LOYOLA UNIVERSITY CHICAGO

THE RICH CHEMISTRY OF CYCLOTRIVERATRYLENE (CTV) AND CTV-INSPIRED REACTIONS: ANTHRACENES WITH ORGANIC LIGHT-EMITTING DIODE (OLED) APPLICATIONS AND THE DISCOVERY OF CASCADE REACTIONS

A DISSERTATION SUBMITTED TO
THE FACULTY OF THE GRADUATE SCHOOL
IN THE CANDIDACY FOR THE DEGREE OF
DOCTOR OF PHILOSOPHY

PROGRAM IN CHEMISTRY

BY
SAMUEL ROBERT SMITH SARSAD
CHICAGO, ILLINOIS
AUGUST 2013
ACKNOWLEDGEMENTS

I wish to thank my supervisor Daniel Becker, Ph.D for working with me and assisting me in my research and taking time to read through my manuscript carefully and correcting my mistakes. I also wish to thank my committee members for their effort and time in reading and analyzing my work. Special thanks go to David Crumrine, Ph.D who also read through my manuscripts and assisted with the spectral characterization for my first publication article. Finally I wish to thank all those in my research group as well as those in the department who worked with me and contributed to the success of my work.
This goes to all those who have encouraged and assisted me throughout my education from childhood up to this level.
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<th>Description</th>
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<tbody>
<tr>
<td>HOMO</td>
<td>Highest Occupied Molecular Orbital</td>
</tr>
<tr>
<td>LUMO</td>
<td>Lowest Unoccupied Molecular Orbital</td>
</tr>
<tr>
<td>OLED</td>
<td>Organic Light Emitting Diode</td>
</tr>
<tr>
<td>LCD</td>
<td>Liquid Crystal Device</td>
</tr>
<tr>
<td>HTL</td>
<td>Hole Transport Layer</td>
</tr>
<tr>
<td>EML</td>
<td>Light Emission Layer</td>
</tr>
<tr>
<td>ETL</td>
<td>Electron Transport Layer</td>
</tr>
<tr>
<td>ND</td>
<td>Not Determined</td>
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<tr>
<td>DME-OH</td>
<td>2-methoxyethanol</td>
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<tr>
<td>TFMSA</td>
<td>Trifluoromethanesulfonic Anhydride</td>
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<td>TMEDA</td>
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</tr>
<tr>
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<td>Tetrahydrofuran</td>
</tr>
<tr>
<td>TLC</td>
<td>Thin Layer Chromatography</td>
</tr>
<tr>
<td>Na$_2$SO$_4$</td>
<td>Sodium Sulfate</td>
</tr>
<tr>
<td>MgSO$_4$</td>
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<tr>
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<td>Electron Injection Layer</td>
</tr>
<tr>
<td>HIL</td>
<td>Hole Injection Layer</td>
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<tr>
<td>ITO</td>
<td>Indium Thin Oxide</td>
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ABSTRACT

Cyclotrimeratrylene (CTV) is a supramolecular scaffold with applications in host-guest chemistry, analytical detection, drug delivery and liquid crystals. We have discovered that CTV rearranges to a highly functionalized anthracene derivative that is ideal for the synthesis of 9,10-disubstituted anthracene derivatives that are useful for the construction of organic light-emitting diodes (OLEDs). Several diaryl anthracene derivatives have been synthesized and analyzed, and were found to have excellent electroluminescent properties, including one analog that exhibits an exceptionally high quantum yield. Red, green and blue are the primary colors needed for full color display, but blue fluorescence emitting organic compounds used in OLEDs degrade rapidly and do not last long due to the high energy required for blue fluorescence emission. Most of the recent research in OLED compounds has been focused on finding a compound that will be an ideal candidate for the construction of blue OLEDs.

Further, while exploring the chemistry of CTV, we have also discovered cascade reaction sequences, where one reaction sets up the subsequent reaction in a domino fashion, enabling the construction of highly complex molecules in a synthetic single operation. We have discovered that CTV undergoes a dual reaction sequence involving a Beckmann rearrangement followed by an electrophilic aromatic addition, two classic reactions that have never been seen combined into a powerful tandem sequence, enabling
the direct construction of ketones, imines, or amines simply through varying the reaction conditions. We have now demonstrated that this tandem reaction sequence is general through success with a series of substrates. Finally, while exploring this Tandem Beckmann sequence, an even more useful cascade reaction was discovered involving the Beckmann reaction, followed by a Ritter reaction, and finally an electrophilic aromatic substitution. This triple cascade reaction sequence affords pharmaceutically important quinazolines and is presently being explored for its generality with very encouraging results.
CHAPTER 1
HIGHLY FUNCTIONALIZED ANTHRACENE DERIVATIVES FROM CTV
WITH OLED APPLICATIONS

Introduction

Demand for ease and comfort of displaying electronic information is highly desirable in this modern day. Research into the chemistry of materials used in displaying electronic information has been useful in flat panel displays in portable devices such as cell phones and car audio players.\(^1\) Flat panel displays are constructed commercially from two main types of devices, namely Liquid Crystals Devices (LCDs)\(^2\) which require backlighting, and organic light emitting diodes (OLEDs) which do not require any backlighting. The difference in backlighting gives OLEDs advantage over LCDs with regards to low power consumption, a wider viewing angle, thin width, light-weight, flexibility, and high image quality. Considering these advantages, OLEDs are in high demand for everyday applications and might replace LCDs and other electronic displays in the future. These make OLEDs the lighting of the future and more research is focused on these devices. OLEDs work by emission of light from electronically excited chemical compounds in the device; therefore the light emission comes directly from the thin OLED device. Large molecular weight aromatic organic compounds have been widely used in this area because they are easily applied as a thin film while maintaining their electronic functionality. The emission of light energy after absorption of incident light energy is
called photoluminescence and this occurs when molecules absorb certain wavelength of light energy and electrons are promoted to a higher electronic level energy level (excited state $S_1$, Fig 1). The electron falls back to the ground state by emitting light energy of characteristic wavelength. This process is called photoluminescence. The electron usually loses some energy by non-radiative relaxation processes and falls to a lower vibrational energy level before falling to the ground state ($S_0$), so the emitted light energy is lower than the incident light energy. This process is called fluorescence. A change of electron spin to a lower energy triplet level ($T_2$) can occur through a process called intersystem crossing from the excited singlet state of the molecule by a non-radiative process. The electron may fall to a lower triplet excited state ($T_1$) and then to the electronic ground state by emitting light of much lower energy or longer wavelength than fluorescence emission and this process is called phosphorescence.

Emission of light energy after absorption of electrical energy is called electroluminescence. The use of organic compounds in OLEDs is an additional advantage because organic materials are cheaper to produce and they can give electroluminescence at comparatively low voltages. These advantages make them very useful in electronic devices.
Organic light emitting diodes (OLEDs) consist of an organic material sandwiched between a positive electrode (anode) and a negative electrode (cathode). A closed circuit results in generation of positive charge carriers (holes) near the anode and negative carriers (electrons) near the cathode. The anode is at a high positive potential resulting in electron migration from the highest occupied molecular orbital (HOMO) of an adjacent organic layer to the conduction band of the metal electrode (anode) shown below (Fig 2).
Figure 2. Electroluminescence in organic compounds

The organic HTL (hole transport layer) layer must have a high level HOMO that is close in energy to the Fermi level of the metal electrode so that less energy will be required to
remove its electrons into the conduction band of the anode. The HTL should also have a high energy or high level lowest unoccupied molecular orbital (LUMO) so that electrons are not dumped into it, so this is called the electron blocking layer. Certain OLED devices have separate layers for hole injection, hole transport and electron blocking. The negative electrode (cathode) dumps electrons into the LUMO of the adjacent organic layer. The organic layer must have a low level LUMO close to the energy level of the cathode. It must also have a very low-lying HOMO to prevent formation of holes, as energy required to remove electron pairs from it will be too high. This is called the hole blocking layer. In certain OLED devices there are different compounds for electron injection, electron transport and hole blocking layers. These are designed to ensure that the maximum and balanced number of polarons is obtained from the OLED device.

Electrons migrate to combine with holes, resulting in emission of light energy (electroluminescence) at the emission layer. The combination of holes and electrons are called excitons, which consist of singlet and triplet excitons depending on the electron spin.\(^5\)

Anthracene crystals (Fig. 3) were among the first organic compounds to be used for electroluminescence experiments. Unfortunately the electroluminescence occurred at a very high voltage for a short period of time, therefore the anthracene crystals were not sufficiently robust for application in commercial OLEDs.\(^6\) This could be due to the low density of charge carriers that are generated from the crystal causing poor electroluminescence.\(^3\) A lower voltage OLED was constructed using an aluminum
hydroquinoline complex as the hole transport layer and a diamine organic compound (Fig. 3) as electron transport layer (ETL).\textsuperscript{7}

**Figure 3.** Structure of anthracene and first multi-OLED compounds

This gave the insight that improvement in low voltage OLED fabrication could be made by using different materials that function as hole injection layer (HIL), hole transport layer (HTL), light emission layer (EML), electron transport layer (ETL), and electron injection layer (EIL).\textsuperscript{8,9} Suitable materials are chosen for HIL and EIL such that the HOMO and LUMO of the HIL has high energy (high level) so that less energy is required to remove electron to create holes while the EIL is low lying (low level).\textsuperscript{9,10} LUMO and HOMO must be closer in energy so that less energy is required to move electrons into the lower energy LUMO. This reduces the energy gap between anode and the HIL as well as the cathode and the EIL, therefore it requires less voltage to create charge carriers. The ease of transport of charge carriers is facilitated by the fact that the HIL and HTL have comparable HOMO energy values or ionization potentials. Therefore holes can be easily generated from HIL to HTL. The EIL and ETL must also have similar LUMO energy values or electron affinities, such that electrons can easily move from EIL and ETL.
without requiring much energy from an external source. The transport of a hole is blocked at the ETL because the ETL has a HOMO with a very high ionization potential and therefore creates a high energy barrier for the creation of holes. This can also be called hole-blocking layer even though some OLED devices may have a separate layer for this. The energy values of the HOMO and LUMO of the EML is suitable for generating holes and electrons in equal proportions. A high concentration of holes and electrons form in the EML resulting in an intense and long lasting electroluminescence. The density or concentration of charge carriers is proportional to the intensity of the electroluminescence in a functioning OLED.

An OLED device that has one transport layer that also functions as an emission layer is called a Double Layer OLED, but a Triple Layered device has separate transport layers in addition to the emission layer (Fig. 4). The electrodes in OLED devices are usually transparent or opaque, depending on the side of the OLED that is used as the light emitting source. The most commonly used cathode is a Mg-Ag alloy, and while transparent indium thin oxide (ITO) is the most common anode which is usually coated on a transparent carbon glass substrate.

**Figure 4.** Schematic diagram of two layered and three layered OLED
It is desirable that compounds used in OLEDs have good morphological properties such as amorphous or non-crystalline thin films, good thermal stability (high glass transition temperatures, melting points and decomposition temperatures), and a narrow HOMO-LUMO energy band gap in order to function successfully in OLEDs. Red and green electroluminescence colors are easy to obtain from OLEDs, but blue color emitters are rare and degrade rapidly due to the larger energy band gap required for blue color emission. This has triggered research into finding more stable organic compounds that can be used for making efficient OLED devices.

Compounds used in OLEDs can be divided into two main categories: polymer OLEDs made of polymer compounds and small molecule OLEDs. The method of OLED fabrication usually gives one type of OLED an advantage over the other and vice versa. Polymer compounds are usually applied by spin coating, screen printing, or an ink-jetting process. This is less expensive and less complicated for single-layer OLEDs as well as being useful for wider-area applications. Small molecules are applied by thermal evaporation, which cannot be used for polymers due to their large molecular weights. Small-molecule OLEDs also have the advantage of being amenable to incorporation in very efficient complex multilayered OLEDs and they are easier to derivatize than polymers, and this affords many opportunities for modulating both physical and optical properties of OLEDs. Several small molecules have been used in OLED fabrication although the most common examples are OLED devices based on anthracene derivatives. Anthracene is a very useful core structure because manifold derivatives can be
synthesized, each with its own unique color emission. Many colors have been obtained employing anthracene derivatives including the primary colors (red, blue and green).

A few examples of anthracene compounds used in OLED include 9,10-bis (arylethenyl)anthracene (BAA), 9,10-di(2-naphthyl) anthracene (ADN), and 9,10-diphenyl anthracene (DPA) and their derivatives (Fig. 5). DPA is a good blue emitter with a very high quantum yield close to one, but it forms crystals in thin films and is therefore not suitable for OLED fabrication since crystalline thin films cause the formation of grain boundaries. Grain boundaries lead to fluorescence quenching in the solid state because holes accumulate behind the boundaries since the energy barrier required to cross is very high, so any electron that forms an exciton interacts rapidly with holes and the energy is lost non-radiatively as heat. Excess heat contributes to rapid degradation of thin film OLED materials and also ADN has low color purity because it emits a blue-green color with a slightly broader emission spectrum and tends to form crystals in thin films; therefore it is important to find anthracene derivatives that have more improved color purity and desirable physical characteristics.

One synthetic strategy is to make anthracene derivatives with substituents that prevent crystal formation in thin films. This has been done by putting alkyl substituents on the anthracene core structure to disrupt the efficiency of packing into crystals in thin films. Amorphous thin film forming derivatives are made by introducing alkyl substituents in the compounds to prevent the molecules from easily packing to form crystals in thin film. The first reported derivative was methylADN (MADN) which is a
commercial blue emitter and a host for dopants which is more amorphous and has better device performance. However, other more amorphous derivatives were subsequently made including tert-butyl ADN (TBADN). Anthracene derivatives with bulky aromatic substituents such as tert-butylidiphenylen Anthracene (TBDPA) and tert-butyl diphenanthryl Anthracene (TBDHA) have improved thermal stability due to their increase in molecular weight.\textsuperscript{14}

\textbf{Figure 5.} Anthracene derivatives employed in OLEDs

The anthracene derivatives are usually made by carbon-carbon bond formation in palladium metal-catalyzed coupling reactions such as Suzuki, Negeshi, or Sonogashira coupling reactions. They are also made by aldol coupling reaction by nucleophilic attack
of aryllithium on an anthraquinone\textsuperscript{14} or by Wittig reaction.\textsuperscript{12} The anthracene derivatives can have different color emission based on the substituents attached at the 9- and 10-positions. All of the primary colors, red, blue and green, have been obtained from different derivatives of anthracene. An additional advantage of anthracene is that there are different derivatives that can have different functions in OLEDs such as hole transport layer, light emission layer, electron transport layer, hole blocking, or electron blocking layer.\textsuperscript{15} Therefore one can have a blue OLED made entirely from anthracene derivatives. This will enhance structure compatibility at the interface between the compounds in an OLED. MADN has been found to be good for light emission as well as hole transport due to its high HOMO energy values and it has been found to have very slow hole drift properties and this prevents formation of excess holes leading to formation of balanced amounts of charge carriers in the light emission layer for good OLEDs performance. However, it was perceived that the addition of oxygen atoms in the form of methoxy substituents would further elevate the HOMO and LUMO energy levels and gave much better OLED performance MADN.\textsuperscript{16}

Tetramethoxy derivatives of anthracene (Fig 6.) such as tetra(methoxy)-9,10-di(mesityl) anthracene (TMOADS) and tetra(methoxy)-9,10-di(1-naphthyl)anthracene (TMOADN) have been used for hole transport and electron blocking materials and these had high thermal stability and better OLED performance compared to the common commercial hole transport material 4,4’-bis[N-(1-naphthyl)-N-phenylamino]biphenyl (NPB) which has low glass transition temperature of 95°C.\textsuperscript{17} The OLED performance
was better in these anthracene derivatives due to slower hole carrier drift leading to formation of charge balance for light emission and good OLED performance. The common nitrogen containing transport materials such as NPB have very high hole carrier drift properties and cause charge imbalance in the light emission layer.\textsuperscript{17,16}

**Figure 6.** Tetramethoxyanthracene derivatives and NPB

Electroluminescent anthracene compounds have been synthesized from many starting materials but synthesis from cyclotriveratrylene (CTV) (Fig 7.) starting material has not being previously reported.

**Figure 7.** Structure of CTV
CTV and its derivatives have important uses in synthesis and in material chemistry. CTV has been used as a host molecule for smaller guest molecules such as acetonitrile or larger molecules such as fullerenes. Other uses of CTV include making more complex molecular hosts, as starting materials for making cryptophanes and extended arm cavitands, for hydrogen bonding coordination networks, and in 3D capsule and metallo-supramolecular structures. Traditional methods for making CTV involve the use of veratrole with formaldehyde and an acid. Additionally CTV can be synthesized from veratryl alcohol (3,4-dimethoxybenzyl alcohol) in acid (such as acetic acid, sulfuric acid, or formic acid). Most CTV derivatization has been done on the methoxy substituents along the periphery, but very little work has been done on the apical methylene bridging carbons. These methylene groups can be oxidized using sodium dichromate or KMnO₄/MnO₂ to the monoketone, or to the diketone that can serve as precursors for making other CTV derivatives. The CTV saddle oxime, CTV amide and the CTV amine have been made from the CTV monoketone. We have discovered that bromination of CTV diketone results in an unexpected rearrangement into a phenyl bromoanthracene compound structurally similar to the precursors of many anthracene compounds currently used in organic light emitting diodes.

The aim of this part of my research is to make highly functionalized anthracene compounds from CTV which are useful synthetic intermediates and supramolecular scaffolds. It was found that the oxidative bromination of CTV diketone resulted in an unexpected rearrangement into a bromoanthracene derivative. This was used to make
other anthracene derivatives that have blue photoluminescence that is needed for applications in OLEDs. Based on this, the UV absorption and fluorescence and the maximum wavelengths for absorption and emission as well as the optical band gap and quantum yields were determined from the spectra. Quantum mechanical calculations were done by using Spartan software to determine the HOMO and LUMO energies and compare them to values from known compounds. Additionally, the HOMO and LUMO energies of the compounds can be measured experimentally by using UV-photoelectron spectroscopy.\(^1\) In this experiment, an incident UV radiation of known energy is used to irradiate an organic compound under high vacuum and then the kinetic energies (\(E_k\)) of ejected electrons are measured. The kinetic energy of ejected electrons is measured by the difference between the maximum cut off energy (highest peak for maximum number of ejected electrons \(E_{\text{ct}}\)) and the energy of the minimum number of ejected electrons (Fermi edge, \(E_{\text{fe}}\)). The difference between the energy of the incident radiation and kinetic energy gives the ionization potential (\(I_P\)) of the material (Eqn. 1 and 2). The \(I_P\) is equivalent to the energy of the HOMO. The optical energy band gap (Eqn 3 and 4) is the wavelength in the UV spectrum at which the absorbance just edges out (absorption edge). The energy value of the HOMO is subtracted from the bandgap energy to get the LUMO energy.

\[
E_k = (E_{\text{ct}} - E_{\text{fe}}) \quad (1) \quad I_P = E_{\text{in}} - E_k \quad (2)
\]

\[
v = \frac{c}{\lambda} \quad (3) \quad h\nu = E_{\text{LUMO}} - E_{\text{HOMO}} \quad (4)
\]

The symbol \(c\) is the velocity of light, \(\lambda\) is the wavelength of the absorption edge, and \(h\) is Plank’s constant.
I was able to determine the thermal properties such as glass transition temperature, the melting points and decomposition temperatures by using differential scanning calorimetry (DSC) and the meltemp apparatus. In DSC a sample is heated with a reference sample in a separate inert gas (N\textsubscript{2} or Ar) chamber. The rate and amount of heat supplied is the same for both the sample and reference compound. There is a linear increase in temperature of sample and reference which is measured by a thermocouple. The difference in energy flow between sample and reference is plotted against temperature of the sample. The shape of the graph is used to determine the thermal properties of the compound. The glass transition temperature (T\textsubscript{g}) occurs when sample absorbs heat to form a glassy or rubber-like texture without a change in phase. This is an endothermic process and causes a depression in the plotted graph. A continual supply of heat causes the sample to absorb heat energy and changes phase to liquid. This endothermic process causes a negative (or downward) depression in the graph that indicates the melting temperature (T\textsubscript{m}). Decomposition occurs when a sample absorbs enough energy to completely overcome all intermolecular forces and the covalent bonds. This occurs as a depression in the plot since the energy difference of sample compared to reference is now negative, and the measured temperature is called the decomposition temperature (T\textsubscript{d}).

Finally, with the compounds that have been synthesized and characterized it is now possible to build an OLED device and measure the electroluminescence spectrum of the compounds that I have synthesized. Device fabrication is done in a clean inert
vacuum chamber. The anode metal electrode is cleaned with acetone, dried and then treated with UV light and ozone and then mounted onto a transparent glass support (substrate). The organic materials are evaporated sequentially onto the electrode at constant rate, temperature and pressure. This is allowed to dry after which the cathode is mounted to complete the OLED fabrication. The electrodes are then connected to an external circuit and the voltage at which light is emitted from the device is plotted against the measured wavelength.

**Results and Discussion**

The synthesis of apex modified CTV derivatives was accomplished by synthesis of CTV as the starting material. This was done by trimerization of veratryl alcohol in formic acid which gave a clean white solid CTV (52%) after recrystallization from toluene (Scheme 1).

**Scheme 1. Synthesis of CTV**

Oxidation of CTV was done (Scheme 2) by using potassium permanganate to obtain CTV diketone (2b) and CTV monoketone (2a) in comparable amounts (41% diketone and 32% monoketone). The modest yields of these oxidation products could be due to
insufficient time needed for the reaction to reach completion. Higher temperatures could be utilized to enable all CTV to be converted to CTV diketone.²⁶

**Scheme 2.** Synthesis of CTV mono- and diketone

Scheme 3. Synthesis of 2-(10-bromo-2, 3, 6, 7-tetramethoxyanthracen-9-yl) -4,5-dimethoxybenzoic acid (3a)
The oxidative bromination\textsuperscript{29} of the CTV diketone 2b resulted in unexpected rearrangement to a functionalized 10-bromo-9-phenyl anthracene derivative (3a) as illustrated in Scheme 3. The structure of the product was confirmed conclusively by X-ray crystallography (Fig 8). This reaction could be initiated by acidic side products of the bromination reaction (HBr) that protonates the carbonyl oxygen followed by electron donation from the methoxy groups to enable nucleophilic attack by the aryl ring of the electron deficient carbonyl carbon (Scheme 4). Nucleophilic attack on the carbonyl by a hydroxyl group leads to formation of a neutral intermediate which contains the activated allylic carbon that undergoes free radical bromination reaction with N-bromosuccinimide. Dehydrogenation followed by dehydration regenerates aromaticity in the final step.

**Scheme 4.** Proposed mechanism for oxidative bromination of CTV diketone
Spirolactone 3c was obtained as a side reaction product. Formation of this product is catalyzed by acids produced from the bromination reaction.\textsuperscript{41}

**Figure 8.** Single crystal X-ray structure of bromoanthracene benzoic acid 3a

Suzuki coupling was utilized in the reaction between the bromoanthracene 3a and boronic acids (phenyl boronic, naphthyl-2-boronic acid and pyrene-1-boronic acid) to form the 9,10-substituted anthracene compounds 4a, 4b, and 4c respectively.
**Scheme 5.** Synthesis of 4,5-dimethoxy-2-(2,3,6,7-tetramethoxy-10-arylanthracen-9-yl) benzoic acid derivatives 4a, 4b, and 4c
Figure 9. General mechanism of the Suzuki coupling reaction

The mechanism of the Suzuki coupling reaction (Fig. 9).\textsuperscript{30,31} involves oxidative addition of the palladium to the aryl halide to form a palladium (II) complex, followed by transmetallation with the aryl boronate ion complex. Reductive elimination completes the reaction and regenerates the palladium (0).\textsuperscript{32} The carboxylic acid group on compounds \textbf{4a}, \textbf{4b}, and \textbf{4c} was then reduced with lithium aluminum hydride (LAH) to form the corresponding alcohols \textbf{5a}, \textbf{5b}, and \textbf{5c} respectively (Scheme 6).
Scheme 6. Synthesis of 4,5-dimethoxy-2-(2,3,6,7-tetramethoxy-10-arylanthracen-9-yl) benzylic alcohols 5a, 5b, and 5c

<table>
<thead>
<tr>
<th>Product</th>
<th>Structure</th>
<th>Yield</th>
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<td>100%</td>
</tr>
<tr>
<td>5b</td>
<td><img src="image" alt="Structure 5b" /></td>
<td>100%</td>
</tr>
<tr>
<td>5c</td>
<td><img src="image" alt="Structure 5c" /></td>
<td>96%</td>
</tr>
</tbody>
</table>

Ar
- 4a phenyl
- 4b 2-naphthyl
- 4c 1-pyrenyl
The Suzuki coupling of bromoanthracene 3a with boronic acids was very challenging and many conditions were tried with very little success (Table 1).

**Table 1.** Coupling reactions of arylboronic acids with bromoanthracene.

<table>
<thead>
<tr>
<th>Compound</th>
<th>Base</th>
<th>Solvent</th>
<th>T/C</th>
<th>Time (hours)</th>
<th>% Yield</th>
<th>Side reaction</th>
</tr>
</thead>
<tbody>
<tr>
<td>4a</td>
<td>Na₂CO₃</td>
<td>Toluene</td>
<td>115</td>
<td>24</td>
<td>no</td>
<td>not detected</td>
</tr>
<tr>
<td></td>
<td>Na₂CO₃</td>
<td>Toluene/ethanol</td>
<td>115</td>
<td>24</td>
<td>no</td>
<td>not detected</td>
</tr>
<tr>
<td></td>
<td>NaOH</td>
<td>ethanol</td>
<td>25</td>
<td>24</td>
<td>trace</td>
<td>not detected</td>
</tr>
<tr>
<td></td>
<td>NaOH</td>
<td>ethanol</td>
<td>90</td>
<td>24</td>
<td>29</td>
<td>not detected</td>
</tr>
<tr>
<td>4b</td>
<td>NaOH</td>
<td>ethanol</td>
<td>90</td>
<td>48</td>
<td>21</td>
<td>Deboronation</td>
</tr>
<tr>
<td></td>
<td>KF/Ag₂O</td>
<td>THF/2-methoxyethanol</td>
<td>100</td>
<td>24</td>
<td>88</td>
<td>Deboronation</td>
</tr>
<tr>
<td>4c</td>
<td>NaOH</td>
<td>ethanol</td>
<td>90</td>
<td>48</td>
<td>trace</td>
<td>Deboronation/debromination</td>
</tr>
<tr>
<td></td>
<td>NaOH</td>
<td>ethanol/n-butanol</td>
<td>140</td>
<td>48</td>
<td>trace</td>
<td>Deboronation/debromination</td>
</tr>
<tr>
<td></td>
<td>NaOH</td>
<td>ethanol/dimethoxyethane</td>
<td>100</td>
<td>48</td>
<td>trace</td>
<td>Deboronation/debromination</td>
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<tr>
<td></td>
<td>K'BuO</td>
<td>ethanol/dimethoxyethane</td>
<td>100</td>
<td>48</td>
<td>trace</td>
<td>Deboronation/debromination</td>
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<tr>
<td></td>
<td>KF/Ag₂O</td>
<td>THF/2-methoxy ethanol</td>
<td>100</td>
<td>48</td>
<td>48</td>
<td>Deboronation/debromination</td>
</tr>
<tr>
<td></td>
<td>KF/Ag₂O</td>
<td>THF/2-methoxy ethanol</td>
<td>100</td>
<td>48</td>
<td>79</td>
<td>Deboronation/debromination</td>
</tr>
</tbody>
</table>

The first coupling reaction of bromoanthracene 3a with the phenylboronic acid that was done with aqueous sodium carbonate and toluene gave back the starting material and just
a trace of the product. However, a modest yield of the product was obtained when sodium hydroxide in ethanol was used. This was easy to identity because the product has a blue fluorescence. This difference in yield between the former and latter conditions could be due to issues relating to strength and solubility of the base or simply the amount of boronic acid, palladium catalyst and base was not enough to push the reaction to form enough products in each case. The coupling reaction with naphthylene-2-boronic acid with the sodium hydroxide base also resulted in low yields and there were deboronated side reaction products. The coupling of the pyrene-1-boronic acid was more challenging reaction because several attempts resulted in only starting materials, deboronated products, and debrominated anthracene compound. The strength of the base was increased by using potassium tert-butoxide but this gave similar results. A weaker base sodium bicarbonate was used with almost the same results. Previous coupling reactions that have been done using 9,10-dibromoanthracene$^{79,80}$ might lead one to think that the same conditions can work or higher yield should be obtained in these reactions. However, this is not the case, and the reason could be due to the electron donating methoxy substituents that make the bromoanthracene core very electron rich and reduce the reactivity at the 10-position of the anthracene. This severely slows the palladium insertion reaction and weakens the palladium carbon bond but strengthens the palladium bromide bond.$^{33}$ The rate limiting step is the removal of the bromine from the palladium intermediate complex making it very important to have conditions that will enable the reaction to go faster than other side reactions so that maximum yield of the desired
product could be obtained in a reasonable amount of time. In this regard, the removal of 
the bromine from the palladium complex would require a good boronate nucleophile and 
a cation with high affinity for bromine. It is very obvious that none of the bases are good 
candidates to provide these conditions. The bases also reacted with the boronic acids and 
resulted in deboronation even though the phenyl deboronation was very difficult to detect 
by TLC.

The base strength was further reduced by using potassium fluoride and silver (I) oxide in THF and 2-methoxyethanol (or ethylene glycol monomethyl ether) in a more 
dilute concentration. This reaction gave a high yield of product together with some 
deboronated and debrominated side products. The silver (I) oxide activates the palladium 
catalyst to accelerate the transmetalation process\textsuperscript{34,35} since silver has a high affinity for halogens. Silver (I) oxide also coordinates to the boronic acid making it more 
nucleophilic and easier for the alkyl nucleophile to bond to the palladium after 
trans-metallation.\textsuperscript{36,37,38} The 2-methoxyethanol was used as a high boiling solvent to aid 
the reaction at high temperatures. THF was added because the starting materials are only 
partially soluble in 2-methoxymethanol but completely soluble in THF. The competing 
debromination\textsuperscript{35} side reaction of the aryl bromide was only observed in reactions 
involving the pyrene-1-boronic acid. This could also be due to steric coupling of 
the bulky pyrenyl group to the highly electron rich bromoanthracene core having four 
electron donating methoxy substituents.\textsuperscript{33} This hinders and slows down the reductive 
elimination step, and allows a competing side reaction involving $\beta$-hydride elimination
on the pyrene bonded to the palladium intermediate complex and release of debrominated anthracene compound and palladium (0).

Three different derivatives (5a-c) were synthesized in high yields by reducing the parent compounds 4a-c containing carboxylic acid groups to the corresponding alcohol with lithium aluminum hydride (LAH) in THF. There is a systematic upfield increase in proton chemical shifts of the methoxy groups due to increase in size and shielding effect of substituents at the 10-position ranging from phenyl, naphthyl and the pyrene respectively.
Scheme 7. Complete linear syntheses of 4a-c and 5a-c

Scheme text and diagram as described in the image.
UV Absorption and Fluorescence Spectroscopy

The UV absorption spectra for all the anthracene derivatives, 4a to 5c, show peaks at 278 nm and 378 nm indicating electronic transitions that are common to anthracene occurring in two different energy states $S_0-S_2$ and $S_0-S_1$ respectively (Fig 10). The fluorescence spectra for all the compounds have a maximum fluorescence emission in the blue region.
Figure 10. UV absorption and fluorescence spectra of 4a, 4b and 4c

The UV-absorption spectrum is shown in blue while the fluorescence emission spectra is shown in pink. Fluorescence spectra of 4a and 4b were normalized by dividing the intensity by 3x10⁶ units, while 4c was normalized by 4x10⁶ units, and 5x10⁶ units for first and second eluted isomers respectively.

The absorption edge was slightly red shifted for compounds 4a and 4b due to poor conjugation with the anthracene while the pyrene adduct 4c was most red shifted and has the smallest energy bandgap due to the large bulky pyrene substituent. The molar extinction coefficients ranging from 9.0 x 10⁻³ M⁻¹ cm⁻¹ to 151.0 x 10³ M⁻¹ cm⁻¹ shows that electronic transitions are mainly occurring from π - π* energy levels in all the
compounds. The spectrum of the pyrene adduct 4c has peaks that correspond to the anthracene as well as the pyrene group and the absorption edge was more red shifted compared to compounds 4a and 4b. There is an increase in the number of double bonds with subsequent decrease in band gap (Table 2). The pyrene adduct 4c blue emission occurs at a much longer wavelength than the naphthyl 4b and phenyl adducts 4a but compound 4a emits at a slightly longer wavelength than compound 4b.

It was also found that the pyrene adduct 4c exhibits atropisomerism due to its formation as two atropisomers that appear as two spots on the TLC plate, and the proton NMR spectra of the atropisomers separated by prep plate TLC show virtually the same chemical shifts. The proton chemical shifts of the methoxy groups around 3.9 ppm differ only by 0.01 ppm in the two atropisomers. This might be due to spatial orientation of the pyrene substituents at 10-position relative to benzoic acid substituent at the opposite 9-position of the anthracene core structure of 4c (Fig 12). The hindered rotation of the pyrene group appears to have locked the molecule in two conformations in which one conformation is slightly higher in energy than the other. Theoretical semi-empirical calculations using AM1 (equilibrium geometry) from SPARTAN software gave two energies of the molecule which consist of one lower energy conformer (-133.178 kcal/mol) with a dipole of 2.82 Debye and a higher energy conformer (-132.973 kcal/mol) with a dipole of 3.35 Debye. These results could be due to the difference in conformation between the isomers such that the carboxylic acid group falls into the aromatic system electron cloud of the anthracene and the pyrene of the lower
energy conformer and decreases its dipole and polarity and makes it slightly more stable. This structure may also hinder the binding interaction of the silica gel to the carboxyl group making it the first to elute from the column. The higher energy conformer has the carboxylic acid pointing away from the aromatic system electron cloud of the anthracene core and the pyrene leading to less stabilization therefore higher dipole and polarity. This isomer could have stronger binding interactions to the silica gel and therefore is the second to elute from the column. Variable temperature NMR experiments revealed that the isomers do not interconvert at temperatures up to 100°C in DMSO.

**Figure 11.** 3D view of 4c

*Chemskech of 4c and calculated minimized energy structures from Spartan showing lower energy conformer and higher energy conformer*

Relative fluorescence quantum yields ($Q_f$) were measured at 365 nm excitation wavelength with an absorbance of about 0.004 for all the compounds in dichloromethane compared to anthracene in ethanol ($Q_f = 0.27$). $Q_f = (A_x/A_s)(I_x/I_s)(n_x/n_s)^2(0.27)$. The symbols $A$, $I$ and $n$ refer to the absorbance, integrated fluorescence intensity which is area under the curve (calculated from originPro software), and refractive index respectively for the unknown compound ($x$) and the anthracene standard ($s$). The low fluorescence quantum yields of 0.063, 0.058 to 0.197 for compounds 4a, 4b and 4c, respectively,
(Table 2) could be due to loss of energy in excited state by the interaction of the π orbitals of the carboxylic acid group with the π aromatic ring systems leading to transfers some of the absorbed excitation energy from singlet excited state of the π aromatic ring systems into a low lying triplet excited state of the carboxylic acid group where the energy is lost as phosphorescence or other non-radiative processes.78

The fluorescence spectra show multiple fine peaks for anthracene (Fig 13), but the anthracene derivatives (4a to 5c) have one unique peak corresponding to one wavelength. This shows that fluorescence emission from anthracene occurs from multiple electronic excited states, but the derivatives emit from only one electronic excited state. This occur because anthracene has a rigid structure so it has less vibrations associated with electronic excitations (vibronic coupling) at the electronic singlet states but the derivatives have substituents and this make them less rigid and have more vibronic coupling in excited states. This cause them to lose some energy non-radiatively to a lower singlet excited electronic state before emission of light to the ground state.40
Figure 12. UV absorption and fluorescence spectra of compounds compared to anthracene

All UV absorption spectra were recorded at concentration of $8.6 \times 10^{-6}$ M in dichloromethane at room temperature. Fluorescence spectra were recorded in dichloromethane at the following concentrations and excitation wavelengths: Phenyl adduct $4a$ is $8.6 \times 10^{-6}$ M excitation wavelength 374 nm, naphthyl adduct $4b$ $4.3 \times 10^{-6}$ M at 374 nm excitation, pyrenyl adduct $4c$ $4.3 \times 10^{-6}$ M at 372 nm excitation wavelength, and anthracene $7.166 \times 10^{-7}$ M at 377 nm excitation wavelength.

Figure 13. Spectra of reduced anthracene adducts 5a-c
Thin films of the compounds were made by spin coating dichloromethane solution (1.0 mM) of each compound on thin glass slides. These were used for measuring the UV absorption spectra and the fluorescence spectra of each compound (Fig 15). The excitation wavelength for the fluorescence was kept constant at 370 nm for all the compounds.

**Figure 14.** Spectra of thin films of anthracene derivatives 4a-c and 5a-c
The fluorescence spectra showed a gradual increase in fluorescence emission wavelength as the size of the 10-position substituent increased in both solution and thin films. However, this was not clearly the same for the UV absorption spectra except that the thin films showed a bathochromic shift compared to those in solution and this is expected to occur since there is more aggregation in solid state than in solution. All the thin films have emission in the blue region and compound 4b has the highest emission intensity of 428 nm compared to all carboxylic acid derivatives, while compound 5a has the highest emission intensity of 428 nm compared to all the alcohols derivatives. The UV absorption spectra show mostly $\pi - \pi^*$ transitions ranging from 276 nm to 381 nm with molar absorptivities of $10 \times 10^3 \text{M}^{-1} \text{cm}^{-1}$ to $150 \times 10^3 \text{M}^{-1} \text{cm}^{-1}$. The optical energy band gap of each compound in solution was calculated from the UV spectrum at the wavelength at which the absorbance just edges out (Eqn 4). The energy band gap calculated was larger for the alcohols than the carboxylic acids since the alcohol functional group is electron donating and elevates the LUMO.

The fluorescent quantum yields were higher for the corresponding alcohols 5a and 5b except for the pyrene adduct 5c which showed a slightly lower value. This is presumably because the carbonyl-containing functional group absorbs some of the excitation wavelength into the triplet state resulting in low fluorescence quantum yields for the compounds 4a and 4b. Compound 4c had a higher quantum yield than 4a and 4b because the restricted rotation of the locked pyrene substituent gives it a more rigid structure than 4a and 4b. However, compounds 4c and 5c had almost the same quantum
yields which were slightly higher for 4c. This might be due to the fact that the parent carboxylic acid compound 4c is slightly more rigid than the alcohol 5c. There are more vibrational degrees of freedom associated with the electronic transitions of the alcohol 5c such that some of the excited energy may be lost as non-radiative heat or the energy may go to the triplet state and be lost as phosphorescence which lowers the fluorescence emission compared to 4c. However, the rigid structure also allows for more intermolecular interactions in the solid state. Sample 4c had very low emission in the solid state compared to the alcohol derivative 5c probably due to the high π-stacking in addition to the presence of the carboxylic acid group.

The melting points that were determined, ranging from 115°C to 240°C (Table 2), were generally higher for the higher molecular weight carboxylic containing compounds (4a and 4b) than the corresponding alcohols (5a and 5b). The pyrene adducts 4c and 5c, have high glass transition temperatures but their melting points were not clearly defined on either the Melttemp or the DSC. This could be due to their highly substituted structure with the bulky pyrene group causing less packing in the solid state making them highly amorphous.

The potential hole transport properties of the compounds 4a-c and 5a-c was analyzed by Spartan theoretical calculation of the HOMO and LUMO energies of the compounds comparing the values to the novel TMOADN and the standard commercial hole transporter NPB (Table 3). The results showed similar energy values for all
compounds and including the standards so this suggests that the compounds should have good hole transport properties.

**Table 2.** Optical properties and melting points of 9,10-diarylanthracenes 4a-c and 5a-c

<table>
<thead>
<tr>
<th>Compd</th>
<th>UV-Vis (absorption) Max $\lambda_{\text{max}}$ (nm) (molar absorptivity x $10^3$)</th>
<th>UV-Vis (absorption) Max $\lambda_{\text{max}}$ (nm) Absorbance Thin films</th>
<th>Fluorescence maxima $\lambda_{\text{max}}$ (nm) Soln,[thin films]</th>
<th>Rel fluor (quantum yield) $Q_f$</th>
<th>Abs energy band gap (nm), (eV)</th>
<th>Mp (°C)</th>
</tr>
</thead>
<tbody>
<tr>
<td>4a</td>
<td>276 (96.76) 374 (12.31)</td>
<td>377</td>
<td>446, [411]</td>
<td>0.063</td>
<td>412 (2.91)</td>
<td>228-232</td>
</tr>
<tr>
<td>4b</td>
<td>273 (99.62) 375 (12.44)</td>
<td>378</td>
<td>438, [428]</td>
<td>0.058</td>
<td>418 (2.87)</td>
<td>234-240</td>
</tr>
<tr>
<td>4c</td>
<td>276 (83.79) 339 (18.67) 366 (10.21) 372 (10.79)</td>
<td>346</td>
<td>479, [464]</td>
<td>0.197</td>
<td>426 (2.82)</td>
<td>120-125 (Tg)</td>
</tr>
<tr>
<td>5a</td>
<td>274 (70.30) 359 (10.60)</td>
<td>377</td>
<td>408, [428]</td>
<td>0.325</td>
<td>401 (2.99)</td>
<td>197-203</td>
</tr>
<tr>
<td>5b</td>
<td>276 (122.01) 377 (15.33)</td>
<td>361</td>
<td>417, [437]</td>
<td>0.39</td>
<td>415 (2.89)</td>
<td>202-205</td>
</tr>
<tr>
<td>5c</td>
<td>277 (150.57) 322 (17.59) 338 (26.59) 370 (18.76) 381 (14.55)</td>
<td>346</td>
<td>476, [447]</td>
<td>0.17</td>
<td>420 (2.86)</td>
<td>115-120 (Tg)</td>
</tr>
<tr>
<td>anthracene</td>
<td>ND</td>
<td>ND</td>
<td>ND</td>
<td>ND</td>
<td>ND</td>
<td>ND</td>
</tr>
</tbody>
</table>

*a* Average value for n=3 (except 4b, n=2) with standard deviation. *b* Average value for n=3 (4b, n=2) with standard deviation. ND = not determined. $(\varepsilon)$ is the molar extinction coefficient for each compound in solution ($8.6 \times 10^6$ M)
Table 3. Approximate HOMO and LUMO energies of synthesized anthracene derivatives relative to standards

<table>
<thead>
<tr>
<th>CMPD</th>
<th>HOMO</th>
<th>LUMO</th>
</tr>
</thead>
<tbody>
<tr>
<td>4a</td>
<td>-4.33</td>
<td>-1.55</td>
</tr>
<tr>
<td>4b</td>
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<tr>
<td>4c</td>
<td>-4.77</td>
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<tr>
<td>5c</td>
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<tr>
<td>TMOADN</td>
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<td>-1.54</td>
</tr>
<tr>
<td>NPB</td>
<td>-4.80</td>
<td>-1.15</td>
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</tbody>
</table>

Spartan Density Functional Theory (B3LYP) single point energy calculation

Conclusion

All the anthracene derivatives compounds that were synthesized are stable in air, highly amorphous, and show high thermal stability, and also fluoresce in solid state thin films. These physical properties are very important for organic compounds to be useful in OLEDs. The use of silver (I) oxide in the Suzuki coupling reactions was very important for obtaining high yields of products even though debromination still occurred in the synthesis of compound 4c. This shows that further research needs to be done to prevent debromination from occurring which will improve the yield. I am very confident that this method will be used successfully by other researchers who have problems doing Suzuki coupling reactions with methoxy-substituted bromoanthracene compounds.

The fluorescence emission spectra show the compounds strongly fluoresce in the blue region which is a very important desired primary color for OLED applications. Further studies need to be done to fully understand the differences between the atropisomers of compounds 4c and 5c and this can be done by experiment together with
quantum mechanical calculations. The tetramethoxyanthracene derivatives have been found to be useful as hole transport materials and this suggests that all the anthracene derivatives; (4a, 4b, 4c, 5a, 5b and 5c) are potentially useful as hole transport materials in OLED applications and construction of OLED devices needs be done to prove this. Even though the optical energy bandgap has been determined for all the compounds, the HOMO and LUMO values need to be determined experimentally, as well as the stability of the compounds in an electric field. The level of the HOMO and LUMO energies is the most important compared to other characteristics such as the melting points. The compounds that were synthesized have more \( \pi \)-electron donating oxygen atoms so they will have higher level HOMO and LUMO energies and this will also make them potentially useful for use in OLED as hole injection and electron blocking materials. Finally this research offers a good prospect for OLEDs because the presence of the carboxylic acid group on the bromoanthracene starting compound for the Suzuki coupling is good for designing many synthetic strategies to make more highly functionalized anthracene derivatives for OLEDs. The work in this part of my research project was published in the *Journal of Organic Chemistry*.\(^{41}\)

**Experimental**

The CTV starting materials and all intermediates were synthesized as shown in the reaction schemes above. The solvents used in synthesis of the final compound were distilled and dried but all other reagents and solvents were purchased commercially and
used without purification. The NMR spectra were measured with INOVA 300 and 500 MHz spectrometers. The UV absorbance spectra were measured with a Shimadzu UV-2450 UV-Visible spectrophotometer while the fluorescence in solution was measured with Quanta Master Model QM-1 and Ratio Master from PTI and the fluorescence of the solid thin films was measured HoribaJobnyvon fluorolog-3. High resolution mass spectra of the compounds were done by time-of-flight electrospray ionization.

**Cyclotrimeronone (1)**

Veratryl alcohol (8.13 g, 48.3 mmol) was added to formic acid (124 mL) and stirred at 60°C for 5 hours and then allowed to cool down to room temperature. Cold distilled water (200 mL) was added to the reaction and stirred for an hour in an ice-bath. It was then vacuum filtered and the sample was air dried overnight. The sample was dried in a vacuum at 100°C for 5 h. The crude product was recrystallized from toluene containing a few drops of chloroform and washed with cold toluene and air dried for 48 h to give cyclotrimeronone 1 as white needle crystals (3.59 g, 50%). $^1$H NMR (CDCl$_3$), $\delta$ 6.83 (6H, s), 4.78 (3H, d, J=14.0 Hz), 3.84 (18H, s), 3.56 (3H, d, J=14.0 Hz).

**CTV-Diketone, 2b**

Cyclotrimeronone (CTV), 1 (4.28 g, 9.50 mmol) was placed in a 500-mL reactor and to this was added a finely ground uniform mixture of potassium permanganate (60 g, 380 mmol) and activated manganese dioxide (66.0 g, 760 mmol), and 120 mL of
pyridine. The reaction mixture was stirred vigorously under reflux for 18 h. The reaction mixture was then vacuum filtered hot (90°C) through a bed of Celite. The reactor and Celite bed were rinsed with ethyl acetate followed by dichloromethane (100 mL each). The organic solvent was removed via reduced pressure (50°C, 10 mm Hg). The crude material was further dried in vacuo at 100°C for 1 h to give a pale yellow solid (3.62 g). Chromatography on silica gel (40:1 loading ratio), eluting with methylene chloride, followed by a step gradient of ethyl acetate/methylene chloride (5/95 to 50/50), afforded CTV-monoketone 2a\textsuperscript{26,27} (1.40 g, 32%) followed by CTV-diketone 2b\textsuperscript{12} (1.88 g, 41%): mp 138-144°C. \textsuperscript{1}H NMR δ 7.20 (2H, s), 6.98 (2H, s), 6.52 (2H, s), 3.92 (12H, s), 3.88 (2H, bs), 3.86 (6H, s). \textsuperscript{13}C NMR δ 196.2, 151.7, 150.2, 147.5, 135.2, 133.6, 131.1, 111.7, 111.3, 109.5, 109.4, 55.8, 55.7, 55.7, 55.6, 55.6.

2-(10-Bromo-2,3,6,7-tetramethoxyanthracen-9-yl)-4,5-dimethoxybenzoic acid (3a)

CTV-diketone 2b (256 mg, 0.535 mmol) was added to N-bromosuccinimide (95 mg, 0.53 mmol) and benzoyl peroxide (1.3 mg, 0.0046 mmol) dissolved in 1,2-dichloroethane (3 mL) and heated to 70°C for 2 h and then cooled to room temperature, diluted with 20 mL de-ionized water, and acidified to pH 2-3 using conc hydrochloric acid. The resulting mixture was extracted with dichloromethane (3 × 40 mL) and the combined organic layers were washed with brine (3 × 40 mL) and dried over MgSO₄. Concentration under reduced pressure afforded a residue which was purified by silica gel column chromatography eluting with ethyl acetate/dichloromethane to afford bromoanthracene 3a (231 mg, 77%): mp 224-226°C. \textsuperscript{1}H NMR δ 7.73 (1H, s), 7.51 (2H,
s), 6.73 (1H, s), 6.53 (2H, s), 4.10 (6H, s), 4.03 (3H, s), 3.83 (3H, s), 3.69 (6H, s). ^13^C NMR δ 169.9, 153.0, 150.7, 149.6, 135.2, 132.9, 126.52, 126.48, 122.5, 118.2, 114.9, 114.0, 105.6, 103.9, 56.6, 56.4, 56.2, 56.0. The benzoic acid proton was not observed due to rapid exchange with water. The structure of 3a was ultimately confirmed by X-ray crystallography (CH\textsubscript{2}Cl\textsubscript{2}/heptane) as seen in Fig 8.\textsuperscript{43,26} Spiro lactone derivative 3c (16\%) was also obtained. Repeat of the reaction with chloroform as solvent gave ethyl ester\textsuperscript{41} derivative 3b (18.4\%), 3a (58.3\%) and spiro lactone derivative 3c (2.4\%) reported in the literature.\textsuperscript{44,43,26,41}

4,5-Dimethoxy-2-(2,3,6,7-tetramethoxy-10-phenylanthracen-9-yl) benzoic acid (4a)

Bromo-anthracene 3a (154 mg, 0.28 mmol), Pd(PPh\textsubscript{3})\textsubscript{4}, (971 mg, 30 mol\%), phenyl boronic-acid (102.4 mg, 0.84 mmol) potassium fluoride (97 mg, 1.7 mmol) and silver (I) oxide (71 mg, 0.31 mmol) was added to 2-methoxyethanol (0.5 mL) and THF (0.5 mL). The mixture were degassed by flushing under nitrogen and then heated in a sealed tube at 90-100°C for 24 h. The reaction mixture was allowed to cool to room temperature and diluted with 20 mL cold de-ionized water. It was then acidified with conc HCl to pH 2-3 and extracted four times with 20 mL of dichloromethane. The combined organic layers were washed twice with water (40 mL), dried over anhydrous Na\textsubscript{2}SO\textsubscript{4}, concentrated under reduced pressure and the raw material was purified by silica gel chromatography using methylene chloride/ethyl ether and ethyl ether/ethyl acetate: 100/0 to 10/100 with 10\% increments for each ratio to afford 10-phenyl anthracene 4a as a light orange solid (72 mg, 96\%): ^1^H NMR δ 7.81 (1H, s), 7.75-7.40 (6H, m), 6.83
(1H, s), 6.81 (2H, s), 6.61 (2H, s), 4.07 (3H, s), 3.86 (3H, s), 3.71 (6H, s). $^{13}$C NMR δ 168.5, 152.8, 149.2, 148.8, 148.1, 139.6, 139.1, 135.3, 133.4, 131.3, 131.1, 130.9, 128.68, 128.66, 127.5, 125.80, 125.76, 125.70, 122.4, 114.9, 113.8, 104.1, 103.2, 56.3, 56.1, 55.6, 55.5. ESI Pos m/z calcd for M-1 C$_{33}$H$_{29}$O$_8$ 553.1862, found 553.1833. FTIR (neat): ν 3527 (br), 2999, 2936, 2831, 1491, 1238 cm$^{-1}$; Td = 381.2°C.

4,5-Dimethoxy-2-(2,3,6,7-tetramethoxy-10-(naphthalen-2-yl)anthracen-9-yl)benzoic acid (4b)

Bromo-anthracene 3a (156 mg, 0.280 mmol), Pd(PPh$_3$)$_4$ (97 mg, 0.084 mmol), naphthyl-2- boronic-acid (145 mg, 1.40 mmol) potassium fluoride (60 mg, 1.7 mmol) and silver (I) oxide (71 mg, 0.31 mmol) were added to a mixture of 2-methoxyethanol (4.5 mL) and THF (6.5 mL). The mixture was degassed by flushing under nitrogen and then heated in a sealed tube at 90-100°C for 48 h. The reaction mixture was allowed to cool to room temperature and diluted with cold de-ionized water (20 mL). It was then acidified with conc HCl to pH 2-3 and then extracted with dichloromethane (4 × 20 mL). The combined organic layers were washed with water (2 × 40 mL) and dried with Na$_2$SO$_4$. The solution was then concentrated under reduced pressure and purified by silica gel chromatography using methylene chloride/ethyl ether followed by ethyl ether/ethyl acetate (100% to 10% with 10% increments for each interval) to afford naphthyl derivative 4b as a light tan solid (111 mg, 88%); $^{1}$H NMR δ 8.10–7.90 (4H, m), 7.80 (1H, s), 7.70–7.55 (3H, m), 6.80 (3H, s), 6.60(2H, s), 4.06 (3H, s), 3.9 (3H, s), 3.7 (6H, s), 3.6 (6H,s). $^{13}$C NMR δ 170.2, 153.0, 149.3, 149.2, 148.3, 137.6, 137.4, 135.8, 135.8, 133.9,
133.1, 133.1, 133.0, 132.2, 130.4, 130.2, 129.8, 129.6, 128.5, 128.4, 128.3, 128.2, 128.1, 126.6, 126.5, 126.4, 125.9, 124.0, 104.3, 103.6, 56.6, 56.4, 55.9, 55.8. HRMS-TOF calcd for C$_{37}$H$_{32}$O$_8$ 604.21, found m/z 603.3 (M-1); HRMS ESI calcd for MH$^+$ C$_{37}$H$_{33}$O$_8$ 605.2175, found 605.2163. FTIR (neat): ν 3526 (br) 2935, 2831, 1491, 1237 cm$^{-1}$ Tg = 143.5°C.

**4,5-Dimethoxy-2-(2,3,6,7-tetramethoxy-10-(pyren-1-yl)anthracen-9-yl)benzoic acid (4c)**

Bromo-anthracene 3a (100 mg, 1.0 mmol), Pd (PPh$_3$)$_4$, (75.2 mg, 0.065 mmol), pyrene-1-boronic-acid (199 mg, 0.809 mmol), potassium fluoride (93.9 mg, 1.62 mmol) and silver (I) oxide (50 mg, 0.22 mmol) were added to 2-methoxyethanol (25 mL). The mixture was degassed by flushing with nitrogen and then heated in a sealed tube at 130°C for 48 h. The reaction was allowed to cool to room temperature and diluted with 20 mL cold de-ionized water, and then acidified with concentrated HCl to pH 2-3 and then extracted four times with 20 mL of dichloromethane. The combined organic layers were washed twice with water (40 mL) and dried over anhydrous Na$_2$SO$_4$. Concentration under reduced pressure and purification of the resulting residue by silica gel chromatography eluting with methylene chloride/ethyl ether followed by ethyl ether/ethyl acetate (100% to 10 % with 10 % increments for each interval) afforded pyrenyl derivative 4c (95.5 mg, 79 %) as a light cream-colored solid. $^1$H NMR (mixture of atropisomers; doubled peaks noted) δ 8.42–8.40 and 8.41–8.38 (1H, 2d, J=7.8 Hz), 8.28-8.01 (8H, m), 7.90 (1H, s), 7.86-7.83 and 7.85-7.82 (1H, 2d, J=9.0 Hz), 7.52-7.49 and 7.51-7.48 (1H, 2d, J= 9.0 Hz),
7.00 and 6.99 (1H, 2s), 6.72 (2H, s), 6.51 (2H, s), 4.12 (3H, s), 3.96 and 3.93 (3H, 2s),
3.74 (6H, s), 3.35 (6H, s); $^{13}$C NMR δ 168.8, 168.6, 152.8, 149.28, 149.25, 149.18,
149.14, 148.2, 135.5, 135.4, 134.7, 132.1, 132.0, 131.4, 131.3, 131.24, 131.16, 131.0,
130.43, 129.6, 129.2, 129.0, 128.2, 127.6, 126.9, 126.8, 126.1, 125.8, 125.7,
125.3, 125.2, 125.1, 124.9, 122.6, 122.5, 115.0, 114.9, 113.9, 109.7, 104.3, 104.23,
104.16, 103.4, 56.4, 56.2, 55.7, 55.6, 55.43, 55.37.

HRMS –TOF calcd for C$_{43}$H$_{34}$O$_8$ 678.23, found m/z 677.3 (M-1). HRMS ESI MH$^+$ calcd
for C$_{43}$H$_{35}$O$_8$ 679.2332, found 679.2289. FTIR (neat): ν 3527 (br) 2920, 2851, 1738 and
1717 (atropisomer C=O’s), 1461, 1260 cm$^{-1}$; Tg =130.13°C, Tm=228.78°C,
Td=348.37°C. Tg =120-125°C. The individual atropisomers were separated by
preparative plate chromatography to afford the two separate atropisomers of 4c: $^1$H
NMR for second eluted isomer δ 8.41 (1H, d, J=7.9 Hz), 8.28 (1H, dd, J=7.9, 4.0 Hz, 3.9
Hz), 8.23 (2H, d, J = 4.4 Hz), 8.04 (1H, t, J = 8.0 Hz), 8.12 (2H, m), 7.90 (1H,  s), 7.83
(1H, d, J=9.2 Hz), 7.49 (1H, d, J= 9.2 Hz), 6.99 (1H, s), 6.75 (2H, s), 6.50 (2H, s), 4.12
(3H, s), 3.96 (3H, s), 3.75 (6H, s), 3.35 (6H, s).

(4,5-dimethoxy-2-(2,3,6,7-tetramethoxy-10-phenylanthracen-9-yl)phenyl)methanol
(5a)

Phenyl anthracene derivative 4a (122 mg, 0.22 mmol) was dissolved in THF
(0.4 mL). A solution of lithium aluminum hydride (0.45 mL, 0.45 mmol, 1.0 M in THF)
was added gradually via syringe and the reaction was then heated to reflux under nitrogen
for 19 h. It was then allowed to cool to room temperature and diluted with 15% aqueous
sodium hydroxide (1.0 mL), stirred for 10 min and then diluted with THF (1.0 mL) followed by water (1.0 mL). The reaction was dried over MgSO₄, filtered, and washed successively with THF, dichloromethane and ethyl acetate. Concentration under reduced pressure afforded a residue which was purified by silica gel column chromatography eluting with toluene/dichloromethane and dichloromethane/ether (100% to 10% with 10% increments for each interval) to obtain 5a as a light orange solid product (92.6 mg, 88%): ¹H NMR δ 7.80–7.40 (6H, m), 6.86 (1H, s), 6.82 (2H, s), 6.69 (2H, s), 4.23 (2H, s), 4.05 (3H, s), 3.85 (3H, s), 3.72 (6H, s), 3.71 (6H, s); ¹³C NMR δ 149.0, 148.7, 148.26, 148.2, 139.2, 139.1, 133.1, 132.3, 130.6, 130.1, 129.6, 129.4, 128.3, 127.2, 125.8, 125.5, 113.43, 113.39, 111.0, 103.9, 103.8, 102.94, 102.88, 62.85, 55.5, 55.7, 55.5, 55.4, 55.3, 55.2, 55.1. HRMS-TOF m/z calcd for [C₃₃H₃₂O₇]+Na⁺ 563.2046, found 563.2048 (M+Na⁺); FTIR (neat): ν 3498 (br) 2916, 2848, 1489, 1235 cm⁻¹; Tg =165.6°C. Tm =197-203°C (MeltTemp).

(4,5-Dimethoxy-2-(2,3,6,7-tetramethoxy-10-(naphthalen-2-yl)anthracen-9-yl)phenyl)methanol (5b)

Naphthyl anthracene derivative 4b (88 mg, 0.145 mmol) was dissolved in THF (0.29 mL). A solution of lithium aluminum hydride (0.29 mL, 0.29 mmol, 1.0 M in THF) was added gradually by a syringe and the reaction was heated under reflux under nitrogen for 24 h. The reaction was then allowed to cool to room temperature and diluted with aqueous 15% sodium hydroxide (1.0 mL), stirred for 10 min and then diluted with THF (1.0 mL) followed by 1.0 mL water, dried with MgSO₄, filtered and washed with THF,
dichloromethane and ethyl acetate, then concentrated under reduced pressure and purified by silica gel column chromatography eluting with toluene/dichloromethane and dichloromethane/ether (100% to 10% with 10% increments for each interval) to obtain 5b as a light orange solid product (85.9 mg, 100%). \(^1\)H NMR \(\delta\) 8.06 (1H, dd, \(J = 8\) Hz, \(J = 4\) Hz), 8.04-7.90 (3H, m), 7.68-7.56 (3H, m), 7.31 (1H, s), 7.16 (1H, d, \(J = 8\) Hz), 6.89 (1H, s), 6.86 (2H, s), 6.73 (2H, s), 4.20 (2H, s), 4.07 (3H, s), 3.90 (3H, s), 3.74 (6H, s), 3.60 (6H, s), 2.30 (1H, s); \(^{13}\)C NMR \(\delta\) 149.7, 149.4, 148.90, 148.85, 137.40, 137.37, 134.0, 133.4, 133.0, 132.9, 130.8, 130.3, 130.2, 129.6, 129.3, 128.6, 128.5, 128.4, 128.2, 126.6, 126.5, 126.3, 125.6, 114.0, 114.0, 111.6, 104.5, 104.4, 103.61, 103.57, 63.5, 56.4, 56.2, 55.99, 55.96, 55.9, 55.8; HRMS-ESI calcd for C\(_{37}\)H\(_{34}\)O\(_7\) 590.6620, m/z found 590.2293 (M+)\(^+\), 573.2279 (M-OH)\(^+\), 613.2188 (M+Na\(^+\)). Tm = 202-205°C (MeltTemp).

\((4,5\text{-Dimethoxy-2-(2,3,6,7-tetramethoxy-10-(pyren-1-yl)anthracen-9-yl)phenyl})\) methanol (5c)

Pyrenyl adduct 4c (56.4 mg, 0.085 mmol) was dissolved in THF (0.4 mL). A solution of lithium aluminum hydride (0.37 mL, 0.37 mmol, 1.0 M in THF) was added gradually by a syringe and the reaction was heated under reflux for 24 h. The reaction was then allowed to cool to room temperature and was diluted with 15% aqueous sodium hydroxide (1.0 mL), stirred for 10 minutes and then diluted with THF (1.0 mL) followed by water (1.0 mL). The reaction was dried over MgSO\(_4\), filtered, and washed with THF, dichloromethane, and ethyl acetate, concentrated under reduced pressure and the resulting
residue was purified by silica gel column chromatography eluting with toluene/dichloromethane and ether to obtain a light orange solid product (54.2 mg, 96%):

\(^1\)H NMR (mixture of atropisomers) \(\delta\) 8.44–8.42 and 8.43-8.40 (1H, 2d, J = 8.0 Hz), 8.30-8.00 (6H, m), 7.90 and 7.86 (1H, 2d, J= 9.0 Hz), 7.53- 7.50 and 7.51-7.48 (1H, 2d, J=9.0 Hz ), 7.36-7.34 (1H, d, J = 6.0 Hz ), 7.01 and 6.97 (1H, 2s), 6.80 (2H,s ), 6.52 (2H, s), 4.40 and 4.30 ( 2H, 2s), 4.12 (3H, s), 3.94 and 3.91 (3H, 2s), 3.77 (6H, s), 3.37 (6H, s).

\(^13\)C NMR \(\delta\) 149.7, 149.5, 148.9, 134.8, 132.9, 131.7, 131.6, 131.4, 131.3, 131.2, 130.6, 130.3, 129.5, 127.9, 127.2, 126.5, 126.0, 125.5, 125.3, 125.2, 114.0, 104.5, 103.6, 88.6, 88.1, 87.7, 63.6, 56.4, 56.2, 56.0, 55.7. HRMS-ESI m/z calcd for C\(_{43}\)H\(_{36}\)O\(_7\) 664.742, found 664.2456; calced for C\(_{43}\)H\(_{35}\)O\(_6\) [M-OH]\(^+\) 647.2433, found 647.2446; calculated for C\(_{43}\)H\(_{36}\)O\(_7\)Na [M+Na]\(^+\), found 687.2356. Tg =115-120\(^\circ\)C (MeltTemp)

**Table 4. Quantum yield calculation**

<table>
<thead>
<tr>
<th>Compound</th>
<th>Conc (10(^{-7})M)</th>
<th>Abs at 365 nm(^a)</th>
<th>Integrat Fluor (10(^{-7}))(^b)</th>
<th>Rel fluor (quantum yield) Q(_f)</th>
</tr>
</thead>
<tbody>
<tr>
<td>4a</td>
<td>9.10</td>
<td>0.004(±0.001)</td>
<td>1.82 (±0.16)</td>
<td>0.063</td>
</tr>
<tr>
<td>4b</td>
<td>3.98</td>
<td>0.004(±0.001)</td>
<td>1.89 (±0.21)</td>
<td>0.058</td>
</tr>
<tr>
<td>4c</td>
<td>2.23</td>
<td>0.004(±0.001)</td>
<td>8.36 (±0.82)</td>
<td>0.197</td>
</tr>
<tr>
<td>5a</td>
<td>9.31</td>
<td>0.004(±0.001)</td>
<td>11.4 (±0.78)</td>
<td>0.325</td>
</tr>
<tr>
<td>5b</td>
<td>2.39</td>
<td>0.003(±0.001)</td>
<td>12.6(±1.65)</td>
<td>0.39</td>
</tr>
<tr>
<td>5c</td>
<td>1.26</td>
<td>0.003(±0.001)</td>
<td>6.15(±0.24)</td>
<td>0.17</td>
</tr>
<tr>
<td>anthracene</td>
<td>3.26</td>
<td>0.003(±0.001)</td>
<td>10.8(±0.32)</td>
<td>ND</td>
</tr>
</tbody>
</table>

\(Q_f = (A_s/A_x)(I_x/I_s)(n_x/n_s)^2(0.27)\) \(n_s = 1.4244\) \(n_x = 1.361\)
CHAPTER 2

INTERMOLECULAR TANDEM BECKMANN REARRANGEMENT: SYNTHESIS
OF BENZOPHENONE DERIVATIVES, ARYLAMINES, IMINES AND
QUINAZOLINES

Introduction

The Beckmann rearrangement is a well-known reaction that has been utilized in the synthesis of many organic compounds and the mechanism has been well studied. A recent intramolecular tandem Beckmann rearrangement involving CTV oxime was reported, which gave insights as to how the reaction conditions could be changed to obtain other products. This was utilized in the synthesis of CTV lactam from the oxime in which additionally the nitrilium ion intermediate underwent a trans-annular intramolecular attack from an electron-donating methoxy group to form the tandem product. Dilution of the reaction mixture gave the amide while more concentrated reactions conditions gave the tandem product almost exclusively. The driving force of that reaction is certainly due to the fast intramolecular process; however, it is of interest to investigate if this tandem Beckmann process could occur in an intermolecular reaction between two molecules. The importance of this in organic synthesis is evident since this presents a new methodology for making a number of important organic compounds.
**Scheme 8.** Formation of the normal Beckmann and the tandem Beckmann-EAS product from CTV

The aim of this aspect of my research is to demonstrate the synthesis of organic molecules by using the intermolecular tandem Beckmann reaction mechanism outlined in Scheme 9, showing that the intermolecular reaction can occur between two molecules by using conditions that mimic the intramolecular CTV tandem Beckmann reaction.
**Scheme 9.** Intermolecular products available via the new tandem Beckmann-EAS reaction sequence

R = alkoxy, alkyl, halogen, or hydrogen.

In this regard, the reactivity of different molecules as \( \pi \)-nucleophiles in the Beckmann rearrangement reactions as well as contribution of other factors such as concentration of reactants and temperature has been investigated carefully by using the processes illustrated in above reaction scheme 9. The intermolecular mimic of the CTV-oxime reaction was done by reacting benzophenone oxime with trifluoromethanesulfonic anhydride (TFMSA)\(^{47} \) at higher temperatures to form a planar nitrilium ion intermediate. Induced high temperature nucleophilic attack from \( \pi \)-electrons of an available nucleophilic compound such as a benzene derivative will result in
formation of an imine. The first π-donor nucleophile employed was veratrole, since it mimics the CTV structural environment. The compounds that were utilized as π-nucleophiles to explore reactions are 1,4-dimethoxybenzene, anisole, toluene, xylenes, bromobenzene, chlorobenzene, benzonitrile and nitrobenzene. The intermediate imine could be isolated or converted to a ketone, an amine or a quinazoline. The ketone product is a benzophenone derivative in which one of the phenyl groups of the oxime has been replaced by the nucleophile.

**Scheme 10. Proposed mechanism for intermolecular tandem Beckmann reaction**

This imine is stable to base\textsuperscript{48} but not to acid, so a basic workup was used to enable isolation of the imine. In contrast, acid hydrolysis converts the imine to a ketone. Similar diaryl ketones have been made previously by several metal-catalyzed reactions including Friedel Crafts acylation of aromatic ethers,\textsuperscript{49} palladium catalyzed reactions,\textsuperscript{50,51} by
intermolecular \( N \)-heterocyclic carbene catalyzed hydroacylation of arynes,\(^{52}\) oxidative rhodium catalyzed homocoupling reactions,\(^{53}\) and other methods.\(^{54}\)

We then wished to reduce the imine to the corresponding amine by adding a reducing agent\(^{55,56}\) to the reaction mixture once it is certain that the intermediate imine is formed. This can be done in different solvent media such as THF or in other solvents such as such as toluene, methanol or other alcohols. We also wanted to demonstrate that nucleophiles such as methyllithium and phenyllithium could be added to the electron deficient imines to make new adducts compounds.\(^{57,58}\)

**Scheme 11.** Addition of nucleophiles to imines derived from the Tandem-Beckmann sequence.

![Scheme 11](image)

The synthesis of functionalized ketones,\(^{54}\) amines,\(^{59}\) and imines\(^{60,47}\) and quinazolines\(^{61}\) is significant because they form the basic structural units in the core of many important drugs and medicines for treating inflammations, malaria, cancer and other diseases. The oxime of benzophenone derivatives has been found to have potent anti-inflammatory activity by inhibiting secretory phospholipase A2 enzyme.\(^{62}\) An additional advantage of the tandem-Beckmann methodology is that most of these compounds, especially the ketones, have been made previously from metal catalyzed reactions where metal toxicity and purification of products is a great issue. This makes the present metal-free approach for making these compounds very important.
Results and Discussion

The intramolecular tandem Beckmanns reaction was observed to occur in synthesis alongside the synthesis of CTV-lactam, however we have now shown that the intermolecular tandem Beckmann reaction can to occur enabling the preparation of diarylketones from benzophenone. This occurred by the attack of π-nucleophiles on the nitrilium ion intermediate followed by acid hydrolysis of the imine intermediate to form the corresponding ketone (Schemes 8, 10, 12). The synthesis of diarylketones gave higher yields when methoxy and dimethoxy substituted π-nucleophiles (veratrole, p-methoxyanisole, and anisole) were used (Table 5). The yield from the methyl substituted π-nucleophiles (toluene and para-xylene) were slightly lower, while the halogen substituted π-nucleophiles (chlorobenzene and bromobenzene) gave the lowest yields (higher for bromobenzene than for chlorobenzene). This presumably occurred because the methoxy groups are more electron donating and this increases the nucleophilicity of the aromatic rings which speeds up the reaction compared to the alkyl groups in toluene and xylene. The electron donating ability of the nucleophilic aromatic substrates bearing halogen substituents (Cl and Br) is offset by the electronegativity of the halogens which are π-electron donating and sigma-deactivating substituents. This decreases the nucleophilicity of the π-nucleophile benzene ring resulting in lower yields of product.

All the products are mixtures of ortho and para isomers except for the 1,4-disubstituted π-nucleophiles which mainly react in the ortho position. This was evident in the proton
NMR spectra of the compounds especially for the products of reactions of toluene and anisole $\pi$-nucleophiles which showed traces of the ortho isomer.

The Tandem Beckmann reaction occurred in 1,2-dichloroethane solvent but not in THF as solvent. This could be due to the fact the THF has lone pair of electrons on the oxygen atom and might have acted as a Lewis base and attacked the TFMSA which is a highly reactive Lewis acid. The reactions are very sensitive to moisture and the presence of other nucleophiles. The reactions in solvent were easy to purify compared to the neat reactions, and very similar yields were obtained for the $\pi$-nucleophiles of veratrole and the 1, 4-dimethoxybenzene nucleophiles, toluene and para-xylene even though toluene and p-xylene gave slightly lower yields. The reactions were performed at 1.0 M concentration for the alkoxybenzene nucleophiles and 2.0 M for the alkylbenzenes. However, the bromobenzene and chlorobenzene nucleophiles were much more concentration dependent and did not react at 2.0 M concentration. Lower yields were obtained at 4.0 M concentration with a marked improvement was observed when running the reactions at 8.0 M concentration. Yields of ketone product obtained by acid hydrolysis of the isolated imine were lower than when the imine was hydrolyzed directly in an aqueous workup without attempting to isolate the imine.
Scheme 12. Mechanism of imine hydrolysis

![Reaction Mechanism Diagram]

The deactivating and meta-directing substituents (benzonitrile and nitrobenzene) resulted in formation of different products from what were expected. The benzonitrile formed two compounds after acid hydrolysis; an imine and a quinazoline. The imine intermediate survived the acid hydrolysis because the resonance structures show the location of the positive (+) charge in the ring with nitrile functional group will result in a higher energy intermediate and this prevented the formation of the ketone.

Scheme 13. Resonance structures for mechanism of formation of imine from the nitrile adducts.

![Resonance Structures Diagram]

The quinazoline was formed apparently by nucleophilic attack by the cyano group on the intermediate nitrilium cation leading to formation of another nitrilium cation intermediate which is a cis isomer (Z isomer). Nucleophilic attack by the π-system of the benzene attached to the nitrogen and followed by deprotonation and cyclization to restore aromaticity forms the quinazoline. However only the quinazoline was obtained when the
reaction was done in solvent (Table 5) therefore making this another pathway for the synthesis of quinazolines. Previously, quinazolines have been synthesized by a similar method with amide starting material instead of oxime, whereas the other methods are mostly metal catalyzed reactions such as zinc chloride catalyzed reaction of aldehydes and 2-aminoarylalkanones-\(O\)-phenyl oximes or by air-assisted copper (I) chloride catalyzed reactions. 

**Scheme 14.** Proposed mechanism for formation of quinazolines

The reactions of the nitrobenzene as the \(\pi\)-nucleophile gave a complex aromatic adduct of nitrobenzene that was difficult to analyze. Therefore future work should focus on the detailed study of nitrobenzene \(\pi\)-nucleophiles in Tandem Beckmann reactions to understand how they react and what products are formed.
Table 5. Synthesis of diarylketones via the Tandem-Beckmann sequence

<table>
<thead>
<tr>
<th>π-nucleophile</th>
<th>product</th>
<th>Yield (%) (neat)</th>
<th>Yield (%) (solution)</th>
</tr>
</thead>
<tbody>
<tr>
<td>O</td>
<td>![Product Image]</td>
<td>97</td>
<td>72 (1.0M)</td>
</tr>
<tr>
<td>O</td>
<td>![Product Image]</td>
<td>91</td>
<td>91 (1.0M)</td>
</tr>
<tr>
<td>O</td>
<td>![Product Image]</td>
<td>95</td>
<td>96 (1.0M)</td>
</tr>
<tr>
<td>O</td>
<td>![Product Image]</td>
<td>95</td>
<td>70 (2.0M)</td>
</tr>
<tr>
<td>O</td>
<td>![Product Image]</td>
<td>75</td>
<td>93 (2.0M)</td>
</tr>
<tr>
<td>Br</td>
<td>![Product Image]</td>
<td>75</td>
<td>34 (4M) 64 (8M)</td>
</tr>
<tr>
<td>Cl</td>
<td>![Product Image]</td>
<td>68</td>
<td>19 (4M) 59 (8M)</td>
</tr>
</tbody>
</table>
All neat reactions were done at approximate temperature of 100°C but the reactions in solution were done at reflux temperature of the solvent 1, 2-dichloroethane at 84°C. Reactions were run under the same conditions for 24 hours. All products were obtained as para products with approximately 10% of the otho adduct isomer except those reactions involving 1,4-disubstituted nucleophiles and the nitrile nucleophiles.

None of the imines adducts could be isolated in pure form and were mixed with the corresponding ketones except for the para-xylene imine adduct that was isolated in the pure form (Scheme 15).
Scheme 15. Isolation of imine intermediates from the Tandem-Beckmann sequence

It is believed that some of the imines have reacted with the silica gel during purification resulting in conversion to the ketone. Imines exist as E/Z isomers with the E-isomer\textsuperscript{48} as the most stable predominant form, but isomerization to the Z-isomer occurs in acid media (Scheme 16).\textsuperscript{60} Thus, the reaction with the silica gel depends on the stability of the protonated form compared to the neutral form. Stability is related to the number of stable resonance forms for the E and Z isomers of each adduct. Equilibrium of the neutral and protonated form of each adduct exists so that the protonated forms undergo hydrolysis on the silica gel to form the ketone. This resulted in the isolation of the mixture of imine and ketone from the silica gel column chromatography.
However it was observed that the 1,4-dimethyl imine adduct was isolated in pure form with no ketone contamination based on the $^1$H NMR spectrum. The methyl substituents could have resulted in a structure that is less reactive with silica due to its spatial orientation and its mild reactivity on silica gel. This methyl group at the ortho position might be sterically preventing the protonation of the nitrogen atom of the imine double bond and subsequent isomerization to the Z-isomer (Scheme 17). The steric environment may force the imine out of conjugation with the xylene phenyl group, thus there is very little resonance so the C-N bond maintains short and strong double bond character and therefore is resistant to hydrolysis. This is not important in excess acid solution since the equilibrium is forced to the right resulting in formation of the ketone.
Scheme 17. Steric effect and resistance to hydrolysis of 1,4-dimethyl adduct

All the other compounds have substituents para to the ipso carbon so there is no steric effect in formation of the Z-isomer resulting in almost equal amounts of E and Z isomers and the positive charged Z-isomer intermediate exists long enough to be hydrolysed to the ketone (Scheme 16). It was also found that the 1,4-paradimethoxy imine adduct reacted with the silica gel but not the 1,4-dimethyl imine adduct. This was unexpected since both compounds have the same 1,4-substituted phenyl groups and the methoxy groups are larger than the methyl groups. This might have occurred due to electron donating effect of the oxygen atoms of the methoxy groups leading to increased electron density, basicity and reactivity of the imine nitrogen atom and created extra resonance structures and stabilized the iminium ion intermediate (Scheme 18). This effect might have overridden any effects of the spacial orientation of the substituents so that a significant amount of the ion will exist in equilibrium which will hydrolyze to the ketone.
**Scheme 18.** Proposed mechanism for hydrolysis of the 1,4-dimethoxy adduct

![Scheme 18](image)

**Table 6.** Imine and amine products from the Tandem Beckmann sequence

<table>
<thead>
<tr>
<th>Imine</th>
<th>Yield of imine (%)</th>
<th>Amine</th>
<th>NaBH$_4$/THF Yield (%)</th>
<th>NaBH$_4$/Methanol Yield (%)</th>
<th>LAH/THF Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><img src="image" alt="Imine" /></td>
<td>67</td>
<td><img src="image" alt="Amine" /></td>
<td>57</td>
<td>ND</td>
<td>14$^a$ (8$^b$)</td>
</tr>
<tr>
<td><img src="image" alt="Imine" /></td>
<td>58</td>
<td><img src="image" alt="Amine" /></td>
<td>8</td>
<td>51</td>
<td>28</td>
</tr>
<tr>
<td><img src="image" alt="Imine" /> (para + ortho)</td>
<td>91</td>
<td><img src="image" alt="Amine" /></td>
<td>ND</td>
<td>66</td>
<td>90</td>
</tr>
</tbody>
</table>
All imines contain some ketones as observed in the NMR spectra except the p-xylene adduct. All reactions were run for 24 hours. *Reduction yield 50°C and at †room temperature.

The amines were formed by in situ reduction55 of the corresponding imines with sodium borohydride in THF or methanol.66,67 Methanol gave higher yields than THF when the imine from the veratrole reaction was reduced in situ, presumably due to enhanced solubility of sodium borohydride in methanol compared to THF. The reduction
of the imine adducts of p-xylene and toluene in methanol resulted in hydrolysis of the imine to the corresponding ketone and hence the use of all protic solvents will cause this to happen. The problem was solved by the use of lithium aluminum hydride (LAH) in THF. This gave higher yields for all the amines except compounds with the di-methoxy adduct where O-demethylation\textsuperscript{68} was observed as a major side reaction. The rate of demethylation is highest at the ortho positions followed by meta and least at para positions.\textsuperscript{69} The amine products are racemic, since sodium borohydride and lithium aluminum hydride attack both faces of the imine intermediate.\textsuperscript{70} Yields for reduction generally followed the same trend as hydrolysis which was higher for the \(\pi\)-nucleophiles with electron donating and activating groups than deactivating groups except for the dimethoxy adducts. Reduction of the 1,4-dimethoxy adduct did not yield any desired product at the refluxing temperature but only demethylated product was obtained. However, low yields of products were obtained at 50\(^\circ\)C.

Synthesis of phenanthridines was attempted by in the tandem Beckmann reaction by using fluorenone oxime instead of benzophenone oxime (Scheme 19). However the reaction did not work and this could be due to the rigid planar structure of fluorenone such that the nitrilium ion intermediate will suffer significant strain resulting in the lack of reactivity of fluorenone oxime to undergo the tandem Beckmann’s reaction.
**Scheme 19.** Tandem Beckmann sequence employing fluorenone oxime

Addition of nucleophiles to the 1,4-dimethylimine adduct was done with methyl-lithium and phenyllithium as demonstrated previously for imines in the literature.\textsuperscript{57,58} However this did not work well, because the NMR and mass spectra showed that the reaction gave a mixture of products, with the desired product mixed with a compound that resembles a dimer.

**Conclusion**

These experiments have conclusively demonstrated that the intermolecular tandem Beckmann reaction sequence can be used for the synthesis of aryl ketones and other compounds, and the yields are comparable to other standard methods currently in use. Isolation of imines with electron donating groups proved very challenging a since these are not stable to moisture or the acidic silica. Reduction of the imines to amines gave variable yields depending on solvent and conditions used. This reaction also revealed that each para product formed has a trace of its ortho isomer and these are mainly due to the presence of ortho/para directors. The compounds that were synthesized have potential medicinal activity or are substructures of important synthetic intermediates for compounds with medicinal or pharmaceutical values and this underscores the importance of this methodology since all these compounds can be obtained from the same one-pot
step without isolation of any intermediates. The other advantage of this intermolecular tandem Beckmann reaction over other methods is that, four distinct functional group compounds can be obtained by using the same starting compound or the same reaction intermediate.

Previous synthesis of di-arylketones utilized mostly heavy metal-catalyzed reactions. This shows that the issues such as toxic metal catalysis and metal leaching into important synthetic compounds was completely eliminated in this current method and therefore will make it more preferable than other methods. Suitable conditions for reduction reactions should be found that has very little or no O-demethylation side reactions to maximize the yield of the amines. Similarly, it is possible that addition of nucleophiles to the imine could be improved in future studies.

**Experimental**

All solvents and chemicals were purchased fresh from Aldrich except p-xylene and toluene which were distilled. $^1$H NMR spectra were obtained from Varian INOVA spectrometers at either 300 or 500 MHz and $^{13}$C NMR spectra were obtained from Varian INOVA spectrometers at either 125 or 75 MHz.

**Benzophenone oxime**

Benzophenone (4.0 g, 21.0 mmol) was placed in a 500 mL round bottomed flask and hydroxylamine hydrochloride salt (15.25 g, 219.5 mmol) added to it. Pyridine (200 mL) was added and the reaction was heated to reflux at 130°C for 24 h. The reaction was allowed to cool to room temperature and diluted with 10% HCl (150 mL) and extracted with dichloromethane (5 x 60 mL). The combined organic layers were washed twice with
water (60 mL) and dried with magnesium sulfate and concentrated under reduced pressure. The product was precipitated by adding water and filtered and washed with water. The solid product was recrystallized from 70% ethanol to obtain benzophenone oxime as white crystals (4.2 g, 98%).

**Fluorenone Oxime**

Fluorenone (7.92 g, 44 mmol) was placed in a 500 mL round bottomed flask and hydroxylamine hydrochloride salt (30.6 g, 440 mmol) was added. Pyridine (200 mL) was added and the reaction was heated to reflux for 24 h. The reaction was allowed to cool to room temperature and diluted with 10% HCl (250 mL). It was then extracted with dichloromethane (4 x 200 mL) and washed with 200 mL water. The combined organic layers were dried with magnesium sulfate and concentrated under reduced pressure. It was precipitated by adding water and filtered and washed with water. The yellow solid product was recrystallized from 70% ethanol to obtain fluorenone oxime as yellow solid (8.18 g, 95%).

**Di-arylketones via the Tandem-Beckmann procedure**

Benzophenone oxime (1.0 mmol) was placed in a clean dry reaction tube. The phenyl nucleophilic compound (15.2 mmol) was added and heated under nitrogen gas until all solid was dissolved and then trifluoromethanesulfonic anhydride (2.02 mmol) was added gradually by a syringe. The reaction was heated at 100°C for 24 h and then allowed to cool down to room temperature and then diluted with THF (10 mL) and dilute hydrochloric acid (50 %, 10 mL) was added it was allowed to stir for an hour and then extracted with dichloromethane (4 x 20 mL) and then once with ethyl acetate (20 mL).
The combined organic layers were washed with water and then dried with magnesium sulfate, filtered and concentrated under reduced pressure. It was then purified by silica gel column chromatography using petroleum ether /toluene /methylene chloride and ether).

**Di-arylketones (solution synthesis)**

Benzophenone oxime (1.0 mmol) was dissolved with 1,2-dichloroethane (1.0 mL) in a clean dry reaction tube. The aryl nucleophile (2.0 mmol) was added and heated under nitrogen gas till all solid was dissolved and then trifluoromethanesulfonic anhydride (2.02 mmol) was added gradually by a syringe. The reaction was heated to reflux for 24 h and then allowed to cool down to room temperature and then diluted with THF (10 mL) and dilute hydrochloric acid (50 %, 10 mL). The mixture was then allowed to stir for at least an hour and then extracted with dichloromethane (4 x 20 mL) and then once with ethyl acetate (20 mL). The combined organic layers were washed with water and then dried with magnesium sulfate, filtered and concentrated under reduced pressure. The product was then purified by silica gel column chromatography using petroleum ether /toluene /methylene chloride and ether).

**Synthesis of imines**

Benzophenone oxime (1.0 mmol) was dissolved with 1,2-dichloroethane (1.0 mL) in a clean dry reaction tube. The π-nucleophile (2.0 mmol) was added and heated under nitrogen gas till all solid was dissolved and then trifluoromethanesulfonic anhydride (2.02 mmol) was added gradually by a syringe. The reaction was heated at 100°C for 24 h and then allowed to cool down to room temperature, and then saturated aqueous sodium
bicarbonate (10 mL) was added, after which the mixture was stirred for at least an hour and then extracted with dichloromethane (4 x 20 mL) and then once with ethyl acetate (20 mL). The combined organic layers were dried with magnesium sulfate, filtered and concentrated under reduced pressure. (Do not wash with water or brine in order to avoid imine hydrolysis.). It was then purified by silica gel column chromatography using petroleum ether /toluene /methylene chloride and ether).

**General synthesis of amines**

Benzophenone oxime (1.0 mmol) was placed in a clean dry reaction tube. The phenyl nucleophilic compound (2.0 mmol) was added and heated under nitrogen gas until all solid was dissolved and then trifluoromethanesulfonic anhydride (2.02 mmol) was added gradually by a syringe. The reaction was heated at 100°C for 24 h and allowed to cool to room temperature. Lithium aluminum hydride in THF solution (3.59 mmol, 1.0 M) was added by a syringe and the mixture was heated at 100°C for 15 h under nitrogen. It was allowed to cool to room temperature and carefully diluted with water (0.46 mL in 0.46 mL THF) followed by addition of 15% sodium hydroxide (0.46 mL) and 1.36 mL water. The solid foam was filtered off and washed with THF (5 mL x 3). The combined filtrate was concentrated under reduced pressure. It was then purified by silica gel column chromatography using (petroleum ether /toluene /methylene chloride and ether).

**Nucleophilic Addition to imines**

Solid imine (0.25 mmol) was placed in a clean dry reaction tube flushed with nitrogen gas. Freshly distilled anhydrous toluene (1.25 mL) was added to dissolve it, followed by TMEDA (1.31 mmol) and the mixture was then stirred at 0°C. Phenyllithium
(1.30 mmol) or methyllithium (0.82 mL, 1.31 mmol) was added by a syringe under nitrogen and then the mixture was allowed to warm back to room temperature for 24 h. It was diluted with saturated aqueous ammonium chloride (20 mL) and extracted four times each with dichloromethane (30 mL). The combined organic layers were washed with water and dried with magnesium sulfate, filtered and concentrated under reduced pressure. It was then purified by silica gel column chromatography using petroleum ether /toluene /methylen chloride and ether).

**Benzophenone oxime**

![Benzophenone oxime](image)

$^1$H NMR $\delta$ 9.08 (1H, br s), 7.47-7.31 (10H, m)

**Fluorenone oxime**

![Fluorenone oxime](image)

$^1$H NMR $\delta$ 8.80–8.60 (1 H, br s), 8.42-8.39 (1H, d, J=8.7 Hz), 7.75-7.72 (1H, d, J=8.7 Hz), 7.68-7.61(1H, m), 7.47-7.28 (4H, m)

**(2, 5-Dimethoxyphenyl)(phenyl)methanone**

![Dimethoxyphenyl](image)
$^1$H NMR $\delta$ 7.81–7.78 (2H, dd, J=8.5 Hz, J=1.5 Hz), 7.56-7.53 (1H, m), 7.46-7.41 (2H, m), 7.02-6.99 (1H, dd, J=9.0 Hz, J=3.0 Hz), 6.93-6.92 (2H, m), 3.78 (3H, s), 3.66 (3H, s);

$^{13}$C NMR $\delta$ 196.0, 153.4, 151.3, 137.5, 132.9, 129.7, 129.4, 128.6, 128.1, 117.2, 114.4, 113.0, 56.2, 55.7

(3,4-Dimethoxyphenyl)(phenyl)methanone$^{62}$

$^1$H NMR $\delta$ 7.72–7.69 (2H, m), 7.50-7.30 (6H, m), 6.84-6.82 (1H, d, J=8.4 Hz), 3.88 (3H, s) 2.87 (3H, s); $^{13}$C NMR $\delta$ 195.1, 152.7, 148.6, 137.9, 131.5, 129.8, 129.3, 111.7, 109.4, 55.68, 55.65, 55.60, 55.59

(4-Methoxyphenyl)(phenyl)methanone$^{73,74}$

$^1$H NMR $\delta$ 7.83–7.80 (2H, d, J=7.0 Hz), 7.75–7.74 (2H, d, J=8.0 Hz), 7.56-7.43 (1H, m), 6.95-6.94 (2H, d, J= 9.0 Hz), 3.84 (3H, s)

(2,5-Dimethylphenyl)(phenyl)methanone$^{75,76,77}$

$^1$H NMR $\delta$ 7.83–7.80 (2H, d, J=7.8 Hz), 7.55-7.50 (1H, m), 7.43-7.38 (2H, m), 7.02-6.98 (1H, dd, J=6.0 Hz, J=3.3 Hz), 6.93-6.89 (2H, m), 3.76 (3H, s), 3.63 (3H, s)
Phenyl(p-tolyl)methanone$^{52}$

\[
\begin{array}{c}
\text{O} \\
\text{H} \\
\text{H} \\
\text{H} \\
\end{array}
\]

$^1$H NMR $\delta$ 7.80–7.60 (4H, m), 7.48–7.37 (2H, m), 7.20–7.16 (2H, m), 7.04–7.00 (3H, m), 2.33 (3H, s), 2.23 (3H, s)

(4-Bromophenyl)(phenyl)methanone$^{52,74}$

\[
\begin{array}{c}
\text{O} \\
\text{Br} \\
\text{Br} \\
\end{array}
\]

$^1$H NMR $\delta$ 7.80–7.75 (2H, m), 7.68–7.53 (5H, m), 7.50–7.45 (2H, m)

(4-Chlorophenyl)(phenyl)methanone$^{52,74}$

\[
\begin{array}{c}
\text{O} \\
\text{Cl} \\
\end{array}
\]

$^1$H NMR $\delta$ 7.78–7.72 (3H, m), 7.62–7.55 (1H, m), 7.50–7.42 (4H, m)

(E)-N-((2,5-Dimethylphenyl)(phenyl)methylene)aniline

\[
\begin{array}{c}
\text{N} \\
\end{array}
\]

$^1$H NMR $\delta$ 7.75–7.72 (2H, dd, J=5.1 Hz, J=1.5 Hz), 7.45–7.36 (3H, m), 7.15–7.10 (2H, m), 6.98 (1H, s), 6.94–6.85 (3H, m), 6.77–6.74 (2H, dd, J=8.7 Hz, J=1.2 Hz), 2.24 (3H, s), 1.99 (3H, s) $^{13}$C NMR $\delta$ 168.6, 150.9, 139.3, 136.3, 134.6, 132.1, 130.7, 129.9, 129.5,
129.2, 128.6, 128.34, 128.25, 123.4, 120.7, 20.9, 19.6; HRMS−ESI (m/z): calcd for C_{21}H_{19}N 285.38226; found 286.1591 [M+H]+

**N-((2,5-Dimethoxyphenyl)(phenyl)methyl)aniline**

![Structure](image)

^1H NMR δ 7.37–7.35 (2H, d, J=9.0 Hz), 7.30-7.21 (3H, m), 7.12-7.09 (2H, m), 6.99-6.98 (1H, d, J=3.0 Hz), 6.83 and 6.81 (1H, 2s), 6.76-6.73 (1H, dd, J= 9.0 Hz, J=3.0 Hz), 6.69-6.66 (1H, m), 6.56-6.54 (2H, dd, J=8.5 Hz, J=1.0 Hz), 5.85 (1H, s), 4.27 (1H, br s), 3.72 (3H, s), 3.71 (3H, s); ^13C NMR δ 153.9, 151.0, 147.6, 142.8, 132.3, 129.0, 128.5, 127.4, 127.0, 117.4, 114.4, 113.4, 112.20, 112.04, 56.8, 56.7, 56.17, 56.15, 55.64, 55.62; HRMS-ESI calcd for C_{21}H_{21}NO. 319.3969 m/z found 318.1487 [(M-H)]+.

**N-((3,4-Dimethoxyphenyl)(phenyl)methyl)aniline**

![Structure](image)

^1H NMR δ 7.40–7.20 (5H, m), 7.13-7.08 (2H, m), 6.87 (1H, s), 6.86-6.85 (1H, d, J=2.0 Hz), 6.80-6.78 (1H, d, J=8.5 Hz), 6.56-6.52 (1H, m), 6.54-6.52 (2H, dd, J=9.0 Hz, J=1.0 Hz), 5.44 (1H, s), 4.20 (1H, br s), 3.83 (3H, s), 3.80 (3H, s); ^13C NMR δ 149.2, 148.3, 147.5, 143.1, 135.6, 129.1, 128.8, 127.40, 127.36, 120.9, 119.6, 117.7, 113.5, 111.4,
111.3, 110.7, 62.8, 55.91 HRMS-ESI calcd for C_{21}H_{21}NO_{2}, 319.3969 m/z found 318.1488 [(M-H)]+, 342.1470 [M+Na]+.

**N-((4-Methoxyphenyl)(phenyl)methyl)aniline**

![Chemical Structure]

$^1$H NMR $\delta$ 7.34–7.15 (8H, m), 7.05-7.02 (2H, dd, J=8.5 Hz, J=7.5 Hz), 6.79-6.77 (2H, d, J=9.0 Hz), 6.64-6.60 (1H, dd, J=14.5 Hz, J=7.0 Hz), 6.47-6.46 (1H, d, J=8.0 Hz), 5.44 (1H, s), 4.17 (1H, s), 3.74 (3H, s); $^{13}$C NMR $\delta$ 158.5, 147.1, 142.9, 134.9, 130.0, 129.0, 128.8, 128.4, 128.3, 128.1, 128.0, 127.1, 126.9, 117.3, 113.8, 113.4, 113.2, 62.1, 54.94, 54.92 (isomer) HRMS-ESI calcd for C_{20}H_{19}NO 289.3709 m/z found 288.1384 [(M-H)]$^+$.  

**N-((2,5-Dimethylphenyl)(phenyl)methyl)aniline**

![Chemical Structure]

$^1$H NMR $\delta$ 7.31–7.23 (5H, m), 7.12-7.05 (4H, m), 6.99-6.97 (1H, d, J=7.0 Hz), 6.67-6.64(1H, dd, J=14.5 Hz, J=7.5 Hz), 6.50-6.48 (2H, d, J=7.5 Hz), 5.61 (1H, s), 4.07 (1H, s), 2.26 (3H, s), 2.22 (3H,s) $^{13}$C NMR $\delta$ 147.59, 142.2, 140.4, 135.8, 132.7, 130.6, 129.2, 128.7, 128.0, 127.9, 127.9, 127.3, 117.5, 113.2, 59.6, 21.3, 19.0 HRMS-ESI calcd for C_{21}H_{21}N 278.3981 m/z found 286.1589[(M-H)]$^+$. 
N-(Phenyl (p-tolyl)methyl)aniline

\[
\begin{align*}
\text{N} & \quad \text{H} \\
\text{NH} & \quad \text{H} \\
\text{H} & \quad \text{H}
\end{align*}
\]

\(^1\)H NMR (300 MHz) \(\delta 7.36\)–7.05 (11H, m), 6.68-6.63 (1H, dd, J=14.7 Hz, J=7.2 Hz), 6.54-6.51 (2H, d, J=8.4 Hz), 5.46 (1H, s), 4.20 (1H, s) 2.32 (3H, s); \(^{13}\)C NMR \(\delta 147.5, 143.2, 140.1, 127.4, 127.3, 126.3, 117.6, 113.5, 113.1, 62.8, 59.5, 21.1\) HRMS-ESI calcd for C\(_{20}\)H\(_{19}\)N 273.3715 m/z found 272.1436[M-H]+.

N-((4-Bromophenyl)(phenyl)methyl)aniline

\[
\begin{align*}
\text{N} & \quad \text{H} \\
\text{NH} & \quad \text{H} \\
\text{H} & \quad \text{Br}
\end{align*}
\]

\(^1\)H NMR \(\delta 7.60\)–7.00 (11H, m), 6.80-6.60 (1H, m), 6.50-6.40 (2H, dd, J=8.5 Hz, J=1.0 Hz), 5.40 (1H, s), 4.16 (1H, s). \(^{13}\)C NMR \(\delta 147.1, 142.6, 141.9, 133.3, 131.9, 129.3, 129.2, 129.1, 129.0, 128.8, 128.3, 127.9, 127.8, 127.6, 121.2, 118.0, 117.9, 113.6, 113.4, 113.2, 62.6\). HRMS-ESI calcd for C\(_{19}\)H\(_{16}\)BrN 338.2410 m/z found 338.0366 [M+], 336.0379[(M-2H)]+.

N-((4-Chlorophenyl)(phenyl)methyl)aniline

\[
\begin{align*}
\text{N} & \quad \text{H} \\
\text{NH} & \quad \text{H} \\
\text{H} & \quad \text{Cl}
\end{align*}
\]
$^1$H NMR δ 7.33 - 7.20 (8H, m), 7.13-7.08 (3H, dd, J=15.9 Hz, J=8.1 Hz), 6.72-6.67 (1H, m), 6.52-6.49 (2H, d, J=8.4 Hz), 5.45 (1H, s), 4.16 (1H, s). $^{13}$C NMR δ 147.4, 141.7, 133.3, 129.5, 129.2, 129.0, 128.3, 128.0, 127.8, 118.3, 113.8, 113.6, 62.8; HRMS-ESI calcd for C$_{19}$H$_{16}$ClN 293.7900 m/z found 292.0891 [(M-H)]$^+$. 

2-Methyl-4-phenylquinazoline$^{61}$

\[
\text{\begin{tikzpicture}
\draw[thick] (0,0) -- (0.5,0.5) -- (1,0) -- (1.5,-0.5) -- (2,0) -- (2.5,0.5) -- (3,0);
\draw[thick] (0,0) -- (0,-0.5);
\draw[thick] (1,0) -- (1,-0.5);
\draw[thick] (2,0) -- (2,-0.5);
\draw[thick] (3,0) -- (3,-0.5);
\draw[thick] (2,0) -- (2,0.5);
\draw[thick] (3,0) -- (3,0.5);
\end{tikzpicture}}
\]

$^1$H NMR δ 8.63–8.61 (2H, m), 8.10-8.06 (2H, m), 7.88-7.85 (1H, m), 7.60-7.45 (4H, m), 3.02 (3H, s). $^{13}$C NMR δ 168.2, 160.1, 150.4, 138.3, 133.5, 130.3, 129.3, 128.5, 126.8, 125.0, 123.0, 22.0

2,4-Diphenylquinazoline$^{61}$

\[
\text{\begin{tikzpicture}
\draw[thick] (0,0) -- (0.5,0.5) -- (1,0) -- (1.5,-0.5) -- (2,0) -- (2.5,0.5) -- (3,0);
\draw[thick] (0,0) -- (0,-0.5);
\draw[thick] (1,0) -- (1,-0.5);
\draw[thick] (2,0) -- (2,-0.5);
\draw[thick] (3,0) -- (3,-0.5);
\draw[thick] (2,0) -- (2,0.5);
\draw[thick] (3,0) -- (3,0.5);
\end{tikzpicture}}
\]

$^1$H NMR (500M Hz) δ 8.70–8.66 (2H, m), 8.18-8.11(2H, dd, J=24.0 Hz, J=8.5 Hz), 7.90- 7.87 (3H, m), 7.60-7.51 (7H, m). $^{13}$C NMR δ 168.8, 160.4, 152.0, 138.3, 137.9, 134, 130.9, 130.5, 130.3, 129.2, 129.0, 128.9, 128.8, 127.4, 127.4, 121.9 HRMS-ESI calcd for C$_{20}$H$_{14}$N$_2$ 282.3387 m/z found 283.1237 [M+H]$^+$. 
(Z)-3-(Phenyl(phenylimino)methylbenzonitrile

\[ \text{N} \quad \text{N} \]

\[ \text{N} \quad \text{N} \]

$^1$H NMR (500 MHz) $\delta$ 8.91–8.90 (1H, d, J=8.5 Hz), 8.73-8.8.71 (2H, d, J=7.0 Hz),
8.40-8.39 (1H, d, J=7.5 Hz), 8.30-8.28 (1H, m), 8.03-8.01 (2H, d, J=7.0 Hz), 7.95-7.92
(1H, m), 7.81-7.70 (6H, m). $^{13}$C NMR $\delta$ 176.1, 157.4, 141.9, 139.5, 135.6, 135.2, 133.6,
131.5, 131.2, 130.6, 130.1, 129.6, 129.6, 129.6, 129.2, 129.0, 121.5, 121.3 HRMS-ESI
calcd for C$_{20}$H$_{14}$N$_2$ 282.3387, m/z found 283.1237 [M+H]$^+$. 
APPENDIX A

SUPPLEMENTARY DATA
(E)-N-((2,5-dimethylphenyl)(phenyl)methylene)aniline
N-((2,5-dimethoxyphenyl)(phenyl)methyl)aniline
Pulse Sequence: 4091
Solvent: CDCl3
Temp. 25.0 C / 508.1 K
User: 3-16-B7
Instrument: "Fortessa"

Pulse 90.0 degrees
Acq. time 2.475 sec
Wait 2.032 sec
FID acquisition

OBSERVE: 133, 135.6995536 Hertz
DECouple: 1H, 403.8807279 Hertz

Data collected contiguously on
MULTIVAC multivanes
DATA PROCESSOR
Line broadening 2.3 Hz
FF close 50014
Total time 16 hr, 41 min, 8 sec

ppm
N-((3,4-dimethoxyphenyl)(phenyl)methyl)aniline
N-((4-methoxyphenyl)(phenyl)methyl)aniline
Sample Name: SRS_IL_103  
Inj Vol: 0.3  
Data Filename: SRS_IL_103_04272012_ACQ Method: ESI_ASE_Pos_Main_000  

**Graph:**

- ESI Scan (0.127-0.159 min, 3 scans) Frag=250.0V SRS_IL_103_04272012_ESI.d Subscript

Counts (%) vs. Mass to Charge (m/z)

- 274.1220
- 278.9337
- 282.2785
- 304.3604
- 310.2289
- 318.1863
- 322.0985
N-((2,5-dimethylphenyl)(phenyl)methyl)aniline
Pulse Sequence: G447S
Solvent: CDCl3
Temp. 298 K / 25°C
SECTION 100 "G447S"

Relax. delay 1.093 sec
Pulse FID 180° prep
Acq. time 0.382 sec
Window 0.016 sec
Baseline 0.5 sec

OBSERVED H: 600.1966 MHz
DATA PROGRESS: 0%
FT SIZE 85500
Total time 6 min. 6 sec
Pulse Sequence: s2pul
Solvant: CDCl3
Temp: 25.0 °C / 77.1 K
SOLVENT: 'CDCl3'

Pulse, delay 1.003 sec
Pulse: 90.1 degrees
Frequency: 500.1 MHz
Bandwidth: 6000.0 Hz
Singles scan
DATA PROCESSING
FT size 65536
Total time 5 min, 4 sec

7.5 7.4 7.3 7.2 7.1 7.0 6.9 6.8 6.7 6.6 6.5 6.4 ppm
38.74 30.48 7.49 7.65 15.25
N-(phenyl (p-tolyl)methyl)aniline
ESI Scan (0.149-0.165 min, 2 scans) Frag=250.0V SRS_II_101_04272012_ESI.d Subtract

272.1450
(M+H)^+

288.1387
+ESI Scan (0.149-0.165 min, 2 scans) Frac=250.0V SRS_II_101_04272012_ESI.d Substruct

Counts (%) vs. Mass-to-Charge (m/z)

-166.1085
-181.1397
-116.0643
-141.0608
-153.0694
-195.1160
N-((4-bromophenyl)(phenyl)methyl)aniline
STANDARD PROTON PARAMETERS

Pulse Sequence: ZG
Solvent: CDCl3
Time: 300 K/0.5 sec
Field: 29.47 T/6090.4 Hz
INHIB: 90°

Relax.: delay 1.0 sec
Spin: 45°/100 Hz
Spin: 90°/100 Hz
Sample: 100.6 ml

Single scan:
Number: 1
1.13 PPM
1.24 PPM
6.77 PPM

Total time: 2 min, 4 sec
N-((4-chlorophenyl)(phenyl)methyl)aniline
Proton NMR Spectroscopy

Sample: [Sample Name]
Solvent: [Solvent Name]
Temp: [Temperature]
Field: [Field Strength]

Chemical Shifts:
- [Shift 1] ppm
- [Shift 2] ppm
- [Shift 3] ppm

Other Parameters:
- [Parameter 1]
- [Parameter 2]
- [Parameter 3]
2-methyl-4-phenylquinazoline
2,4-diphenylquinazoline
Pulse Sequence: zgou
Solvents: CDCl3
Temp: 25.0°C / 298.1 K
Field: 500.13 MHz

Relax. delay: 1.09 sec
Pulse: 12.4 degrees
SNR: time 2.612 sec

Single peak

Full rate: 200000 Hz
Data Processing
FF sig. 8000x

Total time: 5 min, 4 sec

ppm
(Z)-3-(phenylimino)methyl)benzonitrile
REFERENCES


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VITA

I have been through the graduate school at Loyola University Chicago for four years going for PhD in chemistry with emphasis in organic chemistry under direction and mentorship of Daniel P. Becker, Ph.D. I also have a master's degree in chemistry from Emporia State University in Kansas under supervision of Eric Trump, Ph.D. My bachelor’s degree is also in chemistry from the University of Ghana, Legon, in Accra, Ghana. Throughout my graduate education I have been working as a graduate teaching assistant mostly involved in teaching and helping students in sophomore organic chemistry laboratory assignments. My research at Loyola University Chicago is mostly focused synthesis of anthracene derivatives for organic light emitting diodes as well as synthetic methodology for making important functional groups presents in compounds that have medicinal and pharmaceutical significance. These functional groups are mainly ketones, imines, amines and quinazolines. I have also worked with undergraduate students in my research, giving direction to help in their independent research.