendix A**). Moreover, the molecular weight of **5** was confirmed by mass spectrometer ESI-MS $[M+H]^+$ m/z = 273.19 (**Figure A.14**, **Appendix A**).

Table 3.4 The conditions for the synthesis of compound **5**

Entry	EDOT (mmol)	Cinnamoyl chloride (eq)	$AlCl_3$ (eq)	Time (h)	%yield
1	5	1.5	2	1	6.5
2	5	2	2	2	53

3.1.2.2 Michael addition



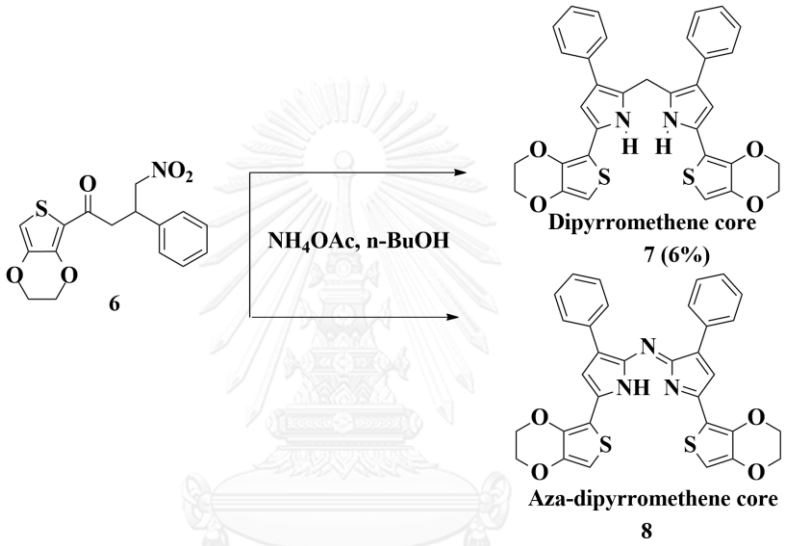
Scheme 3.9 Synthesis of compound **6**

The synthesis of **6** followed the same procedure of Michael addition as in **section 3.1.1.2** to give the product as pale yellow solid up to 86 %yield under reflux EtOH condition (**Table 3.5**). Once again, the more vigorous microwave heating condition gave lower yield of the product. (Entry 2) The success of the nucleophilic addition was evidenced by the appearance in the ^{1}H NMR signals showing the singlet signal of thienyl proton at 6.85 ppm and other signals that well correlated with the expected structure (**Figure A.15**, **Appendix A**). ^{13}C NMR spectrum showed the corresponding five signals of aliphatic carbons (**Figure A.16**, **Appendix A**). Moreover, the molecular weight of **6** was confirmed by mass spectrometer ESI-MS: $[M+H]^+$ m/z = 334.20 (**Figure A.17**, **Appendix A**).

Table 3.5 The conditions for the synthesis of compound **6**

Entry	Reaction condition	Time	%yield
1	Reflux	4 h	86
2	MW 120 ℃	20 min	78

3.1.2.3 Condensation of 6 to dipyrromethene core

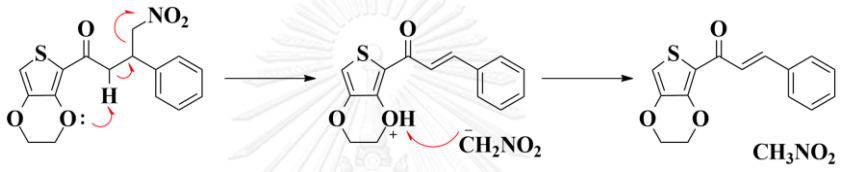


Scheme 3.10 Attempted condensation of **6** to the dipyrromethene cores

Aza-dipyrromethene derivative **8** was planned as the target of condensations of compound **6** and ammonium salt. After long reaction time under reflux or using microwave heating conditions, a pale green solid was obtained. ^{1}H and ^{13}C NMR spectra showed most of the signals that corresponded to the dipyrromethene structure. However, the ^{1}H NMR data showed an extra singlet signal at 6.27 ppm**,** which later be assigned to the methylene protons bridging between the pyrrole rings of the surprisingly unexpected dipyrromethene core of compound **7** (**Figure A.18**, **Appendix A**). ^{13}C NMR also showed the extra signal of this methylene group at 95.7 ppm (**Figure A.19**, **Appendix A**). Furthermore, the HSQC spectroscopy confirmed the correlation between these extra proton and carbon signals, supporting the presence of “non-aza”

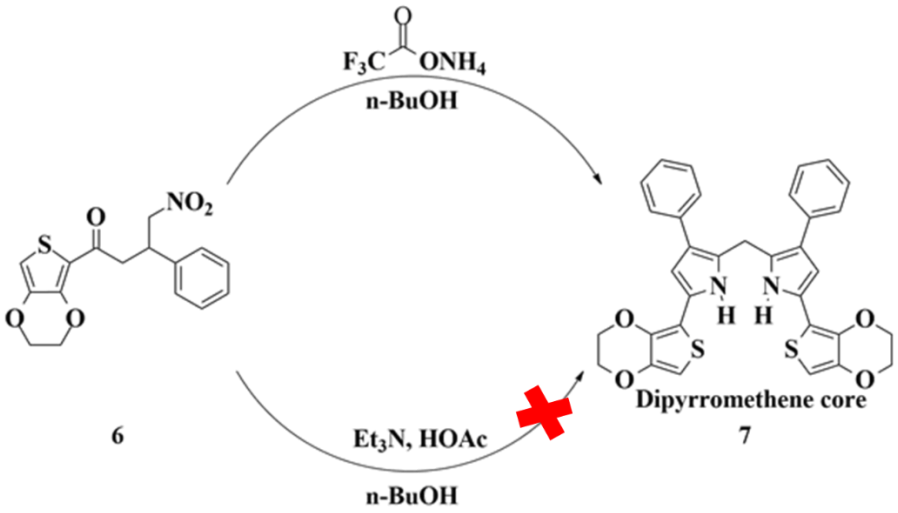
dipyrromethene structure (**Figure A.20**, **Appendix A**). Moreover, the molecular weight of **7** was also confirmed by mass spectrometer MALDI-TOF MS: $[M+H]^+$ m/z = 578.36 (**Figure A.21**, **Appendix A**). The UV-Vis spectrum showed the maximum absorption wavelength (λ_{max}) at 289 nm (**Figure A.22**, **Appendix A**).

It was speculated that in order to form the carbo-dipyrromethene core, a "one-carbon" source capabled of condensations with the fragmented intermediates must be released from the starting material **6** from EDOT-assisted reversed Michael addition as shown in the proposed mechanistic **scheme 3.11**



Scheme 3.11 The proposed mechanism of reversed Michael addition

To help verify the above hypothesis, three model reactions had been performed. First, the ammonium salt with weaker trifluoroacetate counterion was used, expecting the deceleration or even disappearance of the base-induced reversed Michael reaction and instead producing the desired aza-dipyrromethene core (**Scheme 3.12**).

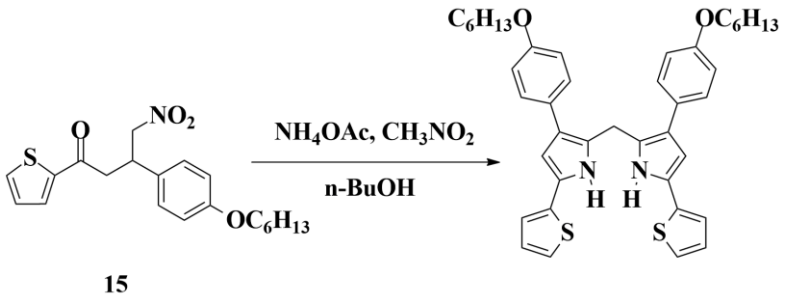


Scheme 3.12 Model reactions to suppress the synthesis of compound **7**

Using the same procedure under microwave condition to synthesize compound **7,** the obtained the crude product gave the ^{1}H NMR spectrum that still mostly corresponded to the dipyrromethene core of compound **7** (**Figure A.23**, **Appendix A**). This result demonstrated that the counterion of the ammonium reagent has no effect on the direction of the reaction.

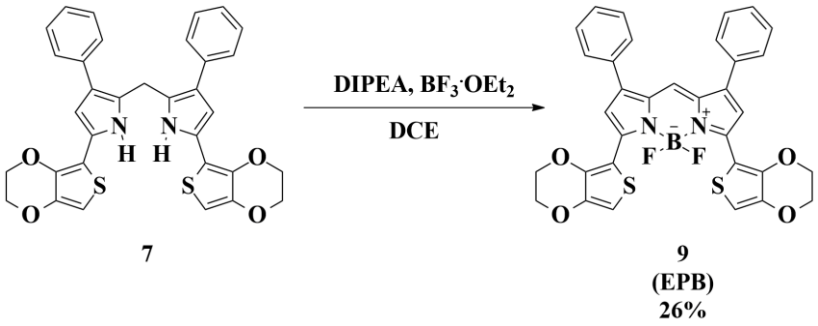
Next, a tertiary amine was used replacing ammonium salt to completely avoid the aza-dipyrromethene formation and perhaps promote the dipyrromethene product (**Scheme 3.12**). Unfortunately, the obtained crude product was a complex mixture in which its ^{1}H NMR spectrum was very complicate and could not be assigned the signals to correspond to either aza- or non-aza-dipyrromethene structures.

Because of the previous success on the synthesis of aza-dipyrromethene core (section 3.1.1.3), the thienyl derivative was then put into the condensation with an external addition of nitromethane (**Scheme 3.13**). Compound **15** (1 mmol) was reacted with ammonium acetate (20 mmol) and nitromethane (1 mmol) using the similar procedure of making derivative of compound **7**. The ^{1}H NMR spectrum of the obtained crude product showed very complicate mixture with a singlet signal that may correspond to the methylene protons of dipyrromethene structure at 6.72 ppm (**Figure A.24**, **Appendix A**). Though not yet conclusive, it partly supported that the added nitromethane was the source of C_1 fragment for the unexpected dipyrromethene formation.



Scheme 3.13 Attempted synthesis of dipyrromethane core from compound **15**

3.1.2.4 Synthesis of EDOT phenyl BODIPY (EPB)

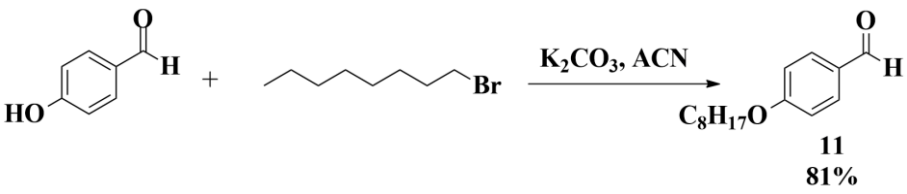


Scheme 3.14 Synthesis of EDOT phenyl BODIPY (**9, EPB**)

Nonetheless with the free ligand **7** in hand, **EPB** was prepared through reaction with boron trifluoride etherate to yield the green solid complex in 26 %yield. The ^{1}H NMR spectrum showed the singlet signal of bridging methine proton at 6.93 ppm (**Figure A.25**, **Appendix A**). Moreover, the molecular weight of **EPB** was confirmed by mass spectrometer MALDI-TOF MS: $[M+H]^{+}$ m/z = 623.64 (**Figure A.26**, **Appendix A**). The UV-Vis spectrum showed the maximum absorption wavelength (λ_{max}) at 660 nm (**Figure A.27**, **Appendix A**), and the single maximum emission wavelength (λ_{max}) at 680 nm (**Figure A.28**, **Appendix A**).

3.1.3 Synthesis and characterization of thiophene alkoxy phenyl aza-BODIPY (TAAB)

3.1.3.1 Synthesis of 4-(octoxy)benzaldehyde (11)

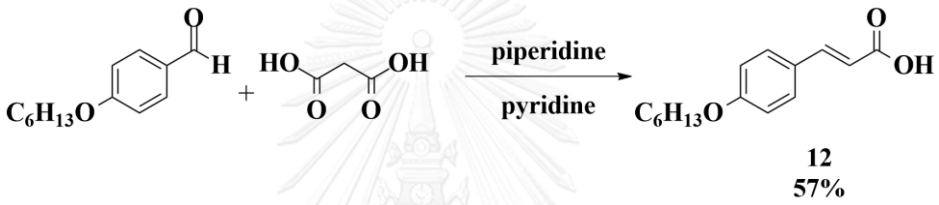


Scheme 3.15 Synthesis of 4-(Octoxy)benzaldehyde

4-Hydroxybenzaldehyde was reacted with 1-bromooctane and potassium carbonate in acetonitrile to provide the product **11** as white solid in 81 %yield. The ^{1}H

NMR signals showed the singlet signal of aldehyde group proton at 9.86 ppm, the two signals of phenyl ring at 7.82, 6.98 ppm and the signal of alkyl group protons at 4.02, 1.78, 1.43, 1.31, 0.88 ppm, respectively (**Figure A.29**, **Appendix A**). Inspite of the success in synthesis, the product was quite easy to be oxidized by air and became a mixture that was difficult to purify. It was then decided that the commercially available analog would be more convenient to use as the starting material for the following series of reactions.

3.1.3.2 Anionic condensation to 4-(hexyloxy)prop-2-enoic acid



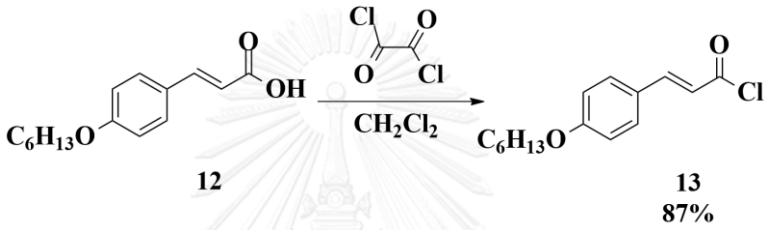
Scheme 3.16 Synthesis of compound **12**

Compound **12** was obtained from reaction of 4-(hexyloxy)benzaldehyde and malonic acid and piperidine in pyridine to yield colorless solid in 57% yield. (Entry 1, **Table 3.6**) Unfortunately, larger scale reaction gave lower yield of the product, (Entry 2) which may be due to longer reaction time that allowed more decomposition of the substrate. The ^{1}H NMR spectrum showed two signals of alkene protons at 7.74, 6.31 ppm and two signals of phenyl ring protons at 7.49, 6.90 ppm and signal of alkyl group at 3.99, 1.79, 1.42, 1.34, 0.90 ppm (**Figure A.30**, **Appendix A**). ^{13}C NMR showed the one signal of carboxylic group at 172.2 ppm and two signals of alkene at 146.8, 114.4 ppm and quarternary carbon at 161.4, 126.6 ppm (**Figure A.31**, **Appendix A**). Finally, the mass spectrum exhibited the corresponding molecular ion peak in the positive mode at 247.38 amu $[M+H]^{+\cdot}$ (**Figure A.32**, **Appendix A**).

Table 3.6 The conditions for synthesis of compound **12**

Entry	4-(Hexyloxy) benzaldehyde (mmol)	Malonic acid (eq)	Piperidine (eq)	Time (h)	%yield
1	5	3	0.34	5.5	57
2	25	15	1.7	6.5	39

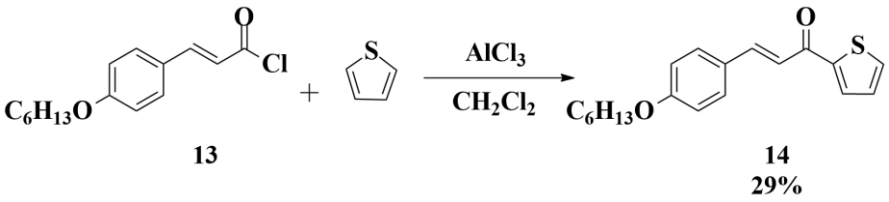
3.1.3.3 Converting carboxylic acid 11 to acid chloride 13



Scheme 3.17 Synthesis of compound **13**

Compound **12** was reacted with oxalyl chloride following a reported procedure [27] to provide the product **13** as yellow oil in 87% yield. The product was used directly without any further purification. The ^{1}H NMR spectrum showed two signals of alkene protons at 7.74, 6.31 ppm and two signals of phenyl protons at 7.49, 6.90 ppm and five signals of alkyl group (**Figure A. 33**, **Appendix A**).

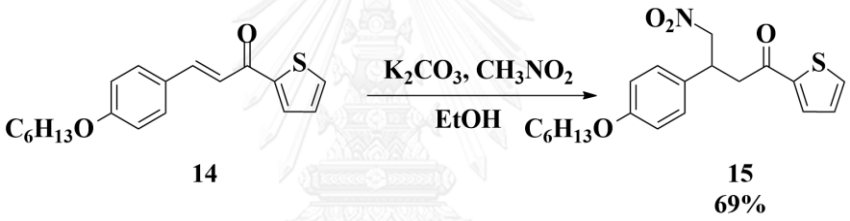
3.1.3.4 Friedel-Crafts acylation



Scheme 3.18 Synthesis of compound **14**

Compound **14** was carried out via electrophilic aromatic substitution using cinnamoyl chloride on thiophene in the presence of aluminium chloride as a catalyst to give the yellow solid product in 29% yield. The ^{1}H NMR showed the signal of thienyl rings protons at 7.84, 7.64, 7.15 ppm and doublet peaks of alkene protons at 7.79, 7.30 ppm (**Figure A. 34**, **Appendix A**). ^{13}C NMR showed signal of thienyl rings at 134.8, 132.9, 131.4 and two signals of alkene at 147.2, 120.2 ppm and twelve types of other carbons (**Figure A.35**, **Appendix A**). Furthermore, the molecular weight of **13** was confirmed by mass spectrometer MALDI-TOF-MS: $[M+H]^{+}$ m/z = 313..33 (**Figure A.36**, **Appendix A**).

3.1.3.5 Michael addition of TAAB

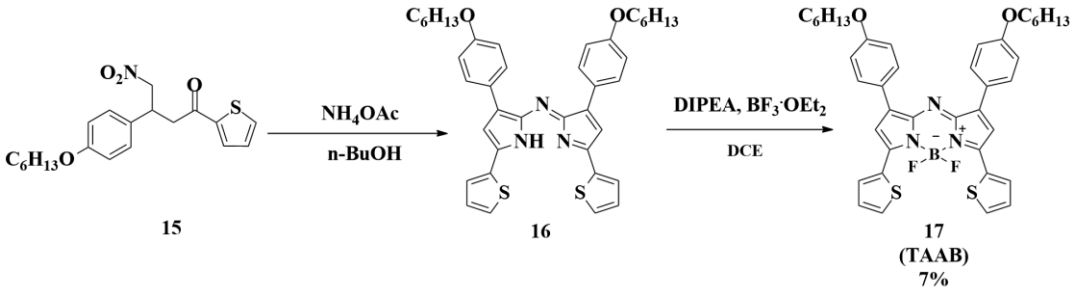


14 **15** 69%

Scheme 3.19 Synthesis of compound **15**

Compound **15** was efficiently obtained via compound **14** reacted with nitromethane in basic condition under microwave heating to give the pale orange solid product in 69 %yield. The ^{1}H NMR showed signals of protons at stereogenic center and adjacent diastereotopic centers at 4.91, 4.17, 3.50 ppm (**Figure A.37**, **Appendix A**). ^{13}C NMR spectrum showed the signals of the expected structure of compound **15** (**Figure A.38**, **Appendix A**).

3.1.3.6 Synthesis of thienyl alkoxy phenyl aza-BODIPY



Scheme 3.20 Synthesis of compound **17 (TAAB)**

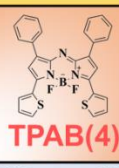
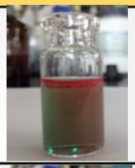
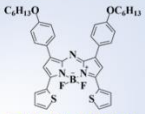
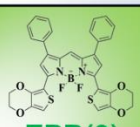
Thienyl alkoxy phenyl aza-BODIPY (**17, TAAB**) was obtained from two-step procedure via dipyrromethene from reaction in section 3.1.1.3, yielding green solid complex in 7 %yield. The ^{1}H NMR of the product showed doublet signals of phenyl ring protons at 7.49, 6.97 ppm, and singlet signal of pyrrole site at 7.33 ppm, and three signals of thiophene rings at 8.13, 7.66, 7.16 ppm which corresponded well with the expected structure (**Figure A. 39**, **Appendix A**). Furthermore, the molecular weight was confirmed by mass spectrometer MALDI-TOF-MS: $[M+H]^{+}$ m/z = 708.11 (**Figure A.40, Appendix A**). The UV-Vis spectrum showed the maximum absorption wavelength (λ_{max}) at 633 nm (**Figure A.41**, **Appendix A**) and the single maximum emission wavelength (λ_{max}) at 649 nm (**Figure A.42**, **Appendix A**).

3.2 Photophysical properties of TPAB, EPB, TAAB

The absorption and emission of **TPAB**, **TAAB** and **EPB** were studied using their ethyl acetate (**Figure 3.2**) and dichloromethane solutions (**Figure 3.3**), respectively. The optical properties are compiled in **Table 3.7**. **TPAB**, **TAAB** and **EPB** exhibited absorption maxima at 627, 633 and 660 nm, respectively (**Figure 3.2**). Each fluorophore showed a single maximum emission wavelength at 650, 649 or 680 nm, resulted in the red, blue or green line. The relative bathochromic shift of absorption maxima for **TAAB** compared to the **TPAB** was because the presence of alkoxy groups substituted on the phenyl rings at 1,7 positions of the core structure. This shift supported the hypothesis that more electrons releasing from these alkoxy phenyl rings decrease the HOMO-

LUMO gap of the aza-BODIPY core, which is related to an enhancement of the electron density and mobility of the π-conjugated system. However, such shift was not large and indicated that electronic effects from these groups at 1,7 positions had only little effect to the aza-BODIPY core, or even none when considered the emission spectra of these 2 compounds, where no shift was observed.

Table 3.7 Optical properties of **TPAB**, **TAAB** and **EPB** in ethyl acetate

Compound	Naked eyes	Black light (λ = 350-400 nm)	λ_{ab} (nm)	λ_{em} (nm)
 TPAB(4)			627	650
 TAAB(17)			633	649
 EPB(9)			660	680

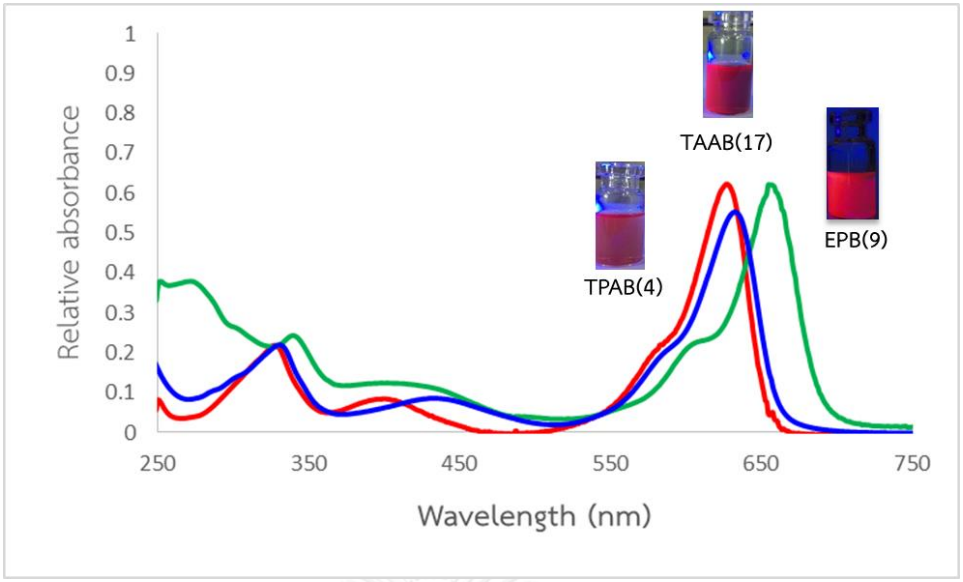


Figure 3.2 Absorption spectra of **TPAB** (red), **TAAB** (blue) and **EPB** (green)

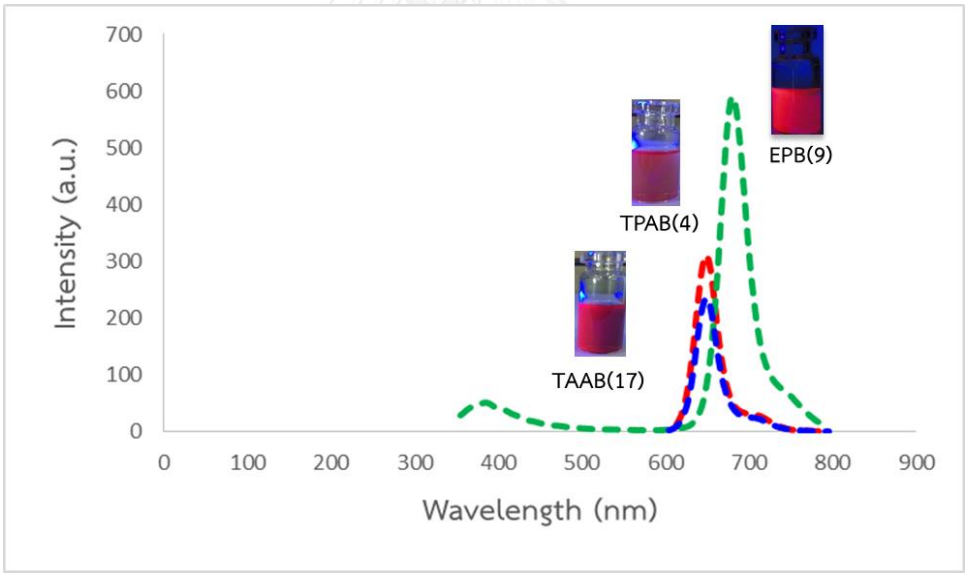


Figure 3.3 Emission spectra of **TPAB** (red), **TAAB** (blue) and **EPB** (green)

Unfortunately, the effect of electron density from the substituted thienyl groups at 3,5 positions of aza-BODIPY could not be directly compared because of the unsuccessful synthesis of the analog **EPAB** (**10**). Nevertheless, the obtained non-aza analog **EPB** (**9**) may be used to compare with other thienyl BODIPY derivatives that

already appeared in literature. The closely related analog thienyl BODIPY **17** has been prepared and found to have the absorption maxima at 597 nm, and emission maxima at 647 nm. [13] Clearly, replacing the unsubstituted thienyl rings with the electron rich EDOT had a strong effect on its optical properties, in which the absorption maxima was bathochromic shifted up to 660 nm, and the emission maxima up to 680 nm. It could be estimated that if the similarly designed **EPAB** was synthetically achieved, its optical properties would even shift further, closer to the near IR region than these non-aza BODIPY derivatives. This result supported our earlier hypothesis that increasing electron releasing property of the substituted thienyl rings at 3,5 positions would, in this case, significantly narrowed down the HOMO-LUMO gap and moved these structures closer towards near IR absorption chromophores or emission fluorophores.

18

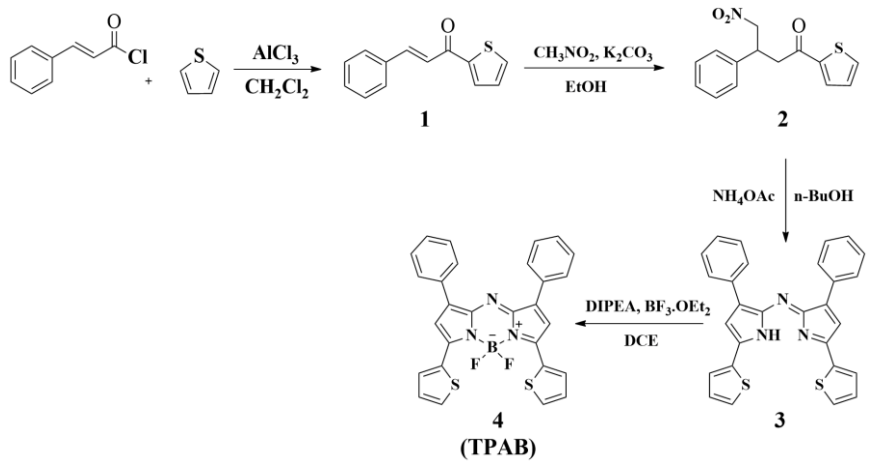
Figure 3.4 Structure of thienyl BODIPY **18**

CHAPTER IV

CONCLUSION

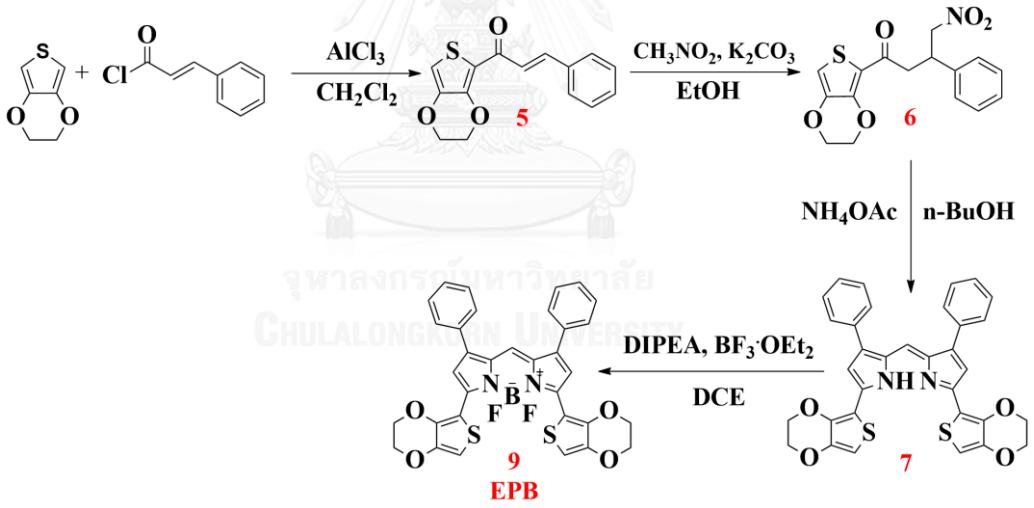
The synthesis of thienyl-substituted aza-BODIPY had been accomplished thienyl phenyl aza-BODIPY (**TPAB**) and thienyl alkoxy-phenyl aza-BODIPY (**TAAB**) were synthesized via 4 steps starting from cinnamoyl chloride derivatives: Friedel-Crafts acylation, Michael addition, and condensation to aza-dipyrromethene, and complexation with boron trifluoride to provide each of the two products. Unfortunately, edot phenyl aza-BODIPY (**EPAB**) could not be synthesized via the same procedure, where edot phenyl BODIPY (**EPB**) was obtained instead.

The synthesis of **TPAB** was achieved via 4 steps as shown in **Scheme 4.1**. Compound **1** was synthesized through Friedel-Crafts acylation from thiophene and cinnamoyl chloride in 65 %yield. It was used in Michael addition with nitromethane to give compound **2** in 88 %yield. Condensation with NH_4OAc yielded aza-dipyrromethene **3** in 6 %yield, which was then complexed with boron trifluoride etherate to provide **TPAB** in 50 %yield. Alternatively, **TPAB** could be synthesized via combined condensation-complexation reaction from compound **2** to yield **TPAB** in 8 %yield. When calculated from all four steps, the overall yields of this process was 2 and 5 %, for the original 4 steps and the combined 3 steps, respectively.



Scheme 4.1 The synthetic procedure for **TPAB**

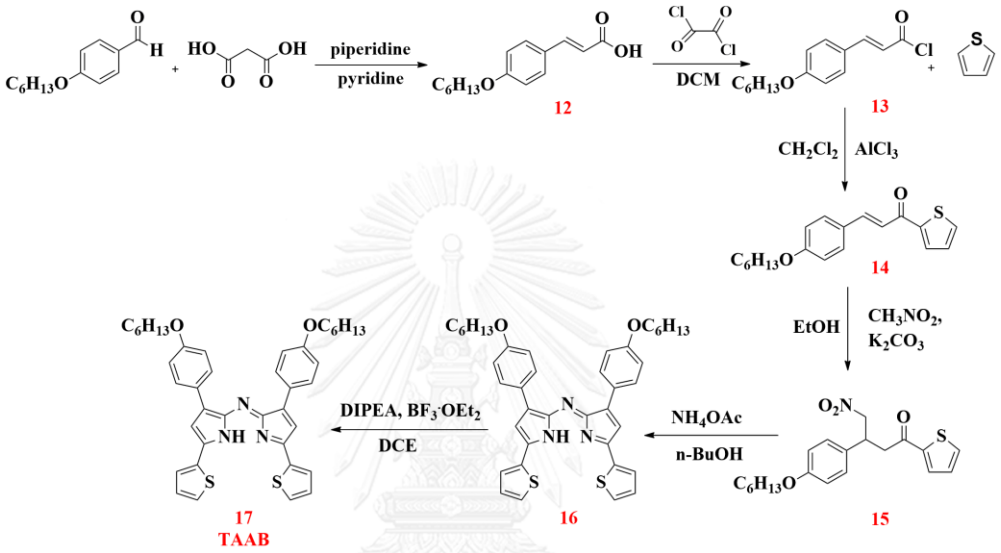
Novel **EPB** was synthesized via 4 steps of the same procedure instead of the expected **EPAB**. Compound **5** was obtained from reaction of cinnamoyl chloride and 3,4-ethylenedioxythiophene (EDOT) via Friedel-Craft acylation in 33 % yield. Next, condensation of compound **6** with nitromethane in *n*-butanol unexpectedly gave dipyrromethane **7** in 6 %yield. Finally, **EPB** was received from dipyrromethane **7** complexed with boron trifluoride etherate in 2.6 yield. When combined all four steps, the overall yield of this process was 0.4 %. The unsuccessful formation of the targeted aza-dipyrromethene in this case was perhaps arised from the possible intramolecular EDOT-assisted reversed Michael addition of the precursor **6** under the reaction condition. Nitromethane by-product generated from this process might be responsible for the unexpected formation of dipyrromethane **7.** (**Scheme 4.2**)



Scheme 4.2 The synthetic procedure for **EPB**

Novel **TAAB** was synthesized via 6 steps as in **Scheme 4.3**. The main precursor *trans*-3-(4-hexyloxy)phenylacryloyl chloride (**13**) was synthesized via two steps. Anionic condensation between 4-(hexyloxy)benzaldehyde with malonic acid yielded the product **12** in 57 %. Then, compound **12** was converted into acid chloride by oxalyl chloride in dichloromethane, which was used without purification in the next step.

Compound **14** was obtained in 29 % from Friedel-Crafts acylation of compound **13** with thiophene and aluminium chloride in dichloroethane. It then underwent Michael addition with nitromethane and potassium carbonate to yield compound **15** in 69 %. Finally, **TAAB** was synthesized via one-pot reaction of condensation and complexation in 7 %yield. When combined all 6 steps, the overall yield of this process was 0.8 %.



Scheme 4.3 The synthetic procedure for **TAAB**

The λ_{max} value in UV-Vis absorption spectra of **TAAB** was found to slightly bathochromic shift from that of **TPAB** around 6 nm. The presence of alkoxy groups on the phenyl ring moieties at 1,7 positions may have added electrons into aza-BODIPY core, decreased the HOMO-LUMO gap and tended to red-shift, although not very significant. The λ_{max} values in the emission spectra of **TPAB** and **TAAB** were rather similar around 650 nm, indicating no contribution from these substituents.

On the other hand, The novel **EPB** substituted with EDOT at 3,5 positions showed the λ_{max} value in UV-Vis absorption spectra significantly bathochromic shift at 660 nm and the emission spectra at 680 nm comparing to its unsubstituted thienyl analog. The electron rich EDOT obviously could enhance of the planarity and electron mobility of the π-conjugated BODIPY system.

Finally, It can be seen that the optical properties of **TAAB** and **EPB** supported the hypothesis that substitutions of electron-rich groups at 1,7- and 3,5-positions tend to give bathochromic shifts of the λ_{max} values in UV-Vis absorption spectra. The substituents on the 3,5 positions may tend to have more effect on the electronic property of the BODIPY core than those on the 1,7 positions.

REFERENCES

[1] Niu, S.L., Massif, C., Ulrich, G., Renard, P.Y., Romieu, A., and Ziessel, R. Water-soluble red-emitting distyryl-borondipyrromethene (BODIPY) dyes for biolabeling. Chemistry 18(23) (2012): 7229-7242.

[2] Qian, Y., Yang, B., Shen, Y., Du, Q., Lin, L., Lin, J., and Zhu, H. A BODIPY–coumarin-based selective fluorescent probe for rapidly detecting hydrogen sulfide in blood plasma and living cells. Sensors and Actuators B: Chemical 182 (2013): 498-503.

[3] Liu, S.R. and Wu, S.P. Hypochlorous acid turn-on fluorescent probe based on oxidation of diphenyl selenide. Organic Letters 15(4) (2013): 878-881.

[4] Kamkaew, A., Lim, S.H., Lee, H.B., Kiew, L.V., Chung, L.Y., and Burgess, K. BODIPY dyes in photodynamic therapy. Chemical Society Reviews 42(1) (2013): 77-88.

[5] Kowada, T., Yamaguchi, S., Fujinaga, H., and Ohe, K. Near-infrared BODIPY dyes modulated with spirofluorene moieties. Tetrahedron 67(17) (2011): 3105-3110.

[6] Kim, D., Yamamoto, K., and Ahn, K.H. A BODIPY-based reactive probe for ratiometric fluorescence sensing of mercury ions. Tetrahedron 68(26) (2012): 5279-5282.

[7] Vedamalai, M. and Wu, S.P. A BODIPY-based highly selective fluorescent chemosensor for Hg2+ ions and Its application in living cell imaging. European Journal of Organic Chemistry 2012(6) (2012): 1158-1163.

[8] Yin, S., Yuan, W., Huang, J., Xie, D., Liu, B., Jiang, K., and Qiu, H. A BODIPY derivative as a colorimetric, near-infrared and turn-on chemosensor for Cu2+. Spectrochimica Acta Part A:Molecular and Biomolecular Spectroscopy 96 (2012): 82-88.

[9] Treibs, A. and Kreuzer, F.H. Difluorboryl-komplexe von di- und tripyrrylmethene. Justus Liebigs Annalen der Chemie 718 (1968): 208-223.

[10] Madras, B.K., Canfield, D.R., Pfaelzer, C., Vittimberga, F.J., Difiglia, M., Aronin, N., Bakthavachalam, V., Baindur, N., and Neumeyer, J.L. Fluorescent and biotin

probes for dopamine receptors: D_1 and D_2 receptor affinity and selectivity. Moleular pharmacology 37(833-839) (1990).

[11] Singh, S.P. and Gayathri, T. Evolution of BODIPY dyes as potential sensitizers for dye-sensitized solar cells. European Journal of Organic Chemistry 2014(22) (2014): 4689-4707.

[12] Loudet, A. and Burgess, K. BODIPY Dyes and Their Derivatives: Syntheses and Spectroscopic Properties. Chemical Reviews 107 (2007): 4891-4932.

[13] Poirel, A., Nicola, A.D., and Ziessel, R. Oligothienyl-BODIPYs: red and near-Infrared emitters. Organic Letters 14(22) (2012): 5696-5699.

[14] Y., C. and U., A.E. Phenylethynyl-BODIPY oligomers: bright dyes and fluorescent building blocks. Organic Letters 11(1) (2009): 85-88.

[15] Rohand, T., Qin, W., Boens, N., and Dehaen, W. Palladium-catalyzed coupling reactions for the functionalization of BODIPY dyes with fluorescence spanning the visible spectrum. European Journal of Organic Chemistry 2006(20) (2006): 4658-4663.

[16] Gresser, R., Hartmann, H., Wrackmeyer, M., Leo, K., and Riede, M. Synthesis of thiophene-substituted aza-BODIPYs and their optical and electrochemical properties. Tetrahedron 67(37) (2011): 7148-7155.

[17] Zhang, X., Yu, H., and Xiao, Y. Replacing phenyl ring with thiophene: an approach to longer wavelength aza-dipyrromethene boron difluoride (Aza-BODIPY) dyes. The Journal of Organic Chemistry 77(1) (2012): 669-673.

[18] Adarsh, N., Krishnan, M.S., and Ramaiah, D. Sensitive naked eye detection of hydrogen sulfide and nitric oxide by aza-BODIPY dyes in aqueous medium. Analytical Chemistry 86(18) (2014): 9335-9342.

[19] Meshkovaya, V.V., Yudashkin, A.V., and Klimochkin, Y.N. Photophysical properties of thiophenes and 2,2′-bithiophenes containing alicyclic moieties. Dyes and Pigments 113 (2015): 435-446.

[20] Lee, W., Yang, Y., Cho, N., Ko, J., and Hong, J.I. Functionalized organic dyes containing a phenanthroimidazole donor for dye-sensitized solar cell applications. Tetrahedron 68(27-28) (2012): 5590-5598.

[21] Wang, C., Liang, M., Huang, J., Cheng, F., Wang, H., Guo, Y., and Xue, S. Redox couple related influences of bulky electron donor as well as spacer in organic dye-sensitized mesoscopic solar cells. Tetrahedron 70(36) (2014): 6203-6210.

[22] Pati, P.B. and Zade, S.S. New panchromatic dyes comprising benzothiadiazole units within a donor–acceptor **π**-conjugated spacer. Synthesis and photophysical properties. Tetrahedron 69(9) (2013): 2167-2174.

[23] Dai, Q., Li, Y., Zhai, L., and Sun, W. 3,4-Ethylenedioxythiophene (EDOT)-based **π**-conjugated oligomers: Facile synthesis and excited-state properties. Journal of Photochemistry and Photobiology A: Chemistry 206(2-3) (2009): 164-168.

[24] Waldvogel, S.R. and Ianni, A. Reliable and versatile synthesis of 2-aryl-substituted cinnamic acid esters. Synthesis 2006(13) (2006): 2103-2112.

[25] Jameson, L.P. and Dzyuba, S.V. Aza-BODIPY: improved synthesis and interaction with soluble Abeta1-42 oligomers. Bioorganic & Medicinal Chemistry Letters 23(6) (2013): 1732-1735.

[26] Vol'eva, V.B., Belostotskaya, I.S., Komissarova, N.L., and Kurkovskaya, L.N. Anionic condensations of 3,5-di-tert-butyl-4(2)-hydroxybenzaldehydes in the presence of weak bases. Russian Journal of Organic Chemistry 44(6) (2008): 803-806.

[27] Srinivasan, R., Tan, L.P., Wu, H., Yang, P.Y., Kalesh, K.A., and Yao, S.Q. High-throughput synthesis of azide libraries suitable for direct "click" chemistry and in situ screening. Organic & Biomolecular Chemistry 7(9) (2009): 1821-1828.

APPENDICES

Appendix A

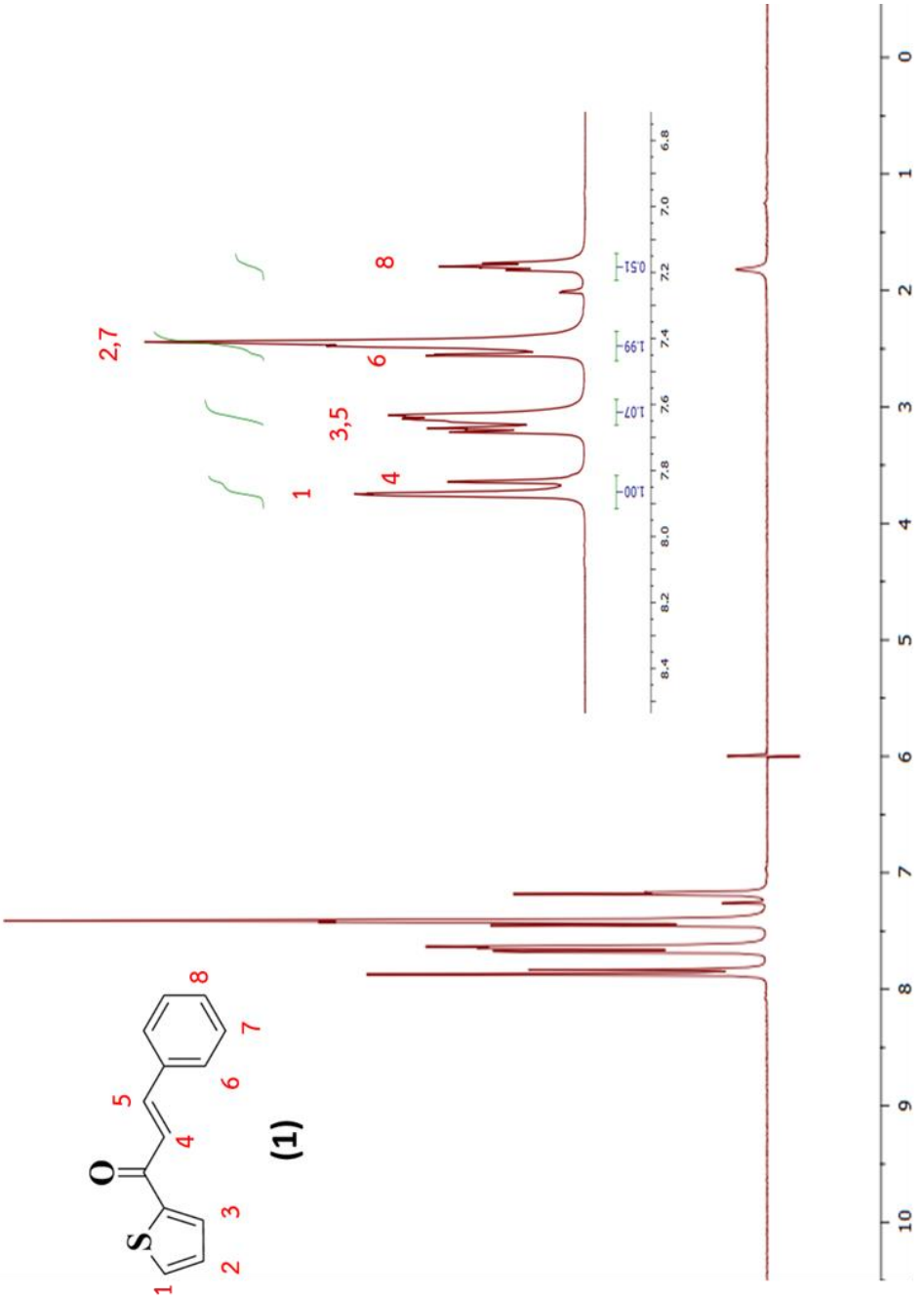


Figure A.1 ^{1}H NMR ($CDCl_3$) spectrum of thienyl-3-phenylprop-2-en-1-one **(1)**

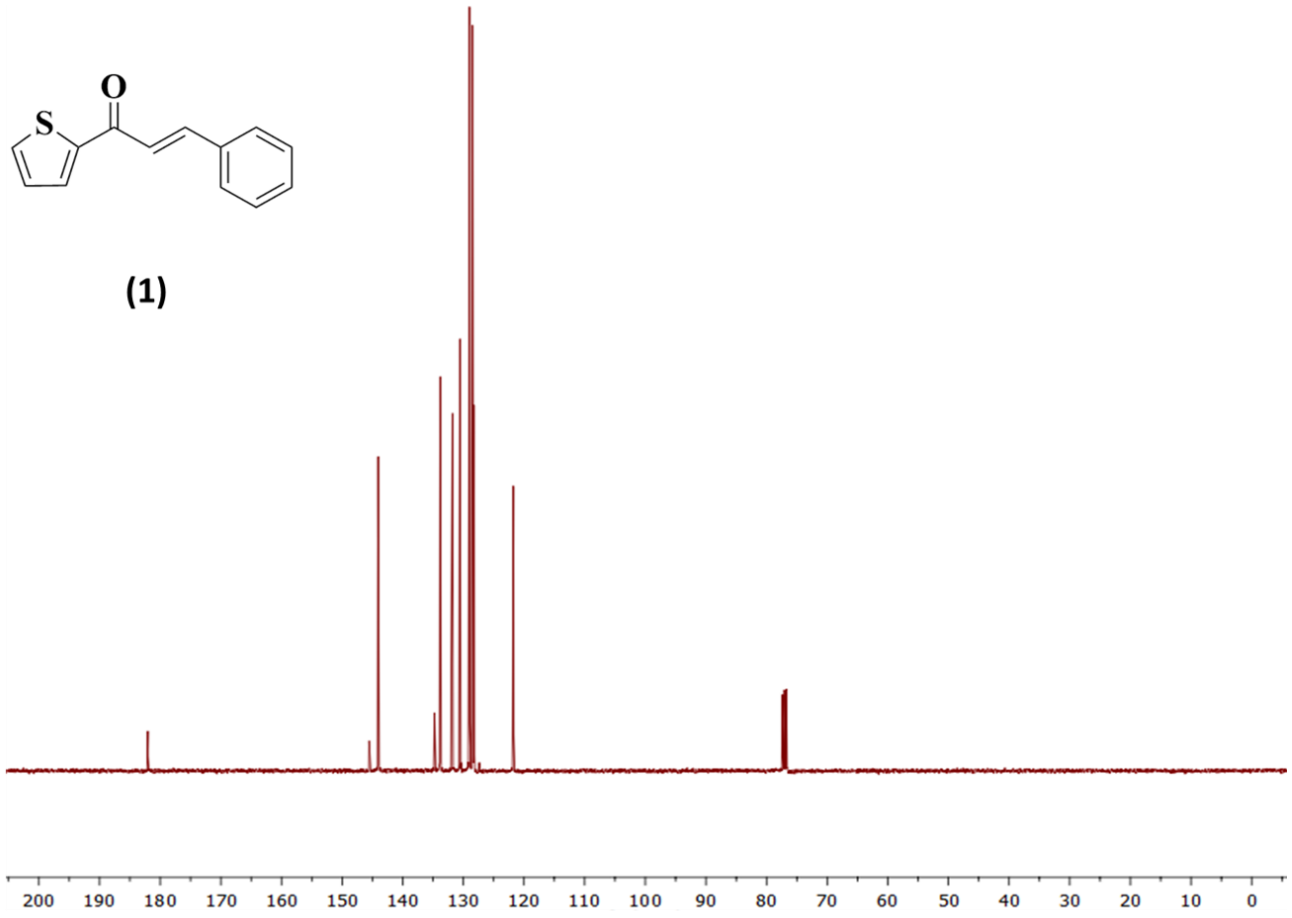


Figure A.2 ^{13}C ($CDCl_3$) spectrum of thienyl-3-henylprop-2-en-one **(1)**

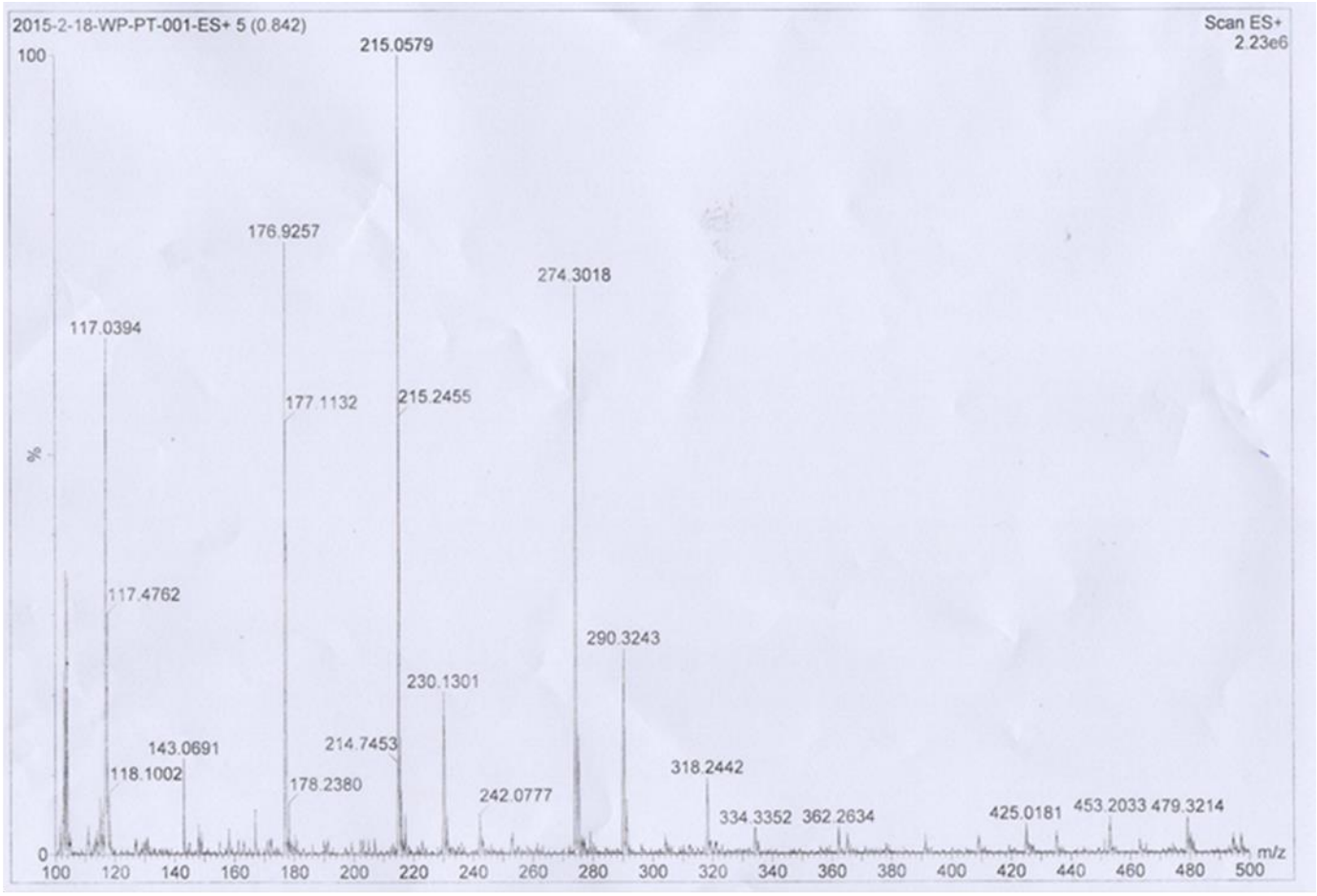


Figure A.3 Mass spectrum of thienyl-3-phenylprop-2-en-1-one **(1)**

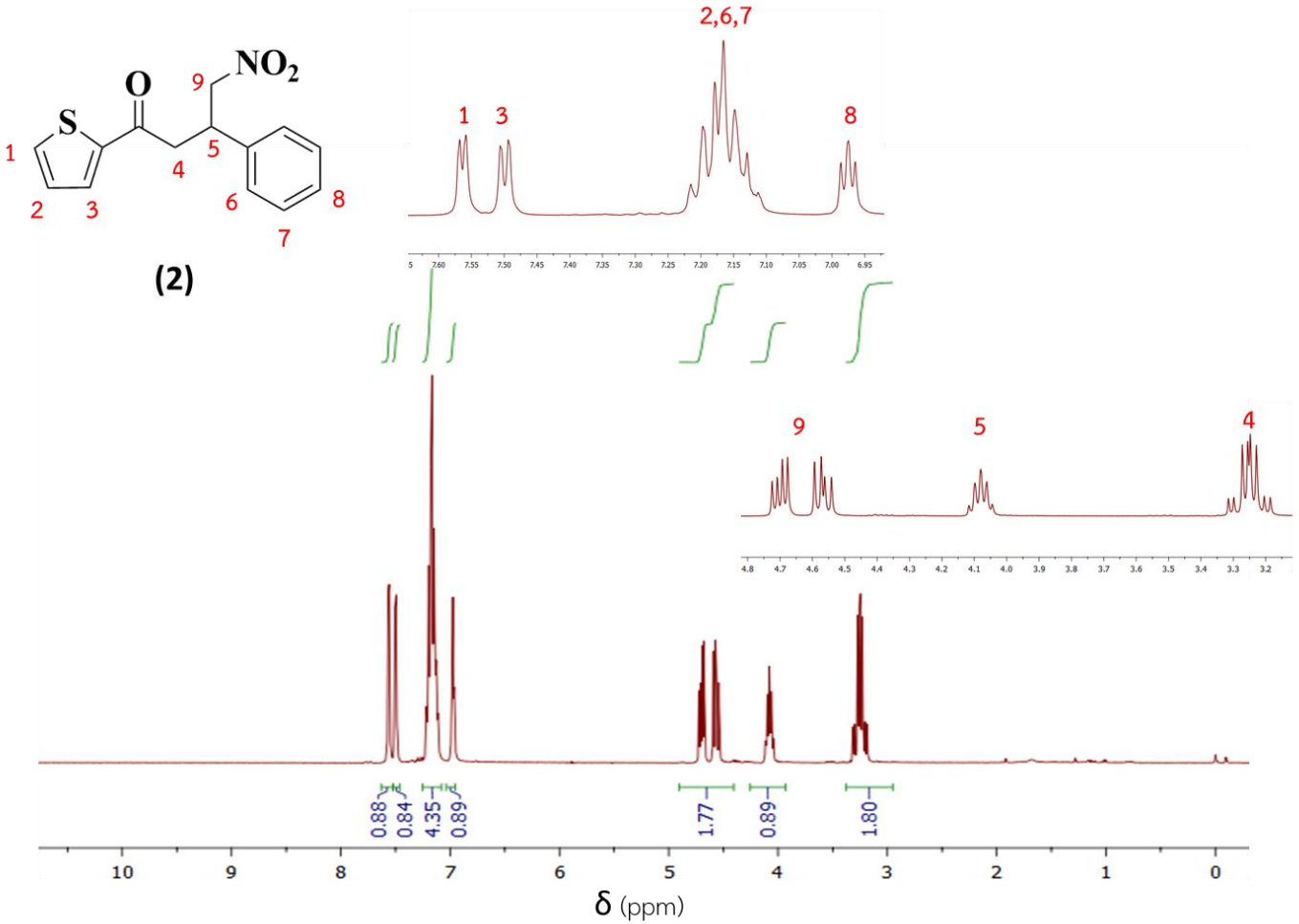


Figure A.4 ^{1}H NMR ($CDCl_3$) spectrum of thienyl-4-nitro-3-phenylbutan-1-one **(2)**

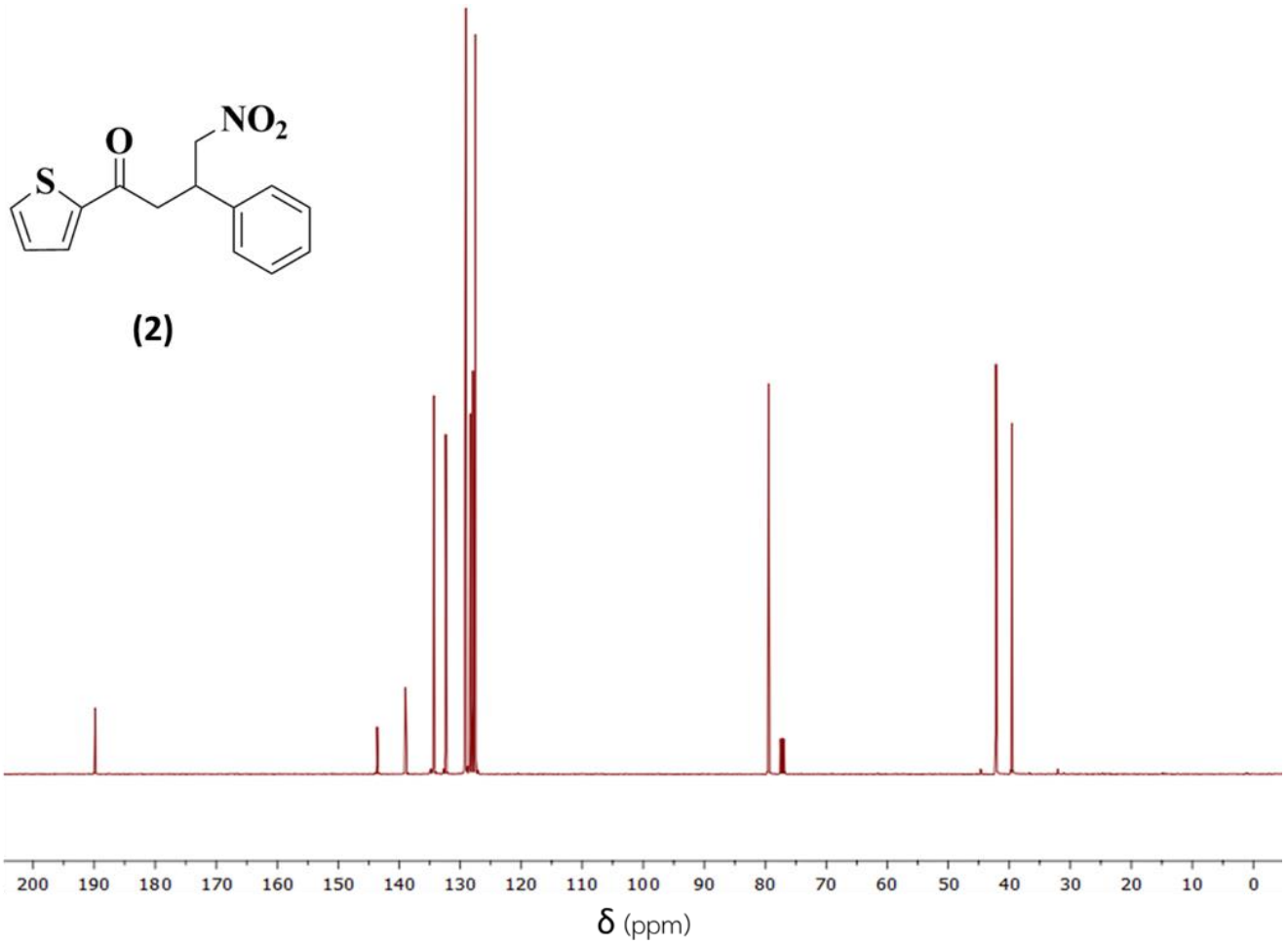


Figure A.5 ^{13}C NMR ($CDCl_3$) spectrum of thienyl-4-nitro-3-phenylbutan-1-one (2)

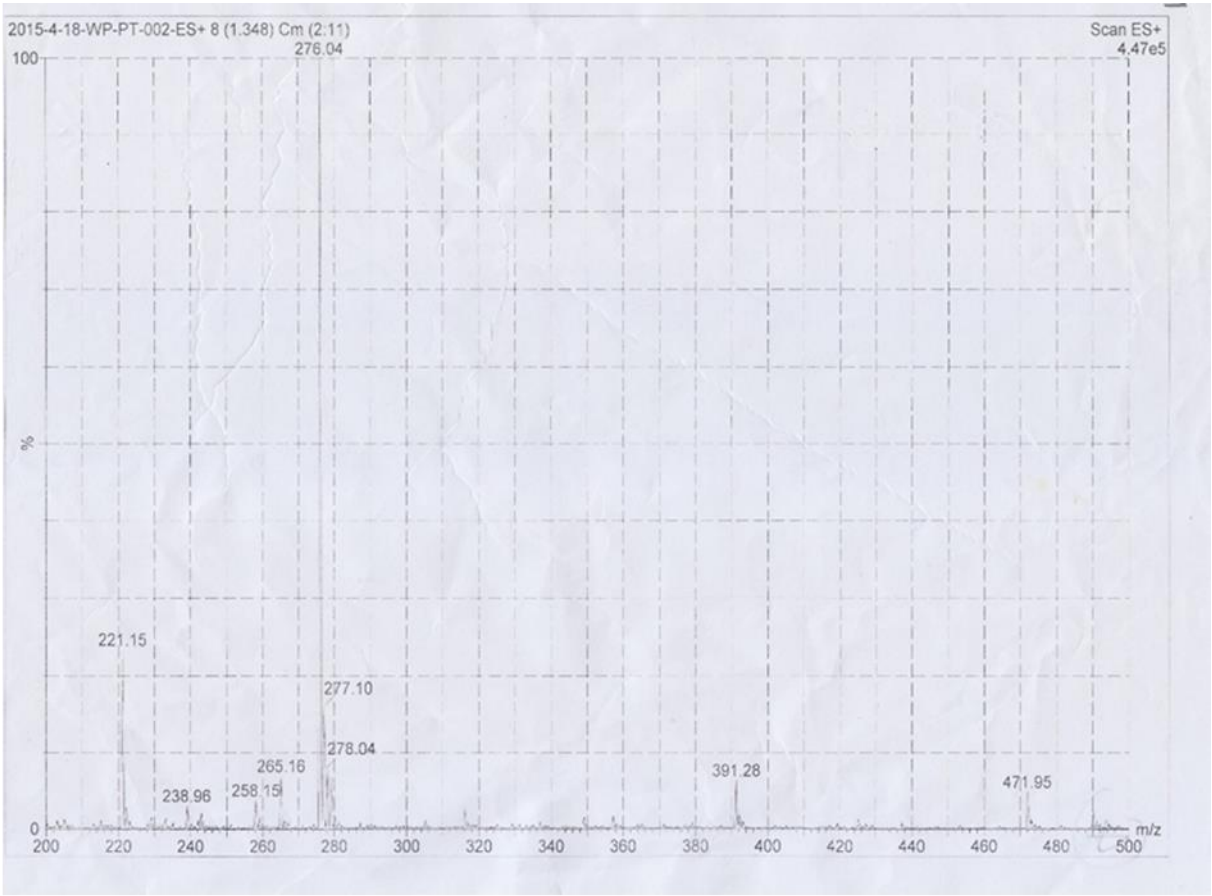


Figure A.6 Mass spectrum of thienyl-4-nitro-3-phenylbutan-1-one **(2)**

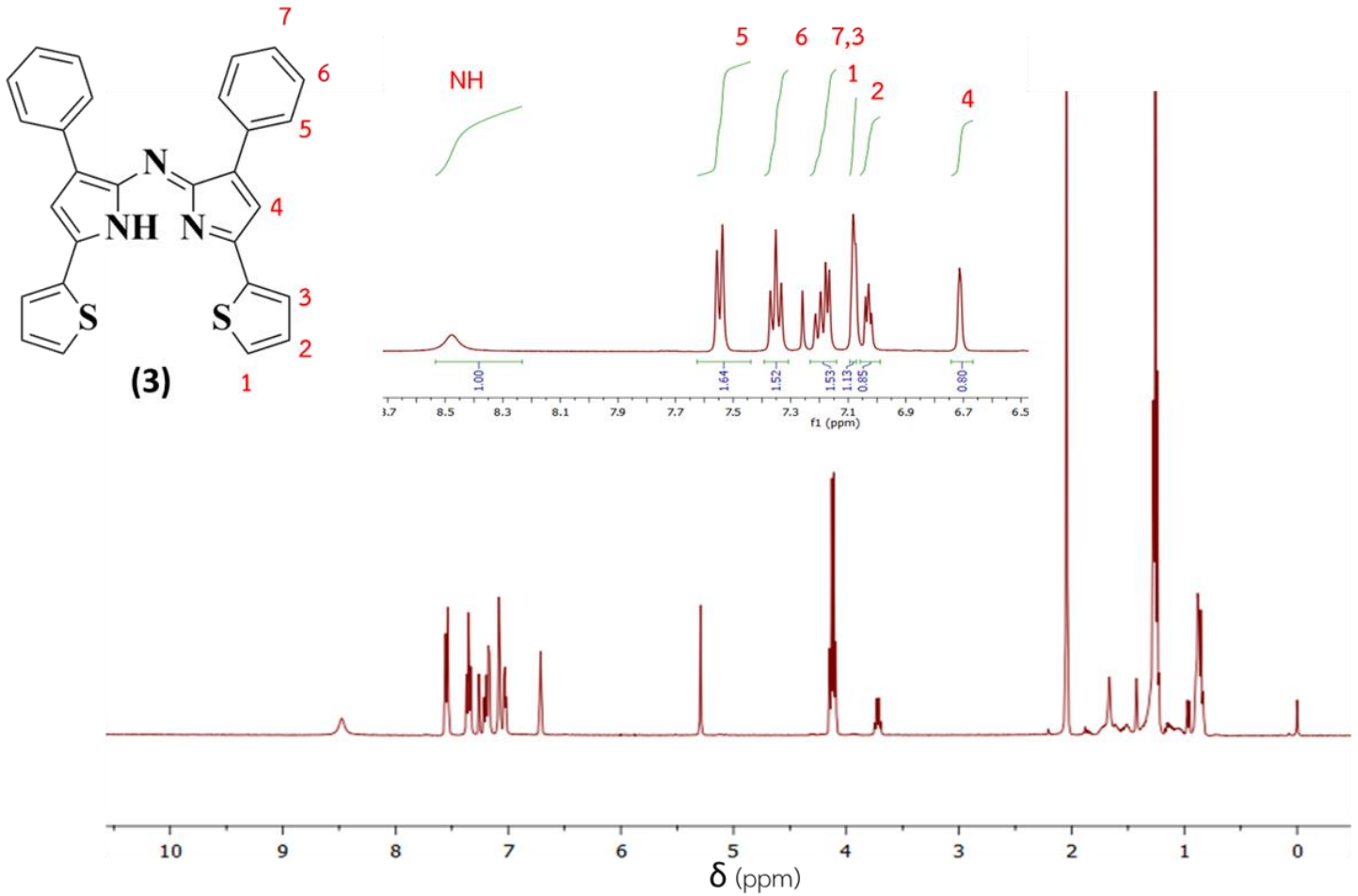


Figure A.7 ^{1}H NMR (Acetone-d_6) spectrum of dipyrromethene of **TPAB (3)**

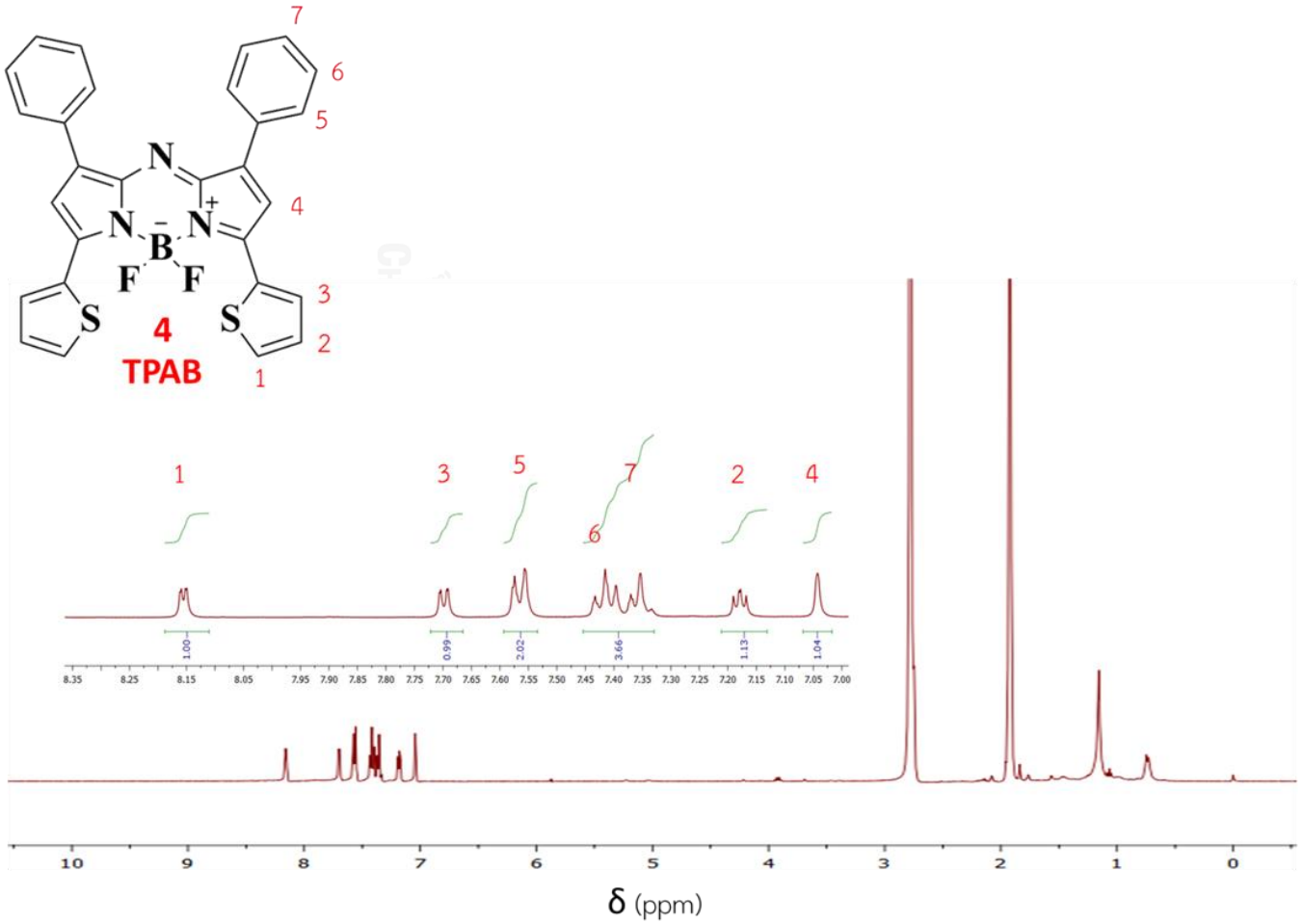


Figure A.8 ^{1}H NMR (Acetone-d_6) spectrum of thiophene phenyl aza-BODIPY **(4, TPAB)**

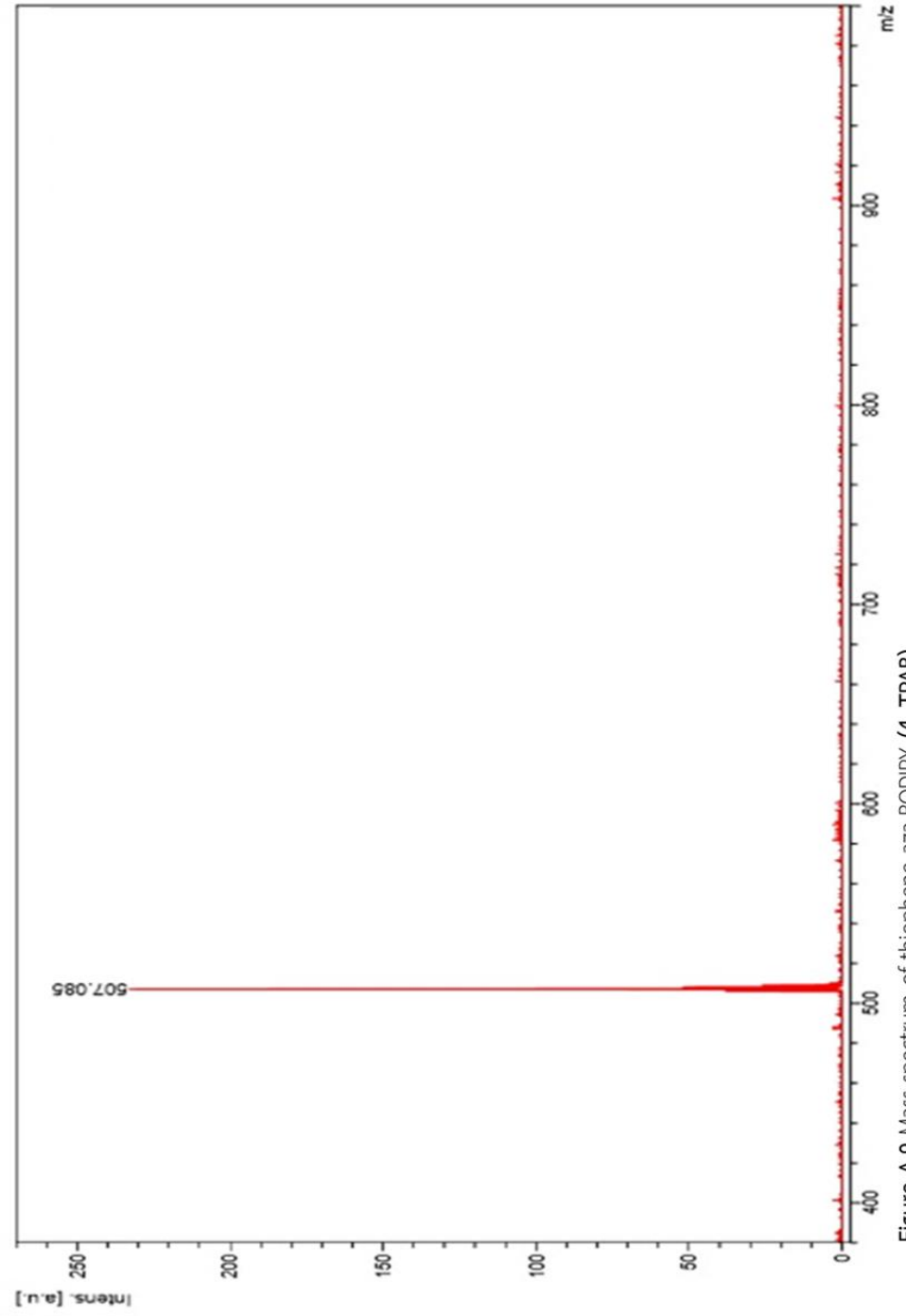


Figure A.9 Mass spectrum of thiophene aza-BODIPY (4, TPAB)

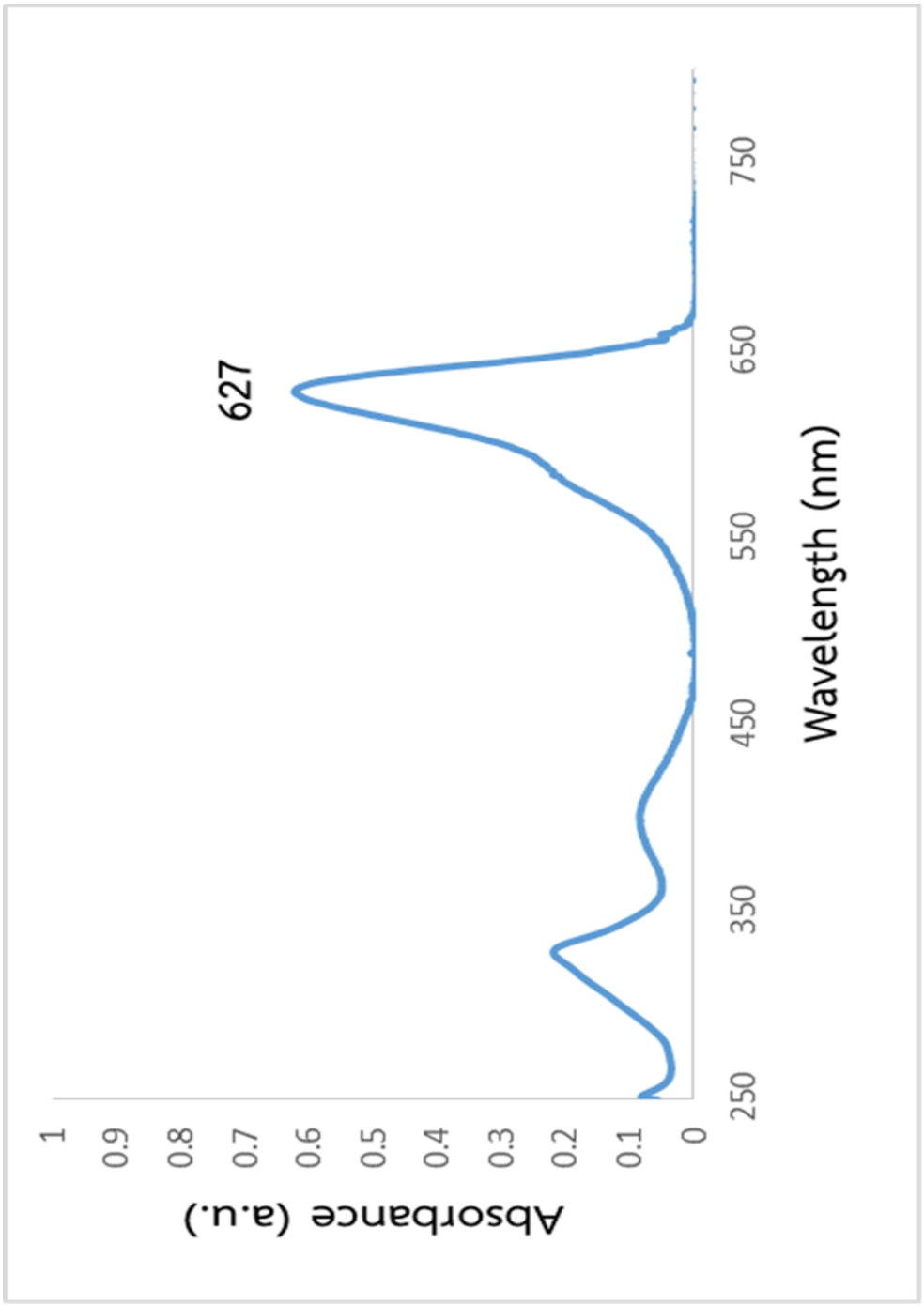


Figure A.10 UV-Visible spectrum of thiophene aza-BODIPY **(4, TPAB)**

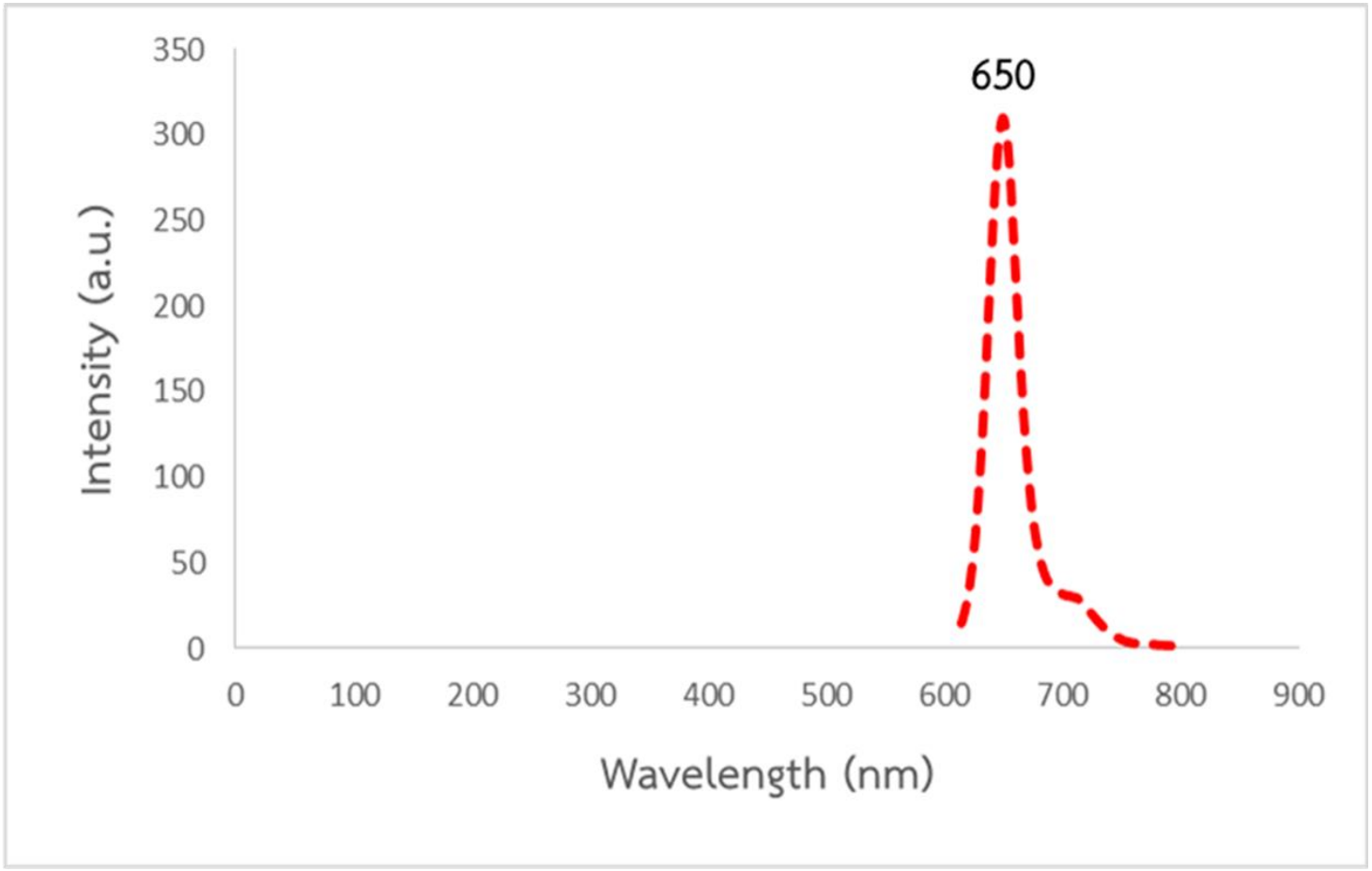


Figure A.11 Fluorescent spectrum of thiophene aza-BODIPY **(4, TPAB)**

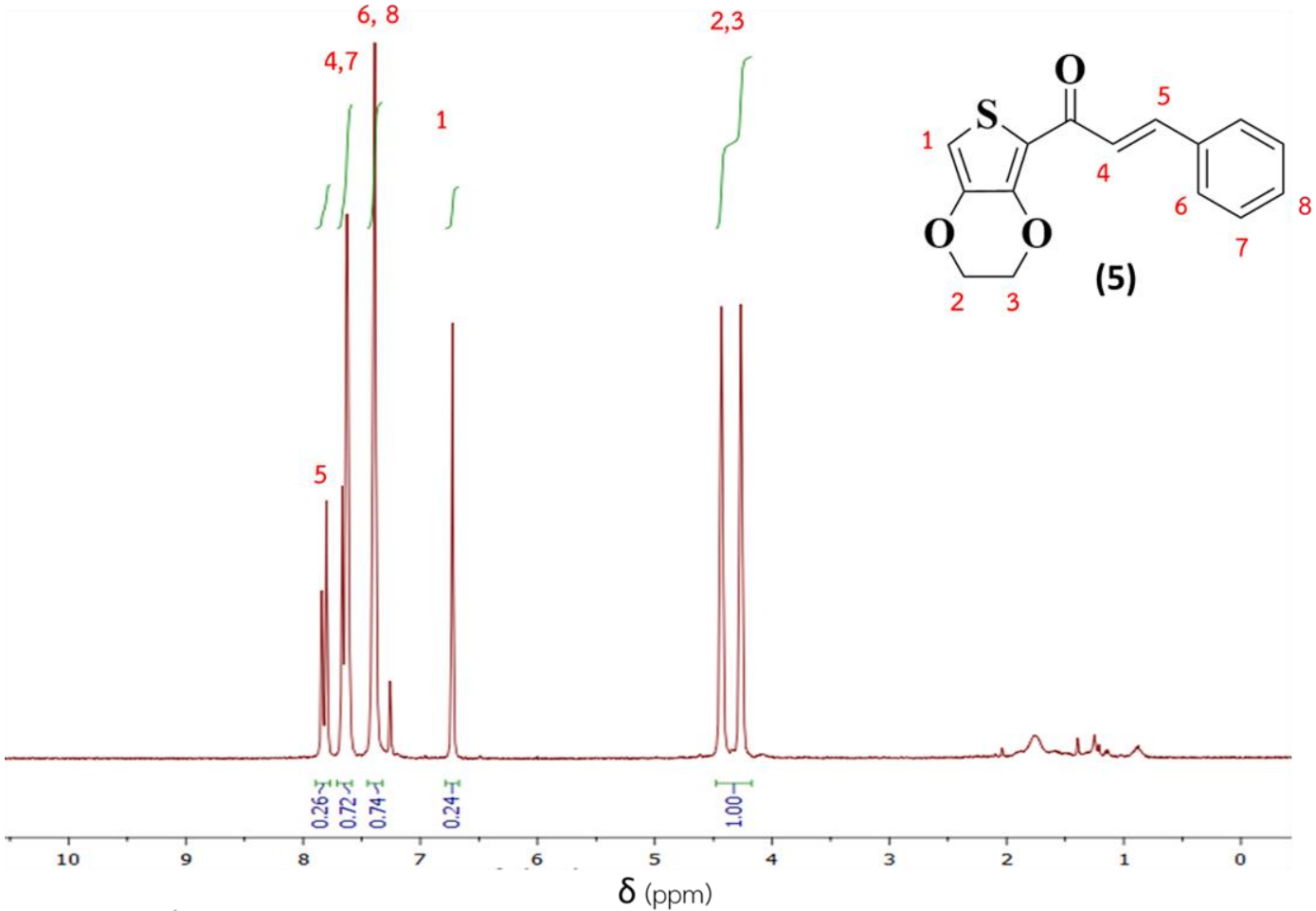


Figure A.12 ^{1}H NMR ($CDCl_3$) spectrum of 3',4'-ethylenedioxy thienyl-3-phenylprop-2-en-1-one **(5)**

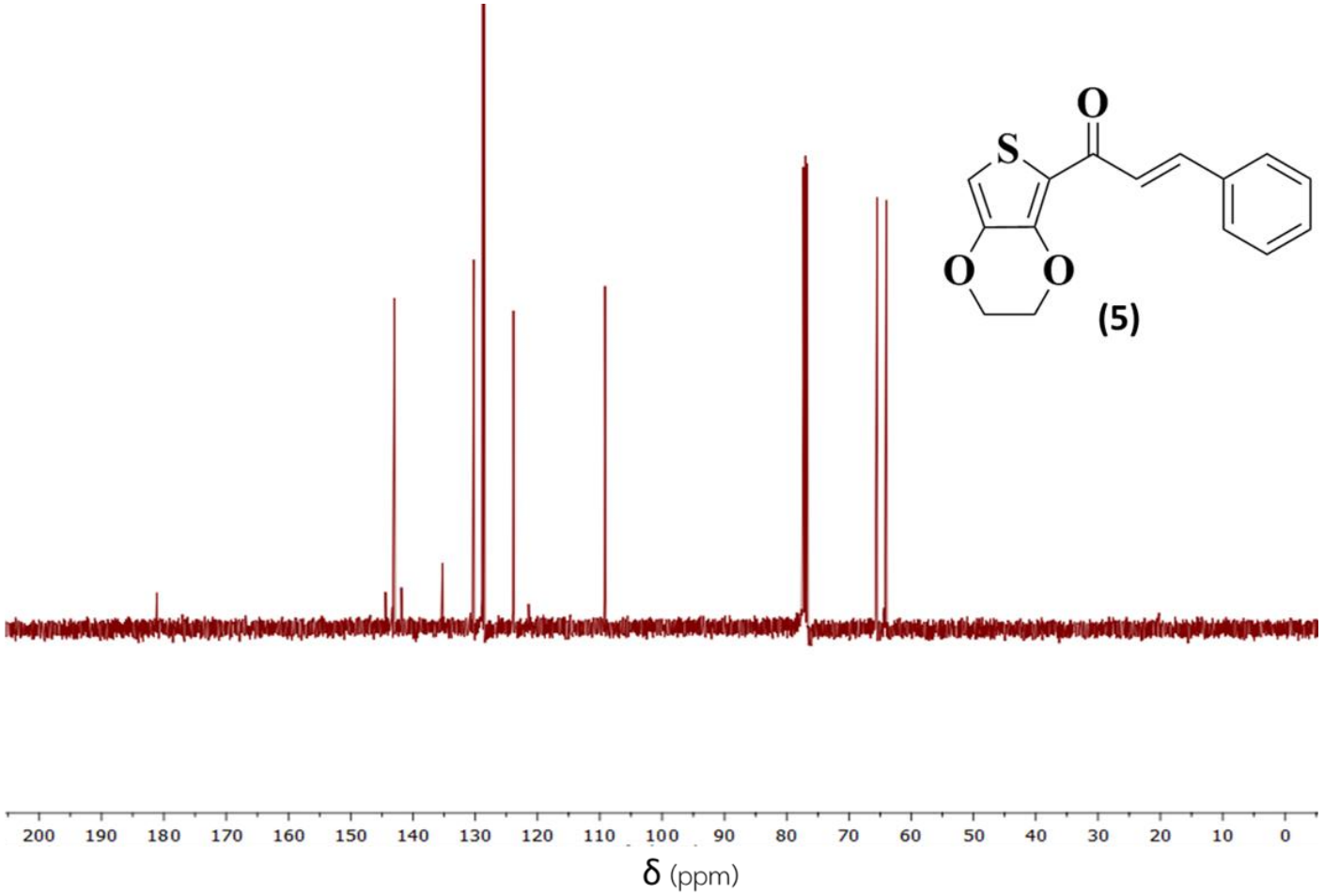


Figure A.13 ^{13}C NMR (Acetone-d6) spectrum of 3',4'-ethylenedioxy thienyl-3-phenylprop-2-en-1-one **(5)**

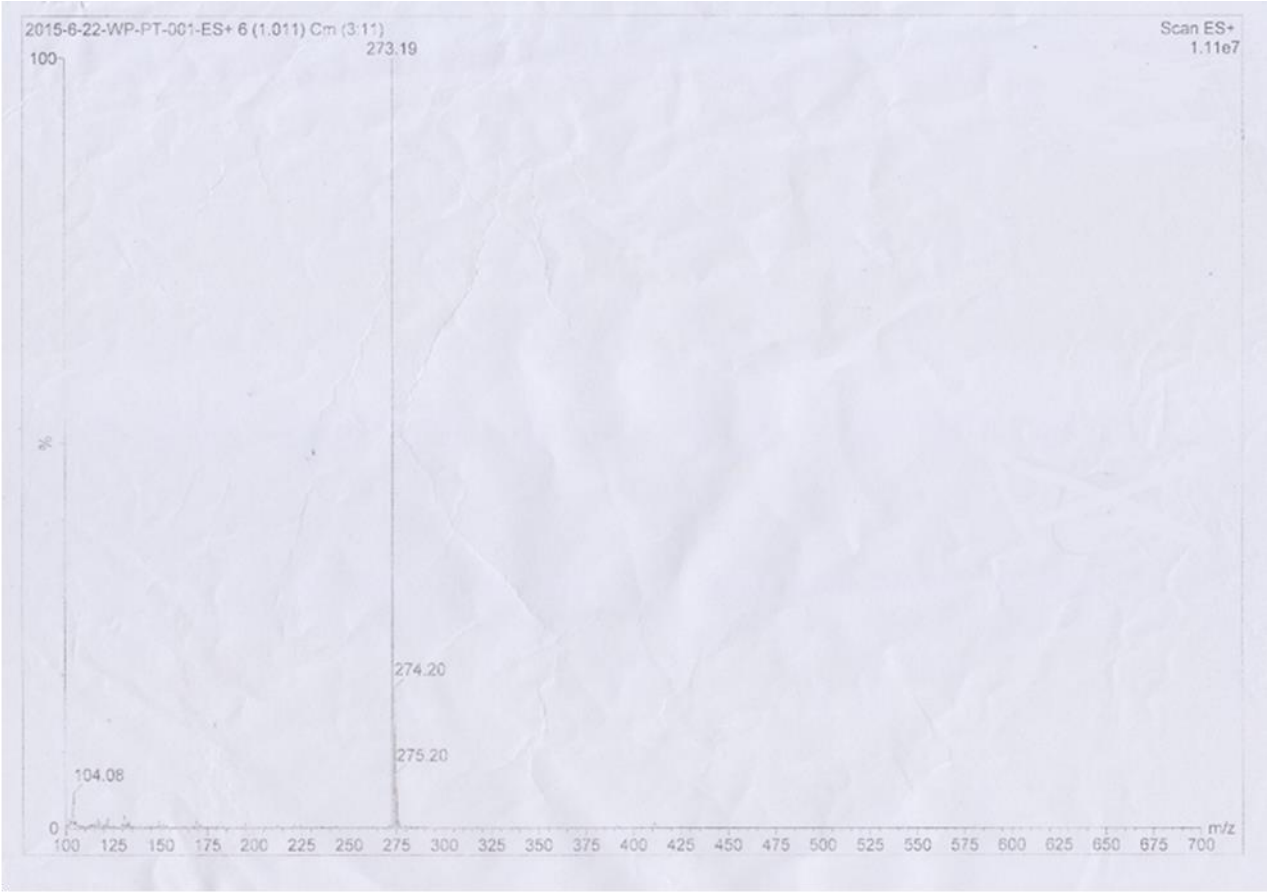


Figure A.14 Mass spectrum of 3',4'-ethylenedioxy thienyl-3-phenylprop-2-en-1-one **(5)**

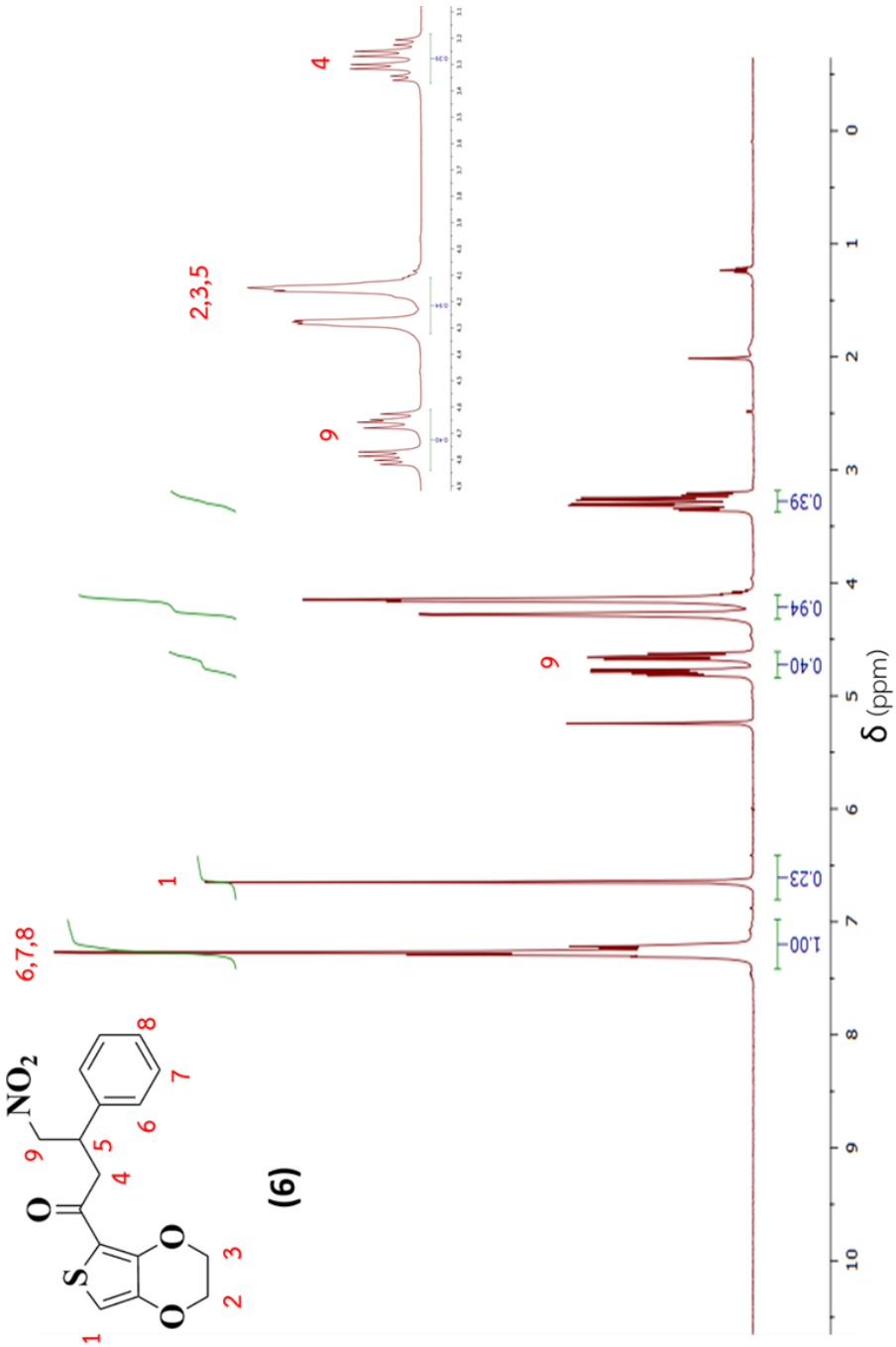


Figure A.15 ^{1}H NMR ($CDCl_3$) spectrum of 3',4'-ethylenedioxy thienyl-4-nitro-3-phenylbutan-1-one **(6)**

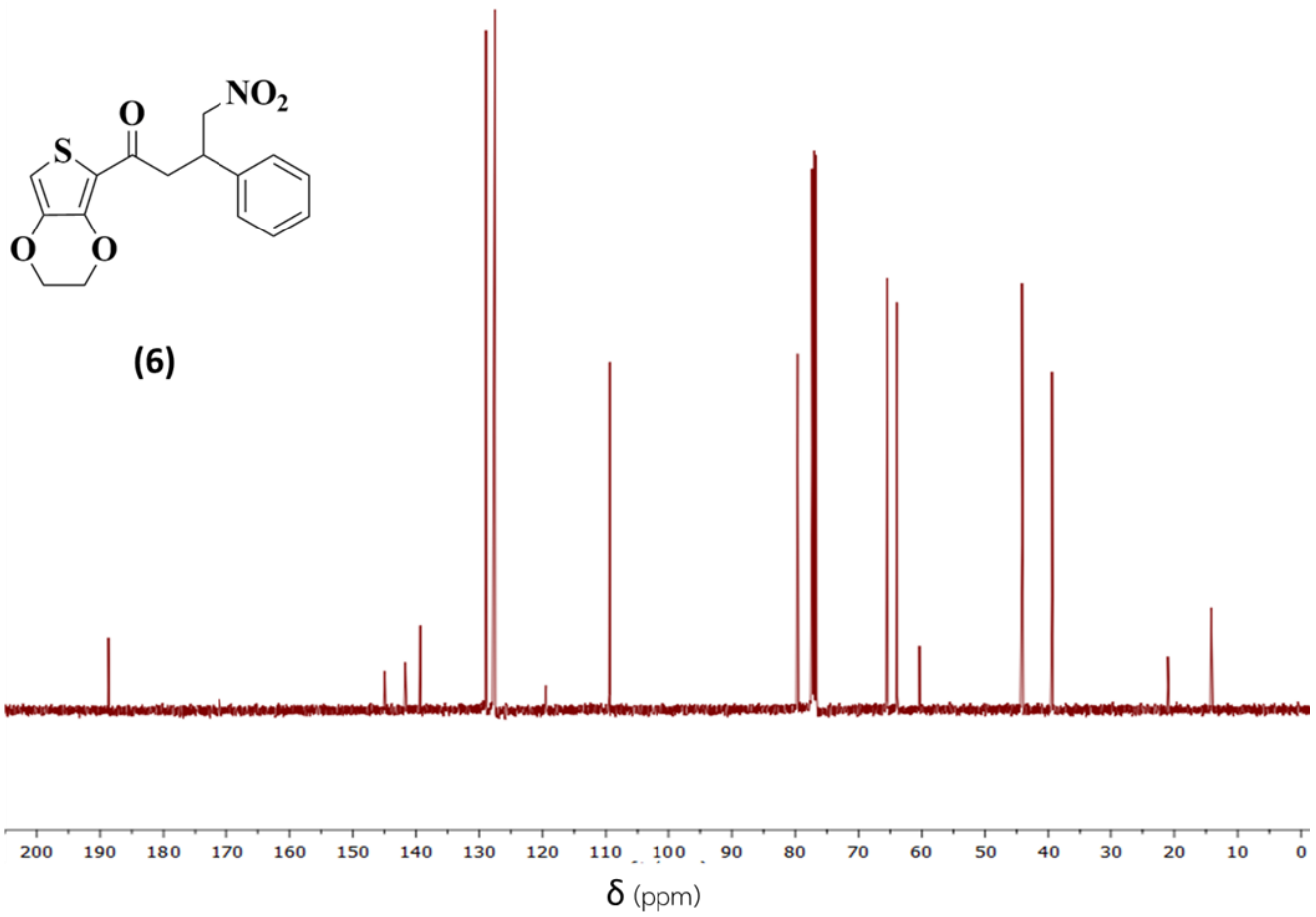


Figure A.16 ^{13}C NMR ($CDCl_3$) spectrum of 3',4'-ethylenedioxy thienyl-4-nitro-3-phenylbutan-1-one **(6)**

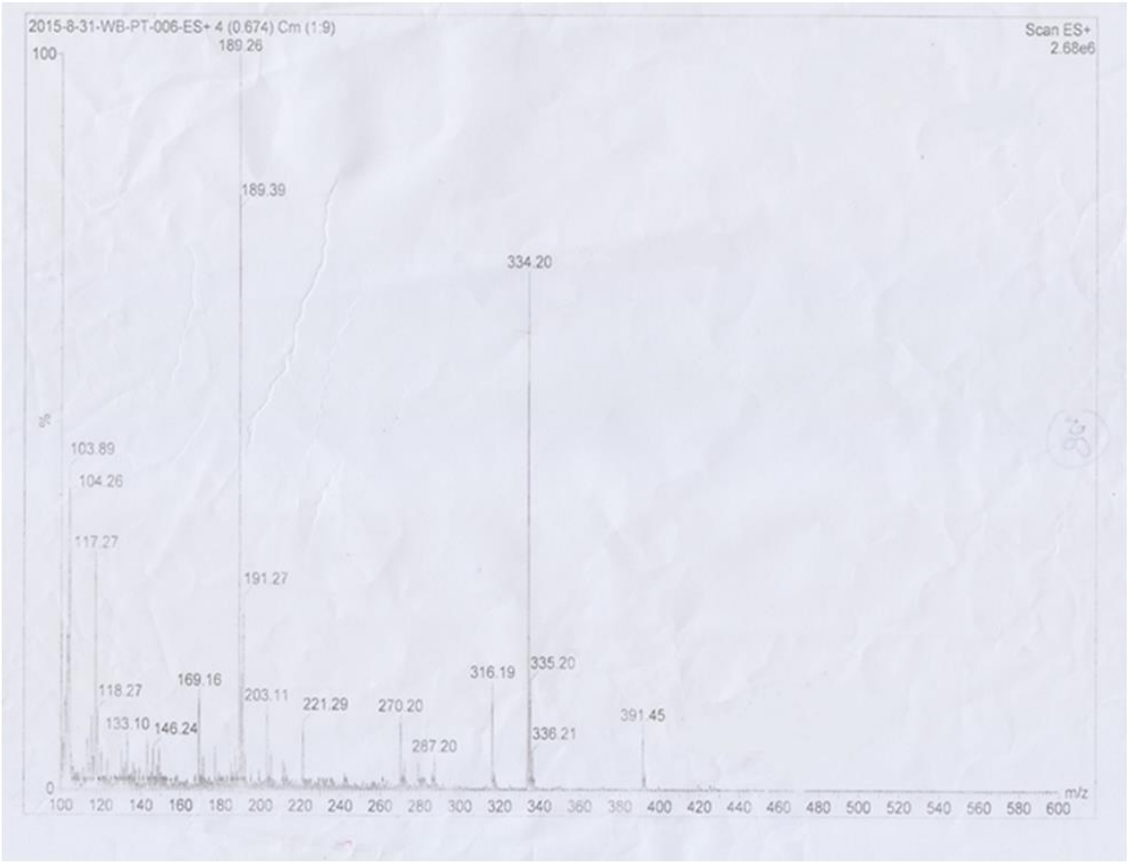


Figure A.17 Mass spectrum of 3',4'-ethylenedioxy thienyl-4-nitro-3-phenylbutan-1-one **(6)**

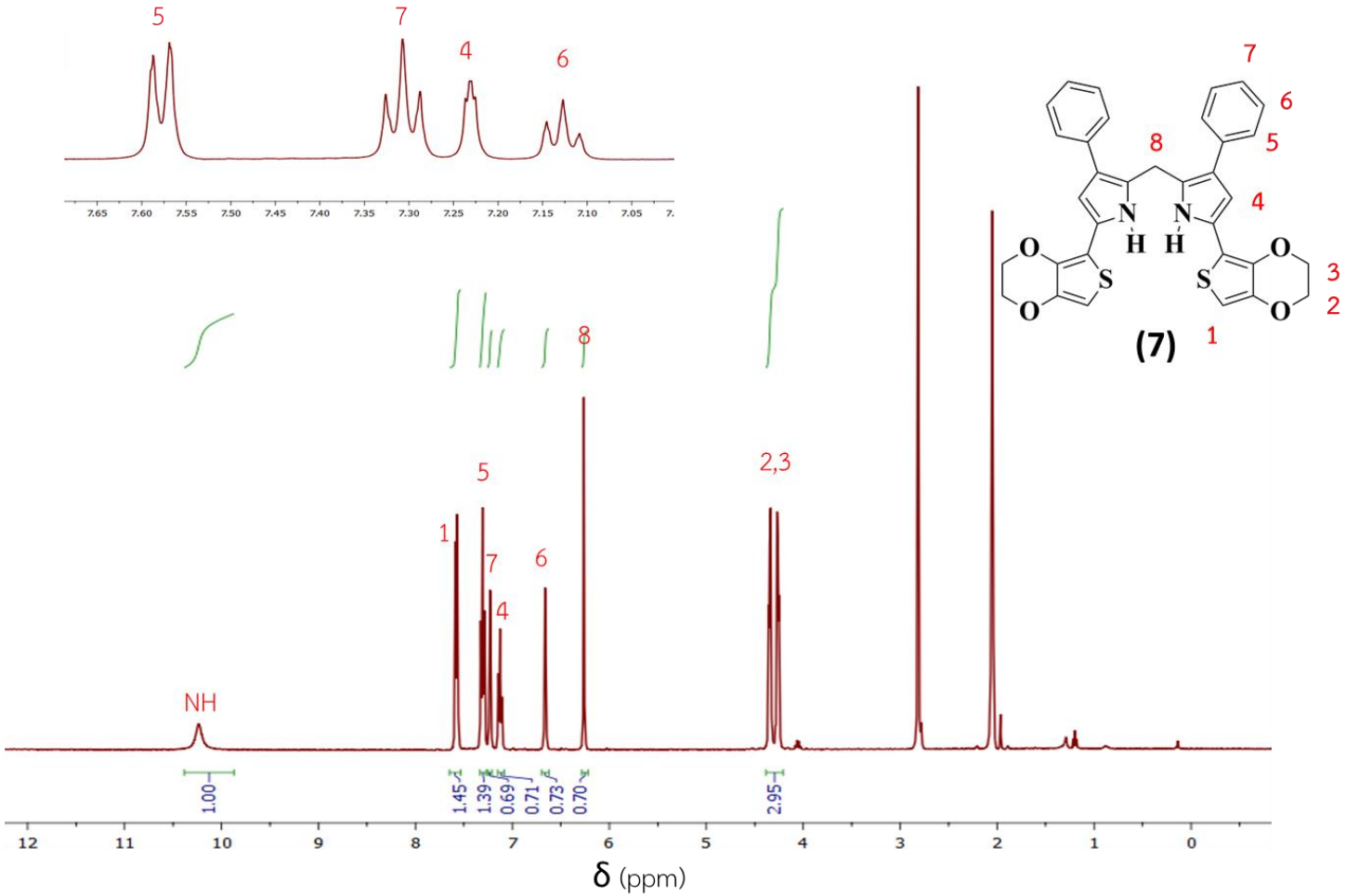


Figure A.18 ^{1}H NMR (Acetone-d_6) spectrum of Dipyrromethene form of **EPB (7)**

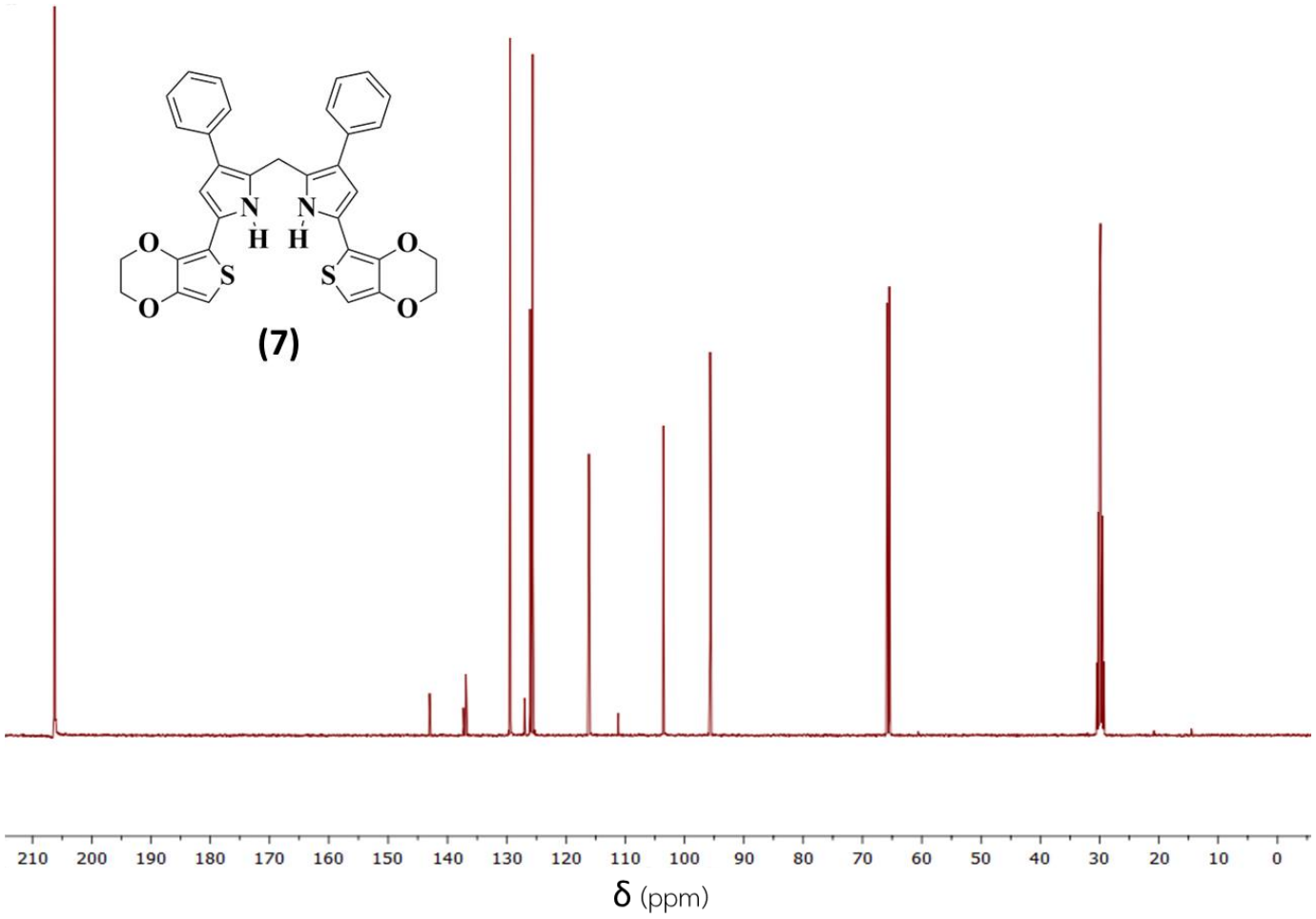


Figure A.19 ^{13}C NMR (Acetone-d_6) spectrum of Dipyrromethene form of **EPB (7)**

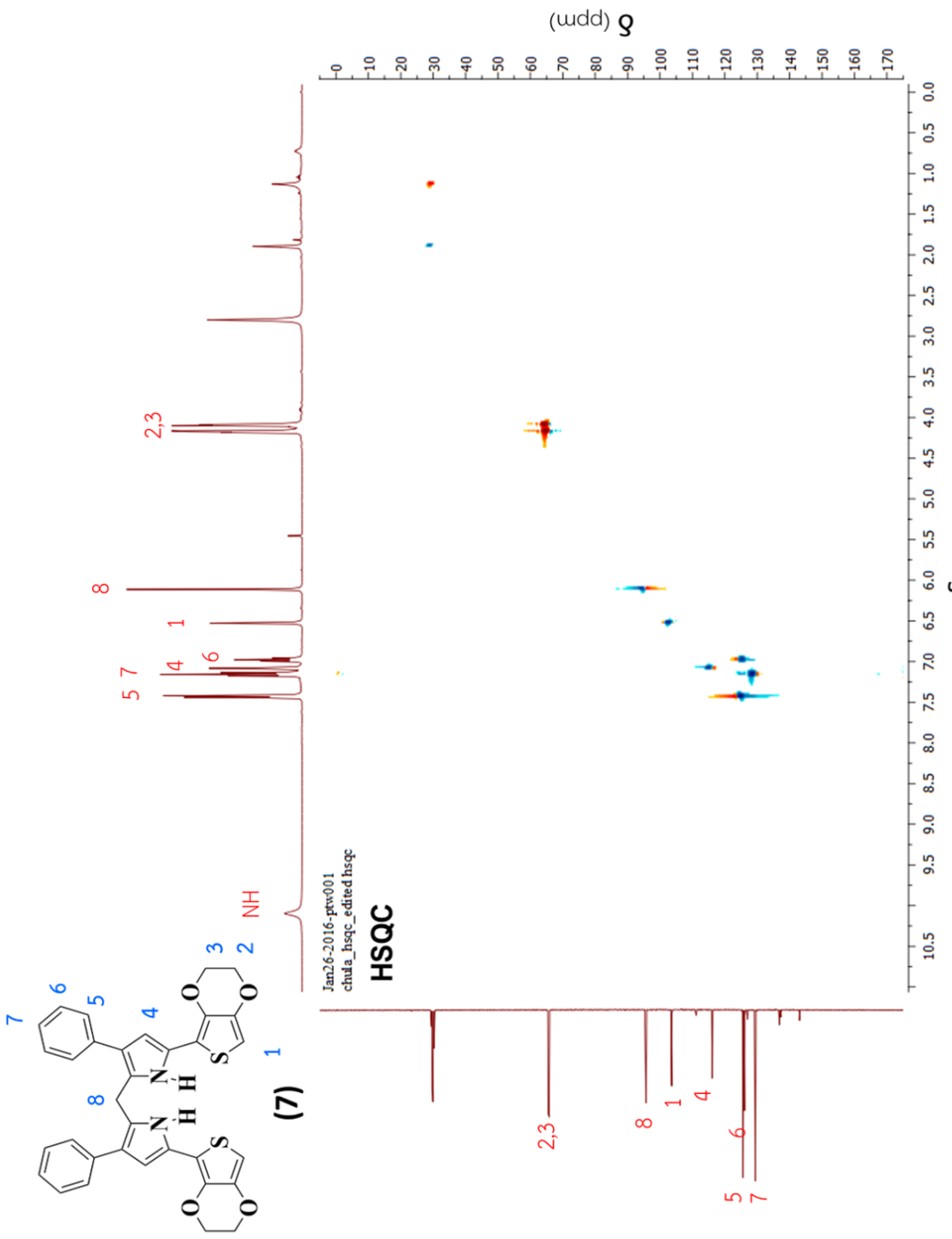


Figure A.20 HSQC spectrum of Dipyrromethene form of **EPB (7)**

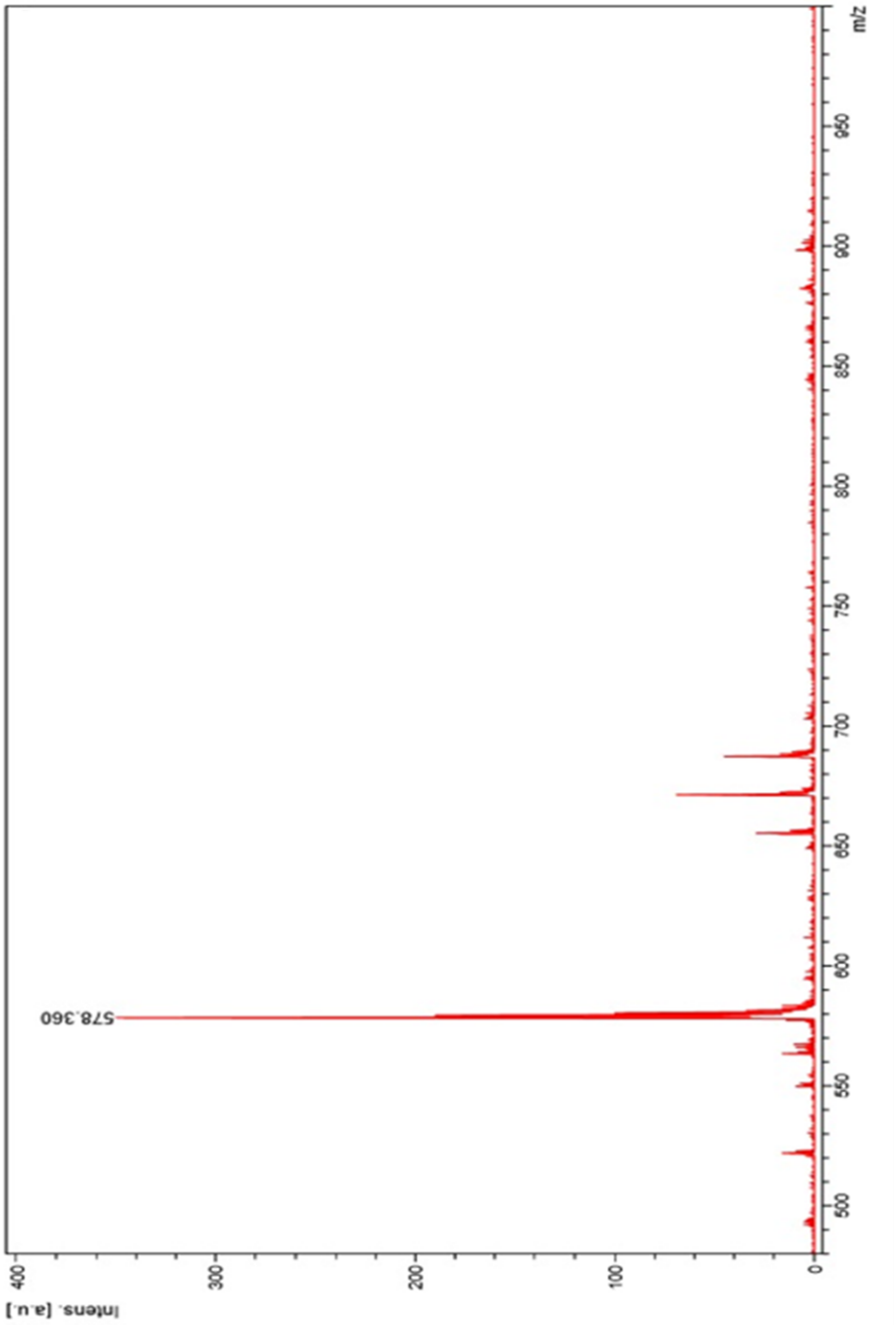


Figure A.21 Mass spectrum of Dipyrromethene form of **EPB (7)**

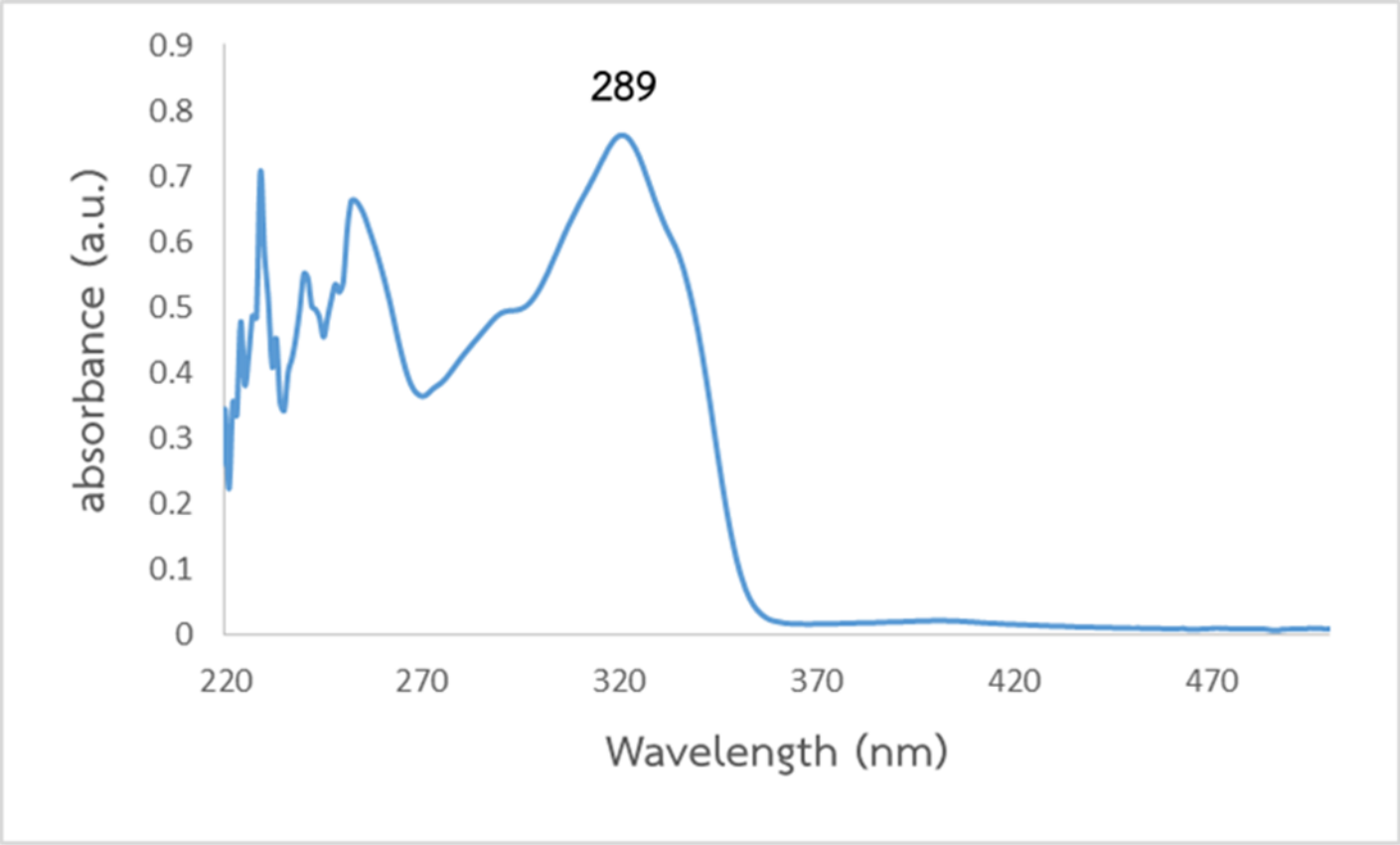


Figure A.22 The UV-Visible spectrum of Dipyrromethene form of **EPB (7)**

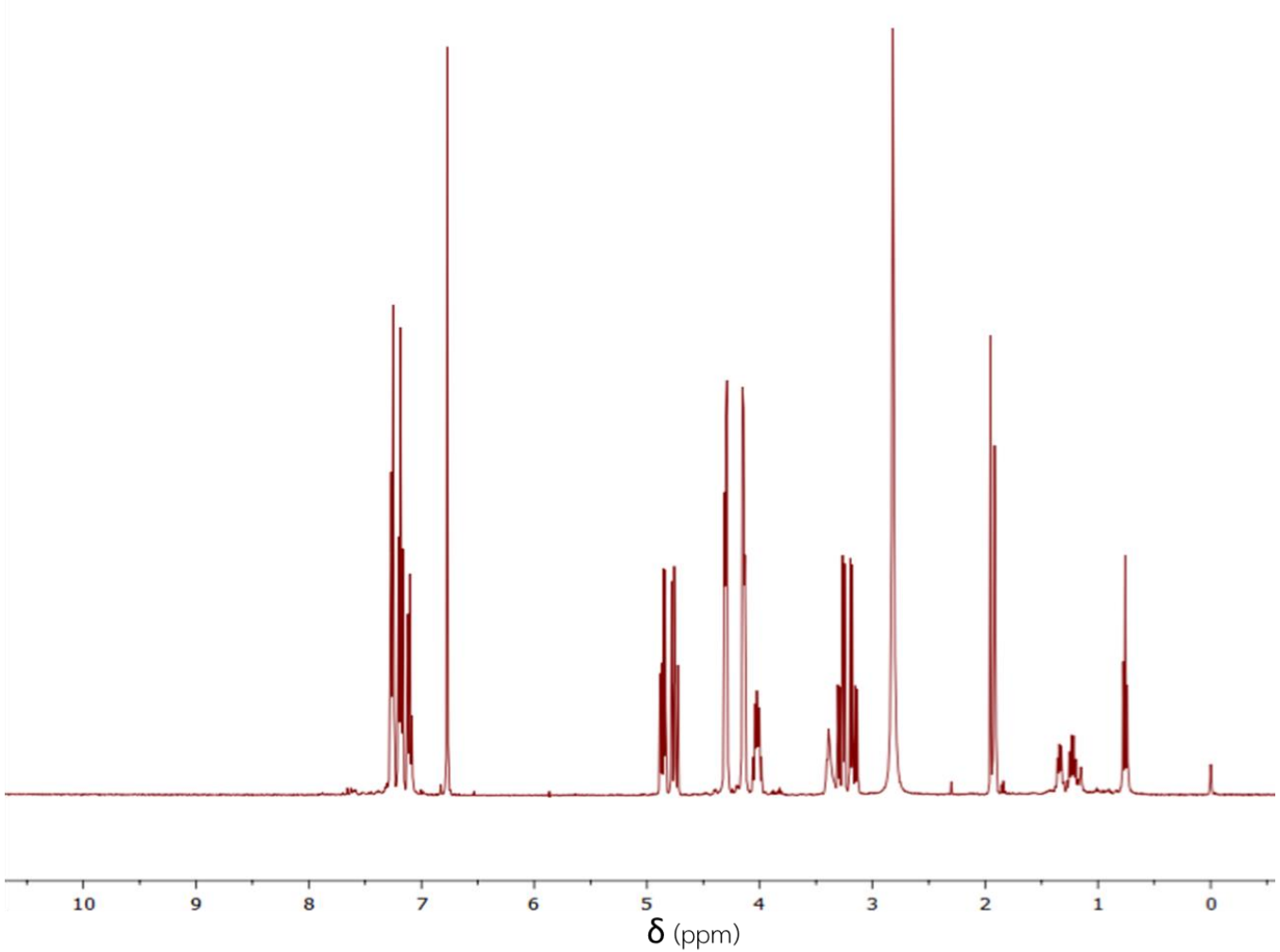


Figure A.23 ^{1}H NMR ($CDCl_3$) spectrum of product mixture from model reaction 1

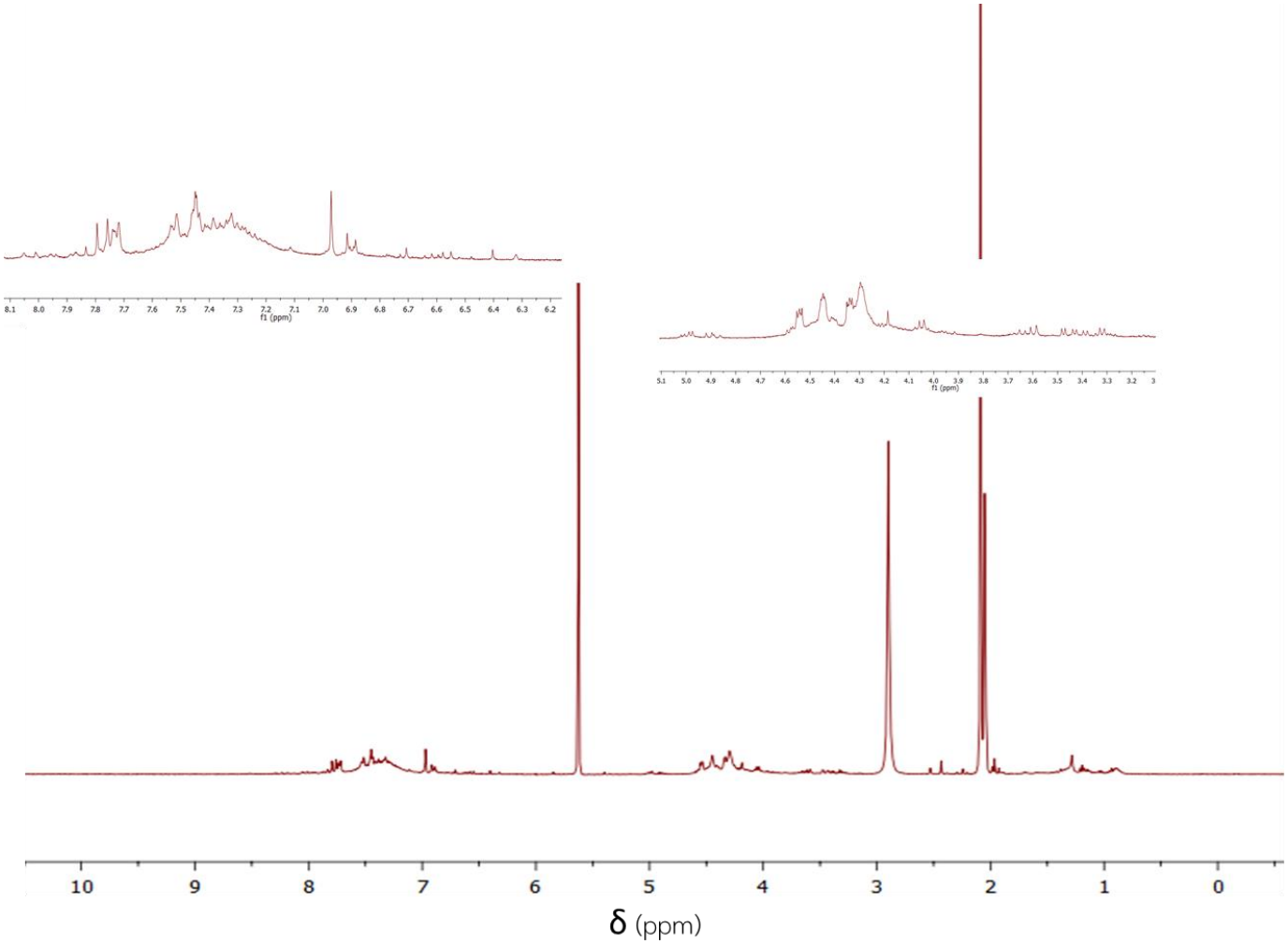


Figure A.24 ^{1}H NMR ($CDCl^{3}$) spectrum of product mixture from model reaction 3

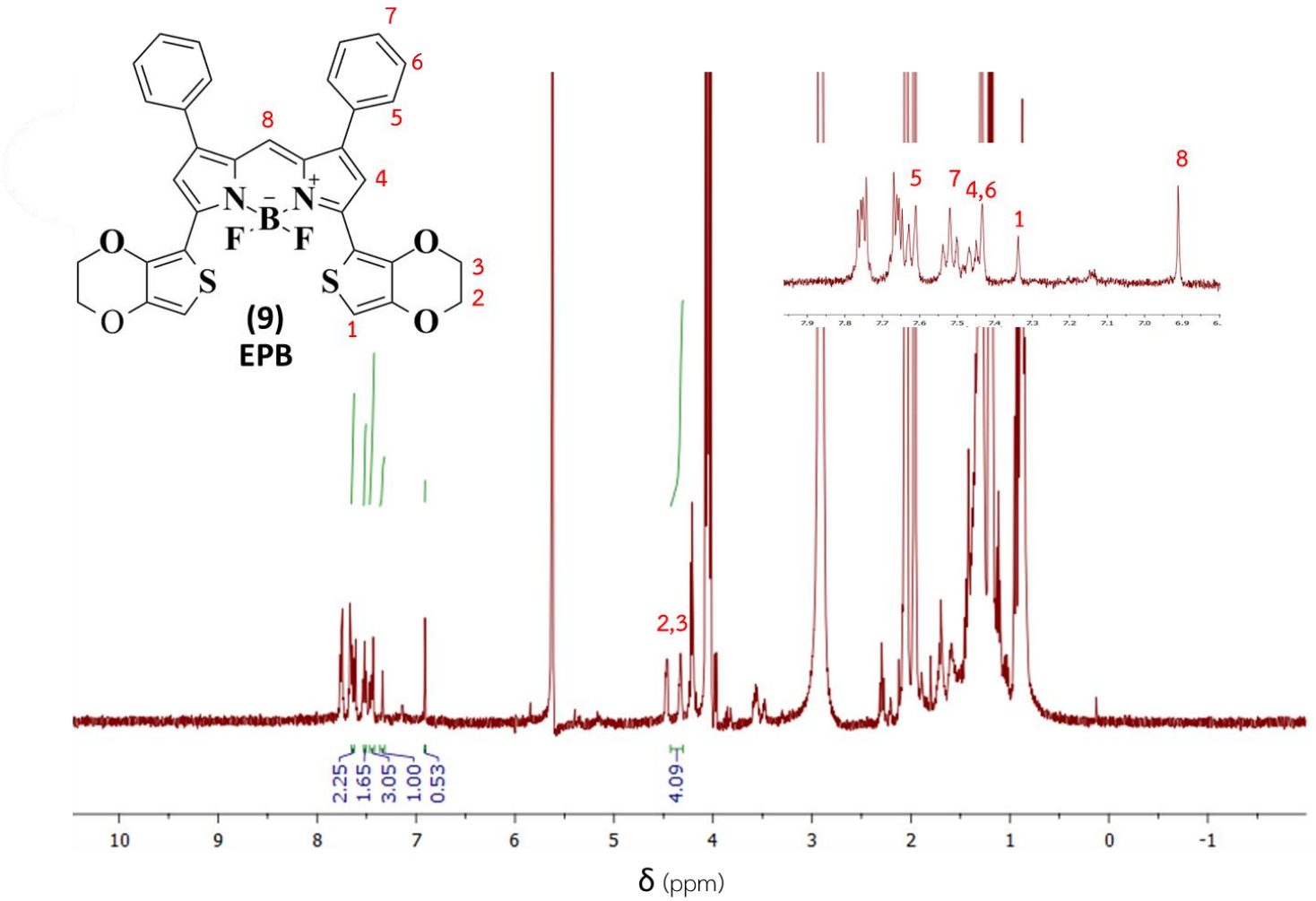


Figure A.25 ^{1}H NMR (Acetone-d_6) spectrum of EDOT phenyl-BODIPY **(EPB)**

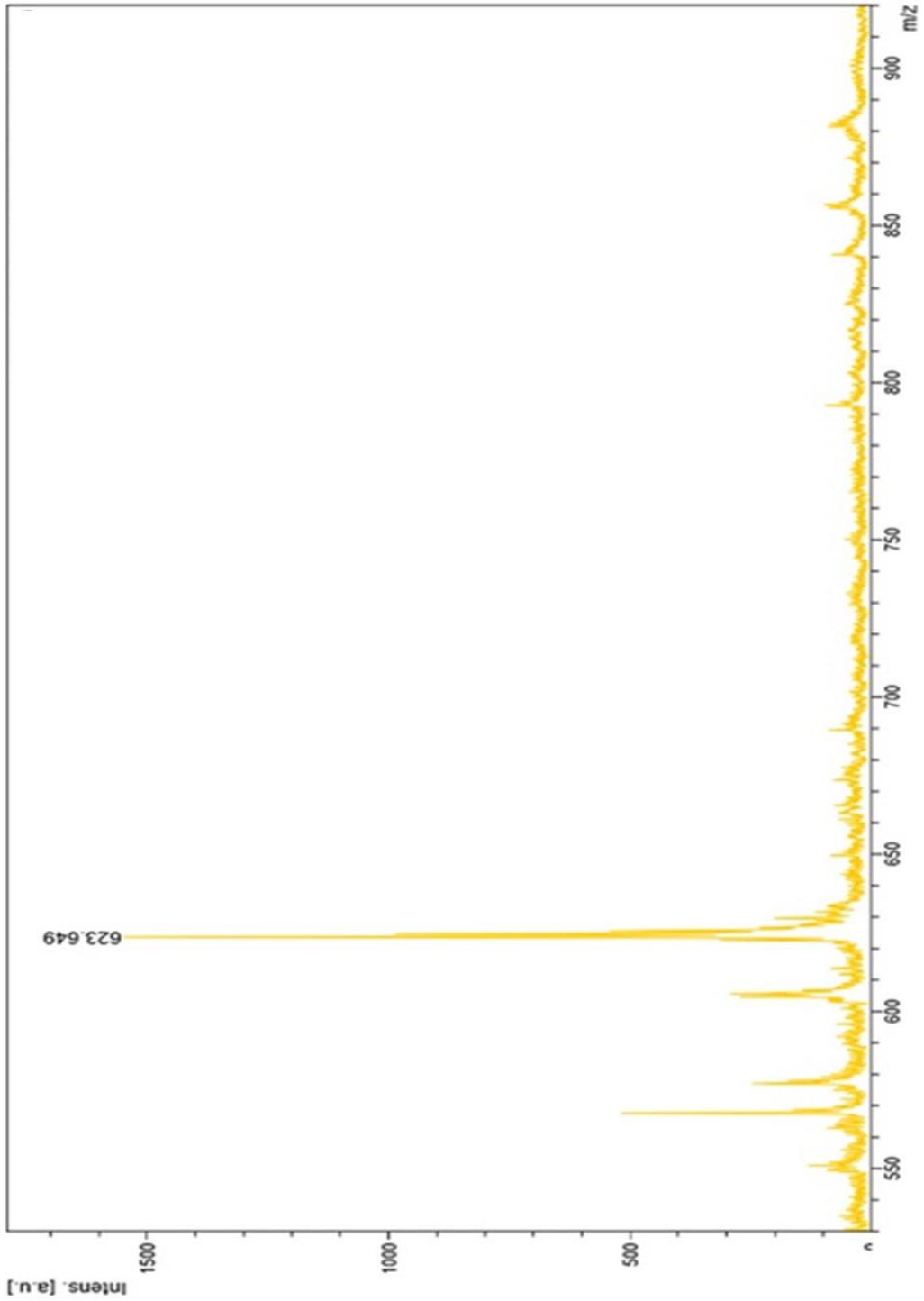


Figure A.26 Mass spectrum of EDOT phenyl BODIPY **(EPB)**

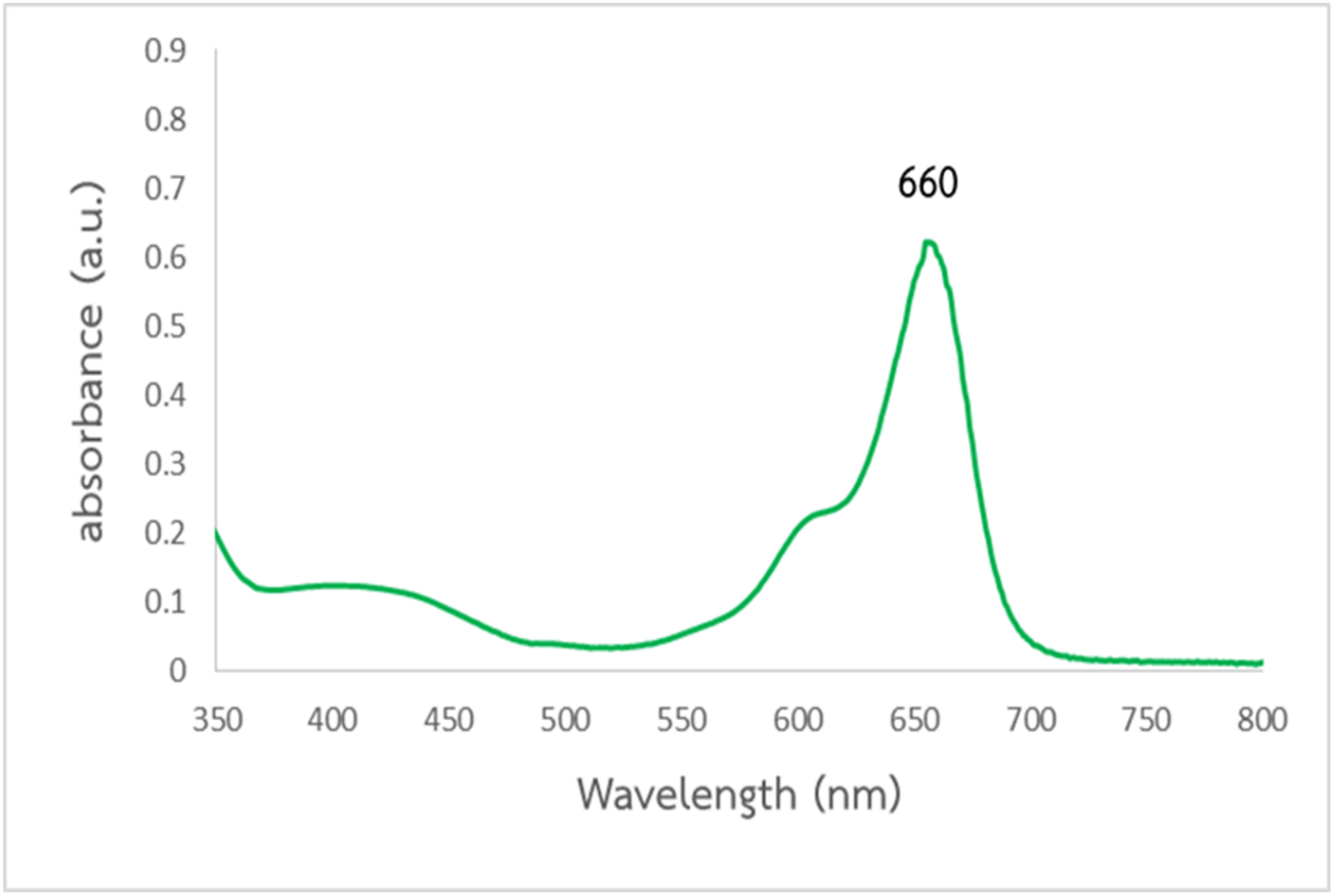


Figure A.27 The UV-Visible spectrum of EDOT phenyl-BODIPY **(EPB)**

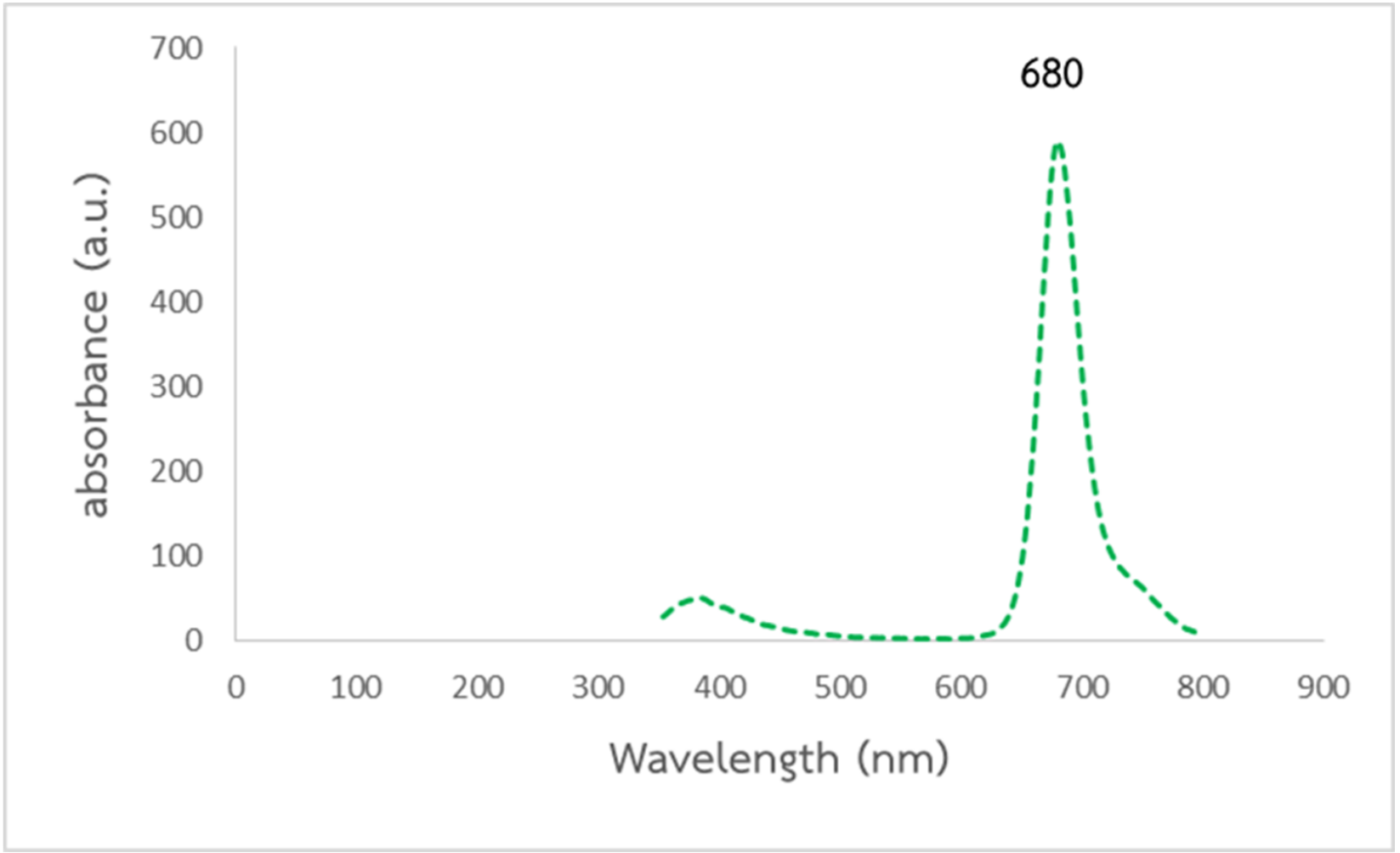


Figure A.28 The fluorescent spectrum of EDOT-phenyl BODIPY **(EPB)**

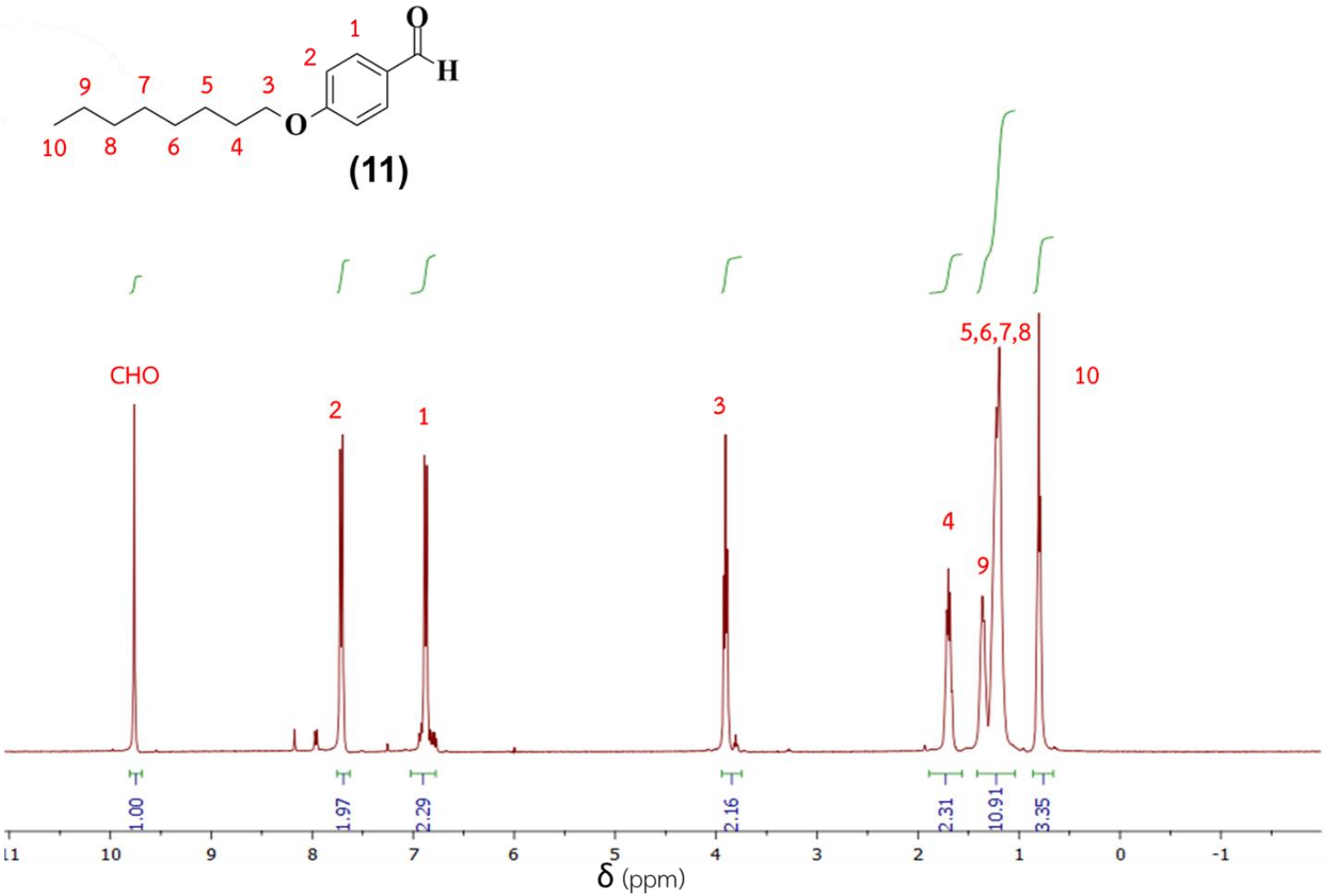


Figure A.29 ^{1}H NMR ($CDCl_3$) spectrum of 4-(octoxy)benzaldehyde **(11)**

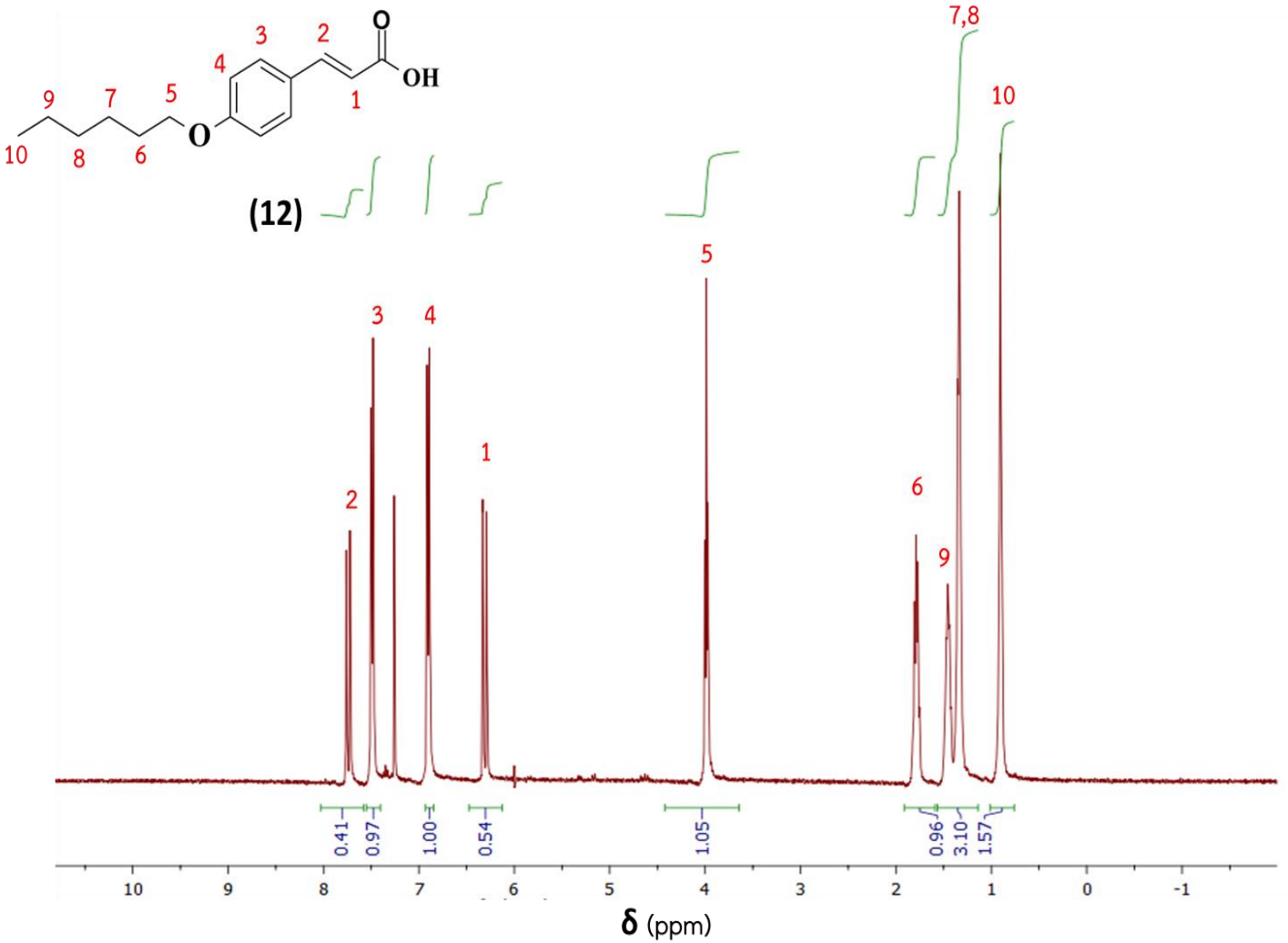


Figure A.30 ^{1}H NMR ($CDCl_3$) spectrum of 4-(hexyloxy)prop-2enoic acid **(12)**

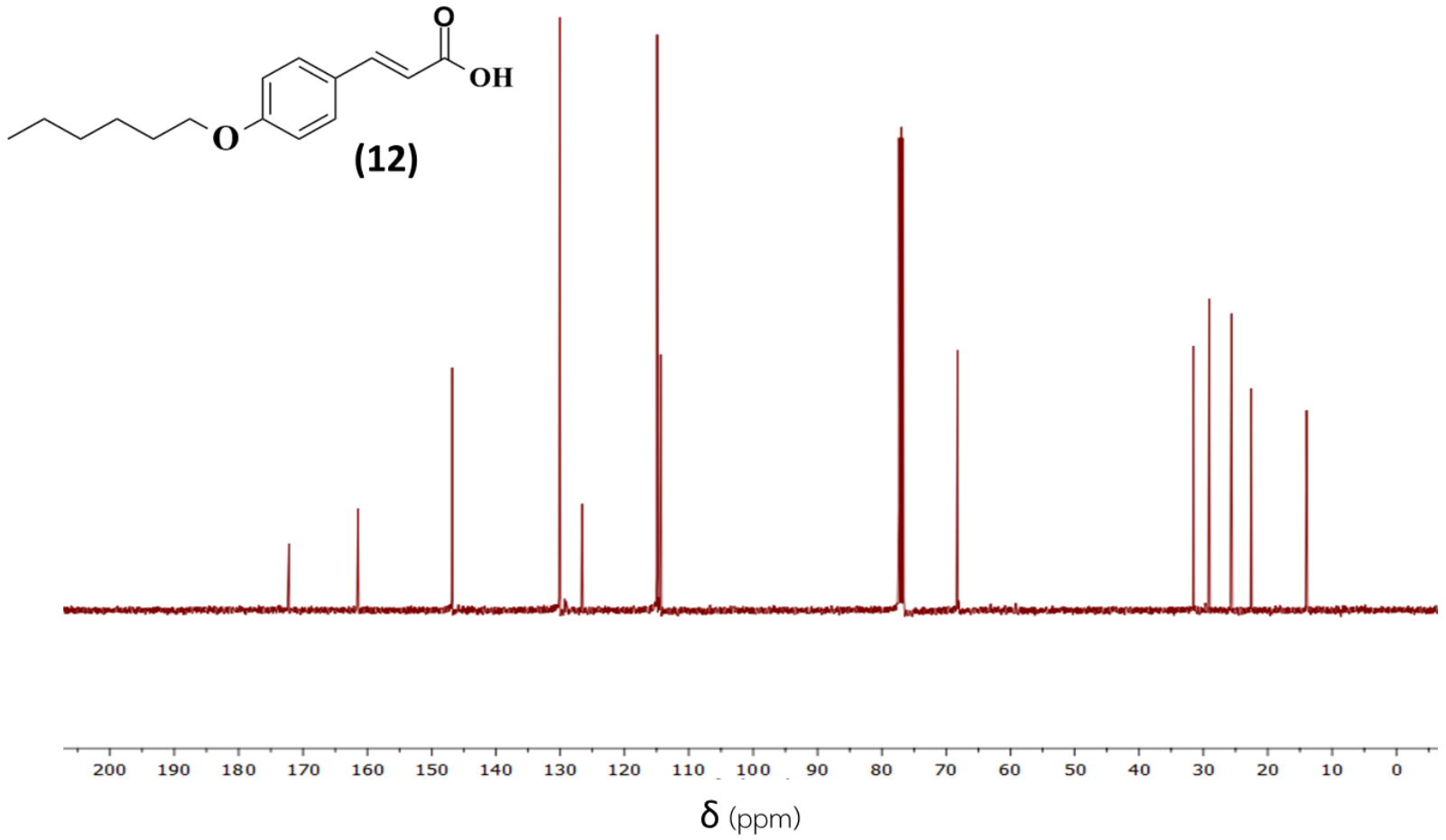


Figure A.31 ^{13}C NMR ($CDCl_3$) spectrum of 4-(hexyloxy)prop-2-enoic acid **(12)**

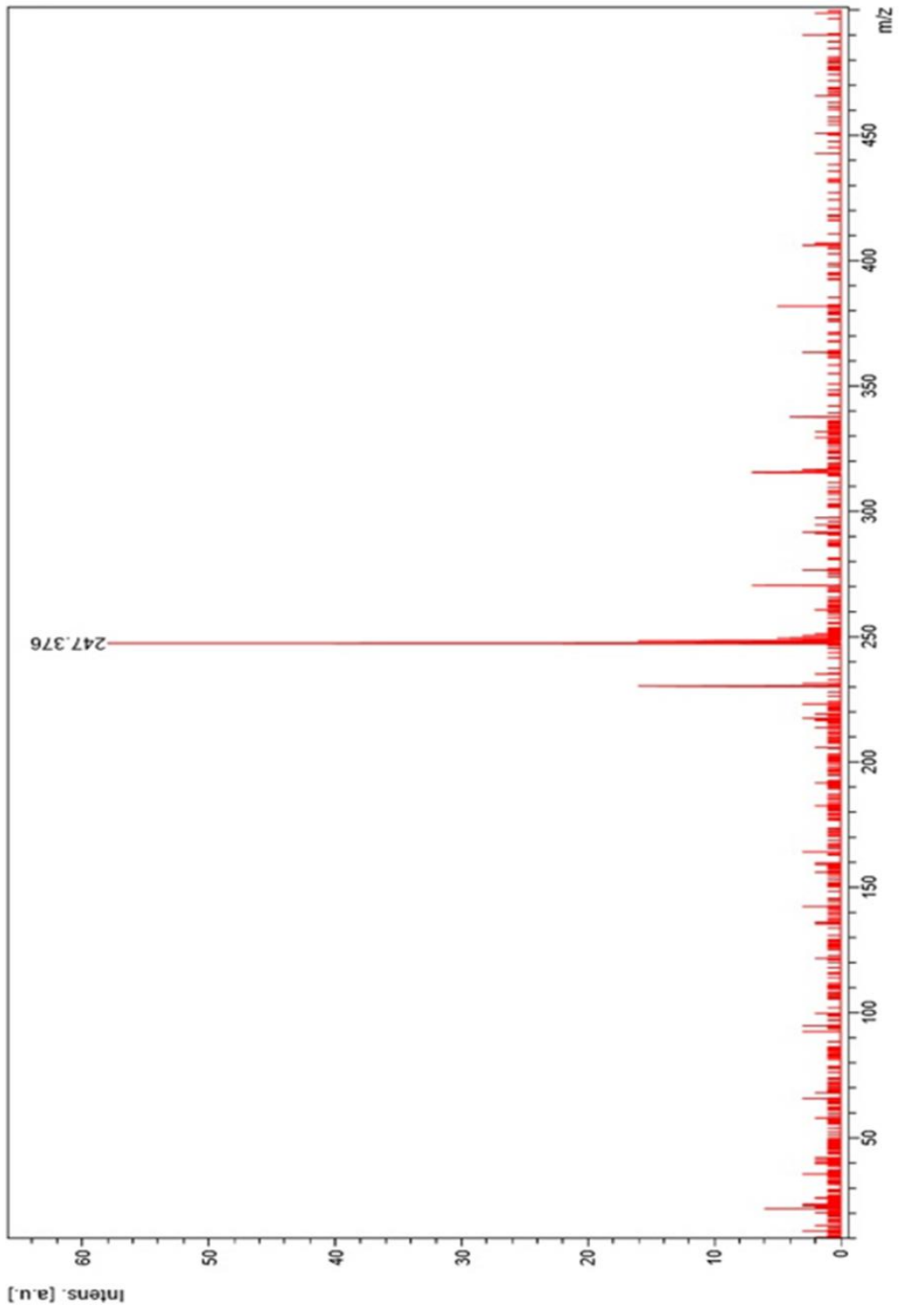


Figure A.32 Mass spectrum of 4-(hexyloxy)prop-2enoic acid **(12)**

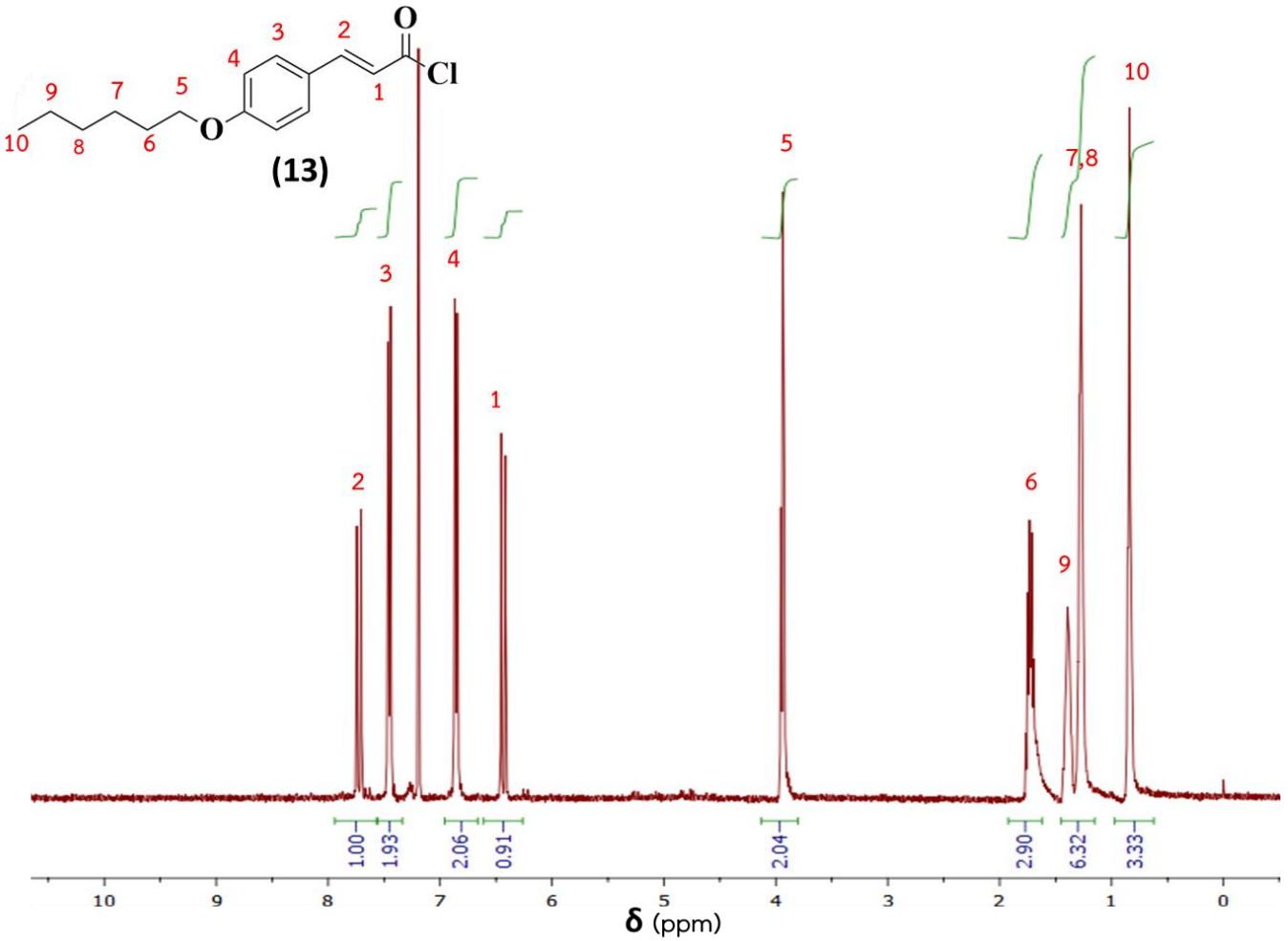


Figure A.33 ^{1}H NMR ($CDCl_3$) spectrum of compound **13**

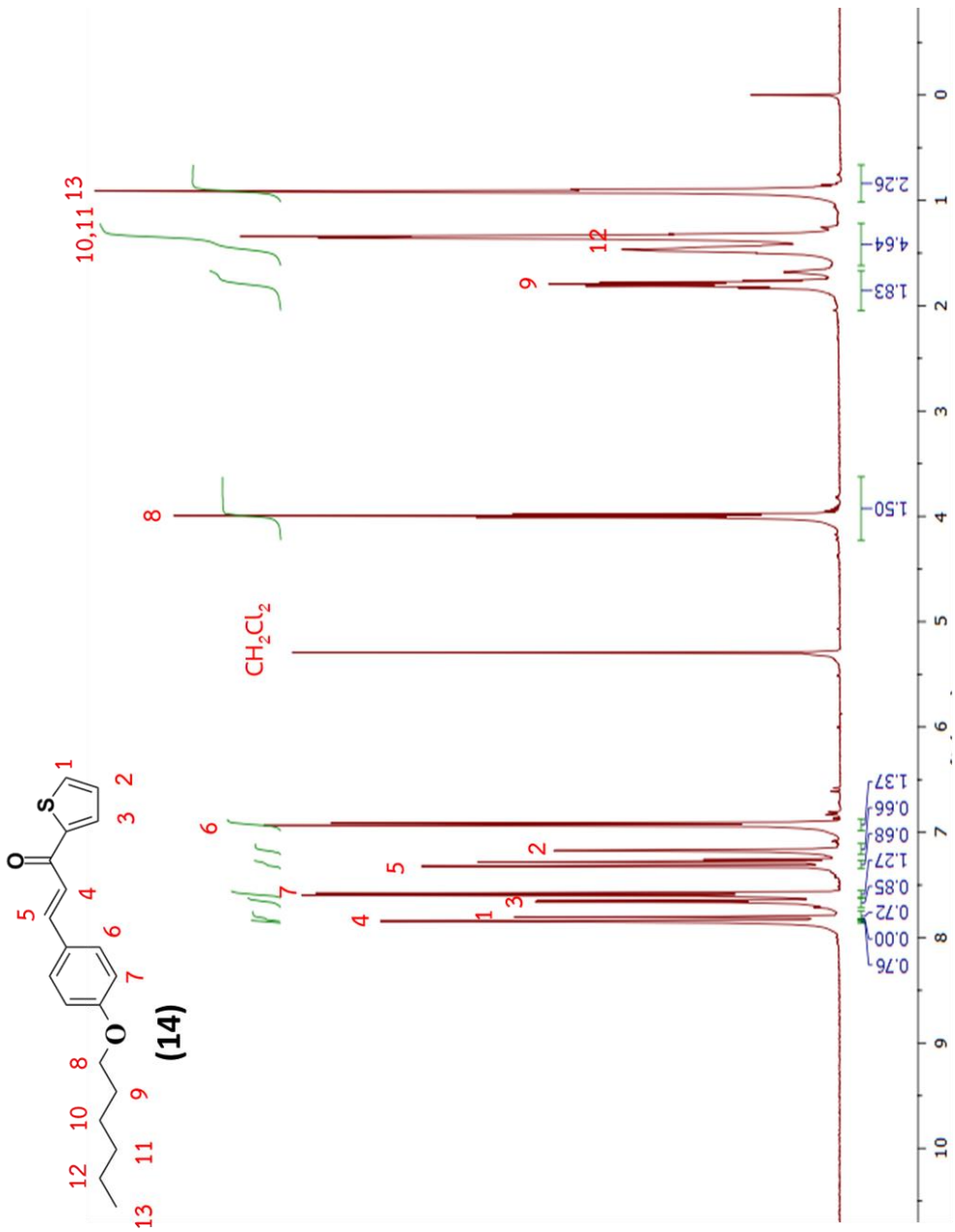


Figure A.34 ^{1}H NMR ($CDCl_3$) spectrum of thienyl-3-4-(hexyloxy)phenylprop-2-en-1-one **(14)**

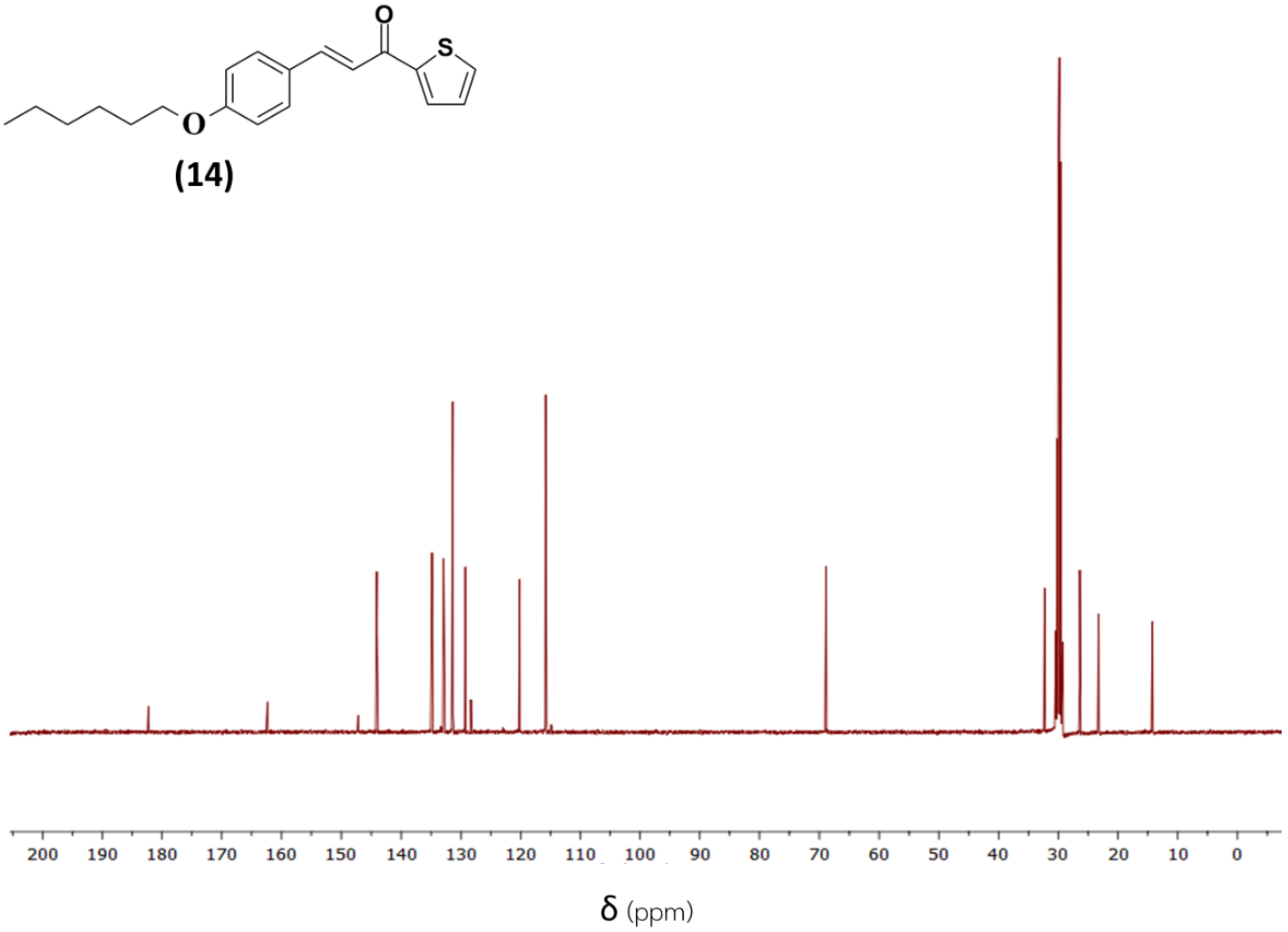


Figure A.35 ^{13}C NMR ($CDCl_3$) spectrum of thienyl-3-4-(hexyloxy)phenylprop-2-en-1-one **(14)**

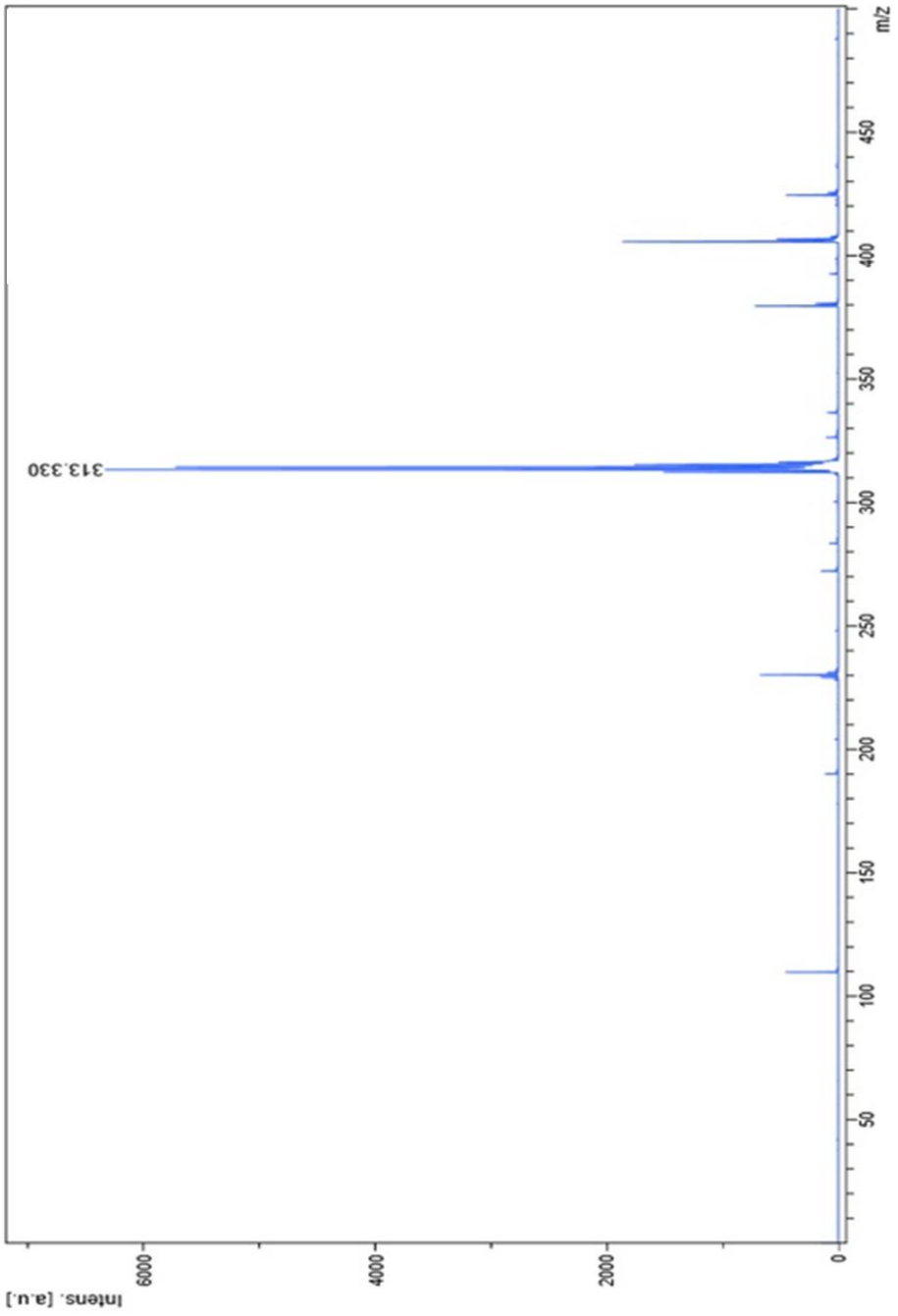


Figure A.36 Mass spectrum of thienyl-3,4-(hexyloxy0phenylprop-2-en-1-one **(14)**

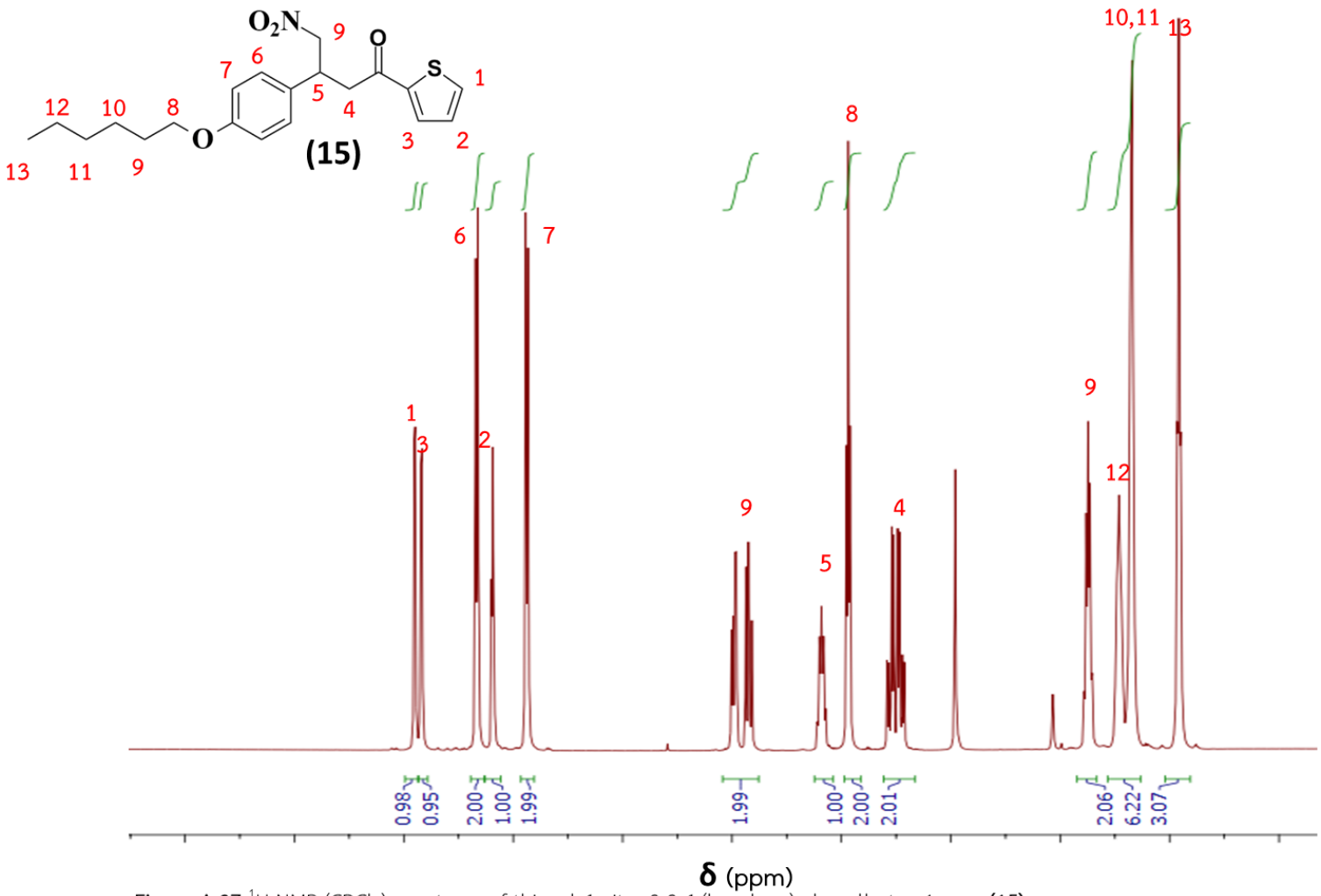


Figure A.37 ^{1}H NMR ($CDCl_3$) spectrum of thienyl-4-nitro-3-3-4-(hexyloxy)-phenylbutan-1-one **(15)**

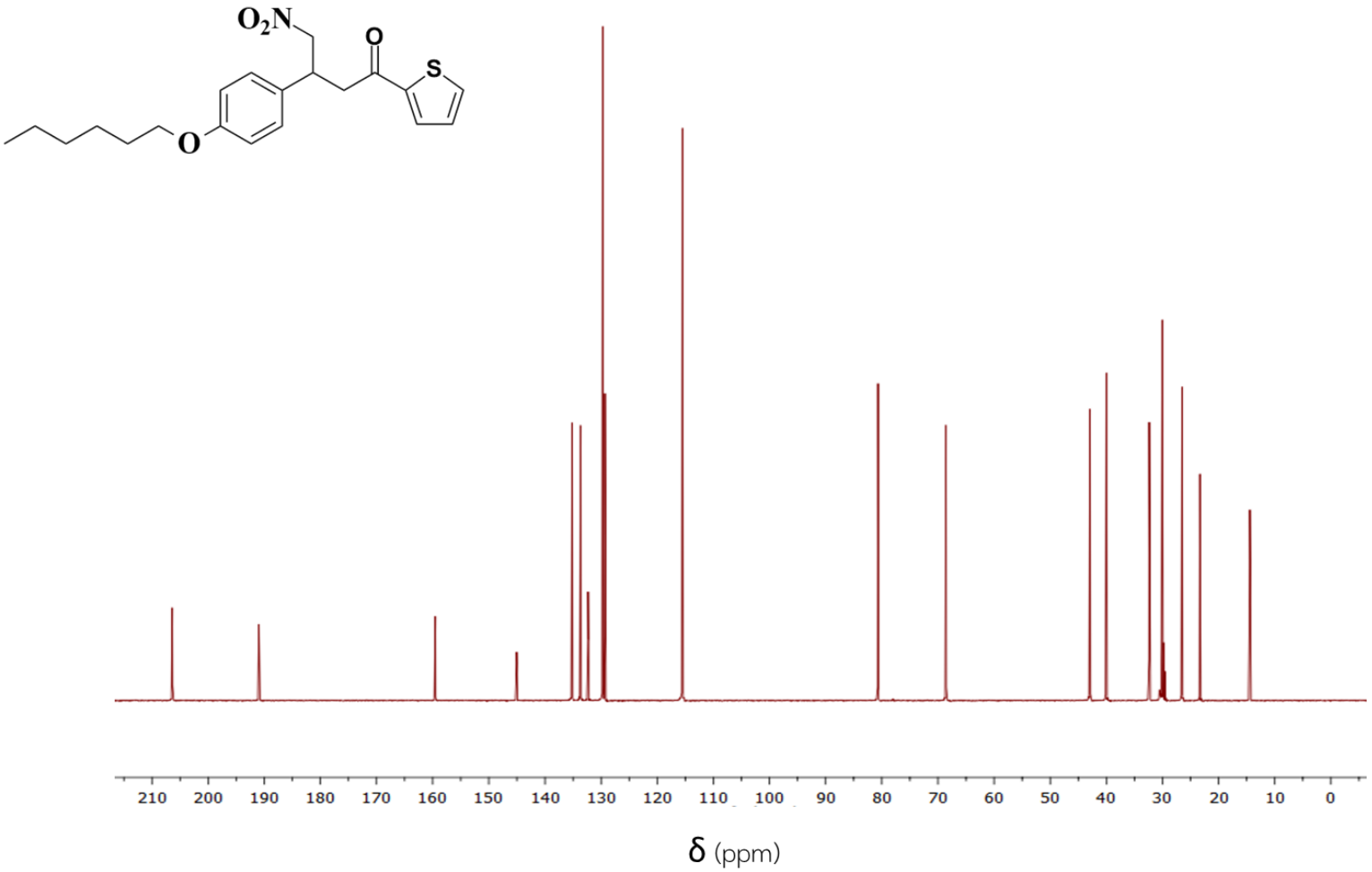


Figure A.38 ^{1}H NMR ($CDCl_3$) spectrum of thienyl-4-nitro-3-3-4-(hexyloxy)-phenylbutan-1-one **(15)**

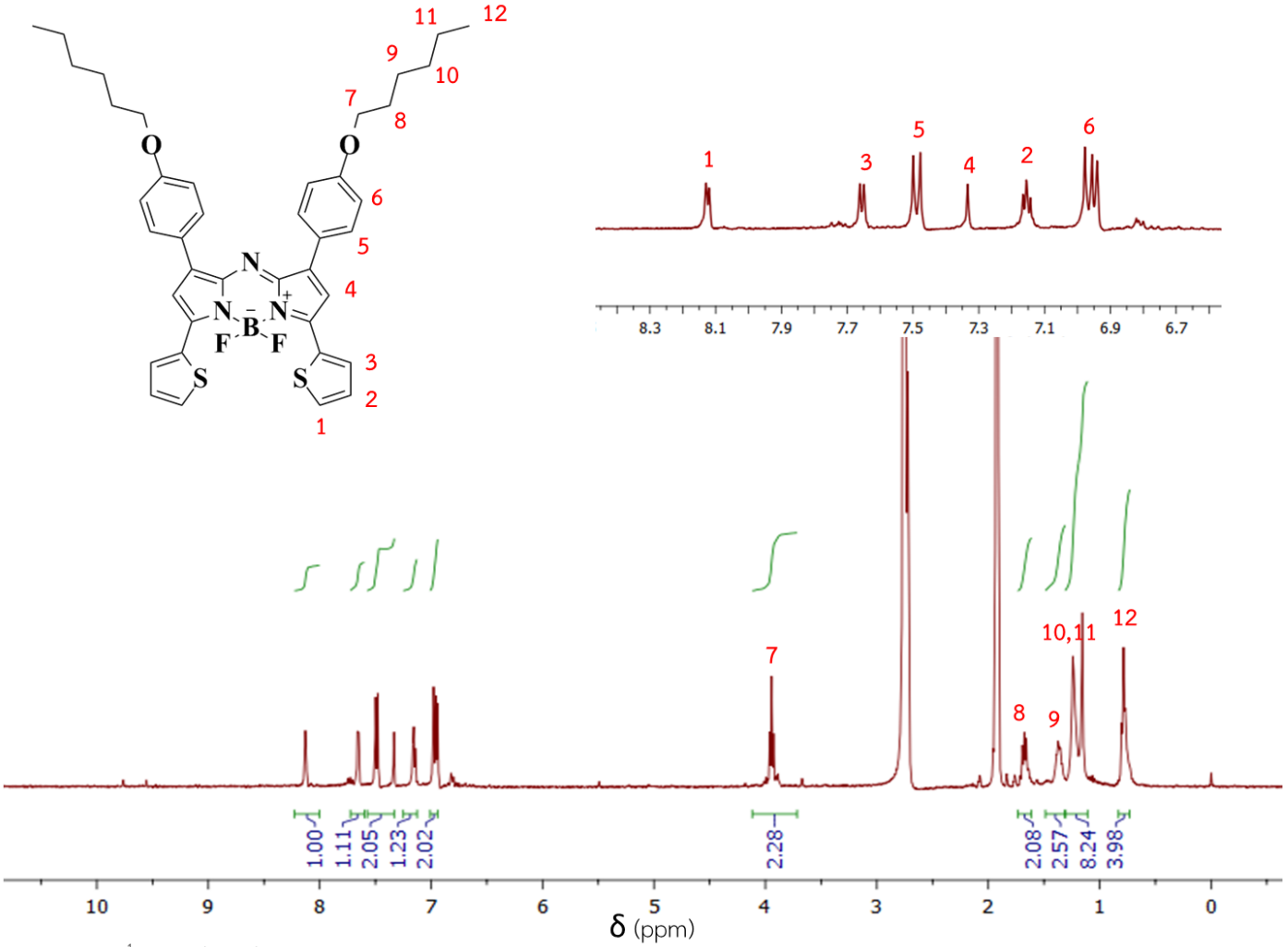


Figure A.39 ^{1}H NMR ($CDCl_3$) spectrum of thienyl alkoxy phenyl azs-BODIPY **(17, TAAB)**

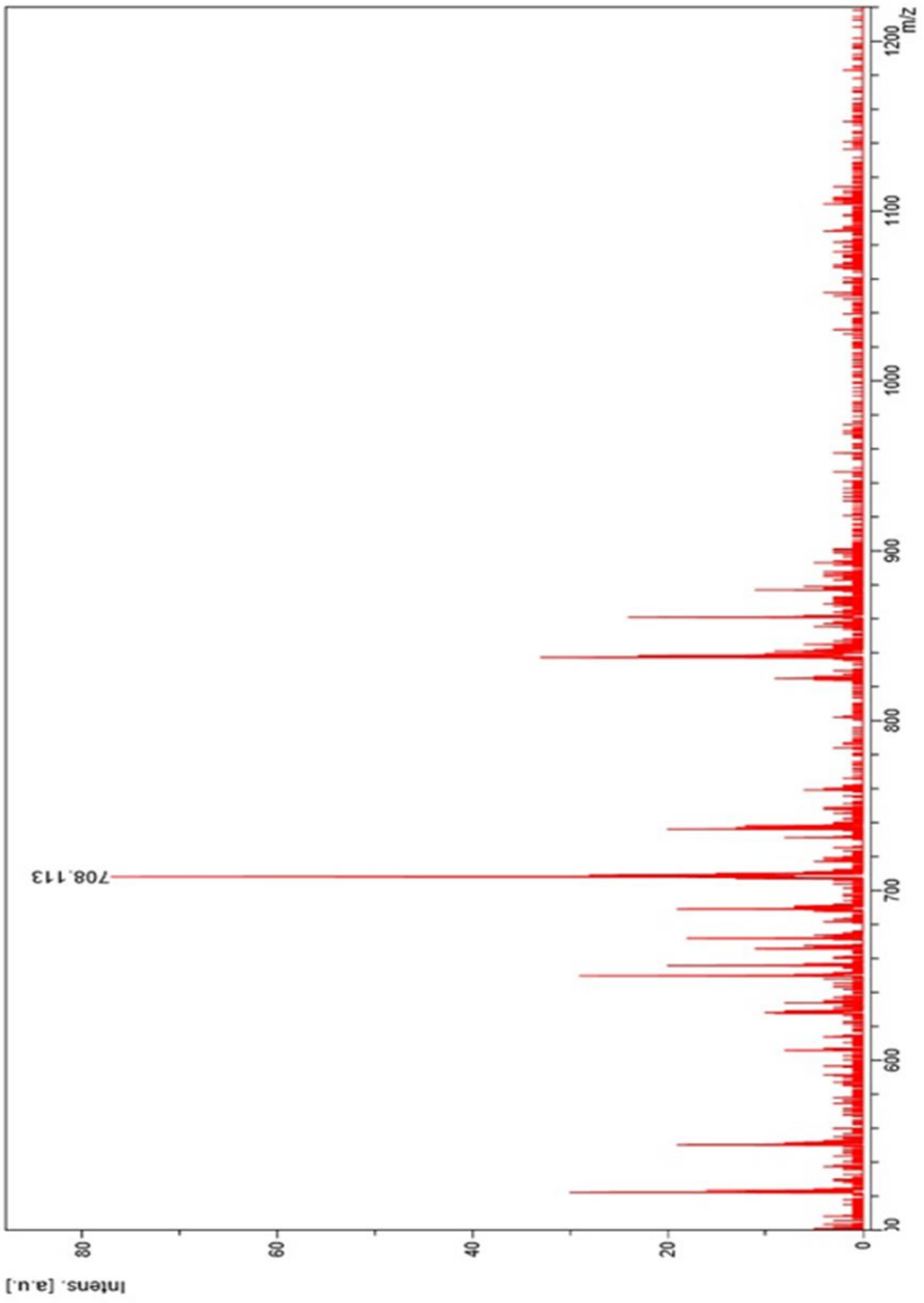


Figure A.40 Mass spectrum of thienyl alkoxy phenyl aza-BODIPY **(17, TAAB)**

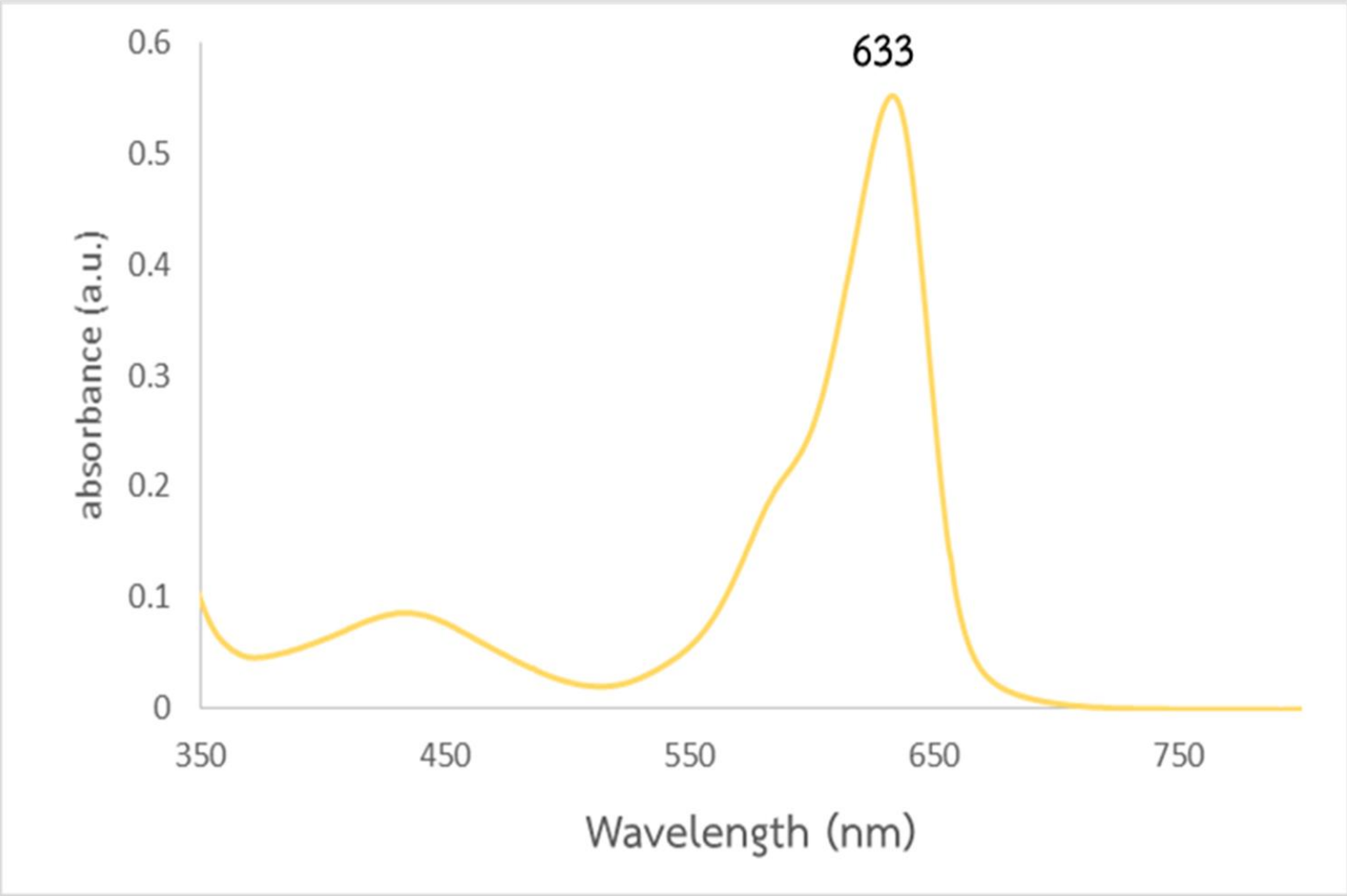


Figure A.41 UV-Visible of thienyl alkoxy phenyl aza-BODIPY **(17, TAAB)**

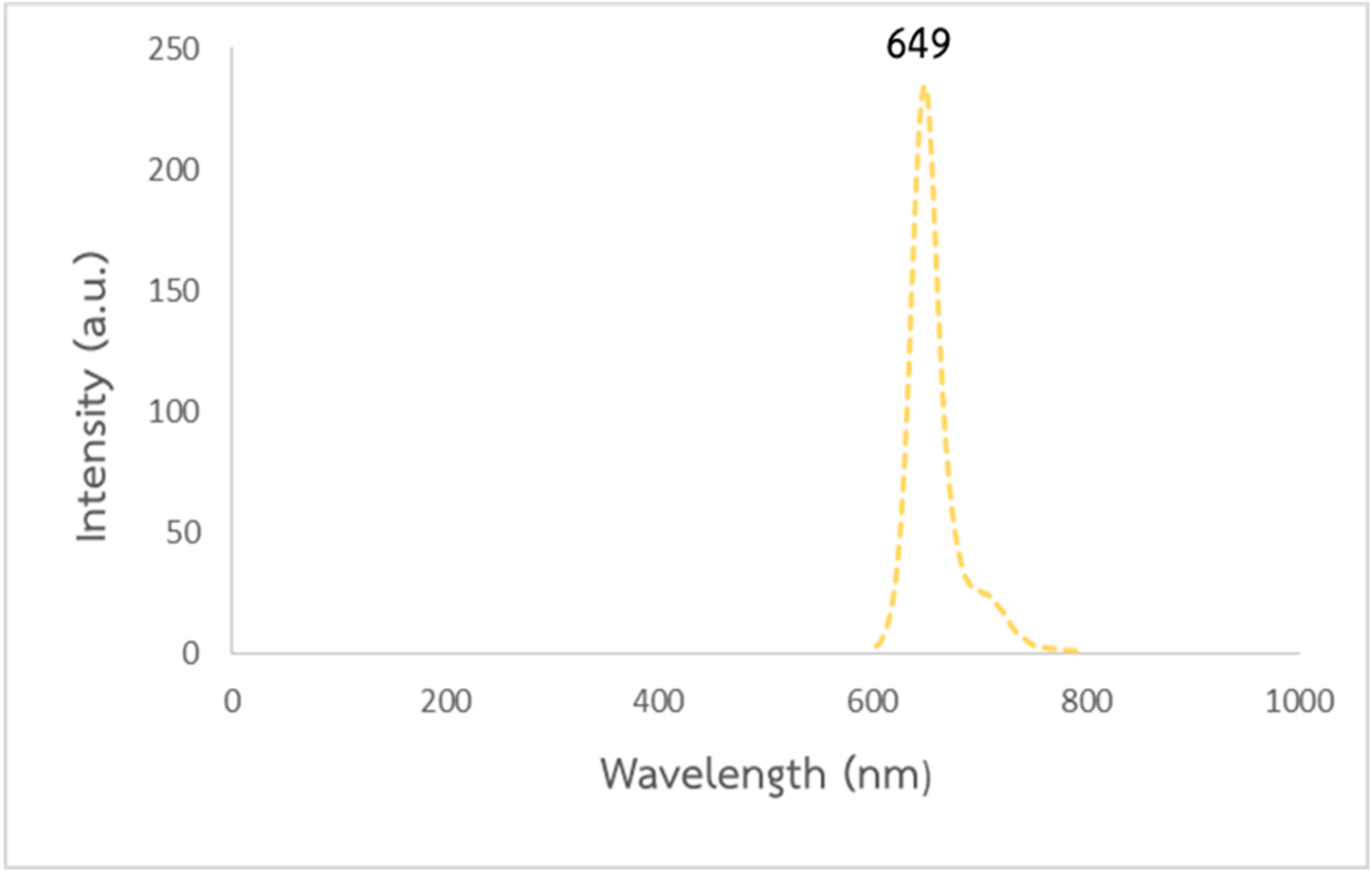


Figure A.42 The UV-Visible spectrum of thienyl alkoxy pheny, aza-BODIPY **(17, TAAB)**

VITA

Miss Pornpana Tepwong was born on June 5, 1991 in Chanthaburi, Thailand. She received a Bachelor's degree of Science from Department of Chemistry, Faculty of Science, Srinakharinwirot University, Thailand, in 2011. She was admitted to a Master's Degree Program in Chemistry, Faculty of Science, Chulalongkorn University and completed the program in 2016. Her address is 108/76, Amphawa road, Watmai sub-district, Chanthaburi, 22000, Thailand.