Scalable and Concise Approaches for the Synthesis of "Archipelago Model" Asphaltene Compounds

by

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A thesis submitted in partial fulfillment of the requirements for the degree of

Doctor of Philosophy

Department of Chemistry
University of Alberta

Abstract

Asphaltenes constitute the most difficult sub-class of bitumen with regards to upgradability. This is due to their complex and variable structure, higher average molecular weight, and inclusion of polar functionalities. These structural traits instigate intermolecular attractions that lead to irreversible aggregation of individual asphaltene molecules and ultimately precipitation from solution. This behavior hampers the ability to efficiently utilize this material and address society's growing energy needs.

At the same time, northern Alberta's Athabasca region has abundant reserves of asphaltene-rich bitumen. There is thus strong interest in developing new technologies for efficient upgrading of this "low quality" crude petroleum. Progress towards this end requires a thorough understanding of asphaltenes at a molecular and supramolecular level. Due to the complex and intractable mixture that comprises asphaltenes, this intimate knowledge has yet to be garnered, despite great effort.

Traditionally, an analytical approach towards deciphering the "micro-structure" of the asphaltenes has been utilized, with limited results that are difficult or impossible to validate. As of yet, no pure asphaltene molecule has been characterized structurally. A reverse-engineering approach towards accurate modeling of theoretical class members is expected to have great potential in unraveling the mysteries that remain.

In this dissertation is described the first concise and scalable synthesis of a range of well-defined asphaltene model compounds obtained in high purity. This new class of synthetic compounds falls within the observed structural guidelines determined for natural samples, both in terms of molecular weight and heteroatom content. These model compounds represent the "archipelago-type" architecture, in

that they are composed of polycyclic aromatic “islands” tethered together by saturated alkyl chains of various lengths, and further decorated with shorter terminal alkyl groups. A range of authentic functionality has been introduced into these compounds, although there remain many variants as yet unprepared.

The foundation of our synthetic approach to these molecules is the traceless cross-coupling of tethers and islands, assembling large carbonaceous skeletons in the terminal step of the synthetic sequence. This feature is pivotal in allowing for simple isolations of otherwise difficult-to-purify targets through extraction and fractional crystallization. All of the reported archipelago model compounds and isolated intermediates have been characterized by ^{1}H- and ^{13}C-NMR spectroscopy, HRMS, and EA. The solid-state structure of one model compound has been determined by X-ray crystallography.

Preface

The 1,3,6,8-Tetrahexylpyrene described herein, whose synthesis was designed and performed by me was provided to the group of our collaborator Murray Gray (then at the Department of Chemical Engineering, University of Alberta). This material was used in oil upgrading experiments that resulted in two publications, which I coauthored as Ali H. Alshareef, Xiaoli Tan, Colin Diner, Jun Zhao, Alexander Scherer, Khalid Azyat, Jeffrey M. Stryker, Rik R. Tykwinski, and Murray R. Gray "Binary Interactions in Coke Formation from Model Compounds and Asphaltenes", Energy Fuels 2014, 28, 1692−1700" and Farhood Karbalaee Habib, Colin Diner, Jeffrey M. Stryker, Natalia Semagina, and Murray R. Gray "Suppression of Addition Reactions during Thermal Cracking Using Hydrogen and Sulfided Iron Catalyst", Energy Fuels 2013, 27, 6637-6645.

Chapter 2 of this thesis has been published as Colin Diner, David E. Scott, Rik R. Tykwinski, Murray R. Gray, and Jeffrey M. Stryker "Scalable, Chromatography-Free Synthesis of Alkyl-Tethered Pyrene-Based Materials. Application to First Generation "Archipelago Model" Asphaltene Compounds", *J. Org. Chem.* 2015, 80, 1719-1726. For this contribution I was the reaction designer and main experimentalist. My colleague, David Scott assisted me in reaction scale-ups. I drafted the original manuscript, which greatly benefitted from the large editing contributions of Jeffrey Stryker, the supervisory author and Rik Tykwinski.

Chapter 3 of this thesis contains information on the uses of, and previous synthesis' of 1-bromopyrene. This information was recently submitted to Org. Synth. as "Improved Synthesis of 1-Bromopyrene and Conversion to 1-Pyrenecarbaldehyde" by Matthias Schulze, Alexander Scherer, Colin Diner, Rik R. Tykwinski. For this contribution, I provided the literature review and wrote the background information. Matthias Schulze and Alexander Scherer developed the experimental procedure. Rik Tykwinski, the supervisory author edited the manuscript.

The remaining results of Chapter 3 will be submitted shortly, to a journal that is yet to be named. For this contribution I was the reaction designer and main experimentalist. This work was done under the supervision of both Rik Tykwinski and my supervisor Jeff Stryker. Matthias Schulze contributed to these synthetic efforts.

"Carbon–hydrogen (C–H) and carbon–carbon (C–C) bonds are ubiquitous in organic molecules."

-Richmond Sarpong

For Clara, Richard, Mary, and Lou

Acknowledgements

I would first like to thank my boss, Prof. Jeffrey Stryker. He has been a reliable, enthusiastic, patient and critical mentor since I joined the group. Jeff was extremely supportive of my research trip to Germany and for that I am so grateful for the opportunity. I was also fortunate to have Jeff's support as I presented my research at various conferences in Western Canada. On these trips, I learned and experienced much. Jeff's support has continued even as my PhD comes to a close and I look forward to future collaborations. Most importantly, I would like to thank Jeff for all of the freedom he lent me while in his group. When in need of help I could always rely on him to steer me in the right direction, but he trusted me to learn, make mistakes, and eventually make less mistakes. This has been fundamental.

I am also very appreciative of my host in Germany, a fellow Minnesotan, Prof. Rik Tykwinski. He was a fantastic host during my stay in Erlangen, and his group was extremely welcoming. I learned a lot about both chemistry and beer throughout my studies in that beautiful city. I look forward to visiting again some day.

I am very thankful to my PhD examination committee members for taking the time to read my thesis, and attend my defense presentation. Prof. Sutherland was kind enough to take some time from his research group in Calgary and I appreciate that. I was very fortunate to have many interactions with Prof. West from the beginning of my studies at the U of A to the present and hopefully into the future. I greatly enjoyed these conversations and learned much about organic synthesis from him in class. I am also very appreciative of Prof. Hall's, Prof. Veinot's, and Prof. McCaffrey's input during my candidacy exam. That was a stressful but memorable experience. Lastly, I would like to thank Prof. Lundgren for being willing to step in as a PhD examiner.

My time at the U of A and my research and productivity have greatly benefitted from the wonderful analytical facilities available. A big thank you goes out to Mark Miskolzie, Ryan McKay and Nupur Dabral from NMR services, I was lucky to access their vast knowledge and impressive skills almost daily. Thank you to Wayne Moffat, Jennifer Jones, Ema Sretenovic, Marc-Andre Hoyle, and Brett Mason for their constant help with elemental analysis, and infrared spectroscopy. The extremely helpful and experienced members of the mass spec facilities were absolutely vital to my success in characterizing my intermediates and products, which required a variety of techniques and different skill sets. Thank you so much Dr. Randy Whittal, Dr. Angie Morales, Dr. Jing Zheng, Dr. Bela Reiz, and Dr. Xiaoxia Ye for all your help. We are very lucky at the U of A to have the "Best in the West" in regards to X-ray data collection and analysis. Dr. Robert McDonald and Dr. Michael Ferguson were able to help me obtain useful data from less than amazing samples, I was lucky to have their help.

Others in the department who have come to my rescue on numerous occasions include Tyler Peterson from the IT department, Bernie Hippel from Stores, Jason Dibbs from the Glass shop, Ryan Lewis from Shipping and Receiving, our administrative help including Lynne Lechelt, Anita Weiler, and Jillian Fell.

A large part of my PhD experience at the U of A was spent "TA'ing". I was lucky to work for people like Prof. West and Prof. Hall as well as Dr. Hayley Wan and Dr. Christine Brzezowski, who were all fantastic bosses. Similarly, I would like to thank Nada Djokic for her help with teaching.

Throughout my time in the group I have developed many friendships with many lab mates. I have learned a lot from them, and they have continued to help me through all of the hurdles of this degree. Thank you to my friends, Dr. Robin Hamilton, Dr. Samuel Mitton, Dr. Kseniya Revunova, Dr. Jeremy Gauthier, Kirsten Tomlin, Devin Reaugh, David Scott, and all the rest of the "Stryke-Force".

I would also like to thank all of my other friends in the department. Their help, advice, interest, and willingness to buy me coffee has been paramount over the past 5 years. Thank you to Jinyue “Jimbo-Slice” Ding, Anushka Jayasuria, Justin Thuss, Chris Berger, Michael Downey, Charles “Chuckwagon” Vaudry, Tran-Tran, Paul Lummis, Roger Ashmus, Ryan Sweeney, Samantha Kwok, and Lindsay Shearer.

A special thanks some of my friends outside of the department who assisted me in editing this thesis, Phyllis Mellman, and Erik Withall.

Finally I would like to thank my family. The support of my parents throughout my education has been essential - emotionally and financially. My uncle Joe was also extremely important in this regard and I cannot thank him enough. I would also like to thank my younger brother Louie for his surprisingly enthusiastic interest and support in my research.

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List of abbreviations

Ac	Acetyl
acac	Acetylacetonyl
ACS	American Chemical Society
APPI	Atmospheric pressure photoionization source
Ar	Aryl group
BINAP	2,2'-Bis(diphenylphosphino)-1,1'-binaphthyl
*t*Boc	*tert*-Butyloxycarbonyl
Bn	Benzyl
br	Broad
n-Bu	Normal Butyl
t-Bu	Tertiary Butyl
cat	Catechol
calcd	Calculated
cm^{-1}	Wavenumbers
COD	1,5-Cyclooctadiene
Cp	Cyclopentadienyl
PMHS	Polymethylhydrosiloxane
Cy	Cyclohexyl
dba	Dibenzylideneacetone
DBT	Dibenzothiophene
DCM	Dichloromethane
CD	Circular dichroism
XRD	X-ray diffraction
BQ	Benzoquinone
dd	Doublet of doublets
DDQ	2,3-Dichloro-5,6-dicyano-1,4-benzoquinone
DFT	Density functional theory
DMA	*N,N*-Dimethylacetamide
DMF	*N,N*-Dimethylformamide
DMSO	Dimethyl sulfoxide

dppe	1,2-Bis(diphenylphosphino)ethane
dppf	1,1'-Bis(diphenylphosphino)ferrocene
dq	Doublet of quartets
dt	Doublet of triplets
ee	Enantiomeric excess
EA	Elemental analysis
EI	Electron impact
eq	Equation
equiv	Equivalents
ESI	Electrospray ionization
Et	Ethyl
Et_2O	Diethyl ether
EtOAc	Ethyl acetate
EtOH	Ethanol
FT	Fourier transform
h	Hour
HPLC	High performance liquid chromatography
HRMS	High resolution mass spectrometry
ICR	Ion cyclotron resonance
IR	Infrared spectroscopy
KAPA	Potassium 1,3-diaminopropanide
LAH	Lithium aluminum hydride
LDA	Lithium diisopropylamide
LiTMP	Lithium 2,2,6,6-tetramethylpiperidide
m	Multiplet
MALDI	Matrix-assisted laser desorption/ionization
Me	Methyl
MeCN	Acetonitrile
MeOH	Methanol
NBS	*N*-Bromo succinimide
NHC	*N*-Heterocyclic carbene

NMR	Nuclear magnetic resonance
Nu	Nucleophile
ORTEP	Oak Ridge Thermal Ellipsoid Plot
O-TMEDA	Bis[2-(*N*,*N*-dimethylamino)ethyl] ether
PEPPSI initaition	Pyridine-enhanced precatalyst preparation stabilization and
Ph	Phenyl
PhMe	Toluene
pin	Pinacolato
PMHS	Polymethylhydrosiloxane
IPr 2-ylidene	1,3-Bis(2,6-diisopropylphenyl)-1,3-dihydro-2*H*-imidazol-
*i*Pr	Isopropyl
q	Quartet
RBF	Round bottom flask
RT	Room temperature
SET	Single electron transfer
RuPhos	2-Dicyclohexylphosphino-2′,6′-diisopropoxybiphenyl
t	Triplet
TBAF	Tetra-*n*-butylammonium fluoride
TFA	Trifluoroacetic acid
THF	Tetrahydrofuran
TMEDA	1,2-Bis(dimethylamino)ethane
TM	Transition metal
TMS	Trimethylsilyl
TOF	Time of Flight
tol	Tolyl
Ts	*para*-Toluenesulfonyl
tt	Triplet of triplets
tq	Triplet of quartet
wt%	Weight perce

1 Introduction: A Brief Rationale for and History of Model Asphaltene Synthesis

Utilizing Alberta's oil sands

As the harvesting rate of conventional crude and natural gas has increased over the past 100 years, ready access to the geologic supply of these materials has decreased. Thus, utilization of less conventional material that is more difficult to upgrade like bitumen has become more attractive. Canada's Oil Sands, located principally in the Athabasca region, are flush with such carbon-rich material. In fact, there are currently over 25 billion m^3 or 165 billion barrels of bitumen remaining in Alberta's reserves.[1] It is in modern society's interest to develop more efficient technologies appropriate for bitumen upgrading and ultimate use as liquid fuels and petrochemical carbon feed stocks.

Bitumen

Bitumen is the organic material isolated from the harvested oil sands and can be separated into two solubility classes based on the SARA method (Figure 1-1). These classes are the maltenes, soluble in n-alkanes, and the asphaltenes, soluble in aromatic solvents like toluene, but insoluble in *n*-alkanes.[2] Maltenes can be categorized further, differentiated by the solvent polarity required to elute them after adsorption onto silica, while the asphaltenes are irreversibly adsorbed. As the polarity of the solvent is increased from alkanes to toluene to methanol, the corresponding sub-classes of maltenes are collected as saturates, aromatics, and resins.[3] It is the asphaltenes within bitumen that both literally and figuratively precipitate issues during upgrading.[4]

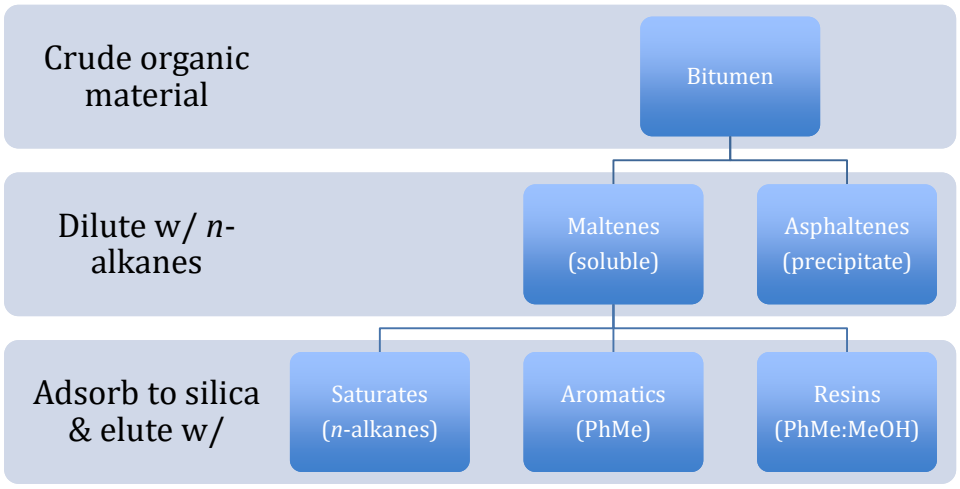


Figure 1-1. SARA analysis for bitumen fractioning.

Along the production line from oil well to upgrading facility, heavy liquid crude petroleum has many opportunities to precipitate solid material. When this happens in flow lines or well bores, the flow of crude product is diminished and profits are lost. When this precipitation happens during the upgrading process of cracking or hydrotreating, it is called coking.[5] Coke buildup not only lowers the yield of usable liquid fuels but also leads to reactor fouling and deactivation of the heterogeneous catalysts currently used to upgrade the crude material.[6]

Petroleum coke is an extremely carbon rich material, and thus when burned releases larger amounts of carbon dioxide relative to other fuels. It is also high in sulfur and metal content and is considered to be a relatively "dirty" energy source. North American refineries are large producers of "petcoke" as a wasteful byproduct of bitumen upgrading. Due to the environmental impact associated with burning such a fuel, the material is generally not used domestically. Rather, petcoke is sold to countries like China, Mexico, and India that follow less stringent environmental impact laws.[7]

1.1.1 Asphaltenes

The problems inherent to the upgrading and transport of asphaltene rich material arise from the more polar nature of the asphaltenes, which allows for more and greater aggregate-inducing intermolecular forces between individual constituents. As these intermolecular associative forces accumulate, precipitation of asphaltene aggregates becomes more likely.[8] The increased polarization of the asphaltene class is a function of its higher C : H ratio (greater unsaturation), as well as an increased heteroatom content, including oxygen, nitrogen, sulfur, and to a lesser extent, nickel and vanadium (the latter two on the ppm scale).[9] Figure 1-2 contains the relative atomic abundances of these elements in typical asphaltenes.[10]

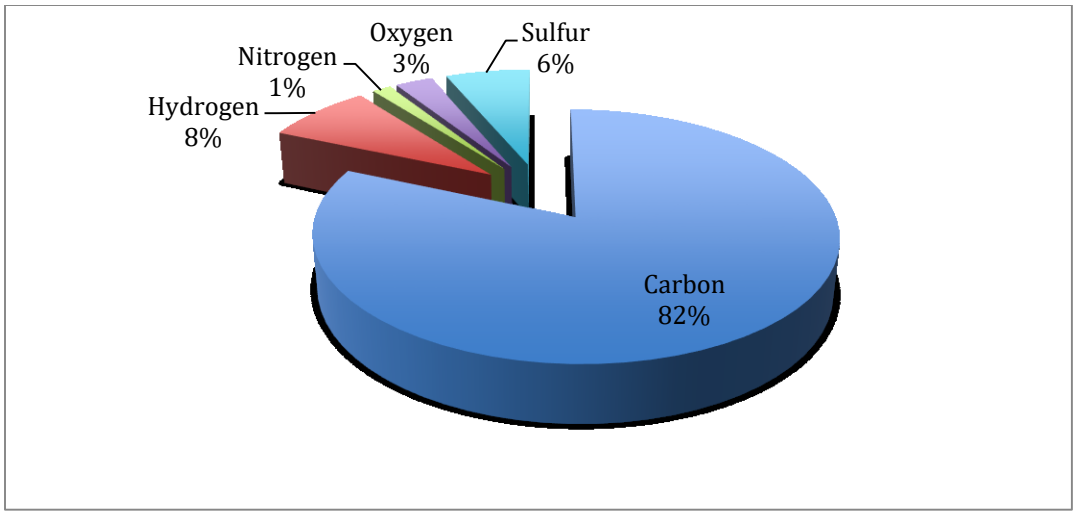


Figure 1-2. Elemental composition of asphaltenes (wt%)

While the exact structure of asphaltenes is unknown – due to its highly complex and varied nature – specific ring systems and functional groups have been identified as constituents. The functional groups include carboxylic acids, thioethers, basic and non-basic nitrogen heteroaromatic compounds such as pyridines/quinolines and pyrroles/indoles, residual biomarker compounds such as metallated porphyrins, and elaborated steroidal polycarbocycles (e.g., hopanes).[11] In this way, strong attractive forces between individual asphaltene molecules can

include hydrogen bonding association as well as both Brønsted and Lewis acid-base interactions.

A brief discussion of the sulfur content within asphaltenes is prudent, as it is the most abundant heteroatom entrenched within this organic material. While the majority of the oxygen content within asphaltenes is believed to manifest itself as alkyl carboxylic acids and esters (exocyclic moieties) and the nitrogen as heteroaromatic constituents (endocyclic moieties), sulfur is found in two drastically different chemical environments within the asphaltene: aliphatic thioethers (primarily exocyclic alkyl-alkyl) and thiophenic aromatic sulfur. Due to the relatively weak C–S bond of alkylthio ethers (approx. 74 kcal/mol),[12] industrial desulfurization via catalytic hydrogenolysis generally proceeds without issue. Removal of thiophenic sulfur is more difficult due to its entrenchment within an aromatic framework. Much of the thiophenic sulfur within asphaltenes exists as larger condensed aromatic polycycles, including alkylated benzo- and dibenzothiophenes.[13] As the molecular weight in this series increases, the rate of desulfurization generally decreases (Figure 1-3).[14]

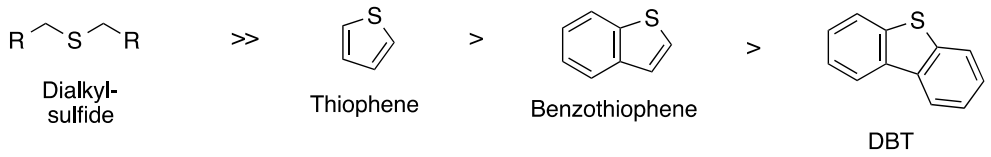


Figure 1-3. Rate of hydrogenolysis of sulfur-containing functionalities within asphaltenes

Catalysis aimed at the hydrogenolysis of 4,6-disubstituted dibenzothiophenes has been termed “deep hydrodesulfurization” (HDS) and is currently a “hot topic” in petroleum research.[15] These efforts are important as governmental guidelines generally mandate that the sulfur content of fuels be in the low ppm range, in order to lower emissions of the acid-rain-inducing gas SO_2.[16]

Illustrative of the intensity of the research effort is the commercial availability of 4,6-dimethyldibenzothiophene (**1-1**) and its ethyl analogue (**1-2**) from Aldrich.[17] The reported synthesis of the former is not trivial on a commercial scale (Figure 1-4).[18]

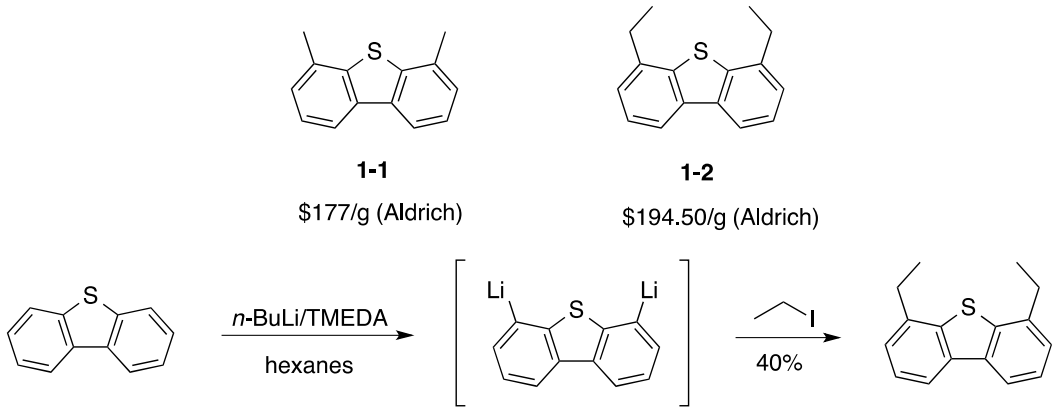


Figure 1-4. Commercial sources and synthesis of thiophenic compounds for "deep HDS" modeling

The increased unsaturation of asphaltenes relative to maltenes, coupled with its higher average molecular weight (approx. 750 Da.),[19] has been proposed to manifest itself structurally in two possible ways: the archipelago model[11,20] and the continental model (Figure 1-5).[19,21] The continental model is characterized by a very large polycyclic (hetero)aromatic core decorated on the periphery with alkyl chains and functionality. In contrast, the archipelago model is described by smaller aromatic "islands" linked together by short (generally two to four methylene units) linear and branched alkyl chains, and further decorated with short terminal alkyl chains. Importantly, both of these models leave room for one potentially important attractive intermolecular force, π-π stacking between aromatic residues.

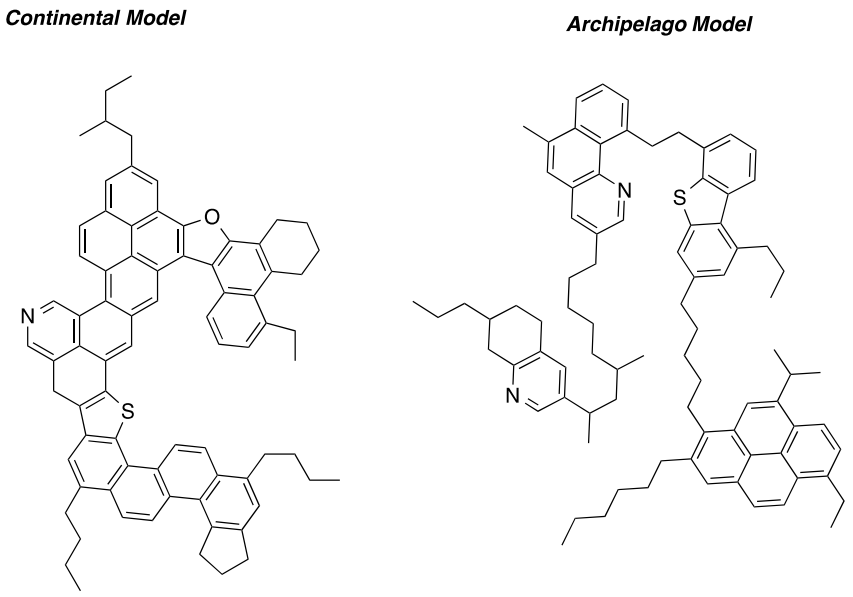


Figure 1-5. Continental vs. archipelago models

Today the actual structural architecture of asphaltenes is accepted, albeit not by everyone, to exist somewhere between these two models. Figure 1-6 is a cartoon of some of the possible associative forces within a fictional asphaltene archipelago sample.[8] Seen in this picture alongside the already mentioned functionalities at play are water clathrates and hydrophobic pockets, some containing small, low molecular weight hydrocarbon components.

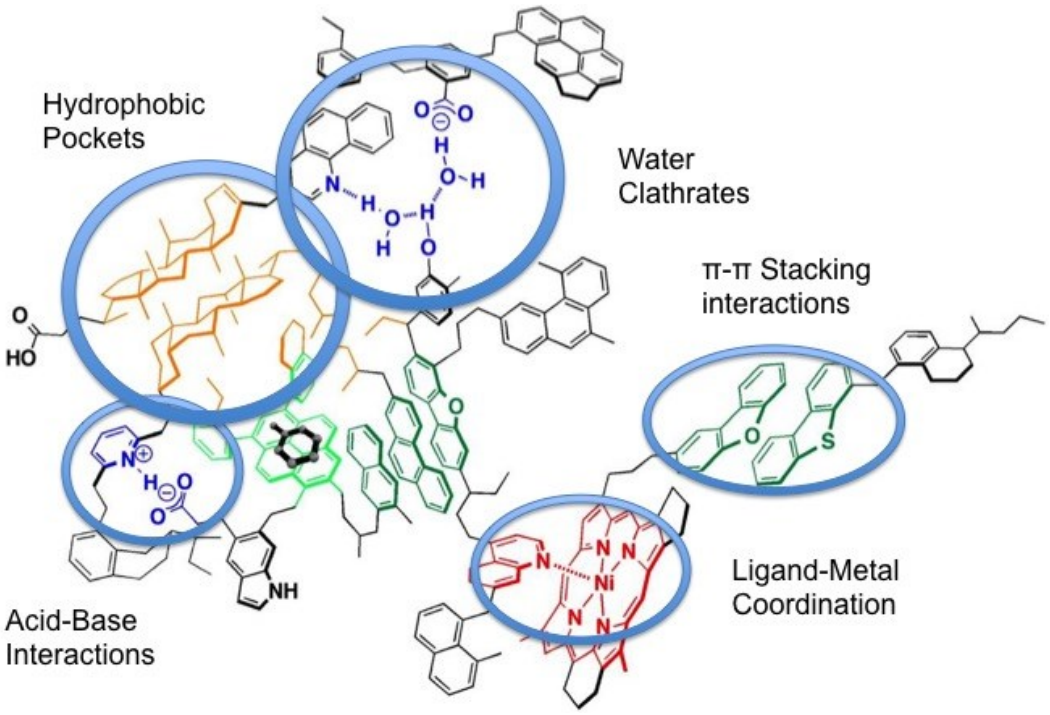


Figure 1-6. Fictional depiction of forces at play within an archipelago model asphaltene.

Asphaltene aggregation studies

1.1.2 Studies on authentic asphaltene samples

To develop robust technologies for the upgrading of asphaltene rich material, a better understanding of the actual structure of these class members is required. Various experimental techniques, including vapor pressure osmometry;[22] infrared spectroscopy;[23] isothermal titration calorimetry;[24] small angle neutron scattering;[25] fluorescence depolarization;[26,27] X-ray diffraction;[28] and, to a very large extent, mass spectroscopy[29-32] on genuine samples, have been used extensively in this regard. A second and increasingly popular approach has been to "reverse engineer" theorized class members, using synthetic model compounds to study their physical attributes as they relate to asphaltene solution structure, aggregation, and coking mechanisms.

1.1.3 Studies on commercially available asphaltene model compounds

Many research groups have utilized commercially available organic molecules bearing structural similarities to a limited range of postulated asphaltene structures, either individually or as a mixture for analytical experiments.[33-37] While this approach has provided some insight, its shortcomings are evident in the simplicity of these compounds (Figure 1-7) relative to the complex proposed structure(s) of actual samples.

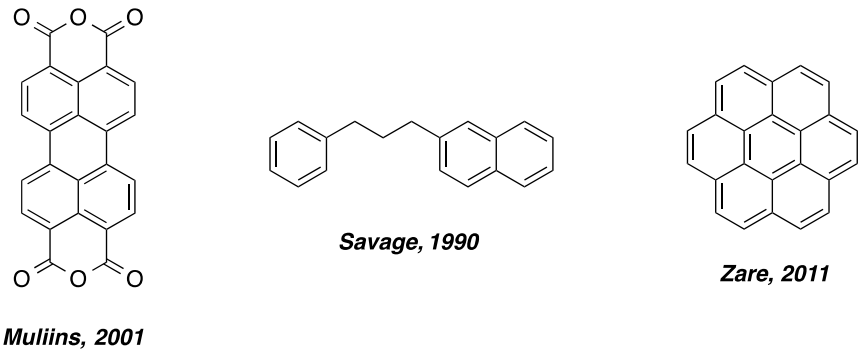


Figure 1-7. Sampled structures of some commercially available asphaltene model compounds

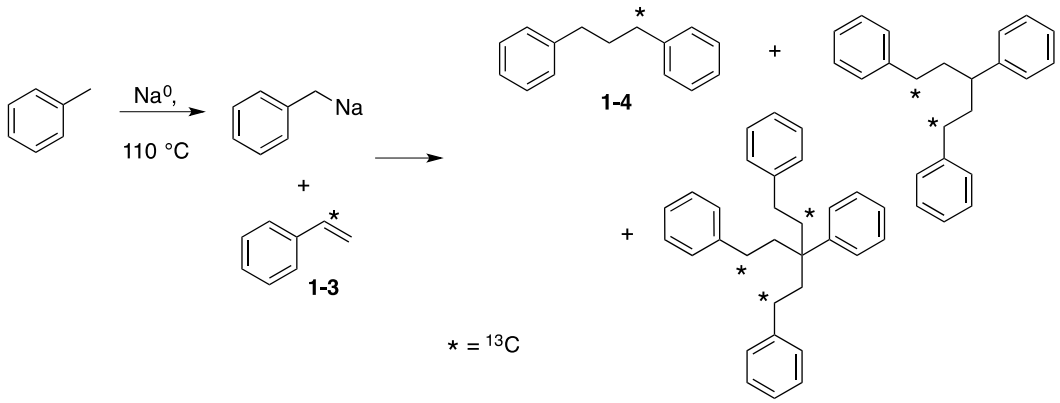
1.1.4 Why advanced synthetic asphaltene model compounds are needed

The only way to study pure samples and defined mixtures of model compounds that more closely resemble the theorized structures within asphaltenes is to synthesize them. In this way, one can more easily control structural variables, including the number and type of functional groups, molecular weight, size of unsaturated moieties (continental vs. archipelago model), and the overall topology of the molecule. Using this approach allows one to study intermolecular aggregation forces individually using the pure model compounds and cumulatively in more complex mixtures. The ultimate goal: synthetic asphaltene.

A decade of asphaltene synthesis

1.1.5 Early approaches towards synthetic asphaltenes

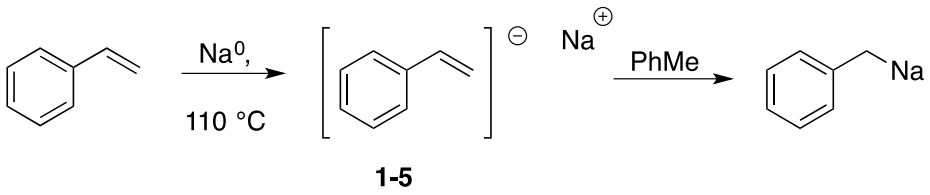
Gray, and co-workers initially studied the coking mechanisms in bitumen utilizing synthetic tracer molecules isotopically enriched in ^{13}C (Scheme 1-1).[38] These model compounds were intended to mimic constituents in gas oil, a lighter, less polarized material than an asphaltene. Thus they were not expected to induce coking (nor did they) as asphaltenes do. One of the main goals of the study was to examine to what extent liquid products were incorporated into coke under variable cracking conditions.



Scheme 1-1. Gray's synthesis of ^{13}C-enriched gas oil coking tracers

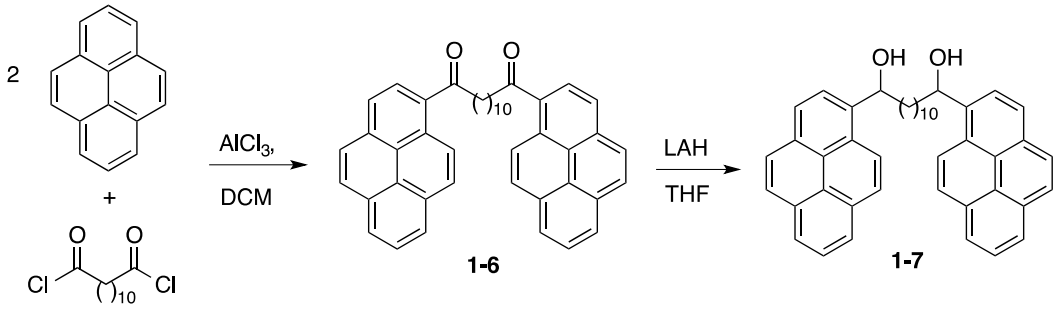
The methodology used for the synthesis of this mixture of model compounds was originally developed by Pines and Wunderlich in the 1950's.[39] This chemistry is reminiscent of the carbolithiations of apolar unsaturated moieties still being studied today,[40] which in turn are remnants of studies into the radical anionic polymerization of styrene.[41] Gray used commercially available α-^{13}C-enriched styrene (**1-3**), treating it with benzylsodium via an anti-Markovnikov addition to make labeled 1-sodio-1,3-diphenyl propane (**1-4**). This intermediate is either quenched upon workup or allowed to continue reacting with styrene to make further addition products, resulting in the observed mixture of compounds after

quenching. Interestingly, the reaction is proposed to be initiated by single electron transfer from sodium to styrene to make the corresponding radical anion, **1-5** (Scheme 1-2). This radical anion then reacts with toluene via hydrogen atom abstraction to make the required benzyl sodium.



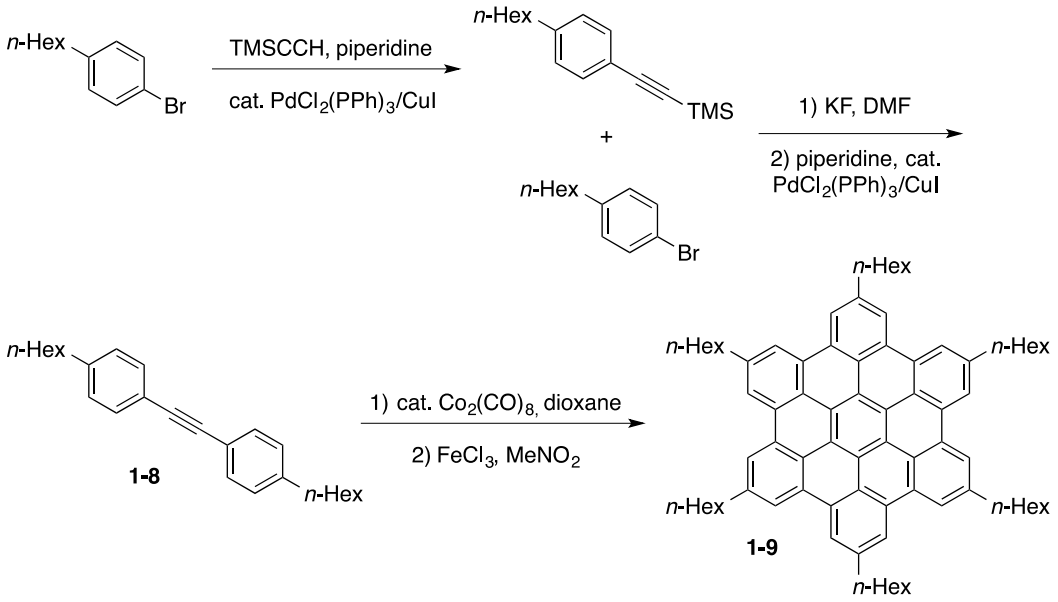
Scheme 1-2. Formation of benzylsodium in the presence of styrene

One of the first syntheses of an archipelago asphaltene model compound (Scheme 1-3) was published by Akbarzadeh, *et al*., in 2005.[42] This group synthesized two pyrene-containing archipelago-type compounds via the double Friedel-Crafts acylation of pyrene with dodecanedioyl dichloride to furnish the dione (**1-6)**. Subsequent reduction presumably provided a mixture of diastereomeric diols (**1-7**). While these simple synthetic compounds provided insight into self-association in solution, their relevance to asphaltene modeling is hampered by the presence of non-ubiquitous polar functional groups (ketones and alcohols).



Scheme 1-3. Early synthesis of pyrene-containing model compounds

Soon after this, investigations into the aggregation of polyalkylated-hexabenzocoronenes (HBC) were undertaken by the Gray group to study the enthalpy of intermolecular associations via π-π stacking interactions.[43] The synthesis of these compounds (Scheme 1-4) was accomplished via Sonagashira coupling[44] of trimethylsilylacetylene with a *p*-bromo-*n*-alkylbenzene, followed by deprotection and subsequent coupling with another equivalent of electrophile to furnish a symmetrical diarylalkyne (**1-8**). The alkyne was then trimerized via cobalt catalysis[45] to give a hexaarylbenzene intermediate primed for the final iron-mediated oxidative cyclodehydrogenation to yield the HBC product **1-9**, as reported by Müllen.[46]



Scheme 1-4. Synthesis of polyalkylated HBCs as model continental compounds

Due to the large number of condensed rings in HBCs, these molecules were expected to serve well as non-polar continental-type model compounds, though their original synthesis was not directed towards asphaltene modeling.[47] The compounds displayed intermolecular aggregation, including liquid crystalline behavior and organogel formation at low concentrations in toluene. However, as

the temperature increased, these higher-order aggregates diminished to dimeric structures, at most. The compounds also showed little adhesion to polar surfaces such as silica or alumina, in contrast to authentic asphaltenes. Thus, asphaltene model compounds clearly require more polar functionalization in order to properly model real material – π-π association is in itself not strong enough to drive asphaltene aggregation.

Other, more highly functionalized continental-type molecules were prepared by Sjoblom and co-workers in Norway (Figure 1-8), for the stated purpose of studying asphaltene film properties, interfacial tension, and emulsion stability as a function of the amount and identity of the polar appendages.[48-50] Most of these compounds incorporate a perylene core aromatic, which has been demonstrated to be a common constituent of asphaltenes.[51]

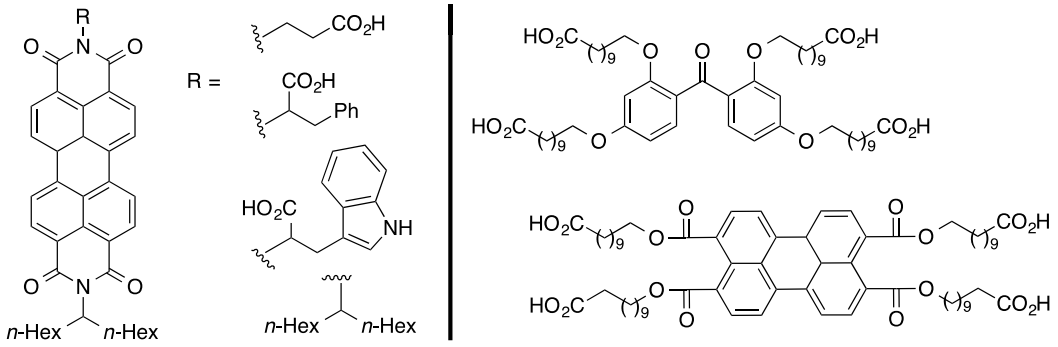
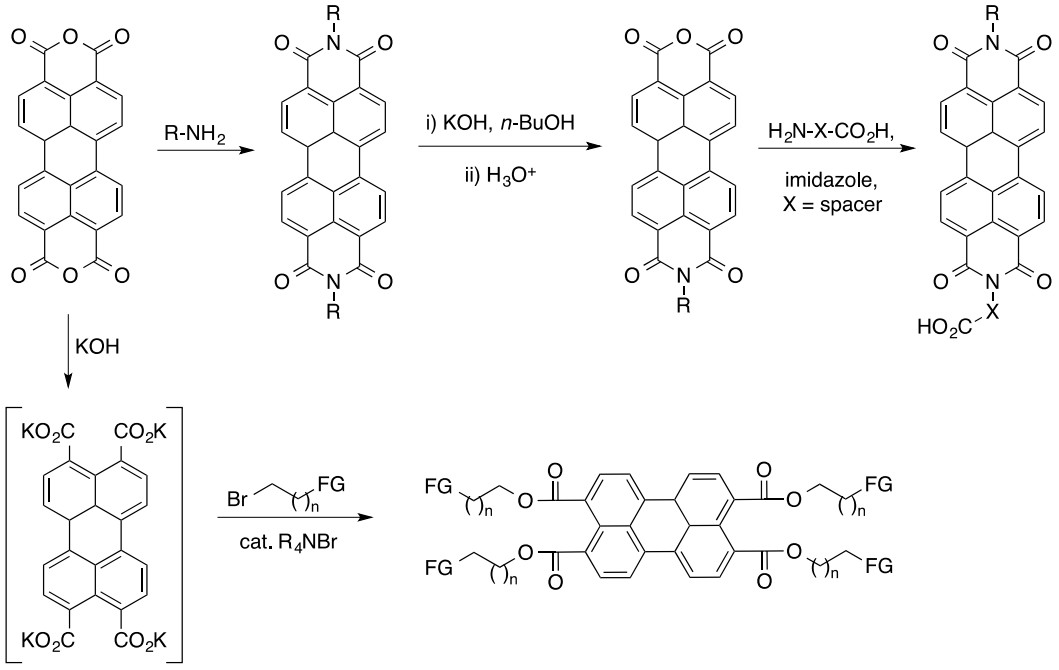


Figure 1-8. Perylene(diimide) based continental model compounds

Notably, very similar compounds bearing both perylenebisimide and carboxylic acid functionalities had been previously synthesized (Scheme 1-5) for biological imaging applications. The syntheses reported were iterative and robust.[52,53] Interestingly, however, the final step was problematic when solvents other than molten imidazole were used. A synthesis of compounds analogous to the tetra-esters was also completed.[54]



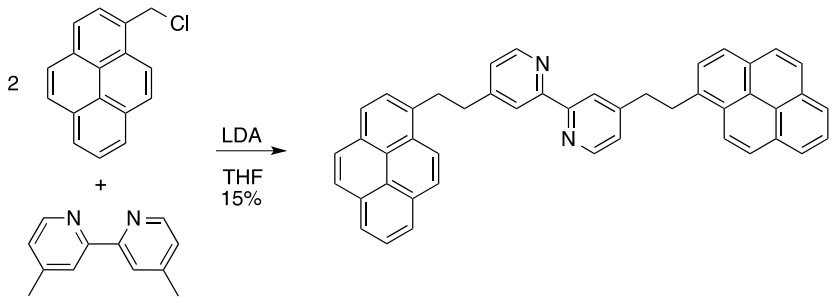
Scheme 1-5. Previous synthesis of perylene(bisimide) based compounds

While Sjoblom's compounds displayed characteristics similar to those of asphaltenes and naphthenic acids (saturated (poly)cyclic carboxylic acids present in crude oil) in terms of interfacial properties, the relevance to asphaltene modeling is similarly hampered (compare, Scheme 1-3) by an inflated heteroatom content and the presence of functional groups (ketones, alcohols, esters, etc.) that are not relevant to or not ubiquitous in asphaltene samples.

1.1.6 "Generation 1" synthetic model compounds

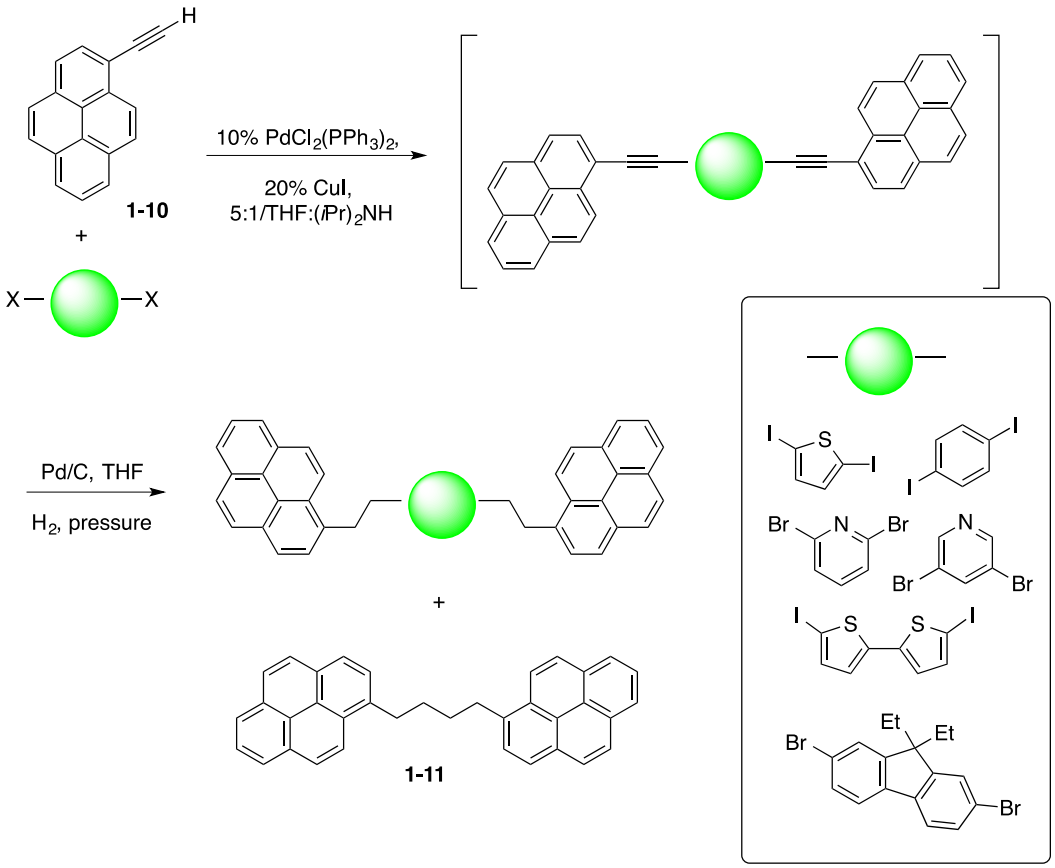
In 2007 the first synthesis of what we now refer to as a first-generation archipelago model compound (G1) was developed by the Fenniri group in collaboration with Gray.[55] This class of model compounds includes archipelago-type structures of two or more polycyclic aromatics linked together by unfunctionalized linear alkyl chains. These compounds are termed "traceless" in their bond forming disconnections, and continue the pyrenyl series started by Akbarzadeh, *et al*.[42] Though the synthesis is concise (Equation 1-1) and elegant in

principle, it is low-yielding and does not provide a "universal" methodology for the assembly of longer congeners and compositionally different central islands.



Equation 1-1. Fenniri's initial Generation 1 archipelago synthesis

The need for a general strategy to prepare other G1 model compounds was soon met by the Tykwinski Group, also in collaboration with Gray.[56] Due to this group's previous success with the Sonagashira alkynylation reaction in assembling HBC-based continental model compounds, the group envisaged using a similar approach to prepare two-carbon tethered archipelago compounds by hydrogenation of the alkynyl bridge (Scheme 1-6). They found that ethynylation of commercially available 1-bromopyrene, as previously reported,[57] provided a bench-stable pronucleophile (**1-10**) that could be used as a cross-coupling partner in combination with various dihalogenated (hetero)aromatic islands to make symmetrical, highly conjugated, alkyne-bridged three-island systems. Upon catalytic hydrogenation, these compounds yielded a library of two-carbon tethered archipelago model compounds that were subsequently studied analytically.

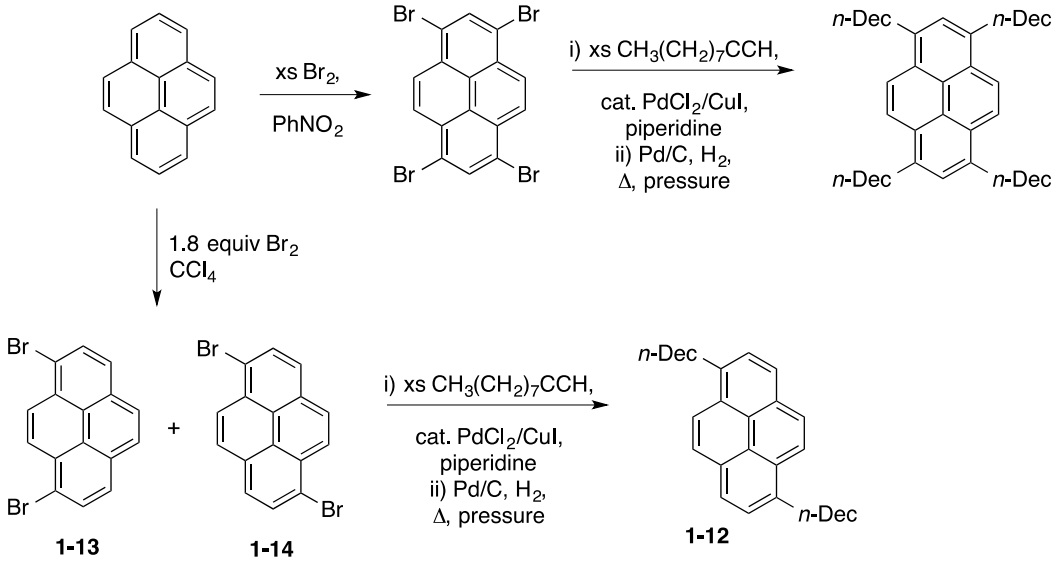


Scheme 1-6. Tykwinski's Sonagashira-inspired G1 methodology

While this approach augmented greatly the scope of accessible model compounds, in practice, the strategy suffers from numerous drawbacks. These issues include (i) competitive homocoupling[58] of the nucleophile, providing a symmetrical butano-bridged system, **1-11** (although this byproduct was used for modeling studies as well); (ii) competitive hydrogenation of the pyrenyl moieties,[59] making purifications tedious or impossible; (iii) no access to archipelagoes with tethers longer than two carbons; (iv) a requirement for the more reactive, but less economical bromo- or iodoarene electrophiles; and (v) the necessity for chromatographic purifications, sometimes repetitively so. This list of issues places practical limits on the scale and applications of the methodology, which are addressed in this thesis.

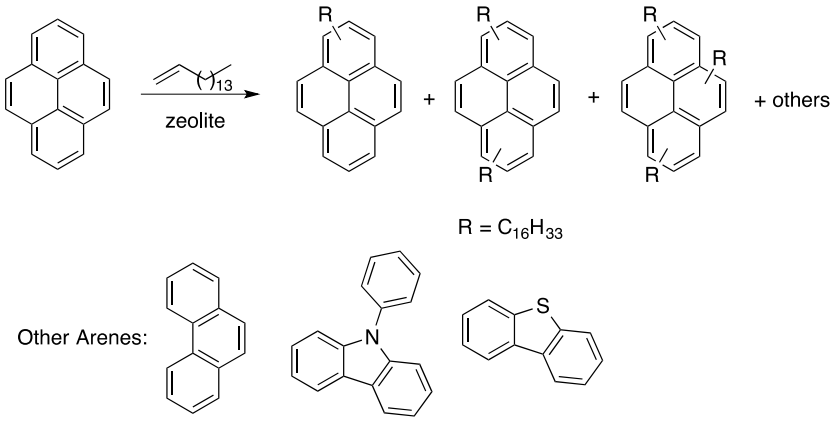
1.1.7 Continental-type model asphaltene compounds

Tykwinski's G1 model compounds mass spectra were compared both to lower molecular weight pyrene based continental model compounds and authentic powdered asphaltene samples. This was done to discern molecular and daughter ions associated with archipelago-type compounds and related but continental-type analogues. These pyrene-based compounds were either di- or tetra-substituted *n*-alkylpyrenes, again synthesized by the Sonagashira coupling of the corresponding polybromopyrenes followed by hydrogenation (Scheme 1-7). Yields were not reported for these compounds, but the synthetic approaches suffer competitive hydrogenation of the bay region of pyrene. Also, the mass balance for the di-alkyl pyrene (**1-12)** is low, due to loss of fully half of the material, as both routes start with a mixture of "cis" (**1-13**) and "trans" (**1-14**) dibromopyrenes, which is carried through the coupling/hydrogenation. Thus **1-14** is presumably converted to the dialkylated derivative, which is then removed in the crystallization of the product.



Scheme 1-7. Tykwinski's synthesis of pyrene based continental model compounds

Francisco, *et al*., also reported the synthesis of a library of polyalkylated small continental model compounds.[60] The group avoided using a cross coupling approach that would necessitate the synthesis of structurally well-defined polyhalogenated (hetero)arenes, which in turn, would maintain the atom connectivity in the polyalkylated products. Instead, they developed an operationally simple semi-random method for the Friedel-Crafts hydroarylation of terminal olefins. The reactions were performed over a zeolite catalyst that could easily be removed via filtration (Scheme 1-8). While this approach uses cheaper, less functionalized starting materials like pyrene, the resulting product mixtures are exceedingly hard to purify (where purified at all), requiring the use of HPLC, and are correspondingly poorly defined in terms of the number and location of alkyl groups on the ring and the ratio of linear/branched products.



Scheme 1-8. Francisco's heterogenous polyalkylation of (hetero)arenes

1.1.8 Model asphaltene compounds incorporating biomarkers

Biomarker-containing synthetic compounds have also been studied with regard to asphaltene modeling. This class of molecules contains structural elements stemming from the remains of biological organisms that have been preserved through catagenesis. Biological structures relevant to asphaltene modeling include diterpenoid relatives of common steroidal compounds and

nickel/oxovanadium porphyrinic compounds. In 2008, the groups of Stryker, Gray, and Tykwinski studied the previously proposed[61] association of nickel/oxovanadium porphyrins with highly condensed compounds in bitumen via π-π stacking or, potentially, axial basic nitrogen coordination.[62] The commercially available petroporphyrins **1-15**–**1-17** were compared alongside previously discussed synthetic samples (Figure 1-8). Experiments to detect association between model compounds via UV-Vis or fluorescence showed no association, leading the groups to assume associative interactions between porphyrins and large aromatics in bitumen were dominated by the interaction of other pendant functional groups. This exposed the need for synthetic and highly functionalized porphyrins for further studies.

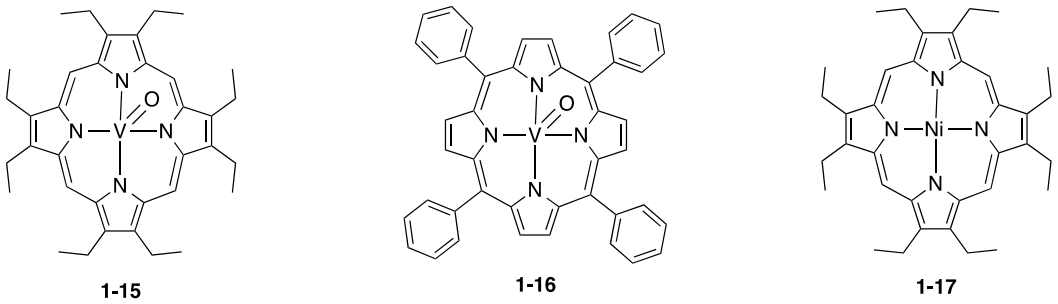


Figure 1-8. Commercial porphyrins used for the detection of π-π stacking

Recently, the Tykwinski group synthesized model nickel porphyrins **1-18**–**1-20** covalently linked by saturated tethers to an increasing number of pyrene moieties (Figure 1-9).[63] Thus the compounds can interact via (at least) two residues capable of π-stacking. The compounds were also studied alongside some high molecular weight aliphatic terminal olefins to test mechanistic hypotheses about cracking kinetics and coke-forming mechanisms. The authors found that these porphyrins underwent radical addition reactions with the alkenes under cracking conditions, forming higher molecular weight compounds.

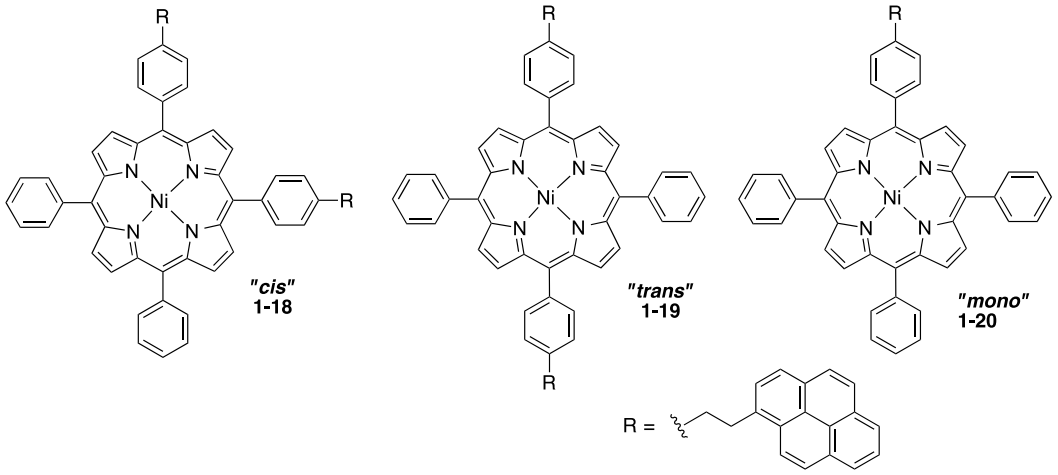
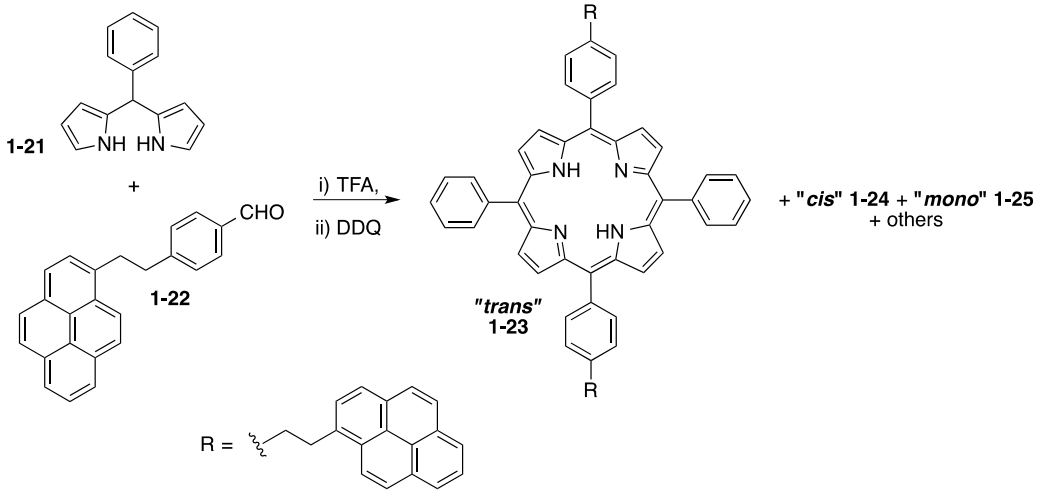


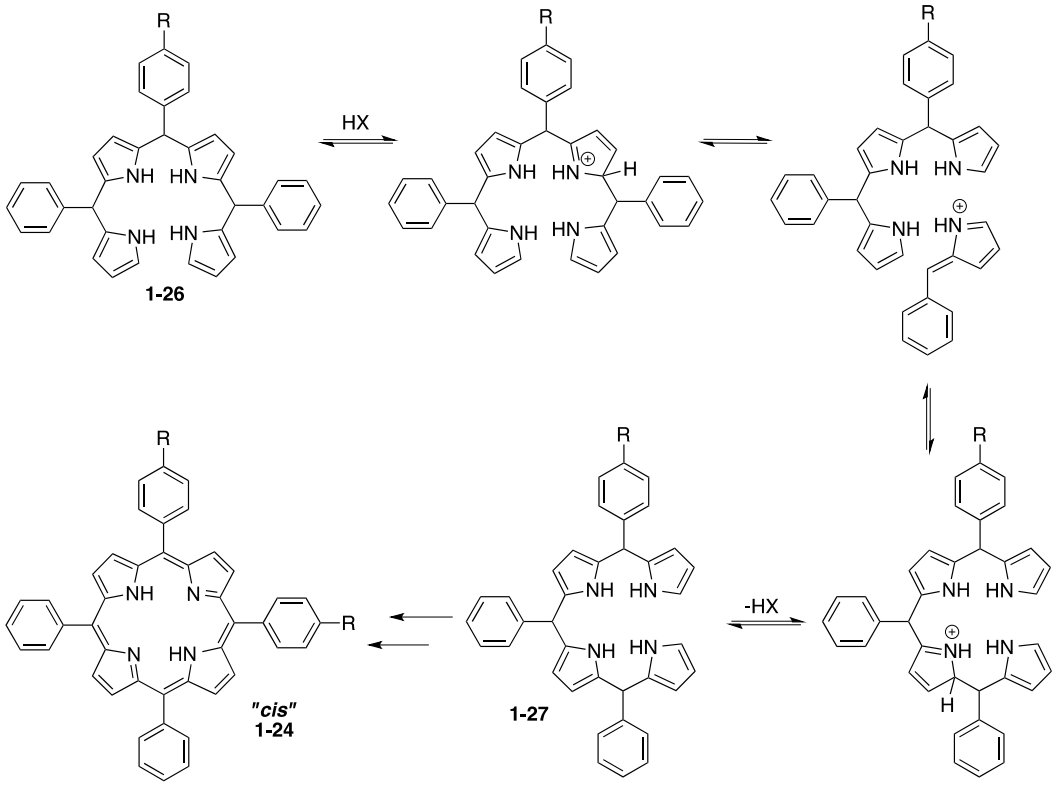
Figure 1-9. Tykwinski's synthetic porphyrins

All of the freebase porphyrin precursors were made in the same reaction pot via acid-catalyzed condensation/aerobic oxidation of 5-phenyldipyrromethane (**1-21**) and aldehyde **1-22** (Equation 1-2).[64] The reaction provides a mixture of porphyrin products incorporating up to four pyrene moieties via some interesting reversible acid catalyzed steps.



Equation 1-2. Synthesis of pyrene bearing porphyrins

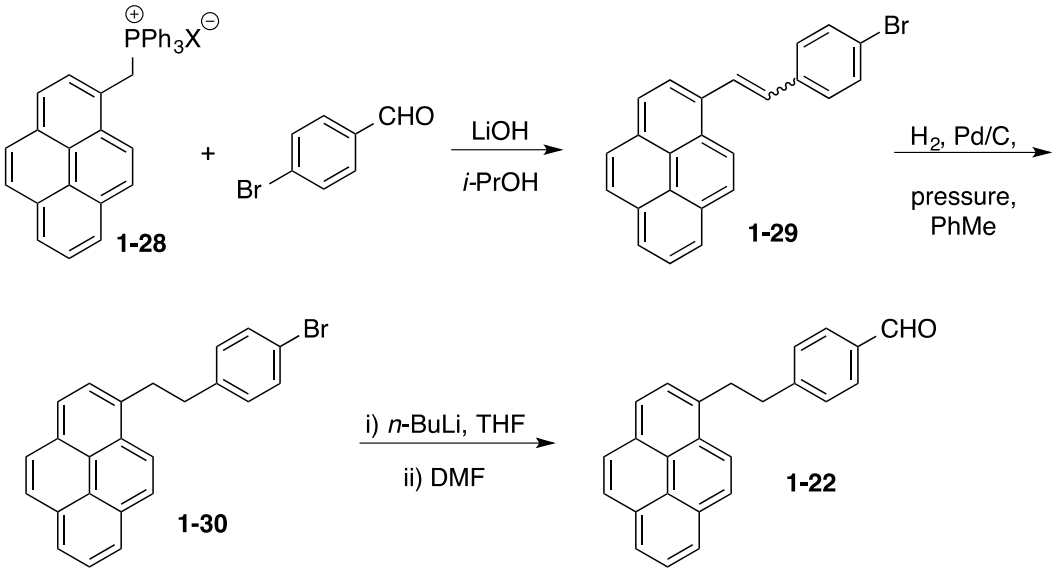
While the formation of the "trans" product, **1-23** is straightforward, the intermediates leading to the "cis" isomer, **1-24**, and the single pyrene-bearing "mono" compound **1-25** are not as obvious. This can be rationalized as follows: Under the reaction conditions, before condensation with the final aldehyde, intermediate **1-26** is formed reversibly under the acidic reaction conditions, resulting in the formation of intermediate **1-27** (Scheme 1-9). This compound condenses with the final aldehyde and aromatizes to provide **1-24**. Similar reversible carbon-carbon bond-forming reactions are responsible for the monopyrenyl adduct **1-25**. The freebase porphyrins are then metallated with $Ni(acac)_2$ in PhMe.[65]



Scheme 1-9. Reversible bond formation in porphyrin assembly mechanism

The required 5-phenyldipyrromethane, **1-21** is made via simple acid catalysis between pyrrole and benzaldehyde.[66] The pyrenyl-appended benzaldehyde, **1-22**

is made via a three-step sequence starting with the ylide derived from 1-halomethylpyrene, **1-28** (Scheme 1-10). This is olefinated via a Wittig reaction[67] with *p*-bromobenzaldehyde, providing an isomeric mixture of olefins (**1-29**). Upon hydrogenation over colloidal palladium on carbon, bromoaryl derivative **1-30** is formed convergently. Following lithium/halogen exchange[68] and DMF quench, aldehyde **1-22** is furnished. Clearly, however, this procedure requires tedious chromatographic purification(s).



Scheme 1-10. Synthesis of pyrene appended benzaldehyde precursor

Asphaltene model compounds containing steroidal biomarkers have also been prepared and studied.[69-72] The Tykwinski Group published the synthesis of some benzoquinoline-fused steroidal compounds as biomarker-containing continental and archipelago model compounds (Figure 1-10). These compounds are interesting in terms of their structural complexity, containing multiple fused rings (saturated and unsaturated), multiple aggregation-inducing functionalities, including basic nitrogen, a large condensed π-system capable of π-stacking, and large hydrophobic alkyl residues.

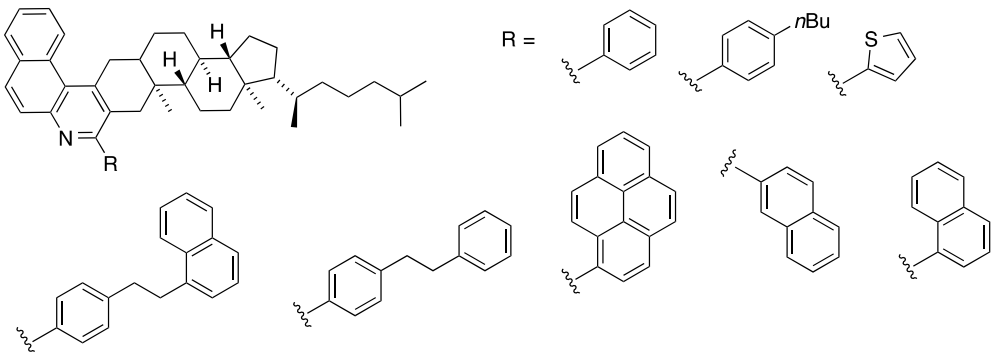
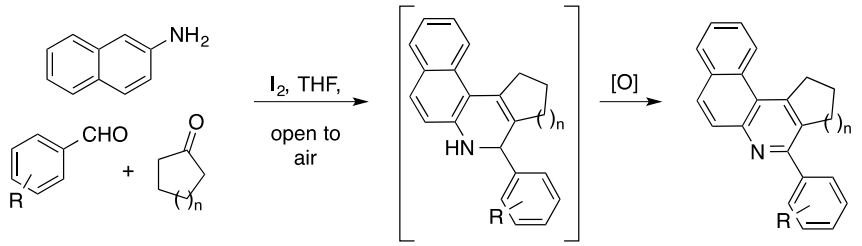


Figure 1-10. Tykwinski's steroidal model compounds

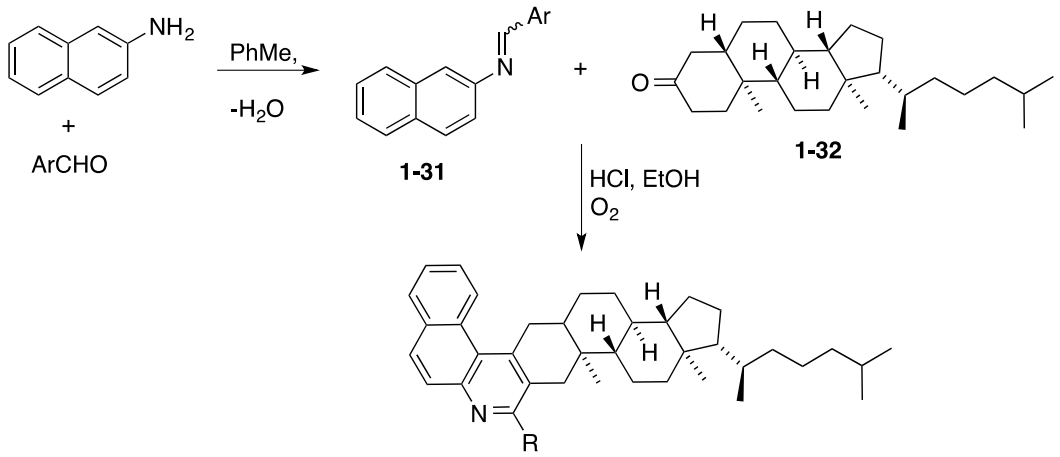
The assembly of these compounds was originally envisioned to arise via the Wang multi-component reaction (MCR) of an aryl amine, an aryl aldehyde, and an enolizable ketone.[73] Wang's procedure nominally provides benzoquinolines in high yields upon iodine-catalyzed condensation of 2-aminonapthalenes with variously-functionalized aldehydes and either acyclic or cyclic ketones of moderate to large ring size (Scheme 1-11). The products are formed with high regioselectivity and are operationally simple due to the aerobic conditions needed for the final aromatization. In addition, the purification of some of the resultant benzoquinolines could be accomplished without chromatography via direct crystallization.



Scheme 1-11. Wang MCR

Unfortunately, when Wang's developed conditions were applied to Tykwinski's steroidal systems, variable yields and complex mixtures were obtained. Given that

the desired products are formed through a "Schiff's base" intermediate (**1-31**),[74] the authors retreated to the stepwise procedure, initially reported by Kozlov and co-workers[75] (Scheme 1-12).



Scheme 1-12. Stepwise approach to steroidal benzoquinolines

The stepwise syntheses are operationally simple, but unfortunately poor yielding. The condensation to give imine could be performed without a catalyst simply by removing water from the system via a Dean-Stark apparatus[76] and the imines could be isolated by simple crystallization. After the acid-mediated cyclocondensation, however, purification required the use of chromatography, providing only enough compound for preliminary study.

Not only is the previously observed high regioselectivity obtained in the cyclization onto naphthylamine notable, the regioselectivity of the cholestanone enolization is nearly complete, a functional of torsional strain transmission in the trans-fused steroidal ketone.[77,78]

This group of synthetic model asphaltene compounds is the first to exhibit chirality (Figure 1-11). Some of these products exist as atropoisomers along the C–C bond joining the two aryl systems; this occurs when the products have

sterically large groups incorporated from the aldehyde component. The pyrene appended compound **1-33**, for example, exhibits this behavior. The compounds also exhibit helical chirality both as solids and in solution, as evidenced by X-ray crystallography and CD spectroscopy. Only one, the "*P*-Isomer" is observed, a function of the stereochemical information contained within the cholestenone component.

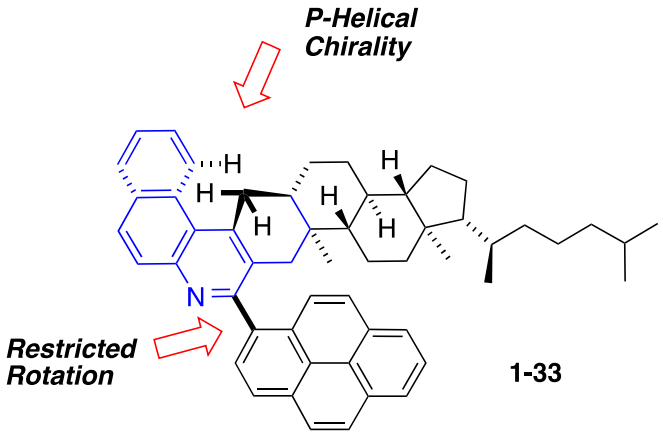


Figure 1-11. Chirality in steroidal model compounds

These compounds, alongside other synthetic model compounds, were studied under thermal cracking conditions to gain insight into the kinetics and mechanisms by which coking both initiates and proceeds.[69,71] These studies indicate that archipelago structures form alongside lighter, cracked compounds via classic radical addition reactions. A very important point, validating the hypothetical existence of archipelago type structures in asphaltenes, was drawn from these studies: "The implication is that such structures will be common in petroleum, where cracking and addition take place by similar mechanisms, albeit over much longer time periods."[69]

A brief discussion on coking

The mechanism by which coking is thought to proceed contains the same elementary steps that cracking follows, with the caveat that high molecular weight olefins in the liquid phase, produced from these thermal reactions, further react by addition reactions with other radicals, affording higher molecular weight material in addition to lower molecular weight cracked fragments. Figure 1-12 displays a rational coking mechanism for 1,3-diphenylpropane (**1-34**), an extremely simplified (and uncharacteristically low molecular weight) asphaltene model. The phenyl groups represent larger aryl systems. While the initiation reaction is highly endothermic, suffering from a high reaction barrier for homolytic cleavage of either C–C or C–H σ-bonds. The initiation step(s), however, only need(s) to occur rarely, as the subsequent chain propagation steps all proceed by considerably lower activation barriers, carrying the conversion efficiently. It is reasonable to assume that in actual bitumen samples weaker bonds such as alkyl thioethers and disulfides are the actual initiators of such chain reactions.

One notable propagation step in the proposed radical coking mechanism is the "radical rearrangement" as shown in Figure 1.12. This apparent 1,2-aryl shift is assumed to operate via a neophyl-type rearrangement (Figure 1-13).[79] The homobenzylic radical (**1-35**) adds to the *ipso* carbon of the arene generating a spirocyclic cyclopropane-cyclohexadienyl radical (**1-36**), an intermediate that can ring open in one of two ways to restore aromaticity prior to further reaction in propagating or terminating steps.

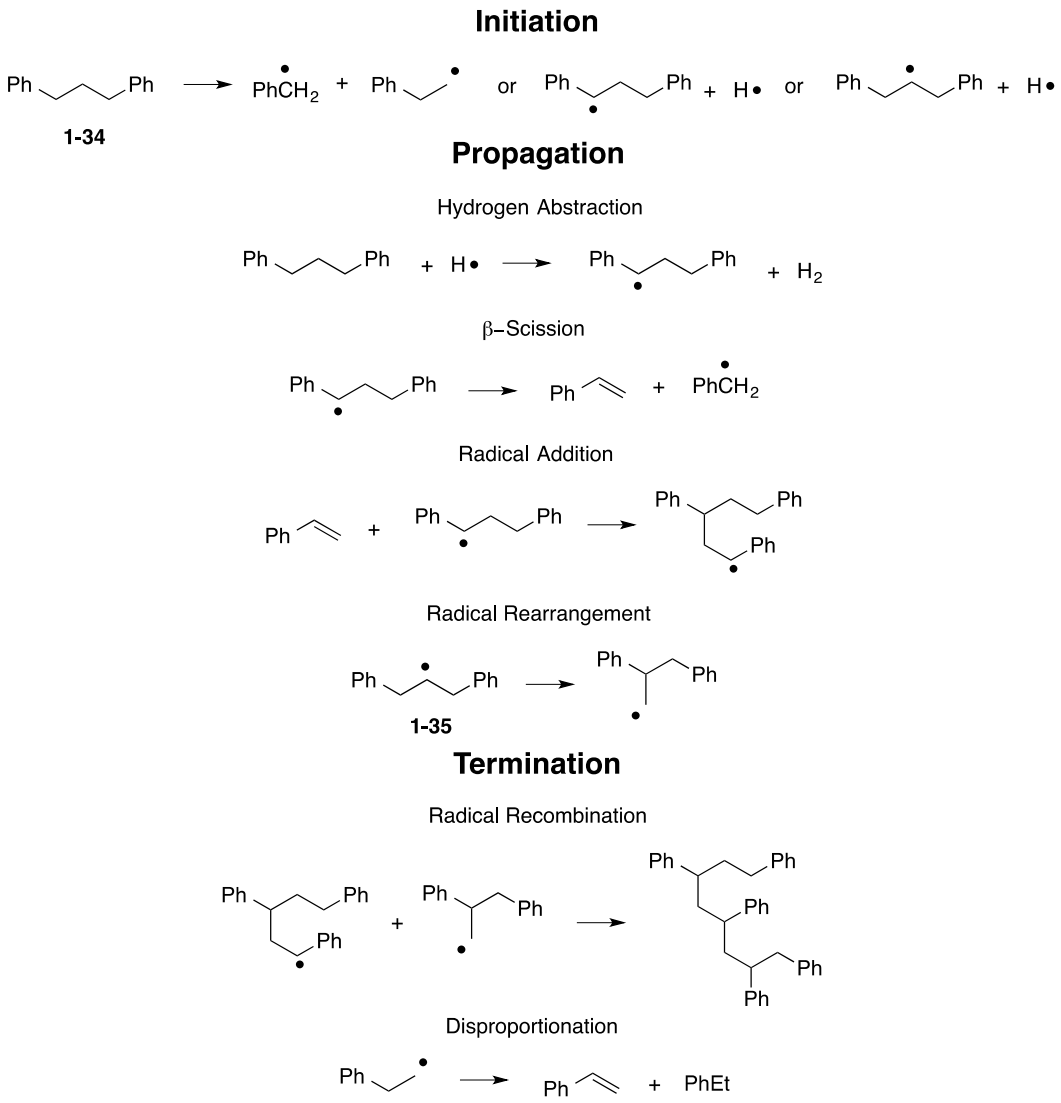


Figure 1-12. Fictional depiction of the coking mechanism for 1,3-diphenylpropane

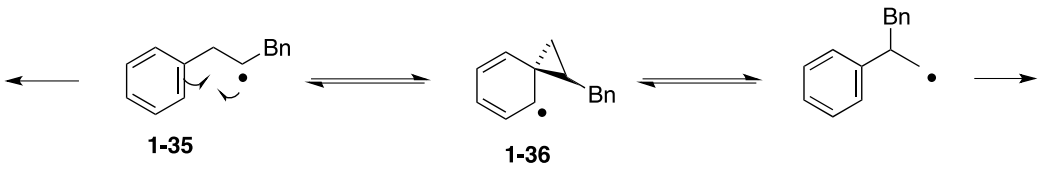


Figure 1-13. Neophyl rearrangement as potential radical propagation step

We and the Tykwinski Group have proposed such rearrangements as a plausible explanation for the observation of α-dealkylated arenes in coking experiments with model asphaltene compounds.[80] For example, when **1-37** was subjected to coking conditions and the product mixture analyzed by mass spectroscopy, pyrene was detected, along with other cracked products (Figure 1-14). It is unlikely that the corresponding pyrenyl radical **1-38** forms via homolysis of the exocyclic C_{sp2}-C bond of **1-37**, due to its high bond dissociation energy relative to the doubly benzylic C–C bond of the ethano-bridge. Instead we expect that it forms via radical rearrangements of the benzylic radical formed from hydrogen atom abstraction from the initial archipelago. While β–scission is a reasonable path from the homobenzylic/benzylic radical **1-39**, another possibility is a neophyl-type rearrangement to form intermediate **1-40**. Following this, a cyclopropane opening and subsequent β–scission will lead to the required aryl radical **1-38** and styrene, **1-42**. It is also possible for **1-40** to undergo a radical addition reaction onto the pendant pyrene moiety forming a strained spirocyclic and highly delocalized radical intermediate **1-41**.

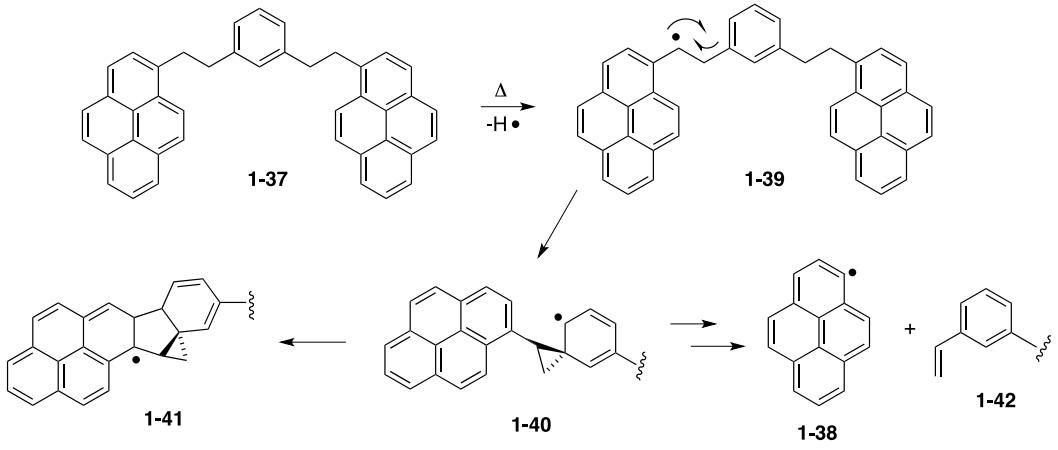


Figure 1-14. Proposed radical rearrangements in model asphaltene coking experiments

Clearly the process of coking is a complex one. Difficulties in deciphering the mechanisms by which this insoluble material is formed are compounded by the vast structural diversity of natural samples. Thus illustrating the importance of model compounds in regards to bitumen upgrading.

Drawbacks of current synthetic approaches

While the synthesis of model asphaltene compounds has clearly advanced over the past two decades, there clearly remains considerable room for improvement and the introduction of more efficient synthetic strategies. Current limitations of model asphaltene synthesis include:

- Many model systems are synthesized as mixtures (regioisomeric mixtures, etc.) rather than discrete (single component) samples. While asphaltenes are certainly a complex mixture of compounds, model compounds should ideally be analytically pure. The purpose of making model compounds is to study first the behavior of individual components when isolated, then cumulatively. While synthetic approaches to model asphaltene mixtures have provided information on bulk properties, pure materials are needed to decipher complex mechanisms.
- Structural relevance. The majority of the model asphaltene compounds synthesized to date were designed to mimic the behavior, not the structure, of the asphaltenes. In order to reverse-engineer model compounds that mimic asphaltene complexity and behaviour, one should mimic both form and function. Model asphaltene compounds should embody the same structural characteristics as they are intended to model. Thus, the desired model compounds should contain ubiquitous asphaltene functional groups and architectures, fall into the correct (broad) molecular weight range, and have cumulative elemental compositions similar to authentic samples.
- Scale. Most of the analytical and experimental work done on asphaltenes to date was done on the milligram scale. This is not desirable for future

work. To perform a great number of experiments involving many controls and have those experiments be industrially relevant, multigram quantities of model compounds must be made available. Bitumen characterization and upgrading is not done on the milligram scale!

- Most synthetic procedures require chromatographic purification(s). As the scale of our syntheses increase, all chromatographic methods begin to become prohibitively expensive and labour-intensive. Also, as model compounds become structurally and functionally more accurate depictions of asphaltene reality, they will irreversibly stick to silica, as authentic asphaltenes do. Ultimately, silica gel chromatography is an unreasonable means of purification for these compounds.

Thesis research objectives

The goal of this research project was to develop and demonstrate concise approaches to the synthesis of structurally relevant model asphaltene compounds that are scalable, chromatography free, and provide analytically pure material. Ideal strategies are also divergent, so that large libraries of representative compounds can be accessed from a relatively small pool of "early-stage" assembly line intermediates.

2 Synthetic Approach Towards Synthetic Asphaltene Compounds

Methodology design

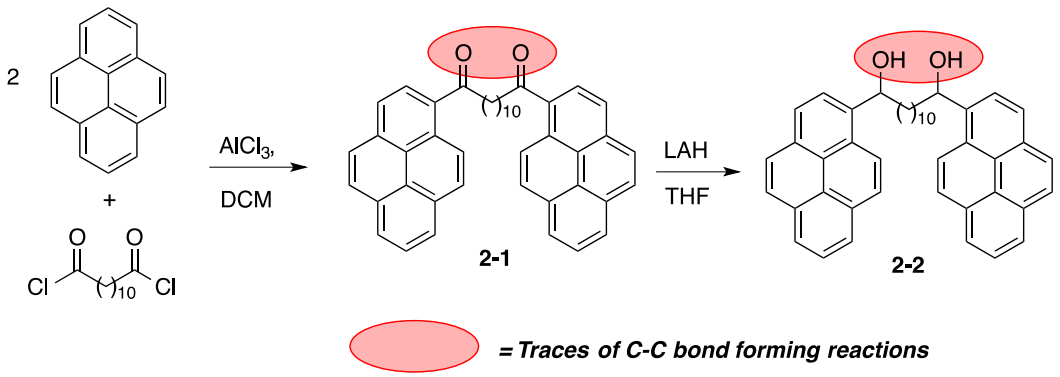
With the drawbacks of previous asphaltene model compound syntheses identified, we are in a position to develop our own synthetic approach, one that avoids those shortcomings. Improvements in the synthesis of these molecules both, raises the bar for future synthetic efforts and will allow us to provide collaborators with more compounds at higher purity and scale.

2.1.1 Prerequisites to our synthetic approach

The attributes of an ideal synthetic approach should include:

- Concise sequences. Because our goal is to eventually develop a large catalog of model compounds, we must be able to furnish final products in as few steps as possible from readily accessible starting materials. In general, efficiency in chemical synthesis is related to ideals such as atom economy[81] and green chemistry.[82] For us, efficiency is more closely related to time management. We cannot afford to spend weeks on the linear synthesis of one compound when there is a demand for multiple different samples.
- Scalability. As the ultimate goal of this project is to study our synthesized model asphaltene compounds through collaborative efforts with other chemists and engineers via potentially destructive methods (e.g., coking simulations or mass spectroscopy studies), our syntheses must be scalable so that we can provide final products at gram-plus scale. Thus, it is in our best interest to develop syntheses of archipelago precursors at decagram-plus scale.

- Chromatography-free. When working within the guidelines above, it follows naturally that our syntheses should be chromatography-free. Products should be isolated via precipitation or crystallization as they generally are in the pharmaceutical industry.[83] It is prohibitively expensive to routinely run reactions at decagram scale (or more) and then purify the isolated intermediates via chromatography.
- Structurally relevant architectures. The goal of most total synthesis projects is to create a single complex molecule found in the environment (usually a secondary metabolite of a living organism). However, our goal is to develop a large catalog of compounds that are *hypothesized* to be in the environment (compounds whose atoms originate from living organisms, but the molecular structures are the result of catagenesis). This lends us the freedom to define the exact structures we choose to target in comparison with a more traditional total synthesis project. Our final products should then fall within the hypothesized themes of asphaltene structure. Therefore, our final products should not incorporate "non-ubiquitous functional groups" that are the result of non-traceless bond forming reactions. Examples of this shortcoming (Scheme 2-1) are the ketones and secondary hydroxyl groups (functional groups that are not representative of the bulk material within asphaltenes) of compounds **2-1** & **2-2** from Gray's early synthesis of model asphaltene compounds.[42]



Scheme 2-1. Examples of undesired "traces" of C-C bond forming reactions in previous model asphaltene syntheses

- Constitutionally relevant molecular formulae. Our final compounds should fall into the assumed correct molecular weight range for asphaltene compounds (500-1500 da.) and the elemental composition of these products should be reflective of natural asphaltene samples as well, i.e. having a C : H ratio approaching unity.

2.1.2 General tenants of synthetic design

The initial class of molecules our group set out to synthesize is termed "second generation archipelago model compounds" (G2) (Figure 2-1), a consequence of joining this project midstream.* These compounds are similar to the G1 compounds except the number of methylene units linking the "islands" of the archipelago system were to be greater than or equal to two. This was desirable as archipelago-type asphaltenes are assumed by most researchers to be dominated by alkyl linkages of lengths between 1-20 methylene units, though predominantly

* This project was originally developed by the Tykwinski Group at the University of Alberta, now at FAU in Germany. The Stryker Group joined these collaborative efforts in 2009.

between 1 and 4.[20] Compared to G1 targets, the total number and type of islands in a given system were projected to be more variable in composition.

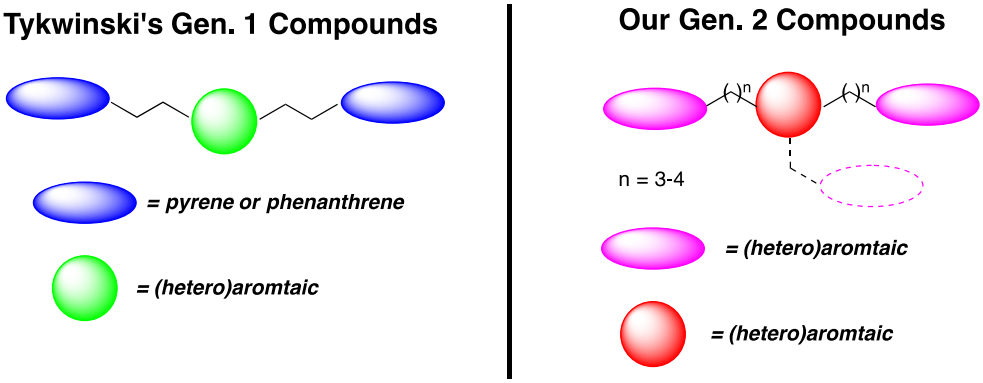
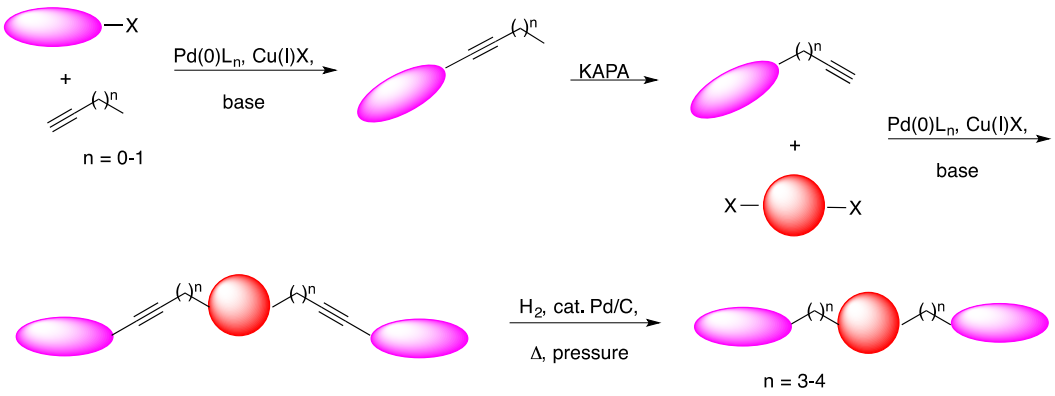


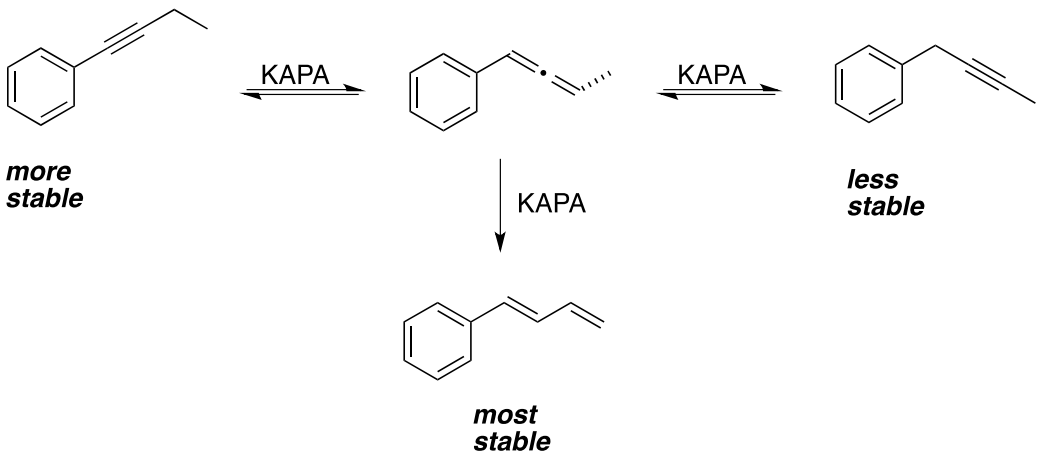
Figure 2-1. G2 compound structural guidelines

While the ethano bridges of G1 compounds clearly lent themselves well (on paper) to assembly via Sonagashira coupling/catalytic hydrogenation, this approach is not directly pertinent to propano- or butano-linked systems. One could, however, envision a synthesis wherein halogenated islands are alkynylated via Sonagashira coupling using propyne or butyne followed by rearrangements via the "alkyne zipper reaction,"[84] to provide the required terminal alkyne for final archipelago assembly (Scheme 2-2).



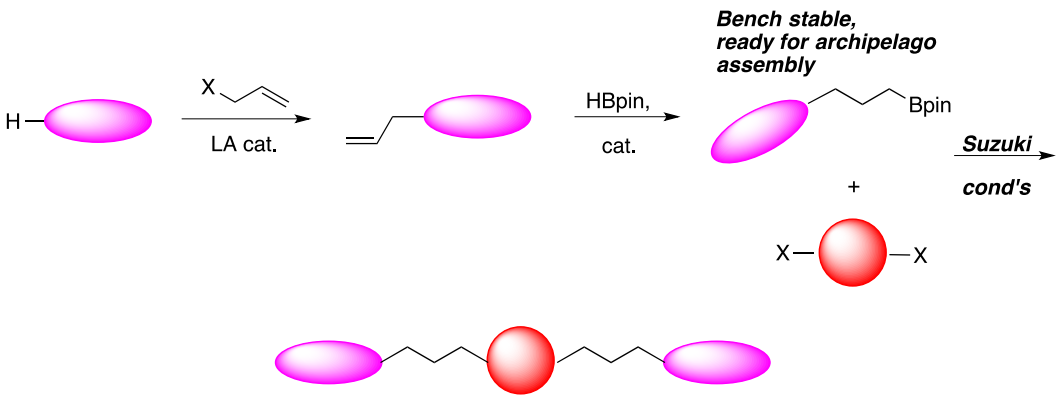
Scheme 2-2. A potential G2 approach utilizing the "alkyne zipper" reaction

Unfortunately, this approach has inherent limitations. Propyne and butyne are gases at room temperature and are thus not easily utilized on the bench. This approach could also potentially suffer from the same nonselective hydrogenation issues suffered by the G1 approach. Most importantly, the zipper reaction is known to have issues in systems wherein the starting material is an aryl alkyne. Once the alkyne has isomerized to its first intermediate along the desired reaction path – an aromatic allene – it is more likely for the intermediate to isomerize to the more conjugated 1-aryl-1,3-butadiene than the next desired intermediate, a propargylic arene[85] (Scheme 2-3). This makes the eventual isomerization to the terminal alkynide (the thermodynamic sink driving product formation) less favorable, as the butadiene formation is itself a thermodynamic sink.



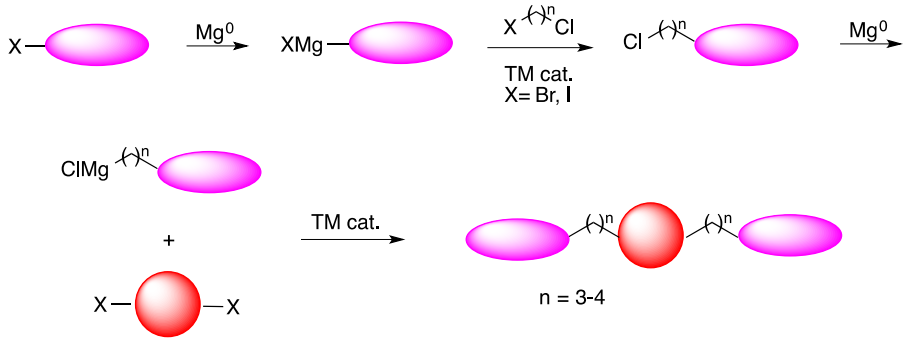
Scheme 2-3. Issues utilizing "zipper" reaction with an aromatic alkyne

Another reasonable approach to these targets can be envisioned by an allylation-hydroboration-Suzuki coupling sequence (Scheme 2-4). One advantage of this strategy is the ability to avoid using a halogenated aromatic building block as the starting material because one could potentially allylate an unfunctionalized arene via Friedel-Crafts type chemistry[86] (assuming selectivity is not an issue). The other advantage is that the hydroborated intermediate could be a bench-stable trifluoroborate, so that the nucleophile could be synthesized at scale and conveniently stored, ready for cross-coupling when needed. Because this approach is limited to propano-linked structures and systems wherein the selectivity of the initial allylation might proceed cleanly, the methodology was shelved.



Scheme 2-4. Potential allylation-hydroboration-Suzuki coupling G2 approach

Instead, the synthetic approach selected featured iterative cross-coupling reactions, wherein a halogenated island is first converted to the corresponding Grignard reagent and subsequently selectively cross-coupled with an α-halo-ω-chloro-*n*-alkane (Scheme 2-5). Assuming the coupling reaction proceeds chemoselectively at the more reactive bromine or iodine, the resulting island-tethered primary alkyl chloride could be similarly metallated by magnesium in preparation for a second cross-coupling. Coupling of this Grignard reagent with an appropriate stoichiometry of a poly-halogenated arene then provides a "homoleptic" archipelago system, analogous to the Tykwinski G1 compounds, with the advantage of greater variability in tether lengths.



Scheme 2-5. Iterative cross coupling approach towards G2 compounds

One advantage of this approach is the simplicity of the assembly. Not only is the carbon framework of the alkyl-tethered product established in the final step of the synthetic sequence, but functional group manipulations (e.g. oxidation/reduction/hydrogenation) are avoided due to the traceless nature of such simple C(sp^3) cross-coupling reactions. This approach, in theory, simplifies compound purifications because the large archipelago products should be much less soluble relative to their smaller by-products.

A review of the pertinent cross-coupling literature

Typically, cross-coupling refers to the transition metal-catalyzed C–C bond formation between an organometallic reagent and an organohalide (or pseudohalide). This general process has revolutionized chemical synthesis in the pharmaceutical industry due to its traceless nature, ever-increasing reliability, and broad functional group compatibility.[87] The importance of this class of reactions is highlighted by the 2010 the Nobel Prize awarded to Richard Heck, Ei-ichi Negishi, and Akira Suzuki "*for palladium-catalyzed cross couplings in organic synthesis*".[88]

The mechanisms of these cross-coupling reactions generally follow the steps of oxidative addition, transmetallation, and reductive elimination, which are outlined in Figure 2-2.[89] The Mizoroki-Heck reaction follows a similar catalytic cycle, though the nucleophile in these reactions is not an organometallic reagent but rather an olefin, and the reaction terminates with a β-hydride elimination instead of a reductive elimination.

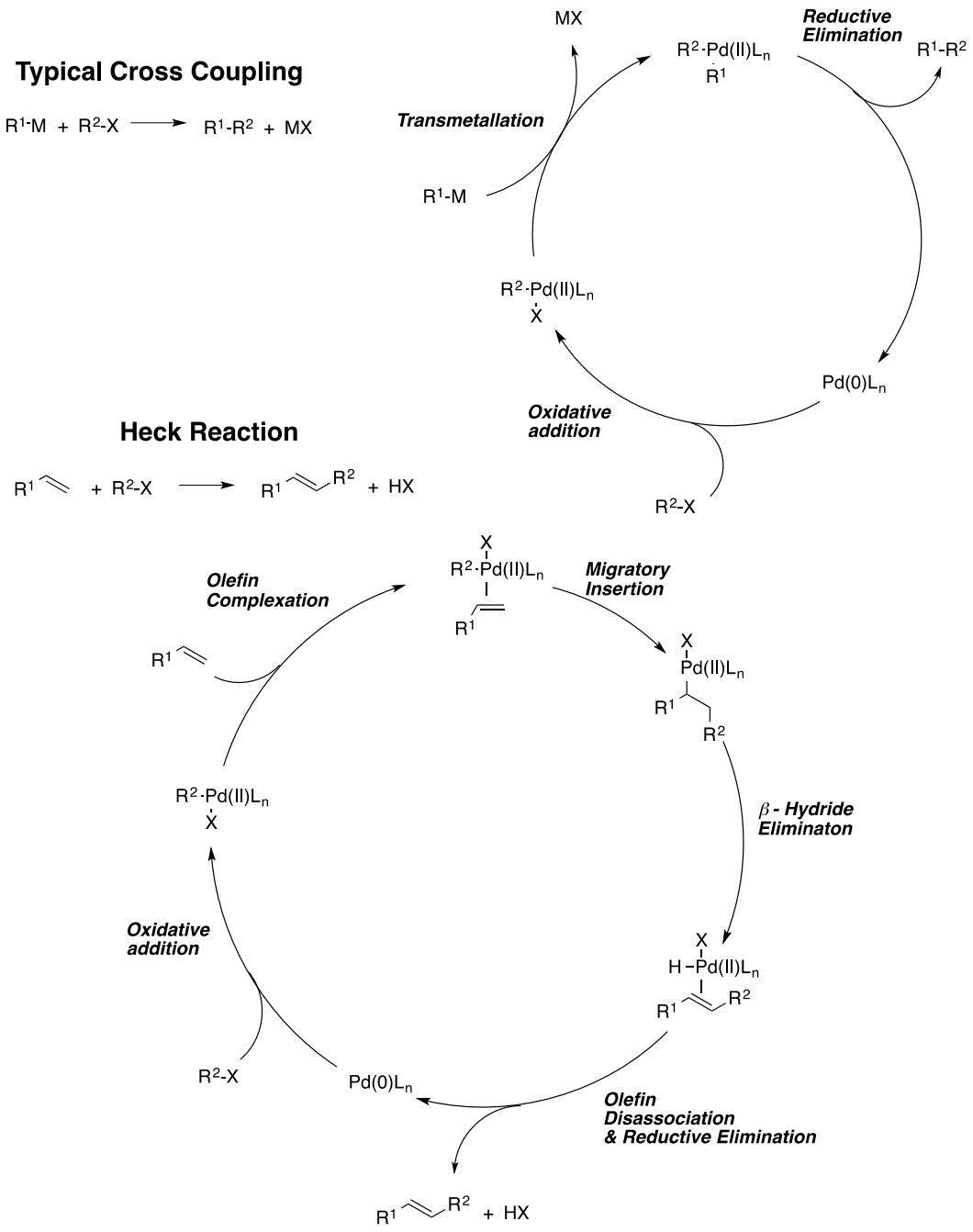
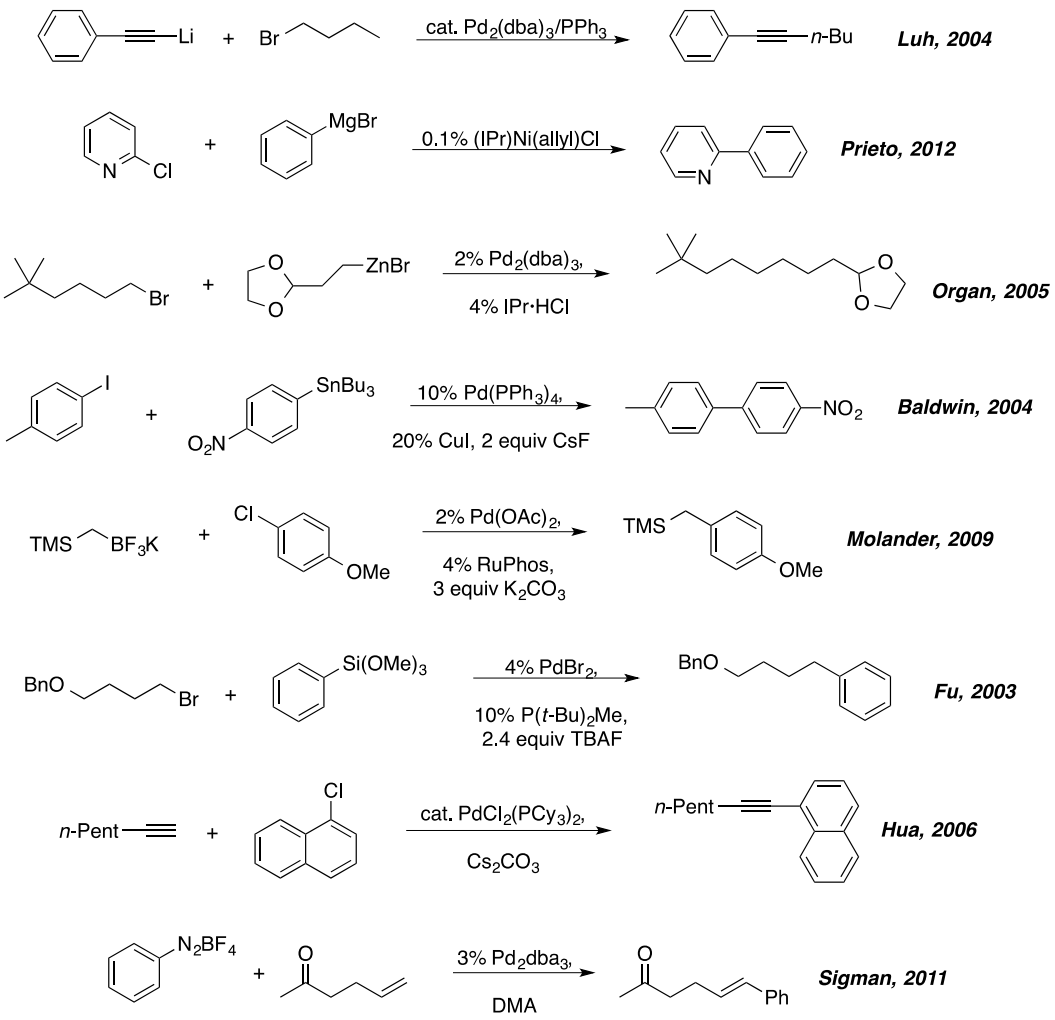


Figure 2-2. General catalytic cycle for Pd catalyzed cross couplings

There is much variability underneath the umbrella of "cross-coupling," both in terms of (but not limited to) the metal used in the nucleophilic component and the hybridization states of the atoms being linked. Main group metals used in these

processes include: lithium, magnesium (Kumada-Tamao-Corriu coupling), zinc (Negishi coupling), tin (Stille coupling), boron (Suzuki-Miyaura coupling), silicon (Hiyama-Denmark coupling), and in-situ formed copper acetylides (Sonagashira coupling) (Scheme 2-6).[90-98] Excluding the Sonagashira and Heck reactions, the hybridization of the nucleophilic carbon atom can vary anywhere from sp to sp^3, although typically the centre is sp^2-hybridized.

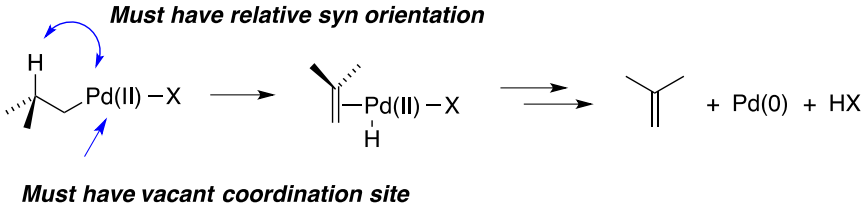


Scheme 2-6. Examples of each class of cross coupling sub-type

2.1.3 Issues limiting cross couplings between alkyl reaction partners

While cross-coupling reactions between sp^2 centers is the standard for this class of reactions, the use of sp^3-hybridized partners remains under active development and is subject to greater limitations. Some of the issues that can plague these processes include:

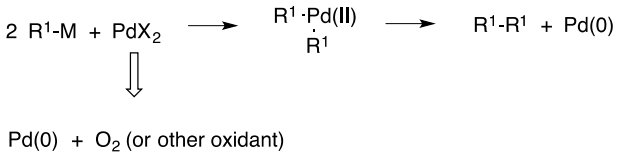
- Uncontrolled β-hydride elimination. Throughout the course of the reaction both the nucleophilic and electrophilic carbon atoms make covalent bonds to palladium. A plausible but counterproductive mechanistic pathway is β-hydride elimination (if indeed β-hydrogen atoms are present) instead of reductive elimination to give the desired product (Scheme 2-7). In order for β-hydride elimination to occur, an open coordination site on the metal is required, and the β-hydrogen in question must be close to "syn-coplanar" relative to the metal. This process is generally facilitated by an agostic interaction of the C-H σ bond with a vacant d-orbital on the metal.[99]



Scheme 2-7. β-hydride elimination from σ-alkyl Pd(II) intermediates

One method of avoiding competitive β-hydride elimination is to use a bulky ancillary ligand, which either does not allow the required geometry for this process to occur, or makes the resulting metal hydride intermediate unfavorable due to steric crowding at the metal.[100] Another approach is to use a multidentate ligand that permanently fills the required vacant site on the metal.[101]

- Homocoupling. Another issue that can lower yields during cross coupling reactions, whether or not one or more of the partners is alkyl, is a process termed "homocoupling." Homocoupling occurs when two electrophilic or two nucleophilic carbon centers self-react, forming an undesired C–C bond. This can occur through various pathways, but most often occurs by sequential transmetallations from the nucleophilic partner to a Pd(II) intermediate, providing an electron rich metal center that reductively eliminates the homocoupled product (Scheme 2-8).[102]



Scheme 2-8. Homocoupling in palladium catalyzed cross couplings

The usual cause of homocoupling is the presence of undesired Pd(II) salts in the reaction mixture. Such salts could originate from the inefficient generation of the active Pd(0) catalyst from a Pd(II) precatalyst and in-situ reductants, or from deleterious oxidants interrupting the catalytic cycle. The former can be addressed by using a Pd(0) precatalyst, while the latter issue can sometimes be suppressed by using more strictly anareobic conditions or even by adding mild reducing agents to the reaction mixture.[103]

- Protodemetallation. Because the nucleophilic coupling partner in these reactions is a preformed organometallic species (excluding the Heck and Sonagashira reactions), the nucleophile can be protonated competitively with transmetallation to the desired RPd(II)X intermediate.[104] When this happens, the nucelophile is sacrificed. In situations wherein the nucleophile is strongly basic, as in the Kumada coupling, the reaction is

generally run under stringently dry conditions to avoid water-mediated protodemetallation.

Interestingly, in some situations, such as most variants of the Suzuki-Miyaura and Hiyama-Denmark couplings, water plays an essential role in the reaction mechanism (viz., base mediated transmetallation) and cannot be avoided.[104] This is not to say protodemetalation does not occour in these reactions; it often does. In fact, for the Suzuki-Miyaura coupling, this process has its own term, "protodeborylation." The problem can often be overcome by using a large excess of the nucleophile relative to the electrophile. Protodemetalation can also occur after transmetallation of the organic fragment to the Pd(II) center, and is termed protodepalladation.[105] Thus, the electrophilic coupling partner can also be reduced via this process (Figure 2-3).

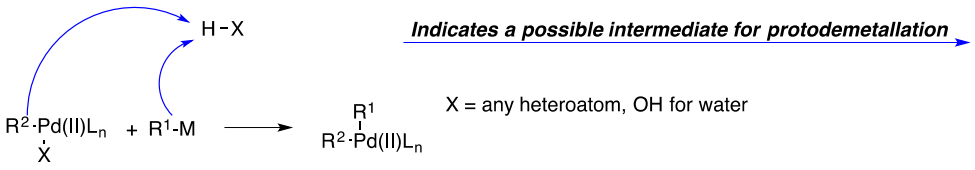


Figure 2-3. Potential protodemetallation processes in cross coupling

- Competitive transmetallations. When performing a cross-coupling reaction with a strong nucleophile, transmetallation between coupling partners can be competitive provided the electrophilic carbon has more s- character than does the nucleophilic carbon. This is not surprising, as transmetallation is a common process for the in-situ formation of complex organometallic reagents from more reactive, commercially available, reagents like *n*-BuLi.[106] As an example, 1-bromothiophene couples quite cleanly with the less reactive phenylmagnesium bromide under Kumada's initial coupling conditions.[107] Transmagnesiation, however, becomes the

dominant pathway when using the more reactive *n*-butylmagnesium bromide (Figure 2-4).

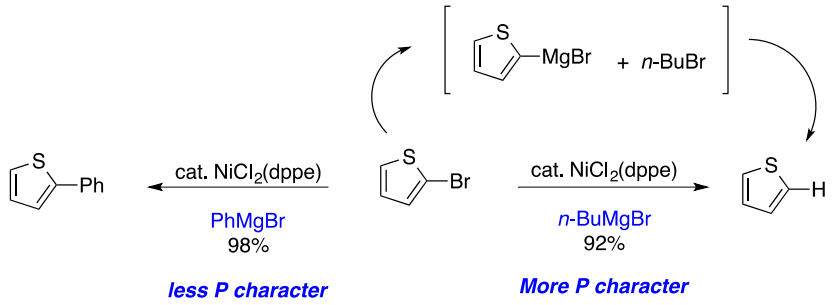
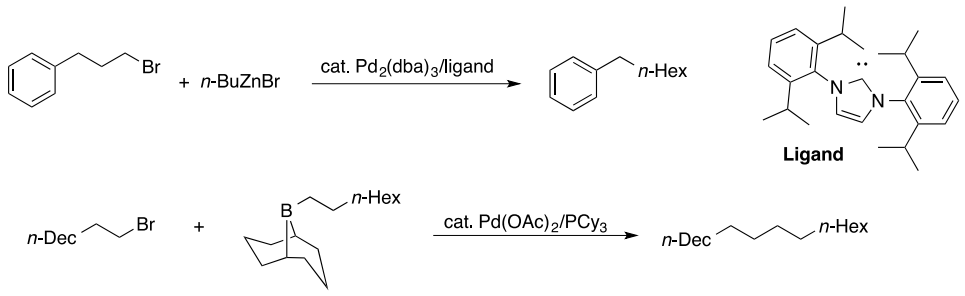


Figure 2-4. Differential reactivity of 1-bromothiophene with different Grignard reagents under coupling conditions

- Slow transmetallation to Pd. While the turnover-limiting step in most cross coupling reactions is oxidative addition of the catalyst into the C-X bond of the electrophile,[104] transmetallation can often have the highest energy barrier in situations where the nucleophile is poorly reactive. In fact, for many coupling reactions, base-assisted transmetallation is used in order to minimize or overcome this barrier.[108] Experimental observations have demonstrated that transmetallation in ***B***–alkyl Suzuki couplings is slow relative to the reaction of unsaturated analogs.[104,109] This is somewhat counterintuitive from a rudimentary point of view, if the C–B bond is viewed as highly ionic in nature like that of a Grignard or lithium reagent. While electronic arguments for this could play a role, the trend is usually ascribed to steric effects.[110] One of the most illustrative reaction classes to exploit this surprising trend is Stille coupling. In general, Stille reactions are used to forge linkages between two sp^2-hybridized atoms. The nucleophilic partner has four organic groups attached to the Sn(IV) atom each theoretically capable of being transferred. Usually, three of them are identical *n*-alkyl groups (*n*-Bu or Me), and the fourth is an olefinic or aryl group. The fourth group is almost invariably the one

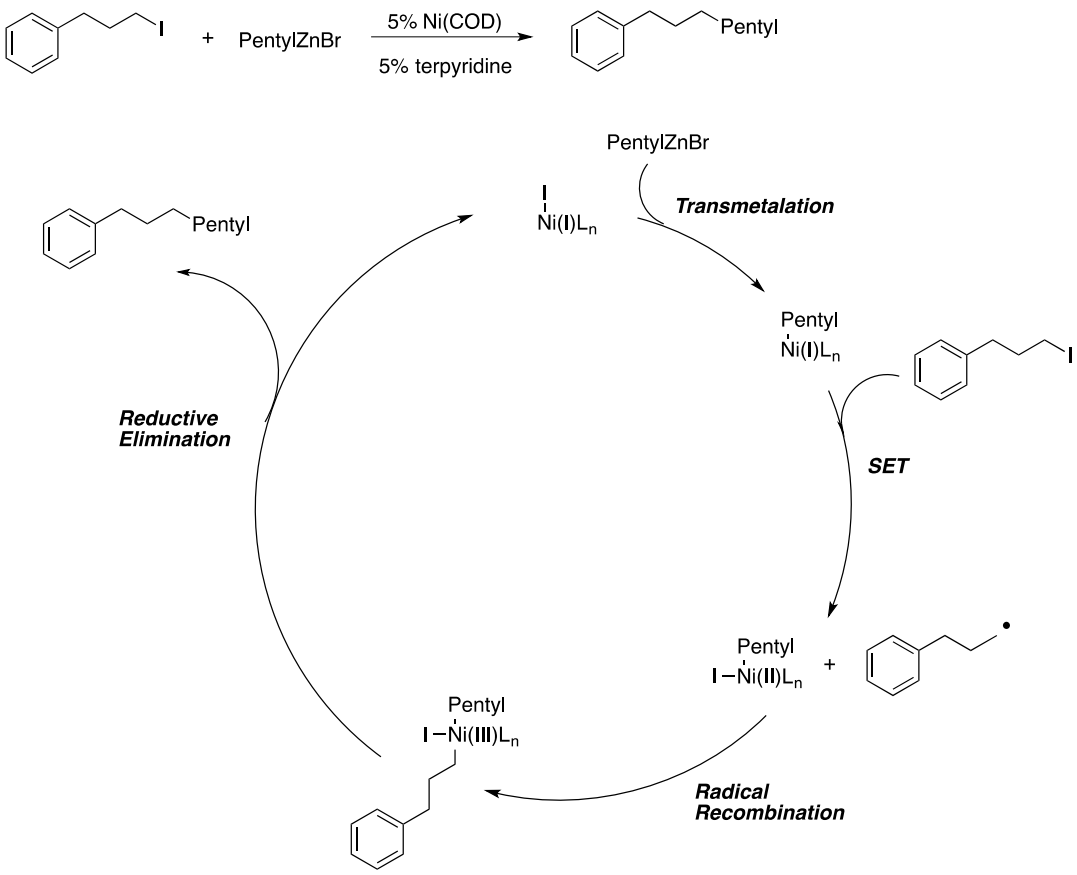
transmetallated to palladium and coupled. Stille has ascribed this to a transition state wherein the carbon atom bonded to tin accumulates a significant amount of charge during transmetallation, which will be stabilized by increasing the s-character of the orbital being cleaved.[111]

- Slow oxidative addition. Cross-coupling reactions wherein the electrophile is sp^3-hybridized can be difficult to control due to many of the deleterious pathways discussed above. But these reactions can also suffer from a relative decrease in the rate of the initial oxidative addition. This can be partially attributed to the absence of a π-system to pre-coordinate with the catalyst before undergoing oxidative addition.[112] The low rates that plague these processes can be often overcome by making the metal more nucleophilic via the incorporation of more strongly electron-donating ligands (Scheme 2-9). This approach has the added advantage of generating a coordinatively unsaturated metal species, which is promoted by metal complexation with bulky ancillary ligands such as NHC's[113] or trialkylphosphines like P(*t*-Bu)$_3$ and PCy$_3$.[114] These intermediates have been shown to be more reactive toward oxidative addition relative to their more coordinately-saturated counterparts.[115]



Scheme 2-9. Some examples of bulky/electron rich strong σ-donors as ligands in cross couplings

Many cross couplings of alkyl halides utilize nickel-based catalyst systems.[116,117] The use of nickel has been proposed to help circumvent the slow rates of oxidative addition by following a radical rebound mechanism, as opposed to an ionic concerted process (Scheme 2-10).[118] A common feature of these coupling reactions is the use of chelating polydentate ligands, which help prevent β-hydride elimination from the σ-alkyl nickel intermediates.



Scheme 2-10. Typical proposal for a Ni(I)-Ni(III) radical rebound type cross coupling mechanism

Results and discussion – development of a G2 synthetic approach.

The desired G2 archipelago model compounds[†] share a scaffold in which the pyrene moiety occupies the central position (in contrast to Tykwinski's G1 compounds). In all cases, the pyrene core is substituted in the 1-, 3-, 6-, and 8-positions, whether by solubilizing *n*-alkyl groups or alkyl-tethered islands (Figure 2-5). This design allows us to study intra- and intermolecular aggregation as a function of the size and number of tethered islands.

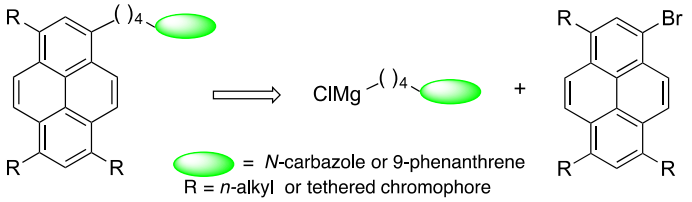


Figure 2-5. General structure of initially-targeted G2 structures

2.1.4 Optimization of the 4-fold Kumada coupling of tetrabromopyrene. A benchmark for archipelago construction

To test the efficacy of the final coupling reaction in our proposed sequence, we hoped to demonstrate efficient conditions for cross-coupling of polybromopyrenes with commercial *n*-alkyl Grignard reagents. Thus, we set out to synthesize 1,3,6,8-tetra-*n*-hexylpyrene (2-3) from tetrabromopyrene (TBP) via the four-fold nickel-catalyzed Kumada coupling using excess *n*-hexylmagnesium chloride (Scheme 2-11). Utilizing this approach eliminates the extra hydrogenation step previously reported for the synthesis of tetra-*n*-alkylpyrenes via Sonagashira coupling/catalytic hydrogenation.[119] In this way, we also thought it possible to

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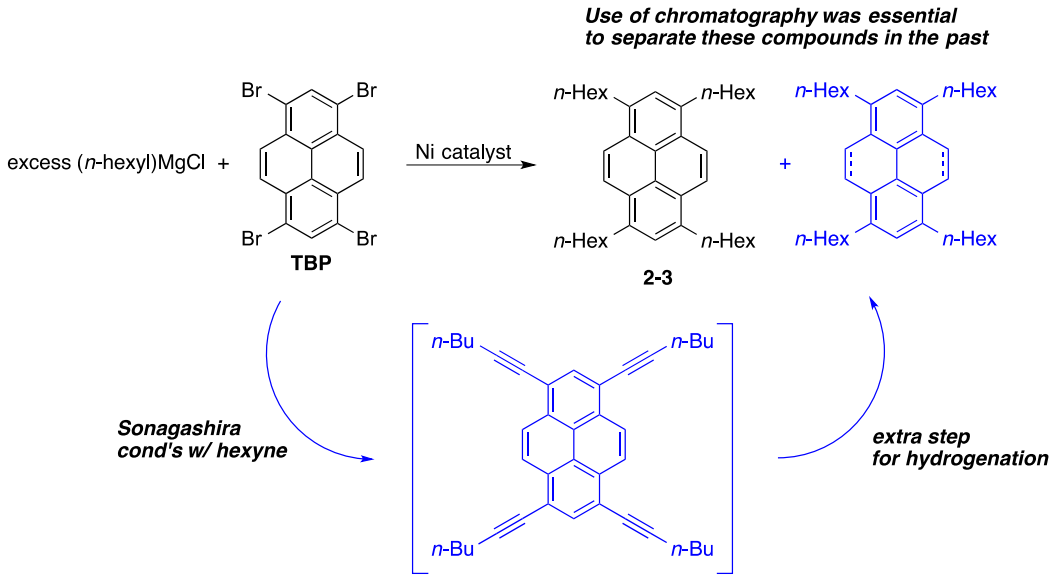
[†] The synthesis of G2 compounds described in the remainder of this chapter was recently published. Diner, C.; Scott, D.; Tykwinski, R.; Gray, M.; and Stryker, J. *J. Org. Chem.* **2015**, *80*, 1719-1726.

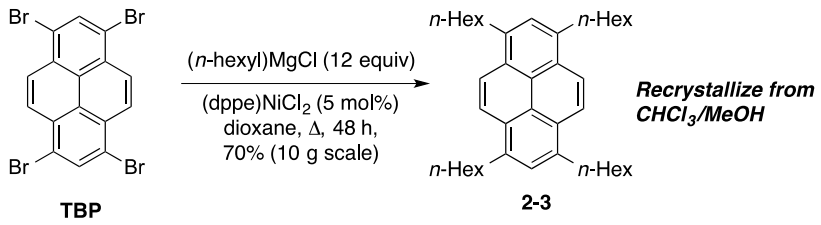
eliminate the previously required chromatographic purification, as we could expect no byproducts suffering from saturation in the pyrene bay region.



Scheme 2-11. Utilization of Kumada coupling for the synthesis of tetra-*n*-alkyl pyrene

A slight variation of Kumada's original procedure proved to be quite effective for this reaction.[120] The complete insolubility of tetrabromopyrene in standard ethereal solvents like THF and ether, led us to adopt hot dioxane as the reaction medium, giving clean conversion when run for a minimum of 48 hours. An excess of the Grignard reagent was used (3 equiv per reaction site) in order to favor product formation; this is less of an issue when using a cheap, commercially available reagent. The main side-product of the reaction, detected in the crude product mixture by ^{1}H NMR spectroscopy, was 1,3,6-tri-*n*-hexylpyrene, which is presumably formed from β-hydride elimination or transmetallation between the alkyl Grignard and the bromoarene. This byproduct was approaching "baseline" in concentration and was removed simply by recrystallization of the crude reaction product from chloroform/methanol. The reaction was scalable to 10 g at

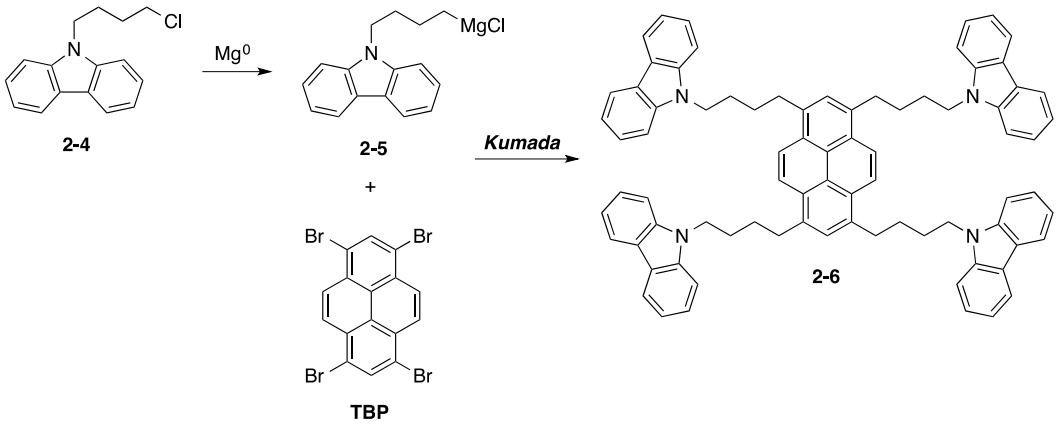
70% yield, while maintaining a chromatography-free process (Equation 2-1). This reaction is quite efficient, demonstrating a 91% reaction yield per coupling site.



Equation 2-1. Optimal conditions for the conversion of **TBP** to **2-3**

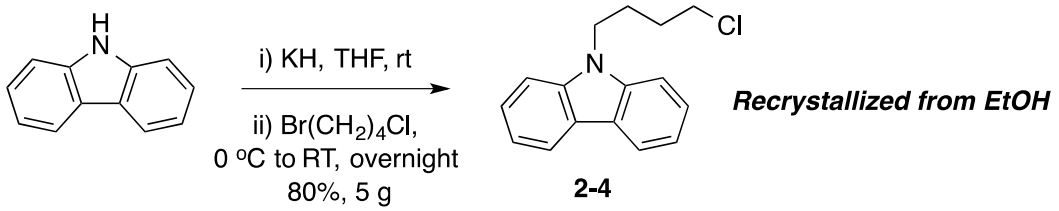
2.1.5 First synthesis of pyrene-centered symmetrical G2 compounds

To demonstrate that the Kumada protocol is adaptable to the synthesis of polycyclic "island-terminated" haloalkyl segments, *N*-(4-chlorobutyl)-carbazole[121] (**2-4**) was targeted as a reasonable entry point into the desired class of compounds, for a number of reasons. For one, a synthesis was already reported,[121] and the use of a modified approach allowed us to prepare this material at multigram scale without chromatography. Also, the carbazole moiety is consistent with the archipelago model of asphaltene structure as a "nonbasic-nitrogenous island." The linkage between the aryl system and the alkyl chain is formed via a simple S_N2 reaction between the corresponding anion of carbazole and an *n*-alkyl halide. In this way we (at least initially) could avoid the potentially problematic cross-coupling reactions with alkyl electrophiles. Our plan was to convert **2-4** to the corresponding Grignard reagent (**2-5**) and exhaustively couple it to a sub-stoichiometric amount of TBP under the vetted Kumada conditions used for the synthesis of **2-3** (Scheme 2-12).



Scheme 2-12. Synthetic plan for our first G2 compound

Our synthesis of **2-4** used slightly different conditions from those reported (Equation 2-2).[121] We found that deprotonation of carbazole by potassium hydride followed by substitution at the more reactive electrophilic center of 1-bromo-4-chlorobutane provided the product in high yield after a recrystallization from hot ethanol.

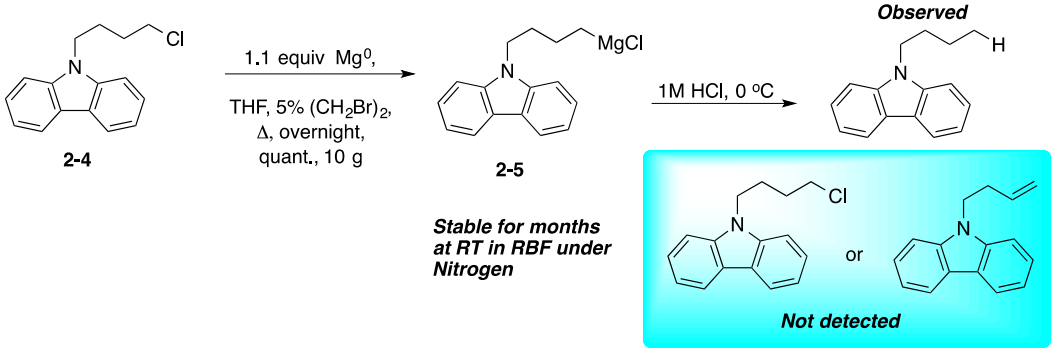


Equation 2-2. Optimized synthesis of archipelago precursor **2-4**

With large amounts of **2-4** in hand, conversion to the corresponding Grignard reagent was undertaken. Due to the relative inertness of *n*-alkyl chlorides to heterogeneous metallation with metallic magnesium, pre-activation of the magnesium was required. Heating a slight excess of magnesium turnings in THF to reflux in the presence of a sub-stoichiometric amount of ethylene bromide provided a more active magnesium surface.[122] Addition of alkyl halide **2-4** to the

activated magnesium in THF, followed by bringing the reaction mixture to reflux and heating overnight, furnished the metallated product cleanly (Scheme 2-13).

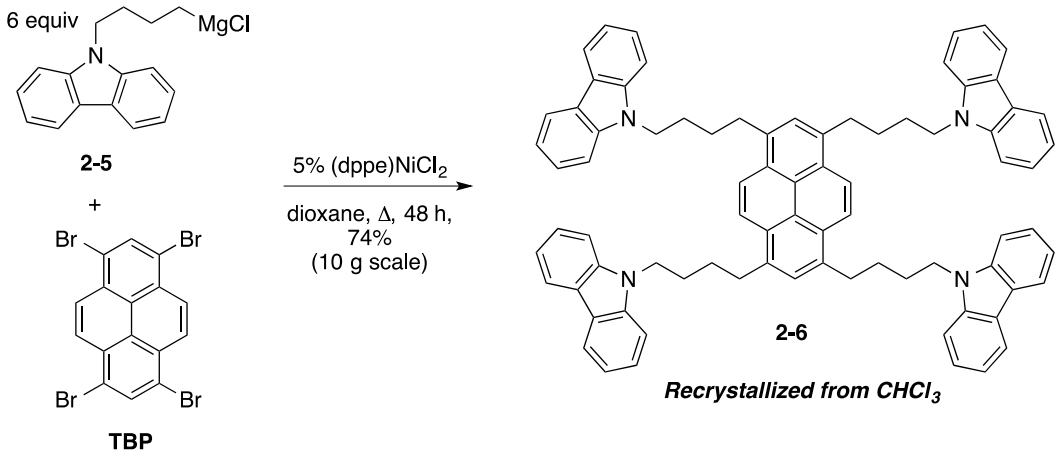
Quenching a small amount of the Grignard reagent with dilute HCl and examining the product mixture by ^{1}H NMR spectroscopy verified the efficiency of the magnesiation reaction (Scheme 2-13). We could not detect any starting material, as well as any olefinic or dimerized products that are often byproducts in such radical electron transfer reactions.[123] The reaction was found to be scalable to decagram quantities and the resultant Grignard solution could be stored for months under inert conditions at room temperature without any observable loss in reactivity.



Scheme 2-13. Optimized conditions for the synthesis of island-tethered Grignard reagent **2-5**

Coupling of **2-5** with TBP under previously established conditions proceeded without issue (Scheme 2-14). As a concession to the greater value of the nucleophile, the excess of Grignard reagent could be reduced to 1.5 equivalents per site without compromising the selectivity or yield. Further reduction in relative stoichiometry was counterproductive. Upon cooling and quenching the reaction mixture, the insoluble crude archipelago compound was obtained as a solid by suction filtration. After rinsing with ether and water to remove both organic impurities and magnesium salts, the nearly colorless crude material was

recrystallized from chloroform. Final drying to constant weight required prolonged treatment under high vacuum to remove persistent residual solvent(s). The five-island, symmetrical first-generation dendrite (**2-6**) was nonetheless obtained analytically pure in 74% yield on a one-gram scale.



Scheme 2-14. Optimized synthesis of our first G2 compound (**2-6**)

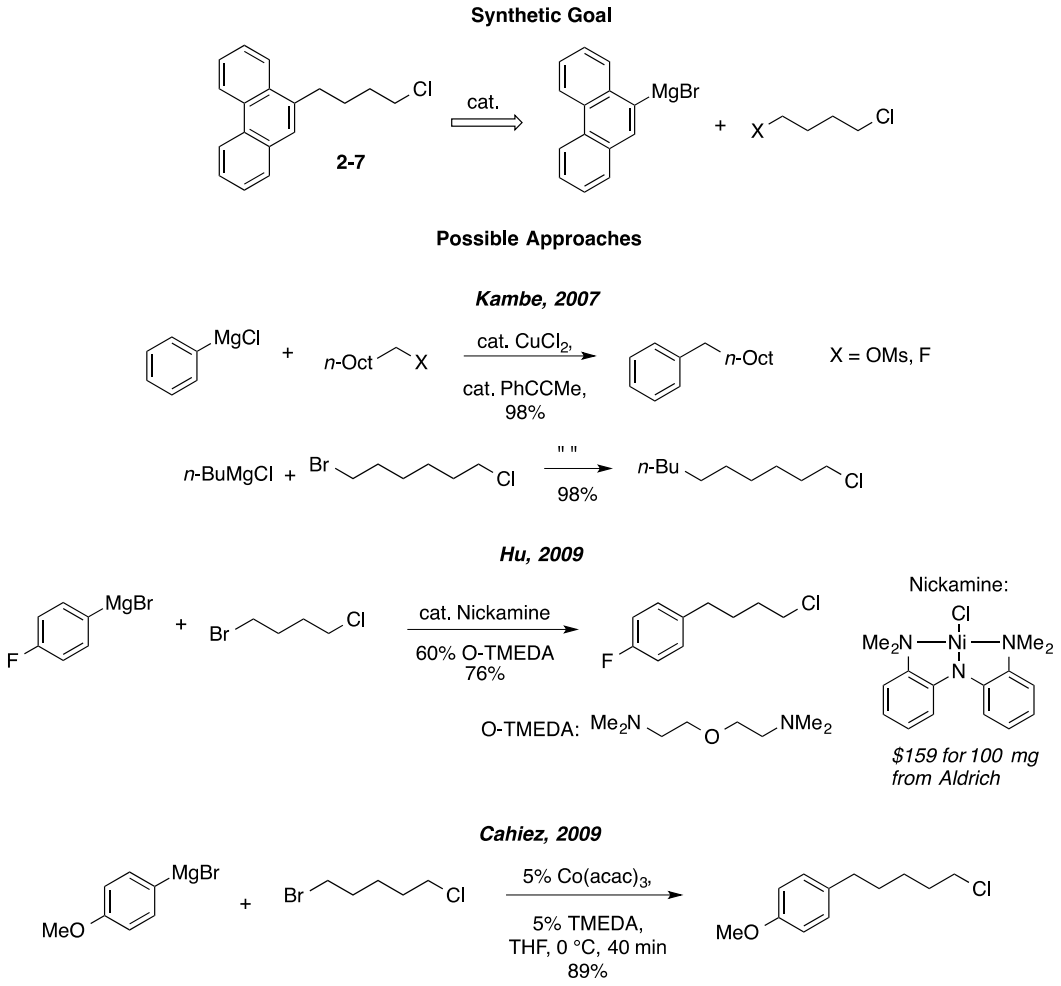
2.1.6 Optimization of a cobalt-catalyzed cross-coupling of primary alkyl halides for the assembly of hydrocarbon archipelago model compounds

Extension of this alkylation protocol to the analogous phenanthrene-terminated derivatives required an efficient synthesis of chloroalkylated phenanthrene **2-7**. As our approach to these chloroalkylated arenes was to cross couple an aromatic Grignard reagent with a difunctionalized electrophile, we surveyed known methodology to accomplish this task (Scheme 2-15), focusing on those catalyzed by copper,[124] nickel,[125] and cobalt, in keeping with our emphasis on base-metal catalysis.[126]

Kambe's copper-catalyzed methodology[44] was intriguing, due to the use of an unconventional ligand system and the high reported yields. Notable in this

methodology is the rare ability of the system to cross-couple primary alkyl fluorides. In contrast to general reactivity trends in precious metal cross-coupling, it is more facile to activate C-F bonds under these conditions than C-Cl bonds, despite their inversely correlated bond strengths. Unfortunately, in our hands, the methodology failed to provide high yields. We were also unable to purify the desired product, despite using chromatography.

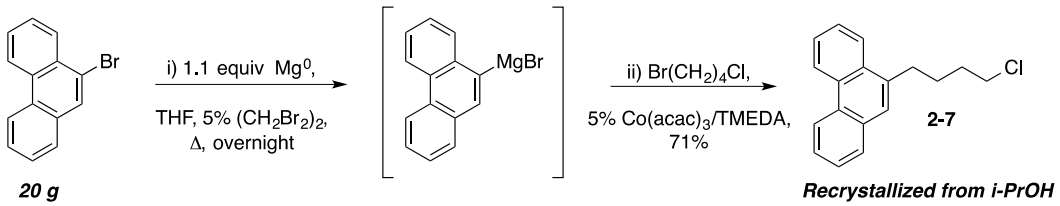
While Hu's reported Ni-catalyzed[125] procedure also seemed amenable to our system, we noted the requirement for "almost stoichiometric" and expensive O-TMEDA in order to couple primary alkyl bromides in the presence of alkyl chlorides. Also, the commercially-available catalyst is prohibitively expensive, although not difficult to make at scale in the laboratory, as we did.[127]



Scheme 2-15. Some potential first-row metal catalyzed approaches to the coupling of aryl Grignard reagents with *n*-alkyl halides

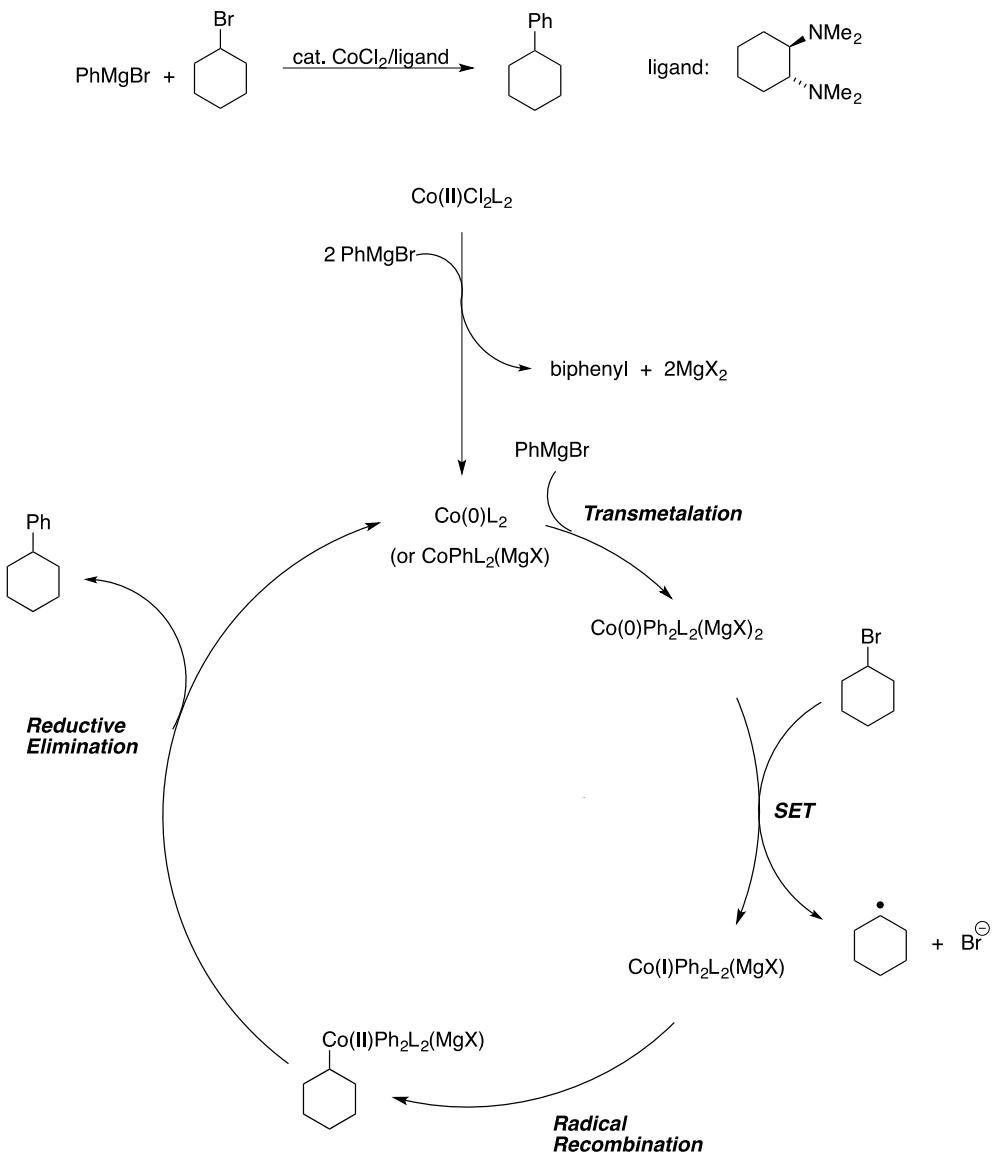
We chose, however, to adopt Cahiez's cobalt-catalyzed methodology.[126] These conditions were appealing for several reasons. The ligand/catalyst system, $Co(acac)_3$/TMEDA is simple, cheap, and used at low loading. The conditions are also simple, using the common solvent THF. In our hands, the reaction proceeds quite smoothly and provides the alkylation product in high yield, provided the reaction is pushed to completion under reflux overnight. We also found that the product readily crystallizes to high purity from isopropanol and the reaction could be readily scaled to 20 g (Scheme 2-16). The required Grignard reagent was then

made from the corresponding aryl bromide and used *in situ* in a similar fashion to the preparation of **2-5** (*vide infra*).



Scheme 2-16. Cobalt-catalyzed synthesis of a phenanthrene-tethered archipelago precursor

This cobalt-catalyzed selective alkylation reaction is certainly worth further mention. In 2001, Oshima presented the first cobalt-catalyzed Grignard cross-coupling reactions involving alkyl halides as the electrophilic component.[128] Based on the interference of tethered olefins in these early domino reactions, a radical rebound mechanism, analogous to the previously cited nickel-catalyzed processes, was proposed. Five years later, the Oshima group provided a system with improved functional group tolerance for simple cross-couplings of aromatic Grignard reagents with alkyl halides.[129] Scheme 2-17 provides a proposed mechanism for this reaction from a more recent report.[128]



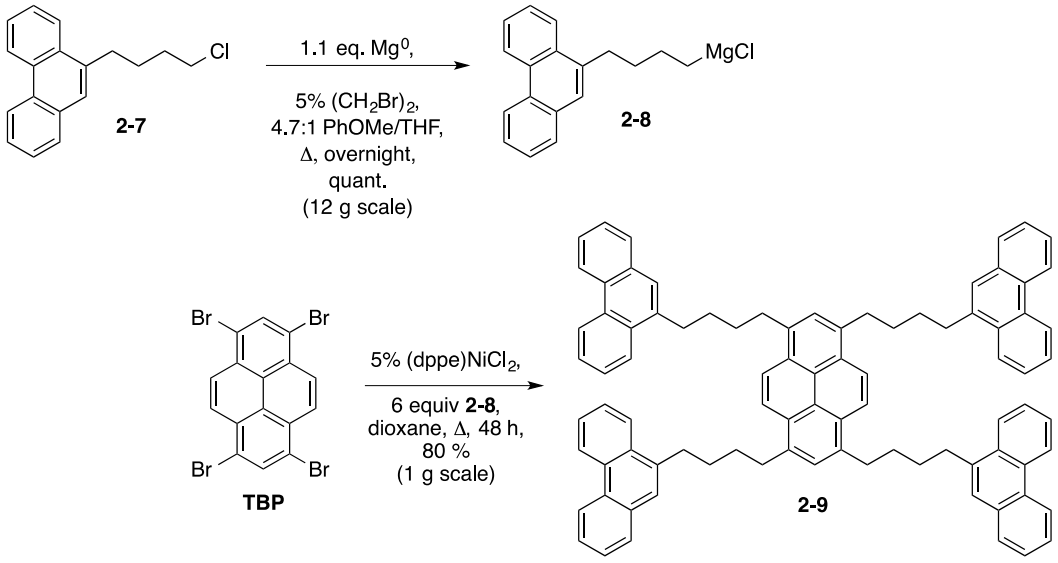
Scheme 2-17. Example and proposed mechanism of cobalt-catalyzed cross-coupling of aromatic Grignard reagents alkyl halides

1-Chloro-4-(9-phenanthryl)butane **2-7** is only sparingly soluble in conventional ethereal solvents, making the conversion to the corresponding Grignard reagent difficult. One possiblity to circumvent this issue is the use of a tertiary amine cosolvent to help solubilize the organohalide.[130] While feasible, we were hesitant to try this becasue of the possibility that the amine might function as a ligand for

nickel in the subsequent cross-coupling reaction, inhibiting the catalytic cycle. Instead, we found that **2-7** dissolves readily in hot anisole, which became the solvent of choice for preparation of the corresponding Grignard reagent.[131]

Thus, metallation of chloroalkyl **2-7** with activated magnesium was performed in analogous fashion to the formation of **2-5**, except using anisole/THF as the optimal reaction solvent). Again, a sample of the product **2-8** was quenched and analyzed by ^{1}H NMR spectroscopy. As before, only the reduced product was observed, no starting chloride, olefin, or dimerized material was detected in the spectrum. This Grignard reagent demonstrated the same stability over time as carbazole derivative **2-5**, when stored rigorously under nitrogen at RT.

In the event of archipelago assembly, the four-fold Kumada cross-coupling with TBP proceeded without issue, yielding the hydrocarbon archipelago **2-9** after a similar workup and crystallization (Scheme 2-18).



Scheme 2-18. Metallation and coupling of **2-7** with **TBP**

The efficiency and reproducibility of this procedure encouraged us to target the complete series of pyrene/carbazole and pyrene/phenanthrene pseudoasphaltenes to make possible a systematic study of intra- and inter-molecular aggregation as a function of the complexity, symmetry, and polarization of the component residues. Thus, all possible two-, three-, and four-island structures in each series have been prepared from the corresponding bromopyrenes, substituting one, two, or three terminal ethyl substituents in place of tethered islands.

2.1.7 Scalable chromatography-free preparation of (poly)brominated-(poly)ethylated pyrene scaffolds

In order to target lower molecular weight archipelagos that follow the architectural guidelines of Figure 2-5, we needed the corresponding (poly)bromo-(poly)-*n*-alkylpyrenes as electrophilic cross coupling precursors. We chose to install ethyl groups as the *n*-alkyl groups, consistent with the "short-chain" terminal alkyl groups that are ubiquitous in natural asphaltenes,[80] and thus we required the pyrene derivatives shown in Figure 2-6. While the compounds bearing one or three bromines provide archipelago products with no symmetry, the two dibrominated isomers **2-11** and **2-12** lead to products bearing symmetry elements. These are the compounds we targeted next, as we assumed that their symmetry properties would aid in their purification via crystallization.[132]

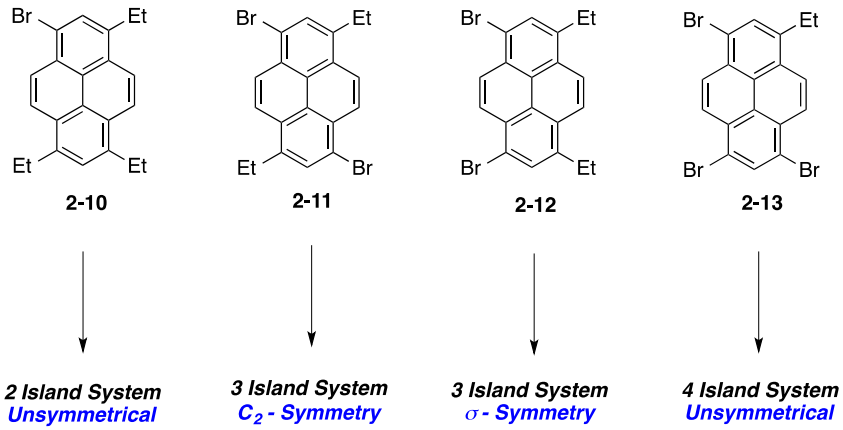


Figure 2-6. Halogenated (poly)ethylpyrene archipelago templates

Regioselective synthesis of specifically brominated pyrene derivatives **2-10** – **2-13** is not a simple problem, particularly on a multigram scale, where chromatography is impractically costly and tedious. Experimental procedures for the preparation of 1-bromopyrene, mixtures of 1,6- and 1,8-dibromopyrenes, and 1,3,6-tribromopyrenes are found in the literature,[133,134] not all of which reliably provide pure materials even after chromatography. While pyrene reacts relatively quickly with electrophilic bromine sources such as NBS and bromine, it is difficult to control the selectivity in terms of the number of bromines added and impossible to control the location of the second bromination. This issue can potentially be circumvented by "blocking" undesired reactive positions of pyrene with inert substituents and then exhaustively brominating the remaining positions. In our case these blocking groups are the ethyl groups, so synthesis of the corresponding ethylated pyrenes **2-14** – **2-17** in pure form should naturally provide the desired archipelago precursors upon electrophilic bromination (Figure 2-7).

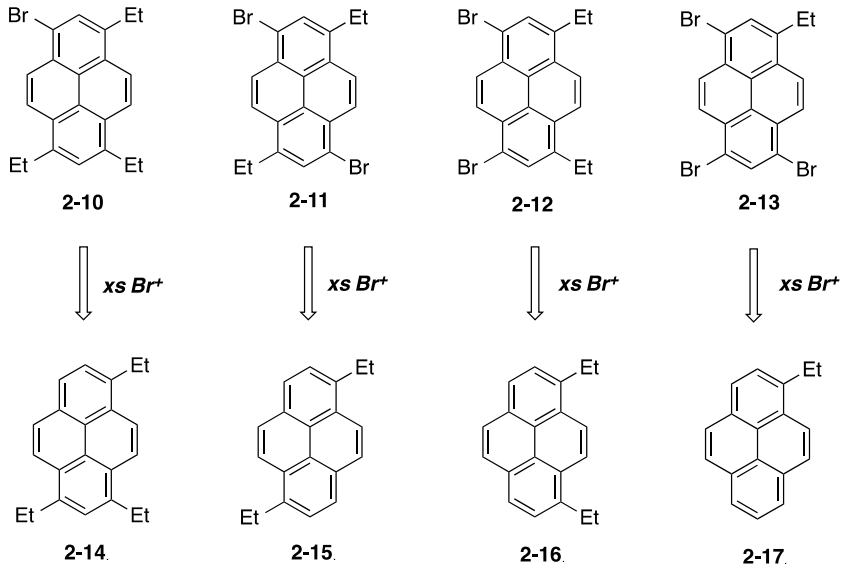
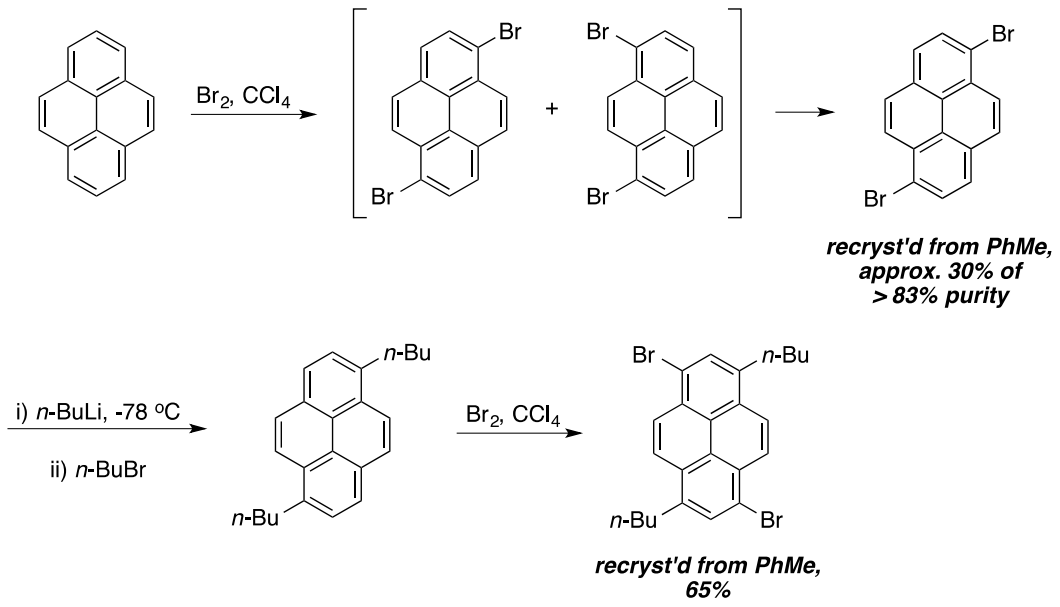


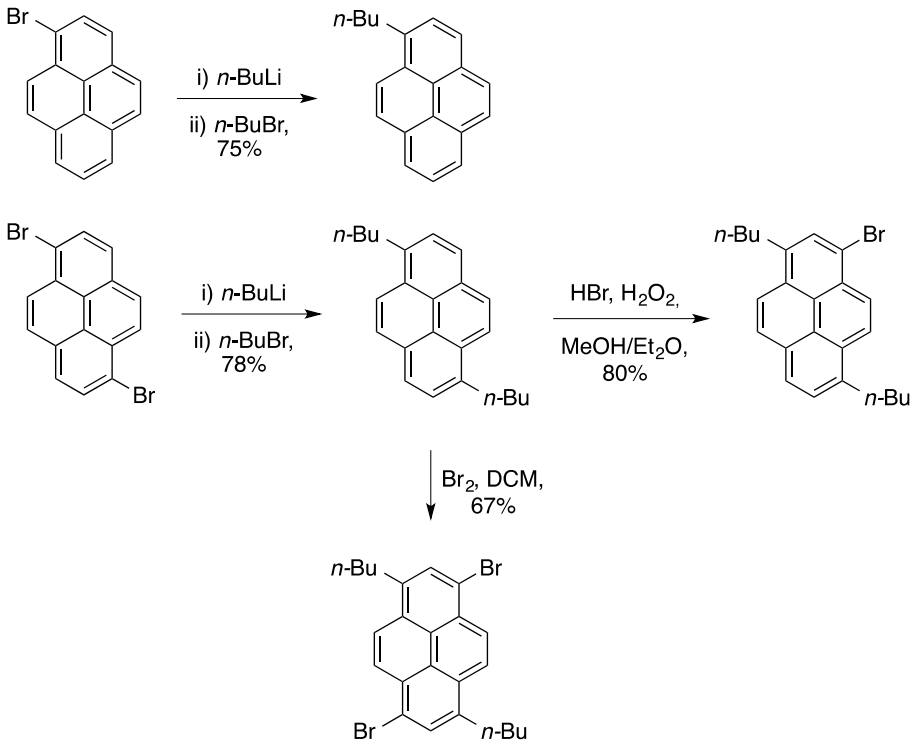
Figure 2-7. Polybrominated archipelago precursors utilizing ethyl groups as **"**blockers**"** in other reactive positions

The Iwasawa group utilized this principle recently, reporting the preparation of 1,6-dibromo-3,8-di-*n*-butylpyrene (Scheme 2-19),[135] which is closely analogous to the diethylated derivatives we targeted for archipelago construction. Bromination of pyrene with two equivalents of bromine provides a 1 : 1 mixture of 1,6- and 1,8-dibromopyrenes, as noted by others.[133,136] Recrystallization of this material from toluene provided an "83% pure" batch of 1,6-dibromopyrene; the corresponding 1,8-isomer was abandoned. This mixture was then lithiated via lithium-halogen exchange and quenched with *n*-bromobutane to provide crude 1,6-di-*n*-butylpyrene. Bromination of this material, and a final recrystallization, provided the product in 65% yield over two steps. Unfortunately, this approach requires multiple steps, use of carbon tetrachloride (a banned substance in many countries),[137] utilization of chromatographic purification, and gives only the C_2-symmetric isomer in purified form in very low overall yield from pyrene.



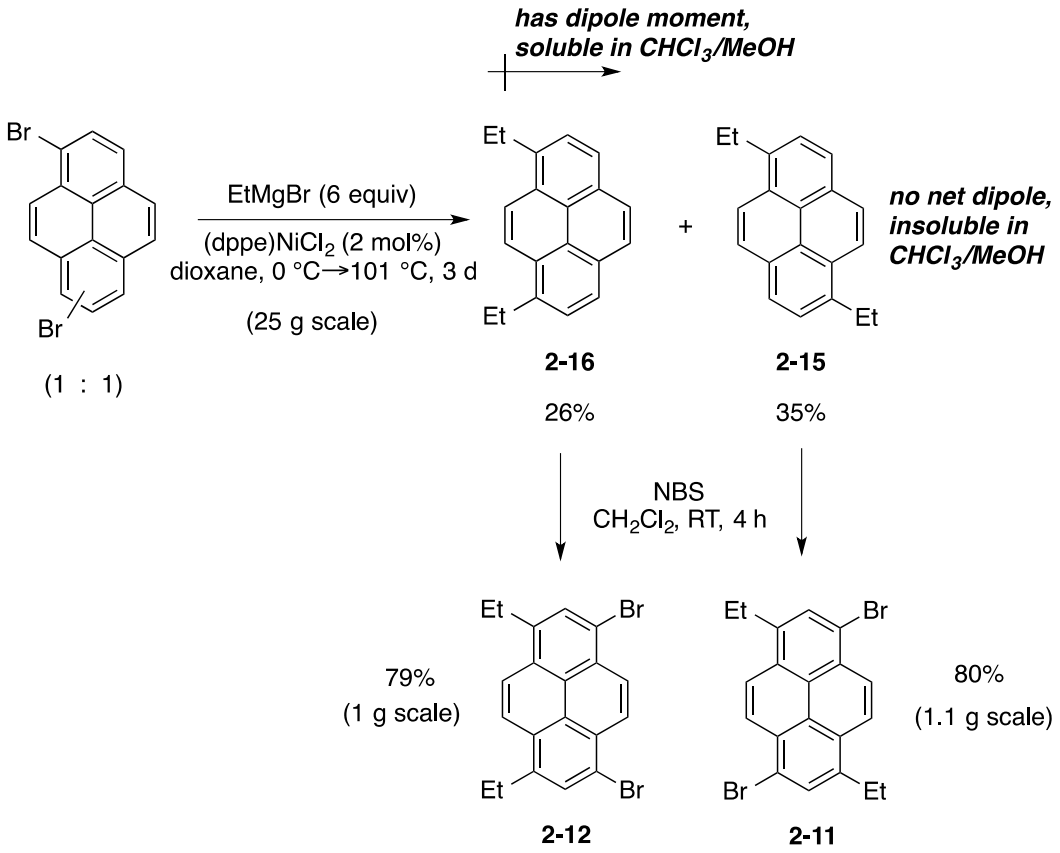
Scheme 2-19. Iwasawa's synthesis of a C_2-symmetric dibromo-di-*n*-butylpyrene

The Konishi group also recently published a synthesis of some polyalkylpyrenes for the purpose of comparing UV/Vis and fluorescence spectroscopic data as a function of the number and type (primary, secondary) of alkyl groups substituted on the pyrene core (Scheme 2-20).[138] Unfortunately, they too only isolated a C_2-symmetric dialkylpyrene, from its brominated precursor (of which they did not provide a source). Only methyl and *n*-butyl chains were installed, groups, made via the same methodology used by the Iwasawa group. The products required "short-plug column chromatography" on silica gel (hexanes), followed by high-performance liquid chromatography and subsequent recrystallization in ethanol to give the target compound.



Scheme 2-20. Konishi group's synthesis of some similar halogenated polybutylpyrenes

To circumvent the issues described above, we have developed an efficient, chromatography-free synthesis of *both* isomerically pure C_2- and C_s-symmetric dibromodialkylpyrenes on a substantial scale. Rather than engage the poorly soluble isomeric dibromides,[139] the 1 : 1 mixture was converted without separation to the more lipophilic diethyl isomers, **2-15** and **2-16** (Scheme 2-21).



Scheme 2-21. Optimized synthesis and separation of dibromodiethylpyrene isomers

Despite the greater solubility of the ethylated derivatives, the polarity difference between the two isomers remains substantial because one isomer has a net dipole moment (C_s-symmetric) and one does not (C_2-symmetric). This leads to a dramatic improvement in the efficiency of fractional crystallization. In this way, both 1,8- and 1,6-diethylpyrenes **2-15** and **2-16** were obtained as pure compounds after a single crystallization. The crude material from the Kumada alkylation was dissolved in dichloromethane and layered with methanol. Conveniently, **2-16** was soluble in this relatively polar solvent system, while **2-15** was not, and the latter crystallized out in lime green colored needles. Crude **2-16** was then harvested from the mother liquor by crystallization from the less polar solvent, hexanes,

again as a pure compound. The material balance is reasonable and can be further improved by manipulation of the mother liquors, if desired.

The compounds were separately identified by their distinctive ^{1}H NMR spectra. Both compounds have chemically equivalent ethyl groups, but compound **2-15** has four chemically unique aryl methine signals each appearing as a doublet. Compound **2-16**, on the other hand, has has four unique aryl methine signals which appear as two symmetry-induced singlets and two doublets (Figure 2-8).

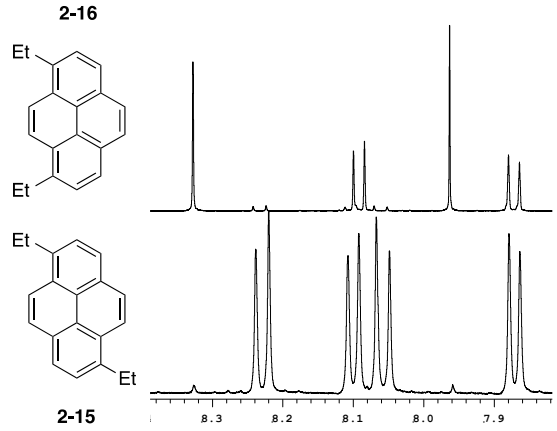


Figure 2-8. Comparing aryl regions of ^{1}H NMR between regioisomers of diethylpyrene

At this stage, double bromination of each diethylpyrene isomer afforded central island templates **2-11** and **2-12** respectively, cleanly, and in high yield. Further evidence for the structural assignment of the isomers was obtained by growing crystals of **2-11** and obtaining the solid state structure by X-ray crystallography (Figure 2-9).

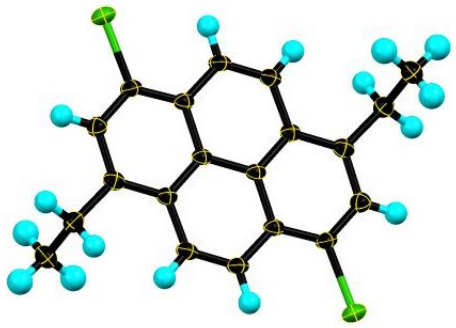


Figure 2-9. ORTEP diagram of the solid-state structure of compound **2-11**, shown with 50% thermal ellipsoids. Hydrogen atoms are shown in aqua, bromine in green

2.1.8 Assembly of remaining symmetrical G2 archipelago model compounds

Archipelago assembly of the corresponding three island systems was facile. The use of dioxane at reflux was not required for these reactions as the dibromopyrenes are more soluble than tetrabromopyrene, although the reaction mixture is still initially heterogenous. Thus, the use of THF at room temperature was sufficient for the reactions to proceed. The reaction mixture became homogenous within ten minutes of addition of either island-bearing nucleophile. Soon after, the reaction mixture again became heterogenous. This behavior is attributed to the initial formation of the soluble nonsymmetrical mono-coupled intermediate followed by the formation and precipitation of the much less soluble dicoupled product.

The crude products from these reactions could again be easily isolated via suction filtration after quenching in almost pure form. Recrystallizations of the materials from hot chloroform provided analytically pure products. The reactions provided good yields at one gram scale and were readily reproducible (Scheme 2-22).

To underscore the purity of the products obtained from these reactions, single crystals of the C_2-symmetric three-island biscarbazole **2-18** were grown from saturated dimethylacetamide and the solid-state structure was determined by X-ray crystallography. ORTEP diagrams of the compound and the extended lattice unit are shown in Figure 2-10. The carbazole units of neighboring molecules show face-to-face π-stacking along the long-molecular axis. The remainder of the close contacts, on the other hand, reveals the dominant role of both intermolecular dispersion interactions and edge-to-face stacking in the crystal packing of the molecule.

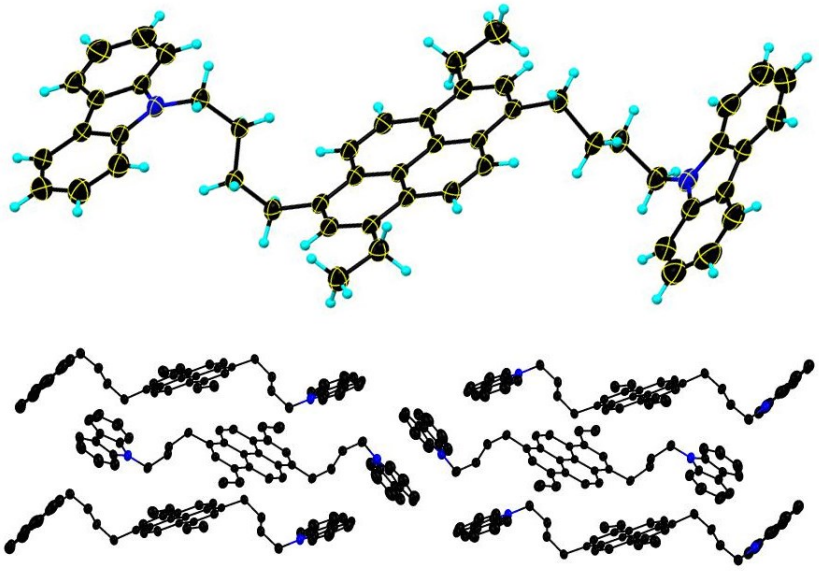
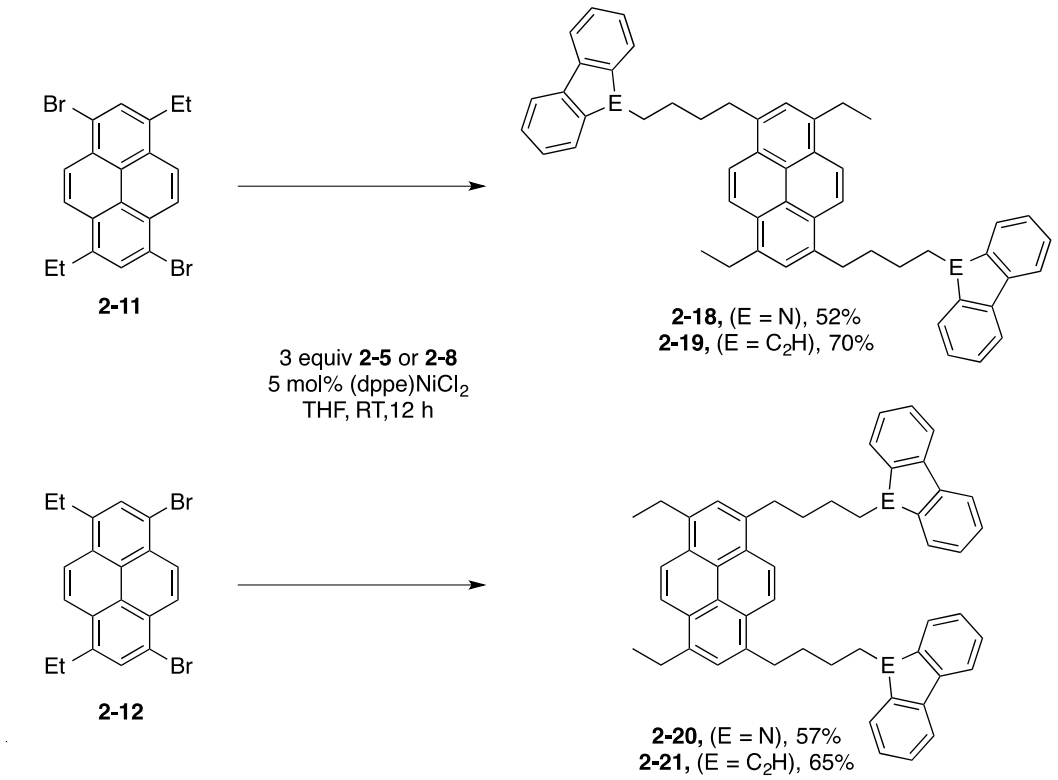


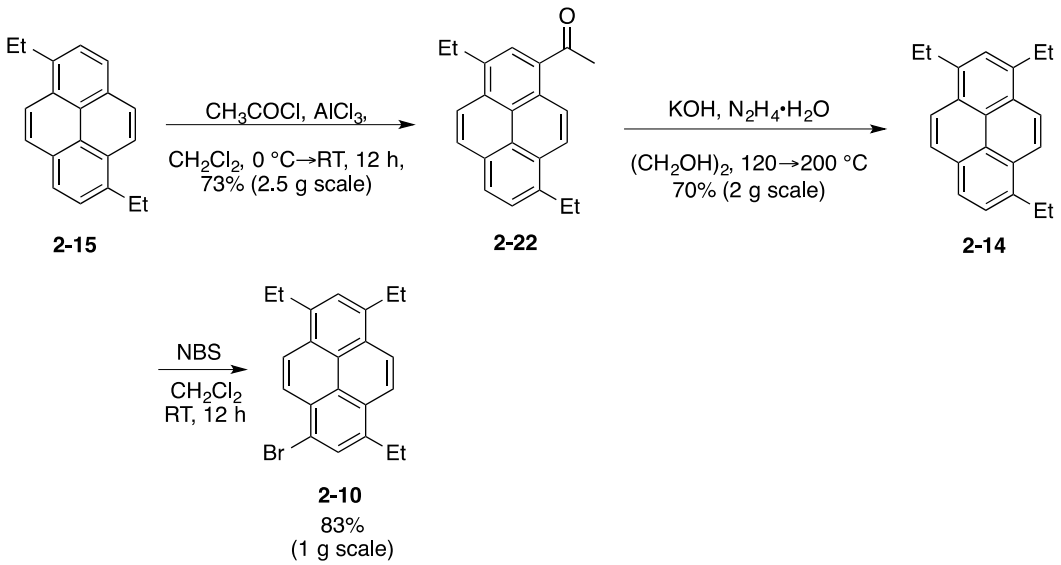
Figure 2-10. (Top) ORTEP diagram of the solid-state structure of compound **2-18**, shown with 50% thermal ellipsoids. Hydrogen atoms are shown in aqua, nitrogen in blue. (Bottom) Extended unit cell with hydrogen atoms omitted for clarity



Scheme 2-22. Assembly of three-island archipelago systems

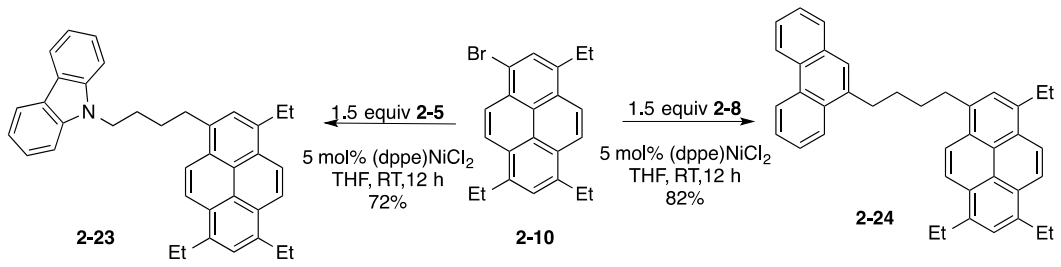
2.1.9 Assembly of non-symmetrical archipelago compounds

For the synthesis of simple two-island archipelago model compounds, the less symmetrical and lower molecular weight precursor **2-10** was prepared by bromination of the 1,3,6-triethylpyrene **2-14** (Scheme 2-23). 1,3,6-Triethylpyrene **2-14** was synthesized from **2-15** via a standard acylation/reduction sequence using a slight variation of the previously reported acylation of pyrene.[140] Clean single acylation reactivity in this case can be attributed to the less nucleophilic product (relative to the starting material). The reduction utilized a variation on a Wolff-Kishner procedure previously reported for the reduction of 1-acetylpyrene.[141] The entire sequence was chromatography free, excluding filtration through a short silica plug required for the purification of triethylpyrene.



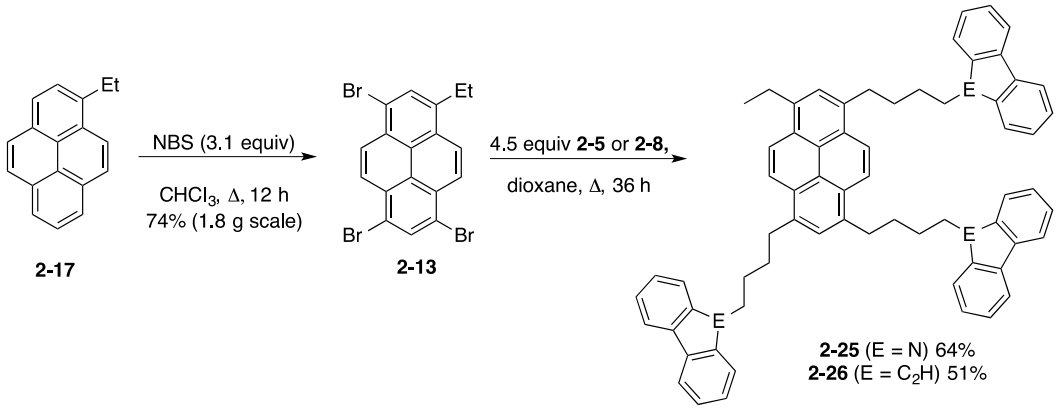
Scheme 2-23. Synthesis of bromotriethylpyrene **2-10**

The corresponding two island archipelagos (**2-23** and **2-24**) were then synthesized under mild Kumada conditions. Due to the lower molecular weight and lack of symmetry, these compounds were readily soluble in THF at room temperature (Scheme 2-24). The reactions were worked up in a more conventional fashion after quenching, using a separatory funnel and multiple washes (see experimental section). The crude material was then recrystallized from isobutanol, providing pure materials **2-23** and **2-24**.



Scheme 2-24. Synthesis of two-island archipelago model compounds

Due to the low solubility of the dibrominated pyrene intermediates, the remaining central island template, tribromoethylpyrene **2-13**, was synthesized from the previously reported 1-ethylpyrene[141] (**2-17**) via exhaustive bromination under marginally forcing conditions. Tribromoethylpyrene **2-13** was highly insoluble in THF, again requiring the use of dioxane under reflux and prolonged reaction times to obtain the corresponding four-island products **2-25** and **2-26** cleanly and in high yield (Scheme 2-25). Although these compounds have a higher molecular weight than the three-island analogues, the products also possess lower symmetry and were surprisingly soluble, requiring a conventional workup following a reaction quench. Purification involved only the recrystallization of the crude materials from chloroform.



Scheme 2-25. Synthesis of four-island Archipelago model compounds

Conclusion

All of the archipelago compounds synthesized via this methodology required drying under high vacuum ($\leq 10^{-5}$ torr) for at least 24 hours in order to obtain solvent-free materials. We attribute this to the semi-dendrimeric nature of the compounds, as some dendrimers have been shown to irreversibly intercalate

solvent molecules. Similarly, many of our archiplego products showed systemically low carbon values by elemental analysis. We attribute this to either residual solvent intercalation[142] or, potentially, incomplete combustion upon analysis. Incomplete combustion is endemic to carbon rich compounds with cumulated quaternary carbon centers and is partly attributable to carbon suboxide formation, which is not detectable.

In summary, efficient, robust, and gram-scale syntheses of alkyl-bridged semi-dendrimeric compounds (Figure 2-11) has been developed, providing G2 model compounds for the investigation of archipelago-model asphaltene structures. This synthetic approach establishes dramatic improvements in efficiency, purity and scalability relative to previous G1 approaches. Also, this methodology is expected to assist developments in a range of materials chemistries based on arrays of chromophores chemically embedded within a single molecular matrix.

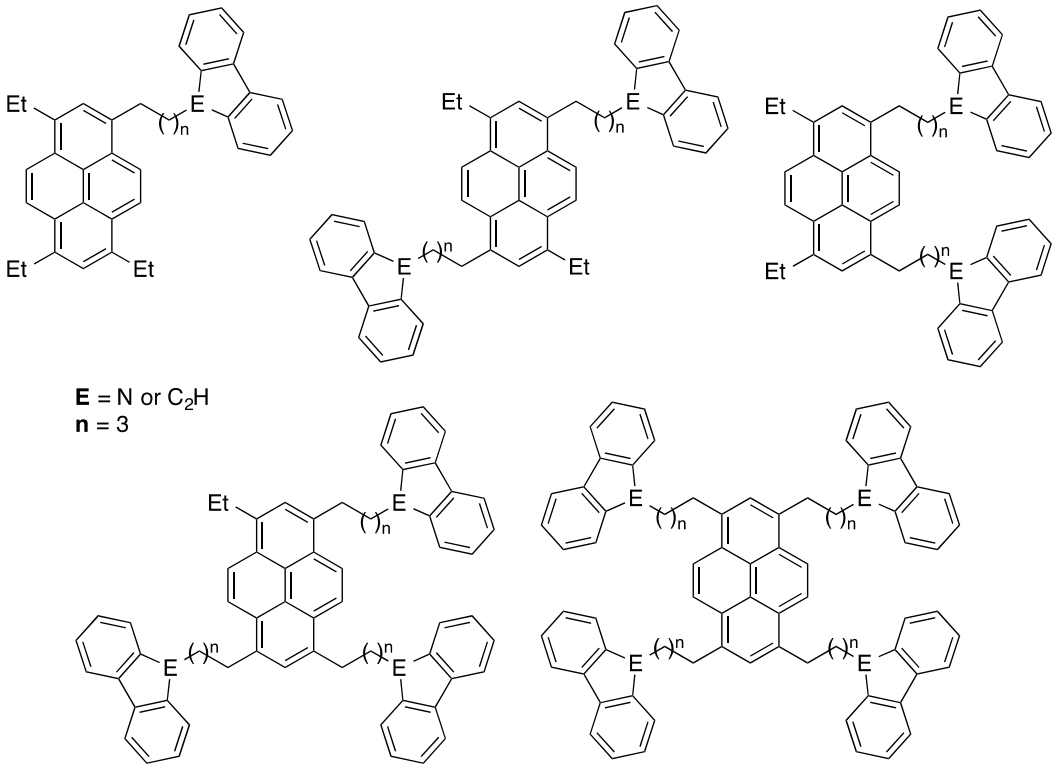


Figure 2-11. Summary of model asphaltene compounds synthesized via G2 approach

Experimental section

2.1.10 General experimental information

All manipulations of air-sensitive compounds were performed under a nitrogen atmosphere using standard Schlenk techniques or in a well-maintained dry box charged with prepurified nitrogen and maintained at <1 ppm oxygen. THF and dioxane solvents were distilled from sodium/benzophenone ketyl under nitrogen. Anisole was dried by heating over stirred CaH_2, then distilled and deoxygenated by purging with N_2. All other solvents and reagents were used without further drying or purification. Infrared spectra were recorded on a ThermoScientific

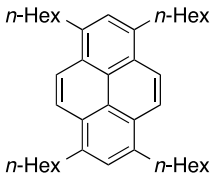
Nicolet 8700 spectrometer attached to a Nicolet Continuum FTIR microscope. ^{1}H and ^{13}C NMR spectra were recorded on either a Varian Unity-Inova 500 (^{1}H, 500 MHz; ^{13}C, 125 MHz) or a Varian Direct Drive 500 (^{1}H, 500 MHz; ^{13}C, 125 MHz). High-resolution mass spectra (HRMS) were obtained on Agilent Technologies 6220 TOF, Bruker 9.4T Apex-Qe FTICR, or Kratos Analytical MS-50G mass spectrometers operated by professional staff. Elemental analyses (C, H, N) were obtained by the Department of Chemistry Instrumentation Laboratory under the supervision of Mr. Wayne Moffat, using a Thermo Carlo Erba EA1108 or ThermoScientific Flash 2000 analyzer. The X-ray crystal structure determination was performed by Michael J. Ferguson of the University of Alberta Molecular Structure Centre using a Bruker D8/APEX II CCD diffractometer with a Cu K□ (1.54178) micro focus source.

^{1}H NMR coupling constants are reported as rounded to nearest 1.0 Hz in this chapter. In the following chapter these values are reported to the nearest 0.1 Hz.

Many compounds bearing multiple cumulated quaternary carbon atoms showed low values for carbon by combustion analysis. In some cases, multiple determinations were run to confirm reproducibility. These compounds were pure by ^{1}H and ^{13}C NMR spectroscopy, and were single component by HRMS.

2.1.11 Experimental, spectroscopic, and analytical data for compounds 2-3 – 2-26

1,3,6,8-Tetrahexylpyrene (2-3)



To a stirred suspension of 1,3,6,8-tetrabromopyrene (10.000 g, 19.311 mmol) and $NiCl_2$(dppe) (0.510 g, 0.966 mmol) in dioxane (600 mL) at 0 °C under nitrogen was added 154 mL of 1.5 M *n*-hexMgCl in THF slowly via cannula. The reaction mixture was warmed to reflux and maintained there for 48 h, after which the resulting solution was cooled to 0 °C and quenched by slow addition of 1 M HCl (150 mL). The reaction mixture was taken up in 400 mL of ether and washed with 400 mL of brine. The organic layer was separated, dried over magnesium sulfate, and filtered. The solvent was removed under vacuum, and the crude product taken up in a minimal amount of hot chloroform. This solution was layered with an equal volume of methanol and allowed to diffuse slowly at RT overnight. The product, lightly colored (lime green), was collected by suction filtration to yield 7.320 g (70%) of spectroscopically and analytically pure compound.

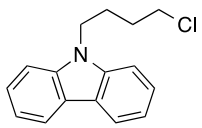
^{1}H NMR (500 MHz, $CDCl_3$): δ 8.23 (s, 4H), 7.71 (s, 2H), 3.32 (t, J = 8 Hz, 8H), 1.87 (m, 8H), 1.52 (m, 8H), 1.44−1.33 (m, 16H), 0.94 (t, J = 7 Hz, 12H).

^{13}C NMR (125 MHz, $CDCl_3$): δ 136.2, 128.7, 127.2, 126.4, 122.3, 33.8, 31.9, 31.9, 29.6, 22.7, 14.1.

HRMS (EI) exact mass calcd for $C_{40}H_{58}$ (M^+) 538.4539, found 538.4546.

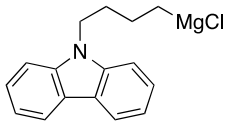
EA anal. calcd for $C_{40}H_{58}$: C, 89.15; H, 10.85. Found: C, 89.36; H, 10.68. Repeat found: C, 89.35; H, 10.72.

9-(4-chlorobutyl)-9*H*-carbazole (2-4)



Carbazole (5.000 g, 29.903 mmol) in THF (45 mL) was slowly added to a slurry of KH (1.314 g, 32.89 mmol) in THF (15 mL) in a round bottom flask fitted with a rubber septum at room temperature under an inert atmosphere. The reaction was allowed to stir for 30 min followed by the slow addition of 1-bromo-4-chlorbutane (4.14 mL, 35.9 mmol) at 0 ^{o}C. The reaction was allowed to warm to RT overnight and was quenched by 1 M HCl (100 mL). The solution was partitioned with ether (100 mL), and the organic layer was washed with brine (100 mL), dried ($MgSO_4$), filtered, and the solvent was removed under reduced pressure. The resulting crude oil was triturated with cold hexane (30 mL) to provide a solid that was recrystalized from hot ethanol in the refrigerator overnight to afford the pure compound as white crystalline needles (6.183 g, 80 %). The product of this reaction matched the analytical and specroscopic data reported in a previous syntheses.[121]

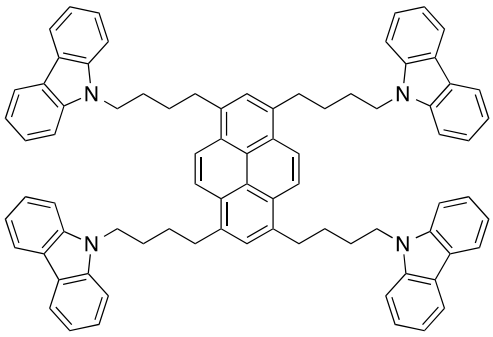
(4-(9H-Carbazol-9-yl)butyl)magnesium Chloride [~0.5 M in THF] (2-5)



In a glass reactor sealed with a high vacuum Teflon stopcock, magnesium turnings (1.040 g, 42.80 mmol) in THF (3 mL) were activated by addition of ethylene bromide (0.17 mL, 1.9 mmol) via syringe under a stream of nitrogen, followed by heating the suspension at reflux for 1 h. To the resulting solution/suspension was added 9-(4-chlorobutyl)-9H-carbazole (10.000 g, 38.895 mmol) in THF (75 mL), and the reactor was resealed and heated to 70 °C overnight. After this time, only a small amount of magnesium remained visible, and the brown solution was used without further purification.

A small amount of this Grignard reagent was quenched with 1 M HCl at 0 °C and subjected to standard workup. Analysis of the crude product by ^{1}H NMR spectroscopy revealed the presence of only N- butylcarbazole, with no evidence for olefinic or dimeric material. Thus, we assumed the magnesiation proceeded to completion and the molarity of the resulting solution was estimated based on quantitative conversion. The Grignard solution was stored in the drybox, remaining stable over months when kept at RT sealed with an unpunctured septum.

1,3,6,8-Tetrakis(4-(9H-carbazol-9-yl)butyl)pyrene (2-6)



In a glass reactor topped by a Teflon high-vacuum stopcock was added a suspension of 1,3,6,8-tetrabromopyrene (1.000 g, 1.931 mmol) and $NiCl_2$(dppe) (0.051 g, 0.097 mmol) in dioxane (60 mL) at rt. To the stirred solution was added (4-(9H-carbazol-9-yl)butyl)magnesium chloride (23 mL of a 0.5 M solution in THF) under a nitrogen atmosphere. The reaction mixture was heated to 100 °C for 48 h, cooled to 0 °C, and quenched with 1 M HCl (5 mL). The product was collected by suction filtration and washed multiple times with hot water, ether, and hexanes, in that order. The remaining material was dissolved in a minimal amount of hot chloroform and placed in the freezer overnight. The product was collected by suction filtration and rinsed with cold dichloromethane. The light yellow, spectroscopically pure powder was dried under high vacuum to yield 1.548 g (74%).

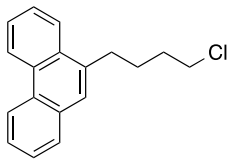
^{1}H NMR (500 MHz, $CDCl_3$): δ 8.08 (ddd, *J* = 8, 1, 1 Hz, 8H), 8.06 (s, 4H), 7.44 (s, 2H), 7.41 (ddd, *J* = 8, 7, 2 Hz, 8H), 7.34 (ddd, *J* = 8, 1, 1 Hz, 8H), 7.20 (ddd, *J* = 7, 7, 1 Hz, 8H).

^{13}C NMR (125 MHz, $CDCl_3$): δ 140.4, 135.5, 128.9, 127.3, 126.4, 125.7, 122.9, 122.4, 120.4, 118.8, 108.7, 43.0, 33.3, 29.2, 28.9.

HRMS (MALDI-FT-ICR) exact mass calcd for (M^+) $C_{80}H_{70}N_4$ 1086.5595, found 1086.5582.

EA anal. calcd for $C_{80}H_{70}N_4$: C, 88.36; H, 6.49; N, 5.15. Found: C, 88.24; H, 6.62; N 5.10. Repeat Found: C, 88.24; H, 6.62; N, 5.10.

9-(4-Chlorobutyl)phenanthrene (2-7)



In a dry 250 mL RBF fitted with a stir bar and condenser attached to a nitrogen pressure inlet were added magnesium turnings (2.080 g, 85.56 mmol) and 80 mL of THF. Ethylene bromide (0.337 mL, 3.89 mmol) was added via syringe and the mixture heated to reflux for 1 h. The reaction mixture was cooled to rt, and 9-bromophenanthrene (20.000 g, 77.782 mmol) in THF (80 mL) was added by cannula transfer. The resulting reaction mixture was heated to reflux overnight and then cooled to rt. In a separate 500 mL RBF fitted with a stir bar and condenser and placed under nitrogen was added $Co(acac)_3$ (1.392 g, 3.907 mmol) in THF (40 mL), followed by TMEDA (0.583 mL, 3.89 mmol) and 4-chlorobromobutane (9.9 mL, 86 mmol). The resulting solution was cooled to 0 °C, and the solution of 9-phenanthrylmagnesium bromide was transferred into the reaction flask via cannula. After 4 h at 0 °C, the reaction mixture was heated to reflux overnight and then cooled to RT and quenched with 1 M HCl (100 mL). To this was added 100 mL of ether in a separatory funnel. After separation of the layers, the organic phase was washed with brine (100 mL) and dried over anhydrous magnesium sulfate. After filtration, the solvent was removed under vacuum and the crude product dissolved in a minimal amount of hot 2-propanol. After slow cooling, 14.823 g (71%) of an off-white product was collected by

suction filtration after rinsing with cold 2-propanol and drying under high vacuum.

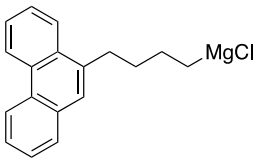
^{1}H NMR (500 MHz, $CDCl_3$): δ 8.76 (dd, *J* = 10, 2 Hz, 1H), 8.67 (d, *J* = 9 Hz, 1H), 8.11 (dd, *J* = 7, 3 Hz, 1H), 7.85 (dd, *J* = 7, 2 Hz, 1H), 7.57-7.70 (m, 5H), 3.63 (t, *J* = 6 Hz, 2H), 3.18 (t, *J* = 7 Hz, 2H), 1.98 (m, 4H).

^{13}C NMR (125 MHz, $CDCl_3$): δ 136.0, 131.9, 131.2, 130.8, 129.8, 128.1, 126.7, 126.6, 126.3, 126.3, 126.1, 124.3, 123.3, 122.5, 44.9, 32.7, 32.6, 27.4.

HRMS (EI) exact mass calcd for $C_{18}H_{17}{}^{35}Cl$ (M^+) 268.1019, found 268.1016.

EA anal. calcd for $C_{18}H_{17}Cl$: C, 80.43; H, 6.38. Found: C, 80.71; H, 6.33. Repeat Found: C, 80.47; H, 6.35.

(4-(Phenanthren-9-yl)butyl)magnesium chloride [~0.3 M in 4.66:1 anisole/THF] (2-8)

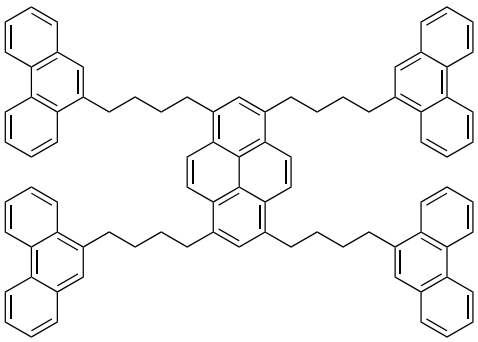


In a glass reactor equipped with a Teflon high vacuum stopcock were placed magnesium turnings (1.193 g, 49.09 mmol), and the vessel was placed under nitrogen. The Mg was suspended in THF (26 mL) and activated by the addition of ethylene bromide (0.193 mL, 2.24 mmol) via syringe under a stream of N_2, followed by heating to reflux for 1 h. In a separate glass reactor, 9-(4-chlorobutyl)phenanthrene (12.000 g, 44.646 mmol) under nitrogen was dissolved in dry, deoxygenated anisole (121 mL). To the activated magnesium suspension was added the solution of 9-(4-chlorobutyl)phenanthrene in anisole. The reactor

was sealed and heated to 70 °C overnight. At this time, only a small amount of magnesium remained visible in the brown solution.

A small amount of this Grignard reagent was quenched with 1 M HCl at 0 °C and subjected to standard workup. Analysis of the crude product by ^{1}H NMR spectroscopy revealed the presence of only 9-butylphenanthrene, with no evidence for olefinic or dimeric material. Thus, we assumed the magnesiation proceeded to completion and the molarity of the resulting solution was estimated on the basis of quantitative conversion. The Grignard solution was stored in the dry box, remaining stable over months when kept at RT under an unpunctured septum.

1,3,6,8-Tetrakis(4-(phenanthren-9-yl)butyl)pyrene (2-9)



To a stirred suspension of 1,3,6,8-tetrabromopyrene (1.000 g, 1.931 mmol, 1 equiv) and $NiCl_2$(dppe) (0.051 g, 0.097 mmol) in dioxane (40 mL) under nitrogen at RT was added (4-(phenanthren-9-yl)butyl)- magnesium chloride (39 mL, 0.3 M in anisole/THF (4.7:1 v/v)). The reactor was sealed and heated to 100 °C for 48 h. The reaction mixture was cooled to 0 °C and quenched by drop wise addition of aq 1 M HCl (5 mL). The crude product was collected by suction filtration, washed multiple times with hot water, and then washed successively with water, ether, and hexanes. The remaining material was dissolved in a minimal amount of hot chloroform and placed in the freezer overnight. The product, a spectroscopically homogeneous white powder, was collected by suction filtration, rinsed with cold

dichloromethane, and dried under vacuum to yield 1.753 g (80%) of compound **2-9**.

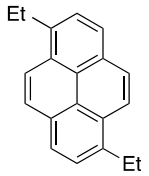
^{1}H NMR (500 MHz, $CDCl_3$): δ 8.71 (dd, *J* = 8, 2 Hz, 4H), 8.63 (d, *J* = 8 Hz, 4H), 8.08 (dd, *J* = 8, 1 Hz, 4H), 7.74 (dd, *J* = 8, 2 Hz, 4H), 7.68 (s, 2H), 7.65-7.5 (m, 20H), 3.36 (t, *J* = 6 Hz, 8H), 3.16 (t, *J* = 6 Hz, 8H), 2.01 (app t, *J* = 4 Hz, 16H).

^{13}C NMR (125 MHz, $CDCl_3$): δ 136.6, 135.9, 132.0, 131.3, 130.8, 129.7, 128.9, 128.1, 127.3, 126.6, 126.5, 126.5, 126.2, 126.1, 125.9, 124.5, 123.3, 122.6, 122.5, 33.6, 33.4, 31.9, 30.2.

HRMS (MALDI-FT-ICR) exact mass calcd for (M^+) $C_{88}H_{74}$: 1130.5785, found 1130.5770.

EA anal calcd for $C_{88}H_{74}$: C, 93.41%; H, 6.59%; found: C, 92.89%; H, 6.61%; repeat found: C, 92.87%; H, 6.63%.

1,6-Diethylpyrene (2-15)



In a dry, three-neck RBF fitted with a condenser and under a nitrogen atmosphere was placed a 1:1 mixture of 1,6- and 1,8-dibromopyrene (25.000 g, 69.852 mmol) and $NiCl_2$(dppe) (0.729 g, 1.38 mmol) in dioxane (500 mL). The solution was cooled to 0 °C, and EtMgBr (138 mL, 3 M in Et_2O) was added slowly. The resultant reaction mixture was heated to 100 °C for 36 h, cooled to 0 °C, and quenched by drop wise addition of saturated NH_4Cl (300 mL) followed by the addition of ether (500 mL) and water (200 mL). This mixture was partitioned in a separatory funnel and the organic layer washed with brine (500 mL), dried over

magnesium sulfate, and filtered. After removal of the solvent under reduced pressure, the crude solid was dissolved in minimum of dichloromethane, and an equal amount of methanol was layered on top. The biphasic mixture was allowed to diffuse overnight in the freezer. 1,6-Diethylpyrene deposited first and was collected by suction filtration. Rinsing with methanol and drying under high vacuum gave a bright yellow solid, 6.167 g (35%), pure by spectroscopic analysis.

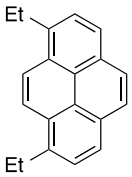
^{1}H NMR (500 MHz, $CDCl_3$): δ 8.27 (d, *J* = 9 Hz, 2H), 8.14 (d, *J* = 8 Hz, 2H), 8.10 (d, *J* = 10 Hz, 2H), 7.91 (d, *J* = 8 Hz, 2H), 3.41 (q, *J* = 8 Hz, 4H), 1.52 (t, *J* = 8 Hz, 6H).

^{13}C NMR (125 MHz, $CDCl_3$): δ 138.4, 129.6, 128.7, 127.4, 126.4, 125.5, 124.7, 122.5, 26.7, 16.1.

HRMS (EI) exact mass calcd for $C_{20}H_{18}$ (M^+) 258.1408; found: 258.1407.

EA anal. calcd for for $C_{20}H_{18}$: C, 92.98%; H, 7.02%; found: C, 92.61%; H, 6.95%.

1,8-Diethylpyrene (2-16)



The filtrate remaining after isolation of 1,6-diethylpyrene was concentrated under reduced pressure. The resulting sludge was dissolved in a minimal amount of hot THF and filtered through a short pad of Florisil. The solvent was removed under vacuum, providing yellow oil, which solidified upon standing overnight at room temperature. The crude solid was dissolved in a minimal amount of hot hexanes and allowed to crystallize in the refrigerator overnight. The 1,6-diethylpyrene was

collected by suction filtration, rinsed with cold hexanes, and dried under high vacuum, giving a spectroscopically pure dark yellow solid, 5.224 g (26%).

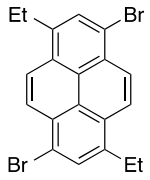
^{1}H NMR (500 MHz, $CDCl_3$): δ 8.34 (s, 2H), 8.09 (d, *J* = 8 Hz, 2H), 7.96 (s, 2H), 7.87 (d, *J* = 8Hz, 2H), 3.39 (q, *J* = 7 Hz, 4H), 1.50 (t, *J* = 7 Hz, 6H).

^{13}C NMR (125 MHz, $CDCl_3$): δ 138.2, 130.1, 128.2, 126.7, 126.3, 125.5, 124.8, 123.1, 26.6, 16.1.

HRMS (EI) exact mass calcd for $C_{20}H_{18}$ (M^+) 258.1408, found 258.1409.

EA anal. calcd for $C_{20}H_{18}$: C, 92.98; H, 7.02. Found: C, 93.11; H, 7.20. Repeat found: C, 92.81; H, 7.03.

1,6-Dibromo-3,8-diethylpyrene (2-11)



A 100 mL RBF open to the atmosphere was charged with a solution of 1,6-diethylpyrene (1.107 g, 4.288 mmol) in DCM (40 mL) at room temperature. To this solution was added NBS (1.601 g, 8.995 mmol) and the reaction mixture stirred magnetically for 4 h. The solvent was removed under vacuum, and the crude product mixture was dissolved in a minimal amount of hot chloroform, layered with an equal volume of ethanol, and allowed to diffuse at RT overnight. The product was collected by suction filtration as a spectroscopically pure, off-white powder (1.432 g, 80%). A sample suitable for X-ray analysis was prepared by crystallizing from a super-saturated solution in DMA.

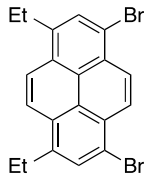
^{1}H NMR (500 MHz, $CDCl_3$): δ 8.45 (d, *J* = 10 Hz, 2H), 8.26 (d, *J* = 10 Hz, 2H), 8.15 (s, 2H), 3.34 (q, *J* = 8 Hz, 4H), 1.48 (t, *J* = 8 Hz, 6H)

^{13}C NMR (125 MHz, $CDCl_3$): δ 139.8, 131.0, 128.2, 128.1, 126.2, 126.2, 123.8, 120.6, 26.5, 15.8.

HRMS (EI) exact mass calcd for $C_{20}H_{16}{}^{79}Br_2$ (M^+) 413.9619; found: 413.9628 (11.05%).

EA anal. calcd for $C_{20}H_{16}Br_2$: C, 57.72%; H, 3.88%; found: C, 57.41%; H, 3.91%.

1,8-dibromo-3,6-diethylpyrene (2-12)



A 100 mL RBF open to the atmosphere was charged with a solution of 1,8-diethylpyrene (1.000 g, 3.874 mmol) in dichloromethane (35 mL) at room temperature. To this solution was added NBS (1.447 g, 8.130 mmol) and the reaction mixture stirred magnetically for 4 h. The solvent was removed under vacuum and the crude product mixture dissolved in a minimal amount of hot chloroform, which was layered with an equal volume of ethanol and allowed to diffuse at RT overnight. The product was collected by suction filtration, rinsed with ethanol and dried under high vacuum providing a spectroscopically pure, off white powder (1.271 g, 79%).

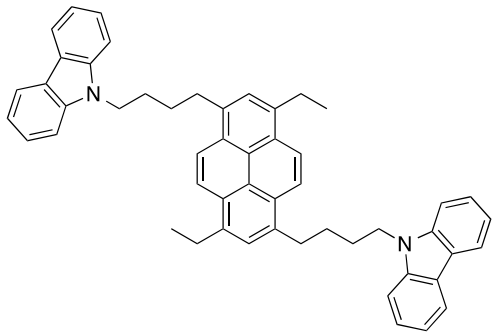
^{1}H NMR (500 MHz, $CDCl_3$): δ 8.44 (s, 2H), 8.29 (s, 2H), 8.17 (s, 2H), 3.35 (q, *J* = 7 Hz, 4H), 1.49 (t, *J* = 7 Hz, 6H).

^{13}C NMR (125 MHz, $CDCl_3$): δ 139.8, 131.0, 128.4, 128.1, 126.8, 126.3, 123.2, 120.5, 26.4, 15.8.

HRMS (EI) exact mass calcd for $C_{20}H_{16}{}^{81}Br_2$ (M^+) 417.9578; found: 417.9583 (48.01%).

EA anal. calcd for $C_{20}H_{16}Br_2$: C, 57.72%; H, 3.88%; found: C, 57.50%; H, 3.77%; repeat found: C, 57.56%; H, 3.89%.

9,9′-((3,8-Diethylpyrene-1,6-diyl)bis(butane-4,1-diyl))bis- (9H-carbazole) (2-18)



A 100 mL RBF was charged with 1,6-dibromo- 3,8-diethylpyrene (1.000 g, 2.403 mmol) and $NiCl_2$(dppe) (0.063 g, 0.12 mmol) in THF (50 mL). To this suspension was added (4-(9H- carbazol-9-yl)butyl)magnesium chloride (14 mL of a 0.5 M solution in THF) at room temperature and the reaction mixture allowed to stir overnight. After being cooled to 0 °C, the reaction was quenched with 1 M HCl (5 mL). The crude product was collected by suction filtration and washed multiple times with hot water, followed by ether, followed by hexanes. This washed product was then dissolved in a minimal amount of hot chloroform and placed in the freezer overnight. The product was collected by suction filtration and rinsed with cold dichloromethane. The resulting white powder was then dried under high vacuum to yield spectroscopically pure. Yield = 0.883 g (52%). A sample suitable

for X-ray analysis was prepared by crystallizing from a super-saturated solution in DMA.

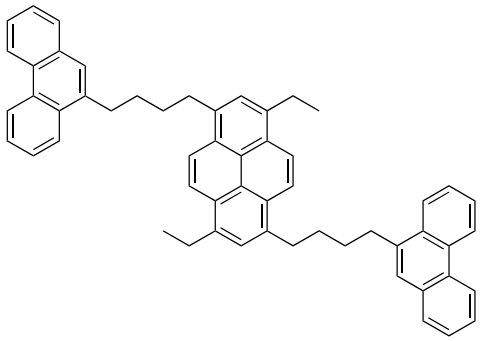
^{1}H NMR (500 MHz, $CDCl_3$): δ 8.17 (d, *J* = 11 Hz, 2H), 8.12 (d, *J* = 11 Hz, 2H), 8.10 (dd, *J* = 8, 1 Hz, 4H), 7.61 (s, 2H), 7.43 (ddd, *J* = 8, 7, 1 Hz, 4H), 7.39 (d, *J* = 8 Hz, 4H), 7.22 (ddd, *J* = 8, 7, 1 Hz, 4H), 4.34 (t, *J* = 7 Hz, 4H), 3.33-3.29 (m, 8H), 2.07 (tt, *J* = 8, 8 Hz, 4H), 1.97 (tt, *J* = 8, 7 Hz, 4H), 1.44 (t, *J* = 8 Hz, 6H).

^{13}C NMR (125 MHz, $CDCl_3$): δ 140.4, 137.7, 135.4, 127.9, 127.2, 127.1, 126.4, 125.6 122.9, 122.4, 122.2, 120.4, 118.8, 108.7, 43.1, 33.4, 29.3, 28.9, 26.7, 16.1.

HRMS (MALDI-FT-ICR) exact mass calcd for (M^+) $C_{52}H_{48}N_2$ 700.3812, found 700.3811.

EA anal. calcd for $C_{52}H_{48}N_2$: C, 89.10; H, 6.90; N, 4.00. Found: C, 88.72; H, 6.87; N, 4.02. Repeat Found: C, 88.79; H, 6.80; N, 4.04.

1,6-Diethyl-3,8-bis(4-(phenanthren-9-yl)butyl)pyrene (2-19)



A 100 mL RBF under nitrogen was charged with 1,6-dibromo-3,8- diethylpyrene (1.000 g, 2.403 mmol) and $NiCl_2$(dppe) (0.063 g, 0.12 mmol) in THF (40 mL) and stirred at room temperature. To this suspension was added (4-(phenanthren-9-yl)butyl)magnesium chloride (24 mL of a 0.3 M in anisole/THF (4.7:1 v/v)). The reaction mixture was allowed to stir overnight at rt, after which time it was cooled

to 0 °C and quenched with 1 M HCl (5 mL). The precipitated product was collected by suction filtration and washed multiple times with hot water, then ether, and then hexanes. The crude product was dissolved in a minimal amount of hot chloroform and allowed to precipitate from solution overnight. The product, a spectroscopically pure white powder, was collected by suction filtration, washed with cold dichloromethane, and dried under high vacuum. Yield = 1.214 g (70%).

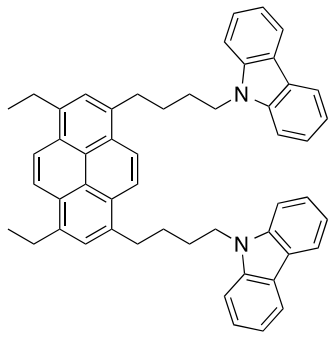
^{1}H NMR (500 MHz, $CDCl_3$): δ 8.74 (dd, *J* = 8, 1 Hz, 2H), 8.65 (d, *J* = 8 Hz, 2H), 8.21 (d, *J* = 10 Hz, 2H), 8.17 (d, *J* = 10 Hz, 2H), 8.12 (d, *J* = 8 Hz, 2H), 7.77 (d, *J* = 8 Hz, 2H), 7.71 (s, 2H), δ 7.68-7.50 (m, 10H), 3.40 (t, *J* = 7 Hz, 4H), 3.32 (q, *J* = 8 Hz, 4H), 3.20 (t, *J* = 8 Hz, 4H), 2.07–2.03 (m, 8H), 1.45 (t, *J* = 5 Hz, 6H);

^{13}C NMR (125 MHz, $CDCl_3$): δ 137.6, 136.7, 136.1, 132.0, 131.4, 130.8, 129.7, 128.1, 128.0, 127.3, 127.1, 126.6, 126.5, 126.5, 126.2, 126.1, 125.9, 124.5, 123.3, 122.5, 122.4, 122.3, 33.7, 33.4, 31.9, 30.3, 26.7, 16.2.

HRMS (APPI-TOF) exact mass calcd for ($[M + H]^+$) $C_{56}H_{51}$: 723.3985, found 723.3971.

EA anal. calcd for $C_{56}H_{50}$: C, 93.03%; H, 6.97%; found: C, 91.38%; H, 6.96%; repeat found: C, 91.39; H, 6.94%.

9,9′-((3,6-Diethylpyrene-1,8-diyl)bis(butane-4,1-diyl))bis- (9H-carbazole) (2-20)



A 100 mL RBF under nitrogen atmosphere was charged with 1,8-dibromo-3,6-diethylpyrene (1.000 g, 2.403 mmol) and $NiCl_2$(dppe) (0.063 g, 0.12 mmol) in THF (50 mL). To this suspension was added (4-(9H-carbazol-9-yl)butyl)magnesium chloride (14 mL of a 0.5 M solution in THF) at room temperature, and the reaction mixture was allowed to stir at RT overnight. The reaction mixture was then cooled to 0 °C and quenched with 1 M HCl (5 mL). The crude product was collected by suction filtration and washed multiple times with hot water, then ether, and then hexanes. The crude product was then dissolved in a minimal amount of warm dichloromethane and allowed to precipitate out of solution overnight. The product, a spectroscopically pure light yellow powder, was collected by suction filtration, washed with cold dichloromethane, and dried under high vacuum. Yield = 0.954 g (57%).

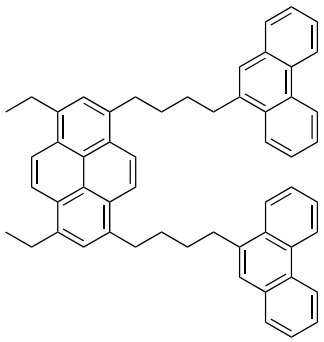
^{1}H NMR (500 MHz, $CDCl_3$): δ 8.21 (s, 2H), 8.10 (ddd, *J* = 8, 1, 1 Hz, 4H), 8.08 (s, 2H), 7.62 (s, 2H), 7.43 (ddd, *J* = 8, 7, 2 Hz, 4H), 7.39 (dd, *J* = 7, 1 Hz, 4H), 7.22 (ddd, *J* = 8, 7, 1 Hz, 4H), 4.35 (t, *J* = 7 Hz, 4H), 3.33–3.28 (m, 8H), 2.11–2.05 (m, 4H), 2.01–1.95 (4, 4H), 1.44 (6, *J* = 7 Hz, 6H).

^{13}C NMR (125 MHz, $CDCl_3$): δ 140.5, 137.8, 135.4, 127.9, 127.2, 127.2, 126.4, 125.7, 122.9, 122.4, 122.3, 120.4, 118.8, 108.7, 43.1, 33.4, 29.4, 29.0, 26.7, 16.2.

HRMS (APPI-TOF) exact mass calcd for ($[M + H]^+$) $C_{52}H_{49}N_2$: 701.3890, found 701.3879.

EA anal. calcd for $C_{52}H_{48}N_2$: C, 89.10%; H, 6.90%; N, 4.00%; found: C, 88.24%; H, 6.96%; N, 4.07%; repeat found: C, 88.35%; H, 6.88%; N, 4.05%.

1,8-Diethyl-3,6-bis(4-(phenanthren-9-yl)butyl)pyrene (2-21)



A 100 mL RBF under nitrogen was charged with 1,8-dibromo-3,6- diethylpyrene (1.000 g, 2.403 mmol) and $NiCl_2$(dppe) (0.063 g, 0.12 mmol) in THF (40 mL). To this suspension was added (4- (phenanthren-9-yl)butyl)magnesium chloride (24 mL of a 0.3 M solution in anisole/THF (4.7:1 v/v)) at room temperature. The reaction mixture was allowed to stir at RT overnight. The reaction mixture was cooled to 0 °C and quenched with 1 M HCl (5 mL). The precipitated product was collected by suction filtration and washed multiple times with hot water, then ether, and then hexanes. This material was then dissolved in a minimal amount of warm dichloromethane and allowed to precipitate from solution overnight in a freezer. The product, a spectroscopically pure white powder, was collected by suction filtration, rinsed with cold dichloromethane, and dried under high vacuum. Yield = 1.136 g (65%).

^{1}H NMR (500 MHz, $CDCl_3$): δ 8.77 (dd, *J* = 8, 1 Hz, 2H), 8.68 (d, *J* = 8 Hz, 2H), 8.25 (s, 2H), 8.20 (s, 2H), 8.15 (dd, *J* = 8, 1 Hz, 2H), 7.80 (dd, *J* = 7, 1 Hz, 2H),

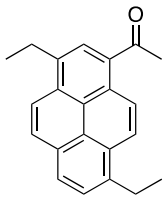
7.75 (s, 2H), 7.70-7.56 (m, 10H), 3.42 (t, J = 7 Hz, 4H), 3.38 (q, J = 7 Hz, 4H), 3.24 (t, J = 7 Hz, 4H), 2.08 (m, 8H), 1.49 (t, J = 8 Hz, 6H).

^{13}C NMR (125 MHz, $CDCl_3$): δ 137.6, 136.7, 136.0, 132.0, 131.4, 130.8, 129.7, 128.1, 128.0, 127.2, 127.1, 126.6, 126.5, 126.5, 126.2, 126.1, 125.9, 124.5, 123.3, 122.5, 122.4, 122.3, 33.7, 33.4, 31.9, 30.3, 26.7, 16.2.

HRMS (APPI-TOF) exact mass calcd for ($[M + H]^+$) $C_{56}H_{51}$: 723.3985, found 723.3977.

EA anal. calcd for $C_{56}H_{50}$: C, 93.03%; H, 6.97%; found: C, 91.27%; H, 7.28%; repeat found: C, 91.49%; H, 6.95%.

1-(3,8-Diethylpyren-1-yl)ethanone (2-22)



A three-necked 250 mL RBF under nitrogen was charged with 1,6-diethylpyrene (3.000 g, 11.61 mmol), dissolved in dichloromethane (60 mL), and cooled to 0 °C. To this stirred solution was added a solution of acetyl chloride (0.83 mL, 12 mmol) and aluminum trichloride (1.548 g, 11.61 mmol) in dichloromethane (30 mL). The reaction mixture was allowed to warm to RT and stirred overnight. The reaction mixture was cooled to 0 °C and quenched by slow addition of 1 M HCl (30 mL). The reaction mixture was allowed to warm to RT over 30 min, at which point 50 mL of water was added, and the resulting two-phase mixture was separated in a separatory funnel. The organic layer was washed with 100 mL of brine and dried over magnesium sulfate. The mixture was filtered, and the solvent was removed under vacuum. The crude product was dissolved in a minimal

amount of hot hexanes and placed in the refrigerator overnight. The product, a spectroscopically pure yellow powder, was collected by suction filtration, rinsed with cold hexanes, and dried under high vacuum. Yield = 2.532 g (73%).

IR (DCM cast, cm^{-1}): 3039 (w), 2990 (s), 2964 (s), 2930 (m), 2878 (m), 1660 (s, C□O).

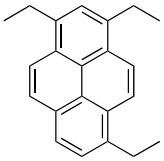
^{1}H NMR (500 MHz, $CDCl_3$): δ 9.00 (d, *J* = 10 Hz, 1H), 8.39 (d, *J* = 10 Hz, 1H), 8.24 (d, *J* = 8 Hz, 1H), 8.23 (s, 1H), 8.17 (d, *J* = 8 Hz, 1H), 8.16 (d, *J* = 9 Hz, 1H), 7.92 (d, *J* = 8 Hz, 1H), 3.41 (q, *J* = 7 Hz, 2H), 3.40 (q, *J* = 8 Hz, 2H), 2.91 (s, 3H); 1.51 (t, *J* = 7 Hz, 3H), 1.50 (t, *J* = 8 Hz, 3H)

^{13}C NMR (125 MHz, $CDCl_3$): δ 202.5, 139.9, 137.1, 131.8, 131.8, 129.7, 129.4, 128.2, 127.8, 127.5, 126.9, 126.1, 126.0, 125.2, 124.8, 124.7, 122.1, 30.6, 26.9, 26.8, 16.3, 16.0.

HRMS (EI) exact mass calcd for $C_{22}H_{20}O$ (M^+) 300.1514; found: 300.1513 (100.0%).

EA anal. calcd for $C_{22}H_{20}O$: C, 87.96%; H, 6.71%; found: C, 87.91%; H, 6.76%; repeat found: C, 87.80%; H, 6.76.

1,3,6-Triethylpyrene (2-14)



To a suspension of 1-(3,8-diethylpyren-1-yl)ethanone **2-22** (2.000 g, 6.658 mmol) and potassium hydroxide (3.883 g, 69.21 mmol) in ethylene glycol (36 mL) in a 100 mL RBF fitted with a reflux condenser and open to the air was added hydrazine hydrate (5.50 mL, 0.113 mol) via syringe. The mixture was heated to 120 °C for 2 h, after which time the condenser was removed and the reaction mixture heated to 200 °C for 1 h to drive off water. At this point, the reaction mixture was cooled to RT and taken up in dichloromethane and water. The organic layer was separated, washed with brine, dried with magnesium sulfate, and filtered, and the solvent was removed under vacuum. The resulting orange sludge was filtered through a short silica pad using hexanes. Removal of the solvent provided a white solid that was dissolved in a minimal amount of hot toluene, diluted with an equal volume 2-propanol, and placed in the freezer overnight. The product, a spectroscopically pure white solid was collected by suction filtration, rinsed with cold 2-propanol, and dried under high vacuum. Yield = 1.13 g (70%).

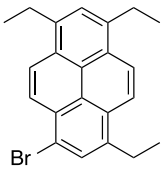
^{1}H NMR (500 MHz, $CDCl_3$): δ 8.29 (d, *J* = 9 Hz, 1H), 8.25 (d, *J* = 9 Hz, 1H), 8.19 (d, *J* = 9 Hz, 1H), 8.06 (d, *J* = 8 Hz, 1H), 7.99 (d, *J* = 9 Hz, 1H), 7.85 (d, *J* = 8 Hz, 1H), 7.75 (s, 1H), 3.40-3.33 (m, 6H, 3 overlapping quartets w/ *J* = 8 Hz each), 1.51-1.46 (m, 9H, 3 overlapping triplets w/ *J* = 8 Hz each);

^{13}C NMR (125 MHz, $CDCl_3$): δ 138.2, 138.0, 138.0, 129.9, 128.5, 127.3, 127.2, 126.8, 126.5, 126.2, 126.0, 125.9, 124.5, 123.2, 122.5, 122.2, 26.8, 26.7, 26.7, 16.2, 16.2, 16.1.

HRMS (EI) exact mass calcd for $C_{22}H_{22}$ (M^+) 286.1722; found: 286.1724 (100%).

EA anal. calcd for $C_{22}H_{22}$: C, 92.26%; H, 7.74%; found: C, 92.18%; H, 7.91%; N, 0.35%.

1-Bromo-3,6,8-triethylpyrene (2-10)



A 50 mL RBF open to the air was charged with 1,3,6-triethylpyrene (1.000 g, 3.494 mmol) dissolved in dichlormethane (30 mL). To this solution was added NBS (0.653 g, 3.67 mmol). The reaction mixture was allowed to stir at RT overnight. The solvent was removed under vacuum and the crude product, a brown sludge, was dissolved in a minimal amount of warm dichloromethane, combined with an equal volume of methanol, and placed in a freezer overnight. The product, a light brown, spectroscopically pure powder, was collected by suction filtration, rinsed with methanol, and dried under high vacuum. Yield = 1.054 g (83%)

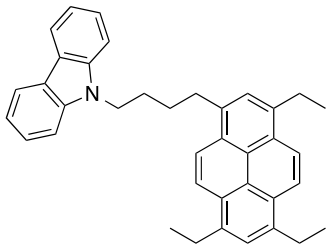
^{1}H NMR (500 MHz, $CDCl_3$): δ 8.37 (d, *J* = 9 Hz, 1H), 8.31 (d, *J* = 8 Hz, 1H), 8.29 (d, *J* = 8 Hz, 1H), 8.20 (d, *J* = 9 Hz, 1H), 8.11 (s, 1H), 7.79 (s, 1H), 3.39-3.31 (6 line m, 6H, 3 overlapping quartets w/ *J* = 8 Hz each), 1.51-1.47 (m, 9H, 3 overlapping triplets w/ *J* = 8 Hz each)

^{13}C NMR (125 MHz, $CDCl_3$): δ 138.9, 138.9, 138.7, 130.2, 128.2, 128.1, 127.8, 127.2, 127.1, 126.9, 125.4, 124.9, 124.1, 123.5, 121.9, 119.4, 26.8, 26.7, 26.4, 16.2, 16.2, 15.8.

HRMS (EI) exact mass calcd for $C_{22}H_{21}{}^{81}Br$ (M^+) 366.0806; found: 366.0822 (97.66%).

EA anal. calcd for $C_{22}H_{21}Br$: C, 72.33%; H, 5.79%; found: C, 72.47%; H, 5.82%.

9-(4-(3,6,8-Triethylpyren-1-yl)butyl)-9H-carbazole (2-23)



A 50 mL RBF under nitrogen was charged with 1-Bromo-3,6,8-triethylpyrene (1.000 g, 2.737 mmol) and $NiCl_2$(dppe) (0.043 g, 0.082 mmol) in THF (20 mL). To the resulting suspension was added (4-(9H- carbazol-9-yl)butyl)magnesium chloride (8 mL of a 0.5 M solution in THF) at room temperature. The reaction mixture was allowed to stir overnight, cooled to 0 °C, and quenched slowly with 1 M HCl (5 mL). The crude reaction mixture was taken up in ether and washed with water and brine. The organic layer was dried over magnesium sulfate and filtered, and the solvent was removed under vacuum. The crude solid was dissolved in a minimal amount of hot sec-butanol and allowed to precipitate from solution overnight at room temperature, providing a yellow, spectroscopically pure powder that was collected by suction filtration, rinsed with sec-butanol, and dried under high vacuum. Yield = 0.995 g (72%).

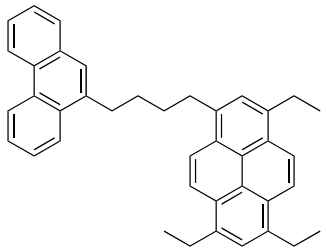
^{1}H NMR (500 MHz, $CDCl_3$): δ 8.23 (d, *J* = 10 Hz, 1H), 8.20 (d, *J* = 10 Hz, 1H), 8.19 (d, *J* = 9 Hz, 1H), 8.12 (d, *J* = 10 Hz, 1H), 8.10 (d, *J* = 8 Hz, 2H), 7.74 (s, 1H), 7.61 (s, 1H), 7.44 (dd, *J* = 6, 1 Hz, 2H), 7.40 (ddd, *J* = 8, 8, 1 Hz, 2H), 7.22 (ddd, *J* = 8, 7, 1 Hz, 2H), 4.35 (t, *J* = 7 Hz, 2H), 3.37-3.28 (m, 8H), 2.07 (m, 2H), 1.98 (m, 2H), 1.49 (t, *J* = 8 Hz, 3H), 1.48 (t, *J* = 8 Hz, 3H), 1.44 (t, *J* = 8 Hz, 3H)

^{13}C NMR (125 MHz, $CDCl_3$): δ 140.5, 137.9, 137.9, 137.6, 135.2, 127.9, 127.2, 127.2, 127.1, 127.0, 127.0, 126.5, 126.4, 125.7, 122.9, 122.4, 122.2, 122.1, 120.4, 118.8, 108.7, 43.1, 33.4, 29.3, 29.0, 26.8, 26.8, 26.7, 16.2, 16.2, 16.1.

HRMS (APPI-TOF) exact mass calcd for ($[M + H]^+$) $C_{38}H_{39}N$: 508.2999, found 508.3003.

EA anal. calcd for $C_{38}H_{37}N$: C, 89.90%; H, 7.35%; N, 2.76%; found: C, 89.63%; H, 7.35%; N, 2.85%; repeat found: C, 89.71%; H, 7.37%; N, 2.83%.

1,3,6-Triethyl-8-(4-(phenanthren-9-yl)butyl)pyrene (2-24)



A 50 mL RBF was charged with 1-bromo-3,6,8-triethylpyrene (1.000 g, 2.737 mmol) and $NiCl_2$(dppe) (0.043 g, 0.082 mmol) and dissolved in THF (15 mL). To this suspension was added (4-(phenanthren-9- yl)butyl)magnesium chloride (14 mL of a 0.3 M in anisole/THF (4.7:1 v/v)). The resulting reaction mixture was allowed to stir overnight at room temperature. The reaction mixture was then cooled to 0 °C and quenched carefully with 1 M HCl (5 mL). The reaction mixture was taken up in chloroform and washed with water, followed by brine. The organic layer was dried over magnesium sulfate and filtered and the solvent removed under vacuum. The crude solid was dissolved in a minimal amount of hot sec-butanol, and the product, a spectroscopically pure white powder, precipitated out of solution at overnight. The product was collected by suction

filtration, rinsed with sec-butanol, and dried under high vacuum. Yield = 1.158 g (82%).

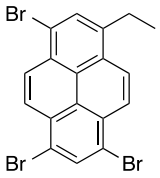
^{1}H NMR (500 MHz, $CDCl_3$): δ 8.74 (dd, *J* = 10, 2 Hz, 1H), 8.65 (d, *J* = 8 Hz, 1H), 8.23 (d, *J* = 10 Hz, 1H), 8.20 (d, *J* = 10 Hz, 1H), 8.20 (d, *J* = 10 Hz, 1H), 8.18 (d, *J* = 10 Hz, 1H), 8.12 (dd, *J* = 8, 1 Hz, 1H), 7.77 (dd, *J* = 7, 1 Hz, 1H), 7.73 (s, 1H) δ 7.71 (s, 1H), 7.67-7.53 (m, 5H), 3.41-3.30 (m, 8H), 3.21 (t, *J* = 7 Hz, 2H), 2.06-2.03 (m, 4H), 1.53-1.44 (m, 9H).

^{13}C NMR (125 MHz, $CDCl_3$): δ 137.8, 137.8, 137.6, 136.7, 136.0, 132.0, 131.4, 130.8, 129.7, 128.1, 127.9, 127.3, 127.1, 127.1, 127.0, 127.0, 126.6, 126.5, 126.5, 126.4, 126.2, 126.1, 125.9, 124.5, 123.3, 122.5, 122.3, 122.3, 122.2.

HRMS (APPI-TOF) exact mass calcd for ($[M + H]^+$) $C_{40}H_{39}$: 519.3046, found 519.3045.

EA anal. calcd for $C_{40}H_{38}$: C, 92.62%; H, 7.38%; found: C, 91.79%; H, 7.38%; repeat found: C, 91.89%; H, 7.41%.

1,3,6-Tribromo-8-ethylpyrene (2-13)



A 100 mL RBF fitted with a condenser and open to the air was charged with a solution of 1- ethylpyrene (1.840 g, 7.990 mmol) in chloroform (60 mL) at rt. To this solution was added NBS (4.408 g, 24.78 mmol), and the reaction mixture was heated overnight at reflux. The reaction mixture was cooled to rt, and the crude product collected by suction filtration, rinsed with cold chloroform and methanol,

and then dried under vacuum to provide 2.758 g (74%) of a spectroscopically pure beige powder.

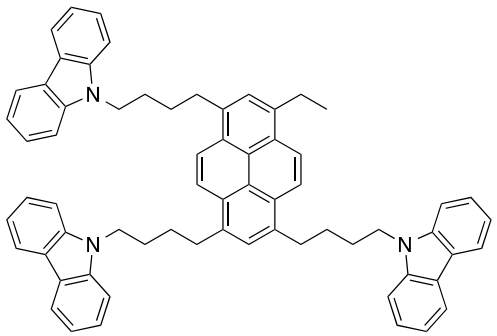
^{1}H NMR (500 MHz, $CDCl_3$): δ 8.53 (s, 1H), 8.52 (d, *J* = 9 Hz, 1H), 8.44 (d, *J* = 9 Hz, 1H), 8.42 (d, *J* = 10 Hz, 1H), 8.35 (d, *J* = 8 Hz, 1H), 8.21 (s, 1H), 3.36 (q, *J* = 8 Hz, 2H), 1.50 (t, *J* = 8 Hz, 3H).

^{13}C NMR (125 MHz, $CDCl_3$): δ 140.8, 134.0, 131.8, 129.4, 129.1, 128.2, 128.1, 128.0, 128.0, 126.5, 125.9, 125.3, 124.9, 121.5, 119.9, 119.8, 26.5, 15.9.

HRMS (EI) exact mass calcd for $C_{18}H_{11}{}^{81}Br_3$ (M^+) 469.8349; found: 469.8346 (36.75%).

EA anal. calcd for $C_{18}H_{11}Br_3$: C, 46.29%; H, 2.37%; found: C, 46.49%; H, 2.42%; repeat found: C, 46.66%; H, 2.43%; N, 0.15%.

9,9′,9′′-((8-Ethylpyrene-1,3,6-triyl)tris(butane-4,1-diyl))tris- (9H-carbazole) (2-25)



To a glass reactor topped by a Teflon high vacuum stopcock under nitrogen were added 1,3,6-tribromo-8- ethylpyrene (1.000 g, 2.141 mmol) and $NiCl_2$(dppe) (0.057 g, 0.11 mmol) in dioxane (60 mL). To this suspension was added (4-(9H-carbazol-9-yl)butyl)magnesium chloride (19 mL of a 0.5 M solution in THF) at room temperature. The reactor was sealed and heated to 100 °C for 36 h. The

resulting reaction mixture was cooled to 0 °C and quenched with 1 M HCl (5 mL). The mixture was taken up in ether and washed with water, followed by brine. The organic layer was dried over magnesium sulfate and filtered, and the solvents were removed under vacuum. The crude product was taken up in a minimal amount of hot chloroform and placed in the freezer overnight, at which point the product, a spectroscopically pure yellow powder, was collected by suction filtration and washed with cold dichloromethane. Yield = 1.224 g (64%).

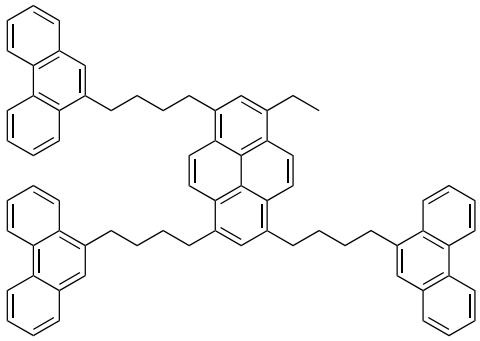
^{1}H NMR (500 MHz, $CDCl_3$): δ 8.18 (d, *J* = 10 Hz, 1H), δ 8.12-8.10 (m, 8H), 8.06 (d, *J* = 9 Hz, 1H), 7.62 (s, 1H), 7.45-7.33 (m, 13H), 7.24-7.19 (m, 6H), 4.36 (t, *J* = 7 Hz, 2H), 4.30-4.26 (m, 4H), 3.33-3.22 (m, 8H), δ 2.11-1.87 (m, 12H), 1.45 (t, *J* = 7 Hz, 3H).

^{13}C NMR (125 MHz, $CDCl_3$): δ 140.4, 140.4, 140.4, 137.9, 135.5, 135.2, 135.1, 128.8, 128.0, 127.4, 127.3, 127.1, 127.1, 126.4, 126.3, 125.6, 125.6, 125.6, 125.6, 125.6, 122.9, 122.9, 122.9, 122.9, 122.5, 122.4, 122.2, 122.2, 120.4, 120.4, 118.8, 118.8, 108.7, 108.7, 43.1, 43.0, 33.4, 33.2, 29.3, 29.2, 29.0, 28.9, 28.9, 26.7, 16.2.

HRMS (APPI-TOF) exact mass calcd for ($[M + H]^+$) $C_{66}H_{60}N_3$: 894.4782, found 894.4774.

EA anal. calcd for $C_{66}H_{59}N_3$: C, 88.65; H, 6.65; N, 4.70. Found: C, 86.04; H, 6.96; N, 4.57. Repeat Found: C, 86.51; H, 6.87; N, 4.62.

1-Ethyl-3,6,8-tris(4-(phenanthren-9-yl)butyl)pyrene (2-26)



To a suspension of 1,3,6-tribromo-8-ethylpyrene (1.000 g, 2.141 mmol) and $NiCl_2$(dppe) (0.057 g, 0.11 mmol) in dioxane (50 mL) in a glass reactor topped by a Teflon vacuum stopcock was added (4- (phenanthren-9-yl)butyl)magnesium chloride (32 mL of a 0.3 M solution in anisole/THF (4.7:1 v/v)) at room temperature. The reactor was sealed and heated to 100 °C for 36 h. The reaction mixture was cooled to 0 °C and quenched carefully with 1 M HCl (5 mL). The resulting mixture was taken up in chloroform and washed with water, followed by brine. The organic layer was dried over magnesium sulfate, filtered, and evaporated to dryness. The crude product was dissolved in a minimal amount of hot chloroform and placed in the freezer overnight. The precipitated product, a light yellow spectroscopically pure powder, was collected by suction filtration, washed with cold dichloromethane, and dried under high vacuum. Yield = 1.022 g (51%).

^{1}H NMR (500 MHz, $CDCl_3$): δ 8.74-8.70 (m, 3H), 8.66-8.62 (m, 3H), 8.20 (d, *J* = 9 Hz, 1H), 8.18 (d, *J* = 9 Hz, 1H), 8.16 (s, 1H), 8.16 (s, 1H), δ 8.12 (dd, *J* = 8, 2 Hz, 1H), δ 8.08-8.06 (m, 2H), 7.77 (dd, *J* = 8, 2 Hz, 1H), 7.75-7.73 (m, 2H), 7.72 (s, 1H), 7.68 (s, 1H), 7.66-7.50 (m, 15H), 3.40-3.30 (m, 8H), 3.22-3.14 (m, 6H), 2.07-2.00 (m, 12H), 1.46 (t, *J* = 8 Hz, 3H).

^{13}C NMR (125 MHz, $CDCl_3$): δ 137.7, 136.6, 136.6, 136.1, 135.9, 135.9, 132.0, 131.4, 131.3, 130.8, 130.8, 129.7, 129.7, 128.9, 128.1, 128.1, 128.0, 127.4, 127.3,

127.2, 127.1, 126.6, 126.6, 126.5, 126.5, 126.5, 126.2, 126.2, 126.1, 126.1, 125.9, 125.9, 124.5, 124.5, 123.3, 123.3, 122.5, 122.5, 122.4, 122.4, 122.3, 33.7, 33.6, 33.4, 33.4, 33.4, 31.9, 31.9, 31.8, 30.3, 30.2, 30.2, 26.7, 16.2.

HRMS (APPI-TOF) exact mass calcd for ($[M + H]^+$) $C_{72}H_{63}$: 927.4924, found 927.4927.

EA anal. calcd for $C_{72}H_{62}$: C, 93.26%; H, 6.74%; found: C, 91.05%; H, 6.62%; repeat found: C, 90.96%; H, 6.62%.

3 Robust, Versatile Total Synthesis of G1 Compounds – an Enhanced Strategy for Alkyl-Bridged Model Asphaltenes

Impetus for an improved G1 approach

In early 2014, the Stryker and Tykwinski groups began a collaborative research effort with Japan Petroleum Energy Center[‡] (JPEC). This incorporated research foundation is interested in developing technologies for the efficient upgrading of asphaltene-rich bitumen, among other energy-related pursuits. Our success in synthesizing G2 model asphaltene compounds at gram scale (Chapter 2) put us in an advantageous position to provide "large" quantities of a broad range of model compounds (multiple grams) to JPEC researchers for "in-house" physical characterization, solubility/aggregation properties, and other bitumen processing studies.

Because our collaborators at JPEC were satisfied with the purity of the materials we provided and the results gained from having access to such compounds, they chose to continue supporting our program. The Tykwinski group's synthetic G1 compounds were important to JPEC because of highly relevant molecular architectures and interesting intermolecular aggregation behavior. Unfortunately, the Tykwinski Group's strategy for the synthesis of G1 compounds was unreliable, failing to afford pure materials, and could not be performed at a functional scale. Thus, we set out to identify and develop a new approach to

[‡] JPEC has business offices in Tokyo, Brussels, and Chicago and a research campus in Chiba prefecture. They are a consortium of industry, government, and academic partners established in 1986. They can be found on the web @ http://www.pecj.or.jp/english/outline/outline02.htmL

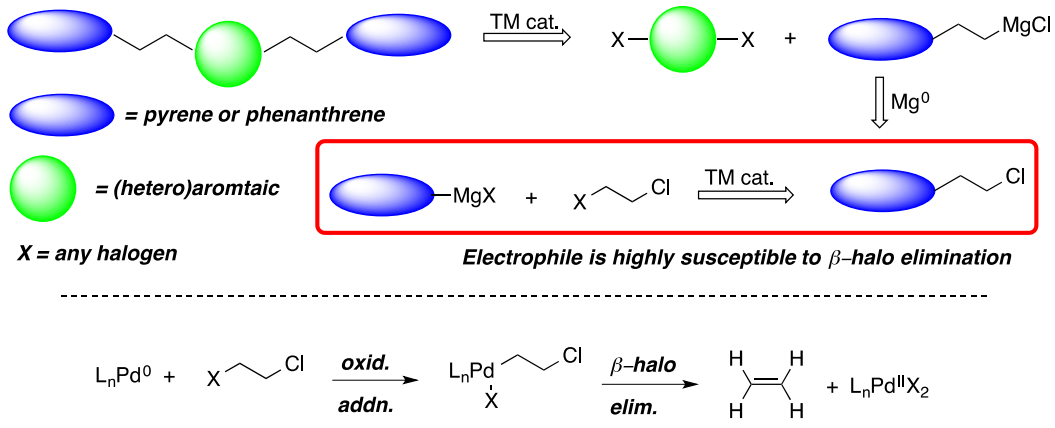
synthesize this class of compounds, with an emphasis on selectivity, substrate scope, and high functional group tolerance, but no sacrifice in convergence or scalability.

Design and background, an improved synthetic approach to G1 compounds

The merits of the approach used to synthesize G2 model compounds are evident in its high yields and scalability. The key to the success of the G2 approach, relative to the methodology used for the synthesis of G1 compounds, is the ability to avoid catalytic hydrogenation. The only obvious drawback to this approach is the lack of bench stability in our nucleophilic cross-coupling partners (i.e., Grignard reagents). Though conveniently stored under nitrogen as ethereal solutions, it would be much more desirable to have bench-stable coupling reagents on hand that are more convenient to handle and weigh.

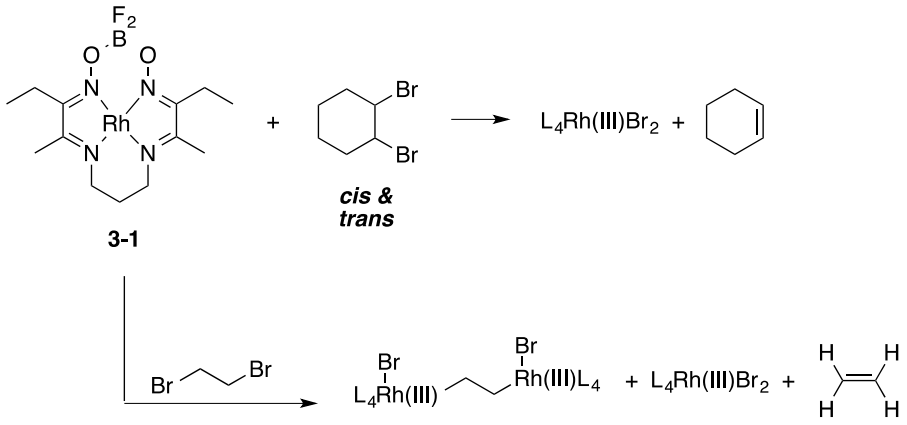
Practicality as a focal point became more pronounced as the project developed, and the need for a greater range of model compounds increased. With this increase in demand for material, we favoured approaches that could easily be reproduced by less-experienced synthetic chemists, including undergraduate researchers. This would allow graduate students working on the project more time to optimize new methodologies directed toward novel model compounds perform aggregation experiments, and interpret data.

Also, a quick analysis of our approach towards the G2 class reveals a prohibitive pitfall in the scope of further applications (Scheme 3-1). The first step in the synthesis of a two-carbon tether is the coupling of an α-halo-β-chloro alkane with an aromatic Grignard reagent. The mechanism of such a reaction (here using Pd as the catalyst) reveals an intermediate wherein a transition metal is bonded to a β-haloalkane fragment. Such an intermediate is highly prone to β-halide elimination,[143] which competes with transmetallation.



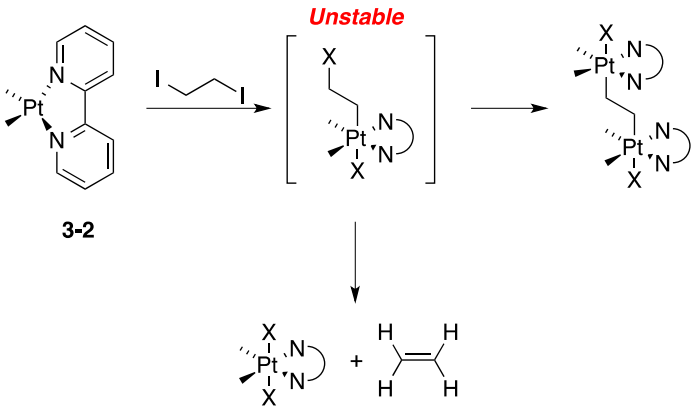
Scheme 3-1. Retrosynthetic analysis of adapting the G2 approach to G1 synthetic compounds

Illustrating this issue, Collman *et al.* reported on the reactivity of vicinal dibromoalkanes with a "superbase" Rh(I) macrocycle complex, **3-1** (Scheme 3-2).[144] Both *cis*- and *trans*-1,2-dibromocyclohexane reacted with **3-1** to form the corresponding Rh(III) dibromide and cyclohexene (albeit at strikingly different rates). Surprisingly, however, when 1,2-dibromoethane was treated with the same complex, a 1 : 1 : 1 mixture of the double oxidative addition product ethylene, and the Rh(III) dibromide was isolated. In this case, β-halo elimination and oxidative addition proceed competitively.



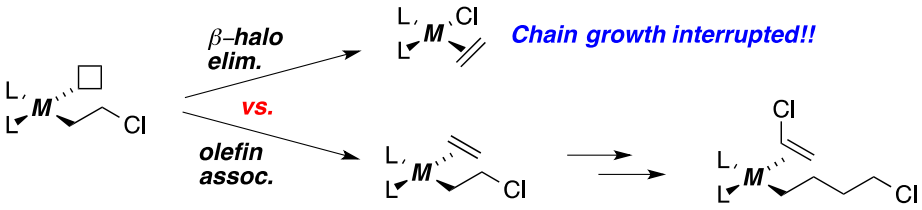
Scheme 3-2. Competitive degradation pathways of a β-halo Rh(III) intermediate

Comparable results were observed by the Puddephatt group when Pt(II) complex **3-2** was treated with 1,2-diiodoethane (Scheme 3-3).[145] Again, no β-haloethyl metal complex was detected or isolated, though it is presumably an intermediate. In both cases, the first metal to add oxidatively into the C–X bond apparently "activates" the neighboring C–X bond towards a second oxidative addition. The bimetallic complex was isolated in a 1 : 2 ratio with the Pt(IV) diiodide complex resulting from β-halo elimination.[146] While analogous experiments with longer chain α,ω-diiodoalkanes provided kinetic analysis consistent with an ionic mechanism, vicinal dihalides revealed free-radical character, slowing down either in the presence of a radical scavenger or when conducted in the dark.



Scheme 3-3. Analogous behavior of a proposed β-iodo-Pt(II) intermediate

β-Chloro elimination is important among organometallic chemists as it relates to the catalytic production of PVC and copolymers bearing polar functionalities.[147] Traditionally, PVC is made via radical-initiated addition-polymerization of vinyl chloride.[148] However, incorporation of vinyl chloride (and other polar monomers) into copolymers via transition metal-catalyzed Ziegler-Natta polymerization is desirable as a means to improve the materials properties of less-functionalized plastics. Unfortunately, this process is inhibited by β-chloro elimination, which is competitive with the chain growth via olefin insertion (Scheme 3-4).[149]



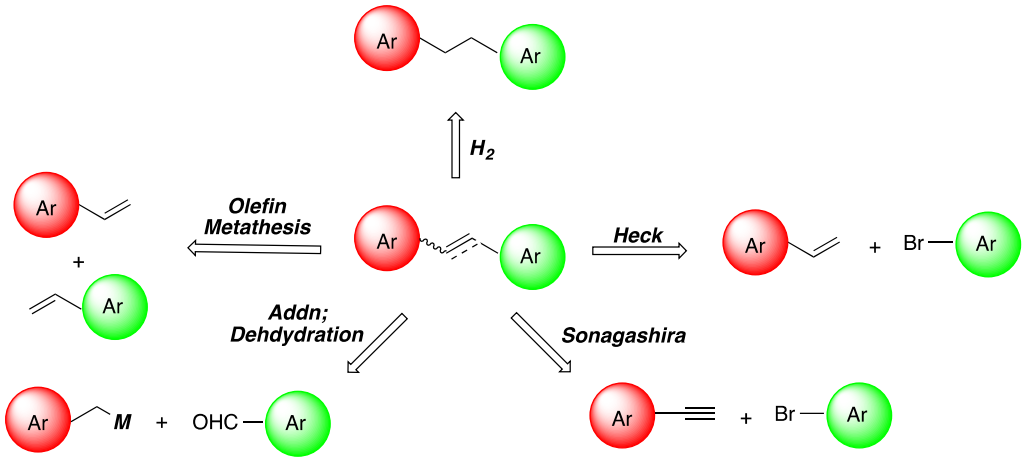
Scheme 3-4. Competitive β-chloro elimination in the copolymerization of ethylene and vinyl chloride

Although isolated examples of β-chloroalkyl ligands bonded to Group 10 metal complexes have been observed,[149-151] the chemistry of such complexes is not yet

robust enough to implement in cross-coupling technology. Thus, we required a different approach to the desired ethano linkages between polycyclic aromatic moieties.

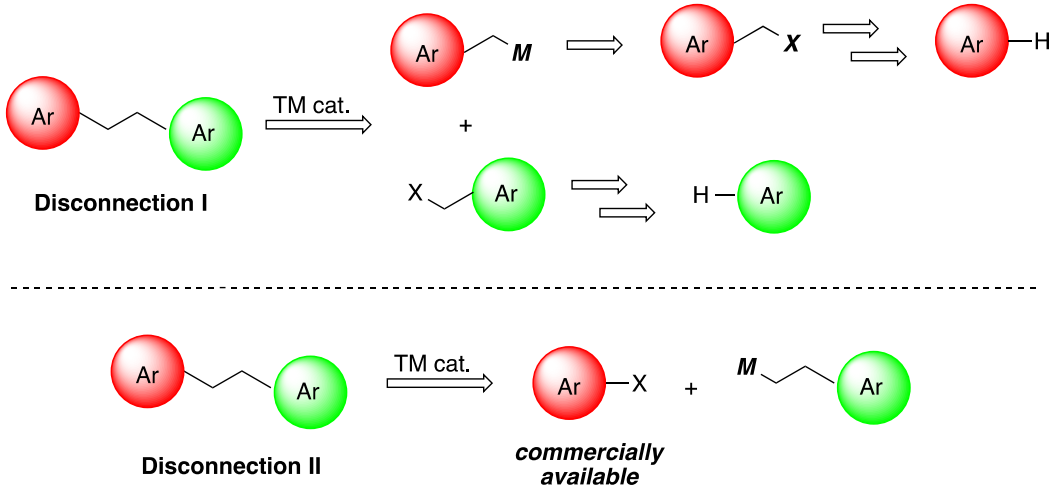
3.1.1 Retrosynthetic analysis. Viable routes to the synthesis of ethano-bridged archipelago compounds

Options for linking two aromatic groups efficiently with an unfunctionalized ethano bridge are dominated by methods proceeding through an unsaturated linkage in the penultimate intermediate (Scheme 3-5). Such methods include the Sonagashira alkynylation reaction, the Heck olefination reaction, various addition/dehydration sequences, and catalytic olefin methathesis. Generally, in small molecule synthesis, these are reliable reactions with extensively demonstrated utility.[152] Subsequent hydrogenation of both alkynes and alkenes is generally routine, using standard heterogeneous or homogeneous catalytic hydrogenation.[153] For our targets, however, catalytic and stoichiometric hydrogenations[56,80] were problematic, and our attention returned to direct methodology for efficient installation of alkano bridges.



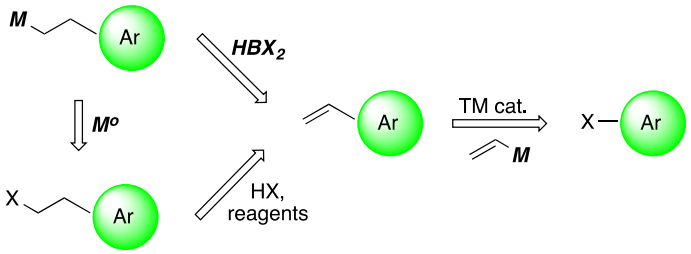
Scheme 3-5. Traditional routes towards ethano-bridged moieties in small molecules

To avoid any approach requiring hydrogenation as the last step, at least one C(sp^3) cross-coupling reaction must be used instead. Coupled with the issue of β-halide elimination in the G2 approach to these compounds, this left us with few options from the existing literature. The potential routes can be separated into two categories based on the position of the final C–C bond formation: (1) between the two benzylic carbons or (2) between the *ipso*-aromatic carbon and the "homobenzylic carbon" of the ethano- fragment (Scheme 3-6). In the former, an sp^3-sp^3 cross-coupling between a benzylic nucleophile and a benzylic electrophile is required. While this is certainly feasible – neither component has potentially problematic β-hydrogens – the scope is limited by its lack of precedence. While there are certainly examples for the cross-coupling of benzyl halides[154,155] with various nucleophilic partners, and benzyl nucleophiles with various electrophilic partners,[156,157] there are very few (if any) examples of the cross-coupling between two primary-benzyl centers for the purpose of installing an ethano-bridge between aryl residues.



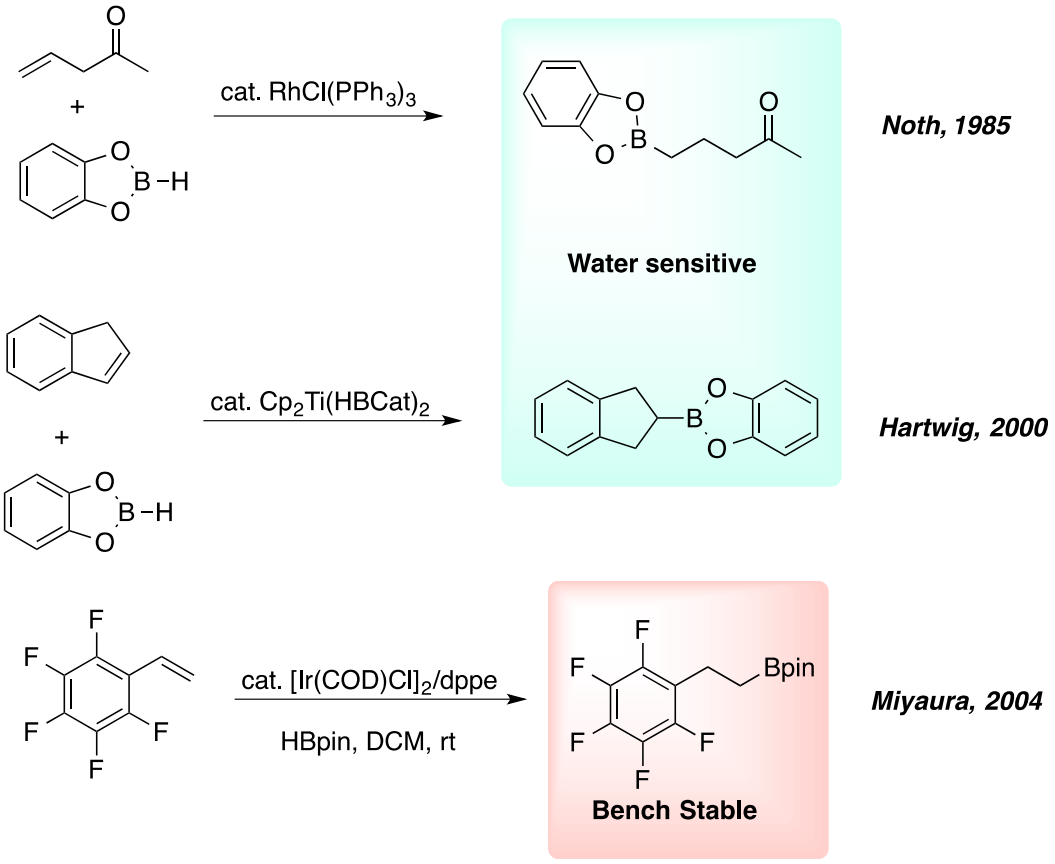
Scheme 3-6. Comparison of potential bond disconnections for the synthesis of ethano-bridged arenes

Thus, key to a new G1 strategy is the preparation of 1-aryl-2-metalloethanes, as shown in disconnection II (Scheme 3-6). In this case, the metal (M) can be a main group metal or metalloid, or, transiently, a transition metal (e.g., Pd). These compounds would most prudently be made from the corresponding styrene derivative via a net anti-Markovnikov hydrometallation (Scheme 3-7). We envisioned the stoichiometric option as more robust, using either a hydroboration or a riskier anti-Markovnikov hydrohalogenation/metallation sequence. The required styrenes would be easily accessible via a standard catalytic vinylation of commercial and synthetic polycyclic aromatic halides.



Scheme 3-7. Potential routes towards the required 1-metallo-2-arylethanes

The hydroboration approach was more attractive for many reasons. For one, the hydrohalogenation/metallation sequence is longer and not as "bench-friendly," as it generally involves the synthesis of sensitive alkyl-metal reagents and intermediates. Also, transition metal-catalyzed hydroboration procedures that have been developed over the past few decades have become increasingly reliable and proceed with high chemo- and regioselectivity. Depending on the boronate, the intermediate can be prepared under mild conditions in bench-stable form (Scheme 3-8).[158-161]



Scheme 3-8. Selected examples of transition metal-catalyzed hydroboration of olefins to form alkylboronates

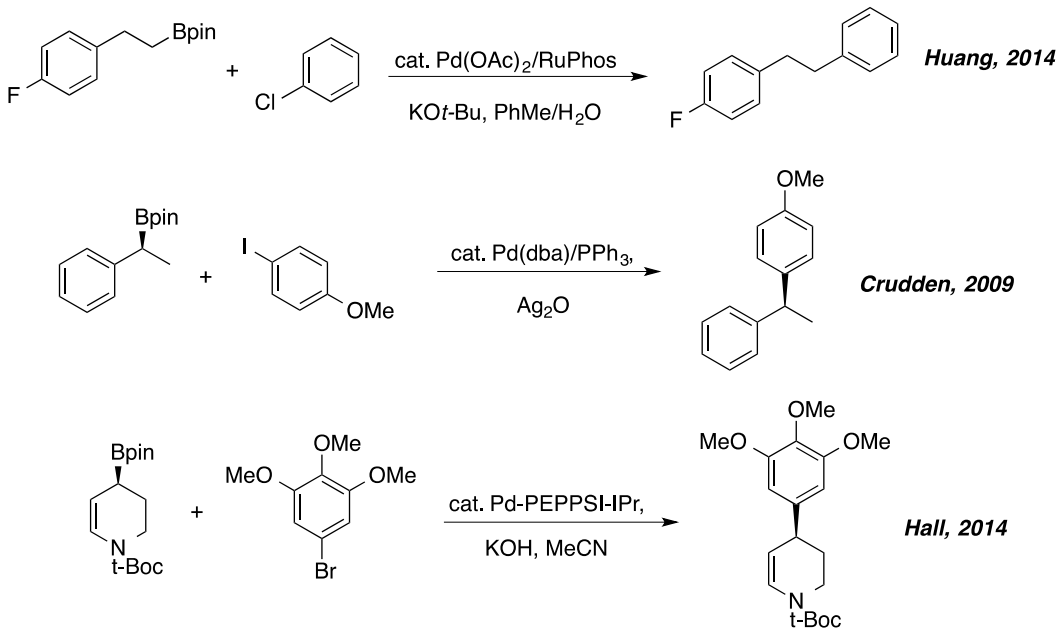
Alkylboronates in synthetic chemistry – preparation and cross-coupling reactivity

With a general idea of how we envisioned making these G1 compounds – vinylation/hydroboration/***B***–alkyl Suzuki cross-coupling – a brief background discussion on the synthesis and cross-coupling of organoboronates seems prudent.

3.1.2 Cross-coupling of sp^3 hybridized organoboronates

The Bpin (pin = 1,1,2,2-tetramethylpinacolato) group in particular enjoys a privileged status among boryl functional groups in organic synthesis. This is due

to an increase in stability toward hydrolysis relative to other boronate esters, including catecholate or neopentanolate relatives.[162] Also, reliable procedures have been developed for the Suzuki-type cross-coupling of these reagents with aryl halides,[163] especially as highly evolved and now commercially-available ligand systems like the Buchwald ligands[164] and Organ's PEPPSI pre-catalysts[165] have become increasingly available, if not reasonably priced (Scheme 3-9).

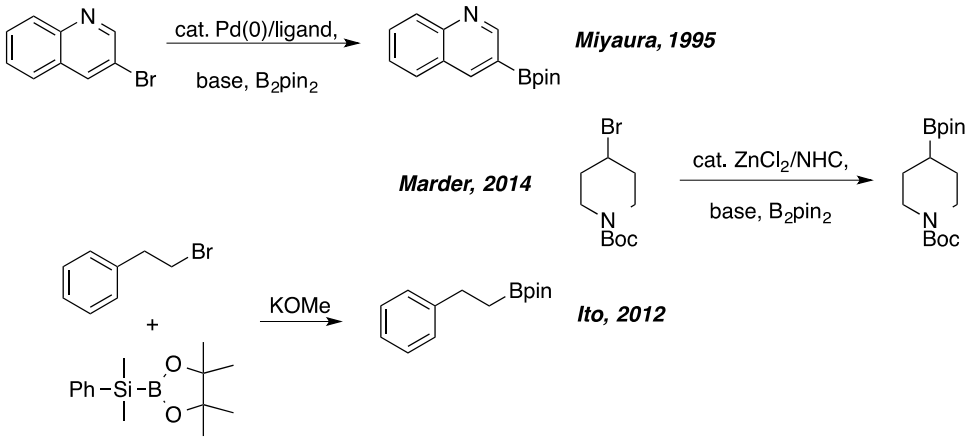


Scheme 3-9. Selected examples of the cross-coupling of alkylboronic acid pinacol esters with aryl halides

3.1.3 Other approaches to the preparation of organoboronate derivatives

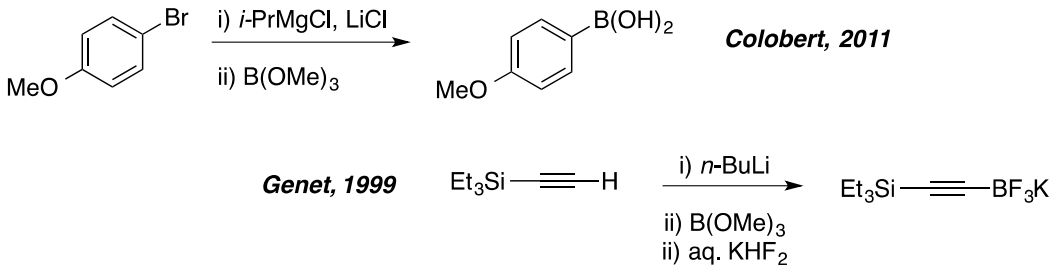
While catalytic hydroboration is a convenient method for the preparation of alkyl boronates from olefins (as well as for making alkenyl boronates from alkynes),[166] many other approaches have been reported, utilizing vastly different boron reagents. Some of the more commonly applied approaches include:

- Miyaura-type borylation (Scheme 3-10). Generally, this is a palladium catalyzed process and is used for the conversion of aryl or alkenyl halides into their corresponding boronic esters.[167] This approach has the advantage of being relatively functional-group-tolerant, but requires access to vinylic halides. In recent years, this approach has been extended to the coupling of alkyl halides via catalysts comprised of base metals, including copper[168] and zinc,[169] as well as by "transition-metal-free" cross-coupling utilizing silylboranes.[170]



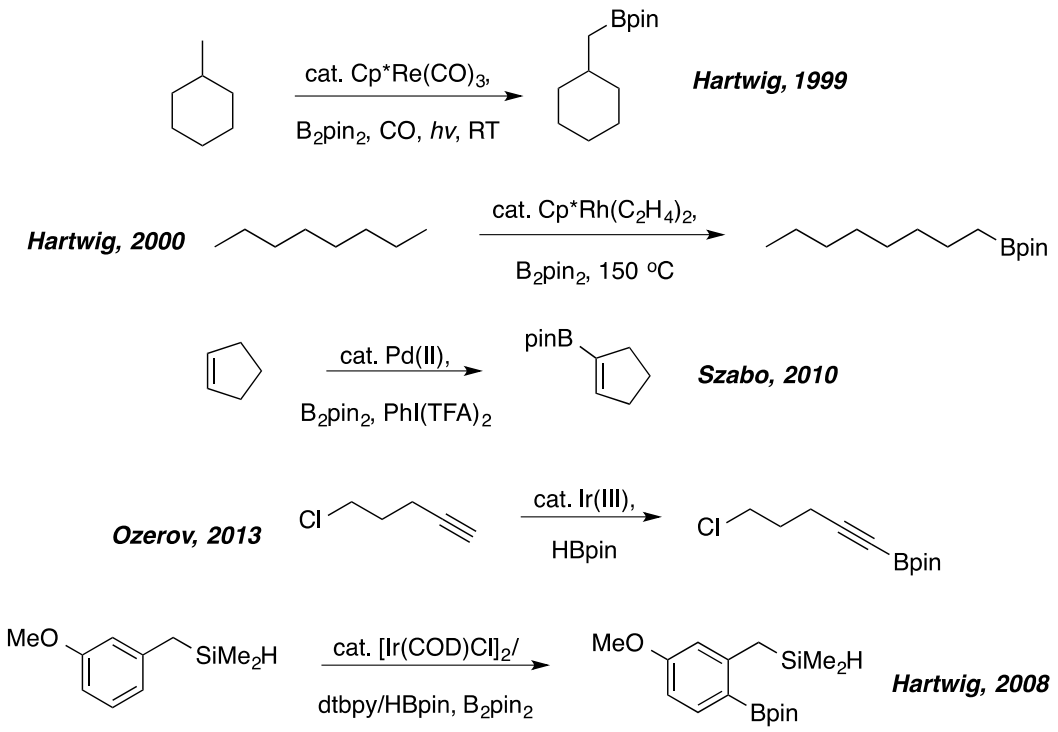
Scheme 3-10. Selected examples of "Miyaura-type" borylations of organohalides

- Borylation via organometallic compounds (Scheme 3-11). Carbon atoms of all hybridizations can form covalent bonds with boron via this approach. Organolithium[171] and Grignard reagents[172] can be quenched with trialkylborates at cryogenic temperatures and variously worked up to make acyclic or cyclic boronates or boronic acids. Although the technique is not functional-group-tolerant, it provides a convenient method for preparing potassium trifluoroborate salts directly from an organometallic precursor in one pot.



Scheme 3-11. Selected examples of organoboronate synthesis via transmetallation

- C-H activation via precious metal catalysis (Scheme 3-12).[173] This approach allows for the borylation of otherwise unreactive C-H bonds, directed either by steric bias or activating (coordinating) functional groups. The technology was originally developed for the regioselective borylation of methyl groups through rhenium catalysis under photolytic conditions[174] and, soon after, under thermal conditions via homogeneous iridium or rhodium catalysis.[175] The field has rapidly matured over the past 15 years and includes high-yielding methods for selective C-H borylations of alkenes,[176] alkynes,[177] and (hetero)arenes[178] with generally low catalyst loadings.



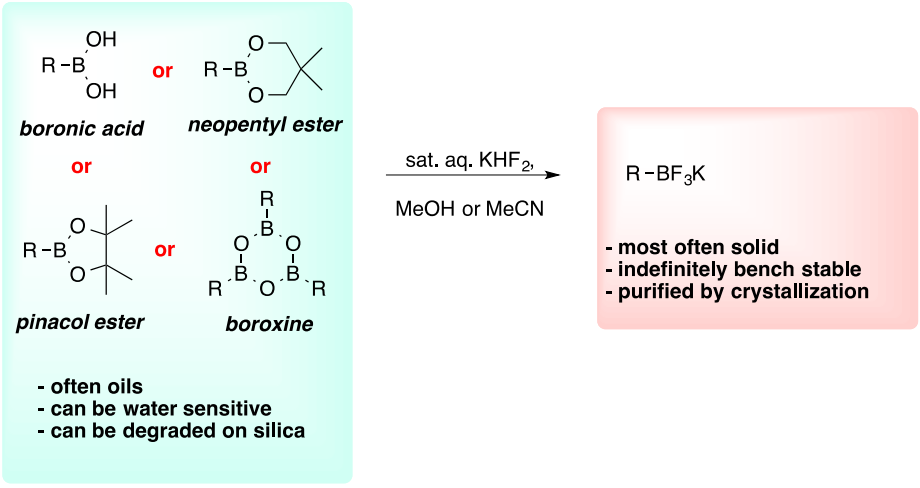
Scheme 3-12. Selected examples of transition-metal catalyzed C-H borylation

3.1.4 Potassium organotrifluoroborates – synthesis and cross-coupling

In 2000, the Molander group reported the first cross-coupling reactions of potassium alkyltrifluoroborates with aryl halides and (pseudo)halides.[179] At the time of publication, this paper was a small triumph within the cross-coupling community. Preceding this contribution, Suzuki and Stille reactions were widely used and appreciated as the "go-to" methodology for functional group tolerant cross-coupling reactions for the construction of sp^2-sp^2 C–C linkages. The Suzuki reaction was also attractive for its environmentally benign nature, especially in comparison with the toxic tin reagents utilized in Stille coupling.[180] Unfortunately, at the time, a reliable procedure for the cross-coupling of bench-stable alkylboron compounds with aryl halides did not exist, except for one report by the Miyaura group involving a highly toxic thallium base.[181]

Molander's new methodology was important for a number of reasons (Scheme 3-13):

- Accessibility. The potassium alkyltrifluoroborates are easily synthesized from the corresponding alkyl boronic acids/esters via treatment with KHF_2[182]; in fact, this process also serves as a convenient purification step for these nucleophiles.
- Stability. The potassium triflouroborate salts are even more stable than their alkylboronate counterparts and are indefinitely stable on the bench. Also, these salts are most often obtained as free-flowing solids imparting not only air and water stability, but also ease of handling relative to the often oily boronate precursors.[183]
- Controlled reactivity. The cross-coupling reaction conditions are often biphasic, requiring water to hydrolyze the borate and release the reactive boronic acid into solution. This is beneficial as it maintains a lower concentration of boronic acid in solution, inhibiting competitive protodeborylation or oxidative homocoupling.[184] This feature also makes the reaction conditions more tolerant, as the organic solvents used need not be stringently dry.



Scheme 3-13. Ease of synthesis and handling of potassium alkyltrifluoroborates

Over the next decade, the Molander group expanded the scope of these coupling reactions to highly functionalized, bench-stable potassium alkyltrifluoroborates,[185-187] as well as adopting Buchwald ligands for the more difficult coupling of the less reactive aryl chlorides.[94]

It is notable that these reactions have drawback as well. Importantly, special reaction apparatii must be used for reactions of trifluoroborates due to the ability of fluoride to etch glass. Also, these reactions are often biphasic or heterogenous, limiting their scalability. Lastly, precautions should always be taken when using fluoride in case the reaction becomes acidic enough to form dangerous HF in situ.

Results and discussion. development of a new G1 approach

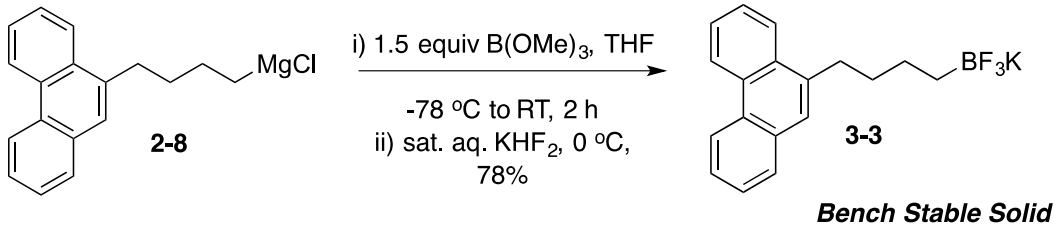
Given the general retrosynthesis proposed for G1 model compounds, the synthesis itself was then demonstrated and optimized. Our targets were "sought-after" asphaltene models, in that JPEC experts requested many of them, making the goal of this work the development of a general approach of broad scope that can be conveniently used as a basis for the synthesis of ethano-bridged model asphaltene compounds with other architectures.[§]

3.1.5 Potassium (4-(phenanthren-9-yl)butyl)trifluoroborate. A proving ground

To test the efficacy of assembling G1 archipelago model compounds via the "***B***-alkyl Suzuki coupling", the reaction was first demonstrated using an easily accessible "island-tethered" primary alkylboronate derivative. The primary alkyl Grignard reagent **2-8** (Equation 3-1), conveniently stored in a drybox, was used

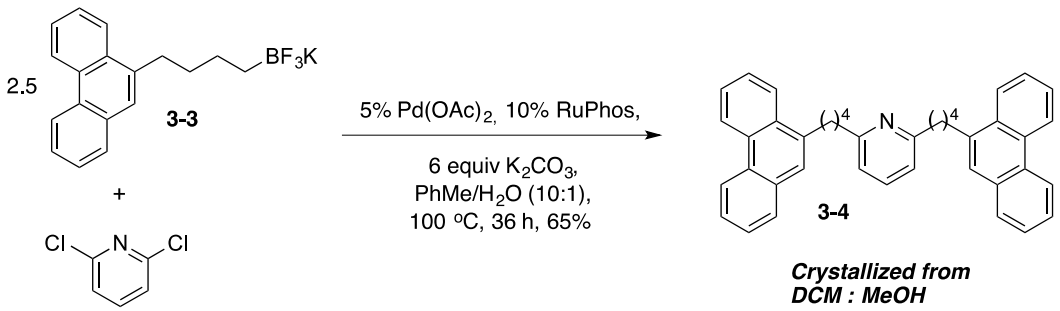
[§]The work described in the remainder of this chapter, excluding the synthesis and discussion of bromopyrene will be submitted for publication shortly.

for this purpose. “Trapping” the Grignard reagent with trimethyl borate at cryogenic temperatures, followed by a saturated potassium bifluoride workup provided trifluoroborate salt **3-3** in good yield and high purity after recrystallization from acetone/ether. This specific procedure was developed by Genet for the synthesis of potassium vinyltrifluoroborate from vinylmagnesium chloride.[171]



Equation 3-1. Conversion of **2-8** to the corresponding potassium alkyltrifluoroborate salt (**3-3**)

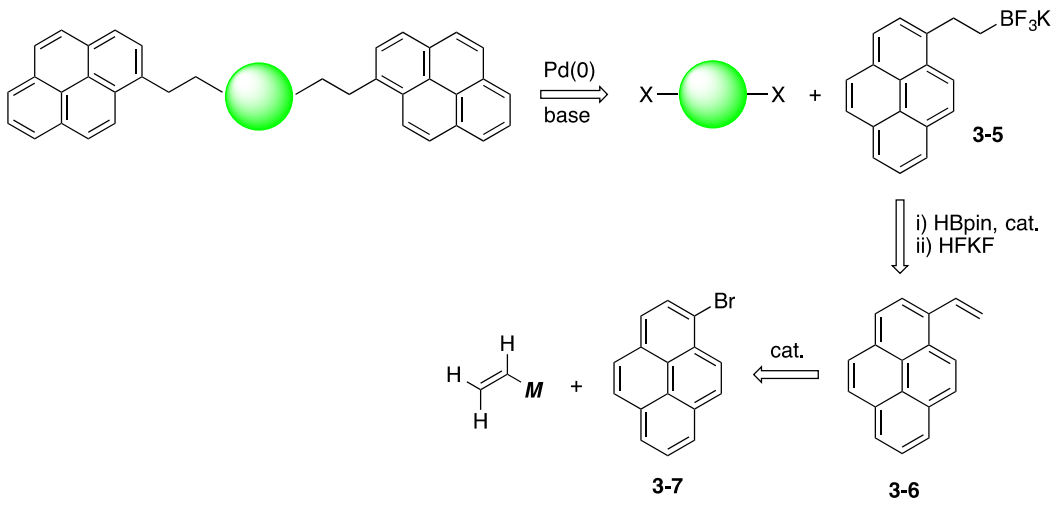
Trifluoroborate salt **3-3** was subjected to the conditions developed by the Molander group for the cross-coupling of primary alkyltrifluoroborate salts with aryl chlorides[94] using 2,6-dichloropyridine as the electrophile and the Buchwald ligand RuPhos (Equation 3-2). The reaction provided the coupled three-island archipelago **3-4** in good yield on the first attempt. Additionally, this compound proved easily purified by crystallization of the crude product mixture from DCM/methanol. Thus, this reaction resolved the question of whether to commit to this strategy for the synthesis of other G1 compounds at scale. At the same time, this demonstration produced a heavier, more flexible four-carbon tethered congener to the targeted “ethano-bridged” analogs.



Equation 3-2. Testing ***B***-alkyl Suzuki coupling for the assembly of G1 compounds

3.1.6 Retrosynthetic considerations for ethano-bridged G1 compounds of pyrene

We initially targeted symmetric G1 model compounds incorporating pyrene moieties as the flanking islands (Scheme 3-14). These compounds were envisioned to arise from the cross-coupling of a dihalogenated arene and potassium (2-(pyren-1-yl)ethyl)trifluoroborate (**3-5**), which in turn would be made via the hydroboration of 1-vinylpyrene (**3-6**), followed by conversion to the corresponding potassium trifluoroborate salt.



Scheme 3-14. Retrosynthesis of pyrenylethyl-tethered G1 compounds

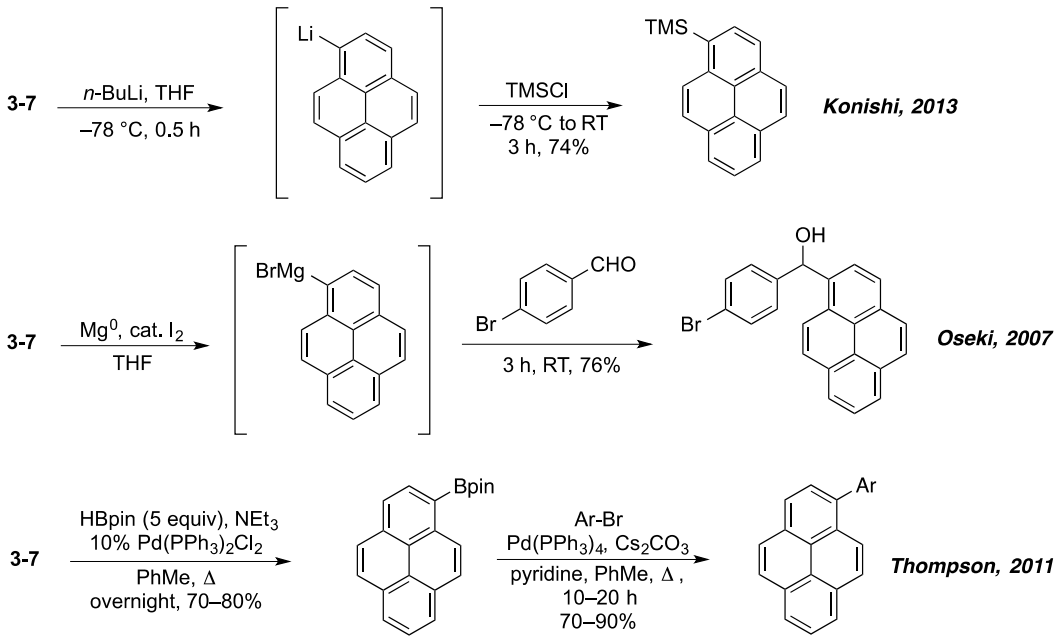
Vinylpyrene is (sometimes) commercially available, but prohibitively expensive because the compound is very sensitive to polymerization. In fact, vinylpyrene can be polymerized under Ziegler-Natta,[188] anionic,[189] cationic,[190] and free radical conditions.[191] The most cited synthesis of vinylpyrene uses a Wittig reaction of methylenetriphenylphosphorane with the corresponding 1-pyrenylaldehyde.[191] However, reproducing the procedure is problematic, giving inconsistent yields. Moreover, chromatography is required for purification, which we need to avoid for early stage intermediates prepared on large scale. We envisioned instead the synthesis starting from bromopyrene (**3-7**) and proceeding via cross-coupling with some vinyl-metal reagent (Scheme 3-14, bottom).

3.1.7 1-Bromopyrene**

Due to the characteristic photophysical attributes of pyrene,[192] it is a desirable component of many functional materials.[133] Thus, 1-bromopyrene (**3-7**) is a key building block for a large subset of the chemical materials community.[193] The first synthesis of bromopyrene was described in 1937 by Lock, via the bromination of pyrene using bromine itself.[194] Similar approaches have since been described using other reagents, including NBS,[195] $CuBr_2$,[196] and HBr/H_2O_2.[197] The necessity of column chromatography in these protocols, however, generally limits the reaction scale. A simple and chromatography-free procedure was reported in 1968 by Gumprecht, fulfilling the demand for 1-bromopyrene in larger quantities.[198] Unfortunately, this procedure (and many others) specify the use of CCl_4 as solvent,[194-196,198] which has more recently been prohibited in many countries[137] due to toxicological[199] and environmental concerns.[200] There is thus considerable demand for a procedure with similar synthetic utility that does not require CCl_4 or column chromatography. The Tykwinski group recently provided such a protocol**,** which has been reliably reproduced on 10–20 g scale by undergraduate chemistry students. Importantly, the procedure tolerates the use of inexpensive, technical grade commercial pyrene as precursor material.

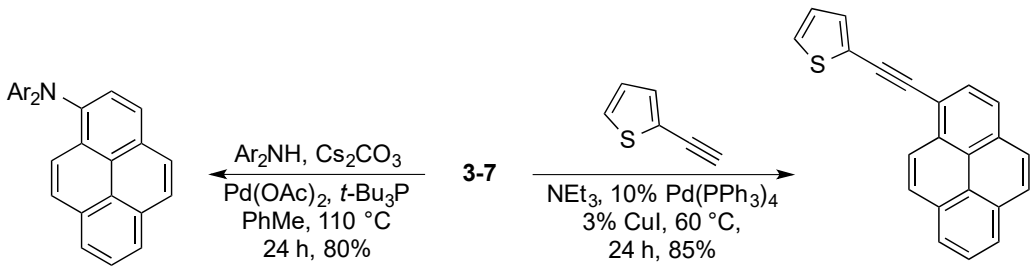
For the preparation of functional materials, 1-bromopyrene is an ordinary haloarene and can be easily transformed into reactive nucleophilic species, for example by lithiation,[138] magnesiation,[201] or borylation.[202] Consequently, 1-bromopyrene has been used for a wide variety of reactions (Scheme 3-15).[138,201,202]

** The information in this chapter regarding bromopyrene and our synthesis of the compound was recently submitted to Org. Syn. as “Improved Synthesis of 1-Bromopyrene and Conversion to 1-Pyrenecarbaldehyde” by Matthias Schulze, Alexander Scherer, Colin Diner, Rik R. Tykwinski



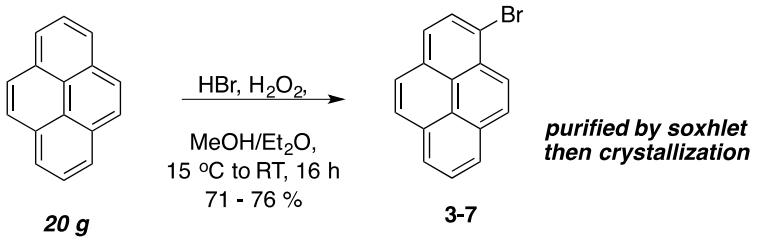
Scheme 3-15. Selected metallations and functionalizations of 1-bromopyrene

Bromopyrene can also be used directly in many transition metal-catalyzed cross-coupling reactions. For example, heteroatomic or organic nucleophiles can be directly linked to pyrene via Buchwald–Hartwig amination[203] or Sonogashira cross-coupling[204] of **3-7** (Scheme 3-16).



Scheme 3-16. Selected examples of utilizing 1-bromopyrene as an electrophile in cross-coupling reactions

The Tykwinski group's preparation of 1-bromopyrene is analogous to that of the Matsumoto group,[197] who reported the reaction on a 2 g scale and purified the crude material via silica gel chromatography. The difference between the two was that the Tykwinski group's procedure was scaled to decagrams and the workup was made more economical by purifying the crude mixture via soxhlet extraction followed by crystallization (Equation 3-3).

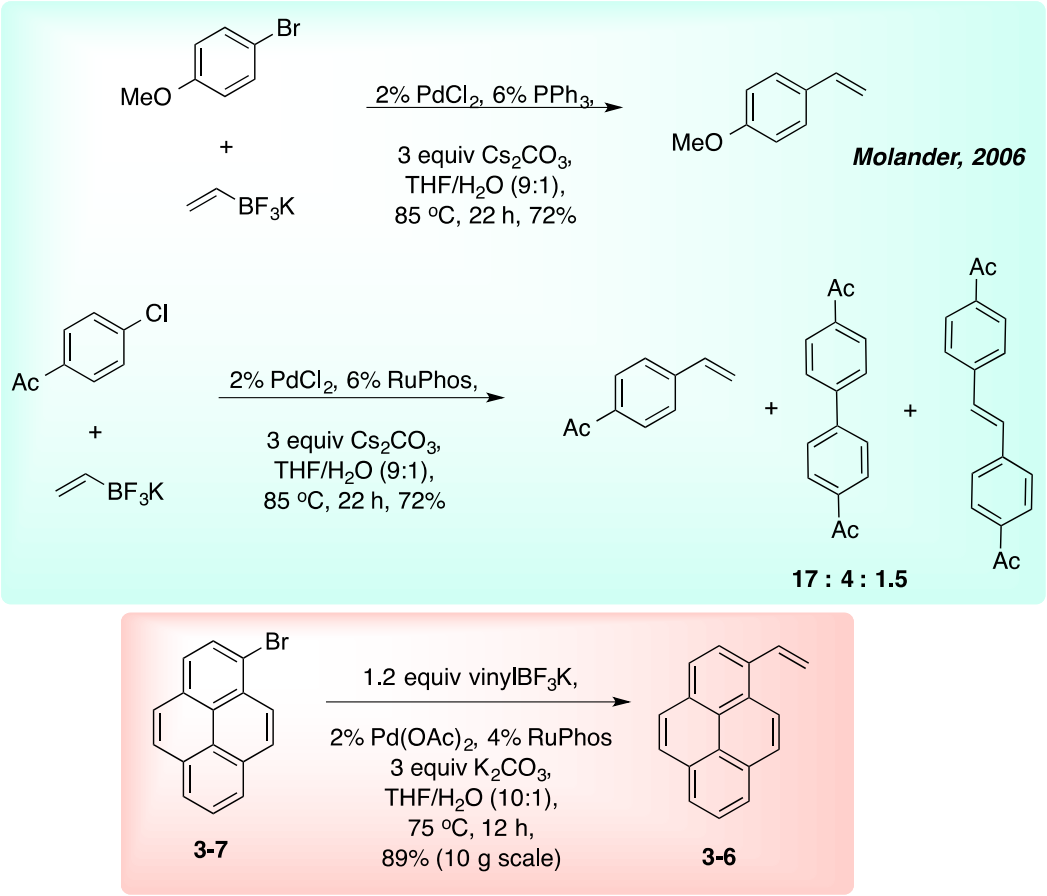


Equation 3-3. Tykwinski group's scalable, chromatography-free preparation of 1-bromopyrene

3.1.8 1-Vinylpyrene

Due to the appealing attributes of potassium organotrifluoroborates (bench stability, free flowing solids) and the fact that potassium vinyltrifluoroborate can be synthesized at large scale in high yield and purity from inexpensive commercial starting materials (vinylmagnesium chloride, trimethyl borate, potassium hydrogen difluoride),[171] we prepared vinylpyrene (**3-6**) via Molander's Suzuki coupling of potassium vinyltrifluoroborate with 1-bromopyrene.[205,206]
Unfortunately, adapting Molander's general optimized conditions for the vinylation of haloarenes, which used triphenylphosphine as the ligand of choice, was initially unfruitful and provided little conversion (Scheme 3-17). However, the reaction was brought to completion by changing the ligand to RuPhos,[207] which the Molander group found optimal for the coupling of an electron-deficient aromatic. We detected no homocoupling or stilbene, the major by-products of this

chemistry. Additionally, we found the reaction was unaffected by changing the base from cesium carbonate to the more economical potassium carbonate.

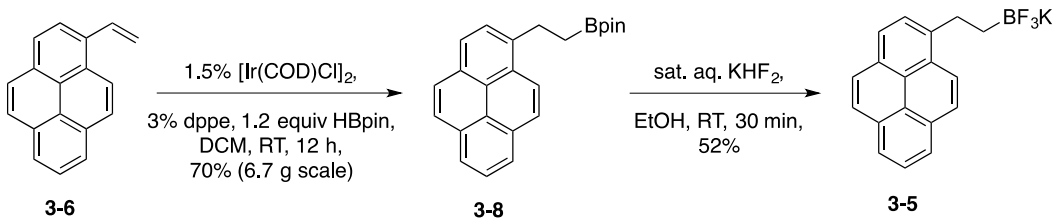


Scheme 3-17. Optimizing the synthesis of **3-6**

When scaling the synthesis to decagram scale, it became increasingly important to inhibit the polymerization of the vinylpyrene. Thus, the reaction was conducted in the presence of trace hydroquinone, a common radical polymerization inhibitor.[208] Also on large scale, the solvent was removed under vacuum at low temperature in the constant presence of hydroquinone.

3.1.9 Hydroboration and archipelago assembly

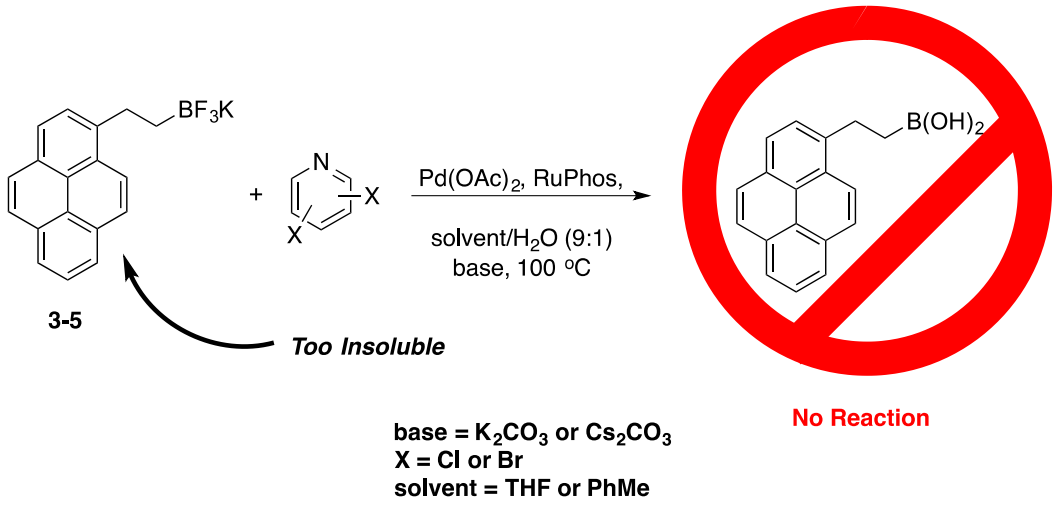
Anti-Markovnikov hydroboration of **3-6** proceeded without issue utilizing Miyaura's procedure (Scheme 3-18), to provide the island tethered primary alkylboronate, **3-8**.[161] The reaction selectivity was high and only the linear product was observed. While the Miyaura group found that dppm was a better ligand for the hydroboration of aryl-alkenes, we found that the less expensive dppe to be sufficient for our purposes. The boronate **3-8** was easily purified via a short silica plug. Flushing with hexanes removed the non-polar byproduct ethylpyrene; subsequent flushing with DCM provided the pure product. Interestingly, the pure compound was obtained as a lime-green oil even after drying under high vacuum overnight, which slowly solidified to a brittle yellow solid over a week's time.



Scheme 3-18. Hydroboration of **3-6** and conversion to the corresponding potassium alkyltrifluoroborate salt **3-5**

The alkylboronate **3-8** was insoluble in methanol but readily soluble in ethanol, which became the preferred solvent for conversion to the potassium alkyltrifluoroborate salt **3-5**.[209] Addition of saturated aqueous KHF_2 into an ethanolic solution of **3-8** at room temperature, open to the air, rapidly precipitated the desired salt. Although the yield was moderate, the reaction was not optimized, deferring this goal until after the pivotal cross-coupling of **3-5** could be demonstrated.

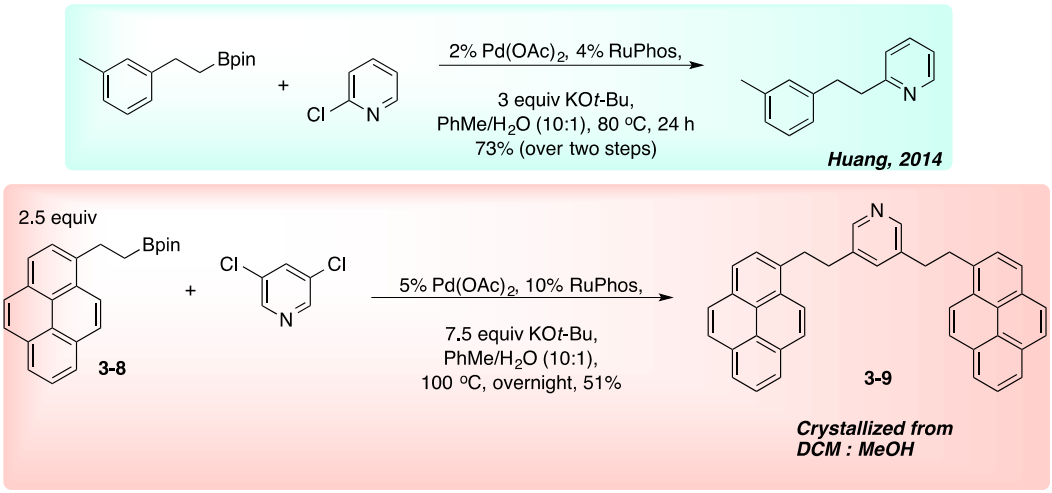
Trifluoroborate **3-5** failed to react with various dihalopyridines[39] under Molander's optimized cross-coupling conditions (Equation 3-4). A range of variables, including solvent (THF, toluene), base (K_2CO_3 and Cs_2CO_3), and heating source (oil bath, microwave reactor), were investigated to no avail. Notably, the reaction always started as a heterogeneous suspension of the unhydrolyzed trifluoroborate **3-5**. This is surprising: even when these reactions fail to provide coupling products, the potassium organotrifluoroborate salt is expected to hydrolyze readily to the more soluble boronic acid under basic, "wet" conditions. We conclude only that the compound is *too insoluble* to undergo in situ hydrolysis, or react under the investigated conditions.



Equation 3-4. Insolubility/reactivity of **3-5** under cross-coupling conditions

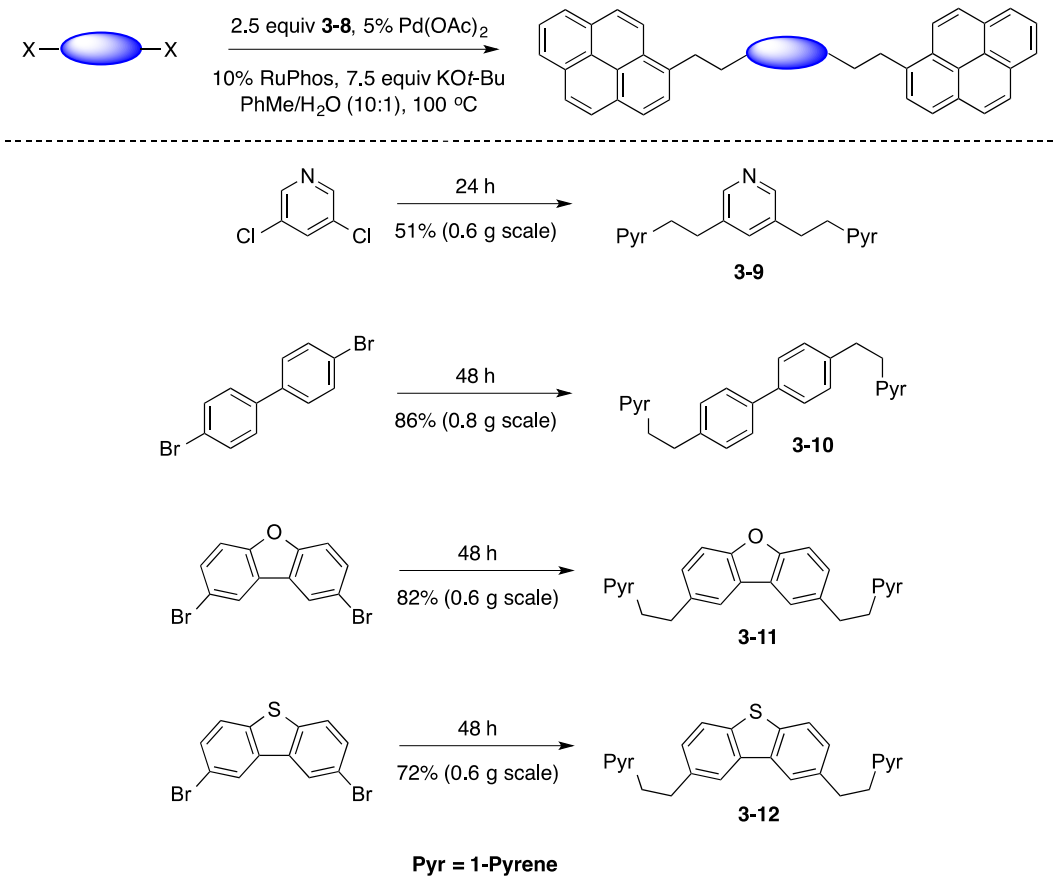
The more soluble pinacol ester **3-8**, however, does react, under Huang's similarly vetted conditons,[164] The reaction of **3-8** with half-stoichiometric amounts of 3,5-dichloropyridine in the presence of a large excess of potassium *tert*-butoxide, and catalytic amounts of $Pd(OAc)_2$ and RuPhos, using a biphasic reaction mixture of toluene and water, provided the G1 model compound **3-9** in moderate yield on a 0.6 g scale (Scheme 3-19). The compound was purified via crystallization of the crude reaction mixture in a similar fashion to that described for archipelago **3-4**.

While we were not sure if the primary alkylboronate, **3-8** would have the same bench stability as **3-5**, boronate **3-8** proved itself bench stable for months when stored in a vial at RT, thus alleviating our concerns.



Scheme 3-19. Adaptation of Huang's cross-coupling conditions to our system

With this success, the reaction was quickly extended to the synthesis of other previously-synthesized-but-never-purified G1 archipelago compounds **3-9**–**3-12** (Scheme 3-20). In these cases, the electrophilic coupling partners were known polycyclic aromatic dibromides, demonstrating a broad scope for the electrophilic coupling partner. In comparison with the relatively soluble pyridyl product, these compounds were completely insoluble, crashing out of the reaction mixture as they formed. The precipitated products were collected by suction filtration directly and washed iteratively with water, ethanol, and hexanes, which removed both inorganic salts and organic by-products, leaving analytically pure powders, in very good yields.

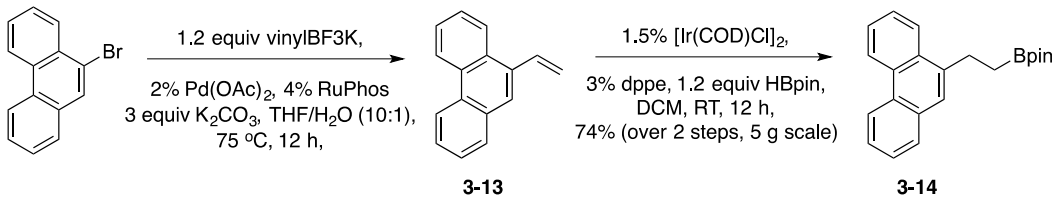


Scheme 3-20. Demonstrating scope and scalability of new approach to the synthesis of G1 archipelago compounds

3.1.10 Phenanthrene-based archipelago compounds

With this novel construction of many pyrene-tethered G1 compounds, extension of this protocol to the corresponding phenanthrene-tethered analogs was soon undertaken. Vinylation of 9-bromophenanthrene proceeded quantitatively to provide 9-vinylphenanthrene **3-13**, a brown oil (Scheme 3-21). This compound was less sensitive than vinylpyrene and did not require any precautions to avoid polymerization. Catalytic hydroboration also proceeds without issue, isolating the product as a colourless oil following flushing through a silica plug, as previously

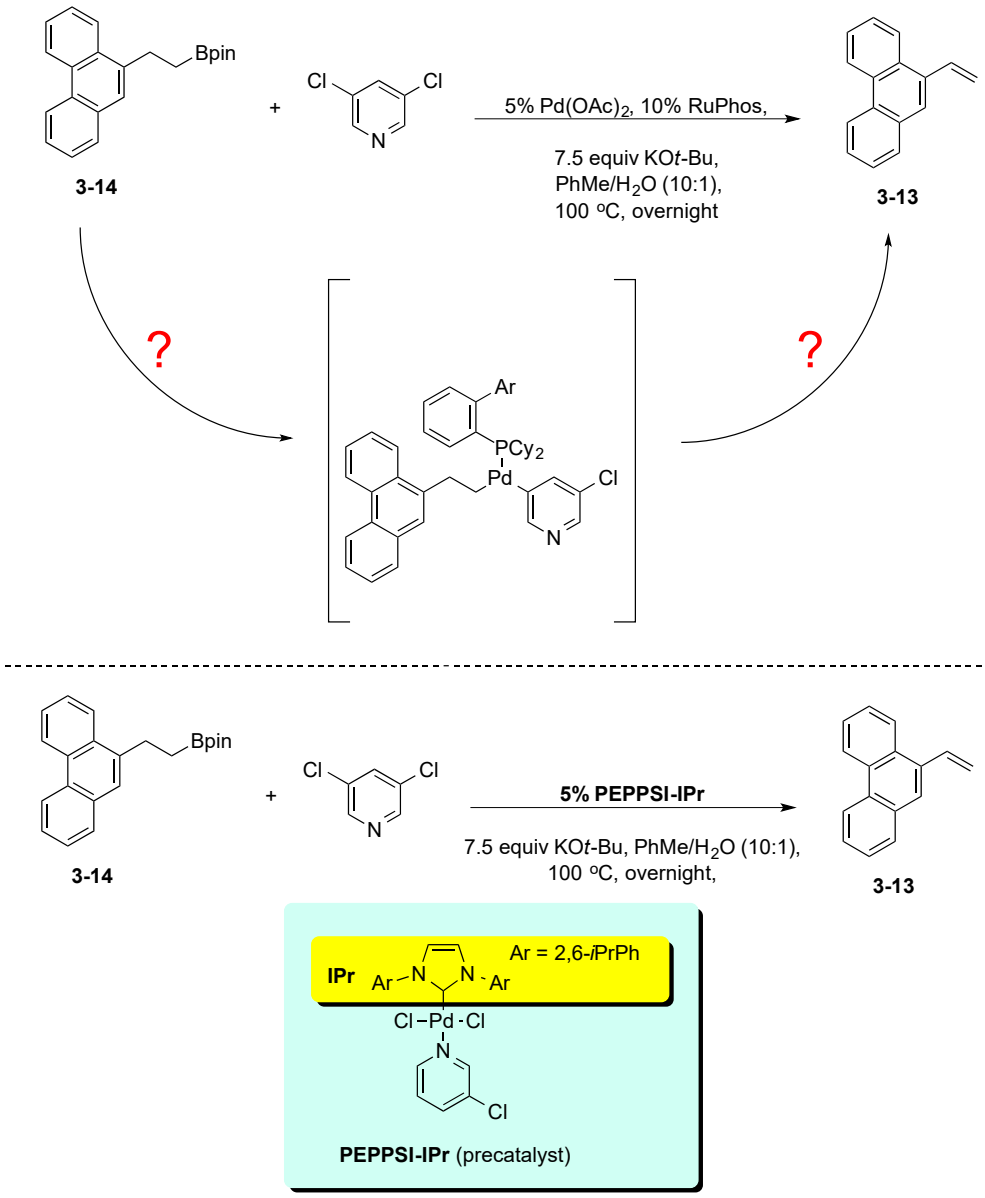
described. In this way, nucleophilic coupling partner **3-14** was isolated in a 74% yield over the two synthetic steps on a five-gram scale.



Scheme 3-21. Analogous synthesis of phenanthrene-tethered nucleophile **3-14**

In contrast to the pyrenyl derivative, the cross-coupling of pinacolatoborate **3-14** with 3,5-dichloropyridine failed completely – only vinylphenanthrene (**3-13**) and starting materials were detected in the crude ^{1}H NMR spectrum (Scheme 3-22). This is presumably the result of an uncontrolled β-hydride elimination from the corresponding phenanthrylethyl Pd(II) intermediate, which does not compete in the pyrenyl series. For this reason, we assumed that both oxidative addition and transmetallation were facile, and concluded that changing the ligand environment might help to favor reductive elimination over β-hydride elimination. Sterically demanding ligands like IPr are generally thought to suppress β-hydride elimination by disfavoring the required geometry (syn coplanar) for such a process to occur. Interestingly, stabilizing agnostic C-H interactions of the methyl groups within the IPr ligand have recently been proposed via computations as the actual source of this tamed reactivity.[113]

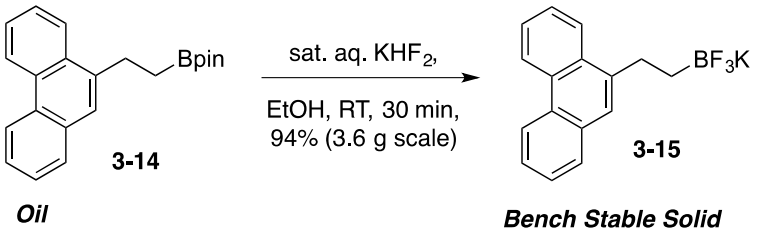
We thus attempted to conduct the same reaction but using Organ's PEPPSI-IPr precatalyst,[210] which has shown broad applicability in cross-coupling reactions of both electrophilic and nucleophilc unactivated primary alkyl partners. Unfortunately, however, this reaction also provided mostly vinylphenanthrene.



Scheme 3-22. Complications in the cross-coupling of **3-14** for archipelago assembly

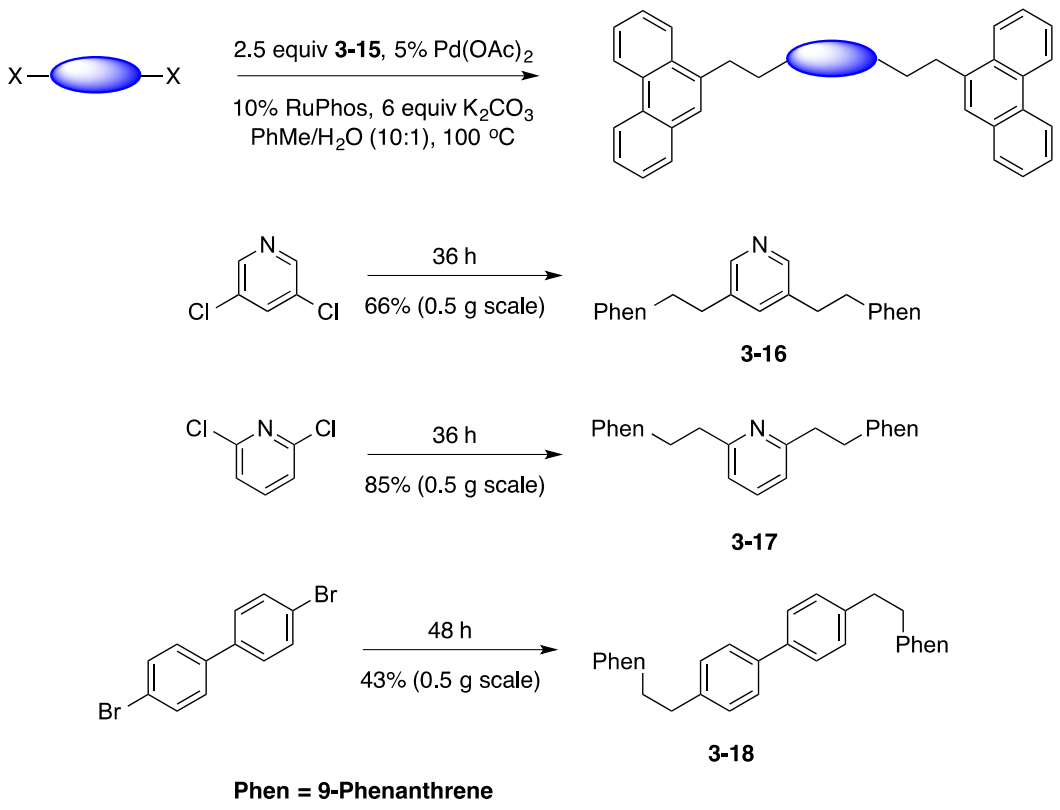
Rather than screening a library of ligands and reaction conditions to overcome this issue, we attempted instead to circumvent the problem via cross-coupling of the corresponding potassium alkyltrifluoroborate (**3-15**), which had not worked in the pyrenyl series. We postulated that cross-coupling would be facilitated if **3-15**

proved to be soluble enough to undergo hydrolysis to the corresponding boronic acid *in situ*. Some researchers have reported the importance of utilizing tetravalent boronate pro-nucleophiles in order to avoid competitive β-hydride elimination.[211] In the event, conversion to the potassium salt under standard conditions proceeded without issue (Equation 3-5).



Equation 3-5. Conversion of **3-14** to its potassium trifluoroborate salt, **3-15**

Cross-coupling of trifluoroborate **3-15** with 3,5-dichloropyridine under Molander's RuPhos conditions was slow but surprisingly successful, providing pyridine-centered archipelago model compound **3-16**. We assume that the less extensive π-system of phenanthrene relative to pyrene reduced intermolecular π-π stacking in the solid state, rendering the phenanthrene derivative sufficiently soluble to promote the reaction. The product could be isolated at scale after a conventional workup and purified by crystallization from DCM/MeOH. The reaction was similary successful using 2,6-dichloropyridine and 4,4'-dibromobiphenyl as reaction electrophiles, providing G1 archipelago targets **3-17** and **3-18** (Scheme 3-23).

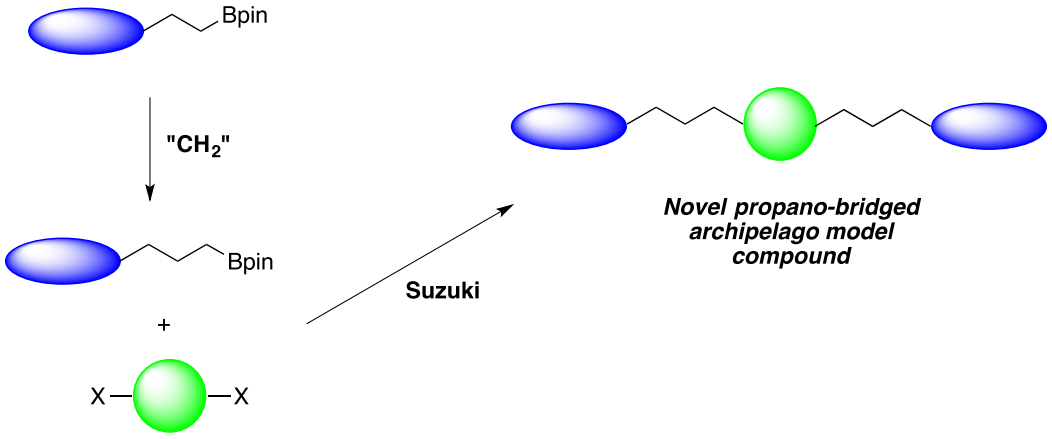


Scheme 3-23. Synthesis of phenanthrene-tethered archipelago compounds **3-16** – **3-18**

At this point, we were satisfied that we had developed a more robust approach to the synthesis and purification of ethano-bridged G1 archipelago model compounds, the primary goal of this synthetic exercise. The compounds are obtained by a concise sequence from inexpensive, commercially available starting materials. Importantly, the pro-nucleophiles used for this archipelago assembly can be bench-stable solids synthesized on a multi-gram scale. Cross-coupling of these privileged precursors with any polyhalogenated aromatic core are expected to provide the corresponding "homoleptic" first-generation dendrimer.

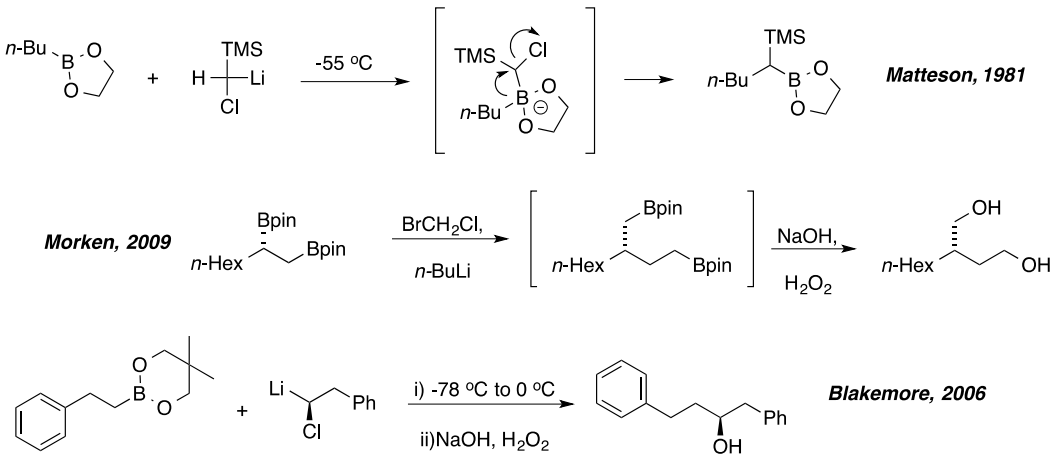
Extension of the B-alkyl Suzuki synthesis. Three-carbon tethered archipelago compounds

Another advantage of this synthetic approach was the potential to extend the tether length between the boron atom and the island by one methylene unit via the Matteson homologation (Scheme 3-24).[212] This reaction would provide propano-bridged archipelago model compounds, "filling out the series" without the need to develop further reactions (e.g., allylation/hydroboration). We would have a unified approach to the synthesis of ethano-, propano-, and via the G2 methodology, butano-bridged archipelago model compounds (Scheme 3-24). This was an intriguing possibility for us as it would then be possible to compare the aggregation properties of otherwise identical model compounds as a function of the tether length between aromatic residues.



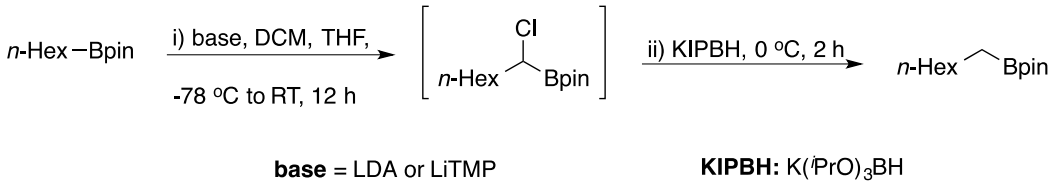
Scheme 3-24. Potential homologation of archipelago precursors for the synthesis of propano-bridged archipelago model compounds

The Matteson homologation has been rigorously developed into a reaction of extensive utility in organic synthesis (Scheme 3-25).[213] Highly stereoselective versions[214] as well as asymmetric variants have been reported.[215] This blossoming technology is currently finding very impressive applications in complex polyketide synthesis,[216] as well as many other synthetic contexts.



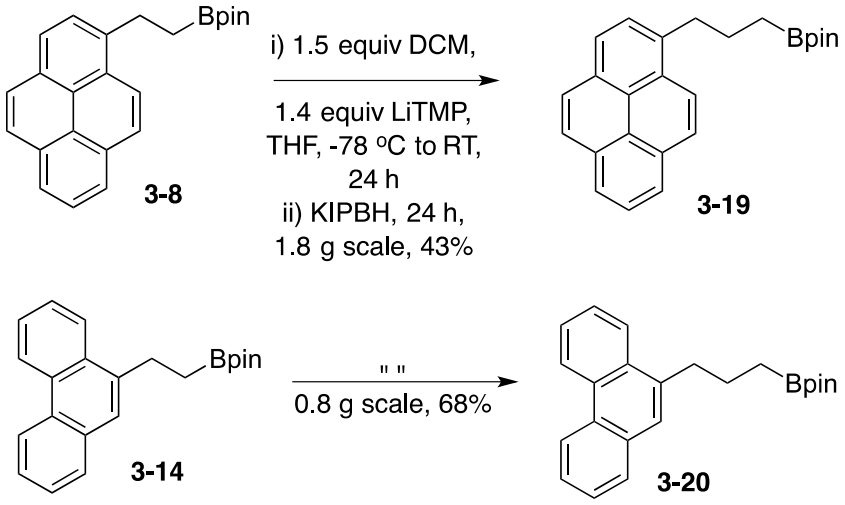
Scheme 3-25. Selected examples of the Matteson homologation in organic synthesis

In recent procedures, the carbenoid reagents used for homologation reactions are generally formed *in situ* from the reaction of a 1,1-dihaloalkane and an alkyl lithium reagent, through either lithium/halogen exchange or deprotonation. We chose to adopt an older but robust procedure developed by Brown, et al., wherein a bulky amide base, typically LDA or LiTMP, is used to deprotonate dichloromethane, which reacts with alkylboronate esters to give the chain-extended α-chloroalkylboronate esters (Equation 3-6).[217] These intermediates are then conveniently reduced *in situ* with potassium tri(isopropoxy)borohydride (KIPBH).[218] Although this reagent is not commercially available, it is readily prepared by the reaction of commercial (^{i}PrO)$_3$B with purified KH.[219] This methodology was preferable for large-scale synthesis, since LiTMP is a free flowing white solid, which is conveniently handled in the glove box.



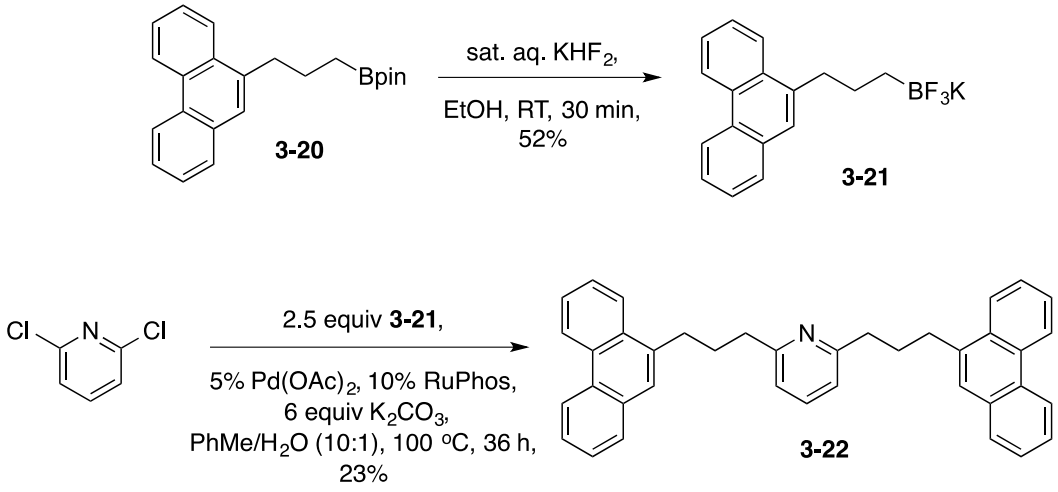
Equation 3-6. Practical Matteson homologation using amide bases

Application of this classic procedure to the homologation of pyrenyl boronate **3-8** proceeded in moderate yield (Scheme 3-26). Longer reaction times were required for both steps of the reaction, a consequence of the poor solubility of our system. Boronate **3-8** is a solid of much higher molecular weight than the substrates reported by Matteson and our reaction did not become homogenous at higher concentration. Purification via a sequential two-solvent plug filtration provided the propano-linked boronate **3-19** in high purity. Gratifyingly, this procedure works similarly to make the phenanthrene-tethered boronate **3-20** as well.



Scheme 3-26. Homologation of archipelago precursors **3-8** and **3-14**

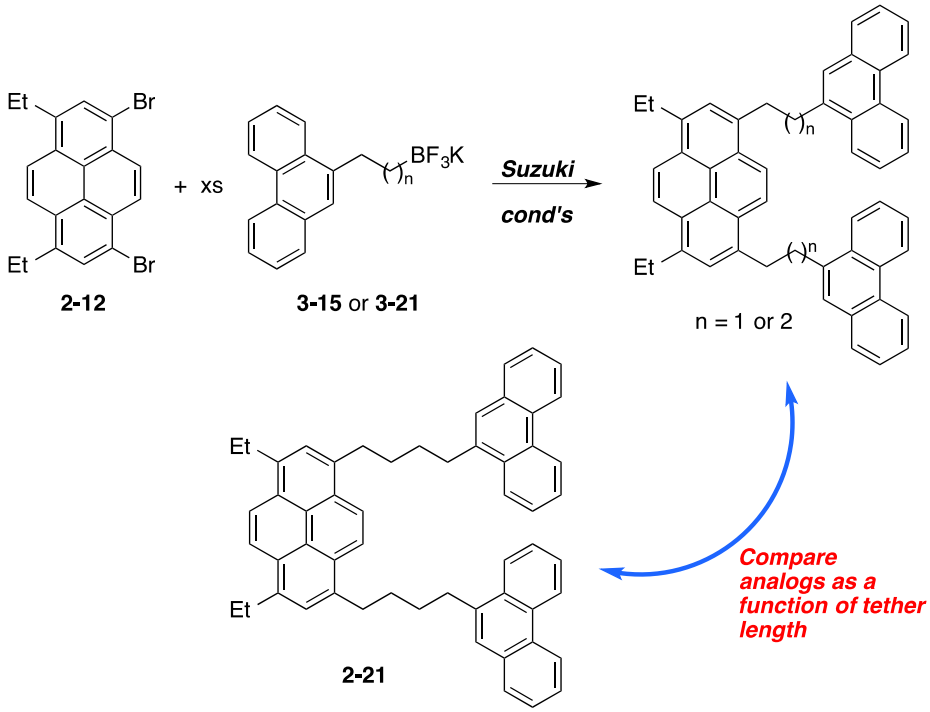
At this point, we had in hand significant amounts of **3-4** and **3-17**, archipelago model compounds differing only by the lengths of the tethers. To complete the homologous series, we targeted the propano-bridged analog, to enable an investigation of aggregation properties of an archipelago compound as a function of "short-alkyl" tether length. Boronate **3-20** was converted to the corresponding potassium trifluoroborate (**3-21**) under standard (unoptimized) conditions and subjected to Suzuki cross-coupling with 2,6-dichloropyridine under vetted conditions (Scheme 3-27), providing a modest yield of the three-carbon tethered analogue **3-22**. While the reaction proceeded with high conversion, as evidenced by the crude ^{1}H NMR spectrum, purification of this homologue was not facile. Crude **3-22** does not crystallize from DCM/methanol or toluene/hexanes, instead "oiling out" at high concentration. Thus, optimization of both reaction conditions and purification protocol is required, possibly involving chromatography.



Scheme 3-27. Synthesis of the first propano-bridged archipelago model asphaltene compound, **3-22**

Future prospects for B-alkyl Suzuki coupling in model asphaltene synthesis

One immediate extension of this approach, would be to use the (poly)brominated pyrenes (**2-10** – **2-13**) as the sub-stoichiometric electrophilic coupling partners in these Suzuki reactions. If successful, we would have access to a whole suite of new hydrocarbon model asphaltene compounds. The phenanthryl analogs of which could be utilized for studying behavior as a function of tether length (Scheme 3-28).



Scheme 3-28 . Potential extension of new G1 approach towards the synthesis of "shorter-chain" G2 analogs

Conclusion

In summary, we have developed an effective alternative approach to the synthesis of two-carbon tethered Generation I model archipelago compounds, which could

not be obtained in pure form from an earlier, alkyne-based synthesis. This catalytic alkylboronate technology allows for archipelago total synthesis on multigram scale, using convenient, bench-stable boronate pro-nucleophiles cross-coupled with dihalogenated polycyclic aromatic ring systems. This chemistry provides general access to symmetrically-substituted "homoleptic" asphaltene model compounds in good yield and, importantly, high purity (Figure 3-1). The synthetic procedures require minimal chromatography; generally, the archipelago products can be purified by crystallization. Extension of the original methodology to propano-bridged compounds has opened up the possibility of comparing analogous systems as a function of tether length.

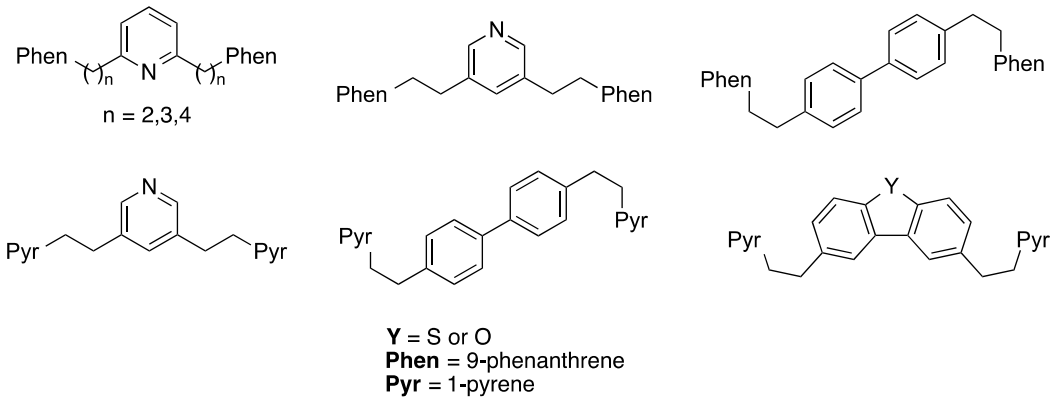


Figure 3-1. Summary of model asphaltene compounds synthesized via new G1 approach

Experimental section

3.1.11 General experimental information

All manipulations of air-sensitive compounds were performed under a nitrogen atmosphere using standard Schlenk techniques or in a well-maintained dry box charged with prepurified nitrogen and maintained at <1 ppm oxygen. THF and dioxane solvents were distilled from sodium/benzophenone ketyl under nitrogen.

Anisole was dried by heating over stirred CaH_2, then distilled and deoxygenated by purging with N_2. All other solvents and reagents were used without further drying or purification (special storage precautions noted). Pinacol borane (stored under nitrogen with a sealed septum in a freezer), Ir(COD)Cl dimer, RuPhos, PEPPSI-IPr, LiTMP (stored in the dry box at RT), and potassium *tert*-butoxide were purchased from Aldrich. Potassium vinyltrifluoroborate was purchased from Oakwood Chemical. Palladium acetate was purchased from Pressure Chemical. Infrared spectra were recorded on a ThermoScientific Nicolet 8700 spectrometer attached to a Nicolet Continuum FTIR microscope. ^{1}H and ^{13}C NMR spectra were recorded on either a Varian Unity-Inova 500 (^{1}H, 500 MHz; ^{13}C, 125 MHz) or a Varian Direct Drive 500 (^{1}H, 500 MHz; ^{13}C, 125 MHz). High-resolution mass spectra (HRMS) were obtained on Agilent Technologies 6220 TOF, Bruker 9.4T Apex-Qe FTICR, or Kratos Analytical MS-50G mass spectrometers operated by professional staff. Elemental analyses (C, H, N) were obtained by the Department of Chemistry Instrumentation Laboratory under the supervision of Mr. Wayne Moffat, using a Thermo Carlo Erba EA1108 or ThermoScientific Flash 2000 analyzer. The X-ray crystal structure determination was performed by Michael J. Ferguson of the University of Alberta Molecular Structure Centre using a Bruker D8/APEX II CCD diffractometer with a Cu K□ (1.54178) micro focus source.

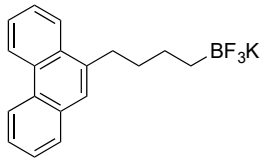
As previously stated, many compounds bearing multiple cumulated quaternary carbon atoms showed low values for carbon by combustion analysis. In some cases, multiple determinations were run to confirm reproducibility. These compounds were pure by ^{1}H and ^{13}C NMR spectroscopy, and were a single component by HRMS.

In the ^{13}C NMR spectra of organoboron compounds, the signals corresponding to the carbon atoms adjacent to boron atoms are not reported due to their broad shape and low visibility (except for compound **3-14**, whose spectrum was

recorded at -60 °C). This phenomena is caused by the quadrupolar relaxation mechanism of the ^{11}B nucleus.[220]

3.1.12 Experimental, spectroscopic, and analytical data for compounds 3-3 – 3-22

Potassium (4-(phenanthren-9-yl)butyl)trifluoroborate (3-3)



In a dry 3-necked RBF fitted with a stir bar and purged under a N_2 bubbler was added trimethylborate (0.13 g, 0.14 mL, 1.2 mmol, 1.5 equiv) and 1 mL of THF via syringes. The flask was cooled to -78 °C and 3.00 mL of a 0.27 M solution of (4-(phenanthren-9-yl)butyl)magnesium chloride (0.81 mmol, 1 equiv) in 4.66 : 1 anisole/THF (v/v) was added dropwise via syringe with stirring. The reaction mixture was allowed to warm to RT over 2 h, at which point it was cooled to 0 °C and aq. KHF_2 (3 mL of a 4.5 M sol'n) was added dropwise, via a syringe. The reaction mixture was again allowed to warm to RT over 4 h, after which the solvent was removed under high vacuum. The crude residue was extracted 3X with 5 mL of hot acetone and filtered through a fritted disk. The solvent was removed from the filtrate under high vacuum. The crude product was dissolved in a minimal amount of hot acetone, at which point 10X this volume of ether was added. The product was allowed to precipitate for 1 h, at which point the white powder was collected by suction filtration, washed with cold ether, and dried in vacuo. The yield was 0.216 g (78%).

^{1}H NMR (500 MHz, DMSO-*d*$_6$): δ 8.84 (dd, *J* = 6.3, 3.5 Hz, 1H), 8.76 (dd, *J* = 7.5, 2.4 Hz, 1H), 8.13 (dd, *J* = 6.5, 3.4 Hz, 1H), 7.89 (dd, *J* = 7.0, 3.0 Hz, 1H),

7.69-7.66 (ddd, *J* – 9.5, 4.0, 4.0 Hz, 2H), 7.64 (s, 1H), 7.61-7.57 (m, 2H), 3.02 (m, 2H), 1.65 (m, 2H), 1.31 (m, 2H), 0.29 (m, 2H).

^{13}C NMR (125 MHz, DMSO-d_6): δ 137.9, 132.0, 131.3, 130.6, 129.4, 128.3, 127.2, 127.2, 126.7, 126.4, 126.0, 125.0, 123.8, 123.1, 34.5, 33.7, 26.5.

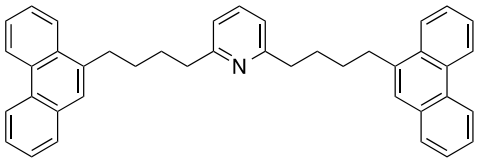
^{19}F NMR (469 MHz, DMSO-d_6) δ -136.7 (m).

^{11}B NMR (160 MHz, DMSO-d_6) δ 4.64 (br s).

HRMS (ESI) exact mass calcd for $C_{18}H_{17}BF_3$ ([M-K]$^-$): 301.1375, found 301.1385.

EA anal. calcd for $C_{18}H_{17}BF_3K$: C, 63.54%; H, 5.04%. Found: C, 61.99%; H, 4.99%; Repeat found: C, 62.07%; H, 5.00%.

2,6-Bis(4-(phenanthren-9-yl)butyl)pyridine (3-4)



In a medium-walled glass tube reactor topped with a high vacuum Teflon stopcock fitted with a stir bar under a nitrogen atmosphere, was combined 2,6-dichloropyridine (0.077 g, 0.520 mmol, 1 equiv), potassium (4-(phenanthren-9-yl)butyl)trifluoroborate (0.444 g, 1.305 mmol, 2.5 equiv), potassium carbonate (0.433 g, 3.13 mmol, 6 equiv), palladium acetate (0.006 g, 0.03 mmol, 0.05 equiv), RuPhos (0.024 g, 0.052 mmol, 0.10 equiv), and toluene (3 mL). The vessel was sealed and under a stream of nitrogen was added deoxygenated water (0.3 mL) via syringe. The vessel was resealed and heated to 100 °C for 36 hours.

The reaction was cooled to RT and was diluted with dichloromethane and washed with water then brine. The organic layer was dried with magnesium sulfate, filtered and the majority of the solvent was removed under vacuum, providing a solution of crude material in toluene. To this was added double its volume of hexane and the flask was placed in the freezer for 48 hours. Crude material was collected by suction filtration, rinsing with hexanes. This material was dissolved in a minimal amount of dichloromethane and to it was layered an equal volume of methanol and the biphasic mixture was placed in the freezer to coalesce overnight. Pure material was collected by suction filtration. Yield = 0.184 g (65%).

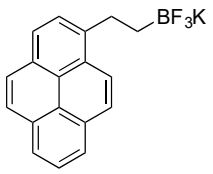
^{1}H NMR (500 MHz, $CDCl_3$): δ 8.74 (dd, *J* = 7.9, 1.5 Hz, 2H), 8.66 (d, *J* = 7.9 Hz, 2H), 8.09 (dd, *J* = 8.0, 2.0 Hz, 2H), 7.81 (dd, *J* = 7.7, 1.4 Hz, 2H), 7.68-7.55 (m, 10H), 7.49 (t, *J* = 7.4 Hz, 1H), 6.97 (d, *J* = 7.7 Hz, 2H), 3.16 (m, 4H), 2.88 (m, 4H), 1.93 (m, 8H).

^{13}C NMR (125 MHz, $CDCl_3$): δ 161.6, 136.7, 136.5, 131.9, 131.3, 130.7, 129.6, 128.0, 126.5, 126.5, 126.1, 126.0, 125.9, 124.5, 123.2, 122.4, 119.8, 38.4, 33.4, 30.3, 30.0.

HRMS (EI) exact mass calcd for $C_{41}H_{37}N$ (M^+) 543.2926, found 543.2920.

EA anal. calcd for $C_{41}H_{37}N$: C, 90.57%; H, 6.86%; N, 2.58%; found: C, 90.05%; H, 6.88%; N, 2.53%. Repeat found: C, 90.05%; H, 6.86%; N, 2.58%.

Potassium (2-(pyren-1-yl)ethyl)trifluoroborate (3-5)



4,4,5,5-Tetramethyl-2-(2-(pyren-1-yl)ethyl)-1,3,2-dioxaborolane (0.948 g, 2.661 mmol, 1 equiv) was dissolved in ethanol (30 mL) in a 100 mL RBF fitted with a stir bar and open to the air at RT. Aq. KHF_2 (6.00 mL of a 4.5 M sol'n) was added dropwise. A precipitate formed immediately and the reaction was allowed to stir at RT for 30 min at which point the solvent was removed under vacuum. The resulting green solid was extracted with hot acetone 3 times with 10 mL and filtered through a fritted disk. The solvent was removed from the filtrate under high vacuum. The crude product was dissolved in a minimal amount of hot acetone, at which point 10x this volume of ether was added. The product was allowed to precipitate for 2 h, at which point the light green powder was collected by suction filtration, washed with cold ether, and dried in vacuo. Yield = 0.465 g (52%)

^{1}H NMR (500 MHz, DMSO-*d*$_6$): δ 8.30 (d, *J* = 9.5 Hz, 1H), 8.20 (d, *J* = 7.4 Hz, 1H), 8.18 (d, *J* = 6.8 Hz, 1H), 8.13 (d, *J* = 9.5 Hz, 1H), 8.13 (d, *J* = 7.9 Hz, 1H), 8.07 (d, *J* = 8.9 Hz, 1H), 8.02 (d, *J* = 8.9 Hz, 1H), 7.99 (m, 1H) , 7.86 (d, *J* = 7.6 Hz, 1H) , 3.12 (m, 2H) , 0.49 (m, 2H)

^{13}C NMR (125 MHz, DMSO-*d*$_6$): δ 143.3, 130.9, 130.5, 128.3, 127.5, 127.5, 126.6, 126.3, 125.8, 125.7, 124.9, 124.4, 124.3, 124.3, 124.2, 123.9, 29.8

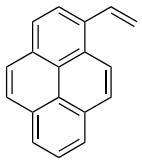
^{19}F NMR (469 MHz, DMSO-*d*$_6$) δ -138.0 (m).

^{11}B NMR (160 MHz, DMSO-*d*$_6$) δ 4.78 (br s).

HRMS (ESI) exact mass calcd for $C_{18}H_{13}BF_3$ ([M-K]$^-$) 297.1071, found 297.1066.

EA anal. calcd for $C_{18}H_{13}BF_3K$: C, 64.31; H, 3.90. Found: C, 62.57; H, 3.87. Repeat found: C, 62.32; H, 3.84.

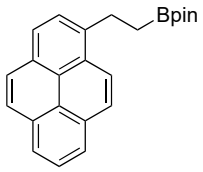
1-Vinylpyrene (3-6)



In a 250 mL 3-necked RBF fitted with a stir bar was combined potassium carbonate (14.747 g, 107 mmol, 3 equiv), potassium vinyltrifluoroborate (5.717 g, 42.68 mmol, 1.2 equiv), palladium acetate (0.160 g, 0.711 mmol, 0.02 equiv), RuPhos (0.664 g, 1.422 mmol, 0.04 equiv), hydroquinone (20 mg), and 1-bromopyrene (10.000 g, 35.568 mmol, 1 equiv). The flask was fitted with a reflux condenser and a nitrogen bubbler, and the flask was purged with nitrogen. 100 mL of THF and 10 mL of deoxygenated water were added via syringe. The flask was heated to 80 °C for 12 hours. The reaction was cooled to RT and diluted with water and ether. The layers were separated and the aqueous layer was extracted again with ether. The organic layers were combined and washed with brine. The organic layer was dried with magnesium sulfate, filtered and the solvent was removed under vacuum. The crude material was taken up in hexane and loaded onto a silica plug that had been flushed with hexanes. Hexanes was run through the plug followed by ether, at which point the product was collected. The solvent was removed under vacuum in the presence of hydroquinone (20 mg) carefully by letting the majority come off at 40 °C to provide a more viscous material, and the remaining solvent was removed under high vacuum at RT to provide pure material. Yield 7.227 g (89%)

The product of this reaction matched the analytical data of previous syntheses.[191]

4,4,5,5-Tetramethyl-2-(2-(pyren-1-yl)ethyl)-1,3,2-dioxaborolane (3-8)



In a dry 250 mL RBF fitted with a stir bar and septum was combined $[Ir(COD)Cl]_2$ (0.294 g, 0.438 mmol, 0.015 equiv), dppe (0.349 g, 0.876 mmol, 0.03 equiv), and dichloromethane (10 mL). The flask was purged with nitrogen. To this was added HBpin (5.03 mL, .035 mol, 1.2 equiv) via syringe followed by 1-vinylpyrene (6.668 g, 0.029 mmol, 1 equiv) in dichloromethane (70 mL) via cannula. The reaction was allowed to stir at RT for 24 hours at which point the septum was removed and methanol (10 mL) was added slowly. The reaction was partitioned between 200 mL of dichloromethane and 200 mL of water. The layers were separated and the aqueous layer was extracted again with 200 mL of dichloromethane. The organic layers were combined and dried with 400 mL of brine, then stirred over magnesium sulfate. This was filtered and the solvent was removed under vacuum to provide a brown sludge. This was taken up in ether and loaded onto a short column that was flushed with ether. After the column was flushed with ether, the column was flushed with dichloromethane at which point a fluorescent green fraction was collected and evaporated, providing a fluorescent green oil which was dried under high vacuum to provide pure material. This material solidified to a brittle yellow solid over a period of a week. Yield = 7.309 g (70%)

^{1}H NMR (500 MHz, $CDCl_3$): δ 8.35 (d, *J* = 9.5 Hz, 1H), 8.17 (d, *J* = 7.5 Hz, 1H), 8.15 (d, *J* = 6.9 Hz, 1H), 8.11 (d, *J* = 7.8 Hz, 1H), 8.10 (d, *J* = 9.0 Hz, 1H), 8.03 (d, *J* = 8.7 Hz, 1H), 8.00 (d, *J* = 8.7 Hz, 1H), 7.98 (app t, *J* = 7.8 Hz, 1H), 7.95 (d, *J* = 8.0 Hz, 1H), 3.49 (t, *J* = 7.9 Hz, 2H), 1.41 (t, *J* = 8.3 Hz, 2H), 1.26 (s, 12H).

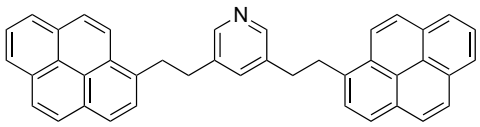
^{13}C NMR (125 MHz, $CDCl_3$): δ 138.9, 131.5, 131.0, 129.7, 128.4, 127.6, 127.0, 126.6, 126.4, 125.7, 125.1, 125.1, 124.8, 124.7, 124.6, 123.7, 83.3, 27.6, 24.9.

^{11}B NMR (160 MHz, $CDCl_3$) δ 33.80 (br s).

HRMS (EI) exact mass calcd for $C_{24}H_{25}BO_2$ (M^+) 356.1948, found 356.1947.

EA anal. calcd for $C_{24}H_{25}BO_2$: C, 80.91%; H, 7.07%; found: C, 81.03%; H, 7.03%; repeat found: C, 80.92%; H, 7.02%.

3,5-Bis(2-(pyren-1-yl)ethyl)pyridine (3-9)



In a 20 mL medium-walled glass tube reactor topped with a high vacuum Teflon stopcock fitted with a stir bar under a nitrogen atmosphere was combined 4,4,5,5-tetramethyl-2-(2-(pyren-1-yl)ethyl)-1,3,2-dioxaborolane (0.674 g, 1.89 mmol, 2.5 equiv), 2,6-dichloropyridine (0.112 g, 0.757 mmol, 1 equiv), and potassium tert-butoxide (0.637 g, 5.68 mmol, 7.5 equiv), and toluene (4.5 mL). To this was added a homogenous solution of palladium acetate (0.008 g, 0.04 mmol, 0.05 equiv) and RuPhos (0.035g, 0.076 mmol, 0.1 equiv) in toluene (1.5 mL). The medium-walled glass tube reactor topped with a high vacuum Teflon stopcock was sealed and removed from the glove box. Deoxygenated water (0.6 mL) was added via syringe under a stream of nitrogen and the reaction was heated to 100 °C for 24 hours. The reaction was cooled to RT and partitioned between dichloromethane and water. The aqueous layer was extracted again and the organic layers were combined. The organic layer was washed with brine, dried with magnesium sulfate and filtered. The solvent was removed under vacuum to provide a light yellow solid. This material was dissolved in a minimal amount of

hot chloroform and then layered with 4X the volume of methanol. This was placed in the freezer overnight. Pure material was collected via suction filtration, rinsing with methanol and drying under high vacuum. Yield = 0.208 g (51%)

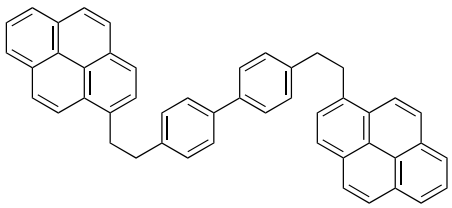
^{1}H NMR (500 MHz, $CDCl_3$): δ 8.40 (br s, 2H), 8.20 (d, *J* = 7.5 Hz, 2H), 8.18 (dd, *J* = 7.9, 1.1 Hz, 2H), 8.10 (d, *J* = 9.4, Hz, 1H), 8.08 (d, *J* = 7.9, Hz, 1H), 8.06-8.01 (m, 10H), 7.64 (d, *J* = 7.6 Hz, 2H), 6.97 (br s, 1H), 3.47 (m, 4H), 3.06 (m, 4H).

^{13}C NMR (125 MHz, $CDCl_3$): δ 147.0, 137.1, 136.7, 134.7, 131.5, 130.9, 130.2, 128.6, 127.6, 127.5, 127.5, 126.9, 126.0, 125.1, 125.0, 124.9, 124.8, 122.9, 35.2, 34.9, One aromatic carbon signal was not observed.

HRMS (ESI) exact mass calcd for $C_{41}H_{30}N$ ($[M + H]^+$): 536.2373, found 536.2373.

EA anal. calcd for $C_{41}H_{29}N$: C, 91.93%; H, 5.46%; N, 2.61%. Found: C, 90.50%; H, 5.39%; N, 2.58%. Repeat found: C, 90.53%; H, 5.44%; N, 2.58%.

4,4'-Bis(2-(pyren-1-yl)ethyl)-1,1'-biphenyl (3-10)



In a 20 mL medium-walled glass tube reactor topped with a high vacuum Teflon stopcock fitted with a stir bar under a nitrogen atmosphere was combined 4,4,5,5-tetramethyl-2-(2-(pyren-1-yl)ethyl)-1,3,2-dioxaborolane (0.884 g, 2.481 mmol, 2.5 equiv), 4,4'-dibromo-1,1'-biphenyl (0.310 g, 0.992 mmol, 1 equiv), potassium tert-butoxide (0.835 g, 7.44 mmol, 7.50 equiv), and toluene (6 mL). To this was added a homogenous solution of palladium acetate (0.011 g, 0.050 mmol, 0.05

equiv) and RuPhos (0.046g, 0.100 mmol, 0.1 equiv) in toluene (1.5 mL). The vessel was sealed and removed from the glove box. Deoxygenated water (0.75 mL) was added via syringe under a stream of nitrogen and the reaction was heated to 100 °C for 24 hours. The reaction was cooled to RT and diluted with 10 mL of methanol. The pure product was collected as a white solid via suction filtration, rinsing with water then hot ethanol then hexanes and dried under high vacuum. Yield = 0.522 g (86%)

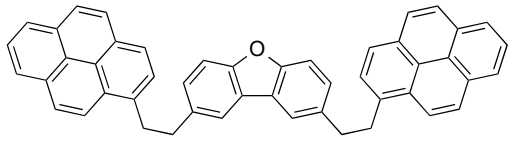
^{1}H NMR (500 MHz, $CDCl_3$): δ 8.39 (d, *J* = 9.6 Hz, 2H), 8.23-8.03 (m, 14H), 7.90 (d, *J* = 8.7 Hz, 2H), 7.59 (d, *J* = 8.7 Hz, 4H), 7.37 (d, *J* = 7.4 Hz, 4H), 3.75-3.72 (m, 4H), 3.26-3.23 (m, 4H).

^{13}C NMR (125 MHz, $CDCl_3$): δ 140.8, 138.9, 136.0, 131.5, 131.0, 130.0, 129.0, 128.7, 127.6, 127.5, 127.4, 127.1, 126.7, 125.9, 125.2, 125.1, 125.0, 124.9, 124.8, 123.3, 37.8, 35.7

HRMS (MALDI-FT-ICR) exact mass calcd for $C_{48}H_{34}$ (M^+) 610.2655, found 610.2659.

EA anal. calcd for $C_{48}H_{34}$: C, 94.39%; H, 5.61%; found: C, 91.49%; H, 5.46%; repeat found: C, 91.08%; H, 5.51%.

2,8-Bis(2-(pyren-1-yl)ethyl)dibenzo[*b*,*d*]furan (3-11)



In a 20 mL medium-walled glass tube reactor topped with a high vacuum Teflon stopcock fitted with a stir bar under a nitrogen atmosphere was combined 4,4,5,5-tetramethyl-2-(2-(pyren-1-yl)ethyl)-1,3,2-dioxaborolane (0.591 g, 1.659 mmol,

2.5 equiv), 2,8-dibromodibenzo[*b*,*d*]furan (0.216 g, 0.664 mmol, 1 equiv), and potassium tert-butoxide (0.559 g, 4.980 mmol, 7.5 equiv), and toluene (3.5 mL). To this was added a homogenous solution of palladium acetate (0.007 g, 0.033 mmol, 0.05 equiv) and RuPhos (0.031g, 0.066 mmol, 0.1 equiv) in toluene (1.5 mL). The medium-walled glass tube reactor topped with a high vacuum Teflon stopcock was sealed and removed from the glove box. Deoxygenated water (0.50 mL) was added via syringe under a stream of nitrogen and the reaction was heated to 100 °C for 24 hours. The reaction was cooled to RT and diluted with 10 mL of methanol. The pure product was collected as a dark green solid via suction filtration, rinsing with water then hot ethanol then hexanes and dried under high vacuum. Yield = 0.340 g (82%)

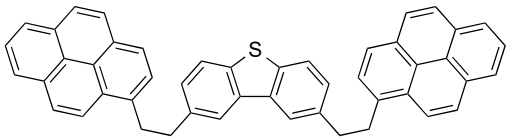
^{1}H NMR (500 MHz, $CDCl_3$): δ 8.40 (d, *J* = 9.2 Hz, 2H), 8.22 (d, *J* = 7.5 Hz, 2H), 8.21 (d, *J* = 7.5 Hz, 2H), 8.17 (d, *J* = 9.2 Hz, 2H), 8.12 (d, *J* = 7.5 Hz, 2H), 8.06 (s, 4H), 8.04 (app t, *J* = 7.5 Hz, 2H), 7.85 (d, *J* = 7.8 Hz, 2H), 7.80 (d, *J* = 1.6 Hz, 2H), 7.51 (d, *J* = 8.3 Hz, 2H), 7.34 (dd, *J* = 8.3, 2.1 Hz, 2H), 3.78-3.74 (m, 4H), 3.36-3.33 (m, 4H).

^{13}C NMR (125 MHz, $CDCl_3$): δ 155.3, 136.3, 135.9, 131.5, 131.0, 130.0, 128.7, 127.7, 127.6, 127.5, 127.5, 126.8, 125.9, 125.2, 125.1, 125.0, 124.9, 124.8, 124.4, 123.3, 120.2, 111.4, 38.1, 36.4.

HRMS (MALDI-FT-ICR) exact mass calcd for $C_{48}H_{32}O$ (M^+) 624.2448, found 624.2450.

EA anal. calcd for $C_{48}H_{32}O$: C, 92.28%; H, 5.16%; Found: C, 88.08%; H, 4.98%; Repeat found: C, 87.73%; H, 4.98%.

2,8-Bis(2-(pyren-1-yl)ethyl)dibenzo[*b*,*d*]thiophene (3-12)



In a 20 mL medium-walled glass tube reactor topped with a high vacuum Teflon stopcock fitted with a stir bar under a nitrogen atmosphere was combined 4,4,5,5-tetramethyl-2-(2-(pyren-1-yl)ethyl)-1,3,2-dioxaborolane (0.674 g, 1.893 mmol, 2.5 equiv), 2,8-dibromodibenzothiophene (0.259 g, 0.757 mmol, 1 equiv), and potassium tert-butoxide (0.637 g, 5.678 mmol, 7.5 equiv), and toluene (4.5 mL). To this was added a homogenous solution of palladium acetate (0.008 g, 0.038 mmol, 0.05 equiv) and RuPhos (0.035 g, 0.076 mmol, 0.1 equiv) in toluene (1.5 mL). The medium-walled glass tube reactor topped with a high vacuum Teflon stopcock was sealed and removed from the glove box. Deoxygenated water (0.5 mL) was added via syringe under a stream of nitrogen and the reaction was heated to 100 °C for 48 hours. The reaction was cooled to RT and diluted with 10 mL of methanol. The pure product was collected as a lime green solid via suction filtration, rinsing with water then hot ethanol then hexanes and dried under high vacuum. Yield = 0.348 g (72%)

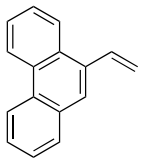
^{1}H NMR (500 MHz, $CDCl_3$): δ 8.37 (d, *J* = 9.3 Hz, 2H), 8.19 (d, *J* = 7.3 Hz, 2H), 8.16 (d, *J* = 7.6 Hz, 2H), 8.14 (d, *J* = 9.8 Hz, 2H), 8.10 (d, *J* = 7.6 Hz, 2H), 8.04 (d, *J* = 8.7 Hz, 2H), 8.02 (d, *J* = 8.7 Hz, 2H), 8.00 (app t, *J* = 7.4 Hz, 2H), 7.90 (d, *J* = 1.4 Hz, 2H), 7.82 (d, *J* = 7.8 Hz, 2H), 7.77 (d, *J* = 8.2 Hz, 2H), 7.33 (dd, *J* = 8.2, 1.9 Hz, 2H), 3.75-3.72 (m, 4H), 3.34-3.31 (m, 4H).

^{13}C NMR (125 MHz, $CDCl_3$): δ 138.1, 137.6, 135.9, 135.8, 131.5, 131.0, 130.1, 128.7, 127.7, 127.6, 127.6, 127.5, 126.8, 125.9, 125.2, 125.1, 125.0, 124.9, 124.9, 123.3, 122.8, 121.4, 38.1, 36.1.

HRMS (MALDI-FT-ICR) exact mass calcd for $C_{48}H_{32}S$ (M^+) 640.2219, found 640.2229.

EA anal. calcd for $C_{48}H_{32}S$: C, 89.96%; H, 5.03%; S, 5.00%. Found: C, 73.50%; H, 4.25%; S, 4.22%. Repeat found: C, 70.14%; H, 4.12%; S, 3.95%.

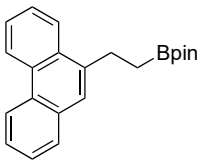
9-Vinylphenanthrene (3-13)



In a 3-necked 100 mL RBF fitted with a stir bar was combined 9-bromophenanthrene (5.530 g, 21.51 mmol, 1.0 equiv), potassium vinyltrifluoroborate (3.456 g, 25.80 mmol, 1.2 equiv), palladium acetate (0.097 g, 0.430 mmol, 0.02 equiv), RuPhos (0.401 g, 0.860 mmol, 0.04 equiv), potassium carbonate (8.917 g, 64.52 mmol, 3 equiv), THF (55 mL), and water (5.5 mL). The system was fitted with a reflux condenser and a nitrogen bubbler. The reaction was purged with nitrogen then heated to 80 °C overnight. The reaction was cooled to RT and partitioned between ether and water. The layers were separated and the aqueous layer was extracted again with ether. The organics were combined and washed with brine. The organic layer was stirred over magnesium sulfate, filtered and the solvent was removed under vacuum to provide a brown oil which was immediately subJected to the next reaction in the sequence.

The product of this reaction was not characterized in depth, a crude ^1H NMR was examined to confirm identity and purity.

4,4,5,5-Tetramethyl-2-(2-(phenanthren-9-yl)ethyl)-1,3,2-dioxaborolane (3-14)



In a dry 100 mL RBF fitted with a septum was combined 9-vinylphenenthrene (4.972 g, 21.78 mmol, 1.0 equiv) and 40 mL of dichloromethane, added via syringe. In a separate 250 mL RBF was combined a stir bar, Bis(1,5-cyclooctadiene)diiridium(I) dichloride (0.146 g, 0.218 mmol, 0.015 equiv), and dppe (0.174 g, 0.436 mmol, 0.03 equiv). The RBF was sealed with a septum and purged with nitrogen. To the reaction was added 8 mL of dichloromethane via syringe followed by HBpin (3.8 mL, 3.3 g, 26 mmol, 1.2 equiv) via syringe. At this point the vinylphenanthtrene solution in dichloromethane was transferred via cannula into the reaction was allowed to stir at RT overnight. The reaction was quenched by removing the septum and adding Methanol (5 mL) dropwise at RT. The reaction was partitioned between dichloromethane and water. The layers were separated and the aqueous layer was extracted again with dichloromethane. The organic layers were combined and washed with brine. The organic layer was dried w/ magnesium sulfate, filtered, and solvent was removed under vacuum to provide a brown oil. This was suspended in ether and loaded on a column that had been flushed with ether. The column is flushed with ether providing material that can be discarded. At this point dichloromethane was run down the column, which provided a pure fraction. The solvent was removed under vacuum to provide a pure clear oil. Yield = 5.289 g (74% over two steps from 9-bromophenanthrene)

^{1}H NMR (500 MHz, $CDCl_3$): δ 8.76 (dd, *J* = 7.4, 2.9 Hz, 1H), 8.68 (dd, *J* = 7.4, 1.6 Hz, 1H), 8.17 (dd, *J* = 7.0, 2.5 Hz, 1H), 7.86 (dd, *J* = 7.0, 2.1 Hz, 1H), 7.70-7.68 (m, 2H), 7.65 (s, 1H), 7.64-7.61 (m, 2H), 3.28 (t, *J* = 7.7 Hz, 2H), 1.40 (t, *J* = 8.2 Hz, 2H), 1.28 (s, 12H).

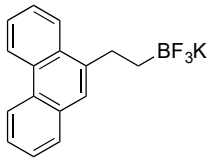
^{13}C NMR (160 MHz, $CDCl_3$, -60 °C): δ 138.0, 131.5, 130.8, 130.0, 129.1, 127.9, 126.5, 126.4, 126.0, 125.7, 124.7, 124.4, 123.0, 122.3, 83.2, 27.1, 24.7, 11.2.

^{11}B NMR (160 MHz, $CDCl_3$) δ 34.07 (br s).

HRMS (EI) exact mass calcd for $C_{22}H_{25}BO_2$ (M^+) 332.1948, found 332.1952.

EA anal. calcd for $C_{22}H_{25}BO_2$: C, 79.53%; H, 7.58%; found: C, 79.92%; H, 7.48%; repeat found: C, 80.11%; H, 7.52%.

Potassium (2-(phenanthrene-9-yl)ethyl)trifluoroborate (3-15)



To a solution of 4,4,5,5-tetramethyl-2-(2-(phenanthren-9-yl)ethyl)-1,3,2-dioxaborolane (3.631 g, 10.93 mmol, 1.0 equiv) in ethanol (150 mL) at RT in a 250 mL RBF fitted with a stir bar and open to the air was added aq. KHF_2 (30 mL of a 4.5 M sol'n). The reaction immediately became heterogeneous and the slurry was allowed to stir for 30 min. The solvent was removed under vacuum leaving behind an off-white residue that was extracted with hot acetone and filtered through a fritted disc 3 times. The solvent was removed under vacuum. The crude material was then dissolved in a minimal amount of hot acetone and layered with 10X that volume of ether. The pure product precipitated as a white powder and was collected by suction filtration rinsing with ether. Yield = 3.204 g (94%)

^{1}H NMR (500 MHz, DMSO-d_6): 8.79 (dd, J = 6.4, 2.9 Hz, 1H), 8.72 (dd, J = 6.4, 4.0 Hz, 1H), 8.13 (dd, J = 5.8, 3.5 Hz, 1H), 7.85 (dd, J = 5.8, 3.5 Hz, 1H), 7.63

(dt, J = 9.8, 2.9 Hz, 2H), 7.58 (s, 1H), 7.56-7.54 (m, 2H), 2.89 (t, J = 5 Hz, 2H), 0.42 (m, 2H).

^{13}C NMR (125 MHz, DMSO-d_6): δ 142.2, 131.9, 131.2, 130.0, 128.6, 127.7, 126.5, 126.3, 125.9, 125.4, 124.7, 123.8, 123.1, 122.5, 29.6.

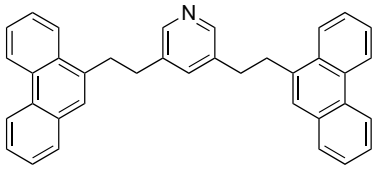
^{19}F NMR (469 MHz, DMSO-d_6) δ -138.0 (m).

^{11}B NMR (160 MHz, DMSO-d_6) δ 4.82 (br s).

HRMS (ESI) exact mass calcd for $C_{16}H_{13}BF_3$ ([M-K]$^-$): 273.1071, found 273.1073.

EA anal. calcd for $C_{16}H_{13}BF_3K$: C, 61.56%; H, 4.20%. Found: C, 57.67%; H, 4.45%. Repeat found: C, 57.72%; H, 4.48%.

3,5-Bis(2-(phenanthren-9-yl)ethyl)pyridine (3-16)



In a 5 mL medium-walled glass tube reactor topped with a high vacuum Teflon stopcock fitted with a stir bar under a nitrogen atmosphere was combined potassium (2-(phenanthrene-9-yl)ethyl)trifluoroborate (0.500 g, 1.602 mmol, 2.5 equiv), 3,5-dichloropyridine (0.095 g, 0.641 mmol, 1.0 equiv), potassium carbonate (0.532 g, 3.846 mmol, 6.0 equiv), and toluene (2.5 mL). To this was added a solution of palladium acetate (0.007 g, 0.032 mmol, 0.05 equiv) and RuPhos (0.030 g, 0.064 mmol, 0.1 equiv) in toluene (1.5 mL). The vessel was sealed and removed from the glove box. Deoxygenated Water (0.4 mL) was added via syringe under a stream of nitrogen and the reaction was heated to 100

°C for 36 hours. The reaction was cooled to RT and partitioned between dichloromethane and water. The aqueous layer was extracted again with dichloromethane and the organic layers were combined. The organic layer was washed with brine, dried with magnesium sulfate and filtered. The solvent was removed under vacuum to provide a white solid, which was taken up in a minimal amount of dichloromethane. This was layered with 2X the volume of methanol and placed in the freezer overnight. Pure material was collected via suction filtration, rinsing with methanol. Yield = 0.207 g (66%)

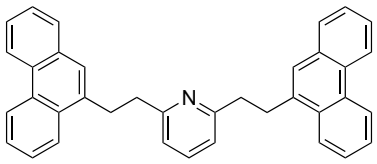
^{1}H NMR (500 MHz, $CDCl_3$): δ 8.79 (dd, *J* = 8.5, 1.9 Hz, 2H), 8.69 (d, *J* = 8.5 Hz, 2H), 8.44 (d, *J* = 2.1 Hz, 2H), 8.06 (dd, *J* = 7.7, 1.3 Hz, 2H), 7.81 (dd, *J* = 8.0, 2.2 Hz, 2H), 7.72 (ddd, *J* = 8.6, 7.7, 1.5 Hz, 2H), 7.67 (ddd, *J* = 8.6, 7.4, 1.5 Hz, 2H), 7.62 (ddd, *J* = 8.3, 6.8, 1.5 Hz, 2H), 7.58 (ddd, *J* = 8.6, 6.8, 1.5 Hz, 2H), 7.46 (s, 2H), 7.14 (t, *J* = 2.2 Hz, 1H), 3.29 (m, 4H), 3.06 (m, 4H).

^{13}C NMR (125 MHz, $CDCl_3$): δ 147.8, 136.6, 136.3, 135.0, 131.7, 130.9, 130.8, 129.8, 128.1, 126.7, 126.7, 126.3, 126.2, 124.1, 123.4, 122.5, 35.2, 33.6, One aromatic carbon signal was not observed.

HRMS (ESI) exact mass calcd for $C_{37}H_{30}N$ ($[M+H]^+$): 488.2373, found 488.2363.

EA anal. calcd for $C_{37}H_{29}N$: C, 91.13%; H, 5.99%; N, 2.87%. Found: C, 89.60%; H, 5.91%; N, 2.71%. Repeat found: C, 89.77%; H, 5.89%; N, 2.72%.

2,6-Bis(2-(phenanthren-9-yl)ethyl)pyridine (3-17)



In a 5 mL medium-walled glass tube reactor topped with a high vacuum Teflon stopcock fitted with a stir bar under a nitrogen atmosphere was combined potassium (2-(phenanthrene-9-yl)ethyl)trifluoroborate (0.500 g, 1.602 mmol, 2.5 equiv), 2,6-dichloropyridine (0.095 g, 0.641 mmol, 1 equiv), potassium carbonate (0.532 g, 3.846 mmol, 6.0 equiv), and toluene (2.5 mL). To this was added a solution of palladium acetate (0.007 g, 0.032 mmol, 0.05 equiv) and RuPhos (0.030 g, 0.064 mmol, 0.1 equiv) in toluene (1.5 mL). The vessel was sealed and removed from the glove box. Deoxygenated Water (0.4 mL) was added via syringe under a stream of nitrogen and the reaction was heated to 100 °C for 36 hours. The reaction was cooled to RT and partitioned between dichloromethane and water. The aqueous layer was extracted again with dichloromethane and the organic layers were combined. The organic layer was washed with brine, dried with magnesium sulfate and filtered. The solvent was removed under vacuum to provide a white solid, which was taken up in a minimal amount of dichloromethane. This was layered with 2X the volume of methanol and placed in the freezer overnight. Pure material was collected via suction filtration, rinsing with methanol. Yield = 0.267 g (85%)

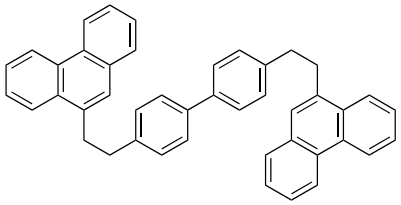
^{1}H NMR (500 MHz, $CDCl_3$): δ 8.77-8.75 (m, 2H), 8.67 (dd, *J* = 8.3, 0.9 Hz, 2H), 8.31-8.30 (m, 2H), 7.81 (dd, *J* = 8.0, 1.6 Hz, 2H), 7.7 (m, 4H), 7.65 (s, 2H), 7.63 (ddd, *J* = 8.3, 6.7, 1.4 Hz, 2H), 7.58 (ddd, *J* = 8.1, 6.7, 1.2 Hz, 2H), 7.47 (t, *J* = 7.5 Hz, 1H), 7.00 (d, *J* = 7.6 Hz, 2H), 3.64 (m, 4H), 3.37 (m, 4H).

^{13}C NMR (125 MHz, $CDCl_3$): δ 161.0, 136.6, 136.0, 132.0, 131.3, 130.8, 129.8, 128.2, 126.7, 126.6, 126.4, 126.2, 126.0, 124.5, 123.3, 122.5, 120.4, 38.9, 33.5.

HRMS (ESI) exact mass calcd for $C_{37}H_{30}N$ ($[M+H]^+$): 488.2373, found 488.2363.

EA anal. calcd for $C_{37}H_{29}N$: C, 91.13%; H, 5.99%; N, 2.87%. Found: C, 76.75%; H, 5.11%; N, 2.34%. Repeat found: C, 76.89%; H, 5.13%; N, 2.36%.

4,4'-Bis(2-(phenanthren-9-yl)ethyl)-1,1'-biphenyl (3-18)



In a 5 mL medium-walled glass tube reactor topped with a high vacuum Teflon stopcock fitted with a stir bar under a nitrogen atmosphere was combined potassium (2-(phenanthrene-9-yl)ethyl)trifluoroborate (0.500 g, 1.602 mmol, 2.5 equiv), 4,4'-dibromo-1,1'-biphenyl (0.200 g, 0.641 mmol, 1 equiv), potassium carbonate (0.532 g, 3.846 mmol, 6.0 equiv), and toluene (2.5 mL). To this was added a solution of palladium acetate (0.007 g, 0.032 mmol, 0.05 equiv) and RuPhos (0.030 g, 0.064 mmol, 0.1 equiv) in toluene (1.5 mL). The vessel was sealed and removed from the glove box. Deoxygenated Water (0.4 mL) was added via syringe under a stream of nitrogen and the reaction was heated to 100 °C for 36 hours. The reaction was cooled to RT and diluted with 10 mL of methanol. The pure product was collected as a white powder via suction filtration, rinsing with water then hot ethanol then hexanes and dried under high vacuum. Yield = 0.155 g (43%)

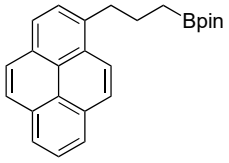
^{1}H NMR (500 MHz, $CDCl_3$): δ 8.80 (dd, *J* = 6.7, 2.4 Hz, 2H), 8.71 (d, *J* = 8.0 Hz, 2H), 8.23 (dd, *J* = 6.0, 3.1 Hz, 2H), 7.86 (d, *J* = 7.5 Hz, 2H), 7.71 (ddd, *J* = 7.5, 6.0, 1.0 Hz, 4H), 7.67-7.62 (m, 6H), 7.60 (d, *J* = 8.0 Hz, 4H), 7.41 (d, *J* = 7.9 Hz, 4H), 3.52-3.49 (m, 4H), 3.23-3.20 (m, 4H).

^{13}C NMR (125 MHz, $CDCl_3$): δ 141.0, 139.0, 135.9, 131.9, 131.2, 130.8, 129.8, 128.9, 128.2, 127.1, 126.7, 126.3, 126.3, 126.1, 124.3, 123.4, 122.5, 36.3, 35.5, One aromatic carbon signal was not observed.

HRMS (MALDI-FT-ICR) exact mass calcd for $C_{44}H_{34}$ (M^+) 562.2655, found 562.2645.

EA anal. calcd for $C_{44}H_{34}$: C, 93.91%; H, 6.09%. Found: C, 85.33%; H, 5.61%; Repeat found: C, 85.36%; H, 5.60%.

4,4,5,5-Tetramethyl-2-(3-(pyren-1-yl)propyl)-1,3,2-dioxaborolane (3-19)



In a 50 mL medium-walled glass tube reactor topped with a high vacuum Teflon stopcock fitted with a stir bar under a nitrogen atmosphere was combined 4,4,5,5-tetramethyl-2-(2-(pyren-1-yl)ethyl)-1,3,2-dioxaborolane (1.815 g, 5.094 mmol, 1.0 equiv) and THF (7 mL). The vessel was sealed and removed from the glove box. Under a stream of nitrogen was added dichloromethane (0.49 mL, 0.65 g, 7.6 mmol, 1.5 equiv) via a Hamilton syringe. The vessel was cooled to -78 °C, and LiTMP (1.050g, 7.132 mmol, 1.4 eq) in THF (5 mL) was added via syringe slowly under a stream of nitrogen. The reaction was allowed to warm to RT over two days at which point it was cooled to 0 °C and potassium triisopropoxyborohydride (4.67 mL of a 1.2 M sol'n in THF) was added dropwise via syringe. The reaction was allowed to warm to RT overnight. The solvent was removed under vacuum and 5 mL of water was added slowly. The reaction was allowed to stir for 1 hour at which point it was extracted twice with ether. The organic layers were combined and washed with brine. The organic layer was

stirred over magnesium sulfate and filtered. The solvent was removed under vacuum to provide a brown oil which was run through a silica plug with dichloromethane. The solvent was removed under vacuum to provide a green oil which solidified upon standing. The solid was dissolved in a minimal amount of hot 2-propanol and placed in the freezer overnight. The precipitated product, a green solid was collected by suction filtration and rinsed with methanol. Yield = 0.811 g (43%).

^{1}H NMR (500 MHz, $CDCl_3$): δ 8.37 (d, *J* = 9.3 Hz, 1H), 8.16-8.13 (m, 2H), 8.10 (d, *J* = 8.0 Hz, 1H), 8.09 (d, *J* = 9.3 Hz, 1H), 8.03 (d, *J* = 9.1 Hz, 1H), 8.00 (d, *J* = 9.3 Hz, 1H), 7.97 (app t, *J* = 7.2 Hz, 1H), 7.87 (d, *J* = 7.8 Hz, 1H), 3.35 (t, *J* = 7.8 Hz, 2H), 1.98 (m, 2H), 1.27 (s, 12H), 0.99 (t, *J* = 7.9 Hz, 2H).

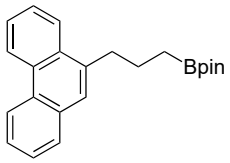
^{13}C NMR (125 MHz, $CDCl_3$): δ 137.3, 131.5, 131.0, 129.7, 128.8, 127.6, 127.5, 127.0, 126.5, 125.7, 125.1, 124.8, 124.7, 124.6, 123.8, 83.1, 36.2, 26.6, 24.9, One aromatic carbon signal was not observed.

^{11}B NMR (160 MHz, $CDCl_3$) δ 34.03 (br s).

HRMS (EI) exact mass calcd for $C_{25}H_{27}BO_2$ (M^+) 370.2104, found 370.2105.

EA anal. calcd for $C_{25}H_{27}BO_2$: C, 81.09%; H, 7.35%. Found: C, 81.26%; H, 7.36%. Repeat found: C, 81.19%; H, 7.28%.

4,4,5,5-Tetramethyl-2-(3-(phenanthren-9-yl)propyl)-1,3,2-dioxaborolane (3-20)



In a 10 mL medium-walled glass tube reactor topped with a high vacuum Teflon stopcock fitted with a stir bar under a nitrogen atmosphere was added 4,4,5,5-tetramethyl-2-(2-(phenanthren-9-yl)ethyl)-1,3,2-dioxaborolane (0.790 g, 2.378 mmol, 1.0 equiv) and THF (3 mL). The vessel was sealed and removed from the glove box. Under a stream of nitrogen was added dichloromethane (0.23 mL, 0.30 g, 3.57 mmol, 1.5 equiv) via a Hamilton syringe. The reaction was cooled to -78 °C and under a stream of nitrogen was added LiTMP (0.490 g, 3.324 mmol, 1.4 equiv) in THF (2 mL). The vessel was allowed to warm to RT over two days. The vessel was cooled to 0 °C and under a stream of nitrogen was added potassium triisopropoxyborohydride (2.180 mL of a 1.2 M solution in THF) via syringe. The vessel and allowed to warm to RT overnight. The solvent was removed under vacuum and 4 mL of water was added and allowed to stir for 1 h at RT. The reaction was partitioned between ether and water. The layers were separated and the organic layer was washed with brine. The layers were separated and the organic layer was dried over magnesium sulfate and filtered. The solvent was removed under vacuum providing a light orange sludge. This was taken up in dichloromethane and run through a silica pad. The solvent was again removed under vacuum to provide pure material. Yield = 0.561 g (68%)

^{1}H NMR (500 MHz, $CDCl_3$): δ 8.73 (dd, *J* = 7.2, 2.4 Hz, 1H), 8.65 (dd, *J* = 6.8, 1.6 Hz, 1H), 8.20 (dd, *J* = 7.6, 2.8 Hz, 1H), 7.82 (dd, *J* = 6.8, 2.0 Hz, 1H), 7.64 (ddd, *J* = 9.6 ,7.6, 2.8 Hz, 2H), 7.59 (s, 1H), 7.57 (ddd, *J* = 7.2, 5.6, 1.6, Hz, 2H), 3.13 (t, *J* = 7.9 Hz, 2H), 1.94 (m, 2H), 1.27 (s, 12H), 0.98 (t, *J* = 8.0 Hz, 2H).

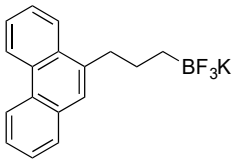
^{13}C NMR (125 MHz, $CDCl_3$): δ 136.9, 132.0, 131.4, 130.7, 129.6, 128.0, 126.5, 126.4, 126.3, 126.0, 125.8, 124.8, 123.1, 122.4, 83.0, 36.1, 25.0, 24.9.

^{11}B NMR (160 MHz, $CDCl_3$) δ 34.02 (br s).

HRMS (EI) exact mass calcd for $C_{23}H_{27}BO_2$ (M^+) 346.2104, found 346.2110.

EA anal. calcd for $C_{23}H_{27}BO_2$: C, 79.78%; H, 7.86%. Found: C, 79.90%; H, 7.81%. Repeat found: C, 80.03%; H, 7.83%.

Potassium (3-(phenanthrene-9-yl)propyl)trifluoroborate (3-21)



To a solution of 4,4,5,5-tetramethyl-2-(3-(phenanthren-9-yl)propyl)-1,3,2-dioxaborolane (1.543 g, 4.456 mmol, 1 equiv) in ethanol (75 mL) at RT in a 250 mL RBF open to the air was added aq. KHF_2 (15 mL of a 4.5 M sol'n). The reaction immediately became heterogeneous and the slurry was allowed to stir for 30 min. The solvent was removed under vacuum leaving behind an off-white residue that was extracted with hot acetone and filtered through a fritted disc 3 times. The solvent was removed under vacuum. The crude material was then dissolved in a minimal amount of hot acetone and layered with 10X that volume of ether. The pure product, a white powder precipitated as pure and was collected by suction filtration rinsing with ether. Yield = 0.758 g (52%)

^{1}H NMR (500 MHz, DMSO-*d*$_6$): δ 8.82 (dd, *J* = 7.1, 2.3 Hz, 1H), 8.75 (dd, *J* = 6.9, 2.7 Hz, 1H), 8.15 (dd, *J* = 7.6, 2.5 Hz, 1H), 7.89-7.87 (m, 1H), 7.68-7.64 (m,

2H), 7.60 (s, 1H), 7.61-7.56 (m, 2H), 2.97, (t, J = 7.8 Hz, 2H), 1.61 (m, 2H), 0.16-0.11 (m, 2H)

^{13}C NMR (125 MHz, DMSO-d_6): δ 138.4, 131.6, 131.1, 130.0, 128.8, 127.8, 126.6, 126.5, 126.1, 125.7, 125.2, 124.7, 123.2, 122.5, 36.6, 27.1.

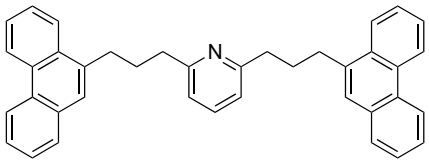
^{19}F NMR (469 MHz, DMSO-d_6) δ -140.8 (m).

^{11}B NMR (160 MHz, DMSO-d_6) δ 5.25 (br s).

HRMS (ESI) exact mass calcd for $C_{17}H_{15}BF_3$ ([M-K]$^-$): 287.1219, found 287.1218.

EA anal. calcd for $C_{17}H_{15}BF_3K$: C, 62.59%; H, 4.64%. Found: C, 62.28%; H, 4.60%. Repeat found: C, 62.36%; H, 4.60%.

2,6-Bis(3-(phenanthren-9-yl)propyl)pyridine (3-22)



In a 5 mL medium-walled glass tube reactor topped with a high vacuum Teflon stopcock fitted with a stir bar under a nitrogen atmosphere was combined potassium potassium (3-(phenanthrene-9-yl)propyl)trifluoroborate (0.500 g, 1.533 mmol, 2.5 equiv), 2,6-dichloropyridine (0.091 g, 0.613 mmol, 1.0 equiv), potassium carbonate (0.508 g, 3.678 mmol, 6.0 equiv), and toluene (4.0 mL). To this was added a solution of palladium acetate (0.007 g, 0.031 mmol, 0.05 equiv) and RuPhos (0.030 g, 0.062 mmol, 0.1 equiv) in toluene (1.5 mL). The vessel was sealed and removed from the glove box. Deoxygenated water (0.4 mL) was added via syringe under a stream of nitrogen and the reaction was heated to 100 °C for 36 hours. The reaction was cooled to RT and partitioned between

dichloromethane and water. The aqueous layer was extracted again with dichloromethane and the organic layers were combined. The organic layer was washed with brine, dried with magnesium sulfate and filtered. The solvent was removed under vacuum to provide a brown oil. This was dissolved in a small amount of dichloromethane and layered with 2X the volume of methanol and placed in the freezer overnight. A tan residue formed and the mother liquor was siphoned off. This was dissolved in a small amount of toluene and layered with 2x the volume of hexanes and placed in the freezer overnight. Again a tan residue was obtained after siphoning off the mother liquor. This residue solidified after drying under high vacuum to provide a solid. Yield = 0.072 g (23%)

^{1}H NMR (500 MHz, $CDCl_3$): δ 8.71 (dd, *J* = 8.1, 1.0 Hz, 2H), 8.64 (d, *J* = 8.2 Hz, 2H), 8.07 (dd, *J* = 8.3, 1.1 Hz, 2H), 7.77 (dd, *J* = 7.7, 1.4 Hz, 2H), 7.60-7.52 (m, 10H), 7.50 (t, *J* = 8.2 Hz, 1H), 7.00 (d, *J* = 7.9 Hz, 2H), 3.19 (t, *J* = 7.0 Hz, 4H), 2.98 (t, *J* = 7.8 Hz), 2.29 (m, 4H).

^{13}C NMR (125 MHz, $CDCl_3$): δ 161.4, 136.5, 131.9, 131.3, 130.7, 129.7, 128.1, 126.5, 126.5, 126.3, 126.1, 125.9, 124.5, 123.2, 122.4, 120.1, 38.4, 33.1, 30.4 (One aromatic signal is missing from the spectrum due to overlap).

HRMS (ESI) exact mass calcd for $C_{39}H_{34}N$ ($[M+H]^+$): 516.2686, found 516.2684.

EA anal. calcd for $C_{39}H_{33}N$: C, 90.83%; H, 6.45%; N, 2.72%. Found: C, 86.13%; H, 6.43%; N, 2.69%. Repeat found: C, 86.32%; H, 6.38%; N, 2.74%.

4 Conclusion and Future perspectives

Project summary

The synthetic contributions described in this document are marked improvements over previous model asphaltene syntheses and provide a high benchmark for future synthetic approaches to this challenging class of molecules. For the first time, a range of G1 and G2 molecules have been synthesized and rigorously purified using robust reactions allowing for the delivery of gram-scale quantities of model compounds. The development of this chemistry fulfilled our promise to provide our collaborators with new required material for aggregation studies. Additionally, this research leaves ample room for future endeavors to assemble large asphaltene model molecules through island/segment coupling and other means such as multi-component reactions.

Our approach towards the preparation of G2 molecules is the first to use sp^3-sp^2 cross-coupling as a means of archipelago assembly, allowing us to avoid the problematic alkyne hydrogenation in the final step. Whereas past attempts were fraught with difficulties arising from scalability and reproducibility issues, this "traceless" bond-forming approach also allows us to synthesize these molecules by a shorter sequence and in a more convergent manner. In terms of brevity, scalability, and reproducibility, this newly developed archipelago model compound synthesis is expected to have great utility in a larger context.

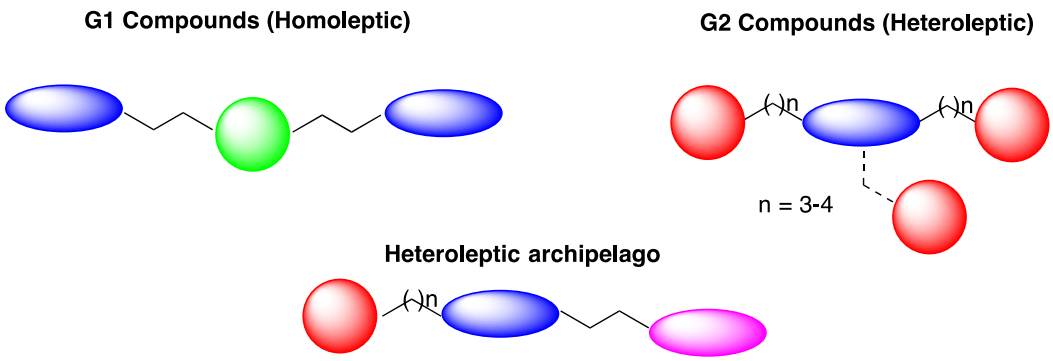
Despite the advancements in G2 model compound synthesis, we are aware of several remaining limitations: (1) The "island-tethered" nucleophiles used in the final step, while made on large scale and stable indefinitely when stored under nitrogen, are not as bench-friendly when compared to air/water resilient reagents

that can be used on the bench. (2) The functional group tolerance of the final Kumada coupling is inherently low because of the highly basic/nucleophilic Grignard reagents required for this transformation. Thus, sensitive functionalities present in actual asphaltenes must be introduced in a later step. This increases the step-count of the synthesis and undermines the simplicity of archipelago purification garnered by assembling the entire carbon skeleton in the final step.

These shortcomings have been addressed in our revamped approach to the preparation of important G1 model compounds. Here, we are unable to construct ethano-bridges between polycyclic aromatic moieties via iterative sp^3-sp^2 cross-coupling reactions, because of unavoidable competitive β-halide elimination, prompting us to develop a vinylation/hydroboration/cross-coupling sequence. Utilization of bench-stable primary alkyl boronates for this purpose is highly effective and very practical, involving bench-stable nucleophiles easily weighed out on the bench. We believe this feature will make reproducibility more facile for less-experienced synthetic chemists.

Unresolved synthetic issues, new targets, and future work

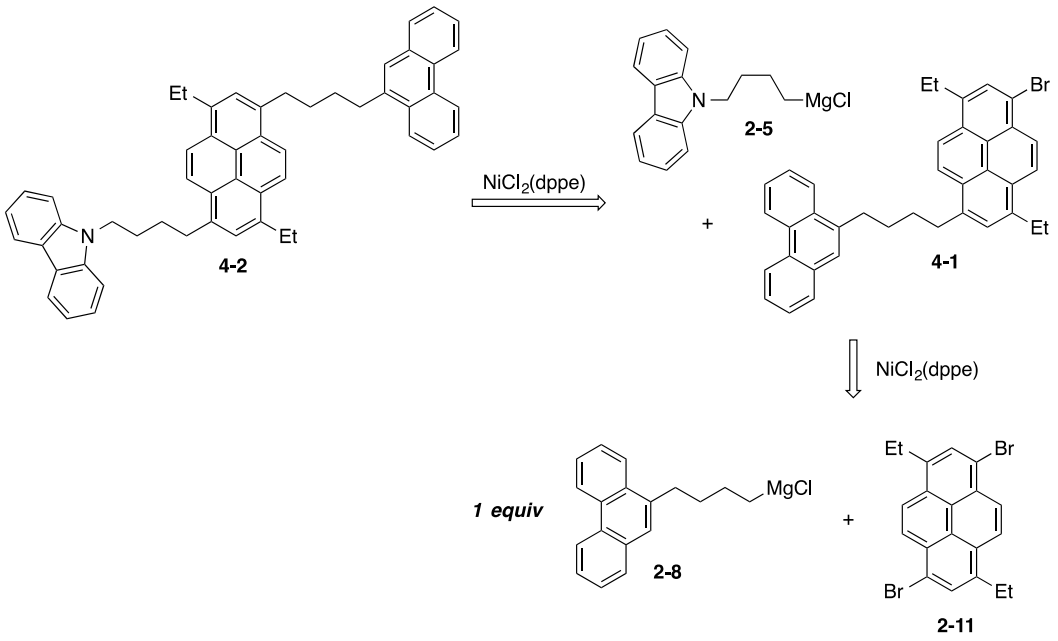
One issue our group has yet to resolve is the synthesis of "heteroleptic" archipelago model compounds, i.e. compounds with multiple different polycyclic terminal residues linked to an internal aromatic "anchor." All of the syntheses of archipelago-type model asphaltene compounds comprising three or more islands provide compounds with matching terminal islands, which we term "homoleptic." This is a function of the manner by which they are synthesized (Scheme 4-1). Thus, a robust approach towards the assembly of three-island systems with three different aromatic residues is highly desirable.



Scheme 4-1. Homoleptic vs. heteroleptic archipelago model asphaltene compounds

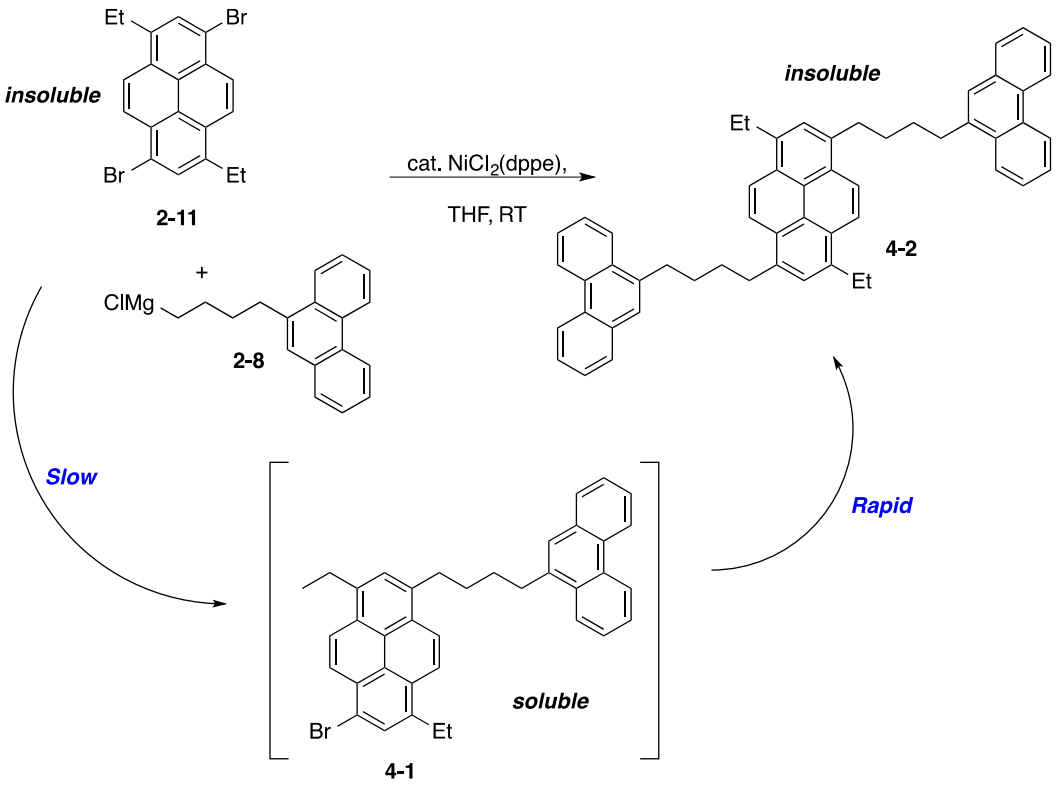
Heteroleptic archipelago synthesis. Sequential cross-coupling?

Preliminary attempts were made to synthesize heteroleptic archipelago-type compounds based on the G2 scaffold via iterative cross-coupling sequences using different aromatic-tethered nucleophiles (Scheme 4-2). Our initial retrosynthetic approach was to isolate the singly cross-coupled product (**4-1**) from a controlled Kumada coupling using a 1 : 1 mixture **2-8** and **2-11**. If successful, a final cross-coupling of monobromide **4-1** with the carbazole-based nucleophile **2-5** would provide the novel, heteroleptic, non-symmetrical, three-island system **4-2**. This strategy requires that there be a substantial rate difference between the two cross-coupling reactions.



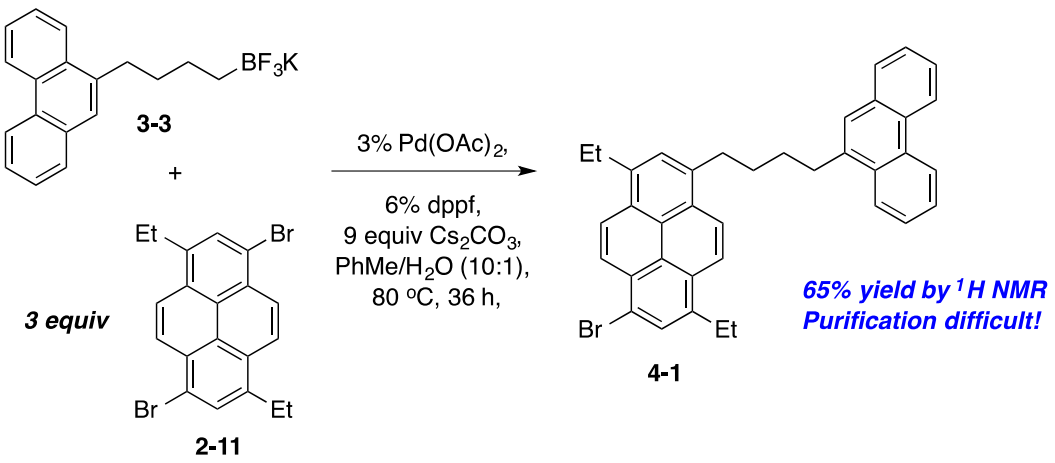
Scheme 4-2. Retrosynthetic analysis for the synthesis of non-nsymmetrical archipelago compound **4-2**

In practice, however, the results were inconsistent with this hypothesis. As previously demonstrated, carbon-carbon bond formation is facile, but controlling the reaction to isolate the "mono-coupled" product proved to be a challenge, arising from the relative solubilities of reactants, products, and intermediates (Scheme 4-3). The reaction begins as heterogeneous due to the insolubility of dibromide **2-11** in ethereal solvents. The reaction ends up heterogeneous as well, because the symmetrical three-island systems precipitate from the product mixture. Yet the reaction briefly becomes homogenous, as the "mono-coupled" adduct **4-1** is more soluble. Thus, the soluble intermediate **4-1** reacts rapidly with another nucleophile to form the symmetrical three-island system, making clean isolation impossible.



Scheme 4-3. Solubility issues hampering the isolation of **4-1**

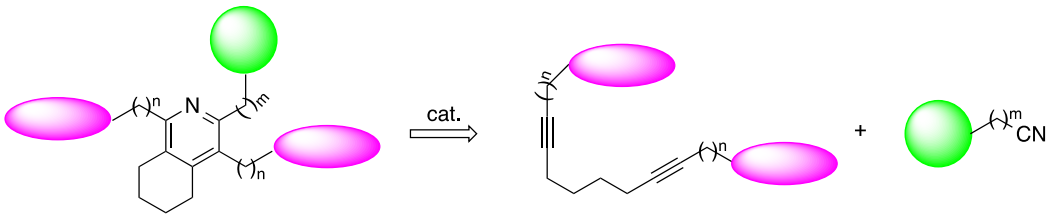
Eventually, the solubility issue was addressed by adopting the heterogeneous, biphasic Suzuki cross-coupling of the analogous boronate (**3-3**), manipulating the stoichiometry to favor the formation of the 1 : 1 adduct **4-1** (Equation 4-1). Unfortunately, purification of the intermediate presented a challenge due to the relative insolubility of the remaining components in the product mixture, prohibiting fractional crystallization or precipitation. Column chromatography was performed, but failed to yield pure **4-1** to carry forward. At this point, recognizing that the synthesis of heteroleptic archipelagos requires introducing orthogonal methodology into the strategy, sequential cross-coupling reactions were abandoned.



Equation 4-1. Utilization of Suzuki coupling for the synthesis of **4-1**

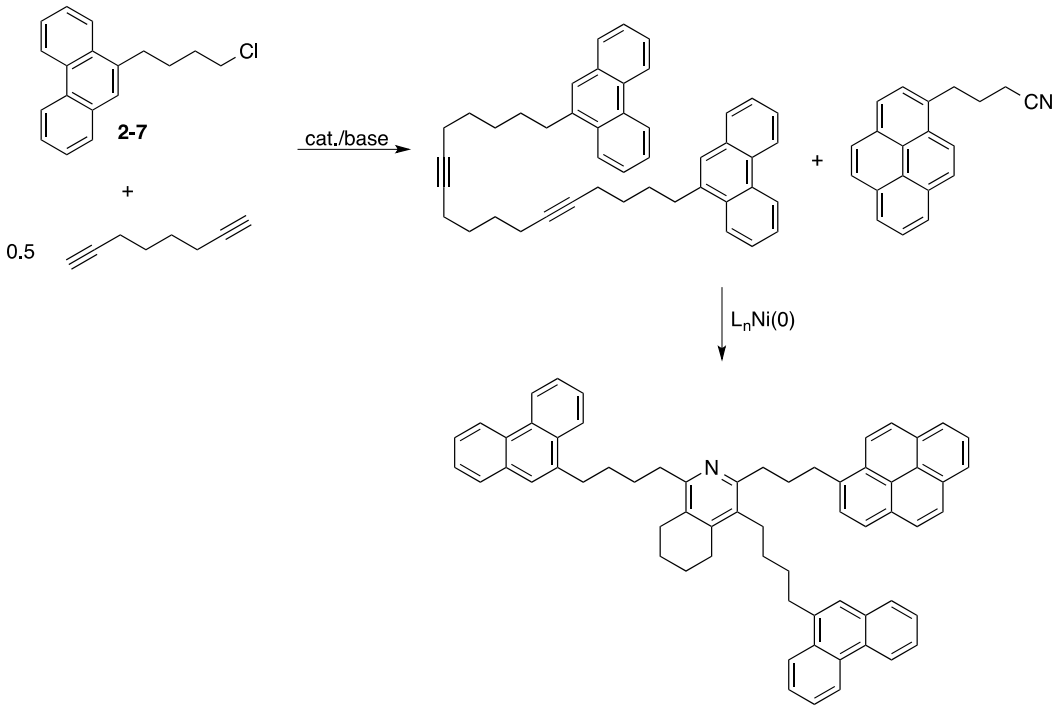
4.1.1 Multi-component reactions as a means towards complex archipelago assembly

Another approach to the synthesis of non-symmetrical or similarly complex archipelagos is to exploit the use of multi-component reactions (MCRs). Given the ubiquity of basic pyridines in natural asphaltene samples, we were enamored with the possibility of assembling heteroleptic archipelago compounds via a formal [2 + 2 + 2] reaction between a symmetrical "island-tethered" diyne and an "island-tethered" alkylnitrile (Equation 4-2).



Equation 4-2. Potential formal [2 + 2 + 2] reaction as a means towards "heteroleptic" archipelago model compounds

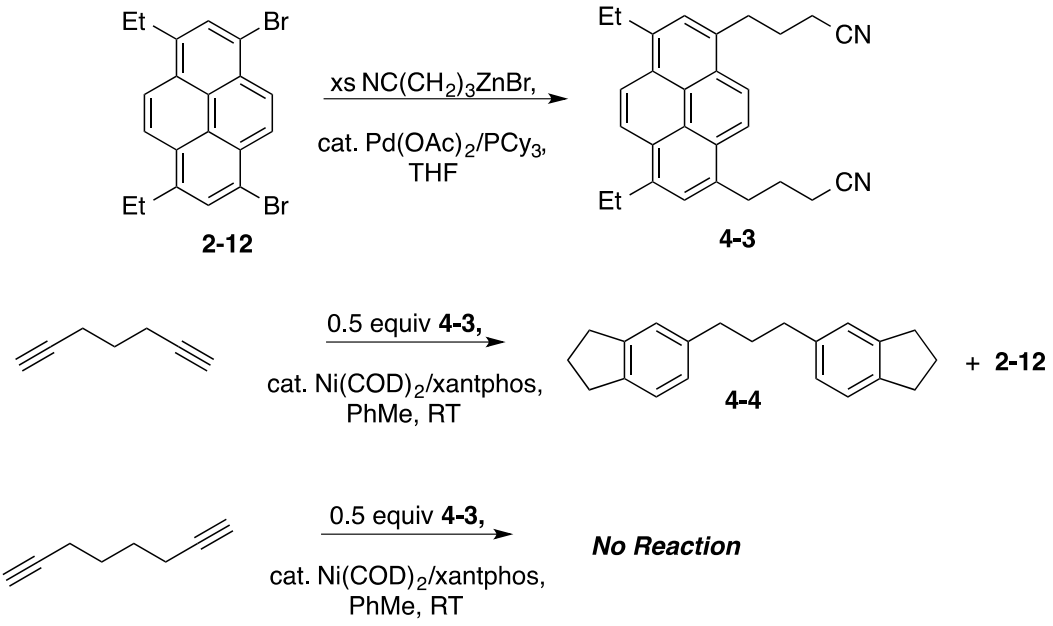
To successfully execute this sequence, we need a robust method for synthesizing the "island-tethered" diynes, as well as a highly efficient metal-catalyzed [2 + 2 + 2] reaction. We envisioned the former being accomplished via a twofold alkyl-Sonagashira reaction (Scheme 4-4), of which attractive palladium-[221] and nickel-[117,222,223]-catalyzed processes have been previously reported. The latter, we predicted, could be accomplished via nickel-catalyzed reactions published by the Louie group.[224-226]



Scheme 4-4. An example of a plausible MCR based route towards pyridine anchored archipelagos

To test the efficacy of such a sequence, we attempted the [2 + 2 + 2] reaction on bis(cyanoalkyl)pyrene **4-3** with simpler, commercially available diynes (Scheme 4-5). Dinitrile **4-3** was made via the two-fold Negishi coupling of dibromide **2-12** with excess of 3-cyanopropylzinc bromide. Unfortunately, using 1,6-heptadiyne

under Louie's optimized conditions, only the alkyne trimerization product **4-4** was isolated, revealing that the terminal alkyne is more reactive than the nitrile. We next used a longer terminal diyne, hoping to allow incorporation of the nitrile into the product. Unfortunately, the reaction with 1,7-octadiyne returned only starting materials.



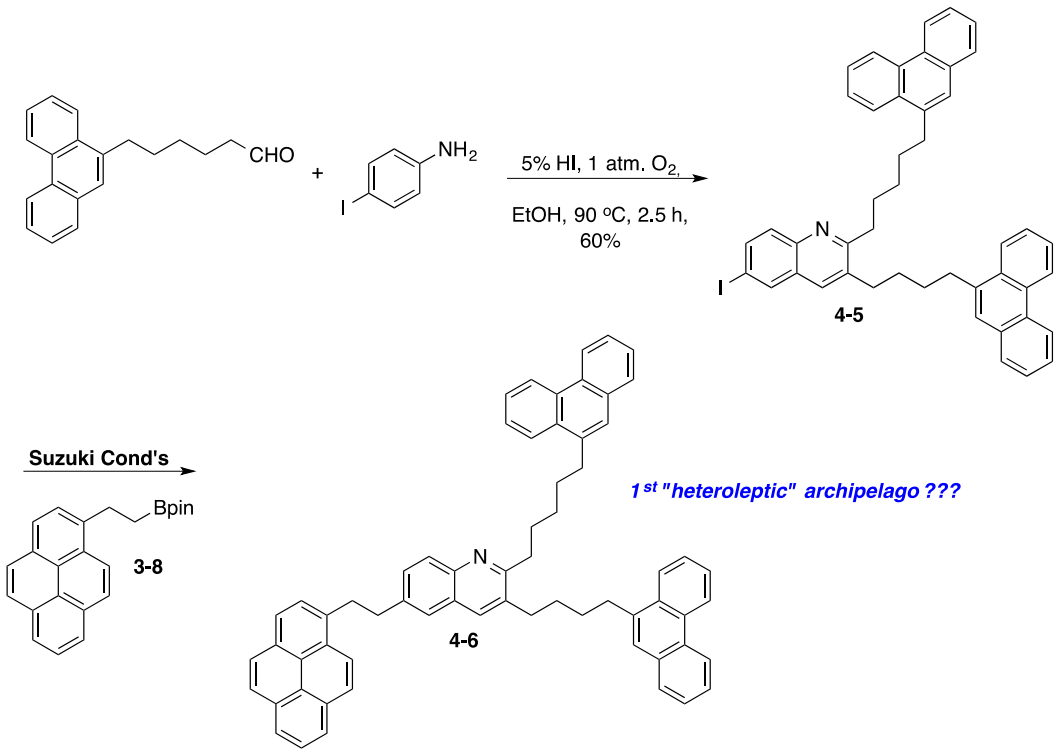
Scheme 4-5. Attempts at Ni(0) catalyzed multi-component reaction of terminal diynes with **4-3**

The literature does suggest that incorporating non-activated alkylnitriles into these reactions would present a challenge,[224-226] as these substrates generally provide lower yields unless paired with less-reactive diynes. It is also possible that these reactions could have worked had an internal diyne been used. Varying the catalyst and/or reaction conditions may yet yield a productive outcome. More straightforward acid-catalyzed cyclocondensation MCRs, which advantageously

avoid the use of transition metal catalysts, are currently used by others in the group for the "one-pot" synthesis of quinoline-anchored archipelagos.[††]

These MCRs tolerate aryl halides and may provide products that can be cross-coupled with one of many island-tethered nucleophiles reported herein. For example, 4-iodoaniline reacts cleanly with two equiv. of 6-(phenanthren-9-yl)hexanal under "oxidative" acid-catalysis to provide the unsymmetrical homoleptic three-island iodoquinoline **4-5** (Scheme 4-6). This compound can be isolated as a pure compound via a conventional workup followed by crystallization from hot ethanol. Archipelago **4-5** is primed for cross coupling with alkylboronates (e.g., **3-8**) to furnish a series of heteroleptic archipelago-type model asphaltene compounds, exemplified by **4-6**.

[††] David Scott, along with contributions from former group members Terry Heidt and Wang Xi, developed these multi-component reactions. Their publication is forthcoming.



Scheme 4-6. Potential approach towards a "heteroleptic" archipelago utilizing a multi-component reaction/cross-coupling sequence

Final remarks

The goal of this thesis research was to develop efficient and scalable approaches to the total synthesis of model asphaltene compounds. These goals were largely met, as a selection of high-purity archipelago model compounds have been delivered to academic and industry collaborators at gram- or near gram-scale via concise, selective reaction sequences. Cross-coupling reactions utilizing sp^3-hybridized carbon centers proved to be the key to our success in assembling these large structures. Major improvements in the genesis of this approach include the use of bench-stable alkylboronates and utilization of the Matteson homologation reaction for conveniently extending the tether length between aromatic residues. The compounds created from these synthetic efforts will help us gain insight into the actual structures present in natural asphaltenes. As the understanding of

asphaltene composition becomes more precise, new synthetic approaches for pertinent model compounds will as well.

5 Bibliography

(1) Teare, M.; Burrowes, A.; Baturin-Pollock, C.; Rokosh, D.; Evans, C.; Marsh, R.; Ashrafi, B.; Tamblyn, C.; Ito, S.; Willwerth, A.; Yemane, M.; Fong, J.; Kirsch, M.-A.; Crowfoot, C.; Board, E. R. C., Ed.; Energy Resources Conservation Board: Calgary, Alberta, 2013. http://pubs.acs.org/doi/pdf/10.1021/bk-2006-STYG.ch014 (accessed Aug 18, 2015)

(2) Pomerantz, A. E.; Hammond, M. R.; Morrow, A. L.; Mullins, O. C.; Zare, R. N. *Energy Fuels* **2009**, *23*, 1162-1168.

(3) Akbarzadeh, K.; Hmmami, A.; Kharrat, A.; Zhang, D.; Allenson, S.; Creek, J.; Kabir, S.; Jamaluddin, A. J.; Marshall, A. G.; Rodgers, R. P.; Mullins, O. C.; Solbakken, T. *Asphaltenes - Problematic but rich in potential*, 2007. https://www.slb.com/~/media/Files/resources/oilfield_review/ors07/sum07/p22_43.pdf (accessed Aug 18, 2015)

(4) Creek, J. L. *Energy Fuels* **2005**, *19*, 1212-1224.

(5) Wiehe, I. A. *Ind. Eng. Chem. Res.* **1993**, *32*, 2447-2454.

(6) Ancheyta, J.; Betancourt, G.; Centeno, G.; Marroquín, G.; Alonso, F.; Garciafigueroa, E. *Energy Fuels* **2002**, *16*, 1438-1443.

(7) Austen, I. In *The New York Times* New York, USA, May 18, 2013, p A1.

(8) Gray, M. R.; Tykwinski, R. R.; Stryker, J. M.; Tan, X. *Energy Fuels* **2011**, *25*, 3125-3134.

(9) Mullins, O. C. S., E. Y.; Hammami, A.; Marshall, A. G. *Asphaltenes, Heavy Oils, and Petroleomics*; Springer: New York, 2007.

(10) Strausz, O. P.; Lown, E. M. *The Chemistry of Alberta Oil Sands, Bitumens and Heavy Oils*; Alberta Energy Research Institute: Calgary, 2003.

(11) Murgich, J.; Abanero, J. A.; Strausz, O. P. *Energy Fuels* **1999**, *13*, 278-286.

(12) McMillen, D. F.; Golden, D. M. *Annu. Rev. Phys. Chem.* **1982**, *33*, 493-532.

(13) Speight, J. G. *Oil Gas Sci. Technol.* **2004**, *59*, 467-477.

(14) Shafi, R.; Hutchings, G. J. *Catal. Today* **2000**, *59*, 423-442.

(15) Bej, S. K.; Maity, S. K.; Turaga, U. T. *Energy Fuels* **2004**, *18*, 1227-1237.

(16) Heavy-Duty Engine and Vehicle Standards and Highway Diesel Fuel Sulfur Control Requirements E.P.A, U. S., Ed. Ann Arbor, Mi, 2000. http://www.epa.gov/otaq/highway-diesel/regs/f00057.pdf (accessed Aug 18, 2015)

(17) sigmaaldrich.com/catalog/product/aldrich/479411?lang=en&region=CA.

(18) Kuehm-Caubère, C.; Adach-Becker, S.; Fort, Y.; Caubère, P. *Tetrahedron* **1996**, *52*, 9087-9092.

(19) Groenzin, H.; Mullins, O. C. *Energy Fuels* **2000**, *14*, 677-684.

(20) Sheremata, J. M.; Gray, M. R.; Dettman, H. D.; McCaffrey, W. C. *Energy Fuels* **2004**, *18*, 1377-1384.

(21) Zhao, S.; Kotlyar, L. S.; Sparks, B. D.; Woods, J. R.; Gao, J.; Chung, K. H. *Fuel* **2001**, *80*, 1907-1914.

(22) Agrawala, M.; Yarranton, H. W. *Ind. Eng. Chem. Res.* **2001**, *40*, 4664-4672.

(23) Moschopedis, S. E.; Speight, J. G. *Fuel* **1976**, *55*, 187-192.

(24) Merino-Garcia, D.; Andersen, S. I. *Pet. Sci. Technol.* **2003**, *21*, 507-525.

(25) Sheu, E. Y.; Liang, K. S.; Sinha, S. K.; Overfield, R. E. *J. Colloid Interface Sci.* **1992**, *153*, 399-410.

(26) Groenzin, H.; Mullins, O. C.; Eser, S.; Mathews, J.; Yang, M.-G.; Jones, D. *Energy Fuels* **2003**, *17*, 498-503.

(27) Ruiz-Morales, Y.; Mullins, O. C. *Energy Fuels* **2007**, *21*, 256-265.

(28) Yen, T. F.; Erdman, J. G.; Pollack, S. S. *Anal. Chem.* **1961**, *33*, 1587-1594.

(29) Müller, H.; Andersson, J. T.; Schrader, W. *Anal. Chem.* **2005**, *77*, 2536-2543.

(30) Panda, S. K.; Schrader, W.; al-Hajji, A.; Andersson, J. T. *Energy Fuels* **2007**, *21*, 1071-1077.

(31) Mullins, O. C.; Martínez-Haya, B.; Marshall, A. G. *Energy Fuels* **2008**, *22*, 1765-1773.

(32) Pinkston, D. S.; Duan, P.; Gallardo, V. A.; Habicht, S. C.; Tan, X.; Qian, K.; Gray, M.; Müllen, K.; Kenttämaa, H. I. *Energy Fuels* **2009**, *23*, 5564-5570.

(33) Sabbah, H.; Morrow, A. L.; Pomerantz, A. E.; Zare, R. N. *Energy Fuels* **2011**, *25*, 1597-1604.

(34) Sharma, A.; Groenzin, H.; Tomita, A.; Mullins, O. C. *Energy Fuels* **2002**, *16*, 490-496.

(35) Smith, C. M.; Savage, P. E. *Ind. Eng. Chem. Res.* **1991**, *30*, 331-339.

(36) Smith, C. M.; Savage, P. E. *Energy Fuels* **1991**, *5*, 146-155.

(37) Smith, C. M.; Savage, P. E. *Energy Fuels* **1994**, *8*, 545-551.

(38) Dutta, R. P.; McCaffrey, W. C.; Gray, M. R.; Muehlenbachs, K. *Energy Fuels* **2001**, *15*, 1087-1093.

(39) Pines, H.; Wunderlich, D. *J. Am. Chem. Soc.* **1958**, *80*, 6001-6004.

(40) Mealy, M. J.; Bailey, W. F. *J. Organomet. Chem.* **2002**, *646*, 59-67.

(41) Waack, R.; Doran, M. A. *J. Org. Chem.* **1967**, *32*, 3395-3399.

(42) Akbarzadeh, K.; Bressler, D. C.; Wang, J.; Gawrys, K. L.; Gray, M. R.; Kilpatrick, P. K.; Yarranton, H. W. *Energy Fuels* **2005**, *19*, 1268-1271.

(43) Rakotondradany, F.; Fenniri, H.; Rahimi, P.; Gawrys, K. L.; Kilpatrick, P. K.; Gray, M. R. *Energy Fuels* **2006**, *20*, 2439-2447.

(44) Chinchilla, R.; Nájera, C. *Chem. Rev.* **2007**, *107*, 874-922.

(45) Kotha, S.; Brahmachary, E.; Lahiri, K. *Eur. J. Org. Chem.* **2005**, *2005*, 4741-4767.

(46) Müller, M.; Kübel, C.; Müllen, K. *Chem. - Eur. J.* **1998**, *4*, 2099-2109.

(47) Ito, S.; Wehmeier, M.; Brand, J. D.; Kübel, C.; Epsch, R.; Rabe, J. P.; Müllen, K. *Chem. - Eur. J.* **2000**, *6*, 4327-4342.

(48) Nordgård, E. L. k.; Sjöblom, J. *J. Dispersion Sci. Technol.* **2008**, *29*, 1114-1122.

(49) Nordgård, E. L.; Landsem, E.; Sjöblom, J. *Langmuir* **2008**, *24*, 8742-8751.

(50) Nordgård, E. L.; Sørland, G.; Sjöblom, J. *Langmuir* **2009**, *26*, 2352-2360.

(51) Fingas, M. In *Handbook of Oil Spill Science and Technology*; John Wiley & Sons, Inc: 2014, p 51-77.

(52) Holman, M. W.; Liu, R.; Adams, D. M. *J. Am. Chem. Soc.* **2003**, *125*, 12649-12654.

(53) Langhals, H.; Lona, W. *Eur. J. Org. Chem.* **1998**, *1998*, 847-851.

(54) Mo, X.; Chen, H.-Z.; Shi, M.-M.; Wang, M. *Chem. Phys. Lett.* **2006**, *417*, 457-460.

(55) Tan, X.; Fenniri, H.; Gray, M. R. *Energy Fuels* **2007**, *22*, 715-720.

(56) Sabbah, H.; Morrow, A. L.; Pomerantz, A. E.; Mullins, O. C.; Tan, X.; Gray, M. R.; Azyat, K.; Tykwinski, R. R.; Zare, R. N. *Energy Fuels* **2010**, *24*, 3589-3594.

(57) Hissler, M.; Harriman, A.; Khatyr, A.; Ziessel, R. *Chem. - Eur. J.* **1999**, *5*, 3366-3381.

(58) Elangovan, A.; Wang, Y.-H.; Ho, T.-I. *Org. Lett.* **2003**, *5*, 1841-1844.

(59) Connor, D. M.; Allen, S. D.; Collard, D. M.; Liotta, C. L.; Schiraldi, D. A. *J. Org. Chem.* **1999**, *64*, 6888-6890.

(60) Francisco, M. A.; Garcia, R.; Chawla, B.; Yung, C.; Qian, K.; Edwards, K. E.; Green, L. A. *Energy Fuels* **2011**, *25*, 4600-4605.

(61) Dickie, J. P.; Yen, T. F. *Anal. Chem.* **1967**, *39*, 1847-1852.

(62) Yin, C.-X.; Tan, X.; Müllen, K.; Stryker, J. M.; Gray, M. R. *Energy Fuels* **2008**, *22*, 2465-2469.

(63) Cardozo, S. D.; Schulze, M.; Tykwinski, R. R.; Gray, M. R. *Energy Fuels* **2015**, *29*, 1494-1502.

(64) Littler, B. J.; Ciringh, Y.; Lindsey, J. S. *J. Org. Chem.* **1999**, *64*, 2864-2872.

(65) Richeter, S.; Hadj-Aissa, A.; Taffin, C.; van der Lee, A.; Leclercq, D. *Chem. Commun.* **2007**, 2148-2150.

(66) Littler, B. J.; Miller, M. A.; Hung, C.-H.; Wagner, R. W.; O'Shea, D. F.; Boyle, P. D.; Lindsey, J. S. *J. Org. Chem.* **1999**, *64*, 1391-1396.

(67) Wittig, G.; Schöllkopf, U. *Chem. Ber.* **1954**, *87*, 1318-1330.

(68) Bailey, W. F.; Patricia, J. J. *J. Organomet. Chem.* **1988**, *352*, 1-46.

(69) Alshareef, A. H.; Scherer, A.; Tan, X.; Azyat, K.; Stryker, J. M.; Tykwinski, R. R.; Gray, M. R. *Energy Fuels* **2011**, *25*, 2130-2136.

(70) Borton, D.; Pinkston, D. S.; Hurt, M. R.; Tan, X.; Azyat, K.; Scherer, A.; Tykwinski, R.; Gray, M.; Qian, K.; Kenttämaa, H. I. *Energy Fuels* **2010**, *24*, 5548-5559.

(71) Alshareef, A. H.; Scherer, A.; Stryker, J. M.; Tykwinski, R. R.; Gray, M. R. *Energy Fuels* **2012**, *26*, 3592-3603.

(72) Scherer, A.; Hampel, F.; Gray, M. R.; Stryker, J. M.; Tykwinski, R. R. *J. Phys. Org. Chem.* **2012**, *25*, 597-606.

(73) Wang, X.-S.; Li, Q.; Yao, C.-S.; Tu, S.-J. *Eur. J. Org. Chem.* **2008**, *2008*, 3513-3518.

(74) Tidwell, T. T. *Angew. Chem., Int. Ed.* **2008**, *47*, 1016-1020.

(75) Kozlov, N. G.; Basalaeva, L. I. *Russ. J. Gen. Chem.* **2001**, *71*, 250-256.

(76) Dean, E. W.; Stark, D. D. *J. Ind. Eng. Chem.* **1920**, *12*, 486-490.

(77) Inhoffen, H. H.; Becker, W.; Kölling, G. *Justus Liebigs Ann. Chem.* **1950**, *568*, 181-184.

(78) Velluz, L.; Valls, J.; Nominé, G. *Angew. Chem., Int. Ed. Engl.* **1965**, *4*, 181-200.

(79) Hamilton, E. J.; Fischer, H. *Helv. Chim. Acta* **1973**, *56*, 795-799.

(80) Alshareef, A. H.; Scherer, A.; Tan, X.; Azyat, K.; Stryker, J. M.; Tykwinski, R. R.; Gray, M. R. *Energy Fuels* **2012**, *26*, 1828-1843.

(81) Trost, B. M. *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 259-281.

(82) Noyori, R. *Chem. Commun.* **2005**, 1807-1811.

(83) McConville, F. X. In *Chemical Engineering in the Pharmaceutical Industry*; John Wiley & Sons, Inc.: 2010, p 407-416.

(84) Brown, C. A.; Yamashita, A. *J. Am. Chem. Soc.* **1975**, *97*, 891-892.

(85) Hoye, R. C.; Baigorria, A. S.; Danielson, M. E.; Pragman, A. A.; Rajapakse, H. A. *J. Org. Chem.* **1999**, *64*, 2450-2453.

(86) Tao, Y.; Wang, B.; Zhao, J.; Song, Y.; Qu, L.; Qu, J. *J. Org. Chem.* **2012**, *77*, 2942-2946.

(87) King, A.; Yasuda, N. In *Organometallics in Process Chemistry*; Springer Berlin Heidelberg: 2004; Vol. 6, p 205-245.

(88) Johansson Seechurn, C. C. C.; Kitching, M. O.; Colacot, T. J.; Snieckus, V. *Angew. Chem., Int. Ed.* **2012**, *51*, 5062-5085.

(89) Bäckvall, J.-E. *Palladium-Catalyzed Cross Couplings in Organic Synthesis*, The Royal Swedish Academy of Sciences, 2010.

(90) Yang, L.-M.; Huang, L.-F.; Luh, T.-Y. *Org. Lett.* **2004**, *6*, 1461-1463.

(91) Iglesias, M. J.; Prieto, A.; Nicasio, M. C. *Org. Lett.* **2012**, *14*, 4318-4321.

(92) Hadei, N.; Kantchev, E. A. B.; O'Brie, C. J.; Organ, M. G. *Org. Lett.* **2005**, *7*, 3805-3807.

(93) Mee, S. P. H.; Lee, V.; Baldwin, J. E. *Angew. Chem., Int. Ed.* **2004**, *43*, 1132-1136.

(94) Dreher, S. D.; Lim, S.-E.; Sandrock, D. L.; Molander, G. A. *J. Org. Chem.* **2009**, *74*, 3626-3631.

(95) Lee, J.-Y.; Fu, G. C. *J. Am. Chem. Soc.* **2003**, *125*, 5616-5617.

(96) Yi, C.; Hua, R. *J. Org. Chem.* **2006**, *71*, 2535-2537.

(97) Cabri, W.; Candiani, I. *Acc. Chem. Res.* **1995**, *28*, 2-7.

(98) Werner, E. W.; Sigman, M. S. *J. Am. Chem. Soc.* **2011**, *133*, 9692-9695.

(99) Koga, N.; Obara, S.; Kitaura, K.; Morokuma, K. *J. Am. Chem. Soc.* **1985**, *107*, 7109-7116.

(100) Pompeo, M.; Froese, R. D. J.; Hadei, N.; Organ, M. G. *Angew. Chem., Int. Ed.* **2012**, *51*, 11354-11357.

(101) Kerber, W. D.; Koh, J. H.; Gagné, M. R. *Org. Lett.* **2004**, *6*, 3013-3015.

(102) Yoshida, H.; Yamaryo, Y.; Ohshita, J.; Kunai, A. *Tetrahedron Lett.* **2003**, *44*, 1541-1544.

(103) Miller, W. D.; Fray, A. H.; Quatroche, J. T.; Sturgill, C. D. *Org. Process Res. Dev.* **2007**, *11*, 359-364.

(104) Jana, R.; Pathak, T. P.; Sigman, M. S. *Chem. Rev.* **2011**, *111*, 1417-1492.

(105) Dickstein, J. S.; Curto, J. M.; Gutierrez, O.; Mulrooney, C. A.; Kozlowski, M. C. *J. Org. Chem.* **2013**, *78*, 4744-4761.

(106) Liu, C.-Y.; Ren, H.; Knochel, P. *Org. Lett.* **2006**, *8*, 617-619.

(107) Tamao, K.; Kodama, S.; Nakajima, I.; Kumada, M.; Minato, A.; Suzuki, K. *Tetrahedron* **1982**, *38*, 3347-3354.

(108) Miyaura, N. *J. Organomet. Chem.* **2002**, *653*, 54-57.

(109) Miyaura, N.; Ishiyama, T.; Sasaki, H.; Ishikawa, M.; Sato, M.; Suzuki, A. *J. Am. Chem. Soc.* **1989**, *111*, 314-321.

(110) Sun, H.-Y.; Hall, D. G. *Nat Chem* **2014**, *6*, 561-562.

(111) Labadie, J. W.; Stille, J. K. *J. Am. Chem. Soc.* **1983**, *105*, 6129-6137.

(112) Green, J. C.; Herbert, B. J.; Lonsdale, R. *J. Organomet. Chem.* **2005**, *690*, 6054-6067.

(113) Valente, C.; Belowich, M. E.; Hadei, N.; Organ, M. G. *Eur. J. Org. Chem.* **2010**, *2010*, 4343-4354.

(114) Netherton, M. R.; Dai, C.; Neuschütz, K.; Fu, G. C. *J. Am. Chem. Soc.* **2001**, *123*, 10099-10100.

(115) Barrios-Landeros, F.; Carrow, B. P.; Hartwig, J. F. *J. Am. Chem. Soc.* **2009**, *131*, 8141-8154.

(116) Schley, N. D.; Fu, G. C. *J. Am. Chem. Soc.* **2014**, *136*, 16588-16593.

(117) Pérez García, P. M.; Ren, P.; Scopelliti, R.; Hu, X. *ACS Catal.* **2015**, *5*, 1164-1171.

(118) Jones, G. D.; Martin, J. L.; McFarland, C.; Allen, O. R.; Hall, R. E.; Haley, A. D.; Brandon, R. J.; Konovalova, T.; Desrochers, P. J.; Pulay, P.; Vicic, D. A. *J. Am. Chem. Soc.* **2006**, *128*, 13175-13183.

(119) Alshareef, A. H.; Azyat, K.; Tykwinski, R. R.; Gray, M. R. *Energy Fuels* **2010**, *24*, 3998-4004.

(120) Tamao, K.; Sumitani, K.; Kiso, Y.; Zembayashi, M.; Fujioka, A.; Kodama, S.-i.; Nakajima, I.; Minato, A.; Kumada, M. *Bull. Chem. Soc. Jpn.* **1976**, *49*, 1958-1969.

(121) Ferorelli, S.; Abate, C.; Colabufo, N. A.; Niso, M.; Inglese, C.; Berardi, F.; Perrone, R. *J. Med. Chem.* **2007**, *50*, 4648-4655.

(122) Pearson, D. E.; Cowan, D.; Beckler, J. D. *J. Org. Chem.* **1959**, *24*, 504-509.

(123) Root, K. S.; Hill, C. L.; Lawrence, L. M.; Whitesides, G. M. *J. Am. Chem. Soc.* **1989**, *111*, 5405-5412.

(124) Terao, J.; Todo, H.; Begum, S. A.; Kuniyasu, H.; Kambe, N. *Angew. Chem., Int. Ed.* **2007**, *46*, 2086-2089.

(125) Vechorkin, O.; Proust, V.; Hu, X. *J. Am. Chem. Soc.* **2009**, *131*, 9756-9766.

(126) Cahiez, G.; Chaboche, C.; Duplais, C.; Moyeux, A. *Org. Lett.* **2009**, *11*, 277-280.

(127) Ren, P.; Vechorkin, O.; Csok, Z.; Salihu, I.; Scopelliti, R.; Hu, X. *Dalton Trans.* **2011**, *40*, 8906-8911.

(128) Wakabayashi, K.; Yorimitsu, H.; Oshima, K. *J. Am. Chem. Soc.* **2001**, *123*, 5374-5375.

(129) Ohmiya, H.; Wakabayashi, K.; Yorimitsu, H.; Oshima, K. *Tetrahedron* **2006**, *62*, 2207-2213.

(130) Ashby, E. C.; Walker, F. W. *J. Org. Chem.* **1968**, *33*, 3821-3828.

(131) Lewis, R. N.; Wright, J. R. *J. Am. Chem. Soc.* **1952**, *74*, 1253-1257.

(132) Pinal, R. *Org. Biomol. Chem.* **2004**, *2*, 2692-2699.

(133) Figueira-Duarte, T. M.; Müllen, K. *Chem. Rev.* **2011**, *111*, 7260-7314.

(134) Grimshaw, J.; Trocha-Grimshaw, J. *J. Chem. Soc., Perkin Trans. 1* **1972**, 1622-1623.

(135) Sato, A. H.; Maeda, M.; Mihara, S.; Iwasawa, T. *Tetrahedron Lett.* **2011**, *52*, 6284-6287.

(136) Bittermann, H.; Siegemund, D.; Malinovskii, V. L.; Häner, R. *J. Am. Chem. Soc.* **2008**, *130*, 15285-15287.

(137) Rae, I. D. *J. Chem. Educ.* **2009**, *86*, 689.

(138) Niko, Y.; Kawauchi, S.; Otsu, S.; Tokumaru, K.; Konishi, G.-i. *J. Org. Chem.* **2013**, *78*, 3196-3207.

(139) Bittermann, H.; Siegemund, D.; Malinovskii, V. L.; Häner, R. *J. Am. Chem. Soc.* **2008**, *130*, 15285-15287.

(140) Weng, J.; Mei, Q.; Ling, Q.; Fan, Q.; Huang, W. *Tetrahedron* **2012**, *68*, 3129-3134.

(141) Babu, P.; Sangeetha, N. M.; Vijaykumar, P.; Maitra, U.; Rissanen, K.; Raju, A. R. *Chem. - Eur. J.* **2003**, *9*, 1922-1932.

(142) Andreitchenko, E. V.; Clark, C. G.; Bauer, R. E.; Lieser, G.; Müllen, K. *Angew. Chem., Int. Ed.* **2005**, *44*, 6348-6354.

(143) Stockland, R. A.; Jordan, R. F. *J. Am. Chem. Soc.* **2000**, *122*, 6315-6316.

(144) Collman, J. P.; Brauman, J. I.; Madonik, A. M. *Organometallics* **1986**, *5*, 218-222.

(145) Monaghan, P. K.; Puddephatt, R. J. *J. Chem. Soc., Dalton Trans.* **1988**, 595-599.

(146) Monaghan, P. K.; Puddephatt, R. J. *Organometallics* **1985**, *4*, 1406-1412.

(147) Stockland, R. A.; Foley, S. R.; Jordan, R. F. *J. Am. Chem. Soc.* **2003**, *125*, 796-809.

(148) Nakamura, A.; Ito, S.; Nozaki, K. *Chem. Rev.* **2009**, *109*, 5215-5244.

(149) Carpenter, A. E.; McNeece, A. J.; Barnett, B. R.; Estrada, A. L.; Mokhtarzadeh, C. C.; Moore, C. E.; Rheingold, A. L.; Perrin, C. L.; Figueroa, J. S. *J. Am. Chem. Soc.* **2014**, *136*, 15481-15484.

(150) Halpern, J.; Jewsbury, R. A. *J. Organomet. Chem.* **1979**, *181*, 223-232.

(151) Fanizzi, F. P.; Maresca, L.; Pacifico, C.; Natile, G.; Lanfranchi, M.; Tiripicchio, A. *Eur. J. Inorg. Chem.* **1999**, *1999*, 1351-1358.

(152) Trnka, T. M.; Morgan, J. P.; Sanford, M. S.; Wilhelm, T. E.; Scholl, M.; Choi, T.-L.; Ding, S.; Day, M. W.; Grubbs, R. H. *J. Am. Chem. Soc.* **2003**, *125*, 2546-2558.

(153) Kelm, H. *Berichte der Bunsengesellschaft für physikalische Chemie* **1974**, *78*, 620-620.

(154) Molander, G. A.; Elia, M. D. *J. Org. Chem.* **2006**, *71*, 9198-9202.

(155) Chen, X.; Zhou, L.; Li, Y.; Xie, T.; Zhou, S. *J. Org. Chem.* **2014**, *79*, 230-239.

(156) Tellis, J. C.; Primer, D. N.; Molander, G. A. *Science* **2014**, *345*, 433-436.

(157) Sase, S.; Jaric, M.; Metzger, A.; Malakhov, V.; Knochel, P. *J. Org. Chem.* **2008**, *73*, 7380-7382.

(158) Männig, D.; Nöth, H. *Angew. Chem., Int. Ed. Engl.* **1985**, *24*, 878-879.

(159) Tucker, C. E.; Davidson, J.; Knochel, P. *J. Org. Chem.* **1992**, *57*, 3482-3485.

(160) Hartwig, J. F.; Muhoro, C. N. *Organometallics* **2000**, *19*, 30-38.

(161) Yamamoto, Y.; Fujikawa, R.; Umemoto, T.; Miyaura, N. *Tetrahedron* **2004**, *60*, 10695-10700.

(162) Hall, D. G. In *Boronic Acids*; Wiley-VCH Verlag GmbH & Co. KGaA: 2011, p 1-133.

(163) Imao, D.; Glasspoole, B. W.; Laberge, V. S.; Crudden, C. M. *J. Am. Chem. Soc.* **2009**, *131*, 5024-5025.

(164) Zhang, L.; Zuo, Z.; Leng, X.; Huang, Z. *Angew. Chem., Int. Ed.* **2014**, *53*, 2696-2700.

(165) Ding, J.; Rybak, T.; Hall, D. G. *Nat. Commun.* **2014**, *5*.

(166) Gunanathan, C.; Hölscher, M.; Pan, F.; Leitner, W. *J. Am. Chem. Soc.* **2012**, *134*, 14349-14352.

(167) Ishiyama, T.; Murata, M.; Miyaura, N. *J. Org. Chem.* **1995**, *60*, 7508-7510.

(168) Yang, C.-T.; Zhang, Z.-Q.; Tajuddin, H.; Wu, C.-C.; Liang, J.; Liu, J.-H.; Fu, Y.; Czyzewska, M.; Steel, P. G.; Marder, T. B.; Liu, L. *Angew. Chem., Int. Ed.* **2012**, *51*, 528-532.

(169) Bose, S. K.; Fucke, K.; Liu, L.; Steel, P. G.; Marder, T. B. *Angew. Chem., Int. Ed.* **2014**, *53*, 1799-1803.

(170) Yamamoto, E.; Izumi, K.; Horita, Y.; Ito, H. *J. Am. Chem. Soc.* **2012**, *134*, 19997-20000.

(171) Darses, S.; Michaud, G.; Genêt, J.-P. *Tetrahedron Lett.* **1998**, *39*, 5045-5048.

(172) Leermann, T.; Leroux, F. R.; Colobert, F. *Org. Lett.* **2011**, *13*, 4479-4481.

(173) Mkhalid, I. A. I.; Barnard, J. H.; Marder, T. B.; Murphy, J. M.; Hartwig, J. F. *Chem. Rev.* **2010**, *110*, 890-931.

(174) Chen, H.; Hartwig, J. F. *Angew. Chem., Int. Ed.* **1999**, *38*, 3391-3393.

(175) Chen, H.; Schlecht, S.; Semple, T. C.; Hartwig, J. F. *Science* **2000**, *287*, 1995-1997.

(176) Selander, N.; Willy, B.; Szabó, K. J. *Angew. Chem., Int. Ed.* **2010**, *49*, 4051-4053.

(177) Lee, C.-I.; Zhou, J.; Ozerov, O. V. *J. Am. Chem. Soc.* **2013**, *135*, 3560-3566.

(178) Boebel, T. A.; Hartwig, J. F. *J. Am. Chem. Soc.* **2008**, *130*, 7534-7535.

(179) Molander, G. A.; Ito, T. *Org. Lett.* **2001**, *3*, 393-396.

(180) Kimbrough, R. D. *Environ. Health Perspect.* **1976**, *14*, 51-56.

(181) Sato, M.; Miyaura, N.; Suzuki, A. *Chem. Lett.* **1989**, *18*, 1405-1408.

(182) Vedejs, E.; Chapman, R. W.; Fields, S. C.; Lin, S.; Schrimpf, M. R. *J. Org. Chem.* **1995**, *60*, 3020-3027.

(183) Lennox, A. J. J.; Lloyd-Jones, G. C. *Chem. Soc. Rev.* **2014**, *43*, 412-443.

(184) Lennox, A. J. J.; Lloyd-Jones, G. C. *J. Am. Chem. Soc.* **2012**, *134*, 7431-7441.

(185) Molander, G. A.; Yun, C.-S.; Ribagorda, M.; Biolatto, B. *J. Org. Chem.* **2003**, *68*, 5534-5539.

(186) Molander, G. A.; Shin, I. *Org. Lett.* **2013**, *15*, 2534-2537.

(187) Fleury-Brégeot, N.; Oehlrich, D.; Rombouts, F.; Molander, G. A. *Org. Lett.* **2013**, *15*, 1536-1539.

(188) Todesco, R. V.; Basheer, R. A.; Kamat, P. V. *Macromolecules* **1986**, *19*, 2390-2397.

(189) O'Malley, J. J.; Yanus, J. F.; Pearson, J. M. *Macromolecules* **1972**, *5*, 158-161.

(190) Tanikawa, K.; Kusabayashi, S.; Hirata, H.; Mikawa, H. *J. Polym. Sci., Part B: Polym. Lett.* **1968**, *6*, 275-280.

(191) Tanikawa, K.; Ishizuka, T.; Suzuki, K.; Kusabayashi, S.; Mikawa, H. *Bull. Chem. Soc. Jpn.* **1968**, *41*, 2719-2722.

(192) Kalyanasundaram, K.; Thomas, J. K. *J. Am. Chem. Soc.* **1977**, *99*, 2039-2044.

(193) Winnik, F. M. *Chem. Rev.* **1993**, *93*, 587-614.

(194) Lock, G. *Ber. Dtsch. Chem. Ges. (A and B Series)* **1937**, *70*, 926-930.

(195) Djerassi, C. *Chem. Rev.* **1948**, *43*, 271-317.

(196) Nonhebel, D. C. *J. Chem. Soc.* **1963**, 1216-1220.

(197) Yukawa, S.; Omayu, A.; Matsumoto, A. *Macromol. Chem. Phys.* **2009**, *210*, 1776-1784.

(198) Gumprecht, W. H. *Org. Synth.* **1968**, *48*, 30.

(199) Agency, U. S. E. P., Ed. Washington DC, 2010.

(200) Water, A. a. C. C. B. In *H128-1/11-661E*; Canada, H., Ed.; Health Canada: Ottawa, Ontario, 2010.

(201) Oseki, Y.; Fujitsuka, M.; Sakamoto, M.; Majima, T. *J. Phys. Chem. A* **2007**, *111*, 9781-9788.

(202) Diev, V. V.; Schlenker, C. W.; Hanson, K.; Zhong, Q.; Zimmerman, J. D.; Forrest, S. R.; Thompson, M. E. *J. Org. Chem.* **2012**, *77*, 143-159.

(203) Jeon, N. J.; Lee, J.; Noh, J. H.; Nazeeruddin, M. K.; Grätzel, M.; Seok, S. I. *J. Am. Chem. Soc.* **2013**, *135*, 19087-19090.

(204) Maeda, H.; Maeda, T.; Mizuno, K.; Fujimoto, K.; Shimizu, H.; Inouye, M. *Chem. - Eur. J.* **2006**, *12*, 824-831.

(205) Molander, G. A.; Brown, A. R. *J. Org. Chem.* **2006**, *71*, 9681-9686.

(206) Molander, G. A.; Rivero, M. R. *Org. Lett.* **2002**, *4*, 107-109.

(207) Molander, G. A.; Canturk, B. *Angew. Chem., Int. Ed.* **2009**, *48*, 9240-9261.

(208) Erbil, Y. H. In *Vinyl Acetate Emulsion Polymerization and Copolymerization with Acrylic Monomers*; CRC Press: 2000.

(209) Yuen, A. K. L.; Hutton, C. A. *Tetrahedron Lett.* **2005**, *46*, 7899-7903.

(210) Organ, M. G.; Avola, S.; Dubovyk, I.; Hadei, N.; Kantchev, E. A. B.; O'Brien, C. J.; Valente, C. *Chem. - Eur. J.* **2006**, *12*, 4749-4755.

(211) St. Denis, J. D.; Scully, C. C. G.; Lee, C. F.; Yudin, A. K. *Org. Lett.* **2014**, *16*, 1338-1341.

(212) Matteson, D. S.; Majumdar, D. *J. Organomet. Chem.* **1980**, *184*, C41-C43.

(213) Matteson, D. S. *Tetrahedron* **1998**, *54*, 10555-10607.

(214) Kliman, L. T.; Mlynarski, S. N.; Morken, J. P. *J. Am. Chem. Soc.* **2009**, *131*, 13210-13211.

(215) Blakemore, P. R.; Marsden, S. P.; Vater, H. D. *Org. Lett.* **2006**, *8*, 773-776.

(216) Burns, M.; Essafi, S.; Bame, J. R.; Bull, S. P.; Webster, M. P.; Balieu, S.; Dale, J. W.; Butts, C. P.; Harvey, J. N.; Aggarwal, V. K. *Nature* **2014**, *513*, 183-188.

(217) Brown, H. C.; Singh, S. M. *Organometallics* **1986**, *5*, 994-997.

(218) Brown, H. C.; Nazer, B.; Sikorski, J. A. *Organometallics* **1983**, *2*, 634-637.

(219) Hubbard, J. L. *Tetrahedron Letters* **1988**, *29*, 3197-3200.

(220) Oliveira, R. A.; Silva, R. O.; Molander, G. A.; Menezes, P. H. *Magnetic Resonance in Chemistry* **2009**, *47*, 873-878.

(221) Eckhardt, M.; Fu, G. C. *J. Am. Chem. Soc.* **2003**, *125*, 13642-13643.

(222) Vechorkin, O.; Godinat, A.; Scopelliti, R.; Hu, X. *Angew. Chem., Int. Ed.* **2011**, *50*, 11777-11781.

(223) Vechorkin, O.; Barmaz, D.; Proust, V.; Hu, X. *J. Am. Chem. Soc.* **2009**, *131*, 12078-12079.

(224) Stolley, R. M.; Duong, H. A.; Louie, J. *Organometallics* **2013**, *32*, 4952-4960.

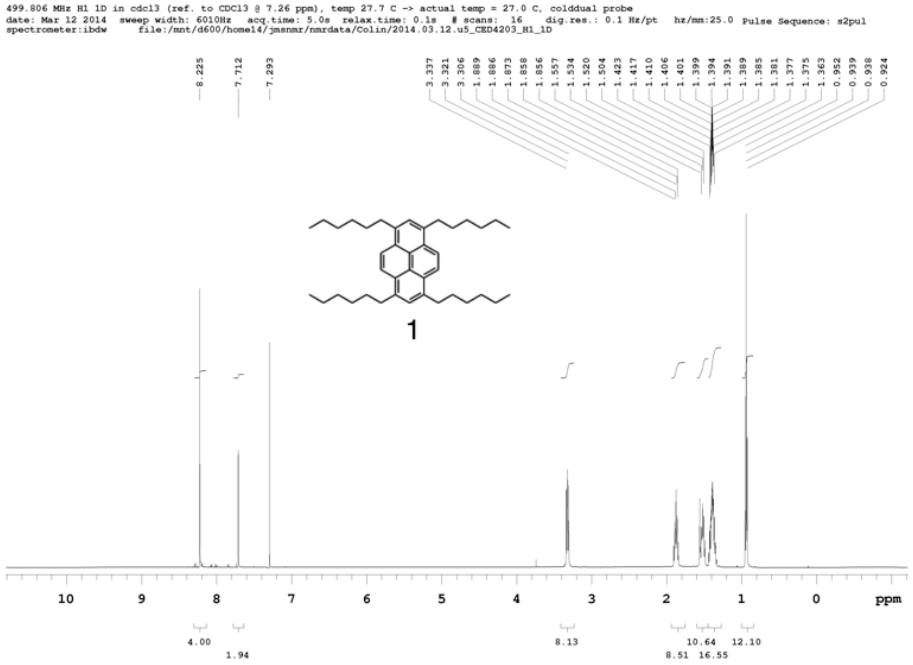
(225) Kumar, P.; Prescher, S.; Louie, J. *Angew. Chem., Int. Ed.* **2011**, *50*, 10694-10698.

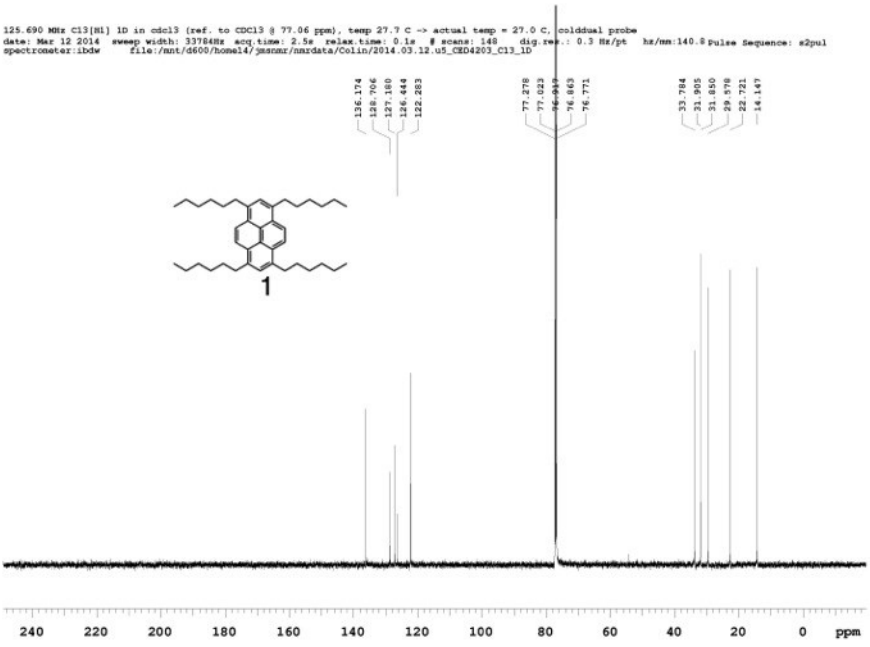
(226) McCormick, M. M.; Duong, H. A.; Zuo, G.; Louie, J. *J. Am. Chem. Soc.* **2005**, *127*, 5030-5031.

Appendix 1: Selected Copies of NMR Spectra

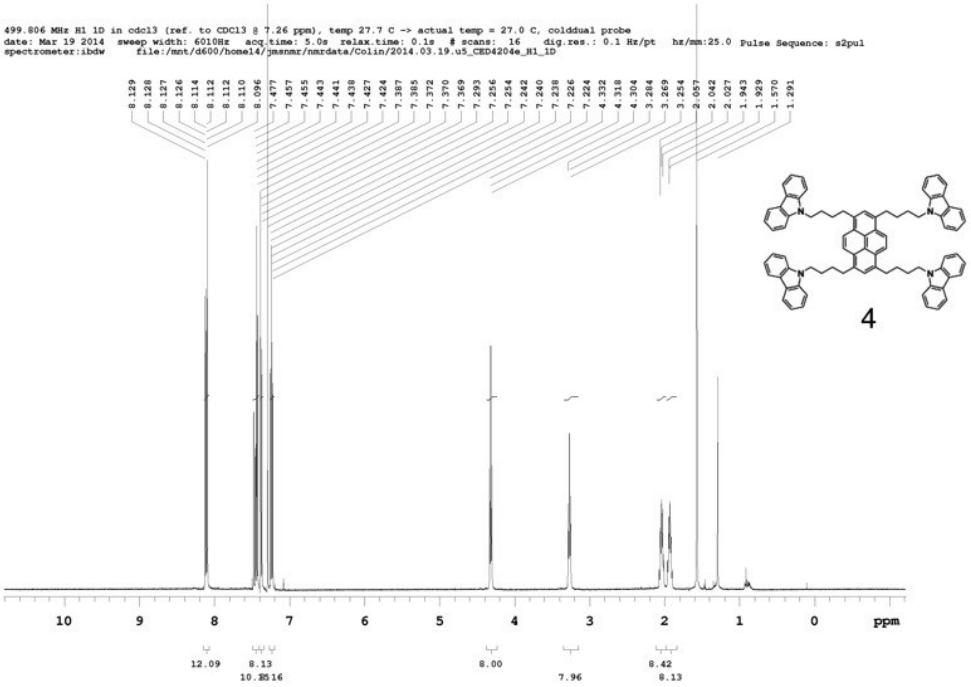
Due to low solubility, some compounds provide ^{13}C Spectra that show poor signal-to-noise ratio.

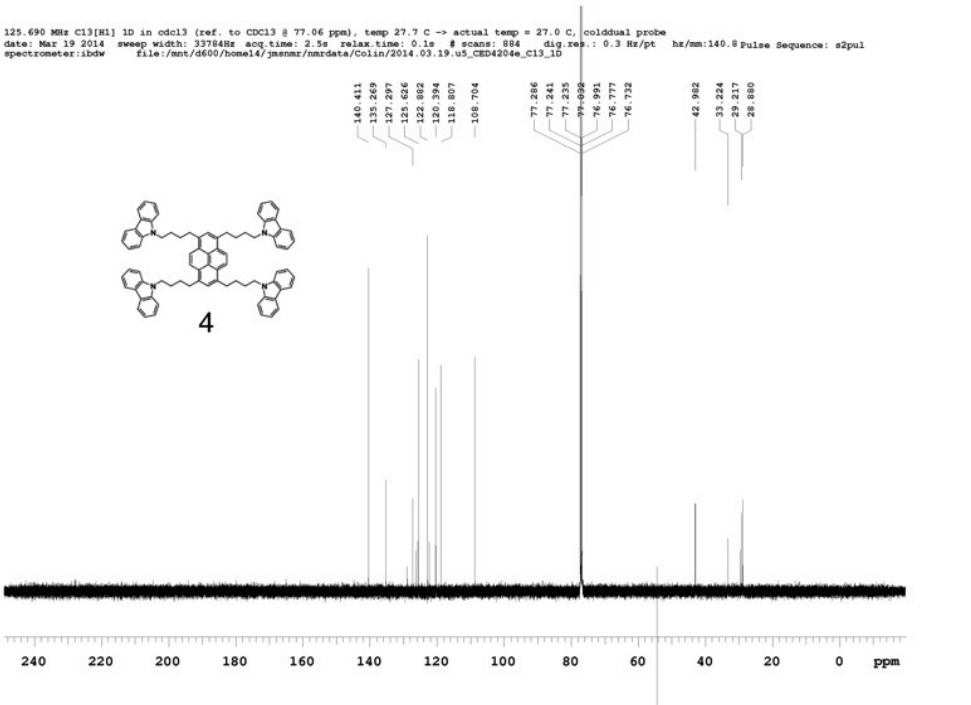
^{1}H (500 MHz) and ^{13}C (126 MHz) NMR of 2-3 in $CDCl_3$ at 25 °C



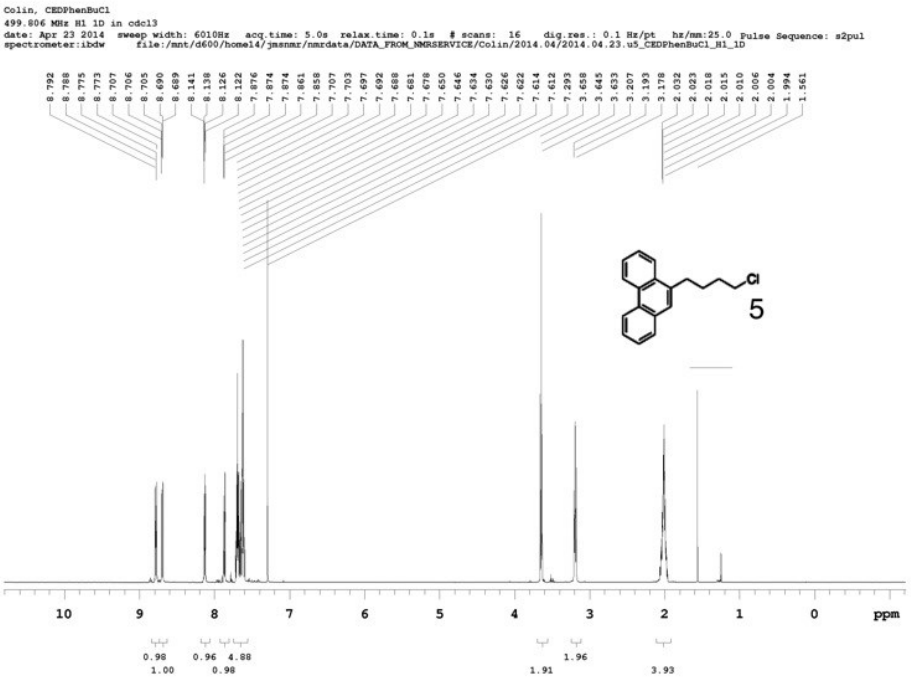


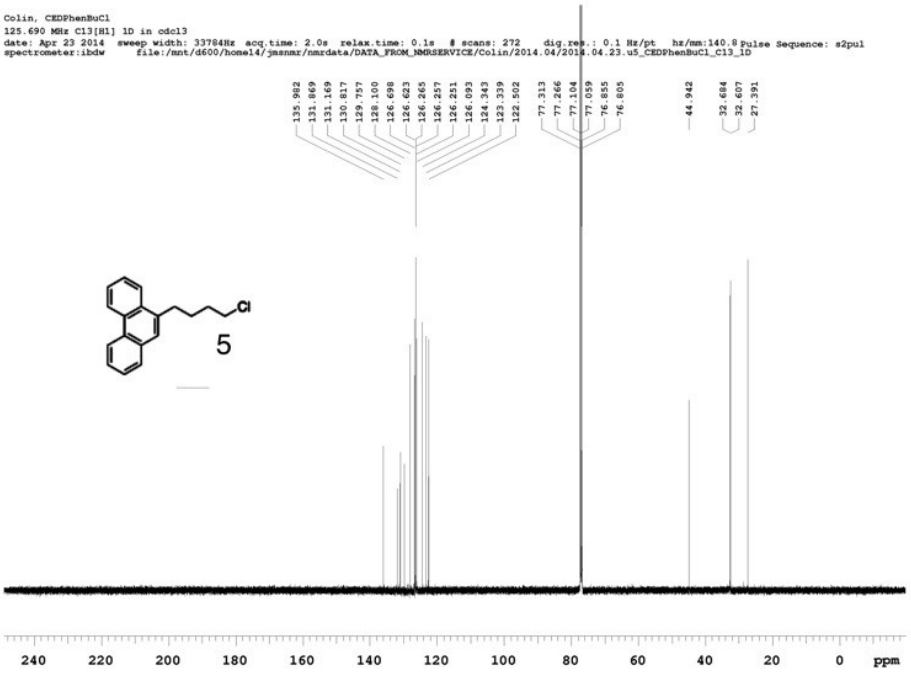
^{1}H (500 MHz) and ^{13}C (126 MHz) NMR of 2-6 in $CDCl_3$ at 25 °C



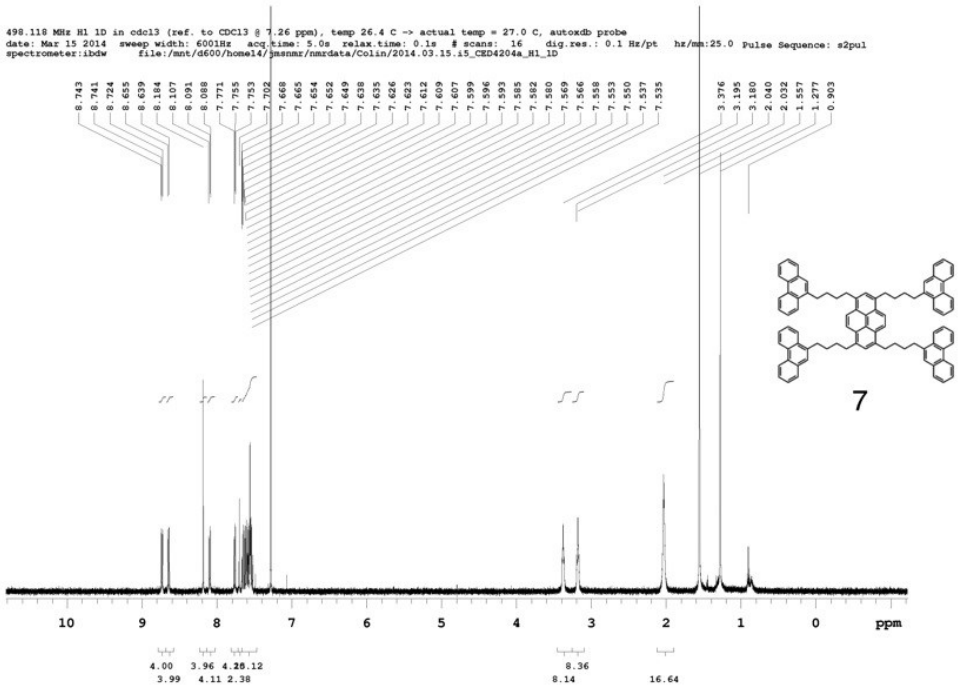


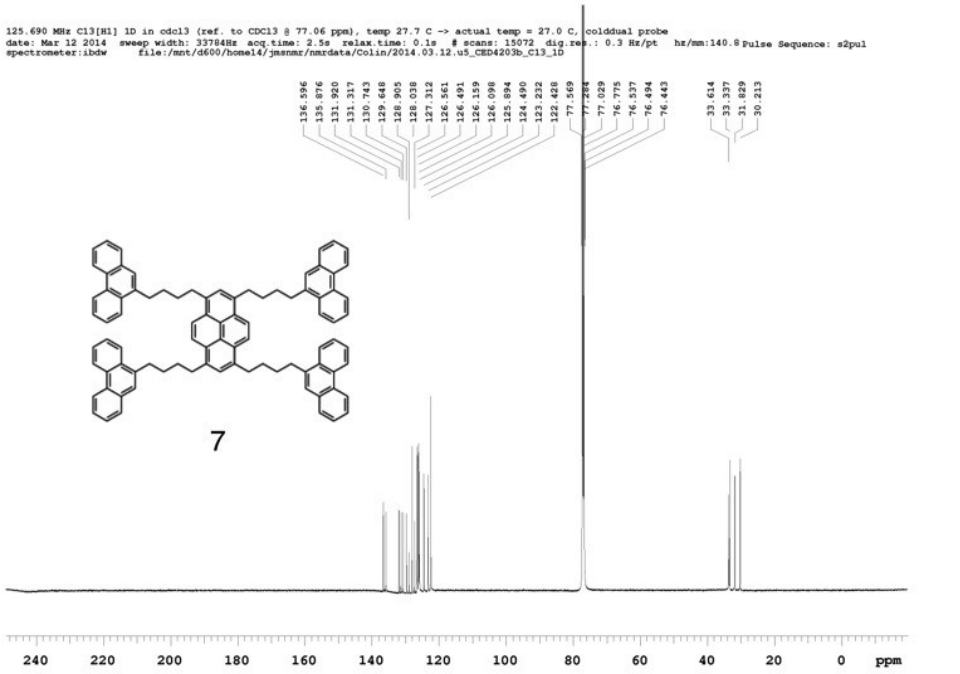
^{1}H (500 MHz) and ^{13}C (126 MHz) NMR of 2-7 in $CDCl_3$ at 25 °C



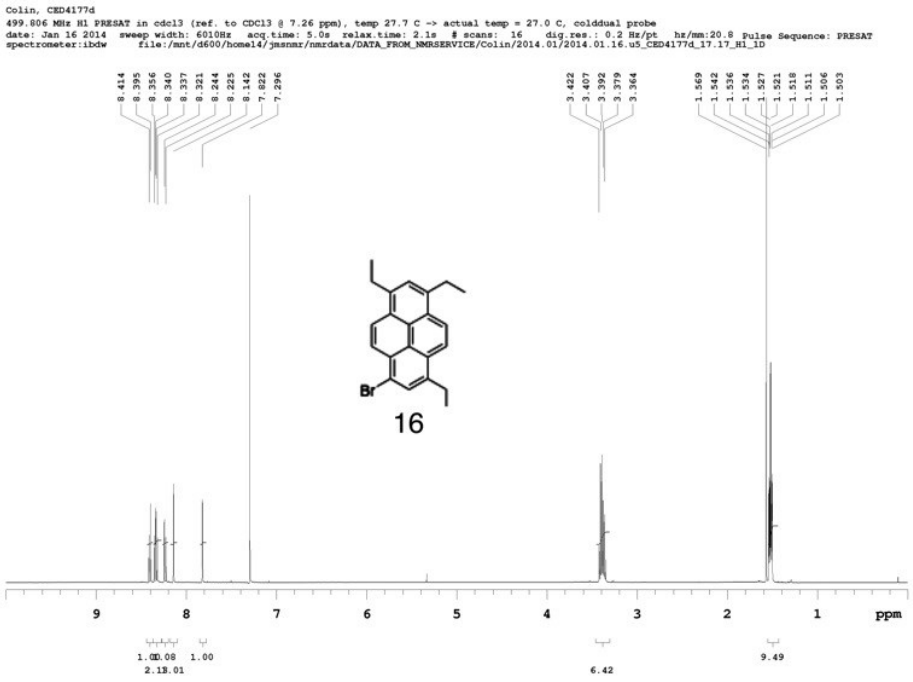


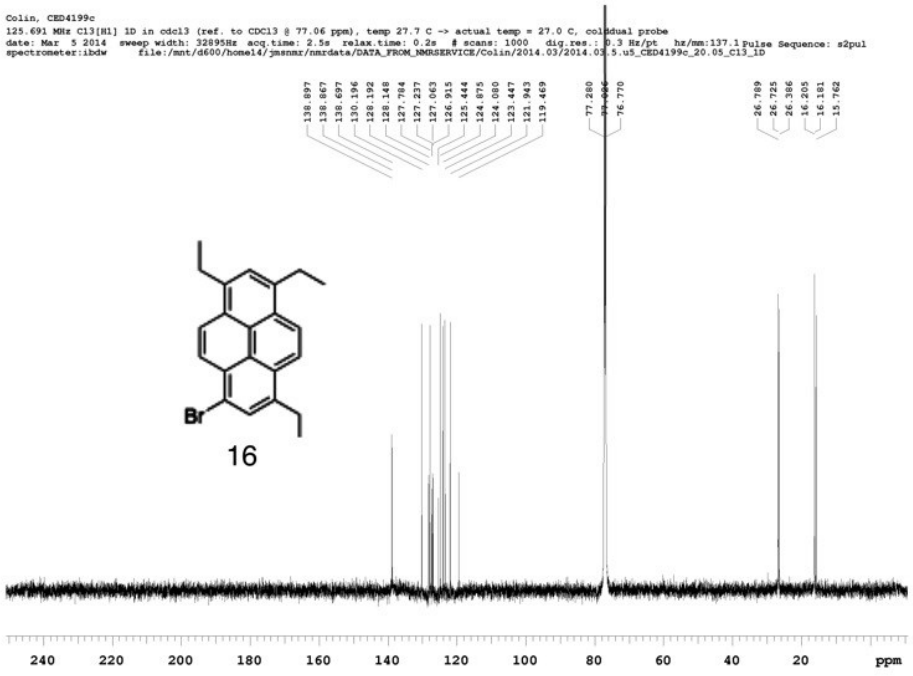
^{1}H (500 MHz) and ^{13}C (126 MHz) NMR of 2-9 in $CDCl_3$ at 25 °C



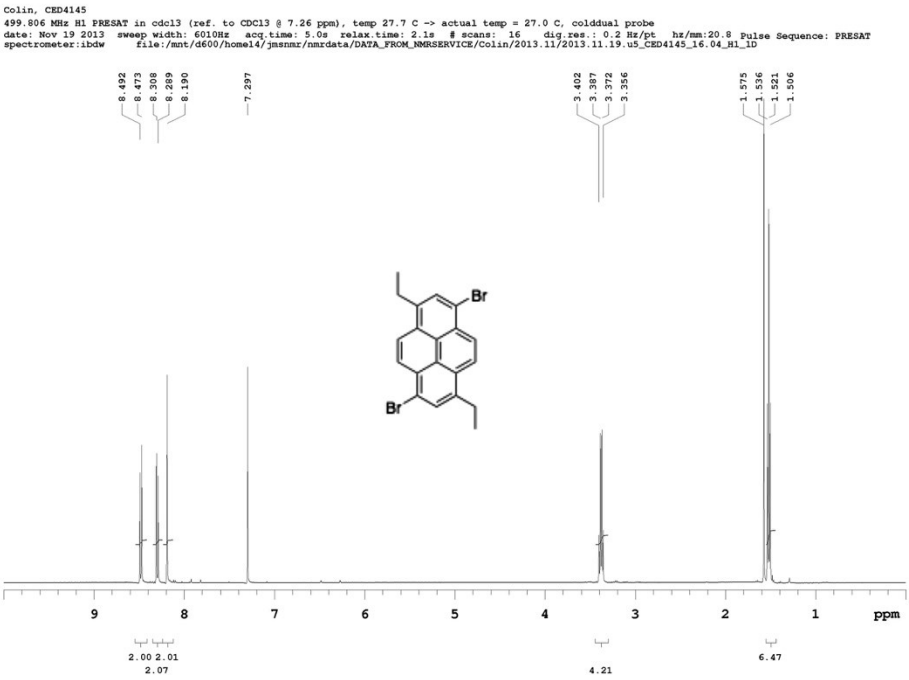


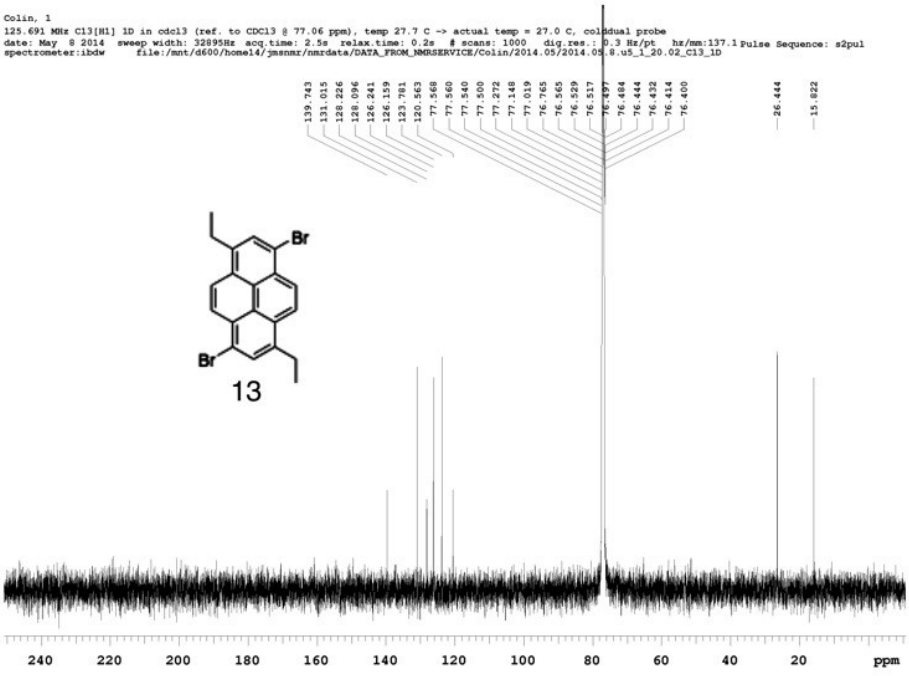
^{1}H (500 MHz) and ^{13}C (126 MHz) NMR of 2-10 in $CDCl_3$ at 25 °C



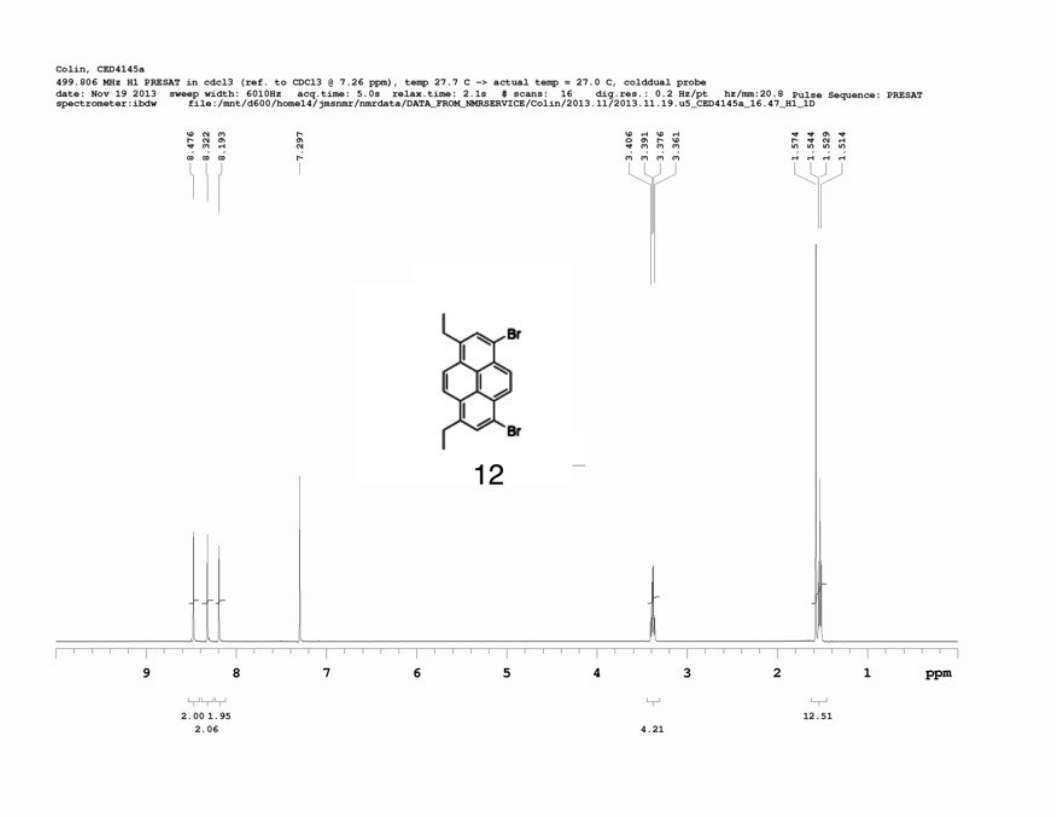


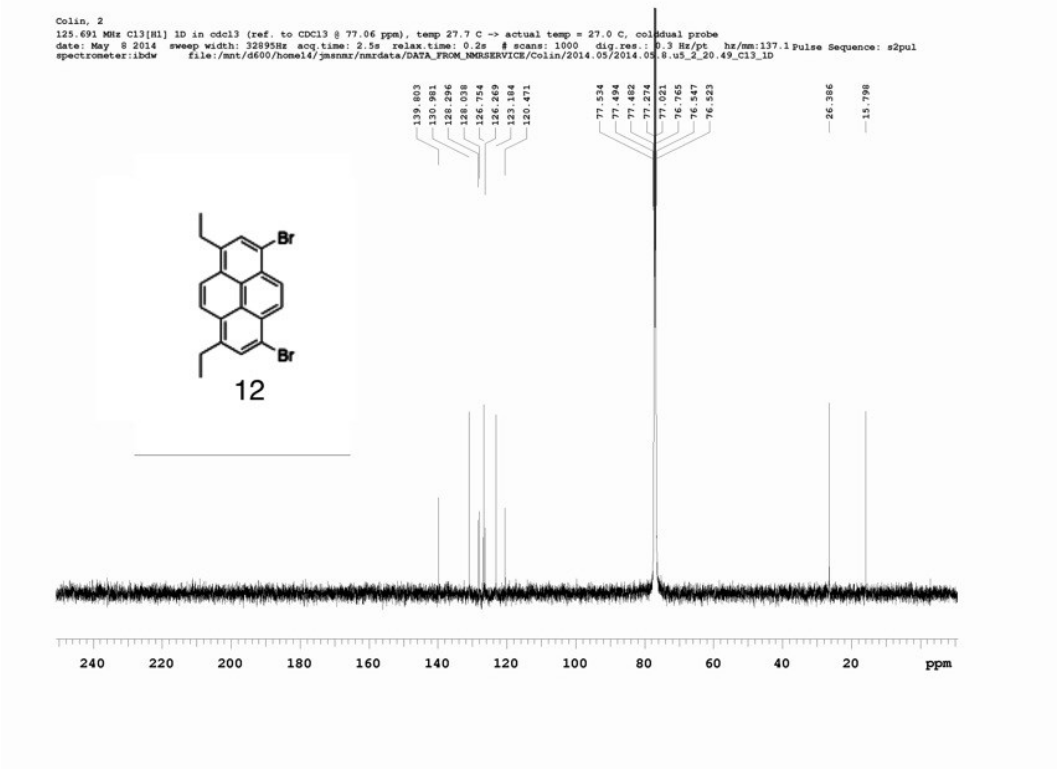
^{1}H (500 MHz) and ^{13}C (126 MHz) NMR of 2-11 in $CDCl_3$ at 25 °C



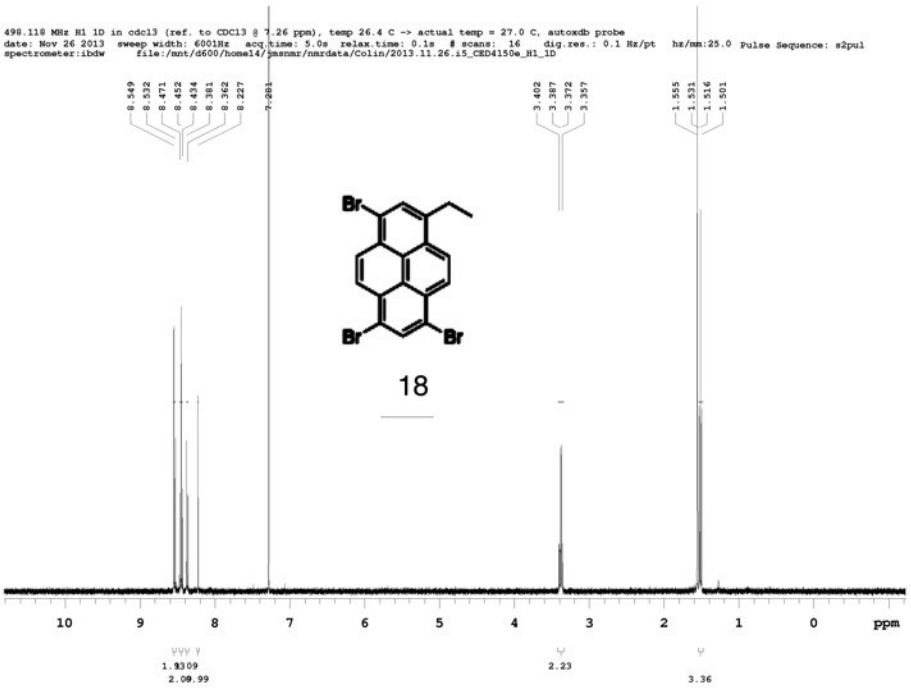


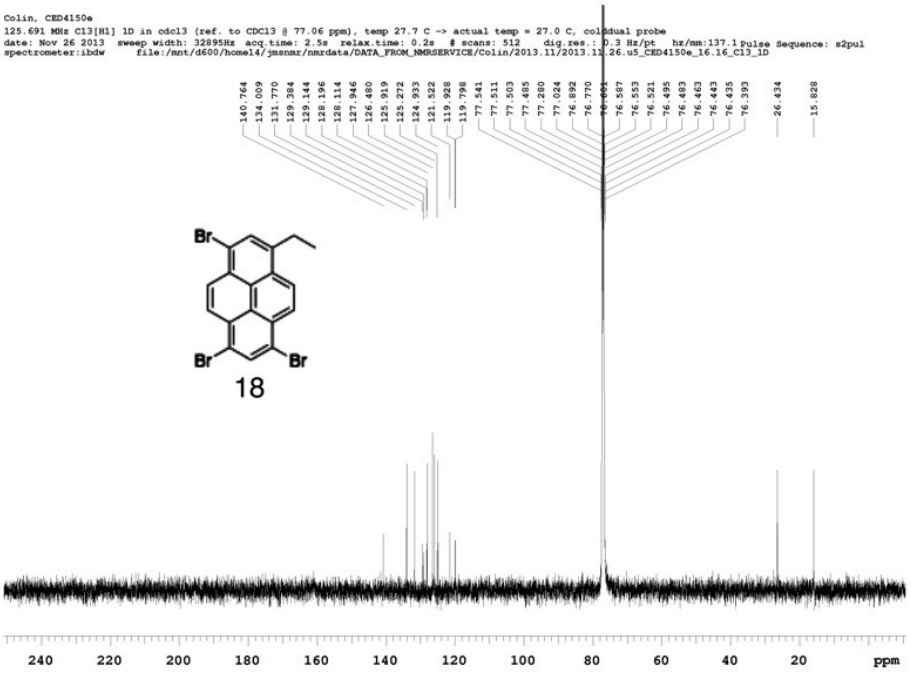
^{1}H (500 MHz) and ^{13}C (126 MHz) NMR of 2-12 in $CDCl_3$ at 25 °C



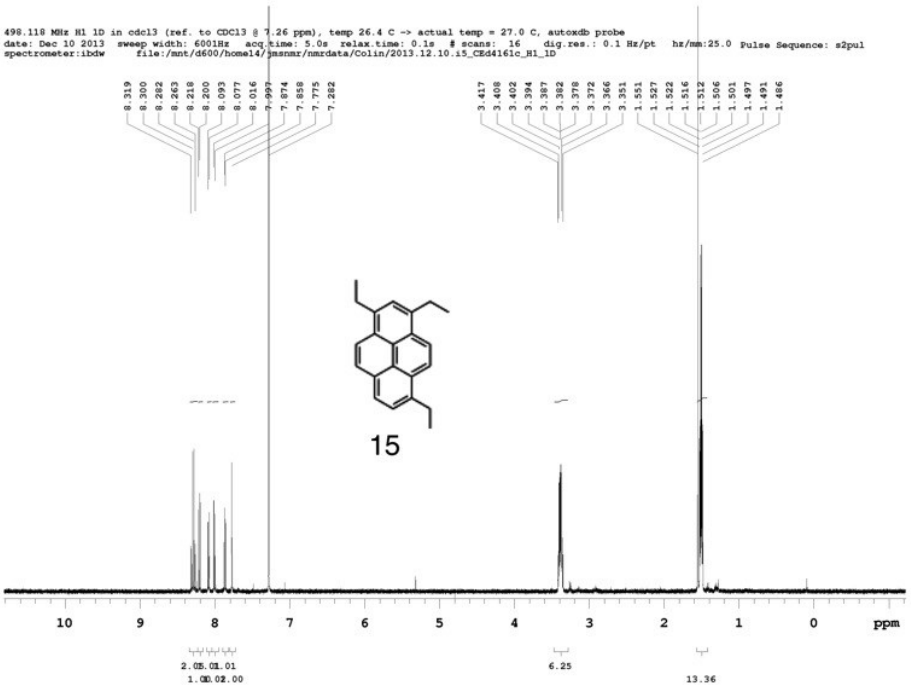


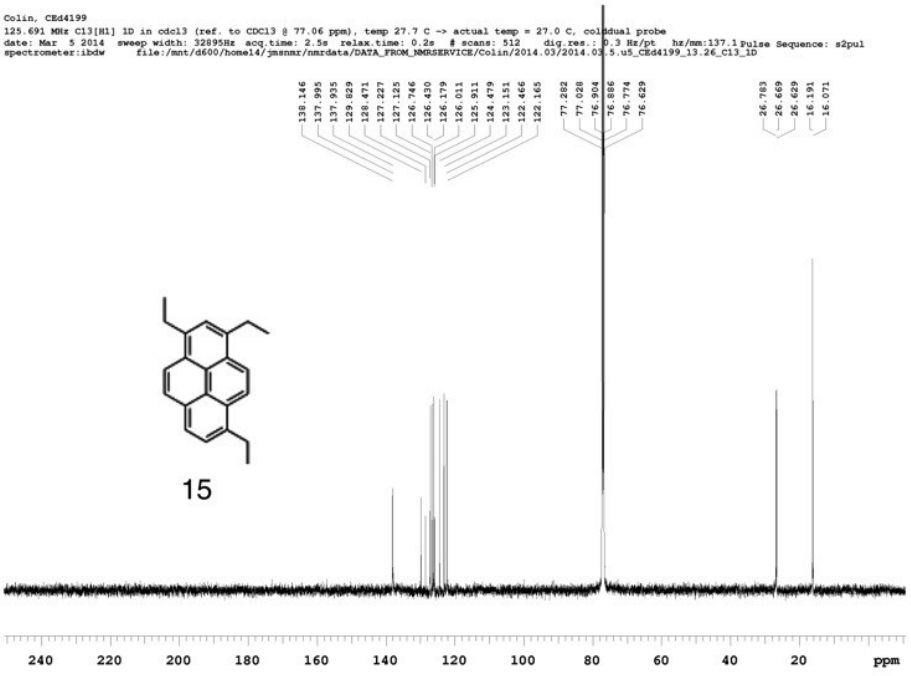
^{1}H (500 MHz) and ^{13}C (126 MHz) NMR of 2-13 in $CDCl_3$ at 25 °C



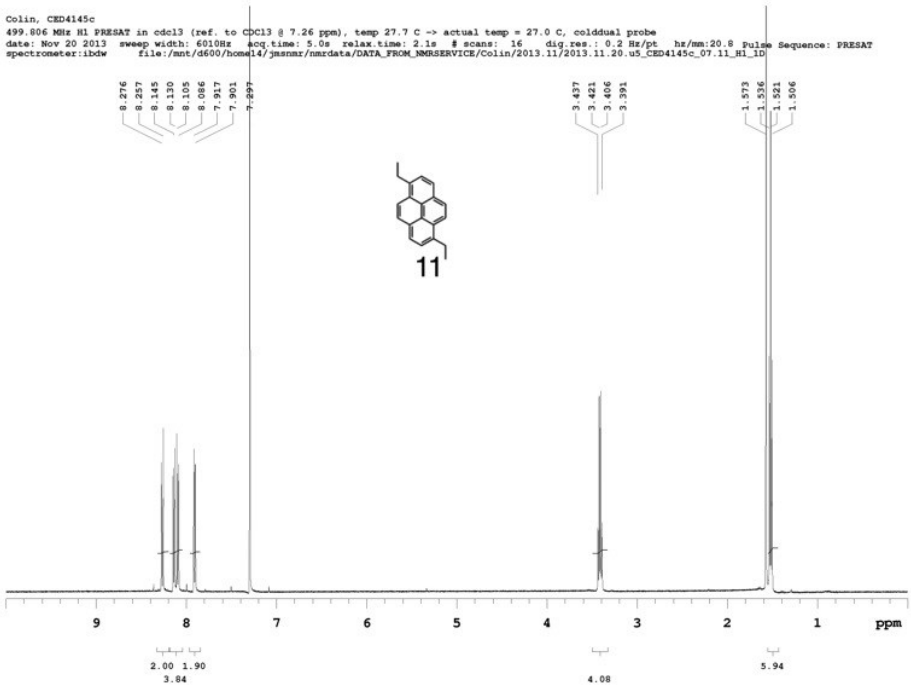


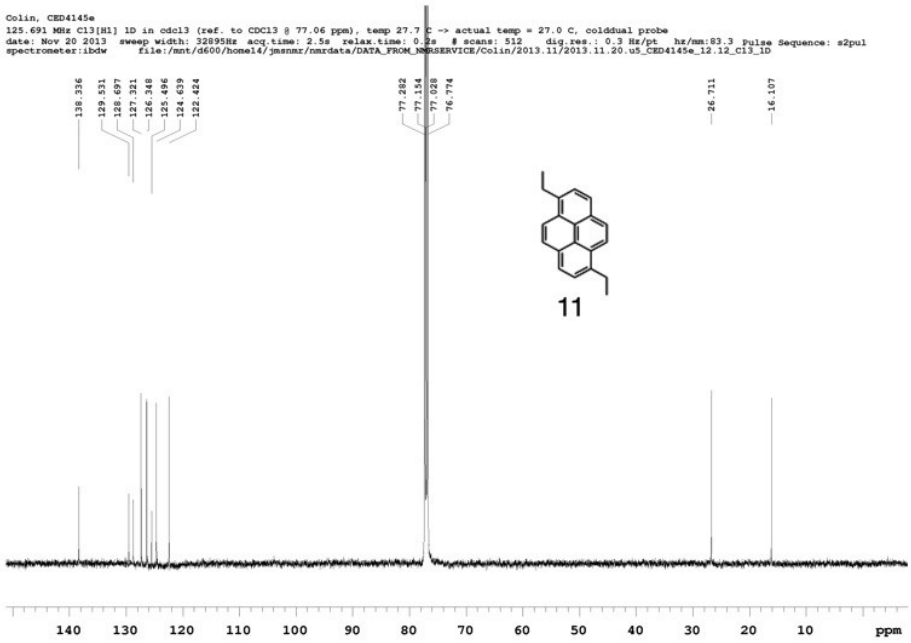
^{1}H (500 MHz) and ^{13}C (126 MHz) NMR of 2-14 in $CDCl_3$ at 25 °C



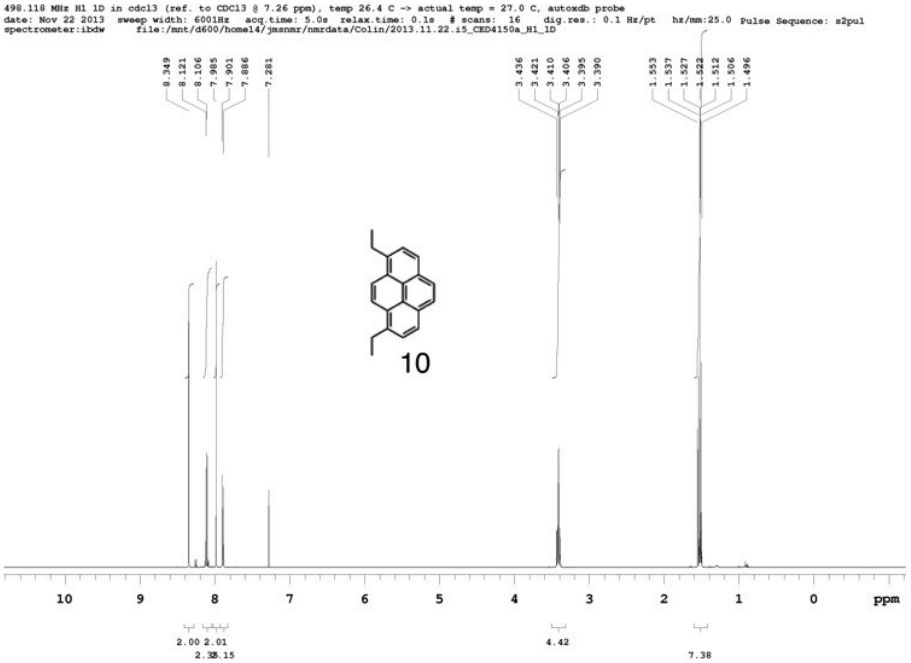


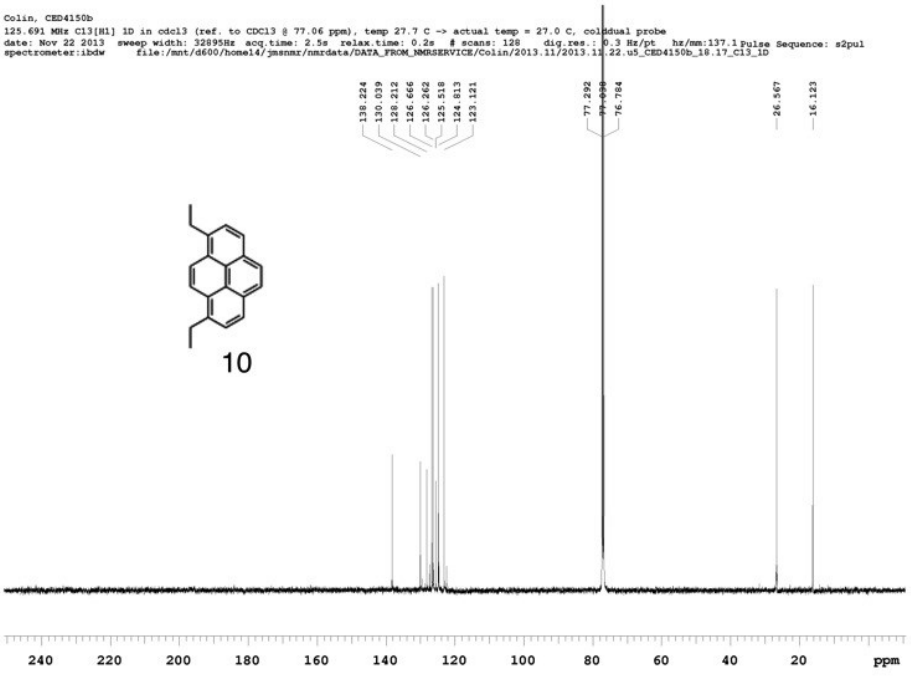
^{1}H (500 MHz) and ^{13}C (126 MHz) NMR of 2-15 in $CDCl_3$ at 25 °C



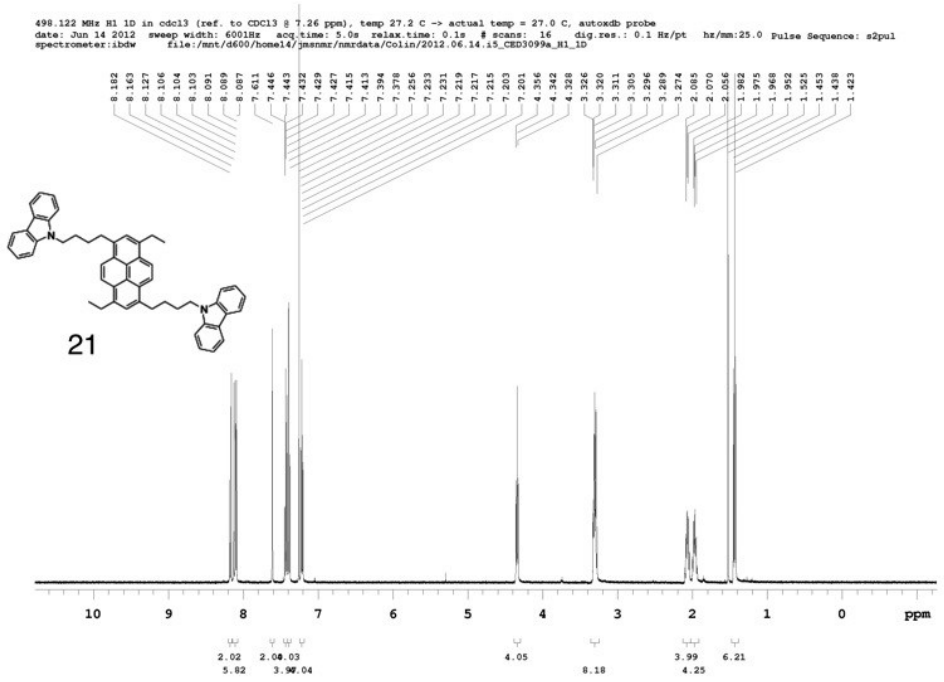


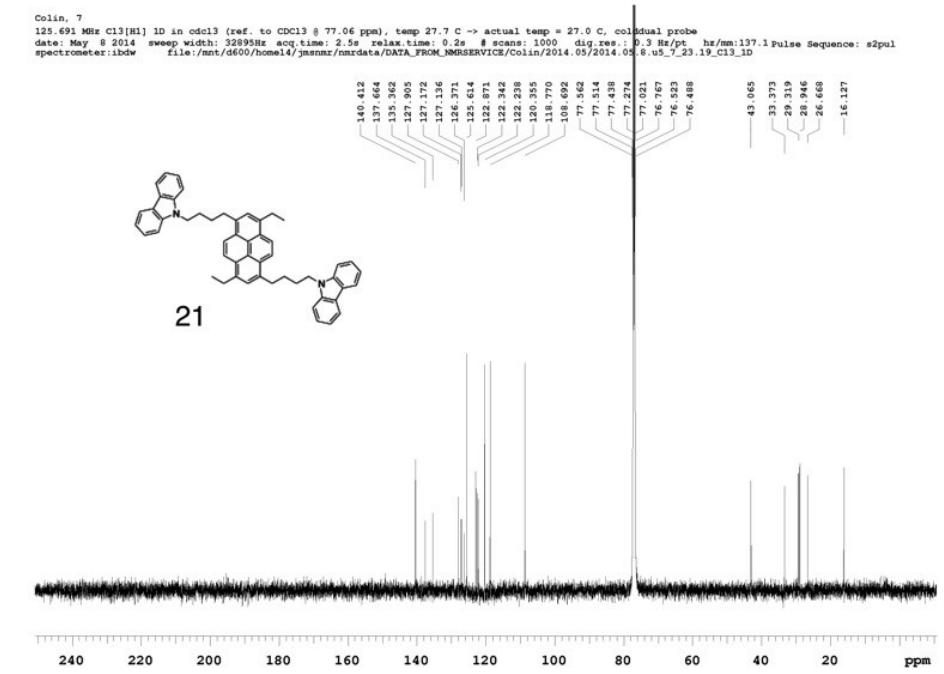
^{1}H (500 MHz) and ^{13}C (126 MHz) NMR of 2-16 in $CDCl_3$ at 25 °C



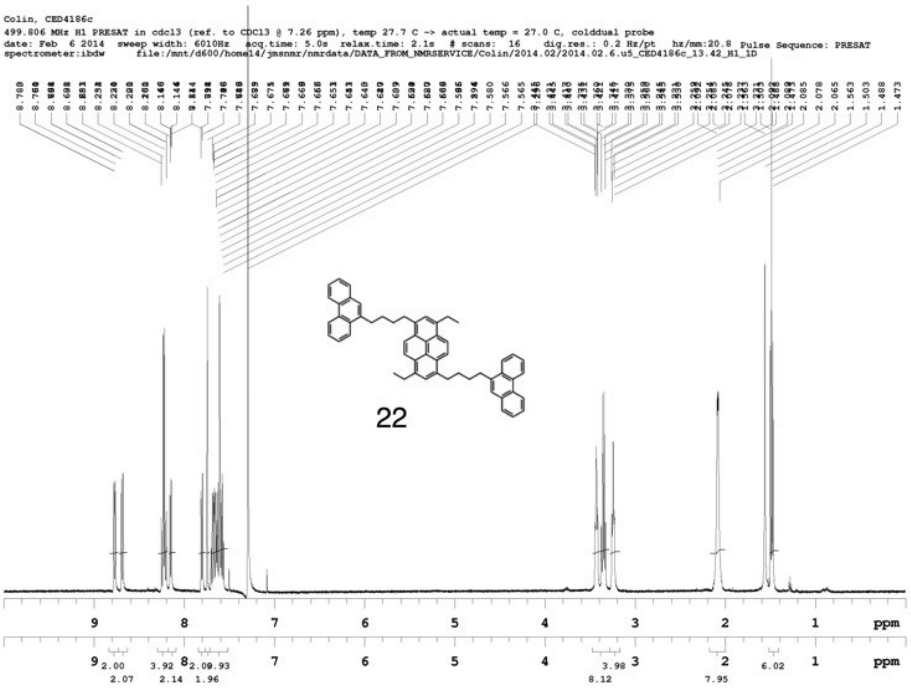


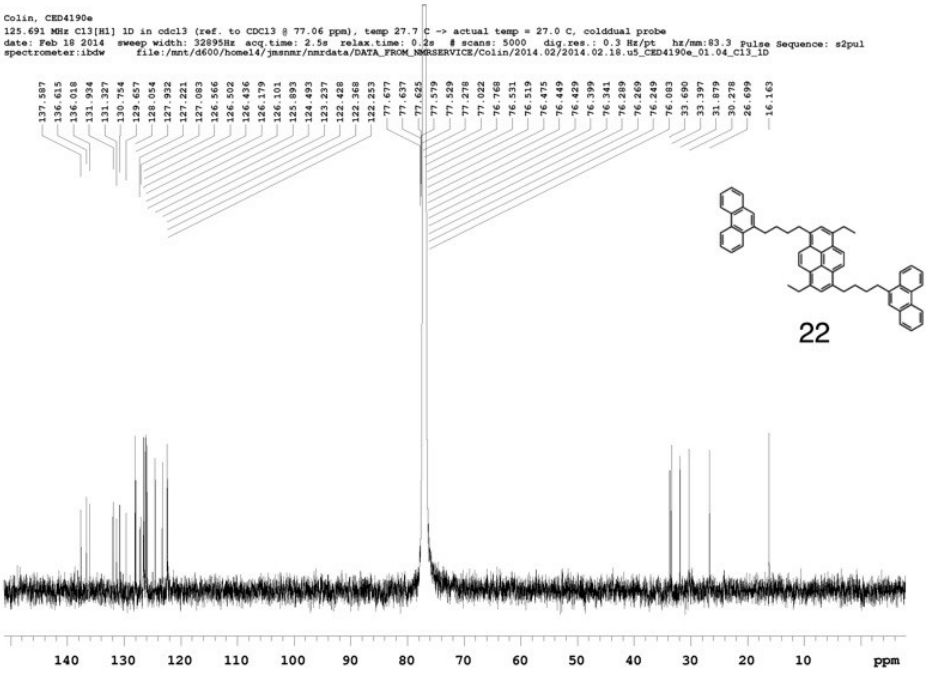
^{1}H (500 MHz) and ^{13}C (126 MHz) NMR of 2-18 in $CDCl_3$ at 25 °C



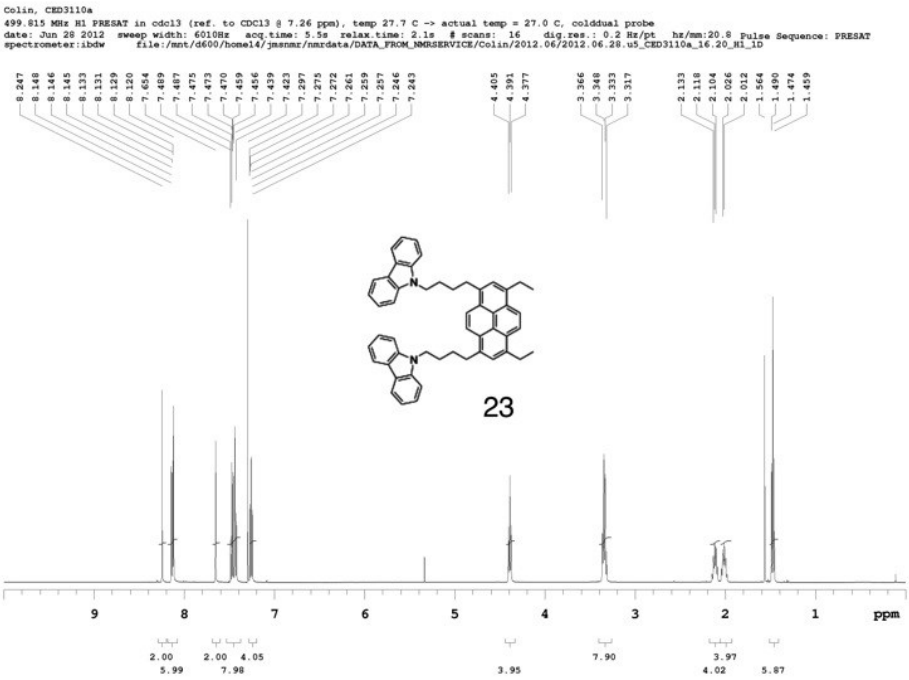


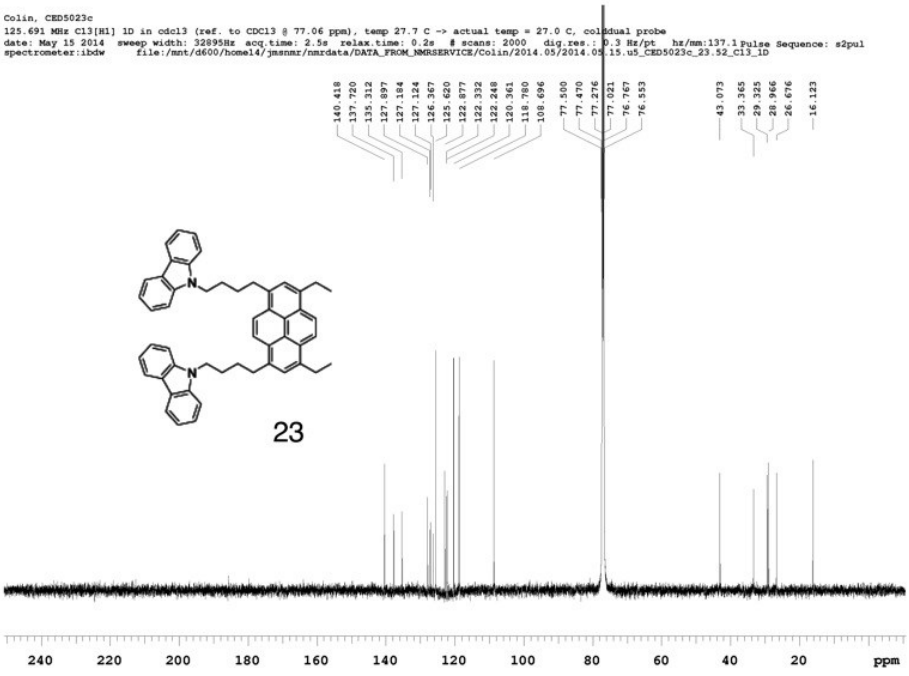
^{1}H (500 MHz) and ^{13}C (126 MHz) NMR of 2-19 in $CDCl_3$ at 25 °C 2-19



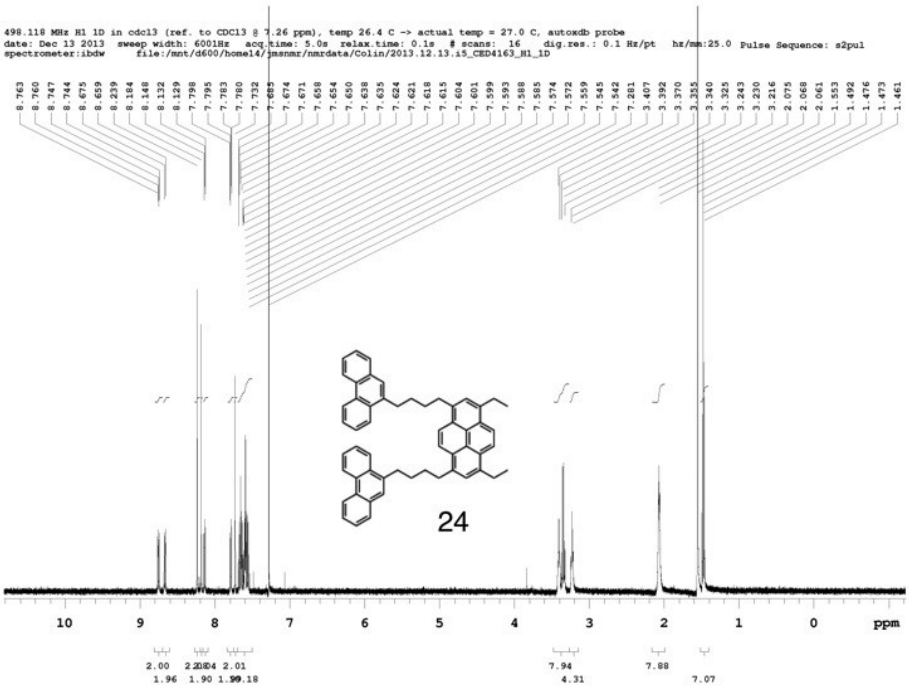


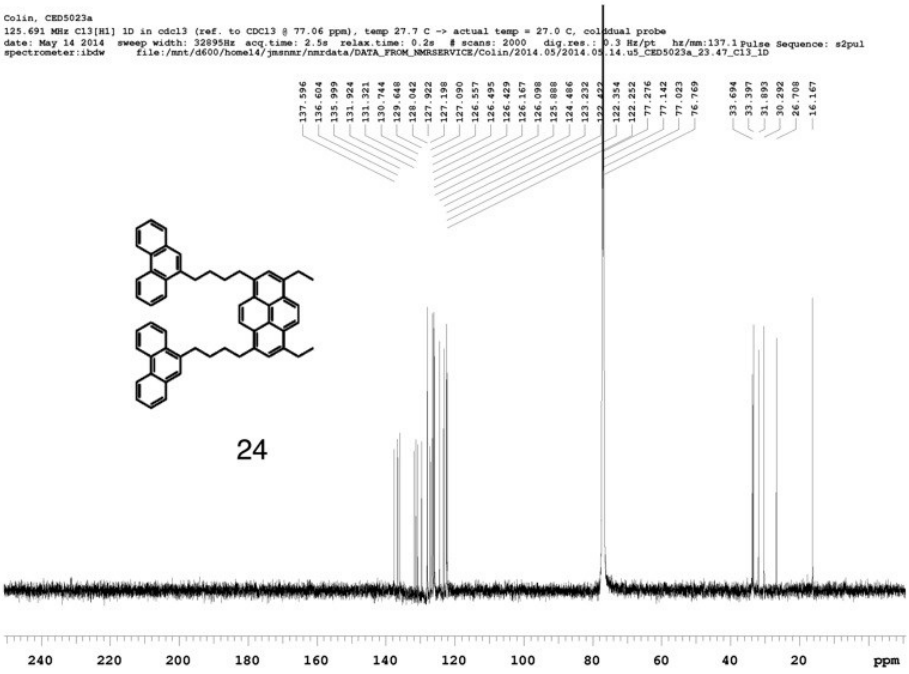
^{1}H (500 MHz) and ^{13}C (126 MHz) NMR of 2-20 in $CDCl_3$ at 25 °C



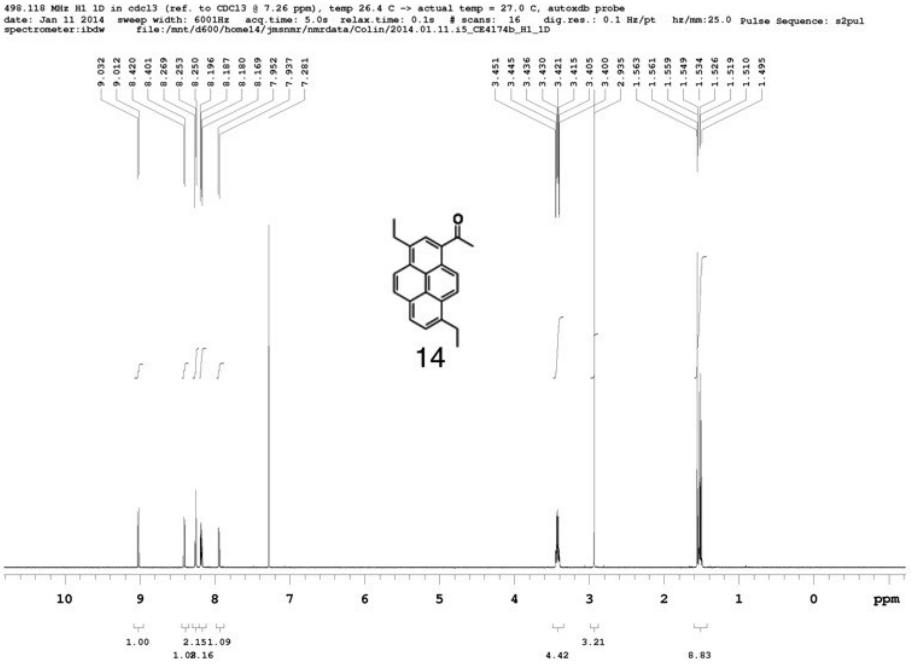


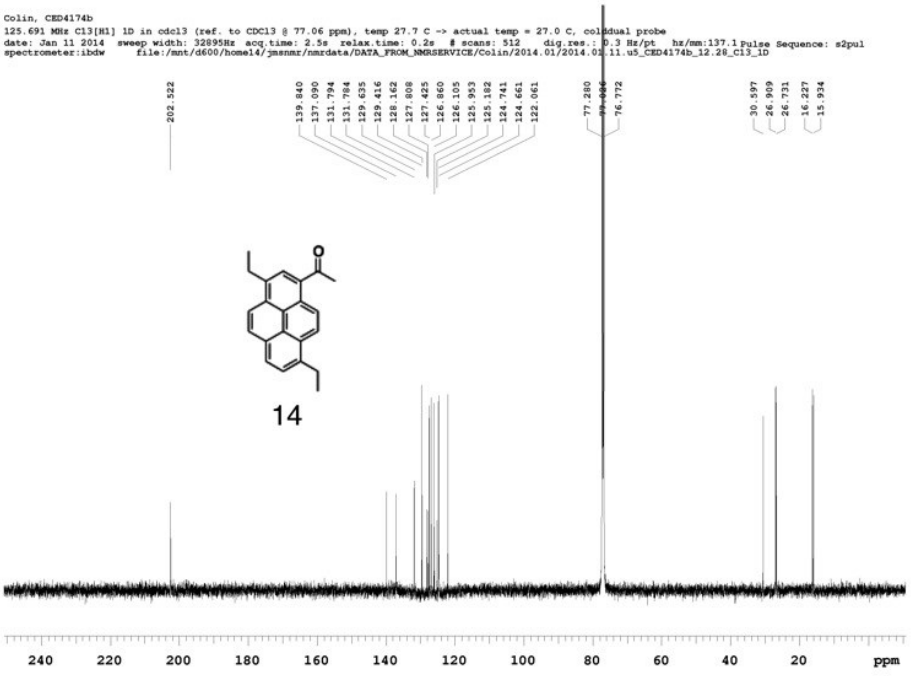
^{1}H (500 MHz) and ^{13}C (126 MHz) NMR of 2-21 in $CDCl_3$ at 25 °C



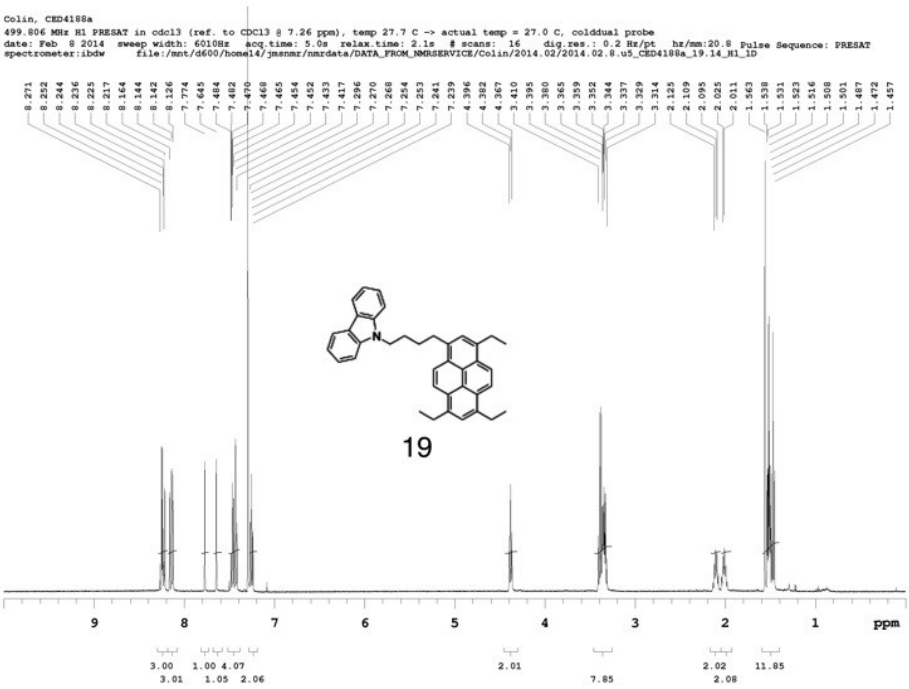


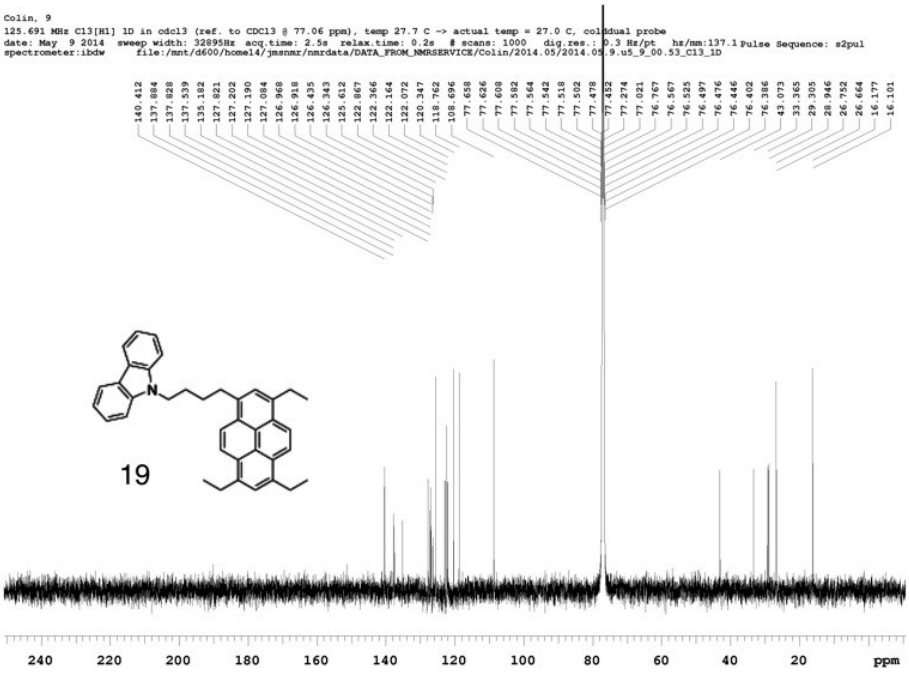
^{1}H (500 MHz) and ^{13}C (126 MHz) NMR of 2-22 in $CDCl_3$ at 25 °C



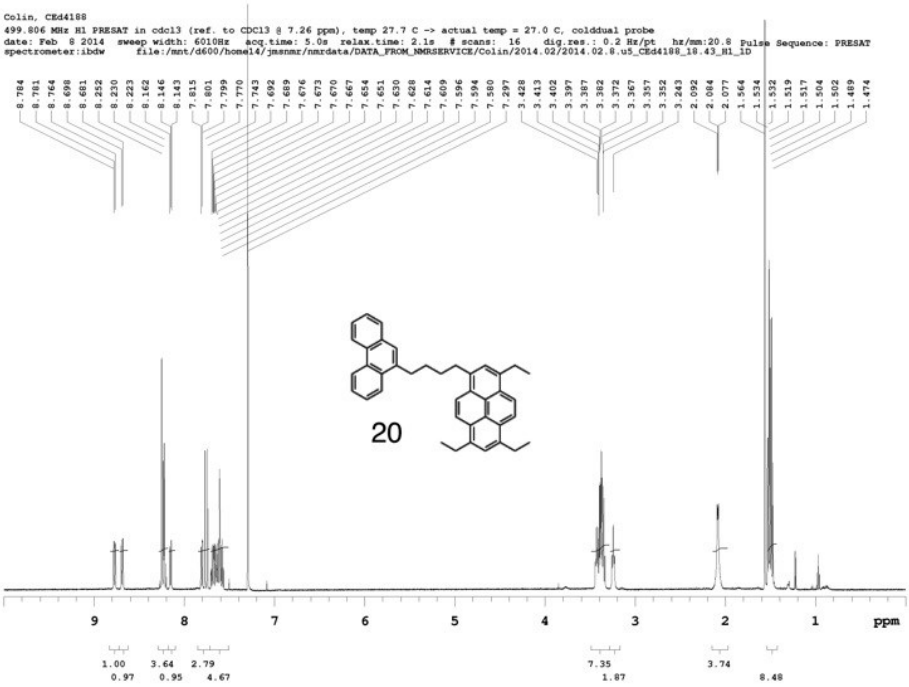


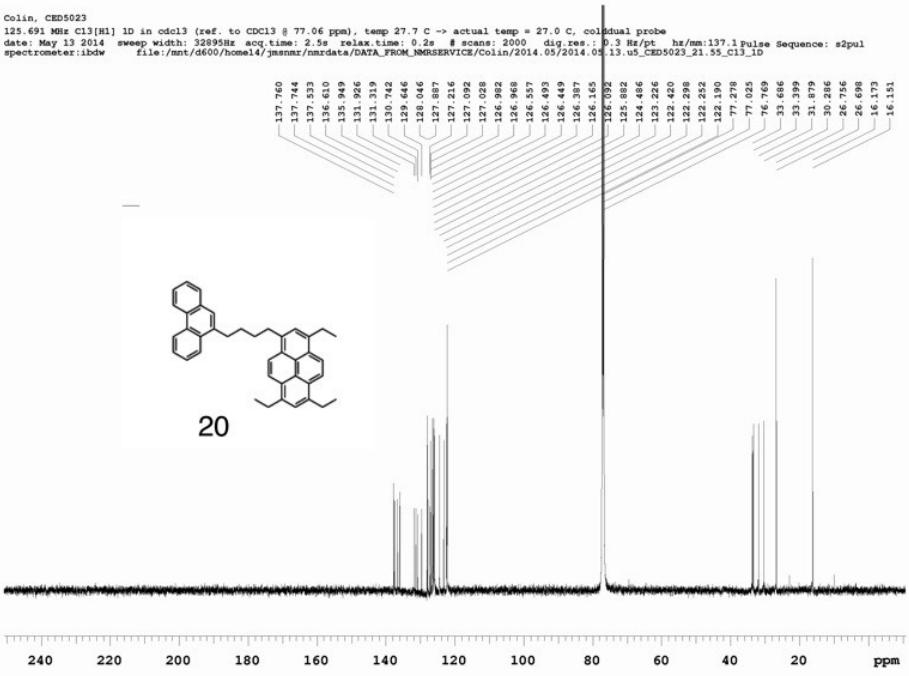
^{1}H (500 MHz) and ^{13}C (126 MHz) NMR of 2-23 in $CDCl_3$ at 25 °C



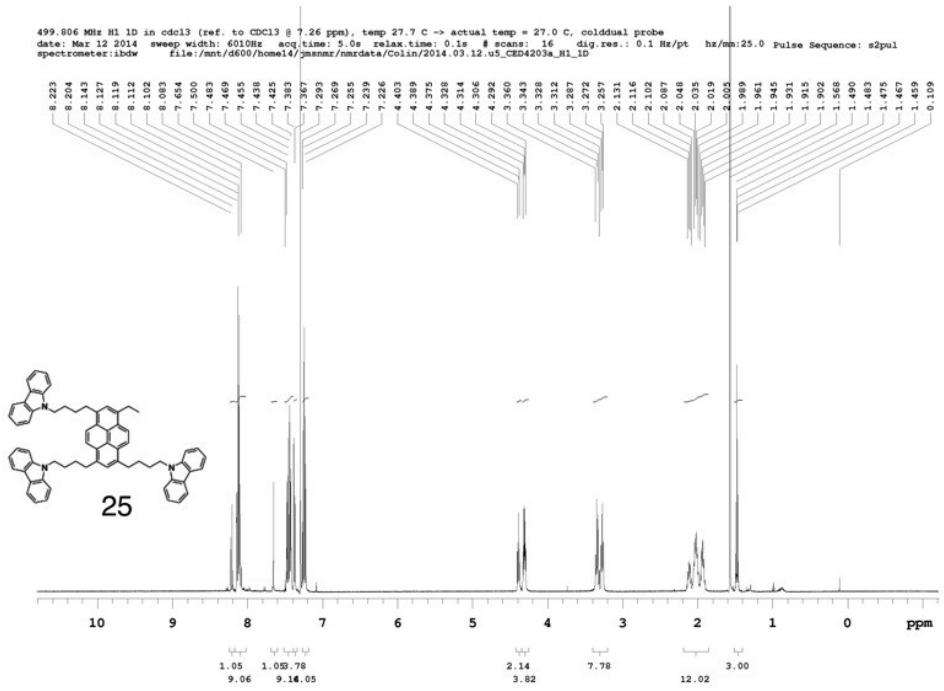


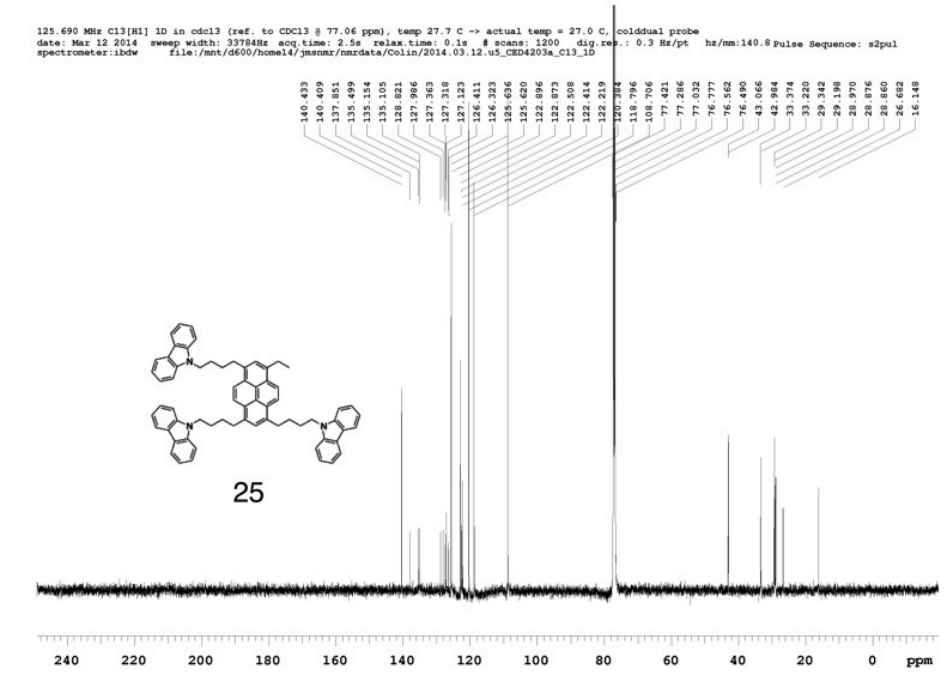
^{1}H (500 MHz) and ^{13}C (126 MHz) NMR of 2-24 in $CDCl_3$ at 25 °C



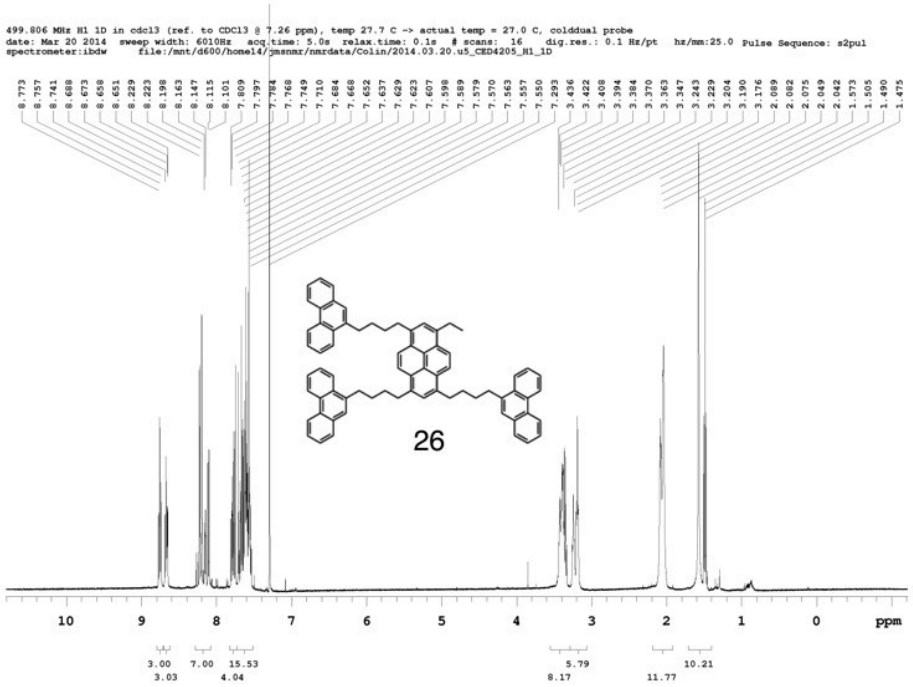


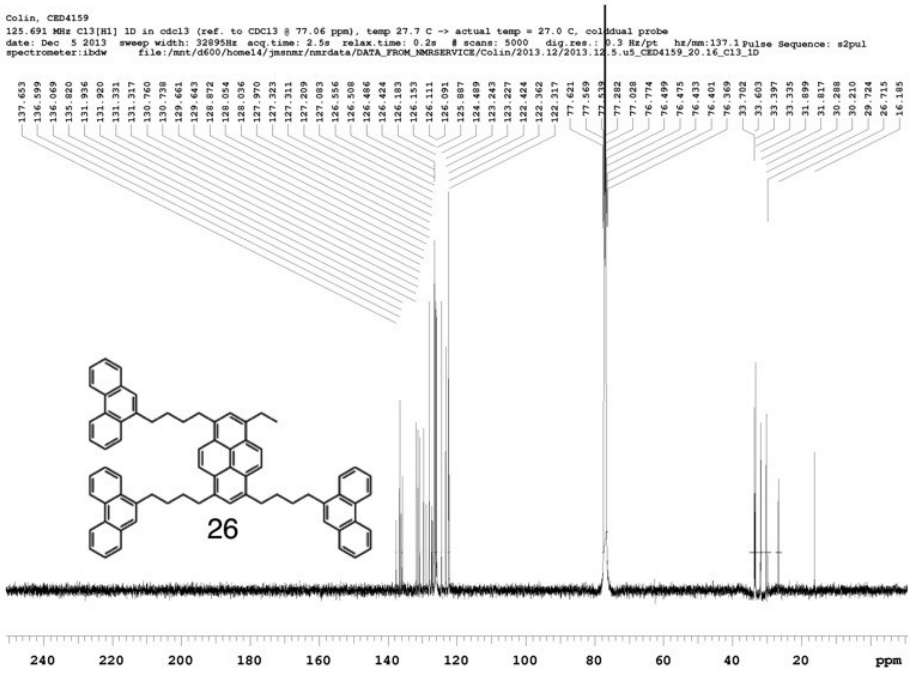
^{1}H (500 MHz) and ^{13}C (126 MHz) NMR of 2-25 in $CDCl_3$ at 25 °C



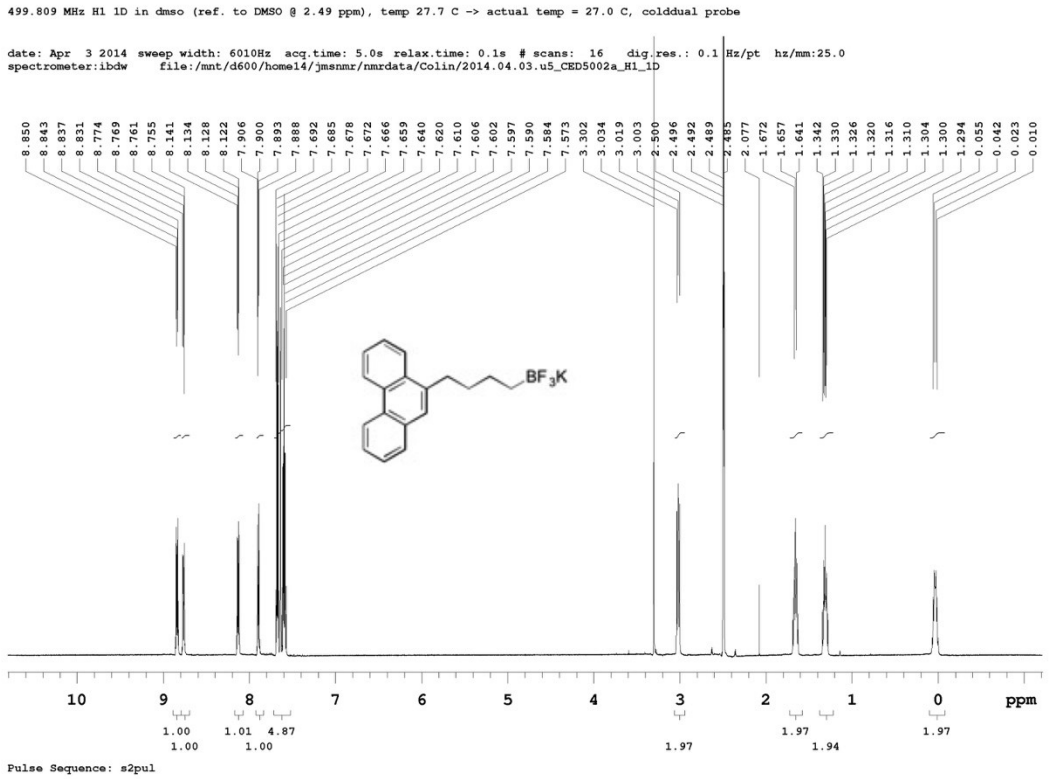


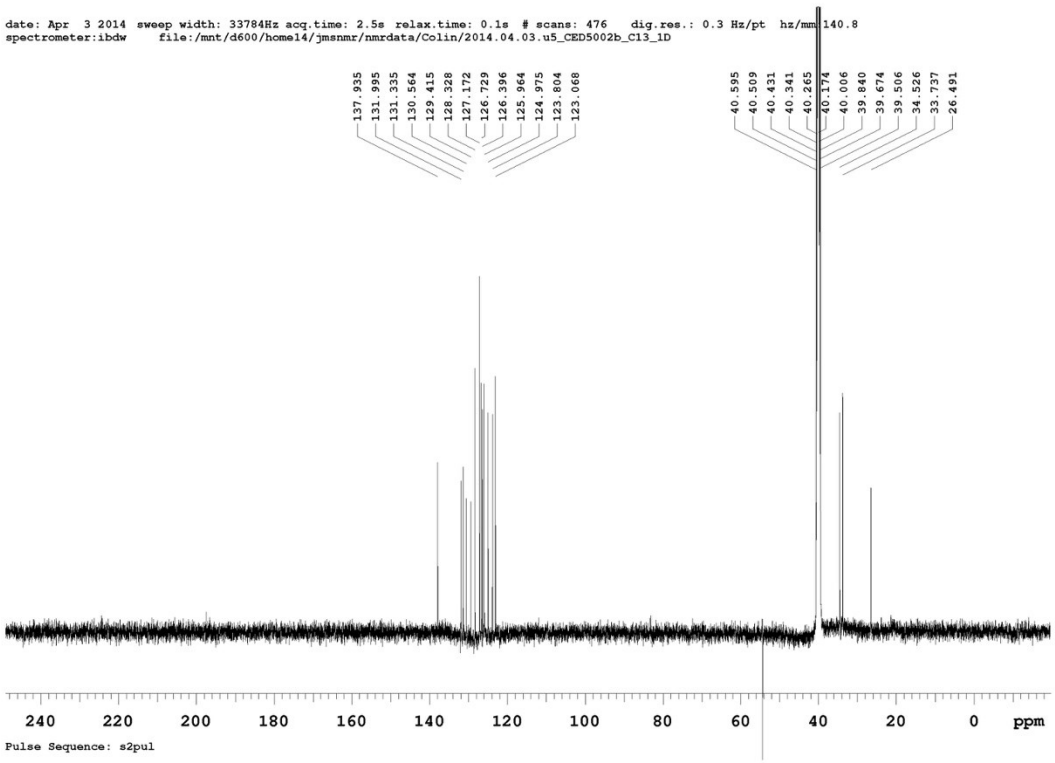
^{1}H (500 MHz) and ^{13}C (126 MHz) NMR of 2-26 in $CDCl_3$ at 25 °C



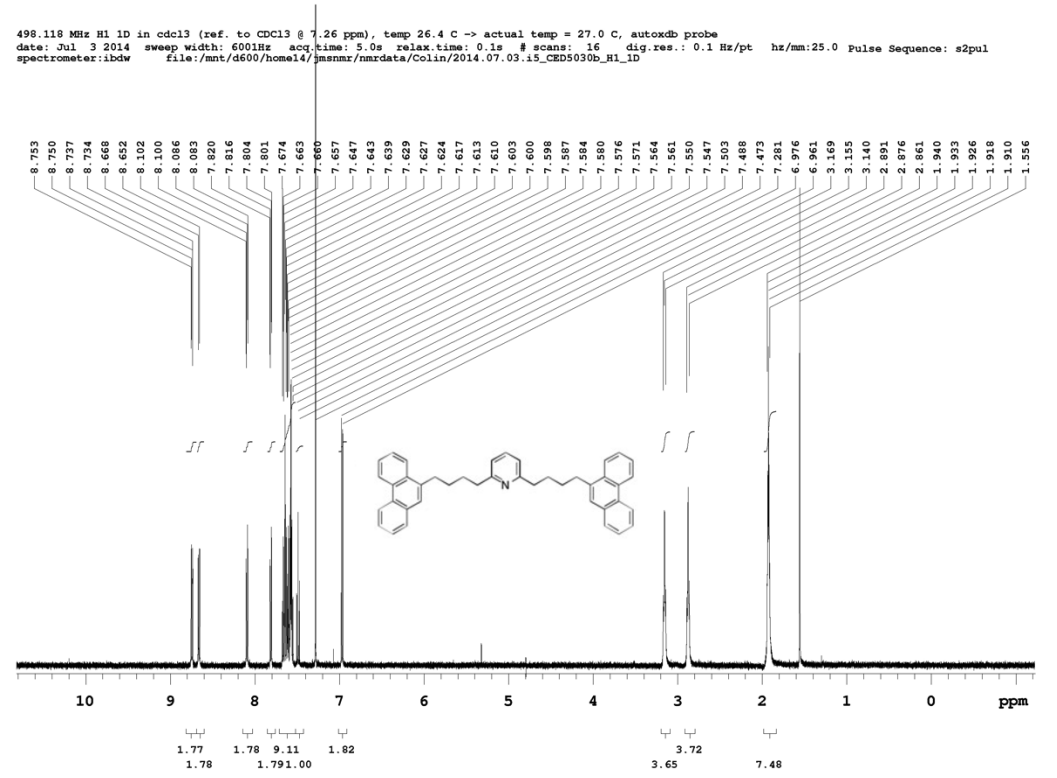


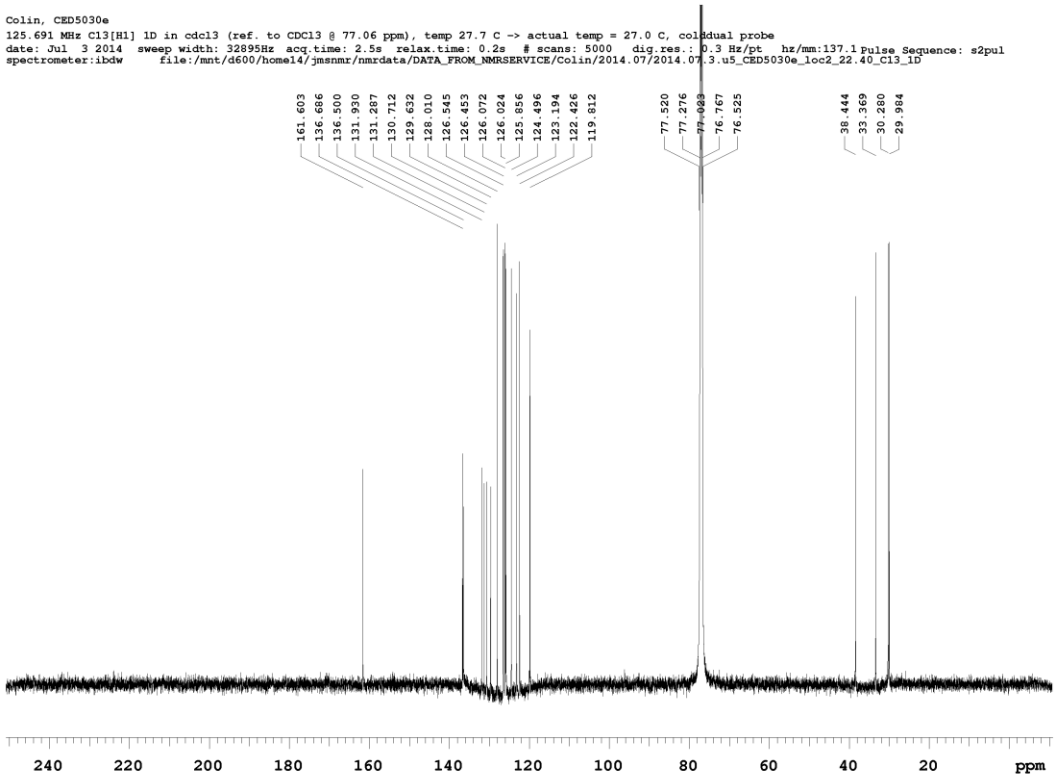
^{1}H (500 MHz) and ^{13}C (126 MHz) NMR of 3-3 in DMSO at 25 °C



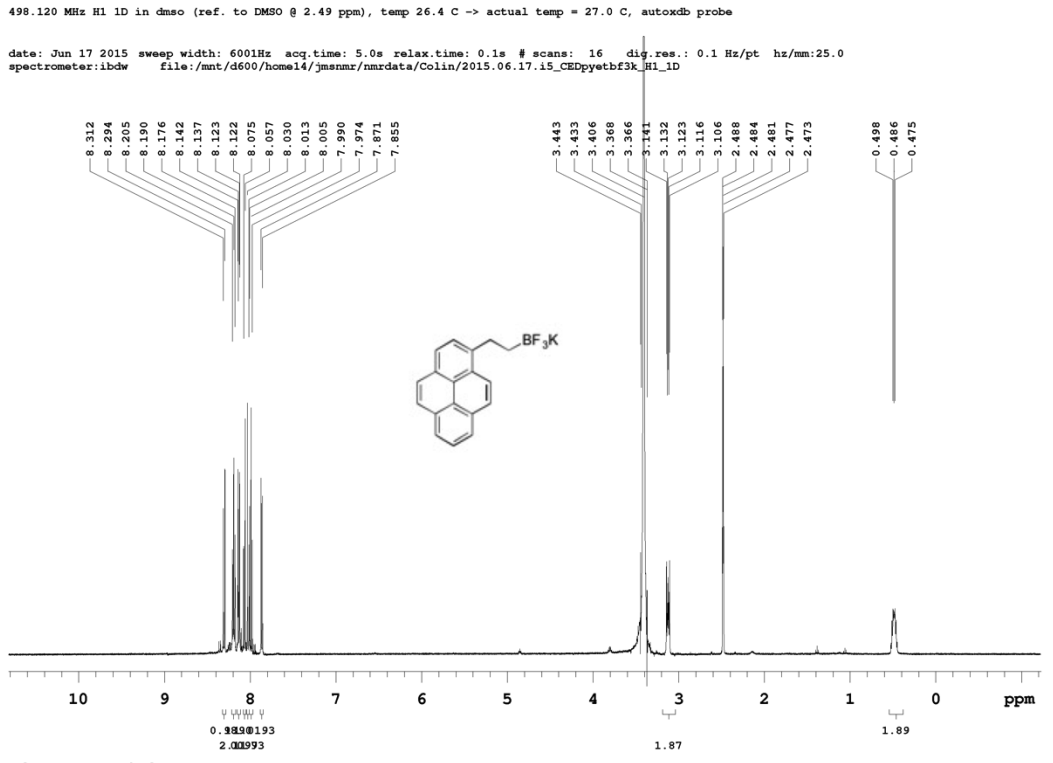


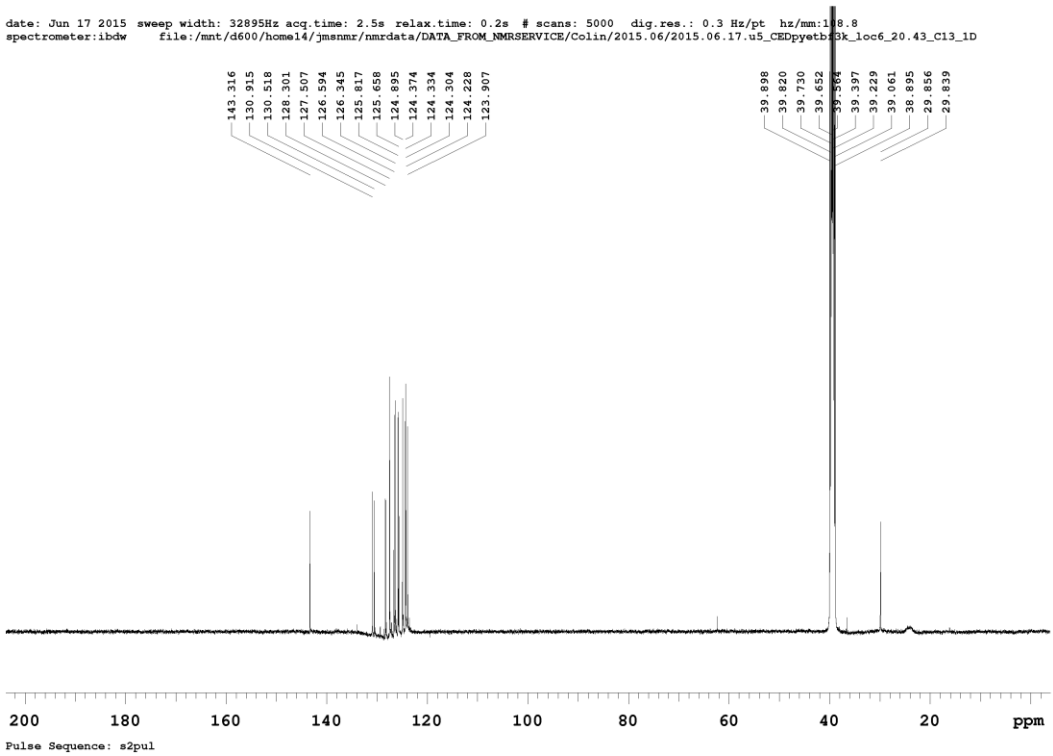
^{1}H (500 MHz) and ^{13}C (126 MHz) NMR of 3-4 in $CDCl_3$ at 25 °C



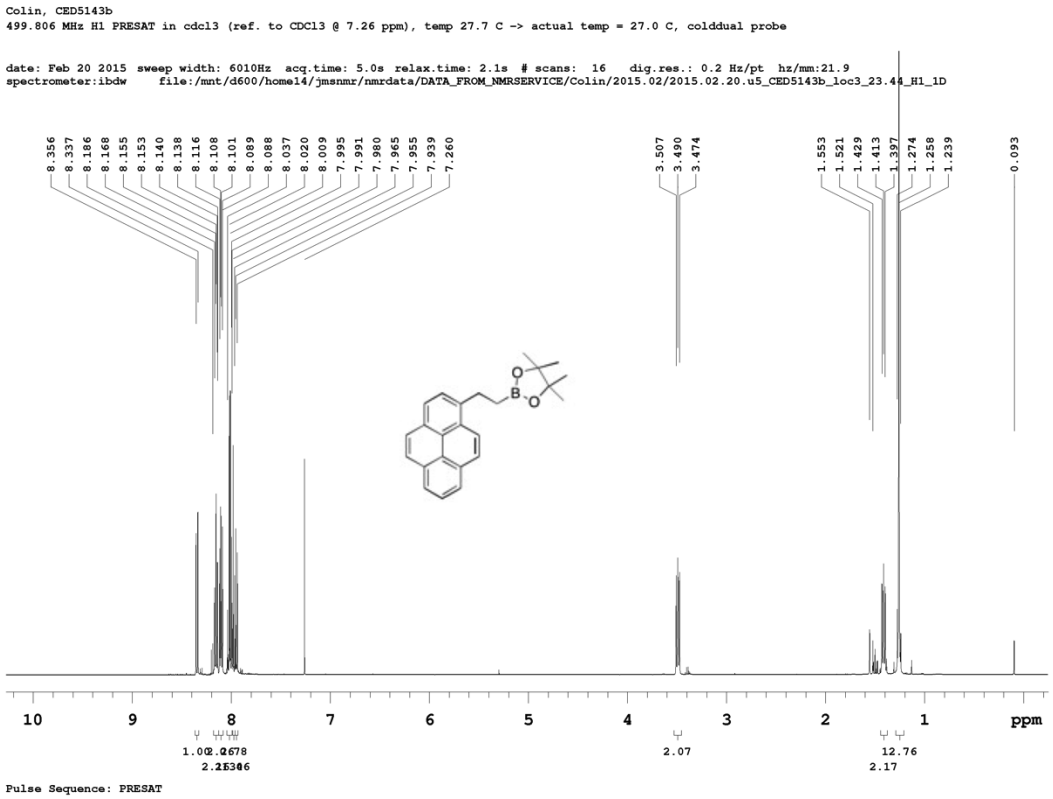


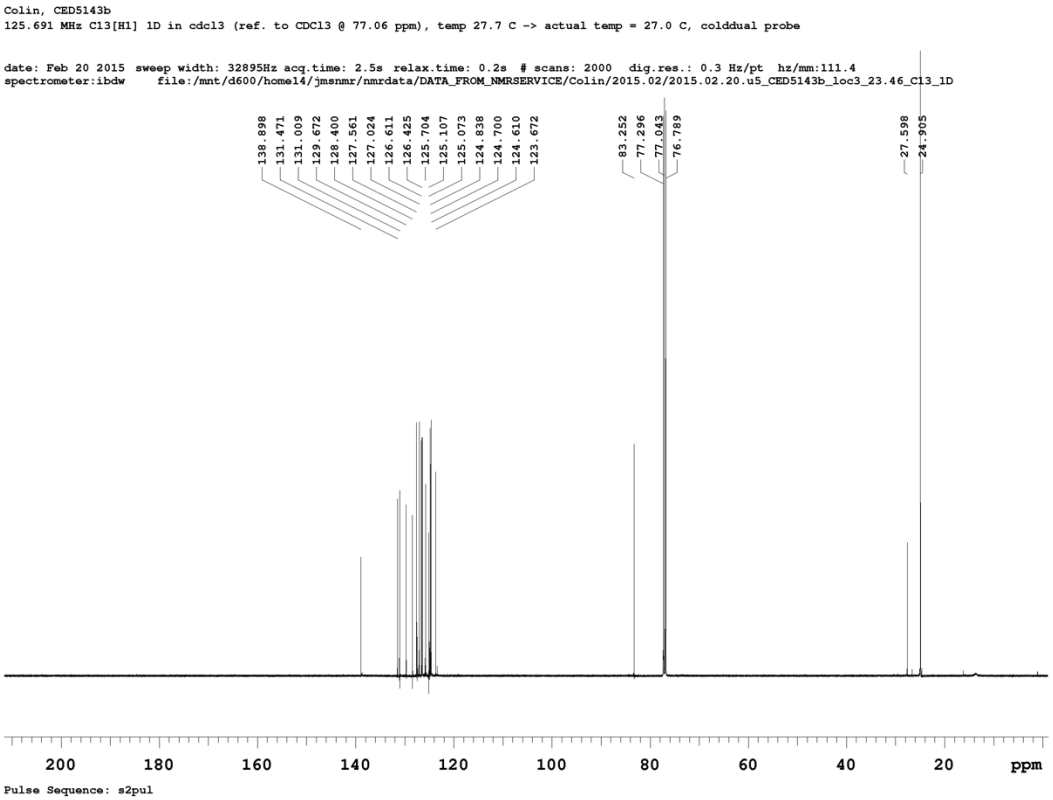
^{1}H (500 MHz) and ^{13}C (126 MHz) NMR of 3-5 in DMSO at 25 °C



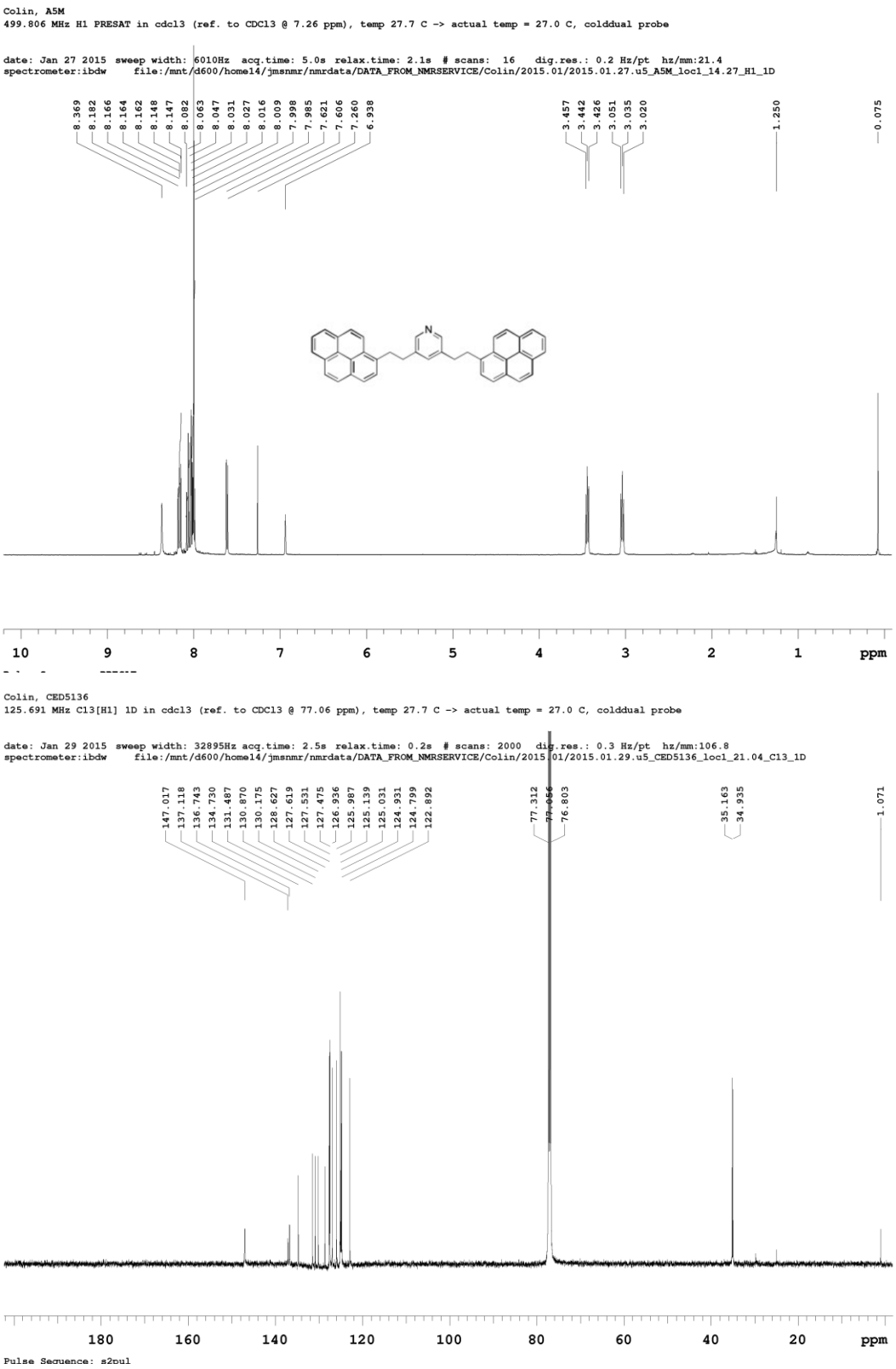


^{1}H (500 MHz) and ^{13}C (126 MHz) NMR of 3-8 in $CDCl_3$ at 25 °C

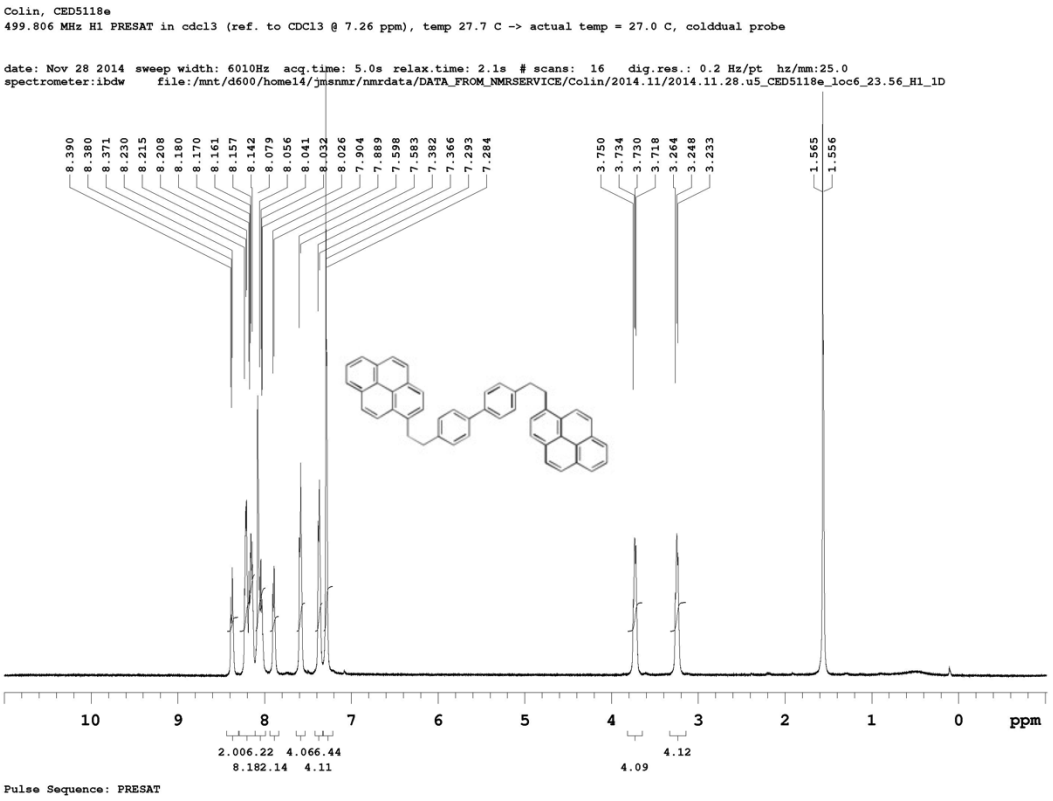


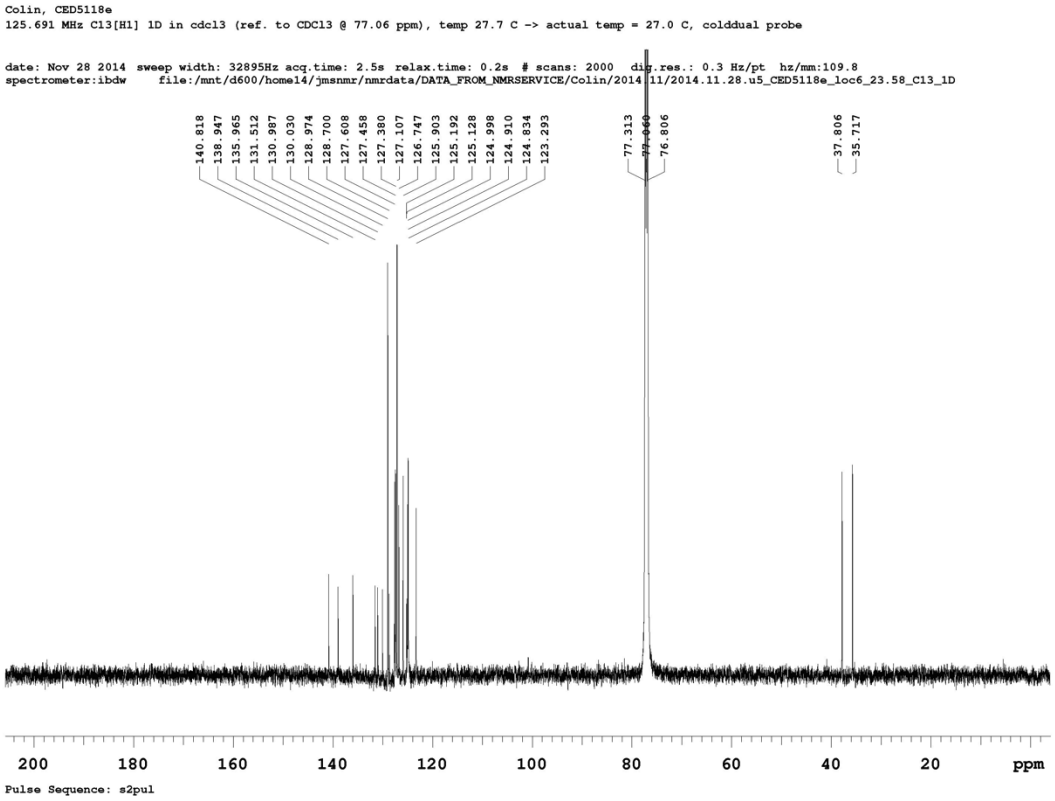


^{1}H (500 MHz) and ^{13}C (126 MHz) NMR of 3-9 in $CDCl_3$ at 25 °C

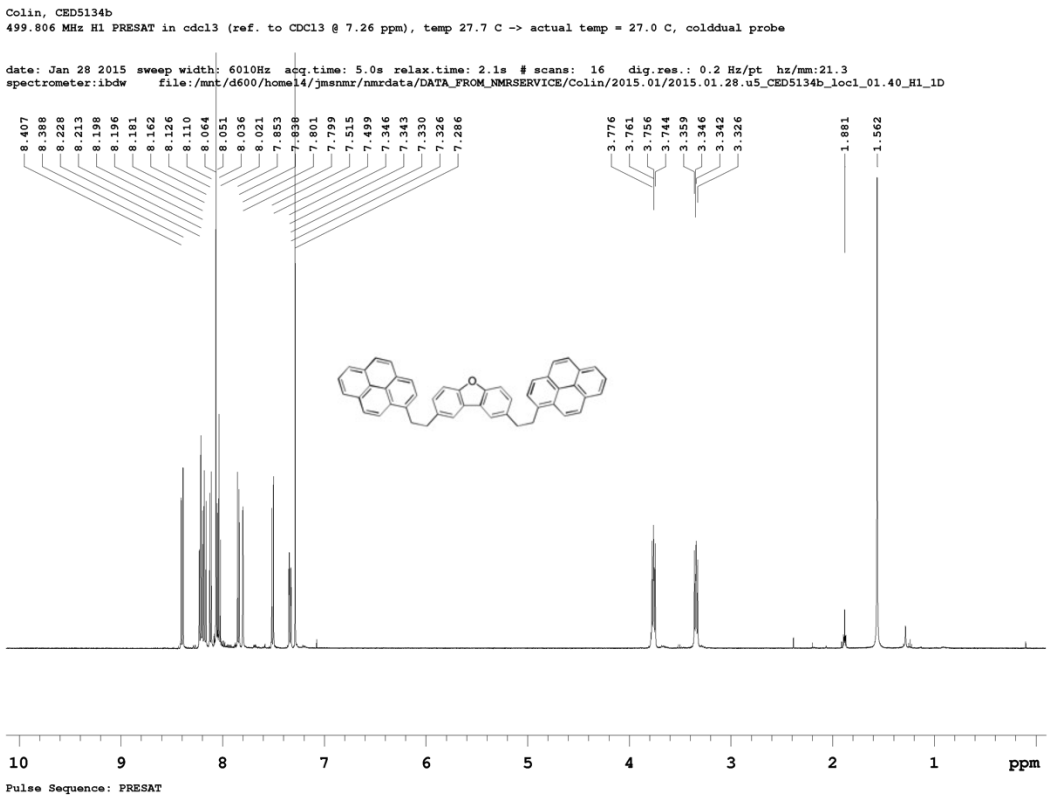


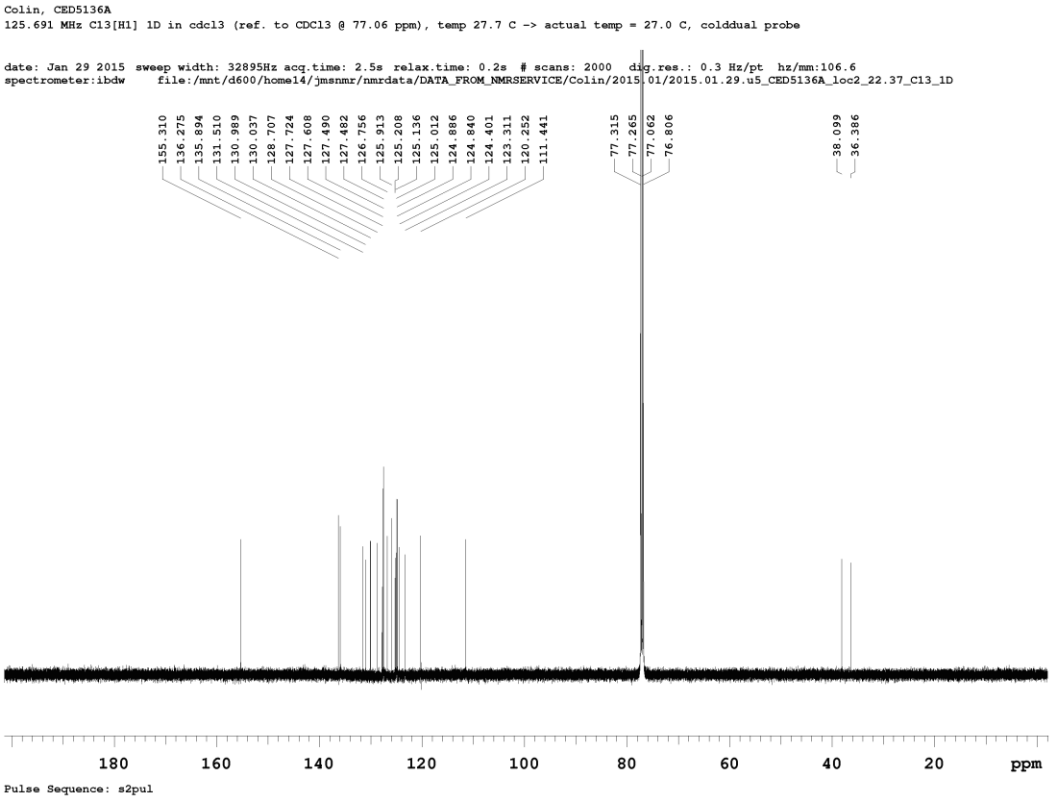
^{1}H (500 MHz) and ^{13}C (126 MHz) NMR of 3-10 in $CDCl_3$ at 25 °C



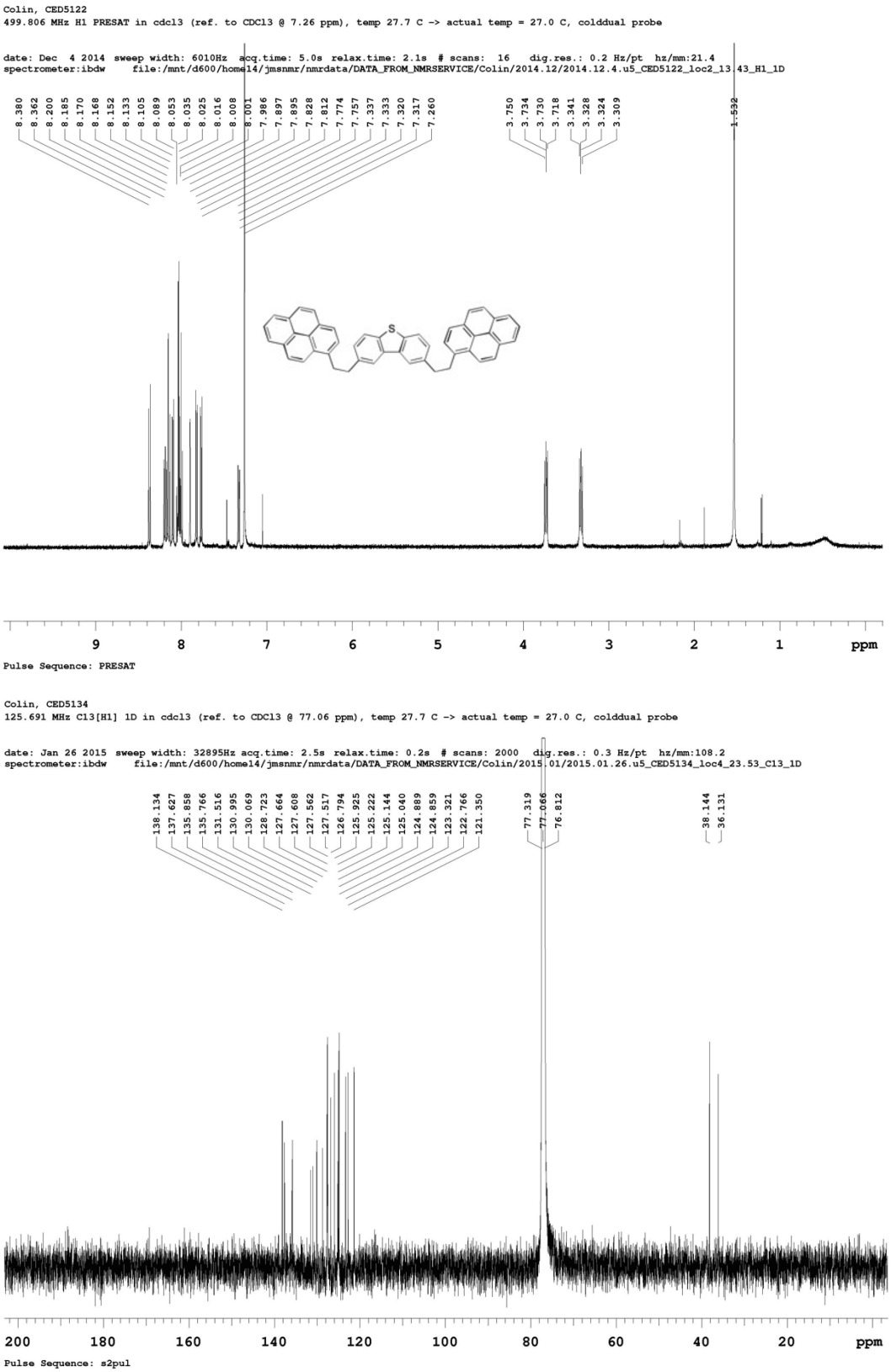


^{1}H (500 MHz) and ^{13}C (126 MHz) NMR of 3-11 in $CDCl_3$ at 25 °C

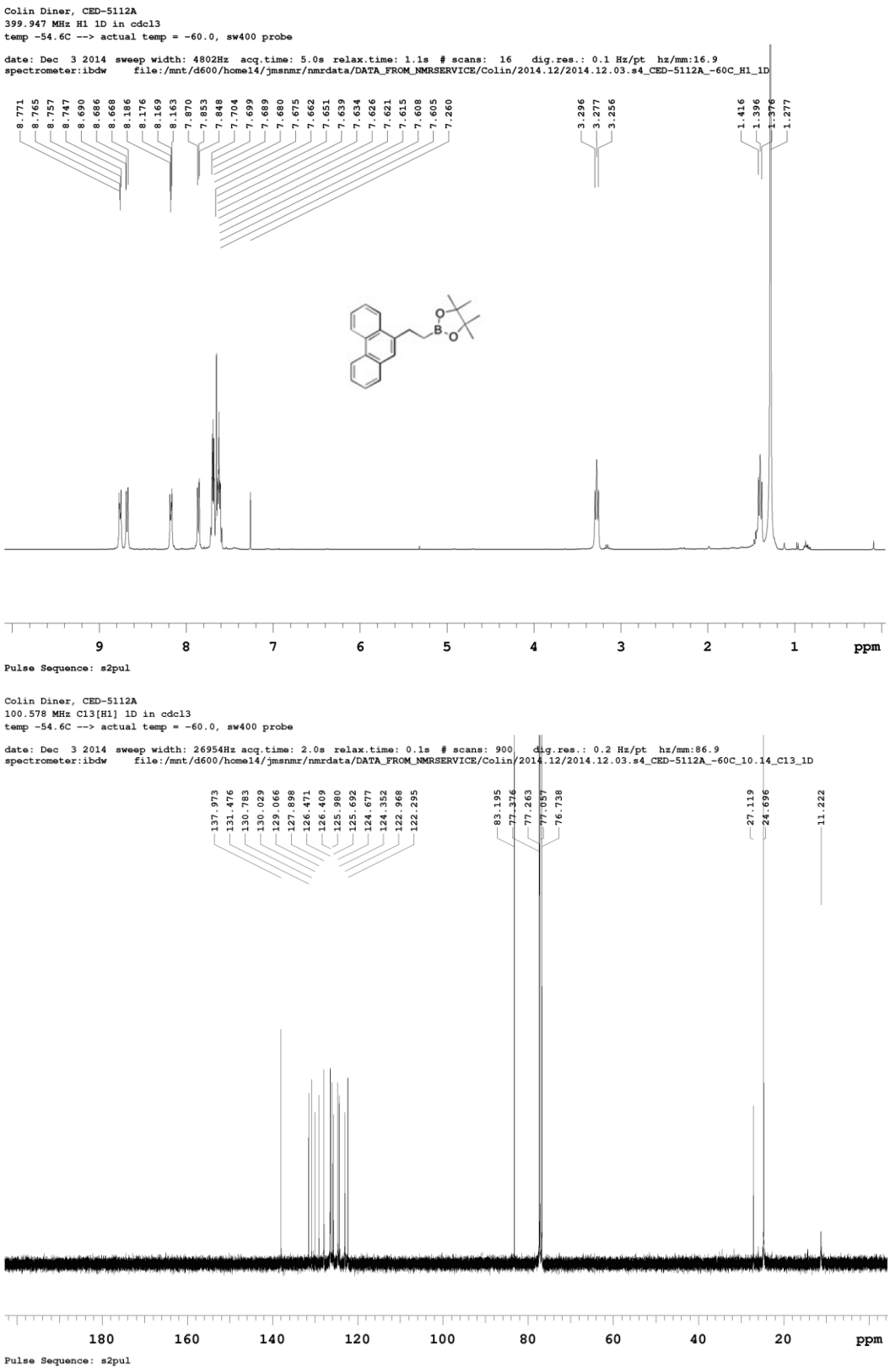




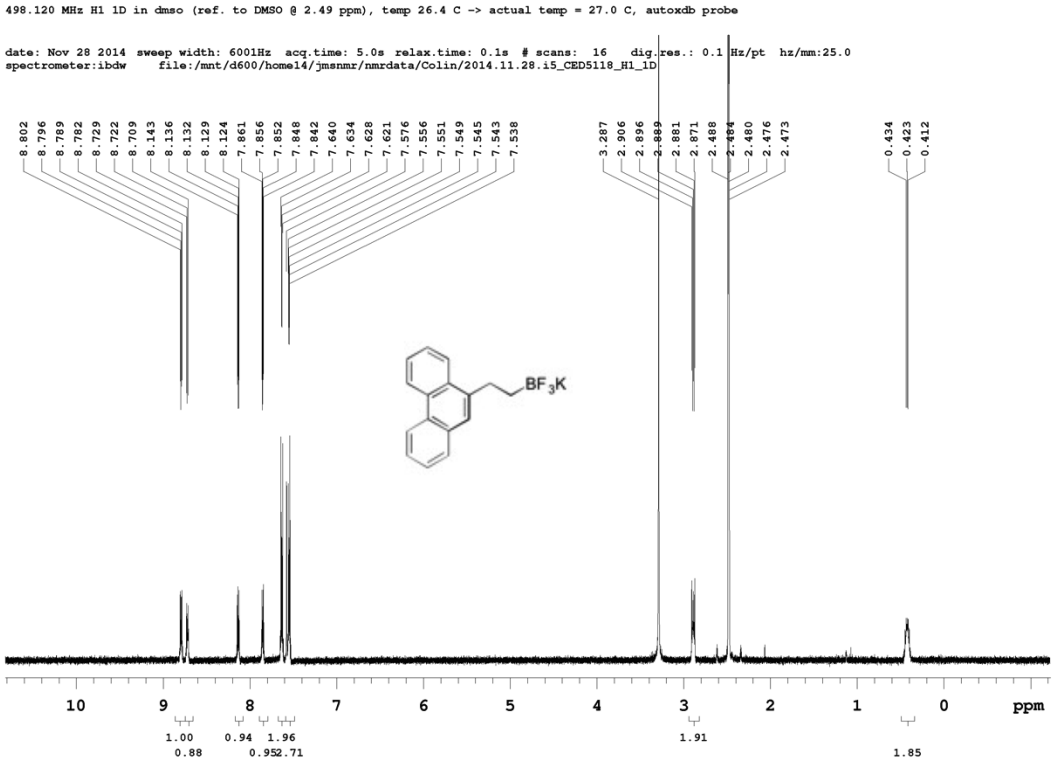
^{1}H (500 MHz) and ^{13}C (126 MHz) NMR of 3-12 in $CDCl_3$ at 25 °C

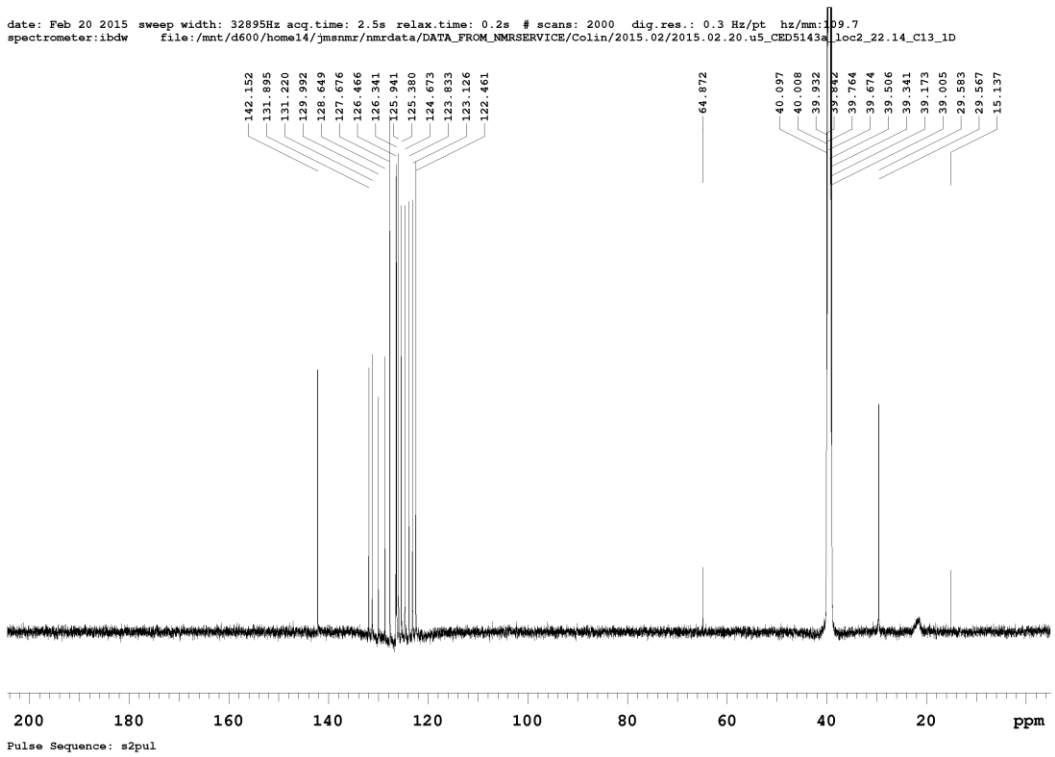


^{1}H (500 MHz) and ^{13}C (126 MHz) NMR of 3-14 in $CDCl_3$ at -60 °C

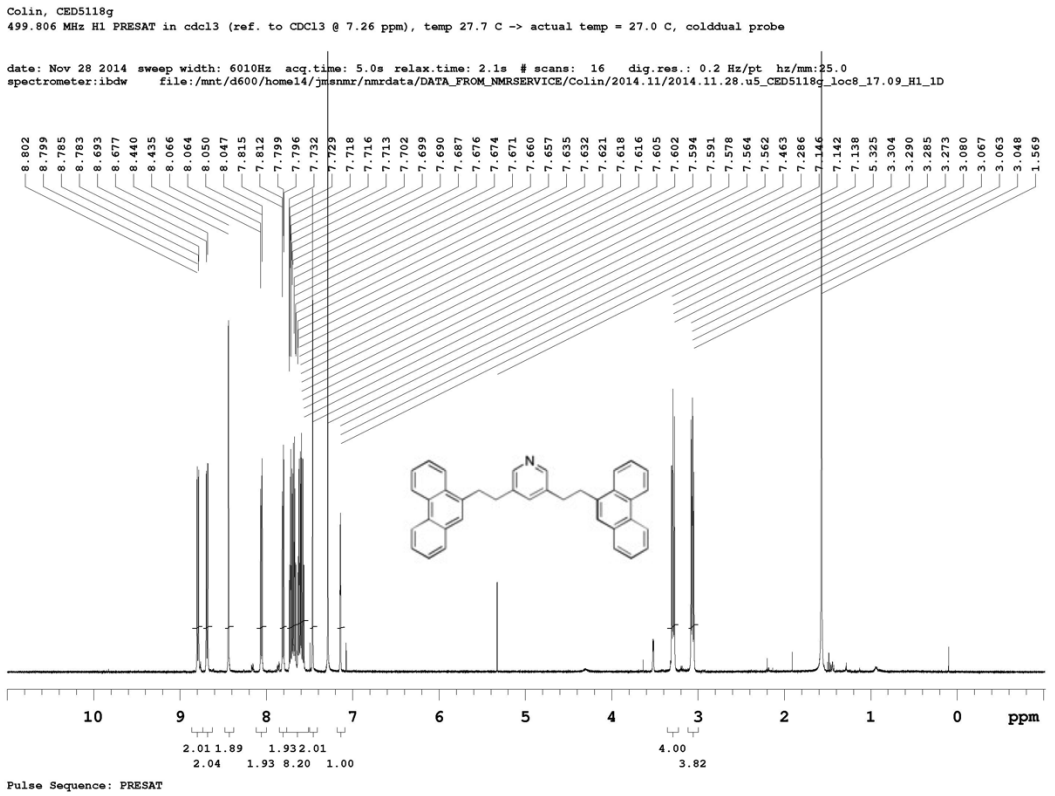


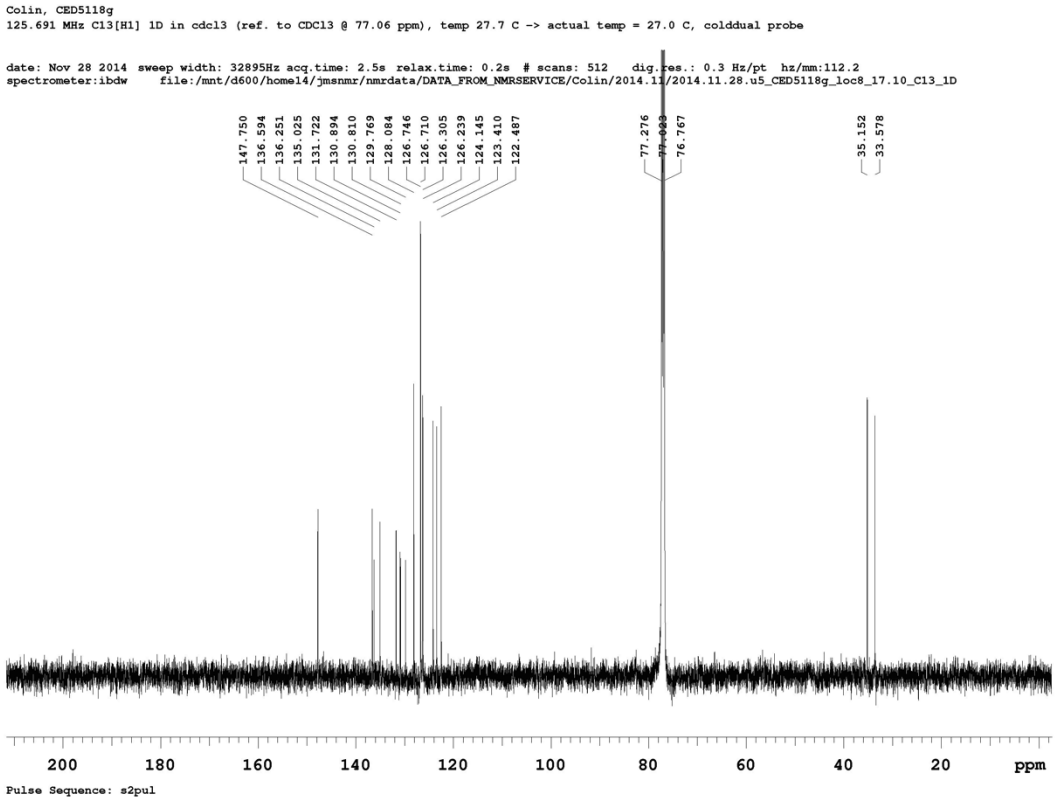
^{1}H (500 MHz) and ^{13}C (126 MHz) NMR of 3-15 in DMSO at 25 °C



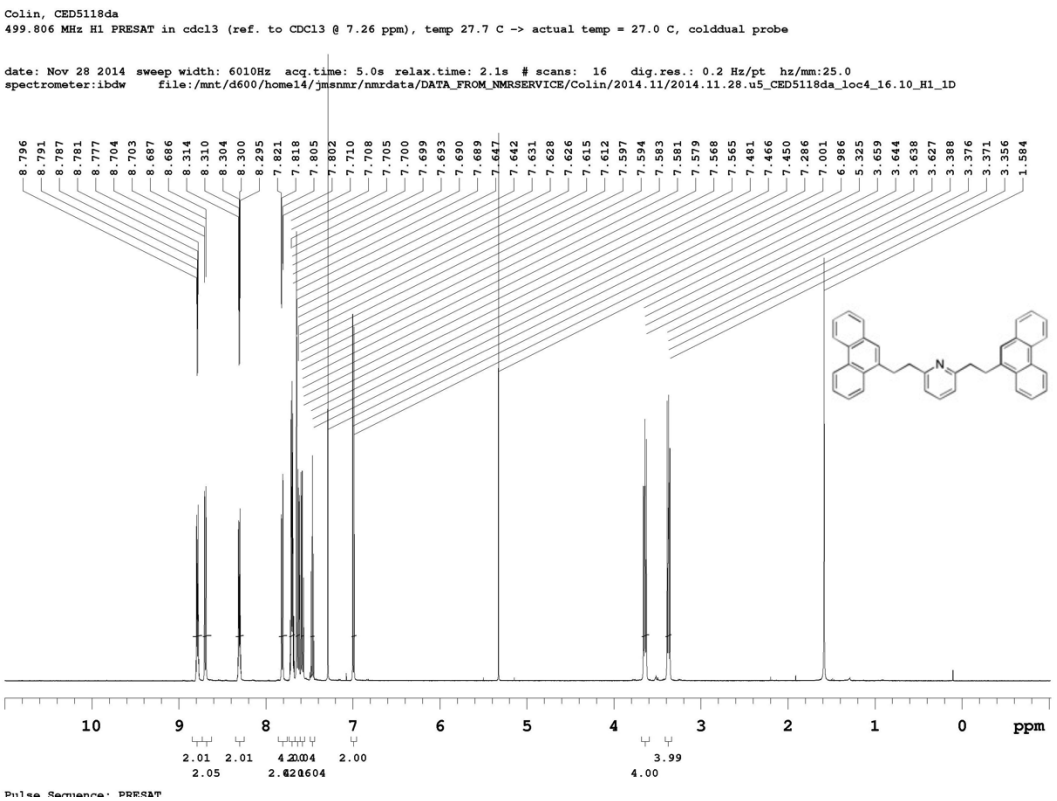


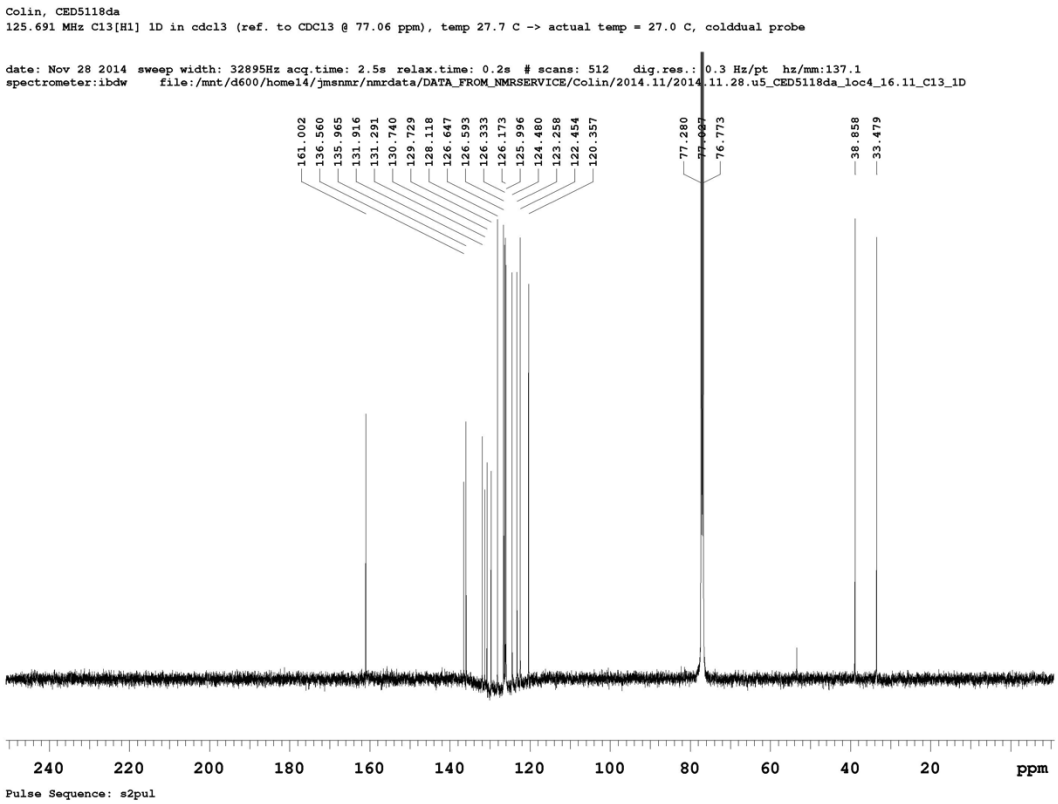
^{1}H (500 MHz) and ^{13}C (126 MHz) NMR of 3-16 in $CDCl_3$ at 25 °C



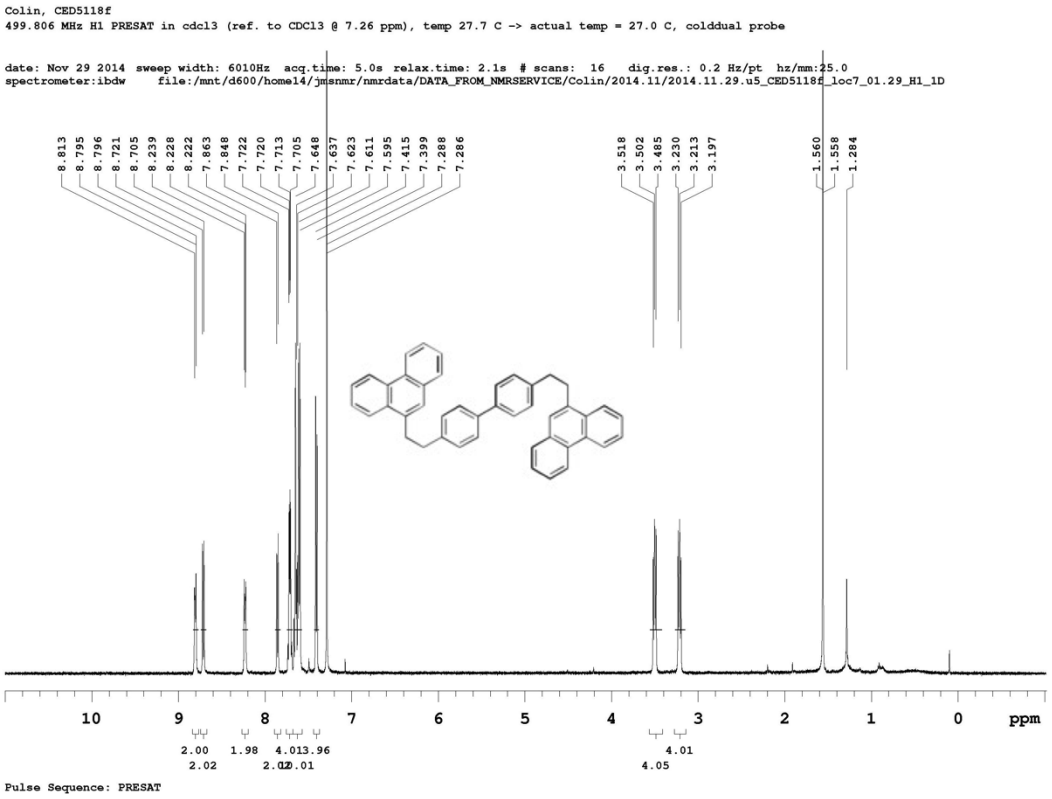


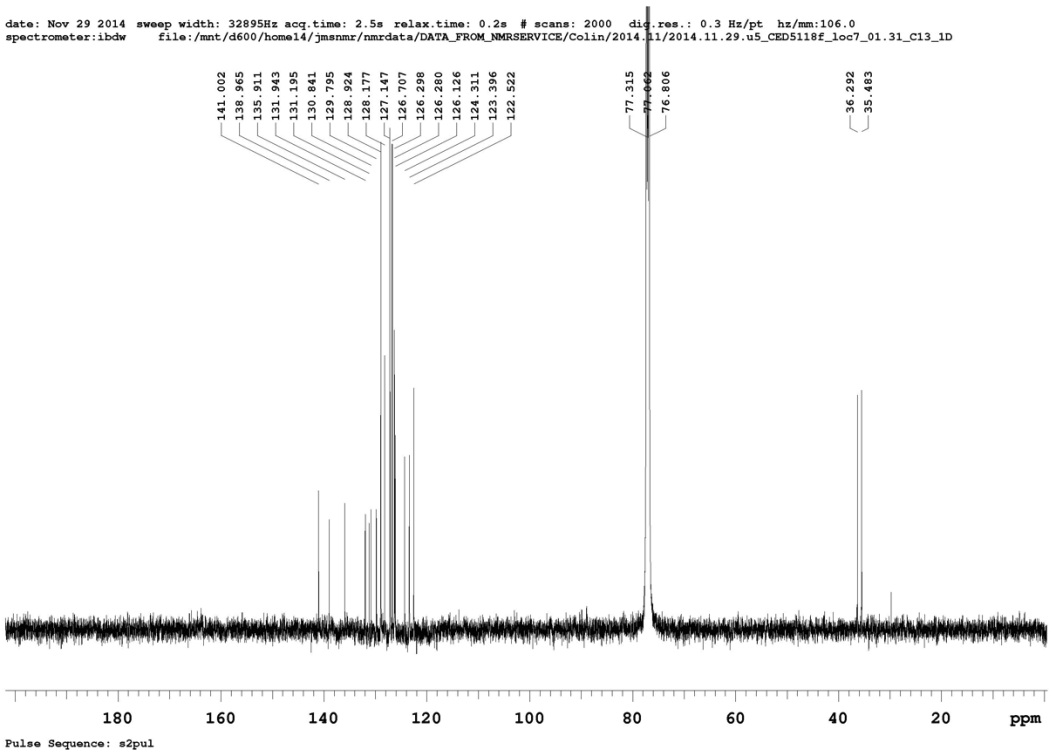
^{1}H (500 MHz) and ^{13}C (126 MHz) NMR of 3-17 in $CDCl_3$ at 25 °C



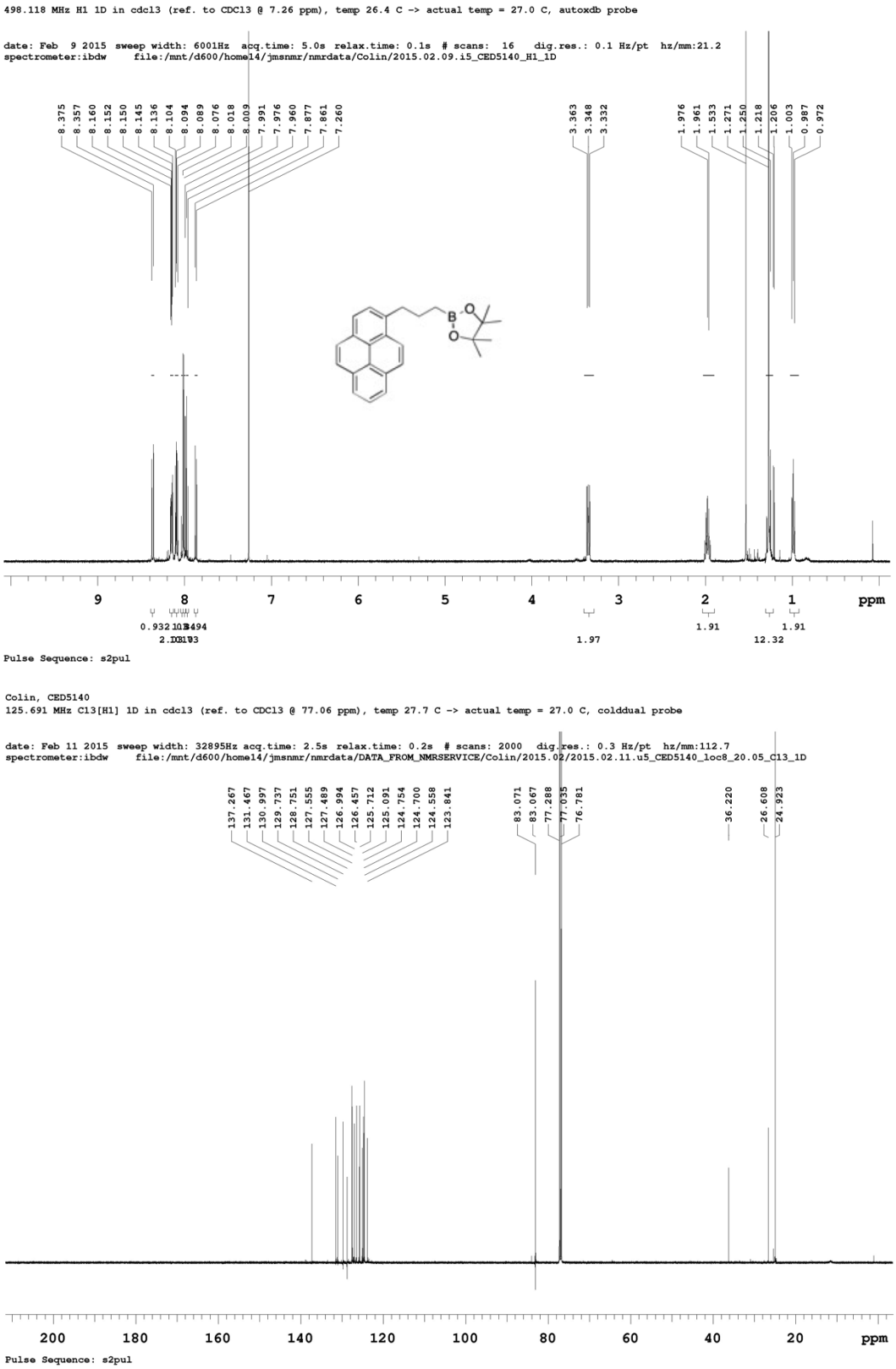


^{1}H (500 MHz) and ^{13}C (126 MHz) NMR of 3-18 in $CDCl_3$ at 25 °C

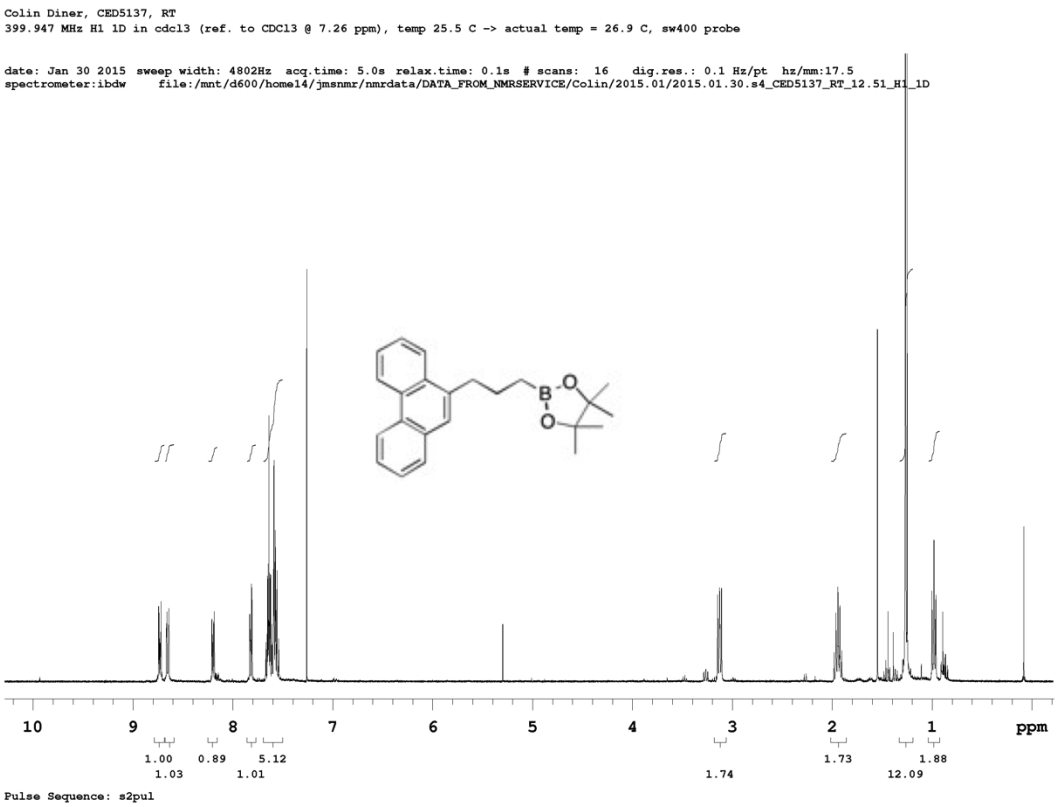


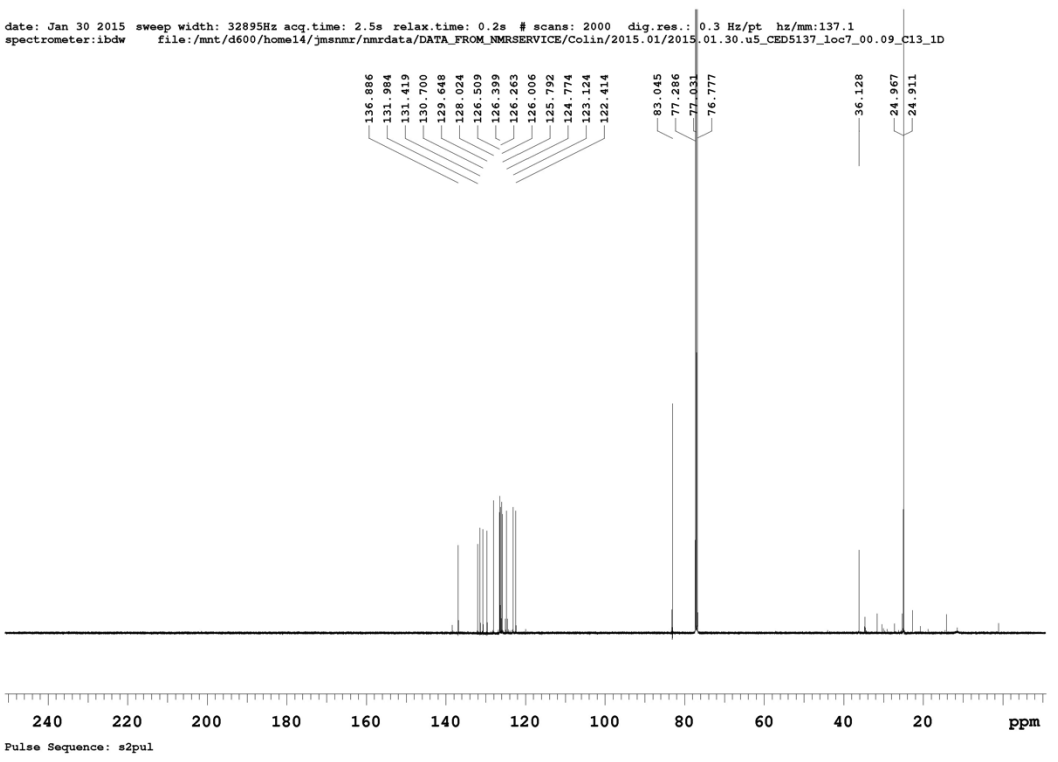


^{1}H (500 MHz) and ^{13}C (126 MHz) NMR of 3-19 in $CDCl_3$ at 25 °C

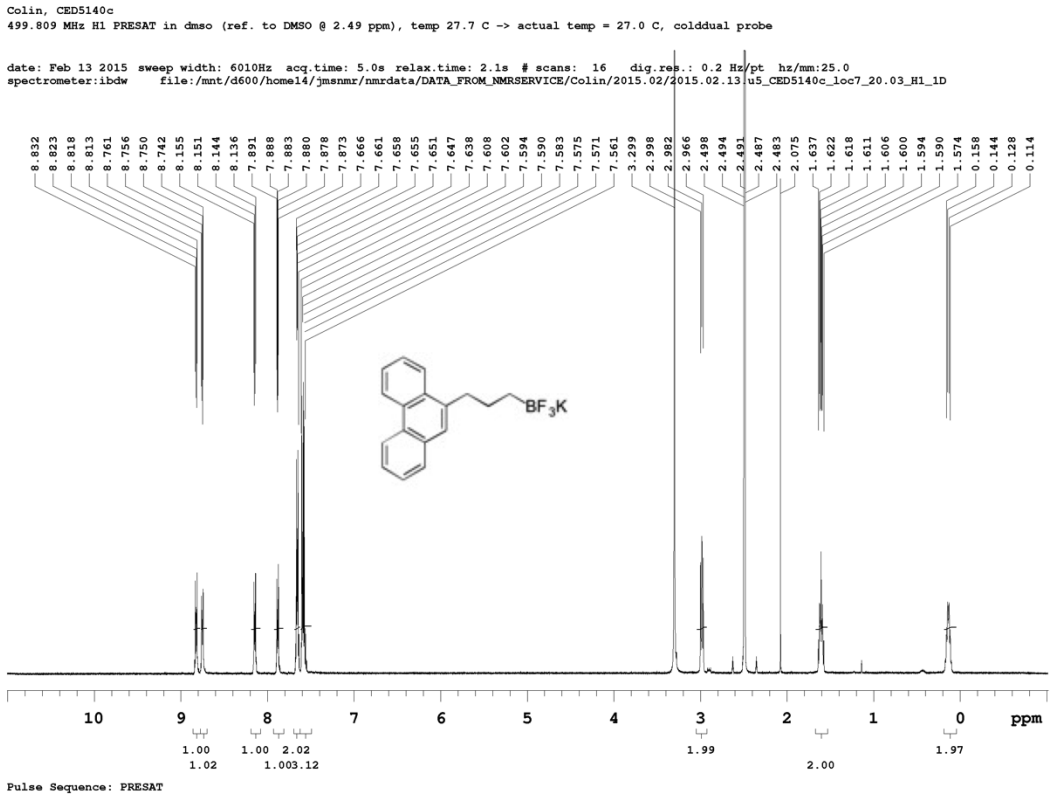


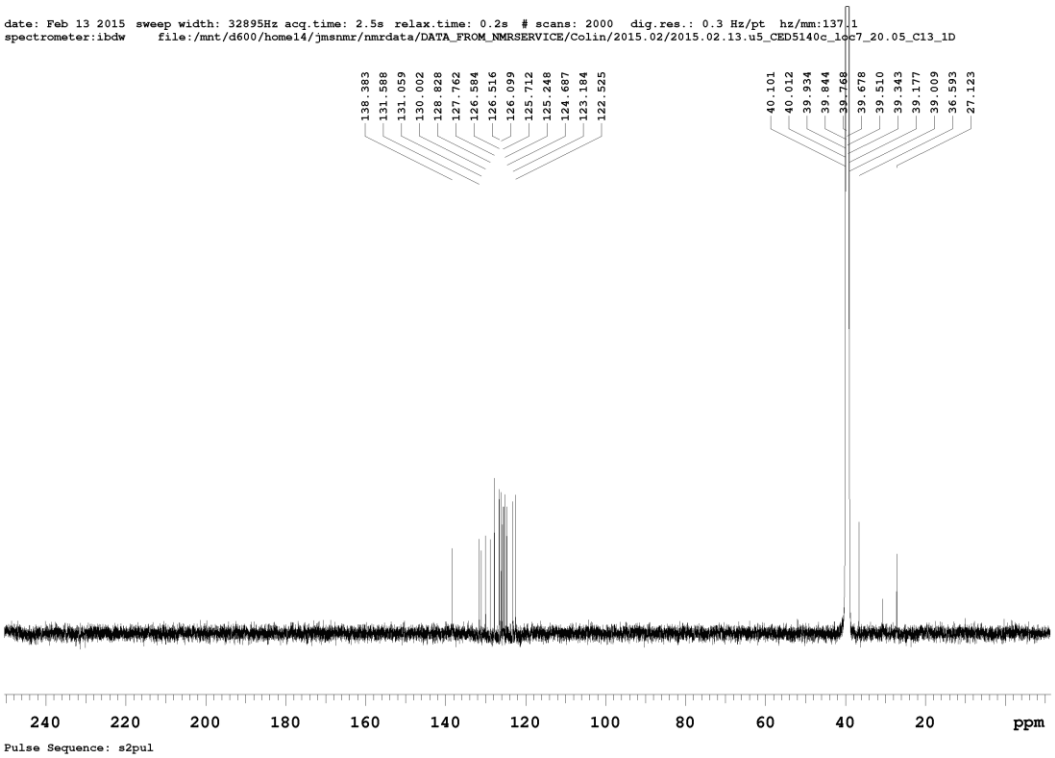
^{1}H (500 MHz) and ^{13}C (126 MHz) NMR of 3-20 in $CDCl_3$ at 25 °C



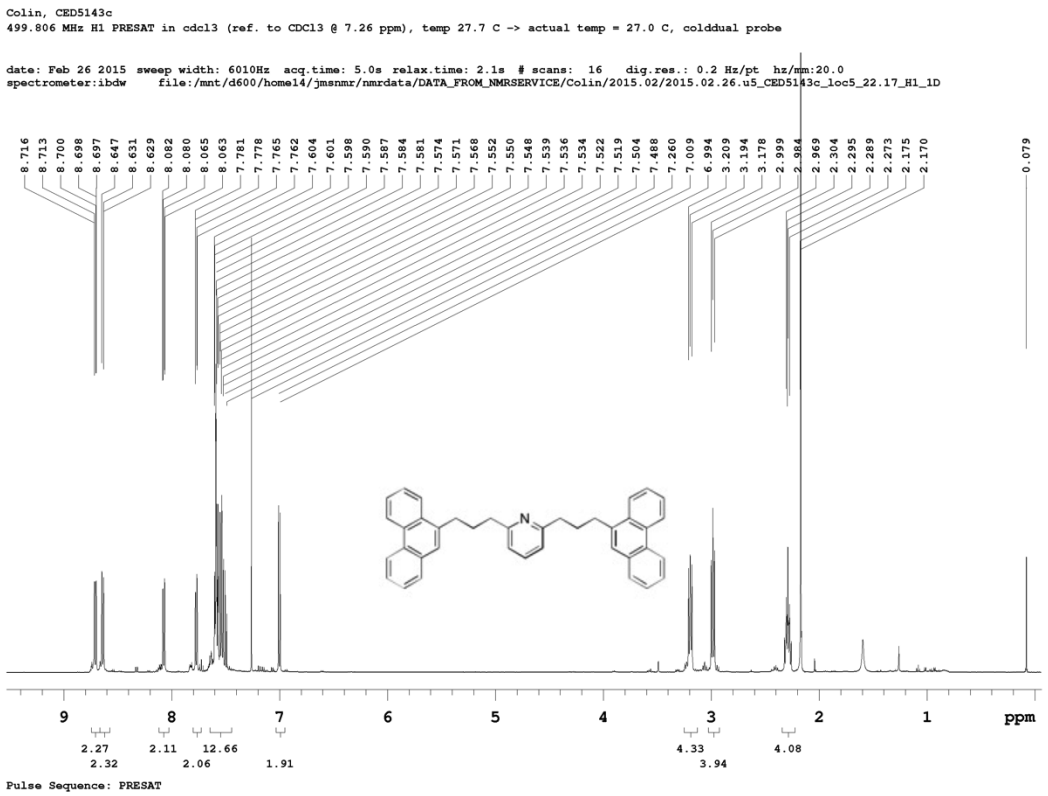


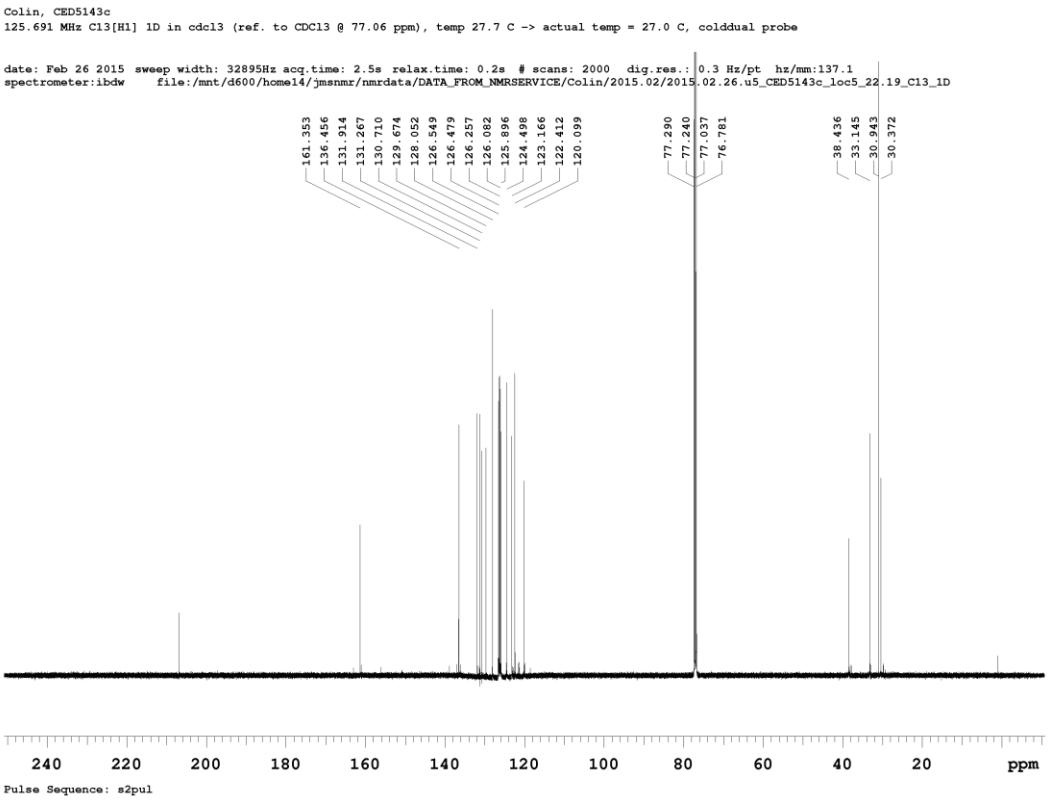
^{1}H (500 MHz) and ^{13}C (126 MHz) NMR of 3-21 in DMSO at 25 °C





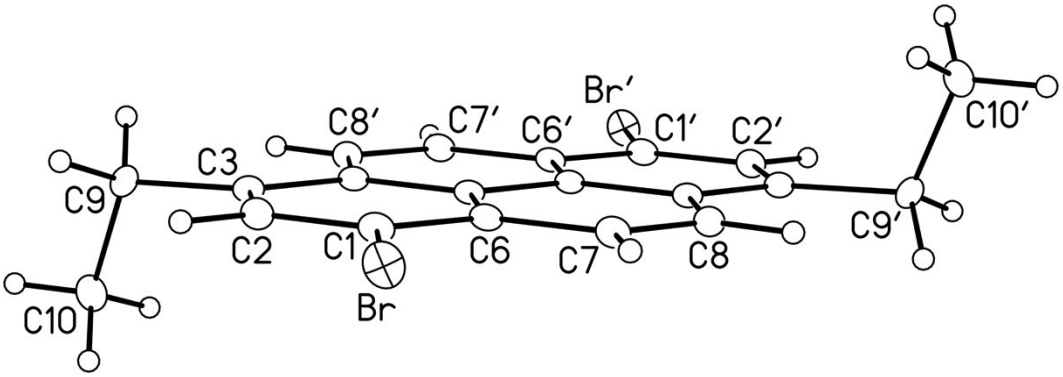
^{1}H (500 MHz) and ^{13}C (126 MHz) NMR of 3-22ca in $CDCl_3$ at 25 °C





Appendix 2: Crystallographic Experimental Details

Crystallographic information for compound 2-11



Perspective view of the 1,6-dibromo-3,8-diethylpyrene molecule showing the atom labelling scheme. Non-hydrogen atoms are represented by Gaussian ellipsoids at the 20% probability level. Hydrogen atoms are shown with arbitrarily small thermal parameters. Primed items are related to unprimed ones via the crystallographic inversion center (0, 0, 1/2) at the midpoint of the C5–C5' bond.

Crystallographic Experimental Details:

A. Crystal Data	
formula	$C_{20}H_{16}Br_2$
formula weight	416.15
crystal dimensions (mm)	0.83 × 0.11 × 0.08
crystal system	monoclinic
space group	$P2_1/c$ (No. 14)
unit cell parameters[a]	
a (Å)	4.6911 (3)
b (Å)	17.4098 (12)
c (Å)	9.8234 (7)
β (deg)	100.4212 (8)
V (Å^3)	789.05 (9)
Z	2
ρ_{calcd} (g cm^{-3})	1.752

μ (mm^{-1})	5.130

B. Data Collection and Refinement Conditions

diffractometer	Bruker PLATFORM/APEX II CCD[b]
radiation (λ [Å])	graphite-monochromated Mo Kα (0.71073)
temperature (°C)	–100
scan type	ω scans (0.3°) (20 s exposures)
data collection 2θ limit (deg)	55.16
total data collected	6945 (-6 ≤ h ≤ 6, -22 ≤ k ≤ 22, -12 ≤ l ≤ 12)
independent reflections	1813 (R_{int} = 0.0131)
number of observed reflections (*NO*)	1654 [$F_o^2 \geq 2\sigma(F_o^2)$]
structure solution method (*DIRDIF–2008*[c])	Patterson/structure expansion
refinement method (*SHELXL–97*[d])	full-matrix least-squares on F^2
absorption correction method	Gaussian integration (face-indexed)
range of transmission factors	0.6934–0.0997
data/restraints/parameters	1813 / 0 / 100
goodness-of-fit (*S*)[e] [all data]	1.099
final *R* indices[f]	
R_1 [$F_o^2 \geq 2\sigma(F_o^2)$]	0.0223
wR_2 [all data]	0.0609
largest difference peak and hole	0.587 and –0.267 e Å^{-3}

[a]Obtained from least-squares refinement of 7130 reflections with 4.68° < 2θ < 55.16°.

[b]Programs for diffractometer operation, data collection, data reduction and absorption correction were those supplied by Bruker.

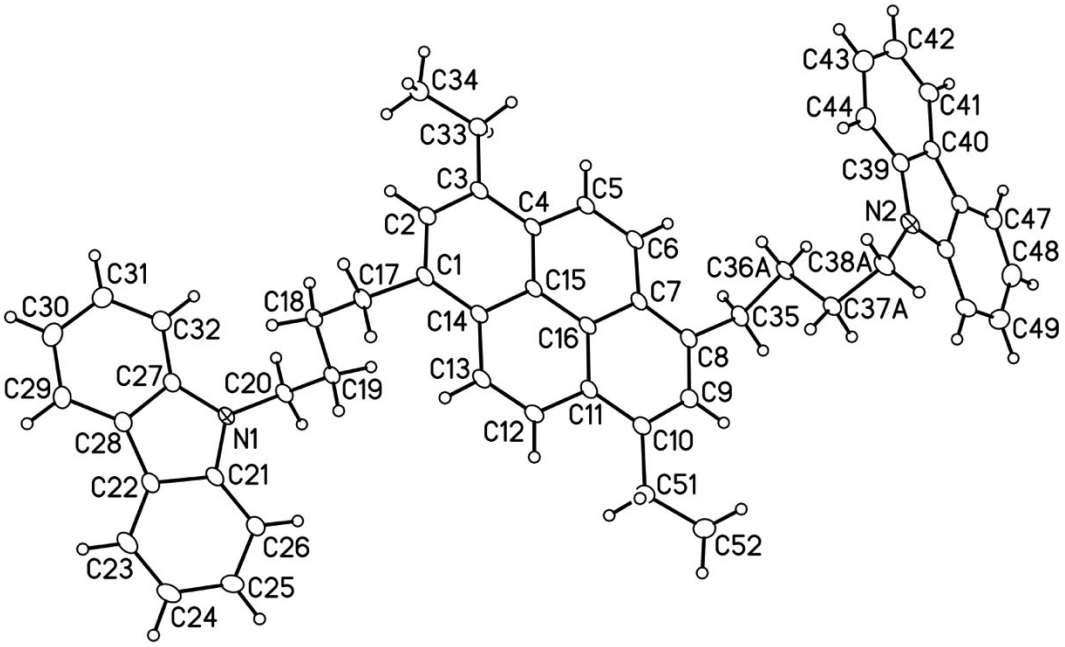
[c]Beurskens, P. T.; Beurskens, G.; de Gelder, R.; Smits, J. M. M.; Garcia-Granda, S.; Gould, R. O. (2008). The *DIRDIF-2008* program system. Crystallography Laboratory, Radboud University Nijmegen, The Netherlands.

[d]Sheldrick, G. M. *Acta Crystallogr.* **2008**, *A64*, 112–122.

[e]$S = [\Sigma w(F_o^2 - F_c^2)^2/(n - p)]^{1/2}$ (n = number of data; p = number of parameters varied; $w = [\sigma^2(F_o^2) + (0.0311P)^2 + 0.4598P]^{-1}$ where $P = [\text{Max}(F_o^2, 0) + 2F_c^2]/3$).

[f]$R_1 = \Sigma||F_o| - |F_c||/\Sigma|F_o|$; $wR_2 = [\Sigma w(F_o^2 - F_c^2)^2/\Sigma w(F_o^4)]^{1/2}$

Crystallographic information for compound 2-18



Perspective view of the 1,6-bis{4-(9*H*-carbazol-9-yl)but-1-yl}-3,8-diethylpyrene molecule showing the atom labelling scheme. Non-hydrogen atoms are represented by Gaussian ellipsoids at the 20% probability level. Hydrogen atoms are shown with arbitrarily small thermal parameters.

Crystallographic Experimental Details

A. Crystal Data

formula	$C_{52}H_{48}N_2$
formula weight	700.92
crystal dimensions (mm)	0.35 × 0.07 × 0.02
crystal system	monoclinic
space group	$P2_1/n$ (an alternate setting of $P2_1/c$ [No. 14])
unit cell parameters[a]	
a (Å)	9.0178 (3)
b (Å)	8.8539 (3)
c (Å)	46.2151 (14)
β (deg)	93.785 (2)
V (Å^3)	3681.9 (2)

Z	4
ρ_{calcd} (g cm^{-3})	1.264
μ (mm^{-1})	0.549

B. Data Collection and Refinement Conditions

diffractometer	Bruker D8/APEX II CCD[b]
radiation (λ [Å])	Cu Kα (1.54178) (microfocus source)
temperature (°C)	–100
scan type	ω and ϕ scans (1.0°) (5 s exposures)
data collection 2θ limit (deg)	135.98
total data collected	20571 (-10 ≤ h ≤ 10, -10 ≤ k ≤ 10, -55 ≤ l ≤ 55)
independent reflections	6383 (R_{int} = 0.0958)
number of observed reflections (*NO*)	3865 [$F_o^2 \geq 2\sigma(F_o^2)$]
structure solution method	direct methods (*SHELXS–97*[c])
refinement method	full-matrix least-squares on F^2 (*SHELXL–97*[c])
absorption correction method	Gaussian integration (face-indexed)
range of transmission factors	0.9869–0.8303
data/restraints/parameters	6383 / 2 / 515
extinction coefficient (x)[d]	0.0018(2)
goodness-of-fit (S)[e] [all data]	1.021
final R indices[f]	
R_1 [$F_o^2 \geq 2\sigma(F_o^2)$]	0.0719
wR_2 [all data]	0.2120
largest difference peak and hole	0.278 and –0.308 e Å^{-3}

[a]Obtained from least-squares refinement of 3692 reflections with 7.66° < 2θ < 133.78°.

[b]Programs for diffractometer operation, data collection, data reduction and absorption correction were those supplied by Bruker.

[c]Sheldrick, G. M. *Acta Crystallogr.* **2008**, *A64*, 112–122.

[d]The following pairs of distances within the disordered 4-(9*H*-carbazol-9-yl)but-1-yl group were constrained to be equal (within 0.03 Å) during refinement: d(N2–C38A) = d(N2–C38B); d(C37A–C38A) = d(C37B–C38B).

[e]$F_c^* = kF_c[1 + x\{0.001F_c^2\lambda^3/\sin(2\theta)\}]^{-1/4}$ where k is the overall scale factor.

[f]$S = [\Sigma w(F_o^2 - F_c^2)^2/(n - p)]^{1/2}$ (n = number of data; p = number of parameters varied; $w = [\sigma^2(F_o^2) + (0.0771P)^2 + 0.4490P]^{-1}$ where $P = [\text{Max}(F_o^2, 0) + 2F_c^2]/3$).

[g]$R_1 = \Sigma||F_o| - |F_c||/\Sigma|F_o|$; $wR_2 = [\Sigma w(F_o^2 - F_c^2)^2/\Sigma w(F_o^4)]^1$