Donor-Acceptor Functionalized Aza-BODIPY Derivatives

M.Sc. Thesis

By

Pratiksha Dad

DEPARTMENT OF CHEMISTRY

INDIAN INSTITUTE OF TECHNOLOGY INDORE

May 2022

Donor-Acceptor Functionalized Aza-BODIPY Derivatives

A THESIS

Submitted in partial fulfilment of the requirements for the award of the degree of

Master of Science

by

Pratiksha Dad

DEPARTMENT OF CHEMISTRY

INDIAN INSTITUTE OF TECHNOLOGY INDORE

May 2022

INDIAN INSTITUTE OF TECHNOLOGY INDORE

CANDIDATE'S DECLARATION

I hereby declare that the work which is being presented in the thesis entitled **Donor–Acceptor Functionalized Aza–BODIPY Derivatives** in the partial fulfilment of the requirements for the award of the degree of **MASTER OF SCIENCE** and submitted to the **DEPARTMENT OF CHEMISTRY, Indian Institute of Technology Indore**, is an authentic record of my own work carried out during the time period from August 2021 of joining the M.Sc. program to May 2022 of M.Sc. Thesis submission under the supervision of Prof. Rajneesh Misra, Professor, IIT Indore.

The matter presented in this thesis has not been submitted by me for the award of any other degree of this or any other institute.

Pratiksha Dad

This is to certify that the above statement made by the candidate is correct to the best of my knowledge.

Prof. Rajneesh Misra

Pratiksha Dad has successfully given her M.Sc. Oral Examination held on **May 25, 2022**.

Signature of Supervisor of M.Sc. thesis

Date: 26-05-2022

Convener, DPGC

Date: 27.05.2022

Signature of PSPC Member #1

Date:

Signature of PSPC Member #2

Date:

ACKNOWLEDGEMENTS

With a great pleasure, I would like to express gratitude to my supervisor Prof. Rajneesh Misra, for giving me an opportunity to pursue research and believing in my research abilities. His guidance, motivation and support have been immensely helpful to complete this M.Sc. project. His enthusiasm and dedication have always inspired me. Further, I want to thank my PSPC members Dr. Selvakumar Sermadurai and Dr. Umesh Kshirsagar for their valuable suggestions and support.

I am grateful to Prof. Biswarup Pathak (Head, Department of Chemistry, IIT Indore). I am also grateful to Prof. Suman Mukhopadhyay, Prof. Sanjay Singh, Prof. Apurba Kumar Das, Prof. Sampak Samantha, Dr. Anjan Chakraborty, Dr. Tridib Kumar Sarma, Dr. Tushar K. Mukherjee, Dr. Venkatesh Chelvam, Dr. Shaikh M. Mobin, Dr. Satya S. Bulusu, Dr. Amrendra Kumar Singh, Dr. Abhinav Raghuvanshi, Dr. Deepak Kumar Roy for their help during various activities. I want to extend my sincere thanks to my mentor Dilip Pinjari and for his supportive, kind and friendly nature. I extend my deep thanks to my group members Indresh Singh Yadav, Faizal Khan, Manju Sheokand, Charu Popli, Pankaj Kumar Gupta, Mohd. Wazid, Nikhilji Tiwari, Ramakant Gavale, Amiy Krishna and Ashwini Mishra for their selfless co-operation and help to make my work successful. I would also like to thank the technical staff from Sophisticated Instrumentation Centre (SIC), IIT Indore, Mr. Kinny Pandey, Mr. Ghanshyam Bhavsar and Mr. Manish Kushwaha for their patience and timely technical support without which it was impossible to continue with my work. I personally want to extend my thanks to my batch mates who were always there and never let me down during these M.Sc. days.

Here, it is to be specially mentioned that, none of this would have been possible without the support of my parents and I express my love and gratitude to my family.

Pratiksha Dad

M.Sc. Student

DEDICATED TO MY PARENTS
AND MY FRIENDS……

For their support in every stage of my life!

ABSTRACT

Aza–boron–dipyrromethene (Aza–BODIPY) is a hetero–atom substituted boron–dipyrromethene (BODIPY), in which a carbon atom present at the *meso*–position is replaced by a nitrogen atom. Aza–BODIPYs show good optical and thermal stability. The donor-acceptor functionalized aza–BODIPY conjugates show lower HOMO–LUMO gap and absorption in near infra–red (NIR) region. Thus, such NIR absorbing materials can be used in various photonic and bio–applications such as bioimaging, sensors, therapeutics, organic light emitting diodes (OLEDs), organic photovoltaics, etc. In present work, we synthesized and characterized β–substituted aza–BODIPY derivatives by Palladium catalyzed Suzuki cross–coupling reaction. Also, the photophysical properties and theoretical calculations have been performed using the density functional theory (DFT) and time–dependent density functional theory (TD–DFT).

TABLE OF CONTENTS

LIST OF FIGURES, SCHEMES AND TABLES

ACRONYMS

HOMO	Highest Occupied Molecular Orbital
LUMO	Lowest Unoccupied Molecular Orbital
OFETs	Organic Field–Effect Transistors
OLEDs	Organic Light–Emitting Diodes

Chapter 1

INTRODUCTION

Boron–dipyrromethene (BODIPY) dyes are the organo–boron compounds which show absorption in ultraviolet (UV)/visible (vis) regions *[1–2]*. Also, BODIPYs show high donor ability, due to which they are used to generate multi–chromophore systems for the studying artificial photosynthetic models. Moreover, BODIPY dyes have good photostability & fluorescence quantum yield. However, the maximum absorptions of BODIPYs are below wavelength 700 nm and that is suboptimal for bio–applications because of the limited penetration depths.

Near–infrared (NIR) absorbing dyes show many applications such as fluorescence imaging used for deep tissue penetration and high resolution. O'Shea's group reported aza–boron–dipyrromethene i.e., aza–BODIPY in 2002 *[3]*. It is a hetero–atom substituted analogue of the conventional BODIPY, in which a carbon atom present at the *meso*–position on the BODIPY ring is replaced by a nitrogen atom (Figure **1**). Such aza–BODIPY dyes retain the optical and thermal stability as well as exhibits bathochromically shifted absorption, and increased absorption coefficient compared to the BODIPY dyes. Aza–BODIPY dyes show fluorescence and absorption in a region with wavelength longer than 650 nm.

Along with the long wavelength absorptions aza–boron–dipyrromethenes have high molar extinction coefficient (ε), high quantum yields as well as narrow emission and absorption peaks *[4]*. Thus, aza–BODIPYs show various applications in sensors *[5–6]*, bioimaging *[7–10]*, OLEDs *[11]*, OFETs, therapeutics *[12–15]*, organic photovoltaics, photosensitizers used in photodynamic therapy *[16–20]*. Aza–BODIPYs can be extensively studied as fluorescent probes as well as phototherapeutic agents.

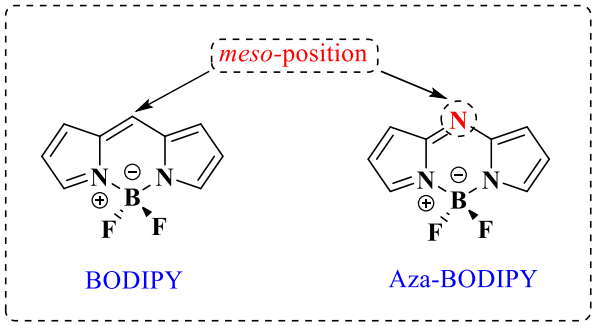


Figure 1. General structures of BODIPY and aza–BODIPY dye.

The significant red–shifted absorption and emission of aza–BODIPYs from those of BODIPYs can be explained by the efficient stabilization of the LUMO due to the presence of nitrogen atom with higher electronegativity in the aza–BODIPY analogue than carbon atom in the BODIPY analogue at the *meso*–position. Since, a HOMO–LUMO transition occurs in case of absorption of BODIPY and aza–BODIPY, it has a longer wavelength absorption than BODIPY because of the narrower band gap *[21–22]*. The structural design of aza–BODIPY dye has an important role for its excellent photophysical properties that ultimately determine its versatile application. Apart from this, a further shift in the maximum absorption of aza–BODIPYs into the NIR–I or NIR–II region becomes a new drift for its application in high performance bio–applications.

Importantly, it has been observed that a significant red–shift of maximum absorption and emission into near–infrared region can be effectively achieved by π–π* conjugated extension, attachment of different donor moieties on the phenyl rings, B-atom chelation, different substitutions on core aza–BODIPY with electron–accepting/donating aromatic rings and replacing the fluorine atom by alkynyl groups or aryl groups *[23–24]*.

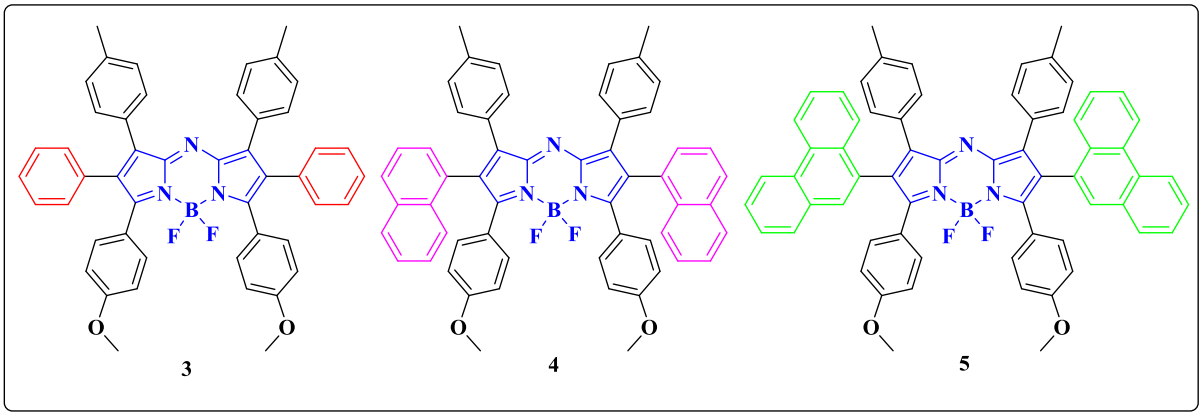


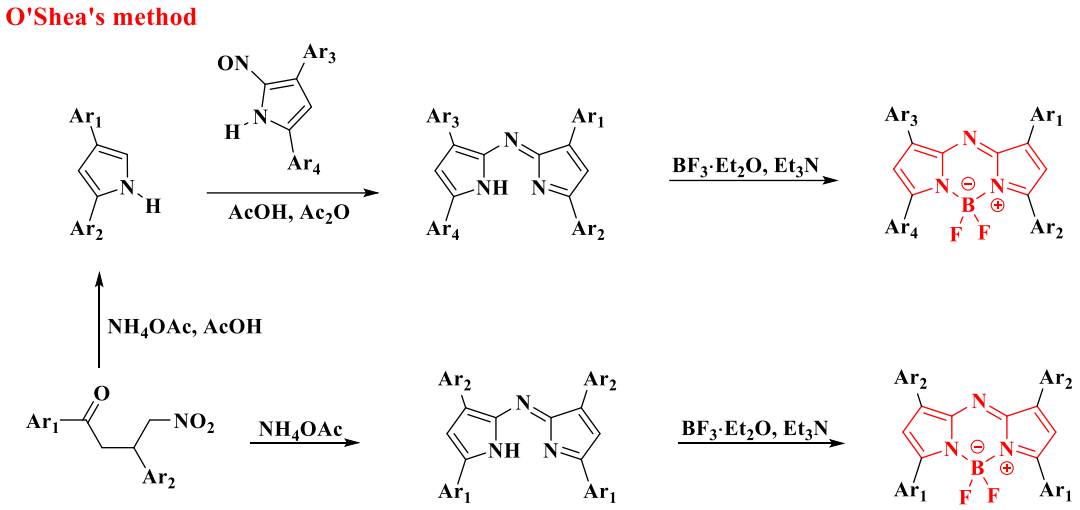
Figure 2. Chemical structures of compounds synthesized.

Herein, we perform the synthesis of the three different β–functionalized aza–BODIPY dyes **3**–**5**. These compounds have been characterized by ^{1}H NMR, ^{13}C NMR, LCMS and HRMS. Also, we have performed the photophysical properties and DFT, TD–DFT studies. These materials can be used in various photonic applications such as solar cell applications, sensing, bioimaging, etc.

Chapter 2

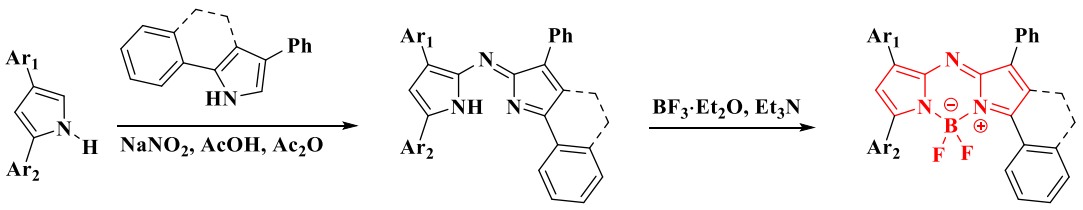
LITERATURE REVIEW

Owing to pioneering the investigations on aza–BODIPY dyes, three major synthetic methods of aza–BODIPY have been reported (Scheme 1–3). O'Shea *et al. [3,25]* proposed a synthetic method for symmetrical and asymmetrical aza–BODIPY products which includes a cyclization reaction of substituted ketones and nitromethane via Michael addition, followed by boron trifluoride complexation to generate the desired products (Scheme 1). Though the synthesis is simple following this method and the conditions used are mild, the yield of the product is quite less (20–50%).



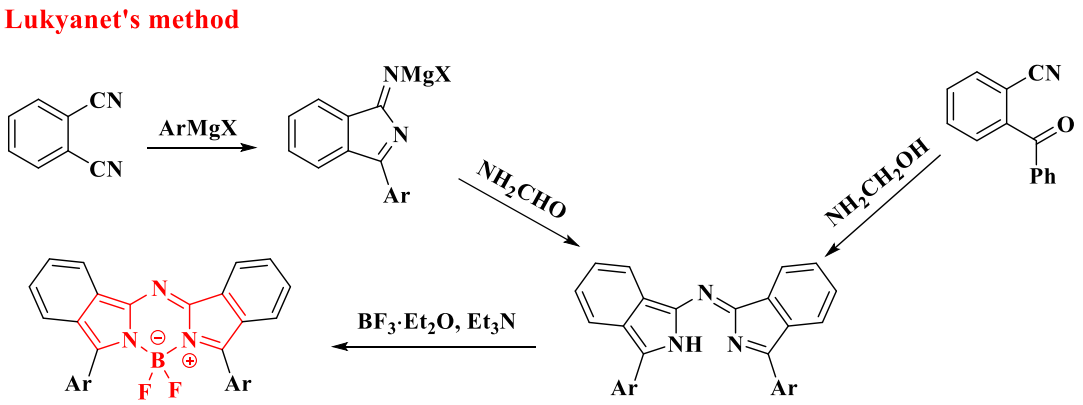
Scheme 1. O'Shea's method for aza–BODIPY synthesis.

Carreira *et al. [25,26]* proposed a synthetic method for symmetrical and asymmetrical aza-BODIPY products which includes a direct cyclization of substituted pyrrole followed by boron trifluoride complexation (Scheme 2). In this case, product yield is higher (>50%). Furthermore, on comparison with the O'Shea's molecular structure, in this case the π–π* conjugated extension could be achieved in the parent molecule as this version can be fused with pyrrole.



Scheme 2. Carreira's method for aza–BODIPY synthesis.

Lukyanets *et al. [25,27]* proposed a synthetic method for symmetrical aza–BODIPY products which includes a reaction of aryl MgBr and phthalonitrile. Further, the desired product can be generated by the boron trifluoride complexation (Scheme 3). However, this synthetic route for aza–BODIPY is having the lowest yield among all the three pathways (10–30%). Conclusively, the three synthetic routes provide a foundation for the synthesis of aza–BODIPY derivatives.



Scheme 3. Lukyanet's method for aza–BODIPY synthesis.

Chapter 3

EXPERIMENTAL SECTION

3.1 General Methods

All the chemicals were used as received unless otherwise indicated. The moisture sensitive reactions were done under argon using Schlenk method. ^{1}H NMR (500 MHz) and ^{13}C NMR (125 MHz) spectra were recorded by using solvent $CDCl_3$. The chemical shifts for ^{1}H NMR are mentioned in parts per million (ppm) relative to the solvent residual peak ($CDCl_3$, 7.26 ppm). The multiplicities are written as singlet (s), doublet (d), multiplet (m), and coupling constants, *J*, are reported in Hz. The chemical shifts for ^{13}C NMR are given in ppm relative to solvent residual peak ($CDCl_3$, 54.0 ppm). LCMS and HRMS were performed on a mass spectrometer (ESI–TOF). The UV–visible absorption spectra of aza–BODIPY were performed on UV–visible Spectrophotometer in DCM (dichloromethane).

3.2 Experimental Procedures

3.2.1 Method for synthesis of aza-BODIPY 1

Aza-BODIPY 1 was synthesized using a four–step literature procedure *[28]*. **^{1}H NMR** (500 MHz, $CDCl_3$, δ in ppm): 8.08–8.07 (4H, d, J = 5 Hz), 8.00–7.98 (4H, d, J = 10 Hz), 7.29–7.26 (4H, m), 7.02–7.00 (6H, d, J = 10 Hz), 3.89 (6H, s), 2.45 (6H, s); **^{13}C NMR** (125 MHz, $CDCl_3$, δ in ppm): 161.8, 158.0, 147.7, 145.3, 143.2, 131.6, 129.9, 129.4, 129.2, 124.3, 118.0, 114.2, 55.4, 53.4, 31.6, 25.3, 22.7, 22.4, 21.5, 18.9; **HRMS** (ESI) *m/z* calcd for $C_{36}H_{30}BF_2N_3O_2$: 586.2478 $[M+nH]^+$, found 586.2479 $[M+nH]^+$.

3.2.2 Method for synthesis of aza-BODIPYs 3–5

2,8-dibromo-5,5-difluoro-3,7-bis(4-methoxyphenyl)-1,9-di-p-tolyl-5H-dipyrrolo[1,2-c:2',1'-f][1,3,5,2]triazaborinin-4-ium-5-uide **2** (100 mg, 0.14 mmol) and an appropriate boronic acid (phenyl boronic acid, naphthalenyl boronic acid and phenanthrenyl boronic acid) (50–100 mg, 0.42 mmol) were taken in a solvent mixture of water/THF/toluene (1:1:1) (20 mL) in a 100 mL one-neck round–bottomed flask. Na_2CO_3 (60 mg, 0.56 mmol) was added further. The RB was fitted with condenser and

stirred for 15 minutes under argon atmosphere. $Pd(PPh_3)_4$ (16 mg, 0.014 mmol) was used as a catalyst and added to the reaction mixture. Further, it was refluxed at 60 °C for 6 to 10 hours. After completion of the reaction, the reaction mixture was quenched with distilled water (5 mL) and it was extracted with DCM. The combined organic layers were further washed with water and brine solution and dried over anhydrous Na_2SO_4. The solvent was evaporated using rota evaporator, and the crude residue was purified by column chromatography (3:2, dichloromethane:hexane) to afford aza–BODIPY **3**–**5**.

Aza–**BODIPY 3:**

Yield: 33%; **^{1}H NMR** (500 MHz, $CDCl_3$, δ in ppm): 8.08–7.98 (3H, m), 7.47–7.37 (6H, m) 7.29 (1H, s), 7.24–7.18 (6H, m), 7.12–7.10 (1H, d, J = 10 Hz), 7.06–7.04 (2H, m), 7.00–6.97 (4H, m), 6.81–6.75 (3H, m), 3.89–3.78 (6H, m), 2.45–2.36 (6H, m); **^{13}C NMR** (125 MHz, $CDCl_3$, δ in ppm): 162.1, 160.7, 159.4, 158.1, 156.6, 146.2, 145.2, 144.4, 143.8, 140.9, 140.0, 139.8, 138.4, 138.2, 135.6, 135.5, 133.0, 1332.4, 131.7, 131.0, 130.9, 130.7, 129.5, 129.4, 129.3, 129.1, 129.0, 128.5, 128.3, 128.2, 127.2, 127.1, 124.0, 123.4, 123.1, 118.1, 114.3, 113.3, 113.2, 55.4, 55.1, 34.7, 31.6, 26.9, 25.3, 22.7, 22.4, 22.5, 21.4, 20.7, 18.8; **HRMS** (ESI) *m/z* calcd for $C_{48}H_{38}BF_2N_3O_2$: 738.3106 $[M+nH]^+$, found 738.3106 $[M+nH]^+$.

Aza–**-BODIPY 4:**

Yield: 27%; **^{1}H NMR** (500 MHz, $CDCl_3$, δ in ppm): 8.08–8.05 (2H, t, J = 7.5 Hz), 7.80–7.74 (4H, m), 7.41–7.28 (11H, m), 7.25–7.22 (5H, m), 7.06–6.98 (2H, m), 6.94–6.88 (3H, m), 6.61–6.56 (3H, m) 3.89–3.66 (6H, m), 2.45–2.17 (6H, m); **^{13}C NMR** (125 MHz, $CDCl_3$, δ in ppm): 162.1, 160.6, 160.4, 142.4, 139.8, 138.5, 138.3, 133.6, 132.4, 131.7, 130.4, 130.3, 129.6, 129.4, 129.3, 129.2, 128.5, 128.2, 128.1, 126.3, 126.2, 126.0, 125.9, 125.5, 124.0, 123.6, 123.3, 114.3, 114.0, 113.1, 113.0, 55.4, 55.0, 21.5, 21.4; **LCMS** (ESI) *m/z* calcd for $C_{56}H_{42}BF_2N_3O_2$: 838.3420 $[M+nH]^+$, found 838.3488 $[M+nH]^+$.

Aza–**BODIPY 5:**

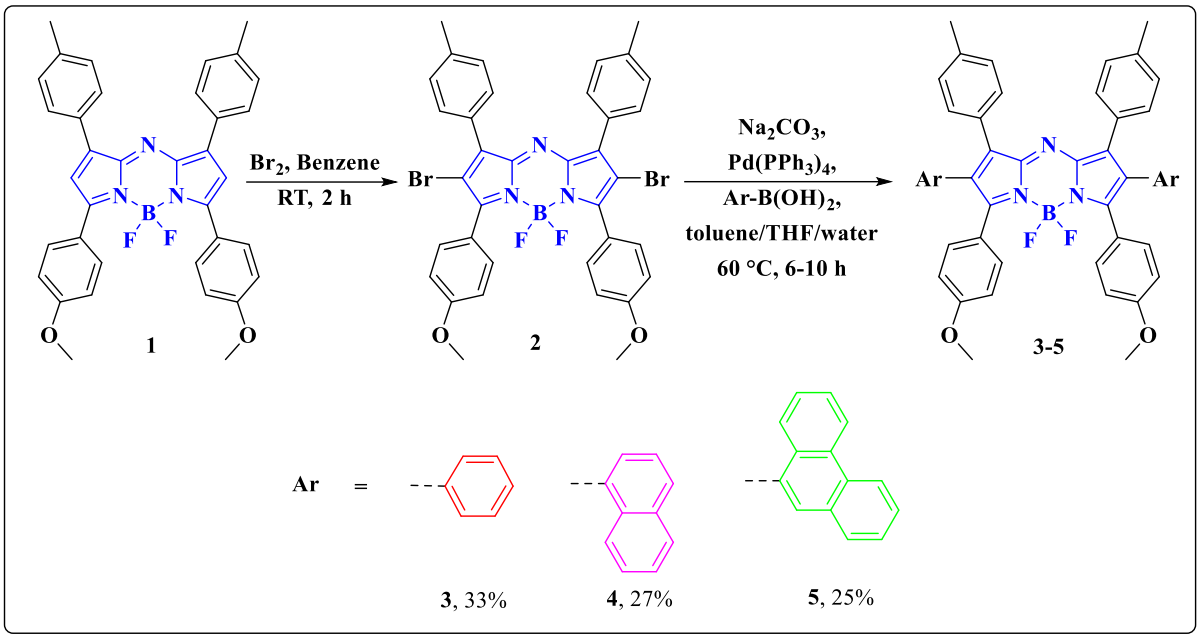
Yield: 25%; **^{1}H NMR** (500 MHz, $CDCl_3$, δ in ppm): 8.69 (4H, s), 8.09 (2H, s), 7.90–7.88 (2H, m), 7.75–7.42 (18H, m), 7.09–6.99 (2H, m), 6.92–6.87 (3H, m), 6.56–6.54 (3H, m), 3.89–3.61 (6H, m), 2.44–2.21 (6H, m); **^{13}C NMR** (125 MHz, $CDCl_3$, δ in ppm): 162.1, 160.6, 160.4, 159.5, 159.1, 145.4, 144.0, 142.6, 139.8, 138.6, 138.4, 136.0, 132.5, 131.8, 131.6, 131.5, 131.4, 131.3, 130.9, 130.7, 130.6, 130.5, 130.4, 130.3,

130.2, 130.1, 129.9, 129.6, 129.5, 129.4, 129.3, 129.2, 128.9, 128.7, 128.6, 128.4, 127.2, 127.0, 126.9, 126.8, 126.7, 126.6, 126.5, 124.3, 124.0, 123.6, 123.3, 123.2, 122.9, 122.8, 122.7, 122.3, 118.2, 115.9, 114.3, 114.2, 114.0, 113.3, 113.2, 106.1, 55.4, 55.0, 34.1, 33.8, 32.0, 31.6, 31.5, 30.2, 29.5, 29.4, 29.2, 29.0, 22.7, 22.4, 21.5, 21.3; **LCMS** (ESI) *m/z* calcd for $C_{56}H_{42}BF_2N_3O_2$: 938.3734 $[M+nH]^+$, found 938.3763 $[M+nH]^+$.

Chapter 4

RESULTS AND DISCUSSION

4.1 Synthesis



Scheme 4. Synthesis route of aza–BODIPY dyes **3**–**5**.

5,5-Difluoro-3,7-bis(4-methoxyphenyl)-1,9-di-p-tolyl-5H-dipyrrolo[1,2-c:2',1'-f][1,3,5,2]triazaborinin-4-ium-5-uide **1** was produced according to the literature procedures for the synthesis of aza–BODIPY dyes *[28]*. Further, the main precursor i.e., 2,8-dibromo-5,5-difluoro-3,7-bis(4-methoxyphenyl)-1,9-di-p-tolyl-5H-dipyrrolo[1,2-c:2',1'-f][1,3,5,2]triazaborinin-4-ium-5-uide **2** was generated by reacting **1** with 2.2 equivalents of bromine in benzene solvent at room tempt for 2 hours *[29]*.

The desired aza–BODIPY dyes **3**–**5** were synthesized by reacting compound **2** with three different aryl boronic acids such as phenyl boronic acid, naphthalenyl boronic acid, phenanthrenyl boronic acid respectively under Suzuki cross–coupling reaction conditions. These reactions were carried out in presence of catalyst $Pd(PPh_3)_4$ and base Na_2CO_3 at 60 °C in toluene/THF/water solvents taken in 1:1:1 ratio. The

reaction mixture was further stirred for 6–10 hours to get the desired products. (Scheme 4)

The crude reaction mixtures were further subjected to column chromatography using neutral activated aluminium oxide to obtain the pure products. All the compounds (**3**–**5)** were characterized by LCMS, HRMS, ^{1}H NMR and ^{13}C NMR techniques. These compounds found to be readily soluble in various organic solvents like toluene, chloroform, dichloromethane, etc.

4.2 Photophysical properties

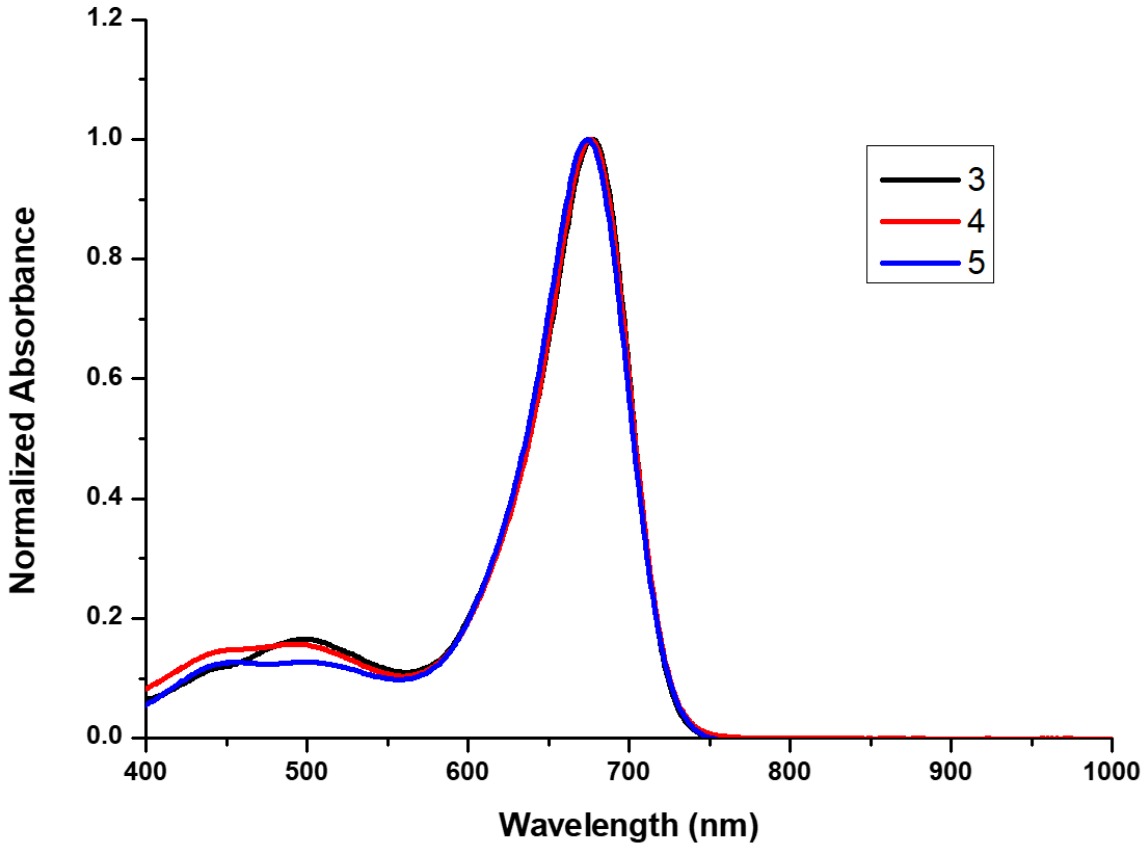


Figure 3. Normalized absorption maxima of aza–BODIPYs **3**–**5** in DCM (1×10^{-5}M).

The photophysical properties of the aza–BODIPYs **3**–**5** in dichloromethane (DCM) are given in Table 1. In general, the aza–BODIPY dyes show absorption in visible to NIR region. Aza–BODIPY dyes **3**–**5** show absorption bands in the wavelength region of 670 to 680 nm owing to intramolecular charge transfer due to the aza–BODIPY core. Whereas, the absorption bands observed in the region of wavelength 430 to 540 nm are because of π–π* transitions.

Table 1. The photophysical properties of aza–BODIPYs **3**–**5**.

Dye	**λ_{abs} (nm)**[a]	**ε ($M^{-1}.cm^{-1}$)**[a]	**E_g**[b] **(eV)**
3	677 498	62,382	2.13
4	676 497	93,623	2.16
5	674 502	51,192	1.52

[a]Absorbance measured in DCM at a concentration of 1×10^{-5} M, *ε*; molar extinction coefficient, [b]Theoretical values of the band calculated by the DFT calculations.

The phenyl substituted aza–BODIPY **3** shows slightly longer wavelength absorption compared to the naphthalene substituted aza–BODIPY **4**, while the aza–BODIPY **4** shows slightly longer wavelength absorption than the phenanthrene substituted aza–BODIPY **5**. Moreover, the molar extinction coefficient for aza–BODIPY **3** is 62,382 $M^{-1}.cm^{-1}$, for aza–BODIPY **4** is 93,623 $M^{-1}.cm^{-1}$ and for aza–BODIPY **5** is 51,192 $M^{-1}.cm^{-1}$.

4.3 Density functional theory

The frontier molecular orbitals of aza–BODIPYs **3**–**5** were investigated with DFT calculations by using Gaussian 09W program, at the B3LYP/6–319G(d, p) and structure optimization was carried out in the gas phase to better understand their structural properties and electronic properties.

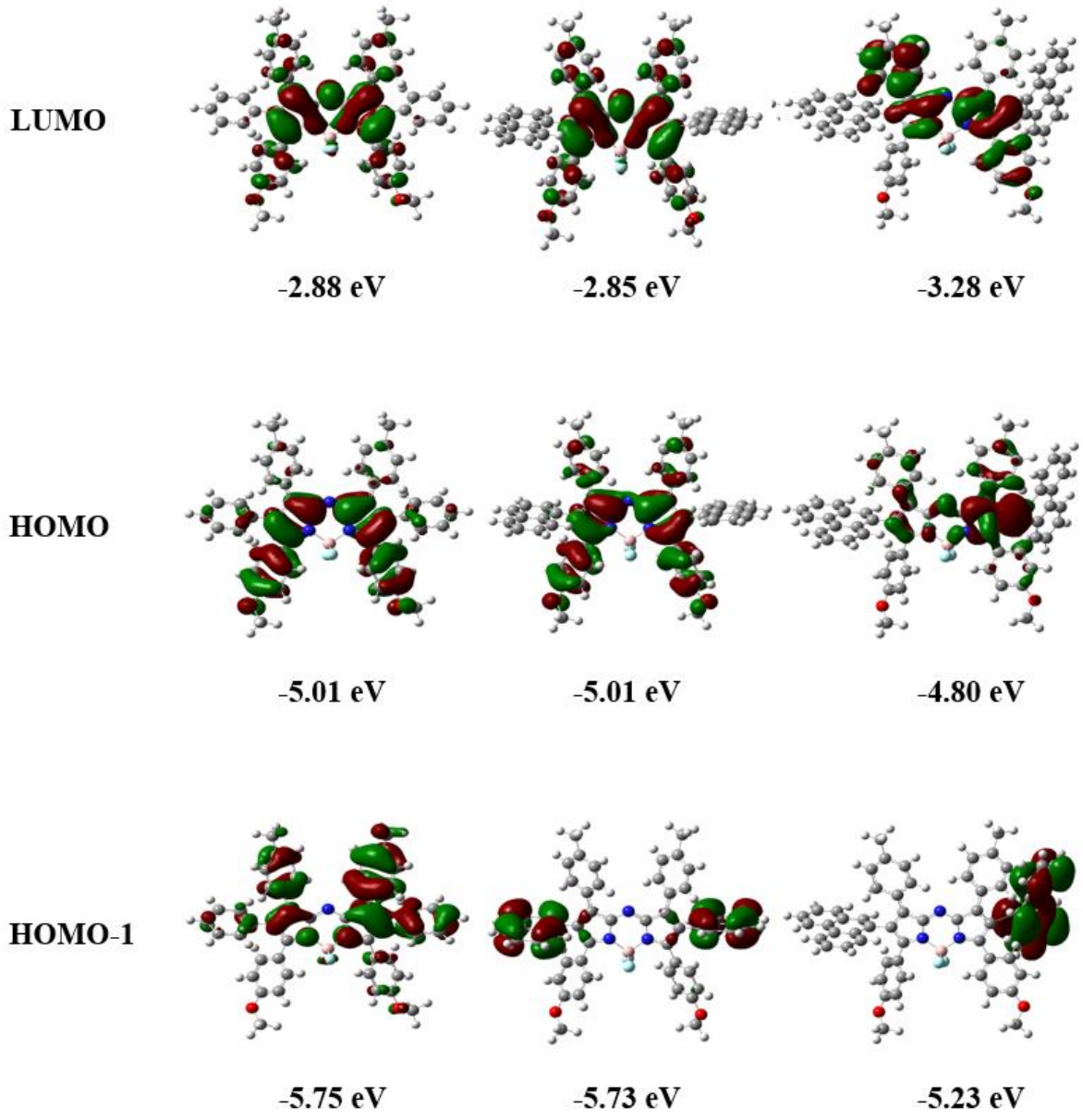


Figure 4. The FMOs of aza–BODIPY dyes **3**–**5** at the B3LYP/6–31G(d, p) level.

The optimized structures of aza–BODIPY dyes **3**–**5** exhibit distorted geometry. The frontier molecular orbitals and the theoretically calculated highest occupied molecular orbitals (HOMOs) and lowest unoccupied molecular orbitals (LUMOs) energy levels are depicted in Figure 4. The HOMOs are localized on the donor as well as acceptor moieties and the LUMOs are localized on the aza–BODIPY core.

According to the computational calculations for aza–BODIPYs **3–5**, the HOMO energy levels are -5.01 eV, -5.01 eV, -4.80 eV and the corresponding LUMO energy levels are -2.88 eV, -2.85 eV, -3.28 eV respectively. Moreover, the TD–DFT approach was used to predict the vertical excitation energies in the aza–BODIPY dyes **3**–**5**. TD–DFT calculations suggest that the aza–BODIPY dyes **3**–**5** show two main transitions

occurring from HOMO to LUMO and HOMO-1 to LUMO in vis–NIR region. The low energy transition in aza–BODIPY dyes is π–π* in nature.

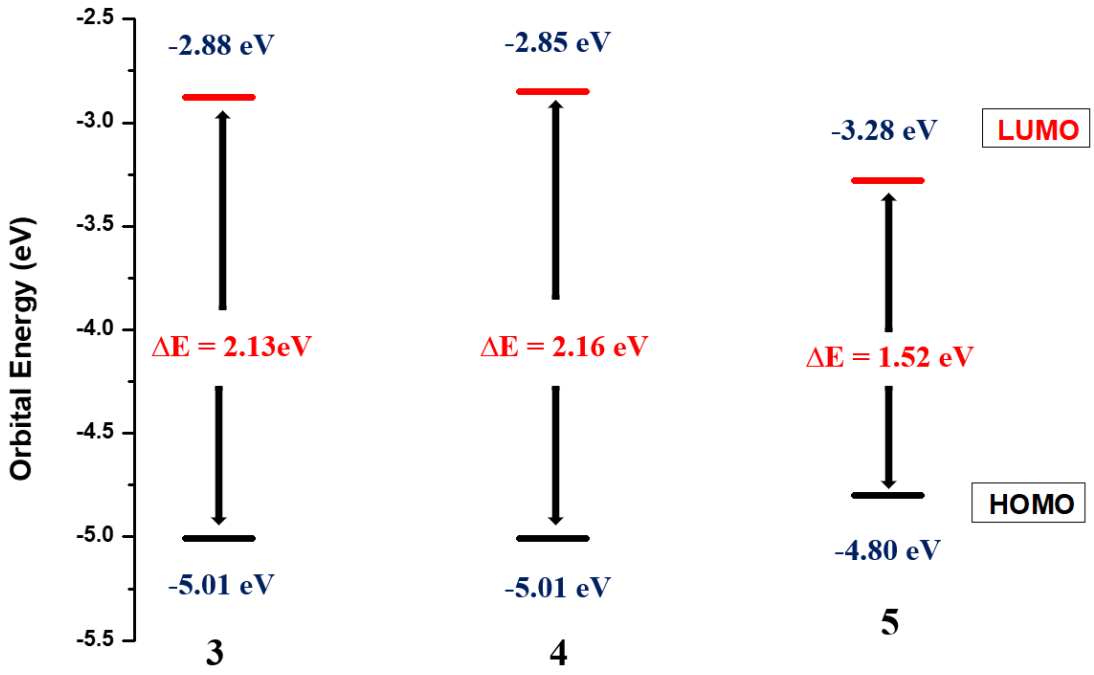


Figure 5. Energy level diagram of aza–BODIPY dyes **3**–**5**.

In order to better understand the photophysical properties of aza–BODIPY dyes, we have performed DFT and TD–DFT calculations. The DFT–predicted molecular orbital diagram is shown in figure **5**. Aza–BODIPY **3** shows band gap of 2.13 eV, aza–BODIPY **4** shows band gap of 2.16 eV whereas, aza–BODIPY **5** shows band gap of 1.52 eV.

Chapter 5

CONCLUSIONS

In conclusion, aza–BODIPY dyes **3**–**5** were synthesized using Palladium catalyzed Suzuki cross–coupling reaction. These dyes are characterized by ^{1}H NMR, ^{13}C NMR and HRMS. In photophysical properties, aza–BODIPY dyes **3**–**5** show absorption in UV–visible region. According to the density functional theory, for compounds **3**–**5**, HOMO is localized on donor as well as acceptor moieties, whereas the LUMO is localized on the acceptor aza–BODIPY core. Incorporating with various donor moieties such as phenothiazine, carbazole, etc., the absorption maxima can be further shifted to near infrared region. Thus, these molecules will be utilized in various applications such as optoelectronic devices, solar cells, sensing, bioimaging, etc.

Chapter 6

SUPPORTING INFORMATION

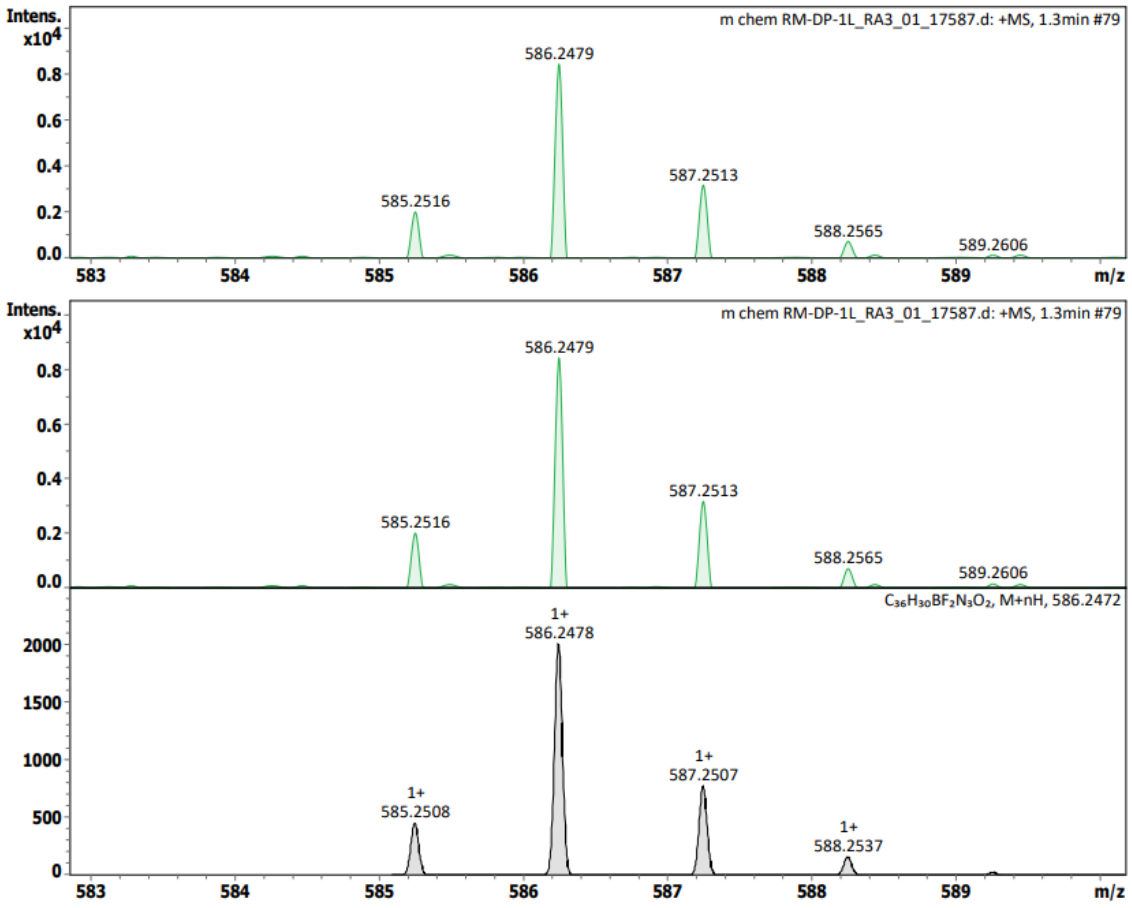


Figure 6. HRMS of aza–BODIPY **1**.

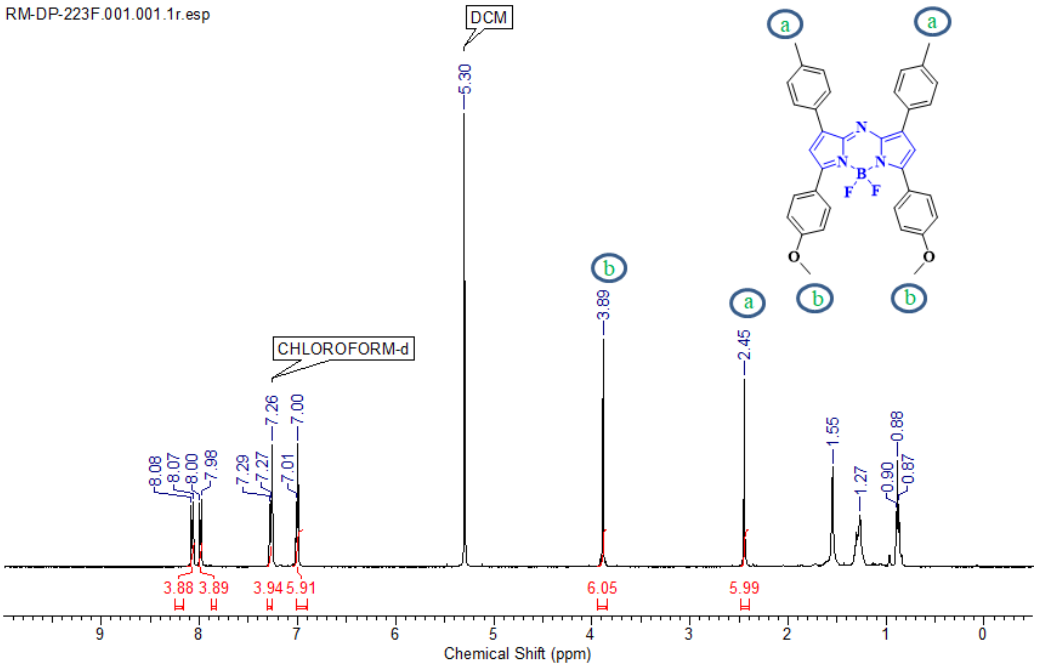


Figure 7. ^{1}H NMR spectrum of aza–BODIPY **1**.

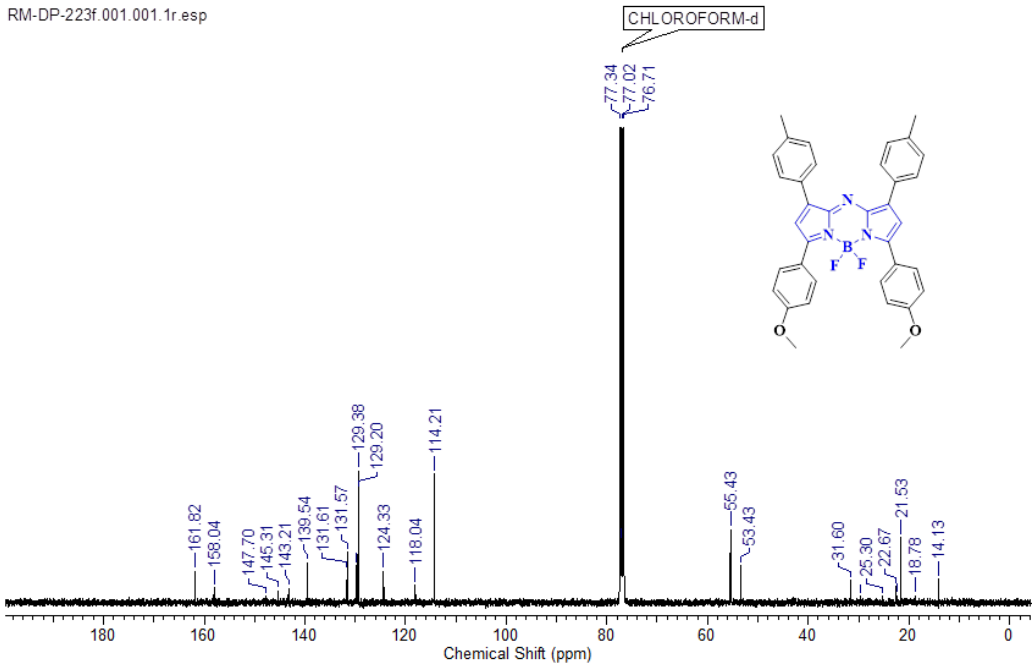


Figure 8. ^{13}C NMR spectrum of aza–BODIPY **1**.

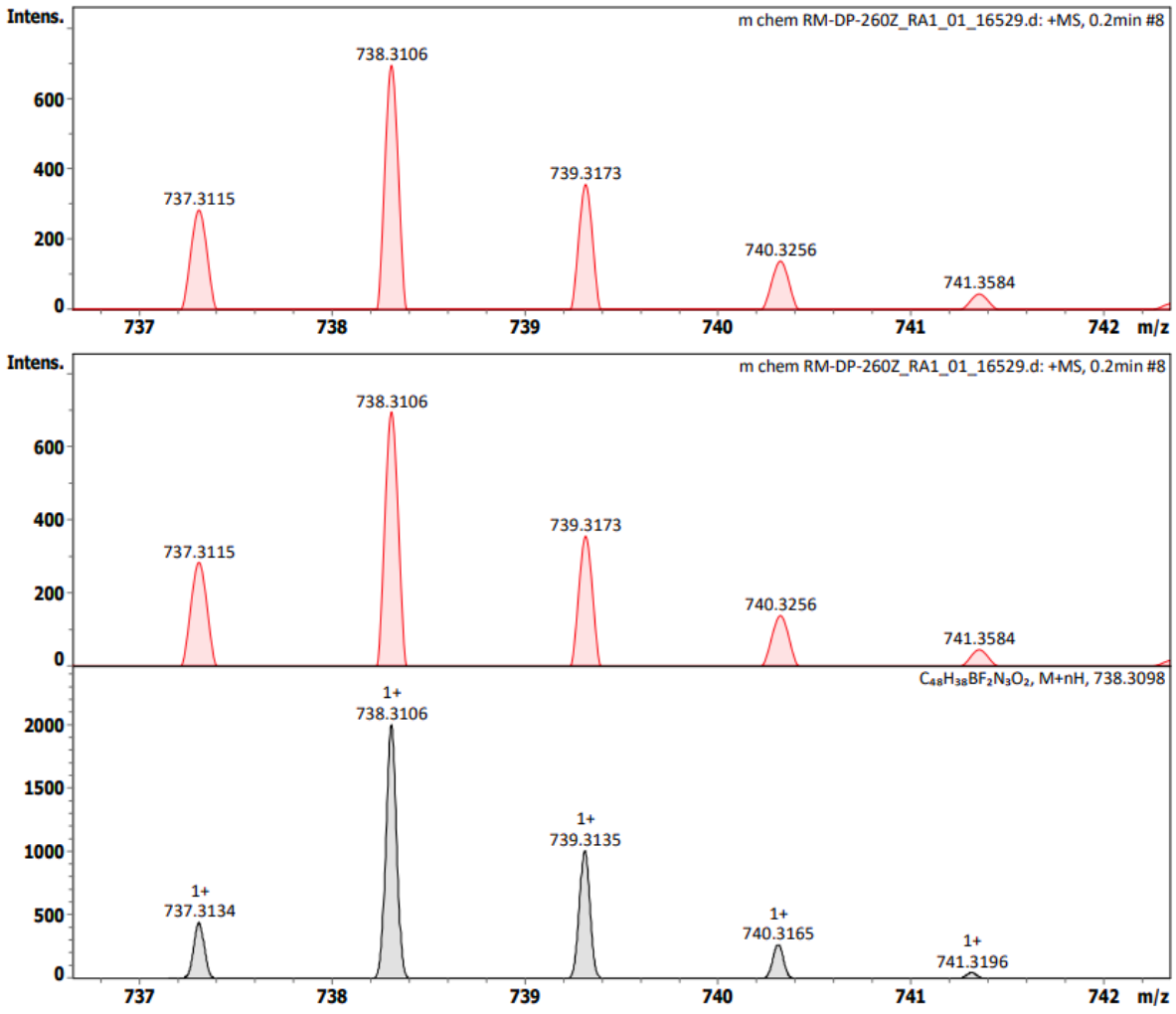


Figure 9. HRMS of aza–BODIPY **3**.

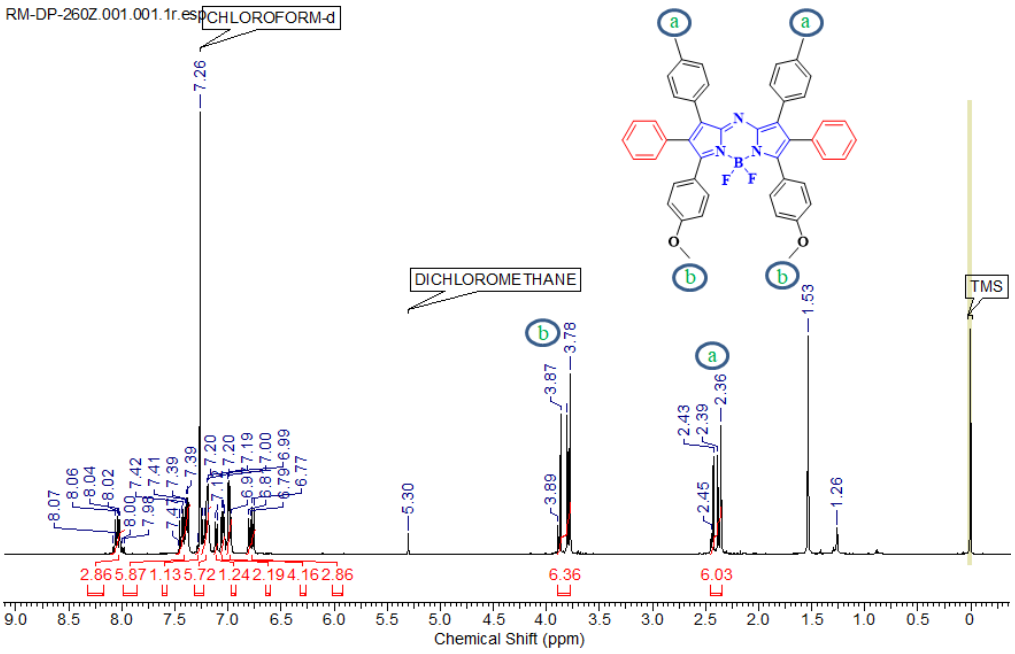


Figure 10. ^{1}H NMR spectrum of aza–BODIPY **3**.

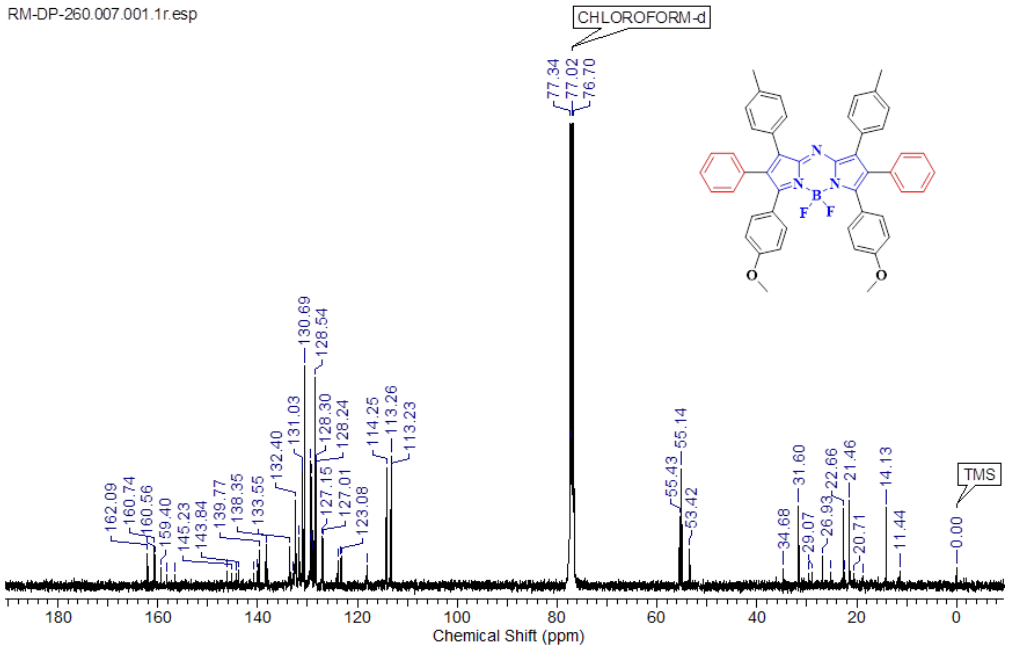


Figure 11. ^{13}C NMR spectrum of aza–BODIPY **3**.

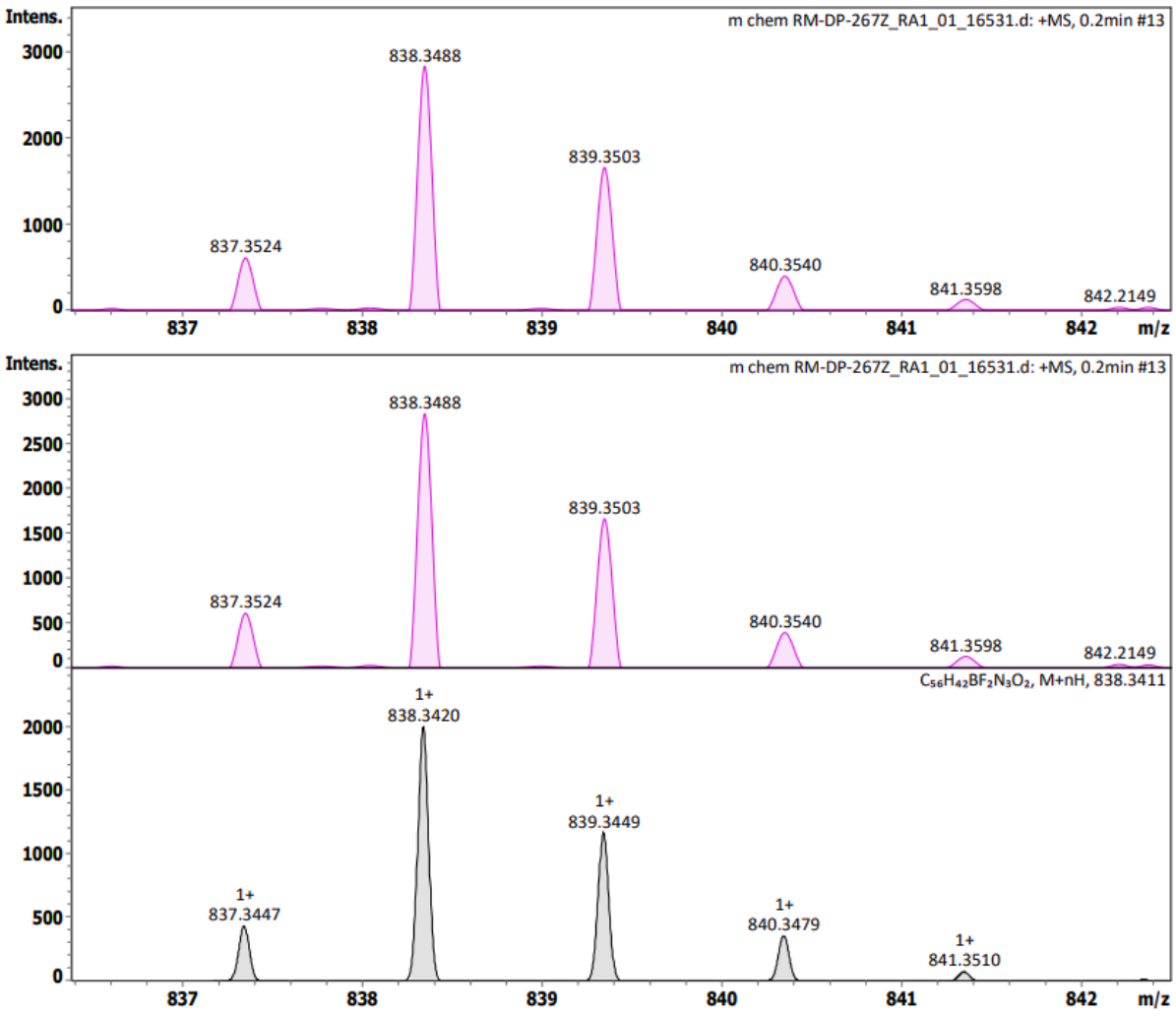


Figure 12. LCMS of aza–BODIPY **4**.

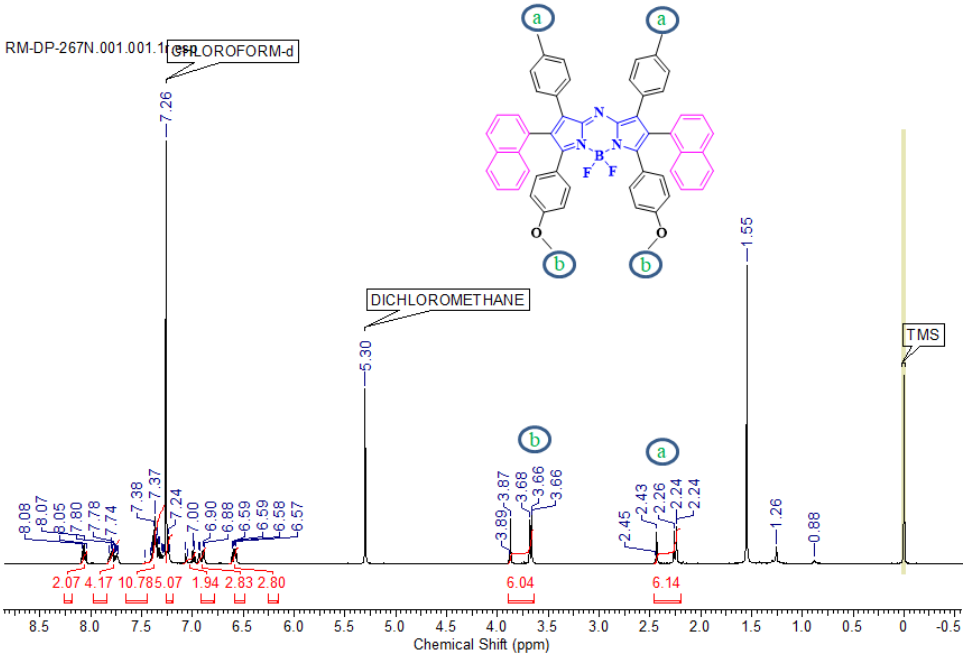


Figure 13. ^{1}H NMR spectrum of aza–BODIPY **4**.

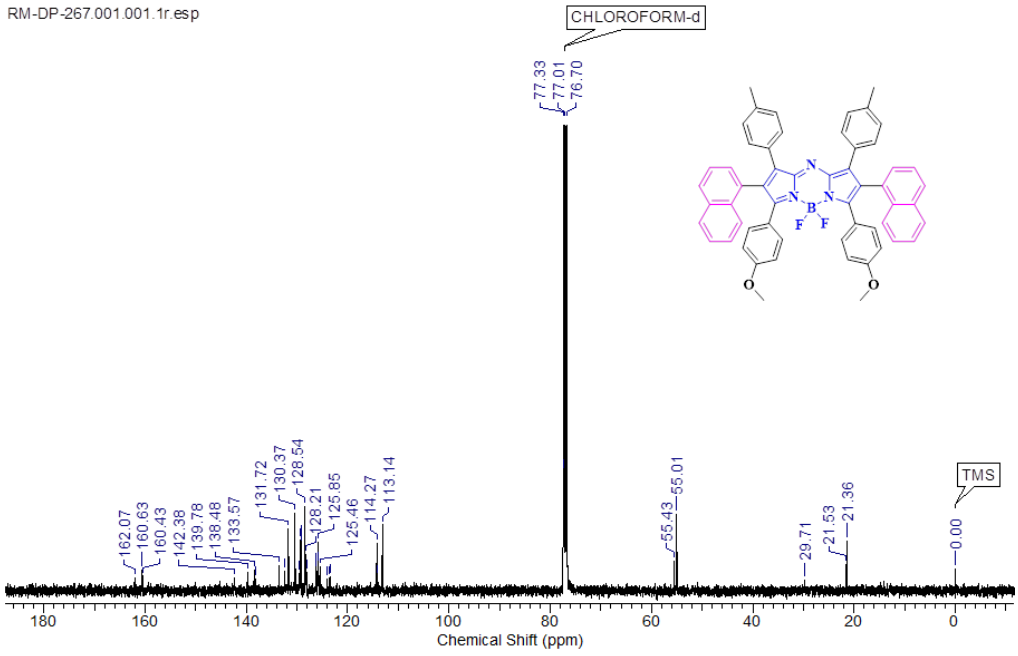


Figure 14. ^{13}C NMR spectrum of aza–BODIPY **4**.

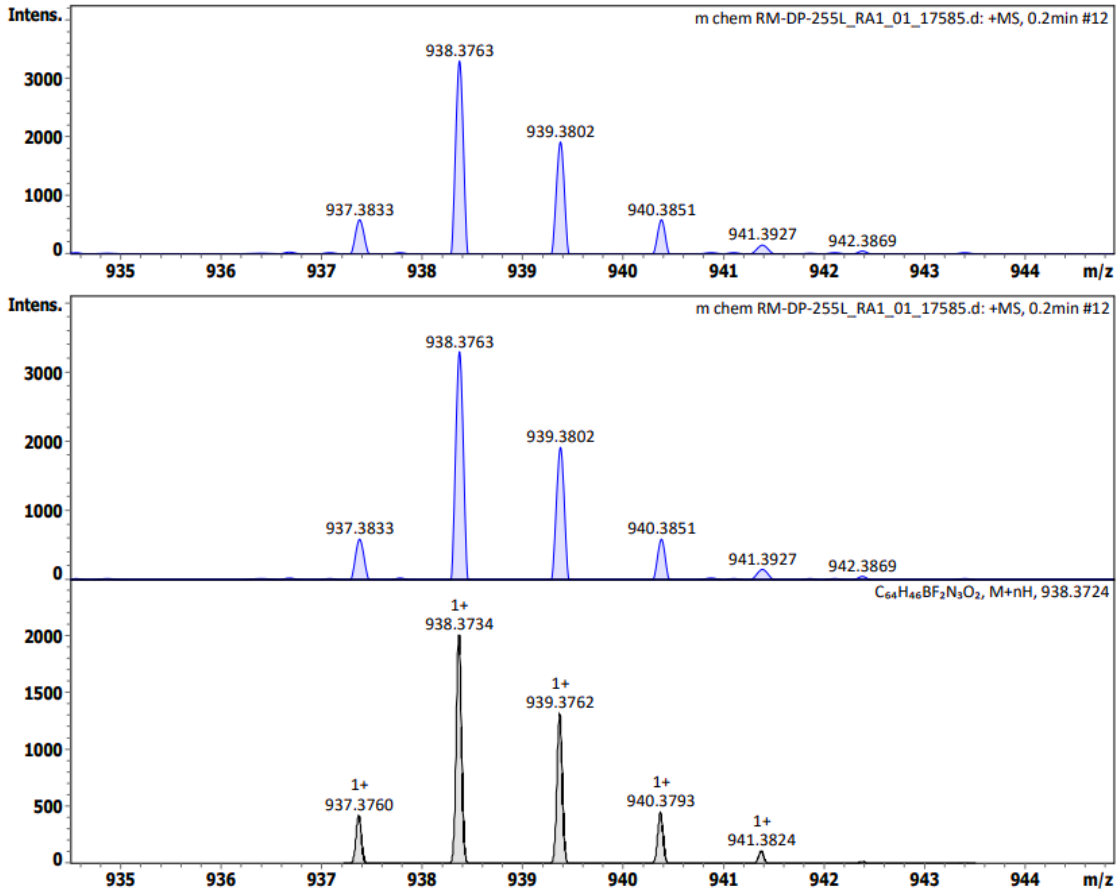


Figure 15. LCMS of aza–BODIPY **5**.

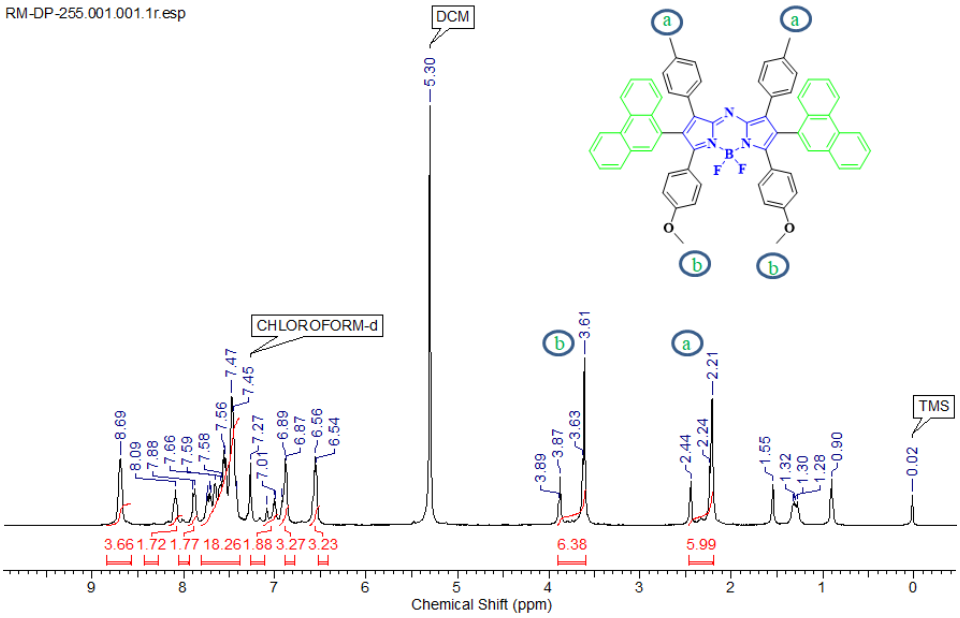


Figure 16. ^{1}H NMR spectrum of aza–BODIPY **5**.

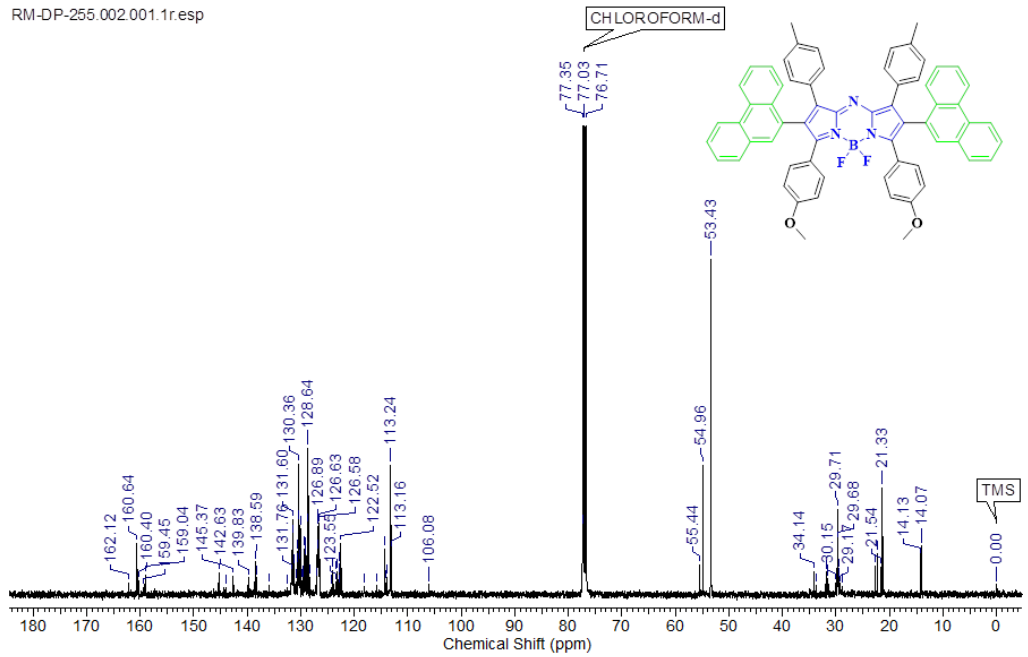


Figure 17. ^{13}C NMR spectrum of aza–BODIPY **5**.

REFERENCES

1. Loudet, A., & Burgess, K. (2007). BODIPY dyes and their derivatives: syntheses and spectroscopic properties. Chemical Reviews, 107, 4891.
2. Ulrich, G., Ziessel, R., & Harriman, A. (2008). The chemistry of fluorescent bodipy dyes: versatility unsurpassed. Angewandte Chemie International Edition, 47,1184.
3. Killoran, J., Allen, L., Gallagher, J. F., Gallagher, W. M., & Donal, F. O. (2002). Synthesis of BF_2 chelates of tetraarylazadipyrromethenes and evidence for their photodynamic therapeutic behaviour. Chemical Communications, 17, 1862.
4. Rogers, M.A.T. (1943). 2: 4-Diarylpyrroles. Part I. Synthesis of 2: 4-diarylpyrroles and 2: 2′: 4: 4′-tetra-arylazadipyrromethines. Journal of the Chemical Society, 590.
5. Lu, P., Zhang, X., Ren, T., & Yuan, L. (2020). Molecular engineering of ultra-sensitive fluorescent probe with large Stokes shift for imaging of basal HOCl in tumor cells and tissues. Chinese Chemical Letters, 31, 2980.
6. Liu, M., Ma, S., She, M., Chen, J., Wang, Z., Liu, P., Zhang, S., & Li, J. (2019). Structural modification of BODIPY: Improve its applicability. Chinese Chemical Letters, 30, 1815.
7. Kolemen, S., & Akkaya, E. U. (2018). Reaction-based BODIPY probes for selective bio-imaging. Coordination Chemistry Reviews, 354, 121.
8. Sheng, W., Lv, F., Tang, B., Hao, E., & Jiao, L. (2019). Toward the most versatile fluorophore: Direct functionalization of BODIPY dyes via regioselective C–H bond activation. Chinese Chemical Letters, 30, 1825.
9. Wang, L., Du, W., Hu, Z., Uvdal, K., Li, L., & Huang, W. (2019). Hybrid rhodamine fluorophores in the visible/NIR region for biological imaging. Angewandte Chemie International Edition, 58, 14026.
10. Weber, J., Beard, P. C., & Bohndiek, S. E. (2016). Contrast agents for molecular photoacoustic imaging. Nature Methods, 13, 639.
11. Chapran, M., Angioni, E., Findlay, N. J., Breig, B., Cherpak, V., Stakhira, P., & Skabara, P. J. (2017). An ambipolar BODIPY derivative for a white exciplex OLED and cholesteric liquid crystal laser toward multifunctional devices. ACS Applied Materials & Interfaces, 9, 4750.
12. Wu, D., Cheung, S., Devocelle, M., Zhang, L. J., Chen, Z. L., & O'Shea, D. F. (2015). Synthesis and assessment of a maleimide functionalized BF_2

azadipyrromethene near-infrared fluorochrome. Chemical Communications, 51, 16667.

13. Palma, A., Alvarez, L. A., Scholz, D., Frimannsson, D. O., Grossi, M., Quinn, S. J., & O'Shea, D. F. (2011). Cellular uptake mediated off/on responsive near-infrared fluorescent nanoparticles. Journal of American Chemical Society, 133, 19618.
14. Palma, A., Tasior, M., Frimannsson, D. O., Vu, T. T., Meallet-Renault, R., & O'Shea, D. F. (2009). New on-bead near-infrared fluorophores and fluorescent sensor constructs. Organic Letters, 11, 3638.
15. Loudet, A., Bandichhor, R., Burgess, K., Palma, A., McDonnell, S. O., Hall, M. J., & O'Shea, D. F. (2008). B, O-chelated azadipyrromethenes as near-IR probes. Organic Letters, 10, 4771.
16. Yan, Y., Zhang, X., Zhang, X., Li, N., Man, H., Chen, L., & Xiao, Y. (2020). Ratiometric sensing lysosomal pH in inflammatory macrophages by a BODIPY-rhodamine dyad with restrained FRET. Chinese Chemical Letters, 31, 1091.
17. Boens, N., Verbelen, B., Ortiz, M. J., Jiao, L., & Dehaen, W. (2019). Synthesis of BODIPY dyes through postfunctionalization of the boron dipyrromethene core. Coordination Chemistry Reviews, 399, 213024.
18. Wang, C., Qiao, Q., Chi, W., Chen, J., Liu, W., Tan, D., & Liu, X. (2020). Quantitative design of bright fluorophores and AIEgens by the accurate prediction of twisted intramolecular charge transfer (TICT). Angewandte Chemie, 132, 10246.
19. Wang, J., Gong, Q., Wang, L., Hao, E., & Jiao, L. (2020). The main strategies for tuning BODIPY fluorophores into photosensitizers. Journal of Porphyrins and Phthalocyanines, 24, 603.
20. Du, J., Xu, N., Fan, J., Sun, W., & Peng, X. (2019). Carbon dots for in vivo bioimaging and theranostics. Small, 15, 1805087.
21. Zhou, N., Huo, F., Yue, Y., Ma, K., & Yin, C. (2020). Rearrangement regulated cysteine fluorescent probe for cellular oxidative stress evaluation induced by copper (II). Chinese Chemical Letters, 31, 2970.
22. Mao, W.L., Zhu, M.M., Yan, C.X. (2020). Rational design of ratiometric near-infrared aza-BODIPY-based fluorescent probe for in vivo imaging of endogenous hydrogen peroxide. ACS Applied Bio Materials, 3, 45.

23. Lu, H., Shimizu, S., Mack, J., Shen, Z., & Kobayashi, N. (2011). Synthesis and spectroscopic properties of fused-ring-expanded Aza-Boradiazaindacenes. Chemistry–An Asian Journal, 6, 1026.
24. Zhang, H., Xu, P., Zhang, X., Cao, X., Han, W., Liu, M., & Zeng, W. (2020). Au nanoparticles based ultra-fast "Turn-On" fluorescent sensor for detection of biothiols and its application in living cell imaging. Chinese Chemical Letters, 31, 1083.
25. A Shi, Z., Han, X., Hu, W., Bai, H., Peng, B., Ji, L., & Huang, W. (2020). Bioapplications of small molecule aza-BODIPY: from rational structural design to in vivo investigations. Chemical Society Reviews, 49, 7533.
26. Zhao, W., & Carreira, E. M. (2006). Conformationally restricted aza-BODIPY: highly fluorescent, stable near-infrared absorbing dyes. Chemistry–A European Journal, 12, 7254.
27. Donyagina, V. F., Shimizu, S., Kobayashi, N., & Lukyanets, E. A. (2008). Synthesis of N, N-difluoroboryl complexes of 3, 3′-diarylazadiisoindolylmethenes. Tetrahedron Letters, 49, 6152.
28. Gorman, A., Killoran, J., O'Shea, C., Kenna, T., Gallagher, W.M., O'Shea, D.F. (2004). In vitro demonstration of the heavy-atom effect for photodynamic therapy. Journal of American Chemical Society, 126, 10619.
29. Killoran, J., Allen, L., Gallagher, J.F., Gallagher, W.M., O′Shea, D.F. (2002). Synthesis of BF_2 chelates of tetraarylazadipyrromethenes and evidence for their photodynamic therapeutic behavior. Chemical Communications, 1862.