Spring 4-14-2021

Preparation of Perylene Bisimide Acceptors with Ethylcarboxyl and Pyrenylcyclohexyl Imide Groups

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PREPARATION OF PERYLENE BISIMIDE ACCEPTORS WITH ETHYLCARBOXYL AND PYRENYLCYCLOHEXYL IMIDE GROUPS

by
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A thesis submitted to the faculty of The University of Mississippi in partial fulfillment of the requirements of the Sally McDonnell Barksdale Honors College

Oxford, MS
May 2021

Approved by

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DEDICATION

For the endless encouragement and support from my friends and family, I dedicate the culmination of this thesis to my parents, Randy and Nanette Stark, and my sisters, Caitlin and Celie Stark; to my grandparents, Marti Stark and Dr. Jeff Roux; to numerous friends; and most importantly to God. My research and work-drive would have been otherwise impossible without the reassurance and faith from those mentioned above. Thank you.

ACKNOWLEDGEMENTS

Throughout the process of my undergraduate research and experimentation, I would like to thank everyone who has helped me along the way; while I may be writing this thesis, it is the result of the combined efforts of many friends and professors. Namely, I would like to wish a sincere thanks to my advisor/mentor Dr. Daniell Mattern for his assistance with my experiments and for his unmatched enthusiasm for organic chemistry. In addition to granting me the enormous opportunity to pursue research under his laboratory, I applaud him for turning such a complex subject as organic chemistry into a topic of passion and curiosity for myself and thousands of other students.

Additionally, I send gratitude and appreciation to my thesis readers, Dr. Susan Pedigo and Dr. Emily Rowland for being willing to assist with my thesis. Furthermore, I would also like to thank past researcher Tarrah Frederick for her extensive information on perylene bisimide (PBI) synthesis products left behind for my research. Finally, I would like to acknowledge my fellow research team, Josh Peltan, Nickie Tiwari, and Tony Lybrand, for their guidance in laboratory techniques and encouragement during my research. My deepest gratitude and appreciation goes to everyone who led me on my way.

ABSTRACT

Multiple attempts were made to deprotect TBDMS-protected (tert-butyldimethylsilyl protected) serinol and swallowtailed PBI (**Compound 2**), synthesized by past researcher Tarrah Frederick, to generate **Compound 1**. The theoretical **Compound 1** product is intended for use in molecular rectification of electricity because the perylene core acts as a good acceptor with high electron affinity, and it does not require an electron donor group. Many rectification molecules are amphiphilic Donor-σ-Acceptor compounds, which allow for electron transfer through localized molecular orbitals when placed between electrodes (Langmuir-Blodgett Method). However, PBIs can transfer electrons from one electrode, through the LUMO of perylene, and to the other electrode at specific voltages by asymmetric rectification. Thus, PBIs have been particular molecules of interest as molecular rectifiers with only an acceptor and no donor.[5]

Several issues arose during the synthesis of **Compound 1** and deprotection of **Compound 2**, such as unknown impurities, byproducts, molecular orientations, intramolecular forces, and other complexities. All of these difficulties resulted in unsuccessful deprotection and ultimately unclear NMR spectra, despite similarly published literature procedures.[5] However, the addition of β-alanine to PMA provided a similar, more concise, and more successful method for addition of a polar, hydrophilic group to PMA (**Compound 4**), though further analysis is needed for confirmation.[4] Continued experimentation with deprotection and β-alanine addition was halted after coordination with other research groups retired. More research is needed moving forward to understand the addition and deprotection of groups on PMA and PBI.[9]

Furthermore, the pursuit of pyrenylcyclohexyl imide (PCHI) group addition to PMA was explored (**Compound 3**). Synthesis of this group and subsequent addition of it to PMA would progress towards the desired product of the Hammer Proposal (**Compound 3**),[7] which seeks to understand and synthesize unimolecular rectifiers with various carbon tethers on PMA. Numerous difficulties were encountered during synthesis of the PCHI with bromine Grignards. Formation of the perylene Grignard with Br proves quite difficult, so synthesis of this Grignard with iodine was explored instead. Iodopyrene was successfully synthesized[3], but the Grignard struggled to form again. Perhaps treatment with butyl lithium offers further investigation of PCHI and the Hammer Proposal.[7]

All in all, the reactions and methods described in this text provide useful information for synthesis and future investigation of targeted PBI molecules for molecular rectification.

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LIST OF ABBREVIATIONS

AR – Aviram-Ratner

Au – gold

Br – bromine

$CDCl_3$ – dueterated chloroform (chloroform-d)

CH_2Cl_2/DCM – methylene chloride or dichloromethane

D-σ-A – Donor-σ-Acceptor

Et_2O – diethyl ether

EtOH – ethanol or ethyl alcohol

g – gram

HCl – hydrochloric acid

HOMO – highest occupied molecular orbital

I – iodine

LUMO – lowest unoccupied molecular orbital

Mg – magnesium metal

mg – milligram

MeOH or CH_3OH – methanol or methyl alcohol

$MgSO_4$ – magnesium sulfate

mL – milliliter

mmols – millimoles

mol – moles

NMR – nuclear magnetic resonance

N_2 – nitrogen gas

PBI – perylene bisimide (same as PDI)

PCHI – pyrenylcyclohexyl imide

PDI – perylene diimide (same as PBI)

PIA – perylene imide anhydride (same as PMA)

PMA – perylene monoanhydride (same as PIA)

PTCDA – perylene-4,5,9,10-bis(dicarboximide)

TBDMSCl – *tert*-butyldimethylsilyl chloride protecting group

THF – tetrahydrofuran

TLC – thin layer chromatography

α – alpha

β – beta (one away from a carbonyl)

Δ – heat/change

π – pi

σ – sigma

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LIST OF COMPOUNDS

Compound 1: PBI with swallowtail and serinol (*cis/trans*)

Compound 2: PBI with swallowtail and silyl ether-protected serinol (*cis/trans*)

Compound 3: PBI with swallowtail and pyrenylcyclohexyl group (*cis/trans*)

Compound 4: PBI with swallowtail and propanoic acid (β-alanine) group

Compound 5: 1,4-cyclohexadione monoethylene ketal

Compound 6: 1-pyrenylcyclohexan-1-ol-4-monoethyleneketal

Compound 7: 4-pyrenylcyclohexan-1-one

Compound 8: 4-pyrenylcyclohexan-1-amine

Compound 9: 1-phenylcyclohexan-1-ol

I. INTRODUCTION

1.1 Background and Rectification

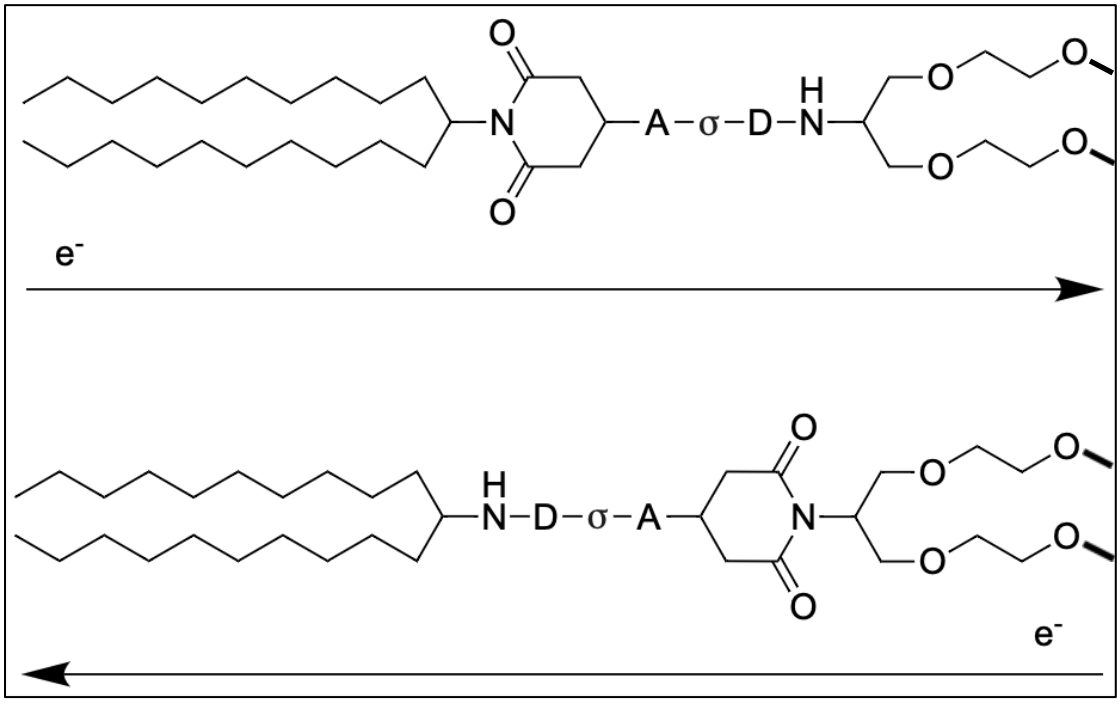


Figure I-1*: When D-σ-A compounds are organized into a monolayer and placed between Au electrodes, they can be rectifiers of electron flow in a single direction.*[10]

As proposed by Ari Aviram and Mark Ratner in 1974, unimolecular rectifiers are single molecules that pass electric current preferentially in one direction. Perhaps the most well-known molecular rectifiers are known as Donor-Sigma-Acceptor (D-σ-A) compounds. As the name suggests, the donor and acceptor groups are bound by a σ bond/bridge that ultimately hinders intermolecular orbital interactions between the two groups, basically insulating them. Ideally, good acceptor groups have a high affinity for electrons, meaning the acquisition of an electron is favorable and increases acceptor stability. The acceptor's ability to obtain electrons results from

its low energy molecular orbitals. On the opposite hand, good donors have lower electron affinity in addition to a low ionization energy. Essentially, a good donor would rather give up or donate electrons, potentially becoming a cation, than accept electrons to achieve stability. As such, donors tend to have high energy molecular orbitals. Between the donor and acceptor, the σ bridge seeks to isolate, decouple, and reduce molecular overlap of the donor and acceptor. Typically, the σ bridge consists of repeated methylene subunits or unsaturated π vinyl bonds, which cause dihedral twist relative to the donor and acceptors and minimize the overlap of molecular orbitals.[5]

For Aviram-Ratner (AR) rectification, D-σ-A compounds rectify electricity when properly aligned in register within a monolayer and sandwiched between two electrodes. Depending on the position of donor and acceptor, electricity can flow preferentially in one of two directions. **Figure I-1** shows individual molecules in two such monolayers. The flow of electrons results from the adjacent acceptor's lowest unoccupied molecular orbital (LUMO) and the donor's highest occupied molecular orbital (HOMO) having different energies. Under electrical bias with enough voltage difference from electrodes (-2 V), electrons flow in a single direction. Therefore, electrons can travel from cathode, to acceptor, to donor, and finally to anode. Without a large enough voltage difference (-1 V or 0 V), no electron flow occurs.[5]

AR rectification occurs due to energy differences between the localized molecular orbital of the acceptor and donor groups. An example by previous researcher Tarrah Frederick explains that an electrical current is possible from acceptor to donor when an electron in the acceptor's LUMO is at a higher energy level than a vacancy (hole) in the donor's HOMO. The D-σ-A molecule can pass electrons through resonance and intramolecular transfer. During this electron

transfer, a D^{+}-σ-A^{-} zwitterion is formed, returning to D^{0}-σ-A^{0} as the electrons travel downhill from cathode to anode.[5]

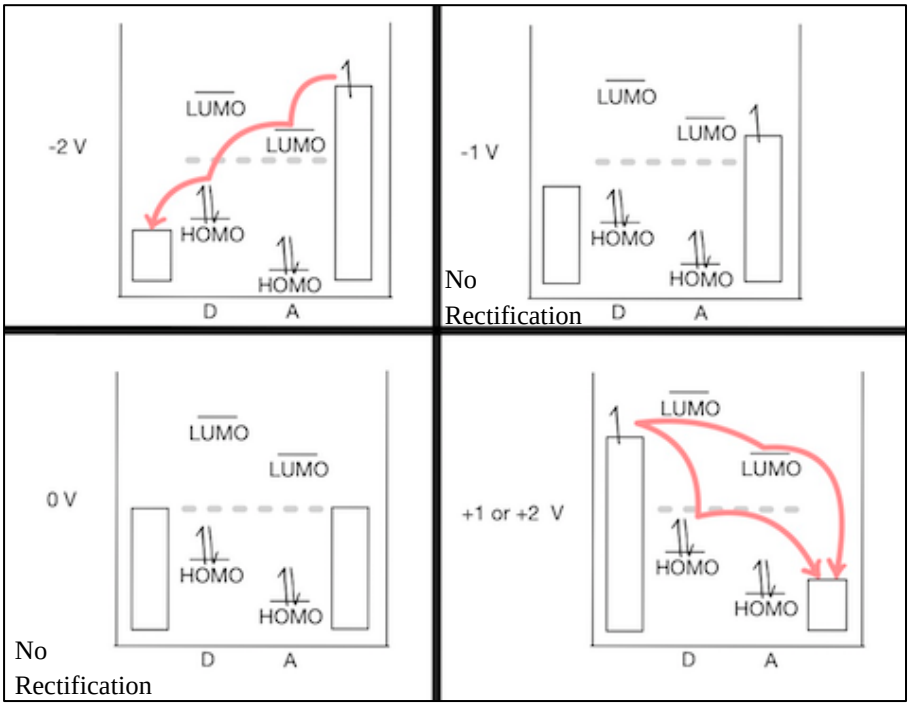


Figure I-2: *Molecular Orbital Diagram of D-σ-A compounds. The height of the bars represents the voltage difference, and molecular orbitals raise in energy next to high-voltage electrodes. Electrons essentially need adjacent "stair-steps" for transfer.*[5, 10]

Despite Aviram and Ratner's molecular rectification proposal, it has also been theorized that rectification can also occur at positive voltages, such as +1 V or +2 V biases, preferentially passing electrons from anode to donor to acceptor to cathode. Thus, this form of electron flow is dubbed Anti-Aviram-Ratner (Anti-AR) rectification. During this type of electrical current flow, electrons can transfer from one electrode to the donor's HOMO or the acceptor's LUMO to the other electrode. The increased, electrical voltage of the electrodes allows for Anti-AR flow of electrons at +1 V and +2 V as opposed to conventional flow in AR rectification at -2 V. Depending on the voltage bias applied and the molecule used, some compounds favor one direction or rectify in both directions (though current flow only occurs in one direction at a time);

for example, some molecules strangely exhibit preferential two-direction Anti-AR rectification at +1 V and AR rectification at -2 V. This effect has been coined the Janus Effect.[5, 10]

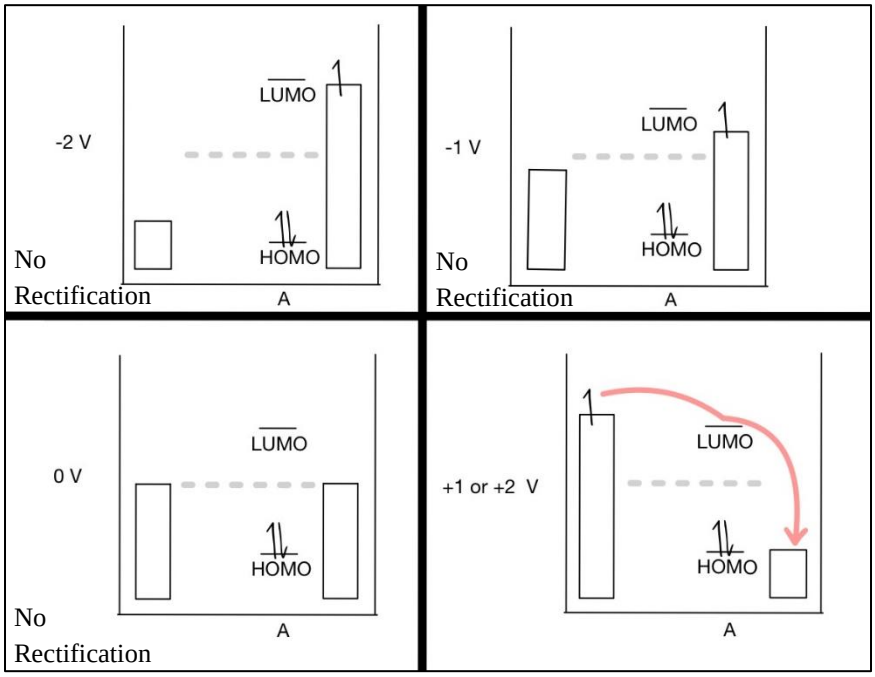


Figure I-3: *Molecular Orbital Diagram of PBIs.* [5, 10]

Many additional factors beyond what have been described are at play in determining if molecular orbitals successfully fall within the appropriate energy gap of the electrodes. These other variables alongside the discovery of preferential two-direction flow have spurred hypotheses of rectification with only an acceptor (no donor group). Instead of flowing through the adjacent HOMO and/or LUMO, a single electro-active acceptor group asymmetrically placed between two electrodes should theoretically rectify current through only the LUMO.[5] Specific candidates of interest have been perylene bisimides (PBIs), which have been pursued in Mattern's lab.

1.2 Langmuir-Blodgett Method

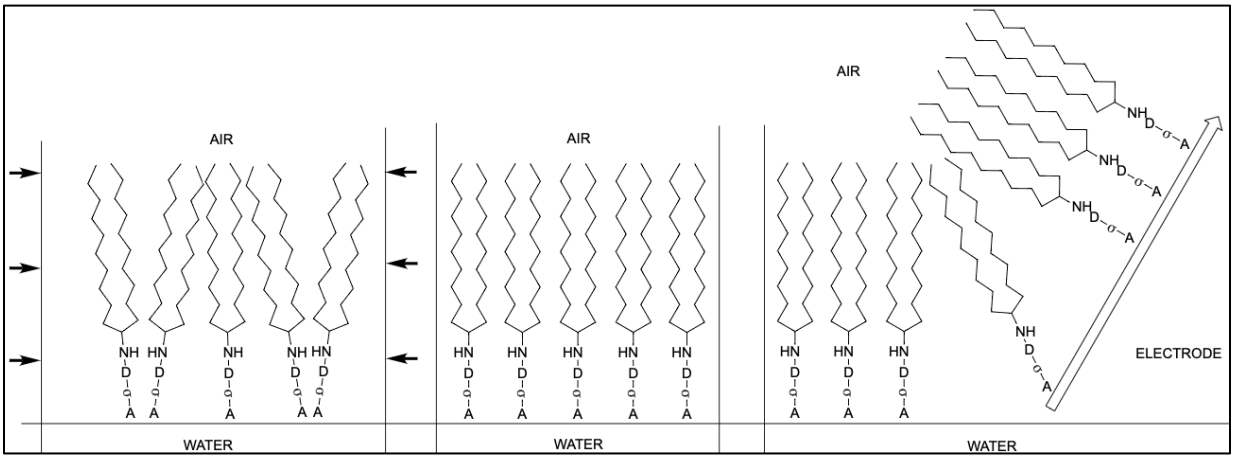


Figure I-4: *Simplified compression and monolayer formation of amphiphilic D-σ-A molecules using the Langmuir-Blodgett technique (left to right).*[5, 10]

The Langmuir-Blodgett (LB) Method can be used to align molecules into a monolayer with the same orientation, such that they can be tested as an ensemble for electrical conductivity. The architecture of compounds for the LB Method is particularly important: one end of the compound must be hydrophilic (seeking a polar substance, such as water), and the other end must be hydrophobic (seeking air, in this case). Molecules with distinct regions of hydrophobicity and hydrophilicity are called amphiphilic. Thus, D-σ-A molecules that are also amphiphilic can be placed onto an aqueous layer like mentioned above (**Figure 1-4**). As a result, the nonpolar, hydrophobic ends (usually hydrocarbon swallowtails) of the molecules stick out of the water while the polar, hydrophilic ends associate with the water. The long molecules can then be compressed together to form a tight monolayer, allowing for π-π orbital stacking. When an electrode is introduced, the monolayer will deposit onto it; with repeated dipping of the electrode, multilayers can form. This procedure has implications with microtechnology, such that thin layers of amphiphilic molecules could be used to pass electric current in devices.[10, 11] The LB Method was also used by research collaborator Robert M. Metzger at the University of

Alabama,[11] where samples from Mattern's laboratory have been sent for measurement of electrical properties.[5]

1.3 Perylene Bisimide (PBI)

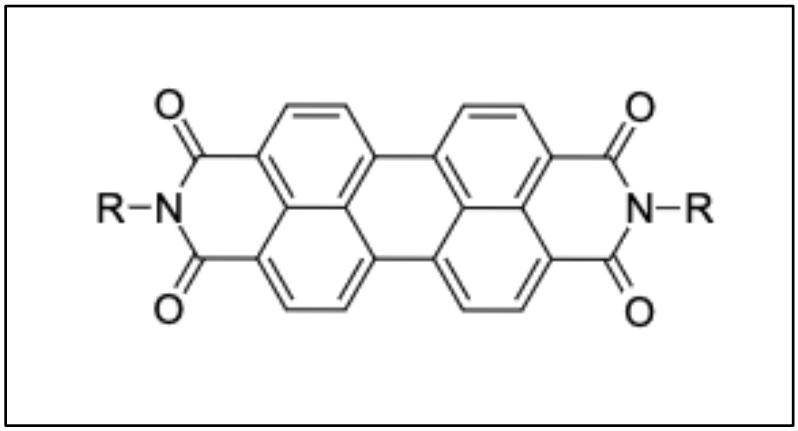
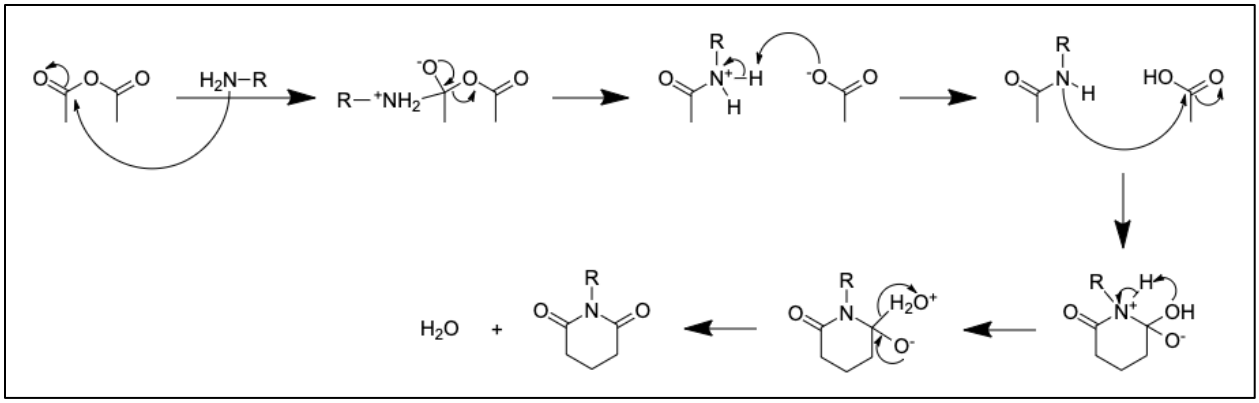


Figure I-5: *Perylene Bisimide as an acceptor without a donor*.

As stated earlier, it has been proposed that rectification with only an acceptor (not through adjacent HOMO and LUMO) that is asymmetrically oriented between two electrodes should conduct electricity, in theory.[5, 11] One particular target of interest has been perylene bisimide (PBI), which lacks a donor group. PBIs are synthesized from perylenetetracarboxylic dianhydride (PTCDA), containing numerous aromatic rings and four carbonyls capable of accepting electrons and withdrawing electron density from π orbitals.[11] Naphthalene subunits make up part of each perylene unit. The opposing anhydrides are available for reactivity, and the R-groups of the imides can vary greatly (**Figure I-5**). One end could be composed of a hydrophobic swallowtail moiety and the other could contain a hydrophilic, polar group, like a carboxylic acid or alcohol. These opposing polar and nonpolar groups make the entire molecule amphiphilic for LB film formation.

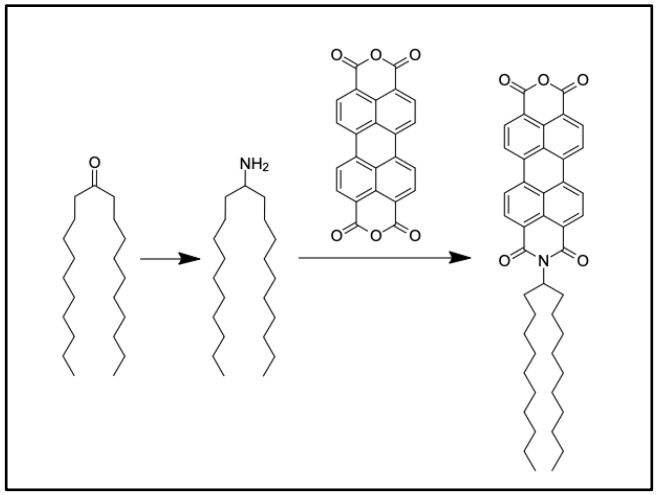


Scheme I-1: *Amines can attack the carbonyls of an anhydride on PTCDA or PMA, thus adding any R group connected to the amine into the ring structure and removing a water*.

1.4 Frederick's Research

Prior to this thesis, previous researcher Tarrah Frederick synthesized and studied many PBI products and protecting groups under Dr. Daniell Mattern.[9] The following is a brief summary of her work which is relevant to the research continued within this thesis. Overall, she successfully synthesized PBIs with swallowtail and silyl ether-protected serinol **(Compound 2)** from PMA and silyl ether-protected serinol. For more information on products synthesized prior to the continuation of Frederick's research, please visit Frederick's thesis.[5]

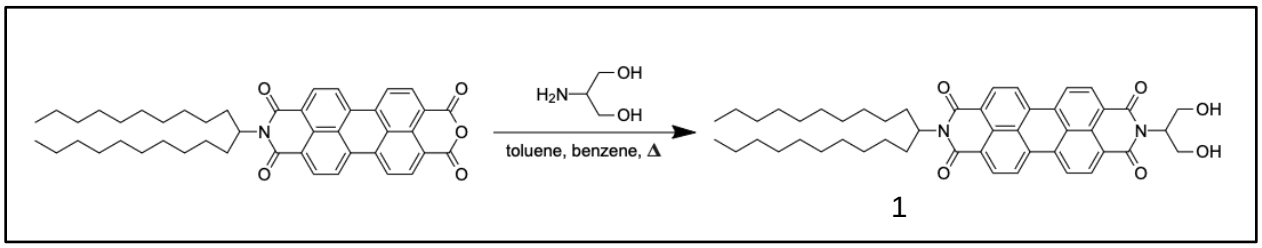
1.4.1 Attempted Synthesis of *N*-(10-Nonadecyl)-*N*'-(1,3-dihydroxypropan-2-yl)perylene-3,4,9,10- bis(dicarboximide), **Compound 1**



Scheme I-2: *Alkylated ketones can become amines, which then add to perylenetetracarboxylic dianhydride (PTCDA) to form PMA/PIA.*[5]*Also see* **Scheme I-1**

According to Frederick's thesis, PMA was "created by refluxing perylene-3,4,9,10-tetracarboxylic dianhydride and a hydrocarbon swallowtailed amine, followed by semi-hydrolysis."[5] The name perylene monoanhydride (PMA), or imide anhydride (PIA), suggests that one of the anhydrides of perylene has been replaced by an imine; in this case, PMA/PIA will refer to perylene with one anhydride available for reactivity and the other replaced with a

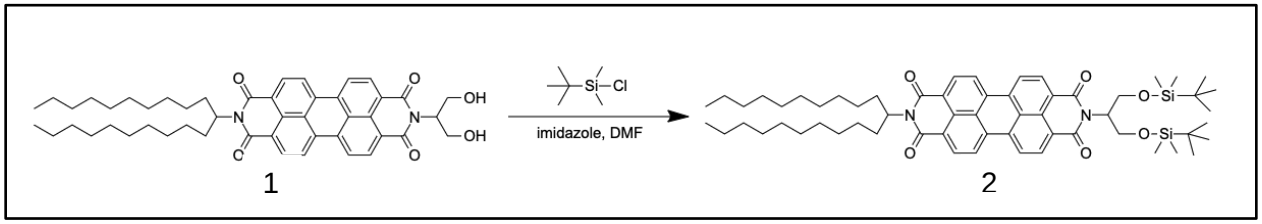
hydrocarbon swallowtail amine (specifically nonadecyl groups).[5]



Scheme I-3: *Reflux of PMA and serinol in toluene and benzene with heat yields* **Compound 1** *PBI with swallowtail and serinol groups.*[5]

After mono-alkylation, PMA was refluxed with serinol, proceeding via acyl substitution to yield **Compound 1**. However, while proton nuclear magnetic resonance (^{1}H-NMR) spectra of the sample did reveal mostly expected peaks for the desired product, 2 unknown peaks were observed. These 2 mysterious peaks were ultimately hypothesized to come from intramolecular reactions between the hydroxyl groups of serinol. In the end, with additional complications from lower than expected integration values from ^{1}H-NMR spectra (even after column chromatography purification) results were inconclusive. Thus, protection of the serinol group was proposed to avoid these obscurities and potential intramolecular interactions.[5, 9]

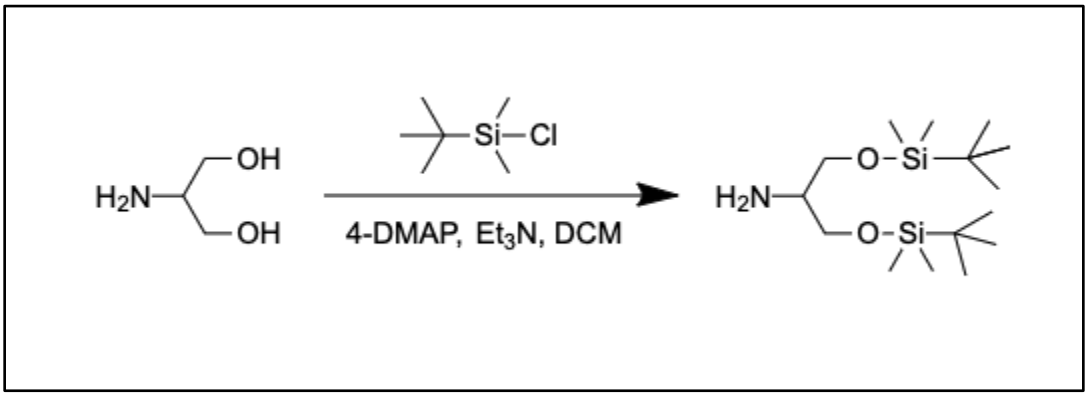
1.4.2 Protection of Hydroxyl Groups of Serinol on **Compound 1** PBI with TBDMSCl



Scheme I-4: *Addition of TBDMSCl to* **Compound 1** *PBI in imidazole and DMF yields TBDMSCl-protected serinol PBI with swallowtails,* **Compound 2**.[5, 9]

Continuing with the product from the previous section, *tert*-butyldimethylsilyl chloride (TBDMSCl) was used to protect the hydroxyls of the serinol group and remedy the unknown ^{1}H-NMR peaks mentioned above. After completion of the reaction, ^{1}H-NMR revealed a low yield of di-protected PBI (**Compound 2**) along with byproducts and unknown impurities. With additional difficulties arising from solubility of PBI products during product extraction, results of successful di-protected product formation became unclear as well. Therefore, attempts were made to protect serinol prior to its addition to PBI for improved synthesis results.[5, 9]

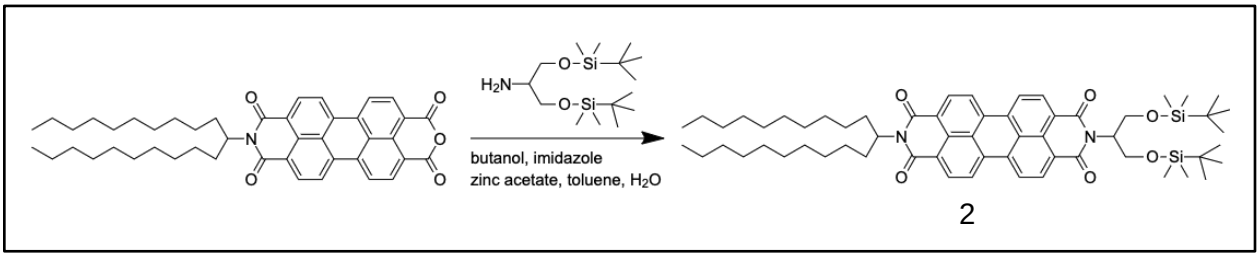
1.4.3 Protection of Serinol (2-amino-1,3-propanediol) using TBDMSCl



Scheme I-5: *Prior protection of serinol before addition to PMA.*[5]

Serinol was reacted with TBDMSCl to form protected serinol before addition to PMA. While some serinol remained unreacted and some was either mono- or tri-protected, a low but significant yield of di-protected serinol was isolated via column chromatography and confirmed with expected peaks from ^{1}H-NMR. With TBDMS-protection of serinol before its addition to PMA, the unclear results from direct addition of TBDMSCl to the serinol on **Compound 1** could be avoided and give more informative results.[5]

1.4.4 Addition of TBDMS-protected Serinol to PMA



Scheme I-6: *Alternative protected synthesis route for* **Compound 2**.[5]

With successful formation of TBDMS-protected serinol, the protected diol was added to PMA to form TBSMD-protected PBI (**Compound 2**). While ^{1}H-NMR did show indicative peaks for the desired product, many unknown impurities remained despite purification by column chromatography. Swallowtail regions on ^{1}H-NMR were also excessively large. These impurities were assumed to be caused by use of impure PMA, so pure PMA was used in a rerun. This time, ^{1}H-NMR spectra were much cleaner and illustrated more reasonable swallowtail integration, though still slightly larger than expected. Some starting material was also noted on ^{1}H-NMR.[5]

Three product spots were observed on thin layer chromatography (TLC). Products with the two highest R_f values contained very similar peaks on ^{1}H-NMR. Depending on the direction of addition, **Compound 2** can have amine R-groups positioned in the same direction outward from the aromatic center (*cis*) or in opposite directions (*trans*) (**Figure I-6**). These isomers could cause differing migration patterns on TLC since positioning of the protected serinol could cause it to migrate on the silica gel differently; more confirmation is needed to confirm this theory though. Moreover, one product with a low R_f appeared on TLC, likely not to be **Compound 2** due to drastically different distance from the two higher R_f products. The low R_f product proved insoluble in the eluting solvent in addition to many other solvents, too. ^{1}H-NMR of this low R_f product yielded no desired product formation and many impurities. Ultimately, the higher R_f

product was isolated via column chromatography to yield TBDMS-protected PBI (**Compound 2**) according to ^{1}H-NMR.[5]

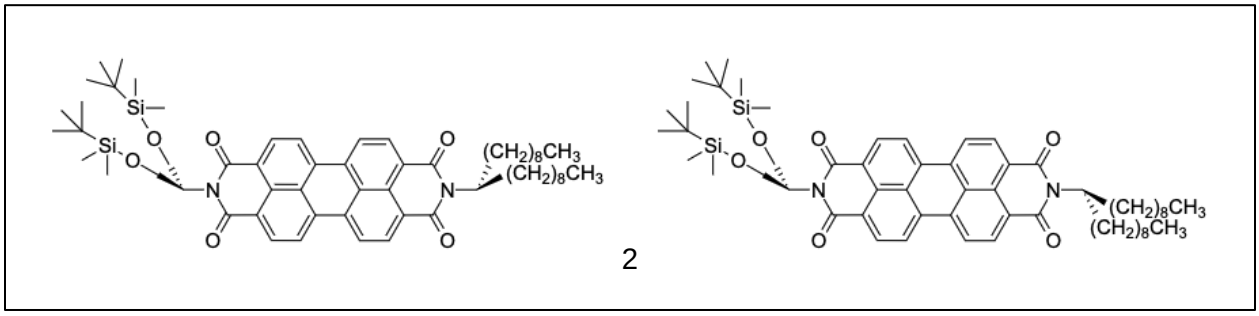
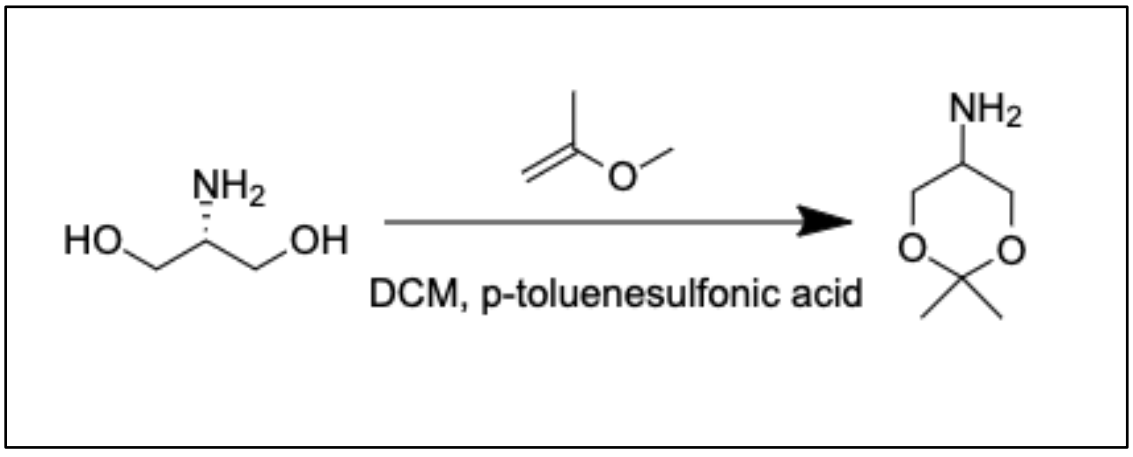


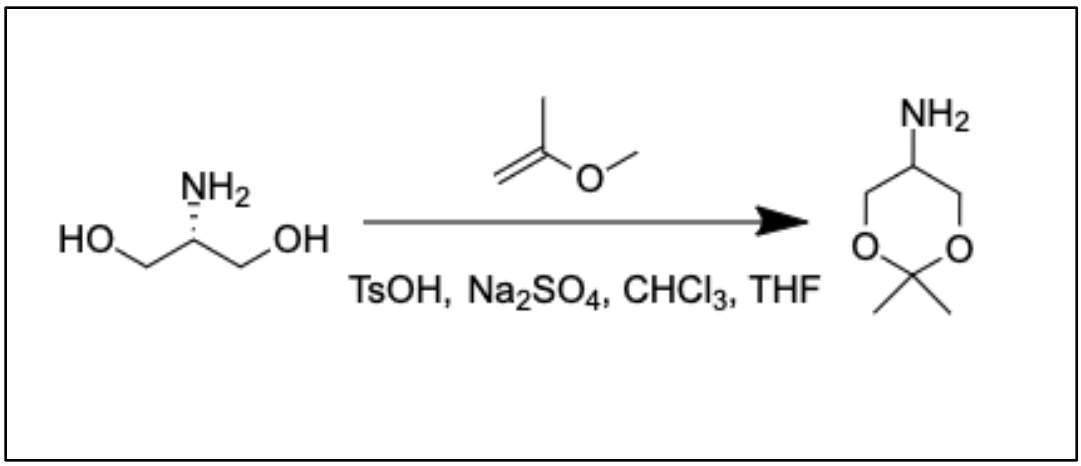
Figure I-6: *Cis and Trans isomers of* **Compound 2**.[5]

1.4.5 Other Serinol Protection Methods

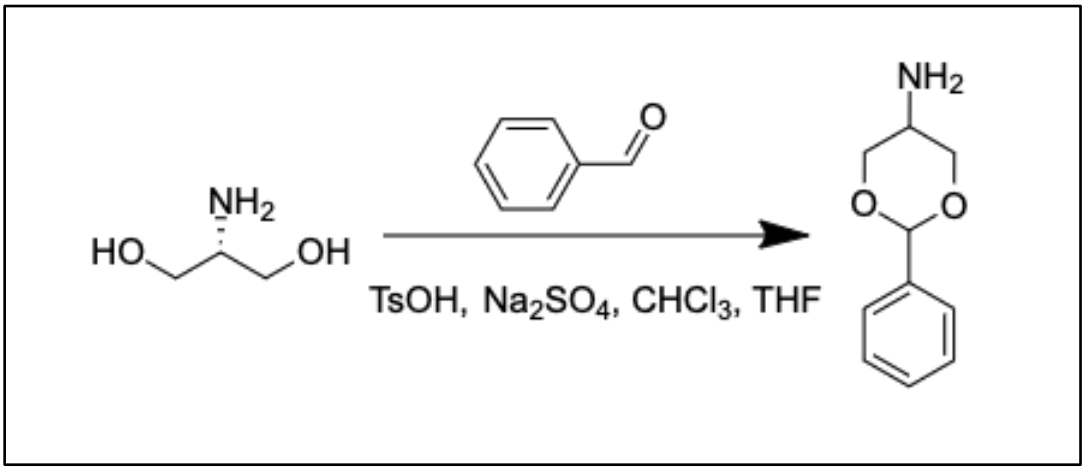
Frederick also explored other serinol protection methods. However, synthesis of these additional protection techniques ultimately provided no desired product formation or destroyed the amino group of serinol.[5] While unsuccessful, these other protection modes still provide significant insight for protection of diols and could provide a protection mechanism if these reactions are better understood in the future.



Scheme I-7: *Cyclo-protection of serinol with 2-methoxypropene*.[5]



Scheme I-8: *Alternate cyclo-protection of serinol with 2-methoxypropene.*[5]



Scheme I-9: *Cyclo-protection of serinol with benzaldehyde.*[5]

For more information regarding serinol protection, rectification, and synthesis of PMA and PBI, Frederick's thesis can be referenced. Her thesis provides more insight into methods used prior to the continued experimentation of PBIs found in this document.[5]

1.5 The Hammer Proposal

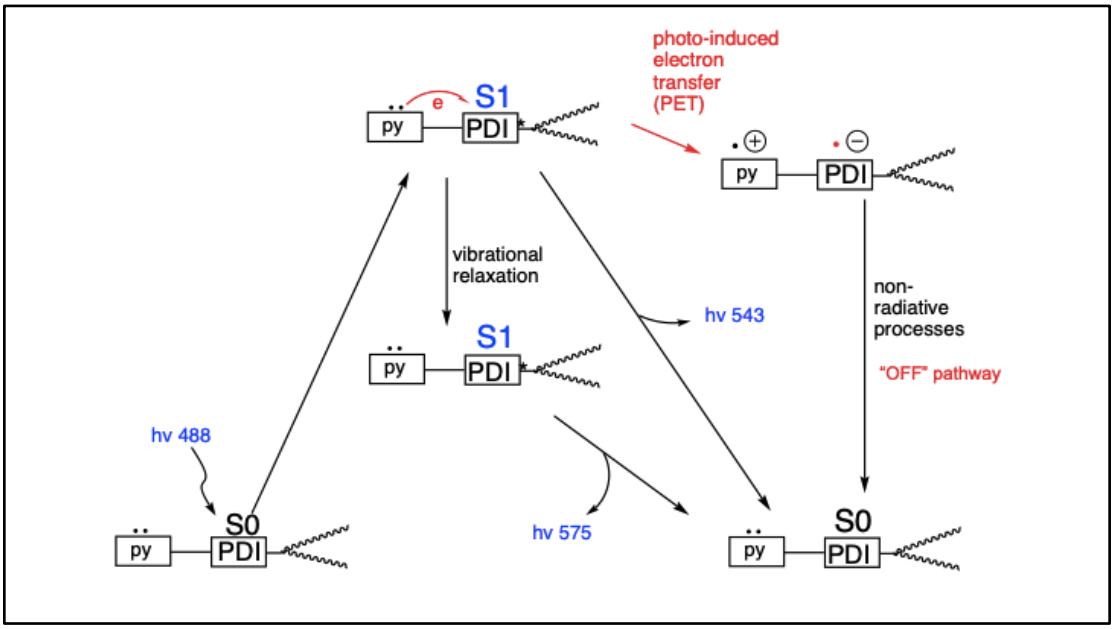


Figure I-7: *Photoexcitation and electron transfer (PET) from pyrene to PBI (also called perylene diimide, or PDI).*

As computer chips quickly approach the limits of miniaturization, perhaps the most challenging progress in electrical innovation is that of single molecule rectifiers. Dr. Nathaniel Hammer and Dr. Daniell Mattern at the University of Mississippi's Department of Chemistry have synthesized and investigated numerous single molecule rectifiers in the past. Most of these rectifiers illustrate Anti-AR electron flow, and more research on these is still needed. However, pyrene-related rectifiers may provide the next step in single-molecule rectification and electrical innovation. The presence of pyrene appears to affect blink-off time and orientation of molecules on thin polymer films. These differences may be related to the tether length and dihedral angles between the aromatic planes of pyrene (**Figure I-7**). Notably, variation in photophysical properties between rectifiers appears to depend on chain length and environment. The open anhydride of PMA allows for a great diversity of carbon tethering through imide addition. This

variability in carbon tethering may also account for variation in chemical/electrical behavior between PBI molecules.[7]

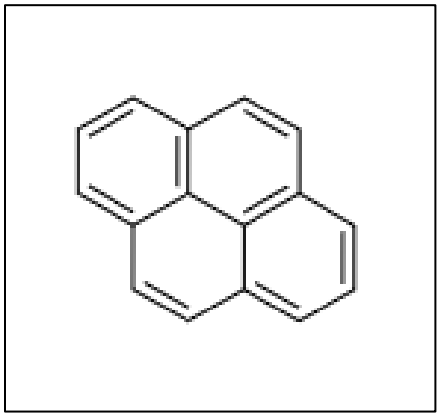


Figure I-8: *Pyrene is a flat, aromatic, 4-ringed compound with significant electron density from conjugated double bonds, consisting of 2 naphthalene subunits.*

The Hammer Proposal suggests four specific perylene-related molecules for testing.[7] These molecules contain the typical alkyl swallowtails on one end and either a *cis*- or *trans*-pyrenylcyclohexyl (**Compound 3**), pyrenylethyl, or methyl group by acyl substitution on the available anhydride of PMA. This text seeks to achieve the pyrenylcyclohexyl imide (PCHI) addition to PMA, generating **Compound 3**. This compound can conform in one of two orientations relative to the cyclohexyl group: *cis* (axial) or *trans* (equatorial), which may also suggest differences in electrical behavior. Electrons from pyrene (**Figure I-8**) have been observed to jump into the empty orbitals of PBI after excitation of PBI by light. Experimentation ultimately seeks to clarify whether the carbon tether distance or bond angle between the pyrene group and PBI molecule affects the electron transfer between the two groups.[7] Synthesis of the **Compound 3** may provide further innovation, understanding, and discovery in microtechnology and PBIs.[10, 11]

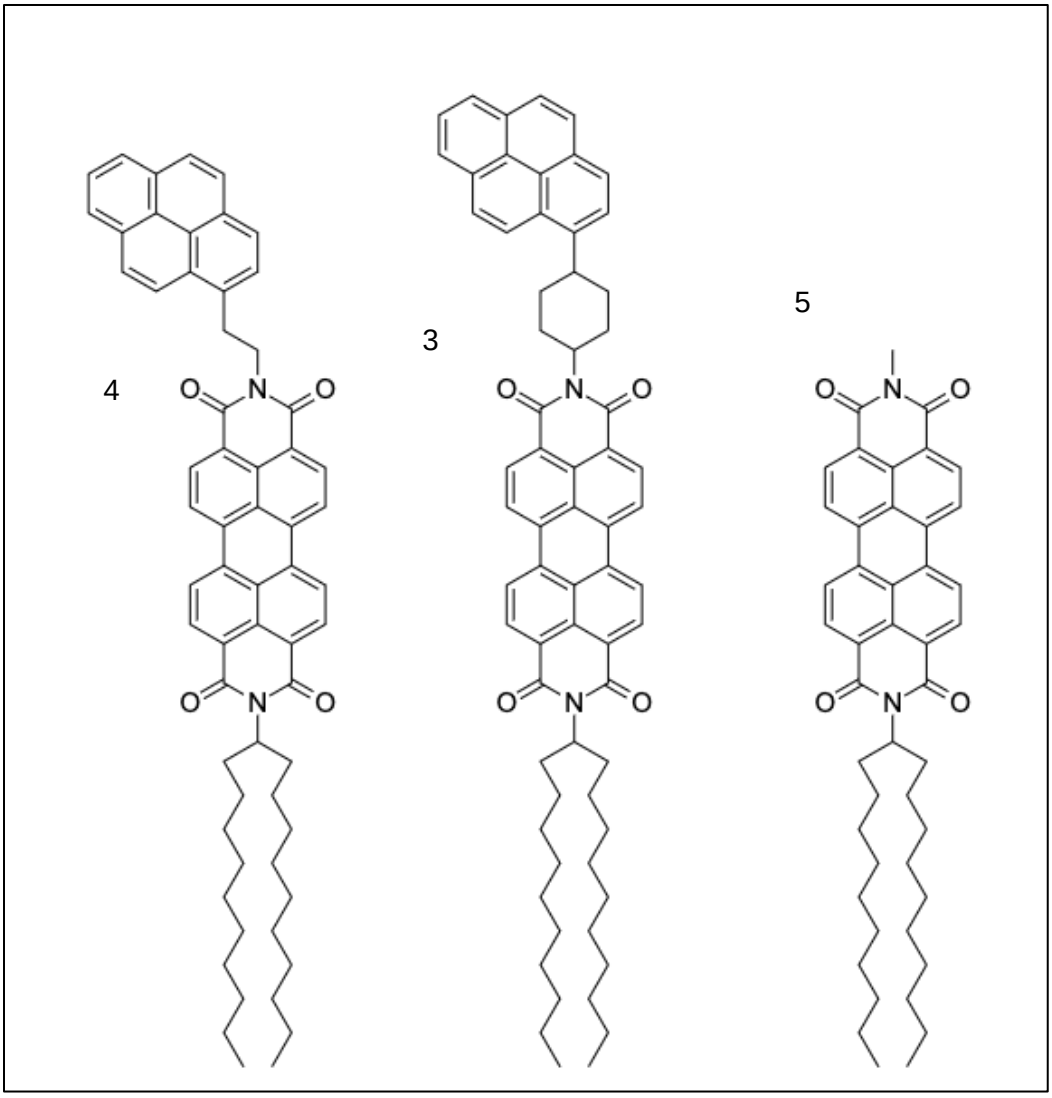
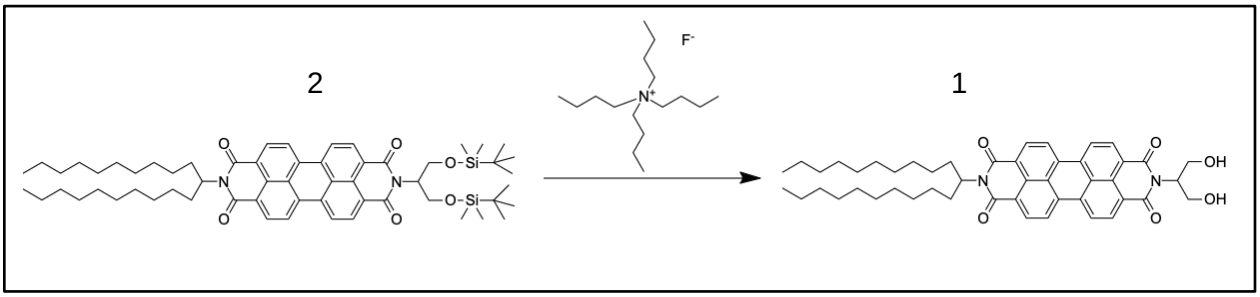


Figure I-9: *Desired perylene-related molecules of the Hammer Proposal, including* **Compound 3**.[7]

II. RESULTS AND DISCUSSION

2.1 Attempted Deprotection of TBDMSCl-protected PBI (**Compound 2**)

2.1.1 Deprotection via TBAF

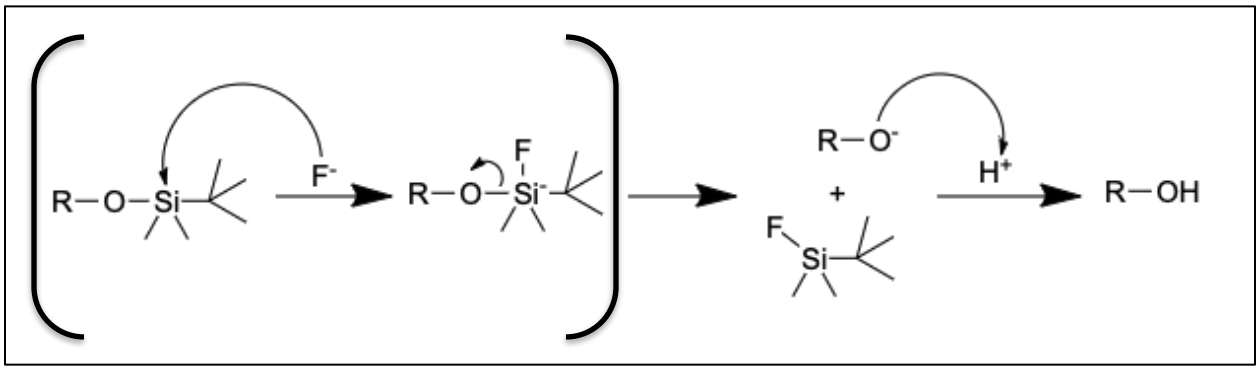


Scheme II-1: *Attempted deprotection of* **Compound 2** *using TBAF*

Experimentation begins with the last synthesized PBI product left by researcher Tarrah Frederick in 2019: **Compound 2**, a PBI with swallowtail and TBDMS-protected serinol.[5] The serinol remains protected until the silyl ether TBDMS group is removed. The proceeding reaction seeks to remove the protecting group on PBI[9] and restore the diol of serinol, generating the desired **Compound 1**. Procedures to remove the silyl ether involved a charged ammonium salt, tetra-n-butylammonium fluoride (TBAF), to liberate the TBDMS group.[9] Half of Frederick's **Compound 2** was used.

In this mechanism, deprotection occurs through a penta-coordinate intermediate. Silyl cations are unstable so the mechanism unlikely proceeds via S_N1-style addition. Instead, this mechanism likely follows a concerted S_N2 mechanism. Firstly, the negatively charged fluoride ion attacks the silicon of the silyl ether protecting group: the Si-F bond is ~30 kcal/mol stronger than the Si-O bond. As a result, the electrons in the bond between silicon and oxygen jump onto oxygen to form a negatively charged oxide, freeing the TBDMS-protecting group from

Compound 2.[9] Oxygen then picks up a proton from the surrounding environment to generate the alcohol. If deprotection with fluoride is performed on both oxygens of the protected-serinol, this mechanism will restore the diol. After removal of TBSMS ether, the protected serinol would then be reverted to the diol, finally yielding the desired **Compound 1**.



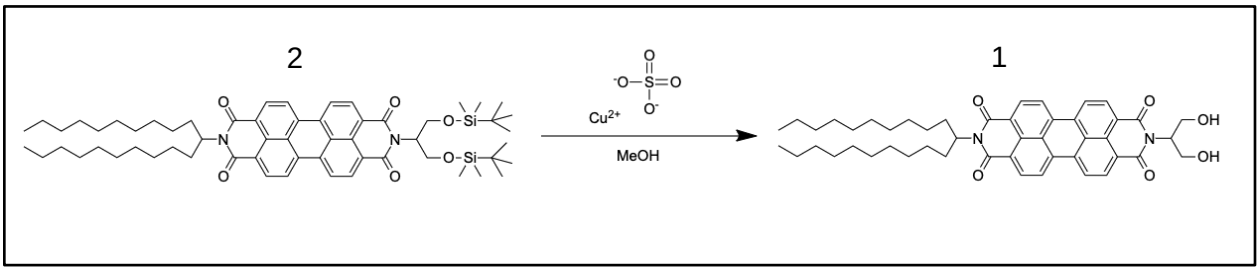
Scheme II-2: *Mechanism for attack by fluoride in TBAF on silyl ether protecting group.*[9]

Thus, **Compound 2** and TBAF were combined and stirred at ambient temperature for over 12 hours, and the solution became deep green and gradually darkened to black. This color change is unusual PBIs which usually have a vibrant red/orange color. To clarify the unexpected resulting color change of this reaction, TLC revealed unpromising migration for deprotection. Successful deprotection would generate the **Compound 1** diol, and the new molecule would contain two highly electronegative oxygens bound to hydrogen. The electronegativity of oxygen and subsequent intermolecular forces from hydrogen bonding would create a more polar compound than the protected species. Thus, **Compound 1** should not migrate as far as **Compound** 2 during TLC in a polar solvent. Nonetheless, migration of the initial and final materials was similar in developing solvent.

To further unveil the unexpected results of the attempted deprotection with TBAF, ^{1}H-NMR spectra of the crude product and compared to spectra of the initial protected molecule left by Frederick. While the crude product spectra did illustrate that some initial signals had

disappeared, these signs were ultimately indicative that the molecule had only decomposed. What occurred to the protected silyl ether group is uncertain, but our leading hypothesis is perhaps that the solution contained a radical, possibly causing expected **Compound 1** to turn an abnormal color as a radical anion and degrade. In a last attempt to scavenge the potentially radical contaminated PBI, a single electron oxidant, Br_2, was used. Bromine was dissolved in chloroform and added to **Compound 1** solution, hoping a bromine radical would pick up the radical of the contaminated PBI. If bromine successfully acquired the radical from PBI, the grayish green color from PBI contamination should revert to the vibrant red/orange from before. However, the resulting solution took on the deep brown color of bromine, providing further uncertainty. Ultimately, this deprotection method with TBAF provided no desired deprotected **Compound 1** PBI product and was abandoned.

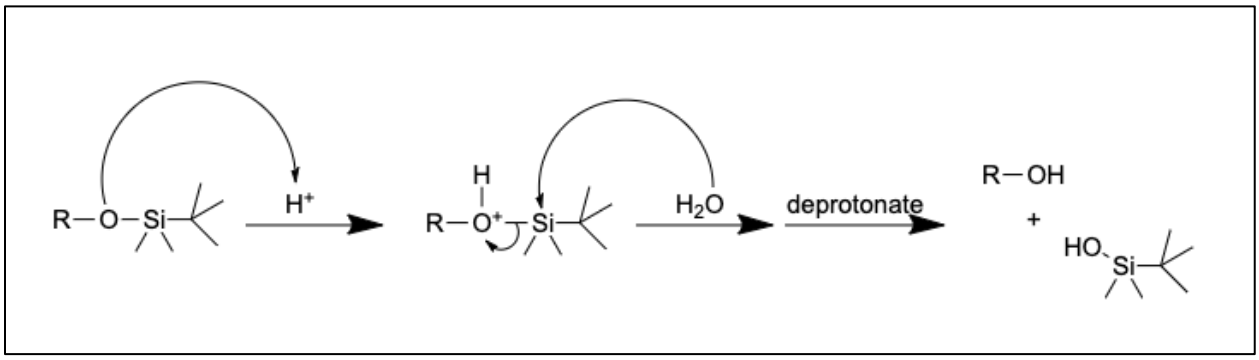
2.1.2 Deprotection via Copper (II) Sulfate



Scheme II-3: *Deprotection of* **Compound 2** *using copper (II) sulfate in methanol*[6, 9, 13]

Moving forward, with only half of protected **Compound 2** PBI remaining, another deprotection method was attempted. This time, **Compound 2** was dissolved in methanol and heated. To this solution, copper (II) sulfate was added, and the mixture was stirred for several hours with a reflux condenser.[6, 13] The mechanism of deprotection with copper (II) sulfate is not completely understood, but it may involve the protonation of the oxygen and attack by water on silicon since copper (II) sulfate tends to associate with water molecules. The ether oxygen could

be protonated to form a positively charged oxygen by an acid or water. Then, the oxygen of another water molecule could attack the silyl ether and kick off electrons onto the positively charged oxygen to generate an alcohol and silyl alcohol. Nonetheless, how copper (II) sulfate removes the silyl ether mechanistically is uncertain.



Scheme II-4: *Acid/Water Deprotection of silyl ether protecting group.*

Notably, upon initiation of the reaction, **Compound 2** and copper (II) sulfate both struggled to dissolve, but over time and with heat, both eventually met dissolution in MeOH. The solution began as a bright orange color and transitioned to maroon after the addition of copper (II) sulfate. This color shift seemed to indicate a chemical change, but the color change may have simply resulted from the orange color of the protected ether and blue color copper (II) sulfate combining. The solution was eventually cooled after several hours of refluxing, and TLC followed.[6, 13]

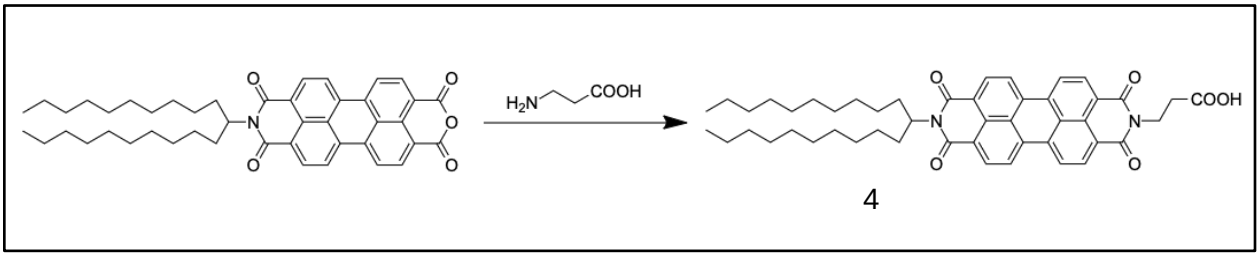
Promisingly, TLC indicated a clear change in migration between starting **Compound 2** and crude product, suggesting that a chemical change had indeed occurred. To purify the crude sample, the product was vacuum filtered, and copper (II) sulfate was separated via solubility in methylene chloride in a separatory funnel.[6, 13] The excess solvent was then removed by rotary evaporation, leaving slightly under 5 mg of concentrated dark red powder as crude product. Despite optimistic indications throughout the reaction, ^{1}H-NMR of the crude sample in

chloroform-d conveyed impurities, decomposition products, some unreacted starting material, and overall uncertain results. No desired **Compound 1** product formation was noted in spectra.

Deprotection of silyl ether-protected serinol on **Compound 2**[9] proved unusually difficult despite such simple procedures detailing silyl ether removal. Failures to produce **Compound 1** with Frederick's penultimate **Compound 2** product[5] ultimately ended with the loss of all **Compound 2** in unsuccessful deprotection attempts. However, the final ~5 mg of dark red product from the copper (II) sulfate deprotection reaction may be purified and further analyzed in the future to provide more definitive answers to the uncertain spectra. At this point, deprotection of **Compound 2** to produce **Compound 1** diol was abandoned for the addition of a different polar group to PMA, namely a carboxylic acid (**Compound 4**). Addition of a carboxylic acid to PMA could prove easier and likewise be just as effective as the diol in the LB Method; thus efforts to add a carboxylic acid group to PMA were subsequently explored.

2.2 Addition of Carboxylic Acid in Lieu of Serinol

2.2.1 Addition of 3-aminopropanoic acid (β -alanine) to PMA, **Compound 4**



Scheme II-5: *Addition of β-alanine (3-aminopropanoic acid) analog to PMA, generating* **Compound 4**.[4]

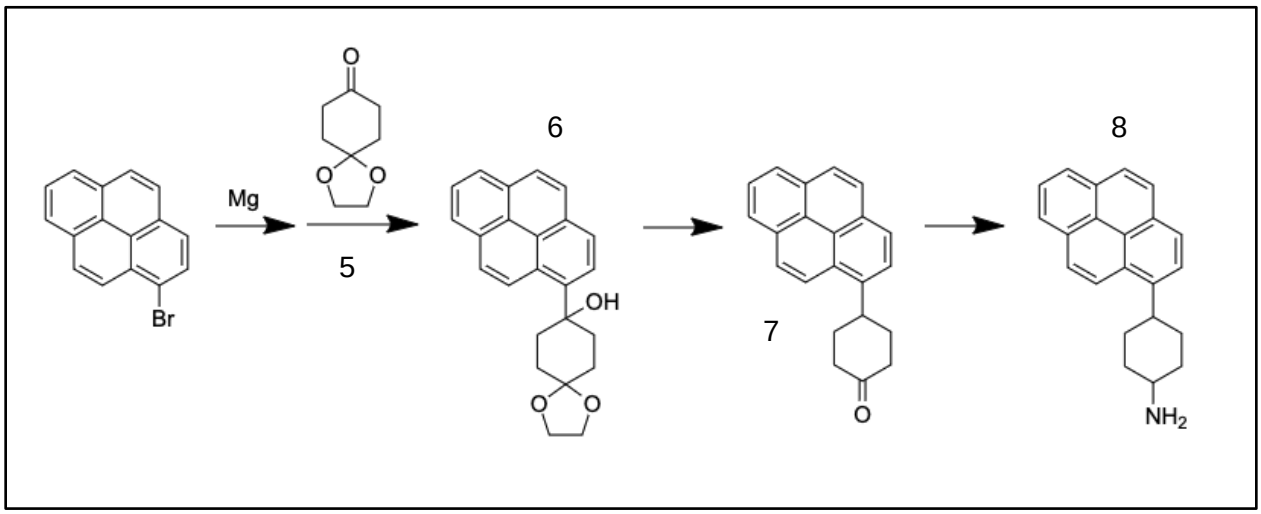
With the TBDMS-protected serinol and swallowtailed **Compound 2** PBI lost, reactions with PMA precursors continued. Several vials of PMA with one swallowtail were left behind by Tarrah and previous researchers. Since deprotection of serinol was unsuccessful previously, another similarly polar/hydrophilic group was attempted on the PMA: a carboxylic acid (via β-alanine). Procedures from **Reference 4** were applied using the β-alanine (3-aminopropanoic acid) analog to PMA, generating **Compound 4**.[4] Though 3-aminobutyric acid (used in the **Reference 4** procedure) and 3-aminopropanoic acid differ by one carbon, reactivity should be similar. Amine addition of β-alanine follows the same mechanism of **Scheme I-1**.Thus, β-alanine and PMA in imidazole solvent were refluxed for several hours. According to TLC, pure PMA with one swallowtail migrated distinctly from PMA reacted with β-alanine, indicating a chemical change did occur. About four notably concentrated products were observed on TLC after PMA reaction with β-alanine.

To separate the products within the crude reaction mixture, column chromatography was performed using methylene chloride and methanol. In total, 46 fractions were acquired, though some stubborn material remained at the origin regardless of various solvents used. Visual analysis of the fractions revealed Fractions 8, 15, 24, and 38 to contain the darkest yellowish

orange/red colors, indicating the highest concentrations of product and likely purest products from the crude mixture. The stubborn products left at the column's origin were successfully re-dissolved and obtained by mixing the sand and silica gel containing the products in methylene chloride and filtering off the sand and silica (Fraction L). Each of the fractions was concentrated by rotary evaporation to remove any excess solvent, yielding a thin, red film on each fraction's flask except for Fraction L, which produced deep red oil. Each of the products was then dissolved in deuterated chloroform and analyzed by ^{1}H-NMR spectra.

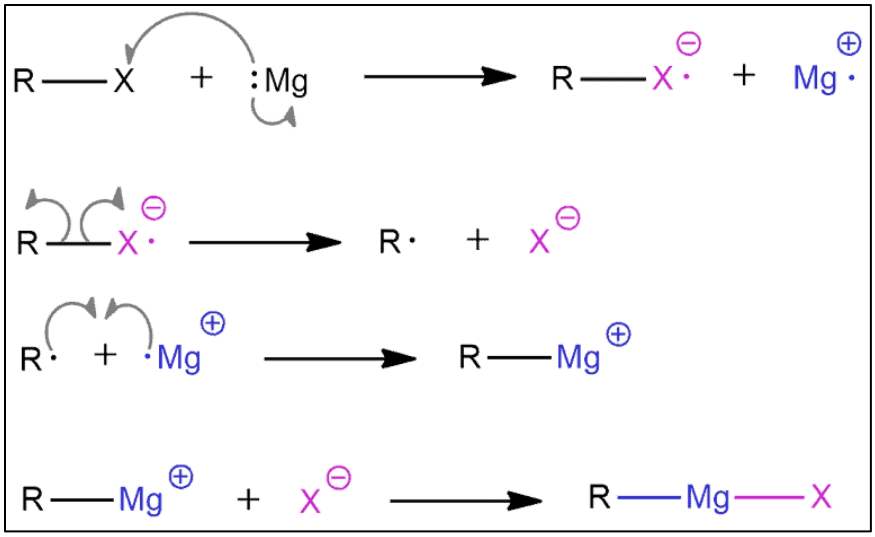
After observation of these spectra, Fractions 8 and 15 seemed to indicate little to no absorbance in the carboxylic acid region (10-12 ppm), intense absorbance in the aromatic region (~7 ppm), intense absorbance in the swallowtail alkane region (~1 ppm), and some other uncertain signals. No desired product was expected in Fractions 8 and 15 as a result. However, Fractions 24 and 38 did reveal expected signals for **Compound 4**, but these fractions contained many unknown impurities as well. Ultimately, it seems the desired **Compound 4** product was made, but it was crowded with other stubborn byproducts and contaminants. Due to these uncertainties alongside the recent retirement of research collaborator Robert Metzger, further purification and analysis of **Compound 4** was halted. While these fractions can be investigated more in future research, definitive confirmation was not pursued. As such, more understanding of carboxylic acid addition to PMA is still needed, but this initial research does pose a potentially optimistic future for future synthesis of **Compound 4**; samples of these fractions have been stored in the lab.

2.3 Bromine Grignard Additions



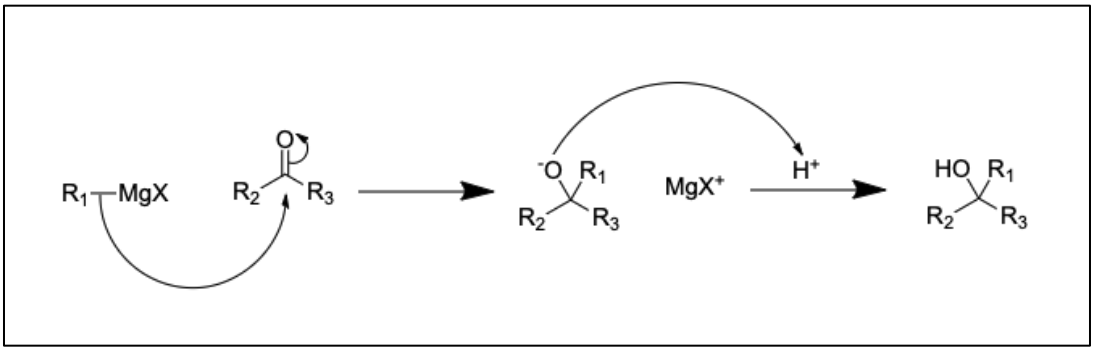
Scheme II-6: *Synthetic Grignard pathway of the Hammer Proposal for the formation of* **Compound 8** *(4-pyrenylcyclohexan-1-amine) from 1-bromopyrene.* **Compound 8** *is a component of* **Compound 3**, *one of the desired products of the Hammer Proposal.*[7]

With deprotection and carboxylic addition of PBI abandoned, research proceeded with Grignard reactions of the Hammer Proposal. This procedure illustrates halopyrene Grignard and 1,4-cyclohexanedione monoethyleneketal (**Compound 5**)[1] synthesizing **Compound 6** alcohol, which is protected by a cyclic monoethyleneketal. This alcohol can then be deprotected and dehydrated to yield **Compound 7** ketone, then aminated to **Compound 8** amine product. The amine could then be used from synthetic addition to perylene molecules, such as PMA to generate **Compound 3**.[7] Since this synthetic scheme used bromine specifically as the primary halogen for Grignard addition, investigation began with brominated compounds for synthetic addition.



Scheme II-7: *Grignard Formation*.

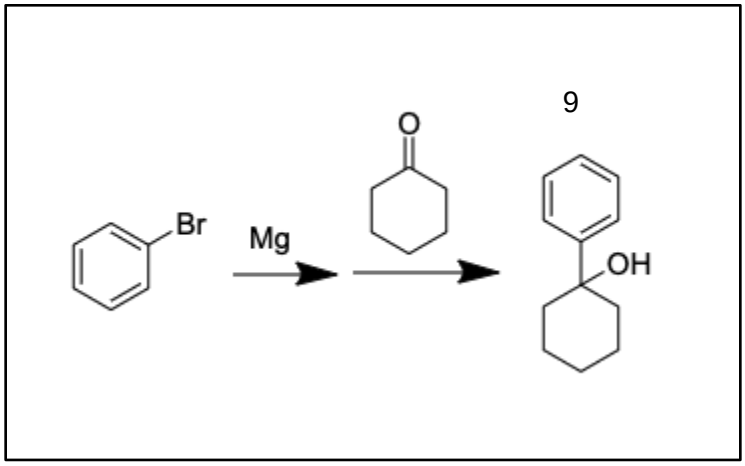
Grignard formation initiates when magnesium donates a single electron to an alkylhalide. The halide picks up this radical electron to form an alkylated halide radical anion and radical magnesium cation. Proceeding, the bond between the alkyl group and halide radical donates a single electron in both directions, generating a halide anion with a lone pair, and an alkyl radical. This alky radical must be stabilized to form, usually by methyl groups on the radical center or resonance (pyrene offers immense radical stabilization through its conjugated aromatic rings). The alkyl radical then bonds with the single electron of the magnesium cation radial, producing a full bond. With the attachment of magnesium to the alkyl group, the halide anion performs nucleophilic attack on the positively charged magnesium to complete the Grignard formation.



Scheme II-8: *Nucleophilic Attack of a Ketone.*

With a successful Grignard reactant formed, the bond between the alkyl group and Mg-X can perform nucleophilic attack on carbonyl groups. Carbonyl groups contain a partial negative charge at the oxygen and a partial positive charge at the carbonyl carbon. Thus, electrons between Mg-X and the alkyl group attack the carbonyl, disassociating MgX from the alkyl group and alkylating the carbonyl species. As the alkyl group bonds to the carbonyl carbon, electrons are kicked up onto the oxygen, which grabs a nearby proton to generate an alcohol. In the proceeding reactions, the carbonyl used for nucleophilic attack will be a ketone, which always produces a tertiary alcohol. This chemical signature can later be used for product verification on NMR spectra. This mechanism will be used in all proceeding Grignard reactions in this text.

2.3.1 Attempted Synthesis of 1-phenylcyclohexan-1-ol



Scheme II-9: *Bromobenzene Grignard addition to cyclohexanone to form 1-phenylcyclohexan-1-ol,* **Compound 9**.[2, 8, 12]

To gauge the viability of future Grignard reactions with brominated compounds and ketones, a model ketone was used first: the smaller, simpler cyclohexanone compared to **Compound 5**. Thus, bromobenzene and cyclohexanone were refluxed to produce **Compound 9**, 1-phenylcyclohexan-1-ol. Firstly, bromobenzene was dissolved in dry THF in a round bottom flask filled with N_2 atmosphere. Following, Mg solid turning were added to the flask with a small

crystal of iodine to initiate the reaction. The iodine helps to clean the surface of the magnesium metal, which contains metal oxides, and initiate reaction. At this point, the benzene Grignard began formation as magnesium was visibly consumed. The solution was allowed to stir on heat for several hours, then cyclohexanone was dissolved dry THF and slowly added to the bromobenzene solution. This reaction was refluxed with continued heat for several more hours before cooling to room temperature.[2, 8, 12]

The solution was then quenched with HCl (donating protons to form the alcohol), and the desired product was separated via separatory funnel using Et_2O solvent. The aqueous layer was drained off, and the organic layer was dried with anhydrous $MgSO_4$ before being vacuum-filtered of the desired product into a separate round bottom flask. The Et_2O solvent was finally concentrated by rotary evaporation, leaving behind crude product.[2, 8, 12] TLC of the starting material and crude product with CH_2Cl_2 as the developing solvent seemed to indicate a successful reaction and alcohol formation from streaking. Synthesis of **Compound 9** was further solidified by NMR spectroscopy. While **Compound 9** is no part of the Hammer Proposal,[7] it can help gauge the viability of more complicated Grignards; thus, no further purification or analysis was performed on the crude product.

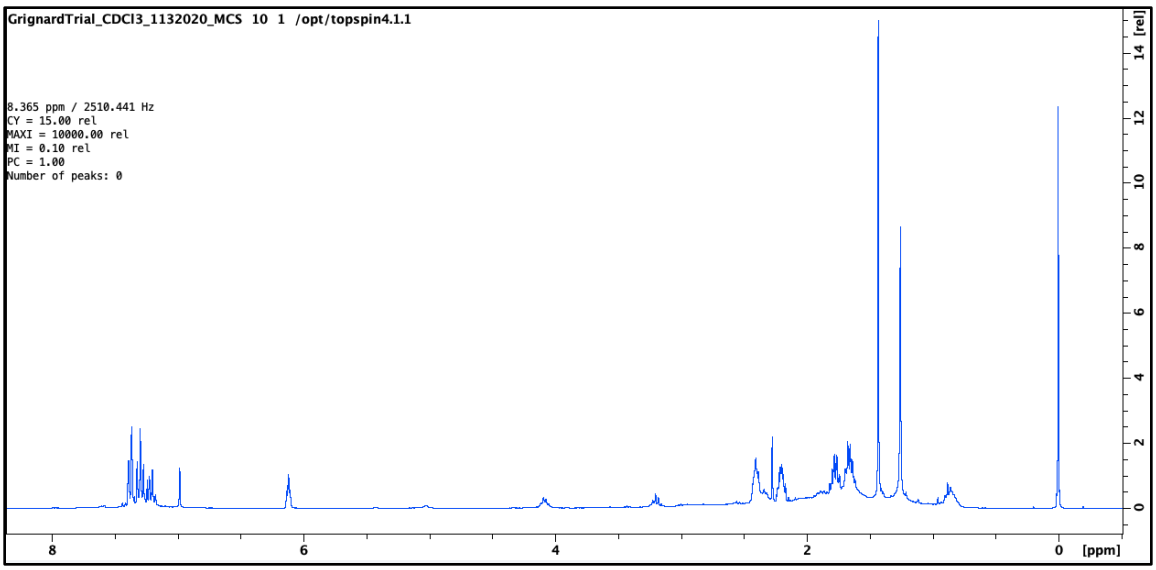
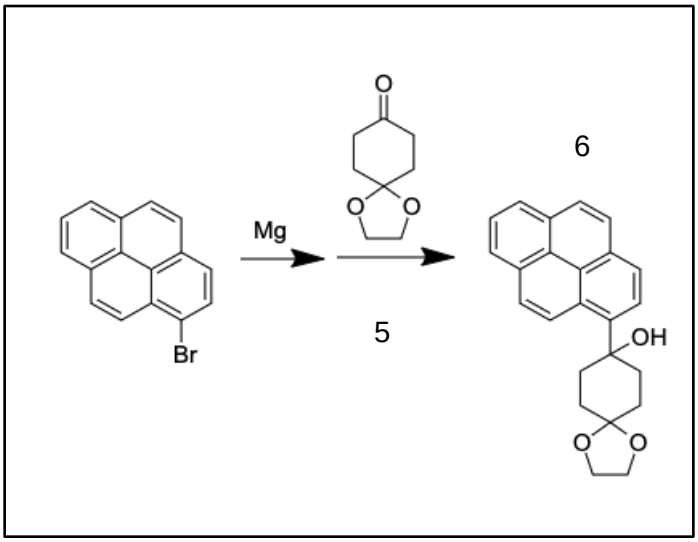


Figure II-1: *^{1}H-NMR spectrum of crude* **Compound 9**, *showing indicative peaks between 7-8 ppm for aromatic hydrogens, and ~2 ppm for hydrogens on cyclohexane; protons closers to the alcohol are more deshielded to 2.1 ppm while protons further on the cyclohexane ring appear around 1.5 ppm.*

2.3.2 Attempted Synthesis of 1-pyreny-4-monoethyleneketalcyclohexan-1-ol (**Compound 6**) with Bromopyrene



Scheme II-10: *Bromopyrene Grignard addition to* **Compound 5**, *generating* **Compound 6**; *the first steps of the Hammer Proposal.*[1, 8, 7]

With successful formation of **Compound 9**, reactions with 1-bromopyrene proceeded. Similar procedures were used as the previous Grignard reaction except the brominated compound and ketone were changed. This experiment aimed to react bromopyrene with **Compound 5** (1,4-cyclohexanedione monoethyleneketal)[1] to form the subsequent **Compound 6** (1-pyrenylcyclohexan-1-ol-4-monoethyleneketal). Synthesis of this product was attempted twice. In the first run, 1-bromopyrene was dissolved dry THF. Following, clean Mg turnings were added to the flask under a N_2 atmosphere. At this point, the solution was clear or extremely pale yellow. To the flask was also added a small crystal of iodine, after which the solution became a light brown color. The subsequent solution was stirred on slight heat for 2 hours.[2, 8]

Next, **Compound 5** was dissolved in dry THF and added to the flask containing 1-bromopyrene and Mg. The reaction was allowed to reflux for several hours before it was cooled, quenched with HCl, dried with $MgSO_4$, and filtered. The desired **Compound 6** product was expected to separate into the organic layer after washing with Et_2O in a separatory funnel. The organic layer was filtered into a flask and concentrated via rotary evaporation to reveal the crude product. TLC of the concentrated crude product illustrated various spots, some similar and some different from the bromopyrene and ketone starting materials.[1, 2, 8]

Furthermore, components of the crude product mixture were separated and purified by column chromatography. Similar fractions were combined into 5 collective super-fractions (**CF1-5**). ^{13}C-NMR and ^{1}H-NMR of each fraction was then taken thereafter. NMR spectroscopy of **CF1** indicated a messy mixture of starting materials and some unknown signals. **CF2** was presumed to be mostly mixed bromopyrene and ketone. **CF3** and **CF5** conveyed weak absorbance and ethanol solvent from NMR, so no useful interpretations of molecular components was deduced. TLC revealed streaking of the components in **CF4**, which is typically

indicative of alcohols such as the desired Grignard product **Compound 6**. However, **CF4** contained disproportional aromatic shifts and a mess of aliphatic absorbances, perhaps from deprotection of the ethyleneketal. A weak but clear carbonyl absorption was also found, indicating incomplete reaction of the starting ketone. There was no obvious peak from the tertiary alcohol of the expected **Compound 6** product either. Ultimately, no indicative results of successful **Compound 6** product were found.

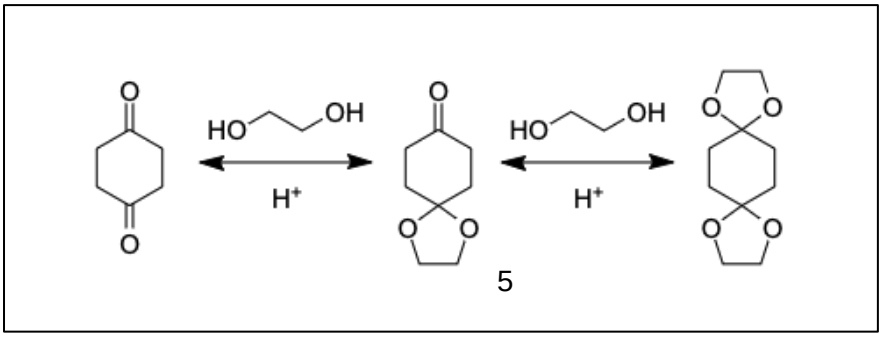
2.3.3 Repeat of Attempted Synthesis of **Compound 6** with Bromopyrene Grignard

After the unclear results from the first attempt of **Compound 6** synthesis, the reaction was repeated with more precaution.[1, 2, 8] All glassware was washed with soap, distilled water, and acetone, then dried in an oven, and isolated in a desiccator. These measures were taken to ensure neither water nor organic contaminants could negatively affect the desired Grignard reaction. The aforementioned procedures for this reaction were repeated with minor adjustments. An oil bath was used to heat the solution instead of a water bath to ensure no water contaminated the Grignard. Additionally, all flasks were filled with inert N_2 atmosphere and covered with film to prevent leaking of N_2. Since atmospheric water vapor could potentially affect the Grignard, this additional precaution was taken. Furthermore, steps where the reaction was allowed to run on heat for a few hours were changed to allowing the reaction to mix on heat for nearly 48 hours. More time may allow the reaction more time to form properly. In the end, magnesium notably struggled to dissolve and no precipitate was formed.

Perhaps one of the most notable observational changes was significantly cleaner NMR spectra. With these cleaner spectra, the components of the expected crude product mixture could be better deduced. Analysis began with the ^{13}C-NMR. Firstly, a particularly important shift that

was expected to disappear was the C-Br absorbance at 119.8 ppm, but this peak was visible. Moreover, the aromatic carbons shown on the ^{13}C-NMR spectrum match the literature values for bromopyrene. Strangely, expected peaks a 265 ppm for the carbonyl carbon of the ketone were missing, suggesting some successful conversion to product. The quaternary carbon containing the alcohol was also missing, however, suggesting no product conversion. With a lack of hydrogens, chemical shifts from the carbonyl carbon and alcohol carbon usually yield small absorbances. These signals were potentially buried in the noise during shift acquisition, but these signals may have been more distinguishable with a long acquisition time. The only unexpected peak occurred around 127 ppm.

Moving to the ^{1}H-NMR spectrum, in the aliphatic region, two triplet signals for the starting ketone matched literature values, indicating that the ketone was not fully consumed. Moreover, three new, unexpected singlets appeared. These singlets may have resulted from protection of the starting ketone **Compound 5** by ethanediol; deprotection would yield 1,4-cyclohexanedione, producing a singlet at 2.7 ppm. Further, the sequestered ethanediol protecting group could re-protect **Compound 5** starting material, creating a di-protected diketone with chemical shifts of 3.9 ppm and 1.8 ppm. Ultimately, no definitive signals for desired **Compound 6** formation were observed (**Figure II-2**).



Scheme II-11: *Protection and deprotection of* **Compound 5** *may explain unknown absorptions on NMR spectra.*

The overall conclusion is that either one of two steps in the Grignard reaction is failing: formation of the pyrene Grignard itself, or nucleophilic attack on the ketone by the Grignard. In analysis of the results and observations noted throughout the experiments, it seems pyrene Grignard is likely very difficult to form. Magnesium struggles to dissolve and form the Mg-Br-R bond. As such, it is presumed that the Grignard formation is the failed step, causing lingering starting materials, such as **Compound 5**, to separate via chromatography. Thus, since the Grignard is not forming at all, no reaction continues from there. From the failure of bromopyrene Grignard formation and with reanalysis of the Hammer Proposal,[7] perhaps another halogen could offer more reactivity and easier Grignard formation. Therefore, focus to using a more reactive halogen for pyrene Grignard formation was explored moving forward. The larger size and reduced electronegativity of another halogen, iodine, may deliver more promising results.

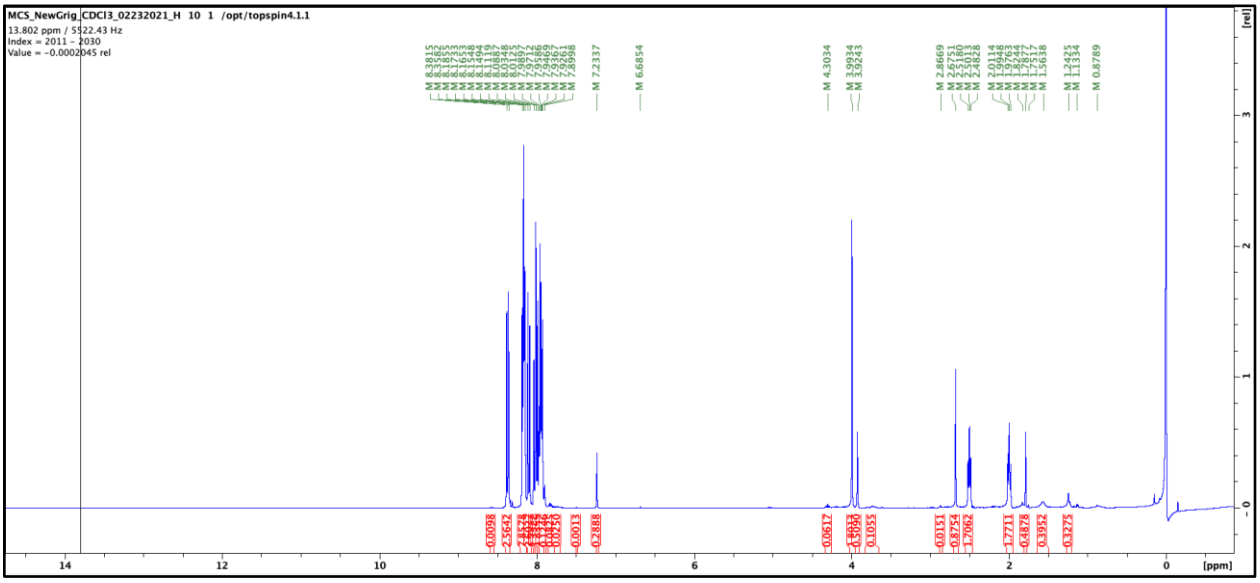
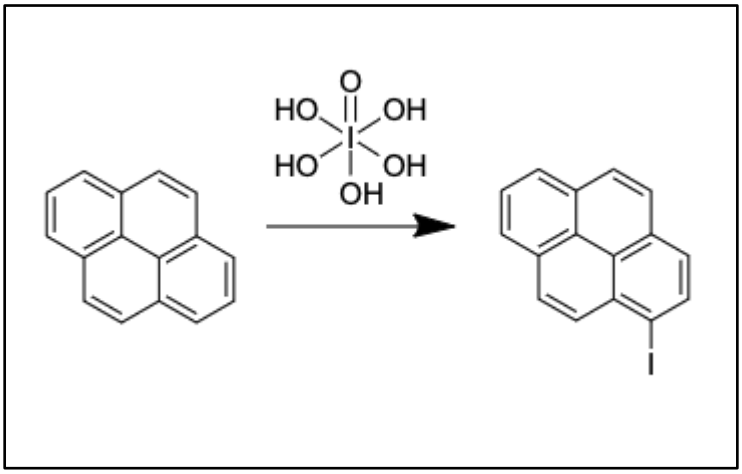


Figure II-2: *^{1}H-NMR spectrum of crude product from attempted bromopyrene Grignard reaction, containing unexpected peaks and no successful* **Compound 6** *formation.*

2.4 Iodine Grignard Additions

2.4.1 Attempted Synthesis of Iodopyrene



Scheme II-12: *Synthesis of iodopyrene from pyrene and periodic acid. While the mechanism is not completely understood, it is presumed that periodic acid adds an iodine to pyrene through electrophilic aromatic substitution, forming iodopyrene.*[3]

Since no iodopyrene was readily available as a starting material, it was synthesized using pyrene and periodic acid.[3] To begin, pyrene and periodic acid were dissolved in 95% EtOH in a round bottom flask. The subsequent solution was maintained on reflux for several hours, during which a pale to dark yellow color change was observed, followed by a transition to a light, vibrant red. Eventually, the solution color became an extremely dark crimson. Some black particulate was visibly noted on the flask, presumed to be polymerized tar. The reaction flask was then cooled, and TLC was performed with the crude product and starting materials.

While migrations between the crude product mixture and the starting materials were similar, new spots also appears. Namely, bromopyrene was used as reference for similar migration as iodopyrene. Thus, NMR was performed to clarify. ^{13}C-NMR of the crude product mixture was taken, and two peaks of particular interest were observed: one at 96.2 ppm and another at 136.7 ppm. These shifts are radically different from those of pyrene. When compared

to literature values for iodopyrene chemical shifts, these peaks indicate successful synthesis of iodopyrene.[3] Moving forward, the crude iodopyrene product was isolated from the polymerized tar and purified via column chromatography.

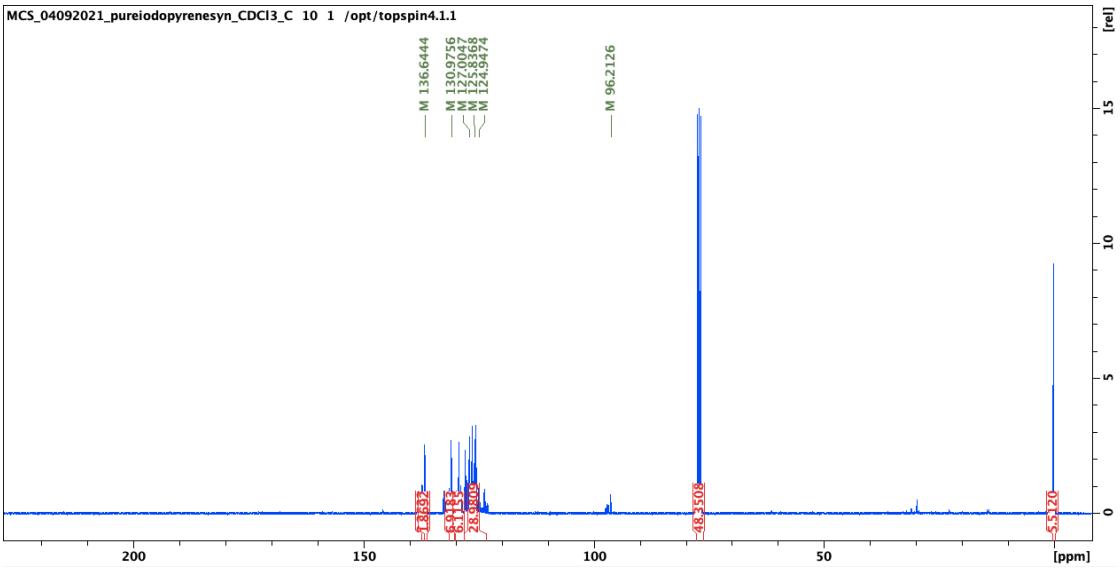
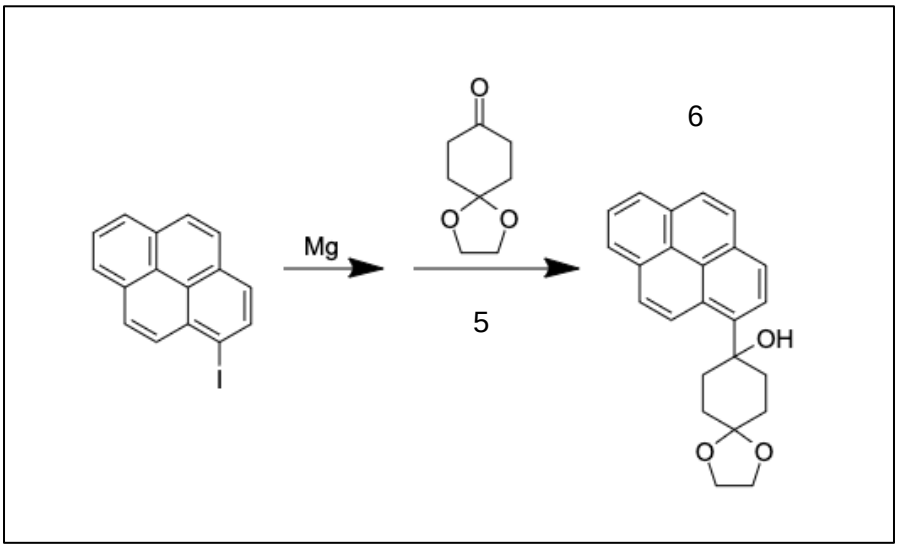


Figure II-3: *^{13}C-NMR spectrum of crude iodopyrene synthesis product, including indicative peaks at 96 ppm and 137 ppm.*[3]

2.4.2 Attempted Synthesis of 1-pyrenyl-4-monoethyleneketalcyclohexan-1-ol (**Compound 6**) with Iodopyrene Grignard

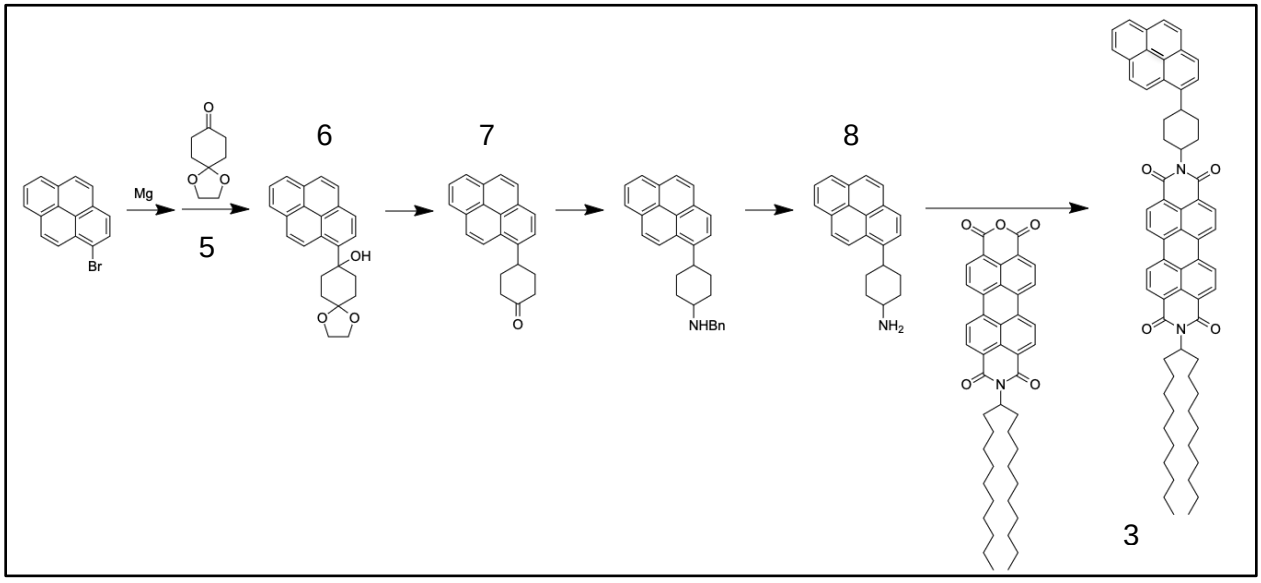


Scheme II-13: *Iodopyrene Grignard addition to* **Compound 5**, *generating* **Compound 6**.[1, 3]

With the successful synthesis, isolation, and purification of iodopyrene, it was combined with clean Mg turnings in dry THF. This solution was refluxed for several hours before addition of **Compound 5** in anhydrous THF, followed by further refluxing. The same procedures and precautions from the second bromopyrene Grignard run were essentially repeated. Again, the Mg struggled to dissolve and form the Grignard reagent. With both bromopyrene and iodopyrene unsuccessful in Grignard formation, perhaps treating either with butyl lithium to generate a pyrenyl lithium species offers more reactivity and optimism for continued research.

III. FUTURE WORK

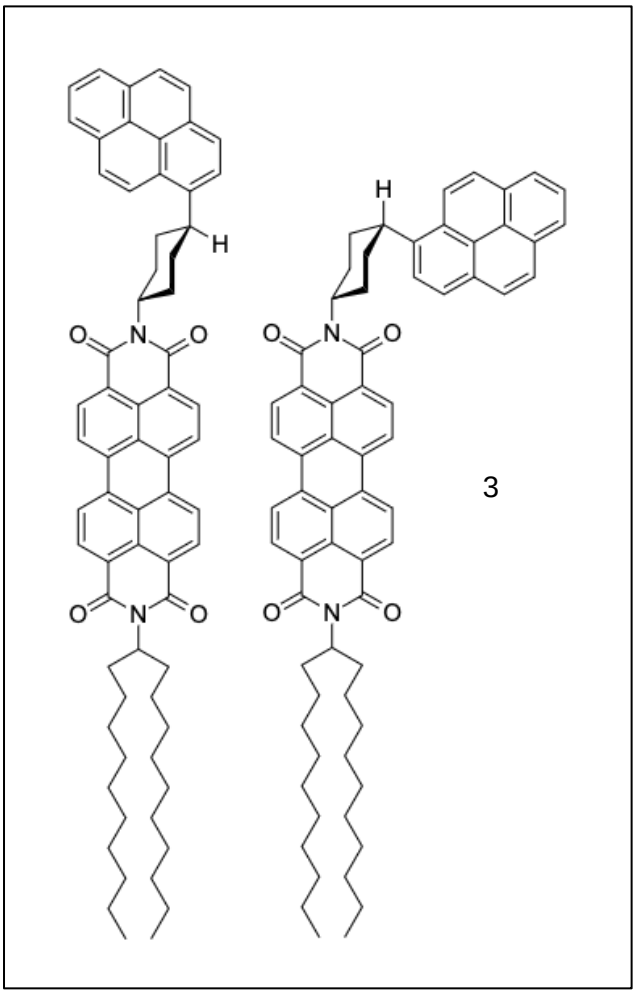
D-σ-A molecules have opened the door to the miniaturization of electronics. Unimolecular electronics from LB films of D-σ-A molecules could unveil new microtechnology innovations. Thus, continued research efforts on PMA, PBI, pyrene, and other D-σ-A molecules offers enormous opportunity and promise for innovation in the field of miniaturized technology.[10, 11]



Scheme III-1: *Complete synthetic pathway of the Hammer Proposal for pyrenylcyclohexyl addition.*[7]

The synthetic products from iodopyrene synthesis and Grignard addition offer optimism for continuing the Hammer Proposal. The last product synthesized in this paper is iodopyrene, which can form a Grignard reagent to add to **Compound 5**, then be deprotected and dehydrated (**Compound 7**), and finally aminated to form 1-pyrenylcyclohexan-4-amine (**Compound 8**). Addition of **Compound 8** to PMA would create the desired **Compound 3** PBI product. As

previously mentioned, depending on the direction of addition to PMA, *cis* and *trans* isomers of **Compound 3** can form. Future research may seek to understand how/why these differences affect electron transfer to excited PBI from pyrene; if significant differences are noted, it may be useful to understand methods to preferentially add specific isomers to PMA.[7]

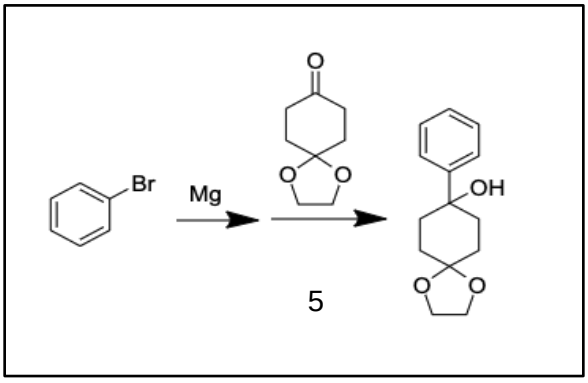


Scheme III-2: *Latter synthesis in Hammer Proposal, illustrating cis/trans orientation of pyrene group based on axial (trans) or equatorial (cis) positions on* **Compound 3**.[7]

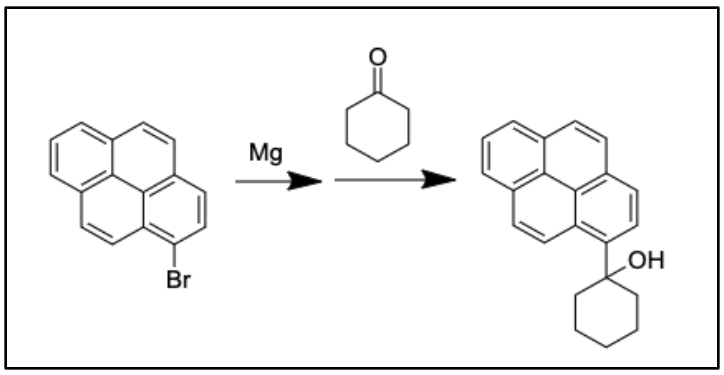
Moreover, the other products of **Figure 7** could be produced: PMA with methyl amine as a no-pyrene control and pyrenylethyl amine addition to introduce a flexible tether. Perhaps these synthetic products hold more success or promising results than does the addition of 1-pyrenylcyclohexan-4-amide to **Compound 3**. The synthesis of **Compounds 1** and **2** could be

reinvestigated to give insight into the aforementioned complexities of spectra from Tarrah and Stark. Clearly, much is still to be learned and understood about the specifics of PBI deprotection and synthesis. Furthermore, other methods of serinol protection could also prove useful to related research. Protecting groups can prevent hydrogen bonding, intramolecular forces, and undesirable functional groups from perturbing spectra, as observed in Frederick's research.[5, 9] Ultimately, many methods of protection are known, but some seem to work only under specific circumstances for certain molecules.

In an attempt to better understand Grignard difficulties experienced in this research thesis, it also may be worthwhile to see if bromobenzene or iodobenzene Grignard will react with **Compound 5** as a model ketone. It's ultimately hypothesized that bromopyrene Grignard formation is too difficult, but perhaps 1,4-cyclohexanediol monoethyleneketal (**Compound 5**) introduces challenges too.[1] Reaction of bromopyrene or iodopyrene with cyclohexanone may also reveal useful information regarding the behavior of this Grignard.



Scheme III-3: *Halobenzene Grignard addition to 1,4-cyclohexanedione monoethyleneketal to form 4-hydroxy-4-phenylcyclohexan-1-one.*[1, 2, 8]



Scheme III-4: *Halopyrene Grignard addition to cyclohexanone to form 1-pyrenylcyclohecxan-1-ol.*

To continue reactions down the Hammer Proposal with the aforementioned bromopyrene and iodopyrene compounds, wither could be treated with butyl lithium in a chemical exhange. The products of this chemical exchange are butyl halide and pyrenyl lithium. Just like the R-MgX bond that seems to struggle formation with pyrene, the bond between pyrene and lithium should be quite reactive. If successfully synthesizes, pyrenyl lithium may offer another mode of nucleophilic attack of ketones, such as **Compound 5**. Future research should pursue use of butyl lithium in an attempt to continue the Hammer Proposal.

IV. CONCLUSION

Though seemingly simple, deprotection of **Compound 2** proved quite difficult. Sometimes reactions regarded as simple have their complexities when accounting for steric hindrance, intramolecular forces, hydrogen bonding, etc. on larger more intricate molecules. What causes these uncertainties on NMR is still not fully understood. While samples of **Compound 2** were ultimately lost, two graces push this research forward. Firstly, PMA can be reacted according to Frederick's procedures to recreate **Compound 2** for further exploration. The protected-serinol PBI that was reacted with copper (II) sulfate[13] could also be purified and pursued further. Secondly, while the serinol diol ultimately proved difficult to deprotect, the addition of β-alanine to PMA forming **Compound 4** appears promising. Though the crude product of β-alanine addition to PMA[4] was not purified and confirmed, many indicators suggest successful formation alongside other impurities and byproducts. If this reaction can be better performed and understood, perhaps the addition of a carboxyl group will behave similarly, more easily, and potentially better in LB Methods. Nonetheless, more research on PBI protection, deprotection, and addition is needed.

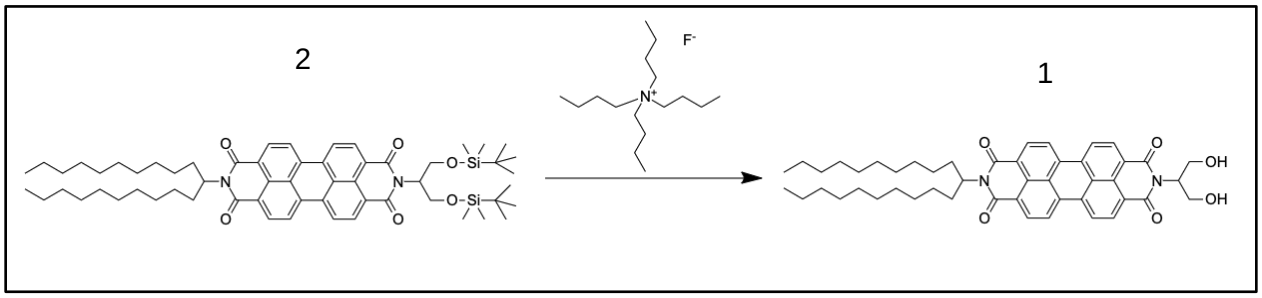
Furthermore, moving from the carboxyl and diol groups, continued synthesis efforts towards **Compounds 3** and **9** could provide another molecule for single-molecule spectroscopy. While bromopyrene ultimately proved too difficult for Grignard formation and addition to **Compound 5** ketone,[1] formation of the more reactive iodopyrene[3] suggests another synthesis route to the desired end molecule of the Hammer Proposal. Perhaps steric hindrance from nearby hydrogen in the aromatic rings blocks the halogen from forming the Grignard, but confirmation

is needed. With the iodopyrene product produced, future experimentation and research can be pursued. Iodopyrene can continue down this synthetic Hammer Proposal pathway to generate **Compound 8**, which can be added to PMA to create **Compound 3**.[7] Synthesis of pyrenyl lithium from halopyrene may also be worthy perusing for an even more reactive pyrene species. Though many difficulties and complexities in the lab and through the COVID-19 pandemic have stunted synthetic progress, iodopyrene and butyl lithium hold promise for future research into unimolecular electric rectification.

V. EXPERIMENTAL

5.1 Procedures for Deprotection of TMDMS-protected PBI

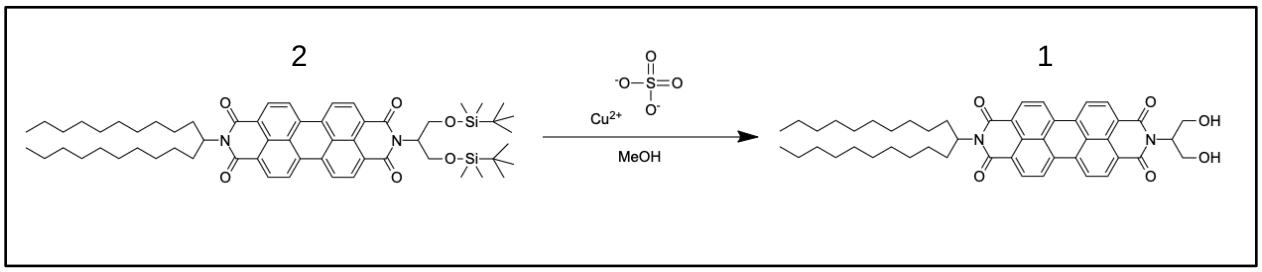
5.1.1 TBAF



Scheme II-1

Compound 2 (10 mg; 0.011 mmol), THF (50 mL), and TBAF (30 mL, 0.03 mmol) were combined in a 100 mL round bottom flask and stirred at ambient temperature for 12 hours. A notable color change from red/orange to grey/green was noted, perhaps from radical contamination. The resulting solution was concentrated via rotary evaporation and developed on TLC; the product illustrated similar migration as the starting material on TLC. While ^{1}H-NMR did show the disappearance of some peaks, none were indicative of deprotection of serinol. No desired **Compound 1** product formation was observed. (Yield: 4 mg; 40%).

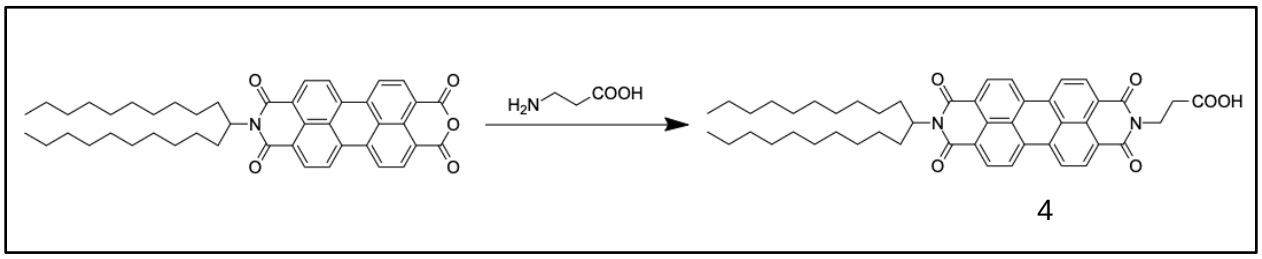
5.1.2 Copper (II) Sulfate



Scheme II-3[13]

Compound 2 (10 mg; 0.011 mmol), MeOH (25 mL), and copper (II) sulfate (2 mg, .012 mmol) were combined into a 50 mL round bottom flask and refluxed at 50℃ for 24 hours. The PBI and copper (II) sulfate were notably hesitant to dissolve but eventually met dissolution. A notable color change from red/orange to a darker maroon was observed. The resulting solution was vacuum filtered, and copper (II) sulfate was removed from solution via solubility in CH_2Cl_2 in a separatory funnel. The organic layer was concentrated via rotary evaporation to yield a dark red powder (~5 mg).[13] TLC indicated the disappearance of starting material and the migration of a new material; however, ^{1}H-NMR revealed unknown impurities and decomposition products. No desired **Compound 1** product formation was observed (Yield: 5 mg; 50%).

5.2 Procedures for Addition of Carboxylic Acid to PMA

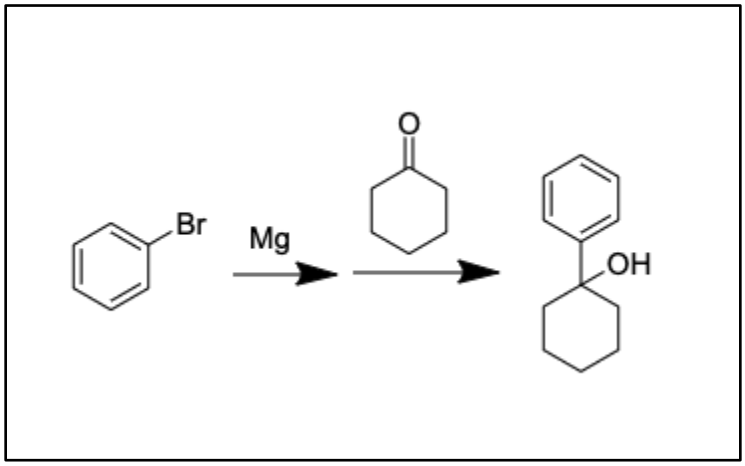


Scheme II-5[4]

PMA (100 mg; 0.7 mmol), β-alanine (45 mg; 0.6 mmol), and imidazole (30 mL) were combined into a 50 mL round bottom flask.[4, 7] TCL and NMR indicated successful synthesis of **Compound 4**, though contaminated with unknown byproducts. With the recent termination of collaborated research with Dr. Metzger's group at the University of Alabama, no further purification or analysis was pursued.

5.3 Bromine Grignard Additions

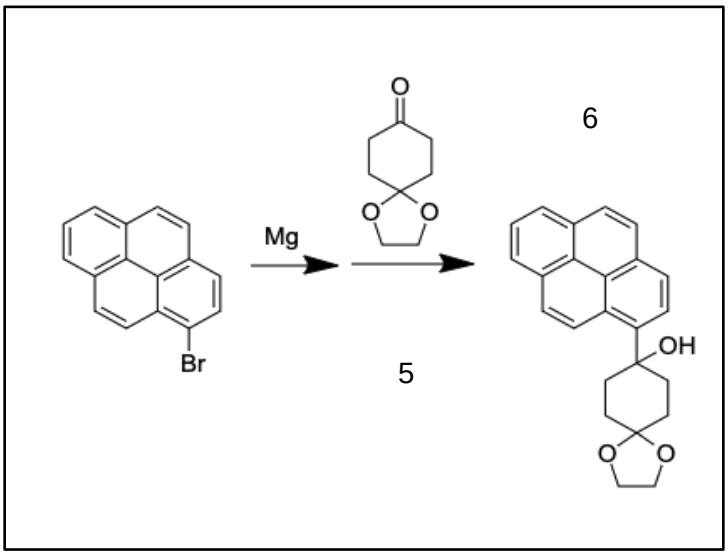
5.3.1 Bromobenzene Grignard Addition to Cyclohexanone



Scheme II-9 [2, 8, 12]

Bromobenzene (1.0 g; 5.50 mmol) and 100 mL of anhydrous THF were added to a 200 mL round bottom flask filled with N_2 atmosphere. Mg turnings (0.155 g; 6.3 mmol) were then added to the flask along with a small crystal of iodine. Mg turnings were visibly consumed. The solution was allowed to reflux at ~65℃ for 6 hours, followed by the slow addition of cyclohexanone (0.446 g; 4 mmol) in 50 mL of THF. The solution was allowed to cool to room temperature before quenching with HCl (5 mmol). The expected product was removed from solution by Et_2O in a separatory funnel, dried with anhydrous $MgSO_4$, and filtered into a round bottom flask.[2, 8, 12] The resulting solution was concentrated by rotary evaporation and used for TLC. Disappearance of starting material and new substance migration was noted. These findings were solidified by ^{1}H-NMR of the crude product. While further purification and isolation of the product is possible, this reaction simply functioned as a model ketone test. The desired 1-phenylcyclohexanol product was formed (0.53 mg; 3 mmol). (Yield: 55%)

5.3.2 Bromopyrene Grignard Addition to 1,4-cyclohexanedione monoethyleneketal, **Compound 5**

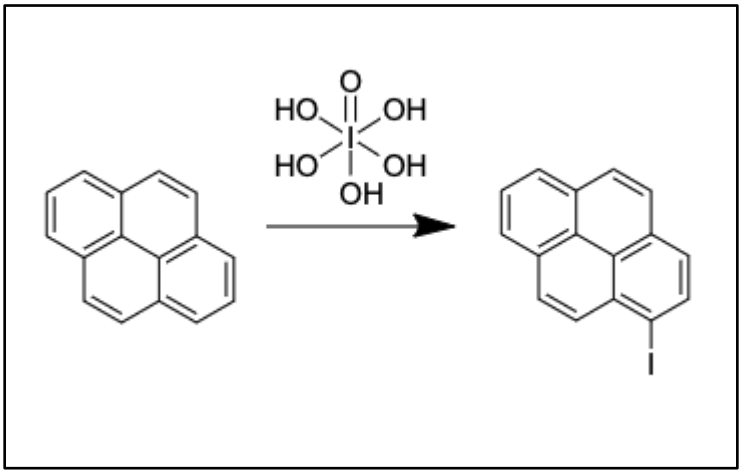


Scheme II-10 [1, 8]

1-Bromopyrene (2.81 g; 10 mmol) was dissolved in 200 mL of anhydrous THF in a 500 mL round bottom flask filled with N_2 atmosphere, followed by clean Mg turnings (0.25 g; 11 mmol) and a crystal of iodine. A notable pale yellow/brown color was observed. The solution was refluxed at 50 ℃ for 2 hours, followed by the addition of **Compound 5** (1,4-cyclohexanedione monoethyleneketal) (1.56 g; 10 mmol) dissolved in 100 mL of dry THF. This solution was refluxed on light heat for 8 hours, then cooled. The expected product was separated from the crude mixture and aqueous layer by 3 washings of 100 mL Et_2O in a separatory funnel.[1, 8] The organic layer was then concentrated by rotary evaporation. TLC of the crude mixture indicated multiple spots. The crude product was then purified via column chromatography with 1% MeOH/DCM elution solvent. Several products were isolated from the crude mixture and clarified by ^{1}H-NMR, such as both starting materials, several unknown impurities, and multi-protected/deprotected ketones. Ultimately, no desired **Compound 6** product formation was observed.[7]

5.4 Iodine Grignard Additions

5.4.1 Synthesis of Iodopyrene



Scheme II-12 [3]

Pyrene (2.00 g; 10 mmols), periodic acid (5.50 g, 9.90 mmol), and 100 mL of 95% EtOH were combined into a 200 mL round bottom flask. The subsequent solution was refluxed with light heat for 48 hours, transitioning from yellow, to red, to black/crimson.[3] The reaction flask was cooled, and TLC revealed disappearance of starting material and new product formation. This was further clarified by ^{13}C-NMR. Thus, the expected product was separated from the tar by warm chloroform and concentrated by rotary evaporation. The concentrated crude product was purified by column chromatography, yielding the desired iodopyrene product. (Yield: 213 mg).

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