Synthesis and Characterization of Fluorophores for the Detection of Lanthanides and Actinides

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SYNTHESIS AND CHARACTERIZATION OF FLUOROPHORES FOR THE DETECTION OF LANTHANIDES AND ACTINIDES

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Interim Dean of the Graduate School
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By

Robinson I. Roacho

2014
This dissertation is dedicated to everybody that has been a part of my life, even if our pathways are not together anymore. I want to thank God for blessing me with a wonderful family and a great life, I must say. This work is the result of all the unconditional love and support that my father Eliseo Roacho and my mother Carmen Baca have shown me since before I was born. This manuscript is also dedicated to my wife Cristina Rivera for helping me in any form she can and cheering me up when I felt disappointed. My sister Kennya Roacho and her family have always encouraged me to push my boundaries, and thus this dissertation is also dedicated to them. Lastly, I want to thank my friends Alfredo Ornelas, Arturo Torres, Edgar Garia, Mario Fierro, Edgar Gutierrez, Carlos Rodriguez, Elias Fraire, Lee Walker, Dr. Renzo Arias, and their families for all the nice experiences we have been through. We shall remain friends forever.

To all,

Thank you!
SYNTHESIS AND CHARACTERIZATION OF FLUOROPHORES FOR THE DETECTION OF LANTHANIDES AND ACTINIDES

By

ROBINSON ROACHO

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Abstract

A series of fluorophores based in the boron dipyrromethene (BODIPY) family were synthesized and characterized. These fluorophores have the capacity of being introduced to a carbamoyl methyl phosphine oxide (CMPO) lanthanide/actinide extractant. These blue, green and red emission fluorophores show high thermal/moisture stability and high fluorescence efficiencies. The fluorescence intensity seems to be dependent on the restricted rotation about the C(8)-C bond in 8-Ph-BODIPY. By taking advantage of this feature, a hydroxyl-containing BODIPY with high fluorescence intensity was synthesized to be incorporated to a CMPO carboxylic acid via esterification. Unfortunately, we did not observe an optical response upon the coordination of the single CMPO-fluorophore ligand to various lanthanides.

The generality of the reaction between primary amines and secondary amines and 8-MeS-BODIPY is also discussed along with the optical properties of the new amino-BODIPY fluorophores. The most important feature observed was the significant dependence of their fluorescence intensity with respect to solvent polarity variation.

Following the same nucleophilic substitution type of reaction, we explored the generality of nucleophilic substitution of 8-MeS-BODIPY by several alkyl- and aryl-thiols under mild conditions. We also observed that polysubstitution is possible by changing the solvent. The optical features and x-ray crystal structures are herein described.

Lastly, a mass spectrometric - collision-induced dissociation (MS-CID) study of lanthanides and various CMPOs is described. It was found that a tridentate CMPO has the capacity to form bis(ligand), nitrate-free complexes with several lanthanides.
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Chapter 1 - Introduction

The search for cheaper and cleaner alternative energy sources to fossil fuel combustion is becoming increasingly important due to environmental and economic concerns. Nuclear energy is an example of an alternative energy source that has gained popularity since the second half of the 20th century. According to the European Nuclear Society, 437 nuclear power plants in 31 countries were connected to the power grid, while 68 are under construction.\(^1\)

One of the main concerns regarding this technology is the fate of the nuclear waste generated in the electricity generation process. High level radioactive waste is produced during the “uranium burning” process, which leads to the formation of long-lived actinides such as plutonium, americium, neptunium, and curium. Since transuranic materials are highly toxic and long-lived, they are deposited in deep geological repositories. The Waste Isolation Pilot Plant (WIPP) located in Carlsbad, NM is one of the facilities utilized for such a purpose.\(^2\)

An alternative to depositing the nuclear waste in repositories is to recycle it. Researchers are developing methodologies for the reprocessing of nuclear waste which requires the quantitative extraction of uranium and plutonium from high level waste. In this process, the nuclear waste is dissolved in 3-4M HNO\(_3\) to solubilize the uranium oxide, followed by the liquid-liquid extraction of uranium(IV) and plutonium(IV) by an organic ligand.\(^3\)

Several organic ligands have been studied for their ability to coordinate to lanthanides and actinides. Carbamoyl methyl phosphine oxide (CMPO), tributyl phosphate (TBP), N,N,N',N'-tetra(n-octyl)diglycolamide (TODGA) and thenoyl trifluoroacetone (TTA) are among the most widely researched, Figure 1.\(^4\)
CMPO, TODGA and TTA are bidentate ligands, while the TBP is a monodentate ligand. A key advantage of the CMPO ligand over its peers is that it may be used for the extraction of trivalent actinides such as Am(III) and Cm(III) from high-level waste (HLW) at 3-4M HNO₃, Figure 2. TBP has the limitation of being an extraction ligand only at low acidity (<1 M HNO₃). This means that it is not suitable for HLW reprocessing, where actinides are stored in 3-4M HNO₃ solutions. TODGA ligands show a high affinity for trivalent lanthanides/actinides compared to the hexavalent metal ions. For instance, these ligands show high empathy for La(III) and Yb(III) even at high pHs (~5).⁵

Thenoyltrifluoroacetone (TTA) shows poor extraction properties for U(IV) and Th(IV) according to Lin et al. since only 15% of the metals were extracted from a cellulose-based filter paper.⁶
The CMPO family has also been extensively researched because its extraction properties may be
tweaked by functionalizing the molecules at the phosphine oxide or the amide functional
groups. Several calix[4]arene CMPOs have been developed taking advantage of the
functionalization feasibility in the amide position, Figure 3. These calix[4]arenes may be fixed
to silica particles via amide bridges. Additionally, the substitution in the phosphine oxide site
has been exploited as a pathway to decrease the solubility of the molecule in acidic media.
Therefore, it is common to observe phenyl rings or long aliphatic chains such as n-octyl to
decrease the polarity of the molecule.
In general, the CMPO may be prepared by reacting 3 equivalents of phenyl magnesium bromide (Grignard) with diethylphosphite which produces the diphenyl phosphine oxide, which is reacted with chloro-N-N’-diiso-butyl-acetamide. The CMPO is purified by recrystallization from hot hexanes, Scheme 1. Using this methodology, 80-100 grams of the material may be synthesized per reaction in one-pot, which makes the CMPO readily available.9

Scheme 1. Synthesis of the carbamoyl methyl phosphine oxide (CMPO)

There are relatively few examples of single crystal x-ray structures of metal-CMPO complexes reported in the literature. However, our group was successful in growing crystals of uranyl nitrate –CMPO which provides evidence of bidentate coordination in the solid state, Figure 4.10 It must be noted that growing crystals of a lanthanide/actinide-CMPO complex is not trivial probably due to the high degrees of freedom present in the CMPO molecule and the poor solubility of the metal salts in THF and other mildly polar organic solvents.
Our group began exploring the possibility of introducing functional groups on the methylene carbon atom of the CMPO by reacting the CMPO with sodium hydride to form the CMPO anion. The anion species readily reacts with several organohalides to form the derivatized CMPO, Scheme 2.

The reaction proceeds smoothly and it is generally completed after 3 hours in good-to-high yields. A variety of substituents were introduced to the CMPO using this methodology such as alkyl and allylic chains, esters, thiols, amides and carboxylic acids, Figure 5.
One of the issues with the CMPO is that it is a colorless molecule. Therefore, we hypothesize that the introduction of a chromophore or fluorophore could improve the detection of the metal ion chelated to the ligand. Perhaps the functional groups previously described may be used as bridges to introduce a fluorophore to the CMPO, which would now act as an optical chemosensor for lanthanides and actinides.

Other dyes have been used for the detection of uranyl and plutonyl such as 2,2’-(1,8-dihydroxy-3,6-disulfonaphthylene-2,7-bisazo)-bisbenzenarsonic acid (AzIII)\textsuperscript{13} and and 2-(5-bromo-2-pyridylazo)-5-(diethylamino)phenol (BrPADAP)\textsuperscript{14}, Figure 6. These dyes display relatively low limits of UO\textsubscript{2}\textsuperscript{2+} detection (46 ppb for AzIII and 200 ppm for BrPADAP). One of the drawbacks for AzIII is that it has low selectivity for actinides over lanthanides since it displays similar molar extinction coefficients for Th(IV) or the trivalent lanthanides. BrPADAP complexes strongly to Th(IV); therefore, its detection capabilities for uranyl and plutonyl are hindered in the presence of Th(IV) which is common in nuclear waste.
Sessler et al. reported a potential hexaphyrin-based colorimetric sensor for uranyl, plutonyl and neptunyl. The acid salt of the hexaphyrin is treated with triethylamine followed by metal complexation resulting in a dramatic color change.\textsuperscript{15}

These dyes use the UV/vis absorption spectroscopy as the tool for detection. However, we envisioned that the limits of detection could be lowered by the use of fluorescence spectroscopy since its sensitivity is higher compared to the absorbance spectroscopy. Furthermore, by creating a CMPO-Fl ligand, we eliminate the necessity for the use of bases as observed in the case of the hexaphyrin complex. This thesis aims at exploring the feasibility of this concept.
Chapter 2 - Problem

An emissive CMPO has not been described in the literature to our knowledge. This chemosensor could aid in the detection and/or identification of a metal ion coordinated to the ligand by triggering a response in its optical properties, e.g. emission wavelength and/or fluorescence intensity.

One of the advantages of such a sensor would be the low detection limit capability since fluorescence techniques involve minimal amounts of material to generate a response. The ultimate goal of this project is to link the CMPO ligand and the fluorophore (Fl) to create a CMPO-fluorophore (Fl) material, and to examine the optical response once the ligand interacts with different metal ion species.

The main problem is to design and synthesize a fluorophore which may be incorporated to the CMPO materials available in our laboratory. There are several emissive dyes that have been used as optical chemosensors for the detection and identification of metal ions such as rhodamines, coumarins, fluoresceins and BODIPYs, which will be described below along with several examples.

Therefore, the first task is to choose a potential fluorophore which is air/moisture stable. This is important because we want to design a CMPO-Fl material capable of being utilized in field experiments in ambient atmosphere. Its fluorescence intensity is not a major concern since the CMPO-fluorophore may act as a turn on/off switch. This means that the fluorophore may show fluorescence upon coordination of the metal ion only. Finally, the fluorophore must be readily available so a relatively large-scale production is possible for the industrial application.
In general, a CMPO-functionality is needed as a way to introduce the fluorophore. Therefore, we plan to use the CMPO-carboxylic acid, CMPO-amine, and CMPO-thiol available in our laboratory. We are proposing three plausible synthetic pathways to produce the CMPO-Fl:

A fluorophore containing a hydroxyl-moiety could be reacted with the CMPO-carboxylic acid in an esterification reaction to produce the CMPO-Fl molecule. This ester bridge may be able to communicate the ligand to the fluorophore to produce an optical response when the ligand chelates to metal ions.

Further, the CMPO and the fluorophores may be bridged via amine if the CMPO-amine is reacted with a halogenated fluorophore to form the CMPO-NH-Fl.

Using a similar approach, we may synthesize a CMPO-S-Fl by reacting the CMPO-thiol with a halogenated fluorophore. However, since the nucleophilicity of the sulfur is lower than nitrogen, this methodology may require the formation of a CMPO-thiolate salt which could then react via nucleophilic substitution to form the CMPO-S-Fl product.

These ideas are presented in Scheme 4.
Now that we have described the proposed methodologies, we should choose a fluorophore to carry out the proposed reactions.

Several fluorophores have been utilized as metal ion chemosensors. Among them, coumarins, fluoresceins, rhodamines, and BODIPYs are the most popular, Figure 7. The emission of fluoresceins and rhodamines is activated only in the presence of ethanol. However, the fluorescence intensity of BODIPYs is high in common non-polar and polar organic solvents, and even in aqueous media.

Scheme 4. Proposed pathways for the introduction of the fluorophore to the Ln/Ac extractants using available CMPO materials.
A functionalized coumarin has been reported to exhibit enhanced fluorescence intensity upon coordination to Zn(II) ions, Figure 8. Although the authors do not describe the coordination mode of the ligand to the metal ion, it shows selectivity for Zn(II) probably due to the size of the cation.²⁰

Fluorescein derivatives have found uses as copper ion sensors with high sensitivities. Jun et al. reported a fluorescein-based fluorophore capable of detecting Cu²⁺ in nanomolar concentrations, Figure 9.²¹
Rhodamines, which resemble the structure of fluoresceins, may be functionalized to recognize Cu\(^{2+}\) as well, Figure 10. The mechanism proposed by Zhou et al. involves a ring opening upon Cu\(^{2+}\) coordination which forms the double bond necessary in order for the rhodamine to exhibit fluorescence. Therefore, this chemosensor could be cataloged as on/off sensor\(^{22}\).

In the same fashion, BODIPYs have been modified to act as chemosensors for the detection of several transition metals. Qi et al. reported a photoinduced electron transfer (PET) based chemosensor that coordinates selectively to Cu\(^{2+}\) ions in a tridentate fashion, Figure 11\(^{23}\). The photoinduced electron transfer is a fluorescence quenching mechanism where upon excitation of the fluorophore, the amine donates an electron to the HOMO of the fluorophore, Figure 12, top, step 2. Therefore, the excited electron from the fluorophore cannot go back to the ground state since the space is already occupied by the electron donated by the amine. Subsequently, the
molecule regenerates itself via thermal-back transfer electron from the LUMO of the fluorophore to the HOMO of the amine, a non-radiative relaxation process, Figure 12, top, step 3. Upon coordination of the amine to the metal ion, the energy of the frontier orbital of the amine is below the HOMO of the fluorophore, and the electron transfer is not possible. Therefore, the excited fluorophore returns to the ground state via fluorescence, Figure 12, right.\textsuperscript{23}

Figure 11. BODIPY-based chemosensor for the detection of Cu\textsuperscript{2+} ions

Figure 12. Photoinduced electron transfer (PET) process in the “off” state (top) and “on” state (bottom)

We chose to focus on the BODIPY family as the potential fluorophore candidate for the chemosensor that we envisioned because it is air/moisture stable and it shows high fluorescence under common organic solvents in neutral conditions.
To our knowledge, BODIPYs have been explored only as transition metal ion chemosensors. Therefore, we seek to create the first lanthanide/actinide (Ln/An) chemosensor by combining the CMPO Ln/An selectivity and the BODIPY fluorescence.

The CMPO and the BODIPY may be bridged by a large variety of linkers. However, by taking into consideration the functionalized CMPOs available in our laboratory, we aim at bridging the ligand and the fluorophore by a thioether, ester, or amide.

However, before we try to produce the CMPO-Fl material, it is a good idea to explore the generality of the reactions that we proposed with simpler molecules. This will give us a good idea of what to expect in terms of reaction yields and fluorescence intensity of the new materials. Therefore, we set to explore the chemistry of the BODIPYs.

BODIPY Chemistry

In the 1960s, Treibs and Kreuzer described for the first time the synthesis and some optical properties of 4,4-difluoro-4-bora-3a,4a-diaza,s-indacene (BODIPY) dyes, Figure 13. The novel fluorophores rapidly caught the attention of the scientific community mainly because their optical properties could easily be tweaked by substituting in the positions 1- and 7-, 2- and 6-, 3- and 5-, and 8- (meso). Furthermore, the extinction coefficients of derivatized BODIPYs are generally high ( > 50,000 M$^{-1}$ cm$^{-1}$), and the stability in air and moisture is remarkable. These compounds found several applications which include metal ion sensing,$^{24}$ protein tagging,$^{25}$ light-harvesting,$^{26}$ and laser dyes.$^{27}$
The BODIPY is readily available by reacting 2,4-dialkyl-pyrrole with an acyl halide followed by the treatment with triethylamine/boron trifluoride to introduce the BF$_2$ moiety in yields of 20% to 30%. Although this is a popular synthetic methodology, the high costs of 2,4-dimethylpyrrole should not be discounted, Scheme 5.$^{19}$

![Scheme 5. Synthesis of 1,3,5,7-tetramethyl-BODIPY using acyl chloride and protected pyrrole](image)

In 2006, Biellmann et al. reported the synthesis of 8-methylthio-BODIPY (I),$^{28}$ which our laboratory took interested in because of its synthetic availability and good reactivity. The reaction of pyrrole and thiophosgene produces dipyrrithioketone, which is treated with methyl iodide to form the dipyrrromethene compound, followed by the insertion of the BF$_2$- moiety, Scheme 6. The dipyrrithioketone and the final BODIPY product are moisture stable. However, all efforts to isolate, characterize or crystallize the dipyrrromethene iodide salt failed.
In Biellmann’s report, they briefly explored the aromatic nucleophilic substitution of the 8-MeS-BODIPY by aniline. Although the reaction was carried out in high yields, the resulting material was a non-emissive dye, and further reactivity studies by amines were stopped, Scheme 7.

Peña et al. investigated the C-C bond formation in the meso-site of the BODIPY core by substituting the MeS- via the palladium catalyzed Liebeskind-Srogl cross coupling reaction.\textsuperscript{29,30} The 8-MeS-BODIPY was even used as a metal ion sensor for Hg\textsuperscript{2+}, Figure 14.\textsuperscript{31}
Due to the versatility of the 8-MeS-BODIPY, our laboratory in collaboration with Peña-Cabrera decided to use it as the fluorophore of choice for the incorporation to the CMPO ligand.
Chapter 3 - Solution

Section I: Chemistry of the CMPO-acid and the BODIPY-Alcohol

Hypothesis

The carboxylic acid functional group of the CMPO ligand may undergo esterification with a hydroxyl-BODIPY to form the desired CMPO-fluorophore. The synthesis of the dye should be facile, in high yields, and it should exhibit high fluorescence intensity.

Introduction

A hydroxyl-functionalized BODIPY is a versatile fluorophore that may be incorporated to a larger molecule by an esterification procedure. In 2009, Rao et al. described the synthesis of 8-(o-hydroxyl)phenyl-BODIPY using o-hydroxybenzaldehyde as precursor. While this material may be used as the fluorophore for the CMPO-Fl, the introduction of a methylene-group between the hydroxyl-moiety and the phenyl ring should avoid or reduce any steric hindrance adverse effects during the esterification process. 8-(α-hydroxymethyl)phenyl-BODIPY (2a) was the initial target molecule because the fluorophore could be readily synthesized from commercially available materials following the procedure reported by Peña et al. The molecule should be highly emissive, and the methylene bridge between the fluorophore and the hydroxyl-moiety should reduce the steric hindrance effects in the esterification reaction with the CMPO carboxylic acid, Figure 15.
Carbon-carbon bonds may be formed by treating the 8-MeS-BODIPY with the corresponding alkyl- or aryl- boronic acid in catalytic conditions using the Liebeskind-Srogl cross coupling reaction. Therefore, 2a was synthesized using 8-(o-hydroxymethyl)phenyl boronic acid, commercially available, in quantitative yields. The meta- (2b) and the para- (2c) isomers were also synthesized under the same conditions to study their optical properties. Moreover, in an effort to explore the generality of the emission features with respect to the hydroxyl- functional group, the isomeric ortho- (3a), meta- (3b) and para- (3c) methoxyphenyl-BODIPYs were subsequently synthesized, Scheme 8.

Scheme 8. Reaction of 8-methylthio-BODIPY (1) with commercially available boronic acids
**Experimental**

BODIPY 2a was synthesized following a previously reported procedure. A 100 mL round bottom flask was charged with 0.2 g (0.84 mmol) of 8-MeS-BODIPY and 0.38 g (2.52 mmol) of o-(hydroxymethyl)phenyl boronic acid dissolved in 30 mL of dry THF under inert atmosphere. Then, 0.08 g (0.084 mmol) of Pd$_2$(dba)$_3$, 0.48 g (2.52 mmol) of CuTC and 0.06 g (0.252 mmol) of TFP were added. The mixture was stirred at 55°C for 6 hours. The starting material was not present as per silica gel thin-layer chromatography. The solvent was removed under vacuum, and the product was purified by silica gel column chromatography using silica of 60 Å and size 60-200 µm in a column of 6 inches high by 1 inch wide using a gradient mixture of ethyl acetate and hexane as eluent. The product was recrystallized from a dichloromethane/hexane mixture yielding red crystals in ~ 90% yield. Compounds 2b-c, 3a-c were synthesized using the same procedure.

**2a:** Orange Crystals, yield 90%, m.pt. 101-102 °C. $^1$H NMR (CDCl$_3$): δ 4.59 (s, 2H), 6.48 (d, 2H, J = 4.08 Hz), 6.70 (d, 2H, J = 4.14 Hz), 7.30-7.31 (m, 1H), 7.38-7.41 (m, 1H), 7.54-7.56 (m, 1H), 7.66 (d, 1H, J = 8.28 Hz), 7.92 (s, 2H). $^{13}$C NMR (CDCl$_3$): δ 62.3 (CH$_2$), 118.7 (CH), 127.0 (CH), 128.0 (CH), 129.8 (CH), 130.1 (CH), 131.0 (CH), 131.3, 135.4, 139.3, 145.5 (ipso), 144.6 (CH). $^{19}$F NMR (CDCl$_3$): δ -144.9(q).

**2b:** Orange powder, yield 92%, m.pt. 159-160 °C. $^1$H NMR (CDCl$_3$): δ 4.8 (s, 2H), 6.53 (d, 1H, J = 3.42 Hz), 6.92 (d, 2H, J = 4.08 Hz), 7.50 (m, 2H), 7.58 (m, 2H), 7.93 (s, 2H). $^{13}$C NMR (CDCl$_3$): δ 64.7 (CH$_2$), 118 (CH), 128.7 (CH), 128.8 (CH), 129.2 (CH), 129.7 (CH), 131.7 (CH), 134.1, 135.0, 141.4, 147.0 (ipso), 144.3 (CH). $^{19}$F NMR (CDCl$_3$): δ -144.9(q).

**2c:** Dark red crystals, yield 90%, m.pt. 152-154 °C. $^1$H NMR (CDCl$_3$): δ 4.82 (s, 2H), 6.53 (d, 2H, J = 3.42), 6.92 (d, 2H, J = 4.08 Hz), 7.54 (m, 4H), 7.92 (s, 2H). $^{13}$C NMR (CDCl$_3$): δ 64.6
(CH₂) 118.6 (CH), 126.8 (CH), 130.8 (CH), 131.6 (CH), 133.1, 135.0, 143.9, 147.2 (ipso), 144.1 (CH). ¹⁹F NMR (CDCl₃): δ -144.9(q).

3a: Dark red crystals, yield 91%, ¹H NMR (CDCl₃): δ 3.73 (s, 3H), 6.46 (d, 2H, J = 3.42), 6.78 (d, 2H, J = 4.14), 7.03 (m, 2H), 7.28 (dd, 1H, J = 2.04, 4.68), 7.49 (td, 1H, J = 1.38, 7.92), 7.88 (s, 2H). ¹³C NMR (CDCl₃): δ 55.6 (CH₂), 111.3 (CH), 118.1 (CH), 120.1 (CH), 122.4 (ipso), 131.1 (CH), 131.5 (CH), 131.6 (CH), 135.7 (ipso), 143.5 (CH), 144.5, 157.1 (ipso). ¹⁹F NMR (CDCl₃): δ -147.9(m), -149.0 (m).

3b: Dark red crystals, yield 92%, ¹H NMR (CDCl₃): δ 3.85 (s, 3H), 6.53 (s, 2H, 6.96 (s, 2H), 7.11 (m, 3H), 7.41 (td, 1H, J = 3.60, 7.68), 7.92 (s, 2H). ¹³C NMR (CDCl₃): δ 55.5 (CH₂), 116.1 (CH), 116.4 (CH), 118.6 (CH), 123.0 (CH), 129.6 (CH), 130.1 (ipso), 131.7 (CH), 135.0 (ipso), 144.3 (CH), 147.2, 159.4 (ipso). ¹⁹F NMR (CDCl₃): δ -145.0(s).

3c: Orange Powder, yield 95%, ¹H NMR (CDCl₃): δ 3.90 (s, 3H), 6.54 (d, 2H, J = 2.04), 6.96 (d, 2H, J = 4.14), 7.04 (m, 2H), 7.54 (m, 2H), 7.91 (s, 2H). ¹³C NMR (CDCl₃): δ 55.6 (CH₃), 114.1 (CH), 118.3 (CH), 126.4 (ipso), 131.4 (CH), 132.5 (CH), 134.9 (ipso), 143.5 (CH), 147.5 (ipso), 162.1 (ipso). ¹⁹F NMR (CDCl₃): δ -144.9(m).

Results and Discussion

NMR Spectroscopy

The materials were characterized by nuclear magnetic resonance studies and the data is in concordance with previously reported BODIPY dyes, Figure 16.¹⁹,³³
due to the coupling of the fluorines with boron-11 (also been observed for 8-o-...}, this non-degeneracy of the fluorine atoms has vide infra, observed from the crystal structure (the oxygen, Figure 17, bottom. At first, we thought that the oxygen could be interacting with the hydrogens in the 1- and 7- positions. However, the distance between the O-H is 3.38 Å as observed from the crystal structure (vide infra, Figure 25, left). Although there is not a conclusive reason of this unusual splitting pattern, this non-degeneracy of the fluorine atoms has also been observed for 8-(o-hydroxy)phenyl-BODIPY. The $^{19}$F NMR shows a quartet typical of the BODIPY cores for series 2 and 3b-c, Figure 17, top, due to the coupling of the fluorines with boron-11 ($I = 3/2$), Figure 18. However, BODIPY 3a shows two sets of signals presumably due to the non-degeneracy of the fluorine atoms caused by the oxygen, Figure 17, bottom. At first, we thought that the oxygen could be interacting with the hydrogens in the 1- and 7- positions. However, the distance between the O-H is 3.38 Å as observed from the crystal structure (vide infra, Figure 25, left). Although there is not a conclusive reason of this unusual splitting pattern, this non-degeneracy of the fluorine atoms has also been observed for 8-(o-hydroxy)phenyl-BODIPY.25
In the case of BODIPY 3a where both fluorines are non-equivalent, a fluorine atom is coupled with the second germinal fluorine to give a doublet. Each peak of the doublet is coupled with the boron to give a doublet of quartets, Figure 18.
Benniston *et al.* suggested the restricted rotation about the C(8)-C(aryl) bond, which causes one fluorine to be in a *cis-* fashion with respect to the oxygen and the other fluorine atom adopts a *trans-* position. However, they performed variable temperature NMR experiments and the rotational barrier was not surpassed even at 60°C. Benniston *et al.* conclude that the two sets of signals correspond to two different fluorines, describing the multiplicity as a multiplet.\(^{32b}\)

The two possible scenarios to describe the coupling between the fluorines are described in Figure 19. In both cases the fluorine-fluorine coupling constant is higher than the fluorine-boron coupling constant as noted in the literature.\(^{34c}\) However, the difference lies in the coupling constant of the fluorine.

We have calculated the coupling constants for these possible scenarios. The fluorine-fluorine \(J_{\text{FF}}\) coupling constant would be calculated measuring the distance of the two peaks in terms of hertz. In the first scenario, we obtained a \(J_{\text{FF}}\) coupling constant of 106.4 Hz by measuring the distance between the first and fifth peaks within one set of signals. The \(J_{\text{FF}}\) is well within the ranges observed for germinal F-F systems reported in the literature.\(^{34c}\) If the second case scenario was true, we would need to measure the distance between the first peaks of both signals, which gives a \(J_{\text{FF}}\) value of 660 Hz. This value is higher than the range observed for germinal F\(_2\) systems. Therefore, the first scenario is more likely to occur in this case. Therefore, we may conclude that the \(J_{\text{FF}}\) value for the BODIPY 3a is 106.4 Hz. The \(J_{\text{BF}}\) constant is 32 Hz which is also in the range of known molecules.\(^{34c}\)
Optical Studies

The fluorophore series 2 and 3 show a strong absorption band at ~500 nm with molar extinction coefficients of approximately 65,000, which is typical of other BODIPY dyes. Therefore, the substitution of the MeS- moiety to form carbon-carbon bonds in the meso- site produces no impact in the absorption wavelength. As a powder, each isomer of 2 is orange. However, 2a shows a strong green color when dissolved in tetrahydrofuran (THF), while 2b and 2c show a pale orange-yellow color, Figure 20. The high fluorescence intensity of 2a is detectable by the naked eye, while it was evident that 2b and 2c did not show a detectable fluorescence. This was confirmed by emission spectroscopy using the $\lambda_{\text{max abs}}$ as the excitation wavelength, Figure 21.
The emission of 2a is high, while the emission for 2b and 2c is barely detectable by the fluorometer.

![Absorbance and emission spectra of compound series 2](image)

**Figure 20.** 2a (left), 2b (center), 2c (right). 1x10^{-3} M THF solutions

![Normalized Absorbance and Fluorescence](image)

**Figure 21.** Absorbance and emission spectra of compound series 2

In an effort to provide more evidence regarding the cause for the high fluorescence intensity of 2a compared to the other isomers of 2, we measured the fluorescence intensity of compound series 3, Figure 22. The emission pattern is similar suggesting that the emission intensity is directly related to the position of the substituent in the phenyl ring and not to the hydroxyl-functionality. This indicates that the fluorescence intensity of 2a should remain high upon the esterification with the CMPO carboxylic acid to produce the CMPO-C(O)O-BODIPY chemosensor.
Since the molecule can exhibit restricted rotation about the C(8)-C axis due to the presence of the methylene- (2a) or the methoxide- (3a) in the ortho-site, the radiative relaxation is preferred upon excitation. Hence, these isomers show high fluorescence intensities with quantum yields of 0.68 and 0.85 respectively. Isomers 2b-c, and 3b-c show poor quantum yields in the order of ~0.03 since these fluorophores are free to rotate through the C(8)-C bond, permitting a non-radiative relaxation.

The details of the absorbance and the emission spectra of compound series 2 and 3 are presented in Table 1.

Table 1. Summary of the optical properties of compound series 2 and 3

<table>
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<tr>
<th></th>
<th>2a</th>
<th>2b</th>
<th>2c</th>
<th>3a</th>
<th>3b</th>
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<td>500</td>
<td>500</td>
<td>503</td>
<td>500</td>
<td>498</td>
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<td>61,400</td>
<td>70,100</td>
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<td>66,800</td>
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<td>$\lambda_{\text{max}}$(nm)</td>
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**X-ray Single Crystal Structures**

Crystals suitable for x-ray single crystallography for compound series 2 and 3 were grown from a mixture of dichloromethane and hexane. In each structure, the BODIPY core exhibit typical bond lengths and angles, Figure 23, Table 2 and Table 3.\textsuperscript{19,36} The structures are presented in Figure 24 and Figure 25 respectively.

![Figure 23. BODIPY labeled according to bond lengths and angles measured. The carbons in blue indicate the dihedral (torsion) angle](image-url)
Table 2. Bond lengths of unsubstituted BODIPY, BODIPY 1, and BODIPY series 2 and 3 (Å)

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<th>2a</th>
<th>2b</th>
<th>2c</th>
<th>3a</th>
<th>3b</th>
<th>3c</th>
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<td>1.388</td>
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Table 3. Bond angles of unsubstituted BODIPY, BODIPY 1, and BODIPY series 2 and 3 (°)

<table>
<thead>
<tr>
<th>Bond</th>
<th>Unsubstituted BODIPY</th>
<th>1</th>
<th>2a</th>
<th>2b</th>
<th>2c</th>
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Dihedral

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<td>C4-C5-(ipso)-C(aryl)</td>
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The main structural difference between the three isomers of series 2 and 3 is the dihedral angle between the aryl group and the BODIPY backbone. The trend observed in each series is the same in relation to the substituent position. For BODIPYs 2a and 3a the dihedral angle was 73.6° and
72.6° respectively, while the dihedral angle for BODIPYs 2b-c and 3b-c is approximately 45°, Figure 26 and Figure 27. This implies that the introduction of a substituent in the ortho-position induces an orthogonal geometry with respect to the phenyl and the BODIPY backbone. Moreover, the methylene- and the oxygen impede the rotation about the C(8)-C(ipso) bond. Thus the non-radiative relaxation through rotation is restricted for BODIPYs 2a and 3a resulting in a high fluorescence intensity. Conversely, BODIPYs 2b-c and 3b-c undergo non-radiative relaxation upon excitation due to the rotation about C(8)-C(ipso).

Figure 26. View from the bottom showing the dihedral angle about the C(8)-C(ipso) for BODIPYs 2a (left), 2b (middle), 2c (right)

Figure 27. View from the bottom showing the dihedral angle about the C(8)-C(ipso) for BODIPYs 3a (left), 3b (middle), 3c (right)
Chemistry of CMPO Carboxylic Acid and BODIPY-Alcohol

The esterification reaction of the CMPO Carboxylic Acid and BODIPY 2a was carried out following a methodology reported by Neises and Steglich.\(^{37}\)

\[
\begin{align*}
\text{CMPO} & \quad + \quad \text{BODIPY} \\
\text{HO} & \quad \text{OH} \\
\end{align*}
\]

EDCI, DMAP

\[
\text{CMPO} \quad \text{BODIPY}
\]

1-Ethyl-3-(3-dimethylaminopropyl)carbodiimide
4-dimethylamino-pyridine

Scheme 9. Steglich esterification of the CMPO carboxylic acid and the BODIPY 2a

The CMPO Carboxylic Acid and the BODIPY 2a were dissolved in dry THF under inert atmosphere in a 100 mL round bottom flask. EDCI and DMAP were added and the mixture was refluxed for 5 hours. The reaction was complete as observed by TLC monitoring. The product was purified by silica gel column chromatography using a column eight inches tall and one inch wide using a gradient mixture of THF and hexanes as eluent. The product was a dark red oil material that failed to crystallize in our hands, Figure 28 and Figure 29.
Figure 28. $^1$H NMR of CMPO-ester-BODIPY (top) $^{13}$C NMR of CMPO-ester-BODIPY (bottom)
The optical response of the material was tested against various lanthanides such as La$^{3+}$, Pr$^{3+}$, Nd$^{3+}$ and UO$_2^{2+}$. It was unfortunate to find out that the fluorescence intensity and the wavelength remained unchanged upon metal addition.

![Figure 29. Mass spectra of the CMPO-ester-BODIPY](image)

![Figure 30. Absorbance (left) and emission (right) spectra of a 1 µM solution of CMPO-ester-BODIPY 2a and lanthanum nitrate in THF, where 0% = pure CMPO-ester-BODIPY 2a, and 200% = 2 equivalents of La$^{3+}$](image)
A plausible reason for this unchanged effect in the fluorescence could be that the ester bridge between the CMPO and the BODIPY may be impeding electronic communication between the fluorophore and the ligand. However, perhaps only density functional theory could provide the answer that we seek. No further experiments were carried out with the CMPO-ester-alcohol material, and we decided to move forward with the next proposed CMPO amine chemistry.

Conclusion

We have synthesized and characterized a series of hydroxyl-containing BODIPYs (series 2) dyes in high yields by the Liebeskind-Srogl cross coupling reaction. The ortho-substituted molecule (2a) exhibits a high quantum yield due to the restricted rotation of the aryl ring, which favors a radiative relaxation upon excitation. The hindered rotation was also observed in the x-ray single crystal structure where the dihedral angle between the aryl ring and the BODIPY core was almost orthogonal. We also synthesized the methoxy-BODIPY isomer (3a) to prove that the high quantum yield is independent from the hydroxyl-moiety.

Upon esterification of the BODIPY 2a and the CMPO carboxylic acid, we did not observe any changes in the optical properties of the material. The fluorescence intensity and the emission wavelength remained unchanged upon metal complexation with various lanthanides and uranyl. A possible cause for this effect is that the ester bridge may not be a good electronic conductor between the CMPO and the fluorophore, but we would need to perform ab initio calculations to support this theory.

This work was published in peer-reviewed international chemical journal.

Section II: Chemistry of the CMPO-Amine and the BODIPY-SMe

\[
\text{CMPO} \quad \text{NH}_2 \quad + \quad \text{SMe} \quad \text{BODIPY} \quad \rightarrow \quad \text{CMPO} \quad \text{NH} \quad \text{BODIPY}
\]

**Hypothesis**

The amine functional group of the CMPO may be used as a link between the CMPO and a BODIPY fluorophore. The reaction between the amine and 8-MeS-BODIPY should occur under neutral conditions to produce the CMPO-NH-BODIPY chemosensor, Figure 31.

![Figure 31. CMPO-NH-BODIPY chemosensor targeted](image)

**Introduction**

As an alternative to the hydroxyl- containing BODIPY fluorophore, we explored the possibility of introducing the BODIPY to the CMPO by an amine linkage. The 8-MeS-BODIPY (I), may be a suitable candidate since Biellmann *et al.* reported the nucleophilic substitution reaction of the methylthio- functional group by aniline to form 8-anilino-BODIPY, a non-emissive BODIPY dye.\(^{28}\) Peña *et al.* also reported the introduction of the propargylamino- group by reacting propargylamine and I.\(^{38}\) The reaction seems to occur both with aromatic and aliphatic amines.
The BODIPYs that Peña reported exhibited a hypsochromic shift in the absorbance and emission wavelengths compared to BODIPY 1. As a result, these fluorophores exhibit a blue emission. This was surprising since the substitution of BODIPYs is generally accompanied by a bathochromic shift in the absorbance and emission wavelengths due to a π-conjugation system expansion, which opens the possibility to synthesize yellow, red and near-IR emissive dyes.

Furthermore, they reported a restricted rotation of the amino-moiety through the C(8)-N bond, Figure 32. This was observed by NMR spectroscopy at room temperature. Rotamer A is the preferred structure in CDCl₃ where some degree of rotation exists since the signals belonging to the protons in the BODIPY core were broad. On the contrary, when the molecules are dissolved in more polar solvents such as MeOD, rotamer B is preferred since the NMR signals are sharp.

Figure 32. Rotation on the C(8)-N bond inducing asymmetry in the molecule illustrating the equivalency and non-equivalency of the protons in the BODIPY core

Since more explorations were needed in this area, we decided to investigate further this synthetic methodology to determine if the CMPO-amine could react in the same fashion to form the desired CMPO-Fl.

By following the reported synthetic procedure, we were able to synthesize symmetric and asymmetric 8-amino-BODIPYs, Scheme 10. We explored the rotation restriction of these
BODIPYs by variable temperature nuclear magnetic resonance spectroscopy; we characterized these molecules by x-ray single crystallography, and we studied their optical properties.

![Diagram](image)

Scheme 10. Synthesis of symmetric and asymmetric 8-amino-BODIPY dyes

**Experimental**

BODIPY 5a was synthesized following a previously reported procedure.\(^{28}\) A 100 mL round bottom flask was charged with 50 mg (0.21 mmol) of 8-MeS-BODIPY and 20 µL (0.23 mmol) of isopropylamine. The reaction was stirred for 5 minutes at room temperature. The starting material reacted completely as observed by silica gel thin-layer chromatography. The solvent was removed under vacuum, and the product was purified by silica gel column chromatography using silica of 60Å and size 60-200 µm in a column of 4 inches high and 1 inch wide. The eluent was a gradient mixture of ethyl acetate and hexane. The product was recrystallized from a mixture of dichloromethane/hexane yielding yellow crystals in ~ 90% yield.

Compounds 4, 5b, and 6 were synthesized in a similar fashion.

**5a:** Yellow crystals, yield 88%. \(^1\)H NMR (CDCl\(_3\)): \(\delta\) 1.44-1.47 (m, 6H), 4.40 (m, 1H), 6.36 (s, 1H), 6.43 (s, 1H), 6.50 (s, 1H), 6.90 (s, 1H), 7.14 (s, 1H), 7.49 (s, 1H), 7.64 (s, 1H). \(^1\)C NMR (CDCl\(_3\)): \(\delta\) 22.3(CH3), 48.2 (CH), 114.7 (multiple signals), 121.6 (ipso), 123.5 (CH), 125.1
(ipso), 132.5 (CH), 135.19 (CH), 147.5 (ipso). Anal. Calcd for C_{12}H_{14}N_{3}BF_{2}: C, 57.87; H, 5.67. Found: C, 57.76; H, 5.71.

5b: Yellow crystals, yield 91%. \(^1\)H NMR (CDCl\(_3\)): \(\delta\) 1.01-1.06 (m, 6H), 2.02-2.06 (m, 1H), 3.30-3.33 (m, 1H), 6.28 (m, 1H), 6.49 (m, 1H), 6.62 (m, 1H), 6.80 (m, 1H), 7.06 (m, 1H), 7.43 (m, 1H), 7.66 (m, 1H). \(^{13}\)C NMR (CDCl\(_3\)): \(\delta\) 20.3(CH\(_3\)), 28.2 (CH), 54.5 (CH\(_2\)), 113.8 (CH), 114.4 (CH), 114.8 (CH), 122.4 (ipso), 123.8 (CH), 125.1 (ipso), 132.4 (ipso), 135.6 (ipso), 148.4 (ipso). Anal. Calcd for C\(_{13}\)H\(_{16}\)N\(_3\)BF\(_2\): C, 59.35; H, 6.13. Found: C, 59.09; H, 6.15.

6: Yellow crystals, yield 87%. \(^1\)H NMR (CDCl\(_3\)): \(\delta\) 1.54-1.56 (m, 6H), 4.10-4.11 (m, 4H), 6.40 (d, 2H), 6.97 (d, 2H), 7.53 (s, 2H). \(^{13}\)C NMR (CDCl\(_3\)): \(\delta\) 13.6 (CH\(_3\)), 50.9 (CH\(_2\)), 113.0 (CH), 121.6 (CH), 124.2 (ipso), 132.4 (CH), 153.1 (ipso). Anal. Calcd for C\(_{13}\)H\(_{16}\)N\(_3\)BF\(_2\): C, 59.35; H, 6.13. Found: C, 59.57; H, 6.19.

**Results and Discussion**

**NMR Spectroscopy**

The protons of the BODIPY core in the asymmetric amino-BODIPYs 5a-b are non-equivalent as shown by \(^1\)H NMR experiments, Figure 33. This effect was noted by our collaborator Eduardo Peña in the 8-propargylamino-BODIPY. However, it seems that there is some degree of rotation through the C(8)-N bond since the signals appear broad. Therefore, rotamer A seems to be the preferred conformation. In more polar solvents such as MeOD, these signals are sharp which suggests that there is no rotation through the C(8)-N bond. Therefore, rotamer B is stabilized by polar solvents probably by hydrogen bonding interactions, *vide infra*, Figure 38.
Figure 33. Aromatic region of $^1$H NMR spectrum of $5b$ in CDCl$_3$ (top) and CD$_3$OD (bottom) at ~25 °C. Note: in the CDCl$_3$ spectrum, the NH has been exchanged with ND via treatment with CD$_3$OD. In the CD$_3$OD spectrum there is an overlap of two resonances at 7.3 ppm.

Variable temperature NMR studies on $5a$ and $5b$ confirm the restricted rotation of the C(8)-N bond since the signals are sharp at 5°C. Progressively raising the temperature results in a broadening and final coalescence of the six resonances into three singlets as expected due to the rapid rotation of the C(8)-N bond. By determining the coalescence temperature, we were able to calculate the activation energies at 59.2 KJ/mol for $5a$ and 62.9 KJ/mol for $5b$, Figure 34 and Figure 35 respectively.
Figure 34. Aromatic region $^1$H NMR spectra of 5a in CDCl$_3$ from 55°C (top) to 5°C (bottom). The extra resonance at ~6.45 ppm is due to the NH.

Figure 35. Aromatic region $^1$H NMR spectra of 5b in CDCl$_3$ from 55°C (top) to 5°C (bottom). The extra resonance at ~6.6 is due to the NH.

In the case of BODIPY 6, since there is no asymmetry associated with the disubstituted amine, only three resonances are expected in the $^1$H NMR spectrum regardless of the solvent. The $^{19}$F NMR exhibits a multiplet with a chemical shift of -146 ppm typical of other BODIPY dyes.
Optical Studies

Each of the amino-BODIPYs exhibits a pale yellow color in solution and in the solid state, in contrast with the starting material. Each fluorophore exhibits an absorbance in the range of 400 nm to 430 nm, with molar extinction coefficients at ~ 120,000, Figure 36. The emission spectra for 5a and 5b exhibit a band between 446 nm to 472 nm. Furthermore, the absorption and emission wavelength present hypsochromic shifts as the solvent polarity increases, which is indicative of negative solvatochromism.\textsuperscript{39} This means that the ground-state molecule is better stabilized by solvation than the molecule in the excited state.

![Absorbance spectrum of 5a in different solvents in range suitable for emission spectroscopy](image)

The fluorescence intensity in BODIPYs 5a and 5b is significantly affected by the polarity of the solvent, Figure 37. We observed that the quantum yields are close to 1.00 in non-polar solvent media such as hexane and toluene. However, the fluorescence intensity decays significantly in polar solvents such as acetone and methanol. A summary of the optical features of 8-amino-BODIPYs is presented in Table 4.

42
Figure 37. Emission spectra of 4 (top), 5a (middle), 5b (bottom) in different solvents

Table 4. Summary of the optical properties of BODIPYs 4, 5a-b, 6

<table>
<thead>
<tr>
<th>Solvent</th>
<th>4</th>
<th>5a</th>
<th>5b</th>
<th>6</th>
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<td></td>
<td>Absorbance</td>
<td>Emission φ</td>
<td>Absorbance</td>
<td>Emission φ</td>
</tr>
<tr>
<td></td>
<td>λ_{max}, nm; λ_{em}, nm.</td>
<td>(ε M⁻¹ cm⁻¹)</td>
<td>λ_{max}, nm; λ_{em}, nm.</td>
<td>(ε M⁻¹ cm⁻¹)</td>
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<tr>
<td>Hexane</td>
<td>428 (0.98)</td>
<td>456 0.96</td>
<td>412 (1.09)</td>
<td>472 0.98</td>
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<tr>
<td>Toluene</td>
<td>426 (1.01)</td>
<td>450 0.98</td>
<td>412 (1.29)</td>
<td>474 0.93</td>
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<tr>
<td>DCM</td>
<td>406 (1.02)</td>
<td>440 0.97</td>
<td>408 (1.23)</td>
<td>468 0.80</td>
</tr>
<tr>
<td>THF</td>
<td>404 (1.01)</td>
<td>436 0.95</td>
<td>406 (1.13)</td>
<td>462 0.16</td>
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<tr>
<td>Acetone</td>
<td>399 (1.15)</td>
<td>435 0.97</td>
<td>401 (1.13)</td>
<td>460 0.04</td>
</tr>
<tr>
<td>MeOH</td>
<td>395 (1.12)</td>
<td>435 0.92</td>
<td>401 (1.08)</td>
<td>464 0.02</td>
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The significant solvent dependency may be further illustrated by progressively changing the composition of the solvent system. Thus, systematic change from a DCM/MeOH solvent
composition from 100% DCM to 100% MeOH results in a normalized emission variation illustrated in Figure 39. It is noteworthy to mention that when the solvent composition is 90% DCM – 10% MeOH, the emission resembles the emission of pure MeOH, Figure 40. The reason may be that the methanol molecules are solvating the fluorophore forming a type of micelle where the hydroxyl- group interacts with the BODIPY molecule due to hydrogen bond affinity while the aliphatic carbon interacts with the DCM. In this case, the methanol molecules form a type of micelle by interacting via hydrogen bonding preventing as illustrated in Figure 38.

Figure 38. Vertical cut view of the proposed micelle-type structure of amino-BODIPYs dissolved in a mixture of 10% MeOH : 90% DCM
Figure 39. Emission of 1 uM solutions of 5a (top) and 5b (bottom) of a DCM/MeOH gradient solvent, where 100% is pure DCM, increments by 1%

Figure 40. Emission of 1uM solution of 5a of DCM/MeOH gradient solvent where 100% is pure DCM, increments by 10%

A further demonstration of the sensitivity of the asymmetric amino-BODIPYs is presented in Figure 41, where the emission intensity changes with respect to the several aliphatic alcohols ranging from methanol to hexanol H(CH)\(_n\)OH (n = 1-6). As we expected, the fluorescence...
intensity increases as the aliphatic chain increases. However, in the case of n-hexyl alcohol, the emission resembles more the emission of methanol than the emission of hexane. Therefore, the hydroxyl- group plays the major role in the fluorescence intensity of the amino-BODIPYs compared to the aliphatic chain.

The quenching of emission by polar solvents has been well-established for other systems such as 2-amino-naphthalene where H-bonding in the excited states is believed to be responsible for the quenching leading to non-radiative relaxation. 40

Fluorophores 5a and 5b may be used as polarity probes for biological applications. Several polarity probes have been studied to measure the polarity of certain areas of proteins or to identify pockets of hydrophobicity inside the cell such as 8-anilino-naphthalene-8-sulfonate, is that 5a and 5b have longer excitation wavelengths. 41 One of the drawbacks of this material is that the excitation wavelength of this material is in the UV region, and the UV light could interact with the protein or the cell. BODIPYs 5a and 5b are excited in the visible region of the spectrum. Thus the chances of interaction between the excitation light and the proteins are largely diminished. 42
The fluorescence intensity for BODIPY 4 is not significantly impacted by the polarity of the solvent, and the quantum yields are close to 1.00. This was in concordance with previously reported results by Peña et al.\textsuperscript{43} BODIPY 6 did not exhibit an emission in any solvent probably due to the bent BODIPY core structure, as observed in the x-ray single crystal structure, \textit{vide infra}.

**X-ray Single Crystal Structures**

The new amino-BODIPYS are crystalline materials and their structures were analyzed by single-crystal x-ray diffraction. The structures for BODIPY 4, 5a and 5b are represented in Figure 42. The substituents on the N atom of these materials are coplanar with the BODIPY core, and thus, the N atom has a trigonal planar geometry. This implies that the lone pair electrons from the N atom are delocalized in the $\pi$-system conjugation of the BODIPY core, and a reduction in the C(8)-N bond is expected for all of the structures. Indeed the C(8)-N bond lengths are in the range of 1.31 Å - 1.35 Å, typical of bonds intermediate between a C-N and C=N bond. This is in concordance with resonance contribution B in Figure 32.
The angle between the two pyrrole rings is an important structural parameter since the fluorescence of BODIPYs is primarily associated with the planarity of the core and the $\pi$-system conjugation. Compounds 4, 5a, and 5b have pyrrole-pyrrole dihedral angles of less than 15°.

The crystal structure of BODIPY 6, illustrated in Figure 43, is distinctive to the general structural features of BODIPYs 4, 5a-b. While the N atom shows a trigonal planar geometry, as observed for previously discussed BODIPYs, the BODIPY core is significantly bent. The distorted backbone shows a pyrrole-pyrrole dihedral angle of 34°, which could be the primary reason for the lack of emission of this fluorophore.

Furthermore, the six-membered ring has adopted a “boat” conformation pushing the boron and the nitrogen out of the plane. This behavior demonstrates the significant steric hindrance induced by the diethyl- substituents.
Other bond lengths and angles corresponding to the BODIPY core are in accordance with similar BODIPY dyes, Figure 44, Table 5 and Table 6.

Figure 44. BODIPY labeled according to bond lengths and angles measured. The carbons in blue indicate the dihedral (torsion) angle.
Table 5. Bond lengths of unsubstituted BODIPY, BODIPY 1, and BODIPYs 4, 5a-b, 6 (Å)

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<th>Unsubstituted BODIPY</th>
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<th>4</th>
<th>5a</th>
<th>5b</th>
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<td>1.366</td>
<td>1.376</td>
<td>1.389</td>
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<td>C3-C4</td>
<td>1.392</td>
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<td>1.451</td>
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<td>1.420</td>
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<td>1.415</td>
<td>1.456</td>
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<td>1.390</td>
<td>1.358</td>
<td>1.393</td>
<td>1.403</td>
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<tr>
<td>C7-C8</td>
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<td>1.394</td>
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<td>1.388</td>
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<tr>
<td>C8-C9</td>
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<td>N/A</td>
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<td>1.314</td>
<td>1.343</td>
<td>1.337</td>
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Table 6. Bond angles of unsubstituted BODIPY, BODIPY 1, and BODIPYs 4, 5a-b, 6 (°)

<table>
<thead>
<tr>
<th>Bond Angles</th>
<th>Unsubstituted BODIPY</th>
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<th>5b</th>
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<td>107.2</td>
<td>107.1</td>
<td>106.3</td>
<td>107.0</td>
<td>107.2</td>
</tr>
<tr>
<td>C8-C9-N2</td>
<td>110.7</td>
<td>110.7</td>
<td>110.0</td>
<td>110.1</td>
<td>110.2</td>
<td>109.3</td>
</tr>
</tbody>
</table>

Dihedral

| C4-C5-N1-C(alkyl) | 5.8 | 4.8 | 3.6 | 10.9 |

50
Chemistry of CMPO-Amine and BODIPY-SMe

A CMPO with a secondary amine was available in our laboratory and I decided to use this reagent because there is evidence that this compound should react with the 8-MeS-BODIPY 1. In a 100 mL round bottom flask, 50 mg (0.21 mmol) of BODIPY 1 and 63 mg (0.20 mmol) of CMPO-amine were dissolved in 30 mL of dry tetrahydrofuran under nitrogen atmosphere. The reaction was stirred overnight at room temperature. However, the reaction did not proceed as expected, Scheme 11. The mixture was stirred at reflux temperature, but the reaction also failed to go forward after 24 hours, as observed by silica gel thin-layer chromatography. We believe the reaction did not proceed since there is a tautomeric resonance in the amide, Scheme 12. Therefore, the lone pair electrons are delocalized through the carboxyl- group. For future work, we need to develop a methodology to synthesize a primary amine-CMPO to repeat the reaction to produce the CMPO-NH-BODIPY chemosensor.
We synthesized and characterized three new 8-R2N-BODIPY dyes, (R2 = HPr, HBu, Et2). The study illustrates for the first the restricted rotation through the C(8)-N bond that was studied by variable temperature NMR. The crystal structures further describe the significant steric hindrance induced by the substituents in the N atom, which significantly modifies the emission properties of these dyes. The emission of the materials R2 = HPr, HBu are extremely sensitive to solvent polarity, and they may be used as fluorescence polar probes for biological applications.

This work was published in an international peer-reviewed chemistry journal.

Section III: Chemistry of the CMPO-Thiol and the BODIPY-SMe

Hypothesis

The thiol-moiety may serve as a thioether link between the CMPO and the BODIPY. Since the CMPO-SH is available in our laboratory, we wanted to explore the possibility of direct nucleophilic substitution of the 8-MeS-BODIPY by the thiol group of the CMPO in a similar fashion as reported for amines. In the literature, there are no reports of nucleophilic substitution of the 8-MeS-BODIPY by thiols, so we decided to explore this chemistry with simple alkylthiols and arylthiols before trying a more complex molecule such as the CMPO-SH.

Introduction

Following the same procedure as for the preparation of 8-amino-BODIPYs, we explored the possibility of the nucleophilic substitution reaction of 1 by several alkyl- and aryl-thiols under mild conditions, Scheme 14. If the substitution takes place, the new methodology could serve to introduce the BODIPY to the CMPO by forming a thioester bridge.

Previous reports in the literature regarding the synthesis of thio-BODIPYs involve the nucleophilic substitution of BODIPY halides by several alkyl- and aryl-thiols. However, these reactions usually require high temperatures and the presence of a base such as triethylamine with reaction yields of 53% starting from the dipyrrroketone, Scheme 13.44
In this chapter, the synthetic methodology and the complete characterization of 8-alkylthio-BODIPYs and 8-arylthio-BODIPYs using a new direct substitution methodology is presented.

BODIPY 7 was synthesized by dissolving 50 mg (0.21 mmol) of 8-methylthio-BODIPY and 24 µL (0.23 mmol) of thiophenol in 30 mL of dry dichloromethane in a 100 mL round bottom flask under nitrogen atmosphere. The reaction was stirred at room temperature, and it was completed after 6 hours as confirmed by the disappearance of the starting material in the silica gel thin-layer chromatography using a mixture of 20% ethyl acetate and 80% hexane. The solvent was removed under vacuum, and the product was purified by silica gel column chromatography using
silica of 60 Å and size 60-200 µm in a column 5 inches high and 1 inch wide. The eluent was a gradient mixture of ethyl acetate and hexane. The product was recrystallized from a mixture of dichloromethane/hexane yielding orange crystals in ~90% yield.

BODIPYs 8-10,12 and 13 were synthesized by the same produce using the corresponding thiol. BODIPYs 11, 14 and 15 were synthesized by reacting 40 mg of the corresponding thiol.

7: Orange crystals, yield 82%, 43.3 mg (0.17 mmol); m.p. 92-93°C; ¹H NMR (CDCl₃) δ 1.40–1.42 (t, 3H, J = 7.74 Hz), 3.34-3.38 (q, 2H, J = 7.56 Hz), 6.51 (d, 2H, J = 4.14 Hz), 7.41 (d, 2H, J = 4.14 Hz), 7.79 (s, 2H). ¹³C NMR (CDCl₃) δ 14.9 (CH₃), 32.5 (CH₂), 118.0 (CH), 128.5 (CH), 135.1 (C), 142.2 (CH), 151.4 (C). ¹⁹F NMR (CDCl₃) -145.8 (m). Anal. Cald for C₁₁H₁₁BF₂N₂S: C, 52.41; H, 4.40. Found: C, 52.74; H,4.25.

8: Orange crystals, yield 86%, 48.0 mg (0.18 mmol); m.p. 95-96 °C; ¹H NMR (CDCl₃) δ 1.05-1.07 (t, 3H, J = 7.56 Hz), 1.74-1.80 (h, 3H, J = 7.56 Hz), 3.30-3.32 (t, 2H, J = 7.56 Hz), 6.51 (d, 2H, J = 4.14 Hz), 7.42 (d, 2H, J = 4.14 Hz), 7.79 (s, 2H). ¹³C NMR (CDCl₃) 13.3 (CH₃), 23.4 (CH₂), 40.3 (CH₂), 118.0 (CH), 128.5 (CH), 135.5 (C), 142.2 (CH), 152.0 (C). ¹⁹F NMR (CDCl₃) -145.8 (m). Anal. Cald for C₁₂H₁₃BF₂N₂S: C, 54.16; H, 4.92. Found: C, 54.04; H,5.16.

9: Orange crystals, yield 89%, 52.3 mg (0.18 mmol); m.p. 98-99°C; ¹H NMR (CDCl₃) δ 0.92-0.95 (t, 3H, J = 7.50 Hz), 1.49 (sextet, 2H, J = 7.56 Hz), 1.70-1.74 (quintet, 2H, J = 6.84), 3.32-3.35 (t, 2H, J = 7.50 Hz). 6.51 (s, 2H), 7.41 (s, 2H), 7.79 (s, 2H). ¹³C NMR (CDCl₃) 13.6 (CH₃), 21.8 (CH₂), 31.8 (CH₂), 38.1 (CH₂), 117.9 (CH), 128.4 (CH), 135.0 (C), 142.0 (CH), 152.1 (C). ¹⁹F NMR (CDCl₃) -145.8 (m). Anal. Cald for C₁₃H₁₃BF₂N₂S: C, 55.74; H, 5.40. Found: C, 55.36; H, 5.32.

10: Red powder, yield 74%, 43.5 mg (0.15 mmol); m.p. 96-97°C; ¹H NMR (CDCl₃) δ 1.39 (s, 9H), 6.51 (d, 2H, J = 4.08 Hz), 7.48 (d, 2H, J = 4.08 Hz), 7.87 (s, 2H). ¹³C NMR (CDCl₃) 32.10
Orange powder, yield 30%; 20 mg (0.05 mmol); m.p. 58-59 °C; $^1$H NMR (CDCl$_3$): $\delta$ 7.80 (s, 2H), 7.42 (d, $J$ = 4.1 Hz, 2H), 6.52 (d, $J$ = 3.3 Hz, 2H), 3.33 (t, $J$ = 7.4 Hz, 2H), 1.81 - 1.68 (m, 2H), 1.51 - 1.40 (m, 2H), 1.36 - 1.18 (m, 2H), 0.88 (t, $J$=6.9 Hz, 3H); $^{13}$C NMR (CDCl$_3$) 152.2, 141.9, 135.1, 128.3, 117.9, 117.8, 38.4, 29.8, 29.6, 29.5, 29.4, 29.3, 29.0, 28.6, 14.1. Anal. Caled for C$_{21}$H$_{31}$BF$_2$N$_2$S: C, 64.28; H, 7.96. Found: C, 64.18; H, 7.82.

Orange crystals, yield 94%; 59.2 mg (0.19 mmol); m.p. 134-135°C; $^1$H NMR (CDCl$_3$) δ 6.37-6.38 (d, 2H, $J$ = 5.28 Hz), 6.95 (d, 2H, $J$ = 4.08 Hz), 7.40-7.45 (m, 3H), 7.60 (d, 2H, $J$ = 7.56 Hz), 7.75 (s, 2H). $^{13}$C NMR (CDCl$_3$) 118.0 (CH), 126.8 (CH), 130.0 (CH), 130.3 (CH), 131.9 (C), 133.1 (CH), 134.2 (C), 142.1 (CH), 150.0 (C). $^{19}$F NMR (CDCl$_3$) -145.5 (m). Anal. Caled for C$_{15}$H$_{11}$BF$_2$N$_2$: C, 60.03; H, 3.69. Found: C, 60.14; H, 3.95. The NMR analysis is in accordance with the results obtained by Leen et al. 44

Red crystals, yield 85%; 58.5 mg (0.17 mmol); m.p. 151-152°C; $^1$H NMR (CDCl$_3$) δ 2.84 (s, 6H), 6.34-6.35 (m, 2H), 2.74 (s, 1H), 7.24 (m, 2H), 7.35-7.38 (t, 1H, $J$ = 7.56 Hz), 7.71 (s, 1H). $^{13}$C NMR (CDCl$_3$) . 21.7 (CH$_3$), 117.5 (CH), 126.0 (CH), 128.2 (C), 129.5 (CH), 131.4 (CH), 132.5 (C), 140.5 (CH), 143.3(CH), 153.7 (C). $^{19}$F NMR (CDCl$_3$) -145.8 (m). HRMS [M + H]: Calcd. for C$_{16}$H$_{13}$BF$_2$N$_2$: 329.1095, Fnd. 329.1083.

Orange crystals; yield= 66%; 35 mg (0.11 mmol); m.p.143-144 °C; $^1$H NMR (CDCl$_3$) δ 7.75 (s, 2H), 7.51 (d, $J$ = 8.1 Hz, 2H), 7.25 (d, $J$ = 8.7 Hz, 2H), 6.93 (d, $J$ = 4.1 Hz, 2H), 6.38 (d, $J$ = 3.6 Hz, 2H), 2.41 (s, 3H). $^{13}$C NMR (CDCl$_3$): 151.8, 141.6, 140.8, 133.8, 133.4, 131.1, 128.1, 127.7, 117.7, 21.4. Anal Caled for C$_{16}$H$_{13}$BF$_2$N$_2$: C, 61.17; H, 4.17. Found: C, 61.29; H, 4.25.
**Results and Discussion**

The MeS- group in 1 was substituted by a range of alkyl- and aryl-thiols, by simply mixing 1 with the corresponding thiol in dichloromethane for 6 hours at room temperature. The reaction does not require acidic or basic conditions, nor the presence of a catalyst or co-reagent,\(^{45}\) therefore, it is a simple and convenient process that provide derivatives in high yields.

The trans-thioesterification is a well-established transformation, and since the 8-thio-BODIPY possesses the R-S-C(sp\(^2\)) group, and it is attached to an electron withdrawing group (the BODIPY core), it is electronically similar to other thioesters.\(^{46}\) Therefore, we propose a mechanism similar to that transformation, Scheme 15.

A driving force in this mechanism is the production of mercaptan gas, thereby reducing the possibility of the reformation of 1.
NMR Spectroscopy

For the 8-RS-BODIPY materials reported both the $^1$H and $^{13}$C NMR spectra exhibit sharp resonances with no broadening due to any restricted rotation about the C(8)-S bond at 298 °K as observed for the 8-amino-BODIPYs (Section II, *vide supra*), Figure 45. This suggests that there is no strong multiple bond character in the structure of these dyes, Scheme 16. The $^{19}$F NMR shows the expected quartet resonance located at ~ -145nm, which is in concordance with other BODIPY fluorophores.\(^{19}\)

![NMR Spectroscopy](image)

Figure 45. $^1$H NMR comparison of the aromatic region for 8-isopropylamino-BODIPY 5a (top) and 8-ethylthio-BODIPY 7 (bottom)
Optical Studies

In general, the absorption and emission wavelengths of the new 8-alkylthio-BODIPYs are little changed with respect to 1 indicating that the length of the alkyl-chain bonded to the S atom does not modify the \(\pi\)-system conjugation in the BODIPY core. The absorbance shape of the 8-alkylthio-BODIPYs is, however, different compared to the other BODIPYs reported.\(^{19}\) BODIPYs 7-11 exhibit two absorption bands at \(\sim 495\) nm and \(\sim 515\) nm when recorded in hexane. Upon solvation of the fluorophores in polar media, the absorption band at \(\sim 515\) nm decreases, while the absorption band at \(\sim 495\) nm remains unchanged, Figure 46. Therefore, there is no evident isosbestic point. The absorption band at \(\sim 515\) nm does not seem to participate in the fluorescence process since the fluorescence intensity sharply decreases upon excitation at 515 nm. This effect is probably due to convolution of the 495 nm and 515 nm absorption bands.

At this point, it is unknown to us what is the electronic transition associated with the absorption band at 515 nm. This is the first time, to our knowledge, that there is a report of a BODIPY showing two absorption bands in this area. This effect seems to be associated to the presence of the sulfur in the 8-site. Substitutions by oxygen or nitrogen do not show this effect. \textit{Ab initio} calculations may be the only plausible way to associate this transition band with the molecule.
The molar extinction coefficients for alkylthio-BODIPYs 7-11 range from 20,000 to 40,000 cm$^{-1}$ M$^{-1}$, in accordance with observations made by Biellmann to the 8-MeS-BODIPY 1.$^{28}$

![Figure 46. Absorbance spectra of 7 in various solvents](image)

Their emission wavelengths remain at ~530 nm upon excitation at ~495 nm, and as previously noted for 8-amino-BODIPYs, the fluorescence intensity decreases as the solvent polarity increases, Figure 47. However, the effect is not as pronounced as in the case of the 8-amino-BODIPYs.
The 8-arylthio-BODIPYs 12-15 behave differently to the 8-alkylthio-BODIPYs 7-11, Figure 48. One difference in the absorbance spectra is the lack of the pronounced absorption band at ~515 nm. Furthermore, the vibronic shoulder is still not present, as it is the case for other BODIPY dyes. It is unknown to us at this point why this absorption band is not present. Upon excitation, BODIPY 12 exhibits a bright fluorescence in hexane, with a quantum yield calculated at 0.61, Figure 48, right. However, the emission is not detected when the molecule is dissolved in more polar solvents. The absence of emission in tetrahydrofuran was observed by Leen et al. Compounds 13-15 do not exhibit fluorescence in any organic solvent tested. The analogous 8-anilino-BODIPY has been reported to show a similar absence of emission in tetrahydrofuran, and it was described as a non-emissive dye by Goud et al. However, we are unsure if the molecule exhibits an emission in hexane as it was observed for BODIPY 12. The rest of the arylthio-BODIPYs 13-15 do not show an emission in any common organic solvent.
The summary of the optical properties of the new 8-organothio-BODIPYs is described in Table 7.
Table 7. Summary of the optical properties of the new 8-organothio-BODIPYs

<table>
<thead>
<tr>
<th>Solvent</th>
<th>Absorbance</th>
<th>Emission</th>
<th>Absorbance</th>
<th>Emission</th>
<th>Absorbance</th>
<th>Emission</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>λmax nm</td>
<td>λmax (nm)</td>
<td>ε, M-1 cm-1</td>
<td>φ</td>
<td>λmax nm</td>
<td>λmax (nm)</td>
</tr>
<tr>
<td>Hexane</td>
<td>493 (4.0)</td>
<td>532</td>
<td>0.4</td>
<td>494 (2.5)</td>
<td>530</td>
<td>0.45</td>
</tr>
<tr>
<td>DCM</td>
<td>491 (4.5)</td>
<td>532</td>
<td>0.26</td>
<td>491 (2.9)</td>
<td>532</td>
<td>0.3</td>
</tr>
<tr>
<td>THF</td>
<td>490 (4.0)</td>
<td>528</td>
<td>0.23</td>
<td>491 (2.7)</td>
<td>530</td>
<td>0.28</td>
</tr>
<tr>
<td>Acetone</td>
<td>486 (4.4)</td>
<td>528</td>
<td>0.18</td>
<td>489 (2.7)</td>
<td>530</td>
<td>0.19</td>
</tr>
<tr>
<td>MeOH</td>
<td>486 (3.5)</td>
<td>528</td>
<td>0.16</td>
<td>489 (2.8)</td>
<td>528</td>
<td>0.17</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
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<td></td>
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<tr>
<td></td>
<td>9</td>
<td>10</td>
<td>11</td>
<td></td>
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<tr>
<td></td>
<td>Absorbance</td>
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<tr>
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<td>λmax (nm)</td>
<td>ε, M-1 cm-1</td>
<td>φ</td>
<td>λmax nm</td>
<td>λmax (nm)</td>
</tr>
<tr>
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<td>0.23</td>
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<td>0.16</td>
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<td>N.A.</td>
</tr>
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<td>0.16</td>
<td>491 (2.0)</td>
<td>N.A.</td>
<td>N.A.</td>
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<tr>
<td>Acetone</td>
<td>493 (3.3)</td>
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<td>0.12</td>
<td>488 (2.1)</td>
<td>N.A.</td>
<td>N.A.</td>
</tr>
<tr>
<td>MeOH</td>
<td>491 (3.4)</td>
<td>528</td>
<td>0.11</td>
<td>499 (1.9)</td>
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<td>N.A.</td>
</tr>
<tr>
<td>Solvent</td>
<td>Absorbance</td>
<td>λmax nm</td>
<td>λmax (nm)</td>
<td>φ</td>
<td>Emission</td>
<td>λmax nm</td>
</tr>
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<td>491 (4.1)</td>
<td>N.D.</td>
</tr>
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<td>N.D.</td>
<td>N.D.</td>
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<td>490 (4.0)</td>
<td>N.D.</td>
</tr>
<tr>
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<td>N.D.</td>
<td>N.D.</td>
<td></td>
<td>490 (4.3)</td>
<td>N.D.</td>
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<th>Solvent</th>
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<th>λmax nm</th>
<th>λmax (nm)</th>
<th>φ</th>
<th>Emission</th>
<th>λmax nm</th>
<th>λmax (nm)</th>
<th>φ</th>
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<tr>
<td>Hexane</td>
<td>495 (2.4)</td>
<td>N.D.</td>
<td>N.D.</td>
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<td>793 (2.7)</td>
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<td>DCM</td>
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<td>N.D.</td>
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<td>493 (2.6)</td>
<td>N.D.</td>
<td>N.D.</td>
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<tr>
<td>THF</td>
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<td>N.D.</td>
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<tr>
<td>Acetone</td>
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<td>N.D.</td>
<td>N.D.</td>
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<td>N.D.</td>
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<tr>
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<td>N.D.</td>
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<td>491 (2.6)</td>
<td>N.D.</td>
<td>N.D.</td>
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</table>

**X-ray Single Crystal Structures**

Several of the new 8-organothio-BODIPYs were readily crystallized to provide crystals suitable for X-ray structural analysis. The crystal refinement data for these structures is beyond the scope of this dissertation, but it has been published as supplementary material elsewhere.

In the case of 8-ethylthio-BODIPY 7 and 8-propylthio-BODIPY 8, the planarity of the BODIPY core is significantly maintained despite any possible steric effect induced by the alkyl chain, Figure 49, with pyrrole-pyrrole dihedral angle in the range of 3° to 5°. Moreover, the thio-
groups are essentially coplanar with the BODIPY core, similar to the 8-isopropylamino-BODIPY 5a and 8-isobutylamino-BODIPY 5b.

Figure 49. Structures of 7 (left) and 8 (right)

The 8-arylthio-BODIPYs 12 and 13 differ in the general geometry from the alkyl analogs above. Firstly, the planarity of the BODIPY core is now moderately disturbed probably due to the steric induced by the phenyl ring in the meso-site. The pyrrole-pyrrole dihedral angles vary between 11° and 16°. Secondly, the substituents on the S atom are not coplanar to the BODIPY core. The dihedral angles for the C(8)-S-C plane are 22° and 31° for 12 and 13 respectively, which is remarkable different to the 8-anilino-BODIPY reported by Goud et al. where the dihedral angle is 2° due to the trigonal planar geometry of the nitrogen.19 Additionally, the phenyl rings are twisted about the S-C(aryl ipso) bond to further reduce the steric congestion by 57° and 66°. These effects are more evident for BODIPY 13, where the methyl-groups induce a larger steric effect, Figure 50 and Figure 51.
Figure 50. Structures of 12 (left) and 13 (right)

Figure 51. View from the bottom showing the dihedral angle about the C(8)-N for 8-anilino-BODIPY (left), C(8)-S BODIPY 12 (middle), BODIPY 13 (right)

Other bond lengths and angles are in accordance with other BODIPY dyes, Figure 52, Table 8 and Table 9.\textsuperscript{19}

Figure 52. BODIPY labeled according to bond lengths and angles measured. The carbons in blue indicate the dihedral (torsion) angle
Table 8. Bond lengths of unsubstituted BODIPY, BODIPY 1, and BODIPYs 7, 8, 12 and 13 (Å)

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<tr>
<th>Bond lengths</th>
<th>Unsubstituted BODIPY 16</th>
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<th>7</th>
<th>8</th>
<th>12</th>
<th>13</th>
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<td>C1-C2</td>
<td>1.381</td>
<td>1.386</td>
<td>1.362</td>
<td>1.387</td>
<td>1.379</td>
<td>1.382</td>
</tr>
<tr>
<td>C2-C3</td>
<td>1.367</td>
<td>1.369</td>
<td>1.399</td>
<td>1.359</td>
<td>1.373</td>
<td>1.377</td>
</tr>
<tr>
<td>C3-C4</td>
<td>1.392</td>
<td>1.409</td>
<td>1.396</td>
<td>1.410</td>
<td>1.407</td>
<td>1.412</td>
</tr>
<tr>
<td>C4-C5</td>
<td>1.373</td>
<td>1.405</td>
<td>1.443</td>
<td>1.403</td>
<td>1.405</td>
<td>1.396</td>
</tr>
<tr>
<td>C5-C6</td>
<td>1.380</td>
<td>1.408</td>
<td>1.389</td>
<td>1.422</td>
<td>1.403</td>
<td>1.406</td>
</tr>
<tr>
<td>C6-C7</td>
<td>1.381</td>
<td>1.405</td>
<td>1.404</td>
<td>1.396</td>
<td>1.402</td>
<td>1.407</td>
</tr>
<tr>
<td>C7-C8</td>
<td>1.376</td>
<td>1.374</td>
<td>1.371</td>
<td>1.382</td>
<td>1.367</td>
<td>1.374</td>
</tr>
<tr>
<td>C8-C9</td>
<td>1.401</td>
<td>1.378</td>
<td>1.398</td>
<td>1.371</td>
<td>1.380</td>
<td>1.377</td>
</tr>
<tr>
<td>C5-S1</td>
<td>N/A</td>
<td>1.730</td>
<td>1.730</td>
<td>1.725</td>
<td>1.735</td>
<td>1.747</td>
</tr>
</tbody>
</table>

Table 9. Bond angles of unsubstituted BODIPY, BODIPY 1, and BODIPYs 7, 8, 12 and 13 (°)

<table>
<thead>
<tr>
<th>Bond Angles</th>
<th>Unsubstituted BODIPY 16</th>
<th>1</th>
<th>7</th>
<th>8</th>
<th>12</th>
<th>13</th>
</tr>
</thead>
<tbody>
<tr>
<td>N1-C1-C2</td>
<td>111.8</td>
<td>110.2</td>
<td>107.3</td>
<td>110.4</td>
<td>110.3</td>
<td>110.2</td>
</tr>
<tr>
<td>C1-C2-C3</td>
<td>105.7</td>
<td>107.6</td>
<td>110.2</td>
<td>107.2</td>
<td>107.4</td>
<td>107.9</td>
</tr>
<tr>
<td>C2-C3-C4</td>
<td>107.7</td>
<td>107.4</td>
<td>104.7</td>
<td>107.9</td>
<td>107.1</td>
<td>106.3</td>
</tr>
<tr>
<td>C4-C5-C6</td>
<td>123.3</td>
<td>120.0</td>
<td>120.7</td>
<td>120.0</td>
<td>120.4</td>
<td>120.7</td>
</tr>
<tr>
<td>C6-C7-C8</td>
<td>108.4</td>
<td>107.8</td>
<td>107.4</td>
<td>107.1</td>
<td>107.1</td>
<td>107.3</td>
</tr>
<tr>
<td>C7-C8-C9</td>
<td>105.4</td>
<td>107.2</td>
<td>107.9</td>
<td>107.2</td>
<td>107.5</td>
<td>107.3</td>
</tr>
<tr>
<td>C8-C9-N2</td>
<td>110.7</td>
<td>110.7</td>
<td>109.8</td>
<td>110.2</td>
<td>110.1</td>
<td>110.5</td>
</tr>
</tbody>
</table>

Dihedral

| C4-C5-S1-(alkyl) | 0.9 | 0.4 | 25.7 | 34.3 |
Chemistry of CMPO-Thiol and BODIPY-SMe

50 mg (0.21 mmol) of 8-MeS-BODIPY and 89 mg (0.20 mmol) of thiopropyl-CMPO were dissolved in 30 mL of dry tetrahydrofuran under ambient atmosphere in a 100 mL round bottom flask. The mixture was stirred at room temperature for 24 hours, and no reaction was observed from the silica gel thin-layer chromatography. The temperature was increased, and the reaction was stirred for 24 hours at reflux temperature, Scheme 17. However, no reaction was evident from the TLC. It may be possible that the thiopropyl-group is not long enough and the steric hindrance induced by the phenols prevents the reaction to occur. Therefore, we decided to react 10 mg (0.018 mmol) of thiononyl-CMPO and 5 mg (0.02 mmol) of 8-MeS-BODIPY in tetrahydrofuran at room temperature under nitrogen atmosphere. The reaction seemed to proceed based on silica gel thin-layer chromatography. However, the amount of product was not enough for the purification process using silica gel column chromatography. Therefore, for future work, I plan to reproduce the synthesis using at least 200 mg of the thiononyl-CMPO to obtain enough material for the complete characterization.
Conclusion

I synthesized and characterized several 8-organothio-BODIPYs in high yields. The 8-alkylthio-BODIPYs exhibit two absorption bands. However, only the absorption band at ~495 nm is responsible for the fluorescence of the dye. The band at ~515 nm tends to disappear as the compounds are dissolved in more polar media. These molecules also exhibit a good fluorescence intensity with quantum yields of ~0.20–0.40.

Contrary, in general, 8-aryllthio-BODIPYs do not show a detectable fluorescence in any organic solvent, except for 8-phenylthio-BODIPY which is emissive only when dissolved in hexane.

There is no evidence of a restricted rotation at room temperature about the C(8)-S bond as per NMR experiments, which show sharp resonance signals in the $^1$H and $^{13}$C NMR.

Lastly, this methodology may be used to react the CMPO-SH with 8-MeS-BODIPY to produce the CMPO-S-BODIPY.

This work has been submitted to *Tetrahedron*
Section IV: Multiple Substitution of the BODIPY Core by Thiophenol

Introduction

As noted above, the substitution in the meso-site of the 8-MeSBODIPY by organothiols was performed in dichloromethane at room temperature. In an effort to improve reaction times, the same reaction was carried out in tetrahydrofuran at room temperature without the presence of a catalyst or co-reagent in neutral conditions. To our surprise, the reaction produces a double and triple substitution in the 3,5- and 3,5,8- sites with thiophenol, Scheme 20. A similar multi-substitution reaction does not seem to work with alkylthiols.

Currently, the only methodologies reported in the literature for the introduction of phenylthio-moieties in the 3- and 3-,5- positions involve the substitution of 3-chloro-BODIPY in overall yields of 66% starting from the 2-acetyl-5-chloropyrrole, or 3,5-dichloro-BODIPY with thiophenol in the presence of a base at 80°C in yields of 87% starting from the 3,5-dichloro-BODIPY, Scheme 18, Scheme 19.48,49
This simple chemistry opens a new methodology for the introduction of arylthio- moieties to the BODIPY core in the 3- and 5- sites without the need of a halogenated BODIPY.
Experimental

Compound 16 was synthesized by dissolving 50 mg (0.21 mmol) of 8-MeS-BODIPY and 80 µL (0.73 mmol) of thiophenol in 50 mL of dry tetrahydrofuran in a 100 mL round bottom flask under nitrogen atmosphere. The mixture was stirred for 6 hours at room temperature, and the reaction was monitored by silica gel thin-layer chromatography. After 6 hours, the reaction was completed, and the product was purified by silica gel column chromatography using silica of 60 Å and size 60-200 µm in a column 8 inches tall by 1 inch wide. The eluent was a gradient mixture of tetrahydrofuran and hexane. The final product was recrystallized from a dichloromethane/hexane mixture.

BODIPY 17 was synthesized using the same procedure, and it was stirred for 48 hours at room temperature. The purification was performed using procedure previously described.

16: Red crystals, yield 85%, 51.4 mg; m.p. 163-164°C; ¹H NMR (CDCl₃) δ 5.78 (d, 1H, J = 4.8 Hz), 6.34 (s, 1H), 6.92 (d, 1H, J = 3.42 Hz), 7.07 (d, 1H, 4.8 Hz), 7.30-7.32 (m, 3H), 7.42-7.47 (m, 5H), 7.62-7.65 (m, 3H). ¹³C NMR (CDCl₃) 116.7 (CH), 119.7 (CH), 126.2 (CH), 128.5
(CH), 128.9 (C), 129.8 (CH), 129.9 (CH), 130.3 (CH), 130.4 (CH), 131.2 (CH), 134.3 (C), 134.4 (C), 135.3 (CH), 138.7 (C), 139.1 (CH), 139.9 (C), 162.4 (C). \(^{19}\)F NMR (CDCl\(_3\)) -147.6 (m).


17: Red crystals, yield 31%, 20.5 mg; m.pt. 92-93\(^\circ\)C; \(^1\)H NMR (CDCl\(_3\)) \(\delta\) 5.79 (d, 2H, \(J = 4.8\) Hz), 6.98 (d, 2H, \(J = 4.14\) Hz), 7.22 (d, 1H, \(J = 7.56\) Hz), 7.25-7.27 (m, 2H), 7.36-7.37 (d, 2H, \(J = 8.22\) Hz), 7.40-7.44 (m, 6H), 7.65 (d, 2H, \(J = 8.64\) Hz). \(^{13}\)C NMR (CDCl\(_3\)) \(\delta\) 118.5 (CH), 127.8 (CH), 128.1 (CH), 129.6 (CH), 129.7 (CH), 129.8 (CH), 129.9 (CH), 130.0 (CH), 133.3 (C), 135.0 (CH), 135.5 (C), 138.1 (C), 157.5 (C). \(^{19}\)F NMR (CDCl\(_3\)) \(\delta\) -147.5 (m). Anal. Cald for C\(_{27}\)H\(_{19}\)BF\(_2\)N\(_2\)S\(_3\): C, 62.79; H, 3.71. Found: C, 61.41; H, 3.66.

Results and Discussion

BODIPYs 16 and 17 were synthesized by mixing thiophenol and 1 in THF at room temperature under nitrogen atmosphere. BODIPY 16 is produced after 6 hours of stirring, while longer reaction times yield BODIPY 17. In our experiments, we did not notice the formation of BODIPY 12, which suggests that the intermediate is a highly reactive species. Substitution at the 1,7- and 2,6- sites of the BODIPY core was not observed after 1 week of stirring and large excess of thiophenol. This indicates that the reaction is highly selective for the 3- and 5- sites. Leen et al. described that the determining step of the reaction for the substitution at the 3- and 5- sites was an oxidation process. Therefore, we carried out the reaction in open atmosphere, \(i.e.\) non N\(_2\), Ar. However, the reaction rate was much slower, and the formation of BODIPY 17 was not observed. Therefore, the reaction must be carried under inert atmosphere to achieve a triple substitution.

Further experiments are underway to determine the generality of the reaction.
NMR Spectroscopy

The NMR experiments did not show a rotation about the C(8)-S for BODIPY bond in accordance with the 8-arylthio-BODIPYs, and the resonance signals are sharp in the $^1$H and $^{13}$C spectra, Figure 53. The $^{19}$F NMR shows the expected quarter at ~ -145 ppm.

![Figure 53. Aromatic region of the 1H NMR of BODIPY 12 (top), BODIPY 16 (middle), BODIPY 17 (bottom) showing sharp signals for the pyrrole-hydrogens, which indicate the absence of restricted rotation about the C(8)-S bond.]

Optical Studies

The introduction of the phenylthio-moieties in the 3- and 5- sites induces a bathochromic shift in the absorbance spectra due to an expansion in the $\pi$-system conjugation when compared to 8-PhS-BODIPY 12. BODIPY 16 shows an absorption band at ~ 560 nm, and an emission band at ~ 600 nm, giving it a bright orange fluorescence color, Figure 54. BODIPY 17 has an absorption band at ~ 600 nm and an emission band at ~ 630 nm, Figure 55. BODIPY 16 shows a solvent dependency in its emission properties as observed for the asymmetric 8-alkylamino-BODIPYs,
where the fluorescence intensity significantly decreases as the solvent polarity increases. The phenythio- group in the 8- position seems to be the primary factor for this effect since it has been reported that there is no fluorescence intensity change for 3-phenylthio-BODIPY with respect to solvent polarity.\textsuperscript{47}

Contrary, the fluorescence intensity of BODIPY 17 does not suffer a significant variation as the solvent polarity increases. At this point, it is unknown to us why BODIPY 16 is susceptible to solvent polarity while BODIPY 17 is not. The summary of the optical properties for BODIPY 16 and 17 are illustrated in Table 10.
Table 10. Summary of the optical properties of BODIPYs 12, 16, and 17

<table>
<thead>
<tr>
<th>Solvent</th>
<th>λ_{max} Abs (nm)</th>
<th>ε (M^{-1} cm^{-1})</th>
<th>λ_{max} Fl (nm)</th>
<th>Φ</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hexane</td>
<td>497</td>
<td>24,000</td>
<td>542</td>
<td>0.61</td>
</tr>
<tr>
<td>DCM</td>
<td>495</td>
<td>24,000</td>
<td>N.D.</td>
<td>N.D.</td>
</tr>
<tr>
<td>THF</td>
<td>493</td>
<td>21,000</td>
<td>N.D.</td>
<td>N.D.</td>
</tr>
<tr>
<td>Acetone</td>
<td>493</td>
<td>23,000</td>
<td>N.D.</td>
<td>N.D.</td>
</tr>
<tr>
<td>MeOH</td>
<td>497</td>
<td>24,000</td>
<td>N.D.</td>
<td>N.D.</td>
</tr>
</tbody>
</table>

X-ray Single Crystal Structures

The crystal structures for BODIPY 16 and 17 are illustrated in Figure 56. One of the similarities of the structures of the bis- 16 and tris- 17 substituted BODIPYs with mono- substituted 12 is the
twisted rotation about the S-C(aryl ipso) in the 8- position to reduce the steric effect induced by the phenyl ring. This feature is observed for the 3- and 5- S-C(aryl ipso) as well. A significant difference between the bis- and tris- substituted BODIPYs with respect to the mono- substituted is that the BODIPY core remains planar for BODIPYs 16 and 17, while the distortion is larger for BODIPY 12. This effect may provide an explanation for the emission observed for these dyes as opposed to the non-fluorescence BODIPY 12.

Figure 56. Structures of 16 (left) and 17 (right)

The bond lengths and bond angles for the BODIPY core are illustrated in Figure 57, Table 11, and Table 12.

Figure 57. BODIPY labeled according to bond lengths and angles measured. The carbons in blue, green, and red indicate the dihedral (torsion) angles
Table 11. Bond lengths of unsubstituted BODIPY, BODIPY 12, and BODIPYs 16-17 (Å)

<table>
<thead>
<tr>
<th>Bond lengths</th>
<th>Unsubstituted BODIPY 36</th>
<th>12</th>
<th>16</th>
<th>17</th>
</tr>
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<tbody>
<tr>
<td>C1-C2</td>
<td>1.381</td>
<td>1.379</td>
<td>1.420</td>
<td>1.397</td>
</tr>
<tr>
<td>C2-C3</td>
<td>1.367</td>
<td>1.373</td>
<td>1.340</td>
<td>1.366</td>
</tr>
<tr>
<td>C3-C4</td>
<td>1.392</td>
<td>1.407</td>
<td>1.413</td>
<td>1.404</td>
</tr>
<tr>
<td>C4-C5</td>
<td>1.373</td>
<td>1.405</td>
<td>1.370</td>
<td>1.392</td>
</tr>
<tr>
<td>C5-C6</td>
<td>1.380</td>
<td>1.403</td>
<td>1.410</td>
<td>1.383</td>
</tr>
<tr>
<td>C6-C7</td>
<td>1.381</td>
<td>1.402</td>
<td>1.390</td>
<td>1.400</td>
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<tr>
<td>C7-C8</td>
<td>1.376</td>
<td>1.367</td>
<td>1.370</td>
<td>1.356</td>
</tr>
<tr>
<td>C8-C9</td>
<td>1.401</td>
<td>1.380</td>
<td>1.360</td>
<td>1.414</td>
</tr>
<tr>
<td>C5-S1</td>
<td>N/A</td>
<td>1.735</td>
<td>1.750</td>
<td>1.758</td>
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<tr>
<td>C5-S2</td>
<td>N/A</td>
<td>N/A</td>
<td>1.730</td>
<td>1.744</td>
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<tr>
<td>C5-S3</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
<td>1.726</td>
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</table>

Table 12. Bond lengths of unsubstituted BODIPY, BODIPY 12, and BODIPYs 16-17 (°)

<table>
<thead>
<tr>
<th>Bond Angles</th>
<th>Unsubstituted BODIPY 36</th>
<th>12</th>
<th>16</th>
<th>17</th>
</tr>
</thead>
<tbody>
<tr>
<td>N1-C1-C2</td>
<td>111.8</td>
<td>110.3</td>
<td>109.4</td>
<td>109.9</td>
</tr>
<tr>
<td>C1-C2-C3</td>
<td>105.7</td>
<td>107.4</td>
<td>107.3</td>
<td>107.1</td>
</tr>
<tr>
<td>C2-C3-C4</td>
<td>107.7</td>
<td>107.1</td>
<td>108.1</td>
<td>107.9</td>
</tr>
<tr>
<td>C4-C5-C6</td>
<td>123.3</td>
<td>120.4</td>
<td>121.1</td>
<td>121.6</td>
</tr>
<tr>
<td>C6-C7-C8</td>
<td>108.4</td>
<td>107.1</td>
<td>107.4</td>
<td>109.1</td>
</tr>
<tr>
<td>C7-C8-C9</td>
<td>105.4</td>
<td>107.5</td>
<td>107.3</td>
<td>107.1</td>
</tr>
<tr>
<td>C8-C9-N2</td>
<td>110.7</td>
<td>110.1</td>
<td>110.3</td>
<td>108.8</td>
</tr>
</tbody>
</table>

Dihedral

| C4-C5-S1-C(alkyl) | 25.7 | 54.3 | 47.8 |

Dihedral

| C4-C5-S2-C(alkyl) | N/A | 6.8 | 15.3 |

Dihedral

| C4-C5-S3-C(alkyl) | N/A | N/A | 7.2 |

Conclusion

We have been able to synthesize the bis- and tris- substituted phenylthio-BODIPY dyes in the 3- and 5- sites under neutral conditions without the presence of a catalyst or a co-reagent. The
yields range from moderate to good. BODIPY 16 shows a high fluorescence in hexane, but it is significantly quenched when the fluorophore is dissolved in polar media. This behavior is similar to that of BODIPY 12. On the contrary, BODIPY 17 maintains its high fluorescence intensity regardless of the solvent.
Section VA: CMPO – Metal Ion Coordination Chemistry

This dissertation has been focusing in developing a fluorophore to be introduced to a CMPO ligand to produce a low limit detector for lanthanides and actinides. However, from a fundamental point of view, the coordination chemistry between the metal ion and various substituted CMPO ligands is unknown to us at this stage.

It is important that this feature is investigated since it could lead to a better ligand design in the near future with the purpose of enhancing the detection capabilities of our CMPO-fluorophore or to enhance the extraction capability or metal ion selectivity of the CMPO.

One of the techniques that has been employed for the study of metal – ligand complexes is by ion-trap mass spectrometry. Crowe et al. studied the binding properties of rare-earth metals and two hydrophobic CMPO ligands finding that the unsubstituted CMPO formed ligands of the type 2:1:2 (ligand : metal ion: nitrate ion). Contrary, the CMPO-amide (vide supra) formed ionic species of the type 1:1:2. The coordination chemistry for the CMPO carboxylic acid (used for the reaction of the hydroxyl-containing BODIPY) was unknown.

Upon isolation of the ions of interest, the fragmentation pathways can be studied by collision-induced dissociation. The process involves the collision of highly energetic helium molecules with the ions of interest resulting in “daughter” ions. The study illustrated in section VB involves the mass-spectrometric collision induced dissociation of several CMPOs including the CMPO carboxylic acid with the theory that we may observe the free nitrate ion species of the type 2:1 (ligand : metal ion) due to the extra carboxylate functional group.
Section VB: A Mass Spectrometric – Collision-Induced Dissociation Study of the Interactions of Selected CMPO Ligands with UO$_2^{2+}$, La$^{3+}$, Ce$^{3+}$ and Eu$^{3+}$ Ions.

Hypothesis

The mass spectrometric study of the interactions of CMPO ligands with UO$_2^{2+}$, La$^{3+}$, Ce$^{3+}$ and Eu$^{3+}$ should provide with insights about the binding of the ligands to the metal ions in the solution phase. The CMPO carboxylic acid ligand contains an extra carboxylate-functional group which could act as a third binding site giving the ligand a tridentate functionality. This could improve its extraction properties or metal ion selectivity by forming nitrate-free complexes. The collision-induced dissociation study may illustrate the solvation mechanism of the ionic species.

Introduction

The fundamental study of the coordination between metal ions and the Ln/Ac extractants is of importance for the design of novel ligands with enhanced extraction capabilities. While the CMPOs described in the literature are bidentate ligands, other tridentate extractants are being developed since there is evidence suggesting that tridentate ligands may show higher selectivity towards heavier lanthanides as opposed to early lanthanides. For instance, Caravan et al. reported that H$_3$TRNS had higher formation constants for 2:1 (Ligand : Metal) complexes with heavier lanthanides such as ytterbium(III) compared to 1:1 (L:M), Figure 58. Furthermore, the stability constants are also higher for 2:1 (L:M) complexes as opposed to 1:1.
Among the several CMPOs available in our laboratory, the CMPO carboxylic acid and the CMPO amide possess an extra carbonyl group which could potentially coordinate to the metal ion making them tridentate ligands, Figure 59. Therefore, we explored the feasibility of these molecules to 2:1 (L:M) complexes in a similar fashion to the report made by Caravan et al.

A plausible methodology for the study of the metal ion – ligand complexes involves ion trap mass spectrometry because we may identify the solution complexes formed, as well as study
their fragmentation pathways by collision-induced dissociation (CID).\textsuperscript{52} The proposed technique has been used to identify the various ion species including lanthanide and uranyl complexes where the authors describe the coordination of acetone molecules to fulfill the coordination spheres of the uranyl and lanthanide ions.\textsuperscript{12,53}

In the present study, we describe the results of a mass spectroscopic – collision induced dissociation comparing the binding ability of a bidentate and two potentially tridentate CMPO ligands.

\section*{Results and Discussion}

\subsection*{Uranyl nitrate and CMPOs A-C solutions}

Our laboratory previously reported that the uranyl nitrate forms a 1:1 complex with the unsubstituted CMPO A acting as a bidentate ligand \textit{via} the P=O and C=O functionalities with the additional coordination of two nitrate ions to achieve charge neutrality.\textsuperscript{10} For the mass spectrometric – CID experiments, a mixture of uranyl nitrate and the corresponding CMPOs A-C were dissolved in acetone/water 50:50. The full-scan mass spectra are illustrated in Figure 60, and the ions of interest are represented in Table 13.

The solution of uranyl nitrate and the unsubstituted CMPO A forms the major species [\(\text{UO}_2(\text{A})(\text{Acetone})_2\)]\(^{2+}\) at 378.5 m/z with a relative intensity of 100%. The \(^{13}\text{C}\) isotopic peak was found at 379.0 m/z confirming a 2+ charge state for the ion. Both acetone ligands are readily dissociated and the loss of the acetone ligands is followed by the solvation of the ion species by a water molecule to yield [\(\text{UO}_2(\text{A})(\text{Acetone})(\text{Water})\)]\(^{2+}\) at 358.5 m/z and [\(\text{UO}_2(\text{A})(\text{Water})_2\)]\(^{2+}\) at \(~338.5\) m/z with relative intensities of 45\% and 25\%, respectively. We also observed a bis(ligand) uranyl complex [\(\text{UO}_2(\text{A})_2\)]\(^{2+}\) at 506.3 m/z and the isotopic \(^{13}\text{C}\) signal 0.5 mass units
higher at 506.8 m/z with a relative intensity of 39%. This suggests that both CMPO A ligands are coordinated to the uranyl in a neutral fashion. The only single charged species was observed at 720.0 m/z corresponding to the \([\text{UO}_2\text{NO}_3(\text{A})(\text{Water})]^+\) with a relative intensity of 22%, Figure 61.

The CMPOs B and C mainly form complexes of the type \([\text{UO}_2(\text{B})(\text{Acetone})_2]^{2+}\) and \([\text{UO}_2(\text{C})(\text{Water})_2]^{2+}\), respectively, with relative abundances of 100%. However, no evidence of the formation of \([\text{UO}_2(\text{B or C})_2]^{2+}\) was observed as in the case of CMPO A probably due to the significant steric effects induced by the carboxylic acid and amide functional groups. Also, the fixed trans- geometry of the uranyl oxygen atoms may hinder the coordination of the third carboxylate- group.

CMPOs B and C also formed the mono charged species \([\text{UO}_2\text{NO}_3(\text{B-C})(\text{Water})]^+\) in low abundances of 15% and 20% respectively where a nitrate ion acts as the counter-ion, Figure 61.
Figure 60. Mass spectra of UO$_2^{2+}$ and CMPOs A (top), B (middle), C (bottom)
Table 13. Summary of the CMPO-Uranyl ion species in the gas phase

<table>
<thead>
<tr>
<th>CMPO A Ion</th>
<th>R.I. (%)</th>
<th>CMPO B Ion</th>
<th>R.I. (%)</th>
<th>CMPO C Ion</th>
<th>R.I. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>[UO2(A)(Water)]²⁺</td>
<td>338.5</td>
<td>[UO2(NO3)(A)(Water)]²⁻</td>
<td>720.0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>-Acetone + Water</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>[UO2(A)(Acetone)(Water)]²⁻</td>
<td>358.5</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>-Acetone + Water</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>[UO2(A)(Water)]²⁻</td>
<td>338.5</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>-Acetone + Water</td>
<td></td>
<td></td>
<td></td>
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<td></td>
</tr>
</tbody>
</table>

Figure 61. Ion species of interest formed from solutions of uranyl nirate and CMPOs A-C
In brief, the behavior of the unsubstituted CMPO A, and the potential tridentate CMPOs B and C follows the same pattern in the presence of uranyl. Perhaps the fixed trans-oxo geometry does not allow for the coordination of the extra carbonyl group in the case of CMPOs B-C. Therefore, we explored this chemistry with several lanthanides since these ions do not have a predetermined geometry.

**Lanthanum nitrate and CMPO (A-C) solutions**

Solutions of lanthanum nitrate with CMPO A produce complexes of the type [La(NO$_3$)$_2$(A)]$^+$ (634.1 m/z) and [La(NO$_3$)$_2$(A)$_2$]$^+$ (1005.0 m/z) with relative intensities of 100% and 50%, respectively, Figure 62. The coordination sphere of the [La(NO$_3$)$_2$(A)]$^+$ ion is not complete, and adducts of water (652.7 m/z) and methanol (665.1 m/z) to form [La(NO$_3$)$_2$(A)(S)]$^+$ (S = water, methanol) are observed with relative intensities of 36% and 44%.

![Figure 62. Mass spectra of a solution of La(NO$_3$)$_3$ and CMPO A](image-url)
The \([\text{La(NO}_3\text{)}_2\text{(A)}]^{+}\) was isolated and dissociated through collision with helium gas resulting in the loss of nitric acid. However, the species is rapidly solvated by water (589.0 m/z) or methanol (603 m/z) adducts to form species of the type \([\text{LaNO}_3\text{(A)}(\text{S})]^{+}\), (\(\text{S} = \text{H}_2\text{O}, \text{MeOH}\)) Figure 63. The isolation and CID analysis of \([\text{La(NO}_3\text{)}_2\text{(A)}_2]^{+}\) also results in the loss of nitric acid. However, contrary to the monoligated species, \([\text{La(NO}_3\text{)}_2\text{(A)}]^{+}\) (942 m/z) is observed along with the water (960 m/z) and methanol (973 m/z) adducts, Figure 64. A summary of the CIDs is illustrated in Figure 65.

![Figure 63. CID spectra of \([\text{La(NO}_3\text{)}_2\text{(A)}]^{+}\)](image1)

![Figure 64. CID spectra of \([\text{La(NO}_3\text{)}_2\text{(A)}_2]^{+}\)](image2)
Interactions of La\(^{3+}\) and CMPO result in the formation of \([\text{La(NO}_3\text{)}_2(B)]^+\) (691.6 m/z) with a relative intensity of 100% as observed for the CMPO A. However, we also observed the ion peak corresponding to \([\text{La(B)}_2]^+\) (995 m/z) with a relative abundance of 50%, Figure 66. This suggests that both CMPO B ligands are coordinated to the metal ion while also acting as counter-ions. Therefore, the carboxylic acid may have been deprotonated to the carboxylate functional group.

The dissociation of \([\text{La(NO}_3\text{)}_2(B)]^+\) (692 m/z) results in the loss of nitric acid to produce \([\text{La(NO}_3\text{)}(B)]^+\) (629 m/z). Therefore, the CMPO B acts as a bidentate ligand and as an anion at the same time, i.e. tridentate. This species is also solvated by water and methanol to form \([\text{La(NO}_3\text{)}(B)(S)]^+\), Figure 67. This is in accordance with the observations made for CMPO A.
Lastly, the interactions of La$^{3+}$ and CMPO C result in the formation of [La(NO$_3$)$_2$(C)]$^+$ (915 m/z) and [La(NO$_3$)$_2$(C)$_2$]$^+$ (1597 m/z) with a relative abundances of 100% and 38% respectively. This pattern was observed for La$^{3+}$ and CMPO A. The dissociation of [La(NO$_3$)$_2$(C)$_2$]$^+$ results in the
loss of a CMPO C ligand (915 m/z), or the loss of nitric acid in equal proportions (1504 m/z), which suggests that the CMPO C is labile probably due to steric effects, Figure 68 and Figure 69.

Figure 68. Mass spectra of a solution of La(NO$_3$)$_3$ and CMPO C (left), and the CID of [La(NO$_3$)$_2$(C)$_2$]$^+$ (right)

Figure 69. CID of La(III) and CMPO C

Overall, the interactions between the CMPOs A and C and La$^{3+}$ produce ions of the type [La(NO$_3$)$_2$(CMPO A/C)]$^+$ and [La(NO$_3$)$_2$(CMPO A/C)$_2$]$^+$. However, the CMPO carboxylic acid B produces ions of the type [La(CMPO B)$_2$], with the CMPO B acting as a tridentate ligand, Figure 70.
$\text{Ln}^{3+}$ (Ln = Ce, Eu) + CMPO (A-C) solutions

The interactions of cerium(III) and europium(III) and CMPO A produce the ions $[\text{Ln(NO}_3^\text{2}(\text{A})]^{+}$ and $[\text{Ln(NO}_3^\text{2}(\text{A})_2]^{+}$, a similar behavior to that of lanthanum(III). Upon dissociation of $[\text{Ln(NO}_3^\text{2}(\text{A})]^{+}$ (635.0 m/z for Ce and 648.2 m/z for Eu), nitric acid is lost to produce $[\text{LnNO}_3(\text{A})]^{+}$. However, the species is solvated by water or molecule as observed for lanthanum(III). The dissociation of $[\text{Ln(NO}_3^\text{2}(\text{A})_2]^{+}$ (1006.1 m/z for Ce and 1019.2 m/z for Eu) also results in the loss of nitric acid and the production of the stable ion $[\text{LnNO}_3(\text{A})_2]^{+}$. This behavior is in accordance with La$^{3+}$ and CMPO A as discussed above, Figure 71, Figure 72 and Figure 73.

We also observed the ion $[\text{CeNO}_3(\text{A})_2]^{2+}$ at 472.2 m/z with a relative abundance of 23%. In the case of europium(III), the ion peak $[\text{CeNO}_3(\text{A})_2]^{2+}$ had a relative abundance of 5%.
Figure 71. Mass spectra of the solutions of Ln(NO$_3$)$_3$ (Ln = Ce (left), Eu (right)) and CMPO A

472 - [Ce(NO$_3$)$_2$ . 2 A]$^+$

1006 - [Ce(NO$_3$)$_3$ . 2 A]$^+$

634 - [Ce(NO$_3$)$_2$ . A]$^+$

1017 - [Eu(NO$_3$)$_2$ . 2 A]$^+$

646 - [Eu(NO$_3$)$_3$ . A]$^+$

Figure 72. CID of Ce(III) and CMPO A

- [Ce(NO$_3$)$_3$(A)]$^+$

+ Nitric Acid

[Ce(NO$_3$)$_3$(A)]$^+$

- Not detected

+ Water

[Ce(NO$_3$)$_3$(A)(Water)]$^+$

635.5 m/z
R.L. 24 %

590.5 m/z
R.L. 100 %

1096.1 m/z
R.L. 100 %

943.1 m/z
R.L. 82 %

973.8 m/z
R.L. 32 %

- Nitric Acid

[Ce(NO$_3$)$_3$(A)]$^+$

+ Water

[Ce(NO$_3$)$_3$(A)(Water)]$^+$

959.7 m/z
R.L. 100 %

[Ce(NO$_3$)$_3$(A)(MeOH)]$^+$

973.8 m/z
R.L. 32 %
The interactions between cerium(III) and CMPO result in the formation of [Ce(NO$_3$)$_2$(B)]$^+$ at 692.7 m/z with a relative intensity of 50%. Upon isolation and collision-induced dissociation of this ion, a molecule of nitric acid is loss to form [CeNO$_3$(B)]$^+$ (630.0 m/z) along with the water (647.2 m/z) and methanol (661.3 m/z) adducts to form ions of the type [CeNO$_3$(B)(S)]$^+$, Figure 74.

The bis(ligand) complex [Ce(B)$_2$]$^+$ (996.1 m/z) with a relative intensity of 100% was also observed. In this case, the CMPOs B are acting as bidentate ions and counter-ions, i.e. tridentate ligands. Furthermore, the species [Ce(B)$_2$]$^{2+}$ (498.7 m/z) was observed with a low relative intensity ~20%. In this case, only one CMPO B is also acting as a counter-ion while the other ligand is neutral, Figure 76.
The same types of ions were observed for europium(III) and CMPO B. However, the ions $[\text{Eu(B)}_2]^{2+}$, $[\text{Eu(NO}_3)_2\text{(B)}]^{2+}$ and $[\text{Eu(B)}_2]^{+}$ are in close relative intensities with one another, Figure 75 and Figure 77.

Figure 74. Mass spectra of the solutions of Ce(NO$_3$)$_3$ and CMPO B (left), and zoom in at 500-750 m/z range (right)

Figure 75. Mass spectra of the solutions of Eu(NO$_3$)$_3$ and CMPO B
Figure 76. CID of Ce(III) and CMPO B

Figure 77. CID of Eu(III) and CMPO B
Lastly, we investigated the ionic species formed by the interaction of cerium nitrate and europium nitrate with CMPO C. The ions observed follow the same pattern as in the case of lanthanum(III) and CMPO C. In the case of cerium, the major species observed are $[\text{Ce(NO}_3\text{)}_2(\text{C})]^+$ (916.2 m/z) and $[\text{Ce(NO}_3\text{)}_2(\text{C})_2]^+$ (1567.6 m/z) with relative intensities of 100% and 70%, Figure 78, left. The dissociation of the bis-CMPO coordinated ion results in the loss of nitric acid or the loss of a CMPO ligand, in accordance with the observations made for La(III) and CMPO C where we observed that the CMPO C is readily dissociated, Figure 78, right, Figure 80.

Europium and CMPO C produce the same ions as observed for lanthanum(III) and cerium(III), Figure 79 and Figure 81.
Figure 78. Mass spectra of a solution of Ce(NO$_3$)$_3$ and CMPO C (left), and the CID of [Ce(NO$_3$)$_3$C]$^+$ (right).

Figure 79. Mass spectra of a solution of Eu(NO$_3$)$_3$ and CMPO C (top), zoom out of the peak at 1567 shows both isotopes for Europium (bottom).
We suspect that the behavior of these CMPO ligands with other lanthanides will follow a similar pattern. However, since other lanthanides have several isotopes, the identification of the charges of the ionic species is complex.

The summary of the ion peaks identified and their CIDs for Ln(NO₃)₃ and CMPOs A-C solutions are illustrated in Table 14 and Table 15.
Table 14. Summary of the ion peaks for Ln(NO\textsubscript{3})\textsubscript{3} (Ln = La, Ce, Eu) and CMPOs A-C solutions

<table>
<thead>
<tr>
<th>Ligand A</th>
<th>La(III) (m/z)</th>
<th>R.I. (%)</th>
<th>Ce(III) (m/z)</th>
<th>R.I. (%)</th>
<th>Eu(III) (m/z)</th>
<th>R.I. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>[M(NO\textsubscript{3})\textsubscript{2}(A)]\textsuperscript{+}</td>
<td>634.13</td>
<td>100</td>
<td>635.01</td>
<td>24</td>
<td>648.20</td>
<td>35</td>
</tr>
<tr>
<td>[M(NO\textsubscript{3})\textsubscript{2}(A)(Water)]\textsuperscript{+}</td>
<td>652.73</td>
<td>30</td>
<td>N.D.</td>
<td>N.D.</td>
<td>665.21</td>
<td>40</td>
</tr>
<tr>
<td>[M(NO\textsubscript{3})\textsubscript{2}(A)(MeOH)]\textsuperscript{+}</td>
<td>665.27</td>
<td>44</td>
<td>N.D.</td>
<td>N.D.</td>
<td>679.33</td>
<td>50</td>
</tr>
<tr>
<td>[M(NO\textsubscript{3})\textsubscript{2}(A)]\textsuperscript{2+}</td>
<td>1005.07</td>
<td>40</td>
<td>1006.14</td>
<td>100</td>
<td>1019.26</td>
<td>100</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Ligand B</th>
<th>La(III) (m/z)</th>
<th>R.I. (%)</th>
<th>Ce(III) (m/z)</th>
<th>R.I. (%)</th>
<th>Eu(III) (m/z)</th>
<th>R.I. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>[M(B)\textsubscript{2}]\textsuperscript{2+}</td>
<td>498.22</td>
<td>30</td>
<td>498.70</td>
<td>23</td>
<td>505.27</td>
<td>80</td>
</tr>
<tr>
<td>[M(NO\textsubscript{3})\textsubscript{2}(B)]\textsuperscript{+}</td>
<td>691.63</td>
<td>100</td>
<td>692.77</td>
<td>30</td>
<td>705.89</td>
<td>100</td>
</tr>
<tr>
<td>[M(NO\textsubscript{3})(B)(MeOH)]\textsuperscript{+}</td>
<td>660.42</td>
<td>30</td>
<td>661.38</td>
<td>25</td>
<td>692.37</td>
<td>30</td>
</tr>
<tr>
<td>[M(NO\textsubscript{3})(B)(Water)]\textsuperscript{+}</td>
<td>646.24</td>
<td>92</td>
<td>647.12</td>
<td>55</td>
<td>678.15</td>
<td>55</td>
</tr>
<tr>
<td>[M(NO\textsubscript{3})(B)]\textsuperscript{+}</td>
<td>629.06</td>
<td>100</td>
<td>630.08</td>
<td>42</td>
<td>660.47</td>
<td>70</td>
</tr>
<tr>
<td>[M(NO\textsubscript{3})(B)]\textsuperscript{2+}</td>
<td>N.D.</td>
<td>N.D.</td>
<td>N.D.</td>
<td>N.D.</td>
<td>N.D.</td>
<td>N.D.</td>
</tr>
<tr>
<td>[M(B)\textsubscript{2}]\textsuperscript{3+}</td>
<td>995.07</td>
<td>60</td>
<td>996.18</td>
<td>100</td>
<td>1009.11</td>
<td>85</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Ligand C</th>
<th>La(III) (m/z)</th>
<th>R.I. (%)</th>
<th>Ce(III) (m/z)</th>
<th>R.I. (%)</th>
<th>Eu(III) (m/z)</th>
<th>R.I. (%)</th>
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<tbody>
<tr>
<td>[M(NO\textsubscript{3})(C)\textsubscript{2}]\textsuperscript{2+}</td>
<td>N.D.</td>
<td>N.D.</td>
<td>753.41</td>
<td>40</td>
<td>760.04</td>
<td>25</td>
</tr>
<tr>
<td>[M(NO\textsubscript{3})(C)]\textsuperscript{2+}</td>
<td>915.41</td>
<td>100</td>
<td>916.21</td>
<td>100</td>
<td>929.35</td>
<td>100</td>
</tr>
<tr>
<td>[M(NO\textsubscript{3})(C)\textsubscript{2}]\textsuperscript{3+}</td>
<td>1567.60</td>
<td>35</td>
<td>1568.50</td>
<td>70</td>
<td>1581.69</td>
<td>30</td>
</tr>
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Table 15. Summary of the collision-induced dissociation peaks for Ln(NO$_3$)$_3$ (Ln = La, Ce, Eu) and CMPOs A-C solutions

<table>
<thead>
<tr>
<th>Ligand A</th>
<th>La(III) (m/z)</th>
<th>La(III) R.I. (%)</th>
<th>Ce(III) (m/z)</th>
<th>Ce(III) R.I. (%)</th>
<th>Eu(III) (m/z)</th>
<th>Eu(III) R.I. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>[M(NO$_3$)$_2$(A)]$^+$</td>
<td>634.11</td>
<td>635.05</td>
<td>648.25</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>[M(NO$_3$)$_3$(A)(MeOH)]$^+$</td>
<td>603.08</td>
<td>100</td>
<td>N.D.</td>
<td>N.D.</td>
<td>N.D.</td>
<td>N.D.</td>
</tr>
<tr>
<td>[M(NO$_3$)$_3$(A)(Water)]$^+$</td>
<td>589.05</td>
<td>20</td>
<td>590.50</td>
<td>100</td>
<td>N.D.</td>
<td>N.D.</td>
</tr>
<tr>
<td>[M(NO$_3$)$_3$(B)]$^+$</td>
<td>N.D.</td>
<td>N.D.</td>
<td>N.D.</td>
<td>N.D.</td>
<td>N.D.</td>
<td>N.D.</td>
</tr>
<tr>
<td>[M(NO$_3$)$_3$(B)$_2$]$^+$</td>
<td>1005.07</td>
<td></td>
<td>1006.14</td>
<td></td>
<td>1019.27</td>
<td></td>
</tr>
<tr>
<td>[M(NO$_3$)$_3$(B)(MeOH)]$^+$</td>
<td>972.85</td>
<td>60</td>
<td>973.84</td>
<td>32</td>
<td>986.95</td>
<td>50</td>
</tr>
<tr>
<td>[M(NO$_3$)$_3$(B)(Water)]$^+$</td>
<td>958.63</td>
<td>100</td>
<td>959.71</td>
<td>100</td>
<td>972.19</td>
<td>75</td>
</tr>
<tr>
<td>[M(NO$_3$)$_3$(C)]$^+$</td>
<td>942.11</td>
<td>50</td>
<td>943.12</td>
<td>82</td>
<td>956.23</td>
<td>100</td>
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</table>

<table>
<thead>
<tr>
<th>Ligand B</th>
<th>La(III) (m/z)</th>
<th>La(III) R.I. (%)</th>
<th>Ce(III) (m/z)</th>
<th>Ce(III) R.I. (%)</th>
<th>Eu(III) (m/z)</th>
<th>Eu(III) R.I. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>[M(NO$_3$)$_3$(B)]$^+$</td>
<td>691.63</td>
<td></td>
<td>692.72</td>
<td></td>
<td>705.87</td>
<td></td>
</tr>
<tr>
<td>[M(NO$_3$)$_3$(B)(MeOH)]$^+$</td>
<td>660.44</td>
<td>30</td>
<td>661.35</td>
<td>25</td>
<td>692.36</td>
<td>30</td>
</tr>
<tr>
<td>[M(NO$_3$)$_3$(B)(Water)]$^+$</td>
<td>646.27</td>
<td>92</td>
<td>647.11</td>
<td>55</td>
<td>678.16</td>
<td>55</td>
</tr>
<tr>
<td>[M(NO$_3$)$_3$(C)]$^+$</td>
<td>629.07</td>
<td>100</td>
<td>630.02</td>
<td>42</td>
<td>660.42</td>
<td>70</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Ligand C</th>
<th>La(III) (m/z)</th>
<th>La(III) R.I. (%)</th>
<th>Ce(III) (m/z)</th>
<th>Ce(III) R.I. (%)</th>
<th>Eu(III) (m/z)</th>
<th>Eu(III) R.I. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>[M(NO$_3$)$_3$(C)$_2$]$^+$</td>
<td>1567.61</td>
<td></td>
<td>1568.51</td>
<td></td>
<td>1581.66</td>
<td></td>
</tr>
<tr>
<td>[M(NO$_3$)$_3$(C)]$^+$</td>
<td>1504.67</td>
<td>90</td>
<td>1505.60</td>
<td>50</td>
<td>1518.65</td>
<td>30</td>
</tr>
<tr>
<td>[M(NO$_3$)$_3$(C)]$^+$</td>
<td>915.45</td>
<td>100</td>
<td>916.20</td>
<td>100</td>
<td>929.32</td>
<td>100</td>
</tr>
</tbody>
</table>

Conclusion

The synthesis of potential tridentate CMPO ligands could eliminate the need for nitrates as counter-ions in various extraction processes. The main species observed for the uranyl and the CMPOs A-C was [UO$_2$(CMPO)(S)$_2$]$^+$. We only observed a bis(ligand)-uranyl species in the case of CMPO A. Perhaps the steric effects induced by the larger CMPOs B-C prevent the formation of a bis(ligand)-uranyl since the geometry of uranyl is fixed in a trans-oxo fashion. The unsubstituted CMPO A and the CMPO amide C in the presence of lanthanides yield ions of the type [Ln(NO$_3$)$_3$(L)]$^+$ and [Ln(NO$_3$)$_3$(L)$_2$]$^+$. In this case, the ligands act as neutral coordination molecules. However, the CMPO carboxylic acid B is able to act as a bidentate coordination
ligand and as a counter-ion forming ions of the type $[\text{Ln(L)}_2]^+$ where both ligands are negatively charged and $[\text{Ln(L)}_2]^{2+}$ where one ligand is neutral and the other is negatively charged. Due to the capacity of forming bis(ligand)-lanthanide species, the CMPO carboxylic acid could show high selectivity towards heavier lanthanides as observed by Caravan \textit{et al.}\textsuperscript{51}

A manuscript describing this work is in preparation.
Chapter 4 - Conclusions

We have synthesized and characterized several BODIPY fluorophores with the purpose of utilizing them as the fluorophores in a CMPO-Fl molecule. We designed a highly emissive hydroxyl-containing BODIPY which could be introduced to the CMPO by an esterification reaction. Further, we explored the generality of the reaction between amines and 8-MeS-BODIPY where we found interesting properties. One of them was the restricted rotation about the C(8)-N bond, and we determined their activation energies by using variable temperature NMR experiments. We are confident that we can react the CMPO-NH$_2$ with the 8-MeS-BODIPY to produce the CMPO-NH-BODIPY.

After our experiments with amines, we decided to try the same reaction with thiols. The reaction proceeds at a slower rate but in high yields. The solvent has a significant impact in driving the reaction to produce the mono-, bis-, and tris- substituted species. We may be able to react the CMPO-SH with 8-MeS-BODIPY to create the CMPO-S-BODIPY.

Lastly, we conducted a mass spectrometric – collision induced dissociation study to analyze the binding of several CMPO ligands with uranyl or several lanthanides. We observed that the CMPO – carboxylic acid is capable of producing nitrate free ion species by forming bis(ligand) – metal ion species, which according to other reports in the literature, the CMPO carboxylic acid may show high selectivity for late lanthanides.
Future Work

One of the near future goals is to synthesize a CMPO with a free amine to react it with the 8-MeS-BODIPY. A plausible methodology is illustrated in Scheme 21 which involves the synthesis of N-aminoethyl-cloroacetamide. We may only hope that the CMPO-NH-BODIPY complex will exhibit an optical response upon coordination to lanthanides and/or actinides.

Scheme 21. Proposed synthesis of the amine-free CMPO


Appendix 1. \(^1\)H NMR of BODIPY 2a in CDCl\(_3\)

Appendix 2. \(^{19}\)F NMR of BODIPY 2a in CDCl\(_3\)
Appendix 3. $^{13}$C NMR of BODIPY 2a in CDCl$_3$

Appendix 4. $^1$H NMR of BODIPY 2b in CDCl$_3$
Appendix 5. $^{13}$C NMR of BODIPY 2b in CDCl$_3$

Appendix 6. $^1$H NMR of BODIPY 2c in CDCl$_3$
Appendix 7. $^{19}$F NMR of BODIPY 2c in CDCl$_3$

Appendix 8. $^{13}$C NMR of BODIPY 2c in CDCl$_3$
Appendix 9. $^1$H NMR of BODIPY 3a in CDCl$_3$

Appendix 10. $^{19}$F NMR of BODIPY 3a in CDCl$_3$
Appendix 11. $^{13}$C NMR of BODIPY 3a in CDCl$_3$

Appendix 12. $^1$H NMR of BODIPY 3b in CDCl$_3$
Appendix 13. $^{19}$F NMR of BODIPY 3b in CDCl$_3$

Appendix 14. $^{13}$C NMR of BODIPY 3b in CDCl$_3$
Appendix 15. $^1$H NMR of BODIPY 3c in CDCl$_3$

Appendix 16. $^{19}$F NMR of BODIPY 3c in CDCl$_3$
Appendix 17. $^{13}$C NMR of BODIPY 3c in CDCl$_3$

Appendix 18. $^1$H NMR of BODIPY 4 in Methanol-d$_4$, spectrum in accordance with Osorio et al.$^{38}$
Appendix 19. $^1$H NMR of BODIPY 5a in CDCl$_3$

Appendix 20. $^{19}$F NMR of BODIPY 5a in CDCl$_3$
Appendix 21. $^{13}$C NMR of BODIPY 5a in CDCl$_3$

Appendix 22. $^1$H NMR of BODIPY 5b in CDCl$_3$
Appendix 23. $^{19}$F NMR of BODIPY 5b in CDCl$_3$

Appendix 24. $^{13}$C NMR of BODIPY 5b in CDCl$_3$
Appendix 25. $^1$H NMR of BODIPY 6 in CDCl$_3$

Appendix 26. $^{19}$F NMR of BODIPY 6 in CDCl$_3$
Appendix 27. $^{13}$C NMR of BODIPY 6 in CDCl$_3$

Appendix 28. $^1$H NMR of BODIPY 7 in CDCl$_3$
Appendix 29. $^{19}$F NMR of BODIPY 7 in CDCl$_3$

Appendix 30. $^{13}$C NMR of BODIPY 7 in CDCl$_3$
Appendix 31. $^1$H NMR of BODIPY 8 in CDCl$_3$

Appendix 32. $^{19}$F NMR of BODIPY 8 in CDCl$_3$
Appendix 33. $^{13}$C NMR of BODIPY 8 in CDCl$_3$

Appendix 34. $^1$H NMR of BODIPY 9 in CDCl$_3$

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Appendix 35. $^1$H NMR of BODIPY 9 in CDCl$_3$

Appendix 36. $^{13}$C NMR of BODIPY 9 in CDCl$_3$
Appendix 37. $^1$H NMR of BODIPY 10 in CDCl$_3$

Appendix 38. $^{19}$F NMR of BODIPY 10 in CDCl$_3$
Appendix 39. $^{13}$C NMR of BODIPY 10 in CDCl$_3$

Appendix 40. $^1$H NMR of BODIPY 11 in CDCl$_3$
Appendix 41. $^{13}$C NMR of BODIPY 11 in CDCl$_3$

Appendix 42. $^1$H NMR of BODIPY 12 in CDCl$_3$
Appendix 43. $^{19}$F NMR of BODIPY 12 in CDCl$_3$

Appendix 44. $^{13}$C NMR of BODIPY 12 in CDCl$_3$
Appendix 45. \(^1\)H NMR of BODIPY 13 in CDCl\(_3\)

Appendix 46. \(^{13}\)C NMR of BODIPY 13 in CDCl\(_3\)
Appendix 47. $^1$H NMR of BODIPY 14 in CDCl₃

Appendix 48. $^{13}$C NMR of BODIPY 14 in CDCl₃
Appendix 49. $^1$H NMR of BODIPY 15 in CDCl$_3$

Appendix 50. $^{13}$H NMR of BODIPY 15 in CDCl$_3$
Appendix 51. $^1$H NMR of BODIPY 16 in CDCl$_3$
Appendix 53. $^{13}$C NMR of BODIPY 16 in CDCl$_3$

Appendix 54. $^1$H NMR of BODIPY 17 in CDCl$_3$
Appendix 55. $^{19}$F NMR of BODIPY 17 in CDCl$_3$

Appendix 56. $^{13}$C NMR of BODIPY 17 in CDCl$_3$
Curriculum Vita

Robinson Roacho earned his Bachelor in Science of Chemistry from The University of Texas at El Paso in El Paso, Texas in 2008 where he met Professor Keith Pannell. Robinson believed that Professor Pannell was a unique mentor, so he decided to continue his postgraduate studies under his direction.

During his postgraduate studies, Robinson traveled to Wichita State University where he met Professor Michael Van Stipdonk performing research in a completely new area of chemistry to him. He was fortunate to travel to the Netherlands in 2011 to continue this research using state-of-the-art instrumentation.

He later on traveled to Japan where he performed research on silicon carbide thin films under the direction of Professor Haruhiko Ito. While in the far east lands, he even learned snowboard and to eat sushi. He practices both activities as often as he cans and with huge passion.

His research work has been presented to fellow scientists in regional and national chemistry conferences. Furthermore, this work has been published in several peer-reviewed journals.

Robinson wants to pursue a career in industry.

Robinson’s dissertation “SYNTHESIS AND DESIGN OF FLUOROPHORES FOR THE DETECTION OF LANTHANIDES AND ACTINIDES” was supervised by Professor Keith Pannell.

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