Synthesis of Polycyclic Aromatic Hydrocarbon Containing Cyclophanes: New and Improved Methodologies

By

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Abstract

Cyclophanes are a vast class of compounds that can be defined as any system containing an aromatic system bridged by at least one *n*-membered bridge ($n \geq 0$). This description encompasses a large number of compounds, but relatively few examples in which the aromatic system is more complex than benzene exist. This is largely due to the increase is synthetic difficulty and a lack of universal methodologies. The work described in this thesis includes improvements in the synthesis of pyrenophanes and the introduction of new methodology for cyclophane formation in which the aromatic unit is peropyrene.

Chapter 1 serves as an introduction to the concept of non-planarity in aromatic systems and the strategies for incorporating such morphologies into structures. Focus has been placed primarily on cyclophanes containing one aromatic system and one bridge and their advantages in structural modulation.

Chapter 2 contains a review of the history of pyrenophanes and strategies towards their preparation. Improvements to the synthesis of the 1,*n*-dioxa-[*n*](2,7)pyrenophanes and [*n*](2,7)pyrenophanes are discussed in detail. Additionally, the reactivity of these systems is briefly discussed.

Chapter 3 introduces peropyrene and discusses its properties and limited synthetic accessibility. The synthesis of a series of new cyclophanes is discussed which takes advantage of the dimerization of phenalenlyl radicals generated phenalene. Characterization of resulting [*n*](2,6)peropyrenophanes is briefly discussed.

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List of Abbreviations

2D EXSY	2D exchange spectroscopy
Å	Ångstrom(s)
Ac	acetyl
AcOH	acetic acid
AM1	Austin Model 1
APPIMS	atmospheric pressure photoionization mass spectrometry
ASE	aromatic stabilization energy
B3LYP	Becke, 3-parameter, Lee–Yang–Parr
Bn	benzyl
B_2pin_2	bis(pinacoloto)diboron
Bu	butyl
°C	Degree(s) Celcius
CAD	Canadian dollar
CFA	coal fly ash
COSY	correlation spectroscopy
d	doublet
D	Dalton(s)
DBU	1,8-diazabicyclo[5.4.0]undec-7-ene
DDQ	2,3-dichloro-5,6-dicyano-1,4-benzoquinone
DFT	density functional theory
DIBAL	diisobutylaluminium hydride
DME	dimethoxyethane
DMF	dimethylformamide
DMSO	dimethyl sulfoxide
dppf	1,1’-bis(diphenylphosphino)ferrocene

ESR	electron spin resonance
Et	ethyl
eV	electronvolt
FVP	flash vacuum pyrolysis
$\Delta G^{\ddagger}$	Gibbs free energy of activation
g	gram(s)
h	hour(s)
HMPT	hexemethylphosphoramide
HOMA	harmonic oscillator model of aromaticity
HPLC	high-performance liquid chromatography
HRMS	high-resolution mass spectrometry
HWE	Horner-Wadsworth-Emmons
i	iso
K	Kelvin
kcal	kilocalorie
LDA	lithium diisopropylamide
m	multiplet
m	*meta*
m-CPBA	*meta*-chloroperoxybenzoic acid
Me	methyl
mg	milligram(s)
MHz	megahertz
min	minute(s)
mL	milliliter(s)
mm	millimeter(s)
MM2	molecular mechanics
mmol	millimole(s)
mol	mole(s)
m.p.	melting point

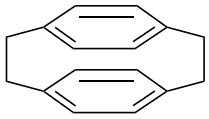
NBS	*N*-bromosuccinimide
NIS	*N*-iodosuccinimide
nm	nanometer(s)
NMI	*N*-methylimidazole
NMP	*N*-methyl-2-pyrrolidone
NMR	nuclear magnetic resonance
NOESY	nuclear Overhauser effect spectroscopy
o	*ortho*
p	*para*
PAH	polycyclic aromatic hydrocarbon
PCC	pyridinium chlorochromate
Ph	phenyl
PPA	polyphosphoric acid
ppm	parts per million
Py	pyridine
q	quartet
R_f	retention factor
rt	room temperature
s	singlet
SOMO	singly occupied molecular orbital
t	triplet
t	tertiary
TBAB	tetra-*n*-butylammonium bromide
TBAI	tetra-*n*-butylammonium iodide
TCNE	tetracyanoethylene
TDAE	tetrakis(dimethylamino)ethylene
Tf	trifluoromethanesulfonyl
TFA	trifluoroacetic acid
THF	tetrahydrofuran

TLC	thin-layer chromatography
TMSA	trimethylsilylacetylene
TMS	trimethylsilyl
Torr	Torricelli (1 Torr = 1 mm Hg)
Ts	tosyl or 4-toluenesulfonyl
UV	ultraviolet
VID	valence isomerization/dehydrogenation
Vis	visible
VT-NMR	variable temperature nuclear magnetic resonance

Chapter 1: Introduction

1.1: Nonplanar Aromatic Hydrocarbons

When encountering the subject of aromaticity for the first time, students of organic chemistry are usually presented with a set of criteria that a molecule must fulfill in order to be considered aromatic. Typical criteria are: 1) the compound must be cyclic, 2) the compound must be planar, 3) the cycle must contain an uninterrupted set of conjugated double bonds, 4) the pi system must obey Hückel's rule. By any yardstick, the introductory definition of aromaticity is nebulous, and this is compounded by the fact that no way of measuring aromaticity is presented. Thus, when a compound such as [2.2]paracyclophane (**1.01**), which contains nonplanar aromatic rings, many students will conclude that it is not aromatic. Other parameters sometimes mentioned include the propensity for aromatic compounds to undergo substitution reactions rather than addition reactions, however, this is less of a criterion for aromaticity than a consequence of it. Additionally, the issues of energy and magnetism may also come into the discussion at introductory level, but they are reserved as the focal point at higher levels.



1.01

Figure 1.1 [2.2]Paracyclophane (**1.01**).

Hückel published his first paper on the electronic structure of benzene in 1931[1], but its concise formulation as the 4*n*+2 rule, which is often attributed to Doering, came two decades later in 1951.[2] This coincided with Cram's report of a rational synthesis of [2.2]paracyclophane (**1.01**),[3] just two years after Brown and Farthing's discovery of this remarkable compound in the pyrolysate of *p*-xylene.[4] The boat conformations of the

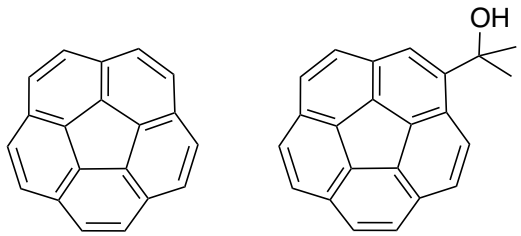
benzene rings in [2.2]paracyclophane (**1.01**) not only marked the dawn of cyclophane chemistry, but also sparked broad interest in the nature of aromaticity and the consequences of distorting aromatic systems from their ideal planar conformations.

In a large majority of cases, the lowest energy structure of an aromatic system is planar. Deviations from planarity, or whatever the lowest energy geometry is, naturally require energy and this begs the question of how structure and the energy of the system are related. Answering this question requires the synthesis of compounds with aromatic systems that are forced to adopt nonplanar geometries. Over the past seven decades, much effort has been invested into doing so and the general approaches can be categorized under three main headings: the incorporation of embedded non-6-membered rings, steric crowding and bridging.

1.1.1: Nonplanar Aromatic Hydrocarbons with Embedded Non-6-membered rings

The strategy of incorporating embedded non-6-membered rings to produce nonplanar aromatic systems can be exemplified in the structure of corannulene (**1.02**), which has as a bowl-shaped lowest energy structure owing to the circumannulated 5-membered ring (**Figure 1.2**). Corannulene (**1.02**) is conformationally dynamic, undergoing a bowl-to-bowl inversion. This process has not yet been directly observed for corannulene itself, but rather in suitably functionalized systems where there is a means to differentiate between the two bowl conformations. In 1992, Scott *et al.* synthesized corannulenyl-dimethylbarbinol (**1.03**), the methyl protons of which are diastereotopic in either bowl conformation but exchange their environments upon inversion.[5] The two methyl groups of **1.03** appear as a single peak in its ^{1}H NMR spectrum at room temperature in acetone-d_6, indicating that inversion is rapid at this temperature.[3] When the ^{1}H NMR spectrum was measured at –90 °C, two well-resolved singlets were observable from the two distinct diastereotopic methyl groups. The temperature of

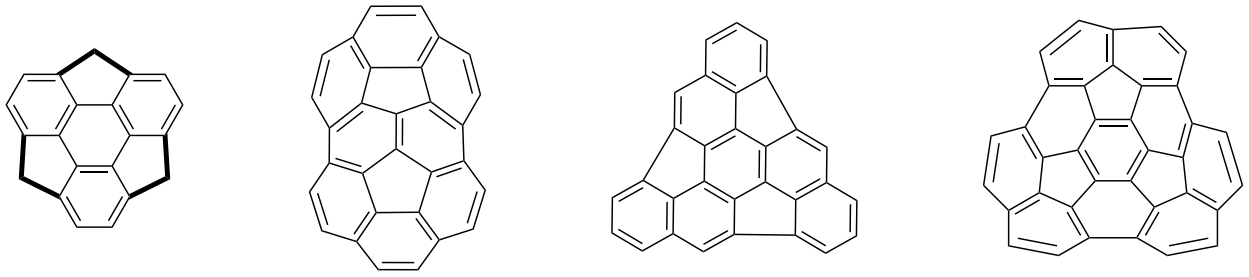
coalescence was found to be –64 °C, which allowed to the bowl-to-bowl inversion barrier to be calculated ($\Delta G^{\ddagger}$ = 10.2 $\pm$ 0.2 kcal/mol). This value is comparable to the to the chair-to-chair inversion of cyclohexane ($\Delta G^{\ddagger}$ = 10.3 kcal/mol at –67 °C).



1.02 **1.03**

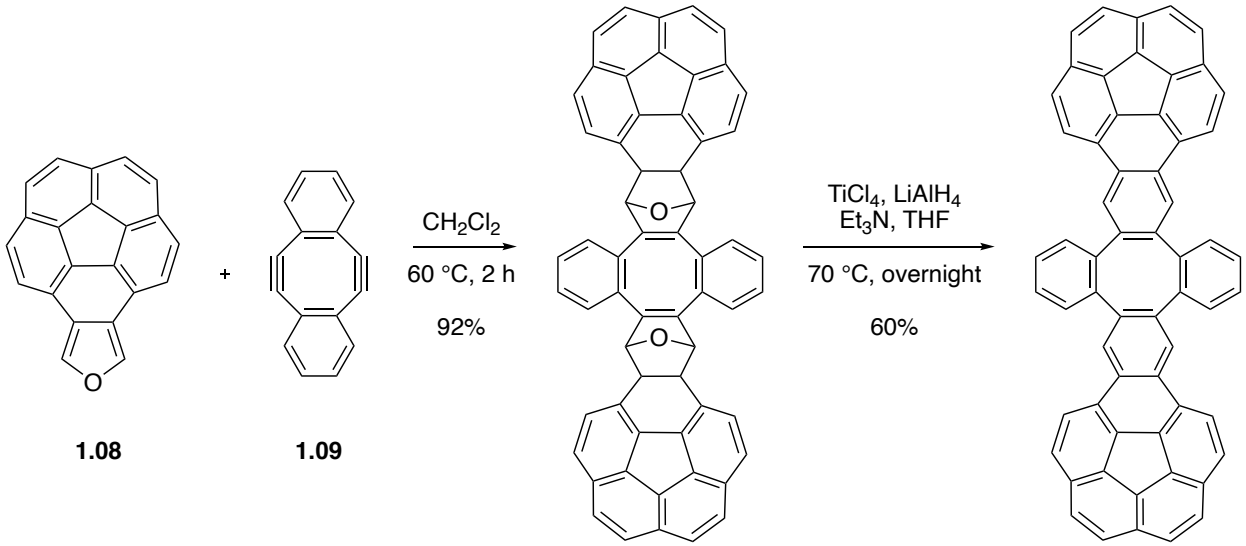
Figure 1.2. Corannulene (**1.02**) and corannulenyl-dimethylcarbinol (**1.03**).

Other notable nonplanar aromatic systems containing 5-membered rings include sumanene (**1.04**), and two isomeric semibuckminsterfullerenes ($C_{30}H_{12}$) **1.05** and **1.06**, circumtriindene (**1.07**) and numerous other corannulene containing systems (**Figure 1.3**). Numerous other corannulene-based systems have been reported and they are often described as buckybowls because they map onto the surface of buckminsterfullerenes. Some corannulene-based systems have found use in supramolecular chemistry as host molecules for fullerenes since their bowl-shaped cavities are appropriately sized. Corannulene (**1.02**) itself is not one of these – mixing it with fullerenes gives no evidence of complexation, likely due to the entropic and solvation energetic costs associated with it. More complex systems, such as those that contain two peripheral corannulene units connected by some a rigid spacer are more effective hosts. For example, Sygula *et al.* designed and synthesized a "buckycatcher".[6] Isofuranocorannulene (**1.08**) was treated with dibenzocyclooctadiyne (**1.09**) in a Diels-Alder reaction to give bis-corannulenyl system **1.10**. This mixture of isomers was deoxygenated with low-valent titanium to give buckybowl **1.11**, which could exist as a mixture of 4 isomers (**Scheme 1.1**). A 1:1 mixture of buckybowl **1.11** and C_{60} afforded the C_{60}@**1.11** inclusion complex, which has a calculated binding energy of 43.1 kcal/mol (B97-D/TZVP level of theory).[7]



1.04 **1.05** **1.06** **1.07**

Figure 1.3 Other bowl-shaped polycyclic aromatic hydrocarbons.



1.08 **1.09** **1.10** **1.11**

Scheme 1.1. Synthesis of Sygula's "buckycatcher".

These corannulene-based inclusion complexes with fullerenes have potential applications. For example, buckycatchers could conceivably be attached to stationary phases in chromatography for the separation of particular fullerenes from complex mixtures. Tuning the cavity size of the buckycatchers might then provide a means to target fullerenes of different sizes. Another potential area of research into applications is their use in molecular electronics. Buckycatchers attached to a surface in a regular

fashion would allow for deposition of fullerenes onto these surfaces in a controlled fashion. This is an attractive research avenue because fullerene and its derivatives have already found utility in photovoltaic devices since they readily absorb light and are excellent electron acceptors.

In comparison to the corannulene (**1.02**), it took much longer for a synthesis of sumanene (**1.04**) to be realized.[8] Sumanene (**1.04**), which was first synthesized in 2003, also has a bowl-shaped lowest energy conformation that can undergo bowl-to-bowl inversion. Trideuteriosumanene (**1.12**) was synthesized to measure the energetics of the bowl-to-bowl inversion using 2D EXSY NMR experiments. The activation energy for inversion was found to be 20.4 kcal/mol ($CDCl_3$), which is about twice that of corannulene.[9] Most of the continuing work on sumanene-based systems has been aimed at the synthesis of pi extended systems such as naphthosumanenes (**1.13**, **1.14**, and **1.15**) (**Figure 1.4**).[10]

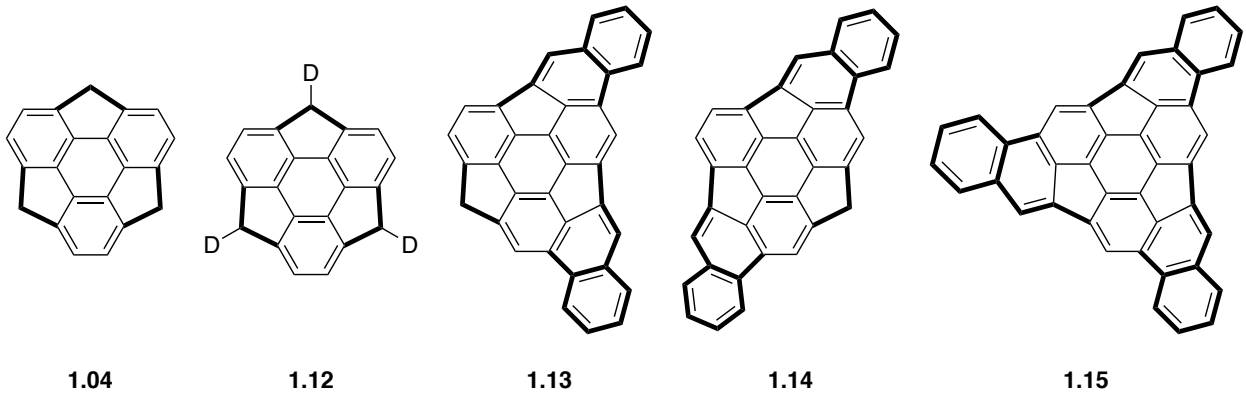
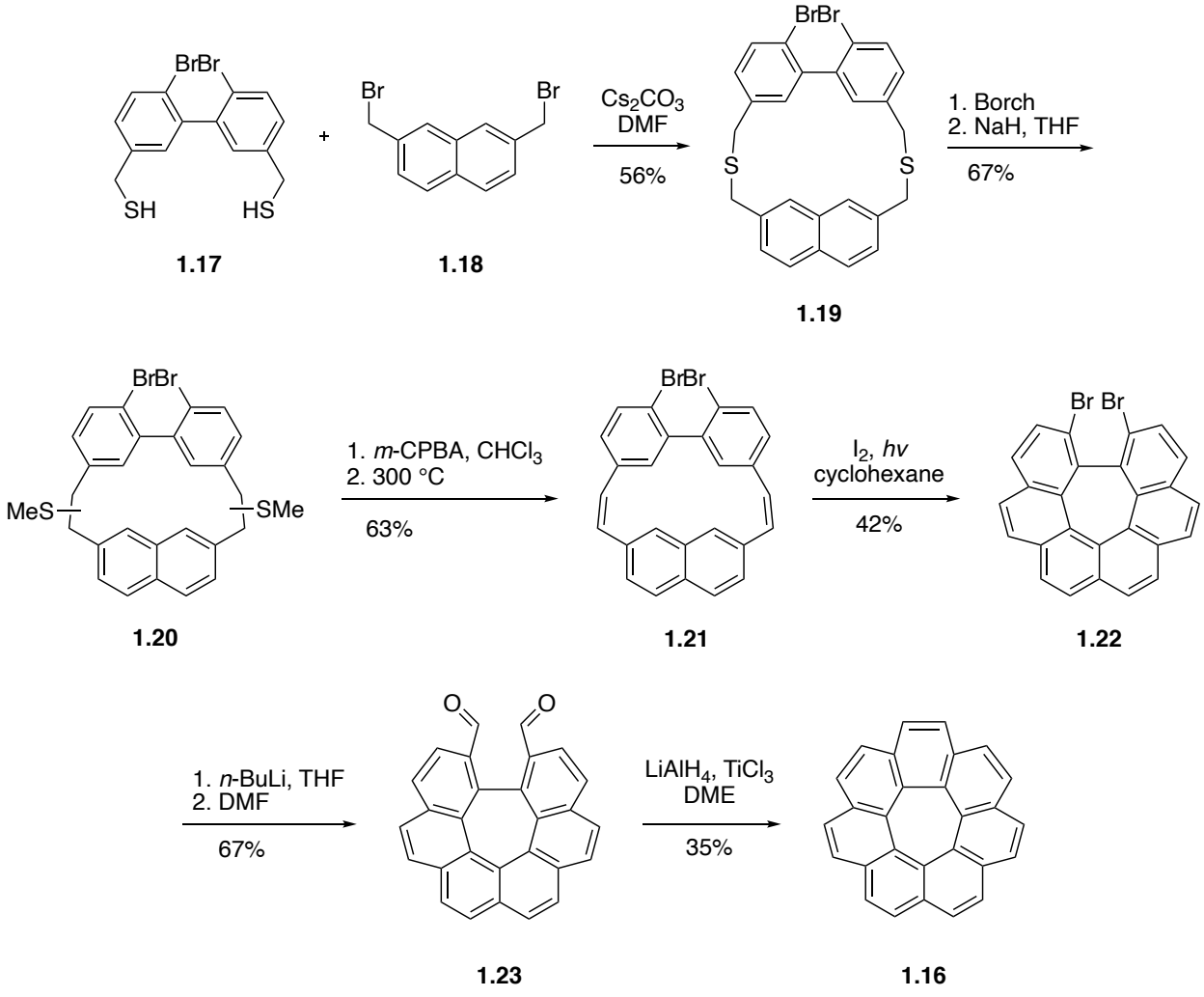


Figure 1.4. Sumanene (**1.04**) and some of its derivatives.

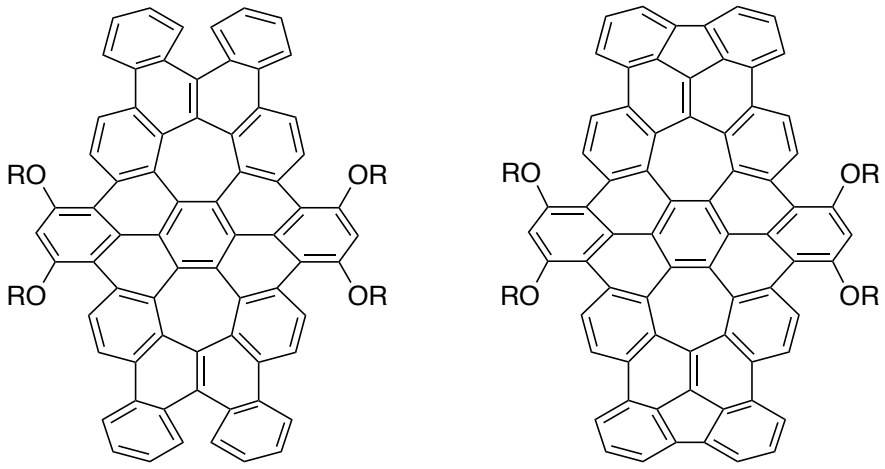
Less common are systems that incorporate 7 or 8-membered rings. The simplest 7-membered ring system is [7]circulene (**1.16**), which was first synthesized in the 1980s by Yamamoto *et al.* using a dithiacyclophane approach (**Scheme 1.2**).[11] A biphenyl dithiol **1.17** and 2,7-bis(bromomethyl)naphthalene (**1.18**) were coupled in the presence of Cs_2CO_3 under high dilution conditions to give dithiacyclophane **1.19** in 56% yield. This was treated with Borch reagent to give a bis(methylsulfonium) salt, which was subjected

to a thia-Stevens rearrangement upon reaction with NaH to give **1.20**. This system was oxidized to give a disulfoxide, which was pyrolyzed at 300 °C to bring about sulfoxide elimination and give cyclophanediene **1.21**. A stilbene/phenanthrene-type photocyclization then gave **1.22**. The remaining bromide substituents were converted into formyl groups by a lithiation/formylation protocol to afford **1.23**. The final closure was accomplished by an intramolecular McMurry reaction to give [7]circulene (**1.16**). Other synthetic routes to [7]circulene (**1.16**) have appeared in the literature over the years.[12,13]



Scheme 1.2 First synthesis of [7]circulene (**1.16**) by Yamamoto.

[7]Circulene containing PAHs have recently been synthesized that adopt saddle-shaped molecular geometries. Miao's carbon nanostructure (**1.24a-b** and **1.25a-b**) contain negative curvature owing to their saddle-shape (**Figure 1.5**).[14] On first glance, one might expect these extended π-system to be extremely rigid, but they are in fact quite flexible as evidenced by their weak to non-existent fluorescence in solution. The flexibility makes radiationless internal conversion more facile and consumes the absorbed energy. The authors compared the level of non-planarity for individual rings with the harmonic oscillator model of aromaticity (HOMA) values and found a rough correlation between higher non-planarity and lower aromaticity. The rings with lower aromaticity also correspond to those that do not show Clar sextets when drawn to maximize them.



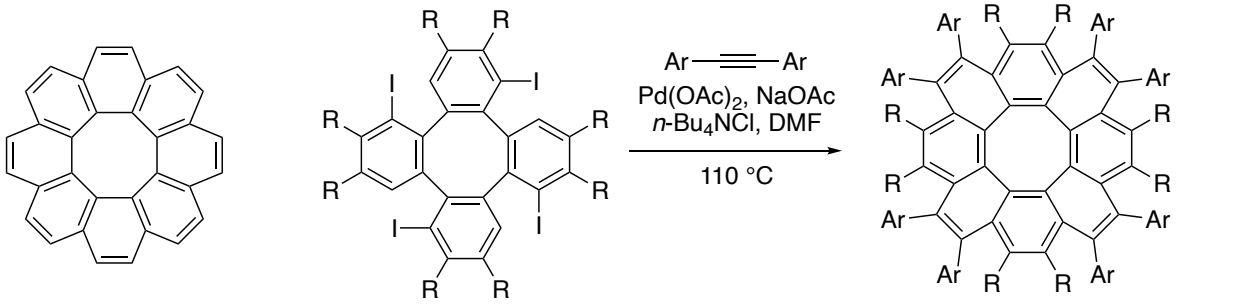
1.24a R = *n*-octyl
1.24b R = *n*-hexyl

1.25a R = *n*-octyl
1.25b R = *n*-hexyl

Figure 1.5 Miao's saddle-shaped carbon nanostructures.

The parent circumannulated 8-membered ring system [8]circulene (**1.26**) has yet to be synthesized, but it is predicted to be of relatively low stability due to concentric aromatic ring currents. In the last few years, the synthesis of [8]circulene derivatives has been realised with the first coming from Wu *et al.* in 2013.[15] They constructed the 8-membered ring system in the early stages to give tetraphenylene derivatives **1.27a-b**.

These compounds were in fact mixtures of different iodo-regioisomers. Palladium catalyzed annulation of this system with diarylethynes gave the highly decorated [8]circulene derivatives (**1.28a-c**) in pretty good yields. The X-ray crystal structure of **1.28a** revealed it to be saddle-shaped and slightly skewed from the D_{2d} point group (**Scheme 1.3**). HOMA values of the different ring systems show that the central 8-membered ring is non-aromatic whereas the rings bearing the aryl groups was slightly more aromatic (0.629) than those bearing the methyl groups (0.369).



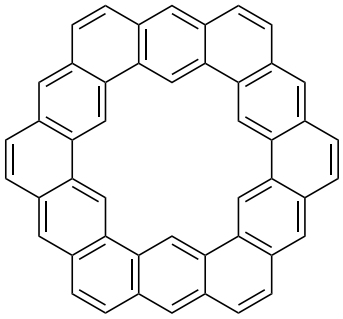
1.26

1.27a R = OMe
1.27b R = Me

1.28a R = OMe, Ar = 4-$(CH_3)C_6H_4$ (75%)
1.28b R = Me, Ar = 4-$(CH_3)C_6H_4$ (60%)
1.28c R = Me, Ar = 3,5-$(CH_3)_2C_6H_4$ (68%)

Scheme 1.3. Structure of [8]circulene and synthesis of [8]circulene derivatives **1.28a-c**.

No higher order circulenes have been successfully synthesized expect for kekulene (**1.28**), which was an early on in 1978 (**Figure 1.6**).[16] This circulene differs from those discussed above in that the annulene it is derived from has *E*-configured alkenes. Kekulene (**1.28**) is circumannulated (*E,E,Z,E,E,Z,E,E,Z,E,E,Z,E,E,Z,E,E,Z*)[18]annulene. The twelve *E*-configured alkenes allow this annulene and the circulene derived from it to adopt a planar conformation.



1.28

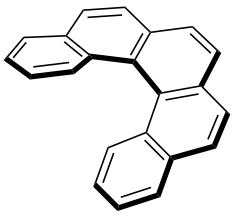
Figure 1.6. Structure of kekulene (**1.28**).

The presence of embedded non-6-membered rings necessarily gives rise to nonplanarity on extended π-systems except as noted above. This distortion manifests itself in the form of pyramidalized quaternary carbon atoms that collectively impart curvature (both positive and negative) to the PAH structure. An important consequence of the deviation from planarity is that it typically leads to good solubility, presumably due to disruption of efficient stacking in the solid state. Although many nonplanar PAHs of this type have been reported, the absence of reliable large-scale syntheses (with the notable exception of corannulene) has limited further research into these systems.

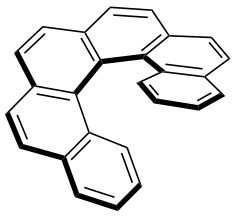
1.1.2: Nonplanar Aromatic Hydrocarbons Through Steric Crowding

Another strategy for the creation of nonplanar aromatic systems is to rely on steric crowding.[17] The high unfavourability of atoms occupying the same space can cause distortion to the geometry of the sigma framework of a PAH. The classical examples are the helicenes, which are screw-shaped molecules comprised of fused arene units that have been *ortho*-condensed. The first carbo-helicene, [5]helicene (**1.29**), was synthesized in 1918[18], but the field was essentially dormant until Newman synthesized and resolved [6]helicene (**1.30**) in the 1950s (**Figure 1.7**).[19] Helicenes have C_2-symmetry and can wind in either direction, which make them chiral even though they possess no centre of

asymmetry. Left-handed helices are denoted by the descriptor *M* and right-handed helices are denoted by the descriptor *P*. Enantiomerically pure helicenes can racemize depending on the structure of the helicene in question. Generally, the free energy barriers for racemization increases as the number of benzene rings increases, meaning that it takes longer for larger helicenes to racemize than the shorter version.



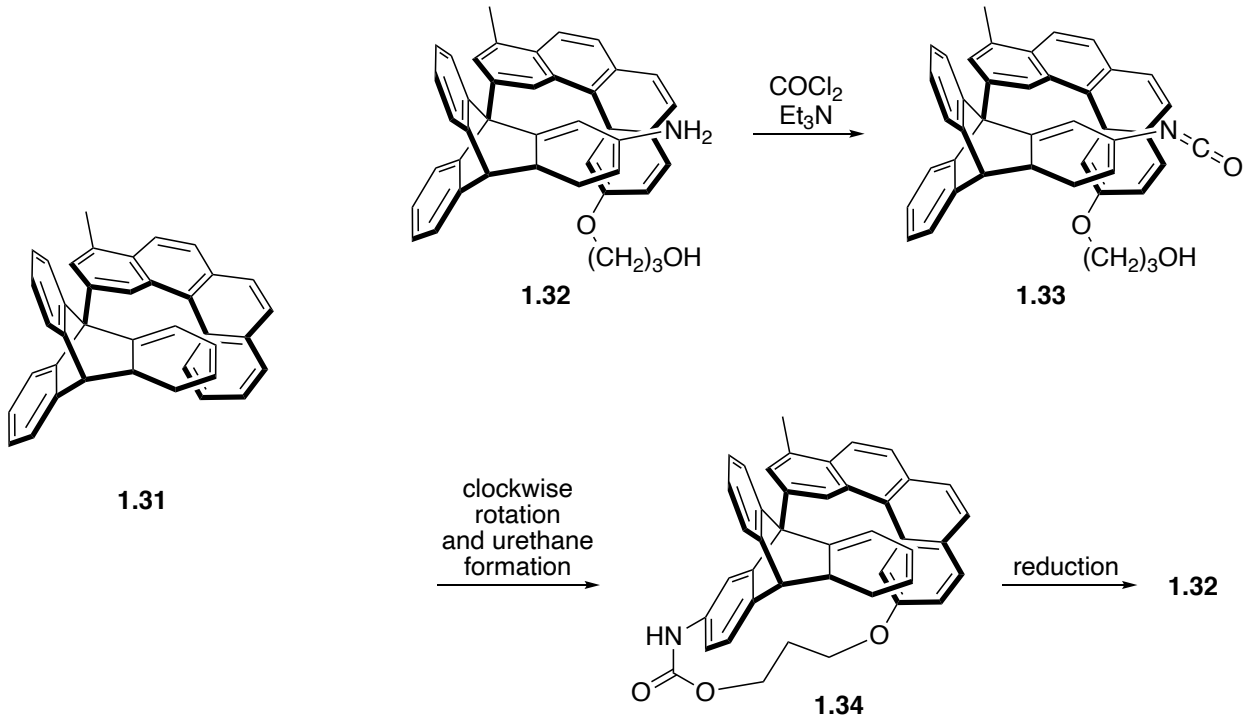
1.29



1.30

Figure 1.7 Structure of (*P*)-[5]helicene (**1.29**) and (*M*)-[6]helicene (**1.30**).

There are numerous strategies for the synthesis of helicenes and related molecules, which include the use of key reactions such as photocyclization, Diels-Alder reactions, Friedel-Crafts-type reactions, and metal-catalyzed cyclizations. Helicenes have been used as components in various molecular machines including molecular ratchets, molecular springs and molecular switches. Kelly *et al.* designed and synthesized a molecular ratchet **1.31**, which incorporated a triptycene unit in conjunction with a [4]helicene (**Scheme 1.4**).[20] Slow rotation of the triptycene could be observed by ^{1}H NMR by peak broadening at 160 °C, but it was found that the movement was not unidirectional. Kelly therefore altered the design of the molecular ratchet slightly by incorporating an amine unit onto the triptycene moiety and an ether-based tether on the helicene component to give **1.32**. This system was converted into an isocyanate **1.33** upon treatment with phosgene. This process promoted clockwise rotation of the triptycene to form a urethane (and cylclophane!) **1.34**, which can rotate through the helicene and then can be reduced back the original ratchet **1.33**.



Scheme 1.4 Kelly's helical molecular ratchets.

Helicenes have found utility in a wide range of other applications including asymmetric catalysis, dyes, molecular recognition, Langmuir-Blodgett films and liquid crystals among others. Helical systems will surely continue to be the subjects of broad and diverse research interest.

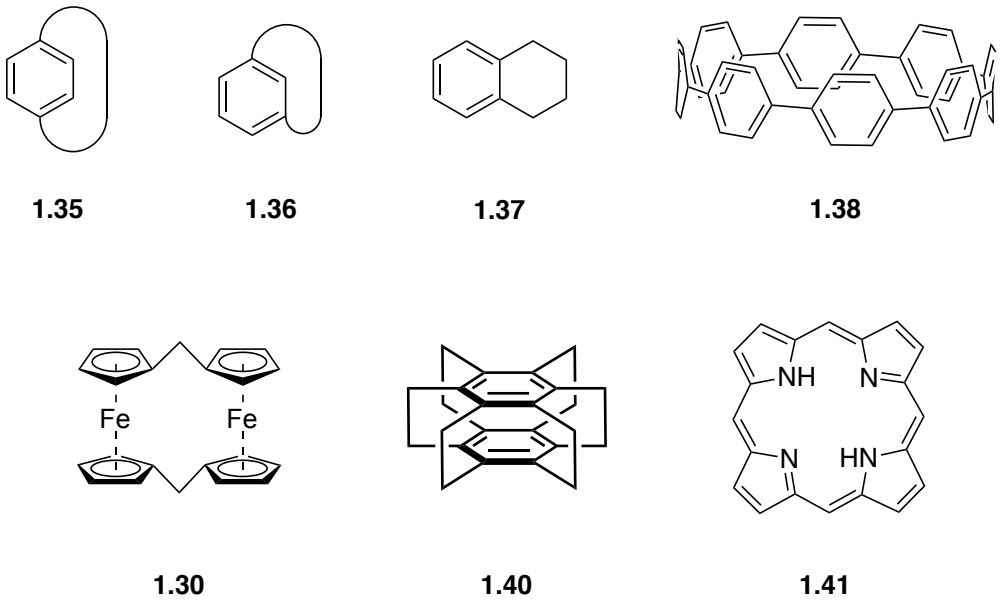
1.1.3: Nonplanar Aromatic Hydrocarbons Through Bridging

The final strategy for creating aromatic systems with non-planarity is to install a bridge across the aromatic system. Such systems are known as cyclophanes. In very broad strokes, the shorter the bridge, the larger the degree of non-planarity. The simplest definition of a cyclophane is: a molecule consisting of one or more aromatic systems bridged by one or more aliphatic chains at non-adjacent positions. If the aromatic system is benzene, two bridging motifs are possible — *para*- (**1.35)** or *meta*-cyclophanes (**1.36**) (**Figure 1.8**). The *ortho*-bridging motif in benzene (and other arenes) is equivalent to ring

fusion, as exemplified by tetralin (**1.37**). Referring to this compound as [4]orthocyclophane would strike most organic chemists as ridiculous.

The simple definition encompasses an enormous breadth of structures. For example, molecules like [8]cycloparaphenylenes **1.38**, ferrocenophane **1.39**, superphane (**1.40**), porphyrins (**1.41**) all fit comfortably under the cyclophane umbrella (**Figure 1.8**). The scope of possible cyclophanes is only limited by imagination.

The focus of this thesis is on cyclophanes with one aromatic system and one bridge, the [*n*]cyclophanes. Since they contain the minimum possible number of aromatic units and bridges to be considered a cyclophane, they are the simplest class of cyclophanes. Members of this family are especially interesting because (below a certain threshold) the bridge can force the aromatic system away from its lowest energy conformation, *i.e.* the one that it prefers when unbridged. More importantly, systematic changes to the length of the bridge will be translated into systematic changes in the structure of the aromatic system and this allows for the study of how the chemical and physical properties of an aromatic system change as it is progressively distorted away from its ideal structure. Of course, structural distortions of aromatic systems are present in many other types of cyclophanes, but arene-arene interactions can complicate structure-property investigations.



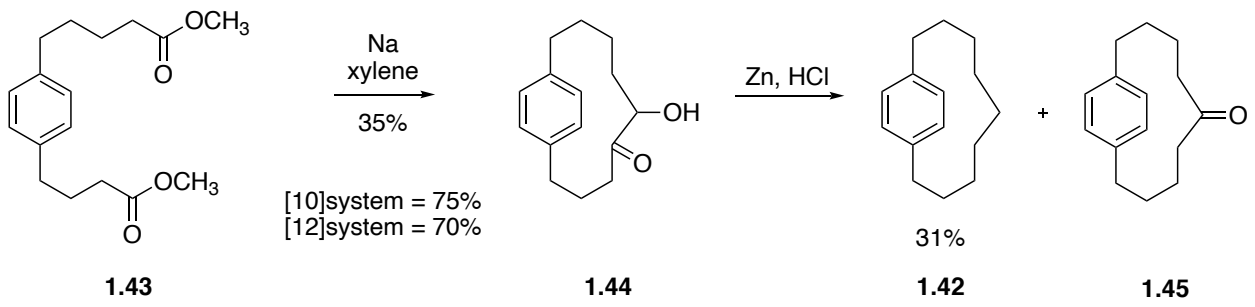
1.35 **1.36** **1.37** **1.38**

1.30 **1.40** **1.41**

Figure 1.8 Selected cyclophanes.

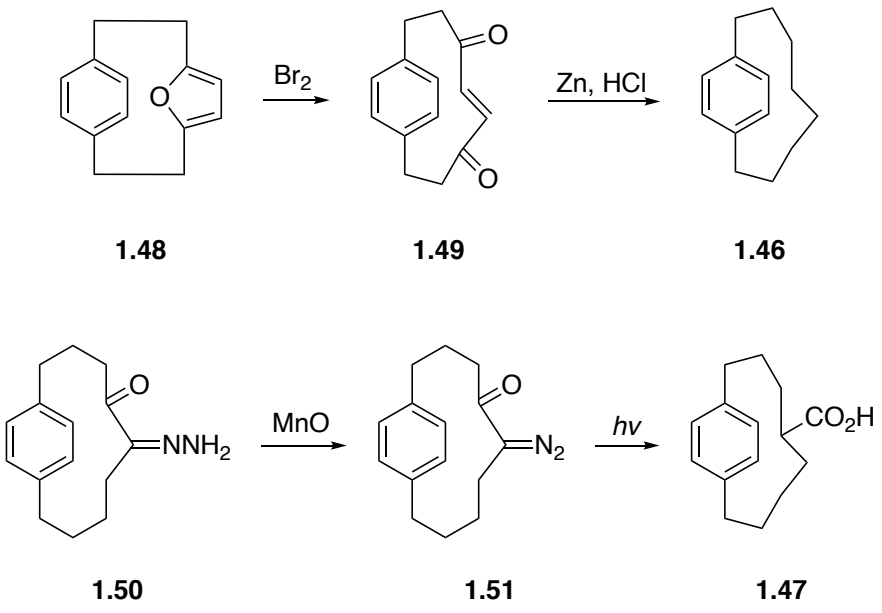
1.1.4: [*n*]Paracyclophanes

The [*n*]paracyclophanes were the first [*n*]cyclophanes to be synthesized. Cram *et al.* reported the synthesis of [12][21], [10][22] and [9]paracyclophane[23] (**1.42**) in the early 1950s. [9]Paracylcophane (**1.42**) may also have been synthesized serendipitously in 1952 by Bartlett *et al.* as a by-product.[24] However, in their manuscript its structure is drawn with only a question mark above it and no mention of it in the text. Cram's rational synthesis of [9]paracyclophane (**1.42**) commenced with the construction of 1,4-disubstitued benzene system **1.43** (**Scheme 1.5**). The bridge-closing step was accomplished by an intramolecular acyloin condensation to give α-hydroxy ketone **1.44** in 35% yield. This yield is much lower than what was observed for the corresponding [10]- and [12]paracyclophanes (75% and 70%, respectively), which is not surprising since the shorter bridge would be expected to result in the development of more strain at the transition of the acyloin condensation. Compound **1.44** could then be deoxygenated with zinc in HCl to give a mixture of [9]paracyclophane (**1.42**) and ketone **1.45** (31%).



Scheme 1.5 Cram's synthesis of [9]paracyclophane (**1.42**).

This strategy of directly forming the bridge failed when the acyloin condensation *en route* toward [8]paracyclophane (**1.46**) was attempted. Two other approaches to the [8]paracyclophane framework were then published in quick succession, one leading to the parent [8]paracylophane (**1.46**)[25] and the other to 4-carboxy[8]paracyclophane (**1.47**).[26] Cram's synthesis appeared first and took inspiration from their synthesis of [2.2]paracyclophane (**1.1**). The mixed [2.2]cyclophane **1.48**, which was obtained through a crossed *p*-xylylene coupling, was treated with bromine to give a *cis/trans* mixture of unsaturated diketone **1.49**. The *trans* isomer could be reduced to [8]paracyclophane (**1.46**) by subjection to Clemmensen reduction conditions (**Scheme 1.6**). The other strategy, reported by Allinger, involved the bridge contraction of an appropriate [9]paracyclophane derivative **1.50.** Conversion of **1.50** to α-diazaketone **1.51** set the stage for ring contraction via Wolff rearrangement to give 4-carboxy-[8]paracyclophane (**1.47**). The degree to which the benzene ring is bent was quantified as $\alpha = 9°$, however this crystallographic data comes from a derivative 4-carboxy[8]paracyclophane. The definition of the bend angle appears on p. 18.

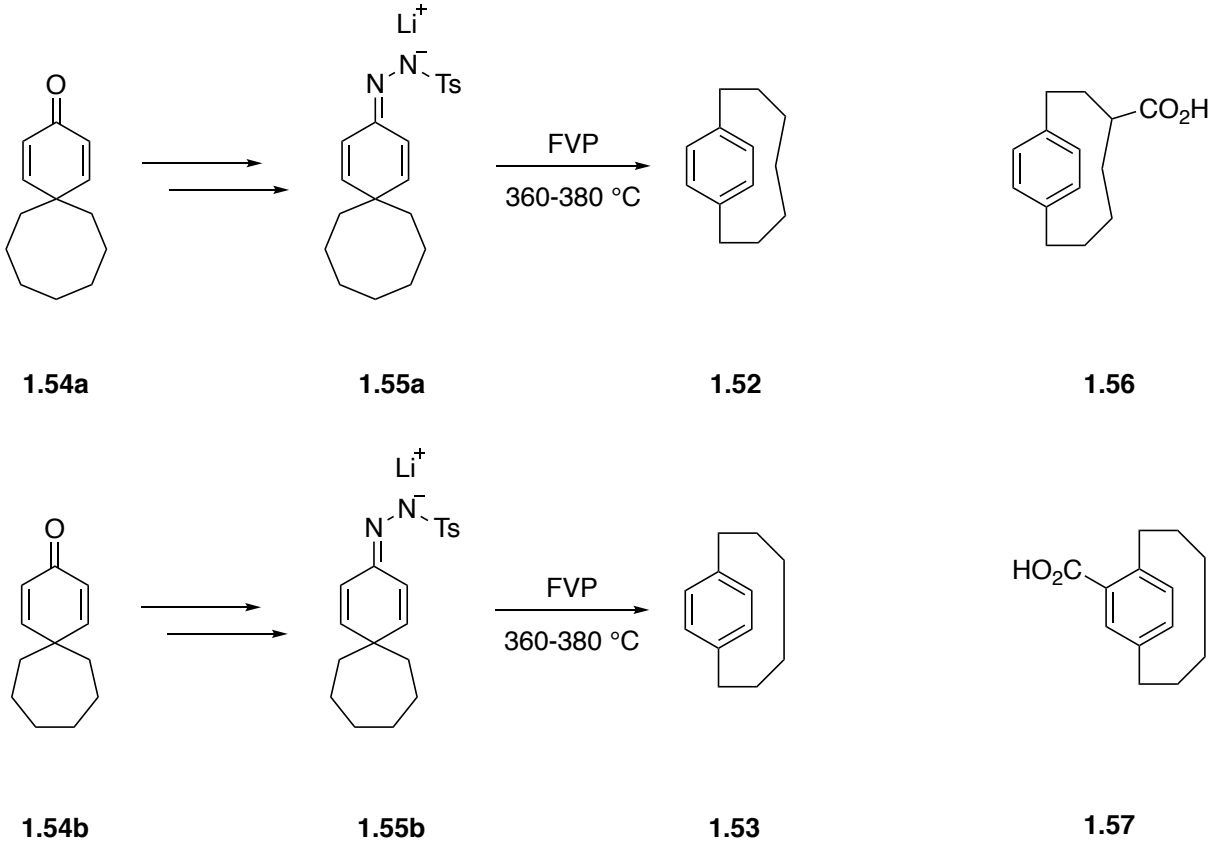


1.48 **1.49** **1.46**

1.50 **1.51** **1.47**

Scheme 1.6 Back-to-back syntheses of [8]paracylophanes.

The synthesis of the two next smaller homologues [7]paracyclophane (**1.52**)[27] and [6]paracyclophane (**1.53**)[28] required another new strategy to more effectively offset the large buildup of strain in the increasingly distorted aromatic ring. The key feature of this strategy is that the benzene ring is formed at the same step as the strain is building up. The substantial amount of aromatic stabilization energy (*ca.* 30 kcal/mol) gained from the formation of a benzene ring serves to sufficiently offset the developing strain. Spirocyclic ketones (**1.54a-b**) were first synthesized using a multi-step sequence. They were then converted in the corresponding tosylhydrazones and deprotonated to afford the lithium salts **1.55a-b**. These lithium salts **1.55a-b** were subjected to flash-vacuum pyrolysis (FVP), which presumably led to the formation of carbene intermediates that rearranged to paracyclophanes **1.52** and **1.53**. To determine the degree to which the benzene ring is distorted from planarity in the [7] system, a crystal structure of 3-carboxy[7]paracyclophane (**1.56**) was obtained which revealed a bend angle of α = 17°.[29] A bend angle for the [6] system of α = 20.7° was determined from a crystal structure of 8-carboxy[6]paracyclophane (**1.57)**.[30]

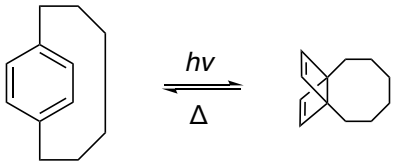


1.54a **1.55a** **1.52** **1.56**

1.54b **1.55b** **1.53** **1.57**

Scheme 1.7 Synthesis of [7]paracyclophane (**1.52**) and [6]paracyclophane (**1.53**).

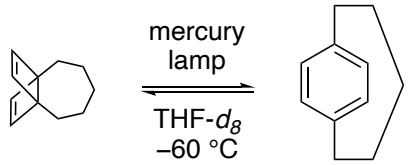
[6]Paracyclophane (**1.53**) can be converted to the corresponding 1,4-hexamethylene(Dewar benzene) (**1.58**) by irradiation with a medium-pressure mercury lamp. Its structure was confirmed by comparison of its structural data with another sample of **1.58** prepared by a different synthetic route.[31] The Dewar benzene system **1.58** could be reverted back to [6]paracyclophane (**1.53**) upon heating between 50 and 90 °C cleanly.



1.53 **1.58**

Scheme 1.8 Conversion between [6]paracyclophane (**1.53**) and Dewar benzenophane **1.58**.

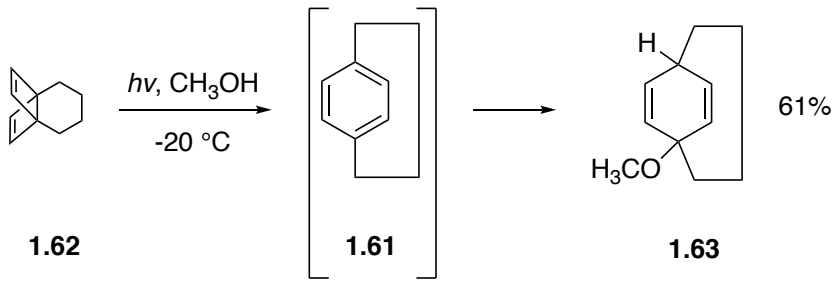
The next lower homologue, [5]paracyclophane (**1.59**) could be formed by photoisomerization of Dewar benzene **1.60** at –60 °C. This very strained cyclophane could be studied by ^{1}H NMR and UV spectroscopy, both of which suggested that the benzene rings retains much of its aromatic character even in this extreme case.[32] Since [5]paracyclophane could not be isolated, the bend angle could only be calculated using *ab initio* computational methods to give a value of α= 23.7°.



1.60 **1.59**

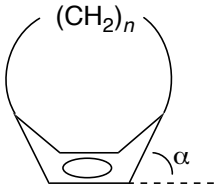
Scheme 1.9 Generation of [5]paracyclophane (**1.59**).

[4]Paracyclophane (**1.61**) has so far proven to be too strained to be isolated directly, but evidence of its formation and trapping by alcoholic solvent has been obtained.[33] Photolysis of **1.62** at –20 °C in MeOH, initially gives [4]paracyclophane (**1.61**), which immediately reacts with MeOH to give bridgehead-substituted compound **1.63**. Further evidence for the formation of [4]paracyclophane was obtained by electronic absorption spectroscopy when the photolysis was performed in an EtOH matrix at 77 K. The spectrum was different from than that of **1.62** and **1.63** with maxima at *ca.* 260 nm and 340 nm which was assigned to [4]paracyclophane (**1.61**).



Scheme 1.10 Evidence of the presence [4]paracyclophane (**1.61**).

The substitution pattern of the benzene ring in the [*n*]paracyclophanes imparts a very specific mode of bending where the benzene is forced to adopt a boat-like conformation (**Figure 1.9**).[34] By removing one methylene unit at a time the effect on the benzene ring can be systematically studied. The extent of the distortion from planarity is quantified using the bend angle α, which is an envelope flap angle. More precisely, it is the smallest angle formed between a plane of three atoms at the end of the benzene unit (envelope flap) and a plane of four atoms in the middle (the body of the envelope). Regarding the physical properties, of the benzene system as it becomes more bent, general trends include a move to higher field chemical shifts of the methylene protons as the bridge gets shorter, and a red shift of the longest wavelength absorption maximum in the UV/Vis spectrum.

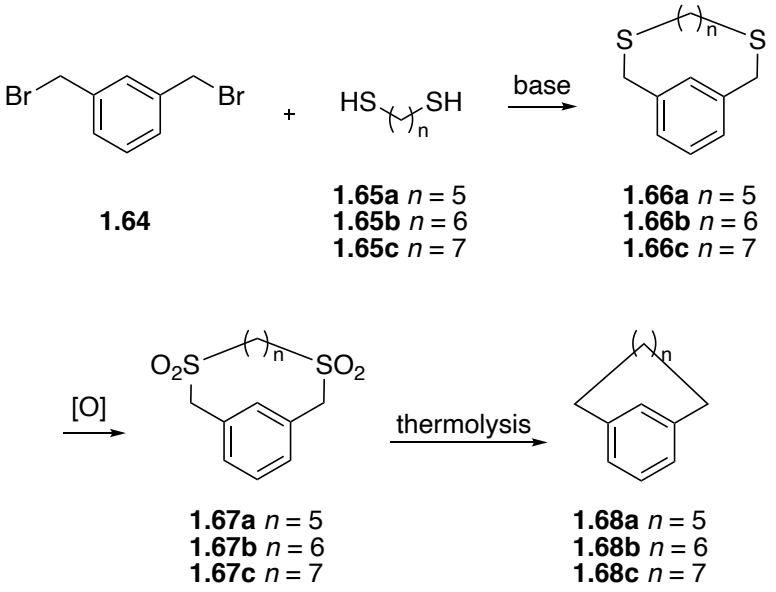


n	α [°]
8	8
7	13
6	17
5	23
4	28

Figure 1.9 Calculated (MNDO) bend angles (α) of [*n*]paracyclophanes .

1.1.5: [*n*]Metacyclophanes

The synthesis of the [*n*]metacyclophanes was occurring during the same period as many of the [*n*]paracyclophanes. The longer bridged [*n*]metacyclophane where *n* = 7-9 could be synthesized by reaction of 1,3-bis(bromomethyl)benzene (**1.64**) with appropriately sized aliphatic dithiols **1.65a-c** under basic conditions to give dithiacyclophanes **1.66a-c** (**Scheme 1.11**). The sulfur atoms could then be oxidized to sulfones **1.67a-c** and SO_2 could be extruded by flash vacuum thermolysis to give [*n*]metacyclophanes (**1.68a-c**).[35] The fact that these systems can be synthesized in this fashion showcases, at least at the dithiacyclophanes stage, the relatively low level of strain.



1.64

1.65a *n* = 5
1.65b *n* = 6
1.65c *n* = 7

1.66a *n* = 5
1.66b *n* = 6
1.66c *n* = 7

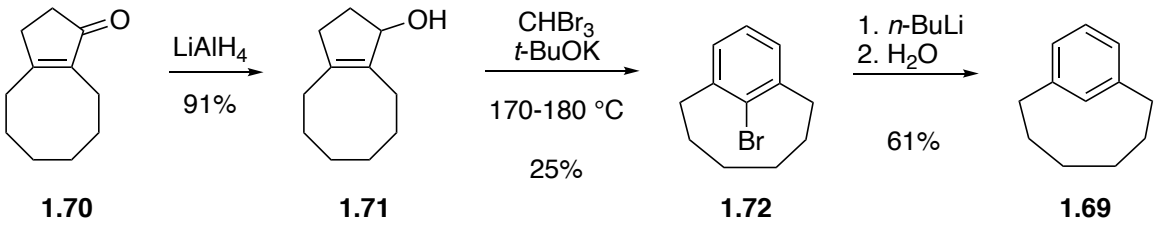
1.67a *n* = 5
1.67b *n* = 6
1.67c *n* = 7

1.68a *n* = 5
1.68b *n* = 6
1.68c *n* = 7

Scheme 1.11 Synthesis of [*n*]metacyclophanes (**1.68a-c**) where *n* = 7-9.

Unsurprisingly, as the bridges get shorter their synthesis becomes more difficult and different synthetic approached were required. The next lower homologue, [6]metacyclophane (**1.69**), was first synthesized in 1972 (**Scheme 1.12**).[36] Cyclopentenone **1.70** was reduced with $LiAlH_4$ to give the corresponding alcohol **1.71**. Treatment of **1.71** with $CHBr_3$-^{t}BuOK at elevated temperature gave the brominated derivative of the desired product **1.72**. This very productive reaction involves the

formation of dibromocarbene, which adds to the double bond of **1.71** to give a propellane that rearranges and loses an equivalent of both H_2O and HBr under the conditions of its formation. Lithiation of **1.72** with *n*-BuLi followed by quenching with H_2O gave [6]metacyclophane (**1.69**).

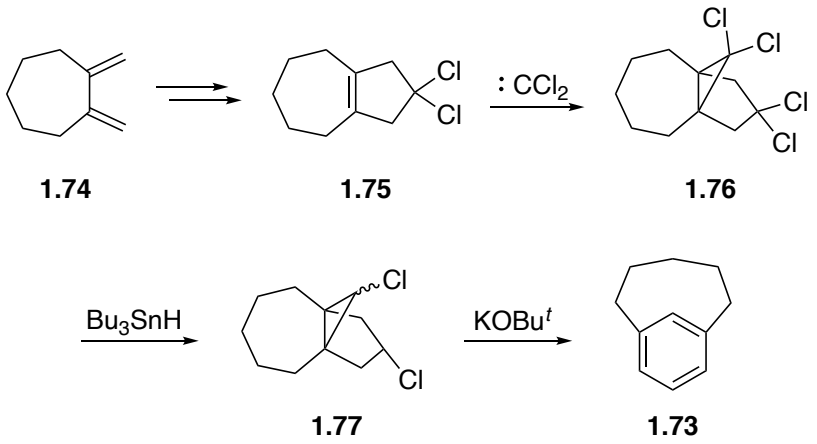


1.70 **1.71** **1.72** **1.69**

Scheme 1.12 First synthesis of [6]metacyclophane (**1.69**).

In the end, the [*n*]metacyclophanes where $n \geq 6$ have been synthesized through a number of different iterations. Some of these other strategies include, acid catalyzed rearrangements of [*n*]paracyclophanes, intramolecular Diels-Alder reactions, and dehydrogenation chemistry and the rearrangements of [*n*.3.1] of propellanes, which was the method used for the synthesis of both **1.69** and its next lower homologue [5]metacyclophane (**1.73**).

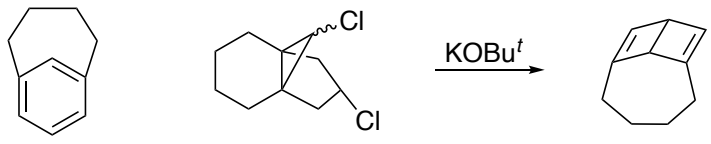
[5]Metacyclophane (**1.73**) was synthesized in several steps from 1,2-bismethylenecyclopheptane (**1.74**) (**Scheme 1.13**).[37,38] Treatment of **1.74** with dichlorocarbene, followed by rearrangement gave the dichloride **1.75**, which was treated with another equivalent of dichlorocarbene to give [5.3.1]propellane **1.76**. This propellane system could then be converted into the parent [5]metacyclophane (**1.73**) in a step-wise manner. The geminal dichlorides were mono-dechlorinated using Bu_3SnH to give **1.77**, as a mixture of isomers, which upon treatment with *t*-BuOK gave the desired product **1.73**.



1.74 **1.75** **1.76** **1.77** **1.73**

Scheme 1.13 Bickelhaupt's synthesis of [5]metacyclophane (**1.73**).

[4]Metacyclophane (**1.78**) proved to be a new challenge (**Scheme 1.14**).[39,40] When the [4.3.1]propellane system **1.79**, which is very similar to propellane **1.77** (**Scheme 1.13**), was treated with KOBu^t only the Dewar benzene isomer **1.80** could be isolated. However, some evidence for the formation of [4]metacyclophane (**1.78**) was obtained upon irradiation of **1.80** at –50 °C in a sealed ampoule. Products that would arise form a [4+2] dimerization of two [4]metacyclophane systems were obtained. It would seem that the strain limit in the [*n*]metacyclopahanes is reached when moving from [5]metacyclophane (**1.73**) to [4]metacyclophane (**1.78**)



1.78 **1.79** **1.80**

Scheme 1.14 Attempted synthesis of [4]metacyclophane (**1.80**).

1.1.6: The Advantages and Disadvantages of [*n*]Cyclophanes

While [*n*]cyclophanes are the simplest class of cyclophanes, their synthesis can often be far from trivial. It took the work of multiple groups over the period of many years to complete the sets of smaller and smaller benzene-based [*n*]cyclophanes that reach their limits of stability.

The relative simplicity of systems that contain only one aromatic system and one bridge present researchers with the unique opportunity to study how incremental changes in bending affects the properties of aromatic units. In addition, the substitution pattern on an aromatic system can be altered to also probe how different bending modes can affect the aromatic unit.

In Chapter 2 of this thesis, the focus moves to the [*n*]pyrenophanes. Pyrene is the only aromatic system beyond benzene that has been progressively bent to the limit of its stability using bridging. After a broad recap of the literature of [*n*](2,7)pyrenophanes, details of improvements to the synthesis of 1,n-dioxa[*n*](2,7)pyrenophanes and [*n*](2,7)pyrenophanes are presented. In Chapter 3, the results of studies aimed at the construction of [*n*]cyclophanes that incorporate a new arene unit, peropyrene, are presented.

1.2: References

(1) Hückel, E. Quantum-Theoretical Contributions to the Benzene Problem. I. The Electron Configuration of Benzene and Related Compounds. *Z. Phys.* **1931**, *70*, 204–286.

(2) Doering, W. von E.; Detert, F. L. Cycloheptatrienylium Oxide. *J. Am. Chem. Soc.* **1951**, *73*, 876–877.

(3) Cram, D. J.; Steinberg, H. Macro Rings. I. Preparation and Spectra of the Paracyclophanes. *J. Am. Chem. Soc.* **1951**, *73*, 5691–5704.

(4) Brown, C. J.; Farthing, A. C. Preparation and Structure of Di-p-Xylylene. *Nature* **1949**, *164*, 915–916.

(5) Scott, L. T.; Hashemi, M. M.; Bratcher, M. S. Corannulene Bowl-to-Bowl Inversion Is Rapid at Room Temperature. *J. Am. Chem. Soc.* **1992**, *114*, 1920–1921.

(6) Sygula, A.; Fronczek, F. R.; Sygula, R.; Rabideau, P. W.; Olmstead, M. M. A Double Concave Hydrocarbon Buckycatcher. *J. Am. Chem. Soc.* **2007**, *129*, 3842–3843.

(7) Mück-Lichtenfeld, C.; Grimme, S.; Kobryn, L.; Sygula, A. Inclusion Complexes of Buckycatcher with C_{60} and C_{70}. *Phys. Chem. Chem. Phys.* **2010**, *12*, 7091-7097.

(8) Sakurai, H.; Daiko, T.; Hirao, T. A Synthesis of Sumanene, a Fullerene Fragment. *Science* **2003**, *301*, 1878–1878.

(9) Amaya, T.; Sakane, H.; Muneishi, T.; Hirao, T. Bowl-to-Bowl Inversion of Sumanene Derivatives. *Chem. Commun.* **2008**, 765–767.

(10) Amaya, T.; Nakata, T.; Hirao, T. Synthesis of Highly Strained π-Bowls from Sumanene. *J. Am. Chem. Soc.* **2009**, *131*, 10810–10811.

(11) Yamamoto, K.; Harada, T.; Nakazaki, M.; Naka, T.; Kai, Y.; Harada, S.; Kasai, N. Synthesis and Characterization of [7]Circulene. *J. Am. Chem. Soc.* **1983**, *105*, 7171–7172.

(12) Yamamoto, K.; Harada, T.; Okamoto, Y.; Chikamatsu, H.; Nakazaki, M.; Kai, Y.; Nakao, T.; Tanaka, M.; Harada, S.; Kasai, N. Synthesis and Molecular Structure of [7]Circulene. *J. Am. Chem. Soc.* **1988**, *110*, 3578–3584.

(13) Yamamoto, K.; Sonobe, H.; Matsubara, H.; Sato, M.; Okamoto, S.; Kitaura, K. Convenient New Synthesis of[7]Circulene. *Angew. Chem. Int. Ed. Engl.* **1996**, *35*, 69–70.

(14) Cheung, K. Y.; Xu, X.; Miao, Q. Aromatic Saddles Containing Two Heptagons. *J. Am. Chem. Soc.* **2015**, *137*, 3910–3914.

(15) Feng, C.; Kuo, M.; Wu, Y. Synthesis, Structural Analysis, and Properties of [8]Circulenes . *Angew. Chem. Int. Ed.* **2013**, *52*, 7791–7794.

(16) Diederich, F.; Staab, H. A. Benzoide versus Annulenoide Aromatizität: Synthese Und Eigenschaften Des Kekulens. *Angew. Chem.* **1978**, *90*, 383–385.

(17) Shen, Y.; Chen, C.-F. Helicenes: Synthesis and Applications. *Chem. Rev.* **2012**, *112*, 1463–1535.

(18) Klingler, A.; Weitzenböck, R. Synthese Der Isomeren Kohlenwasserstoffe 1, 2-5, 6-Dibenzanthracen Und 3, 4-5, 6-Dibenzphenanthren. *Monatsh. für Chem.* **1918**, *39*, 315–323.

(19) Newman, M. S.; Lednicer, D. The Synthesis and Resolution of Hexahelicene 1. *J. Am. Chem. Soc.* **1956**, *78*, 4765–4770.

(20) Kelly, T. R. Progress toward a Rationally Designed Molecular Motor †. *Acc. Chem. Res.* **2001**, *34*, 514–522.

(21) Cram, D. J.; Allinger, N. L.; Steinberg, H. Macro Rings. VII. The Spectral Consequences of Bringing Two Benzene Rings Face to Face 1. *J. Am. Chem. Soc.* **1954**, *76*, 6132–6141.

(22) Cram, D. J.; Daeniker, H. U. Macro Rings. V. Transannular Effects in the 1,4-Decamethylenebenzene Series 1. *J. Am. Chem. Soc.* **1954**, *76*, 2743–2752.

(23) Cram, D. J.; Antar, M. F. Macro Rings. XV. The Synthesis and Properties of Six New Paracyclophanes Carrying One Methylene in One of the Bridges 1. *J. Am. Chem. Soc.* **1958**, *80*, 3103–3109.

(24) Bartlett, M. F.; Figdor, S. K.; Wiesner, K. Synthesis of para-Bridged Benzene Compounds. III. *Can. J. Chem.* **1952**, *30*, 291–294.

(25) Cram, D. J.; Knox, G. R. A Cross-breeding Reaction, A Bent Benzene Ring, and a Multiple Diels-Alder Reaction 1. *J. Am. Chem. Soc.* **1961**, *83*, 2204–2205.

(26) Allinger, N.; Freiberg, L. Communications to the Editor: The Synthesis of Highly Strained Medium Rings.1 (8) Paracyclophane-4-Carbolic Acid. *J. Org. Chem.* **1962**, *27*, 1490–1491.

(27) Wolf, A. D.; Kane, V. V.; Levin, R. H.; Jones, M. [7]Paracyclophane. *J. Am. Chem. Soc.* **1973**, *95*, 1680–1680.

(28) Kane, V. V.; Wolf, A. D.; Jones, M. [6]Paracyclophane. *J. Am. Chem. Soc.* **1974**, *96*, 2643–2644.

(29) Allinger, N. L.; Walter, T. J.; Newton, M. G. Synthesis, Structure, and Properties of the [7]Paracyclophane Ring System. *J. Am. Chem. Soc.* **1974**, *96*, 4588–4597.

(30) Tobe, Y.; Kakiuchi, K.; Odaira, Y.; Hosaki, T.; Kai, Y.; Kasai, N. Synthesis and Structure of 8-Carboxy[6]Paracyclophane. *J. Am. Chem. Soc.* **1983**, *105*, 1376–1377.

(31) Kammula, S. L.; Iroff, L. D.; Jones, M.; Straten, J. W. V.; Wolf, W. H. D.; Bickelhaupt, F. Interconversion of [6]Paracyclophane and 1,4-Hexamethylene(Dewar Benzene). *J. Am. Chem. Soc.* **1977**, *99*, 5815–5815.

(32) Jenneskens, L. W.; Kanter, F. J. J. D.; Kraakman, P. A.; Turkenburg, L. A. M.; Koolhaas, W. E.; Wolf, W. H. D.; Bickelhaupt, F.; Tobe, Y.; Kakiuchi, K.; Odaira, Y. [5]Paracyclophane. *J. Am. Chem. Soc.* **1985**, *107*, 3716–3717.

(33) Kostermans, G. B. M.; Bobeldijk, M.; Wolf, W. H. D.; Bickelhaupt, F. [4]Paracyclophane Intercepted. *J. Am. Chem. Soc.* **1987**, *109*, 2471–2475.

(34) Bickelhaupt, F. Small Cyclophanes: The Bent Benzene Business. *Pure Appl. Chem.* **1990**, *62*, 373–382.

(35) Atzmüller, M.; Vögtle, F. Synthese Und Stereochemie Eng Verklammerter Benzophenone Und Diphenylmethan-Systeme. *Chem. Ber.* **1978**, *111*, 2547–2556.

(36) Hirano, S.; Hiyama, T.; Fujita, S.; Nozaki, H. [6]Metacycoplahe and Related Compounds. *Chem. Lett.* **1972**, *1*, 707–708.

(37) Turkenburg, L. A. M.; Blok, P. M. L.; Wolf, W. H. de; Bickelhaupt, F. Studies on the Formation of [5]Metacyclophane. *Tetrahedron Lett.* **1981**, *22*, 3317–3320.

(38) Jenneskens, L. W.; Kanter, F. J. J. D.; Turkenburg, L. A. M.; Boer, H. J. R. D.; Wolf, W. H. D.; Bickelhaupt, F. Synthesis and Conformational Analysis of 8,11-Dihalo[5]Metacyclophanes. *Tetrahedron* **1984**, *40*, 4401–4413.

(39) Kostermans, G. B. M.; Dansik, P. V.; Wolf, W. H. D.; Bickelhaupt, F. Thermal Generation and Dimerization of [4]Metacyclophane. *J. Am. Chem. Soc.* **1987**, *109*, 7887–7888.

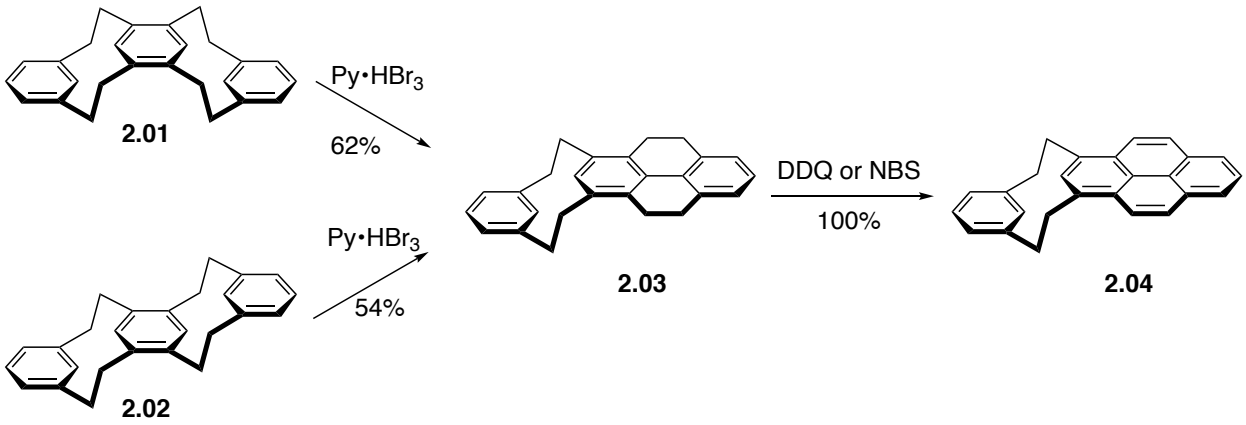
(40) Kostermans, G. B. M.; Dansik, P. V.; Wolf, W. H. D.; Bickelhaupt, F. The Intermediate Formation of [4]Metacyclophane on Flash Vacuum Thermolysis. *J. Org. Chem.* **1988**, *53*, 4531–4534.

Chapter 2: 1,*n*-Dioxa[*n*](2,7)pyrenophanes and [*n*](2,7)Pyrenophanes: Improved Synthesis, Properties and Reactivity

2.1: Introduction

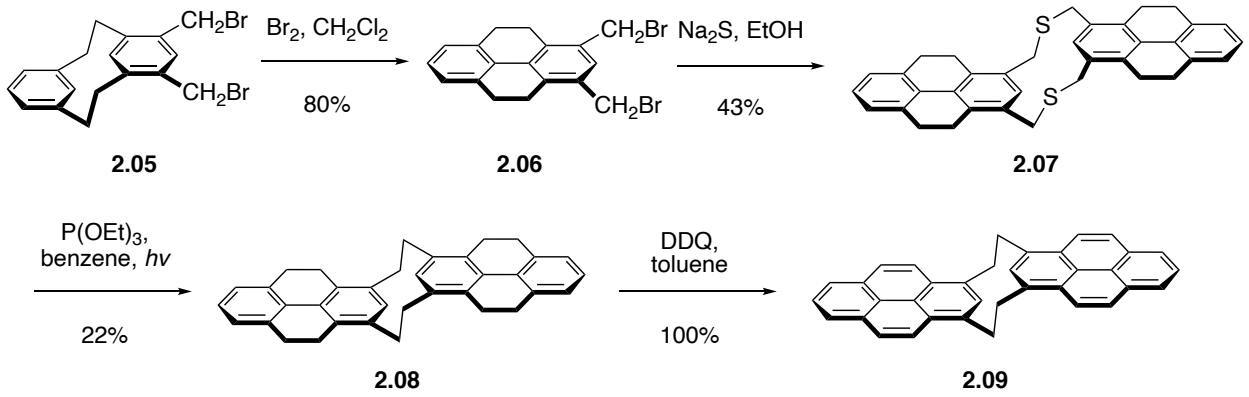
Pyrenophanes are a sub-class of cyclophanes where at least one of the aromatic systems contained within is a pyrene unit. Pyrenophanes are especially interesting because of their photophysical and photochemical properties, which arise from the presence of the pyrene system. The fluorescence of pyrene systems is very sensitive to its microenvironment, and this has led to its widespread use as a fluorescent probe. In the book Advanced Concepts in Fluorescence Sensing Part B: Macromolecular Sensing, Jones *et al.* state in Chapter 7: Excimer Sensing, pp 211-239 that "the pyrene structure has been elevated to the status of gold standard as a molecular probe of microenvironments".[1] This point was reiterated several years later by Müllen *et al.*[2]

Pyrenophanes hold a privileged status in cyclophane chemistry as the only large PAH containing class with a considerable number of examples. The bridging motifs of reported pyrenophanes are (1,3), (1,6), (1,7), (1,8), (2,4), (2,7) and (4,9) while the other 5 bridging motifs have yet to be realized. The first pyrenophane was reported in 1975 by Misumi *et al.* and this paved the way for what would become a commonly-used strategy for the construction of pyrene units in cyclophanes (**Scheme 2.1**).[3] Treatment of any mixture of conformers of layered [2.2]metacyclophanes **2.01** and **2.02** with pyridinium perbromide afforded tetrahydropyrenophane **2.03**. This system was then aromatized under oxidative conditions using NBS or DDQ to quantitatively give pyrenophane **2.04**.



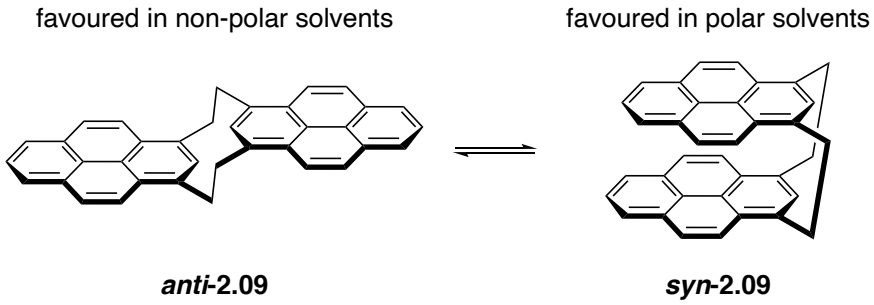
Scheme 2.1 Synthesis of the first pyrenophane.

Later that year, the same researchers reported on the synthesis of a second pyrenophane which contained two pyrene units (**Scheme 2.2**).[4] The authors' previous strategy in synthesizing pyrenophane **2.04** failed in the synthesis of [2.2](1,3)pyrenophane (**2.09**) because the layered metacyclophane system (not shown) that was required as a synthetic precursor did not smoothly undergo the desired transformation under the same conditions. In order to work around this issue, the authors developed a strategy utilizing a sodium sulfide coupling reaction. Dibromide **2.05** was treated with Br_2 to afford bis(bromomethyl)tetrahydropyrene **2.06**, which was coupled with sodium sulfide under high dilution in ethanol to give dithiacyclophane **2.07**. Ring contraction by desulfurization was accomplished photochemically by irradiation of **2.07** in an 8:1 mixture of triethyl phosphite and benzene. Over the course of the reaction, octahydro[2.2](1,3)pyrenophane **2.08** precipitated from the reaction mixture. Compound **2.08** was then treated with an excess of DDQ to quantitatively yield [2.2](1,3)pyrenophane (**2.09**).



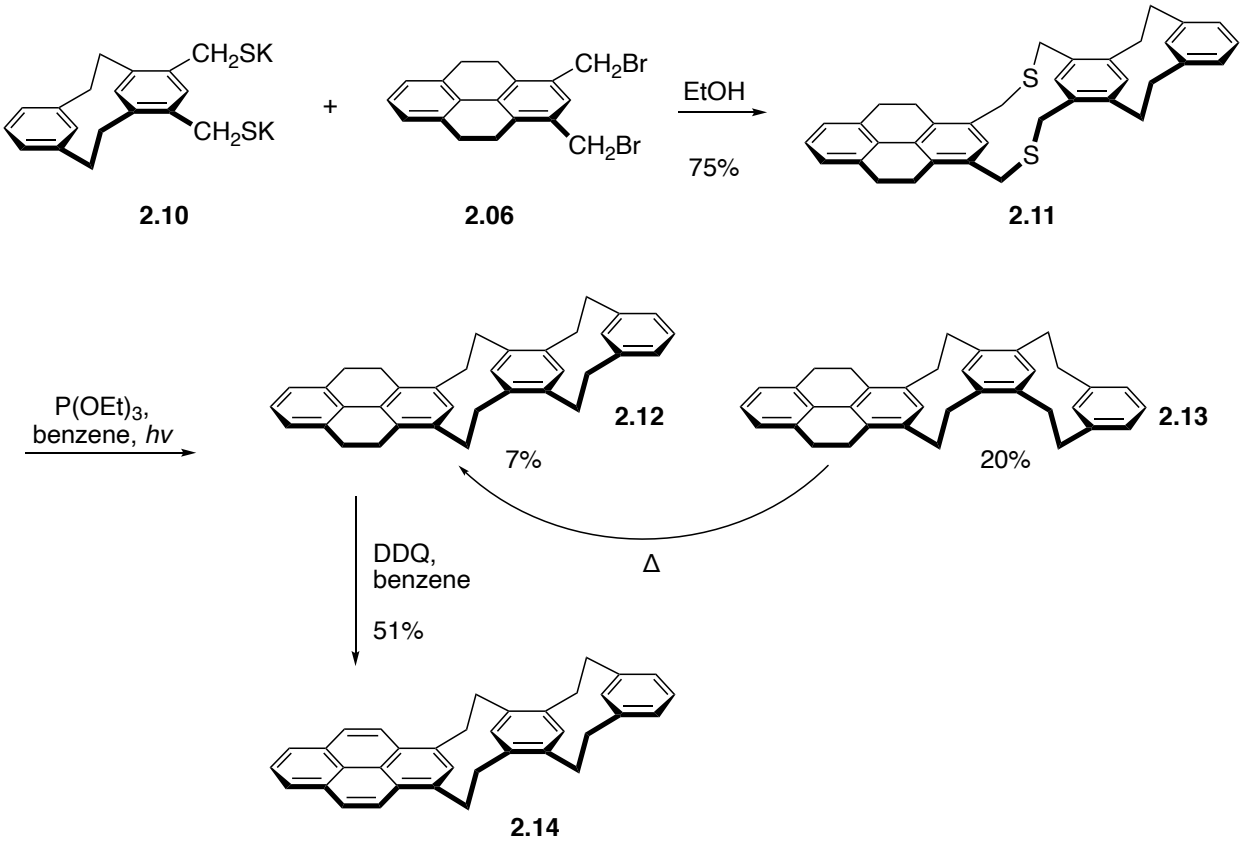
Scheme 2.2 Misumi's synthesis of the first pyrenophane with two pyrene units.

From the very beginning, researchers were interested in the photophysical properties of these pyrenophanes. The absorption spectra of pyrenophanes **2.04** and **2.09** are similar to that of pyrene, although the absorption maxima are slightly broadened and red-shifted. Interestingly, the fluorescence behaviour of **2.09** was found to be highly dependent on the solvent. In methylcyclohexane, a nonpolar solvent, the fluorescence spectrum of **2.09** shows a band at λ_{max} = 410 nm, which has been attributed to monomer emission. On the other hand, in acetonitrile, a polar solvent, the fluorescence spectrum contained a broad featureless band at 475 nm attributed to intramolecular excimer emission, in addition to the band at 410 nm. The interpretation of this observation was that a conformational flip from an *anti* to *syn* occurs (**Scheme 2.3**).[5]



Scheme 2.3 Conformations of pyrenophane **2.09**.

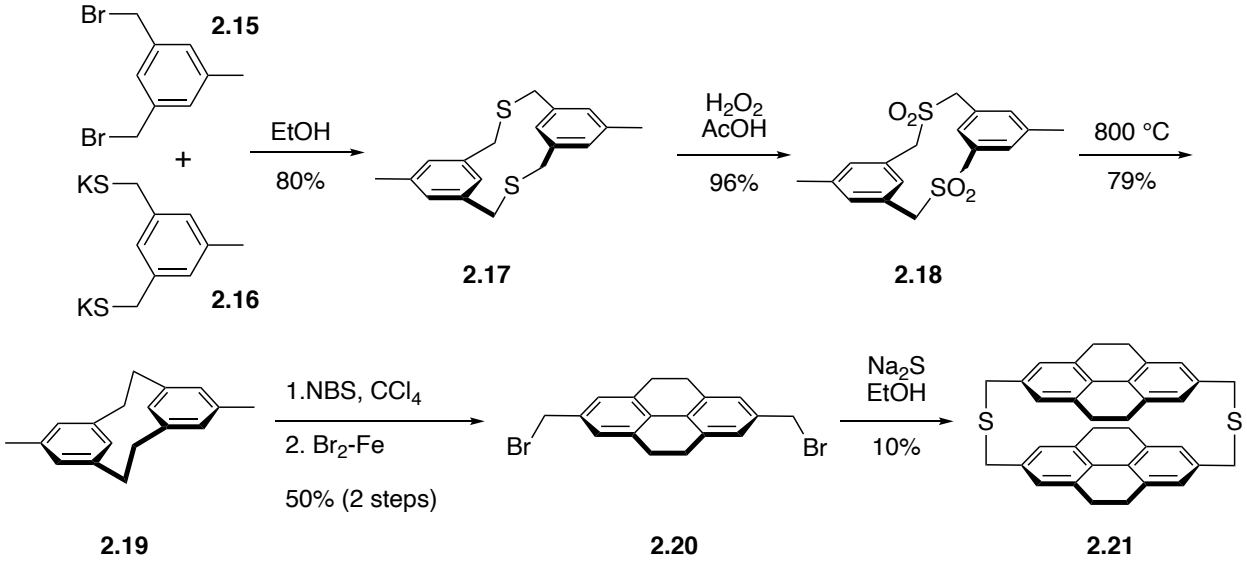
In the same publication, Misumi *et al.* reported the synthesis of another layered cyclophane containing one pyrene unit and a metacylclophane unit (**Scheme 2.4**). Coupling of metacyclophane derivative **2.10** with tetrahydropyrene dibromide **2.06** in EtOH afforded thiacyclophane **2.11** in an impressive 75% yield. This dithiacyclophane was then irradiated in a 40:1 triethylphosphite/benzene mixture to yield a mixture of isomeric meta-cyclotetrahydropyrenophanes, the *up,up* (**2.12**) and *up,down* (**2.13**) systems. The *up,down* isomer could be interconverted to the *up,up* isomer with heating. Compound **2.12** was then aromatized with DDQ in refluxing benzene to give the fully dehydrogenated metacyclo-pyrenophane **2.14** in 51% yield.



Scheme 2.4 Misumi's synthesis of metacyclo-pyrenophane **2.14**.

Misumi pyrenophane synthesizing days in 1975 were still no over. He also reported the synthesis of [2.2](2,7)pyrenophane (**2.25**) and its alkene-bridged derivative (**2.26**) using a similar dithiacyclophane/bridge contraction strategy (**Scheme 2.6**).[6] A

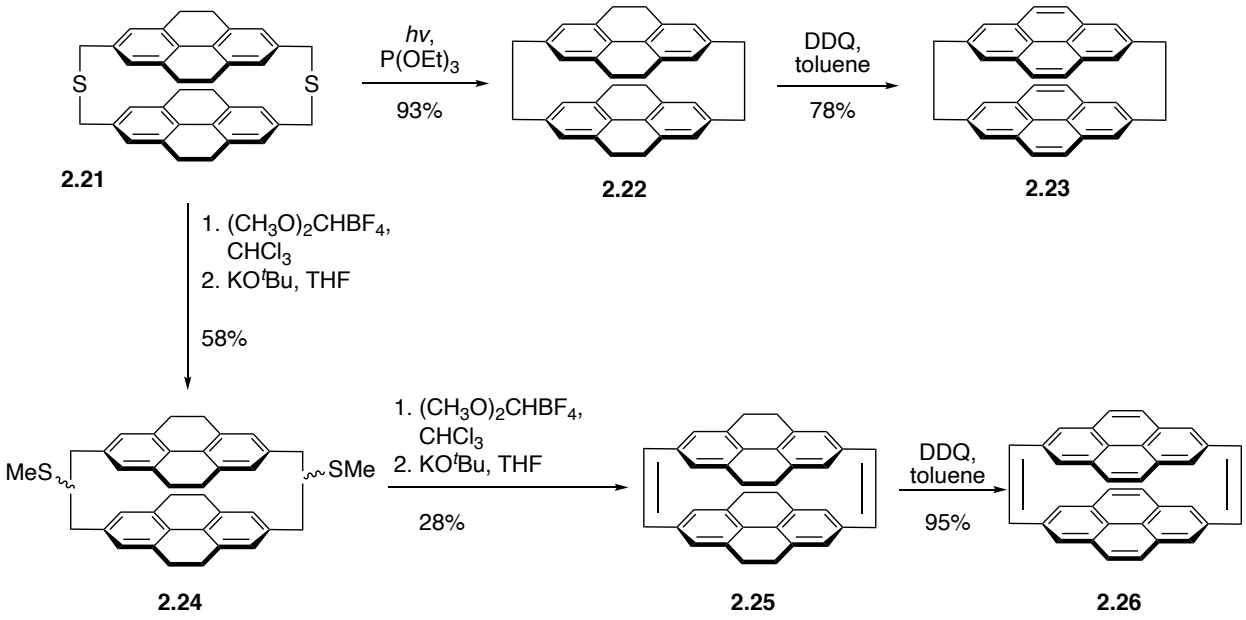
major motivation for the design and synthesis of these compounds was their utility as models for excimer fluorescence due to the enforced closeness of the two aromatic units in a face-to-face fashion. Additionally, one can see the aesthetic appeal of these quite highly symmetric systems and their synthetic challenges, which were no doubt additional motivators. The synthesis began with the formation of a functionalized [2.2]metacyclophane (**2.19**), which was converted into a tetrahydropyrene and subsequently mono-brominated at both benzylic positions to afford dibromide **2.20**. Two dibromide units could then be coupled together by treatment with Na_2S in ethanol to give dithiacyclophane **2.21** in 10% yield. This dithiacyclophane system could be used as a common precursor to both the target molecules **2.23** and **2.26** (**Scheme 2.6**).



Scheme 2.5 Misumi's synthesis of dithiacyclophanes **2.21**.

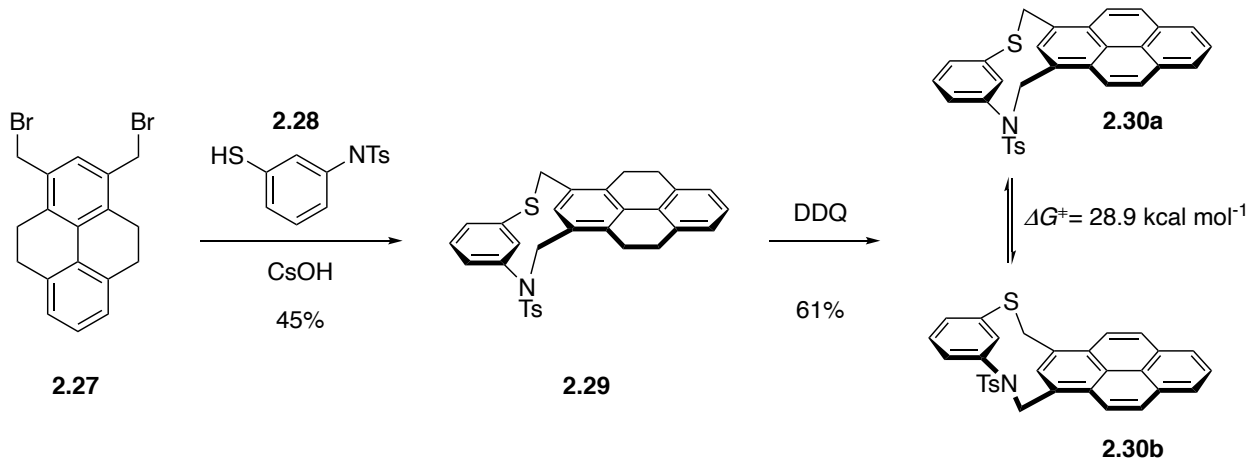
[2.2](2,7)Pyrenophane (**2.23**) was obtained upon desulfurization by irradiation of **2.21** in triethyl phosphite to give tetrahydropyrenophane **2.22**, which was aromatizated with DDQ. Both of these transformations proceeded in good yields. [2.2](2,7)Pyrenophane-1,13-diene (**2.26**) was prepared by *S*-methylation of **2.21** using Borch reagent followed by thia-Stevens rearrangement with potassium *tert*-butoxide to give thioether **2.24** (mixture of isomers) which was *S*-methylated again with Borch reagent and then subjected to Hoffman elimination upon treatment with potassium *tert*-

butoxide to give cyclophane **2.25** in 28% yield. This system was then aromatized by treatment with DDQ to give [2.2](2,7)pyrenophane-1,3-diene **2.26** in 95% yield (**Scheme 2.5**). Shortly after this report, Both Mitchell[7] and Staab[8] also succeeded in the synthesis of pyrenophanes **2.23** and **2.26** using similar chemistry.



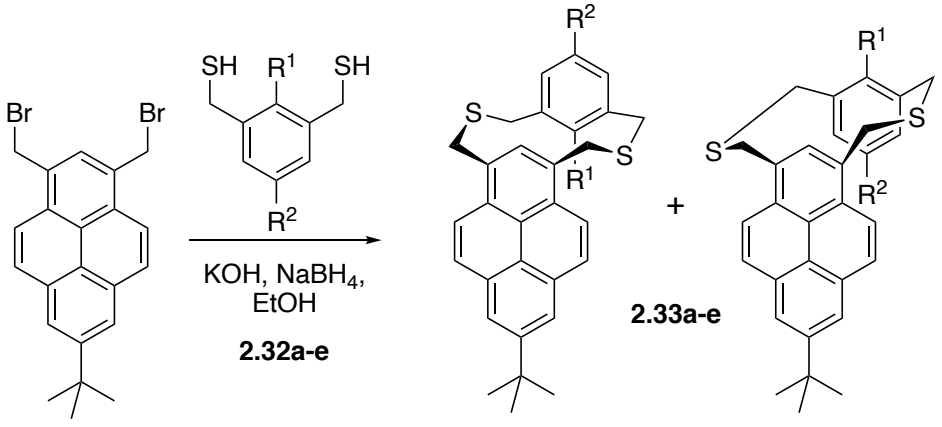
Scheme 2.6 Misumi's synthesis of [2.2](2,7)pyrenophane (**2.23**) and its 1,13-diene derivative **2.26**.

In 1990, Vögtle and co-workers reported on the synthesis of a (1,3)pyrenophane that displays helical chirality.[9] Dibromide **2.27** was treated with 3-thio-*N*-tosylaniline **2.20** and CsOH to give tetrahydropyrenophane **2.29** (**Scheme 2.7**). This system was then aromatized using DDQ to give pyrenophane **2.30a-b** as a mixture of isomers. Partial separation by chiral HPLC allowed the authors to study the racemization and its kinetics to determine a barrier of 28.9 kcal mol^{-1} for interconversion, which occurs through an *anti-anti'* conformation process.



Scheme 2.7 Vögtle's synthesis of helically chiral pyrenophane **2.30**.

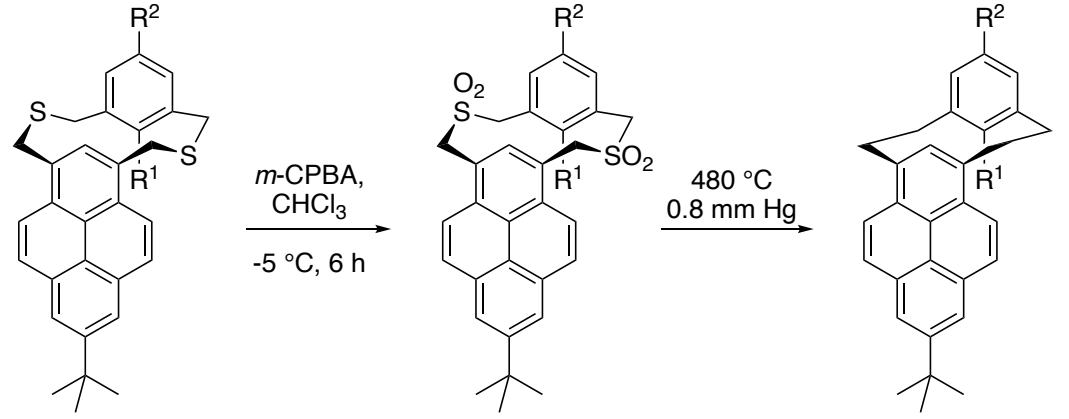
Another example of a (1,3)pyrenophane, reported in 1993, was the first that did not require the utilization of tetrahydropyrene intermediates for solubility reasons.[10] In order to avoid the solubility issue, *tert*-butyl groups were installed on the pyrene core, which proved to be an effective solubilizing strategy. The bis(bromomethyl)pyrene system **2.33** was reacted with a series of dithiols **2.34a-e** under high dilution conditions in ethanolic potassium hydroxide to form exclusively one of either the *syn*- or *anti*-pyrenophanes (**2.35a-e**) depending on the starting dithiol (**Scheme 2.8**).



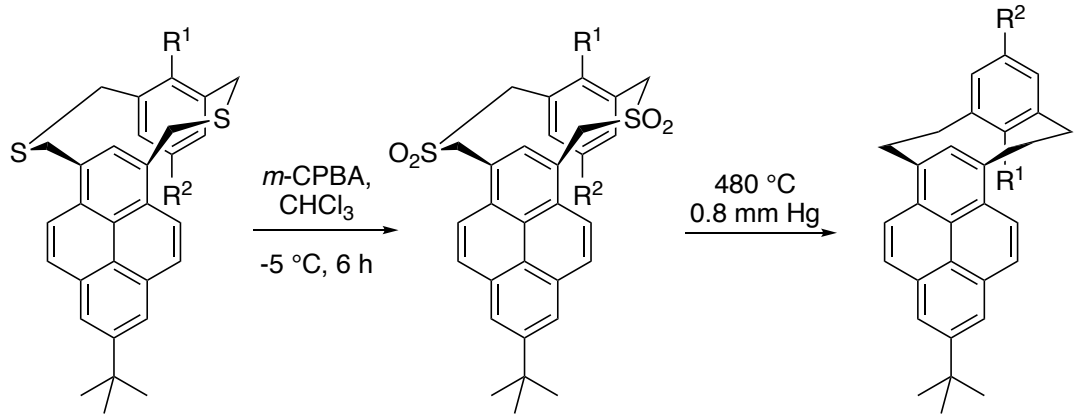
R^1 = R^2 = H (**a**)	0%	38%
R^1 = Me, R^2 = ^{t}Bu (**b**)	35%	0%
R^1 = Et, R^2 = ^{t}Bu (**c**)	44%	0%
R^1 = OMe, R^2 = ^{t}Bu (**d**)	0%	25%
R^1 = F, R^2 = ^{t}Bu (**e**)	0%	41%

Scheme 2.8 Synthesis of pyrenophanes **2.33a-e**.

These pyrenophanes were further manipulated by oxidation of the sulfur atoms with *m*-chloroperoxybenzoic acid. *Anti*-**2.33b** and *anti*-**2.33c** were oxidized to the sulfone products **2.34b,c** quantitatively while retaining their *anti* geometry. The *syn*-**2.33a**, *syn*-**2.33d** and *syn*-**2.33e** pyrenophanes could also be oxidized to form the corresponding sulfones quantitatively without any change in the conformation (**Scheme 2.9**). All of these sulfones were then flash vacuum pyrolyzed at 480 °C to give a series of [2]metacyclo[2](1,3)pyrenophanes (**2.35a-e**). These systems were all shown to exist exclusively in their *anti*-conformations.



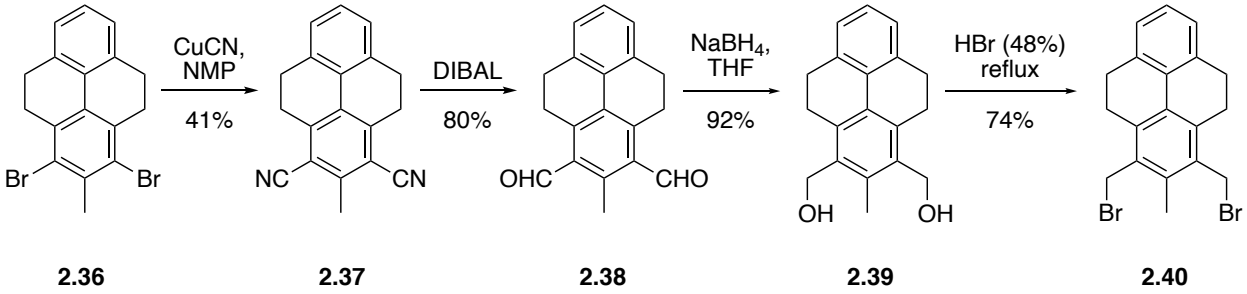
R^1 = Me, R^2 = ^{t}Bu (**2.33b**) — quant. (**2.34b**) — 68% (**2.35b**)
R^1 = Et, R^2 = ^{t}Bu (**2.33c**) — quant. (**2.34c**) — 44% (**2.35c**)



R^1 = R^2 = H (**2.33a**) — quant. (**2.34a**) — 48% (**2.35a**)
R^1 = OMe, R^2 = ^{t}Bu (**2.33d**) — quant. (**2.34d**) — 41% (**2.35d**)
R^1 = F, R^2 = ^{t}Bu (**2.33e**) — quant. (**2.34e**) — 55% (**2.35e**)

Scheme 2.9 Yamato's synthesis of (1,3)pyrenophanes **2.35a-e**.

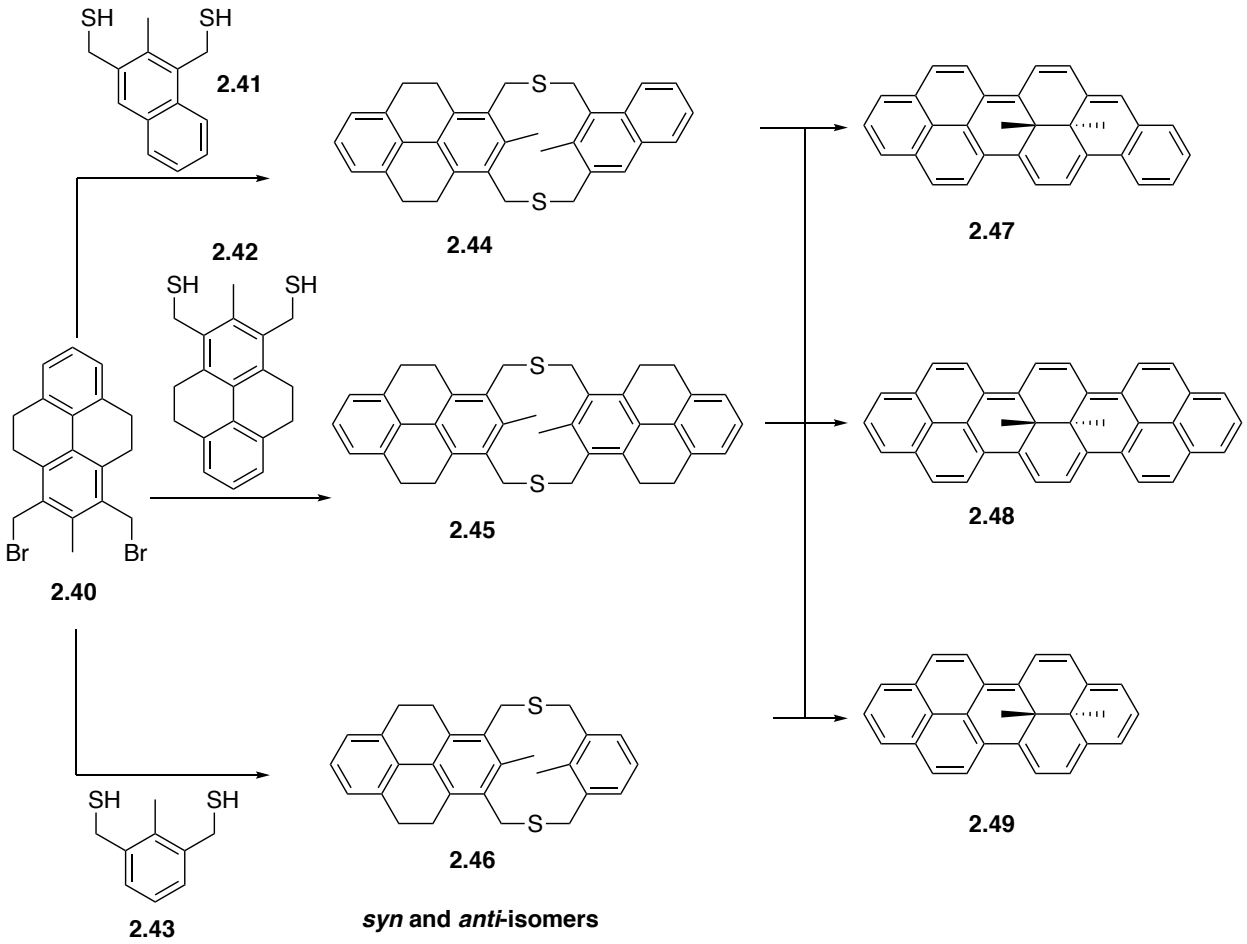
A few years later, Mitchell *et al*. reported the synthesis of new (1,3)pyrenophanes, which were synthesized in order to experimentally probe the aromaticity of annulated dimethyldihydropyrenes in relation to benzene.[11] The synthesis of these systems relied on the construction of a (1,3)bis(bromomethyl)dihydropyrene system **2.40**, which was achieved through a four-step series of transformations starting from compound **2.36**. Firstly, **2.36** was subjected to a Rosenmund-von Braun reaction to give dinitrile **2.37**. This system was then reduced with DIBAL to the corresponding dialdehyde **2.38**, which was then further reduced to the diol **2.39**. These benzyic alcohols were finally converted into benzyl bromides in refluxing HBr to give the pyrenophane precursor **2.40** (**Scheme 2.10**).



Scheme 2.10 Mitchell's synthesis of pyrenophane precursor **2.40**.

Dibromide system **2.40** was treated with various dithiols (**2.41-2.43**) to give three dithiacyclophanes (**2.44-2.46**), which existed as a mixture of the *syn* and *anti*-isomers that could be separated by flash column chromatography (**Scheme 2.11**). The ring conformation of a cyclophane of this type was accomplished by ^{1}H NMR analysis. The chemical shifts of the internal methyl groups in an *anti* conformer were observed at significantly higher field than those of the corresponding *syn* conformers. The bridges of the *anti* conformers were then contacted by desulfurization following a multi-step protocol. Wittig rearrangement was induced by treatment with *n*-BuLi. Quenching of the products with MeI gave the ring-contracted cyclophanes bearing SMe substituents. According to a well-established cyclophane methodology, these SMe groups were converted into good leaving groups by methylation with Borch reagent and subsequent

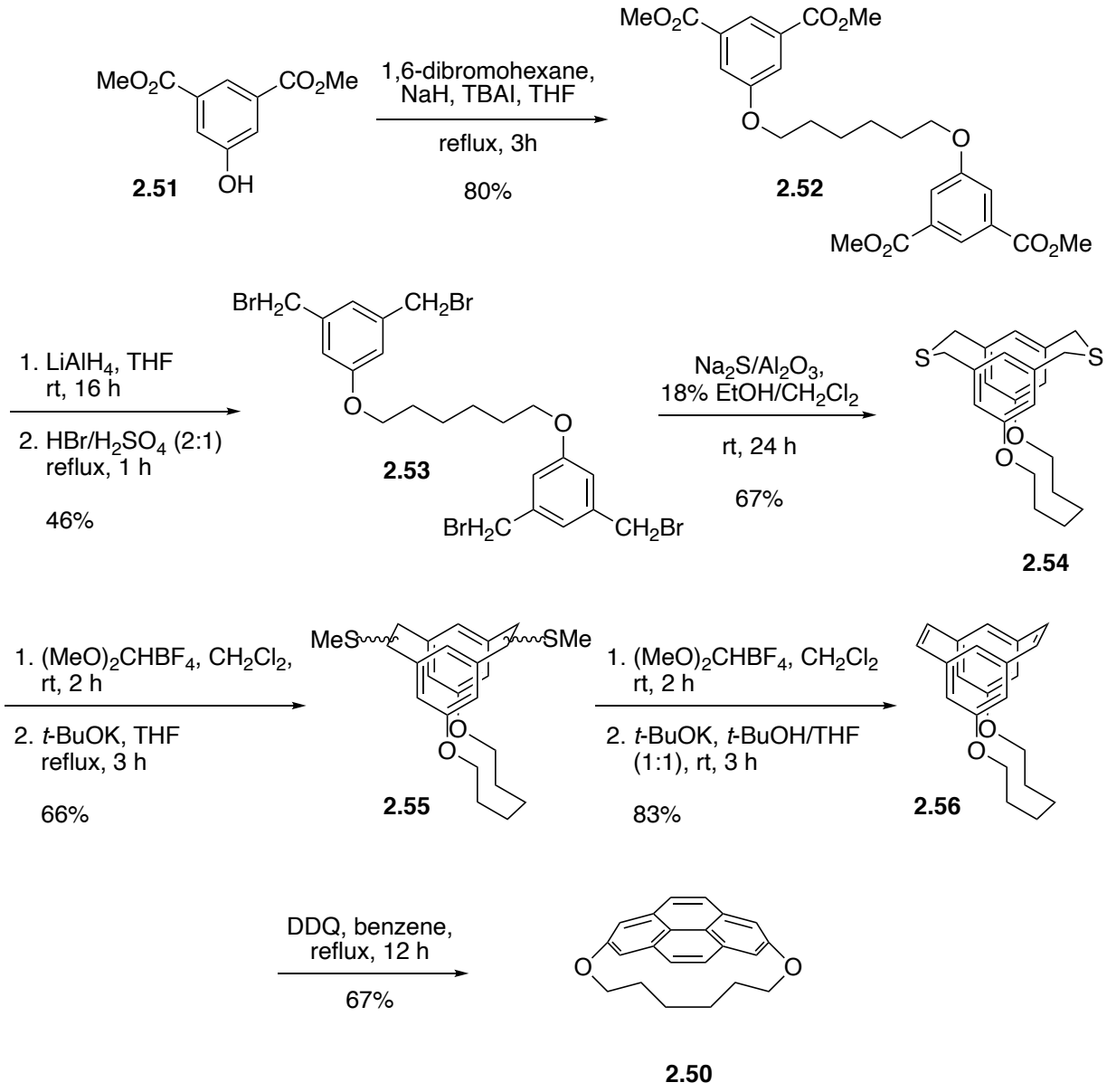
reaction with potassium *tert*-butoxide brought about Hoffman elimination to yield **2.47-2.49**.



Scheme 2.11 Synthesis of dimethyldihydropyrenes **2.47-2.49**.

In the following year, the Bodwell group reported the synthesis its first pyrenophane, 1,8-dioxa[8](2,7)pyrenophane **2.50** (**Scheme 2.12**).[12] Small cyclophanes such as this one are of interest because they contain highly nonplanar aromatic systems, in which the severe distortion from planarity can lead to unusual spectroscopic and chemical properties. Synthetically, two units of dimethyl 5-hydroxyisophthalate (**2.51**)

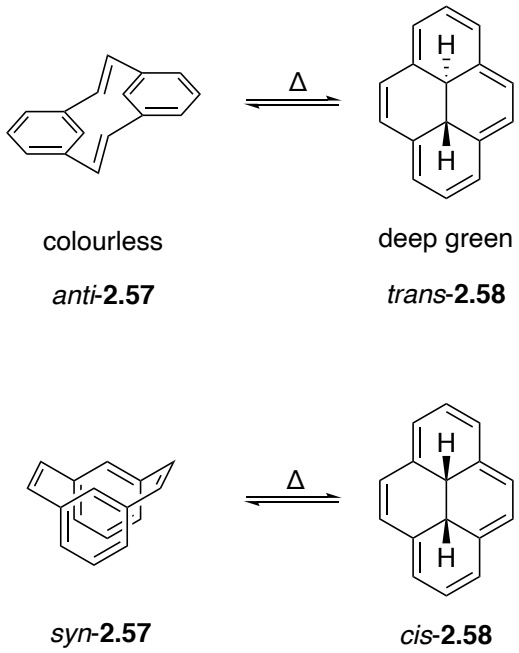
were tethered under Williamson ether synthesis conditions by treatment with TBAI, NaH and 1,6-dibromohexane in benzene at reflux to afford tetraester **2.52** in 67% yield. This tetraester was then reduced with $LiAlH_4$ to give the corresponding tetraol which was converted in crude form to the corresponding tetrabromide **2.53** in 46% yield over two steps. The cyclophane-forming step involved the coupling of the benzylic bromides with Na_2S supported on Al_2O_3, which yielded 1,8-dioxa-16,25-dithia[8.3.3](1,3,5)dioxadithiacyclophane **2.54** in good yield (67%). This system was then ring contracted and desulfurized using a series of transformations that will be discussed in greater detail later to give cyclophanediene **2.56** in 75% yield over 4 steps. Cyclophanediene **2.56** was then treated with DDQ (2,3-dichloro-5,6-dicyanobenzoquinone) in benzene at reflux and this cleanly induced cyclodehydrogenation to give 1,8-dioxa[8](2,7)pyrenophane (**2.50**) in 67% yield.



Scheme 2.12 Bodwell's first synthesis of a pyrenophane **2.50**.

The transformation from cyclophanediene to pyrenophane in the presence of an oxidant was inspired by the work of Boekelheide and Mitchell and their work on [2.2]metacyclophane-1,9-diene (**2.57**) and its valence isomerization.[13] When **2.57** (colourless) is irradiated with ultraviolet light (or heated), a valence isomerization leading to dihydropyrene **2.58** (deep green) occurs. The equilibrium between these systems

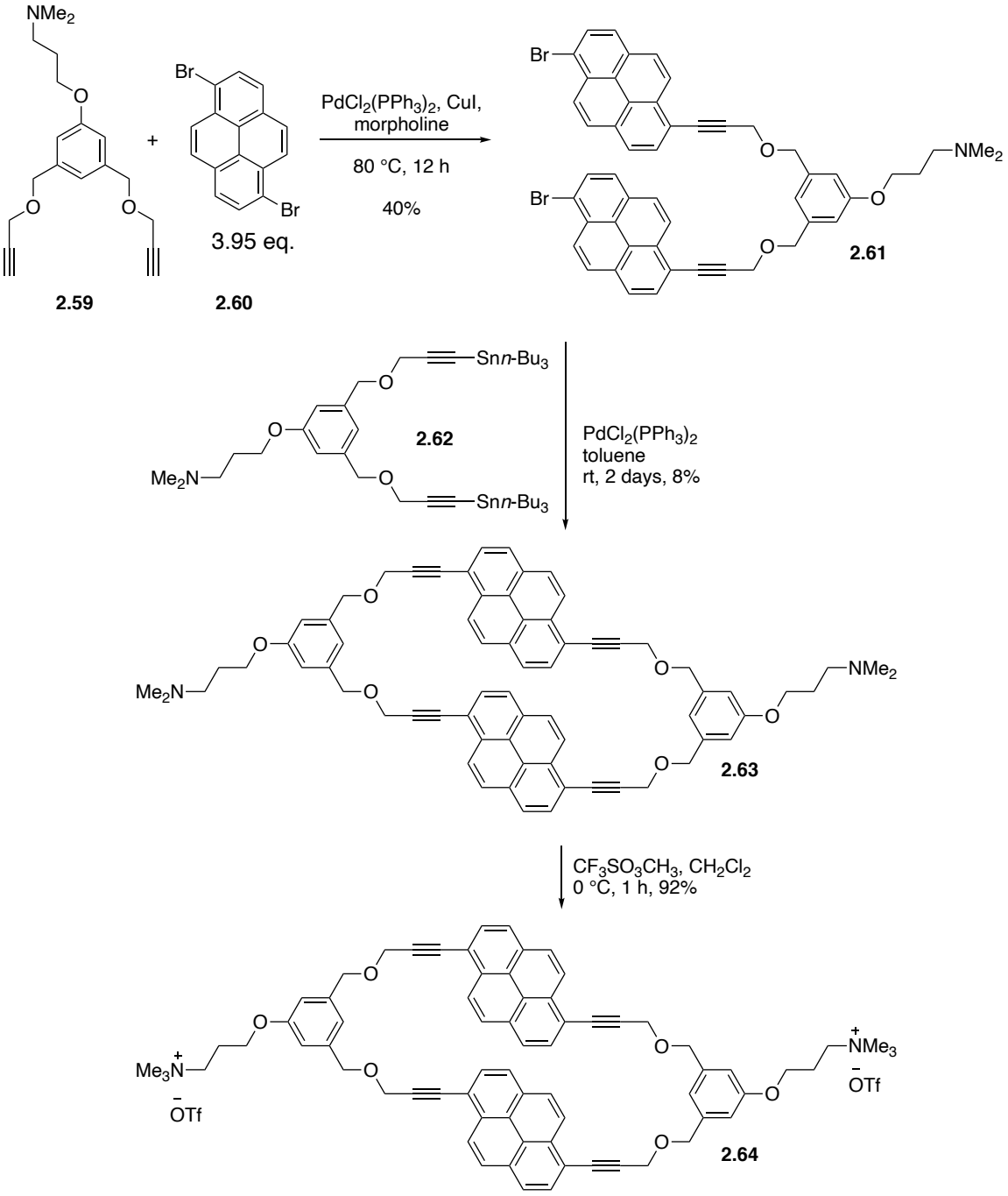
favours the 14π-electron dihydropyrene **2.58**, but upon irradiation with visible light the equilibrium can be pushed back towards [2.2]metacyclophane-1,9-diene (**2.57**).



Scheme 2.13 Valence isomerization of [2.2]metacyclophane-1,9-diene (**2.57**).

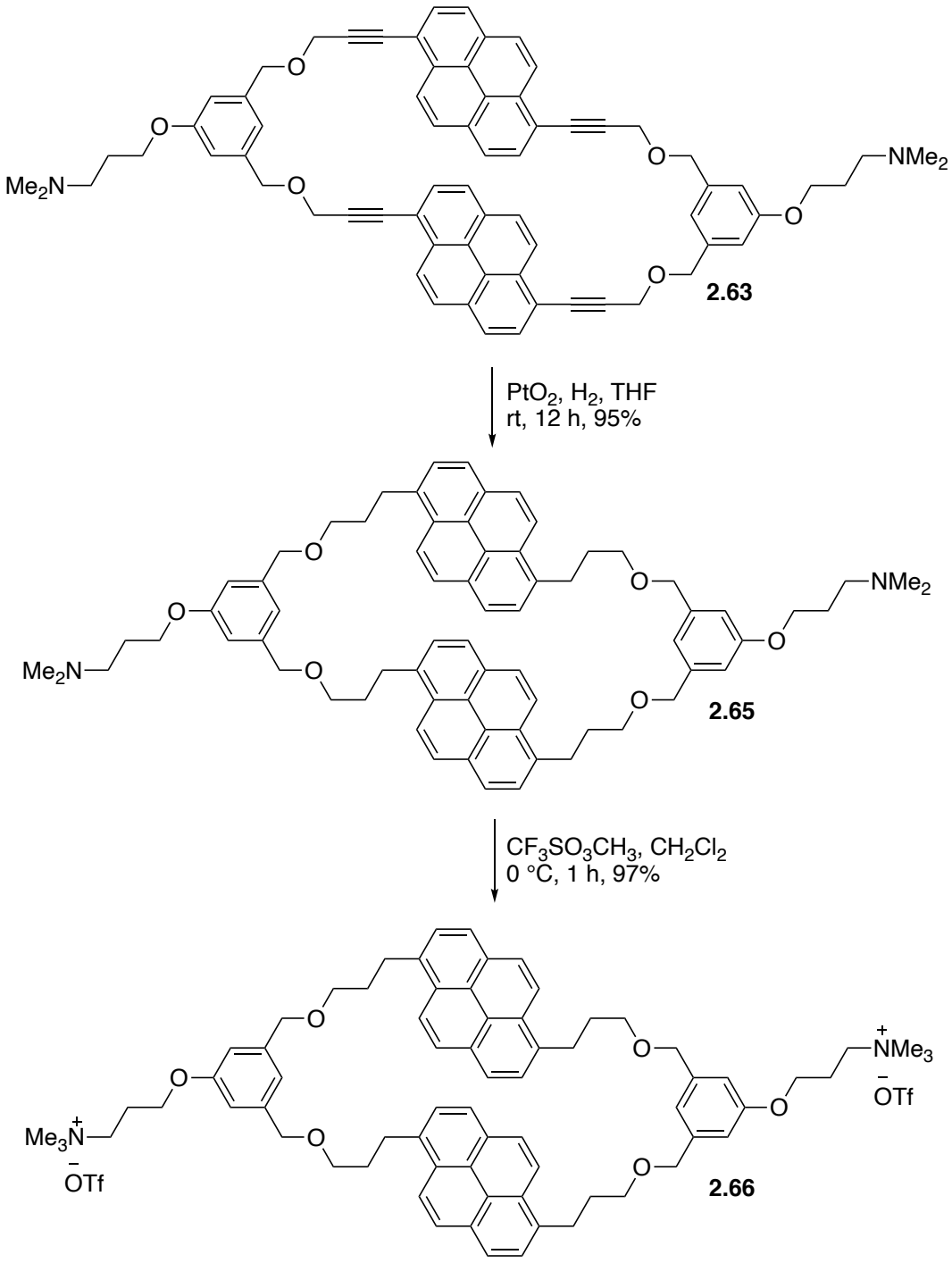
The valence isomerization between *anti*-**2.57** and *trans*-**2.58** is a 6π antarafacial electrocyclic ring closure / ring opening, which is photochemically "allowed". In Bodwell's diithiacyclophane **2.56**, the conformation of the [2.2]metacyclophanediene system is held in the *syn* conformation, which renders the electrocyclic ring closue / ring opening suprafacial and thus thermally "allowed". The purpose of adding DDQ was to dehydrogenate the dihydropyrene system after the valence isomerization to give a pyrene system. It is noteworthy that this reaction was able to afford a rather highly strained system 1,8-dioxa[8](2,7)pyrenophane (**2.50**). The success of this reaction is in large part due to the gain in aromatic stabilization energy (ASE) that comes from forming a pyrene system (ASE = 74.6 kcal/mol) from a dihydropyrene (ASE ≈ 20 kcal/mol) in the dehydrogenation step, which offsets the development of strain.[14]

A few years later, in 1999, Inouye and co-workers reported the synthesis and properties two pyrene-containing water-soluble cyclophanes, **2.64** and **2.66**, that displayed molecular recognition (**Scheme 2.14** and **Scheme 2.15**).[15] Terminal alkyne **2.59** was coupled with 1,6-dibromopyrene (**2.60**) under Sonogashira cross-coupling conditions to give pyrene system **2.61** in 40% yield. The first cyclophane was obtained by a two-fold Stille coupling between the aromatic bromides in **2.61** and a bis(stannylalkyne) derived from diyne) **2.59** in 8% yield. In order to make this cyclophane water-soluble, the free amines were reacted with methyl trifluoromethanesulfonate to give quaternary ammonium salts **2.64.**



Scheme 2.14 Inouye's synthesis of water-soluble pyrenophane **2.64**.

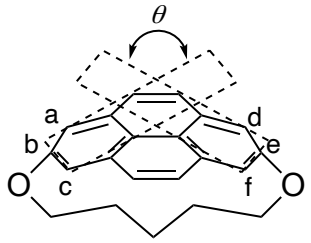
They also prepared another water-soluble pyrenophane by hydrogenating the C-C triple bonds in **2.63** by treatment with hydrogen in the presence of PtO_2 (**Scheme 2.15**). The hydrogenated system **2.65** was also treated with methyl trifluoromethanesulfonate to give the quaternary ammonium salt-bearing pyrenophane **2.66**.



Scheme 2.15 Inouye's synthesis of water-soluble pyrenophane **2.66**.

The ^{1}H NMR spectrum of pyrenophane **2.63** showed similar upfield shifts (δ 7.51-7.78) to those of the pyrene protons reported by Misumi for pyrenophanes (**2.23** and **2.26**) (7.20-7.47 and 7.22-7.51 ppm), although they are not quite as upfield shifted. This suggests that, in the absence of a guest, the pyrene moieties in **2.63** lie close to each other, but not as close as they lie in Misumi's pyrenophanes.

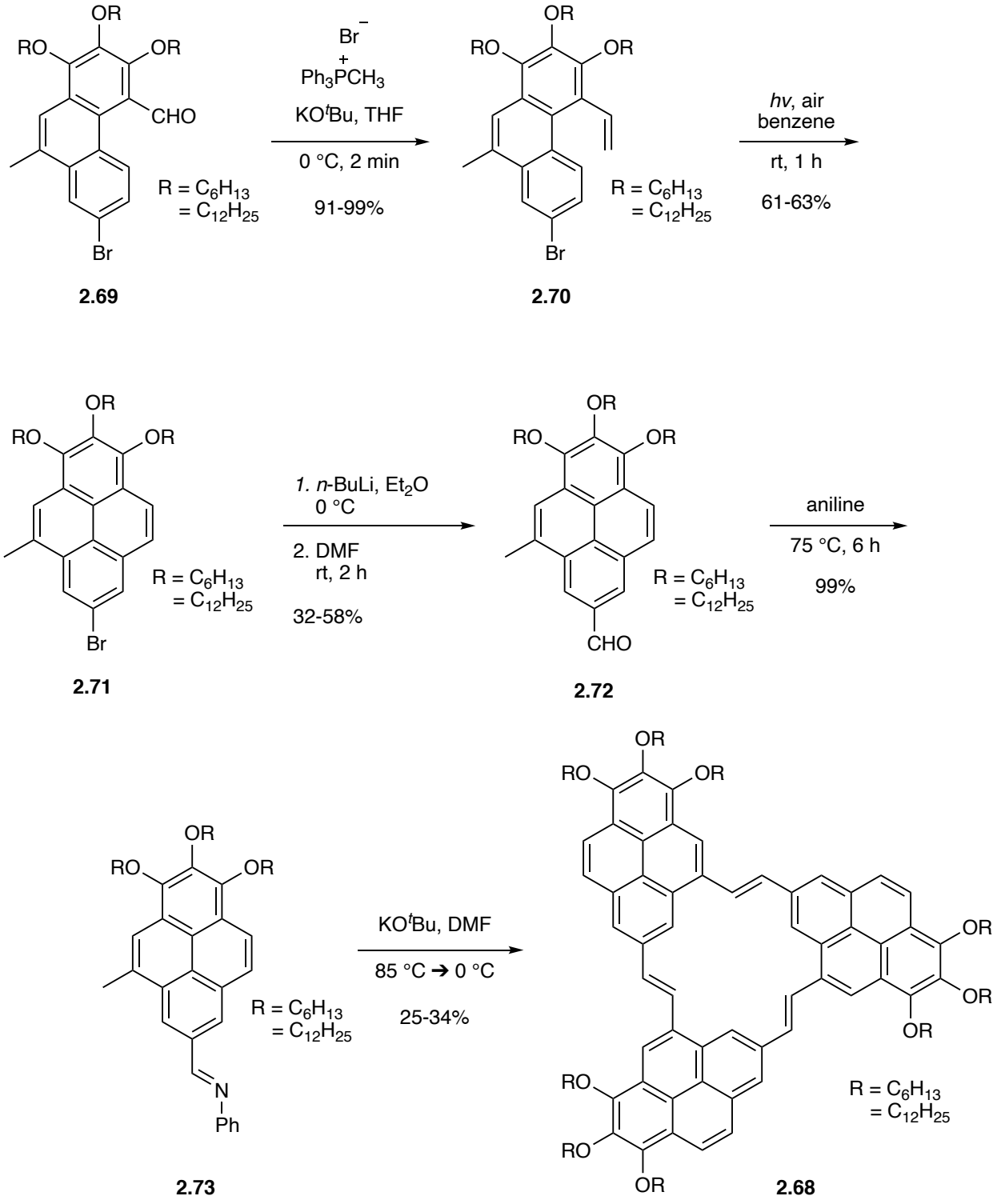
In that same year, the Bodwell group published its second pyrenophane **2.67** using the same strategies employed in the synthesis of **2.50**.[16] In this report the length of the bridged was shortened by one methylene unit to give 1,7-dioxa[7](2,7)pyrenophane **2.67**. Single crystal X-ray analysis of pyrenophane **2.67** showed a pyrene system that was far more distorted then the previously reported pyrenophane **2.50**, which at the time of its synthesis set the record for pyrene distortion from planarity (end-to-end bend). In order to quantify the amount of distortion, the angle θ was defined as the smallest angles between two planes of atoms, one formed by C_a-C_b-C_c and the other by C_d-C_e-C_f (**Scheme 2.16**). Using this metric, the bend angle (θ) of 1,8-dioxa[8](2,7)pyrenophane (**2.50**) was determined to be 87.8° and the bend angle of 1,7-dioxa[7](2,7)pyrenophane (**2.67**) was determined to be 109.1° (more than 20° larger than its lower homologoue) using X-ray data. The repeating pyrene unit around the equator of D_{5h}-C_{70} has a bend angle of 108.0°, making pyrenophane **2.67** slightly more bent. The pyrene-forming methodology is clearly quite powerful.



2.67

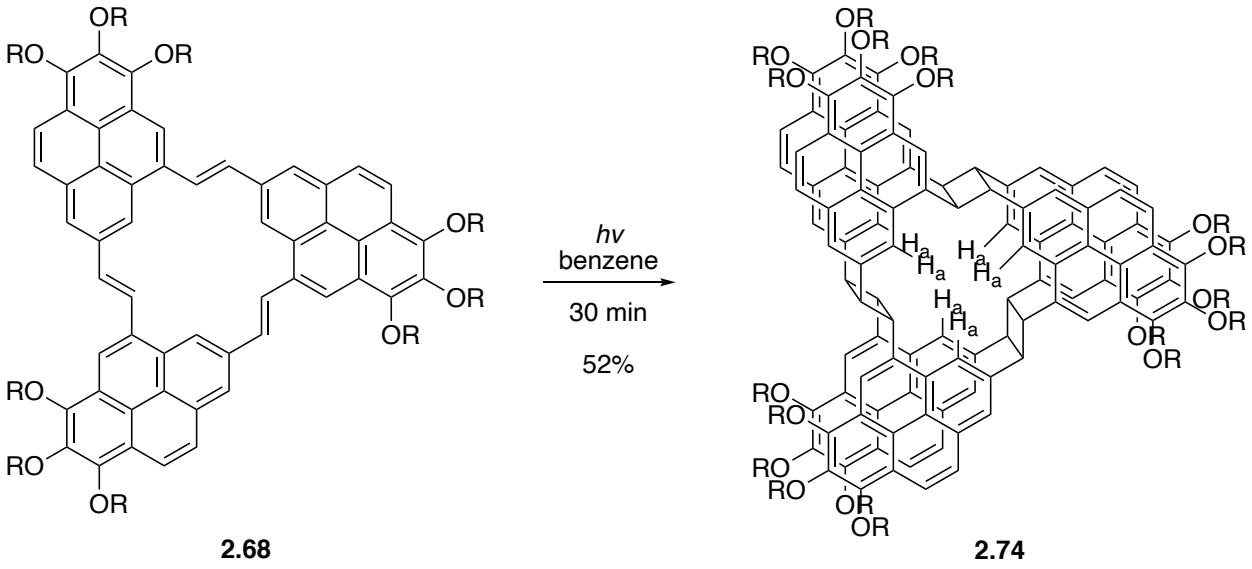
Scheme 2.16 Bend angle (θ) of the pyrene system in 1,7-dioxa[7](2,7)pyrenophane (**2.67**).

In the following year, Meier *et al.* synthesized a highly conjugated (2,4)pyrenophane **2.68**, which contains three pyrene units bridged by alkenes.[17] The synthesis begins with 1,2,3-trialkoxybenzenes, but this discussion will begin from phenanthryl aldehyde **2.69** (**Scheme 2.17**). Aldehyde **2.69** was subjected to a Wittig reaction with methyltriphenylphosphonium bromide and KO^{t}Bu to give alkene **2.70**, which was oxidatively photocyclized to give pyrene **2.71**. This system was subjected to lithium-halogen exchange with *n*-BuLi and then quenched with DMF to give pyrenyl aldehyde **2.72**. This aldehyde was then converted into imine **2.73** by condensation with aniline. The methyl group attached to the 4-position of pyrene is activated by the electron withdrawing imine group and could be deprotonated with potassium *tert*-butoxide. The resulting anion reacts with the imino group of another molecule resulting in overall in an *E*-selective cyclocondensation to give pyrenophane **2.68** (25-34%) as well as linear condensation products. These pure pyrenophanes were found to aggregate to form discotic liquid crystals.



Scheme 2.17 Meier's synthesis of pyrenophane **2.68**.

Meier and co-workers followed up their paper on the synthesis of pyrenophane **2.68** by further investigating its aggregation properties and discovering that it underwent a spectacular photodimerization (**Scheme 2.18**).[18] Irradiation of **2.68** induces a three-fold [2+2] cycloaddition which yields the dimerized pyrenophane **2.74** in 52% yield as a thick oil with only a hint of colour. The inner aromatic protons (H_a) show a significant downfield chemical shift of 10.56 ppm which the authors attribute to extended ring currents of the pyrene units.

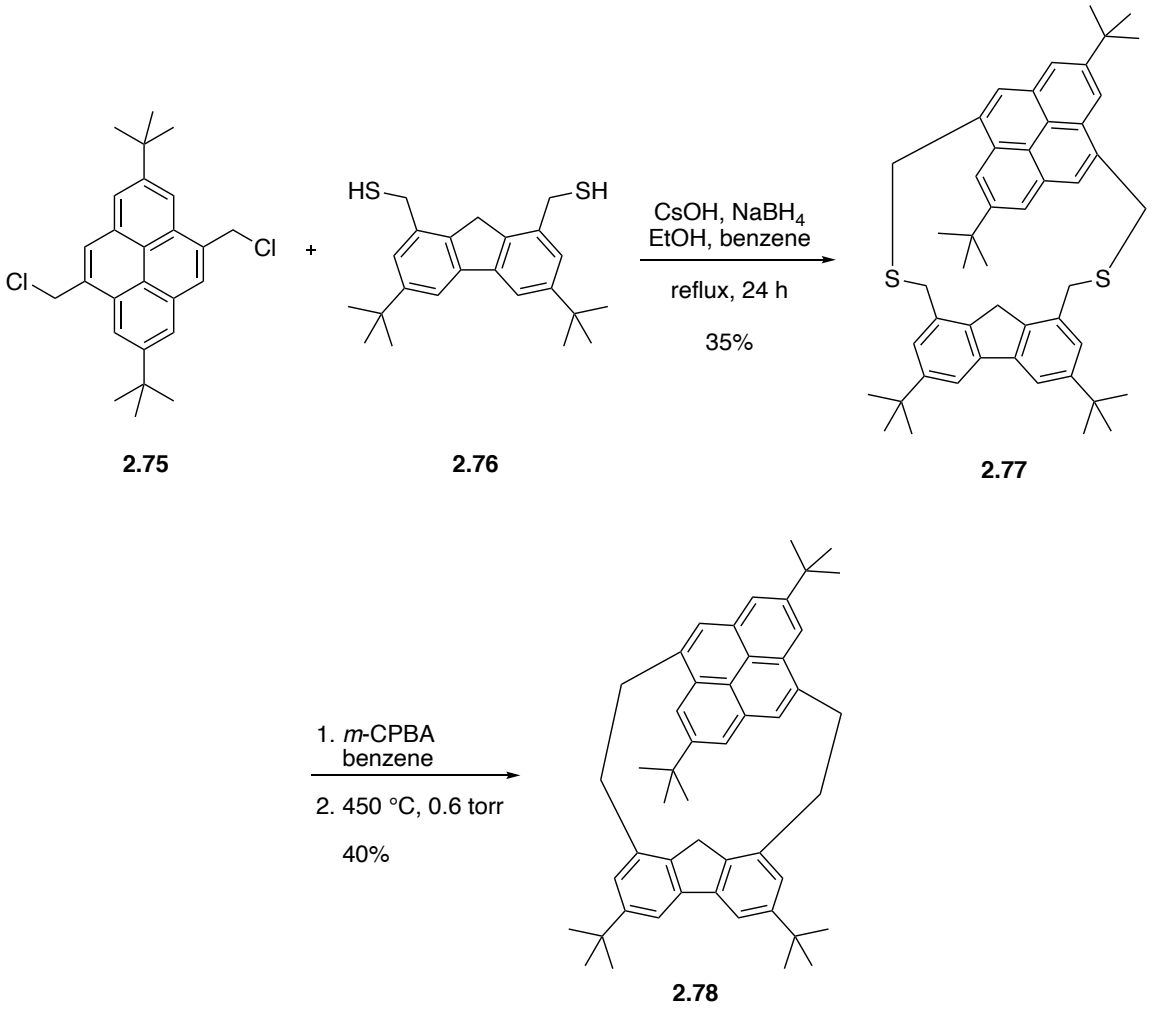


2.68 **2.74**

Scheme 2.18 Dimerization of Meier's pyrenophane **2.68**.

Also in 2001, Tsuge and co-workers reported on the synthesis of the first (4,9)pyrenophane **2.77**, which was formed by the reaction of a bis(chloromethyl)pyrene **2.75** with a bis(methanethiol)fluorene **2.76** under basic conditions (CsOH) and high dilution (**Scheme 2.19**).[19] The resulting dithiacyclophane **2.76** was obtained in 35% yield. The ^{1}H NMR chemical shifts of the methylene protons in the fluorene unit proved interesting. Firstly, in the product they are diastereotopic and easily distinguishable and, secondly, the proton pointing towards the pyrene system is firmly entrentched within its shielding zone as evidenced by its upfield shift to –0.80 ppm. By comparison, its geminal

neighbour points away from the opposite π-system and appears at 1.59 ppm. As expected, these protons showed large geminal coupling constants of 21 Hz. Even upon heating to 150 °C, no coalescence was observed indicating a high energy barrier to flipping of one aromatic system to the other. The bridges of pyrenophane **2.77** could be contracted via sulfur extrusion using sulfone pyrolysis. This was accomplished by first oxidizing the thioethers to the corresponding sulfones and then pyrolyzing at 450 °C to give the bridge-contracted pyrenophane **2.78** in 40% yield. The NMR spectrum of this pyrenophane exhibited similar traits to those of the parent pyrenophane **2.77**.



2.75 **2.76** **2.77** **2.78**

Figure 2.19 Tsuge's synthesis of the first (4,9)pyrenophanes **2.77** and **2.78**.

In 2002, Tsuge and co-workers reported another synthesis of (4,9)pyrenophanes (**Scheme 2.20**).[20] Their synthesis began with a bis(chloromethyl)pyrene **2.75** system and reacted it with bis(thiomethyl)benzenes **2.79** under basic conditions (Cs_2CO_3) and high dilution to give dithiacyclophanes **2.80a-b** in moderate yields. The nitro-containing cyclophane **2.80a** was also reduced to the corresponding amine **2.81** by catalytic hydrogenation with Pd/C and H_2, albeit in low yield (15%), which the authors attributed to steric congestion around the nitro group. The crystal structure of **2.80a** demonstrated that the nitrobenzene moeity is nearly parallel to the pyrene unit, which was also supported by the desymmetrized ^{1}H NMR spectrum of the pyrene resonances.

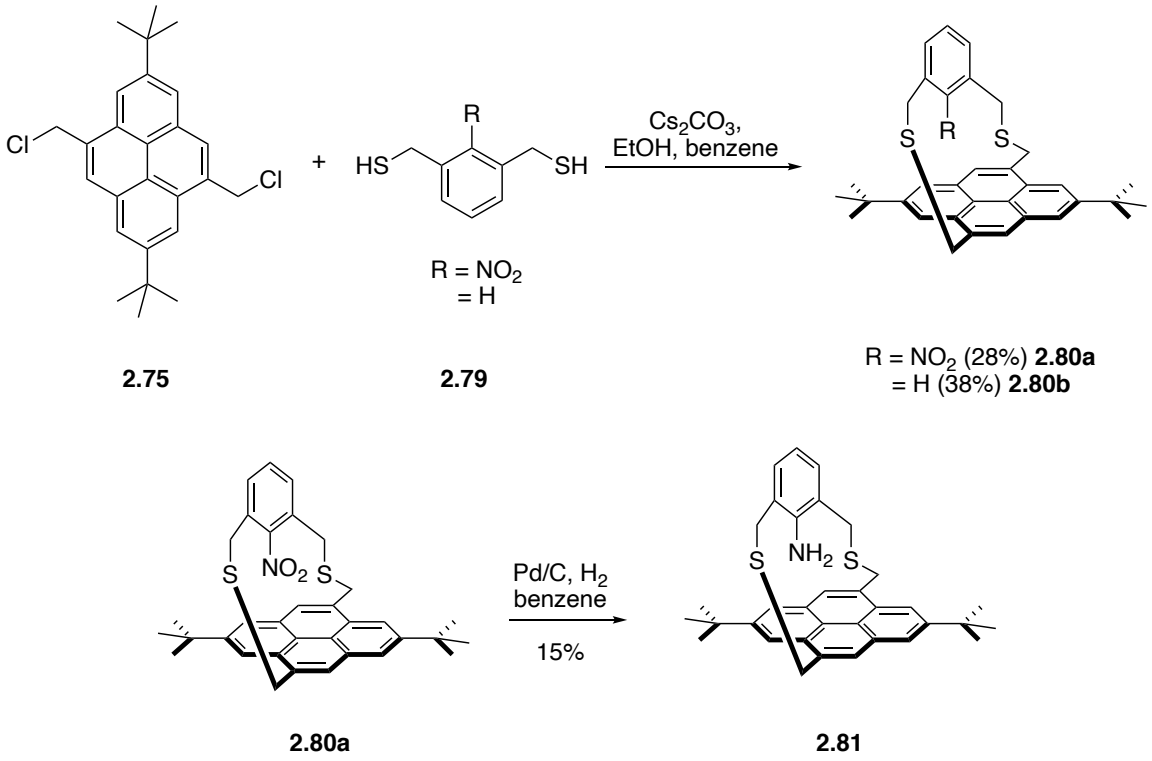
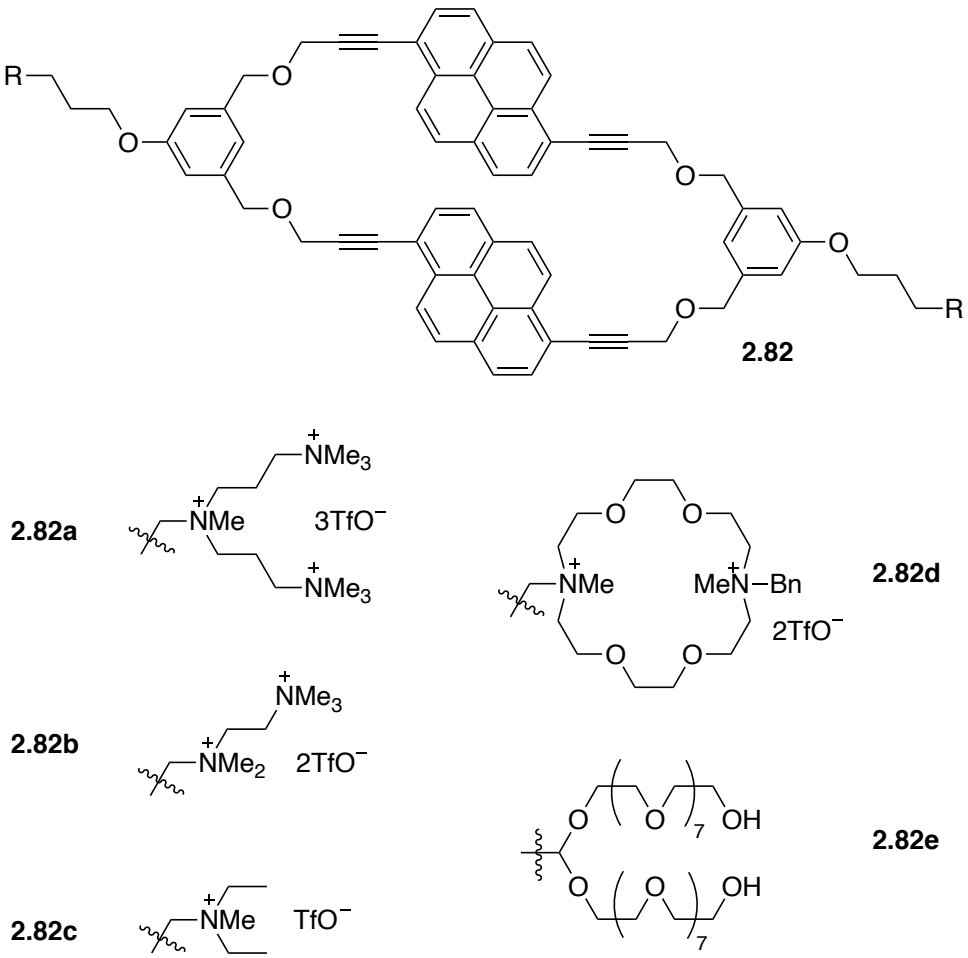


Figure 2.19 Tsuge's synthesis of pyrenophanes **2.81** and **2.82**.

In 2003, The Bodwell group completed the synthesis of a series of syntheses of 1,*n*-dioxa[*n*](2,7)pyrenophanes with *n* = 7,10 using the same synthetic approach as previously mentioned.[21] The original synthesis of these systems is discussed later in this

Chapter and the development of an improved synthesis forms the basis of the new results presented at the end of this Chapter.

In 2004, Inouye *et al.* revisited their work on the search for water soluble pyrenohane systems (**Scheme 2.21**).[22] Utilizing the same scaffold as **2.66w**, they varied the nature of the ether appended to the phenyl group in an effort to improve the water solubility. Introducing polyammonium, diazoniumcrown and octa(oxyethylene) groups afforded pyrenophanes **2.82a-e** of which **2.82a**, **2.82d**, and **2.82e** were pure-water soluble. The authors investigated the host-guest properties of the water-soluble pyrenophanes with a number of different guest molecules such as: monomeric pyrenes which were either neutral, cationic or anionic, naphthaleno-disulfonates, adenosine, and several nucleotides. Octa(oxyethylene) pyrenophane **2.82e** showed good binding affinities for any monomeric pyrene system regardless of charge. Pyrenophane **2.82d** preferred to bind with anionic species. The authors made no further mention of the host-guest properties of pyrenophane **2.82a**.



Scheme 2.21 Inouye's water soluble pyrenophanes.

In 2005, Tsuge and co-workers continued to expand the scope of (4,9)pyrenophanes using the same strategy of coupling bis(chloromethyl)pyrene **2.75** with various new bis(methanethiol)benzenes **2.83** to give a series of pyrenophanes **2.84** (**Scheme 2.22**).[23] In all cases, the ^{1}H NMR spectra showed the methylene signals as doublets which indicates that the systems are conformationally rigid at room temperature on the NMR time-scale. When R_1 is a proton the benzene ring adopts a perpendicular conformation in relation to the pyrene system. In these systems the inner R_1 proton appears very high-field shifted (3.44-3.96 ppm), which is consistent with it being situated over the middle of the pyrene system. The authors claimed that this was evidence of a perpendicular arrangement of the two aromatic systems, but it is also

possible that the benzene deck is flipping rapildly between degenerate parallel conformations (the average of these two conformation is a perpendicular conformation). When the inner R_1 group is not a proton (R_1 = OCH_3, NO_2, F) the system adopts a different conformation where the two aromatic systems are now parallel to each other.

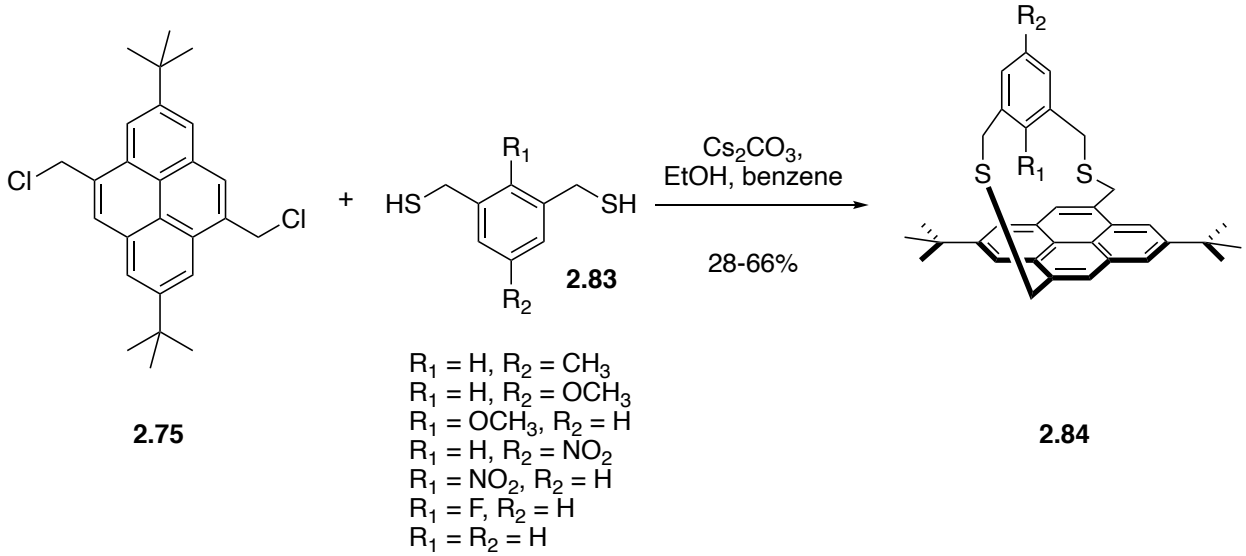
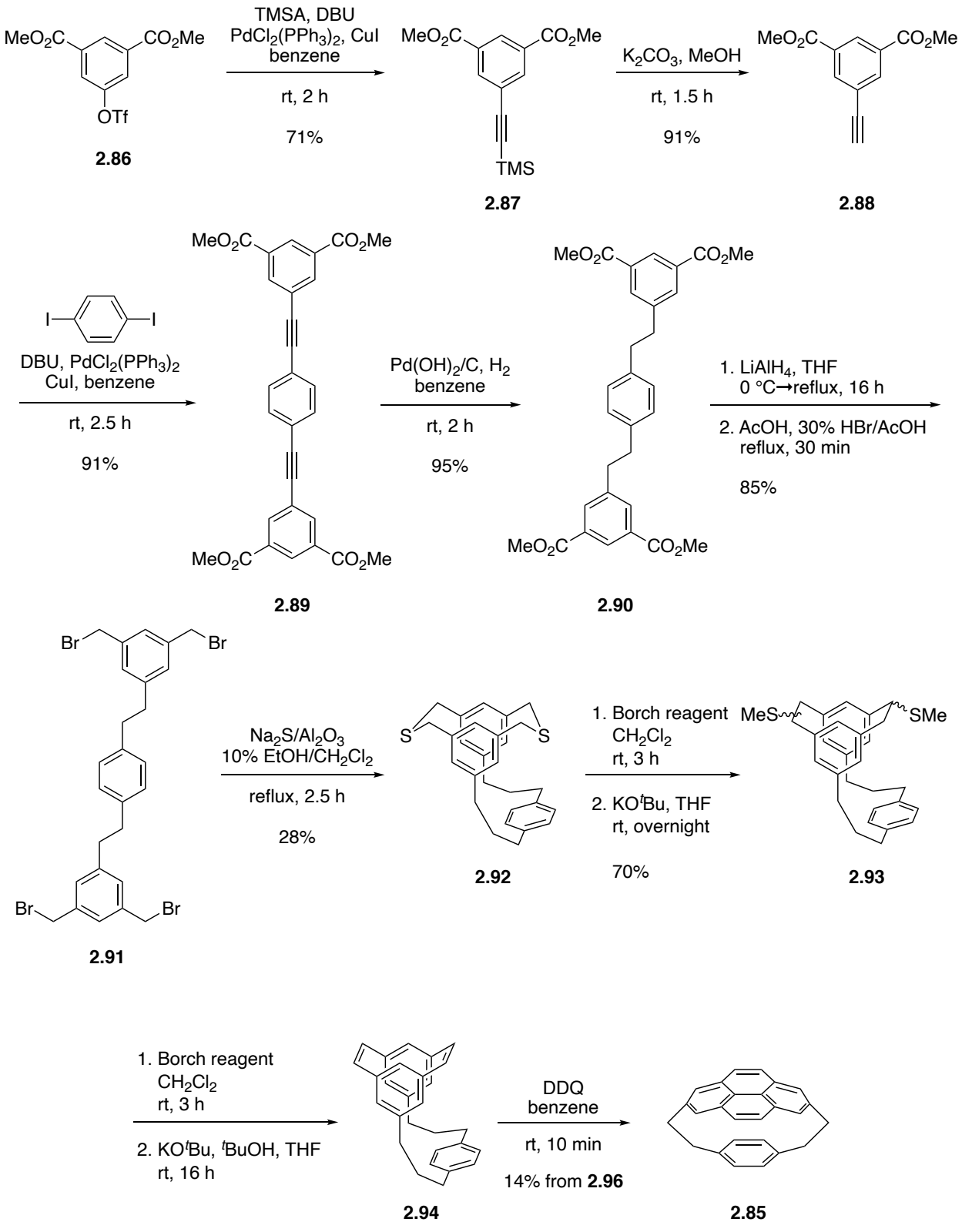


Figure 2.22 Tsuge's final syntheses of (4,9)pyrenophanes.

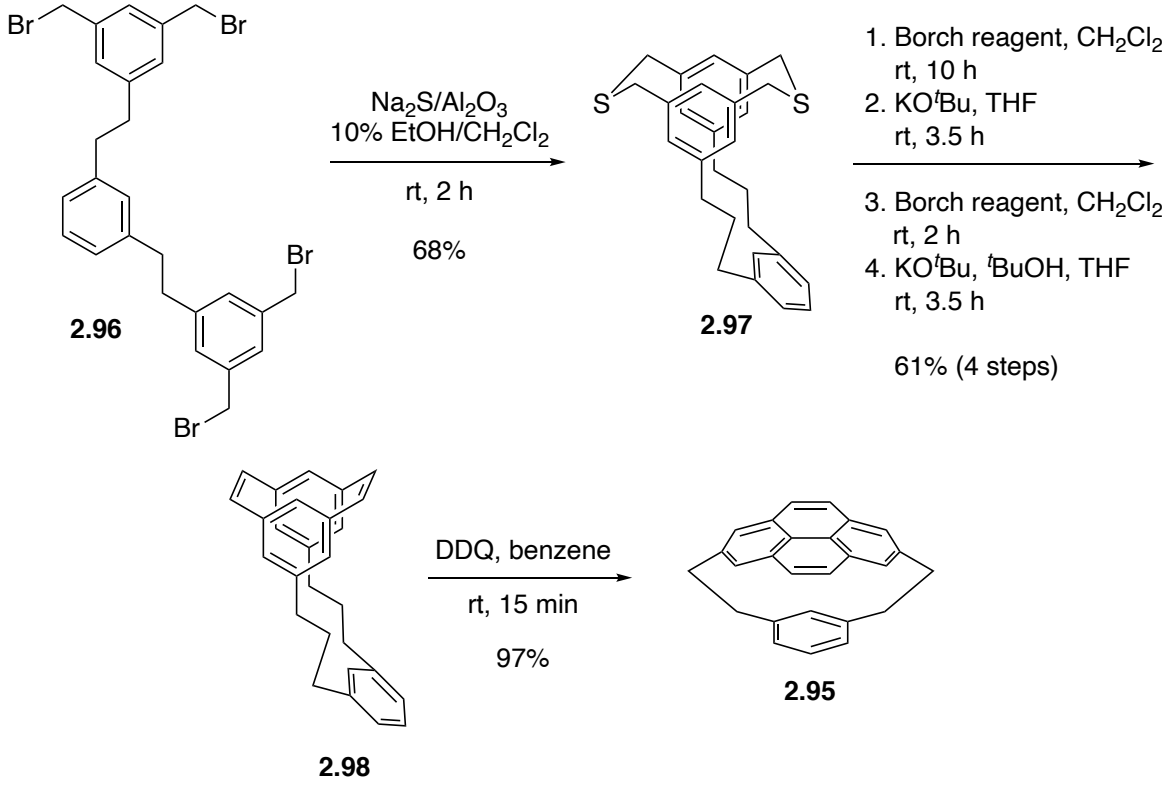
Around the same time, the Bodwell group reported on the synthesis of new (2,7)pyrenophanes that contained a second aromatic system. The first one, [2]paracyclo[2](2,7)pyrenophane **2.85**, was reported in 2001 (**Scheme 2.23**).[24] Strategically, cyclophane formation was accomplished in a similar fashion to the previously reported (2,7)pyrenophane syntheses. In this case, the synthesis began with a Sonogashira coupling between trimethylsilylacetylene and triflate **2.86** to give the TMS-protected alkyne **2.87**, which was smoothly deprotected with K_2CO_3 in MeOH to give alkyne **2.88**. This alkyne was then two-fold coupled under Sonogashira conditions with 1,4-diiodobenzene to give dialkyne **2.89** which quickly installed all the carbon atoms present in the product pyrenophane. The alkynes were subsequently hydrogenated using Pearlman's catalyst under a H_2 atmosphere to give tetraester **2.90**, which was reduced to the corresponding tetraol and then brominated in refluxing HBr/AcOH to give tetrabromide **2.91**. Dithiacyclophane **2.92** formation proceeded in a lower yield (28%)

than has been typical for these systems. This result was rationalized as being due to the presence of the *p*-phenylene system in the bridge, which introduced more rigidity into the bridge and caused an increase in strain in the dithiacyclophane system **2.92**. Methylation with Borch reagent followed by thia-Stevens rearragnement gave isomeric mixture **2.93** in good yield (70%). Methylation once again followed by Hofmann elimination gave a 1:1 mixture of cyclophandiene **2.94** and pyrenophane **2.85**. This mixture could be converted to pyrenophane by treatment with DDQ in benzene at room temperature.



Scheme 2.23 Bodwell's synthesis of [2]paracyclo[2](2,7)pyrenophane **2.85**.

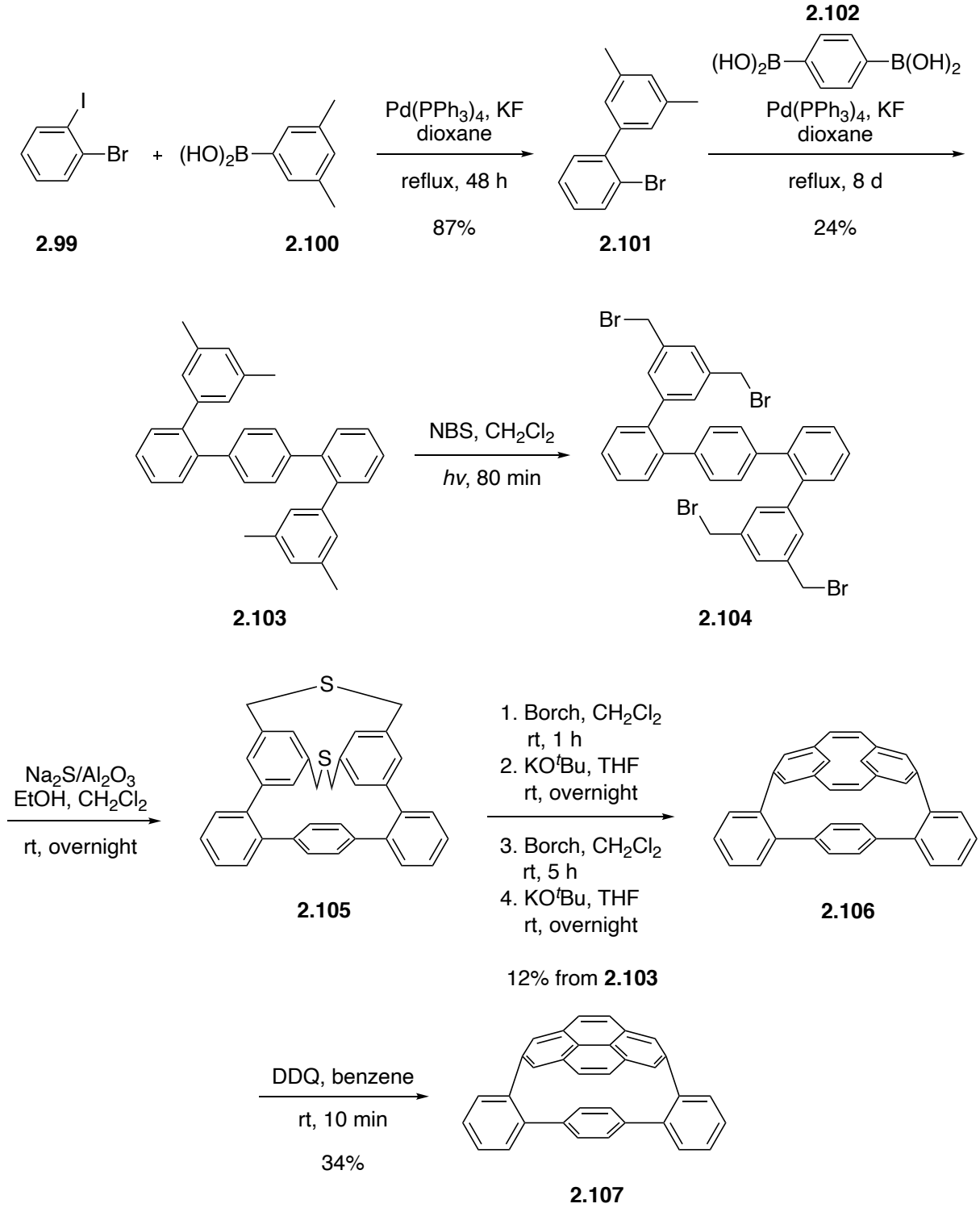
In the same vein, the Bodwell group also reported on the synthesis of [2]metacyclo[2](2,7)pyrenophane (**2.95**) (**Scheme 2.24**).[25] With the introduction of the *meta*-substituted arene into the bridge, the sodium sulfide coupling of tetrabromide **2.96** proceeded in much higher yield (68%) to give dithiacyclophanes **2.97**, which is less strained than the *para*-dithiacyclophane **2.92**. The yield of this sodium sulfide coupling falls more in line with the other examples from the Bodwell group. The dithiacyclophane **2.97** was taken through the same series of transformations as the previous example to afford cyclophanediene **2.98** in 61% yield over four steps from **2.97**. This was cleanly converted into [2]metacyclo[2](2,7)pyrenophane (**2.95**) by treatment with DDQ at room temperature in an impressive yield of 97%.



Scheme 2.24 Bodwell's synthesis of [2]metacyclo[2](2,7)pyrenophane (**2.95**).

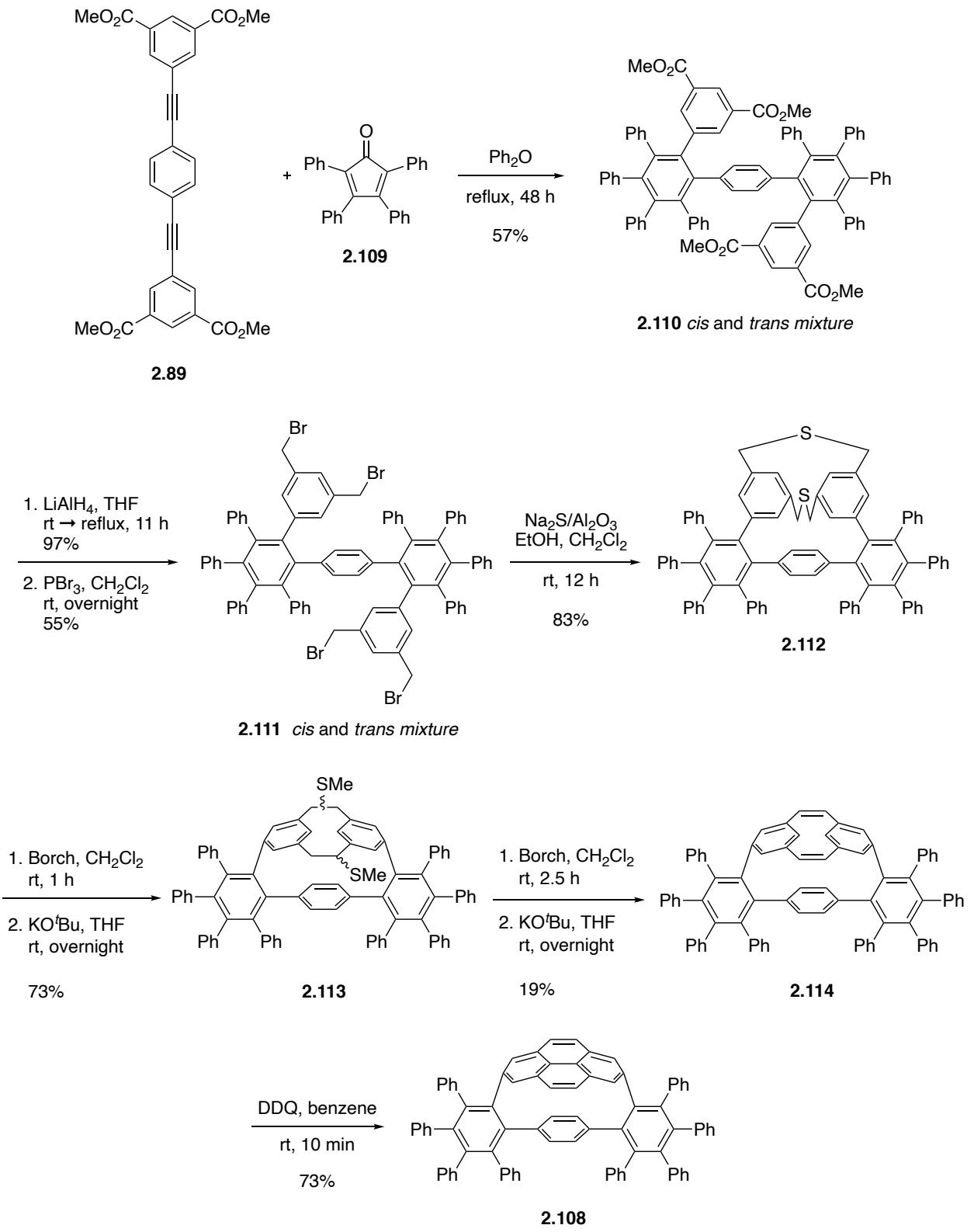
In the following years, other (2,7)pyrenophanes with aromatic systems were synthesized in the Bodwell group.[26] Dibenzo[2]paracyclo[2](2,7)pyrenophane (**2.107**),

which utilizes a terphenyl bridge, was the first to have a skeleton composed entirely of sp^2-C atoms (**Scheme 2.25**). Putting together the carbon skeleton of the product relied heavily on Suzuki-Miyaura cross-coupling chemistry. 1-Bromo-2-iodobenzene (**2.99**) was coupled chemoselectively with (3,5-dimethylphenyl)boronic acid (**2.100**) to produce functionalized biphenyl **2.101**. The biphenyl system was then subjected to Suzuki-Miyaura coupling with 1,4-phenylenebis(boronic acid) (**2.102**), which only gave the terphenyl system **2.103** in 24% yield along with numerous other compounds that were not identified. The benzylic positions were brominated with NBS under visible light irradiation to give a mixture of products, *ca*. 70% of which was estimated to be the desired tetrabromide **2.104** by ^{1}H NMR analysis. The crude product was carried forward as all attempts to purify the product failed. This system was then converted in dithiacyclophanes **2.105** using Na_2S/Al_2O_3 and the crude product of this reaction was also carried through without any purification. Crude dithiacyclophane **2.105** was subjected to the previously discussed 4-step protocol to afford cyclophanediene **2.106** in 6% overall yield from terphenyl **2.103**, which contained a small amount of the target pyrenophane **2.107**. This mixture was then treated with DDQ at room temperature to give pyrenophane **2.107**.



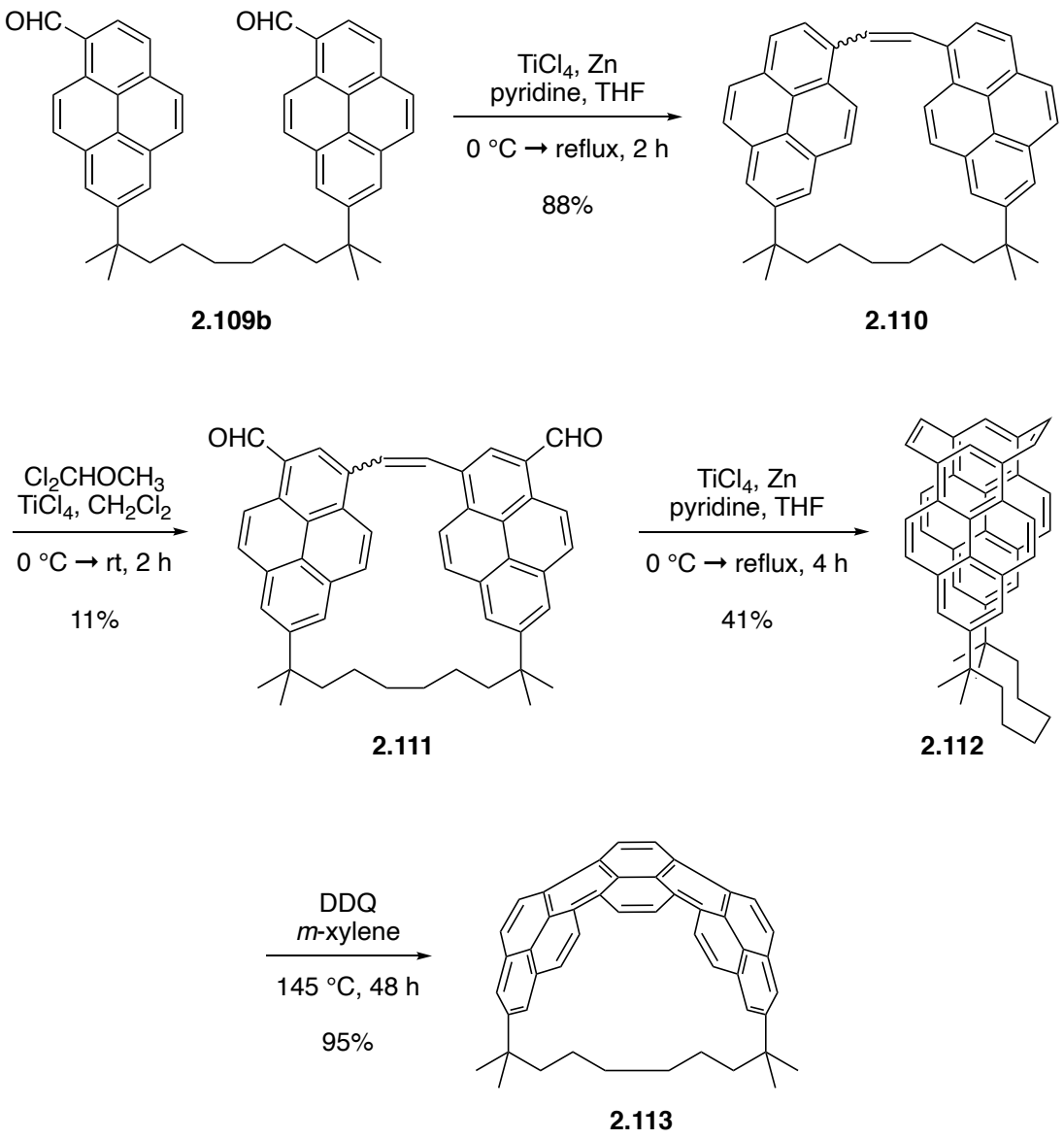
Scheme 2.25 Bodwell's synthesis of all-aromatic bridged pyrenophane **2.107**.

The low overall yield (0.8%) of pyrenophane **2.107** led to a shift in target molecule for study into the properties of these types of systems. An octaphenyl derivative **2.108** was synthesized from the synthetic intermediate **2.89** from the synthesis of [2]paracyclo[2](2,7)pyrenophane (**2.85**) (**Scheme 2.26**). Diyne **2.89** was subjected to Diels-Alder reaction conditions with tetraphenylcyclopentadienone (**2.109**) to give tetraester **2.110** (65%), which was found to exist as a slowly equilibrating mixture of *cis* and *trans* isomers. This tetraester was reduced with $LiAlH_4$ and then brominated with PBr_3 to give tetrabromide **2.111** in 55% yield. The sulfide coupling of **2.111** with Na_2S/Al_2O_3 gave an impressive yield of 83% (the highest yet with this reagent) of dithiacyclophanes **2.112**. Methylation and thia-Stevens rearrangement gave a mixture of thioethers **2.113** (73%), which was subsequently methylated again and eliminated to give cyclophanediene **2.114** in 19% yield. Diene **2.114** was cleanly converted to octaphenyl pyrenophane **2.108** in a 73% yield upon reaction with DDQ.



Scheme 2.26 Synthesis of octaphenylpyrenophane **2.108**.

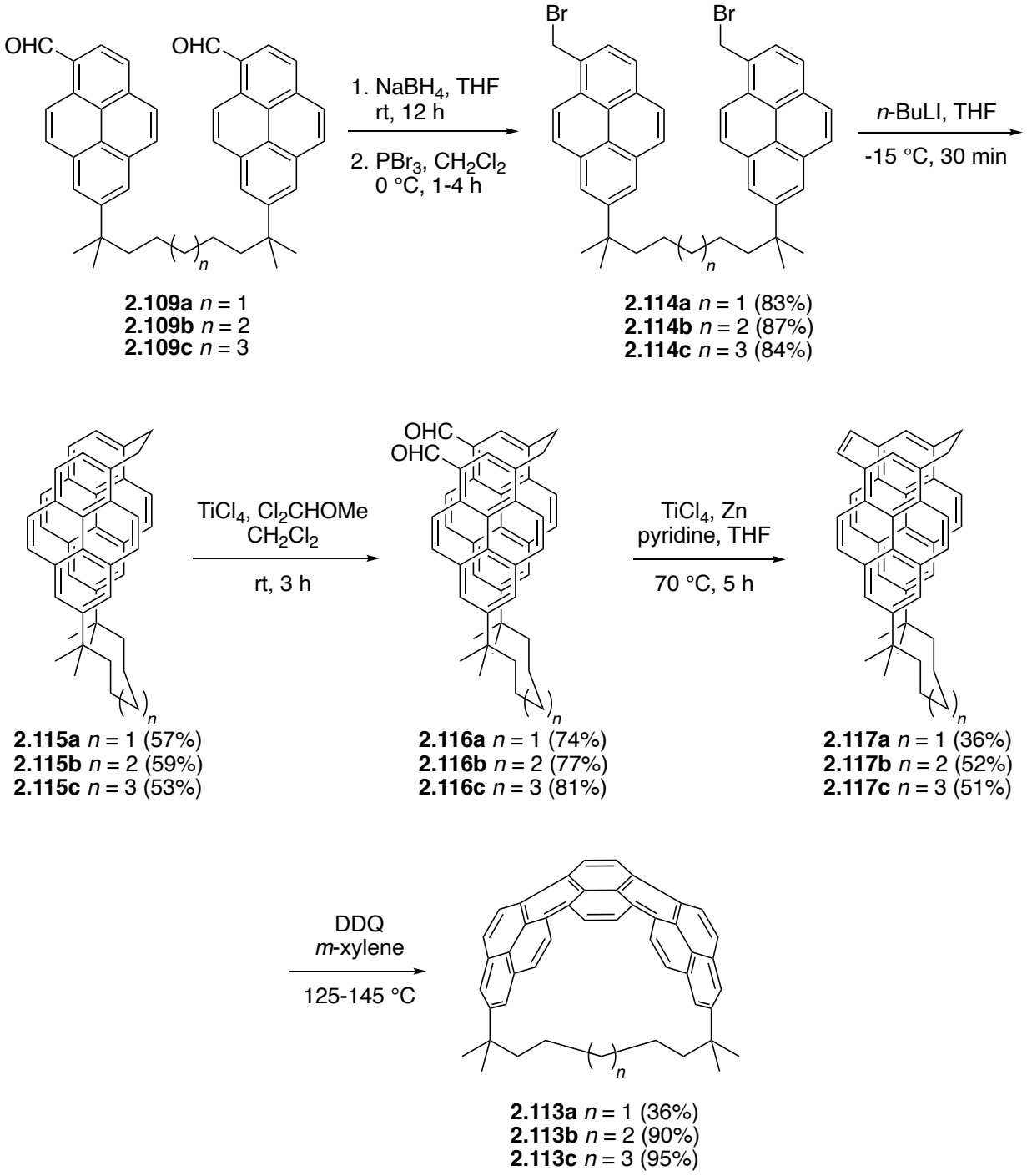
Later, the Bodwell group reported the synthesis of a new type of pyrenophane that served as a synthetic intermediate *en route* to a series of [*n*](2,11)teropyrenophanes. The first reported teropyrenophane synthesis involved an intramolecular McMurry coupling of pyrene aldehyde **2.109b** to give [8.2](7,1)pyrenophane-mono-ene **2.110** as an inseparable mixture of *E/Z* isomers.[27] This pyrenophane was the first example of a 1,7-bridged pyrenophane. This system was then formylated to give dialdehyde **2.111**, where the *E* and *Z* isomers were separable by column chromatography. (*Z*)-**2.111** was subsequently subjected to McMurry coupling conditions to give another new pyrenophane **2.112**, which was the first example of a triply bridged pyrenophane. This cyclophanediene (**2.112**), which contains the previously discussed cyclophanediene structural motif was converted in very high yield (95%) into 1,1,8,8-tetramethyl[8](2,11)teropyrenophane (**2.113**) upon reaction with DDQ in hot *m*-xylene.



Scheme 2.27 First synthesis of a teropyrenophane **2.113**.

The syntheses of the 7- and 9- atom bridged teropyrenophane system (not shown) were also reported in follow-up papers, which included a modified synthesis for the 8-atom bridged system.[28-30] The original double-McMurry route was unsuitable for the synthesis of the next higher homologue (9 atom bridge) as only the *trans*-configured olefin was formed in the first McMurry reaction. It was also reported to be unsuitable for

the next lower homologue because the second McMurry reaction failed (original report), but this obstacle was later overcome. To overcome this drawback, the dialdehydes **2.109a-c** were reduced to the corresponding diols and then converted to benzylic bromides **2.114a-c**, which were cyclized to pyrenophanes **2.113a-c** using Wurtz-type coupling with *n*-BuLi. These systems possess greater conformational flexibility than olefin **2.110** and can still be formylated efficiently under Rieche conditions to give dialdehydes **2.116a-c**. McMurry coupling then successfully afforded cyclophanemonoenes **2.117a-c**. It was unknown at the time whether the VID reaction with DDQ would be successful with the saturated nature of one bridge, however it turned out the unsaturated bridges are not necessary for dehydrogenation leading to the fully aromatized product teropyrenophanes **2.113a-c**. The teropyrene units in **2.113a-c** can be viewed as three pyrene substructures, in which the middle pyrene moiety showed the most severe bend, based on X-ray crystallographic analysis, in comparison to the two flanking moieties. In other words, the profile of the teropyrene system is semielliptical rather than semicircular. An interesting photophysical property of these system is the blue shift observed in the absorption spectra as the aromatic system becomes more bent. This contrasts what is observed for a benzene ring as it becomes more bent.



2.109a *n* = 1
2.109b *n* = 2
2.109c *n* = 3

2.114a *n* = 1 (83%)
2.114b *n* = 2 (87%)
2.114c *n* = 3 (84%)

2.115a *n* = 1 (57%)
2.115b *n* = 2 (59%)
2.115c *n* = 3 (53%)

2.116a *n* = 1 (74%)
2.116b *n* = 2 (77%)
2.116c *n* = 3 (81%)

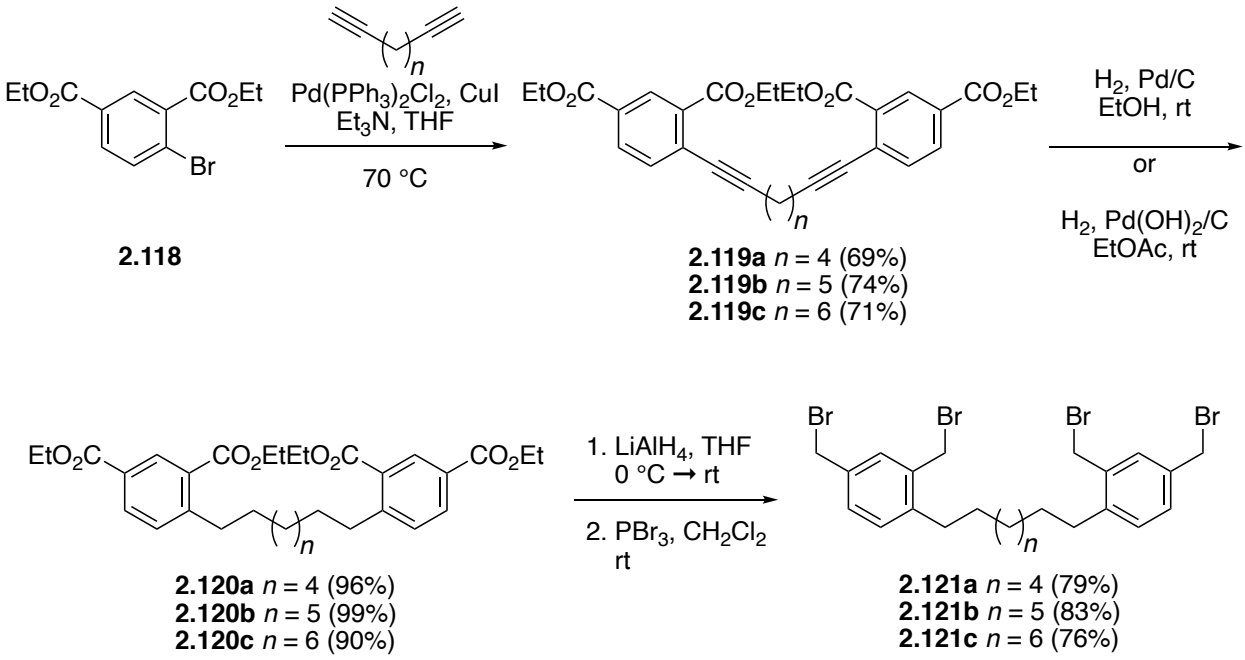
2.117a *n* = 1 (36%)
2.117b *n* = 2 (52%)
2.117c *n* = 3 (51%)

2.113a *n* = 1 (36%)
2.113b *n* = 2 (90%)
2.113c *n* = 3 (95%)

Scheme 2.28 Synthesis of a series of [n](2,11)teropyrenophanes **2.113a-c**.

The Bodwell group also synthesized a 1,6-bridged pyrenophane **2.124**, which due to the nature of the bridging motif is C_2-symmetric and therefore chiral.[31] Synthetically,

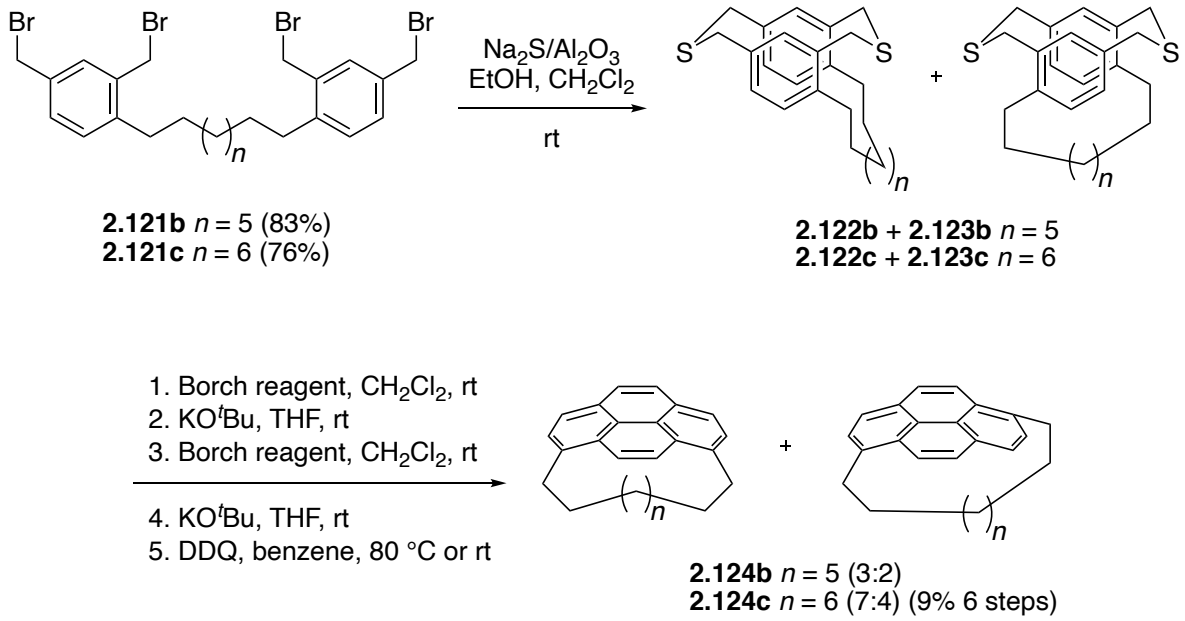
the strategy towards this pyrenophane was similar to that utilized in the synthesis of [*n*](2,7)pyrenophanes. Instead of using as 1,3,5-trisubstituted building block, which was used in the synthesis of [*n*](2,7)pyrenophanes, a 1,2,4-trisubstituted building block was employed to enable access to the appropriate pyrene substitution pattern. Diethyl 4-bromoisophthalate (**2.118**) was coupled with various diynes to give tetraesters **2.119a-c**, which were then hydrogenated using either Pd/C or Pd(OH)/C as the catalyst to give the fully saturated tether tetraesters **2.120a-c**. These tetratesters were then converted into tetrabromides **2.121a-c**.



Scheme 2.29 Synthesis of 1,3,4-substituted cyclophane precursors.

The standard formation of dithiacyclophanes by coupling with Na_2S/Al_2O_3 would be expected to give a mixture of two isomers because the approaching benzene rings have prochiral faces and can be coupled in either a face-to-face or face-to-back fashion. This would lead to a [*n*](1,8)- and [*n*](1,6)pyrenophanes, respectively. In practice, the sodium sulfide coupling of these systems gave very little to none of the either dithiacyclophane **2.122a** or **2.123a**. On the other hand, useable amounts **2.122b-c** and **2.122b-c** were obtained from the sodium sulfide coupling of tetrabromides **2.121b-c**. The

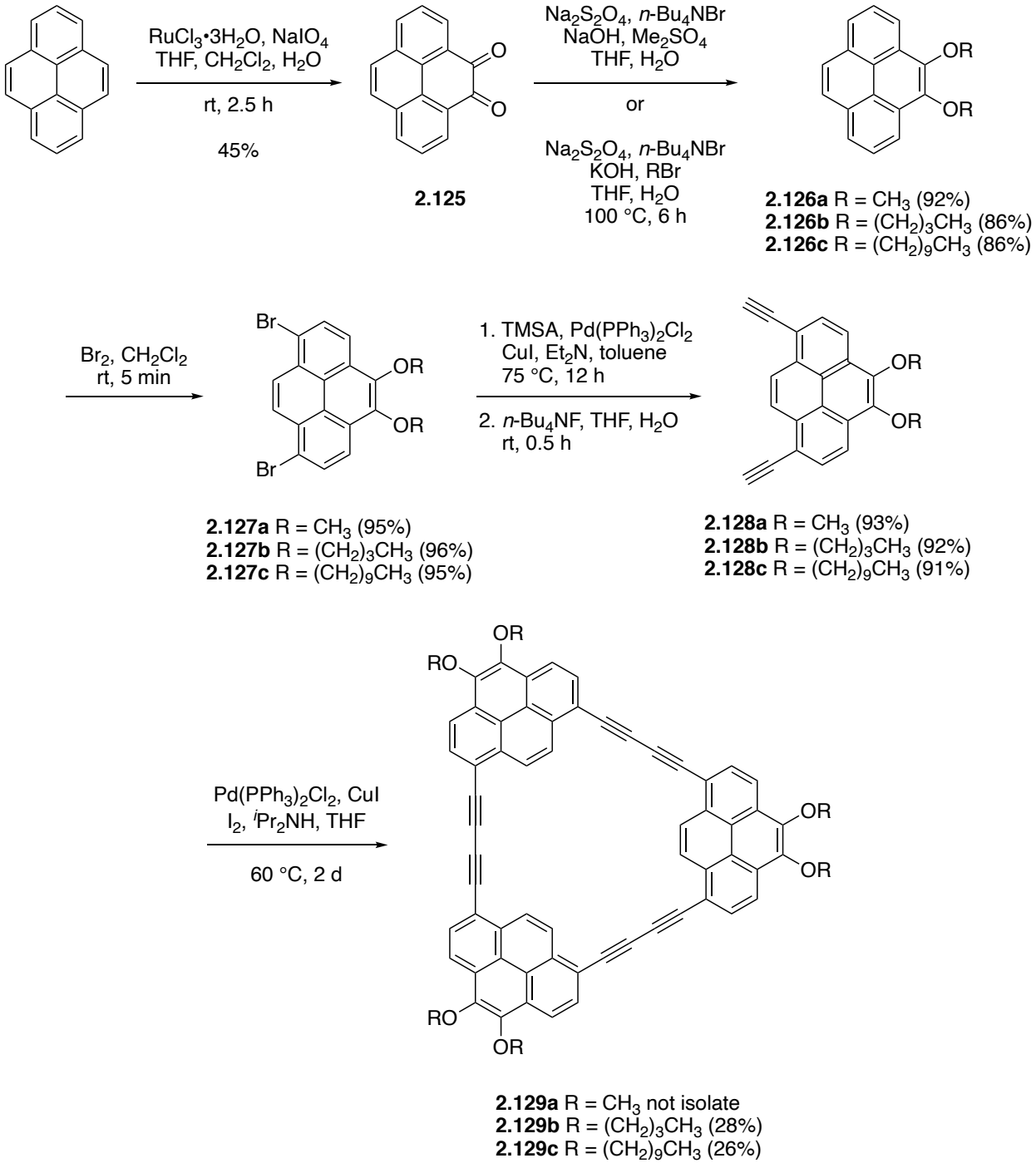
^{1}H NMR spectra of both mixtures suggested the presence of a *ca.* 3:1 mixture, but it could not be determined which isomer was the major product. The mixtures were carried through the familiar steps to give a mixture of [*n*](1,8)- and [*n*](1,6)pyrenophanes (**2.124b-c**).



Scheme 2.30 Synthesis of [*n*](1,6) and [*n*](1,8)pyrenophanes **2.124**.

A series of non-strained pyrenophanes, called pyrenylene-ethynylene macrocycles in the report, were created from a regioselective desymmetrization of pyrene that was developed in the Bodwell group.[32] Pyrene can be oxidized by treatment with $RuCl_3 \cdot 3H_2O$ and $NaIO_4$ at the 4,5-position to give pyrene-4,5-dione (**2.125**), The synthesis of which has been improved in the intervening years.[33] This diketone was then reductively alkylated with linear alkyl chains if various lengths to give 4,5-alkoxy pyrene **2.126a-b**. Installation of the alkoxy groups at these positions served two purposes. Firstly, they served as solubilizing groups in order to maintain the solution processability of all compounds. Secondly, these alkoxy groups, even methoxy, completely block any reaction occurring on that side of the pyrene system, as evidenced by bromination with Br_2, which produced dibrominated products **2.127a-b** in very high yields and with complete regioselectively.

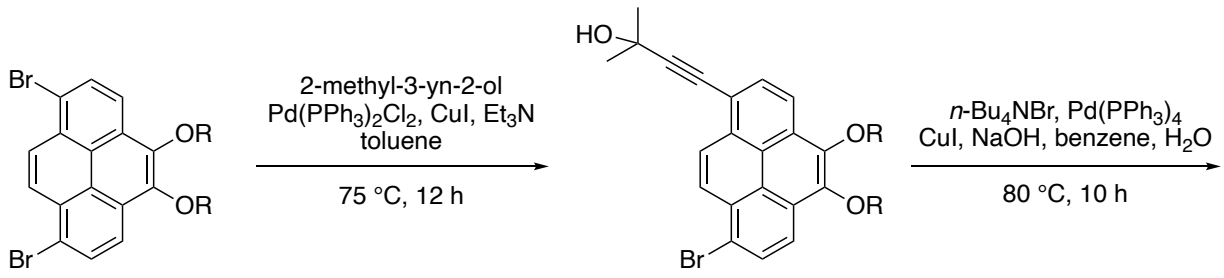
The presence of halides at the 1,8-positions of pyrene allow for the opportunity to build further on these systems using cross-coupling chemistry. A two-fold Sonogashira cross-coupling with trimethylsiliyl acetylene followed by deprotection gave dialkynes **2.128a-b**. These dialkynes were oxidatively homo-coupled to give cyclic trimers **2.129b-c**, although cyclic trimer **2.129a** could not be fished out of the reaction mixture. While many would describe these systems as macrocyclic in nature, they are also cyclophanes by definition. Most synthetic chemists would look at highly delocalized planar systems such as these and be wary of their solubilities, however, the alkoxy groups proved to be very effective, rendering these systems completely soluble in common organic solvents.



Scheme 2.31 Bodwell's synthesis of pyrene macrocycles **2.129a-c**.

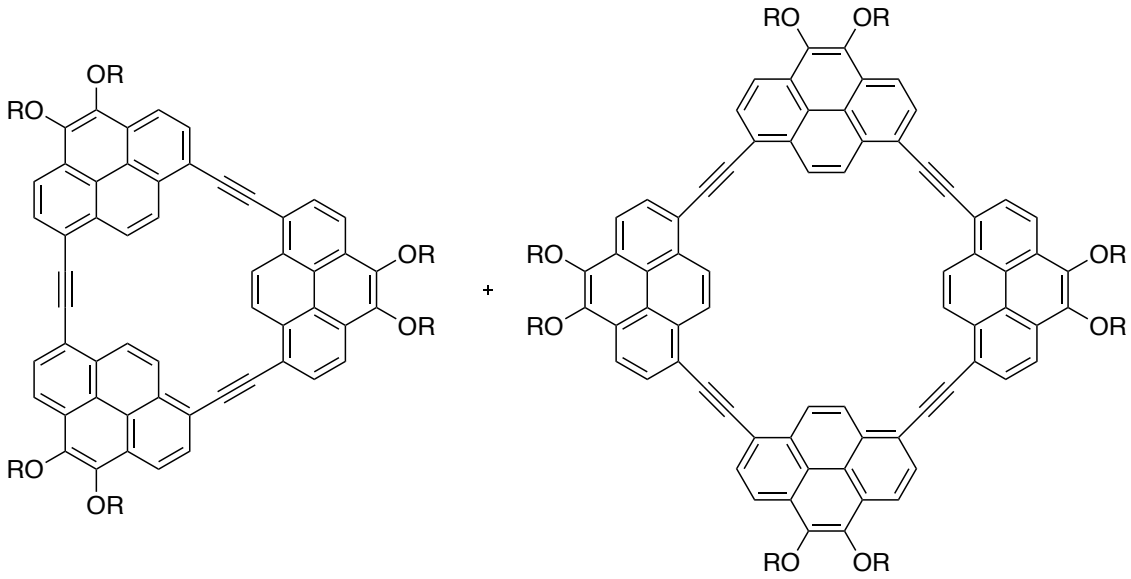
Systems with single ethynylene bridges could also be accessed starting from the common dibromides **2.137a-c** by Sonogahira cross-coupling with 1.1 eq of 2-methyl-3-

butyn-1-ol to give monoynes **2.140a-c**. *In situ* deprotection and Sonogashira cross-coupling provided two cyclophane products, which come from cyclic trimerization (22-23%) (**2.141b-c**) and tetramization (23-25%) (**2.142b-c**) modes. No product could be isolated from the methoxy systems, presumably due to low solubility. All of the isolated macrocycles (pyrenophanes) (**2.141b-c** and **2.142b-c**) were soluble in common organic solvents.



2.127a R = CH_3
2.127b R = $(CH_2)_3CH_3$
2.127c R = $(CH_2)_9CH_3$

2.130a R = CH_3 (66%)
2.130b R = $(CH_2)_3CH_3$ (68%)
2.130c R = $(CH_2)_9CH_3$ (65%)



2.131a R = CH_3 not isolated
2.131b R = $(CH_2)_3CH_3$ (23%)
2.131c R = $(CH_2)_9CH_3$ (22%)

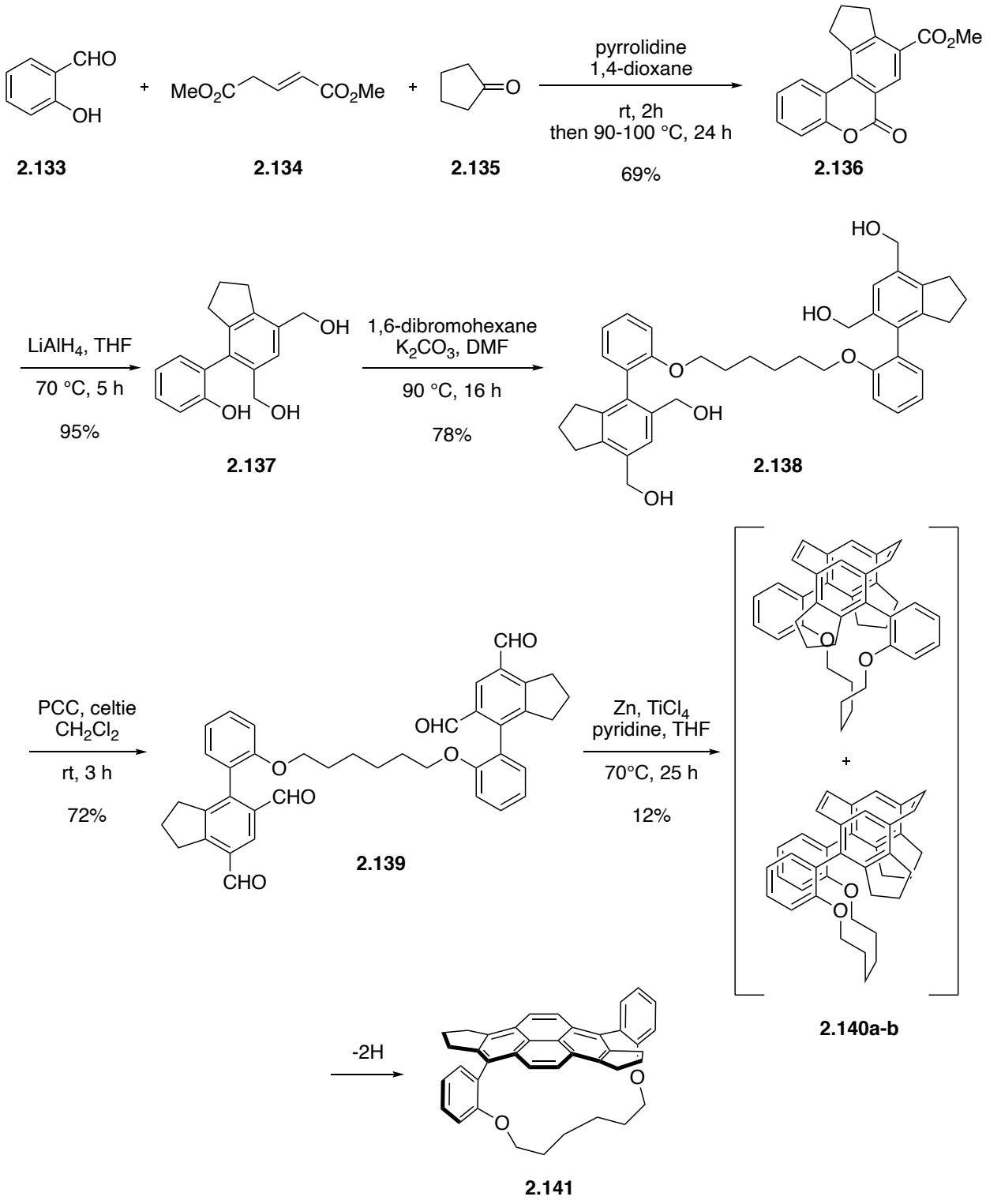
2.132a R = CH_3 not isolated
2.132b R = $(CH_2)_3CH_3$ (30%)
2.132c R = $(CH_2)_9CH_3$ (25%)

Scheme 2.32 Bodwell's synthesis of pyrene macrocycles **2.131b-c** and **2.132b-c**.

Closer inspection of the structural features of **2.129b-c**, **2.131b-c** and **2.132b-c** reveals that the π-electron count of **2.129b-c** correspond to Hückel aromatic electron counts whereas **2.131b-c** and **2.132b-c** correspond to Hückel antiaromatic electron counts. However, the ^{1}H NMR spectra of the decoxy macrocycles are inconsistent with the presence of macrocyclic ring current. The NMR data in addition to NICS calculations suggest that the pyrene moieties are essentially islands of aromaticity connected through ethynylenes with little to no macrocyclic delocalization.

A different chiral pyrenophane synthesis was reported by the Bodwell group, whereby a cyclophanediene **2.140** was created in one shot from a double-McMurry coupling of a tetraaldehyde system **2.141**.[34] The synthesis of this system was inspired by work in the Bodwell group on multicomponent reactions and inverse-electron demand Diels-Alder (IEDDA) reactions.[35-38] A multicomponent reaction between salicylaldehyde (**2.133**), dimethyl glutaconante (**2.134**) and cyclopentanone (**2.135**) gave coumarin **2.136**, which was reduced to triol **2.137** using $LiAlH_4$. Two triol units were tethered through the phenolic hydroxy groups via a Williamson ether synthesis with 1,6-dibromohexane to give tetraol **2.138**, which was oxidized up to tetraaldehyde **2.139** using PCC. McMurry coupling of this tetraaldehyde could, in theory, give rise to two isomeric cyclophanedienes (**2.140a-b**) resulting from either a face-to-face or face-to-back approach, but the only product isolated was a [12](1,6)pyrenophane **2.141** in 12% yield. Not only did two intramolecular McMurry reactions take place, but the resulting cyclophanediene **2.140a** underwent cyclodehydrogenation under reductive conditions. As with many other of the pyrenophanes reported by the Bodwell group, the bridge protons were observed at anomalously high field (δ = 0.36, 0.14, –0.39, –0.51 ppm) because they lie across the face of the pyrene system, *i.e.* in its shielding zone. This is a rare example, along with the synthesis of teropyrenophanes, of the McMurry reaction being utilized in the synthesis of [2.2]metacyclophane systems and the first one that was used to from both bridges at once. Due to the substitution pattern of pyrenophane **2.141,** it is formed as a mixture of enantiomers, which were successfully separated by preparative chiral phase HPLC

(Chiralpak OD-H column: 40% EtOH(0.1% diethylamine)/O_2, 100 bar) to give approximately 10 mg samples of (+)-**2.141** (>99% *ee*) and (-)-**2.141** (>99% *ee*), which gave nearly identical mirror image CD spectra. This is the first, and currently only, chiral pyrenophane synthesized by the Bodwell group to be separated into enatiomerically pure samples.

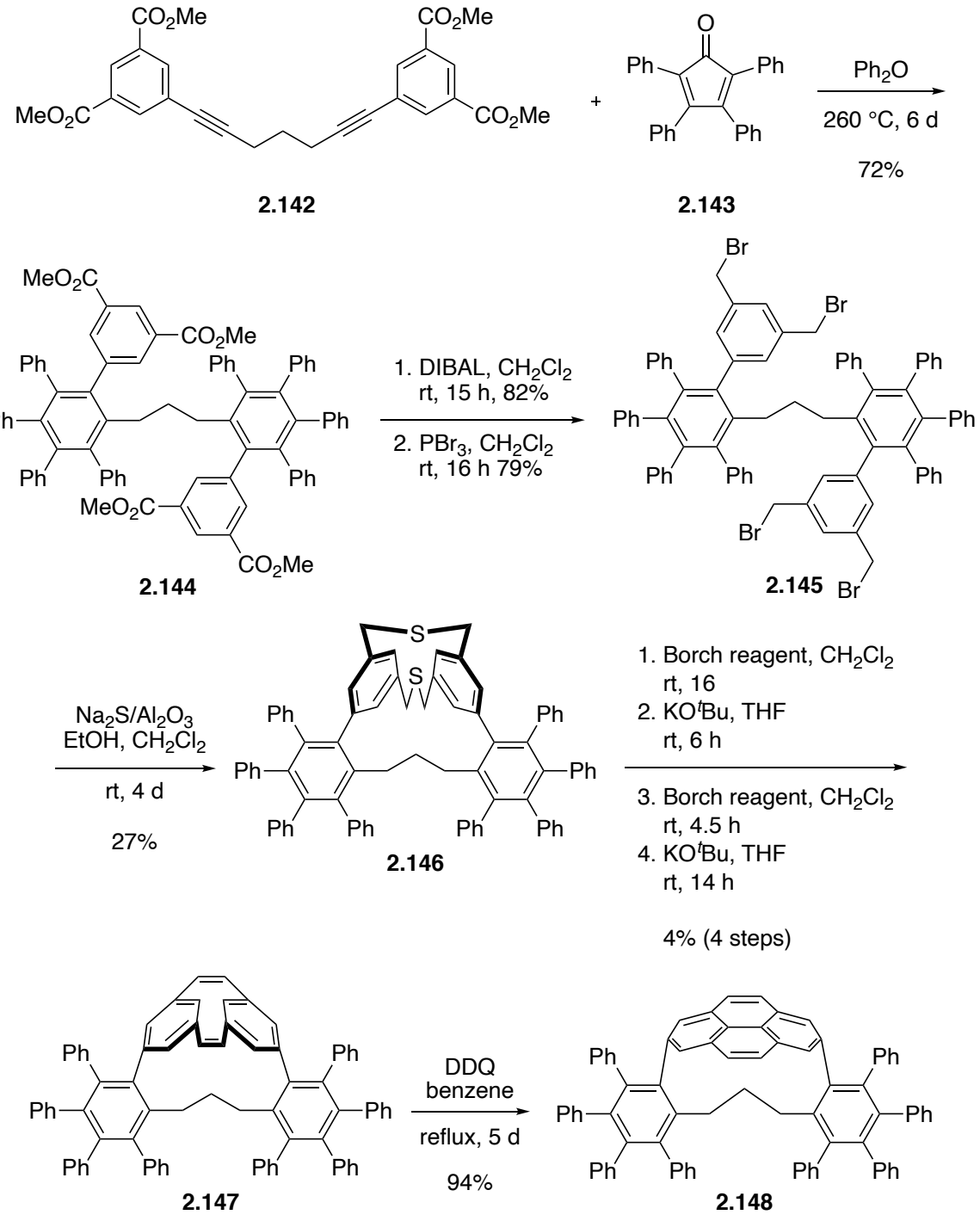


Scheme 2.33 Synthesis of C_2-symmetric pyrenophane **2.151** by double McMurry coupling.

The majority of the pyrenophanes already described in this thesis so far were covered in a 2015 review article by Ghods Ghasemabadi, Yao and Bodwell.[39] In the intervening years, more pyrenophanes have appeared in the literature and these will be briefly discussed below.

The last [*n*](2,7)pyrenophane system to be reported from the Bodwell group borrows structural elements from the methylene-bridged and octaphenyl pyrenophanes **2.208a-d** and **2.108**, respectively. The goal of this work was to set a new record holder for highest degree of end-to-end bend (θ) of the pyrene system.[40] The calculated bend angle for pyreneophane **2.148** (AM1) is 116.2°, which is nearly 3° greater than the calculated bend for the previous record holder 1,7-dioxa[7](2,7)pyrenophane (**2.67**) (113.3°). The synthesis began with the Diels-Alder reaction of diyne **2.142** cyclopentadienone **2.143** to give tetraester **2.144**. Reduction of the ester groups with DIBAL and bromination of the resulting tetraol with PBr_3 gave the tetrabrominated product **2.145**, which was slated for the classic dithiacyclophane-based approach to the formation of the pyrene system. The reaction of **2.145** with Na_2S/Al_2O_3 proceeded in relatively low yield (27%) to afford **2.146,** most likely due to steric constraints provided by the external phenyl rings. The standard four-step ring contraction/elimination procedure provided cyclophanediene **2.147** in 4% overall yield from the dithiacyclophane **2.146**. The VID reaction for the transformation of cyclophanediene **2.147** to pyrenophane **2.148** proved to be non-trivial, however, this was not unsurprising since the intended product contained the most bent pyrene to date. The VID did proceed efficiently, but over a period of 5 days in refluxing benzene to give a 94% yield of the desired pyrenophane **2.148**. This impressive yield and stability of the highly-strained product throughout isolation and purification suggested that the bulky phenyl groups (especially those closest to the pyrene system) provided a substantial amount of kinetic stabilization. Unfortunately, no single crystal suitable for X-ray crystallographic analysis could be grown. The calculated (B3LYP/6-31G(d)) bend angle (θ) using the gas-phase structure was 107.6°, which is 1.6° less than that for the experimentally determined record holder

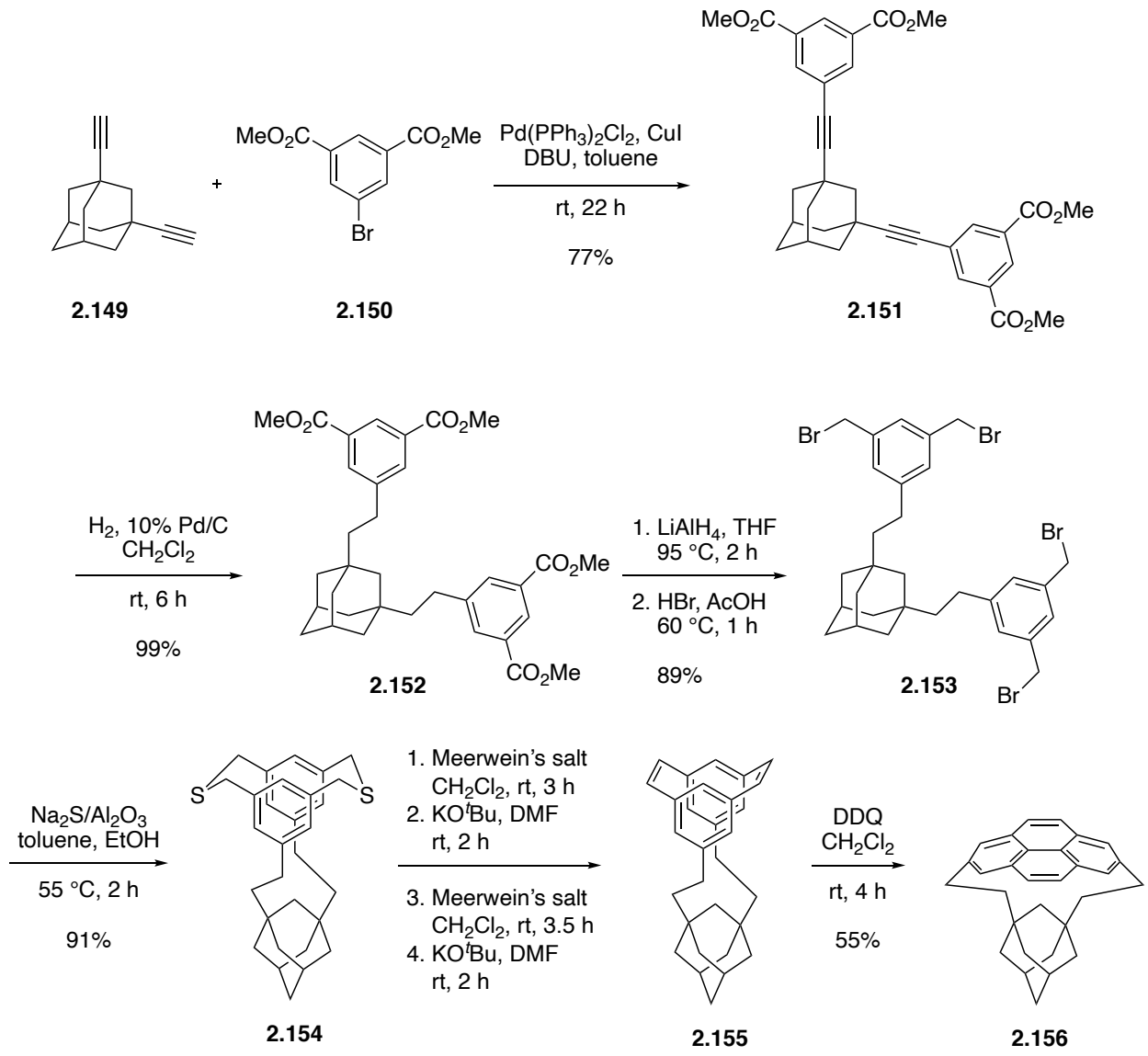
(109.2°) so the question as to whether a new record holder had been synthesized was left unanswered. A follow-up to this paper followed the same synthetic route to create the same pyrenophane systems with longer methylene bridges of 3-6 carbon atoms.[41] Also in this report was work aimed at synthesizing a system with a 2 carbon atom methyl bridge whose calculated (DFT) bend angle (θ) was 130.4°. Heating the corresponding cyclophanediene in the presence of DDQ for four weeks provided evidence for the formation of the pyrenophane by TLC analysis. Analytical HPLC analysis followed by mass spectrometry on the isolated fractions showed the presence of peaks that correspond to the desired product in addition to a Diels-Alder adduct between DDQ and the pyrenophane. Unfortunately, further attempts to isolate pure pyrenophane proved unfruitful.



Scheme 2.34 Kinetically stabilized highly bent pyrenophane **2.148**.

The newest (2,7)pyrenophane reported in the literature was reported by Schreiner *et al.*, in which a portion of the bridge contained an adamantane unit (**2.156**).[42]

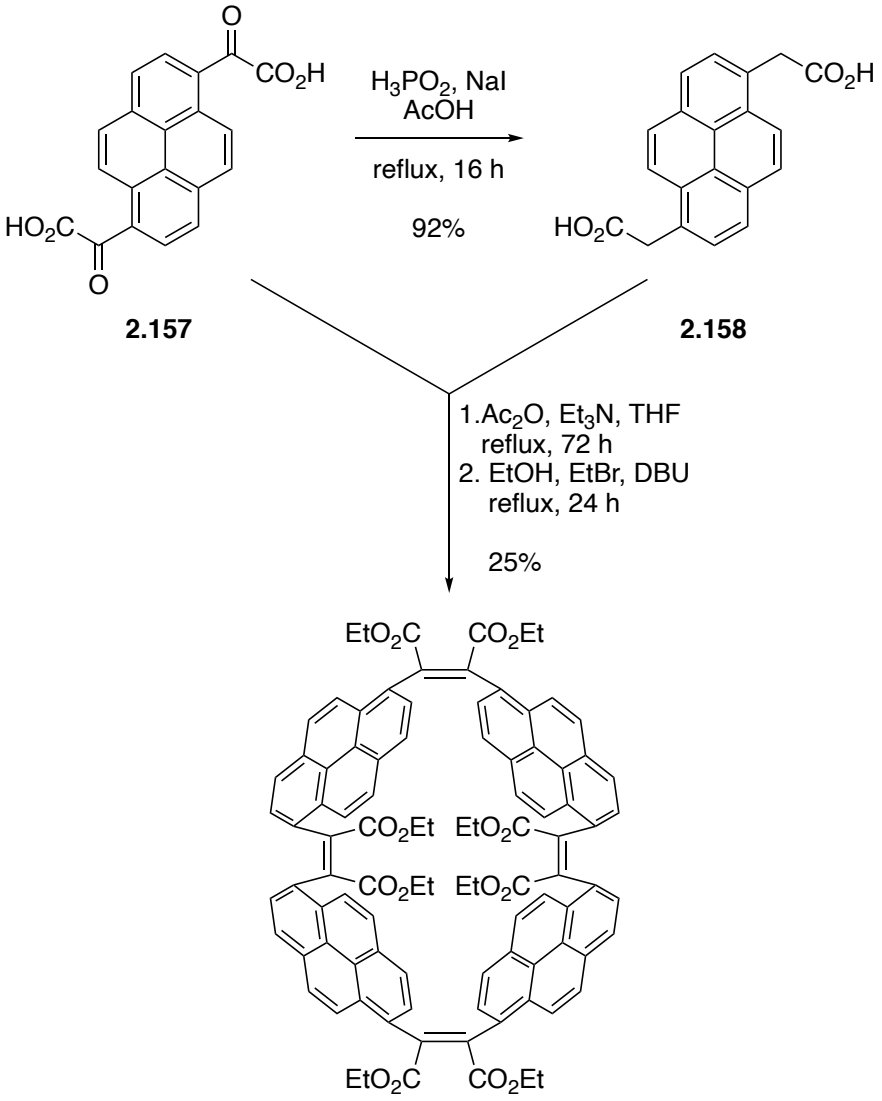
Adamantane is the simplest diamondoid system that retains many of the electrochemical properties of larger diamondoid structures, such as its ability to act as an electron emitter. An advantage of using smaller diamondoids as opposed to large diamond structure is reproducibility of the compounds one makes in addition to their ability to be selectively functionalized. For example, adamantane can be selectively functionalized at the 1,3 positions, which are taken advantage of in this synthesis. The synthesis started with 1,3-diethynyladamantane (**2.149**), which was coupled under Sonogashira conditions with dimethyl 5-bromoisophthalate (**2.150**) to give tetraester **2.151**. This compound already has all of the carbon atoms required for the synthesis of the final product. The alkynes were hydrogenated to give a fully saturated adamantane-containing tether **2.152**. The steps from here are consistent with those already discussed for the synthesis of (2,7)pyrenophanes. Tetraester **2.152** was reduced and brominated to give **2.153**. Dithiacyclophane formation to give **2.154** proceeded in an impressive 91% yield. Modifications to the standard conditions included the use of a higher proportion of EtOH (7:3 instead of 1:9) and the use of toluene in lieu of CH_2Cl_2. This system was then subjected to *S*-methylation, thia-Stevens rearrangement, *S*-methylation and Hofmann elimination to afford diithiacyclophane **2.155**. In this instance, Meerwein's salt was employed instead of the Borch reagent because it was found to give higher yields. The VID reaction proceeded nicely at room temperature in CH_2Cl_2 with DDQ to give [2](1,3)adamantano[2](2,7)pyrenophane (**2.156**) in 25% total yield over 10 steps. The X-ray crystal structure allowed the bend angle (θ) of the pyrene unit to be determined (104.3°). As expected, the methylene protons from the dithiacyclophane group pointing up towards pyrene system are significantly shielded and appear as a broad signal (δ = –2.09 ppm). The authors also computed (M06-2X/cc-pVDZ) the dipole moment to be 2.3 D, which they noted is rather large, even for a dipolar hydrocarbon (*cf.* azulene, μ = 1.2 D).[43] The charge separation was computed to be 0.9 *e*, which means that the dithiacyclophane system bears a partial charge of *ca.* +0.45 *e* and the pyrene system bears a partial charge of *ca.* –0.45 *e*. This property implies that **2.156** may be a good candidate to be a molecular rectifier (a one-way conductor).



Scheme 2.35 Synthesis of adamantyl-pyrenophane **2.156**.

A recent report on the synthesis of a new (1,6)pyrenophane used a new glyoxylic Perkin condensation strategy by reacting a 1,6-substituted pyrene diglyoxylic acid **2.157** and 1,6-subsituted pyrenylenediacetic acid **2.158**.[44] The diglyoxylic acid **2.167** was accessed by lithium-halogen exchange of 1,6-dibromopyrene and quenching of the

resulting dianion with diethyl oxalate. A portion of the product was then reduced upon treatment with H_3PO_2 and NaI to afford pyrenylenediacetic acid **2.158**. These two compounds were then subjected to Perkin condensation conditions (Ac_2O, Et_3N, THF, reflux, 3 d) to presumably give an octaacid, which was esterified directly to give (1,6)pyrenophane **2.159** in 25% yield along with unidentified linear oligomers. The X-ray crystal structure revealed that the pyrene units are only slightly bent. The ^1H NMR spectrum of pyrenophane **2.159** was simple and sharp which indicated that the pyrenophane is either conformationally stable at the temperature at which the spectrum was measured, or that any conformational processes are very fast. The absorption spectrum of **2.159** was similar to that of a linear oligomer, the longest wavelength maximum of pyrenophane **2.159** (363 nm) was only slightly bathochromically shifted from that of the linear oligomer (347 nm). This suggested that the individual pyrene units do not communicate electronically to any appreciable amount.



Scheme 2.36 Formation of pyrenophane **2.159** by Perkin condensation.

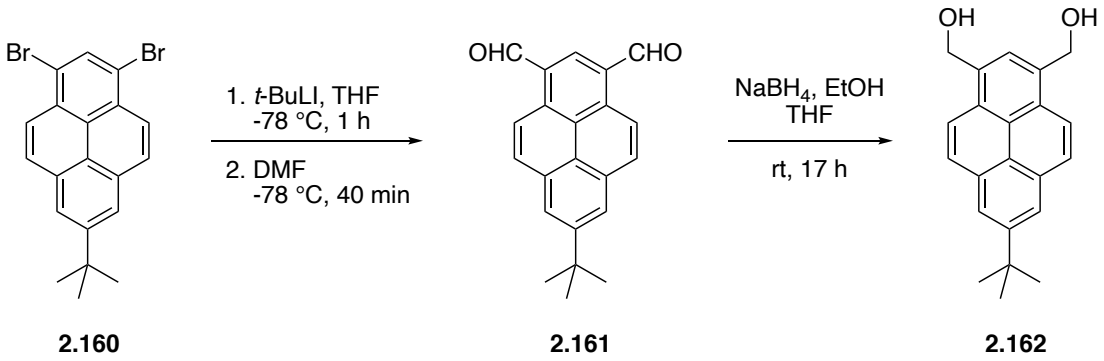
In 2017, Maeda *et al.* reported the synthesis and properties of [3.3](1,3)pyrenophanes **2.165**, **2.166**, and **2.167**, which contain oxygen, sulfur and selenium atoms in the bridges (**Scheme 2.37**).[45] The goal of this work was to investigate the conformational behaviour between the *syn* and *anti*-conformers. The syntheses all began from 1,3-dibromo-7-*tert*-butylpyrene (**2.160**), which was doubly formylated by sequential lithiation and quenching with DMF to give 2-*tert*-butyl-6,8-diformylpyrene (**2.161**). This system was reduced with $NaBH_4$ to give diol **2.162**, which could be

brominated to give dibromide **2.163**. Dithiacyclophane **2.166** was synthesized by coupling dibromide **2.163** in the presence of Na_2S/Al_2O_3 in 14% yield. The oxygen-containing pyrenophane **2.165** was prepared by Williamson ether synthesis between diol **2.162** and dibromide **2.163** in 5% yield. In order the synthesize the selenium-linked pyrenophane **2.167**, dibromide **2.163** was converted into bis(selenocyanate) **2.164**, which was then treated with dibromide **2.163** under reducing conditions ($NaBH_4$) to give **2.167**. The UV/Vis absorbance spectra of **2.165** and **2.166** both showed broad absorption bands at relatively long wavelengths (400-430 nm), which have previously been attributed to ^1L_b and ^1L_a transitions that arise from two stacked pyrene rings. This provided some evidence for the presence of *syn*-conformers in solution. In the fluorescence spectra of **2.165** and **2.166**, increasing the polarity of the solvent (toluene $\rightarrow$ CH_2Cl_2 $\rightarrow$ DMF) resulted in a decrease in the intensity of the monomer emission (401 nm) with a concomitant increase in intramolecular excimer emission (497-500 nm). This effect was also observed for **2.167**, but it was less pronounced. An explanation for a shift in the equilibrium towards the *syn*-conformation is more polar solvent involves the difference in polarity between the conformers. The *anti*-conformations expected to be less polar and therefore favoured less in polar solvents.

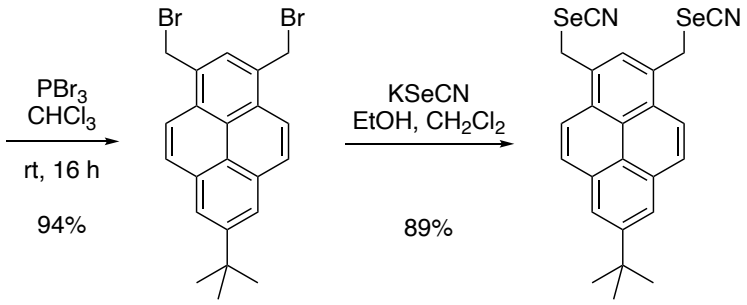
Additionally, excitation at longer wavelength (360-370 nm) led to the observation of more intense monomer emission, whereas excitation at shorter wavelengths (340-350 nm) led to enhancement of the excimer emission. The authors explain this phenomenon by commenting that the *syn*-conformer (which would be expected to exhibit excimer emission) absorbs more strongly at the shorter wavelength.

The ^1H NMR spectra of all three pyrenophanes **2.165**, **2.166**, and **2.167** display only 3 singlets and 2 doublets, which indicates that the *syn/anti* flip is occurring rapidly on the NMR time scale. A ^1H VT-NMR (in $CDCl_3$) studied revealed that the doublets began to broaden at lower temperatures. The coalescence temperature of **2.165** was measured to be –50 °C, that of **2.166** was –30 °C and **2.167** had not yet reached coalescence at –60

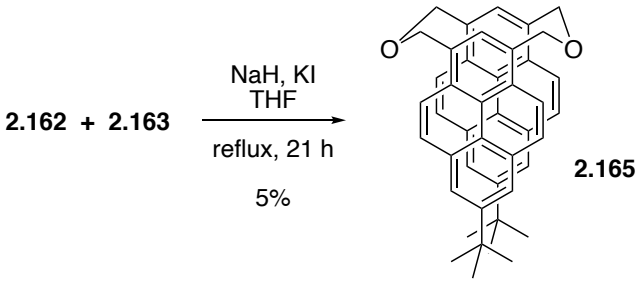
°C. The trend in coalescence temperature follows the length of the C–chalcogen bond. An increase in the effective length of the bridge means that the internal protons (H_i) can more easily pass through the middle of the macrocyclic ring of the cyclophane during a conformational flip.



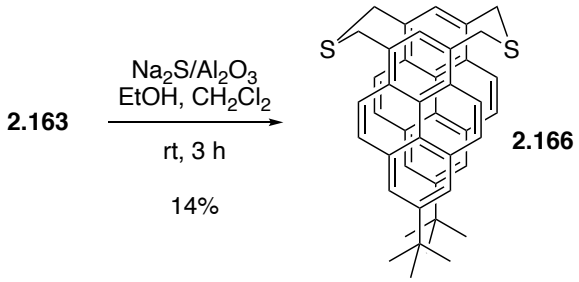
2.160 **2.161** **2.162**



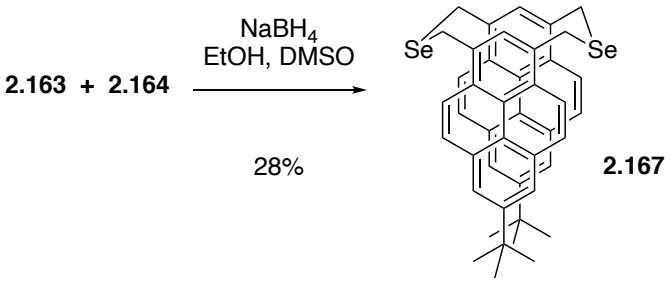
2.163 **2.164**



2.165



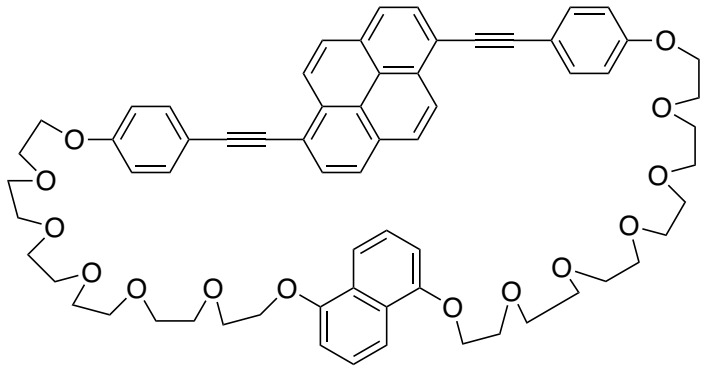
2.166



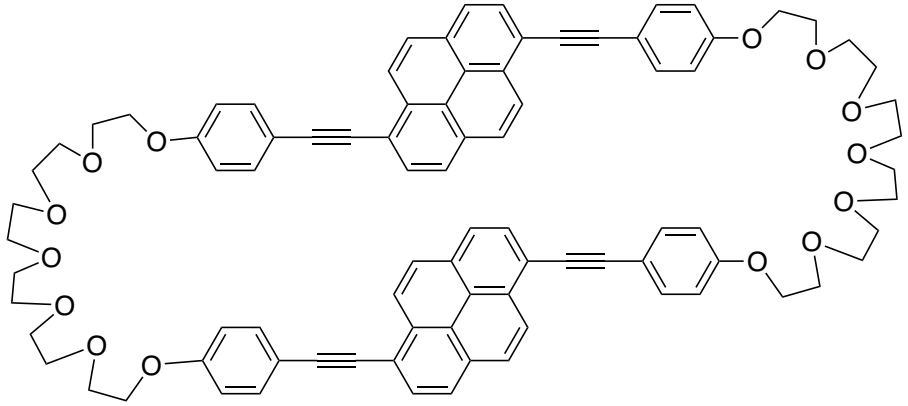
2.167

Scheme 2.37 Maeda's synthesis of (1,3)pyrenophanes **2.165**, **2.166**, and **2.157**.

In 2017, Tamaoki and Sagara synthesized a set of photoluminescent pyrenophanes (**2.169** and **2.170**) displaying mechanoresponsive luminescence.[46] Theses pyrenophanes were designed to include 1,6-bis(phenylethynyl)pyrene groups to act as luminophores and oligo(ethylene glycol) bridges to give these systems nematic liquid-crystalline phases. Pyrenophane **2.168** was found to exhibit a broad nematic liquid crystal phase (at 106.9 °C) with green photoluminescence, which could be maintained or converted to a blue-emitting form depending on the mode of cooling (rapid versus slow, respectively). The phase-change dynamics were studied in detail by polarized optical microscopy and differential scanning calorimetry. Mechanical stimulation of the blue-emissive form of **2.168** at 25 °C caused the colour of emission to change to green and, upon cessation of mechanical stimulation, the system returned to its blue-emissive state. The green-emissive state was determined to be a kinetically trapped metastable nematic phase. Pyrenophane **2.169** also exhibited a phase transition to a nematic liquid-crystallize phase at 227 °C. Unlike **2.168**, super-cooling of this phase does not maintain any of the LC-phase properties. When solid-state pyrenophane **2.169** (sky-blue emission) is mechanically stimulated, the colour of emission changes to green-yellow, which reverts back to blue emission upon cessation of mechanical stimulation. The authors determined that in this case the change in emission is a result of excimer formation in the condensed states upon grinding.



2.168

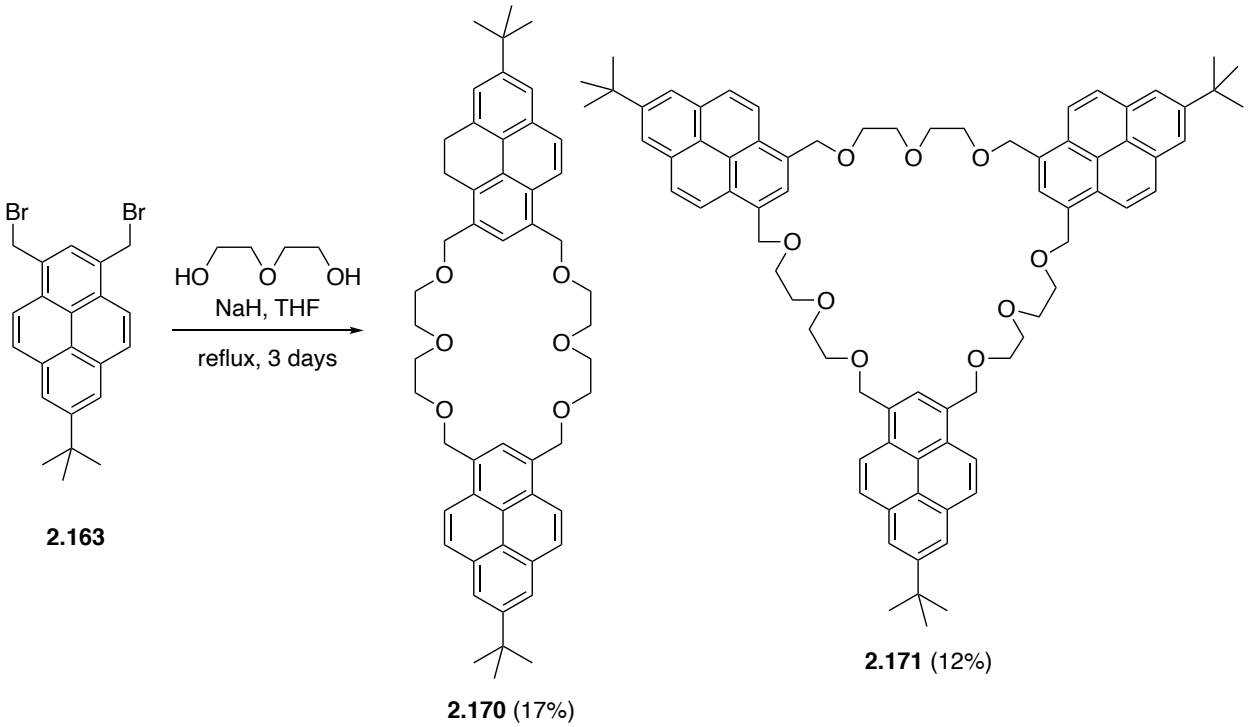


2.169

Scheme 2.38 Sagara's synthesis of photoluminescent pyrenophanes **2.168** and **2.169**.

Two of the most recent pyrenophane publications are further contributions from the Maeda group. Utilizing dibromide **2.163** as a starting material, the authors aimed to create cyclophanes with crown ether bridges for use as cationic sensors.[47] When dibromide **2.163** was treated with diethylene glycol under basic conditions, two pyrenophanes, **2.170** (17%) and **2.171** (12%) were formed (**Scheme 2.39**). Treatment of dibromide **2.163** with triethylene glycol gave pyrenophanes **2.172** (37%) and **2.173** (9%), and treatment with tetraethylene glycol gave pyrenophanes **2.174** (28%) and **2.175** (4%). The absorbtion spectra of the pyrenophanes were nearly identical, except that the molar

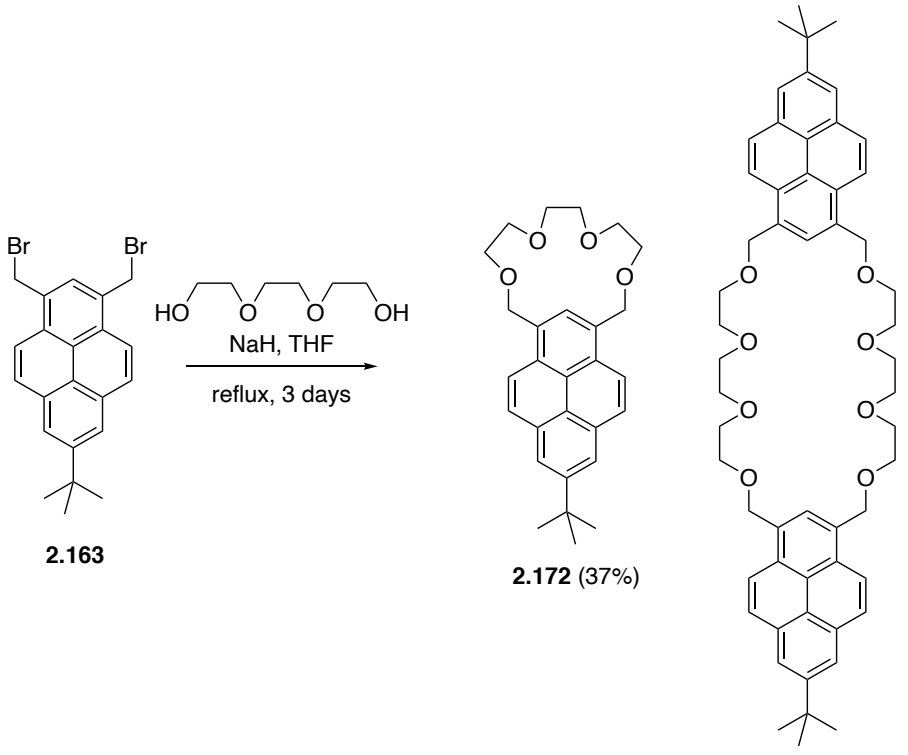
extinction coefficients increased with the number of pyrene units present. In contrast, there were stark differences in the fluorescence spectra of the pyrenophanes depending on the number of pyrene units present. Pyrenophanes **2.172** and **2.173**, which have only 1 pyrene unit display monomer emission bands (380-410 nm), whereas, **2.170**, **2.171**, **2.173** and **2.175**, which have multiple pyrene units, displayed intense intramolecular excimer emission bands (*ca.* 470 nm) with only weak bands in the area of monomer emission.



2.163

2.170 (17%)

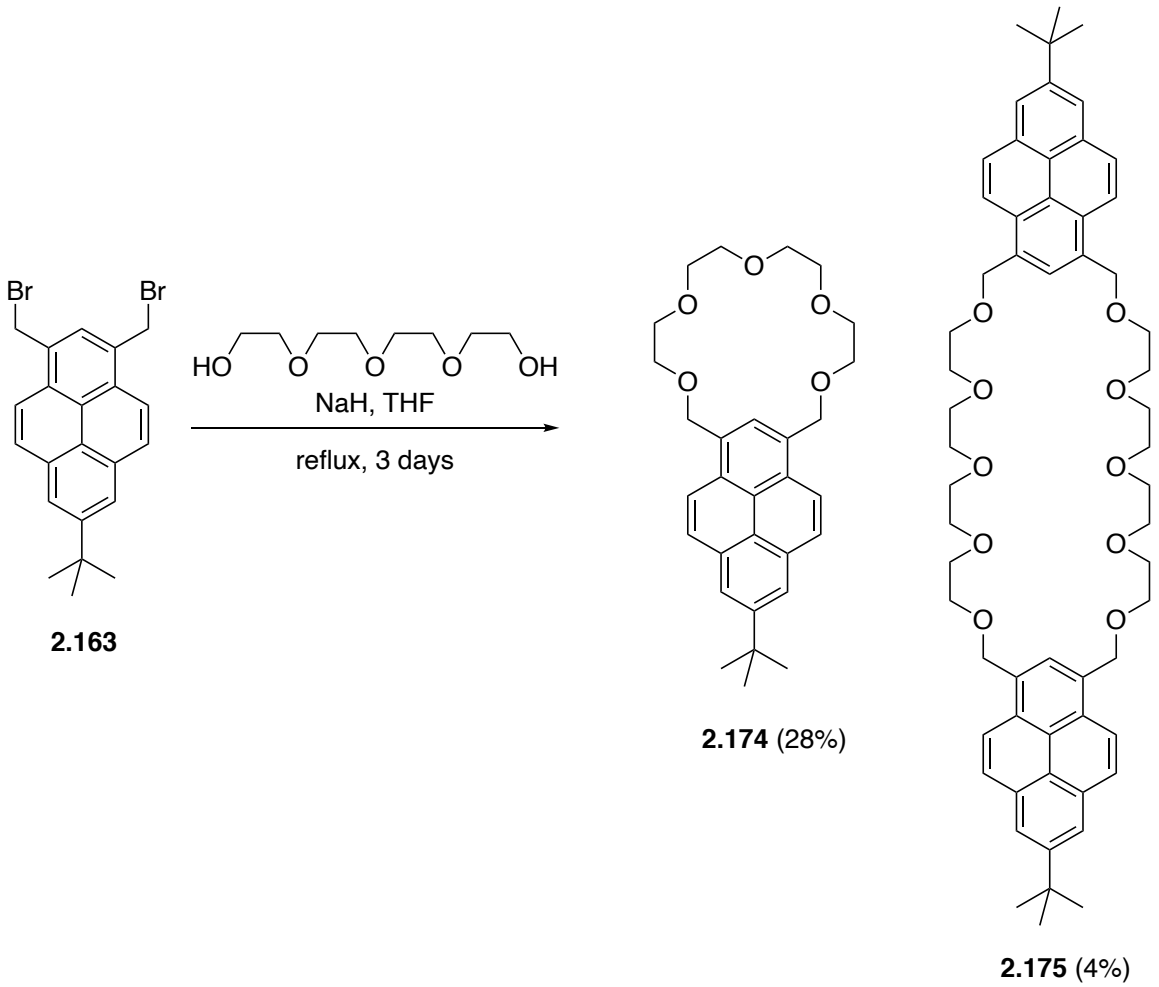
2.171 (12%)



2.163

2.172 (37%)

2.173 (9%)



2.163

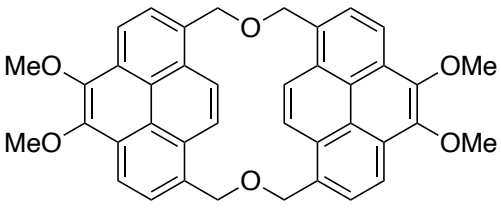
2.174 (28%)

2.175 (4%)

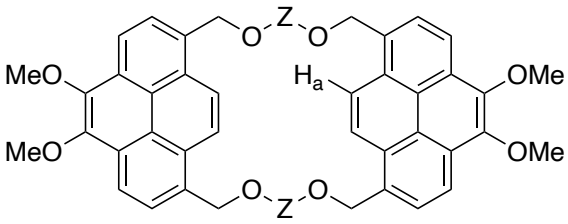
Scheme 2.39 Maeda's synthesis of (1,3)pyrenophanes.

The other most recent contribution from Maeda *et al.* utilizes chemistry developed in the Bodwell group (see **Scheme 2.31**), which allows for complete regiochemical control of pyrene functionalization. The (1,8)pyrenophanes synthesized **2.176**, **2.177a-f** and a pyrenophane by-product **2.178** were synthesized in an effort to create novel fluorescence switching sensors (**Scheme 2.40**).[48] Pyrenophane **2.176** only displayed monomer emission, which suggests that a *syn* conformation in which the two pyrene units adopt a face-to-face orientation is not easily accessible. Only monomer emission was observed for pyrenophanes **2.177a-d** as well. The emission spectra for pyrenophanes **2.177e-f** displayed both monomer and intramolecular excimer emission.

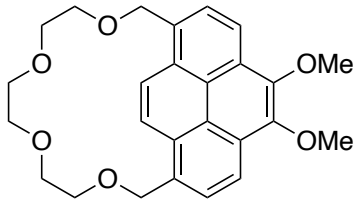
The ratios of excimer/monomer emission increased with increasing solvent polarity. Interestingly, **2.177d** and **2.177e** both have the same number of atoms in their respective bridges, but one shows excimer emission (**2.177e**) while the other (**2.177d**) does not. The authors rationalize this experimental observation by mentioning that the largely methylene bridged system **2.177d** should favour an all-*anti* conformation whereas the ethylene glycol bridged system **2.177e** would prefer to exist in an all-*gauche* conformation. The dynamic behaviour of the conformations of **2.177e-f** were investigated by measuring the emission spectra at different temperatures and variable-temperature ^{1}H NMR spectra. The emission spectra of **2.177e-f** measured in toluene displayed in increase in the amount of monomer emission with cooling. The chemical shift for H_a was shifted more downfield when the ^{1}H NMR was measured at colder temperatures in toluene-d_8. Therefore, the conformation responsible for monomer emission is more favourable at cooler temperatures and the conformation responsible for excimer emission becomes more populated at higher temperatures.



2.176



2.177a Z = $(CH_2)_2$
2.177b Z = $(CH_2)_3$
2.177c Z = $(CH_2)_4$
2.177d Z = $(CH_2)_5$
2.177e Z = $(CH_2)_2O(CH_2)_2$
2.177f Z = $(CH_2)_2O(CH_2)_2O(CH_2)_2$

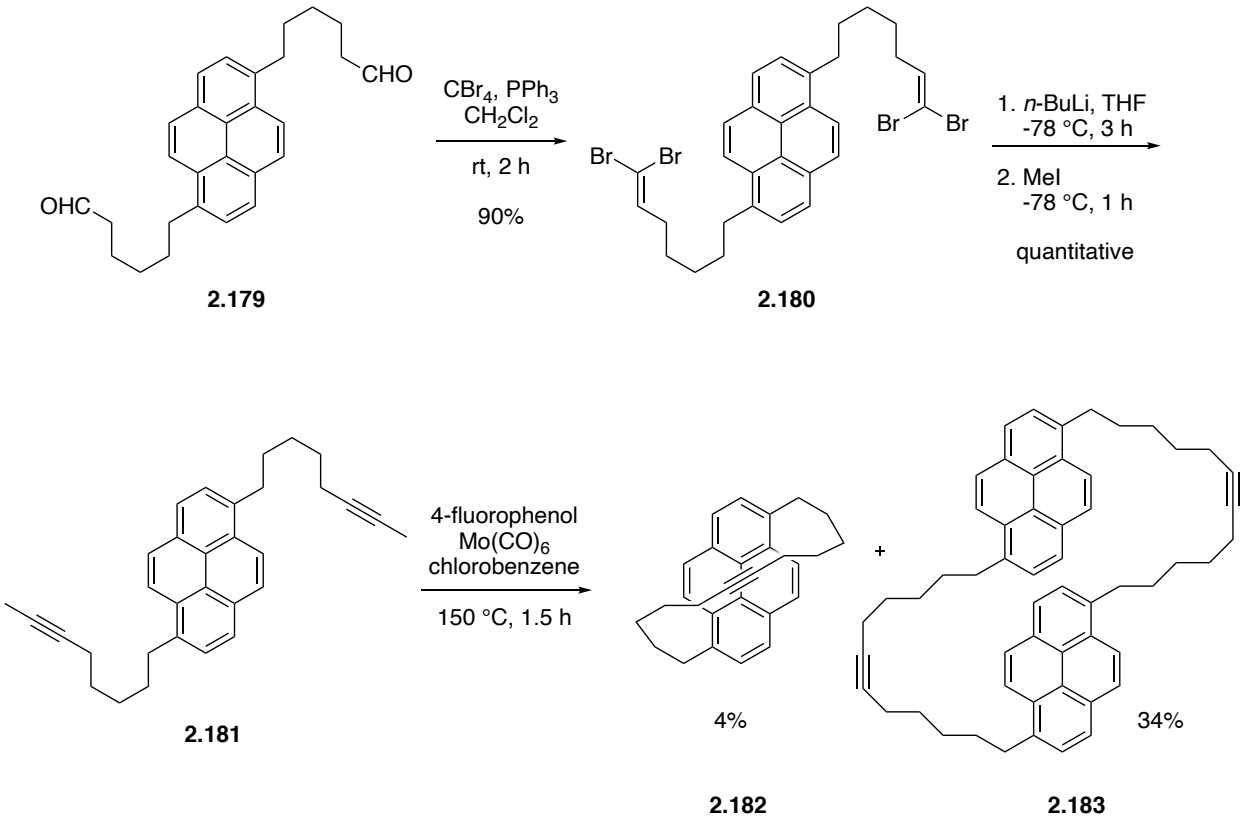


2.178

Scheme 2.40 Maeda's synthesis of (1,8)pyrenophanes.

A final pyrenophane recently reported by Mayor *et al.* was designed to be inherently chiral through construction of a 1,6-substituted pyrene (**Scheme 2.41**).[49]

Pyrene dialdehyde **2.179** was subjected to Ramirez dibromo olefination with CBr_4 and PPh_3 to give tetrabromide **2.180**. Treatment of **2.180** with excess *n*-BuLi, followed by quenching of the acetylide anion with MeI gave methyl-capped dialkyne **2.181**. While students are often taught that this entire transformation is the Corey-Fuchs reaction, it was in fact Ramirez *et al.* a decade earlier who discovered the transformation of aldehydes and ketones into dibromo olefins.[50] Later on, Corey and Fuchs disclosed that treatment of the dibromoolefins with *n*-BuLi gives the corresponding lithium acetylides, which can be quenched with a variety of electrophiles.[51] The next transformation, ring-closing alkyne metathesis, required non-terminal alkynes and was accomplished using Morteux's catalyst, which contains a $Mo(CO)_6$ pre-catalyst with 2-fluorophenol as co-catalyst. A small amount of the desired [12](1,6)pyrenophane **2.182** (4% yield) was isolated as a racemic mixture in addition to a 34% yield of dimeric pyrenophane **2.183**. Pyrenophane **2.182** was produced in low of a yield likely due to the build-up of strain required for its formation, even with a 12-membered bridge. Unfortunately, suitable crystals for X-ray analysis could not be grown so the degree to which the pyrene core is distorted is unknown. The enantiomers of **2.182** were successfully separated by chiral-HPLC. Enantiomerically pure samples were configurationally stable up until 250 °C when decomposition began to occur without any evidence of racemization.



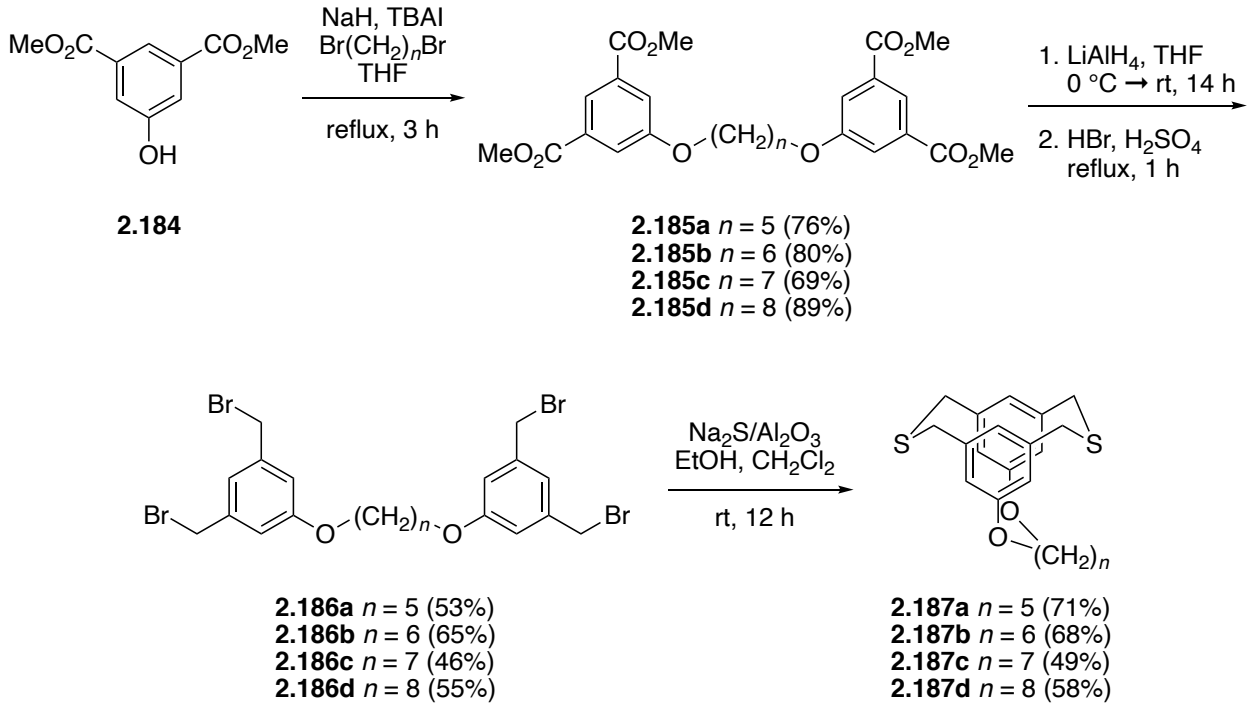
Scheme 2.41 Mayor's chiral (1,6)pyrenophane **2.182**.

A lot of real estate has been covered in the preceding discussion of the 50-year history of pyrenophane chemistry in a roughly chronological order, but it has hopefully accomplished several things. Firstly, it should serve as a jumping off point for any future students entering into this area of research. Secondly, the breadth of structural features that have been explored should serve to illustrate that the limit to pyrenophane chemistry is one's imagination and it is certain that pyrenophanes will continue to be designed, synthesized and studied long into the future.

2.2: The Synthesis of 1,*n*-Dioxa[*n*](2,7)pyrenophanes and the Development of Improved Protocols

In this Section, the focus turns to the original synthesis of the 1,*n*-dioxa[*n*](2,7)pyrenophanes (**2.47a-d**), which has been repeated on several occasions in the Bodwell group since its original development, usually to provide samples for collaborators. One of the main objectives of the work described in this thesis was to further explore the chemistry of these and other pyrenophanes and this required the synthesis of synthetically useful amounts of the pyrenophanes. Along the way, it became apparent that there was room for improvement at several stages. The results of this work are outlined in Sections 2.3 and 2.5 and this is prefaced below by a detailed consideration of the original synthetic pathway.

Bodwell first reported the synthesis of 1,*n*-dioxa[*n*](2,7)pyrenophanes (**2.47a-d**) and successfully synthesized pyrenophanes where *n* = 7-12.[12,16,21] The synthesis began with a Williamson ether synthesis between methyl 5-hydroxyisophthalate (**2.184**) with a series of 1,*n*-dibromoalkanes using NaH and tetra-*n*-butylammonium iodide (TBAI) in THF at reflux (**Scheme 2.42**). These conditions afforded the tethered tetraesters (**2.185a-d**) in yields ranging from 69-89%. The major drawback of this approach was the relatively low solubility of these compounds, which made purification on larger scales difficult. Therefore, crude mixtures of these compounds were carried through without purification. Tetraesters (**2.185a-d**) were reduced completely to the corresponding tetraols with $LiAlH_4$ and the crude mixtures were brominated with refluxing HBr/H_2SO_4 to give the series of tetrabromides (**2.186a-d**) in 42-65% yields over 2 steps. The tethered tetrabromides were self-coupled using sodium sulfide on a solid support of Al_2O_3 (basic) to afford dithiacyclophanes (**2.187a-d**) in moderate yields (49-66%). No correlation between tether length and yield was observed. It should be noted that the Na_2S/Al_2O_3 reagent was developed specifically for the purpose of synthesizing such dithiacyclophanes.[52] It was most effective when freshly prepared but remained active for several weeks when stored in a sealed vial in the freezer. The next series of transformations are also classics in the area of cyclophane chemistry and have been utilized in numerous pyrenophane syntheses from the Bodwell group.



2.184

2.185a *n* = 5 (76%)
2.185b *n* = 6 (80%)
2.185c *n* = 7 (69%)
2.185d *n* = 8 (89%)

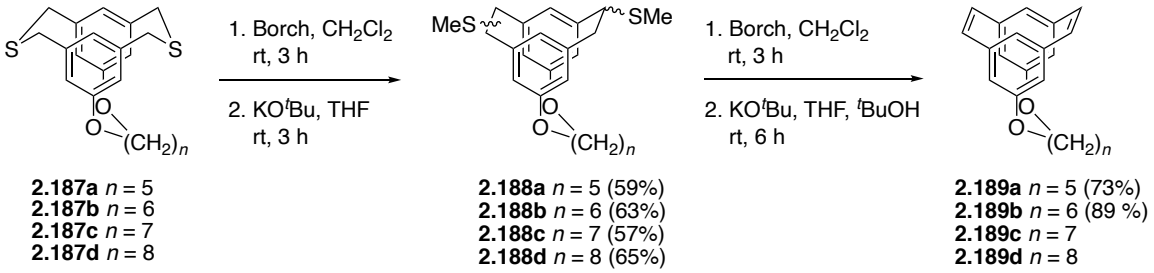
2.186a *n* = 5 (53%)
2.186b *n* = 6 (65%)
2.186c *n* = 7 (46%)
2.186d *n* = 8 (55%)

2.187a *n* = 5 (71%)
2.187b *n* = 6 (68%)
2.187c *n* = 7 (49%)
2.187d *n* = 8 (58%)

Scheme 2.42 Bodwell's original synthesis of dithiacyclophanes **2.187a-d**.

The sulfur atoms of dithiacyclophanes **2.187a-d** were methylated using Borch reagent ($(MeO)_2CHBF_4$) followed by a two-fold thia-Stevens rearrangement with potassium *tert*-butoxide to give a mixture of isomeric products **2.188a-d** in yields ranging from 57% to 65% (**Scheme 2.43**). No attempt was ever made to separate the isomers because all of them conceivably lead to the same product. Accordingly, this mixture was *S*-methylated again with Borch reagent and then subjected to a double elimination reaction by treatment with potassium *tert*-butoxide. In the shortest bridged systems, the elimination afforded cyclophanediene **2.189a-b** in 73% and 89% yields from **2.188a-b**, respectively. The longer bridged systems gave mixtures of compounds which are likely cyclophanedienes **2.189c-d**, dihydropyrenophanes and pyrenophanes. In terms of cyclophane strategies, this falls under the umbrella of bridge contraction. The

dithiacyclophanes are relatively low-strain [3.3]cyclophanes, which are then converted into moderately strained [2.2]cyclophanes.



2.187a n = 5
2.187b n = 6
2.187c n = 7
2.187d n = 8

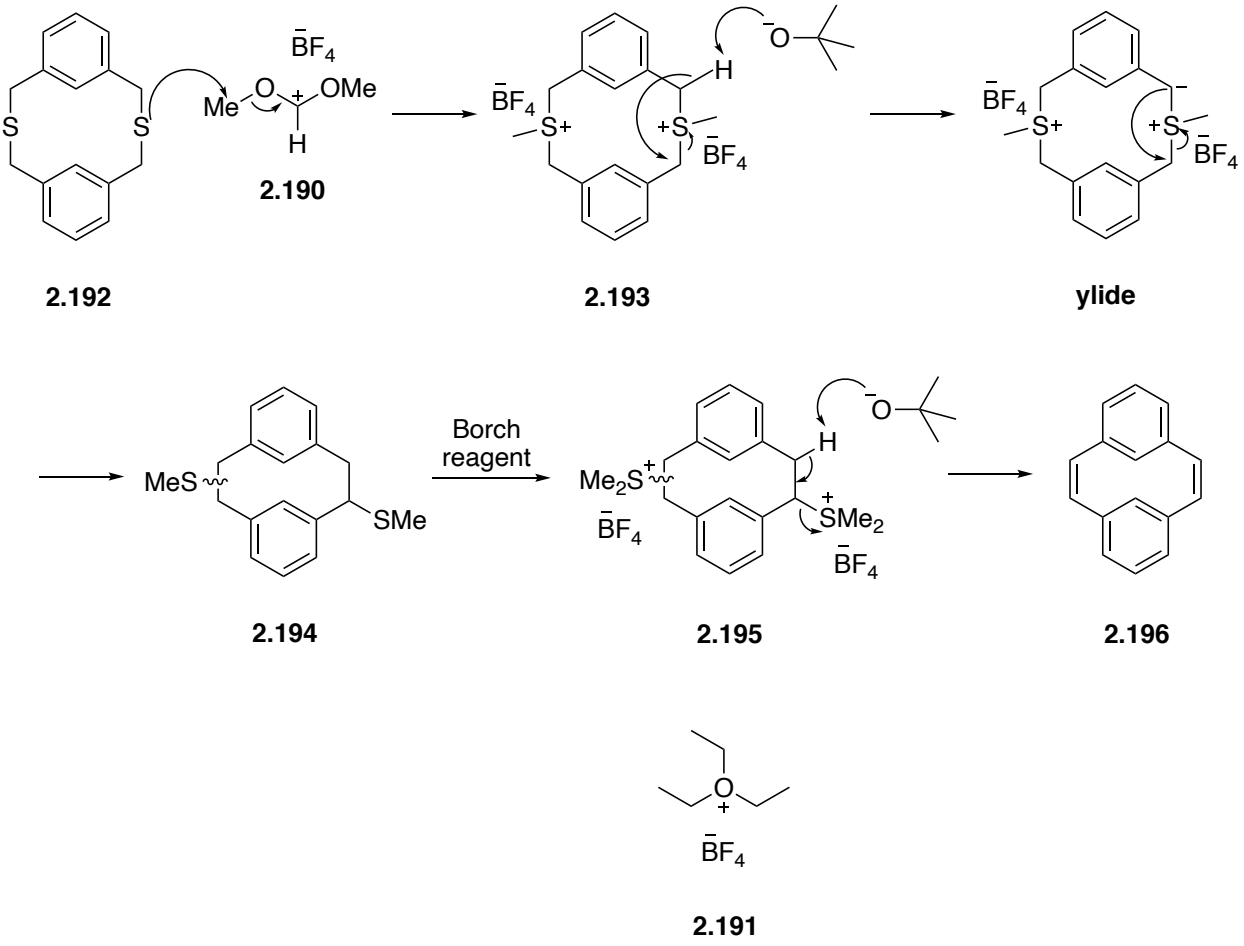
2.188a n = 5 (59%)
2.188b n = 6 (63%)
2.188c n = 7 (57%)
2.188d n = 8 (65%)

2.189a n = 5 (73%)
2.189b n = 6 (89 %)
2.189c n = 7
2.189d n = 8

Scheme 2.43 Step-wise procedure for cyclophanediene procedure **2.189a-d**.

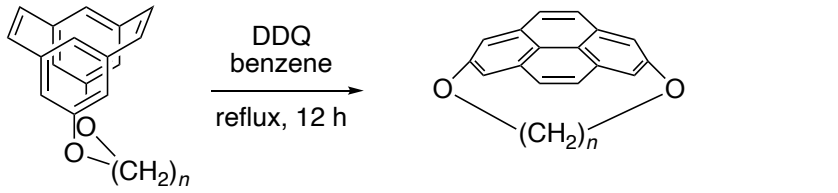
It is instructive to consider the details of the four-step conversion of dithiacyclophanes **2.187a-d** to the cyclophanedienes **2.189a-d**. The Borch reagent (**2.190**) is a source of powerfully electrophilic alkyl groups (usually methyl). It was first reported by Richard F. Borch in 1968 as a new method for synthesizing nitrilium salts which come from the alkylation of nitriles.[53] While Meerwein's salt (**2.191**)[54], another source of electrophilic alkyl groups, can accomplish similar transformations, it does suffer the drawback of being a hygroscopic solid which can be more difficult to handle. Borch reagent (**2.190**) is prepared by the reaction of orthoformates with boron trifluoride, which gives dialkoxycarbonium fluoroborates, in this case the alkyl groups are methyl. Mechanistically, using dithia[3.3]metacyclophane (**2.192**) as an example, the sulfur atoms undergo nucleophilic attack (S_N2) on a methyl group, with methyl formate acting as a leaving group to afford a methylsulfonium tetrafluoroborate salt (**2.193**) (**Scheme 2.44**). This salt, when treated with potassium *tert*-butoxide affords a sulfur ylide, which then undergoes a modified Stevens rearrangement. The result is contraction of the cyclophane bridges from 3 atoms to 2 and the movement of the sulfur atom from an endocyclic position to an exocyclic one, as in **2.194**. Several isomers can form. The [2.2]metacyclophane structure can adopt a *syn* or an *anti* conformation (*anti* is usually favoured, but only *syn* isomers are possible for **2,189a-d**), and each of these conformers have six possible isomers that can form: a set of three stereoisomers where the two sulfur

atoms are adjacent to the same benzene ring and a second set of stereoisomers where the two sulfur atoms are adjacent to opposite benzene rings. These two sets of isomers are constitutionally isomeric to one another. Typically, these isomers are isolated together, because they all lead to the same product. The sulfur atoms of the methylthio groups are then methylated again with Borch reagent to form bis(dimethylsulfonium tetrafluoroborate) salts **2.195**. With a good leaving group in place, treatment of this salt with potassium *tert*-butoxide induces a Hofmann elimination to give cyclophanediene **2.196.**



Scheme 2.44 Mechanism of bridge contraction of dithiacyclophanes.

Returning to the synthesis of the pyrenophanes, the pure cyclophanedienes (**2.189a-b**) and the mixtures (**2.189c-d**) could both by converted into pure 1,*n*-dioxa[*n*](2,7)pyrenophanes (**2.47a-d**) by treatment with DDQ in benzene at reflux in yields ranging from 35% to 81% (**Scheme 2.45**). This reaction has often been referred to as the valence isomerization/dehydrogenation (VID) reaction.

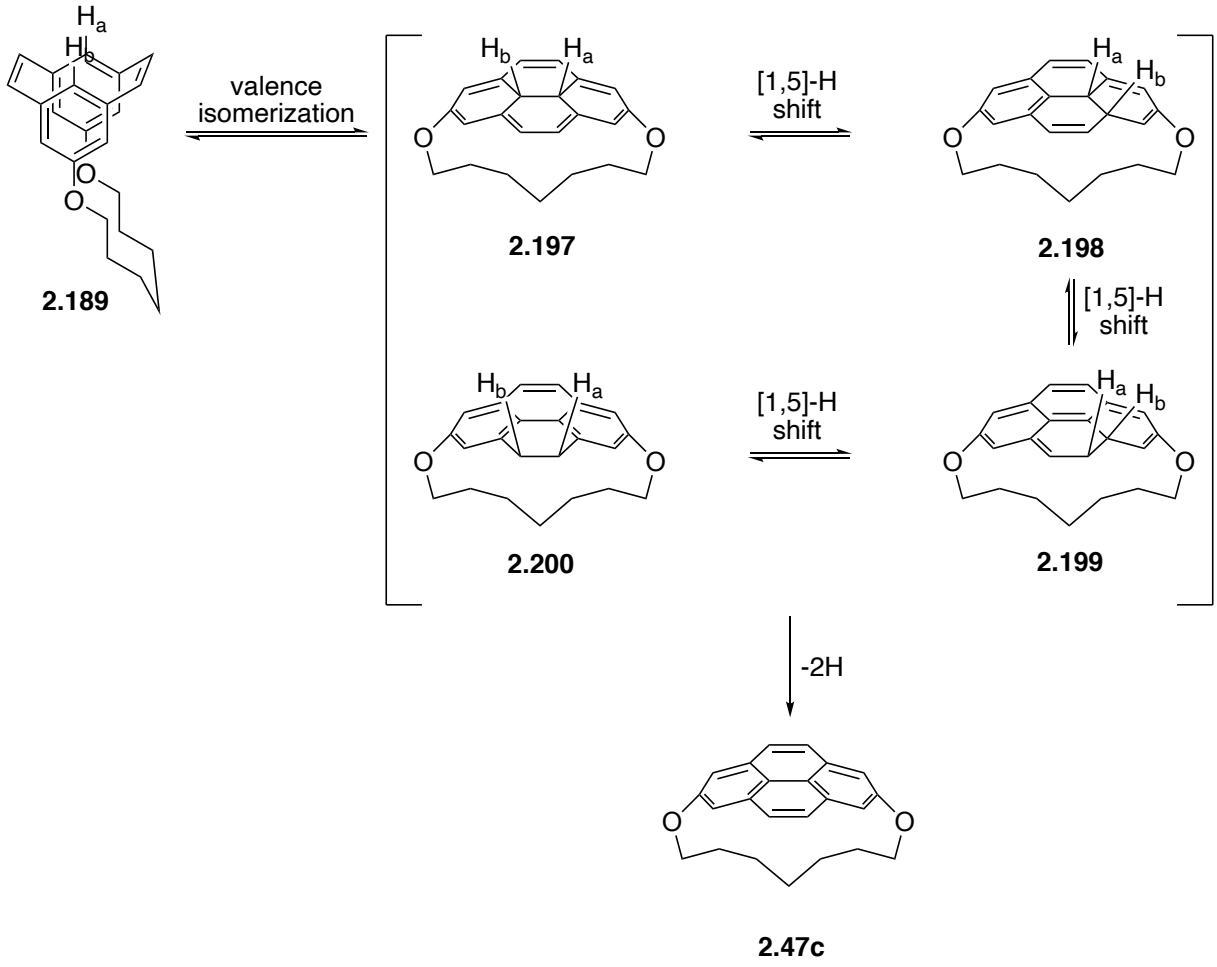


2.189a *n* = 5
2.189b *n* = 6
2.189c *n* = 7
2.189d *n* = 8

2.47a *n* = 5 (35%)
2.47b *n* = 6 (81%)
2.47c *n* = 7 (23% from **2.188c**)
2.47d *n* = 8 (50% from **2.188d**)

Scheme 2.45 VID reaction of cyclophanedienes **2.189a-d**.

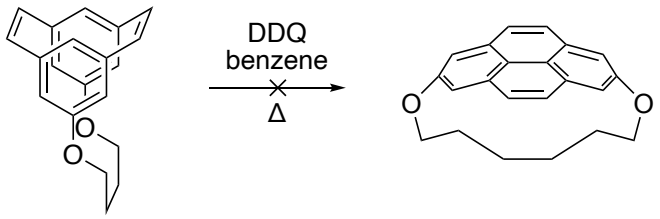
The mechanism for VID reactions has not been unambiguously determined, but It was originally proposed to follow the known valence isomerization between [2.2]metacyclophane-1,9-dienes and 10b,10c-dihydropyrenes.[55-57] Using cyclophanediene **2.189c** as an example, the first step is a thermally allowed valence isomerization (it is a suprafacial, thermal 4n+2 π electron electrocyclic reaction), which provides bridged cis-10b,10c-dihydropyrenophane **2.197** (**Scheme 2.46**). The dihydropyrenophane that is initially formed, **2.197,** can undergo a series of [1,5]-H shifts to give compounds **2.198**, **2.199** and **2.200**, which would help to explain the complicated ^{1}H NMR spectrum obtained for the formation of cyclophanediene **2.189c**.[58] Any of the possible dihydropyrenophanes could undergo dehydrogentation upon reaction with DDQ, which leads to aromatization of the entire pyrene system to give pyrenophane **2.47c**.



Scheme 2.46 Valence isomerization/dehydrogenation reaction of cyclophanediene **2.187c**.

Even though systems are being formed that should have considerable strain, and therefore has an energetic cost associated with it, the aromatic stabilization energy gained from forming a new pyrene system balances out the associated gain in strain energy. While it is difficult to arrive at a value for the aromatic stabilization energy (ASE) for pyrene with complete confidence, it has been computed using a homodesmotic equation to be 74.5 kcal/mol at the B3LYP/6-311+G** level of theory.[14] Obviously, a new pyrene moiety is not being constructed from a system devoid of aromatic components so the actual stabilization gained will be less than 74.5 kcal/mol. Nature seems content with the trade-off of strain energy for aromatic stabilization gained.

The synthesis of 1,6-dioxa[6](2,7)pyrenophane **2.47e** was attempted following the same procedure as above (**Scheme 2.47**). However, the final transformation failed during the attempted conversion of cyclophanediene **2.189e** to the corresponding pyrenophane with DDQ. No reaction was observed in benzene at reflux and raising the temperature (reflux in xylenes) led to decomposition of starting material without any evidence of the desired product. Therefore, it can be concluded that the buildup of strain energy in 1,6-dioxa[6](2,7)pyrenophane (**2.47e**) is not sufficiently offset by the gain of aromatic stabilization energy afforded by creation of a highly distorted pyrene system. This appears to be the limit to which nature is willing to make the trade-off. No attempt has yet been made to revisit this system.



2.189e **2.47e**

Scheme 2.47 Attempted VID reaction of cyclophanediene **2.189e**.

2.3: Improvements in the Early Stages of the Synthesis of 1,n-Dioxa[*n*](2,7)pyrenophanes (2.47a-d) (This Work)

The Williamson ether syntheses to give the tethered tetraesters **2.185a-d** (methyl esters) were fairly high yielding in the original scheme, but it was noted that the methyl esters gave products that were somewhat difficult to purify, especially as the scale became larger. Therefore, the first alteration to be made was to replace the methyl esters with ethyl esters. The resulting tetraester systems (**2.202a-d**) exhibited improved solubility, which eased the purification and allowed for reactions to be performed on a larger scale (5-10 g) with relative ease. The isolated yields of pure tetraesters (84-90%)

were also improved (cf. 76-89%), most likely due to the minimization of losses during purification and not because the ethyl esters were inherently better substrates for this transformation than the methyl esters.

$$\text{Atom economy} = \frac{\text{Molecular weight of product}}{\text{Molecular weight of all reactants}} \times 100\%$$

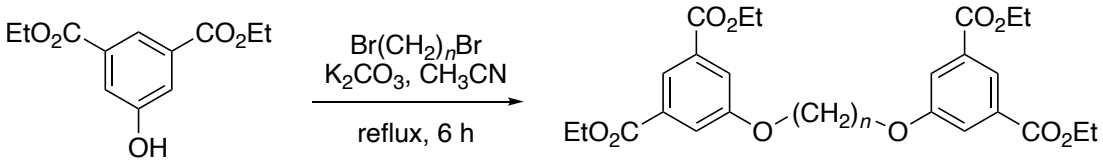
Equation 2.1. How to calculate atom economy for a chemical reaction.

Another step taken to improve this particular reaction was to look at the atom economy of the transformation.[59] Simply switching from methyl to ethyl esters has only a marginal impact on the atom economy of the transformation (**Table 1**). On the other hand, changing the reaction conditions from isophthalate, dibromide, NaH (40% in mineral oil) and TBAI in THF to isophthalate, dibromide and K_2CO_3 in CH_3CN greatly increased the efficiency of the transformation (**Table 1**), but had little effect on yield (**Scheme 2.48**). Not only did the use of K_2CO_3 instead of NaH and TBAI result in improved atom economy, but this new protocol was also arguably safer and more dollar economical.

	O-C_5-O tetraester	**O-C_6-O tetraester**	**O-C_7-O tetraester**	**O-C_8-O tetraester**
Methyl ester, dibromide, NaH, TBAI	57%	58%	59%	59%
Ethyl ester, dibromide, NaH, TBAI	62%	63%	63%	64%

Ethyl ester, dibromide, K_2CO_3	90%	90%	90%	90%

Table 2.1. Atom economy values for Williamson ether synthesis.

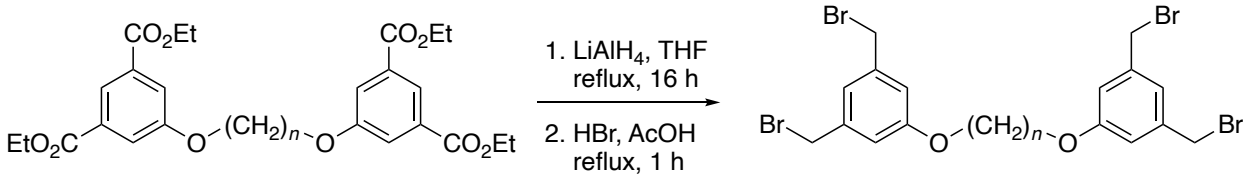


2.201

2.202a n = 5 (84%)
2.202b n = 6 (89%)
2.202c n = 7 (90%)
2.202d n = 8 (86%)

Scheme 2.48 Improved Williamson ether synthesis.

Reduction of the ethyl esters was still carried by treatment with $LiAlH_4$ in THF to give a grey solid which was dissolved in 2:1 HBr/H_2SO_4 mixture and refluxed for 1 h to give tetrabromides (**2.186a-d**) in 55-65% (**Scheme 2.49**). The yields were similar to those previously reported from the Bodwell group.



2.202a n = 5
2.202b n = 6
2.202c n = 7
2.202d n = 8

2.186a n = 5 (58%)
2.186b n = 6 (75%)
2.186c n = 7 (78%)
2.186d n = 8 (72%)

Scheme 2.49 Reduction and bromination of tetraesters **2.202a-d**.

The formation of dithiacyclophanes **2.187a-d** is one of the key steps in the synthetic pathway and significant improvements to this reaction were achieved. The results of this work are discussed in Section 2.7.

The conversion of dithiacyclophanes **2.187a-d** to cyclophanedienes **2.189** was performed using the same set of transformations as before with similar results. The use of a Wittig rearrangement / Hofmann elimination sequence was considered, but previous work in the Bodwell group had found that this methodology was clearly inferior to the existing Stevens rearrangement / Hofmann elimination sequence. (Bodwell, G. J.; Zhang, B. unpublished results)

The final VID reaction of cyclophanedienes **2.189a-d** to pyrenophanes were previously carried out in refluxing benzene. Under these conditions, the reactions worked well for the 1,*n*-dioxa[*n*](2,7)pyrenophanes (**2.47b-d**) where *n* = 8-10, but the yield suffered in the case of 1,7-dioxa[7](2,7)pyrenophane (35%) (**2.47a**). In addition to the low yield for the VID reaction, several side products[60] were present, none of which were unambiguously identified. One of the side products was believed to be a Diels-Alder adduct that results from a reaction with 1,7-dioxa[7](2,7)pyrenophane and DDQ. In this case, the structural assignment was based solely on the similarity of the (complicated) ^{1}H NMR spectrum of the side product to a known Diels-Alder adduct of [7](2,7)pyrenophane with TCNE.[61]

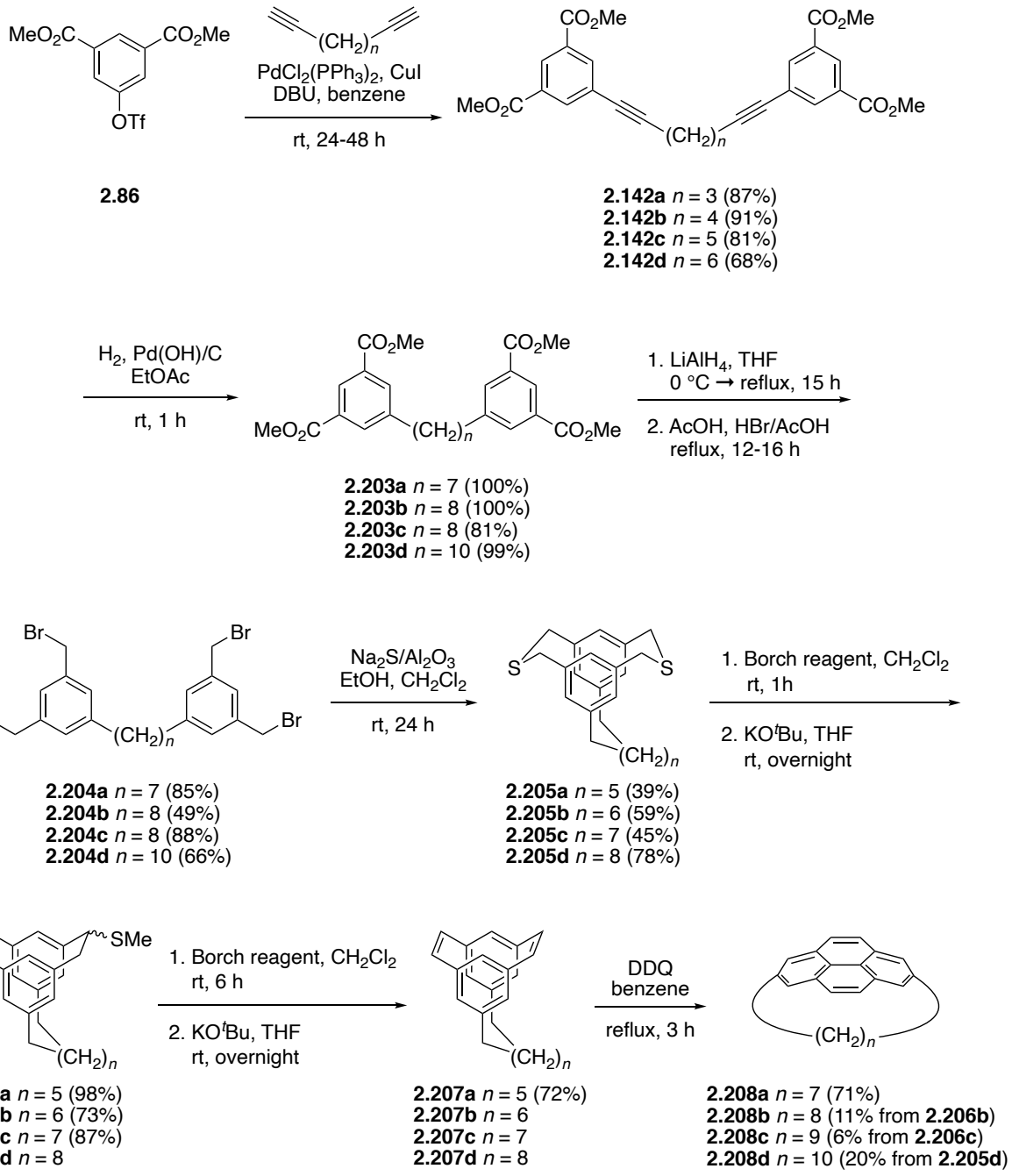
Since at least one of the side products came from a follow-on reaction of the intended product, it was envisaged that lowering the temperature might prevent them from taking place. When the VID reaction leading to 1,7-dioxa[7](2,7)pyrenophane (**2.47a**) was performed at room temperature, it proceeded in a much-improved 85% yield with no evidence of any side products (TLC analysis). The reaction leading to the higher homologues, 1,*n*-dioxa[*n*](2,7)pyrenophanes (**2.47b-d**), worked just as well at room temperature as they did at reflux in benzene without the need for longer reaction times. It therefore seems clear that the problem with the reaction leading to the smallest pyrenophane **2.47a** was that the product was not stable under the conditions of its formation.

2.4: Original Synthesis of [*n*](2,7)Pyrenophanes

The all-carbon bridged systems were also reported by the Bodwell group (**Scheme 2.50**).[61,62] This series of compounds was also required for further studies of their chemistry and their use as starting points for the construction of more elaborate cyclophanes. Their original syntheses are considered in detail below and this is followed (Section 2.5) by the presentation of an improved synthetic pathway (Section 2.6). The original synthesis began with a two-fold Sonogashira cross-coupling between 3,5-bis(methoxycarbonyl)phenyl triflate (**2.86**) and a series of terminal diynes to give a series of 7-10 carbon tethered diyne tetraesters **2.142a-d**. This reaction worked well in all cases with yields >80%. The alkynes could then be hydrogenated using H_2 in the presence of Pearlman's catalyst ($Pd(OH)_2/C$) to give the tetraesters **2.203a-d** with fully saturated tethers. Although they appear to be the most straightforward of reactions, they have long suffered from a lack of consistency according to Bodwell group lore. This includes long periods of time elapsing (e.g. most of a Summer) without a single transformation being successful. The cause(s) for the inconsistency have never been clearly identified, although some combination of improperly cleaned glassware (poisoning the catalyst), inactive catalyst, and starting material purity haven entered into the discussion. Interestingly, Derek Lowe, in his "In The Pipeline" blog, frequently mentions the voodoo or witchcraft of catalytic hydrogenations. While the experimental procedures for this class of reaction are typically very simple, they can often be the most finicky to reproduce.

Tetraesters **2.203a-d** were then reduced to the corresponding tetraols with $LiAlH_4$ and the products were extracted with large quantities of ethyl acetate from the salt byprodcuts. Practically, this synthetic step could result in large losses of product due to low solubility of the alcohol products. The aqueous layer needed to be extracted multiple times to ensure a high yield. The tetraols were not purified further, but rather slurried in glacial acetic acid. HBr in acetic acid was added to this slurry, which was heated at reflux

overnight to give tetrabromides **2.204a-d**. Tetrabromides **2.204a-d** were then converted into the dithiacyclophanes **2.205a-d** upon reaction with Na_2S/Al_2O_3**.** The yields of these sodium sulfide couplings were lower than those of the dioxa series. It was posited that the drop in yield from the dioxa series was due to the absence of oxygen atoms in the bridge, which may have been able to chelate a sodium atom and thus predispose the benzylic bromides to ring closure. With the series of dithiacyclophanes in hand, the same ring contraction protocol was used to gain accees to the corresponding cyclophanedienes **2.207a-d**. *S*-Methylation of dithiacyclophanes **2.205a-d** with Borch reagent afforded the corresponding bis(methylsulfonium tetrafluoroborate) salts, which were subjected to thia-Stevens rearrangement with potassium *tert*-butoxide to afford a mixture bis(thiomethyl)cyclophanes (**2.206a-d**) isomers. In the case of the 7-carbon bridged system, *S*-methylation and Hoffman elimination afforded cyclophanediene **2.207a** in 29% overall yield over the four steps. Pure cyclophanediene (**2.207a**) could be cleanly converted into [7](2,7)pyrenophane (**2.208a**) by treatment with DDQ in benzene at reflux in 71% yield. In the case of the 8,9 an 10-carbon bridged systems **2.206b-d**, the second *S*-methylation and Hoffman elimination afforded a mixture of products which included cyclophanedienes **2.207b-d**, [*n*](2,7)pyrenophanes (**2.208b-d**) and other byproducts. This mixture was treated with DDQ in benzene at reflux, which nicely gave [8](2,7)pyrenophane (**2.190b**) and [9](2,7)pyrenophane (**2.190c**), and [10](2,7)pyrenophane (**2.190d**) in 11%, 6% and 20% yields, respectively, from the dithiacyclophanes **2.206b-d** over five steps.

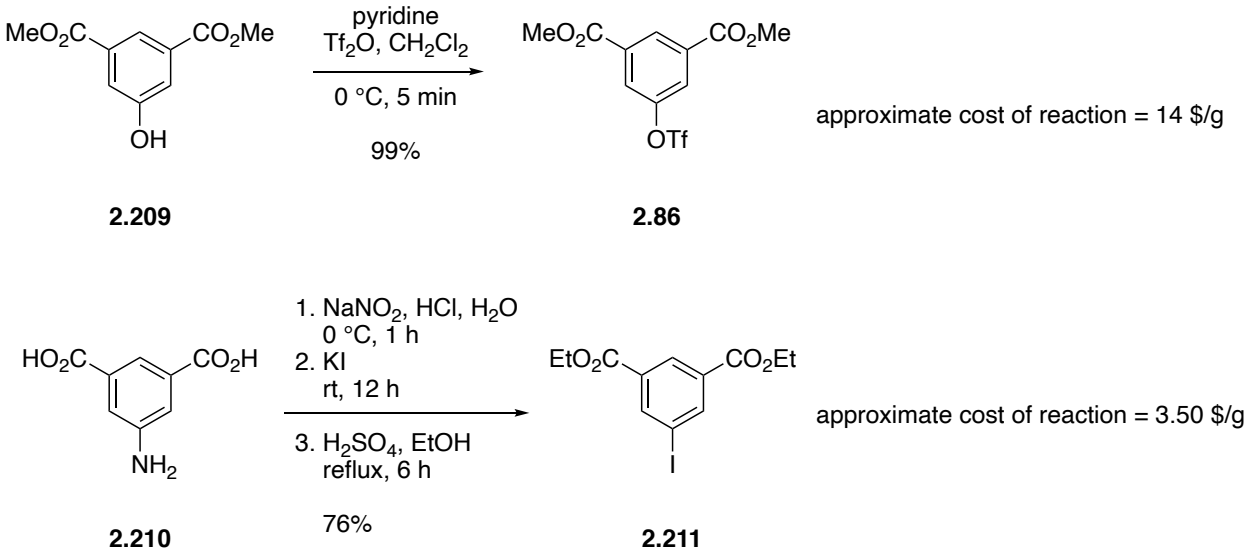


Scheme 2.50 Bodwell's original synthesis of [*n*](2,7)pyrenophanes (**2.208a-d**).

2.5: Improvements to the synthesis of [*n*](2,7)pyrenophanes (2.208a-d) (This Work)

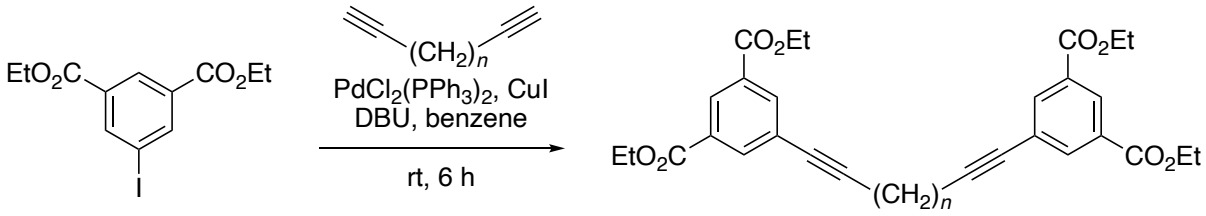
Several improvements were made to the synthetic steps leading towards the [*n*](2,7)pyrenophanes (**2.208a-d**). These improvements were made for several reasons including reproducibility, safety, economy, and improvements in yield.

The first modification was to alter the isophathalate component in the double Sonogashira cross-coupling with the 1,*n*-alkyldiynes. Based on previous work performed in the Bodwell group, a procedure was developed for the multi-gram conversion of 5-aminoisophthalic acid (**2.210**) into 5-iodoisophthalates (**2.211**) (**Scheme 2.51**).[63] This was accomplished through diazotization of 5-amino isophthalic (**2.210**) with $NaNO_2$ followed by quenching with an excess of potassium iodide to afford crude 5-iodoisophthalic acid, which was collected by filtration, dried, then dissolved in EtOH and heated to reflux with catalytic sulfuric acid to give diethyl 5-iodoisophthalate (**2.211**) in 76% over twosteps on scales up to 5 g. Performing the diazotization on scales larger than 5 grams is not advisable due to potential for explosive decomposition of diazo compounds, however, multiple diazotization reactions could be performed in series to give access to relatively large quantities of diethyl 5-iodoisophthalate (**2.211**). While the formation of triflate **2.86** is relatively straight forward and very high yielding, the use of Tf_2O makes this an unnecessarily costly step at the beginning of a synthesis. Based on the cost of reagents (excluding solvents) and commodity chemicals, from MilliporeSigma Canada Co. the cost to synthesize 1 gram of triflate **2.86** is approximately 14.00$ CAD, whereas the cost to synthesize 1 gram of 5-iodoisophthalate **2.221** is approximately 3.50 $ CAD. For a common starting material that was required in large quantities, it is far more cost effective to work with diethyl 5-iodoisophthalate (**2.211**). Additionally, iodides are often superior substrates for cross-coupling reactions.



Scheme 2.51 Synthesis of substituted isophthalates.

The use of 5-iodoisophthalate (**2.211**) has little effect on the yields of the Sonogashira cross-coupling reactions, with every example proceeding at over 80% yield and being completed within 6 h on scales up to 5 g to give alkynes **2.212a-d** (**Scheme 2.52**). Additionally, these reactions proceeded cleanly enough that the crude reaction mixture could be recrystallized from EtOH to give product of sufficient purity to be carried forward.



2.211

2.212a *n* = 3 (85%)
2.212b *n* = 4 (80%)
2.212c *n* = 5 (92%)
2.212d *n* = 6 (82%)

Scheme 2.52 Sonogashira cross-couplings with diethyl 5-iodoisophthalate (**2.211**).

As discussed above, the hydrogenation of carbon-carbon triple bonds seems straightforward, but can actually be a problematic reaction. Experience in the Bodwell

group has demonstrated that these reactions can either work beautifully, proceed partially or fail completely. In the case of the catalytic hydrogenations of alkynes **2.212a-d**, they were originally found to be successful using with 10% Pd/C and Pearlman's catalyst (Pd(OH)/C), but these results were not reproducible and would stop working for weeks at a time (and never work for some students). Several factors may contribute to why these reactions are so mercurial. Suppliers have a myriad of different hydrogenation catalysts available that range from affordable to prohibitively expensive, especially in an academic research setting. Focusing solely on solid-supported palladium catalysts, a quick search of the MilliporeSigma catalogue produced over 30 unique catalyst systems. Screening all possible catalysts, suppliers, and reaction conditions to find the "Goldilocks" zone for any system is both time-consuming and expensive.

Felpin has spent considerable time studying the properties, preparations and uses of Pd/C catalysts and has outlined the results in two microreview articles.[64,65] A paragraph in one of these reviews rings true with anyone who has battled with these catalystic systems:

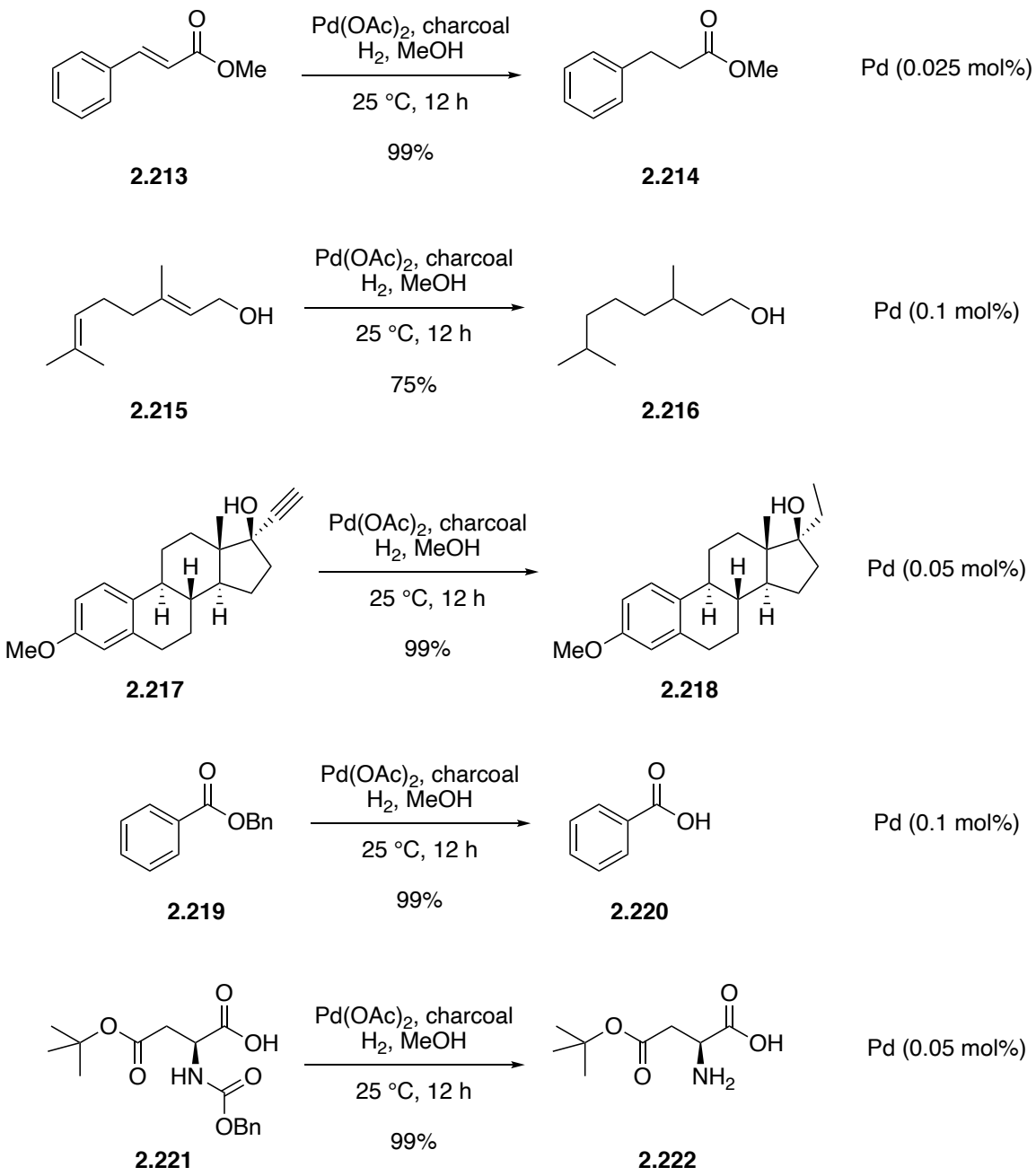
"*Although we and others appreciated the peculiar reactivites of Pd/C for the creation of C-C and C-X bonds, we face many reproducibility issues, especially in our early-stage projects, and we learned from these failures that the use of Pd/C requires a good knowledge of properties governing its reactivity"*

The authors mention that the term "Pd/C" is really a catch-all for any combination of palladium metal supported on some form activated carbon. However, the variations that exist under this umbrella are expansive. There are five main considerations a researcher should bear in mind when looking at different Pd/C catalysts:

1. When one purchases Pd/C from a commercial source it is a mixture of Pd^{II} and Pd^{0}, the ratio of which depends on the method of preparation and supplier, and has a profound effect on the catalyst's reactivity.
2. The dispersion pattern of the palladium is important and includes eggshell (on the surface of carbon), thickshell (inside the porous carbon) and uniform as a mixture.
3. The size of the palladium nanoparticles plays a huge role in its catalytic activity.
4. The nature of the carbon support in use has significant implications on the reactivity of the catalyst. Activated charcoal is not purely carbon, it contains other trace elements, the ratios of which depend on the source of the carbonized material. The effect of these trace elements is still poorly understood.
5. Dry Pd/C is highly flammable and dangerous to handle so it often wetted, the degree to which can have a profound effect on reactivity.

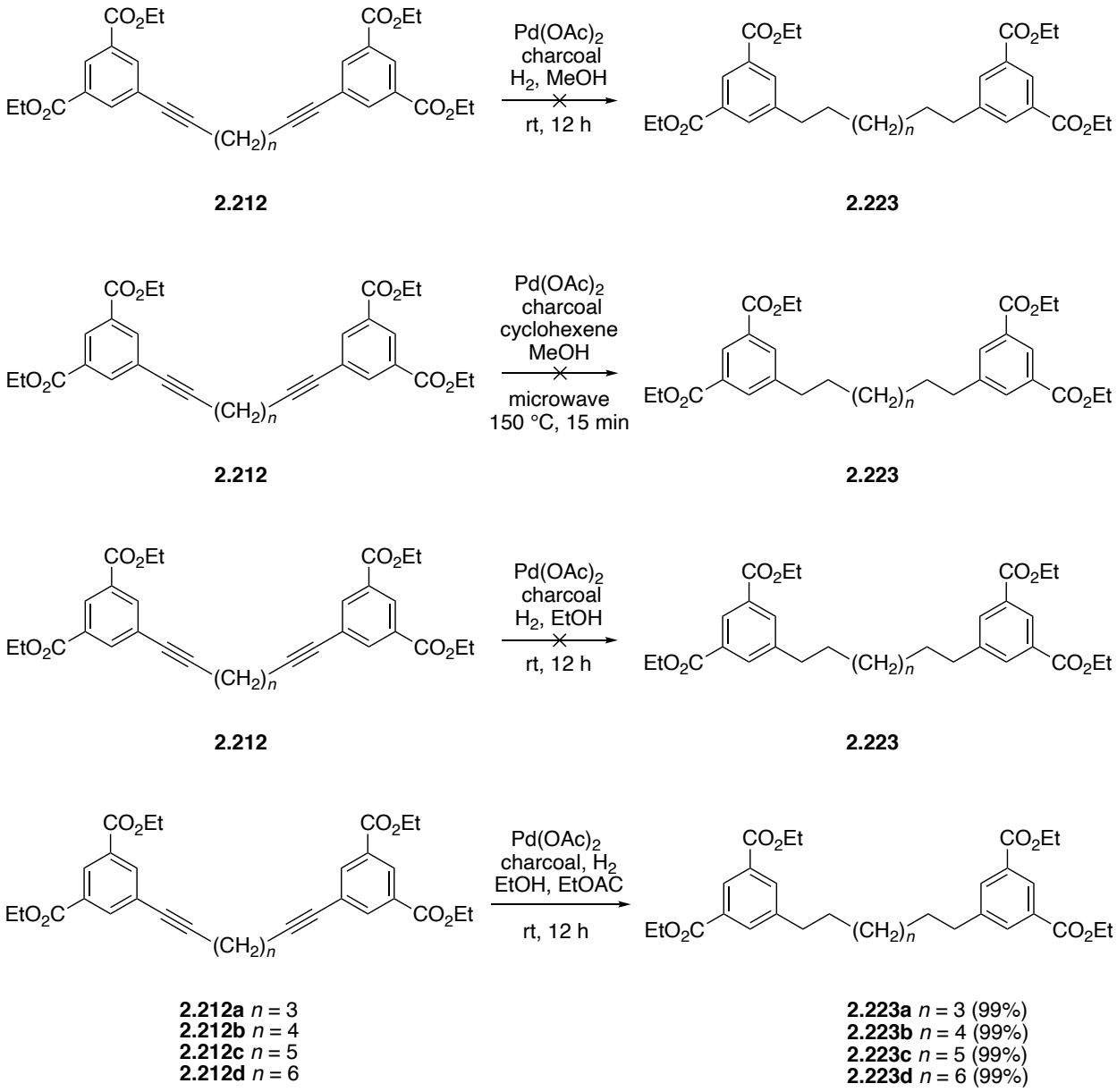
These factors are impossible to control when buying these catalyst from commercial suppliers, so the Felpin group decided to explore homemeade Pd/C catalysts. They hypothesized that they could control the nature of the palladium species (Pd^{0} versus Pd^{II}) by generating it *in situ* in the presence of an appropriate carbon source. They discovered that highly stable $Pd(OAc)_2$ could be used as a pre-catalyst and that it could be reduced to Pd^{0} by H_2 gas and MeOH in the presence of charcoal. The charcoal served two purposes: as both a support and a stabilizer for the palladium nanoparticles that were generated. The nanoparticles formed using this procedure were shown to be fairly uniform in size (3-6 nm) (X-ray photoelectron spectroscopy) and fully adsorbed onto the charcoal (ICP-MS analysis). Additionally, the palladium species present were determined to be comprised of 70% Pd^{0} and 30% Pd^{II}. The catalyst was prepared by mixing $Pd(OAc)_2$ (10% w/w) with charcoal (90% w/w) in MeOH under a H_2 atmosphere. This *in situ* generation of Pd/C was shown to be an effective catalyst for the hydrogenation of olefins, e.g. **2.213** and **2.215**, the hydrogenation of alkynes, e.g. **2.217**, and the hydrogenolysis of *O*-benzyl groups, e.g. **2.219** and **2.220** (**Scheme 2.53**).[66] These reactions were found to be easily scalable to multi-gram levels and the recovered catalyst (by filtration) could be

reused up to 8 times without appreciable loss of reactivity. Interestingly, the catalytic system could also be generated by transfer hydrogenation of cyclohexene with microwave activation at 150 °C.



Scheme 2.53 Selected examples of *in situ* Pd/C reactions by Felpin.

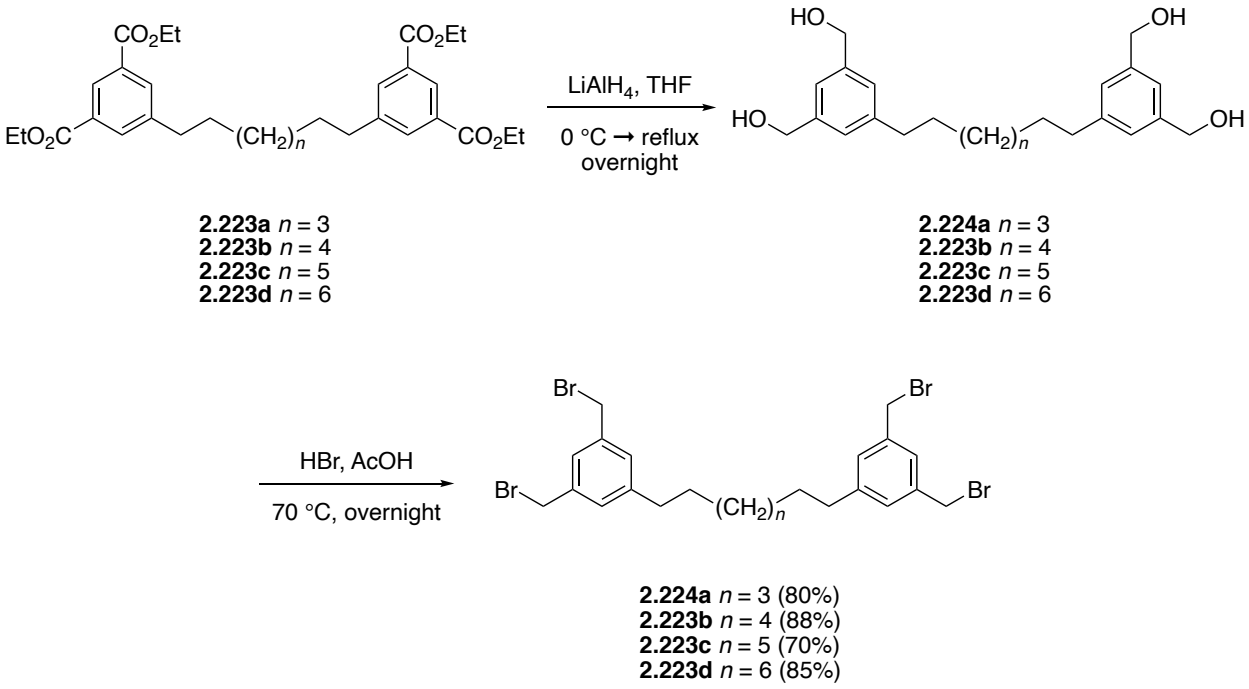
The possibility of using this catalytic hydrogenation system for the hydrogenation of alkynes **2.212a-d** was then investigated (**Scheme 2.54**). Initially, the general conditions outlined in **Scheme 2.53** were investigated. However, no product was formed, which was almost certainly due to the low solubility of the starting material in MeOH. The reaction also failed when microwave conditions (using cyclohexene as a hydrogen source) were employed with only recovery of the starting material. In all of the work published by Felpin, only MeOH was ever used as the solvent for the *in situ* generation of Pd/C. The authors mention that MeOH and H_2 gas are required in order to reduced Pd^{II} to Pd^0. Having observed that the alkynes **2.212a-d** were soluble in hot EtOH, the hydrongenation reactions of alkynes **2.212c** and **2.212d** were attempted. Unfortunately, while alkynes **2.212a-d** were sparingly soluble in room temperature EtOH, this was not sufficient for the reaction to be proceed successfully. Gratifyingly, when a mixed solvent system of 1:1 EtOH/EtOAc was used, the hydrogenation proceeded in quantitative yields!



Scheme 2.54 Optimization of catalytic hydrogenation of alkynes **2.212a-d**.

The change from methyl ester to ethyl esters had little effect on the reduction to benzylic alcohols **2.224a-d**, which were isolated without purification (**Scheme 2.55**). The bromination could be accomplished under simpler conditions without the need to use the rather expensive HBr in acetic acid. Crude alcohols **2.224a-d** were dissolved in warm glacial acetic acid and a 1:1 mixture of HBr (48%)/AcOH was added. The reaction was gently heated overnight then quickly worked-up and purified by column chromatography.

If the crude oily brown mixture is not purified shortly after work-up the yield of the reaction drops off significantly. The purified tetrabromides **2.204a-d** are bench stable and have shown no level of degradation over periods of several months to a year.



2.223a *n* = 3
2.223b *n* = 4
2.223c *n* = 5
2.223d *n* = 6

2.224a *n* = 3
2.223b *n* = 4
2.223c *n* = 5
2.223d *n* = 6

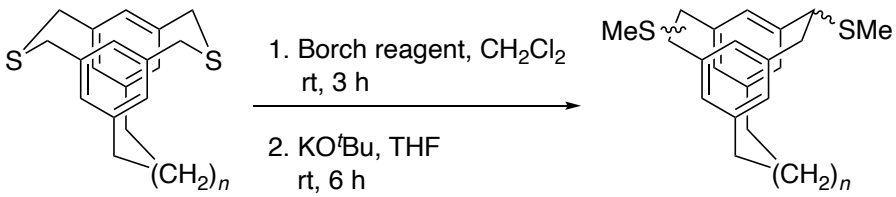
2.224a *n* = 3 (80%)
2.223b *n* = 4 (88%)
2.223c *n* = 5 (70%)
2.223d *n* = 6 (85%)

Scheme 2.55 Reduction and bromination of tetraesters **2.223a-d**.

As in the case of the dioxapyrenophane series, the conversion of the dibromides **2.223a-d** into the corresponding dithiacyclophanes **2.205a-d** is a key step in the synthetic sequence. The major improvements to this transformation are discussed in Section 2.7.

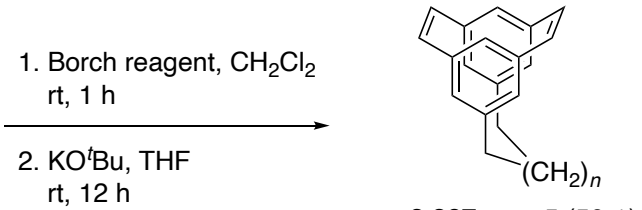
The conversion of dithiacyclophanes **2.205a-d** into cyclophanedienes **2.207a-d** was accomplished using the same procedures outlined previously, but with slightly improved yields in some cases (**Scheme 2.56**). Dithiacyclophanes were *S*-methylated using Borch reagent to give the corresponding (methylsulfonium tetrafluoroborate) salts that were then subjected to a thia-Stevens rearrangement with potassium *tert*-butoxide to afford bis(thioethers) **2.206a-d** in good yields (74-85%). These mixtures of isomers were passed through a plug of silica gel, but as usual no further effort was made to

separate the isomers. Compounds **2.206a-d** were again *S*-methylated with Borch reagent then subjected to Hofmann elimination with potassium *tert*-butoxide to give cyclophanedienes **2.207a-d**. Only the 7-atom bridged system gave pure dithiacyclophan **2.207a** (in 50 % yield from **2.206a**). The other 3 systems (8-,9-,and 10-atom bridged) all gave a mixture of cyclophanediene, dihydropyrenophanes and pyrenophane.



2.205a *n* = 5
2.205b *n* = 6
2.205c *n* = 7
2.205d *n* = 8

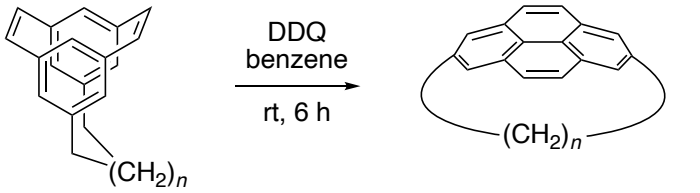
2.206a *n* = 5 (74%)
2.206b *n* = 6 (80%)
2.206c *n* = 7 (85%)
2.206d *n* = 8 (82%)



2.207a *n* = 5 (50%)
2.207b *n* = 6
2.207c *n* = 7
2.207d *n* = 8

Scheme 2.56 Transformation of dithiacyclophanes **2.205a-d** into cyclophanedienes **2.207a-d**.

As was the case for the VID reaction used to form 1,*n*-dioxa[*n*](2,7)pyrenophanes (**2.24a-d**) the initial procedure in refluxing benzene proved to be overkill. All cyclophanediene **2.207a** and mixtures **2.207b-d** were cleanly converted to [*n*](2,7)pyrenophanes **2.208a-d** upon exposure to DDQ in benzene at room temperature (**Scheme 2.58**).



2.207a *n* = 5
2.207b *n* = 6
2.207c *n* = 7
2.207d *n* = 8

2.208a *n* = 7 (71%)
2.208b *n* = 8 (20% 5 steps)
2.208c *n* = 9 (30% 5 steps)
2.208d *n* = 10 (40% 5 steps)

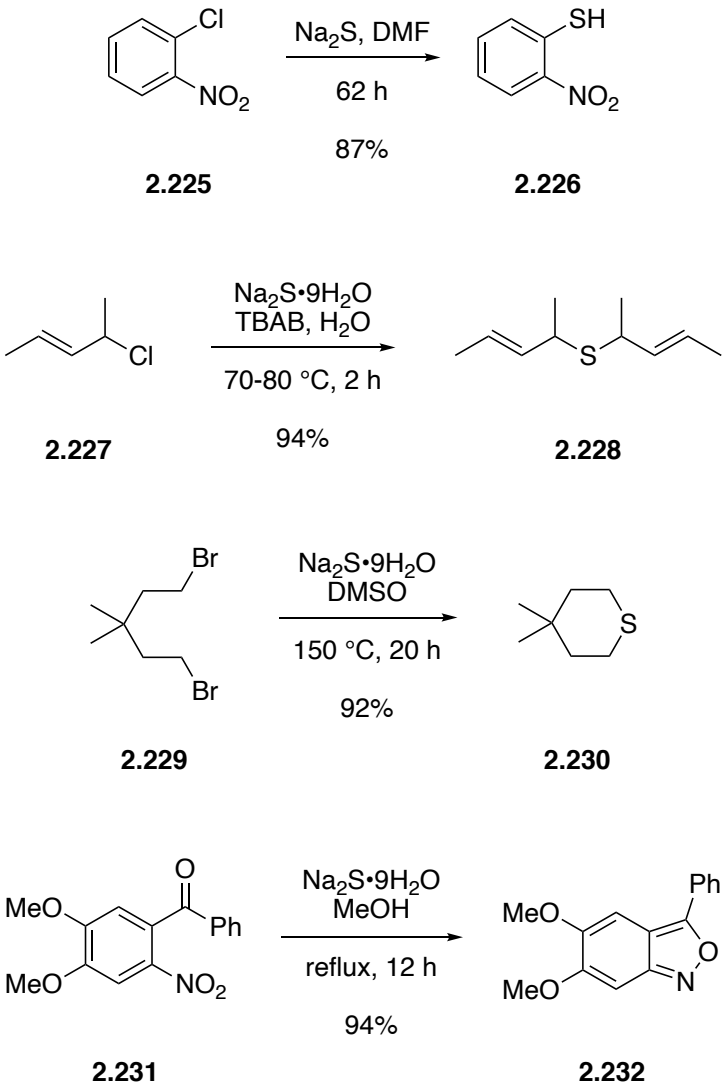
Scheme 2.57 VID reaction of cyclophanedienes **2.207a-d**.

2.6: A Brief History of Na_2S as a Reagent

Returning to the dithiacyclophane-forming reactions, Na_2S (in various forms, see below) has been used extensively as a reagent for this purpose. Attempts to improve this reaction were directed to the way in which the reagent was introduced to the reaction. To provide context for this work, some background regarding Na_2S is provided here. Na_2S is largely used as an industrial chemical in areas such as wastewater treatment, photography and rubber manufacturing. Its greatest use is in the Kraft process, which converts wood into wood pulp.[67] Briefly, this process involves treatment of wood chips with a hot mixture of water, NaOH and Na_2S which breaks down lignin and cellulose.[68] Any who travles through a city with a pulp and paper mill will quickly become intimate with the sulfurous smell associated, in part, with this process.

Sodium sulfide also has many uses in synthetic chemistry, e.g. in the preparation of thiols via nucleophilic aromatic substitution, *e.g.* **2.226,**[69] thioethers via S_N2 reactions, *e.g.* **2.228**,[70] cyclic thioethers via intramolecular S_N2 reactions, *e.g.* **2.230**,[71] and the reduction of aromatic nitro groups to aromatic amines groups (Zinin reaction), *e.g.* **2.232**

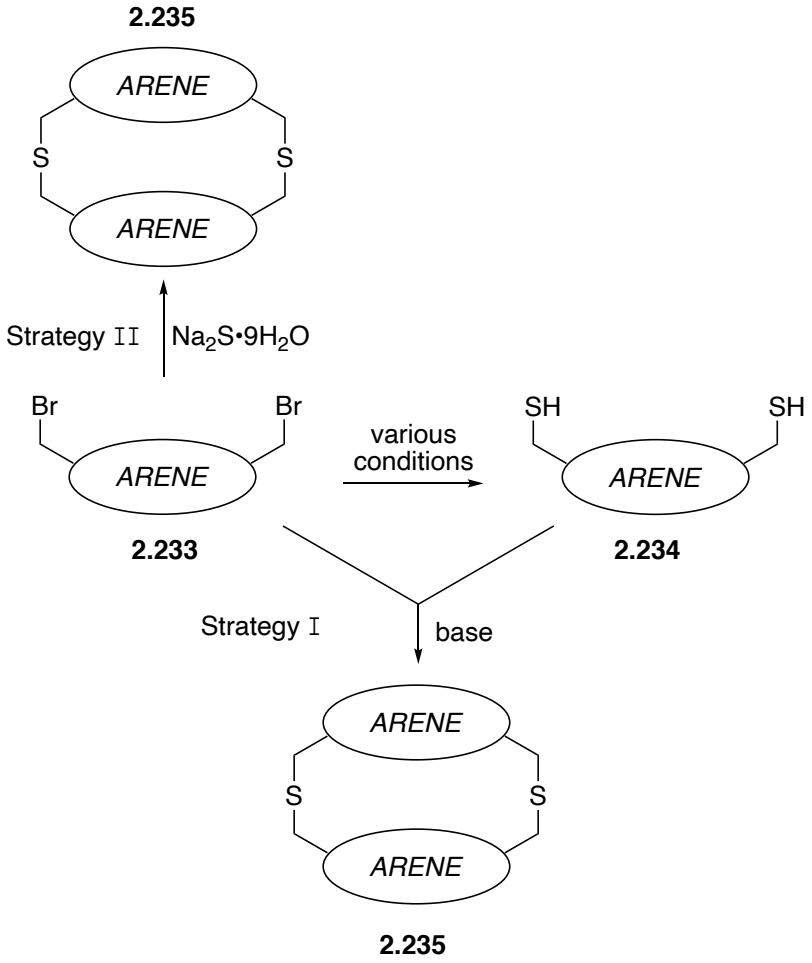
(**Scheme 2.59**).[72] The ability to form cyclic thioethers has been exploited extensively in the synthesis of various cyclophane systems.[73]



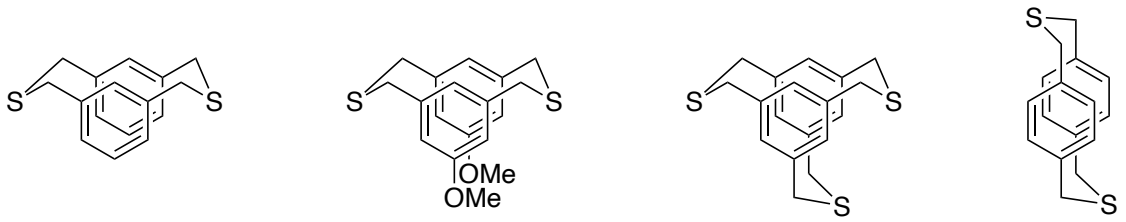
Scheme 2.58 Synthetic uses of sodium sulfide.

Traditionally, the formation of the thioether cyclophanes was accomplished using one of two complementary strategies starting from bis(bromomethyl)arenes (**2.233**) (**Scheme 2.60**). The first strategy (I) converts a bis(bromomethyl)bromide (**2.233**) into a

bis(thiomethyl)arene (**2.234**) using any of the various methods available. Then a mixture of compounds **2.233** and **2.234** are treated with base to afford [3.3]dithiacyclophanes **2.335**. The other strategy (II) is more direct and involves the coupling of bis(bromomethyl)bromide **2.233** by using $Na_2S{\cdot}9H_2O$. While the more direct method II would appear to be advantageous, it often requires long reaction times. Furthermore, the scope is limited to high dilution using identical bis(bromomethyl)arenes. Nevertheless, a large number of thiacyclophanes (**Figure 2.1**) have been synthesized by one or both of these methods (**Table 2.2**).[13,52,74-78]



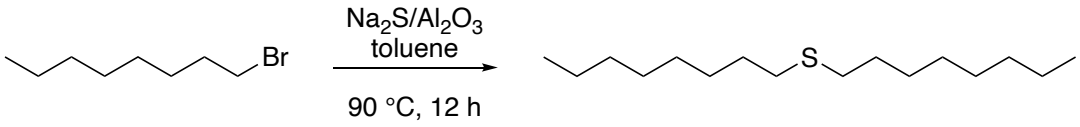
Scheme 2.59 Strategies for the synthesis [3.3]dithiacyclophanes **2.235**.



2.236 **2.237** **2.238** **2.239**

Figure 2.1 A small selection of dithiacyclophanes.

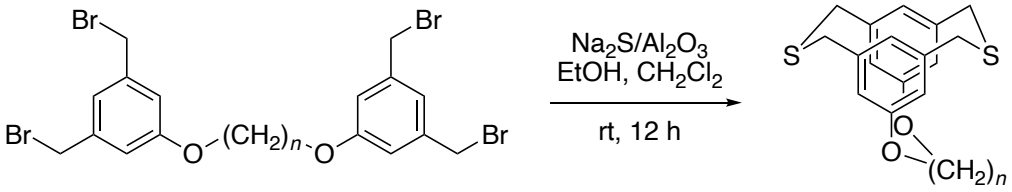
In 1980, Regen *et al.* developed a reagent in which sodium sulfide was adsorbed onto alumina.[80] The authors were interested in converting alkyl bromides into thioethers (**Scheme 2.64**). Coupling of 1-bromooctane (**2.2.40**) with $Na_2S{\cdot}9H_2O$ in hot toluene gave only 20% of the product, whereas, Na_2S-impregnated alumina gave the product in 97% yield. In addition to the improvement in yield, other advantages to this new reagent include lack of odour, shorter reaction times, and the need for only moderate dilution.



2.240 97% **2.241**

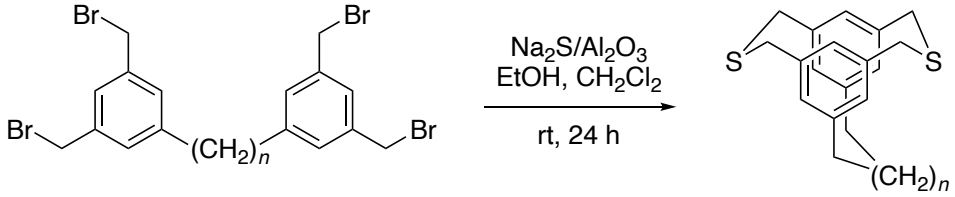
Scheme 2.60 Regen's use of Na_2S/Al_2O_3 for the synthesis of thioether **2.241**.

This reagent was adopted by the Bodwell group for the synthesis of dithiacyclophanes and they have reported numerous examples (**Scheme 2.62**). Examples include the conversion of the previously discussed tetrabromides **2.186a-d** and **2.204a-d** into the corresponding dithiacyclophanes **2.187a-d** and **2.205a-d**. Another [3.3]dithiacyclophane synthesized by the Bodwell group is the iodo-substituted system **2.243**, which came from the homocoupling of **2.242**.[81] As previously shown (**Scheme 2.37**), pyrenophane **2.166** was obtained from dibromide **2.163**.[44]



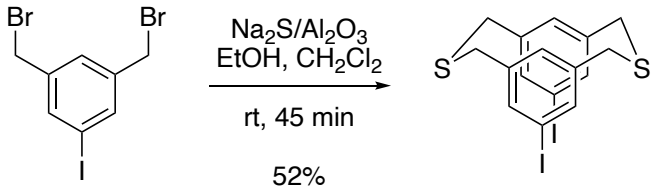
2.186a *n* = 5
2.186b *n* = 6
2.186c *n* = 7
2.186d *n* = 8

2.187a *n* = 5 (71%)
2.187b *n* = 6 (68%)
2.187c *n* = 7 (49%)
2.187d *n* = 8 (58%)

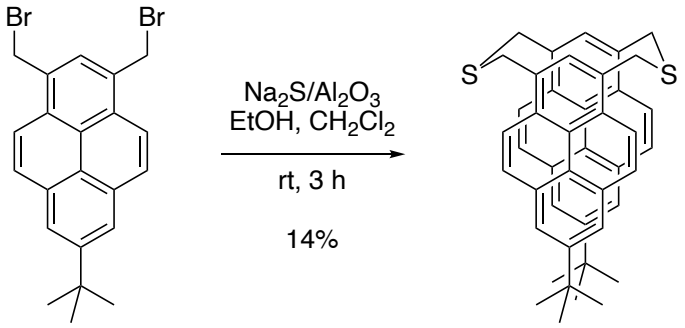


2.204a *n* = 7
2.204b *n* = 8
2.204c *n* = 8
2.204d *n* = 10

2.205a *n* = 5 (39%)
2.205b *n* = 6 (59%)
2.205c *n* = 7 (45%)
2.205d *n* = 8 (49%)



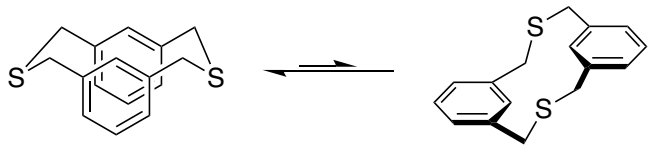
2.242 **2.243**



2.163 **2.166**

Scheme 2.61 [3.3]Dithiacyclophane formation by Na_2S/Al_2O_3.

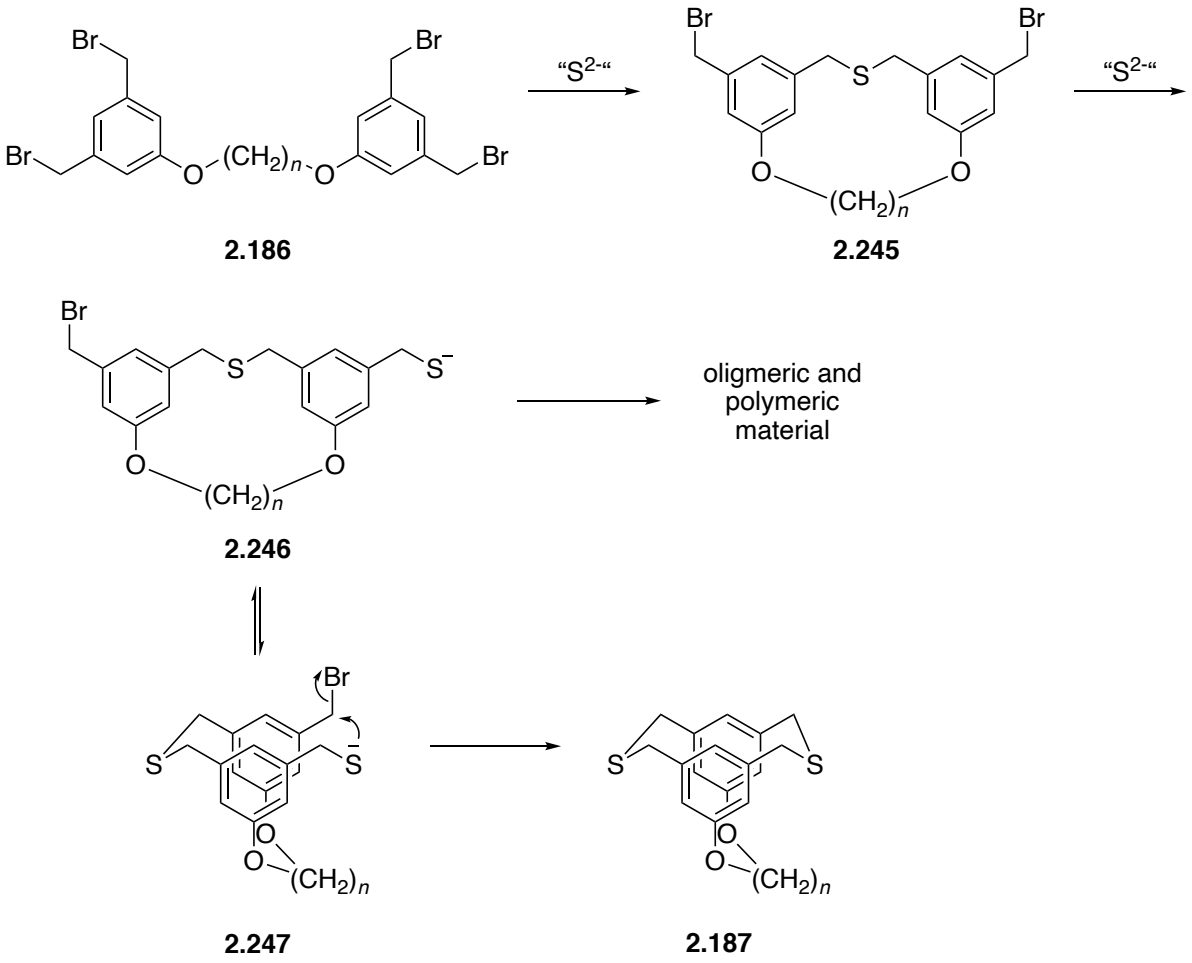
The two conformations of 2,11-dithia[3.3]metacyclophane are *syn*-**2.244** and *anti*-**2.244** (**Scheme 2.63**). In the solid state the only conformation present is *syn*-**2.244a** by X-ray crystallographic analysis, and calculations have indicated that the *syn*-conformer is more stable by 3-5 kcal/mol. The energy barrier for *syn* to *anti* conversion was determing to be 9.3-9.6 kcal/mol using VT ^{13}C NMR experiments.[82]



syn-**2.244** *anti*-**2.244**

Scheme 2.62 Conformational behaviour of 2,11-dithia[3.3]metacyclophane (**2.244**).

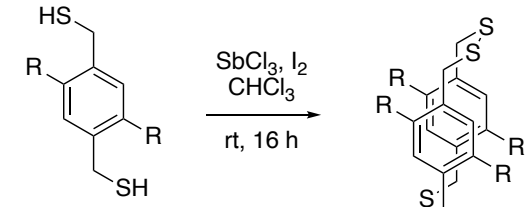
The point is that as *meta*-[3.3]dithiacyclophanes are being formed their propensity to adopt *syn*-conformations analogous to **2.244a** would impact the yields of their formations. The two thioether bridges presumably form stepwise and it is the ease with which the second thioether formation occurs that dictates the yield of the reaction (**Scheme 2.64**). Once the first thioether bridge is installed the second thioether formation can proceed intramolecularly (to give the desired product **2.187**) or intermolecularly to produce oligomeric and polymeric thioether materials. For the bridge to be formed, the mono-bridged system must exist in a conformation, such as **2.247**, where the two aromatic units are in proximity and face-to-face.



Scheme 2.63 Stepwise formation of dioxa[n.3.3]dithiacyclophanes.

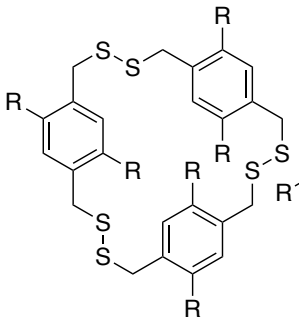
The only identifiable trend in the case of [3.3]dithiacyclophanes **2.205a-d**, where the bridges are comprised entirely of methylene units, is that the two members of the series with an even number of atoms in the long bridge, **2.205b** and **2.205d** (where *n* = 6 and 8, **Scheme 2.56**) have slightly higher yields than their odd counterparts **2.205a** and **2.205c** (where *n* = 5 and 7, **Scheme 2.56**). Na_2S/Al_2O_3 has been a workhorse for dithiacyclophane synthesis in the Bodwell group and the reagent has been prepared and used in exactly the same way since its initial use in the group. This reagent has been successful in the synthesis of numerous thioethers, especially cyclophanes, however, the yields of these reactions often have room for improvement.

A more recent approach in the synthesis [3.3]dithiacyclophanes was reported by Johnson *et al.*, which relies on dynamic disulfide bond formation from the homocoupling of dithiols (**Scheme 2.65**).[83] They demonstrated that some new and classic cyclophanes could be synthesized using this approach. When dithiol **2.248a-b** is treated with $SbCl_3$ and I_2 in chloroform, 5 different cyclized disulfide cyclophanes could be isolated (**2.249a-b**, **2.250a-b**, **2.251a-b**, **2.252a-b**, **2.253a-b**) with the smallest cyclophanes being isolated in the highest yields. As a proof of concept, the authors took cyclophanes **2.250a-b** and subjected them to sulfur extrusion with hexamethylphosphorous triamide (HMPT), which gave [3.3.3]trithiacyclophanes **2.254a-b** in good yields 72-82%. The authors made no mention of attempting the desulfurization procedure for any of the other isolated disulfide cyclophanes. To further expand the synthetic utility of this approach, the authors subjected trithiol **2.255** to their pnictogen-promoted cyclophane-forming protocol and this afforded **2.256** and **2.257** in 69% and 29% yields, respectively. Satisfyingly, both of these systems were amenable to sulfur extrusion with HMPT to give thiacyclophanes **2.238** (95%) and **2.258** (94%). While this approach is likely to have many useful applications in the synthesis of larger cyclophanes, the additional synthetic steps to access the required thiol systems makes this approach less appealing for the synthesis of pyrenophanes.

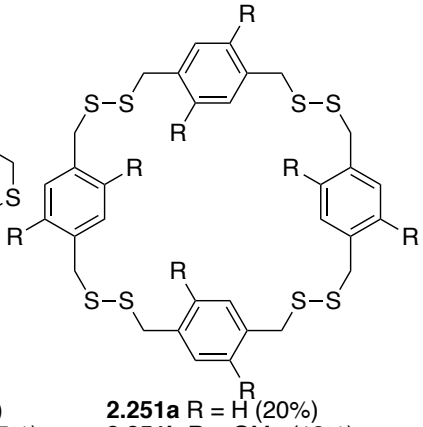


2.248a R = H
2.248b R = OMe

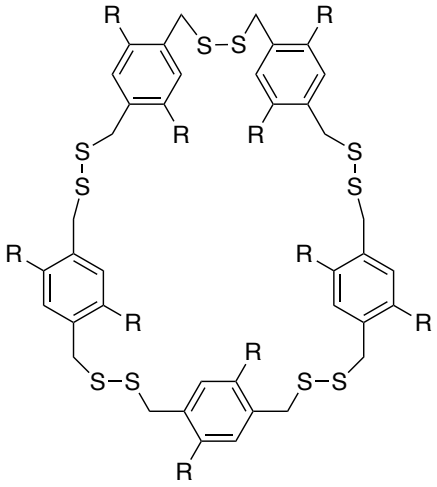
2.249a R = H (9%)
2.249b R = OMe (37%)



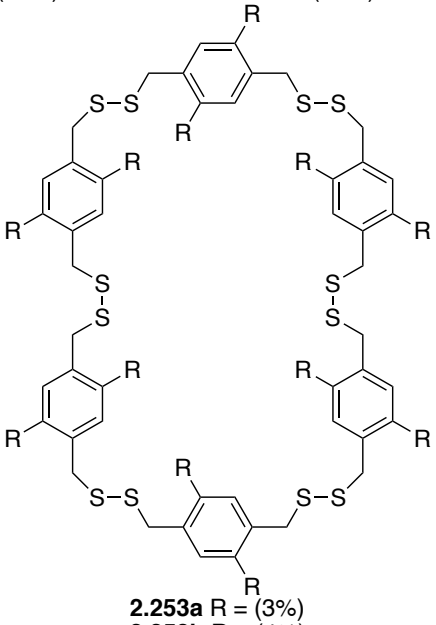
2.250a R = H (45%)
2.250b R = OMe (35%)



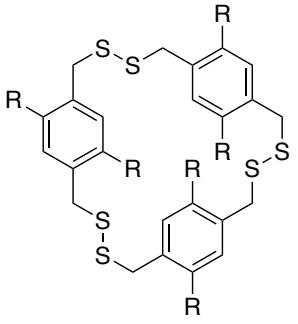
2.251a R = H (20%)
2.251b R = OMe (13%)



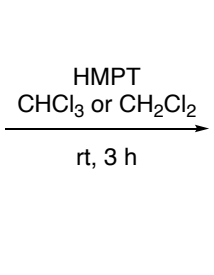
2.252a R = (7%)
2.252b R = (4%)

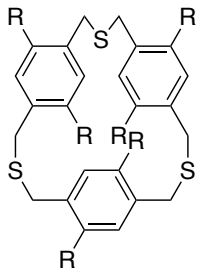


2.253a R = (3%)
2.253b R = (4%)

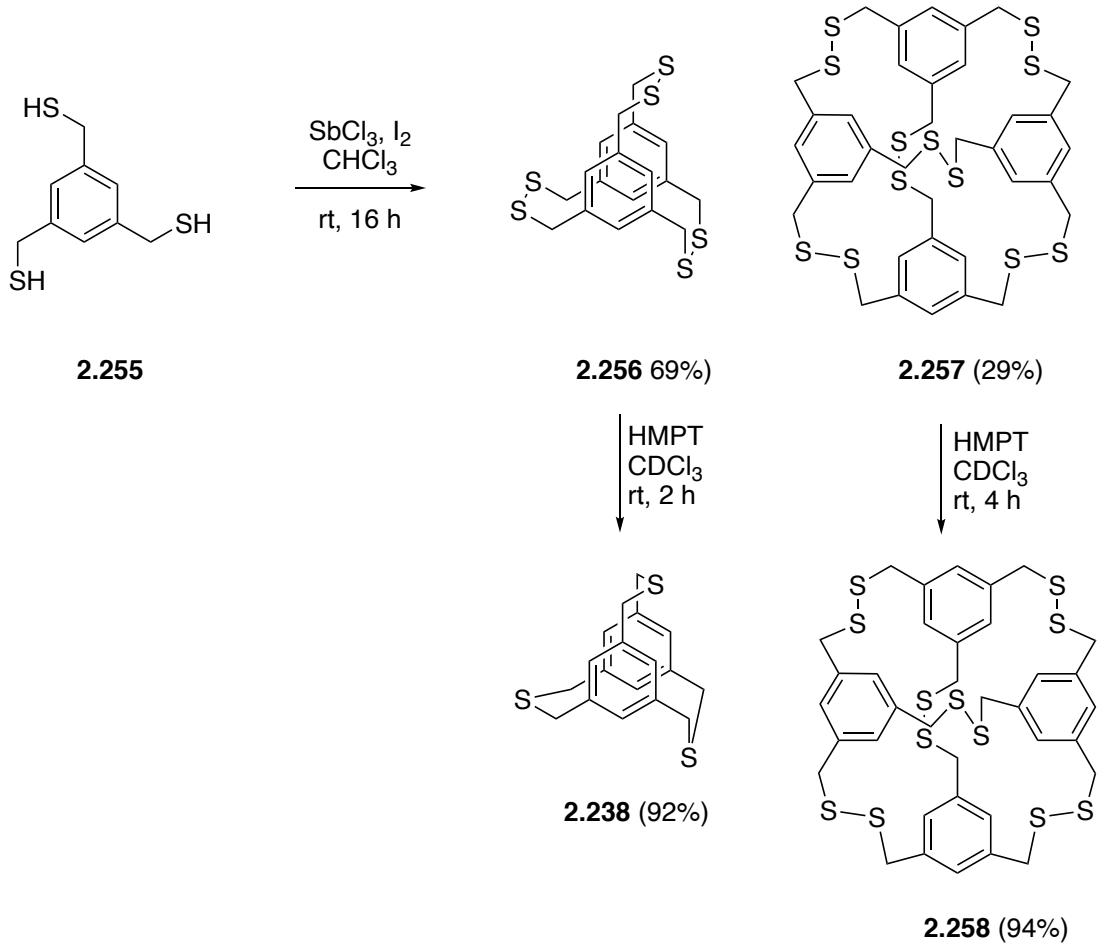


2.250a R = H
2.250b R = OMe





2.254a R = H (82%)
2.254b R = OMe (72%)



Scheme 2.64 Johnson's approach to [3.3]thiacyclophanes.

The Bodwell group also used disulfide linkages in the synthesis of dithiacyclophanes when it was found that the Na_2S/Al_2O_3 reagent proved unsuitable due to steric congestion around the benzylic positions.[84] Tethered thiol **2.259** was oxidatively coupled by reaction with I_2 and pyridine under high dilution conditions gave disulfide cyclophane **2.260** in 31% (**Scheme 2.66**). Desulfurization was accomplished by reaction with HMPT in benzene at reflux to give dithiacyclophane **2.261** in 21% yield. This methodology was inferior to the direct dithiacyclophane formation mentioned above.

Since introduction of a solid support for Na_2S saw an increase in yields and utility of sodium sulfide couplings, efforts were made to envision a new solid support material.

Based on ease of acquisition and increased interest into coal fly ash (CFA) the investigation centered around it as a replacement for alumina.

2.7: Coal Fly Ash as a New Solid Support

Coal fly ash (CFA) is the by-product that is collected from the flue gasses emitted from coal-fired boilers in thermal power plants. It has been described as one of the most complex anthropogenic materials.[85] The large quantity of CFA being produced has become an environmental concern, which has prompted worldwide efforts aimed at reuse and recycling efforts. In a review published in 2010, it was estimated that global production of CFA was 500 million tonnes, and the total utilization lay at approximately 16% (meaning 84% is waste).[86] Of all the countries using coal-fired electricity generation, China (50.2%), USA (11.7%) and India (8%) account for much of the global consumption of coal and therefore produce the most CFA. Approximately 20% of recycled CFA is utilized in the production of cement, construction of roads and brick manufacturing. Other uses for recycled CFA include ceramics,[85] zeolite synthesis,[85] gas absorption[87] and wastewater treatment,[88] among others.[89]

The chemical properties and composition of CFA is highly dependent on the coal source from which it is derived. In all cases, the major chemical components are silica (SiO_2), alumina (Al_2O_3), Fe_2O_3 and CaO in addition to smaller amounts of MgO, Na_2O, K_2O and carbonaceous materials. CFA exists as fine particles, which are mostly spherical in shape and are, for the most part, ≤75 μm in diameter. The small particle sizes translate into high surface areas (300-500 m^2/kg).[90]

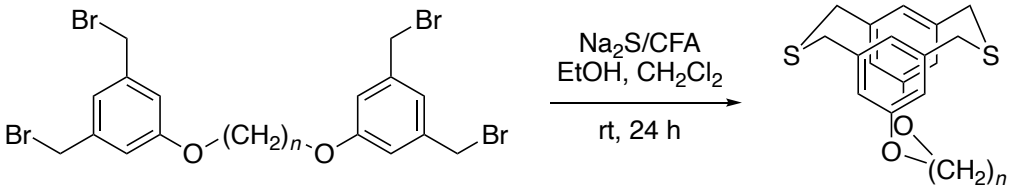
CFA has been used as a support material for catalysis and most of the catalytic CFA-supported systems have only appeared in the chemical literature in the last decade. One example is the CFA-supported CaO base catalyst for Knoevenagel condensation reactions.[91] A similar catalyst has also been utilized for transesterifications of soybean oil

turning it into fuel-grade biodiesels.[92] Another catalyst consisting of $Zr(SO_4)_2$ on CFA was used for benzylation reactions.[93] At the present moment, no studies have been published on using CFA as a solid support material for reagents instead of catalysts.

To explore this new avenue of inquiry into the uses of CFA, the use of Al_2O_3 as a solid support for Na_2S was revisited. It was thought that CFA could be a suitable replacement for alumina without the loss of any reactivity since Al_2O_3 is a major component of CFA. Therefore, a new reagent (Na_2S/CFA) was prepared in a similar fashion to Na_2S/Al_2O_3. The Na_2S loading of this reagent was calculated as moles of Na_2S per gram of material. It is worth noting that the new reagent appeared to be very hygroscopic, even more so than Na_2S/Al_2O_3. The reason is likely two-fold. Firstly, due to the deliquescent nature of sodium sulfide and secondly, CFA itself is hygroscopic and reacts readily with water. After storing for a few days, the reagent would turn into a cement-like grey solid which showed no more reactivity. For the best results, fresh reagent should be prepared just before use.

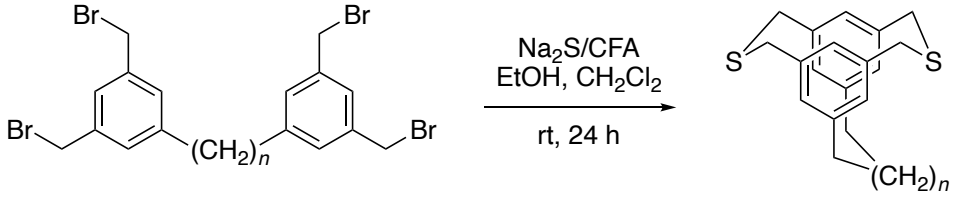
The yields of [3.3]dithiacyclophane formation using this new reagent were tested against those already reported in the synthesis of 1,*n*-dioxa[*n*](2,7)pyrenophanes (**Scheme 2.42**), [*n*](2,7)pyrenophanes (**Scheme 2.50**), 2,11-dithia[3.3]metacyclophane (**2.236**), 6,15-dimethoxy-2,11-dithia[3.3]metacyclophane (**2.237**) and 2,11-dithia[3.3]paracyclophane (**2.239**), which were previously synthesized using one or more of the previously mentioned classical approaches (**Scheme 2.66**).[94] The use of this reagent for the synthesis of a few other [3.3]dithiacyclophanes was performed by other individuals and appear in the referenced report (**Scheme 2.42**).[93] In every case, the yield was improved compared to when Na_2S/Al_2O_3 was used (**Table 2.2**). The yields for [3.3]dithiacyclophanes **2.187a-d** improved moderately for the shorter dioxa-bridged systems with 7- and 8-atoms **2.187a-b**, whereas a much larger improvement was observed in the formation of the 9- and 10-atoms bridged [3.3]dithiacyclophanes **2.187c-d**. The largest improvement was for **2.187d**, where the yield rose from 58% to 80% yield.

Even better results were obtained for the [3.3]dithiacyclophanes **2.205a-d**, where the yields all improved substantially using Na_2S/CFA. The lowest jump in yield was 26% (**2.205c**) and the largest jump in yield was 35% (**2.205d**). With the promising results for the formation of [3.3]dithiacyclophane **2.187a-d** and **2.205a-d**, the use of Na_2S/CFA for the synthesis of other [3.3]dithiacyclophanes was then investigated. Using Na_2S/CFA, 2,11-dithia[3.3]metacyclophane was obtained in 75% yield from dibromide **2.260**, which is superior to the literature reported yields of 48% (using $Na_2S{\cdot}9H_2O$)[113] and 65% (using Na_2S/Al_2O_3).[52] The new reagent even comes close to rivalling the yield of 80% obtained by thiol-bromide coupling.[13] 6,15-Dimethoxy-2,11-dithia[3.3]metacycloiphane (**2.237**) was synthesized from dibromide **2.261** in 89% yield using Na_2S/CFA, which is substantially higher than the yield obtained from the thiol-bromide coupling (49%).[76] The final system to be examined, 2,11-dithia[3.3]paracyclophane (**2.239**) had previously only been successfully synthesized using the thiol-bromide coupling strategy in 52% yield.[94] When dibromide **2.261** was treated with Na_2S/CFA, [3.3]dithiacyclophanes **2.239** formed in 49% yield, which even rivals the generally higher yielding thiol-bromide coupling (52%).



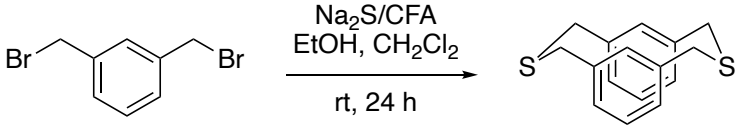
2.186a *n* = 5
2.186b *n* = 6
2.186c *n* = 7
2.186d *n* = 8

2.187a *n* = 5 (75%)
2.187b *n* = 6 (79%)
2.187c *n* = 7 (65%)
2.187d *n* = 8 (80%)

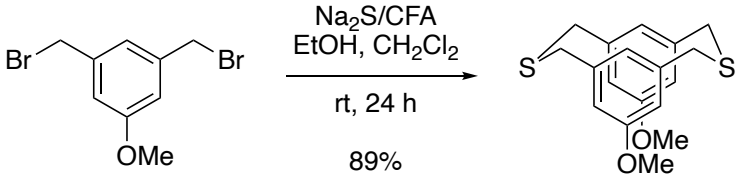


2.204a *n* = 7
2.204b *n* = 8
2.204c *n* = 8
2.204d *n* = 10

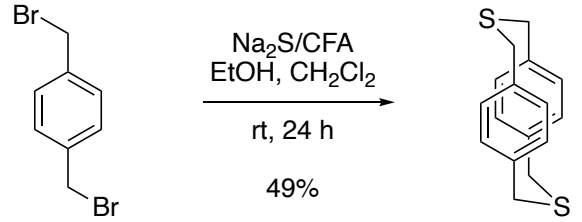
2.205a *n* = 5 (70%)
2.205b *n* = 6 (86%)
2.205c *n* = 7 (71%)
2.205d *n* = 8 (84%)



2.259 **2.236**



2.260 **2.237**



2.261 **2.239**

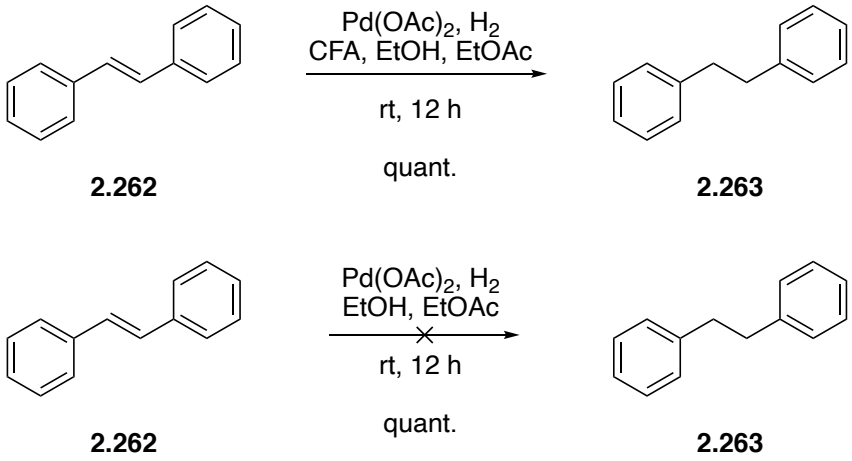
Scheme 2.65 Synthesis of [3.3]dithiacyclophanes with Na_2S/CFA.

		Isolated yields (%)	
Substrate	Product	Using Na_2S/Al_2O_3	Using Na_2S/CFA
2.186a	**2.187a**	71	75
2.186b	**2.187b**	68	79
2.186c	**2.187c**	49	65
2.186d	**2.187d**	58	80
2.204a	**2.205a**	39	70
2.204b	**2.205b**	59	86
2.204c	**2.205c**	45	71
2.205d	**2.205d**	49	84
2.259	**2.236**	65	75
2.260	**2.236**	49 (using thiol-bromide coupling)	89
2.261	**2.239**	52 (using thiol-bromide coupling)	49

Table 2.2 Comparison of yield of dithiacyclophane formation using Na_2S/CFA to other methods.

With the success of coal fly ash (CFA) as a solid support for sodium sulfide in the synthesis of dithiacyclophanes, it seemed like a natural progression to explore what other solid supports used in synthesis could be replaced with CFA. Based on the earlier work utilizing *in situ* generated Pd supported on charcoal for the catalytic hydrogenation of internal alkynes (**Scheme 2.54**), the possibility of replacing charcoal could be replaced with CFA was investigated. As a model system, the catalytic hydrogenation of a simple alkene was investigated (**Scheme 2.67**). Accordingly, *trans*-stilbene (**2.262**) was dissolved in a 1:1 mixture of MeOH/EtOAc and then $Pd(OAc)_2$ (1 mol%) and CFA (10 *w/w* $Pd(OAc)_2$) were added. Two balloons of H_2 gas were bubbled through the stirred reaction mixture

and stirring was continued under a H_2 atmosphere for 12 h. This led to the isolation of dibenzyl (**2.263**) in quantitative yield. To check that the CFA alone was not responsible for the catalytic hydrogenation, a control reaction was performed on *trans*-stilbene in the absence of $Pd(OAc)_2$. No reaction occurred and *trans*-stilbene was recovered quantitatively.

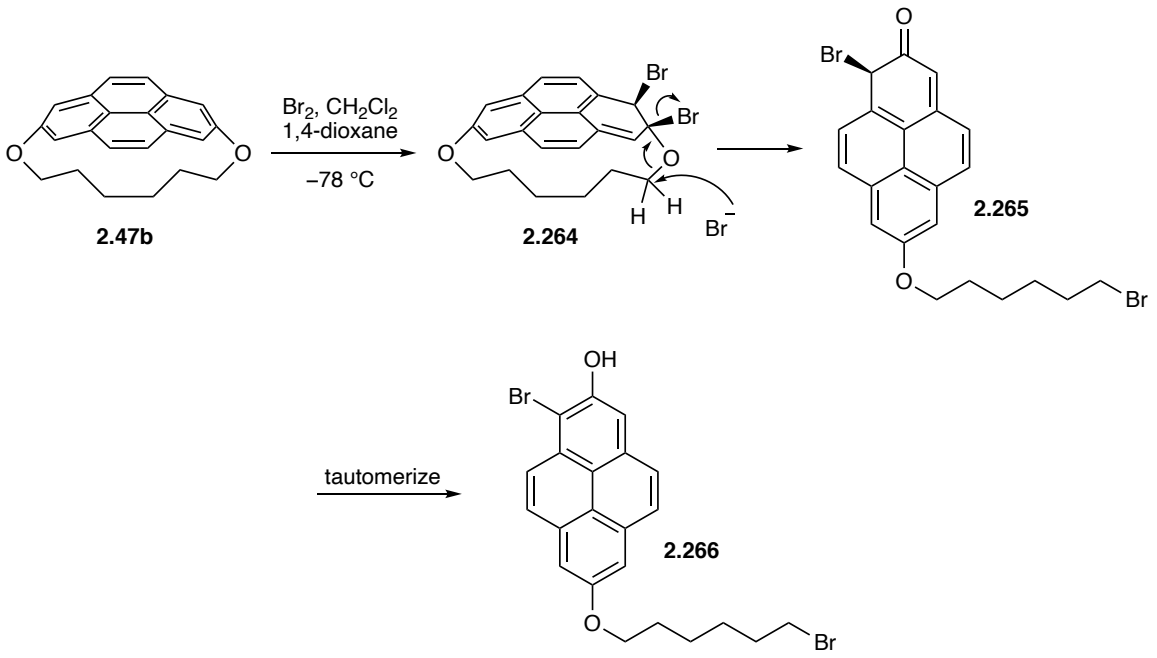


Scheme 2.66 CFA as a solid-support for catalytic hydrogenations.

Based on these preliminary results on the utility of CFA as a solid support, it would appear that there are abundant oppurtunites for future wotk with CFA to be undertaken.

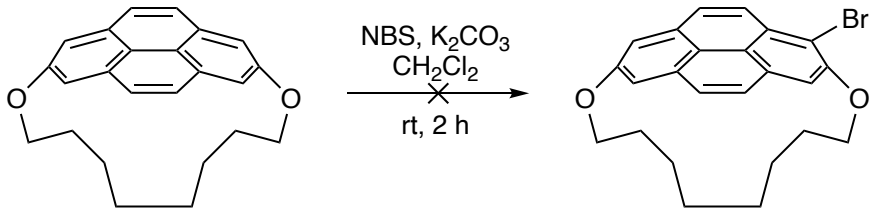
2.8: Reactivity of 1,*n*-Dioxa[*n*](2,7)pyrenophanes (2.47a-b)

The Bodwell group briefly investigated some reactivity of the 1,*n*-dioxa[*n*](2,7)pyrenophanes towards bromine, acids and *t*-BuLi with little success in maintaining the pyrenophane structure. The dioxa-bridges appear to be especially susceptible to bridge rupture to alleviate molecular strain. For example, when 1,8-dioxa[8](2,7)pyrenophane (**2.47b**) was treated with molecular bromine in a mixed solvent system of 1,4-dioxane and CH_2Cl_2 at -78 °C the ring opened and dibromide **2.266** was the only isolated product (**Scheme 2.68**). A mechanism for the formation of this product was proposed, which first involved Br_2 addition across the 1 and 2 positions of the pyrene system from the top side to give dihydropyrenophane **2.264**. Attack of a bromide ion in an S_N2 fashion could then lead to the rupture of the bridge. Tautomerism of the resulting α-bromoketone **2.265** would then afford the rearomatized bromohydroxypyrene **2.266**. In retrospect, there does not appear to be any need to invoke the addition of two Br atoms, but rather just one at the 1 position akin to normal electrophilic aromatic substitution.



Scheme 2.67 Bodwell's bromination of 1,8-dioxa[8](2,7)pyrenophane (**2.47b**).

The improved synthesis of the 1,*n*-dioxa[*n*](2,7)pyrenophanes (**Section 2.3**) allowed easier access to the synthetically useful amounts of material and this provided an opportunity to extend the scope of the study of their chemistry. This started with the bromination of the least strained member of the series, 1,10-dioxa[10](2,7)pyrenophane (**2.47d**). The first question to be addressed was whether the lower amount of strain in this compound would result in electrophilic aromatic substitution instead of bridge cleavage. When 1,10-dioxa[10](2,7)pyrenophane (**2.47d**) was treated with NBS in the presence of K_2CO_3 (to neutralize HBr generated in the reaction) in CH_2Cl_2, no reaction occurred and the starting pyrenophane was completely recovered (**Scheme 2.69**). The non-reactivity of the pyrenophane system with NBS was surprising for two reasons. Firstly, the pyrene core should be relatively electron rich and activated towards electrophilic aromatic substitution. Secondly, in MacKinnon's MSc thesis it was shown that 2-hydroxypyrene derivatives were readily *ortho*-substituted via electrophilic aromatic system with NBS in CH_2Cl.[96] Although the oxygen lone pairs in the dioxa-pyrenophanes do not overlap with the pi system in the same way. The next logical experiments to conduct would be to run the reaction at elevated temperature, and to run the reaction in DMF instead of CH_2Cl_2, which has been shown to cleanly mono-brominate various aromatic systems at room temperature, especially for phenols and anisoles.

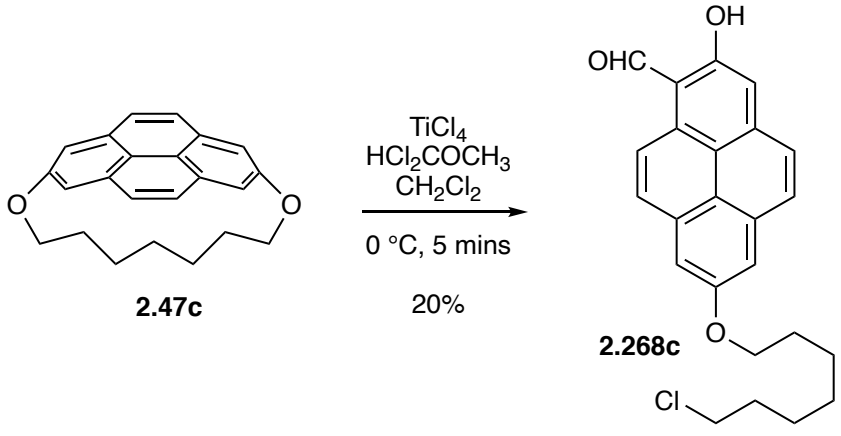


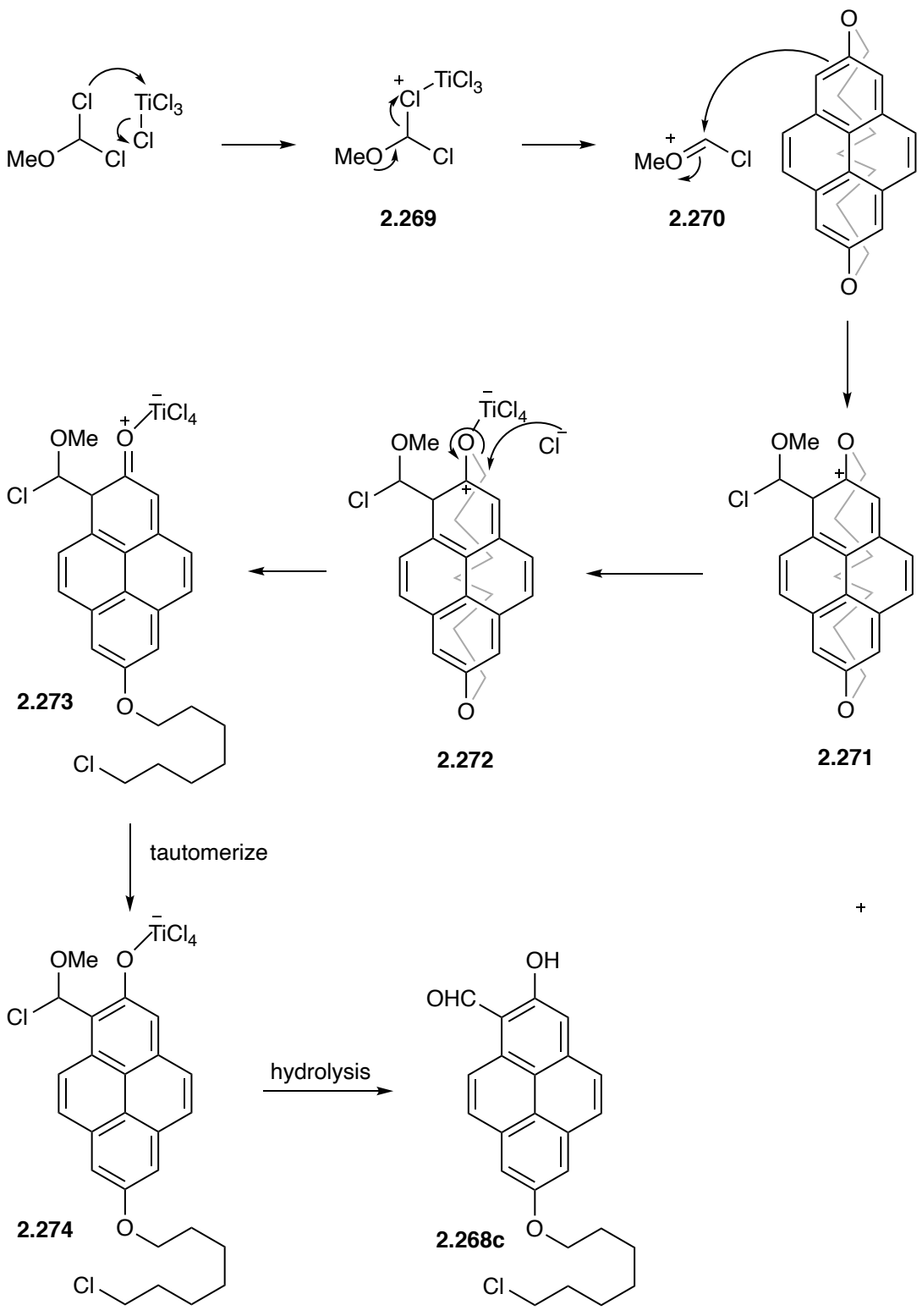
2.47d **2.267**

Scheme 2.68 Attempted bromination of 1,10-dioxa[10](2,7)pyrenophane (**2.47d**).

Cracking the bromination conundrum would be extremely interesting because it would allow extension of the pyrene aromatic core through cross-coupling chemistry.

Another sought-after way of functionalizing the 1,*n*-dioxa[*n*](2,7)pyrenophanes was formylation. Rieche formylation at the position adjacent to the bridgehead was attempted. 1,9-Dioxa[*n*](2,7)pyrenophane (**2.47c**) in CH_2Cl_2 was treated with $TiCl_4$ and dichloromethyl methyl ether in CH_2Cl_2 at 0 °C. Complete consumption of the starting material occurred after 5 min (TLC analysis) and a new vibrantly yellow spot was formed. The compound was isolated and found to be a bridge-ruptured hydroxyaldehyde **2.268c** (20%). When the reaction was run at –78 °C, no reaction was observed by TLC after 1 h. When this reaction was allowed to gradually warm up to 0 °C, the only TLC mobile product that formed was the previously isolated **2.268c**. A potential mechanism to account for the formation of **2.268c** is outlined in **Scheme 2.70**. Dichloromethyl methyl ether reacts with $TiCl_4$ to form Lewis acid-base pair **2.269** which then expels $TiCl_4$ to give methylated acid chloride **2.270** as the reactive electrophile. Nucleophilic attack of the aromatic system on electrophilic **2.270** aided by the bridge-oxygen to give intermediate **2.271**, whose resonance structure can coordinate to $TiCl_4$ (**2.272**). A chloride ion can attack the bridge methylene, which ruptures the bridge to give "opened" system **2.273**, which can tautomerize to rearomatize the pyrene system to afford **2.274**. Upon acidic aqueous work-up the α-chloroalkyl methyl ether is hydrolyzed to the corresponding aldehyde and final product **2.268c**.

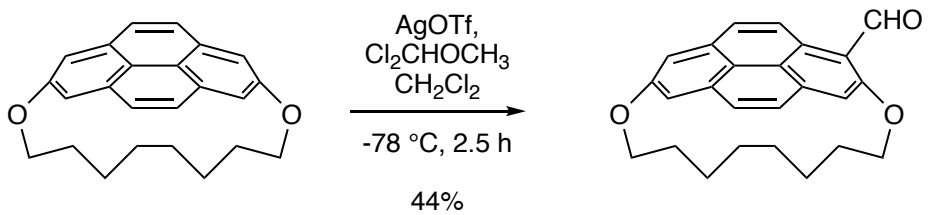




Scheme 2.69 Attempted Rieche formylation of 1,9-dioxa[9](2,7)pyrenophane (**2.47c**).

The same reaction was performed on the longer-bridged, less strained 1,10-dioxa[10](2,7)pyrenophane (**2.47d**) on a small scale and TLC analysis indicated that the outcome was the same.

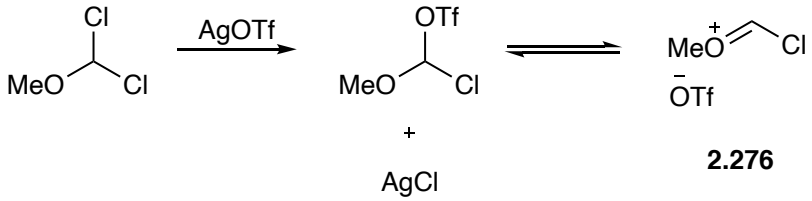
$TiCl_4$ promoted Rieche formylation is not the only tool in the organic chemist's arsenal. Numerous aromatic systems have been formylated by the Reimer-Tiemann reaction, Gatterman reaction, Vilsmeier-Haack reaction and Duff reaction among others. A lot of formylation reactions require the use of strongly basic conditions, strongly Lewis acidic conditions or elevated temperatures, all of which could be troublesome to 1,*n*-dioxa[*n*](2,7)pyrenophanes. A report by Doi *et al.* on the direct formylation of anisoles with a highly reactive formylating agent, Cl_2CHOMe-AgOTf, showed good formylation yields without dealkylation of the alkoxy groups.[97] When 1,10-dioxa[10](2,7)pyrenophane (**2.47d**) was treated with 3 equiv. of both dichloromethyl methyl ether and silver triflate, formylated pyrenophane **2.275d** was isolated in 44% yield (**Scheme 2.71**). The ^{1}H NMR spectrum of **2.275d** clearly shows the desymmetrization of the pyrene system and presence of an aldehyde proton (δ 10.94 ppm). Desymmetrization of the geminal methylene protons in the bridge was also observed and the presence of some highly shielded signals (–0.60 - –1.17 ppm) clearly indicated that the system retained its cyclophane structure. Unfortunately, when 1,9-dioxa[9](2,7)pyrenophane was subjected to these reaction conditions it was quickly consumed at –78 °C in 5 mins by TLC analysis, but no evidence of the formylated pyrenophane was present. Based on this data, it seems the 1,10-dioxa[10](2,7)pyrenophane (**2.47d**) is the limit at which non-destructive formylation is possible using this chemistry.



2.47d **2.275d**

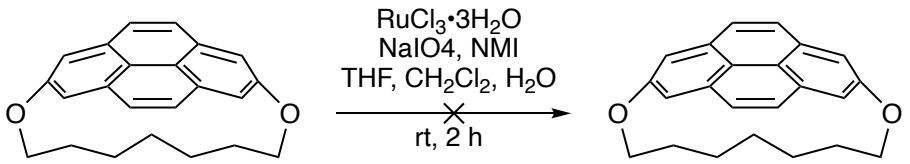
Scheme 2.70 Successful formylation of 1,10-dioxa[10](2,7)pyrenophane (**2.47d**).

A possible explanation for the formylation success under these reaction conditions is outlined in Doi *et al.'s* report (**Scheme 2.72**). Silver triflate reacts with dichloromethyl methyl ether by substitution of a chloride with triflate to afford **2.276a**, which exists in equilibrium with the highly electrophilic species **2.276b**. This species reacts with the aromatic system in much the same way as in the Rieche formylation with $TiCl_4$, but Ag^+ should interact less with the bridge-oxygen atoms due to the mismatch of hard base with soft acid from hard-soft acid-base (HSAB) theory.



Scheme 2.71 Possible mechanism involving AgOTf and Cl_2CHOCH_3.

Another pyrenophane functionalization of interest was *K*-region oxidation to give a 4,5-diketone system. A previously shown in **Scheme 2.31**, our group has had repeated success with this transformation on numerous non-pyrenophane pyrene derivatives as well with [10](2,7)pyrenophane. When a pyrene derivative is treated with a catalytic amount of $RuCl_3 \cdot 3H_2O$ (10 mol%), in the presence of a stoichiometric oxidant $NaIO_4$ along with a small amount of the additive *N*-methylimidazole (5 mol%) in the mixed solvent system THF, CH_2Cl_2 and water, the 4,5-diketone is obtained in around 50% yield, depending on the substrate. When 1,9-dioxa[9](2,7)pyrenophane (**2.47c**) was subjected to these reaction conditions no change occurred and only starting material was recovered, with no evidence of the formation of diketone **2.277c** (**Scheme 2.73**). It is not immediately obvious why this reaction should fail in the dioxa-pyrenophane system.



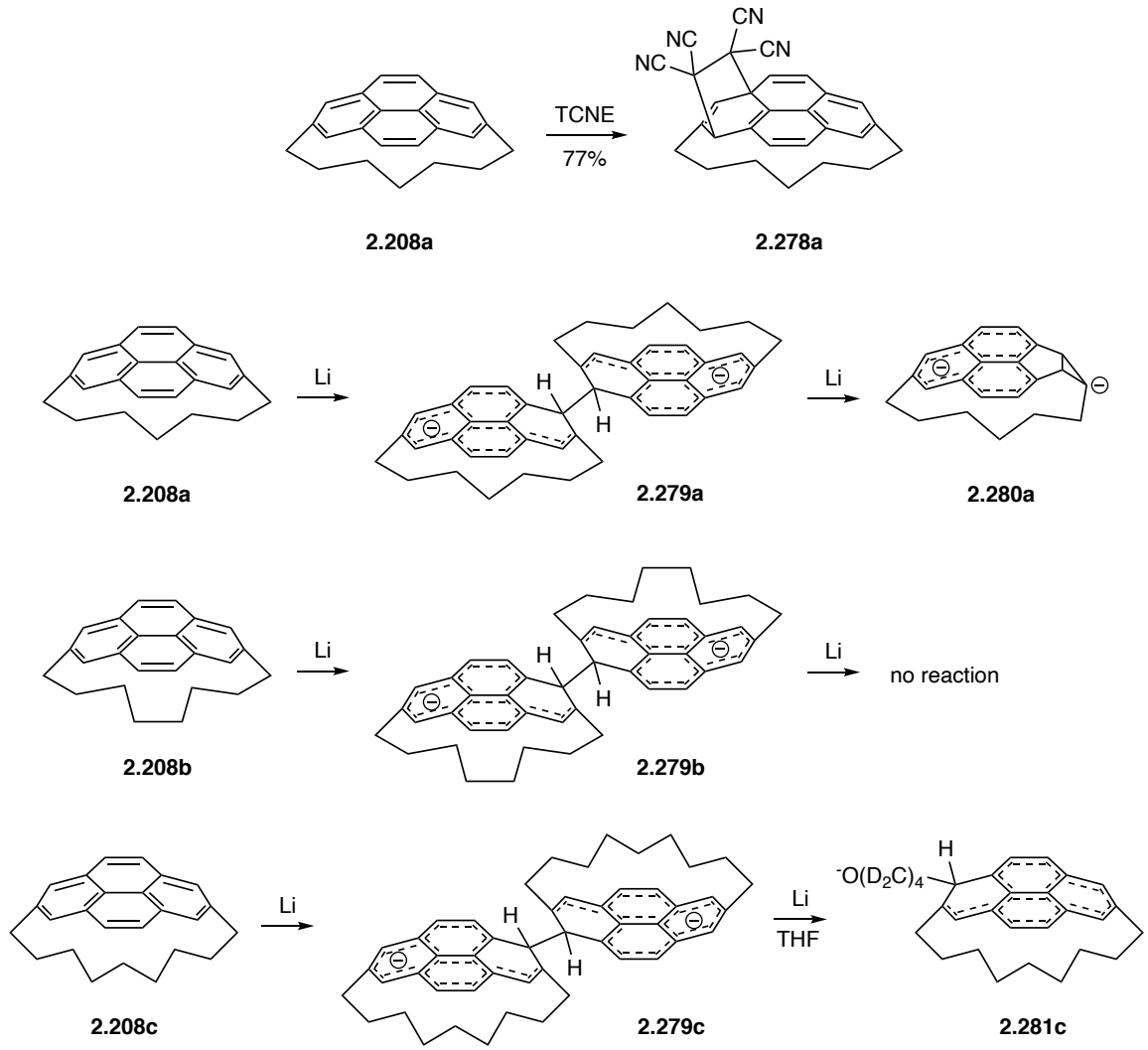
2.47c **2.277c**

Scheme 2.72 Attempted *K*-region oxidation of 1,9-dioxa[9](2,7)pyrenophane (**2.47c**).

With very little success, previously and in this work, the 1,*n*-dioxa[*n*](2,7)pyrenophane (**2.47a-d**) series appears to be poor substrates for further modification. ThIS seems to be especially true for the more strained members of the series. Attention was therefore turned to the [*n*](2,7)pyrenophanes **2.208a-d**, which were expected to be far less prone to bridge cleavage.

2.9: Reactions of the [*n*](2,7)Pyrenophanes (2.208a-d)

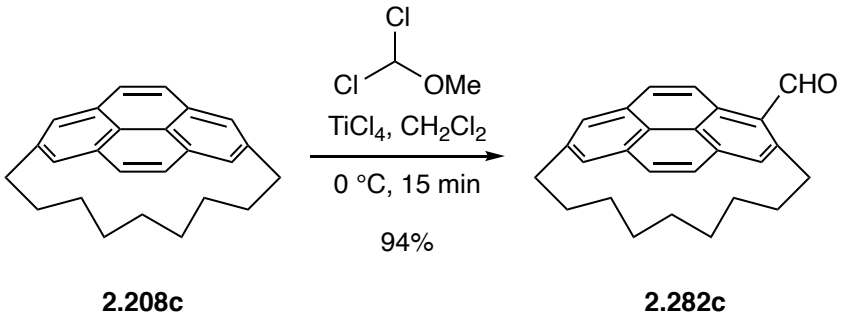
To date, very little of the chemistry of [*n*](2,7)pyrenophanes (**2.208a-d**) has been reported in the literature. When these pyrenophanes were treated with tetracyanoethylene (TCNE), only the most strained [7](2,7)pyrenophane (**2.208a**) showed any reactivity, forming adduct **2.278a** in 77% yield (**Scheme 2.74**).[61] The reduction of these pyrenophane systems with alkali metals was also explored (**Scheme 2.74**).[98] All of the [*n*](2,7)pyrenophanes (**2.208a-d**) underwent one-electron reduction with lithium or potassium and the resulting radical anions dimerized to give dianions **2.279a-d**. The shortest-bridged [7](2,7)pyrenophane (**2.208a**) could be further reduced, which resulted in the unique transformation of a benzene ring into a cyclopropano-cyclopentano ring system fused to a phenalenyl anion system **2.280a**. [8](2,7)Pyrenophane (**2.208b**) could not be further reduced. [9](2,7)pyrenophane (**2.208c**) and [10](2,7)pyrenophane (**2.208d**) behaved like pyrene upon a second reduction to give formally antiaromatic dianions, which ultimately reacted with a solvent molecule to give **2.281c-d**.



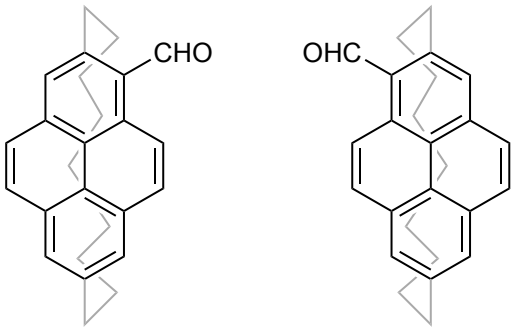
Scheme 2.73 Known reactivity of [*n*](2,7)pyrenophane with alkali metals (**2.208a-d**).

To date, the reactivity of [*n*](2,7)pyrenophanes towards electrophilic aromatic substitution reactions has not been explored. Direct formylation using Rieche conditions was investigated first because the all-methylene bridges should be more resistant to rupture. Reaction of [9](2,7)pyrenophane (**2.208c**) with dichloromethyl methyl ether in the presence of $TiCl_4$ in CH_2Cl_2 at 0 °C for 15 min afforded functionalized pyrenophane **2.208c** in an excellent 94% yield (**Scheme 2.75**). In addition to the high yield, no evidence of any bridge ruptured product was observable by TLC analysis (based on previous experience with **2.268c**). Functionalization of the pyrene core desymmeterizes the

product formyl-pyrenophane **2.208c**, which is C_1-symmetric and therefore chiral. No efforts were made to separate the enantiomers. In the future, the aldehyde handle might be used for an attempt at classical resolution with a chiral amine.



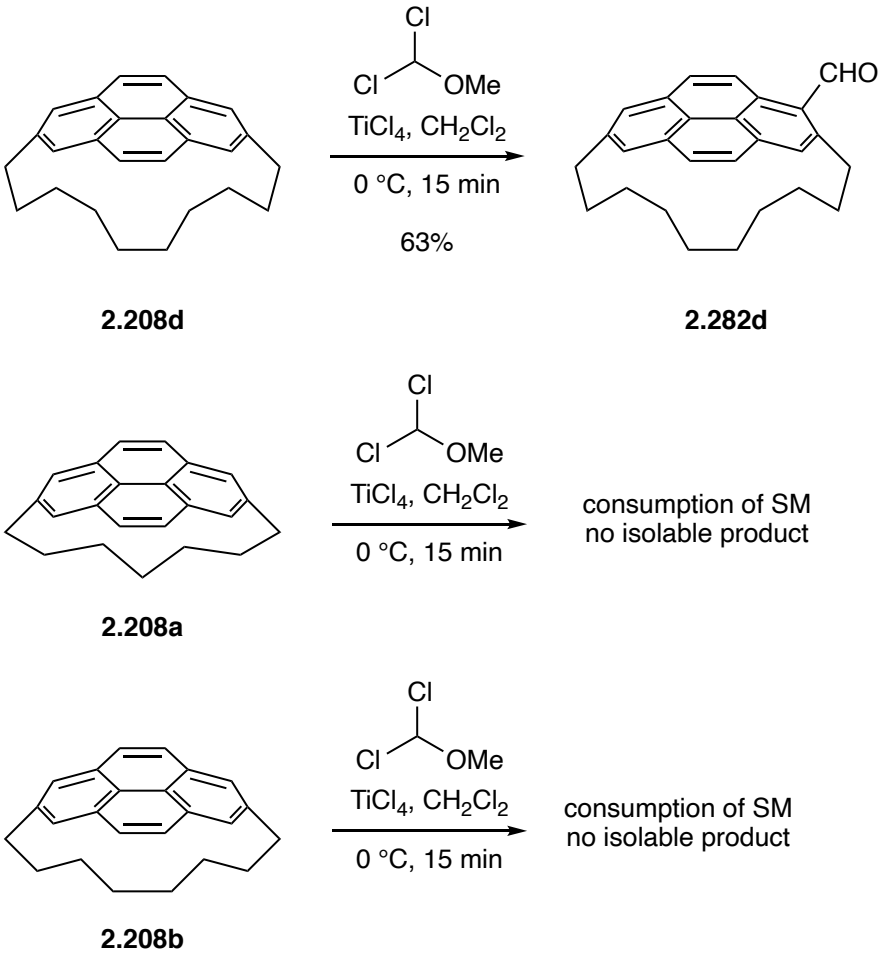
2.208c **2.282c**



enantiomers of **2.282c**

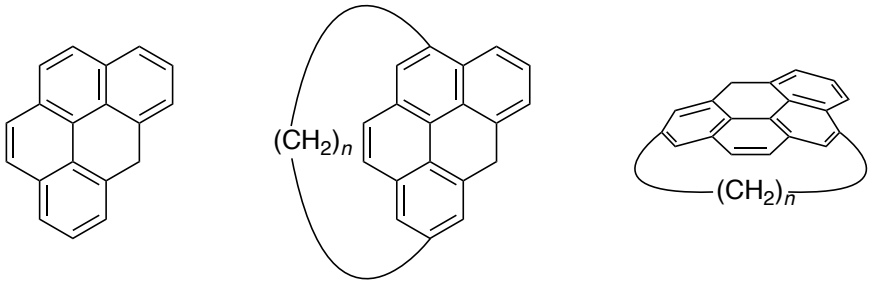
Scheme 2.74 Rieche formylation of [9](2,7)pyrenophane (**2.208c**).

Rieche formylation proceeded smoothly with [10](2,7)pyrenophane (**2.208d**) to give formyl-pyrenophane **2.282d**, albeit in a slightly lower yield (63%) than was the case for the [9](2,7)pyrenophane system (**Scheme 2.76**). The shorter-bridged pyrenophanes, [7](2,7)pyrenophane and [8](2,7)pyrenophanes (**2.208a** and **2.208b**), were completely consumed in a few minutes under these reaction conditions but no mobile spots were observed (TLC analysis). Based on these preliminary results it appears as if [9](2,7)pyrenophane (**2.208c**) may be the "goldilocks" molecule for further investigations into post-synthetic modifications.



Scheme 2.75 Formylation reactions of other [*n*](2,7)pyrenophanes **2.208a**, **2.208b** and **2.208d**.

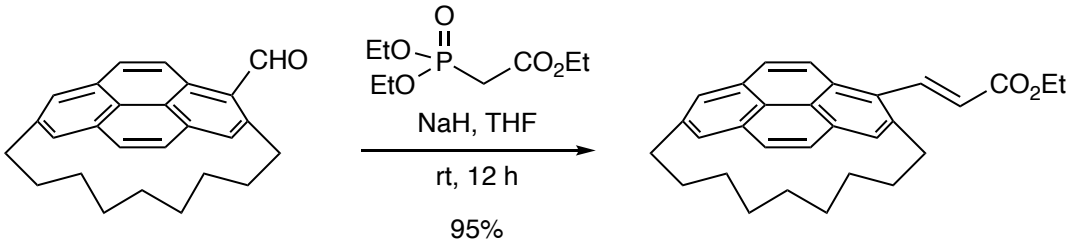
With access to reasonable quantities of formyl-pyrenophane **2.208c** (*ca.* 100 mg), further structural modification was undertaken with the goal of growing the aromatic system and thus furnishing a cyclophane with an aromatic system that is not only larger, but also new to cyclophane chemistry. Specifically, annulation of *peri*-region would result in the expansion of the pyrene system into olympicene (**2.283**). The resulting cyclophane would be an [*n*]olympicenophane (**2.284**) (**Scheme 2.77**).



2.283 **2.284**

Scheme 2.76 Olympicene (**2.283**) and proposed [*n*]olympicenophane (**2.284**).

In an effort to synthesize [9](4,10)olympicenophane **2.284**, the first step was a Horner-Wadsworth-Emmons reaction of aldehyde **2.282c** using triethyl phosphonoacetate / NaH which gave the *E*-configured α,β-unsaturated ester **2.285c** (95%). It is likely that this reaction went to completion long before the 12 hours of reaction time, but the starting material and product have the same R_f values and appear identical on TLC.

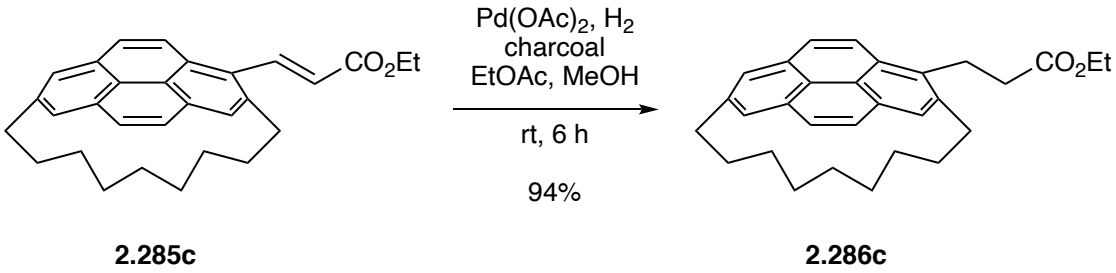


2.282c **2.285c**

Scheme 2.77 Horner-Wadsworth-Emmons olefination of aldehyde **2.282c**.

Hydrogenation of the olefin proved to be more difficult than expected. It was found to be resistant to conjugate reduction with $NaBH_4$ (a method that was employed successfully in other systems reported in this thesis (Section 3.7)). The HOMO of pyrene has a large orbital coefficient at the 1 position and this contributes to the strong preference for electrophilic aromatic substitution at this position. It may also serve to lower the reactivity of the alkene toward conjugate reduction by acting as an electron

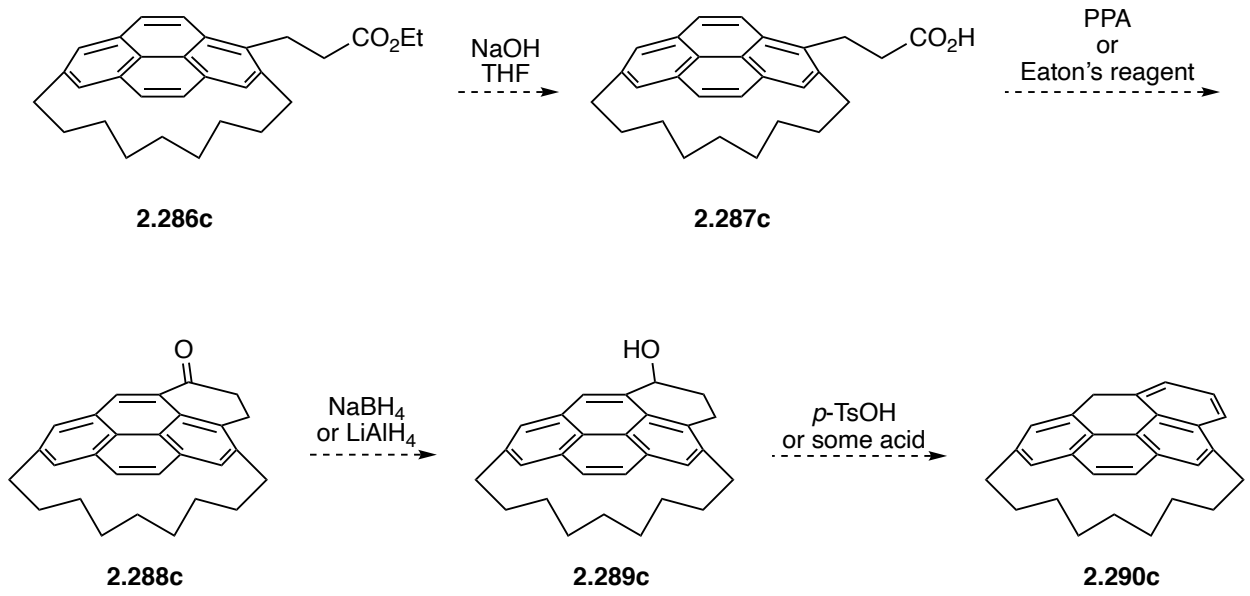
donating group. Catalytic hydrogenation with Pd/C and H_2 gas proved meddlesome giving incomplete reaction. Once again, Felpin's *in situ* method (Section 2.5) showed itself to be very effective. The use of $Pd(OAc)_2$, H_2 gas and charcoal in a mixture of EtOH and EtOAc (for solubility) resulted in clean hydrogenation of **2.283c** to give 2.286c in 94% yield.



2.285c **2.286c**

Scheme 2.78 Hydrogenation of olefin **2.285c**.

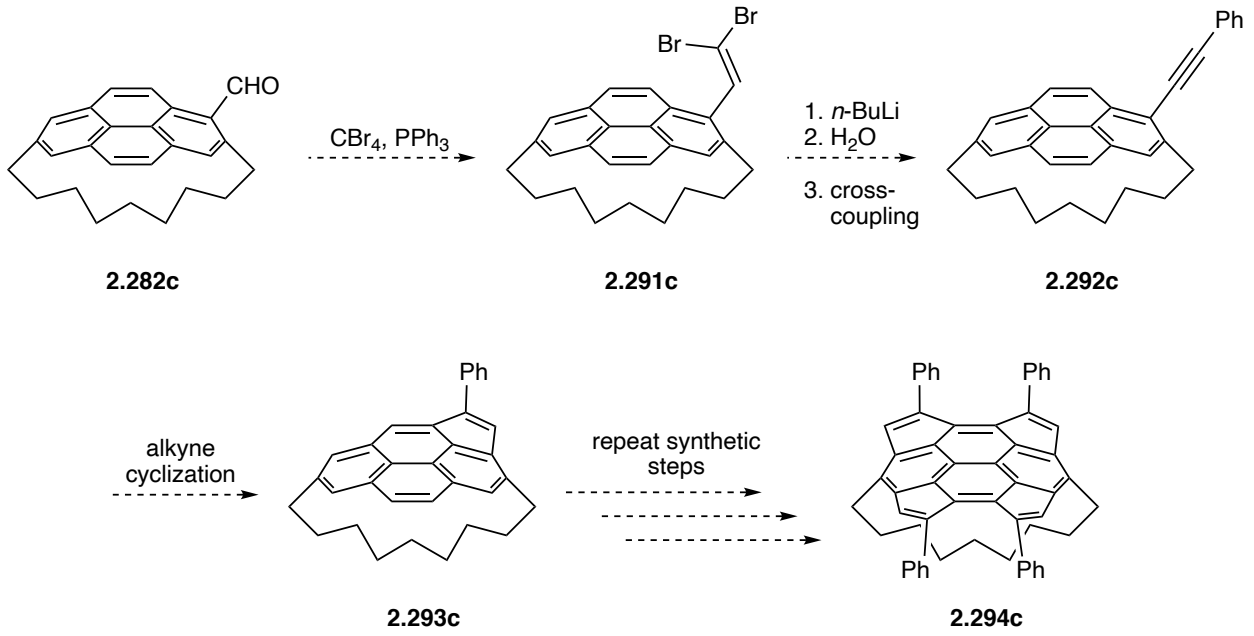
No further progress toward [9](4,10)olympicenophane was made, but the final few steps could conceivably follow a synthetic route akin to the one taken in the synthesis of the parent olympicene (**2.283**). Hydrolysis of the ester would afford acid **2.287c** and a subsequent Friedel-Crafts acylation-type cyclization, either directly from the acid with a dehydrating reagent such as polyphosphoric acid or Eaton's reagent or from the corresponding acid chloride using $AlCl_3$, would give ketone **2.288c**. This system would then be reduced to the corresponding alcohol **2.289c** and then dehydrated under acidic conditions to give the final [9](4,10)olympicenophane (**2.290c**) product. The methylene group of the olympicene system has been drawn in the centre of the aromatic core because this is where it was found to reside in the parent compound **2.283**. It was also calculated to be the lowest energy isomer.



Scheme 2.79 Possible synthetic route to [9](4,10)olympicenophane (**2.290c**).

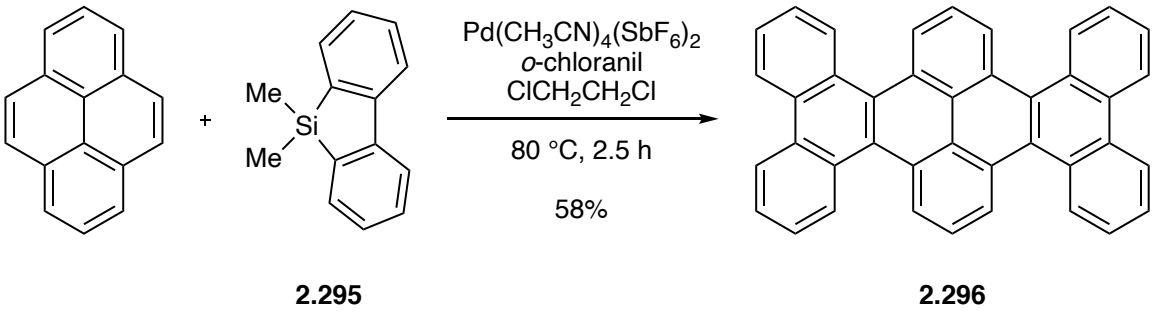
2.10: Other Future Work on the Synthetic Modification of [*n*](2,7)Pyrenophanes

Since the features of non-planarity and therefore strain is already present in [*n*](2,7)pyrenophanes, it may allow one the opportunity to build the pyrene structure further and create large PAH cyclophane systems. For example an iterative approach, outlined below, may give access to a multiple cyclopenta-fused pyrene systems potentially before a synthesis of the parent compounds is realized. Formyl-pyrenophane **2.282c** could be subjected to Ramirez dibromoolefination to give compound **2.291c** which could be then be converted to the corresponding alkyne **2.292c** under Corey-Fuchs reaction conditions. *Peri* fusions by alkyne cyclizations are known in the literature, but the complete cyclopentannulated pyrene system is unknown.[137] In the case of the pyrenophanes, the aromatic system in the starting material is already non-planar, so there may be a better chance that alkyne cyclization could be successful to give compound **2.293c**, which contains one cyclopenta-fused ring system. Repeating this procedure 3 more time (or accessing four-fold functionalized pyrenes) may give access to four-fold cyclopenta-fused pyrenophane **2.294**.



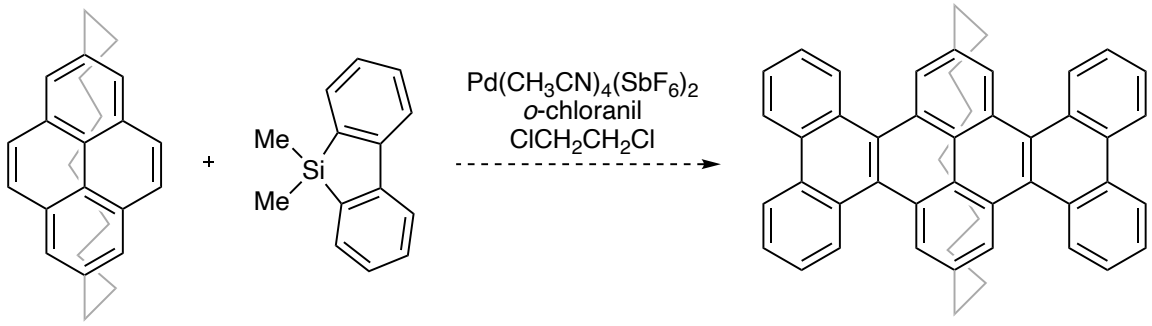
Scheme 2.80 Formyl-pyrenophanes as scaffolds for further modifications.

Another possibility lies in the utilization of annulative π-extension (APEX) chemistry on the *K*-regions of the pyrene system. Itami has shown that *K*-regions, including those of pyrene, can be π-extended using dibenzosiloles (**2.295**) in the presence of a cationic Pd catalyst and an oxidant such as *o*-chloranil to give, in the case of pyrene, compound **2.296** (**Scheme 2.82**).[100]



Scheme 2.81 Itami's *K*-region APEX chemistry.

APEX chemistry on the [*n*](2,7)pyrenophanes would provide access to a new set of cyclophanes, the aromatic system of which would contain 40 carbon atoms (**Scheme 2.83**). This would be just two carbons shy of the largest aromatic system (hexabenzocoronene, C_{42}) to ever have been incorporated in a cyclophane.[39]



2.208c **2.295** **2.296**

Scheme 2.82 Proposed APEX reaction of [9](2,7)pyrenophane.

2.11: Conclusions

This Chapter has outlined the long history of pyrenophane chemistry and its wide breadth of structural motifs, properties and applications in the greater field of cyclophane chemistry. The syntheses of the 1,*n*-dioxa-[*n*](2,7)pyrenophanes and [*n*](2,7)pyrenophanes have been improved and the creation of a new reagent for thiacyclophane formation has been introduced. This reagent has the potential to become another workhouse in the field of cyclophane chemistry. Coal fly ash has the potential to become more widely used as a solid support for other reagents due to its complex chemical nature and wide availability. Finally, some exploration into the feasibility of (2,7)pyrenophane system towards electrophilic aromatic substitution reactions was conducted. Even in the parent [*n*](2,7)pyrenophanes, which lack ether groups that are prone to cleavage, the smaller members of the series do not undergo formylation as cleanly as the less strained higher homologues. The side reactions that are occurring in the smaller systems deserve further attention.

2.12: References

(1) Geddes, C. D.; Lakowicz, J. R.; Vullev, V. I.; Jiang, H.; II, G. J. *Excimer Sensing*; Boston, MA: Springer US: Boston, MA, 2005; Vol. 10.

(2) Figueira-Duarte, T. M.; Müllen, K. Pyrene-Based Materials for Organic Electronics. *Chem. Rev.* **2011**, *111*, 7260–7314.

(3) Umemoto, T.; Kawashima, T.; Sakata, Y.; Misumi, S. Layered Compounds. XXXIV. The Synthesis of Metacyclopolynuclear Carbophanes via Transannular Reaction of Multilayered Metacyclophanes. *Tetrahedron Lett.* **1975**, *16*, 463–466.

(4) Umemoto, T.; Kawashima, T.; Sakata, Y.; Misumi, S. Layered Compunds. XXVIII. [2.2](1,3)Pyrenophane and Another Triple-layered Metacyclo-pyrenophane. *Chem. Lett.* **1975**, *4*, 837–840.

(5) Hayashi, T.; Mataga, N.; Umemoto, T.; Sakata, Y.; Misumi, S. Solvent-Induced Polarization Phenomena in the Excited State of Composite Systems with Identical Halves. 2. Effects of Solvent Polarity upon the Fluorescence of [2.2](1,3)Pyrenophane. *J. Phys. Chem.* **1977**, *81*, 424–429.

(6) Umemoto, T.; Satani, S.; Sakata, Y.; Misumi, S. Layered Compounds. XXIX. [2.2](2,7)Pyrenophane and Its 1,13-Diene. *Tetrahedron Lett.* **1975**, *16*, 3159–3162.

(7) Mitchell, R. H.; Carruthers, R. J.; Zwinkels, J. C. Straining Strained Molecules — I. The Synthesis of the First Cyclophane within a Cyclophane — [2,2]Paracyclo ([2,2]Metacyclophane). *Tetrahedron Lett.* **1976**, *17*, 2585–2588.

(8) (a) Schweitzer, D.; Hausser, K. H.; Kirrstetter, R. G. H.; Staab, H. A. Transanular Interaction in [2.2]Phanes: [2.2](2,7)Pyrenophane. *Zeitschrift für Naturforschung.* **1976**,

No. 10, 1189–1192, (b) Irnagartinger, H.; Kirrstetter, R. G. H.; Krieger, C.; Rodewald, H.; Staab, H. A. *Tetrahedron Lett.* **1977**, 1425-1428.

(9) Vögtle, F.; Ostrowicki, A.; Begemann, B.; Jansen, M.; Nieger, M.; Niecke, E. Chirale dreilagige und kondensierte [2.2]Cyclophane Synthese, Struktur, Chiroptik. *Eur. J. Inorg. Chem.* **1990**, *123*, 169-176.

(10) Yamato, T.; Miyazawa, A.; Tashiro, M. Medium-Sized Cyclophanes. Part 31. Synthesis and Electrophilic Substitution of 8-Substituted [2]Metacyclo[2](1,3)Pyrenophanes. *J. Chem. Soc., Perkin Trans. 1* **1993**, 3127.

(11) Mitchell, R. H.; Iyer, V. S.; Khalifa, N.; Mahadevan, R.; Venugopalan, S.; Weerawarna, S. A.; Zhou, P. An Experimental Estimation of Aromaticity Relative to That of Benzene. The Synthesis and NMR Properties of a Series of Highly Annelated Dimethyldihydropyrenes: Bridged Benzannulenes. *J. Am. Chem. Soc.* **1995**, *117*, 1514–1532.

(12) Bodwell, G. J.; Bridson, J. N.; Houghton, T. J.; Kennedy, J. W. J.; Mannion, M. R. 1,8-Dioxa[8](2,7)Pyrenophane, a Severely Distorted Polycyclic Aromatic Hydrocarbon. *Angew. Chem. Int. Ed. Engl.* **1996**, *35*, 1320–1321.

(13) Mitchell, R. H.; Boekelheide, V. Transformation of Sulfide Linkages to Carbon-Carbon Double Bond. Syntheses of Cis- and Trans-15,16-Dimethyldihydropyrene and Trans-15,16-Dihydropyrene. *J. Am. Chem. Soc.* **1974**, *96*, 1547–1557.

(14) Wu, J. I.; Dobrowolski, M. A.; Cyrański, M. K.; Merner, B. L.; Bodwell, G. J.; Mo, Y.; Schleyer, P. v. R. On the Aromatic Stabilization Energy of the 4N π Electron Pyrene. *Mo.l Phys.* **2009**, *107*, 1177–1186.

(15) Inouye, M.; Fujimoto, K.; Furusyo, M.; Nakazumi, H. Molecular Recognition Abilities of a New Class of Water-Soluble Cyclophanes Capable of Encompassing a Neutral Cavity. *J. Am. Chem. Soc.* **1999**, *121*, 1452–1458.

(16) Bodwell, G. J.; Bridson, J. N.; Houghton, T. J.; Kennedy, J. W. J.; Mannion, M. R. 1,7-Dioxa[7](2,7)Pyrenophane: The Pyrene Moiety Is More Bent than That of C70. *Chem. Eur. J.* **1999**, *5*, 1823–1827.

(17) Schnorpfeil, C.; Fetten, M.; Meier, H. Synthesis of Tripyreno[2,3,4-Abc: 2,3,4-Ghi: 2,3,4-Mno][18]Annulenes. *J. Für Prak. Chem.* **2000**, *342*, 785–790.

(18) Schnorpfeil, C.; Meier, H.; Irie, M. Aggregation and Photodimerization of Areno-Condensed Annulenes. *Helv. Chim. Acta* **2001**, *84*, 2467.

(19) Tsuge, A.; Nada, R.; Moriguchi, T.; Sakata, K. Synthesis and Spectral Properties of 1,8-Bridged Fluorenophanes Consisting of Polynuclear Aromatic Component. *J. Org. Chem.* **2001**, *66*, 9023–9025.

(20) Tsuge, A.; Tanba, Y.; Moriguchi, T.; Sakata, K. Preparation and Molecular Arrangement of Novel Pyrenophanes. *Chem. Lett.* **2002**, *31*, 384–385.

(21) Bodwell, G. J.; Bridson, J. N.; Cyrañski, M. K.; Kennedy, J. W. J.; Krygowski, T. M.; Mannion, M. R.; Miller, D. O. Nonplanar Aromatic Compounds. 8.1Synthesis, Crystal Structures, and Aromaticity Investigations of the 1,n-Dioxa[n](2,7)Pyrenophanes. How Does Bending Affect the Cyclic π-Electron Delocalization of the Pyrene System? *J. Org. Chem.* **2003**, *68*, 2089–2098.

(22) Abe, H.; Mawatari, Y.; Teraoka, H.; Fujimoto, K.; Inouye, M. Synthesis and Molecular Recognition of Pyrenophanes with Polycationic or Amphiphilic Functionalities: Artificial Plate-Shaped Cavitant Incorporating Arenes and Nucleotides in Water. *J. Org. Chem.* **2004**, *69*, 495–504.

(23) Tsuge, A.; Otsuka, M.; Moriguch, T.; Sakata, K. Syntheses, Structural Properties, and Charge-Transfer Complexes of Pyrenophanes. *Org. Biomol. Chem.* **2005**, *3*, 3590–3593.

(24) Bodwell, G. J.; Miller, D. O.; Vermeij, R. J. Nonplanar Aromatic Compounds. 6. [2]Paracyclo[2](2,7)Pyrenophane. A Novel Strained Cyclophane and a First Step on the Road to a “Vögtle” Belt. *Org. Lett.* **2001**, *3*, 2093–2096.

(25) Vermeij, R. J.; Miller, D. O.; Dawe, L. N.; Aprahamian, I.; Sheradsky, T.; Rabinovitz, M.; Bodwell, G. J. Mixed [2.2]Cyclophanes of Pyrene and Benzene. *Aust. J. Chem.* **2010**, *63*, 1703–1716.

(26) Zhang, B.; Manning, G. P.; Dobrowolski, M. A.; Cyrański, M. K.; Bodwell, G. J. Nonplanar Aromatic Compounds. 9. Synthesis, Structure, and Aromaticity of 1:2,13:14-Dibenzo[2]Paracyclo[2](2,7)- Pyrenophane-1,13-Diene. *Org. Lett.* **2008**, *10*, 273–276.

(27) Merner, B. L.; Dawe, L. N.; Bodwell, G. J. 1,1,8,8-Tetramethyl[8](2,11)Teropyrenophane: Half of an Aromatic Belt and a Segment of an (8,8) Single-Walled Carbon Nanotube. *Angew. Chem. Int. Ed.* **2009**, *48*, 5487–5491.

(28) Merner, B. L.; Unikela, K. S.; Dawe, L. N.; Thompson, D. W.; Bodwell, G. J. 1,1, n , n -Tetramethyl[n](2,11)Teropyrenophanes (n = 7–9): A Series of Armchair SWCNT Segments. *Chem. Commun.* **2013**, *49*, 5930–5932.

(29) Unikela, K. S.; Roemmele, T. L.; Houska, V.; McGrath, K. E.; Tobin, D. M.; Dawe, L. N.; Boeré, R. T.; Bodwell, G. J. Gram-Scale Synthesis and Highly Regioselective Bromination of 1,1,9,9-Tetramethyl[9](2,11)Teropyrenophane. *Angew. Chem. Int. Ed.* **2018**, *57*, 1707–1711.

(30) Unikela, K. S.; Merner, B. L.; Ghasemabadi, P. G.; Warford, C. C.; Qiu, C. S.; Dawe, L. N.; Zhao, Y.; Bodwell, G. J. The Development of Synthetic Routes to 1,1,n,N-Tetramethyl[n](2,11)Teropyrenophanes. *Eur. J. Org. Chem.* **2019**, 4546–4560.

(31) Yang, Y.; Mannion, M. R.; Dawe, L. N.; Kraml, C. M.; Pascal, R. A.; Bodwell, G. J. Synthesis, Crystal Structure, and Resolution of [10](1,6)Pyrenophane: An Inherently Chiral [n]Cyclophane. *J. Org. Chem.* **2011**, *77*, 57–67.

(32) Venkataramana, G.; Dongare, P.; Dawe, L. N.; Thompson, D. W.; Zhao, Y.; Bodwell, G. J. 1,8-Pyrenylene−Ethynylene Macrocycles. *Org. Lett.* **2011**, *13*, 2240–2243.

(33) Walsh, J. C.; Williams, K. M.; Lungerich, D.; Bodwell, G. J. Synthesis of Pyrene-4,5-dione on a 15 g Scale. *Eur. J. Org. Chem.* **2016**, 5933–5936.

(34) Nandaluru, P. R.; Dongare, P.; Kraml, C. M.; Pascal, R. A.; Dawe, L. N.; Thompson, D. W.; Bodwell, G. J. Concise, Aromatization-Based Approach to an Elaborate C 2 -Symmetric Pyrenophane. *Chem. Commun.* **2012**, *48*, 7747–7749.

(35) Pottie, I. R.; Nandaluru, P. R.; Benoit, W. L.; Miller, D. O.; Dawe, L. N.; Bodwell, G. J. Synthesis of 6 H -Dibenzo[b , d]Pyran-6-Ones Using the Inverse Electron Demand Diels–Alder Reaction. *J. Org. Chem.* **2011**, *76*, 9015–9030.

(36) Pottie, I.; Nandaluru, P.; Bodwell, G. An Inverse Electron-Demand Diels-Alder-Based Total Synthesis of Urolithin M7. *Synlett* **2011**, 2245–2247.

(37) Nandaluru, P. R.; Bodwell, G. J. An Inverse Electron Demand Diels–Alder-Based Total Synthesis of Defucogilvocarcin V and Some C-8 Analogues. *J. Org. Chem.* **2012**, *77*, 8028–8037.

(38) Nandaluru, P. R.; Bodwell, G. J. Multicomponent Synthesis of 6H-Dibenzo[b,d]Pyran-6-Ones and a Total Synthesis of Cannabinol. *Org. Lett.* **2011**, *14*, 310–313.

(39) Ghasemabadi, P. G.; Yao, T.; Bodwell, G. J. Cyclophanes Containing Large Polycyclic Aromatic Hydrocarbons. *Chem. Soc. Rev.* **2015**, *44*, 6494–6518.

(40) Zhang, B.; Zhao, Y.; Bodwell, G. Kinetic Stabilization of a Highly Bent Pyrene System. *Synlett* **2016**, 2113–2116.

(41) Zhang, B.; Pascal, R. A.; Zhao, Y.; Bodwell, G. J. Generation of an Extremely Bent Pyrene System Using Kinetic Stabilization. *Can. J. Chem.* **2017**, *95*, 460–481.

(42) Kahl, P.; Wagner, J. P.; Balestrieri, C.; Becker, J.; Hausmann, H.; Bodwell, G. J.; Schreiner, P. R. [2](1,3)Adamantano[2](2,7)Pyrenophane: A Hydrocarbon with a Large Dipole Moment. *Angew. Chem. Int. Ed.* **2016**, *55*, 9277–9281.

(43) Anderson, A. G.; Steckler, B. M. Azulene. VIII. A Study of the Visible Absorption Spectra and Dipole Moments of Some 1- and 1,3-Substituted Azulenes 1,2. *J. Am. Chem. Soc.* **1959**, *81*, 4941–4946.

(44) Robert, A.; Dechambenoit, P.; Bock, H.; Durola, F. A Carboxyfunctionalized (24)-1,6-Pyrenophane-Tetraene by Glyoxylic Perkin Condensation. *Can. J. Chem.* **2017**, *95*, 450–453.

(45) Maeda, H.; Hironishi, M.; Ishibashi, R.; Mizuno, K.; Segi, M. Synthesis and Fluorescence Properties of Dioxa-, Dithia-, and Diselena-[3.3](1,3)Pyrenophanes. *Photochem. Photobiol. Sci.* **2016**, *16*, 228–237.

(46) Sagara, Y.; Tamaoki, N. Mechanoresponsive Luminescence and Liquid-Crystalline Behaviour of a Cyclophane Featuring Two 1,6-Bis(Phenylethynyl)Pyrene Groups. *RSC Adv.* **2017**, *7*, 47056–47062.

(47) Maeda, H.; Nakamura, K.; Furuyama, T.; Segi, M. (1,3)Pyrenophanes Containing Crown Ether Moieties as Fluorescence Sensors for Metal and Ammonium Ions. *Photochem. Photobiol. Sci.* **2019**, *18*, 2397–2410.

(48) Hajime, M.; Geshi, M.; Hirose, K.; Furuyama, T.; Segi, M. Synthesis, Fluorescence Properties, and Conformational Analysis of Ether-Linked (1,8)Pyrenophanes. *Tetrahedron* **2019**, *75*, 130512.

(49) Mannancherry, R.; Devereux, M.; Häussinger, D.; Mayor, M. Molecular Ansa-Basket: Synthesis of Inherently Chiral All-Carbon [12](1,6)Pyrenophane. *J. Org. Chem.* **2019**, *84*, 5271–5276.

(50) Desai, N. B.; McKelvie, N.; Ramirez, F. A New Synthesis of 1,1-Dibromoölefins via Phosphine-Dibromomethylenes. The Reaction of Triphenylphosphine with Carbon Tetrabromide. *J. Am. Chem. Soc.* **1962**, *84*, 1745–1747.

(51) Corey, E. J.; Fuchs, P. L. A Synthetic Method for Formyl→ethynyl Conversion (RCHO→RC≡CH or RC≡CR'). *Tetrahedron Lett.* **1972**, *13*, 3769–3772.

(52) Bodwell, G. J.; Houghton, T. J.; Koury, H. E.; Yarlagadda, B. Sodium Sulfide Adsorbed on Alumina as a Reagent for the Facile Synthesis of 2,11-Dithia[3.3]Metacyclophanes. *Synlett* **1995**, 751–752.

(53) Borch, R. F. Nitrilium Salts. New Method for the Synthesis of Secondary Amines. *J. Org. Chem.* **1969**, *34*, 627–629.

(54) Meerwein, H.; Hinz, G.; Hofmann, P.; Kroning, E.; Pfeil, E. Tertiary Oxonium Salts. I. *J. Prakt. Chem.* **1937**, *147*, 257–285.

(55) Blattmann, H.-R.; Meuche, D.; Heilbronner, E.; Molyneux, R. J.; Boekelheide, V. Photoisomerization of Trans-15,16-Dimethyldihydropyrene. *J. Am. Chem. Soc.* **1965**, *87*, 130–131.

(56) Blattmann, H.-R.; Schmidt, W. Über Die Phototropie Des Trans-15,16-Dimethyldihydropyrens Und Seiner Derivate. *Tetrahedron* **1970**, *26*, 5885–5899.

(57) Mitchell, R. H.; Boekelheide, V. Syntheses of [2.2]Metacyclophane-1,9-Diene and Trans-15,16-Dihydropyrene. *J. Am. Chem. Soc.* **1970**, *92*, 3510–3512.

(58) Mannion, Michael R. Synthesis and Chemistry of Highly Distorted Polycyclic Aromatic Hydrocarbons. **1999**.

(59) Trost, B. The Atom Economy—a Search for Synthetic Efficiency. *Science* **1991**, *254*, 1471–1477.

(69) Watson, W. On Byproducts and Side Products. *Org. Process Res. Dev.* **2012**, *16*, 1877–1877.

(61) Bodwell, G. J.; Fleming, J. J.; Mannion, M. R.; Miller, D. O. Nonplanar Aromatic Compounds. † 3. A Proposed New Strategy for the Synthesis of Buckybowls. Synthesis, Structure and Reactions of [7]-, [8]- and [9](2,7)Pyrenophanes. *J. Org. Chem.* **2000**, *65*, 5360–5370.

(62) Aprahamian, I.; Bodwell, G. J.; Fleming, J. J.; Manning, G. P.; Mannion, M. R.; Merner, B. L.; Sheradsky, T.; Vermeij, R. J.; Rabinovitz, M. Reduction of Strained Polycycles: How Much Strain Can a Pyrene Anion Take? *J. Am. Chem. Soc.* **2004**, *126*, 6765–6775.

(63) MacKinnon, M. Synthesis of Novel π-Systems Containing Two Pyrene Units, 2014.

(64) Felpin, F.-X. Ten Years of Adventures with Pd/C Catalysts: From Reductive Processes to Coupling Reactions. *Synlett* **2014**, *25*, 1055–1067.

(65) Felpin, F.; Ayad, T.; Mitra, S. Pd/C: An Old Catalyst for New Applications – Its Use for the Suzuki–Miyaura Reaction. *Eur. J. Org. Chem.* **2006**, 2679–2690.

(66) Felpin, F.; Fouquet, E. A Useful, Reliable and Safer Protocol for Hydrogenation and the Hydrogenolysis of O-Benzyl Groups: The In Situ Preparation of an Active Pd0/C Catalyst with Well-Defined Properties. *Chem. Eur. J.* **2010**, *16*, 12440–12445.

(67) Lange, L.; Triebel, W. Sulfides, Polysulfides, and Sulfanes. *Ullmann's Encycl. Ind. Chem. (7th Ed.)* **2000**, a25_443-0.

(68) Ragnar, M.; Henriksson, G.; Lindström, M. E.; Wimby, M.; Blechschmidt, J.; Heinemann, S. Pulp. *Ullmann's Encycl. Ind. Chem. (7th Ed.)* **2014**, 1–92.

(69) Battistoni, P.; Bruni, P.; Fava, G. The Synthesis of O-Nitrobenzenethiols: An Advantageous Nucleophilic Displacement on o-Chloronitrobenzenes. *Gazz. Chim. Ital.* **1980**, *110*, 301–303.

(70) Tolstikov, G. Nucleophilic Conversion of Allylic Halides to Sulfides with Phase-Transfer Catalysts. *Russ. J. Org. Chem.* **1986**, *22*, 1400–1406.

(71) Nagasawa, K.; Yoneta, A. Organosulfur Chemistry. II. Use of Dimethyl Sulfoxide; A Facile Synthesis of Cyclic Sulfides. *Chem. Pharm. Bull.* **1985**, *33*, 5048–5052.

(72) King, F. E.; King, T. J. 216. New Potential Chemotherapeutic Agents. Part II. Derivatives of 2-Aminobenzocinnoline. *J. Chem. Soc.* **1945**, 824–826.

(73) Mitchell, R. H. The Use Thiacyclophanes to Prepare Novel Conjugated Aromatic Compounds. *Heterocycles* **1978**, *11*, 563–586.

(74) Sato, T.; Wakabayashi, M.; Kainosho, M.; Hat, K. Conformational Changes in the Sulfur Analogs of 11- and 12-Membered Metacyclophanes. *Tetrahedron Lett.* **1968**, *9*, 4185–4189.

(75) Vögtle, F.; Schunder, L. Sterische Wechselwirkungen Im Innern Cyclischer Verbindungen, VII. Dithia [3.3]Metacyclophane. *Chem. Ber.* **1969**, *102*, 2677–2683.

(76) Boldt, P.; Bruhnke, D. Chinone. XIII. Synthese von 4,5,9,10-Tetrahydropyren-2,7-Dion Und Versuch Zur Darstellung von Pyren-2,7-Dion. *J. Prakt. Chem.* **1994**, *336*, 110–114.

(77) Boekelheide, V.; Hollins, R. A. [2.2.2](1,3,5)Cyclophane and Its Derivatives. Extreme Example of Face-to-Face Crowding of Aromatic Rings. *J. Am. Chem. Soc.* **1973**, *95*, 3201–3208.

(78) Vögtle, F. Vielfach Verbrückte Aromatische Verbindungen, I 2.11.20-Trithia[3.3.3](1,3,5)Cyclophan1). *Liebigs Ann. Chem.* **1970**, *735*, 193–195.

(79) Montanari, M.; Bugana, A.; Sharma, A. K.; Pasini, D. Mild Preparation of Functionalized [2.2]Paracyclophanes via the Pummerer Rearrangement. *Org. Biomol. Chem.* **2011**, *9*, 5018–5020.

(80) Czech, B.; Quici, S.; Regen, S. L. Convenient Synthesis of Organic Sulfides Using Impregnated Reagents. *Synthesis* **1980**, 113–113.

(81) Zhang, B. Synthesis of Polyphenyl Pyrenophanes and Pyrenylene-Ethynylene Nanorings, **2007**.

(82) Mitchell, R. H. Conformational Changes of 2,11-Dithia[3.3]Metacyclophane. A New Look Using VT NMR and Calculation. *J. Am. Chem. Soc.* **2002**, *124*, 2352–2357.

(83) Collins, M. S.; Carnes, M. E.; Nell, B. P.; Zakharov, L. N.; Johnson, D. W. A Facile Route to Old and New Cyclophanes via Self-Assembly and Capture. *Nat. Commun.* **2016**, *7*, 11052.

(84) Bodwell, G. J.; Bridson, J. N.; Chen, S.-L.; Poirier, R. A. Nonplanar Aromatic Compounds. 5. 1 A Strategy for the Synthesis of Cis -10b,10c-Dimethyl-10b,10c-Dihydropyrenes. First Crystal Structure of a Cis -10b,10c-Dimethyl-10b,10c-Dihydropyrene. *J. Am. Chem. Soc.* **2001**, *123*, 4704–4708.

(85) Yao, Z. T.; Ji, X. S.; Sarker, P. K.; Tang, J. H.; Ge, L. Q.; Xia, M. S.; Xi, Y. Q. A Comprehensive Review on the Applications of Coal Fly Ash. *Earth Sci. Rev.* **2015**, *141*, 105–121.

(86) Singh, R. P.; Gupta, A. K.; Ibrahim, M. H.; Mittal, A. K. Coal Fly Ash Utilization in Agriculture: Its Potential Benefits and Risks. *Rev. Environ. Sci. Biotechnol.* **2010**, *9*, 345–358.

(87) Kim, M. I.; Im, J. S.; Seo, S. W.; Cho, J. H.; Lee, Y.-S.; Kim, S. Preparation of Pitch-Based Activated Carbon with Surface-Treated Fly Ash for SO2 Gas Removal. *Carbon Lett.* **2020**, *30*, 381–387.

(88) Mushtaq, F.; Zahid, M.; Bhatti, I. A.; Nasir, S.; Hussain, T. Possible Applications of Coal Fly Ash in Wastewater Treatment. *J. Environ. Manage.* **2019**, *240*, 27–46.

(89) Ezhilmathi, P.; Thirumalai, K.; Swaminathan, M.; Krishnasamy, K. One-Pot Synthesis of Tetra Substituted Imidazoles Catalyzed by Fly Ash Supported Bi2O3–ZnO. *J. Nanosci. Nanotechnol.* **2019**, *19*, 8163–8171.

(90) Ahmaruzzaman, M. A Review on the Utilization of Fly Ash. *Prog. Energy Combust. Sci.* **2010**, *36*, 327–363.

(91) Jain, D.; Khatri, C.; Rani, A. Fly Ash Supported Calcium Oxide as Recyclable Solid Base Catalyst for Knoevenagel Condensation Reaction. *Fuel Process Technol.* **2010**, *91* (9), 1015–1021.

(92) Chakraborty, R.; Bepari, S.; Banerjee, A. Transesterification of Soybean Oil Catalyzed by Fly Ash and Egg Shell Derived Solid Catalysts. *Chem. Eng. J.* **2010**, *165* (3), 798–805.

(93) Khatri, C.; Mishra, M. K.; Rani, A. Synthesis and Characterization of Fly Ash Supported Sulfated Zirconia Catalyst for Benzylation Reactions. *Fuel Process. Technol.* **2010**, *91*, 1288–1295.

(94) MacKinnon, M. R.; Warren, R. N.; Brake, S.; Zhang, B.; Wang, L.; Bodwell, G. J. Sodium Sulfide on Coal Fly Ash (Na2S/CFA) as a Reagent for the Synthesis of Dithia[3.3]Cyclophanes. *Can. J. Chem.* **2020**, *98*, 322–326.

(95) Montanari, M.; Bugana, A.; Sharma, A. K.; Pasini, D. Mild Preparation of Functionalized [2.2]Paracyclophanes via the Pummerer Rearrangement. *Org. Biomol. Chem.* **2011**, *9*, 5018–5020.

(96) MacKinnon, M. Synthesis of Novel π-Systems Containing Two Pyrene Units. **2014**.

(97) Ohsawa, K.; Yoshida, M.; Doi, T. A Direct and Mild Formylation Method for Substituted Benzenes Utilizing Dichloromethyl Methyl Ether–Silver Trifluoromethanesulfonate. *J. Org. Chem.* **2013**, *78*, 3438–3444.

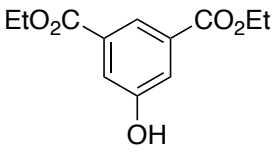
(98) Aprahamian, I.; Bodwell, G. J.; Fleming, J. J.; Manning, G. P.; Mannion, M. R.; Sheradsky, T.; Vermeij, R. J.; Rabinovitz, M. "The Great Escape" from Antiaromaticity: Reduction of Strained Pyrenes. *J. Am. Chem. Soc.* **2003**, *125*, 1720–1721.

(99) Havenith, R. W. A.; Jiao, H.; Jenneskens, L. W.; Lenthe, J. H. van; Sarobe, M.; Schleyer, P. von R.; Kataoka, M.; Necula, A.; Scott, L. T. Stability and Aromaticity of the Cyclopenta-Fused Pyrene Congeners. *J. Am. Chem. Soc.* **2002**, *124*, 2363–2370.

(100) Ito, H.; Ozaki, K.; Itami, K. Annulative π-Extension (APEX): Rapid Access to Fused Arenes, Heteroarenes, and Nanographenes. *Angew. Chem. Int. Ed.* **2018**, *56*, 11144–11164.

2.13: Experimental Procedures and Characterization Data

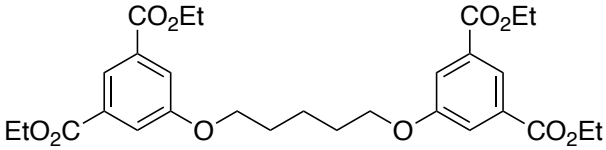
1,9-Diethyl 5-hydroxyisophthalate (2.201)



2.201

5-Hydroxyisophthalic acid (50.0 g, 275 mmol) was dissolved in EtOH (250 mL) and H_2SO_4 (15 mL) was added. The reaction mixture was refluxed for 12 h then cooled to rt and concentrated under reduced pressure. The resulting residue was dissolved in CH_2Cl_2 (200 mL) and washed with H_2O (100 mL), saturated $NaHCO_{3(aq)}$ (100 mL), H_2O (100 ml), and brine (100 mL) then dried ($MgSO_4$), filtered and concentrated under pressure to yield diethyl 5-hydroxyisophthalate (64.1 g, 98%) as a white solid which was used without further purification. R_f = 0.45 (CH_2Cl_2); m.p. 292-294 °C (CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.25 (t, *J* = 1.4 Hz, 1H), 7.80 (d, *J* = 1.4 Hz, 2H), 5.60 (broad s, 1H), 4.41 (q, *J* = 7.14 Hz, 4H), 1.41 (t, *J* = 7.14 Hz, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.17, 156.48, 132.04, 122.60, 120.96, 61.68, 14.25.

1,5-Bis(3,5-bis(ethoxycarbonyl)phenoxy)pentane (2.202a)

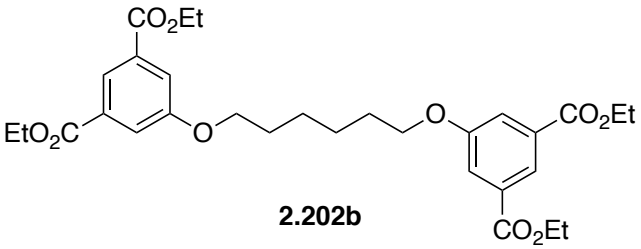


2.202a

Diethyl 5-hydroxyisophthalate (5.00 g, 21.0 mmol) and 1,5-dibromopentane (1.36 mL, 2.30 g, 9.99 mmol) were dissolved in CH_3CN (100 mL) and the reaction mixture was purged with N_2 for 5 mins. K_2CO_3 (3.45 g, 25.0 mmol) was added and the reaction was refluxed under a N_2 atmosphere for 12 h. After cooling to rt the reaction was quenched with saturated aqueous NH_4Cl (50 mL) and volatiles were removed *in vacuo* and redissolved in CH_2Cl_2 (100 mL) and washed with saturated aqueous NH_4Cl (50 mL), H_2O (50 mL) and brine (50 mL). The organic layer was dried ($MgSO_4$), filtered and concentrated under reduced pressure. The resulting residue was subjected to column chromatography (20% ethyl acetate/hexanes) to afford 1,5-bis(3,5-bis(ethoxycarbonyl)phenoxy)pentane (4.57 g, 84%) as a white solid. A small sample was

recrystallized from heptane for analysis. R_f = 0.35 (20% ethyl acetate/hexanes); m.p. 105-107 °C (heptane); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.27 (t, *J* = 1.4 Hz, 2H), 7.74 (d, *J* = 1.4 Hz, 4H) 4.40 (q, *J* = 7.1 Hz, 8H), 4.09 (t, *J* = 6.3 Hz, 4H), 1.90-1.94 (m, 6H), 1.41 (t, *J* = 7.1 Hz, 12H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 165.78, 159.06, 132.09, 122.82, 119.67, 68.31, 61.32, 28.89, 25.95, 14.33; HRMS (LC-APPIMS) calculated for $C_{29}H_{36}O_{10}$ (M^+) 544.2309, found 544.2323.

1,6-Bis(3,5-bis(ethoxycarbonyl)phenoxy)hexane (2.202b)

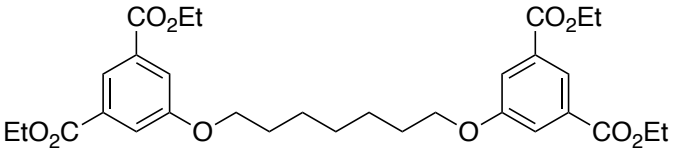


2.202b

Diethyl 5-hydroxyisophthalate (5.00 g, 21.0 mmol) and 1,6-dibromohexane (1.54 mL, 2.44 g, 9.99 mmol) were dissolved in CH_3CN (100 mL) and the reaction mixture was purged with N_2 for 5 mins. K_2CO_3 (3.45 g, 25.0 mmol) was added and the reaction was refluxed under a N_2 atmosphere for 12 h. After cooling to rt the reaction was quenched with saturated aqueous NH_4Cl (50 mL) and volatiles were removed *in vacuo* and redissolved in CH_2Cl_2 (100 mL) and washed with saturated aqueous NH_4Cl (50 mL), H_2O (50 mL) and brine (50 mL). The organic layer was dried ($MgSO_4$), filtered and concentrated under reduced pressure. The resulting residue was subjected to column chromatography (20% ethyl acetate/hexanes) to afford 1,6-bis(3,5-bis(ethoxycarbonyl)phenoxy)hexane (4.97 g, 89%) as a white solid. A small sample was recrystallized from heptane for analysis. R_f = 0.35 (20% ethyl acetate/hexanes); m.p. 115-117 °C (heptane); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.26 (t, *J* = 1.4 Hz, 2H), 7.74 (d, *J* = 1.4 Hz, 4H), 4.40 (q, *J* = 7.1 Hz, 8H) 4.07 (t, *J* = 6.4 Hz, 4H), 1.86-1.88 (m, 4H), 1.57-1.59 (m, 4H), 1.41 (t, *J* = 7.1 Hz, 12H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 165.80, 159.10, 132.05, 122.74, 119.68, 68.38, 61.38, 29.08, 25.79, 14.31; HRMS (LC-APPIMS) calculated for $C_{30}H_{38}O_{10}$ (M^+) 558.2465, found 558.2480.

1,7-Bis(3,5-bis(ethoxycarbonyl)phenoxy)heptane (2.202c)

Diethyl 5-hydroxyisophthalate (5.00 g, 21.0 mmol) and 1,7-dibromoheptane (1.71 mL, 2.58 g, 9.99 mol) were dissolved in CH_3CN

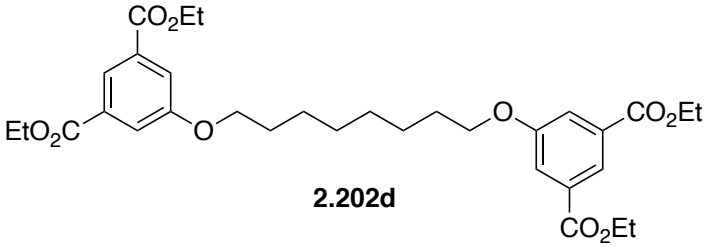


2.202c

(100 mL) and the reaction mixture was purged with N_2 for 5 mins. K_2CO_3 (3.45 g, 25.0 mmol) was added and the reaction was refluxed under a N_2 atmosphere for 12 h. After cooling to rt the reaction was quenched with saturated aqueous NH_4Cl (50 mL) and volatiles were removed *in vacuo* and redissolved in CH_2Cl_2 (100 mL) and washed with saturated aqueous NH_4Cl (50 mL), H_2O (50 mL) and brine (50 mL). The organic layer was dried ($MgSO_4$), filtered and concentrated under reduced pressure. The resulting residue was subjected to column chromatography (20% ethyl acetate/hexanes) to afford 1,7-bis(3,5-bis(ethoxycarbonyl)phenoxy)heptane (5.14 g, 90%) as a white solid. A small sample was recrystallized from heptane for analysis. R_f = 0.35 (20% Ethyl Acetate/hexanes); m.p. 65-69 °C (heptane); ^{1}H NMR (500 MHz, $CDCl_3$) δ8.26 (t, *J* = 1.5 Hz, 2H), 7.74 (d, *J* = 1.5 Hz, 4H), 4.40 (quartet, *J* = 7.1 Hz, 8H), 4.06 (t, *J* = 6.4 Hz, 4H), 1.81-1.87 (m, 4H), 1.49-1.56 (m, 6H), 1.41 (t, *J* = 7.1 Hz, 12H); ^{13}C NMR (75 MHz, $CDCl_3$) δ165.79, 159.13, 132.05, 122.71, 119.67, 68.48, 61.36, 29.07, 25.94, 14.32 (10 of 11 signals observed); HRMS (LC-APPIMS) calculated for $C_{10}H_{40}O_{10}$ (M^+) 572.2621, found 572.2647.

1,8-Bis(3,5-bis(ethoxycarbonyl)phenoxy)octane (2.202d)

Diethyl 5-hydroxyisophthalate (5.00 g, 21.0 mmol) and 1,8-dibromooctane (1.84 mL, 2.72 g, 9.99 mmol) were dissolved in

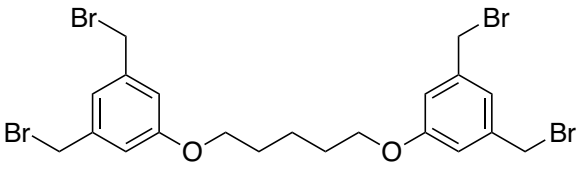


2.202d

CH_3CN (100 mL) and the reaction mixture was purged with N_2 for 5 mins. K_2CO_3 (3.45 g, 25.0 mmol) was added and the reaction was refluxed under a N_2 atmosphere for 12 h. After cooling to rt the reaction was quenched with saturated aqueous NH_4Cl (50 mL) and

volatiles were removed *in vacuo* and redissolved in CH_2Cl_2 (100 mL) and washed with saturated aqueous NH_4Cl (50 mL), H_2O (50 mL) and brine (50 mL). The organic layer was dried ($MgSO_4$), filtered and concentrated under reduced pressure. The resulting residue was subjected to column chromatography (20% ethyl acetate/hexanes) to afford 1,8-bis(3,5-bis(ethoxycarbonyl)phenoxy)octane (4.92 g, 86%) as a white solid. A small sample was recrystallized from heptane for analysis. R_f = 0.35 (20% ethyl acetate/hexanes); m.p. 108-110 °C (heptane); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.26 (t, *J* = 1.4 Hz, 2H), 7.74 (d, *J* = 1.4 Hz, 4H), 4.05 (t, *J* = 6.5 Hz, 4H), 1.80-1.86 (m, 4H), 1.49-1.52 (m, 4H), 1.41 (t, *J* = 7.1 Hz, 12H), 1.27-1.30 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 165.78, 159.15, 132.03, 122.68, 119.68, 68.52, 61.34, 29.11, 29.01, 25.94, 14.31; HRMS (LC-APPIMS) calculated for $C_{32}H_{42}O_{10}$ (M^+) 586.2778, found 586.2798.

1,5-Bis(3,5-bis(bromomethyl)phenoxy)pentane (2.186a)

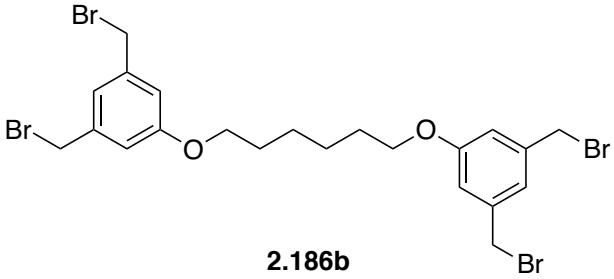


2.186a

$LiAlH_4$ (6.50 g, 171 mmol) was slurried in dry THF (100 mL) and cooled to 0 °C under a N_2 atmosphere. 1,5-bis(3,5-bis(ethoxycarbonyl)phenoxy)pentane (8.34 g, 17.1 mmol) was dissolved in THF (100 mL) and added dropwise via cannula to the cooled $LiAlH_4$ slurry. Upon complete addition the reaction mixture was allowed to gradually warm to rt then stirred for an additional 24 h. Reaction mixture was cooled to 0 °C and quenched by slow addition of EtOAc (50 mL) then 10% $HCl_{(aq)}$ (15 mL) and all volatiles were removed under reduced pressure to obtain a grey solid which was dissolved in 2:1 HBr/H_2SO_4 (150 mL) solution and refluxed for 2 h. Reaction mixture was cooled to rt and diluted with H_2O (200 mL) and extracted with CH_2Cl_2 (4 × 100 mL). The combined organic extracts were washed with saturated aqueous $NaHCO_3$ (100 mL), H_2O (100 mL) and brine (100 mL) then dried ($MgSO_4$), filtered and concentrated under reduced pressure. The resulting residue was purified by column chromatography (40%

CH_2Cl_2/hexanes) to obtain 1,5-bis(3,5-bis(bromomethyl)phenoxy)pentane (6.23 g, 58%) as a white solid, a small portion of which was recrystallized from heptane for analysis. R_f = 0.20 (25% CH_2Cl_2/hexanes); m.p. 105-106 °C (heptane); ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.99 (t, *J* = 1.4 Hz, 2H), 6.86 (d, *J* = 1.4 Hz, 4H), 4.43 (s, 8H), 4.00 (t, *J* = 6.3 Hz, 4H), 1.82-1.91 (m, 4H), 1.63-1.71 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 159.48, 139.60, 121.74, 115.23, 67.91, 32.93, 28.91, 22.71.

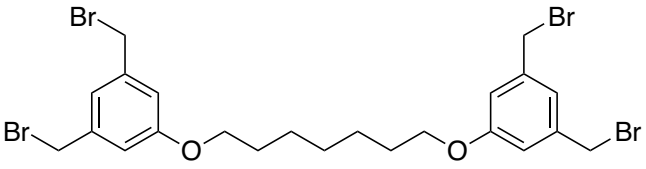
1,6-Bis(3,5-bis(bromomethyl)phenoxy)hexane (2.186b)



2.186b

$LiAlH_4$ (5.40 g, 142 mmol) was slurried in THF (100 mL) and cooled to 0 °C under a N_2 atmosphere. 1,6-bis(3,5-bis(ethoxycarbonyl)phenoxy)hexane (7.12 g, 14.2 mmol) was dissolved in THF (100 mL) and gently warmed for complete dissolution, after which this solution was added dropwise via cannula to the slurried solution. Upon complete addition the reaction was warmed to rt then stirred for 18 h under a N_2 atmosphere. Reaction was cooled to 0 °C and quenched by slow addition of EtOAc (100 mL). Volatiles were removed under reduced pressure, and the residue was dissolved in a 2:1 HBr/H_2SO_4 mixture (150 mL) and refluxed for 1 h. Reaction mixture was cooled to rt, diluted with H_2O (200 mL) and extracted with CH_2Cl_2 (3 × 100 mL). The combined organic extracts were washed with saturated aqueous $NaHCO_3$ (100 mL), saturated aqueous $Na_2S_2O_3$ (100 mL) and brine (100 mL) then dried ($MgSO_4$), filtered and concentrated under reduced pressure. The resulting brown residue was recrystallized from heptane to obtain 1,6-bis(3,5-bis(bromomethyl)phenoxy)hexane (6.82 g, 75%) as a white solid. R_f = 0.20 (25% CH_2Cl_2/hexanes); m.p. 99-101 °C (heptane); ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.99 (t, *J* = 1.4 Hz, 2H), 6.86 (d, *J* = 1.4 Hz, 4H), 4.43 (s, 8H), 3.98 (t, *J* = 6.4 Hz, 4H), 1.80-1.85 (m, 4H), 1.52-1.57 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 159.72, 139.72, 121.83, 115.36, 68.14, 33.08, 29.26, 25.98.

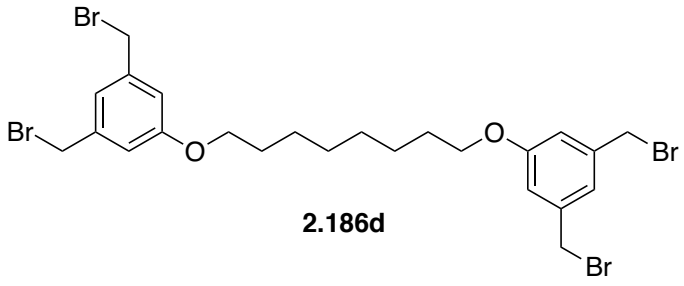
1,7-Bis(3,5-bis(bromomethyl)phenoxy)heptane (2.186c)



2.186c

$LiAlH_4$ (4.51 g, 119 mmol) was slurried in THF (100 mL) and cooled to 0 °C under a N_2 atmosphere. 1,7-bis(3,5-bis(ethoxycarbonyl)phenoxy)heptane (6.50 g, 11.9 mmol) was dissolved in THF (100 mL) and added dropwise to the slurried solution of $LiAlH_4$ *via* cannula. Upon complete addition the reaction mixture was warmed to rt and stirred for an additional 18 h. The reaction mixture was cooled to 0 °C and quenched with slow addition of EtOAc (100 mL). Volatiles were removed under reduced pressure and the resulting grey/white residue was dissolved in a 2:1 HBr/H_2SO_4 mixture (150 mL) and refluxed for 1 h. The reaction mixture was cooled to rt and diluted with H_2O (300 mL) and extracted with CH_2Cl_2 (3 × 100 mL). The combined organic extracts were washed with saturated aqueous $NaHCO_3$ (100 mL), saturated aqueous $Na_2S_2O_3$ (100 mL) and brine (100 mL) then dried ($MgSO_4$), filtered and concentrated under reduced pressure. The resulting brown oily residue was subjected to column chromatography (40% CH_2Cl_2/hexanes) to afford 1,7-bis(3,5-bis)(bromomethyl)phenoxy)heptane (7.79 g, 78%) as a white solid; a small amount of which was recrystallized from heptane for analysis. R_f = 0.20 (25% CH_2Cl_2/hexanes); m. p. 105-106 °C (heptane); ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.98 (t, J = 1.4 Hz, 2H), 6.86 (d, J = 1.4 Hz, 4H), 4.43 (s, 8H), 3.97 (t, J = 6.4 Hz, 4H), 1.78-1.82 (m, 4H), 1.47-1.52 (m, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 159.56, 139.58, 121.66, 115.24, 68.11, 32.96, 29.12, 29.08, 25.97.

1,8-Bis(3,5-bis(bromomethyl)phenoxy)octane (2.186d)

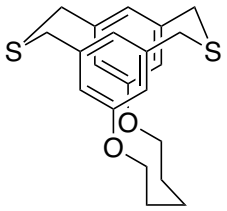


2.186d

$LiAlH_4$ (3.88 g, 102 mmol) was slurried in THF (100 mL) and cooled to 0 °C under a N_2 atmosphere. 1,8-bis(3,5-

bis(ethoxycarbonyl)phenoxy)octane (6.00 g, 10.2 mmol) was dissolved in THF (100 mL) and added dropwise to the slurried solution of $LiAlH_4$ *via* cannula. Upon complete addition the reaction mixture was warmed to rt and stirred for an additional 18 h. The reaction mixture was cooled to 0 °C and quenched with slow addition of EtOAc (100 mL). Volatiles were removed under reduced pressure and the resulting grey/white solid was dissolved in a 2:1 HBr/H_2SO_4 mixture (150 ml) and refluxed for 1 h. The reaction mixture was cooled to rt and diluted with H_2O (300 mL) and extracted with CH_2Cl_2 (3 × 100 mL). The combined organic extracts were washed with saturated aqueous $NaHCO_3$ (100 mL), saturated aqueous $Na_2S_2O_3$ (100 mL) and brine (100 mL) then dried ($MgSO_4$), filtered and concentrated under reduced pressure. The resulting brown oily residue was subjected to column chromatography (40% CH_2Cl_2/hexanes) to afford 1,8-Bis(3,5-bis(bromomethyl)phenoxy)octane (4.93 g, 72 %) as a white solid; a small amount of which was recrystallized from heptane for analysis. R_f = 0.20 (25% CH_2Cl_2/hexanes); m.p. 103-104 °C (heptane); ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.98 (t, *J* = 1.4 Hz, 2H), 6.86 (d, *J* = 1.4 Hz, 4H), 4.43 (s, 8H), 3.96 (t, *J* = 6.4 Hz, 4H), 1.74-1.81 (m, 4H), 1.42-1.52 (m, 8H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 159.56, 139.56, 121.64, 115.22, 68.13, 63.48, 32.98, 29.27, 29.17, 25.96.

syn-1,7-Dioxa-15,24-dithia[7.3.3](1,3,5)benzophane (2.187a)

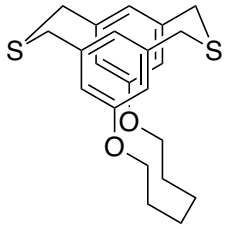


2.187a

1,5-Bis(3,5-bis(bromomethyl)phenoxy)pentane (2.12 g, 3.39 mmol) was dissolved in 18% EtOH/CH_2Cl_2 (1000 mL) with vigorous stirring in an Erlenmeyer flask. Freshly prepared Na_2S/fly ash (2.59 g, 8.49 mmol, 3.27 mmol/g) was added in roughly three equal portions over 1 h. The reaction mixture was stirred vigorously for 23 h at rt. The reaction mixture was filtered and concentrated under reduced pressure. The resulting residue was subjected to column chromatography (CH_2Cl_2) to give *syn*-1,7-dioxa-15,24-dithia[7.3.3](1,3,5)benzophane (940 mg, 75%) as a white solid. R_f = 0.45 (CH_2Cl_2); m.p. 126-128 °C (heptane); ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.75 (s, 2H), 6.40 (s, 4H), 4.11-4.07 (m, 4H), 3.78 (d, *J* = 14.8 Hz, 4H), 3.74 (d, *J* = 14.8 Hz, 4H), 1.76-1.67 (m, 4H), 1.64-1.55 (m,

4H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 158.0, 138.5, 124.2, 113.5, 65.7, 38.8, 27.3, 21.8; HRMS (LC-APPIMS) calculated for $C_{21}H_{24}O_2S_2$ (M^+) 372.1218, found 372.1289.

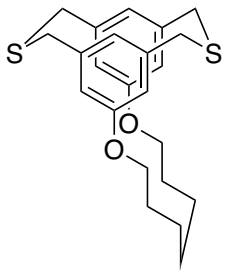
syn-1,8-Dioxa-16,25-dithia[8.3.3](1,3,5)benzophane (2.187b)



2.187b

1,6-Bis(3,5-bis(bromomethyl)phenoxy)hexane (220 mg, 0.343 mmol) was dissolved in 18% EtOH/CH_2Cl_2 (200 mL) with vigorous stirring in an Erlenmeyer flask. Freshly prepared Na_2S/fly ash (343 mg, 0.880 mmol, 2.55 mmol/g) was added in roughly three equal portions over 1 h. The reaction mixture was stirred vigorously for 24 h at rt. The reaction mixture was filtered and concentrated under reduced pressure. The resulting residue was subjected to column chromatography (CH_2Cl_2) to give syn-1,8-dioxa-16,25-dithia[8.3.3](1,3,5)benzophane (105 mg, 75%) as white solid. R_f = 0.40 (CH_2Cl_2); m.p. 165-167 °C (heptane); ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.70 (s, 2H), 6.38 (m, 4H), 3.88-3.84 (m, 4H), 3.79 (d, J = 14.7 Hz, 2H), 3.74 (d, J = 14.7 Hz, 2H), 1.75-1.69 (m, 4H), 1.58-1.55 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 159.07, 138.53, 124.47, 113.31, 64.68, 38.83, 28.05, 20.77; HRMS (LC-APPIMS) calculated for $C_{22}H_{26}O_2S_2$ (M^+) 386.1374, found 386.2384.

syn-1,9-Dioxa,17,26-dithia[9.3.3](1,3,5)cyclophane (2.187c)

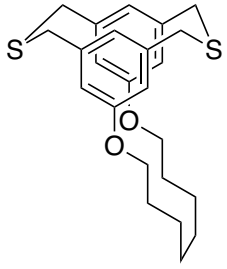


2.187c

1,7-Bis(3,5)-bis(bromomethyl)phenoxy)hexane (200 mg, 0.305 mmol) was dissolved in 18% EtOH/CH_2Cl_2 (200 mL) with vigorous stirring in an Erlenmeyer flask. Freshly prepared Na_2S/fly ash (345 mg, 0.910 mmol, 2.64 mmol/g) was added in roughly four equal portions over 1 h. The reaction mixture was stirred vigorously for 24 h at rt. The reaction mixture was filtered and concentrated under reduced pressure. The resulting residue was subjected to column chromatography (50% CH_2Cl_2/hexanes) to give syn-1,9-dioxa,17,26-dithia[9.3.3](1,3,5)cyclophane (120 mg, 65%)

as a white solid. R_f = 0.40 (50% CH_2Cl_2/hexanes); m.p. 157-160 °C (EtOH); ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.78 (s, 2H), 6.38 (s, 4H), 3.85-3.81 (m, 4H), 3.79 (d, *J* = 14.8 Hz, 4H), 3.75 (d, *J* = 14.8 Hz, 4H), 1.80-1.73 (m, 4H), 1.58-1.52 (m, 4H), 1.40-1.32 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 158.83, 128.42, 124.20, 112.83, 65.48, 38.77, 27.11, 24.69, 24.10; HRMS (LC-APPIMS) calculated for $C_{23}H_{28}O_2S_2$ (M^+) 400.1531, found 400.1591.

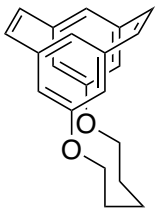
syn-1,10-Dioxa-18,27-dithia[10.3.3](1,3,5)benzophane (2.187d)



2.187d

1,8-Bis(3,5-bis(bromomethyl)phenoxy)octane (203 mg, 0.303 mmol) was dissolved in 18% EtOH/CH_2Cl_2 (200 mL) with vigorous stirring in an Erlenmeyer flask. Freshly prepared Na_2S/fly ash (357 mg, 0.910 mmol, 2.55 mmol/g) was added in roughly three equal portions over 1 h. The reaction mixture was vigorously stirred for 18 h at rt. The reaction mixture was filtered and concentrated under reduced pressure. The resulting residue was subjected to column chromatography (CH_2Cl_2) to give *syn*-1,10-dioxa-18,27-dithia[10.3.3](1,3,5)benzophane (100 mg, 81 %) as a white solid. R_f = 0.40 (50% CH_2Cl_2/hexanes); m.p. 139-141 °C (heptane); ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.81 (s, 2H), 6.37 (s, 4H), 3.82-3.75 (m, 12H), 1.76-1.68 (m, 4H), 1.58-1.48 (m, 4H), 1.42-1.36 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 158.82, 138.43, 124.11, 112.88, 66.35, 38.78, 28.43, 27.10, 23.70; HRMS (LC-APPIMS) calculated for $C_{24}H_{30}O_2S_2$ (M^+) 414.1686, found 414.1742.

1,7-Dioxa[7.2.2](1,3,5)cyclophane-(14,22)diene (2.189a)

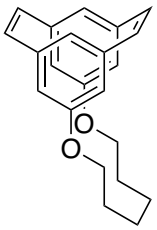


2.189a

syn-1,7-Dioxa-15,24-dithia[7.3.3](1,3,5)benzophane (1.50 g, 4.02 mmol) was dissolved in CH_2Cl_2 (100 mL) to which Borch reagent (1.35 g, 0.80 mL, 8.45 mmol) was added. The reaction was stirred at rt under N_2 for 3 h then volatiles were removed under reduced pressure. The resulting oily residue was quenched with MeOH (50 mL) and stirred for 1 h. The white precipate was collected

by decanting and then drying the remaining solido *in vacuo* to give crude bis(tetrafluoroborate) salt which was immediately slurried in THF (100 mL). *t*-BuOK (2.25 g, 20.1 mmol) was added and the reaction was stirred at rt under N_2 for 3 h. The reaction was quenched with saturated $NH_4Cl_{(aq)}$ (5 mL) and volatiles were removed under reduced pressure then redissolved in CH_2Cl_2 (100 mL). The organic layer was washed with saturated $NH_4Cl_{(aq)}$ (100 mL), H_2O (100 mL), brine (100 mL), dried ($MgSO_4$), filtered and concentrated under reduced pressure. The resulting residue was filtered thorugh a plug of silica and concentrated to give crude isomeric bis-Sme cyclophane as a foamy yellow solid (1.04 g, 2.61 mmol, 65% from dithiacyclophane) which was used without further purification. This isomeric material was dissolved in CH_2Cl_2 (100 mL) and Borch reagent (1.35 g, 0.80 mL, 8.45 mmol) was added. The reaction was stirred at rt under N_2 for 3 h then the solvents were removed to give a black-oily residue which was immediately slurried in THF (100 mL) to which *t*-BuOK (2.25 g, 20.1 mmol) was added. The reaction was stirred at rt under N_2 for 12 h then quenched with saturated $NH_4Cl_{(aq)}$ (5 mL) and volatiles were removed *in vacuo*. This residue was taken up in CH_2Cl_2 (100 mL) and washed with saturated $NH_4Cl_{(aq)}$ (100 mL), H_2O (100 mL), brine (100 mL), dried ($MgSO_4$), filtered and concentrated under reduced pressure. The resulting residue was purified by column chromatopgraphy (CH_2Cl_2) to yield 1,7-dioxa[7.2.2](1,3,5)cyclophane-(14,22)diene (595 mg, 75% from crude isomeric mixture) as a light-yellow solid. R_f = 0.42 (CH_2Cl_2); m.p. 138-140 °C (heptane); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.14 (s, 4H), 6.87 (s, 2H), 6.12 (s, 4H), 4.07 (t, *J* = 5.6 Hz, 4H), 1.51-1.47 (m, 4H), 1.18-1.12 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 155.9, 136.3, 135.9, 134.6, 114.0, 66.7, 29.1, 22.7.

1,6-Dioxa[6.2.2](13,5)cyclophane-14,22-diene (2.189b)

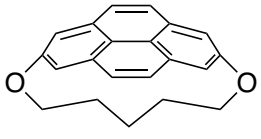


2.189b

syn-1,8-Dioxa-15,24-dithia[7.3.3](1,3,5)benzophane (1.10 g, 2.85 mmol) was dissolved in CH_2Cl_2 (100 mL) to which Borch reagent (958 mg, 0.580 mL, 5.98 mmol) was added. The reaction was stirred at rt under N_2 for 3 h then the volatiles were removed under reduced pressure. The resulting

oliy residue was quenched with MeOH (50 mL) and stirred for 1 h. The white precipitate was collected by decanting off the liquid and then drying *in vacuo* to give crude bis(tetrafluoroborate) salt which was immediately slurried in THF (100 mL). *t*-BuOK (1.60 g, 14.3 mmol) was added and the reaction was stirred at rt under N_2 for 3 h. The reaction was quenched with saturated $NH_4Cl_{(aq)}$ (5 mL) and volatiles were removed under reduced pressure then redissolved in CH_2Cl_2 (100 mL). The organic layer was washed with saturated $NH_4Cl_{(aq)}$ (100 mL), H_2O (100 mL), brine (100 mL), dried ($MgSO_4$), filtered and concentrated under reduced pressure. The resulting residue was filtered through a plug of silica and concentrated to give crude isomeric bis-Sme cyclophane as a foamy yellow solid (0.71 g, 1.7 mmol, 60% from dithiacyclophane) which was used without further purification. This isomeric material was dissolved in CH_2Cl_2 (100 mL) and Borch reagent (958 mg, 0.580 mL, 5.98 mmol) was added. The reaction was stirred at rt under N_2 for 3 h then solvents were removed to a black-oily residue which was immediately slurried in THF (100 mL) to which *t*-BuOK (1.60 g, 14.3 mmol) was added. The reaction was stirred at rt under N_2 for 12 h then quenched with saturated $NH_4Cl_{(aq)}$ (5 mL) and volatiles were removed *in vacuo*. The residue was taken up in CH_2Cl_2 (100 mL) and washed with saturated $NH_4Cl_{(aq)}$ (100 mL), H_2O (100 mL), brine (100 mL), dried ($MgSO_4$), filtered and concentrated under reduced pressure. The resulting residue was purified by column chromatography (CH_2Cl_2) to yield 1,6-dioxa[6.2.2](13,5)cyclophane-14,22-diene (462 mg, 1.45 mmol) as a light yellow solid. R_f = 0.45 (CH_2Cl_2); m.p. 117-118 °C (heptane); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.15 (s, 4H), 6.95 (t, *J* = 1.4 Hz, 2H), 6.11 (d, *J* = 1.4 Hz, 4H), 3.91 (t, *J* = 6.0 Hz, 4H), 1.50-1.54 (m, 4H), 1.26-1.29 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 155.87, 136.22, 135.60, 134.81, 113.99, 67.49, 27.86, 22.90.

1,7-Dioxa[7](2,7)pyrenophane (2.47a)

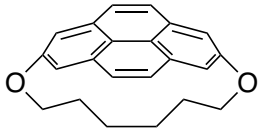


2.47a

1,7-Dioxa[7.2.2](1,3,5)cyclophane-14,22-diene (285 mg, 0.940 mmol) was dissolved in CH_2Cl_2 (40 mmol) to which DDQ (234 mg, 1.03 mmol) was added in one portion. The resulting reaction

mixture was stirred at rt for 24 h then quenched with saturated $NH_4Cl_{(aq)}$ (50 mL) and extracted with CH_2Cl_2 (3 ×. 30 mL). The combined organic extracts were washed with 1M $NaOH_{(aq)}$ (50 mL) and brine (50 mL), then dried ($MgSO_4$), filtered and concentrated under reduced pressure. The resulting residue was purified by column chromatography (CH_2Cl_2) to afford 1,7-dioxa[7](2,7)pyrenophane (245 mg, 86%) as a light yellow solid. R_f = 0.45 (CH_2Cl_2); m.p. 154-156 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.73 (s, 4H), 7.22 (s, 4H), 3.31 (t, *J* = 4.8 Hz, 4H), 0.02- –0.07 (m, 4H), –2.04 - –2.14 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 152.01, 133.42, 126.69, 126.31, 123.14, 76.28, 27.92, 26.87.

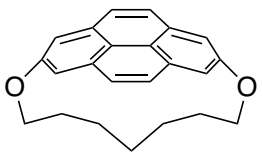
1,8-Dioxa[8](2,6)pyrenophane (2.47b)



2.47b

syn-1,6-Dioxa[6.2.2](1,3,5)cyclophane-14,22-diene (450 mg, 1.42 mmol) was dissolved in CH_2Cl_2 (40 mL) to which DDQ (354 mg, 1.56 mmol) was added in one portion. The resulting reaction mixture was stirred at rt for 18 h then quenched with saturated $NH_4Cl_{(aq)}$ and extracted with CH_2Cl_2 (3 × 30 mL). The combined organic extracts were washed with 1M $NaOH_{(aq)}$ (50 mL) and brine (50 mL), then dried ($MgSO_4$), filtered and concentrated under reduced pressure. The resulting residue was purified by column chromatography (CH_2Cl_2) to afford 1,8-dioxa[8](2,7)pyrenophane (363 mg, 81%) as a light yellow solid. R_f = 0.42 (CH_2Cl_2); m.p. 188-189 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ8 8.84 (s, 4H), 7.44 (s, 4H), 3.58 (t, *J* = 4.5 Hz, 4H), 0.10 (broad s, 4H), −1.46 (broad s, 4H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 153.66, 132.69, 127.41, 126.96, 123.26, 77.75, 27.96, 26.70; HRMS (LC-APPIMS) calculated for $C_{22}H_{20}O_2$ (M+1) 317.1463, found 317.1522.

1,9-Dioxa[9](2,7)pyrenophane (2.47c)



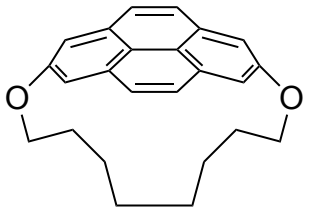
2.47c

syn-1,9-Dioxa,17,26-dithia[9.3.3](1,3,5)cyclophane (800 mg, 2.00 mmol) was dissolved in CH_2Cl_2 (50 mL) to which Borch reagent (961 mg, 0.600 mL, 5.79 mmol) was added via syringe. The reaction was stirred at rt under a

N_2 atmosphere for 3 h, then the volatiles were removed under reduced pressure. The resulting oily residue was quenched with MeOH (50 mL) and stirred for 1 h. The white precipitate was collected by decanting and then drying the remaining solid *in vacuo* to give crude bis(tetrafluoroborate) salt which was immediately slurried in THF (50 mL). *t*-BuOK (600 mg, 4.88 mmol) was added and the reaction was stirred at rt under N_2 for 3h. The reaction was quenched with saturated $NH_4Cl_{(aq)}$ (5 mL) and the volatiles were removed under reduced pressure, then redissolved in CH_2Cl_2 (50 mL). The organic layer was washed with saturated $NH_4Cl_{(aq)}$ (50 mL), H_2O (50 mL), and brine (50 mL) then dried ($MgSO_4$), filtered, and concentrated under reduced pressure. The resulting residue was filtered through a plug of silica and concentrated to give crude isomeric bis-Sme cyclophane as a foamy yellow solid (601 mg, 1.40 mmol, 70% two-steps) which was used without further purification. This isomeric material was dissolved in CH_2Cl_2 (50 mL) and Borch reagent (487 mg, 2.10 mL, 2.94 mmol) was added. The reaction was stirred at rt under N_2 for 3 h then the solvents were removed to give a black-oily residue which was immediately slurried in THF (50 mL) to which *t*-BuOK (600 mg, 4.88 mmol) was added. The reaction was stirred at rt under N_2 for 12 h then quenched with saturated $NH_4Cl_{(aq)}$ (5 mL) and volatiles were removed *in vacuo* This residue was taken up in CH_2Cl_2 (100 mL) and washed with saturated $NH_4Cl_{(aq)}$ (100 mL), H_2O (100 mL), brine (100 mL), dried ($MgSO_4$), filtered and concentrated under reduced pressure. The resulting residue was purified by column chromatopgraphy (CH_2Cl_2) to an inseperable mixture of products. This mixture was dissolved in CH_2Cl_2 (50 mL) was DDQ (499 mg, 2.20 mmol) in one portion and stirred for 12 h at rt. The reaction was quenched with saturated $NH_4Cl_{(aq)}$ (50 mL) and extracted with CH_2Cl_2 (3 ×. 30 mL). The combined organic extracts were washed with 1M $NaOH_{(aq)}$ (50 mL) and brine (50 mL), then dried ($MgSO_4$), filtered and concentrated under reduced pressure. The resulting residue was purified by column chromatography (CH_2Cl_2) to afford 1,9-dioxa[9](2,7)pyrenophane (231 mg, 35% from **2.187c**) as a light yellow solid. R_f = 0.42 (CH_2Cl_2); m.p. 247.5-249.5 (heptane); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.91 (4H), 7.63 (4H), 3.76 (t, *J* = 4.3 Hz, 4H), 0.74-0.65 (m, 4H), −0.67- −0.78 (m, 2H), −1.83- −1.94 (m, 4H);

^{13}C NMR (75 MHz, $CDCl_3$) δ 153.70, 132.75, 127.06, 125.37, 122.06, 75.77, 28.93, 28.80, 28.31.

1,10-Dioxa[10](2,7)pyrenophane (2.47d)

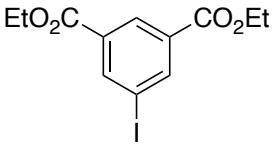


2.47d

syn-1,10-Dioxa,18,27-dithia[10.3.3](1,3,5)cyclophane (950 mg, 2.29 mmol) was dissolved in CH_2Cl_2 (75 mL) to which Borch reagent (1.14 g, 0.700 mL, 6.87 mmol) was added via syringe. The reaction was stirred at rt under a N_2 atmosphere for 3 h, then the volatiles were removed under reduced pressure. The resulting oily residue was quenched with MeOH (50 mL) and stirred for 1 h. The white precipitate was collected by decanting and then drying the remaining solid *in vacuo* to give crude bis(tetrafluoroborate) salt which was immediately slurried in THF (75 mL). *t*-BuOK (642 mg, 5.75 mmol) was added and the reaction was stirred at rt under N_2 for 3h. The reaction was quenched with saturated $NH_4Cl_{(aq)}$ (5 mL) and the volatiles were removed under reduced pressure, then redissolved in CH_2Cl_2 (50 mL). The organic layer was washed with saturated $NH_4Cl_{(aq)}$ (50 mL), H_2O (50 mL), and brine (50 mL) then dried ($MgSO_4$), filtered, and concentrated under reduced pressure. The resulting residue was filtered through a plug of silica and concentrated to give crude isomeric bis-Sme cyclophane as a foamy yellow solid (610 mg, 1.48 mmol, 65% two-steps) which was used without further purification. This isomeric material was dissolved in CH_2Cl_2 (50 mL) and Borch reagent (741 mg, 0.460 mL, 4.46 mmol) was added. The reaction was stirred at rt under N_2 for 3 h then the solvents were removed to give a black-oily residue which was immediately slurried in THF (50 mL) to which *t*-BuOK (600 mg, 4.88 mmol) was added. The reaction was stirred at rt under N_2 for 12 h then quenched with saturated $NH_4Cl_{(aq)}$ (5 mL) and volatiles were removed *in vacuo* This residue was taken up in CH_2Cl_2 (100 mL) and washed with saturated $NH_4Cl_{(aq)}$ (100 mL), H_2O (100 mL), brine (100 mL), dried ($MgSO_4$), filtered and concentrated under reduced pressure. The resulting residue was purified by column chromatopgraphy (CH_2Cl_2) to an inseperable mixture of products. This mixture was dissolved in CH_2Cl_2 (50 mL) was DDQ

(370 mg, 1.63 mmol) in one portion and stirred for 12 h at rt. The reaction was quenched with saturated $NH_4Cl_{(aq)}$ (50 mL) and extracted with CH_2Cl_2 (3 ×. 30 mL). The combined organic extracts were washed with 1M $NaOH_{(aq)}$ (50 mL) and brine (50 mL), then dried ($MgSO_4$), filtered and concentrated under reduced pressure. The resulting residue was purified by column chromatography (CH_2Cl_2) to afford 1,10-dioxa[10](2,7)pyrenophane (283 mg, 36% from **2.187d**) as a light yellow solid. R_f = 0.42 (CH_2Cl_2); m.p. decomposition >250 °C (heptane); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.94 (s, 4H), 7.74 (s, 4H), 4.03 (t, *J* = 4.4 Hz, 4H), 0.90-0.95 (m, 4H), −0.66- −0.72, (m, 4H), −1.13- −1.19 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 154.81, 132.36, 127.16, 123.64, 121.07, 76.36, 30.11, 30.03, 28.34.

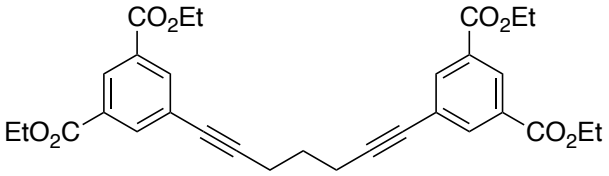
Diethyl 5-iodoisophthalate (2.211)



2.211

5-Aminoisophthalic acid (5.00 g, 27.6 mmol) was slurried in H_2O (10 mL) and 10% HCl (100 mL) and cooled to 0 °C. $NaNO_2$ (2.09 g, 30.4 mmol) was added and the reaction was stirred while maintaining cooling to 1 h. KI (18.3 g, 110 mmol) was added in roughly four equal portions over 1 h after which the reaction mixture was allowed to gradually warm to rt and stirred overnight. The resulting precipitate was collected by suction filtration, washed with plenty of H_2O (500 mL) to obtain crude 5-iodoisophthalic acid as a yellow filter cake which was used without further purification. This product was dissolved in EtOH (150 mL) and conc. H_2SO_4 (10 mL) was added and the reaction mixture was refluxed overnight then cooled to rt. Volatiles were removed *in vacuo* then re-dissolved in CH_2Cl_2 (200 mL) and washed with saturated $NH_4Cl_{(aq)}$ (100 mL), H_2O (100 mL) and brine (100 mL) then dried ($MgSO_4$), filtered and concentrated under reduced pressure. The resulting residue was purified by column chromatography (CH_2Cl_2) to afford diethyl 5-iodoisophthalate (6.53 g, 68%) as a white crystalline solid. R_f = 0.35 (CH_2Cl_2); m.p. 75-76 °C (EtOH); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.63 (t, *J* = 1.5 Hz, , 2H1H), 8.54 (d, *J* = 1.5 Hz, 2H), 4.41 (q, *J* = 7.1 Hz, 4H), 1.42 (t, *J* = 7.1 Hz, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 164.41, 142.33, 132.53, 129.82, 93.40, 61.77, 14.30.

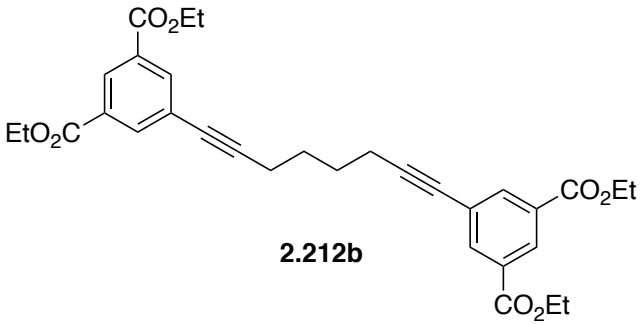
1,7-Bis(3,5-bis(ethoxycarbonyl)phenyl)-1,6-heptadiyne (2.212a)



2.212a

Diethyl 5-iodoisophthalate (2.00 g, 5.74 mmol) was dissolved in benzene (50 mL) and purged with N_2 for 5 mins. 1,6-Heptadiyne (0.31 mL, 250 mg, 2.73 mmol) and DBU (1.02 mL, 1.04 g, 6.83 mmol) were added followed by $PdCl_2(PPh_3)_2$ (77mg, 0.11 mmol) and CuI (42 mg, 0.22 mmol). The reaction mixture was stirred at rt under a N_2 atmosphere for 20 h. The reaction mixture was concentrated under reduced pressure and subjected to column chromatography (20% ethyl acetate/hexanes) to yield 1,7-bis(3,5-bis(ethoxycarbonyl)phenyl)-1,6-heptadiyne (1.24 g, 85%) as a clear colourless oil. R_f = 0.32 (20% ethyl acetate/hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.57 (t, *J* = 1.6 Hz, 2H), 8.24 (d, *J* = 1.6 Hz, 4H), 4.40 (quartet, *J* = 7.1 Hz, 8H), 2.64 (t, *J* = 7.0 Hz, 4H), 1.95 (quintet, *J* = 7.0 Hz, 2H), 1.41 (t, *J* = 7.1 Hz, 12H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 165.21, 136.40, 131.10, 129.51, 124.65, 91.07, 79.75, 61.45, 27.53, 18.64, 14.28.

1,8-Bis(3,5-bis(ethoxycarbonyl)phenyl)1,7-octadiyne (2.212b)



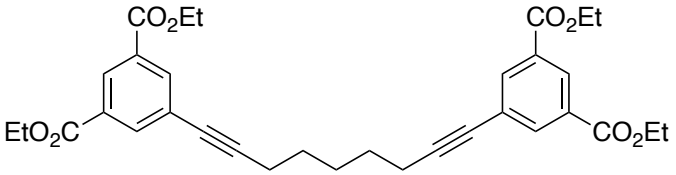
2.212b

Diethyl 5-iodoisophthalate (2.00 g, 5.74 mmol) was dissolved in toluene (50 mL) and purged with N_2 for 5 mins. 1,7-Octadiyne (0.36 mL, 290 mg, 2.74 mL) and DBU (1.02 mL, 1.04 g, 6.45 mmol) were added followed by $PdCl_2(PPh_3)_2$ (77 mg, 0.11 mmol) and CuI (42 mg, 0.22 mmol). The reaction mixture was stirred at rt under a N_2 atmosphere for 20 h. The reaction mixture was concentrated under reduced pressure and subjected to column chromatography (20% ethyl acetate/hexanes) to afford 1,8-bis(3,5-bis(ethoxycarbonyl)phenyl)1,7-octadiyne (1.19 g, 80%) as a white solid. A small sample

was recrystallized from heptane for analysis. R_f = 0.35 (20% ethyl acetate/hexanes; m.p. 88-90 °C (heptane); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.56 (t, *J* = 1.6 Hz, 2H), 8.22 (d, *J* = 1.6 Hz, 4H), 4.40 (q, *J* = 7.1 Hz, 8H), 2.52 (t, *J* = 6.4 Hz, 4H), 1.82 (m, 4H), 1.41 (t, *J* = 7.1 Hz, 12H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 165.24, 136.39, 131.08, 129.41, 124.81, 91.78, 79.38, 61.43, 27.67, 18.97, 14.27.

1,9-Bis(3,5-bis(ethoxycarbonyl)phenyl)-1,8-nonadiyne (2.212c)

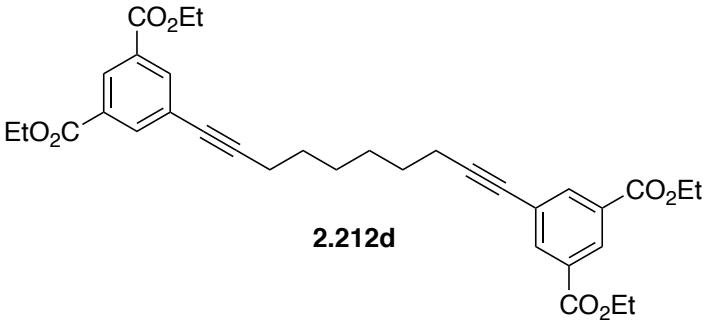
Diethyl 5-iodoisophthalate (3.00 g, 8.62 mmol) was dissolved in toluene (75 mL) and purged with N_2 for 5 mins. 1,8-nonadiyne (0.62 mL, 295 mg, 4.10 mmol) and DBU (1.53 mL, 1.56 g, 10.3 mmol) were added followed by $PdCl_2(PPh_3)_2$ (112 mg, 0.16 mmol) and CuI (61 mg, 0.32 mmol). The reaction mixture was stirred at rt under a N_2 atmosphere for 18 the concentrated under reduced pressure and subjected to column chromatography (20% ethyl acetate/hexanes) to afford 1,9-bis(3,5-bis(ethoxycarbonyl)phenyl)-1,8-nonadiyne (2.11 g, 92%) as a white solid, a small sample was recrystallized from heptane for analysis. R_f = 0.32 (20% ethyl acetate/hexanes); m.p. 110-112 °C (heptane); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.54 (t, *J* = 1.6 Hz, 2H), 8.20 (d, *J* = 1.6 Hz, 4H), 4.40 (q, *J* = 7.1 Hz, 8H), 2.48 (t, *J* = 6.4 Hz, 4H), 1.67-1.70 (m, 6H), 1.41 (t, *J* = 7.1 Hz, 12H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 165.29, 136.40, 131.06, 129.37, 124.89, 92.18, 79.20, 61.45, 28.18, 28.08, 19.30, 14.29.



2.212c

1,10-Bis(3,5-bis(ethoxycarbonyl)phenyl)-1,9-decadiyne (2.212d)

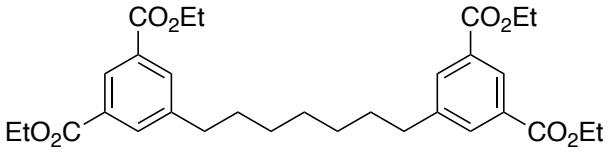
Diethyl 5-iodoisophthalate (4.48 g, 12.9 mmol) was dissolved in toluene (60 mL) and purged with N_2 for 5 mins. 1,9-decadiyne (1.00 mL, 822 mg, 6.12 mmol) and DBU (2.30 mL, 2.33 g, 15.3 mmol) were added followed by $PdCl_2(PPh_3)_2$ (170 mg, 0.24 mmol) and CuI (92 mg, 0.48 mmol). The reaction mixture was stirred at rt under a N_2 atmosphere for 17 h then concentrated under reduced pressure and subjected to column chromatography (20% ethyl acetate/hexane) to afford 1,10-bis(3,5-bis(ethoxycarbonyl)phenyl)-1,9-decadiyne (2.88 g, 82%) as a white solid. A small sample was recrystallized from heptane for analysis. R_f = 0.30 (20% ethyl acetate/hexanes); m.p. 121-123 °C (heptane); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.55 (t, *J* = 1.6 Hz, 2H), 8.22 (d, *J* = 1.6 Hz, 4H), 4.40 (q, *J* = 7.1 Hz, 8H), 2.46 (t, *J* = 6.4 Hz, 4H), 1.65-1.69 (m, 4H), 1.52-1.56 (m, 4H), 1.41 (t, *J* = 7.1 Hz, 12H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 165.35, 136.44, 131.08, 129.39, 124.96, 92.40, 79.11, 61.48, 28.47, 28.44, 19.38, 14.32.



2.212d

1,7-Bis(3,5-bis(ethoxycarbonyl)phenyl)heptane (2.223a)

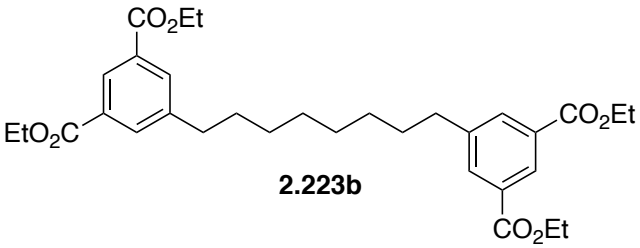
1,7-Bis(3,5-bis(ethoxycarbonyl)phenyl)-1,6-heptadiyne (1.24 g, 2.33 mmol) was dissolved in EtOAc (50 mL) and EtOH (50 mL), then purged with N_2 for 5 mins. $Pd(OAc)_2$ (5 mg, 0.02 mmol) and charcoal (45 mg) were added and 2 balloons of H_2 were bubbled through the reaction mixture, then stirred for 12 h under a H_2 atmosphere. Celite was added to the reaction mixture then filtered. The filter cake was washed with EtOAc (3 × 50 mL). The combined organic washes were concentrated under reduced pressure to afford 1,7-bis(3,5-bis(ethoxycarbonyl)phenyl)heptane (1.26 g, 99%) as a clear colourless oil which was used without further purification. R_f = 0.32 (20% ethyl



2.223a

acetate/hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.50 (t, *J* = 1.5 Hz, 2H), 8.04 (d, *J* = 1.5 Hz, 4H), 4.41 (quartet, *J* = 7.1 Hz, 8H), 2.70 (t, *J* = 7.7 Hz, 4H), 1.63-1.68 (m, 4H), 1.42 (t, *J* = 7.1 Hz, 12H), 1.33-1.38 (m, 6H); ^{13}C NMR (75 MHz, $CDCl_3$)

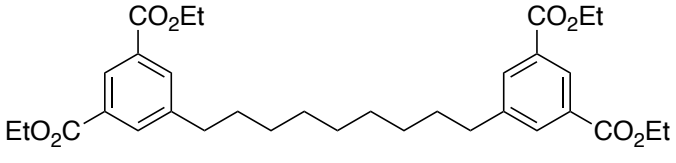
1,8-Bis(3,5-bis(ethoxycarbonyl)phenyl)octane (2.223b)



2.223b

1,8-Bis(3,5-bis(ethoxycarbonyl)phenyl)-1,7-octadiyne (2.26 g, 4.14 mmol) was dissolved in EtOAc (75 ml) and EtOH (75 mL), then purged with N_2 for 5 mins. $Pd(OAc)_2$ (9 mg, 0.04 mmol) and charcoal (81 mg) were added and 2 balloons of H_2 were bubbled through the reaction mixture, then stirred for 12 h under a H_2 atmosphere. Celite was added to the reaction mixture then filtered. The filter cake was washed with EtOAc (3 × 50 mL). The combined organic washes were concentrated under reduced pressure to afford 1,8-bis(3,5-bis(ethoxycarbonyl)phenyl)octane (2.29 g, 99%) as a white solid. A small sample was recrystallized from heptane for analysis. R_f = 0.35 (20% ethyl acetate/hexanes); m.p. 77-79 °C (heptane); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.50 (t, *J* = 1.6 Hz, 2H), 8.04 (d, *J* = 1.6 Hz, 4H), 4.40 (q, *J* = 7.1 Hz, 8H), 2.70 (t, *J* = 7.8 Hz, 4H), 1.62-1.67 (m, 4H), 1.41 (t, *J* = 7.1 Hz, 12H), 1.32 (broad s, 8H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.09, 143.61, 133.69, 130.85, 128.10, 61.24, 35.58, 31.27, 29.34, 29.19, 14.35.

1,9-Bis(3,5-bis(ethoxycarbonyl)phenyl)nonane (2.223c)

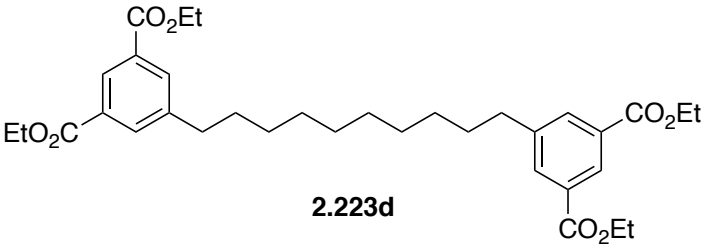


2.223c

1,9-Bis(3,5-bis(ethoxycarbonyl)phenyl)-1,8-nonadiyne (1.74 g, 3.10 mmol) was dissolved in EtOAc (75 mL) and EtOH (75 mL), then purged with N_2 for 5 mins. $Pd(OAc)_2$ (7mg, 0.03 mmol) and charcoal

(63 mg) were added and 2 balloons of H_2 were bubbled through the reaction mixture, then stirred for 12 h under a H_2 atmosphere. Celite was added to the reaction mixture then filtered. The filter cake was washed with EtOAc (3 × 50 mL). The combined organic washes were concentrated under reduced pressure to afford 1,9-bis(3,5-bis(ethoxycarbonyl)phenyl)nonane (1.76 g, 99%) as a white solid. A small was recrystallized from heptane for analysis. R_f = 0.32 (20% ethyl acetate/hexanes); m.p. 58-59°C (heptane); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.50 (t, *J* = 1.5 Hz, 2H), 8.04 (d, *J* = 1.5Hz, 4H), 4.40 (q, *J* = 7.1 Hz, 8H), 2.70 (t, *J* =7.8 Hz, 4H), 1.63-1.66 (m, 4H), 1.42 (t, *J* = 7.1 Hz, 12H), 1.31 (broad s, 10H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.09, 143.64, 133.69, 130.84, 128.08, 61.23, 35.58, 31.28, 29.43, 29.40, 29.19, 14.34.

1,10-Bis(3,5-bis(ethoxycarbonyl)phenyl)decane (2.223d)

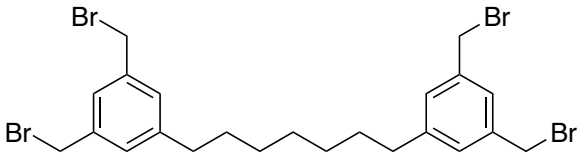


2.223d

1,10-Bis(3,5-bis(ethoxycarbonyl)phenyl)-1,9-decadiyne (820 mg, 1.43 mmol) was dissolved in EtOAc (50 mL) and EtOH (50 mL), then purged with N_2 for 5 mins. $Pd(OAc)_2$ (3 mg, 0.01 mmol) and charcoal (27 mg) were added and 2 ballons of H_2 were bubbled through the reaction mixture then filtered. The filter cake was washed with EtOAc (3 × 50 mL). The combined organic washes were concentrated under reduced pressure to afford 1,10-bis(3,5-bis(ethoxycarbonyl)phenyl)decane (830 mg, 99%) as a white solid. A small sample was recrystallized from heptane for analysis. R_f = 0.30 (30% ethyl acetate/hexanes); m.p. 82-83°C (heptane); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.49 (t, *J* = 1.2 Hz, 2H), 8.04 (d, *J* = 1.2 Hz, 4H), 4.40 (q, *J* = 7.1 Hz, 8H), 2.70 (t, *J* = 7.8 Hz, 4H), 1.63-1.66 (m, 4H), 1.41 (t, *J* = 7.1 Hz, 12H), 1.25-1.32 (m, 12H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.07, 143.65, 133.69, 130.82, 128.07, 61.23, 35.58, 31.29, 29.50, 29.40, 29.20, 14.34.

1,7-Bis(3,5-bis(bromomethyl)phenyl)heptane (2.224a)

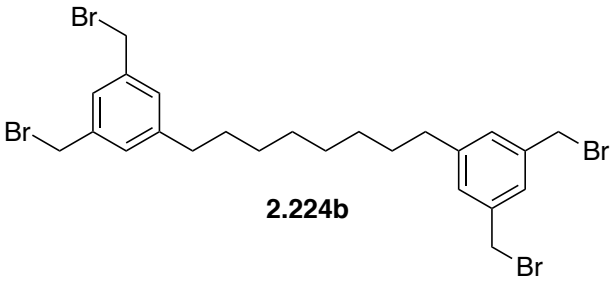
1,7-Bis(3,5-bis(ethoxycarbonyl)phenyl)heptane (2.50 g, 4.62 mmol) was dissolved in THF (150 mL) and cooled to 0 °C under a N_2 atmosphere to which $LiAlH_4$ (2.11 g, 55.5 mmol). The reaction mixture was allowed to gradually warm to rt then stirred overnight. The reaction mixture was cooled to 0 °C and quenched by slow addition of EtOAc (200 mL) and 10% $HCl_{(aq)}$ (200 mL). The reaction mixture was stirred for 1 h and the layers were separated. The aqueous layer was extracted with EtOAc (2 x 100 mL). The combined organic extracts were washed with brine (100 mL), dried ($MgSO_4$), filtered and concentrated under reduced pressure. The resulting tetraalcohol was dissolved in a 2:1 AcOH/HBr mixture (150 mL) and refluxed overnight. The mixture was cooled to rt, diluted with H_2O (100 mL) and extracted with CH_2Cl_2 (3 x 100 mL). The combined organic extracts were washed with saturated aqueous $NaHCO_3$ (100 mL) and brine (100 mL), then dried ($MgSO_4$), filtered and concentrated under reduced pressure. The resulting residue was subjected to column chromatography (40% CH_2Cl_2/hexanes) to afford 1,7-bis(3,5-bis(bromomethyl)phenyl)heptane (2.30 g, 80%) as white solid, a small amount was recrystallized from heptane for analysis. R_f = 0.25 (40% CH_2Cl_2); m.p. 59-61 °C (heptane); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.23 (t, J = 1.5 Hz, 2H), 7.13 (d, J = 1,5 Hz, 4H), 4.45 (s, 8H), 2.58 (t, J = 7.8 Hz, 4H), 1.56-1.65 (m, 8H), 1.34 (broad s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 144.22, 138.27, 129.24, 126.99, 35.60, 33.15, 31.12, 29.22, 29.15.



2.224a

1,8-Bis(3,5-bis(bromomethyl)phenyl)octane (2.224b)

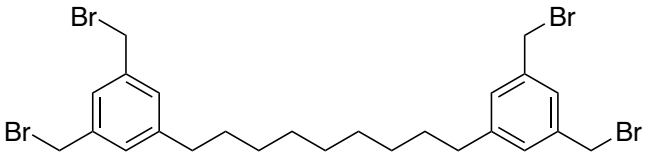
1,8-Bis(3,5-bis(ethoxycarbonyl)phenyl)octane (2.28 g, 4.11 mmol) was dissolved in THF (150mL) and cooled to 0 °C under a N_2 atmosphere to which $LiAlH_4$ (1.87 g, 49.3 mmol) was added. The reaction mixture was allowed to gradually warm to rt then stirred overnight. The reaction mixture was cooled to 0 °C and quenched by slow addition of EtOAc (200 mL) and 10% $HCl_{(aq)}$ (200 mL). The reaction mixture was stirred for 1 h and the layers were separated. The aqueous layer was extracted with EtOAc (2 x 50 mL). The combined organic extracts were washed with brine (100 mL), dried ($MgSO_4$), filtered and concentrated under reduced pressure. The resulting tetraalcohol was dissolved in a 2:1 AcOH/HBr mixture (150 mL) and refluxed for 8 h. The mixture was cooled to rt, diluted with H_2O (100 mL) and extracted with CH_2Cl_2 (3 x 100 mL). The combined organic extracts were washed with saturated aqueous $NaHCO_3$ (100 mL) and brine (100 mL), then dried ($MgSO_4$), filtered and concentrated under reduced pressure. The resulting residue was subjected to column chromatography (40% CH_2Cl_2/hexanes) to afford 1,8-bis(3,5-bis(bromomethyl)phenyl)octane (2.32 g, 88%) as a white solid, a small amount was recrystallized from heptane for analysis. R_f = 0.35 (40% CH_2Cl_2/hexanes); m.p. 85-86 °C (heptane); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.23 (t, J = 1.5 Hz, 2H), 7.14 (d, J = 1.5 H, 4H), 4.45 (s, 8H), 2.58 (t, J = 7.8 Hz, 4H), 1.56-1.64 (m, 4H), 1.32 (broad s, 8H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 144.28, 138.26, 129.24, 126.97, 35.63, 33.15, 31.16, 29.34, 29.26.



2.224b

1,9-Bis(3,5-bis(bromomethyl)phenyl)nonane (2.224c)

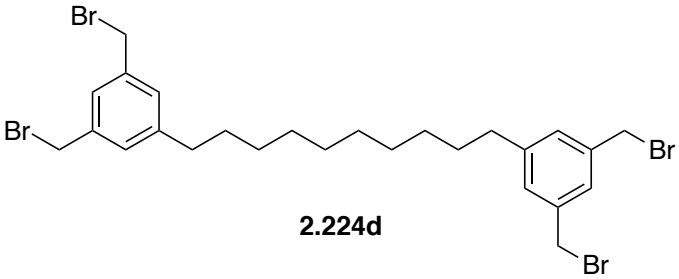
1,9-Bis(3,5-bis(ethoxycarbonyl)phenyl)nonane (1.73 g, 3.04 mmol) was dissolved in THF (100 mL) and cooled to 0 °C



2.224c

under a N_2 atmosphere to which $LiAlH_4$ (1.38 g, 36.5 mmol) was added. The reaction mixture was allowed to gradually warm to rt then stirred overnight. The reaction mixture was cooled to 0 °C and quenched by slow addition of EtOAc (100 mL) and 10% $HCl_{(aq)}$ (100 mL). The mixture was stirred for 1 h and the layers were separated. The aqueous layer was extracted with EtOAc (2 x 50 mL). The combined organic extracts were washed with brine (100 mL), dried ($MgSO_4$), filtered and concentrated under reduced pressure. The resulting tetraalcohol was dissolved in a 2:1 AcOH/HBr mixture (100 mL) and refluxed overnight. The mixture was cooled to rt, diluted with H_2O (100 mL) and extracted with CH_2Cl_2 (3 x 100 mL). The combined organic extracts were washed with saturated aqueous $NaHCO_3$ (100 mL) and brine (100 mL), then dried ($MgSO_4$), filtered and concentrated under reduced pressure. The resulting residue was subjected to column chromatography (40% CH_2Cl_2/hexanes) to afford 1,9-bis(3,5-bis(bromomethyl)phenyl)nonane (1.38 g, 70%) as a white solid, a small amount was recrystallized from heptane for analysis. R_f = 0.35 (40% CH_2Cl_2/hexanes); m.p. 69-71 °C (heptane); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.21 (t, *J* = 1.5 Hz, 2H), 7.12 (d, *J* = 1.5 Hz, 4H), 4.43 (s, 8H), 2.57 (t, *J* = 7.8 Hz, 4H), 1.55-1.63 (m, 4H), 1.29 (broad s, 10H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 144.30, 128.28, 129.27, 127.01, 35.67, 33.24, 31.22, 29.48, 29.45, 29.31.

1,10-Bis(3,5-bis(bromomethyl)phenyl)decane (2.224d)

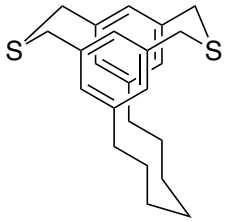


2.224d

1,10-Bis(3,5-bis(ethoxycarbonyl)phenyl)decane (2.50 g, 4.29 mmol) was dissolved in THF (150 mL) and cooled to 0 °C under a N_2 atmosphere to which $LiAlH_4$ (1.95 g, 51.5 mmoL) was added. The reaction mixture was gradually warmed to rt then stirred overnight. The reaction mixture was cooled to 0 °C and quenched by slow addition of EtOAc (50 mL) and 20% $HCl_{(aq)}$ (100 mL) and then stirred for 1 h after which the layers were separated and the aqueous layer was extracted with EtOAc (2 x 75 mL).

The combined organic layers were washed with brine (100 mL), dried ($MgSO_4$), filtered and concentrated under reduced pressure to afford crude 1,10-bis(3,5-bis(methanol)phenyl)decane which was used without purification. The tetraalcohol was dissolved in glacial acetic acid (50 mL), to which was added a solution of 1:1 HBr/AcOH (50 mL). The mixture was refluxed overnight then cooled to rt, diluted with H_2O (100 mL) and extracted with CH_2Cl_2 (3 x 75 mL). The combined organic layers were washed with H_2O (100 mL), saturated aqueous $NaHCO_3$ solution (100 mL), and brine (100 mL) then dried ($MgSO_4$), filtered and concentrated under reduced pressure. The resulting oily brown residue was purified by column chromatography (40% CH_2Cl_2/hexanes) to afford 1,10-bis(3,5-bis(bromomethyl)phenyl)decane (2.43 g, 85%) as a white solid. A small sample was recrystallized from heptane for analysis. R_f = 0.33 (40% CH_2Cl_2/hexanes); m.p. 96-98°C (heptane); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.23 (t, *J* = 1.5 Hz, 2H), 7.13 (d, *J* = 1.5 Hz, 4H), 4.45 (s, 8H), 2.58 (t, *J* = 7.8 Hz, 4H), 1.57-1.65 (m, 4H), 1.25-1.32 (m, 12H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 144.28, 138.26, 129.24, 126.98, 35.63, 33.16, 31.16, 29.34, 29.26 (9 of 10 observed).

syn-15,24-Dithia[7.3.3](1,3,5)benzophane (2.205a)

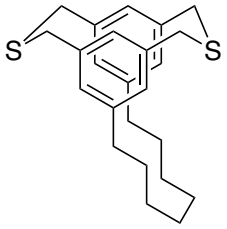


2.205a

1,7-Bis(3,5-bis(bromomethyl)phenyl)heptane (2.12 g, 3.39 mmol) was dissolved in 10% EtOH/CH_2Cl_2 (1000 mL) with vigourous stirring in an Erlenmeyer flask. Freshly prepared Na_2S/fly ash (2.59 g, 8.49 mmol, 3.17 mmol/g) was added in roughly three equal portions over 1 h. The reaction mixture was vigourously stirred for 19 h at rt. The reaction mixture was filtered and concentrated under reduced pressure. The resulting residue was subjected to column chromatopgraphy (40% CH_2Cl_2/hexanes) to give *syn*-15,24-dithia[7.3.3](1,3,5)benzophane (875 mg, 70%) as a white solid. R_f = 0.45 (40% CH_2Cl_2/hexanes); m.p. 119-122 °C (heptane);); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.10 (s, 2H), 6.65 (s, 4H), 3.83 (d, *J* = 15.3 Hz, 4H), 3.77 (d, *J* = 15.3 Hz, 4H), 2.37-2.33 (m, 4H), 1.56-1.52 (m, 4H), 1.16-1.08 (m, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 142.88, 137.03, 128.71, 127.10,

39.22, 34.10, 28.83, 26.49, 26.28; HRMS (LC-APPIMS) calculated for $C_{23}H_{28}S_2$: 368.1632, found: 368.1641.

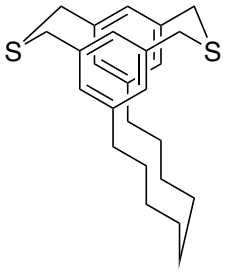
***syn*-16,25-Dithia[8.3.3](1,3,5)benzophane (2.205b)**



2.205b

1,8-Bis(3,5-bis(bromomethyl)phenyl)octane (230 mg, 0.360 mmol) was dissolved in 10% EtOH/CH_2Cl_2 (200 mL) with vigourous stirring in an Erlenmeyer flask. Freshly prepared Na_2S/fly ash (424 mg, 1.08 mmol, 2.55 mmol/g) was added in roughly three equal portions over 1 h. The reaction mixture was vigourously stirred for 19 h at rt. The reaction mixture was filtered and concentrated under reduced pressure. The resulting residue was subjected to column chromatopgraphy (40% CH_2Cl_2/hexanes) to give *syn*-16,25-dithia[8.3.3](1,3,5)benzophane (119 mg, 87%) as a white solid. R_f = 0.47 (40% CH_2Cl_2/hexanes); m.p. 119-122 °C (heptane); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.19 (s, 2H), 6.65 (s, 4H) 3.83 (s, 8H), 2.38 (t, *J* = 6.08 Hz, 4H), 1.43-1.37 (m, 4H), 1.31-1.26 (m, 4H), 1.01-0.97 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 159.04, 138.51, 124.44, 113.32, 64.06, 38.88, 28.03, 20.71; HRMS (LC-APPIMS) calculated for $C_{24}H_{30}S_2$: 382.1789, found: 382.1793.

***syn*-17,26-Dithia[9.3.3](1,3,5)cyclophane (2.205c)**

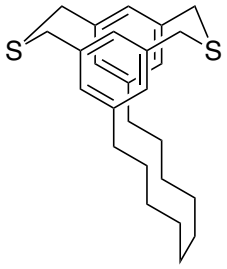


2.205c

1,9-Bis(3,5-bis(bromomethyl)phenyl)nonane (230 mg, 0.352 mmol) was dissolved 10% EtOH/CH_2Cl_2 (200 mL) with vigourous stirring in an Erlenmeyer flask. Freshly prepared Na_2S/fly ash (399 mg, 1.05 mmol, 2.63 mmol/g) was added in roughly three equal portions over 1 h. The reaction mixture was vigourously stirred for 19 h at rt. The reaction mixture was filtered and concentrated under reduced pressure. The resulting residue was subjected to column chromatopgraphy (40% CH_2Cl_2/hexanes) to give *syn*-17,26-dithia[9.3.3](1,3,5)benzophane (99 mg, 72%) as a white solid. R_f = 0.30 (20% CH_2Cl_2/hexanes); m.p 156-159 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.12 (s, 2H), 6.63 (s, 4H),

3.86 (d, *J* = 14.9 Hz, 4H), 3.76 (d, *J* = 14.9 Hz, 4H), 2.36 (t, *J* = 7.7 Hz, 4H), 1.58-1.49 (m, 4H), 1.33-1.28 (m, 10H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 142.54, 137.09, 128.66, 126.44, 39.11, 33.92, 27.39, 26.40, 25.41, 24.88; HRMS (LC-APPIMS) calculated for $C_{25}H_{32}S_2$: 396.1945, found: 396.1948.

syn-18,27-Dithia[10.3.3](1,3,5)cyclophane (2.205d)

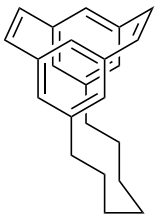


2.205d

1,10-Bis(3,5-bis(bromomethyl)phenyl)decane (202 mg, 0.303 mmol) was dissolved in 10% EtOH/CH_2Cl_2 (200 mL) with vigorous stirring in an Erlenmeyer flask. Freshly prepared Na_2S/fly ash (357 mg, 0.910 mmol, 2.55 mmol/g) was added in roughly three equal portions over 1 h. The reaction mixture was vigorously stirred for 18 h at rt. The reaction mixture was filtered and concentrated under reduced pressure. The resulting residue was subjected to column chromatography (40% CH_2Cl_2/hexanes) to give *syn*-18,27-dithia[10.3.3](1,3,5)benzophane (105 mg, 85%) as a white solid. R_f = 0.30 (20% CH_2Cl_2/hexanes);

m.p. 125-128 °C (heptane); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.11 (s, 2H), 6.63 (s, 4H), 3.82 (d, *J* = 14.9 Hz, 4H), 3.76 (d, *J* = 14.9, 4H), 2.33-2.30 (m, 4H), 1.48-1.25 (m, 14H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 142.71, 137.20, 128.75, 126.48, 38.99, 35.55, 29.56, 28.49, 26.67, 26.33; HRMS (LC-APPIMS) calculated for $C_{26}H_{34}S_2$: 410.2102, found: 410.2088.

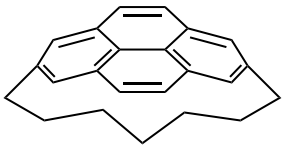
[7.2.2](1,3,5)Benzophane-14,22-diene (2.207a)


2.207a

[7.3.3]-15,24-Dithia(1,3,5)cyclophane (1.27 g, 3.45 mmol) was dissolved in CH_2Cl_2 (50 mL) to which Borch reagent (1.21 g, 0.70 mL, 7.59 mmol) was added via syringe and the reaction mixture was stirred at rt under a N_2 atmosphere for 3 h. The volatiles were removed *in vacuo* and the resulting residue was quenched with EtOAc (50 mL) and stirred for 1 h. The white precipitate was collected by suction filtration (EtOAc) and dried under vacuum to afford crude

bis(tetrafluoroborate) salt (1.45 g, 2.54 mmol, 74%). The *bis*(tetrafluoroborate) salt (1.45 g, 2.54 mmol) was slurried in THF (50 mL) to which *t*-BuOK (1.14 g, 10.2 mmol) was added and the reaction mixture was refluxed under an N_2 atmosphere for 6 h. The reaction mixture was cooled to rt and volatiles were removed *in vacuo* redissolved in CH_2Cl_2 (50 mL) and washed with saturated $NH_4Cl_{(aq)}$ (50 mL), H_2O (50 mL) and brine (50 mL), then dried ($MgSO_4$), filtered and concentrated under reduced pressure to give an isomeric mixture of bis(thiomethyl)cyclophane (958 mg, 2.41 mmol) as an oily light yellow solid which was used without further purification. The bis(thiomethyl)cyclophane (958 mg, 2.41 mmol) was dissolved in CH_2Cl_2 (50 mL) and Borch reagent (809 mg, 0.50 mL, 5.06 mmol) was added via syringe. The reaction mixture was stirred for 1 h at rt under a N_2 atmosphere then the volatiles were removed *in vacuo* to give an oily brown residue which was immediately slurried in THF (50 mL) to which was added *t*-BuOK (1.14 g, 10.2 mmol). The reaction mixture was refluxed under a N_2 atmosphere for 12 h then cooled to rt and concentrated *in vacuo*. The resulting residue was redissolved in CH_2Cl_2 (50 mL) and washed with saturated $NH_4Cl_{(aq)}$ (50 mL), H_2O (50 mL) and brine (50 mL), then dried ($MgSO_4$), filtered and concentrated under reduced pressure which was purified by column chromatography (20% CH_2Cl_2/hexanes) to yield [7.2.2]cyclophane-14,22-diene (3.68 mg, 50% from *bis*(thiomethyl)cyclophane) as a light yellow crystalline solid. R_f = 0.55 (20% CH_2Cl_2/hexanes); m.p. 82-84 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.38 (s, 2H), 7.17 (s, 4H), 6.38 (narrow d, *J* = 1.4 Hz, 4H), 2.25-2.29 (m, 4H), 1.40-1.47 (m, 4H), 0.83-0.85 (m, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 138.38, 137.04, 135.86, 132.91, 125.74, 34.79, 30.76, 27.89, 26.98.

[7](2,7)pyrenophane (2.208a)

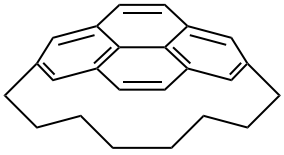


2.208a

[7.2.2](1,3,5)Benzophane-14,22-diene (500 mg, 1.67 mmol) was dissolved in benzene (50 mL) to which DDQ (416 mg, 1.83 mmol) was added in one portion. The reaction mixture was stirred at rt for 6 h then quenched with saturated $NH_4Cl_{(aq)}$ (50 mL) and extracted with CH_2Cl_2 (3 ×. 30

mL). The combined organic extracts were washed with 1M $NaOH_{(aq)}$ (50 mL) and brine (50 mL), then dried ($MgSO_4$), filtered and concentrated under reduced pressure. The resulting residue was purified by column chromatography (hexanes) to afford [7](2,7)pyrenophane (353 mg, 71%) as a light yellow solid. A small sample was recrystallized from heptane for analysis. R_f = 0.55 (20% CH_2Cl_2/hexanes); m.p. 151-153 (heptane); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.77 (s, 4H), 7.43 (s, 4H), 2.39 (t, J = 6.1 Hz, 4), 0.58-0.50 (m, 4H), −1.25- −1.43 (m, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 136.39, 131.77, 130.78, 130.01, 126.45, 35.82, 33.27, 31.52, 23.59.

[8](2,6)Pyrenophane (2.208b)

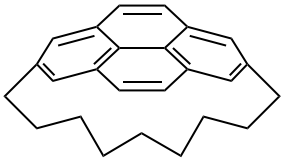


2.208b

16,25-Dithia[8.3.3](1,3,5)cyclophane (980 mg, 2.57 mmol) was dissolved in CH_2Cl_2 (50 mL) and Borch reagent (864 mg, 0.5 mL, 5.40 mmol) was added via syringe and the reaction was stirred at rt under an N_2 atmosphere for 5 h. The volatiles were removed *in vacuo* and then quenched with EtOAc (50 mL) and stirred for 1 h. The resulting precipitate was collected via suction filtration (EtOAc) and dried under vacuum to afford the crude bis(tetrafluoroborate) salt (1.21 g, 80%) as white a solid. The bis(tetrfluoroborate) salt was slurried in THF (50 mL) to which *t*-BuOK (1.15 g, 10.3 mmol) was added and the reaction was refluxed under N_2 for 6 h. The volatiles were removed *in vacuo* and dissolved in CH_2Cl_2 (50 mL) and washed with saturated NH_4Cl (50 mL), H_2O (50 mL) and brine (50 mL), then dried ($MgSO_4$), filtered and concentrated under reduced pressure to yield bis(thiomethyl)cyclophane (740 mg, 1.80 mmol, 70% from 16,25-dithia[8.3.3](1,3,5)cyclophane) which was used without further purification. The bis(thiomethyl)cyclophane was dissolved in CH_2Cl_2 (50 mL) and Borch reagent (605 mg, 0.4 mL) 3.78 mmol) was added via syringe and the reaction was stirred at rt under an N_2 atmosphere for 1 h. The volatiles were removed *in vacuo* and the resulting brown residue was immediately slurried in THF (50 mL) to which *t*-BuOK (808 mg, 7.20 mmol) and the reaction mixture was refluxed under N_2 for 12 h. The volatiles were removed, and the

resulting residue was dissolved in CH_2Cl_2 (50 mL) and washed with saturated $NH_4Cl_{(aq)}$ (50 mL), H_2O (50 mL) and brine (50 mL), then dried ($MgSO_4$), filtered and concentrated under reduced pressure. The resulting residue was subjected to column chromatography (20% CH_2Cl_2/hexanes) to afford a mixture of compounds. This mixture was dissolved in benzene (50 mL) and treated with DDQ (408 mg, 1.80 mmol) and stirred at rt for 6 h. The reaction mixture was concentrated under reduced pressure and redissolved in CH_2Cl_2 (50 mL) and washed with 1 M HCl (50 mL), H_2O (50 mL) and brine (50 mL), then dried ($MgSO_4$), filtered and concentrated under reduced pressure. The resulting residue was subjected to column chromatography (10% CH_2Cl_2/hexanes) to afford [8](2,7)pyrenophane (281 mg, 50% from bis(thiomethyl)cyclophane) as a light yellow crystalline solid. R_f = 0.50 (40% CH_2Cl_2/hexanes); m.p. 175-176.5 °C (heptane); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.84 (s, 4H), 7.60 (s, 4H), 2.60 (t, *J* = 6.4 Hz, 4H), 0.92-0.84 (m, 4H), −0.62- −0.72 (m, 4H) −1.41- −1.48 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 137.53, 131.38, 128.94, 126.66, 35.94, 31.72, 31.17, 23.51;

[9](2,7)Pyrenophane (2.208c)

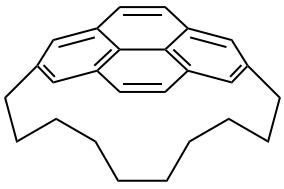


2.208c

17,26-Dithia[9.3.3](1,3,5)cyclophane (1.21 g, 3.10 mmol) was dissolved in CH_2Cl_2 (75 mL) and Borch reagent (1.24 g, 0.75 mL, 7.75 mmol) was added via syringe and the reaction was stirred at rt under an N_2 atmosphere for 5 h. The volatiles were removed *in vacuo* and then quenched with EtOAc (50 mL) and stirred for 1 h. The resulting precipitate was collected via suction filtration (EtOAc) and dried under vacuum to afford the crude bis(tetrafluoroborate) salt (1.65 g) as white a solid. The bis(tetrfluoroborate) salt was slurried in THF (50 mL) to which *t*-BuOK (1.39 g, 12.4 mmol) was added and the reaction was refluxed under N_2 for 6 h. The volatiles were removed *in vacuo* and dissolved in CH_2Cl_2 (50 mL) and washed with saturated NH_4Cl (50 mL), H_2O (50 mL) and brine (50 mL), then dried ($MgSO_4$), filtered and concentrated under reduced pressure to yield bis(thiomethyl)cyclophane (1.15 g, 2.70 mmol, 87% from 15,26-

dithia[9.3.3](1,3,5)cyclophane) which was used without further purification. The bis(thiomethyl)cyclophane was dissolved in CH_2Cl_2 (50 mL) and Borch reagent (1.08 g, 0.65 mL, 6.75 mmol) was added via syringe and the reaction was stirred at rt under an N_2 atmosphere for 1 h. The volatiles were removed *in vacuo* and the resulting brown residue was immediately slurried in THF (50 mL) to which *t*-BuOK (1.21 g, 10.8 mmol) and the reaction mixture was stirred at rt for 12 h. The volatiles were removed and the resulting residue was dissolved in CH_2Cl_2 (50 mL) and washed with saturated $NH_4Cl_{(aq)}$ (50 mL), H_2O (50 mL) and brine (50 mL), then dried ($MgSO_4$), filtered and concentrated under reduced pressure. The resulting residue was subjected to column chromatography (20% CH_2Cl_2/hexanes) to afford a mixture of compounds. This mixture was dissolved in benzene (50 mL) and treated with DDQ (674 mg, 2.97 mmol) and stirred at rt for 6 h. The reaction mixture was concentrated under reduced pressure and dissolved in CH_2Cl_2 (50 mL) then washed with 1 M HCl (50 mL), H_2O (50 mL) and brine (50 mL), then dried ($MgSO_4$), filtered and concentrated under reduced pressure. The resulting residue was subjected to column chromatography (10% CH_2Cl_2/hexanes) to afford [9](2,7)pyrenophane (176 mg, 20% from bis(thiomethyl)cyclophane) as a light yellow crystalline solid. R_f = 0.50 (40% CH_2Cl_2/hexanes); m.p. 213-216 °C (heptane); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.91 (s, 4H), 7.75 (m, 4H), 2.84 (t, *J* = 6.5 Hz, 4H), 1.14-1.07 (m, 4H), 0.29-0.20 (m, 4H), −0.82- −0.97 (m, 2H), −2.03- −2.14 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 136.95, 131.39, 127.70, 126.79, 126.31, 36.30, 30.88, 29.76, 29.36, 25.29.

[10](2,7)Pyrenophane (2.208d)



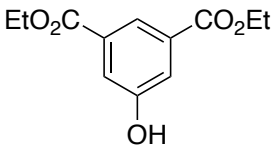
2.208d

18,27-Dithia[10.3.3](1,3,5)cyclophane (1.00 g, 2.44 mmol) was dissolved in CH_2Cl_2 (75 mL) and Borch reagent (976 mg, 0.60 mL, 6.10 mmol) was added via syringe and the reaction was stirred at rt under an N_2 atmosphere for 5 h. The volatiles were removed *in vacuo* and then quenched with EtOAc (50 mL) and stirred for 1 h. The resulting precipitate was collected via suction filtration (EtOAc) and dried under vacuum to afford the crude bis(tetrafluoroborate) salt (1.25 g) as white a solid. The bis(tetrafluoroborate)

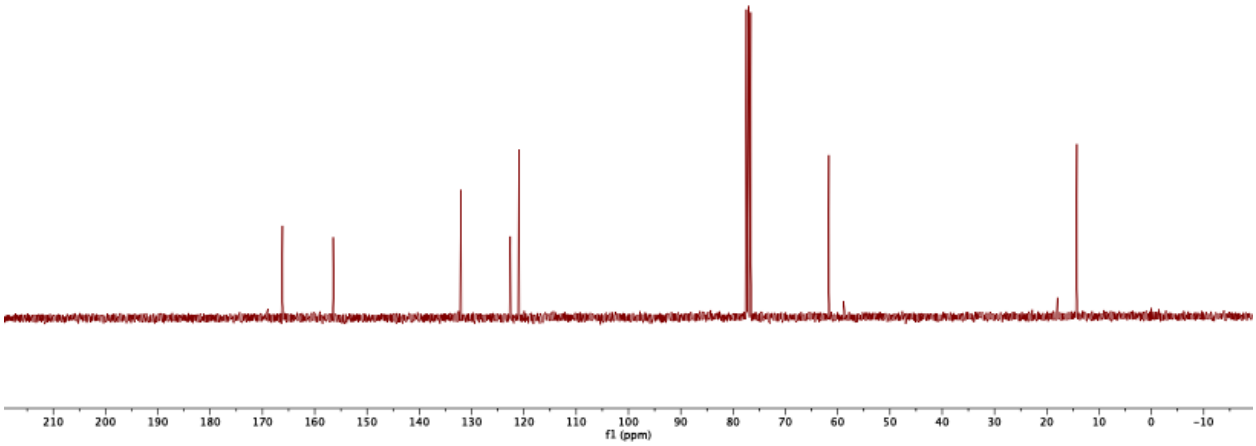
salt was slurried in THF (50 mL) to which *t*-BuOK (1.09 g, 9.76 mmol) was added and the reaction was refluxed under N_2 for 6 h. The volatiles were removed *in vacuo* and dissolved in CH_2Cl_2 (50 mL) and washed with saturated NH_4Cl (50 mL), H_2O (50 mL) and brine (50 mL), then dried ($MgSO_4$), filtered and concentrated under reduced pressure to yield bis(thiomethyl)cyclophane (876 mg, 2.00 mmol, 82% from 18,27-dithia[10.3.3](1,3,5)cyclophane) which was used without further purification. The bis(thiomethyl)cyclophane was dissolved in CH_2Cl_2 (50 mL) and Borch reagent (800 mg, 0.50 mL, 5.00 mmol) was added via syringe and the reaction was stirred at rt under an N_2 atmosphere for 1 h. The volatiles were removed *in vacuo* and the resulting brown residue was immediately slurried in THF (50 mL) to which *t*-BuOK (1.12 g, 10.0 mmol) and the reaction mixture was stirred at rt for 12 h. The volatiles were removed, and the resulting residue was dissolved in CH_2Cl_2 (50 mL) and washed with saturated $NH_4Cl_{(aq)}$ (50 mL), H_2O (50 mL) and brine (50 mL), then dried ($MgSO_4$), filtered and concentrated under reduced pressure. The resulting residue was subjected to column chromatography (20% CH_2Cl_2/hexanes) to afford a mixture of compounds. This mixture was dissolved in benzene (50 mL) and treated with DDQ (476 mg, 2.10 mmol) and stirred at rt for 6 h. The reaction mixture was concentrated under reduced pressure and dissolved in CH_2Cl_2 (50 mL) then washed with 1 M HCl (50 mL), H_2O (50 mL) and brine (50 mL), then dried ($MgSO_4$), filtered and concentrated under reduced pressure. The resulting residue was subjected to column chromatography (10% CH_2Cl_2/hexanes) to afford [10](2,7)pyrenophane (332 mg, 40% from dithiacyclophane) as a light yellow crystalline solid. R_f = 0.50 (40% CH_2Cl_2/hexanes); m.p. 253.5-255 °C (heptane); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.96 (s, 4H), 7.87 (s, 4H), 2.97 (t, *J* = 6.6 Hz, 4H), 1.54-1.40 (m, 4H), 0.46-0.44 (m, 4H), –1.03 - –1.04 (m, 4H), –1.70 (broad s, 4H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 137.42, 131.08, 129.01, 127.59, 126.84, 35.91, 31.49, 25.68, 23.41;

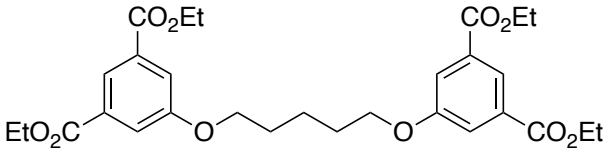
Appendix 1:

Selected ^{1}H and ^{13}C NMR Spectra for Chapter 1



2.201

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O
CO2Et

2.202a

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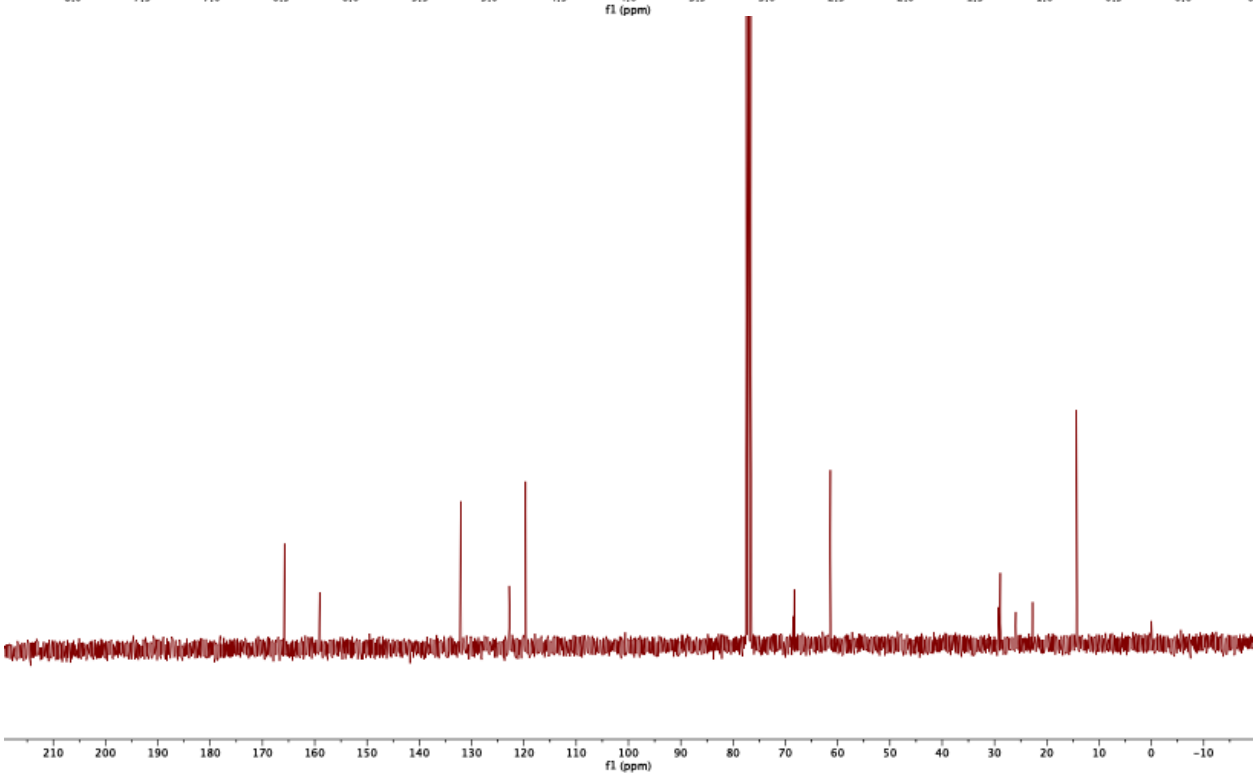
f1 (ppm)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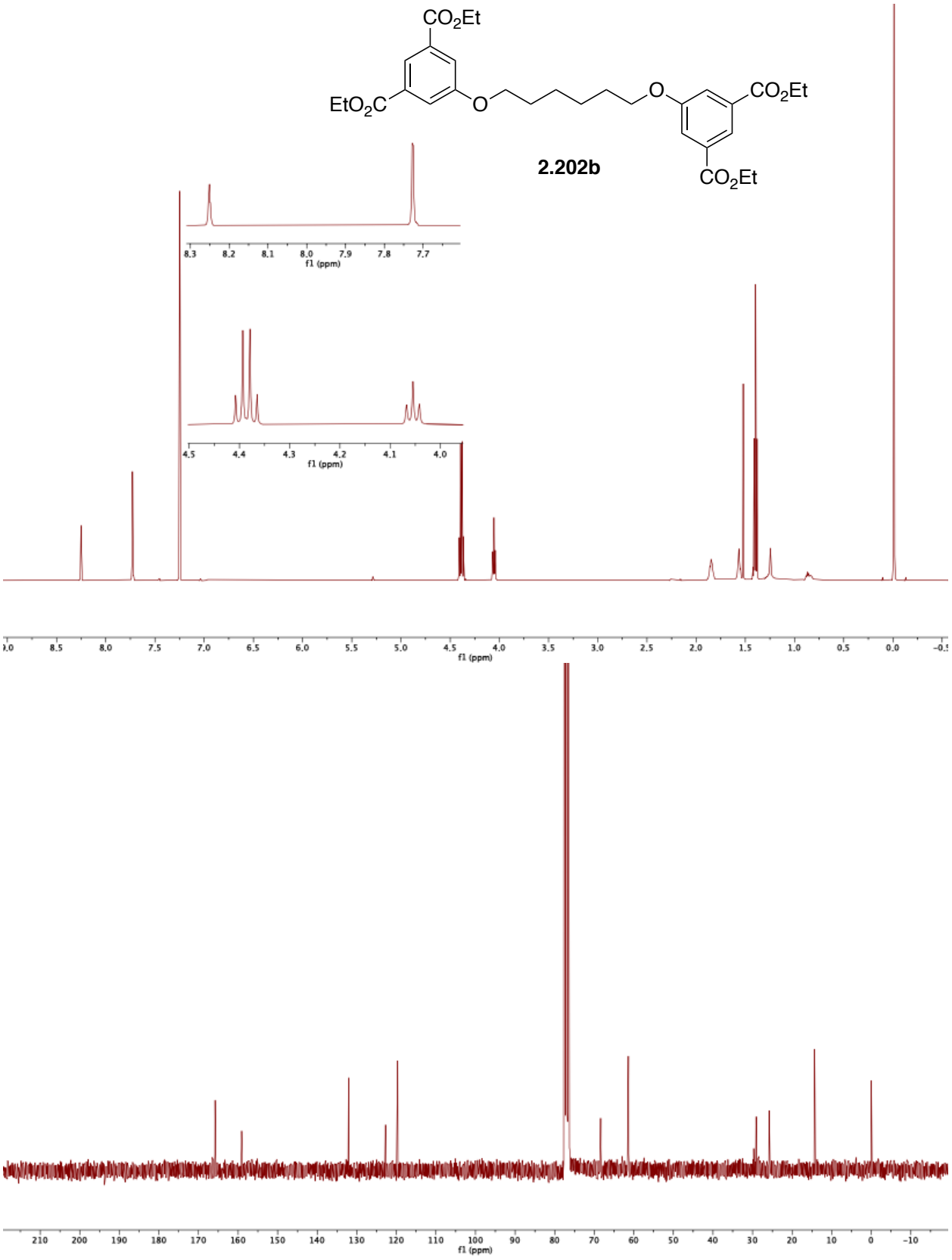
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CO2Et
CO2Et
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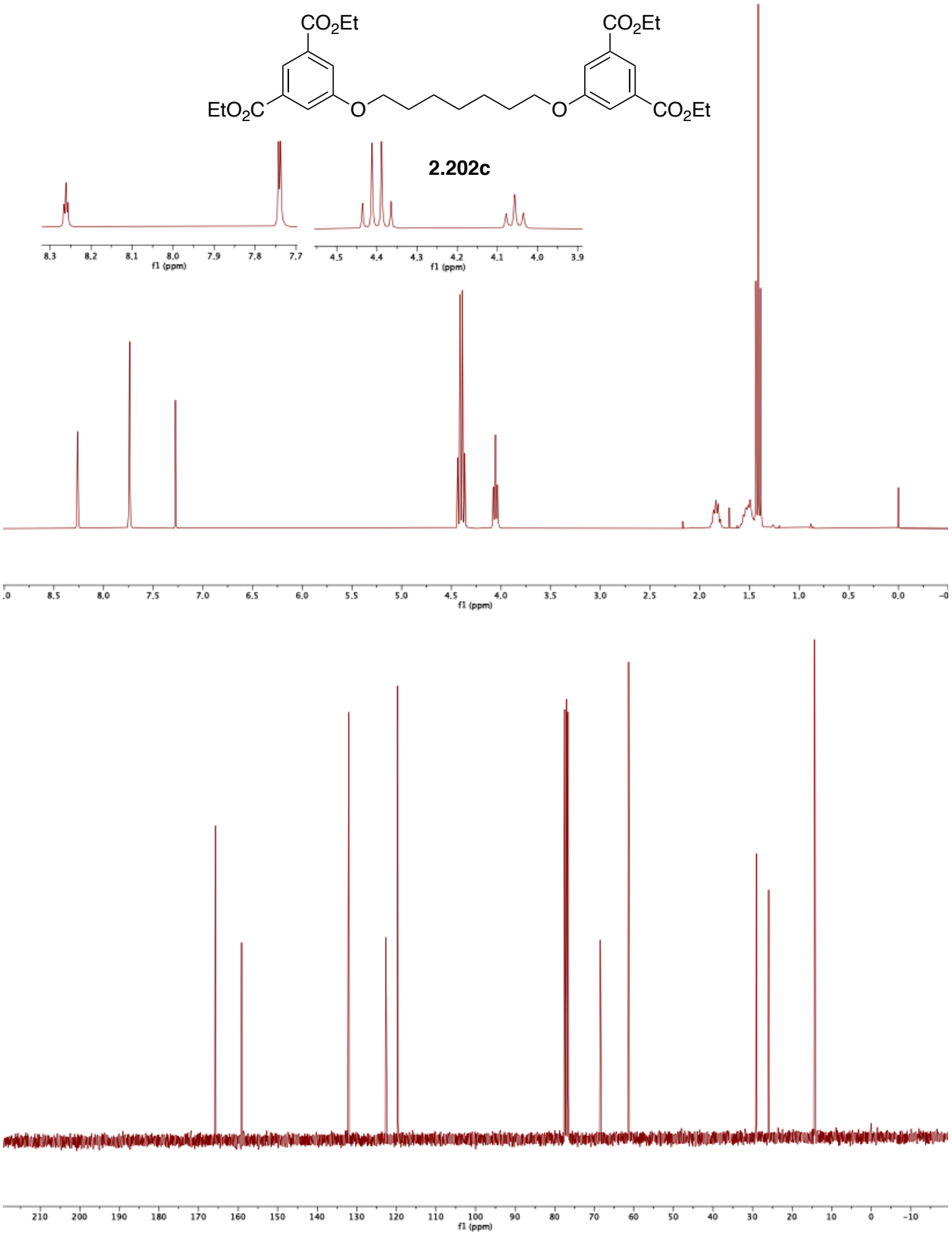
f1 (ppm)
f1 (ppm)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CO2Et
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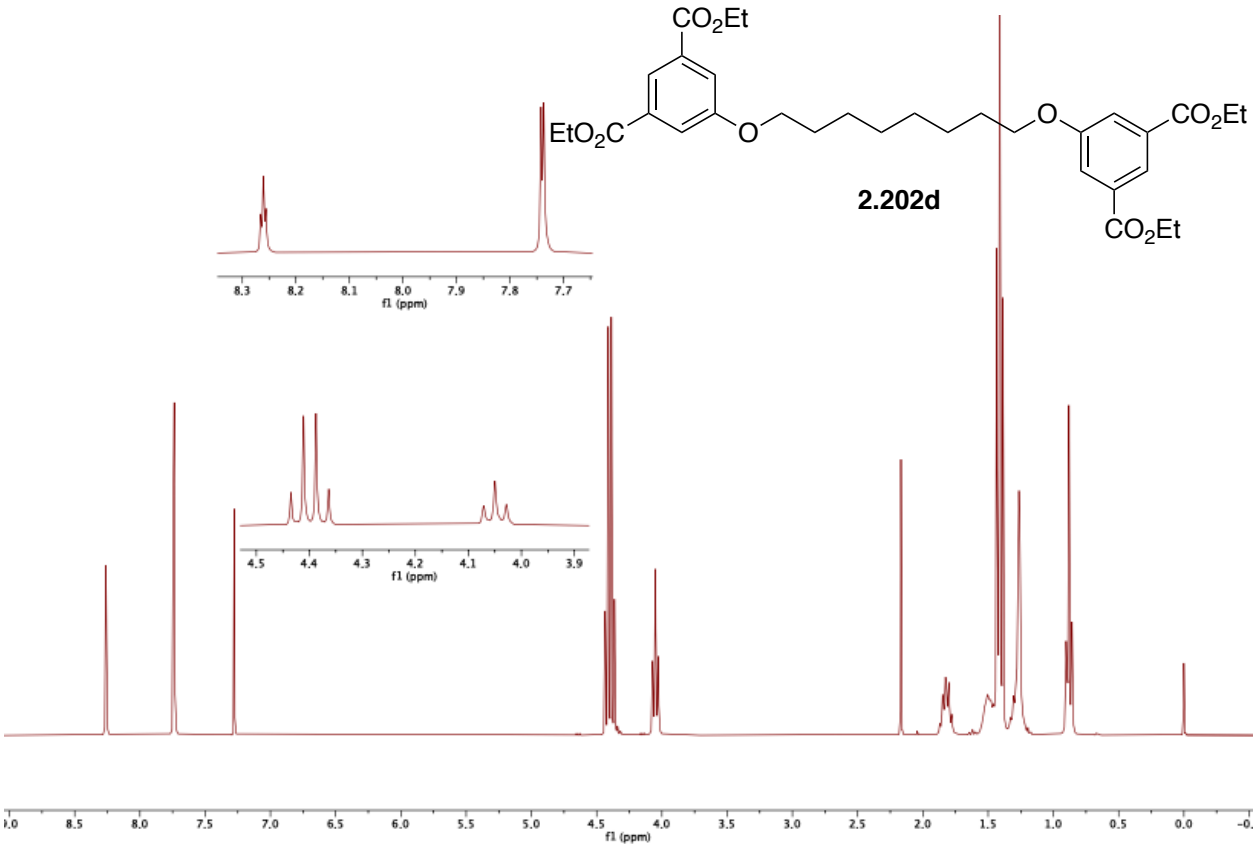
f1 (ppm)
f1 (ppm)
f1 (ppm)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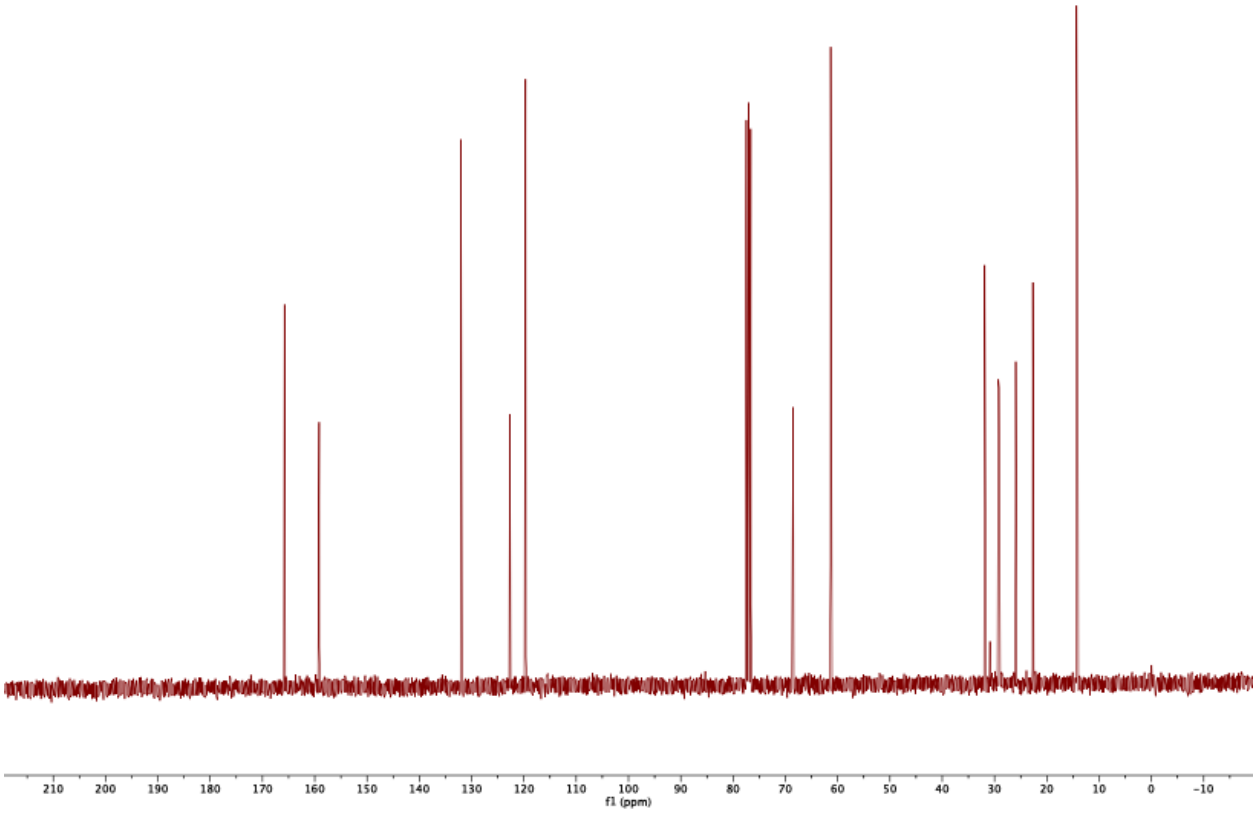
f1 (ppm)
f1 (ppm)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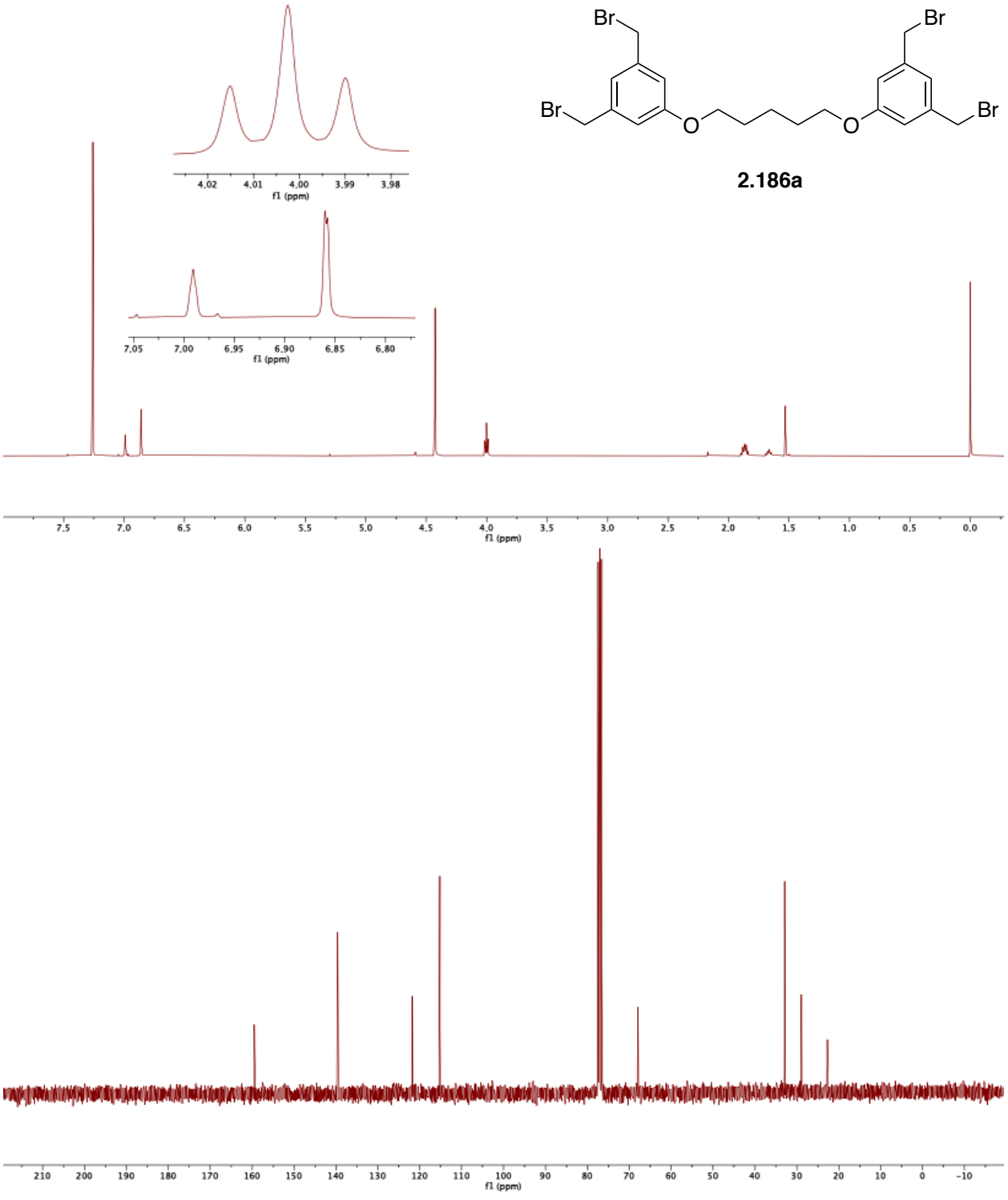
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7.00
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6.85
6.80
f1 (ppm)
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2.0
1.5
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f1 (ppm)
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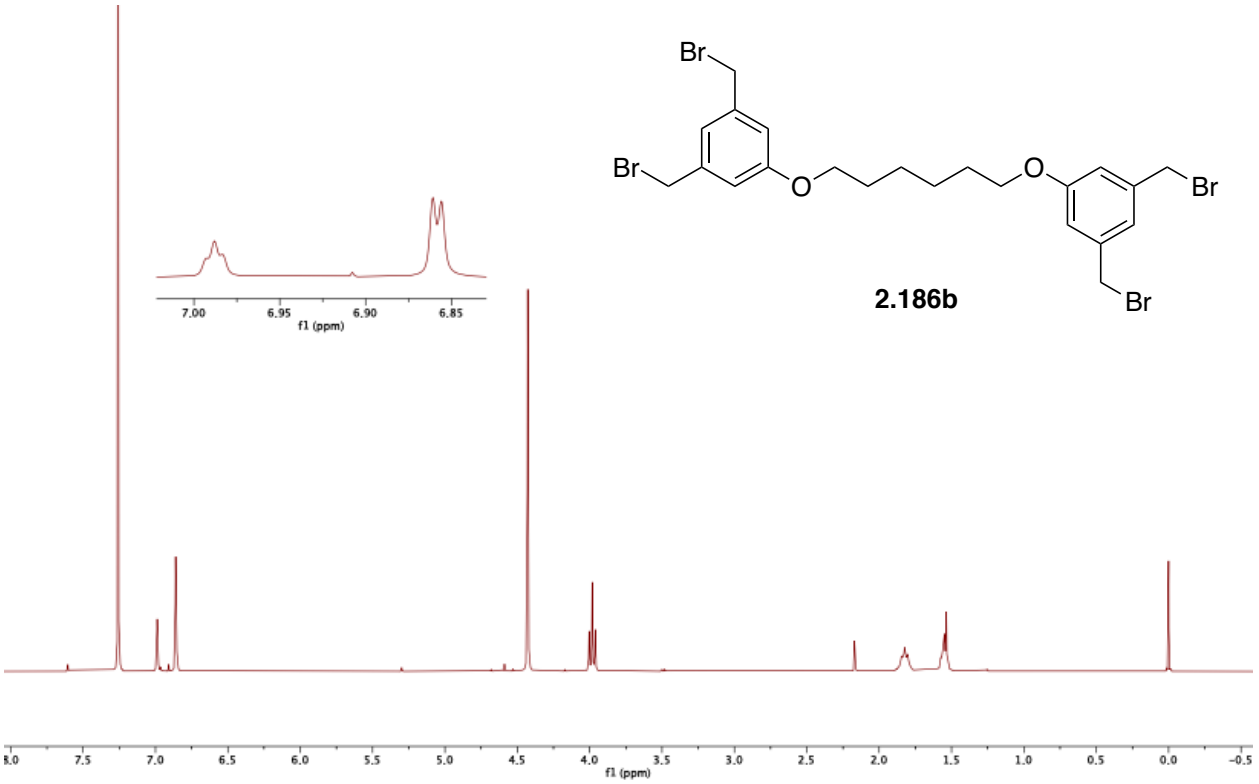
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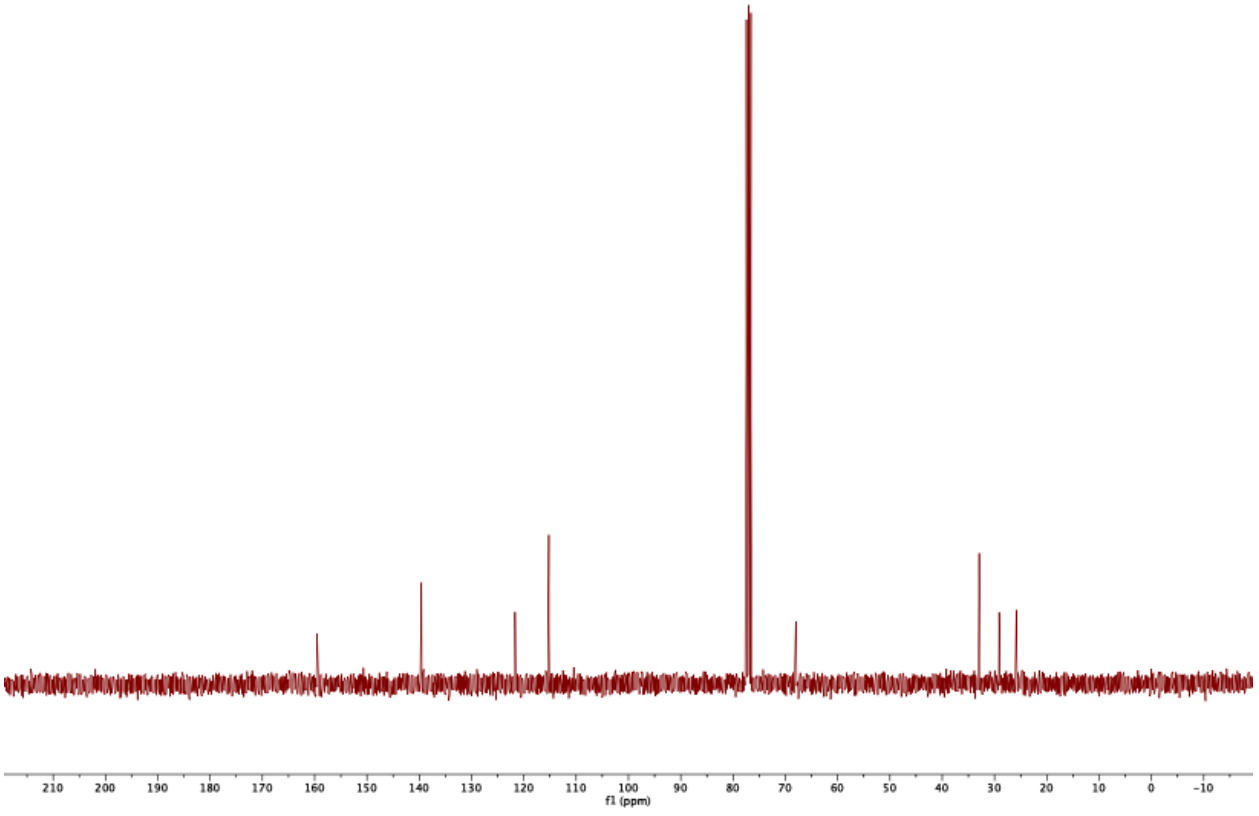
f1 (ppm)

2.186b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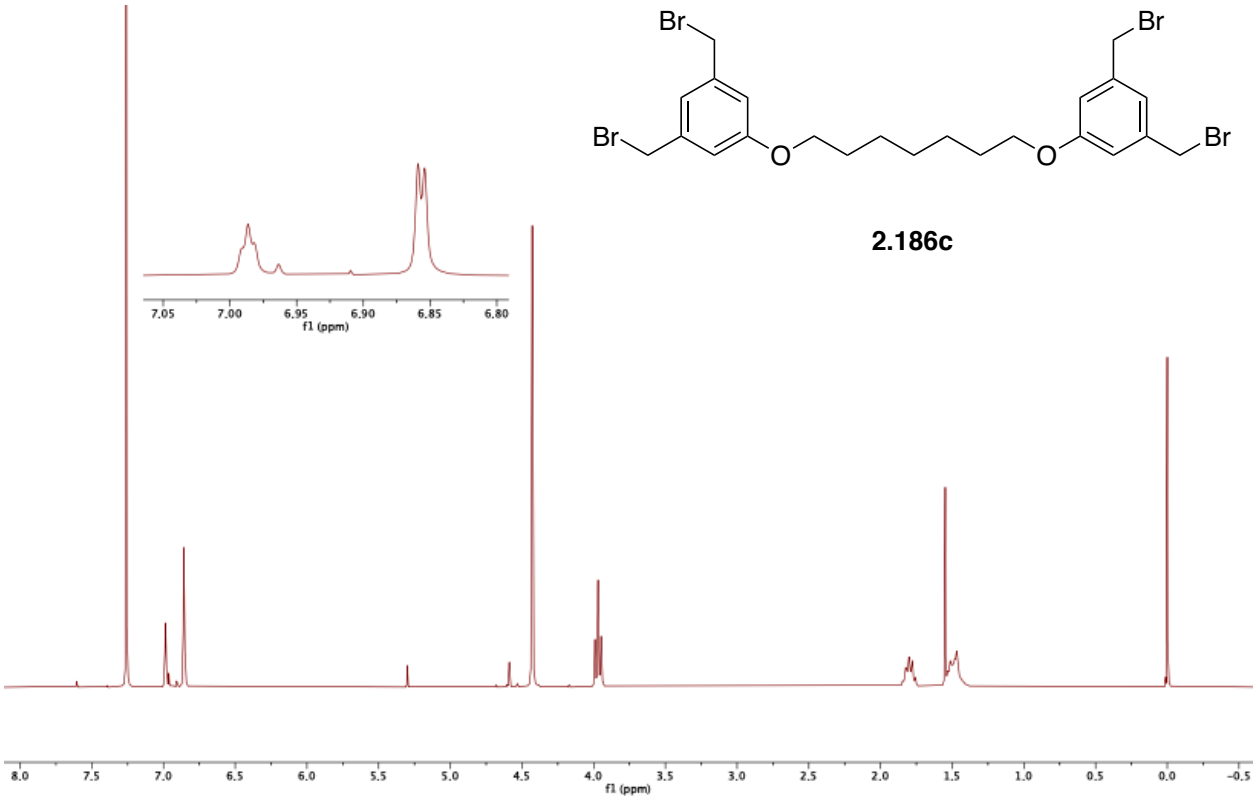
f1 (ppm)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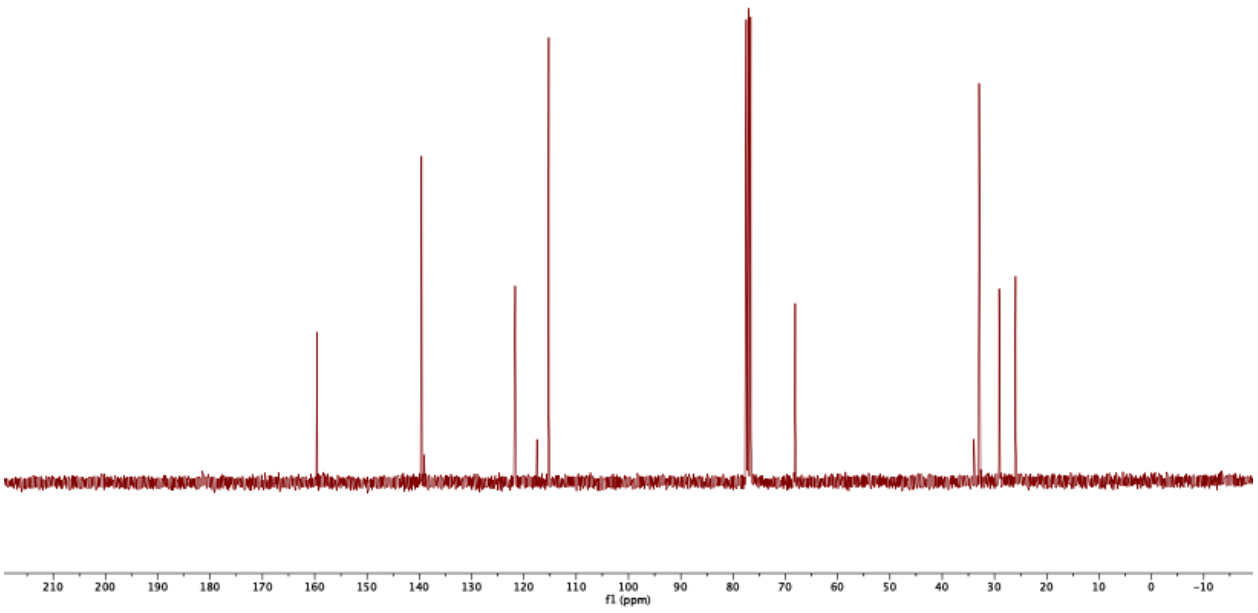
f1 (ppm)

2.186c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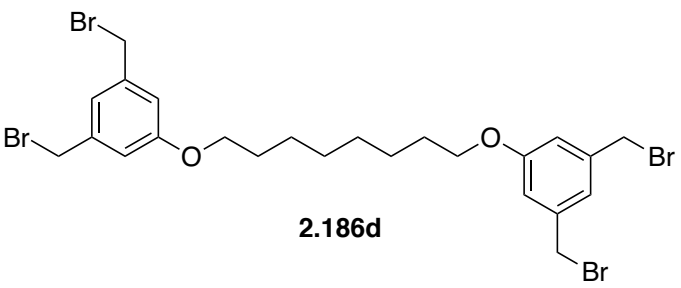
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Br

2.186d

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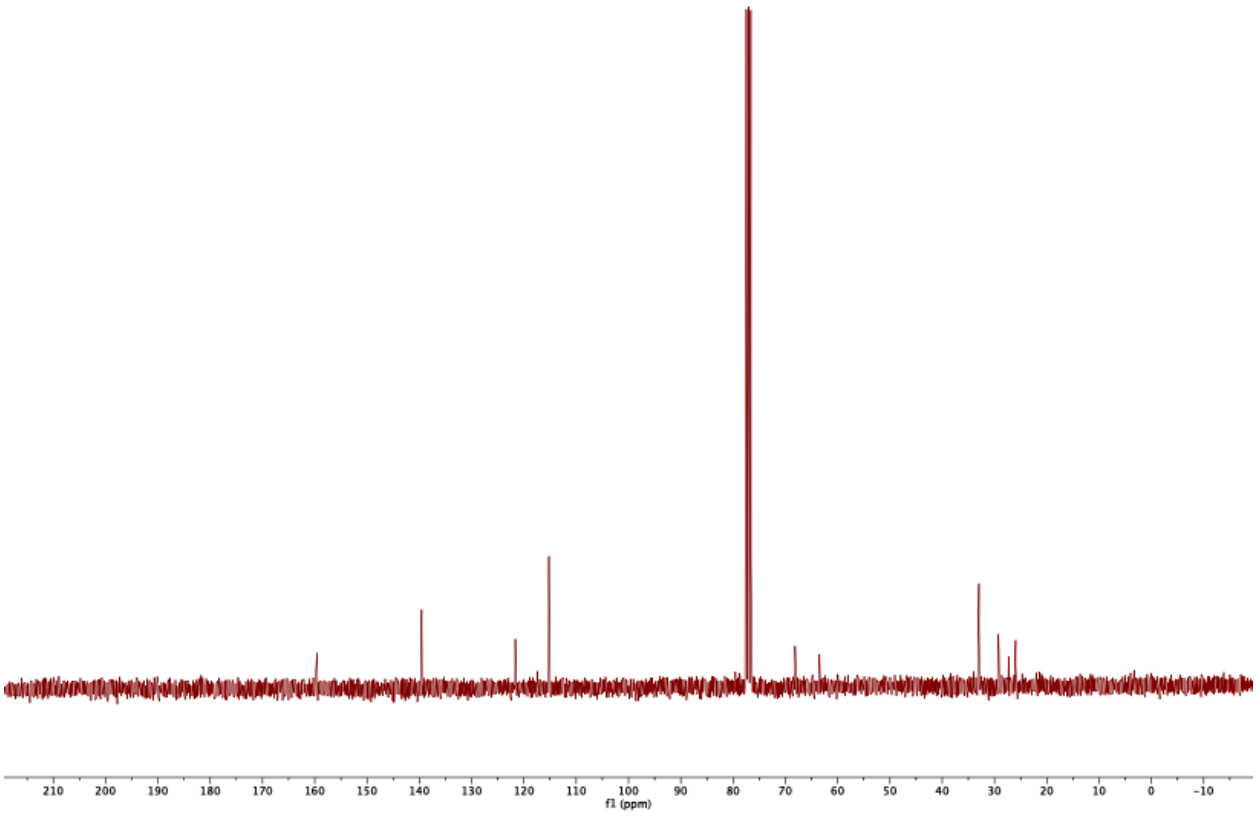
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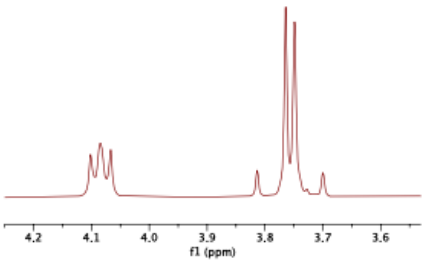
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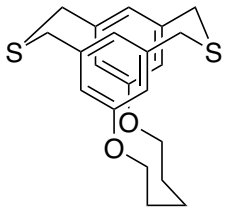
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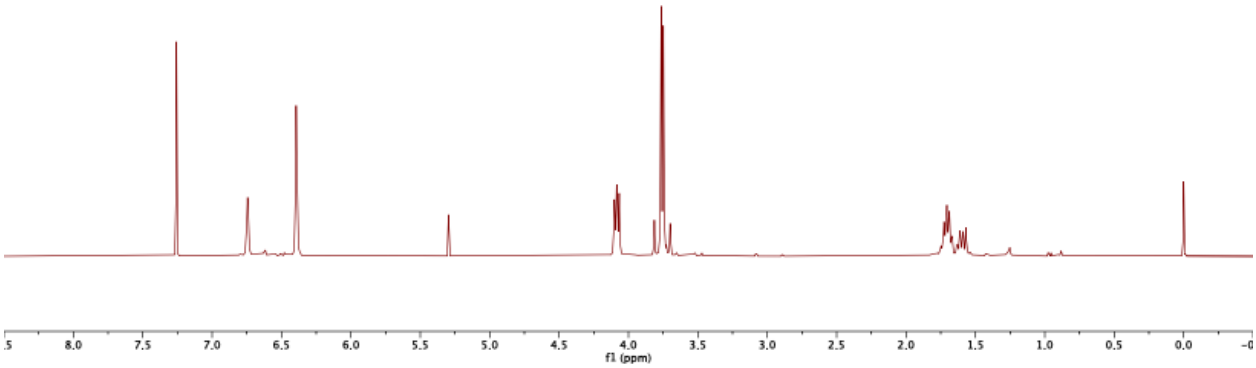
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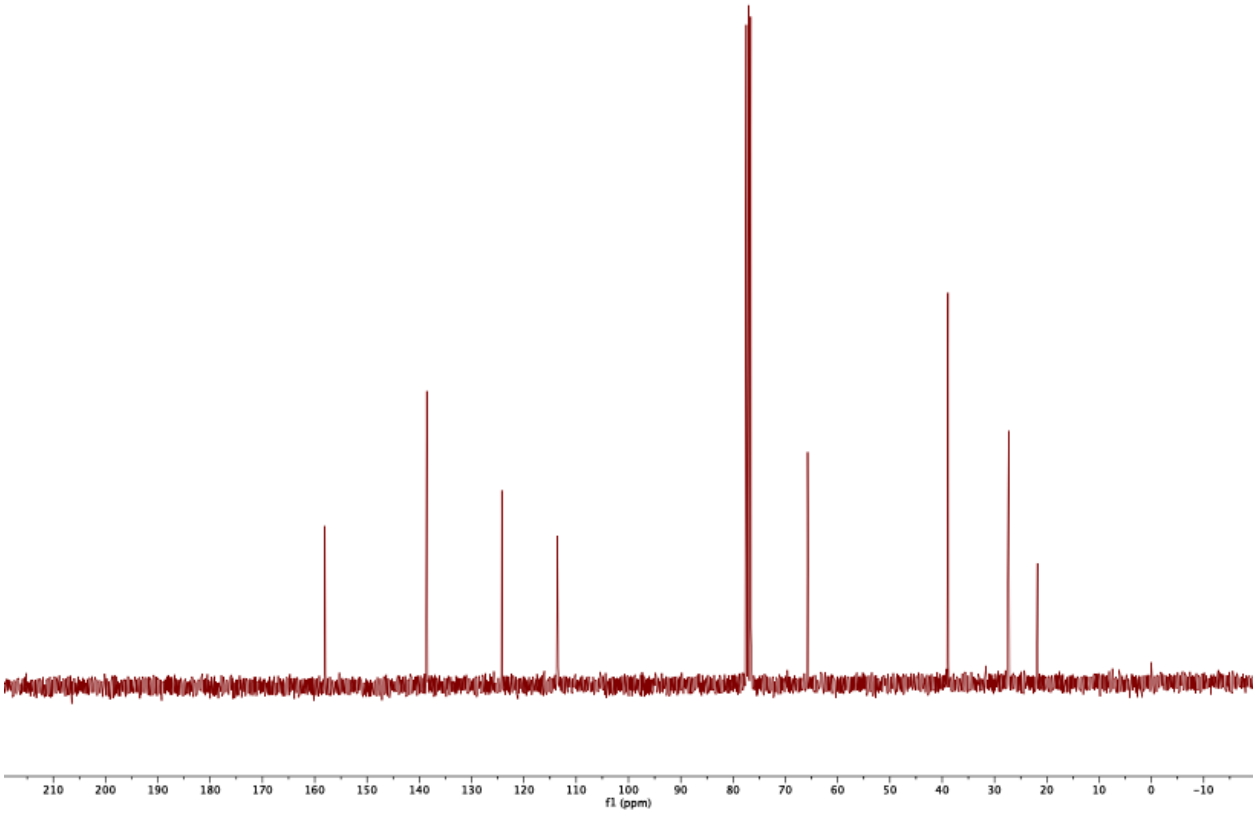
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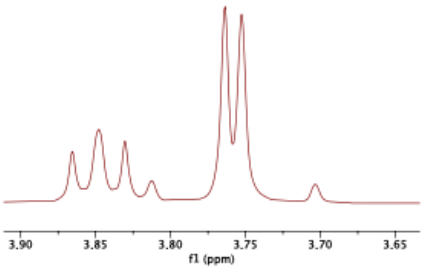
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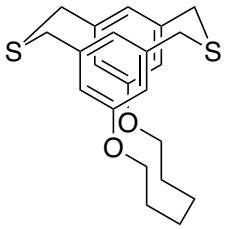
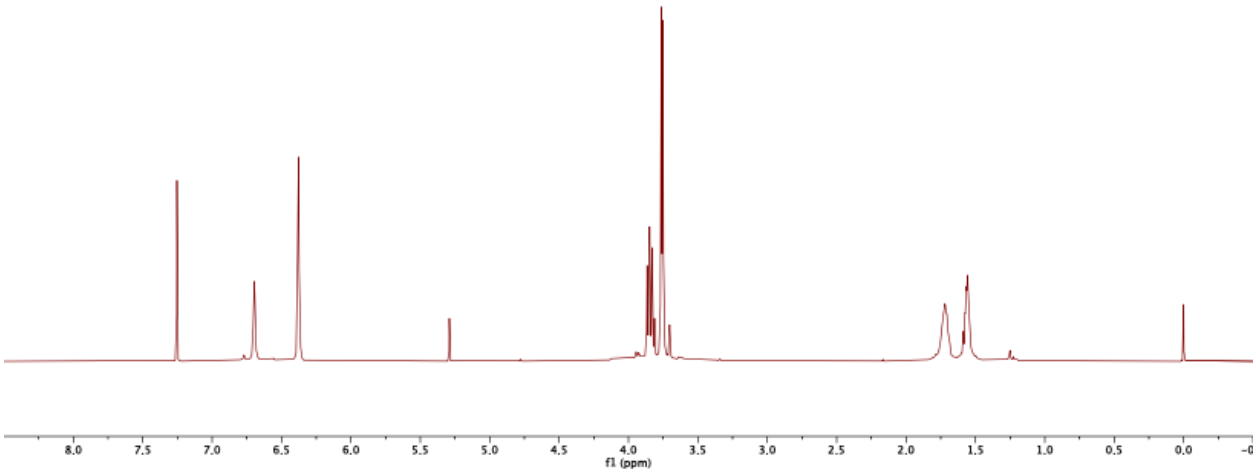

S
S
O
O

2.187b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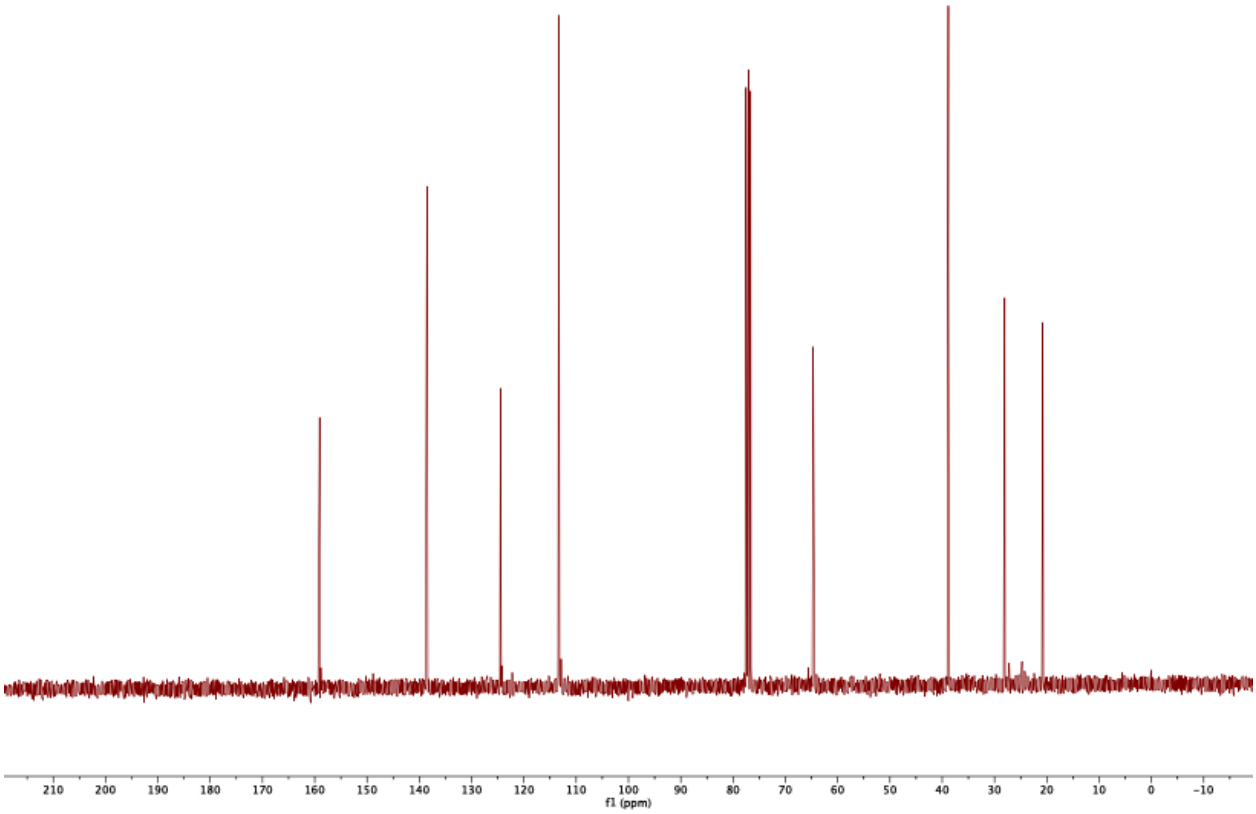
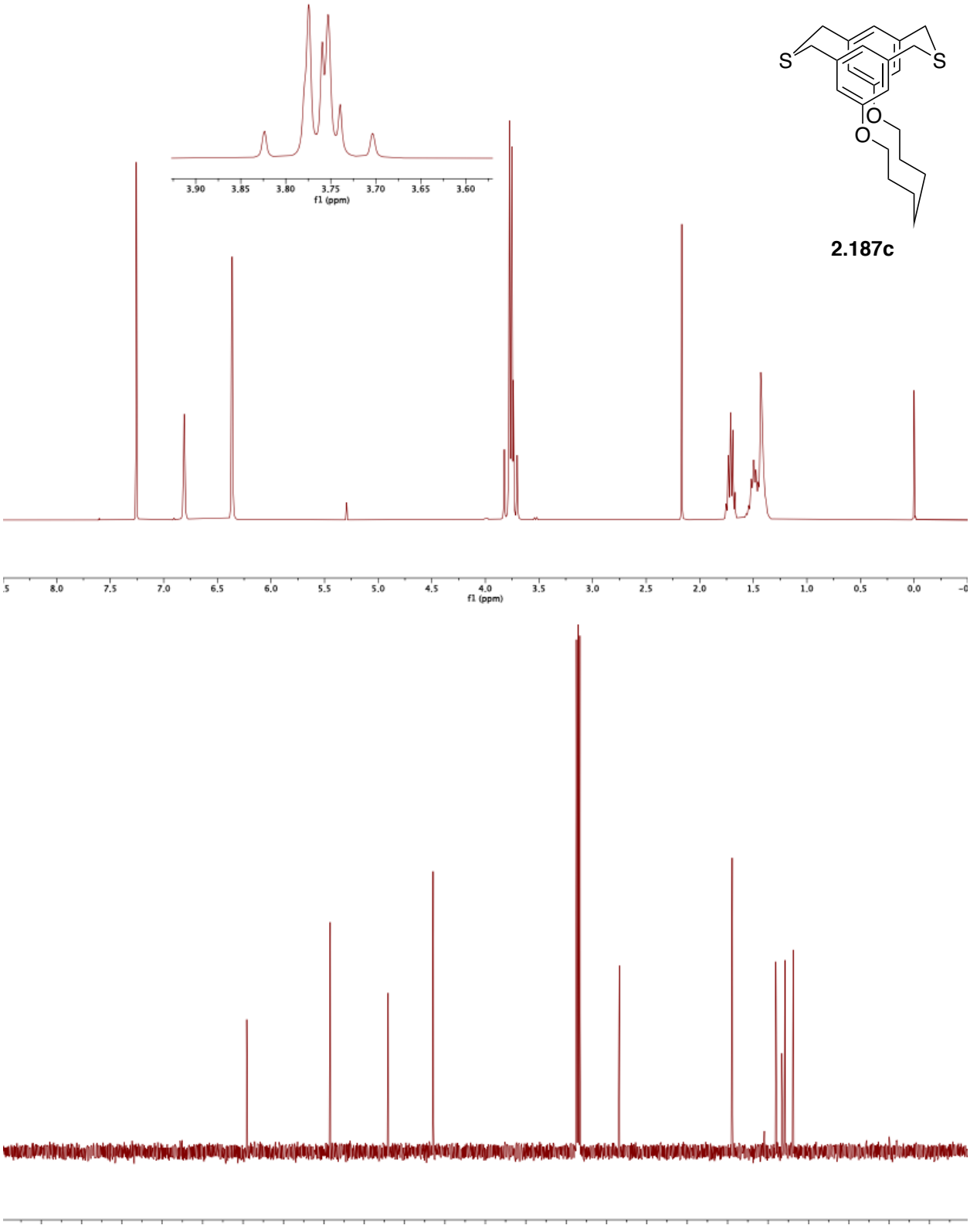
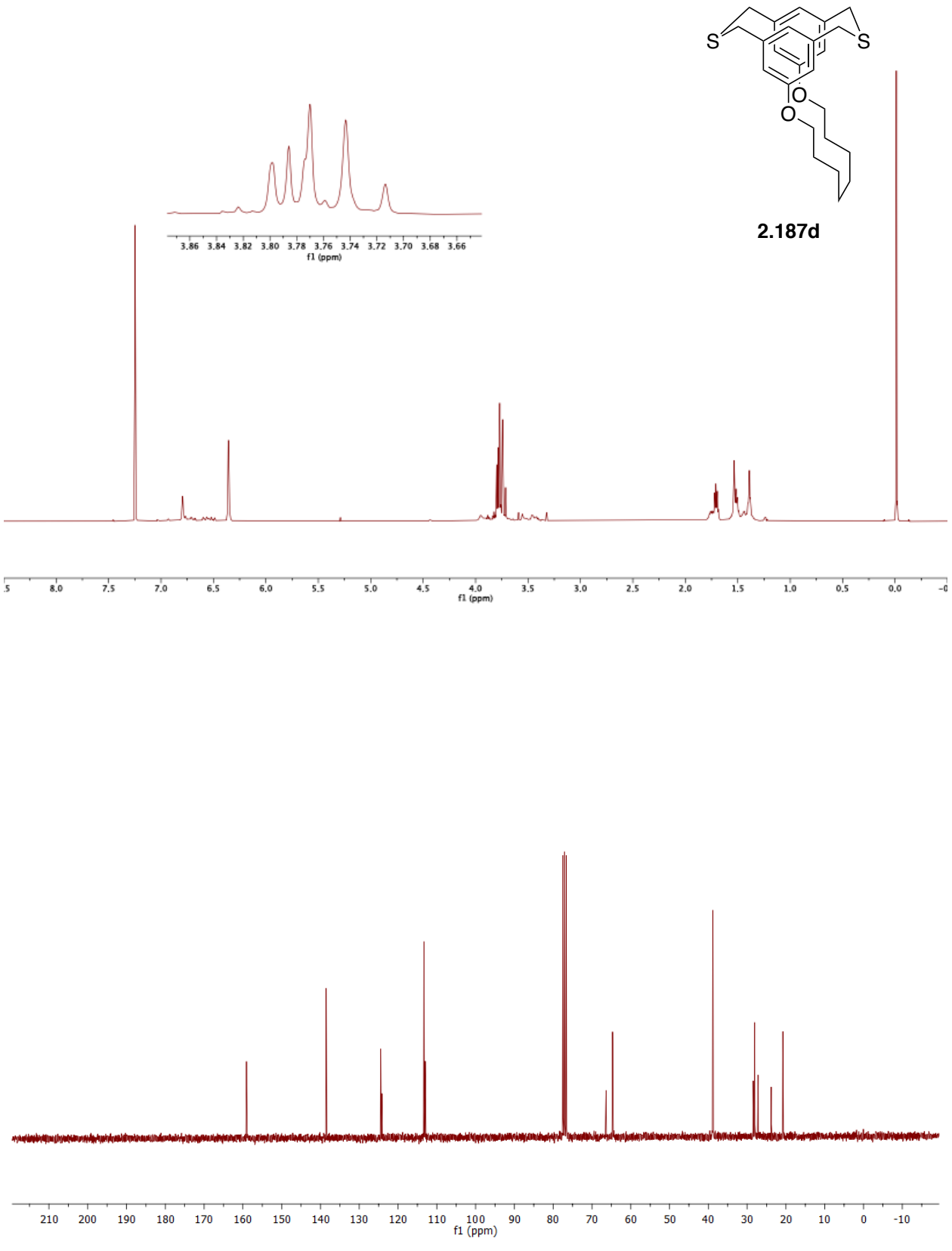
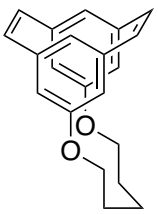
0.5
0.0
f1 (ppm)


210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)


S
S
O
O
3.90
3.85
3.80
3.75
3.70
3.65
3.60
f1 (ppm)
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

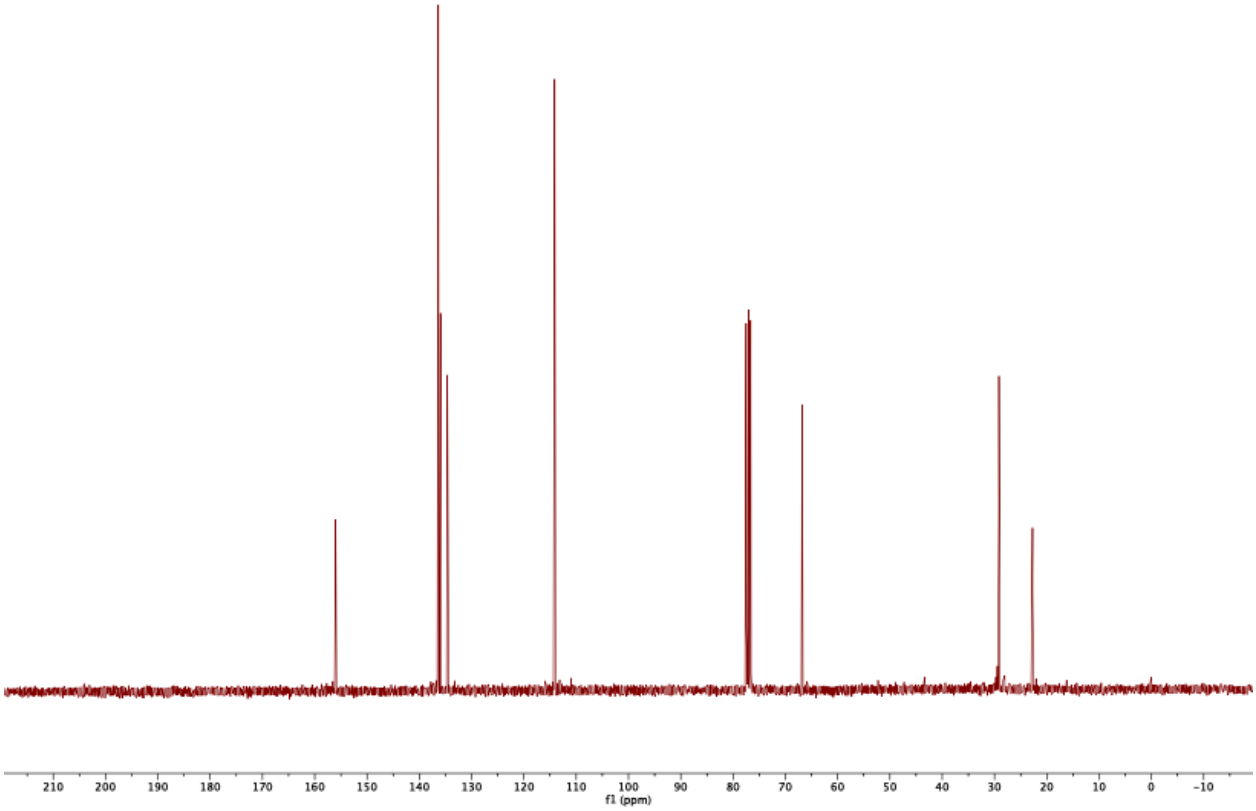
2.187c

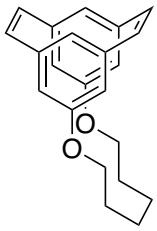

S
S
O
O
2.187d
3.86 3.84 3.82 3.80 3.78 3.76 3.74 3.72 3.70 3.68 3.66
f1 (ppm)
8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


O
O

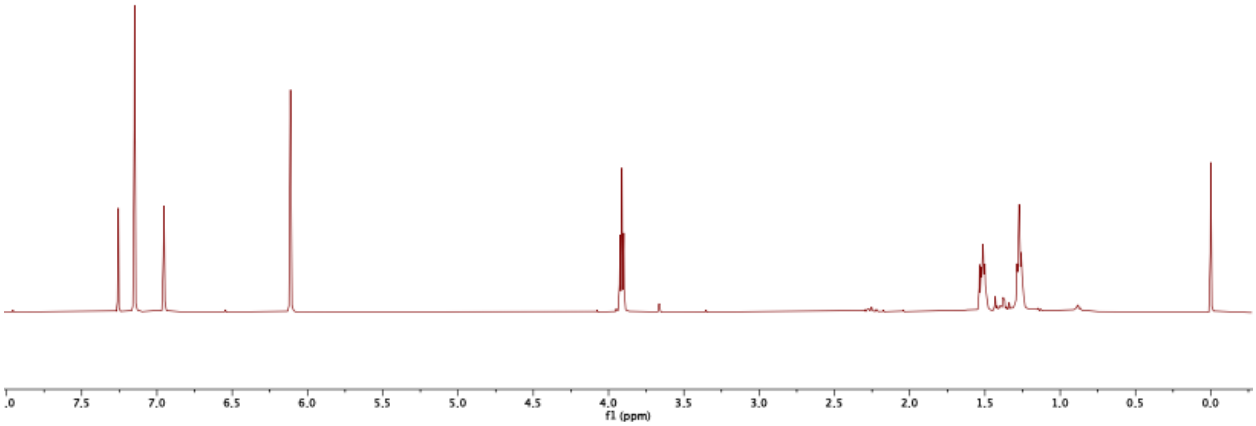
2.189a

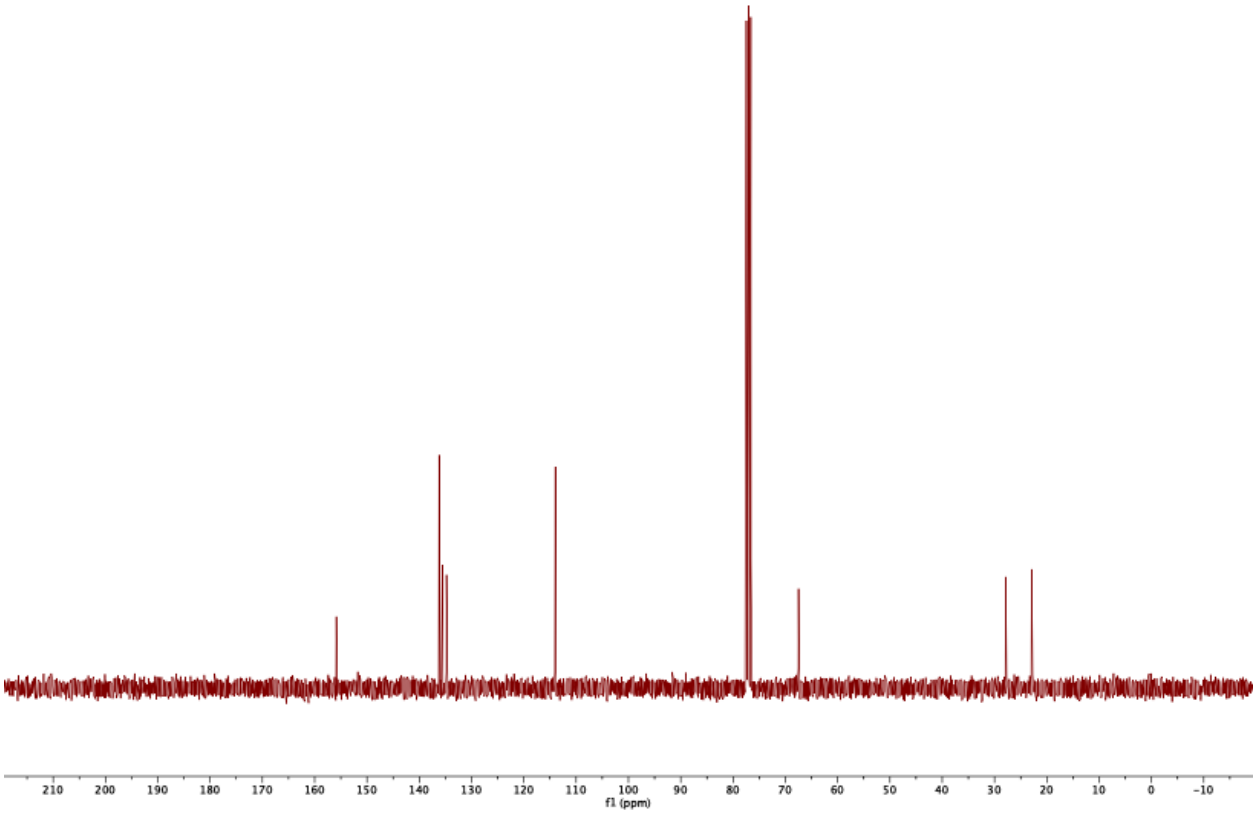
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

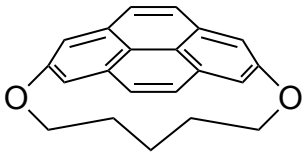

210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)



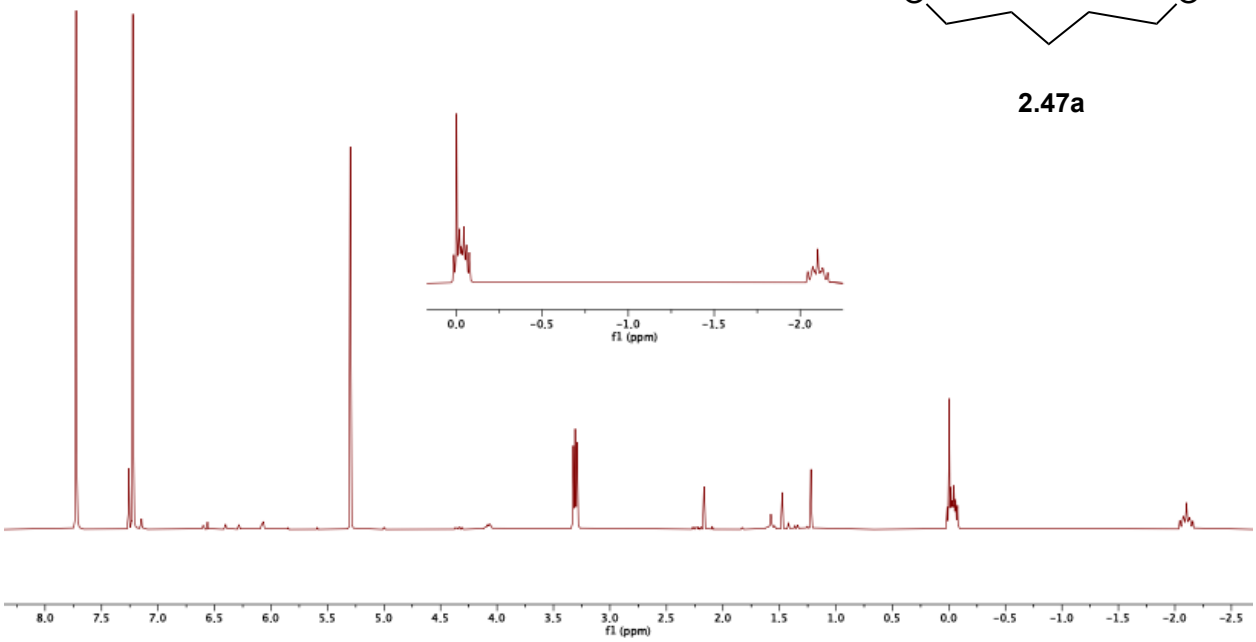
2.189b

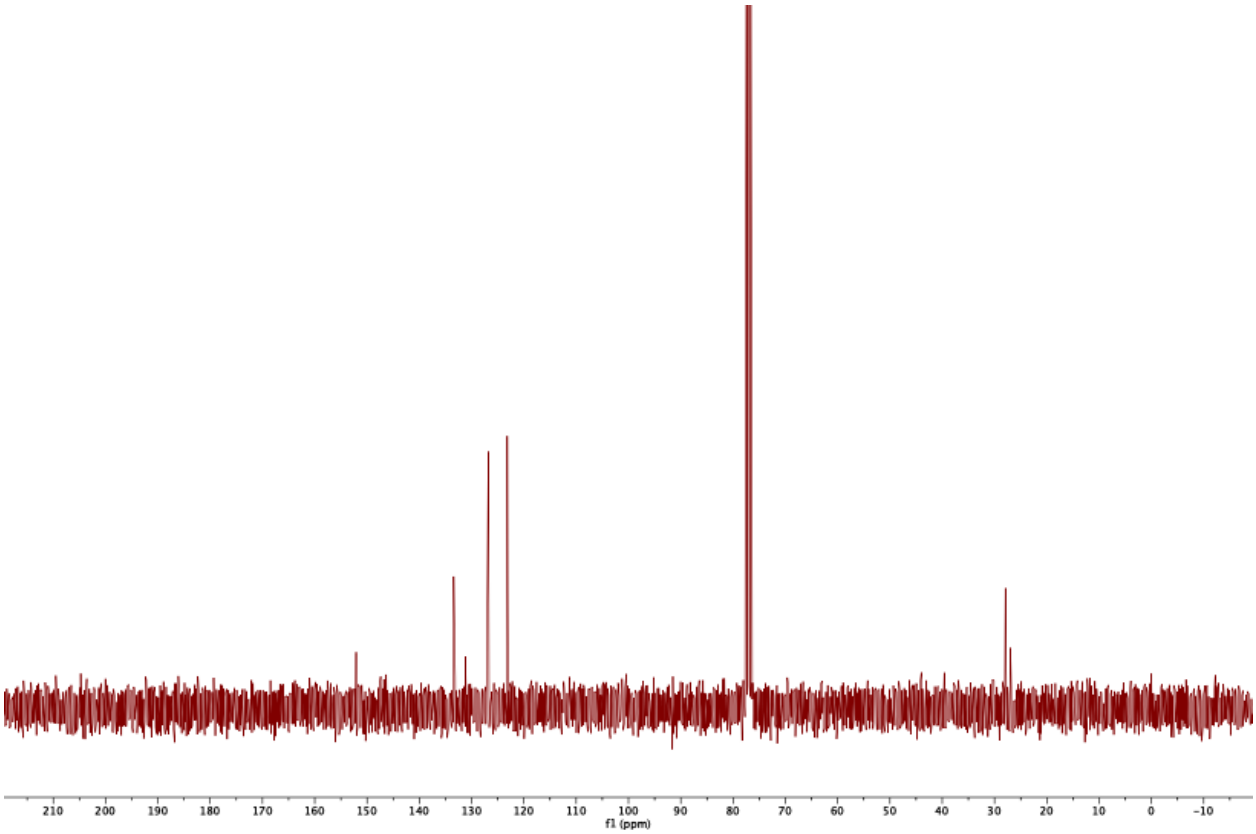

7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

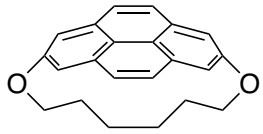

210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)


O
O

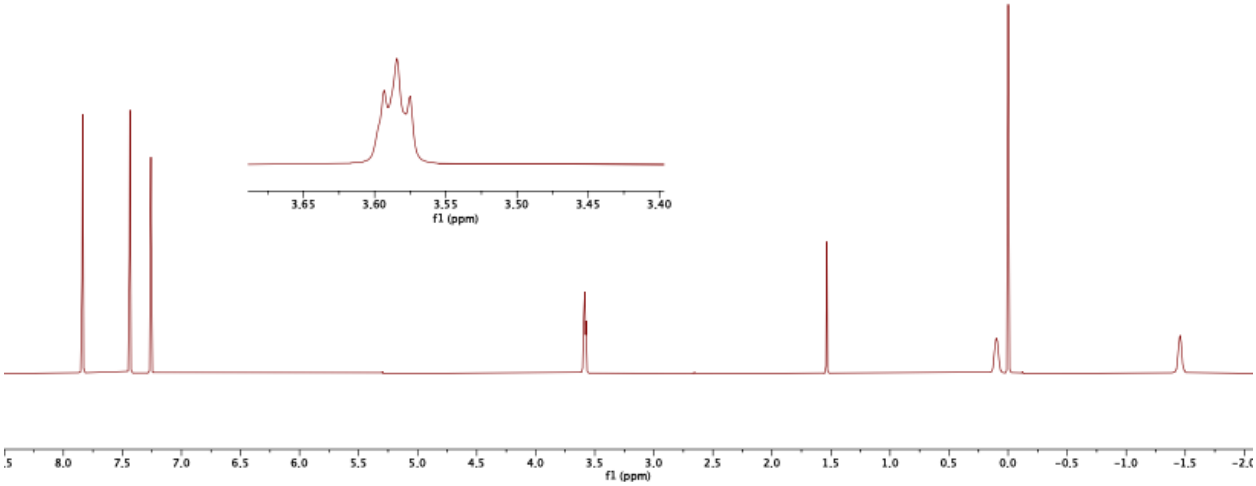
2.47a

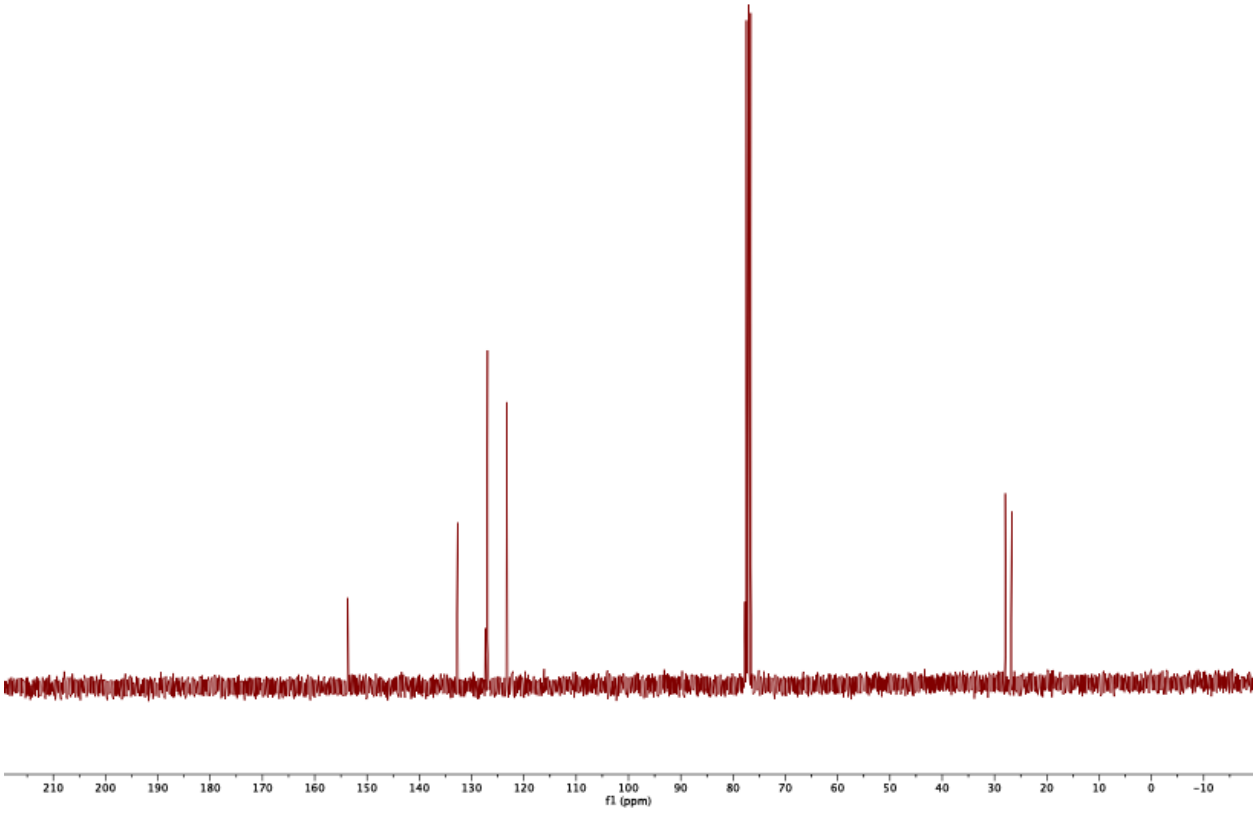

0.0
-0.5
-1.0
-1.5
-2.0
f1 (ppm)
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1.0
-1.5
-2.0
-2.5
f1 (ppm)

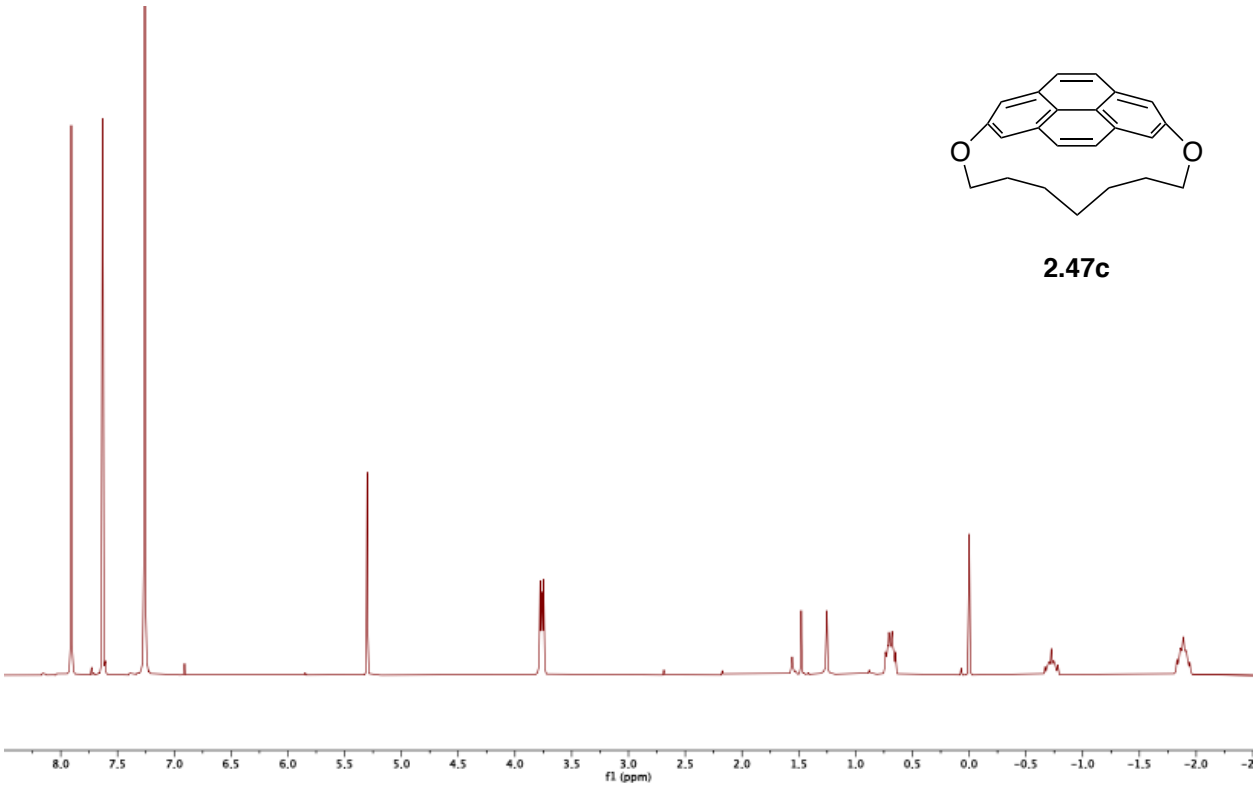

210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

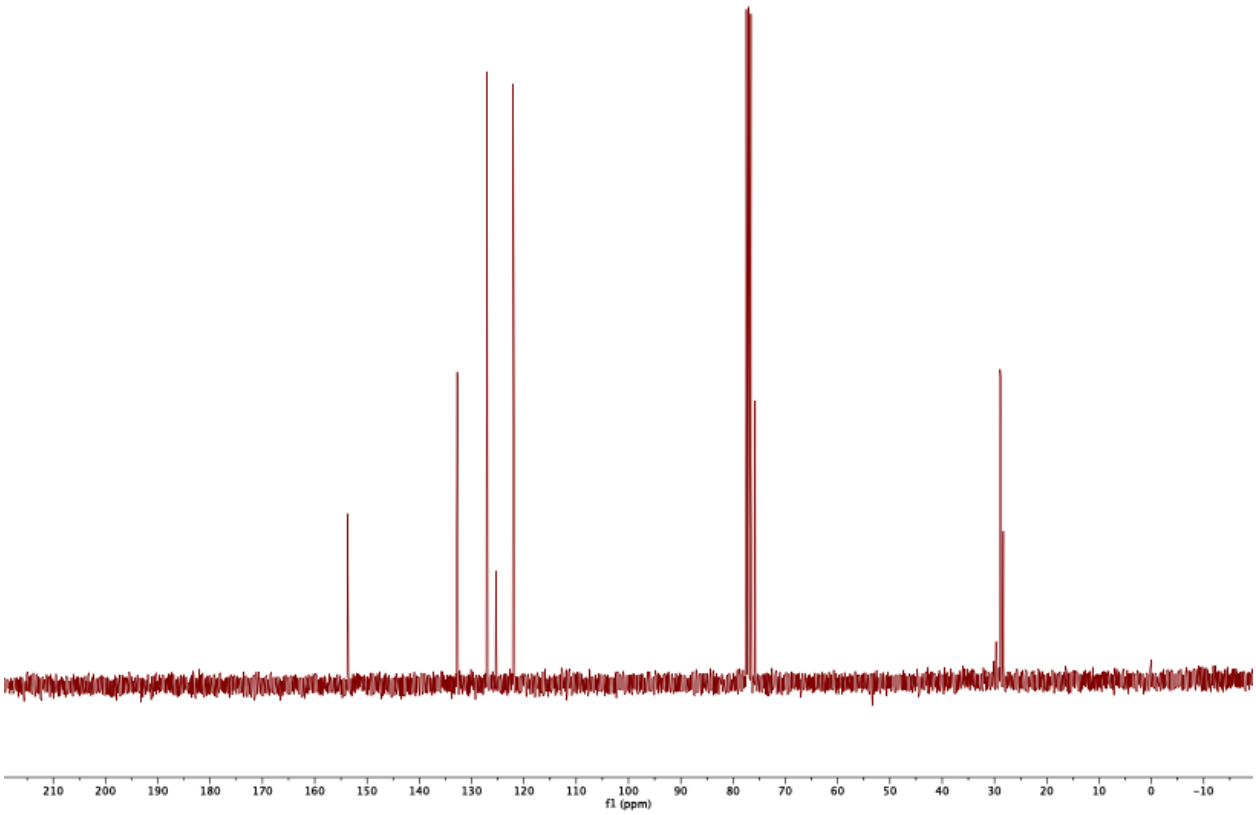

O
O

2.47b


3.65
3.60
3.55
3.50
3.45
3.40
f1 (ppm)
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1.0
-1.5
f1 (ppm)

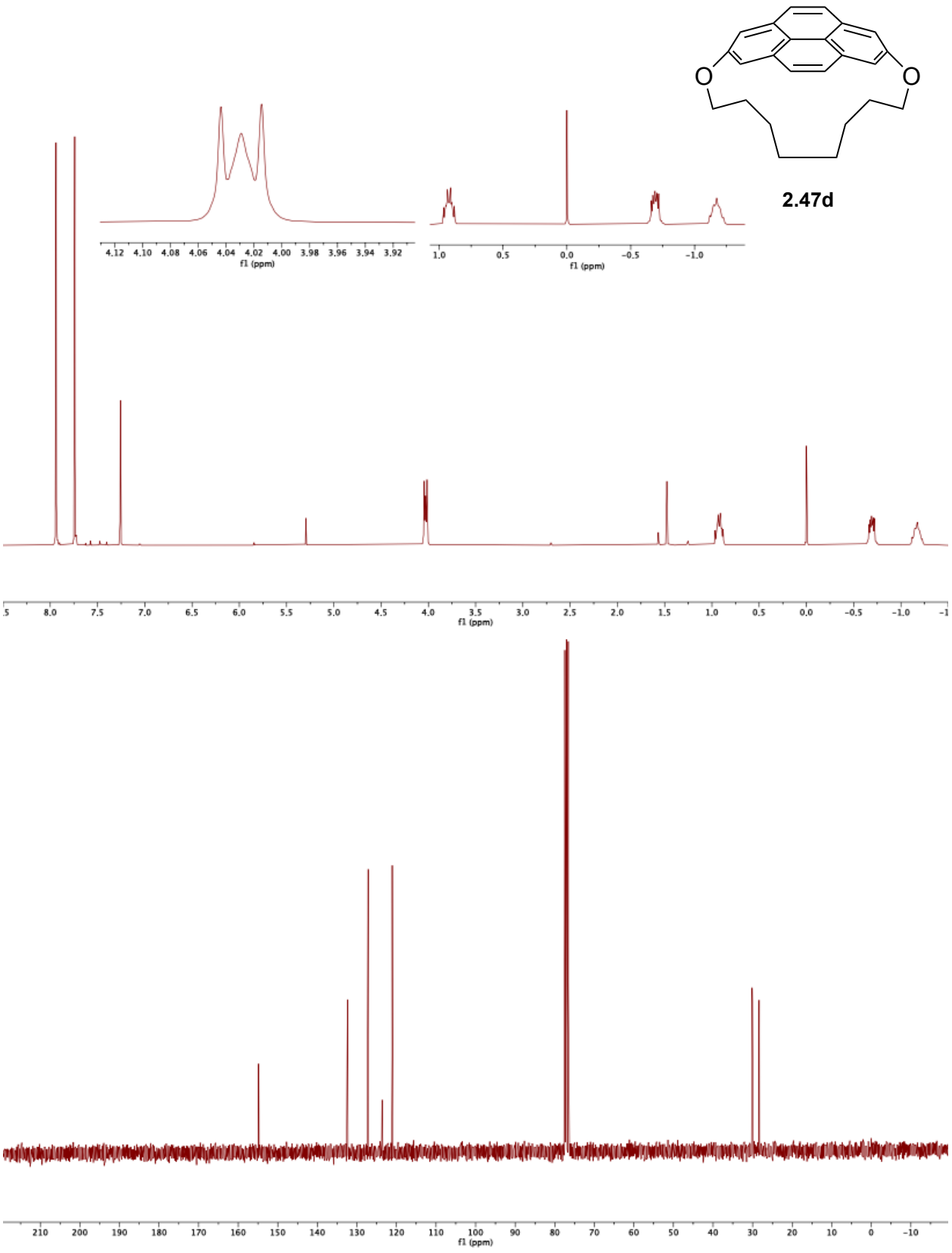

210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

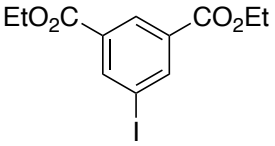

8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1.0
-1.5
-2.0
f1 (ppm)


210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

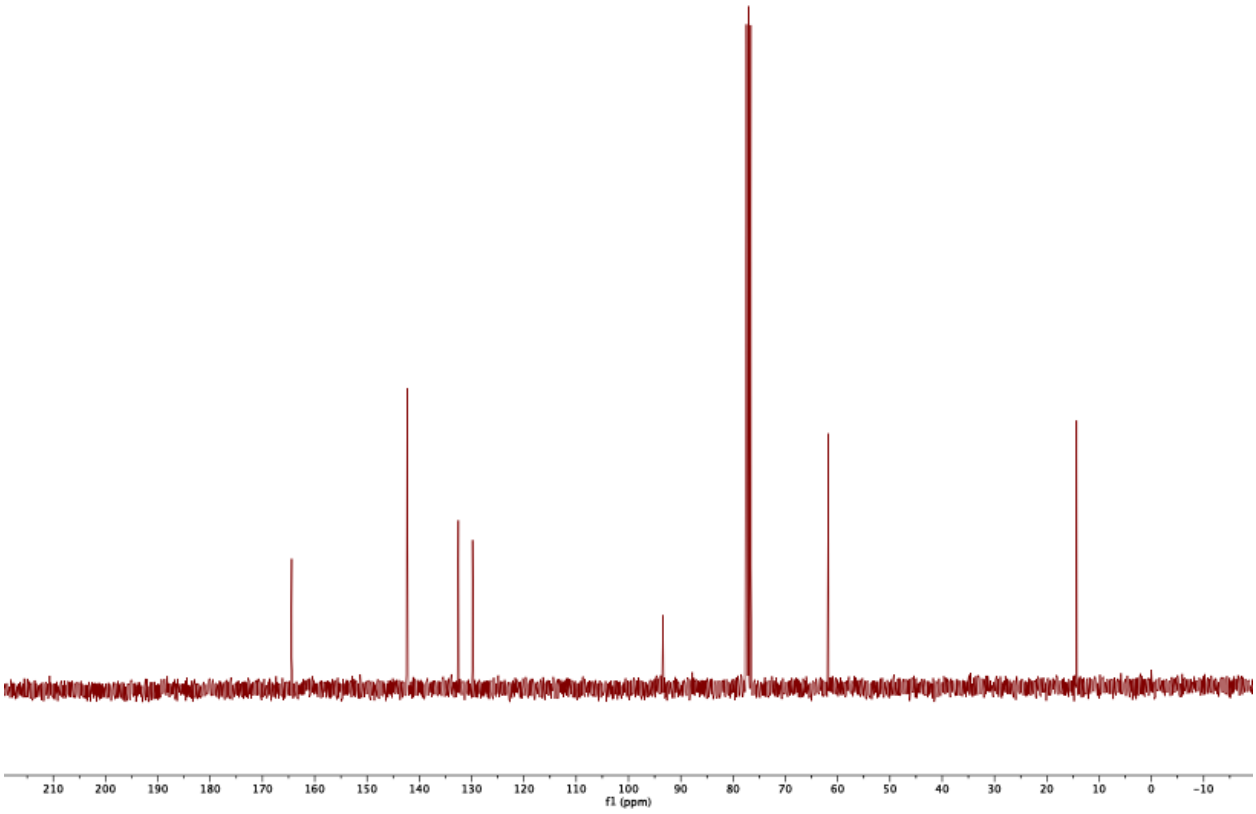
O
O

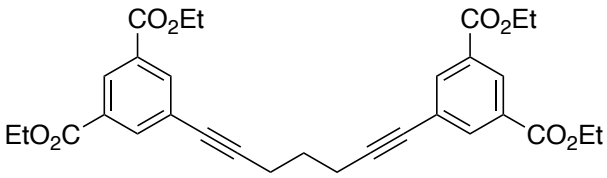
2.47c


O
O
2.47d
4.12 4.10 4.08 4.06 4.04 4.02 4.00 3.98 3.96 3.94 3.92
f1 (ppm)
1.0 0.5 0.0 −0.5 −1.0
f1 (ppm)
f1 (ppm)
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 −10
f1 (ppm)



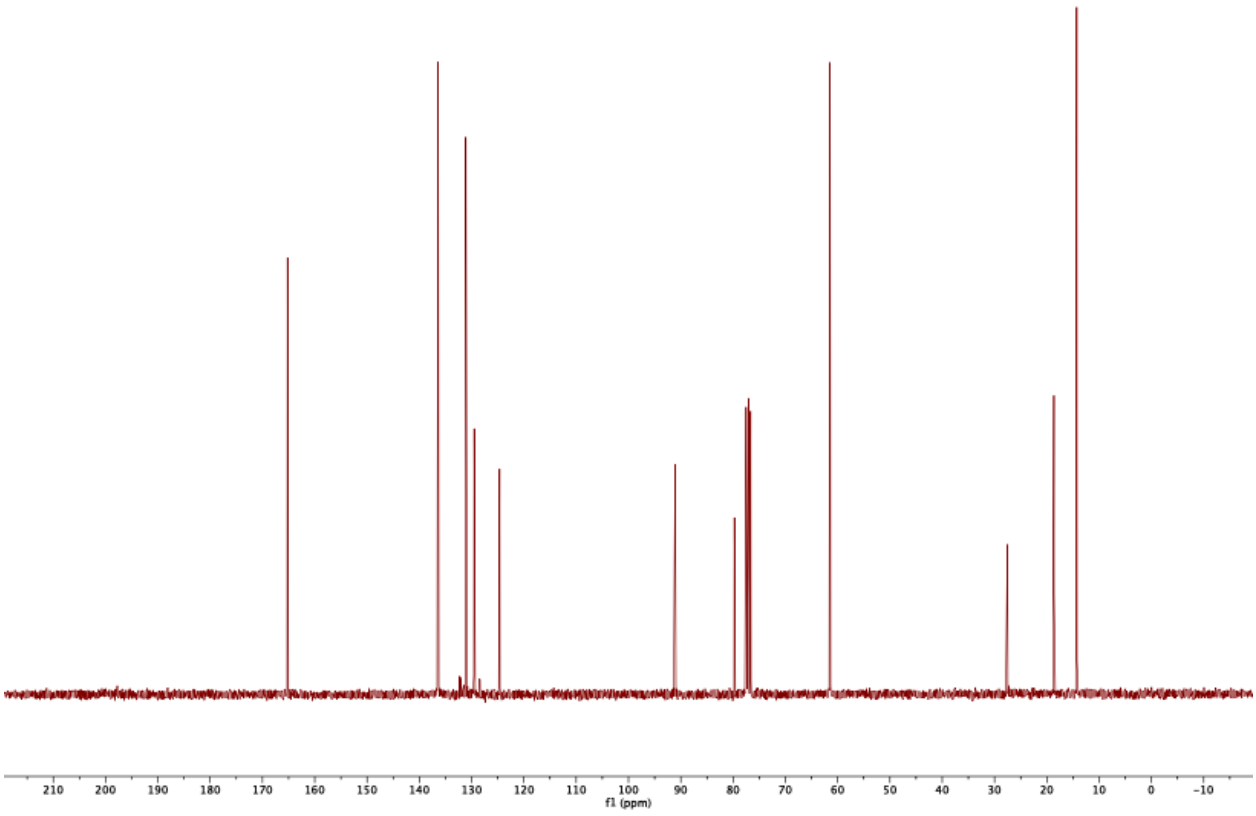
2.211

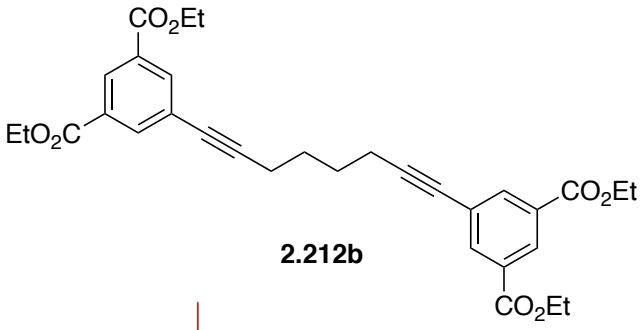



CO2Et
CO2Et
EtO2C
CO2Et

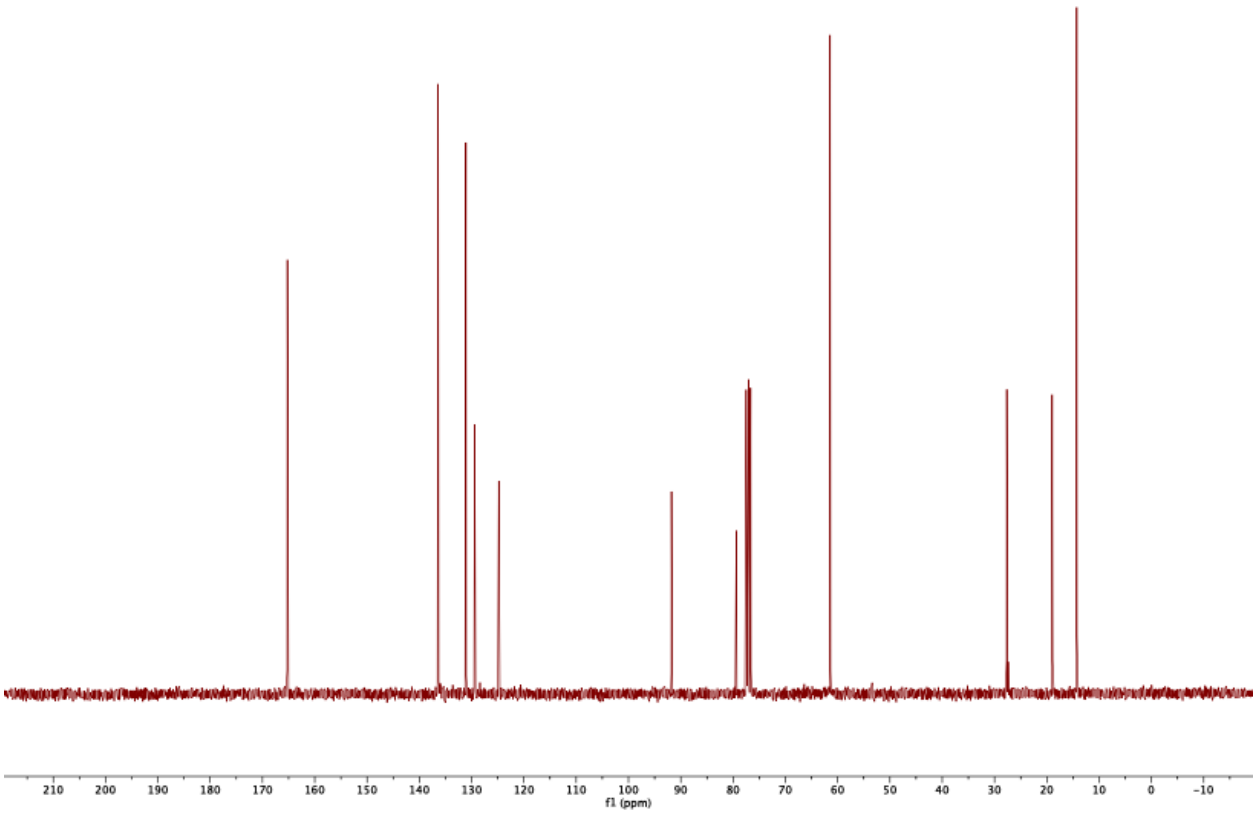
2.212a

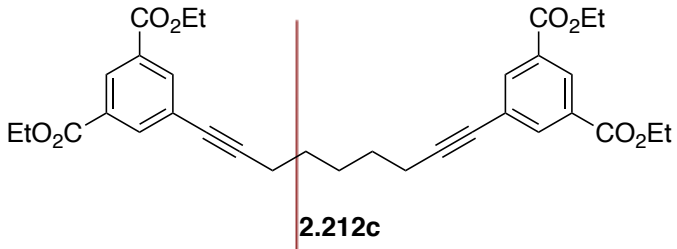
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)



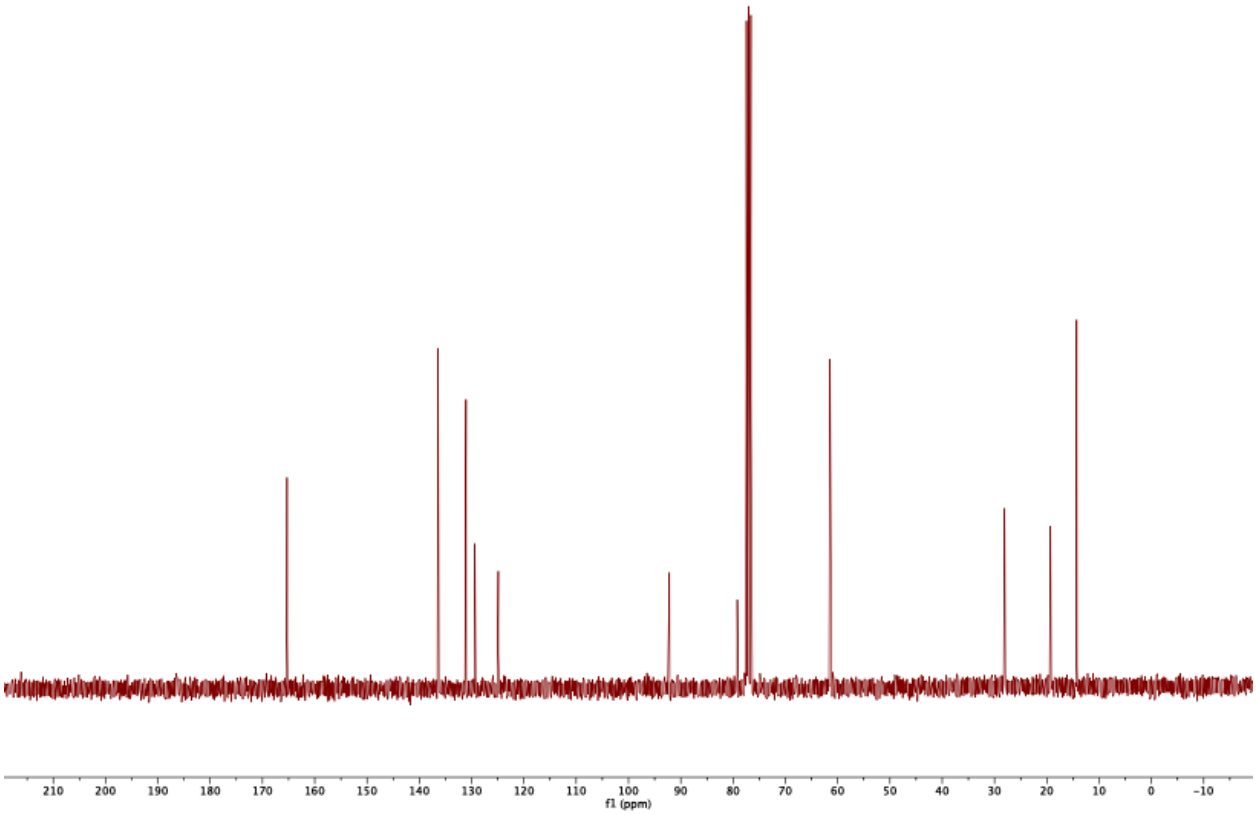
2.212b

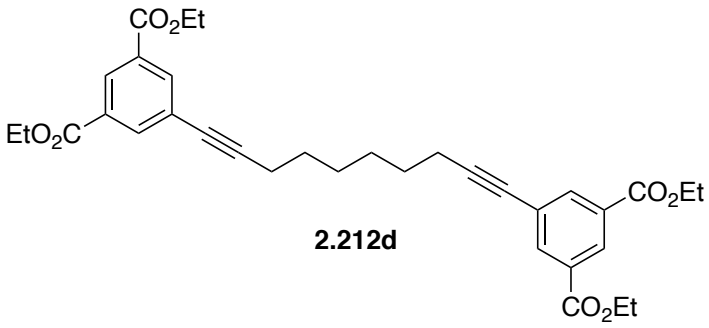



CO2Et
CO2Et
EtO2C
CO2Et

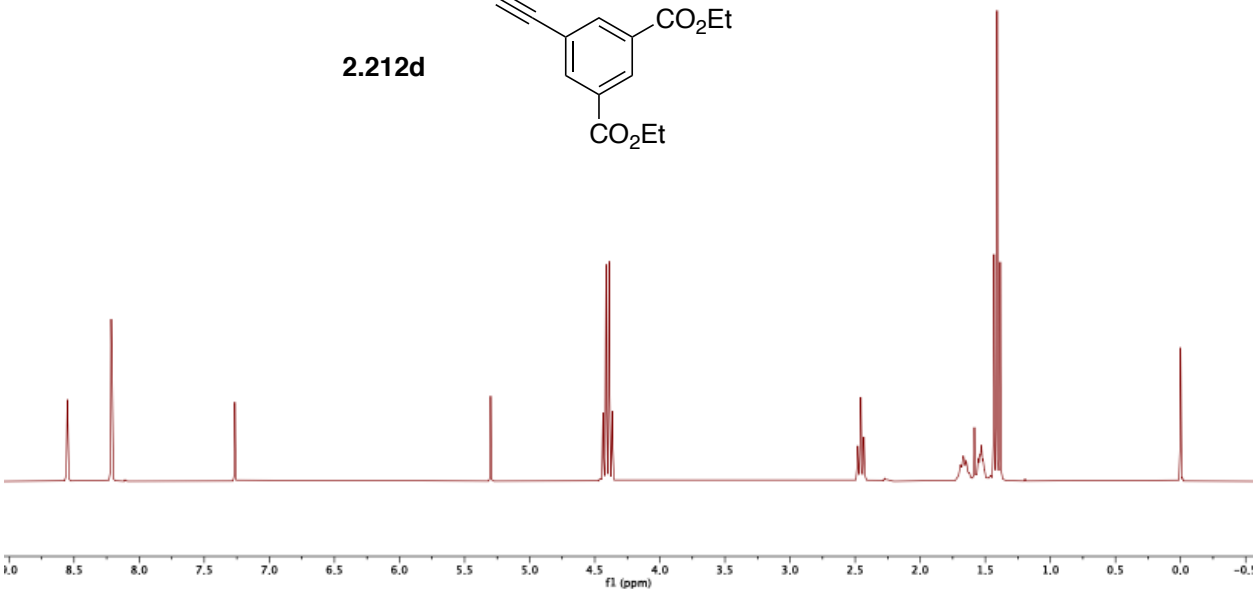
2.212c

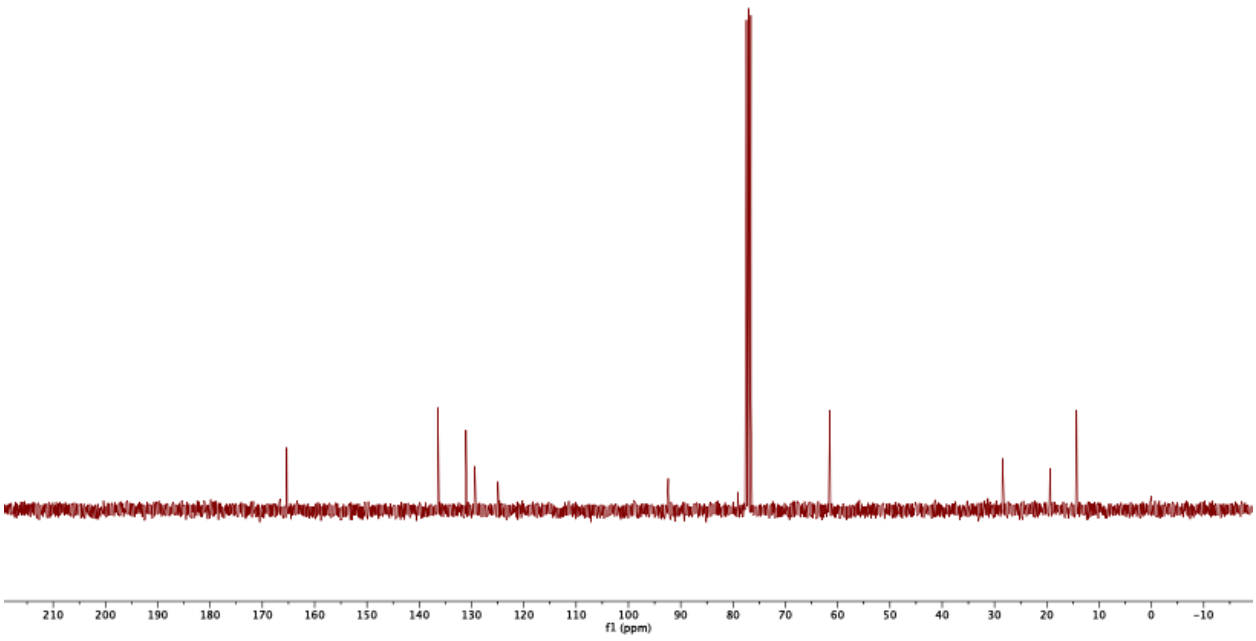
0.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

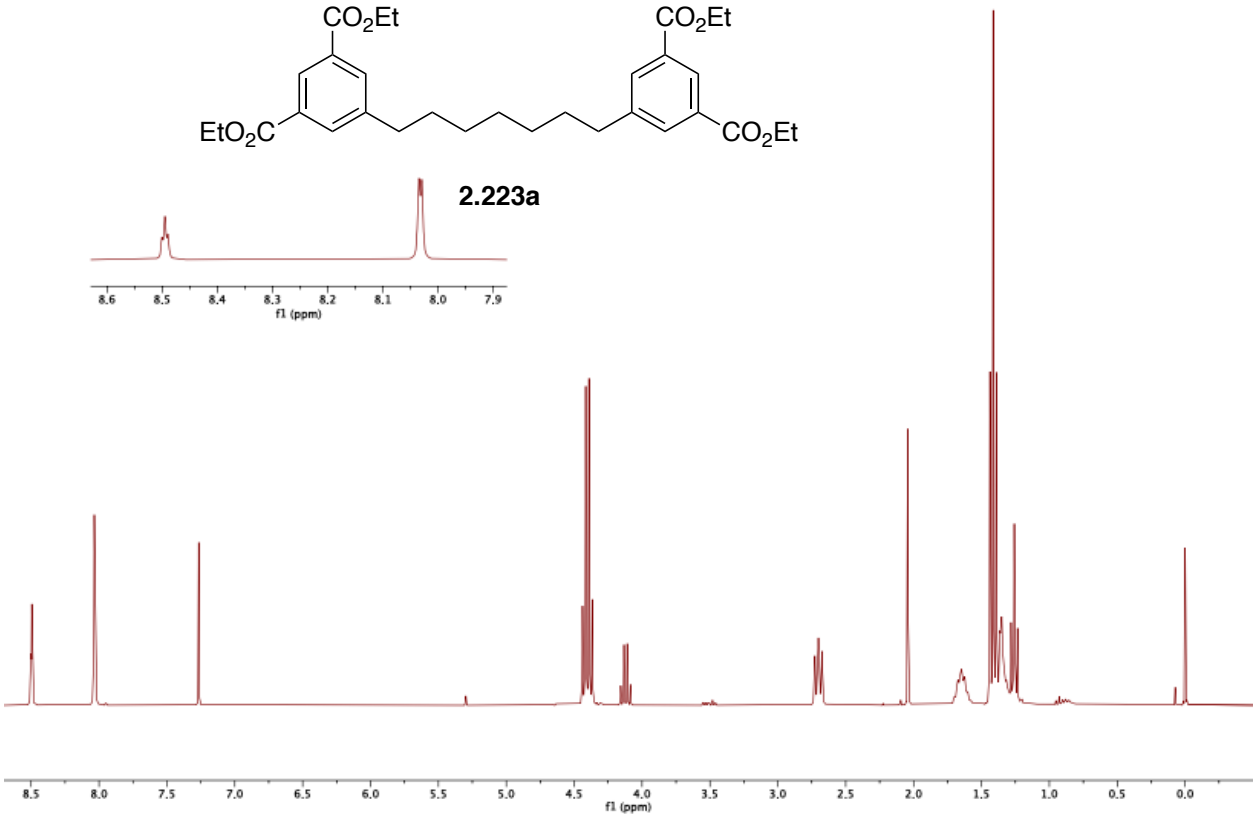

210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

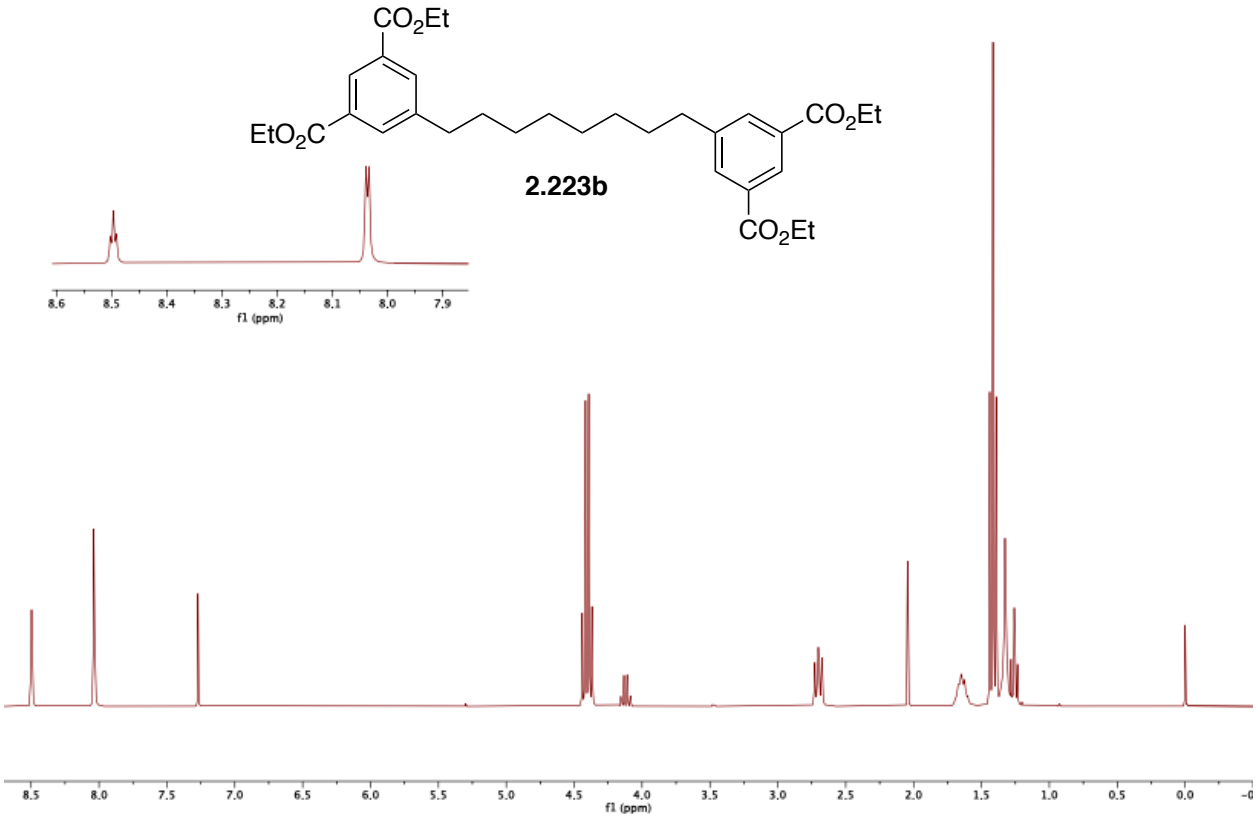


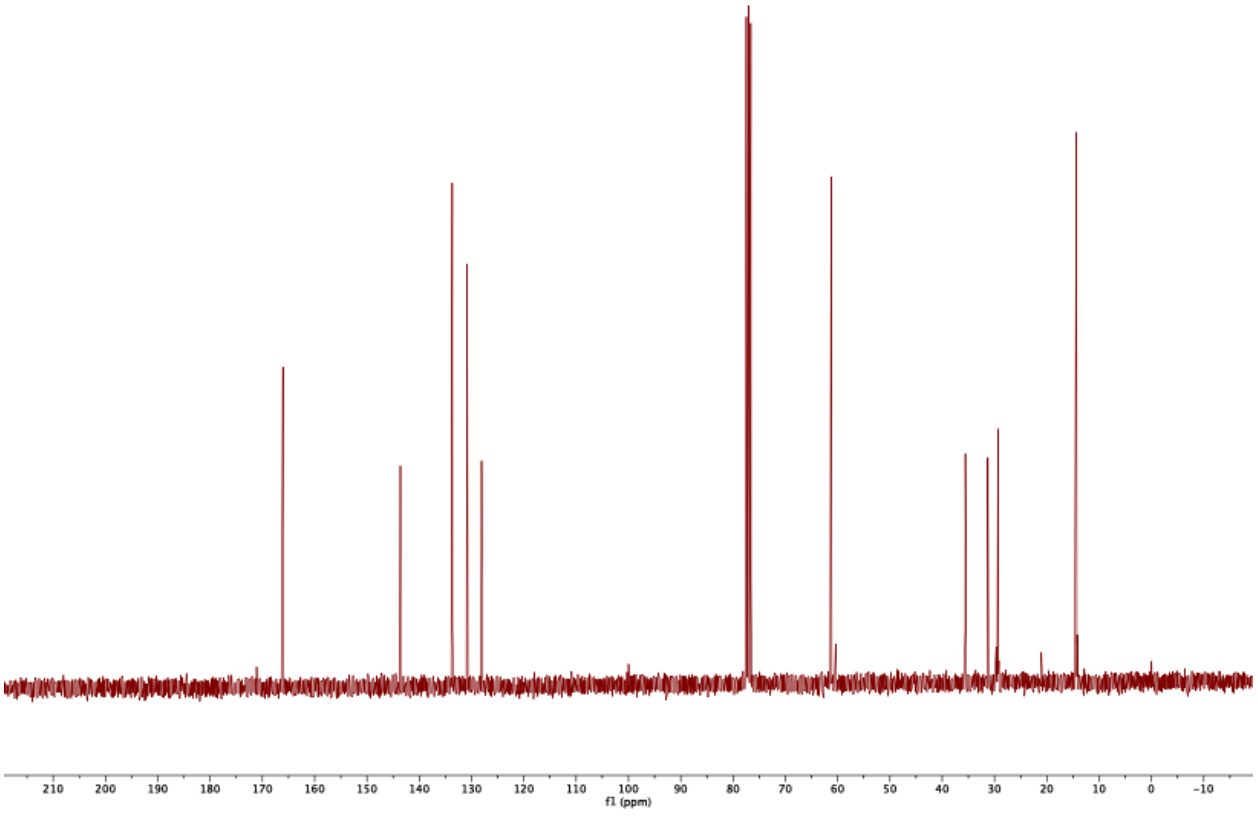
2.212d

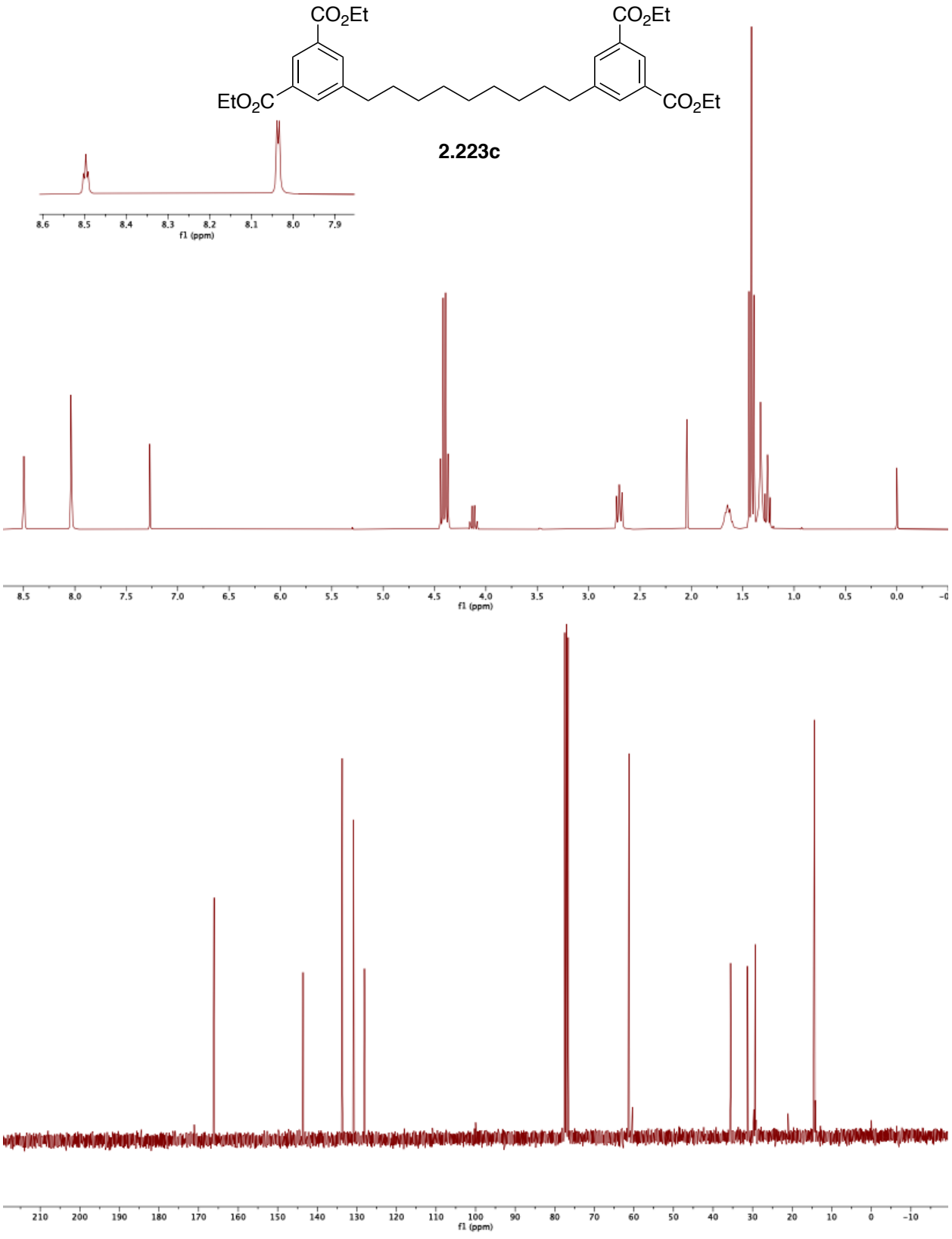


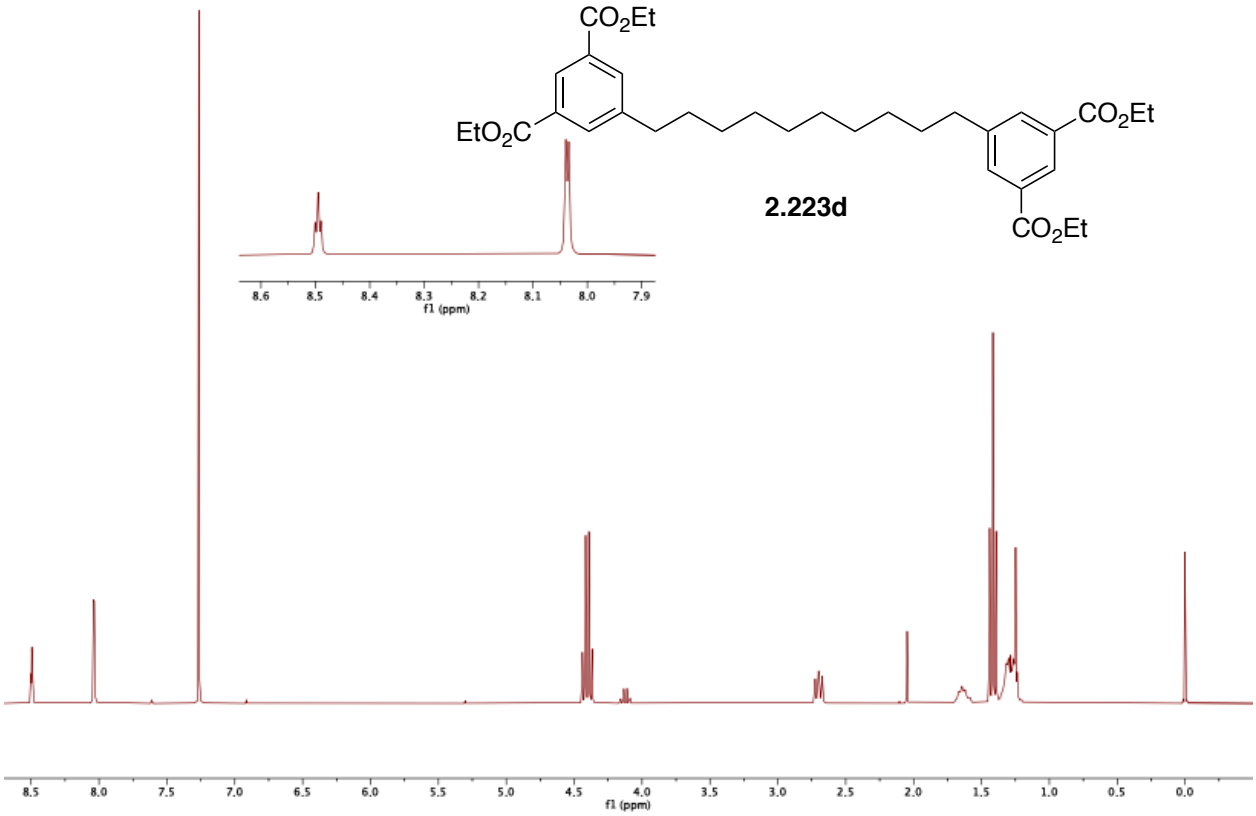


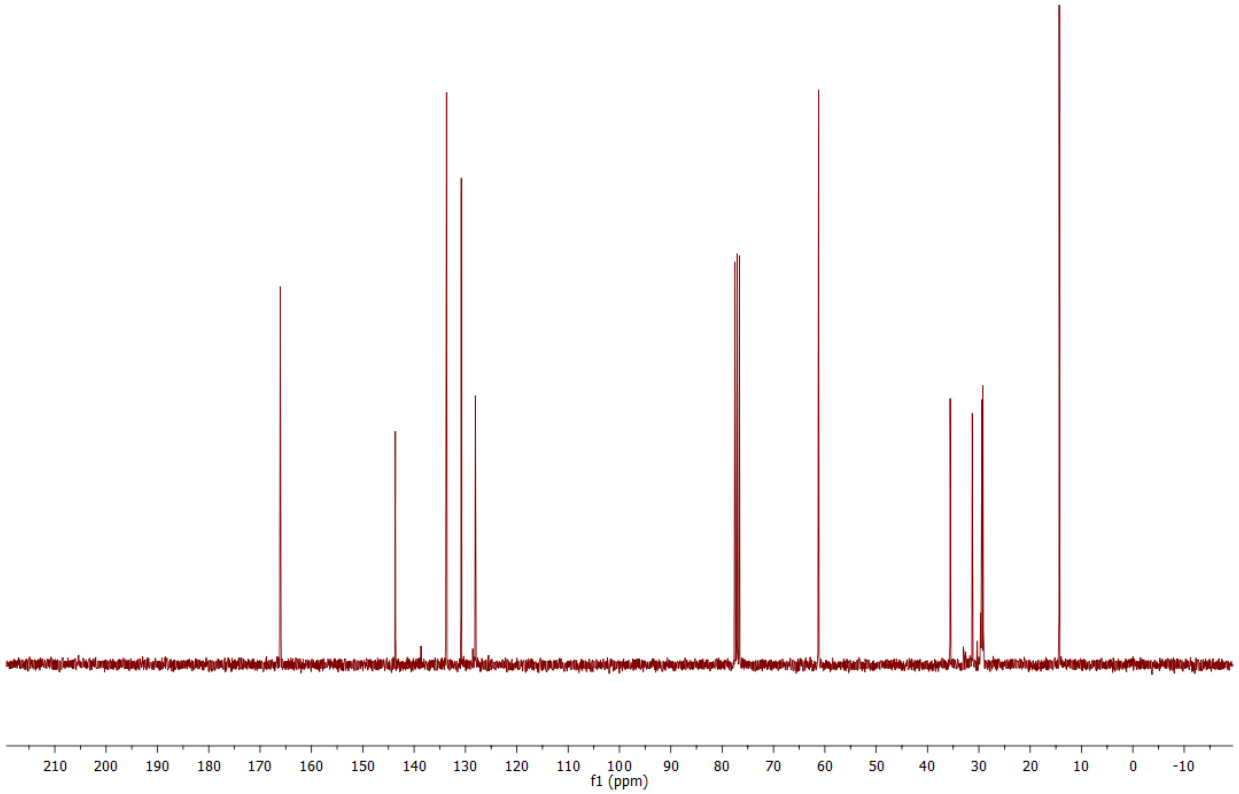

CO2Et
CO2Et
EtO2C
CO2Et
2.223a
8.6
8.5
8.4
8.3
8.2
8.1
8.0
7.9
f1 (ppm)
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

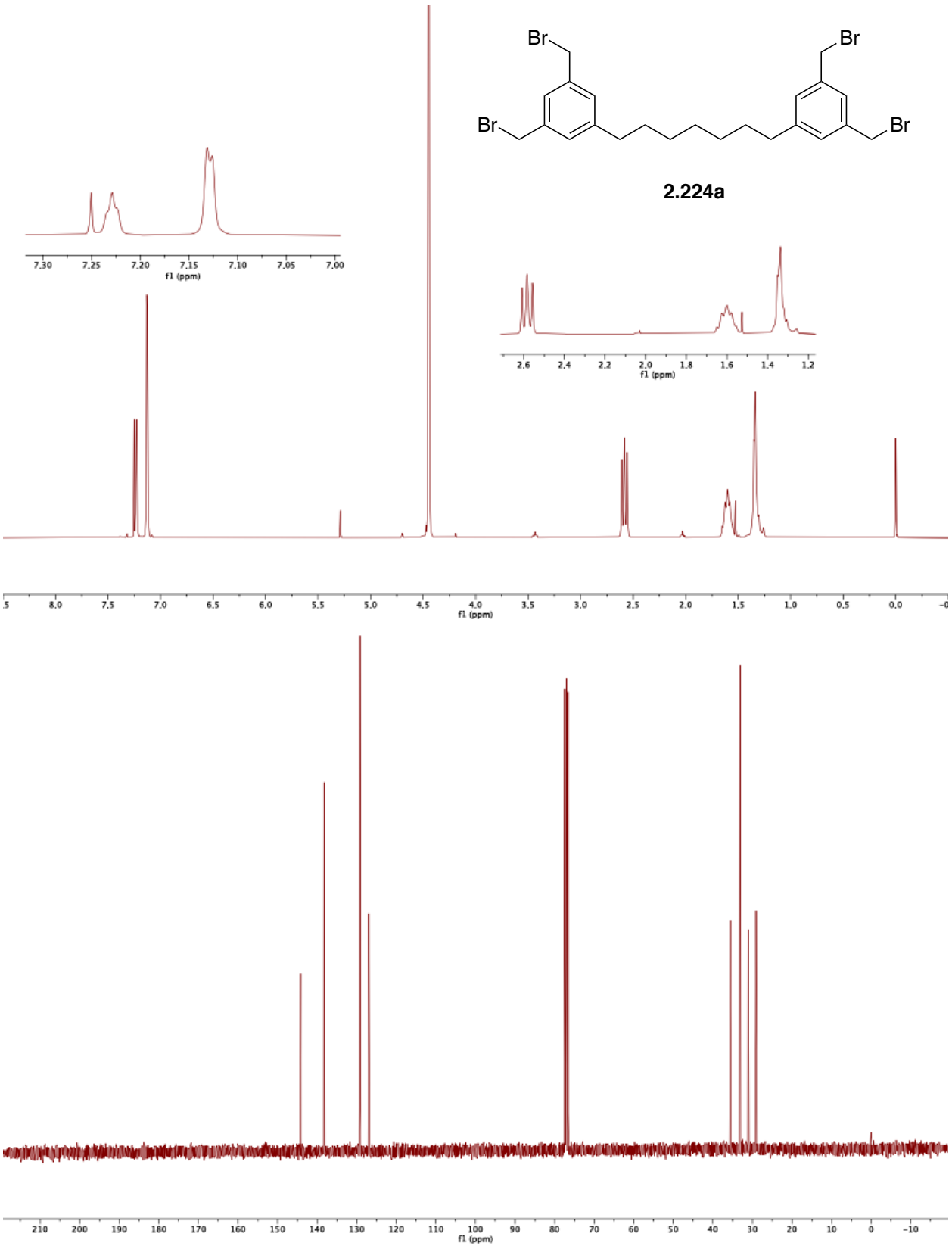

CO2Et
EtO2C
CO2Et
CO2Et
2.223b
f1 (ppm)

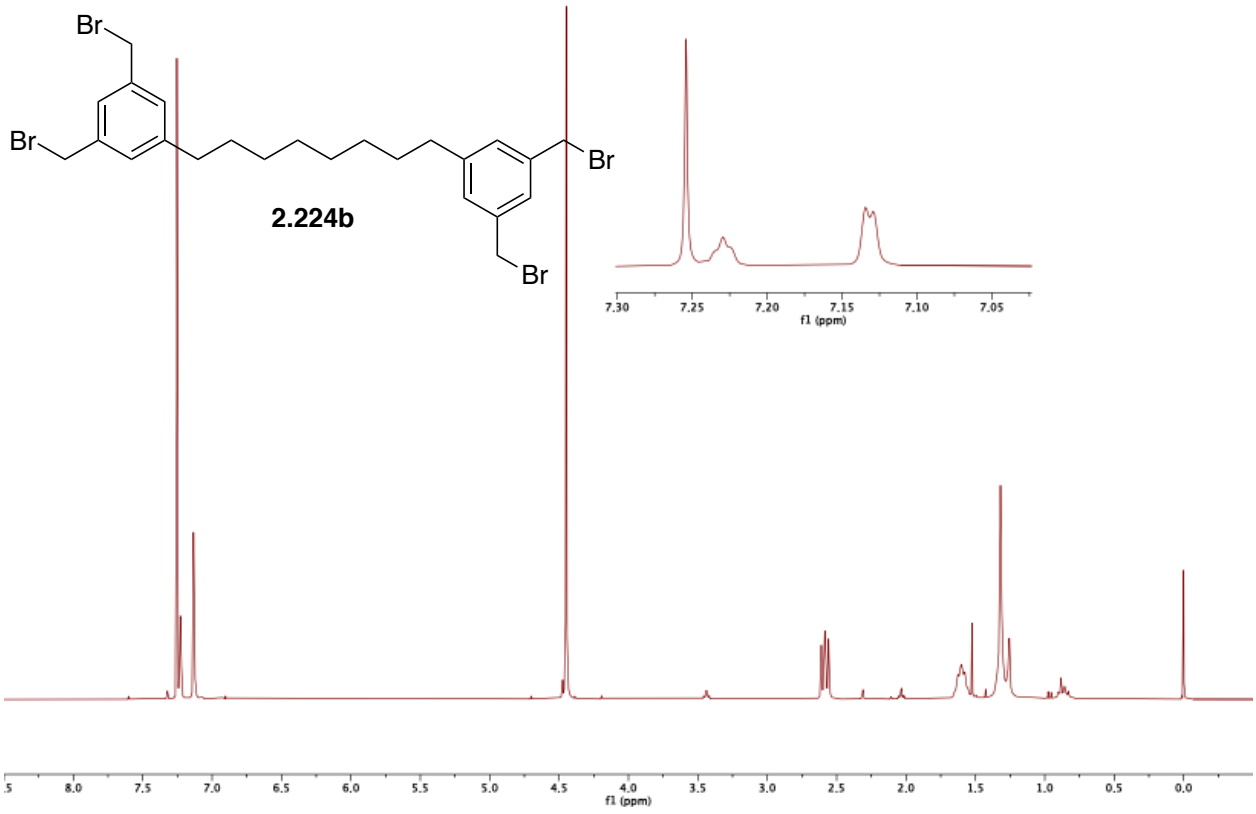

f1 (ppm)


CO2Et
CO2Et
EtO2C
CO2Et
2.223c
f1 (ppm)
f1 (ppm)
f1 (ppm)


CO2Et
EtO2C
CO2Et
CO2Et
2.223d
8.6 8.5 8.4 8.3 8.2 8.1 8.0 7.9
f1 (ppm)
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


Br
Br
Br
Br
2.224a
7.30
7.25
7.20
7.15
7.10
7.05
7.00
f1 (ppm)
2.6
2.4
2.2
2.0
1.8
1.6
1.4
1.2
f1 (ppm)
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)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Br
Br
Br
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7.25
7.20
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7.10
7.05
f1 (ppm)
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7.5
7.0
6.5
6.0
5.5
5.0
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2.5
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1.5
1.0
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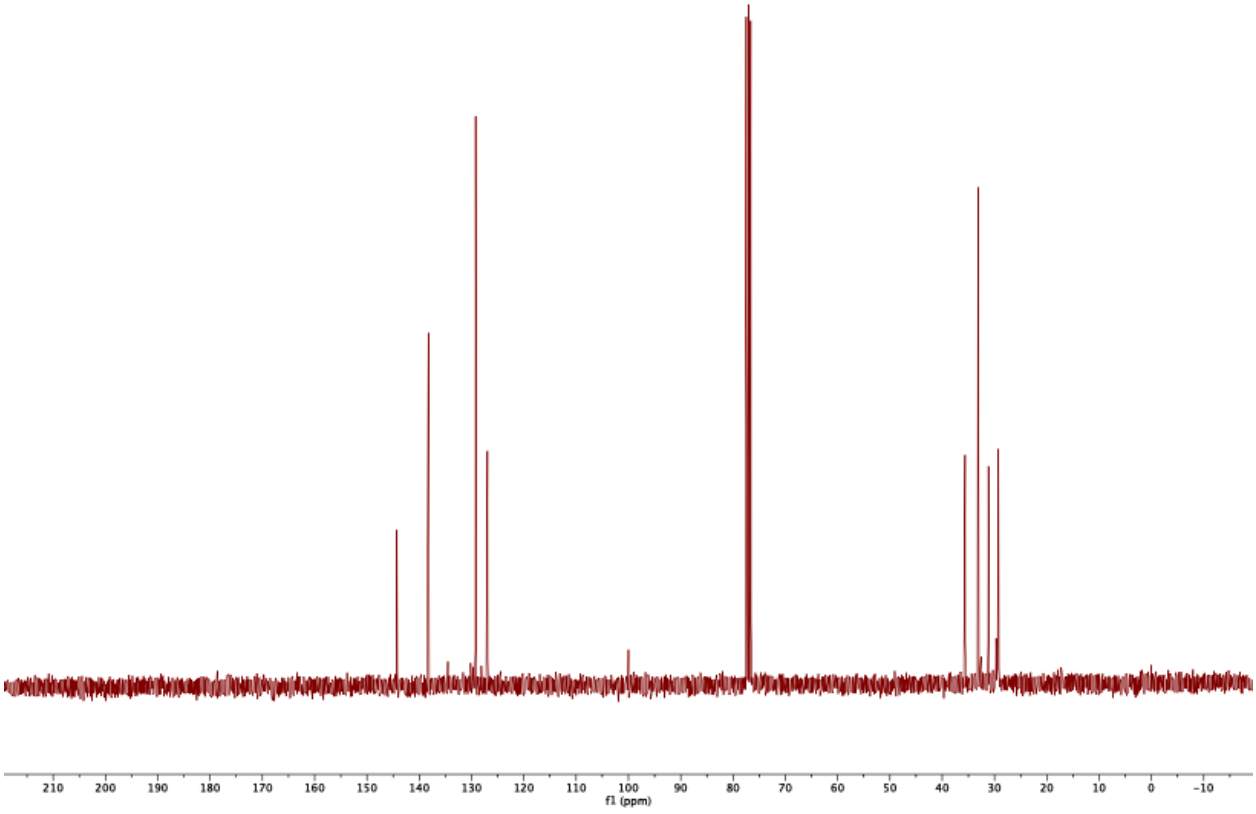
0.0
f1 (ppm)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100
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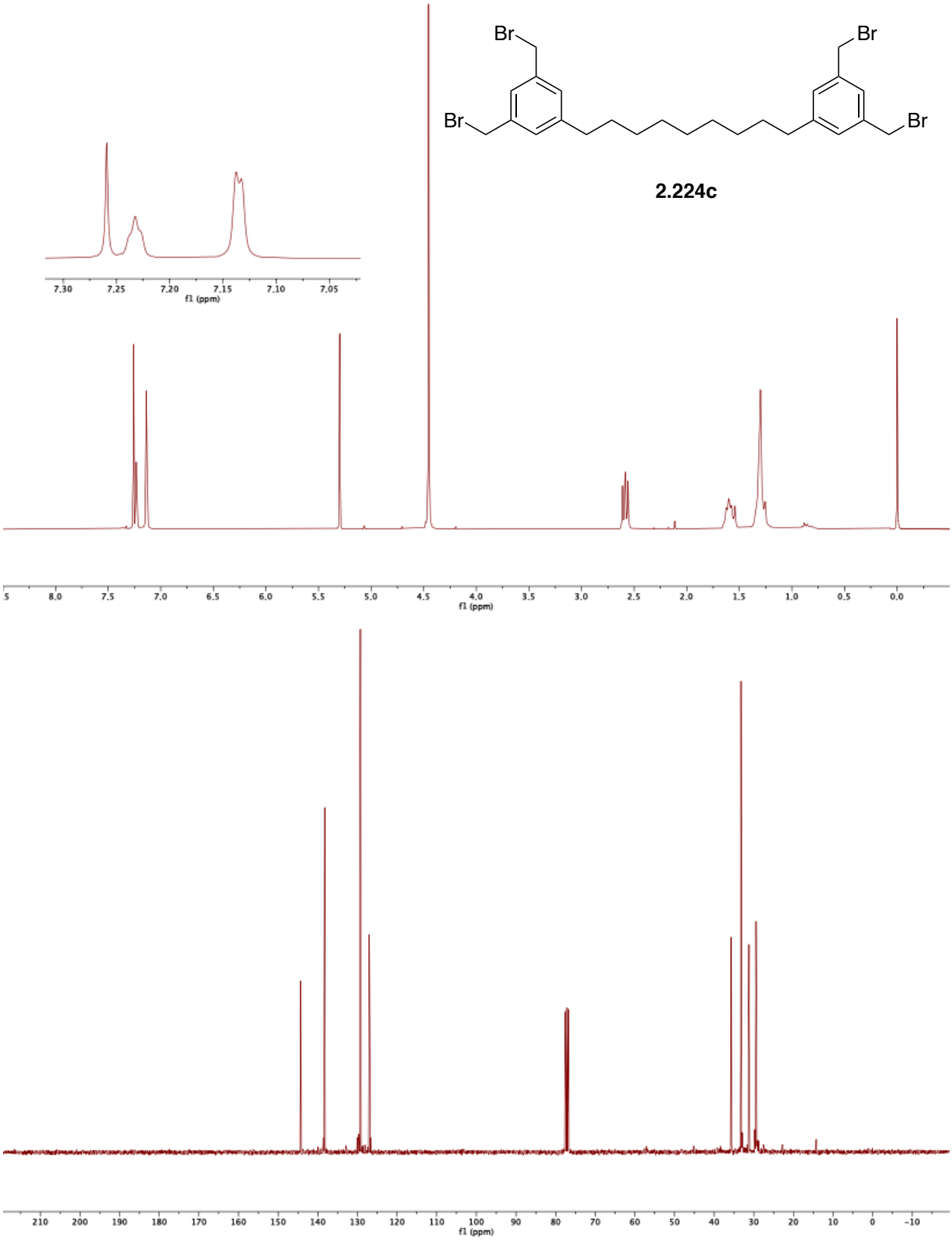
60
50
40
30
20
10
0
-10
f1 (ppm)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Br
Br
Br
2.224c
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7.25
7.20
7.15
7.10
7.05
f1 (ppm)
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7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)
210
200
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180
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100
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80
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60
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40
30
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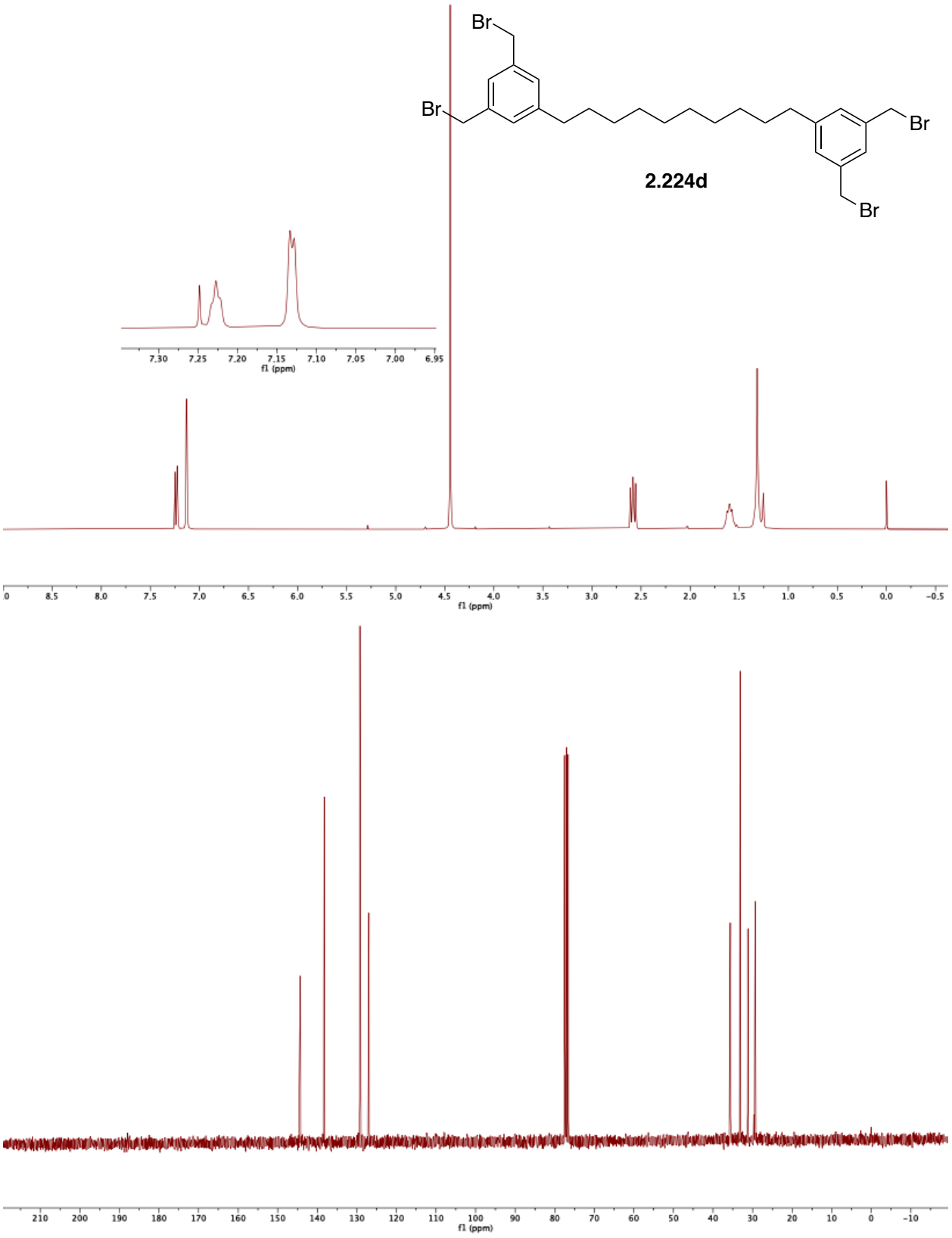
f1 (ppm)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Br
Br
Br
2.224d
7.30 7.25 7.20 7.15 7.10 7.05 7.00 6.95
f1 (ppm)
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f1 (ppm)
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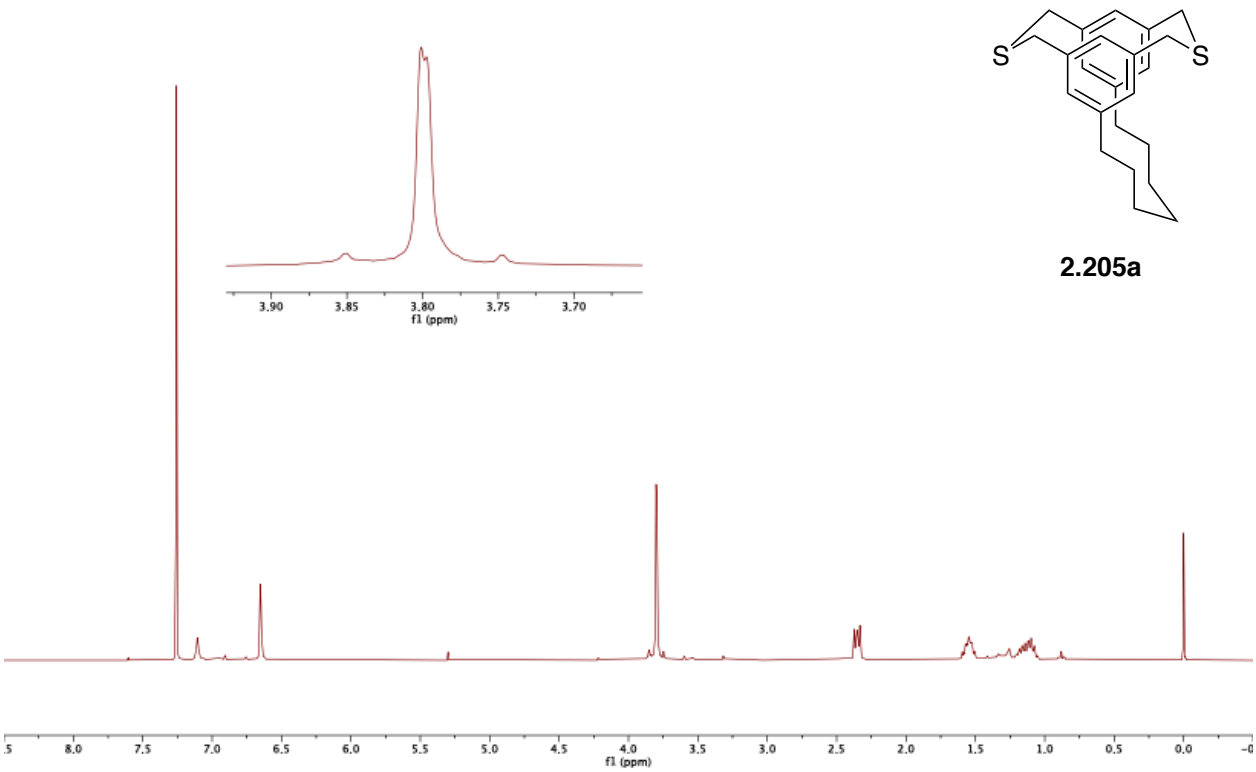
f1 (ppm)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3.5
3.0
2.5
2.0
1.5
1.0
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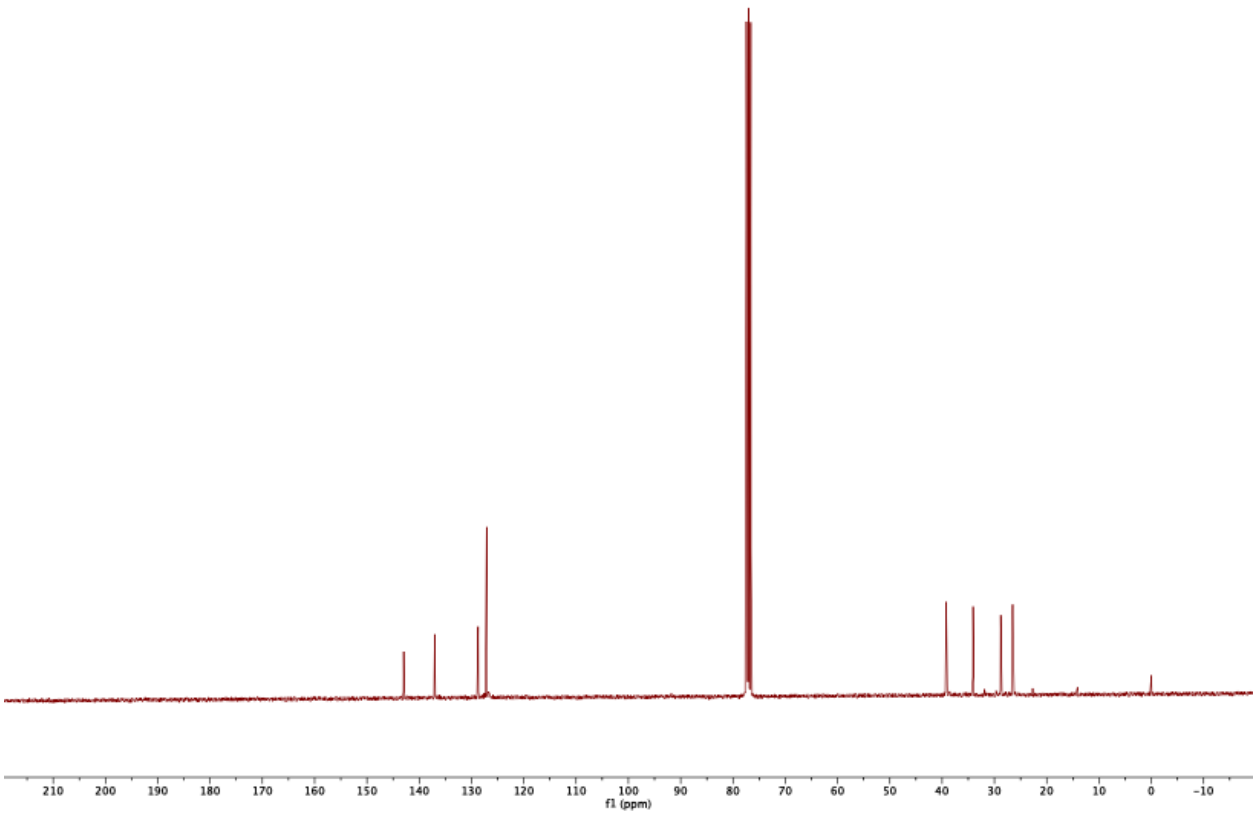
0.0
f1 (ppm)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80
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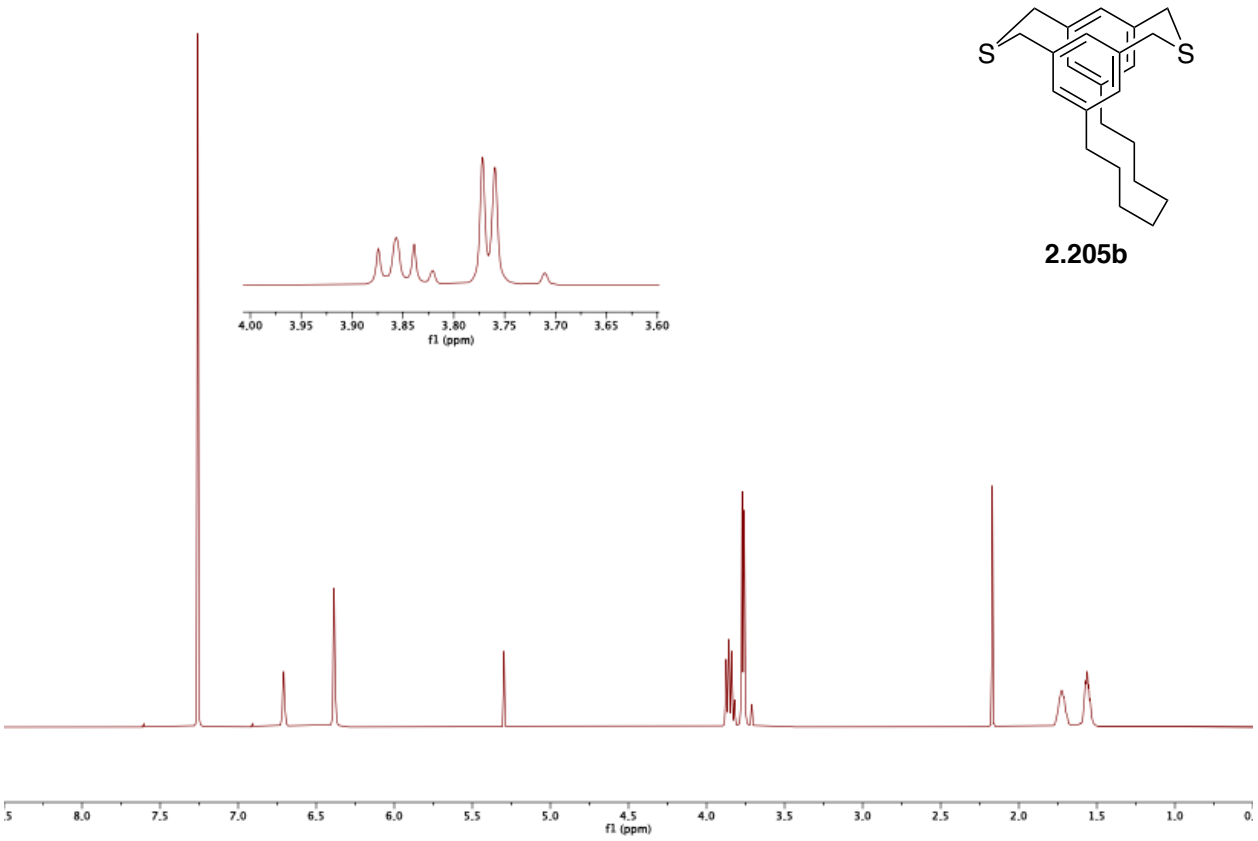
60
50
40
30
20
10
0
-10
f1 (ppm)

S
S

2.205a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S
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3.75
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3.65
3.60
f1 (ppm)
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7.5
7.0
6.5
6.0
5.5
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4.0
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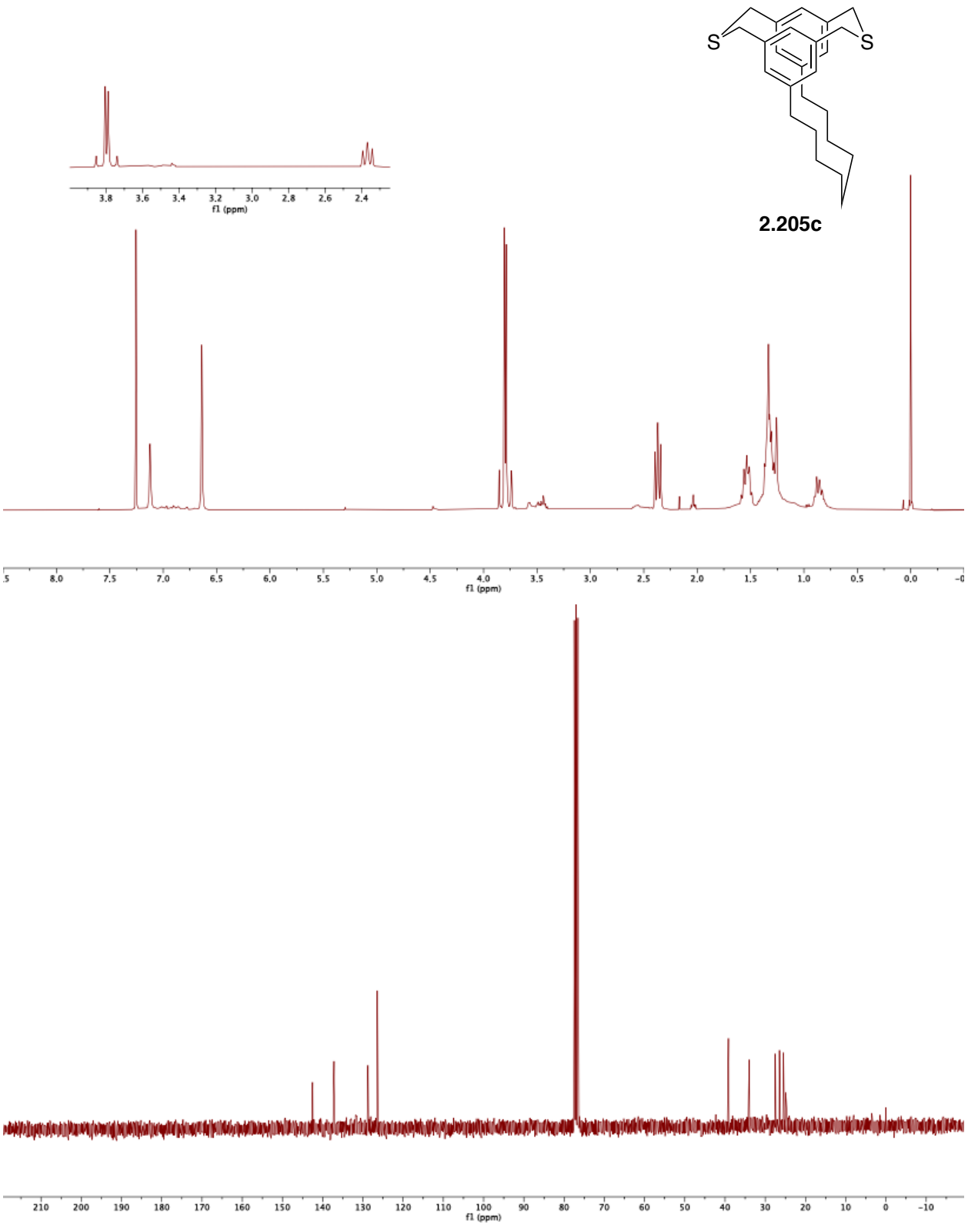
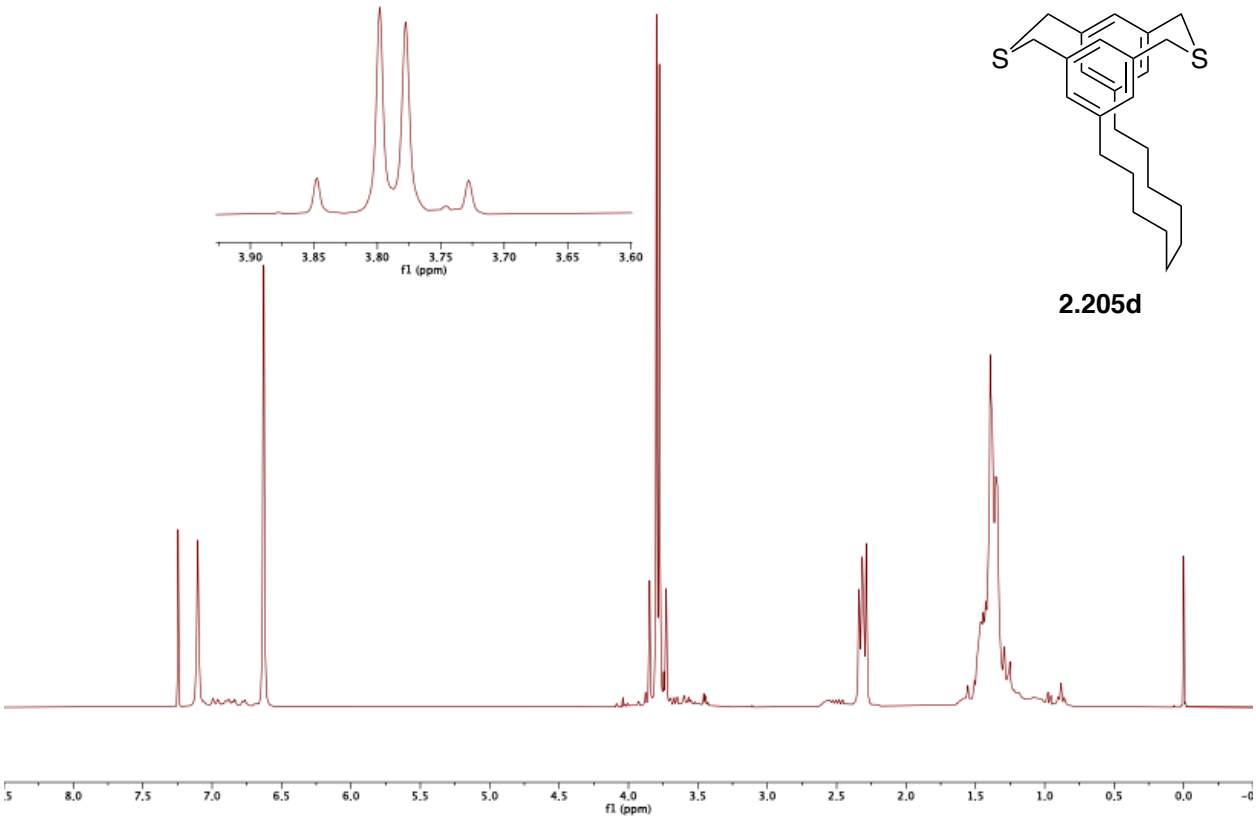
2.5
2.0
1.5
1.0
f1 (ppm)

2.205b


S
S
2.205c
f1 (ppm)
f1 (ppm)
f1 (ppm)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S
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3.85
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3.60
f1 (ppm)
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6.5
6.0
5.5
5.0
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3.0
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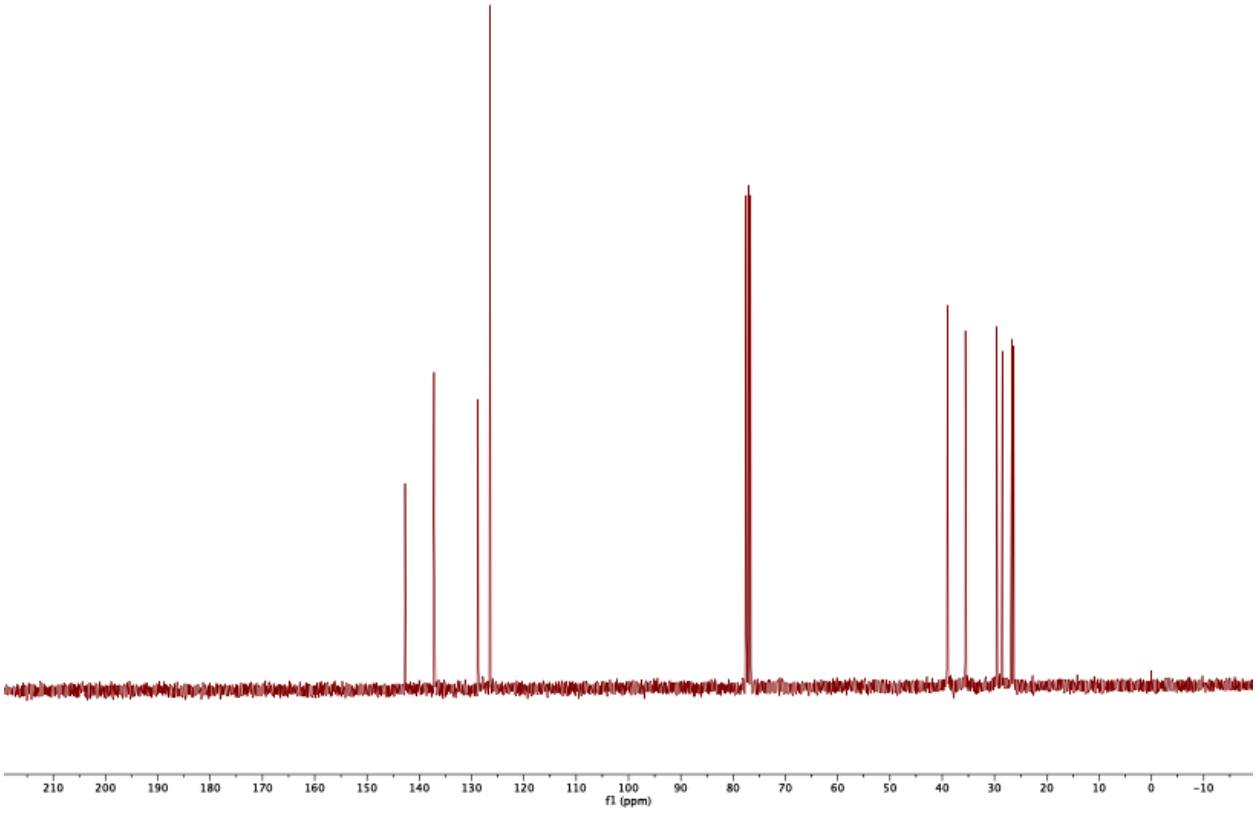
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

2.205d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120
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100
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60
50
40
30
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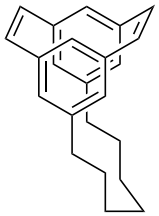
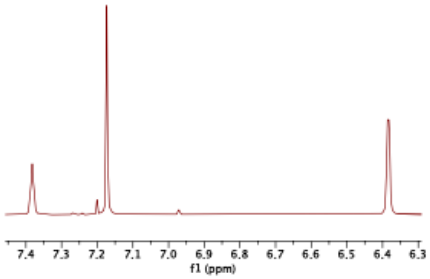
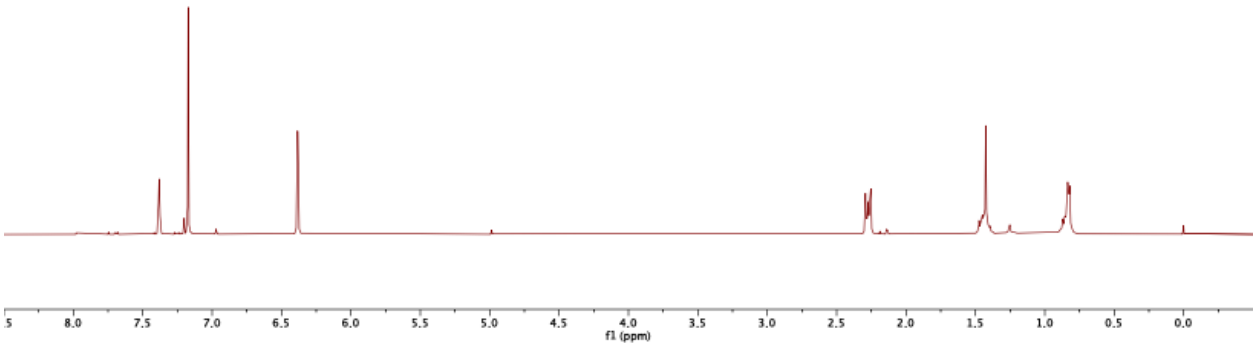
10
0
-10
f1 (ppm)



2.207a


7.4 7.3 7.2 7.1 7.0 6.9 6.8 6.7 6.6 6.5 6.4 6.3
f1 (ppm)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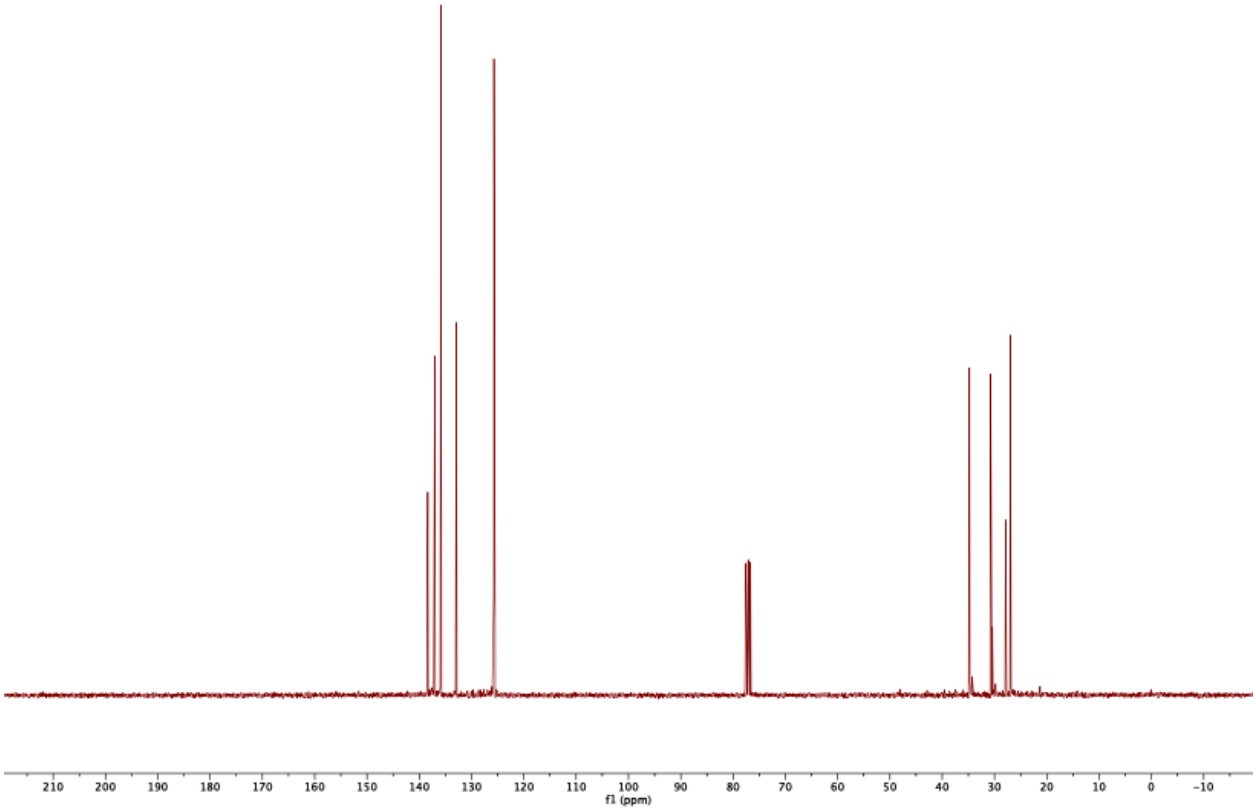
f1 (ppm)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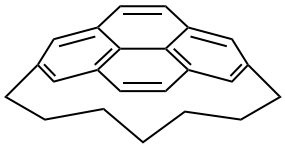

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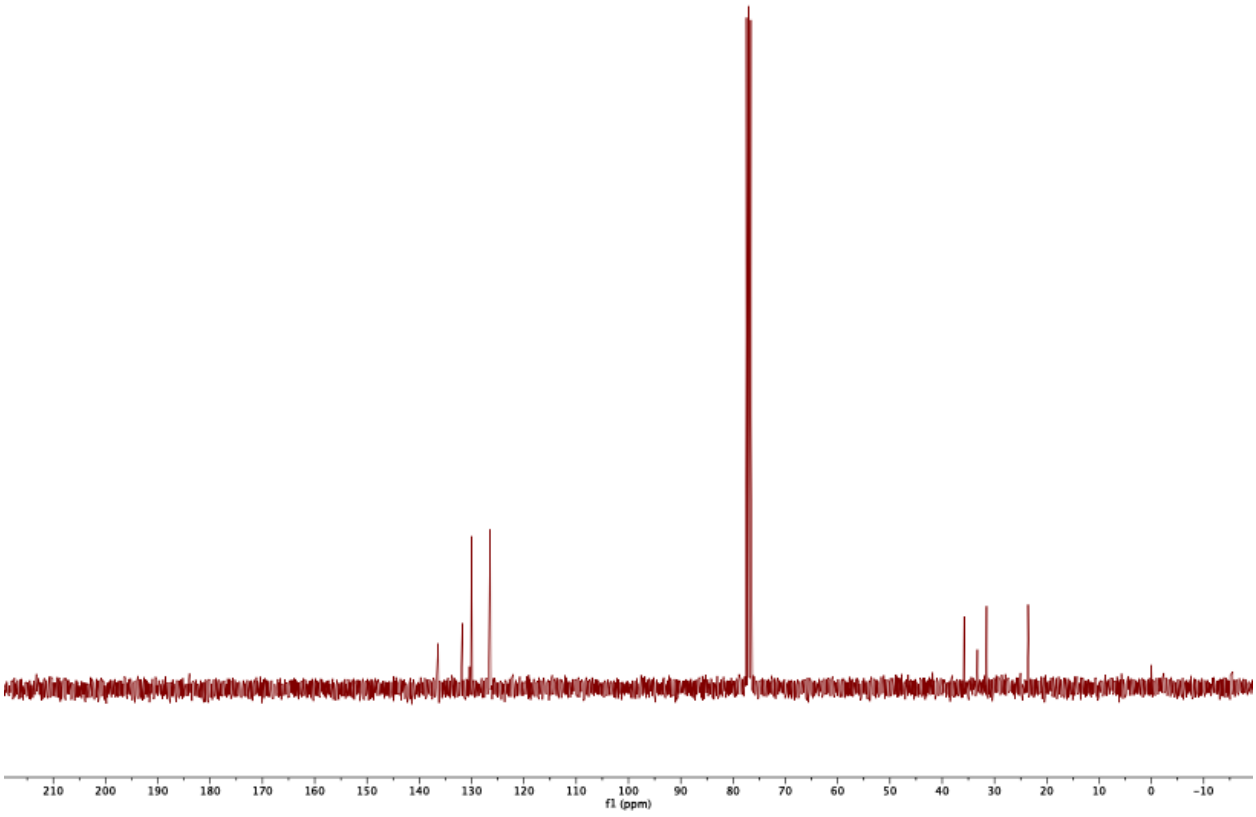

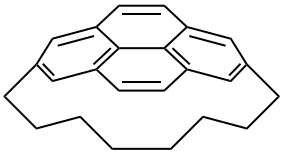

2.208b

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5.0
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4.0
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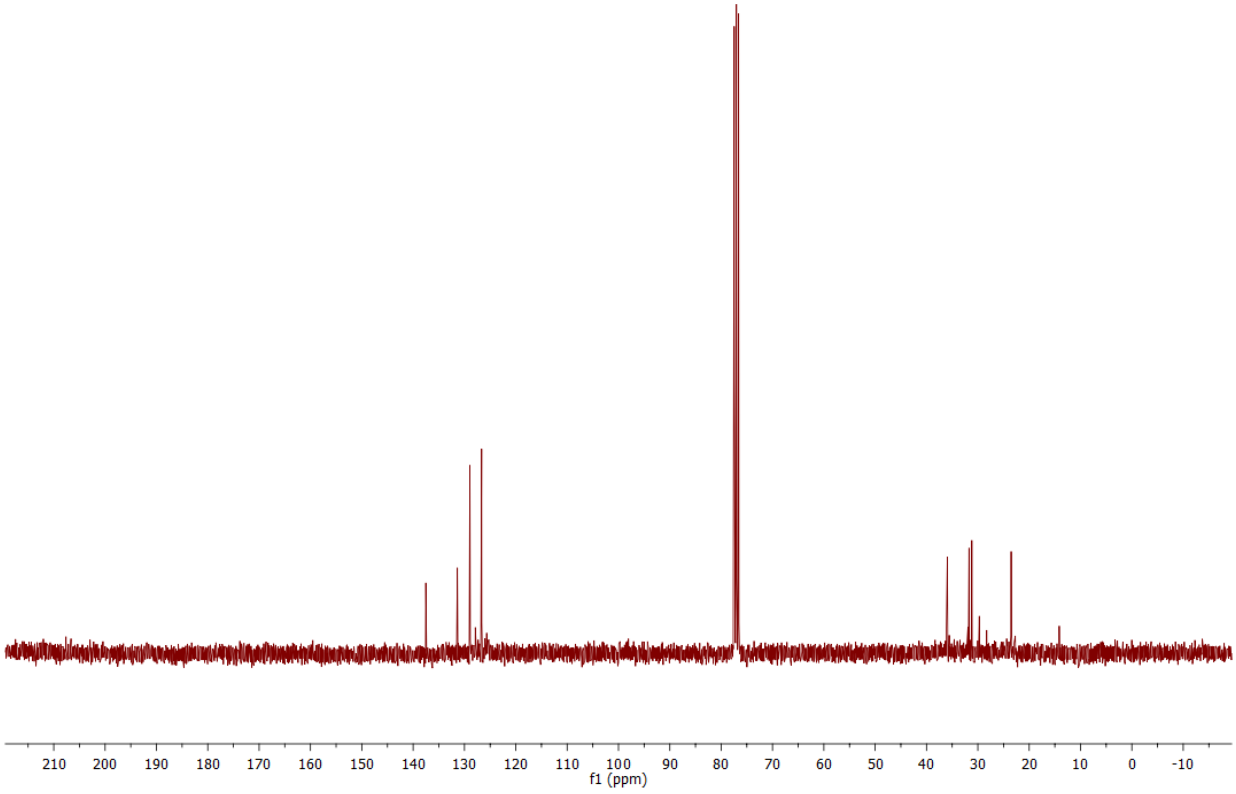
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1.0
-1.5
f1 (ppm)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100
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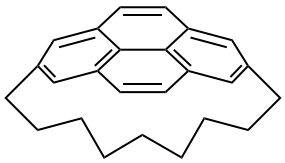
60
50
40
30
20
10
0
-10
f1 (ppm)



2.208c

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7.0
6.5
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5.0
4.5
4.0
3.5
3.0
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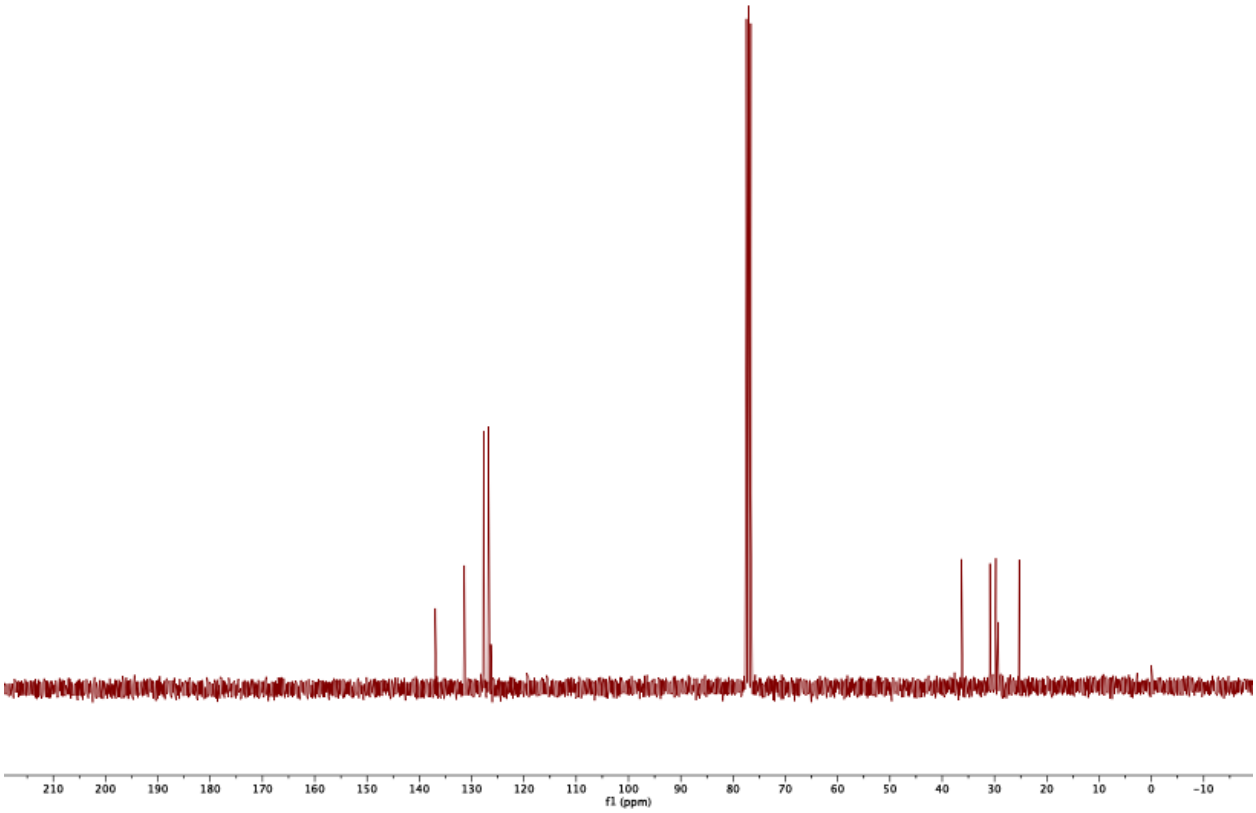
1.5
1.0
0.5
0.0
-0.5
-1.0
-1.5
-2.0
f1 (ppm)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180
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40
30
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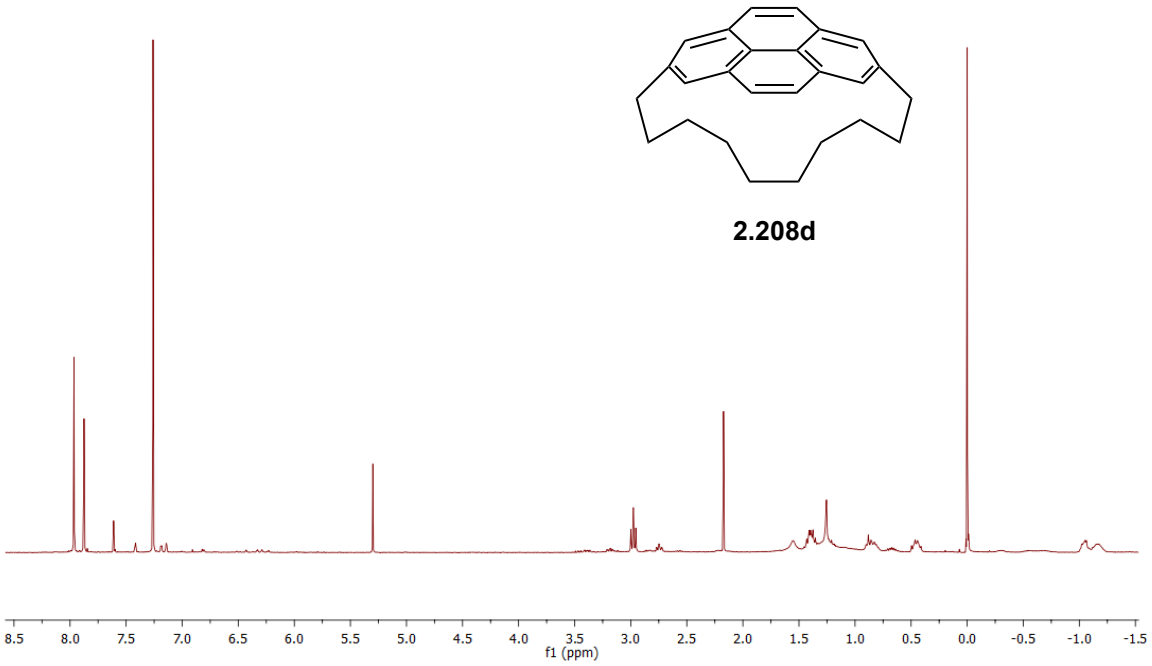
10
0
-10
f1 (ppm)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6.0
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5.0
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4.0
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3.0
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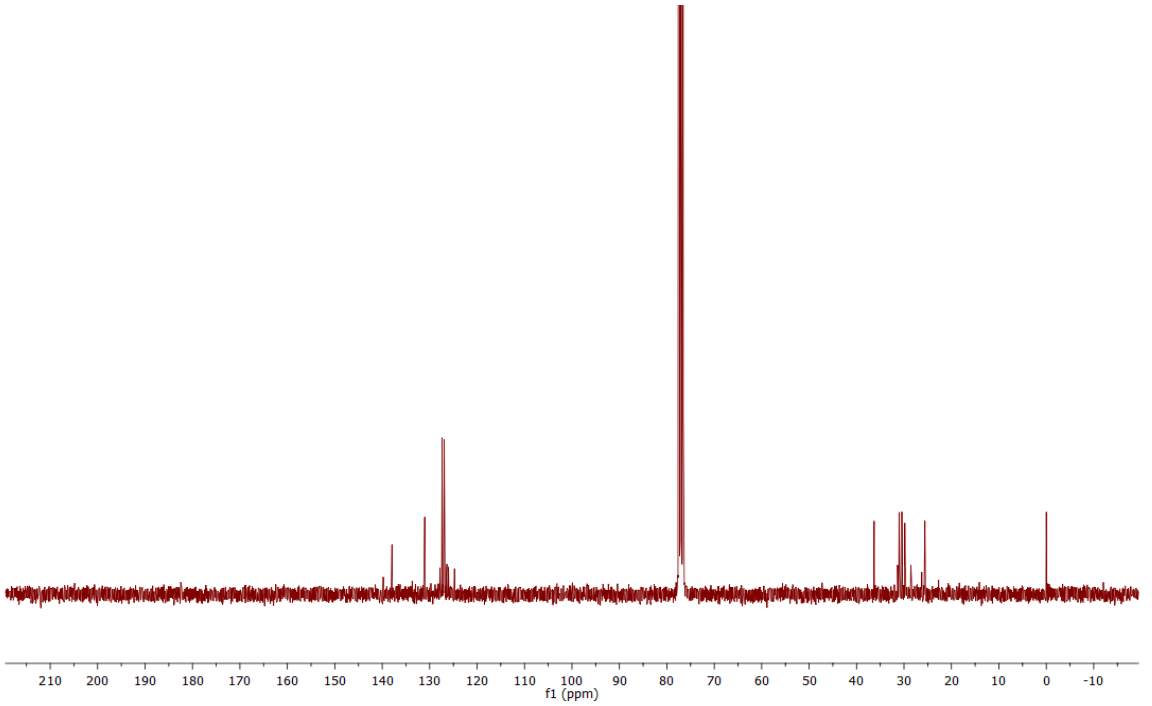
0.0
-0.5
-1.0
-1.5
f1 (ppm)

2.208d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180
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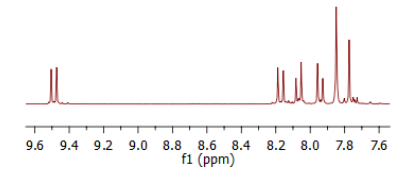
10
0
-10
f1 (ppm)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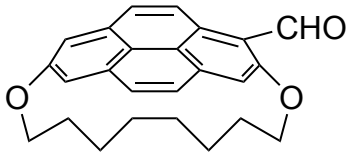
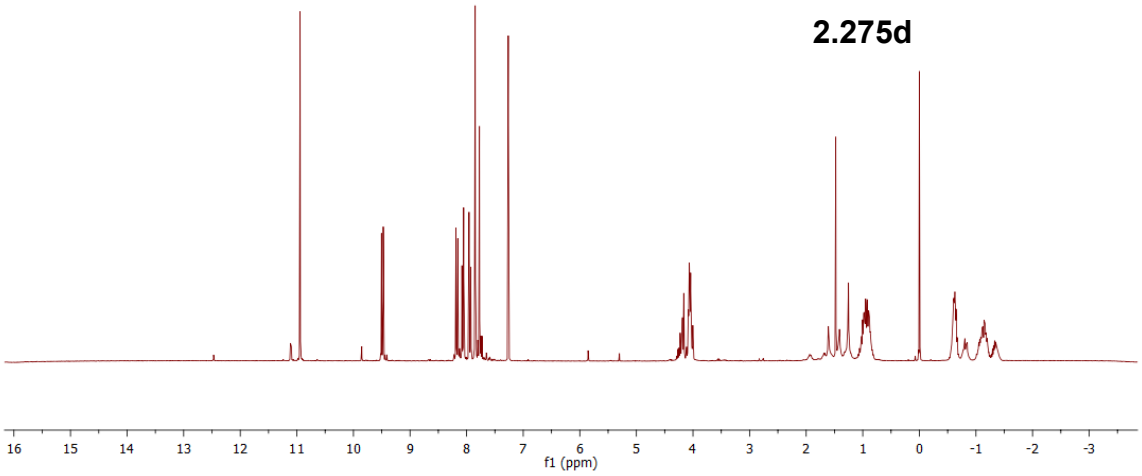
f1 (ppm)


CHO
O
O

2.275d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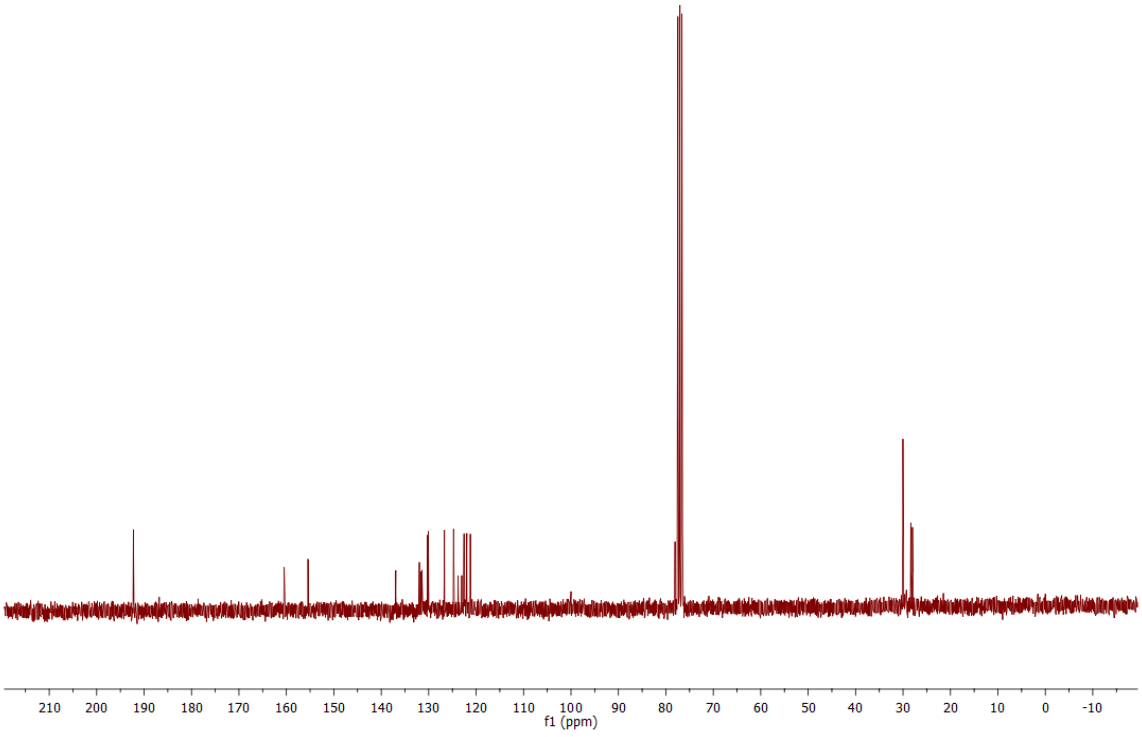
f1 (ppm)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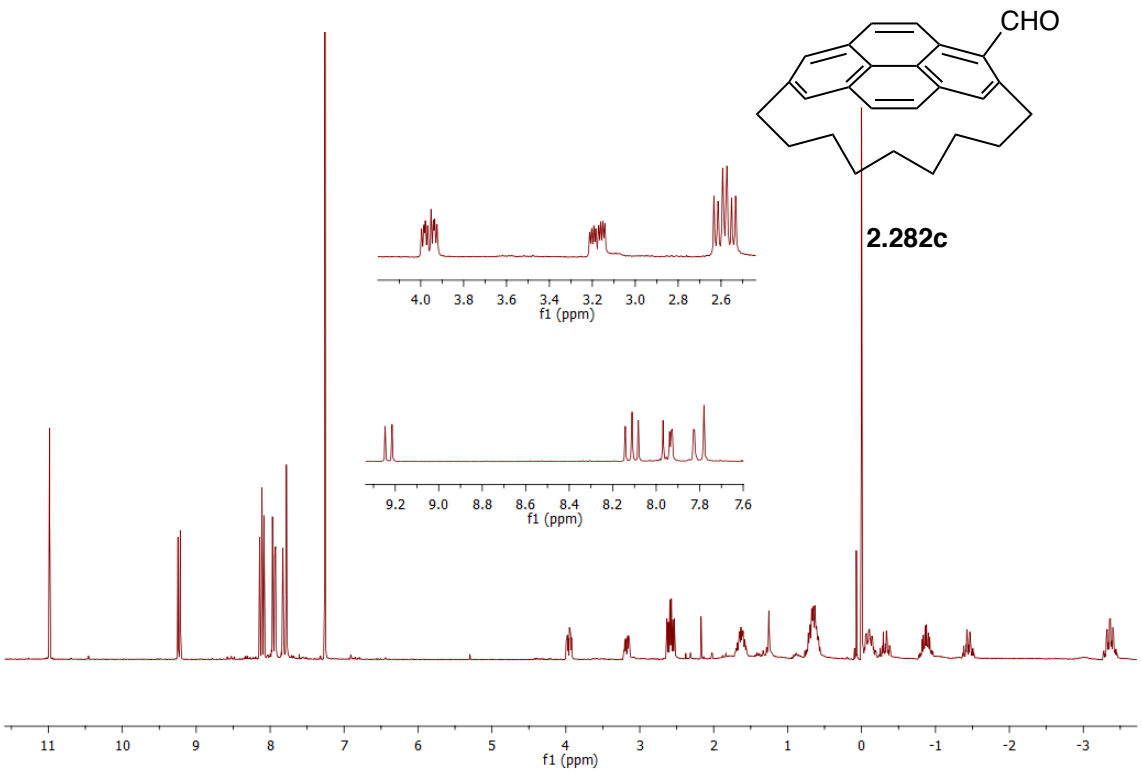
f1 (ppm)


CHO
2.282c
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f1 (ppm)
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f1 (ppm)
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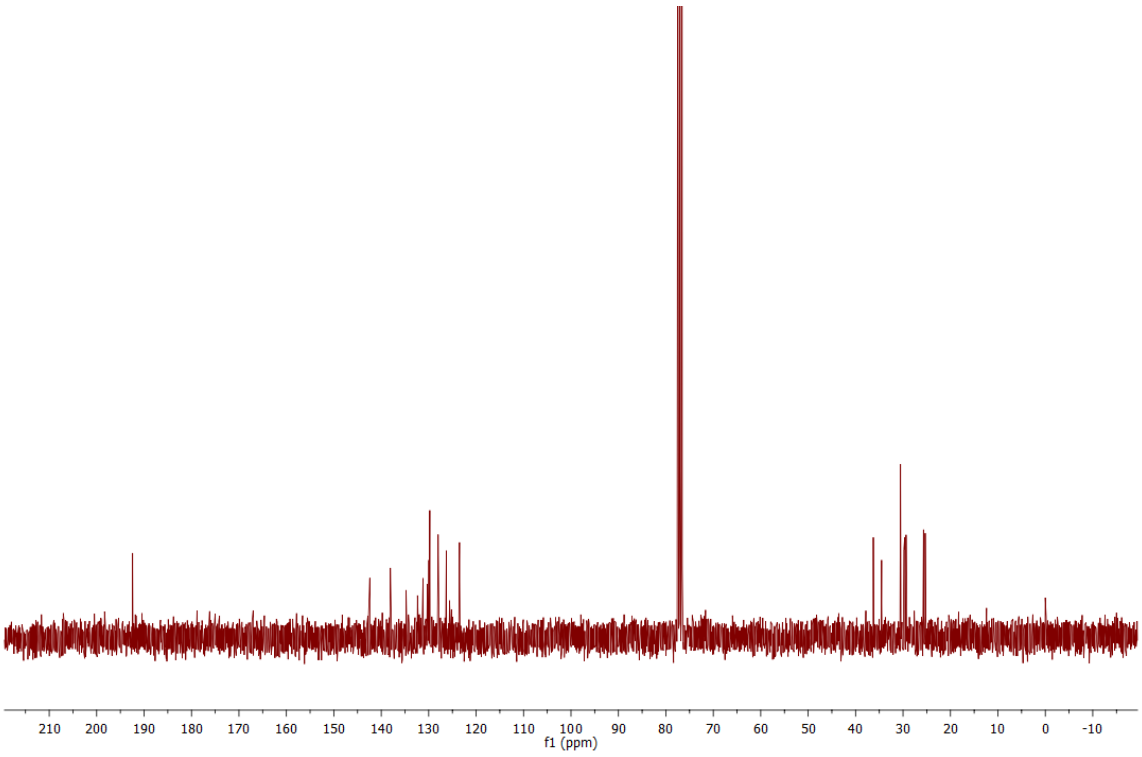
f1 (ppm)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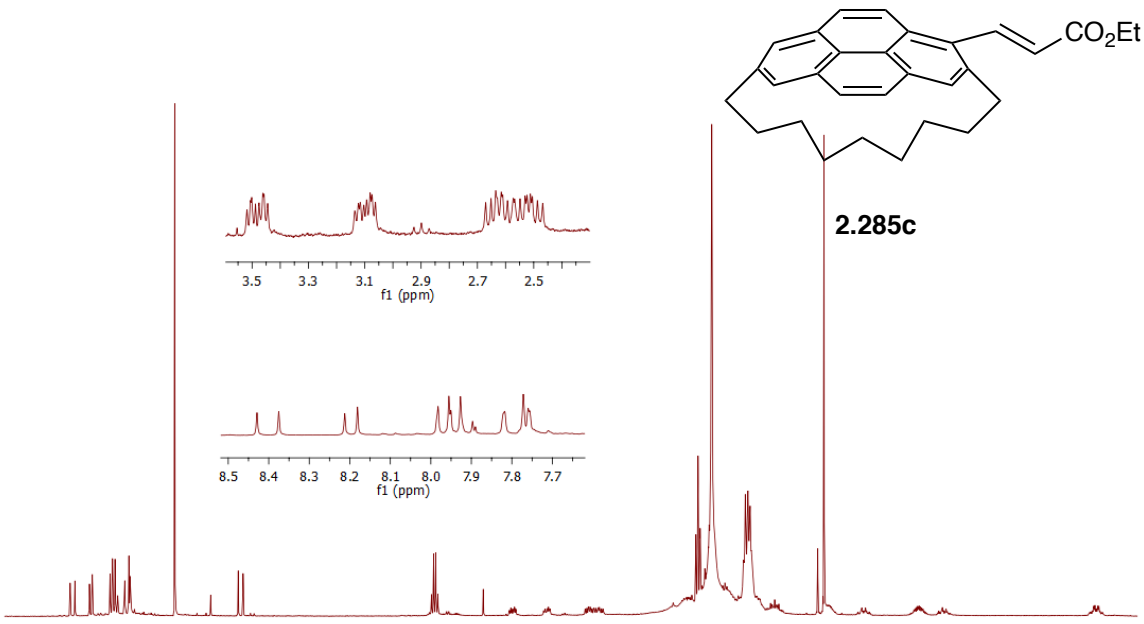
f1 (ppm)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2.285c
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3.3
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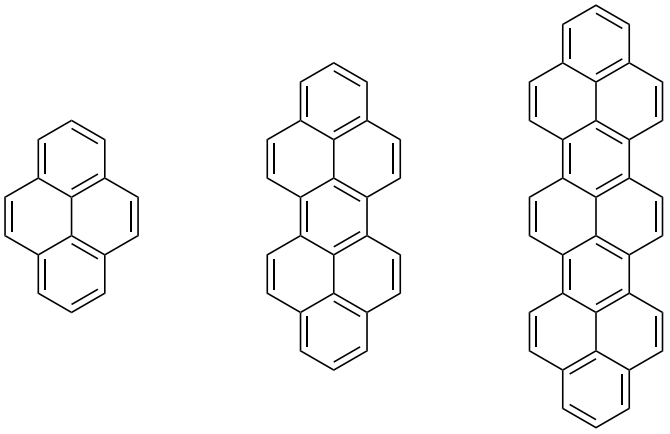
2.9
2.7
2.5
f1 (ppm)
8.5
8.4
8.3
8.2
8.1
8.0
7.9
7.8
7.7
f1 (ppm)

Chapter 3: Synthesis of [*n*](2,6)Peropyrenophanes

3.1: Introduction

Peropyrene (**3.2**) belongs to homologous series of armchair-edged graphene nanoribbons dubbed the "ropyrenes",[1] which also contains pyrene (**3.1**) and teropyrene (**3.3**) as its next lowest and highest homologues, respectively (**Figure 3.1**). It was first synthesized by Clar in 1959[2] and has attracted renewed interest in recent years due to its potential to exhibit singlet fission.



3.1 **3.2** **3.3**

Figure 3.1. Homologous series of armchair-edged graphene nanoribbons.

3.1.1: Photophysical Properties of Peropyrene

Peropyrene (**3.2**) has not been studied to a great extent, most likely due to its limited supply and low solubility. However, some photophysical properties have been studied.[3] The absorption spectrum of peropyrene (**3.2**) in CH_3CN shows a highly-structured absorption band with a longest wavelength absorbance maximum at 445 nm (**Figure 3.2**). The absorption spectrum is not greatly influenced by solvent polarity, which indicates that there is little difference in polarity between the ground and excited states

of the parent peropyrene system. The fluorescence spectrum in CH_3CN is also highly structured and nearly a mirror image of the absorbance spectrum. The near symmetry of the absorption and fluorescence spectra is indicative of a ground state (S_0) and excited singlet state (S_1) that are very similar in geometry and therefore little reorganization occurs upon excitation. Peropyrene (**3.2**) is also an efficient fluorophore that exhibits a quantum yield (Φ_f) of 0.87 in CH_3CN, 0.93 in toluene and about 0.90 in other organic solvents.[4]

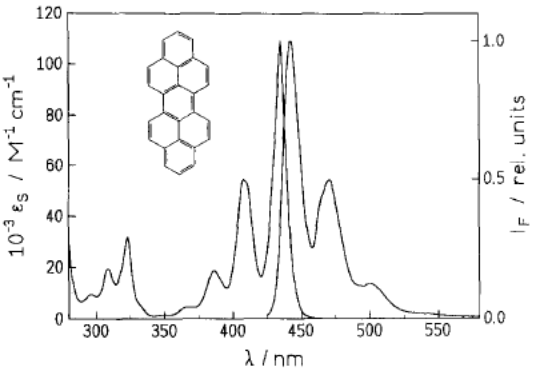


Figure 3.2 UV/Vis absorption and fluorescence spectra of peropyrene (**3.2**) in acetonitrile.[3]

Peropyrene (**3.2**) also exhibits an interesting phenomenon where the energy of the singlet (S_1) excited state lies at more than twice the energy of the triplet (T_1) excited state. The singlet and triplet excited state energies for peropyrene (**3.2**) $E(S_1)$ and $E(T_1)$ have been measured to be 2.79 eV and 1.36 eV, respectively.[5] Molecules that satisfy this particular energy requirement have been shown to demonstrate singlet fission.[142] When molecule **A** absorbs a photon, an electron is excited into the S_1 state, which then interacts with a ground state molecule **B** (**Figure 3.3**) to give two molecules in the T_1 state. This process, which is known as singlet fission, is a spin allowed transition.

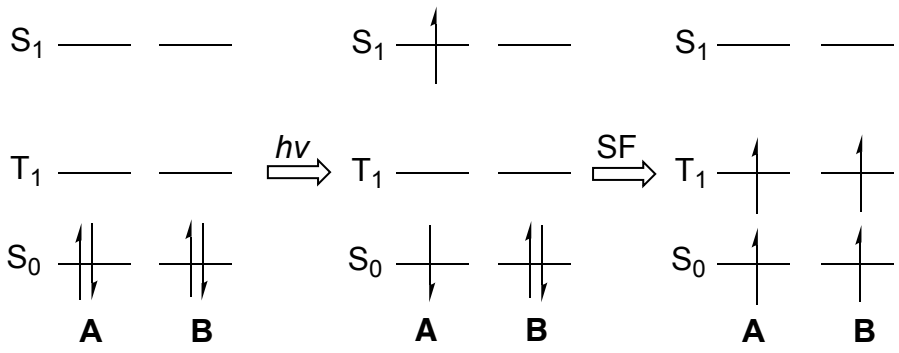


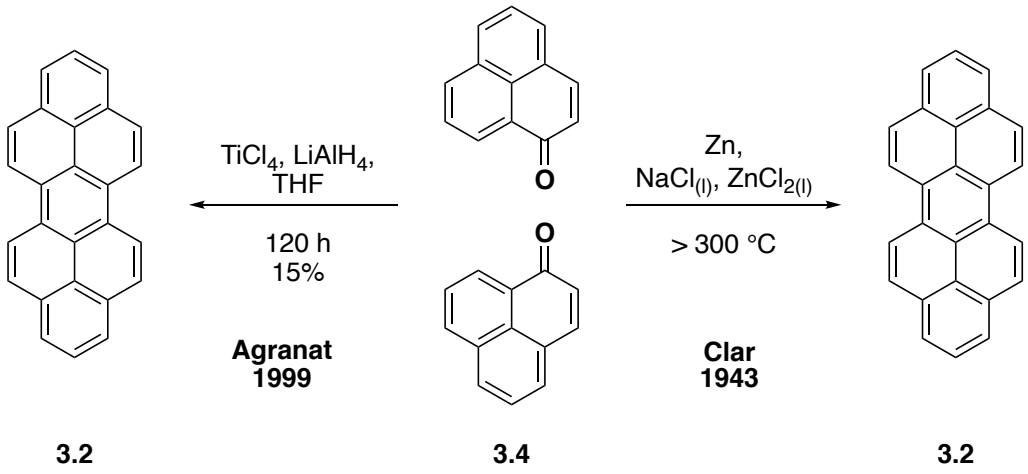
Figure 3.3 Schematic for singlet fission.

One of the potential applications for materials that can exhibit singlet fission behaviour is in organic photovoltaic devices (OPV), *i.e.* solar cells. If a singlet fission organic compound is paired with a low band gap semiconductor, it is conceivable that a system could be created where one high-energy photon is transformed into not one, but two electron-hole pairs. The production of two possible electricity-generating events from one photon would increase the maximum theoretical efficiency limit from 33.3% for single junction solar cells to 50% based on quantitative analysis of the Shockley-Queisser limit.[6]

Although several known systems have the potential to exhibit singlet fission behaviour (they fulfil the energy requirement) it is not necessarily observed, and this is indeed the case for peropyrene (**3.2**) in the solid state. This is because, in the crystalline state, excimer formation outcompetes singlet fission.[4] If one could design a peropyrene containing system in which excimer formation is disfavoured without greatly perturbing the singlet and triplet excited states, it might become possible to observe the singlet fission behaviour.

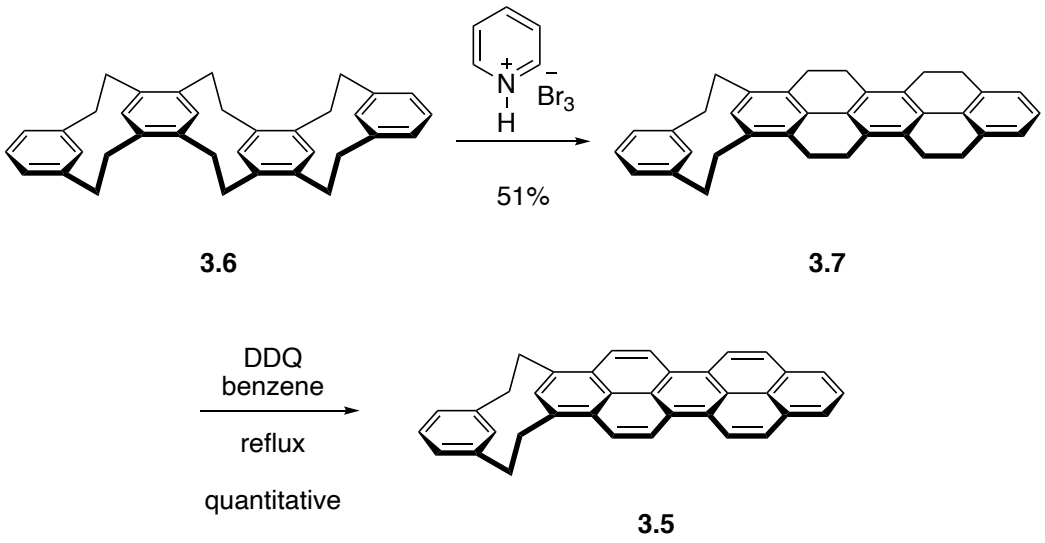
3.1.2: Synthesis of Peropyrene

Clar's original synthesis of peropyrene (**3.2**) involved the reductive coupling of 1*H*-phenalen-1-one (**3.4**) with zinc dust in a molten mixture of NaCl and $ZnCl_2$ at a temperature of >300 °C (**Scheme 3.1**).[2] Although this reaction afforded the desired PAH, the conditions are harsh and lack of regioselectivity could be an issue if the phenalenone bears substituents. Over 50 years later, Agranat *et al.* utilized a McMurry reaction to obtain peropyrene (**3.2**) in 15% yield.[7]



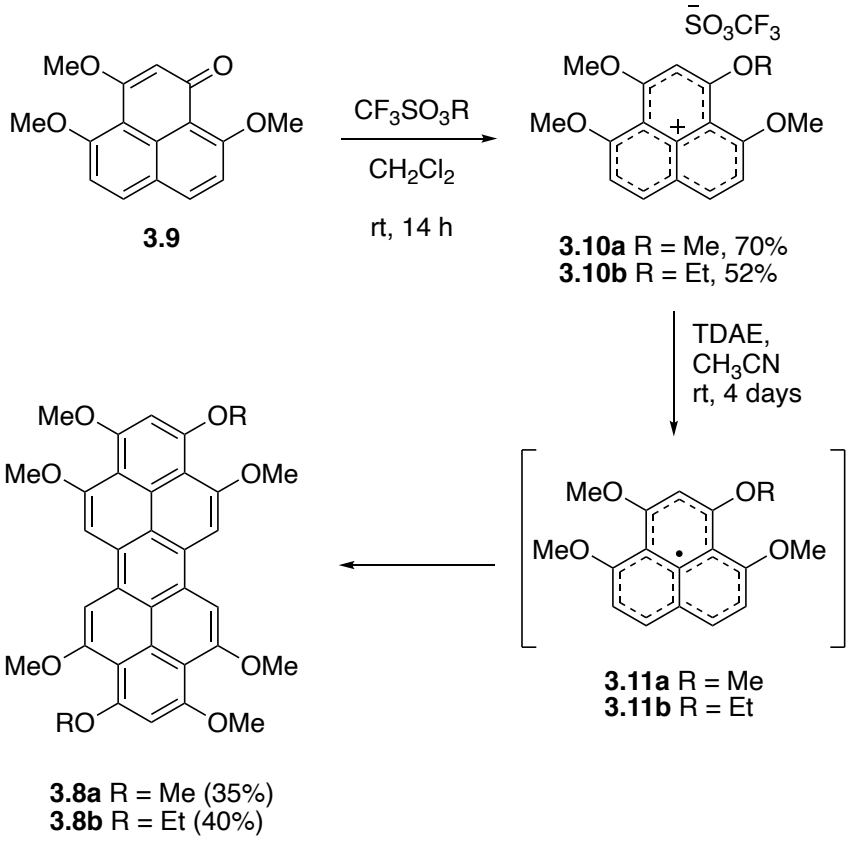
Scheme 3.1 Clar's and Agranat's syntheses of peropyrene (**3.2**).

The peropyrene core has only been assembled a few other ways, one of which was unintentional. In 1975, Misumi *et al*. reported (1,3)peropyrenophane **3.5** as a side product.[8] The layered metacyclophane **3.6** was first converted into octahydroperopyrenophane **3.7** then oxidized in an attempt to synthesize teropyrene (**3.3**), instead (1,3)peropyrenophane **3.5** was obtained (**Scheme 3.2**).



Scheme 3.2 Misumi's serendipitous synthesis of the first peropyrenophane (**3.5**).

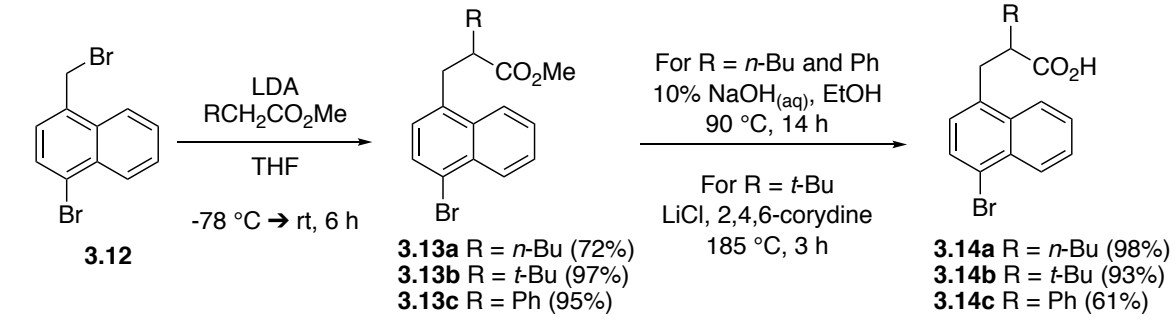
In the last 15 years, a handful of syntheses of substituted peropyrenes have appeared in the literature by Haddon[9], Kubo[10,11], Chalifoux[12-15] and Mateo-Alonso.[16,17] The former two examples rely on the dimerization of phenalenyl radicals, which leads to peropyrenes after several steps. In Haddon's synthesis of highly oxygenated peropyrene derivatives **3.8a** and **3.8b**, the formation of phenalenyl radicals **3.11a** and **3.11b** was observed in solution by both EPR spectroscopy and cyclic voltammetry (**Scheme 3.3**). However, it was found that upon attempted recrystallization, dimerization and aromatization occurred leading to the observed peropyrene derivatives **3.8a** and **3.8b**, as a single regioisomer in the case of **3.8b**.

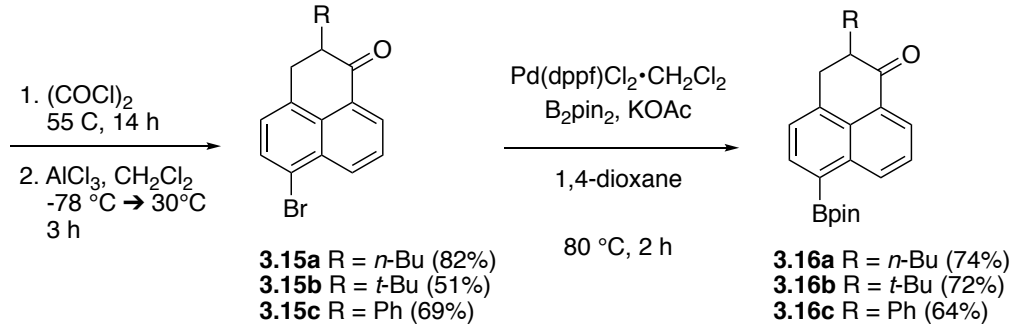


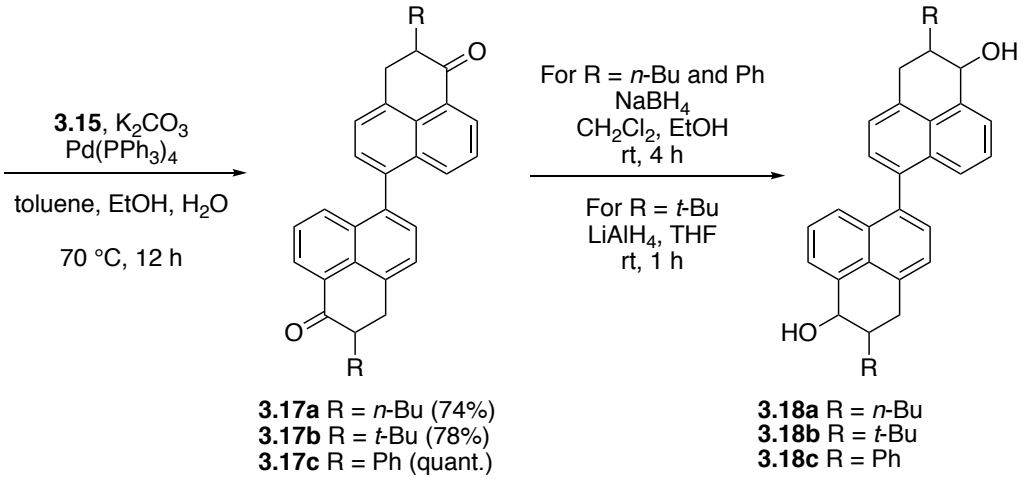
Scheme 3.3 Haddon's phenalenyl radical-based synthesis of peropyrenes **3.8a** and **3.8b**.

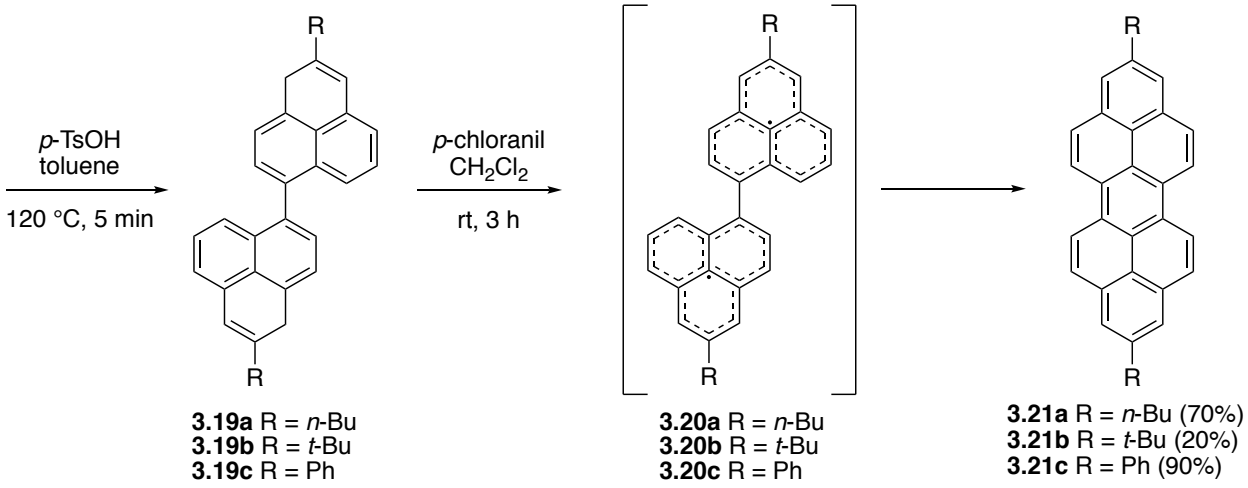
Kubo's synthesis of peropyrene cores also relies on the generation of phenalenyl radicals, but in this case the phenalenyl radical precursors are already connected (**Scheme 3.4**). The enolates of various methyl acetates were alkylated with 1-bromo-4-(bromomethyl)naphthalene (**3.12**) to give naphthyl propanoates **3.13a-c** in good yields (72-97%), where R = *n*-Bu (**3.13a**), *t*-Bu (**3.13b**) and Ph (**3.13c**). Two of the esters (**3.13a** and **3.13c**) were hydrolyzed under basic conditions to give the corresponding acids **3.14a** and **3.14c** in 98% and 61% yields, respectively. The steric hindrance present in the *tert*-butyl system **3.13b** required optimized conditions of LiCl in molten 2,4,6-corydine heated to 185 °C, but ultimately acid **3.14b** was obtained in 93%. This set of conditions, giving **3.14b**, are not conventional, however, the authors provide no further commentary on this choice. All three acids (**3.14a**-**c**) were treated with neat oxalyl chloride at 55 °C to give

the corresponding acid chlorides in preparation for an intramolecular Friedel-Crafts acylation. The acid chlorides were immediately dissolved in CH_2Cl_2 and cooled to –78 °C. The addition of $AlCl_3$ brought about cyclization onto the neighbouring *peri* position to give 2*H*-phenalenones **3.15a**-**c** in moderate to good yields (51-82%). At this point in the synthesis of two 2*H*-phenalenone units needed to be coupled. This was accomplished by converting the bromine atom in **3.15a**-**c** to a Bpin group by Miyaura borylation to give borylated 2*H*-phenalenone **3.16a**-**c** in good yields (64-74%). With the two coupling partners in hand, the bromides **3.15a**-**c** and boronates **3.16a**-**c**, they were subjected to Suzuki-Miyaura cross-coupling to give **3.17a**-**c** as mixtures of diastereomers. No effort was made to separate the stereoisomers because the asymmetric centres were slated for destruction later in the synthetic sequence. At this point of the synthesis it should be noted that the entire carbon scaffold was in place for the final peropyrene products. The ketones in **3.17a** and **3.17c** were reduced to hydroxyl groups and with $NaBH_4$, while those in **3.17b** required the use of $LiAlH_4$ in order to be reduced. All three systems **3.17a**-**c** were rapidly dehydrated by treatment with *p*-toluenesulfonic acid monohydrate in refluxing toluene to give biphenalene derivatives **3.18a**-**c**, which were used in crude form for the final step of the synthesis. Bisphenalenes **3.18a**-**c** were treated with 2 equivalents of *p*-chloranil which promoted oxidative formation of phenalenyl radicals **3.19a**-**c**, which underwent a series of steps to generate peropyrene derivatives **3.20a**-**c**. Details of this transformation are discussed later in this Chapter.


Br
Br
3.12
LDA
RCH2CO2Me
THF
-78 °C ➔ rt, 6 h
R
CO2Me
Br
3.13a R = n-Bu (72%)
3.13b R = t-Bu (97%)
3.13c R = Ph (95%)
For R = n-Bu and Ph
10% NaOH(aq), EtOH
90 °C, 14 h
For R = t-Bu
LiCl, 2,4,6-corydine
185 °C, 3 h
R
CO2H
Br
3.14a R = n-Bu (98%)
3.14b R = t-Bu (93%)
3.14c R = Ph (61%)


1. (COCl)2
55 C, 14 h
2. AlCl3, CH2Cl2
-78 °C ➔ 30°C
3 h
R
O
Br
3.15a R = n-Bu (82%)
3.15b R = t-Bu (51%)
3.15c R = Ph (69%)
Pd(dppf)Cl2•CH2Cl2
B2pin2, KOAc
1,4-dioxane
80 °C, 2 h
R
O
Bpin
3.16a R = n-Bu (74%)
3.16b R = t-Bu (72%)
3.16c R = Ph (64%)

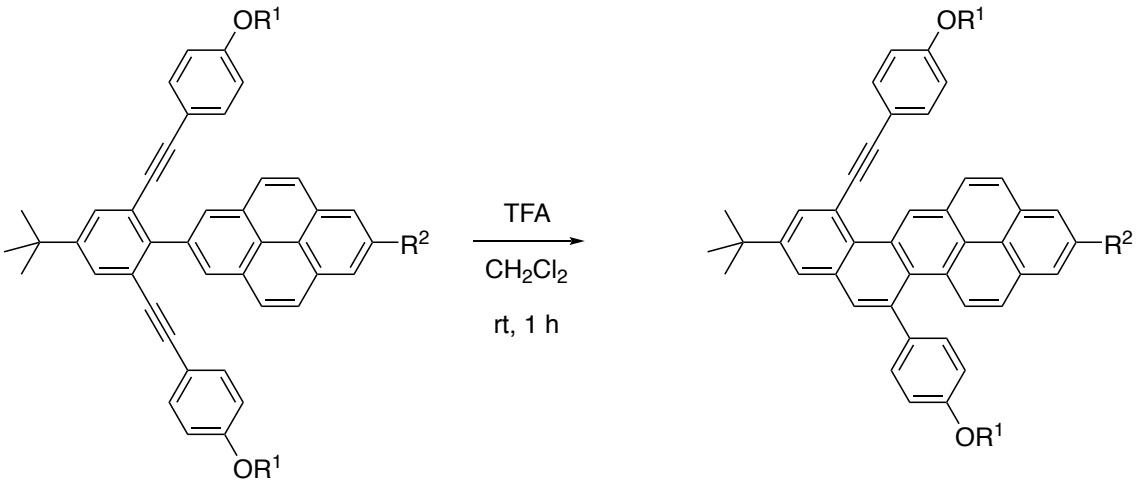

3.15, K2CO3
Pd(PPh3)4
toluene, EtOH, H2O
70 °C, 12 h
R
O
O
R
3.17a R = n-Bu (74%)
3.17b R = t-Bu (78%)
3.17c R = Ph (quant.)
For R = n-Bu and Ph
NaBH4
CH2Cl2, EtOH
rt, 4 h
For R = t-Bu
LiAlH4, THF
rt, 1 h
R
OH
HO
R
3.18a R = n-Bu
3.18b R = t-Bu
3.18c R = Ph


p-TsOH
toluene
120 °C, 5 min
R
R
3.19a R = n-Bu
3.19b R = t-Bu
3.19c R = Ph
p-chloranil
CH2Cl2
rt, 3 h
R
R
3.20a R = n-Bu
3.20b R = t-Bu
3.20c R = Ph
R
R
3.21a R = n-Bu (70%)
3.21b R = t-Bu (20%)
3.21c R = Ph (90%)

Scheme 3.4 Kubo's synthesis of (2,7)peropyrene derivatives **3.21a**-**c**.

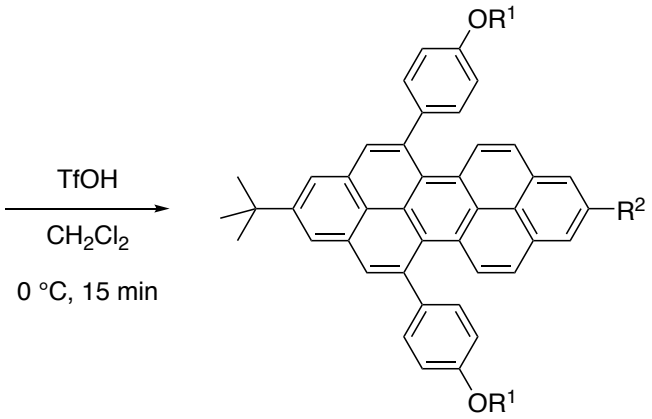
Chalifoux *et al.* took advantage of an acid-promoted alkyne-based benzannulation reaction to access a number of bay-region substituted peropyrenes (**Scheme 3.5**).[12] Their approach involved an initial monocyclization of pyrenes **3.22a**-**c** with TFA to give compounds **3.23a**-**c**, which then underwent a second cyclization on the other side upon treatment with TfOH. The resulting peropyrenes **3.24a**-**c** were obtained in 57-72% yields.

Scheme 3.5. Chalifoux's cyclization approach to peropyrene synthesis.



3.22a $R^1 = CH_3$, R^2 = *t*-butyl
3.22b $R^1 = C_6H_{13}$, R^2 = *t*-butyl
3.22c $R^1 = C_{10}H_{21}$, R^2 = H

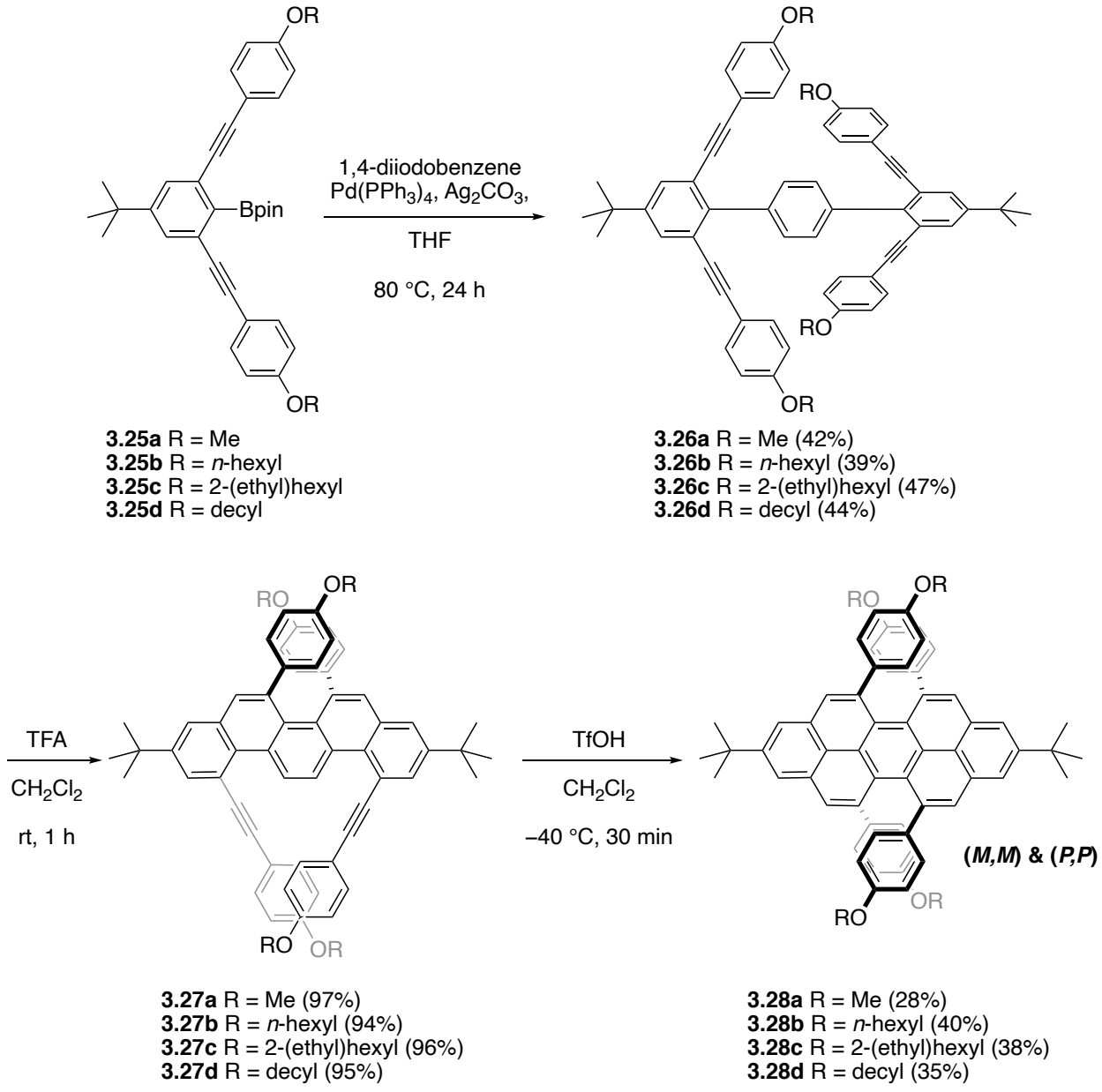
3.23a $R^1 = CH_3$, R^2 = *t*-butyl (98%)
3.23b $R^1 = C_6H_{13}$, R^2 = *t*-butyl
3.23c $R^1 = C_{10}H_{21}$, R^2 = H (99%)



3.24a $R^1 = CH_3$, R^2 = *t*-butyl (57%)
3.24b $R^1 = C_6H_{13}$, R^2 = *t*-butyl (72%)
3.24c $R^1 = C_{10}H_{21}$, R^2 = H (65%)

The crystal structure of peropyrene of **3.24b** revealed a twist of the peropyrene core of 18° to accommodate the steric repulsion between the aryl group and the bay region hydrogens. A consequence of this twist is that compound **3.24b** is axially chiral. The absorption and emission spectra for peropyrene **3.24a** (measured in toluene) show the characteristic vibronic structure of peropyrene, with the emission spectrum being a near-mirror image of the absorption spectrum.

With a proof of concept in hand, Chalifoux *et al*. extended their approach to incorporate two substituents into each bay region of peropyrene.[13] The same alkyne-based benzannulation methodology was utilized, except now a four-fold cyclization around a more highly decorated terphenyl core **3.26a**-**d** was achieved (Scheme 3.6). To synthesize the terphenyl derivative **3.26a**-**d**, 1,4-diiodobenzene was reacted with boronate ester **3.25a**-**b** under Suzuki-Miyaura conditions. After the initial treatment with trifluoroacetic acid, two of the four possible cyclizations occurred. Interestingly, although potentially three doubly cyclized products are possible, only the picene derivatives **3.27a**-**d** were obtained, which results from the cyclization on the same side of the system. Treatment of **3.27a**-**d** with TfOH then promoted the final two alkyne cyclizations. This gave exclusively a racemic mixture of (*M,M*) and (*P,P*) peropyrenes **3.28a**-**d** and none of the *meso* (*P,M*)/(*M,P*) diastereomer.

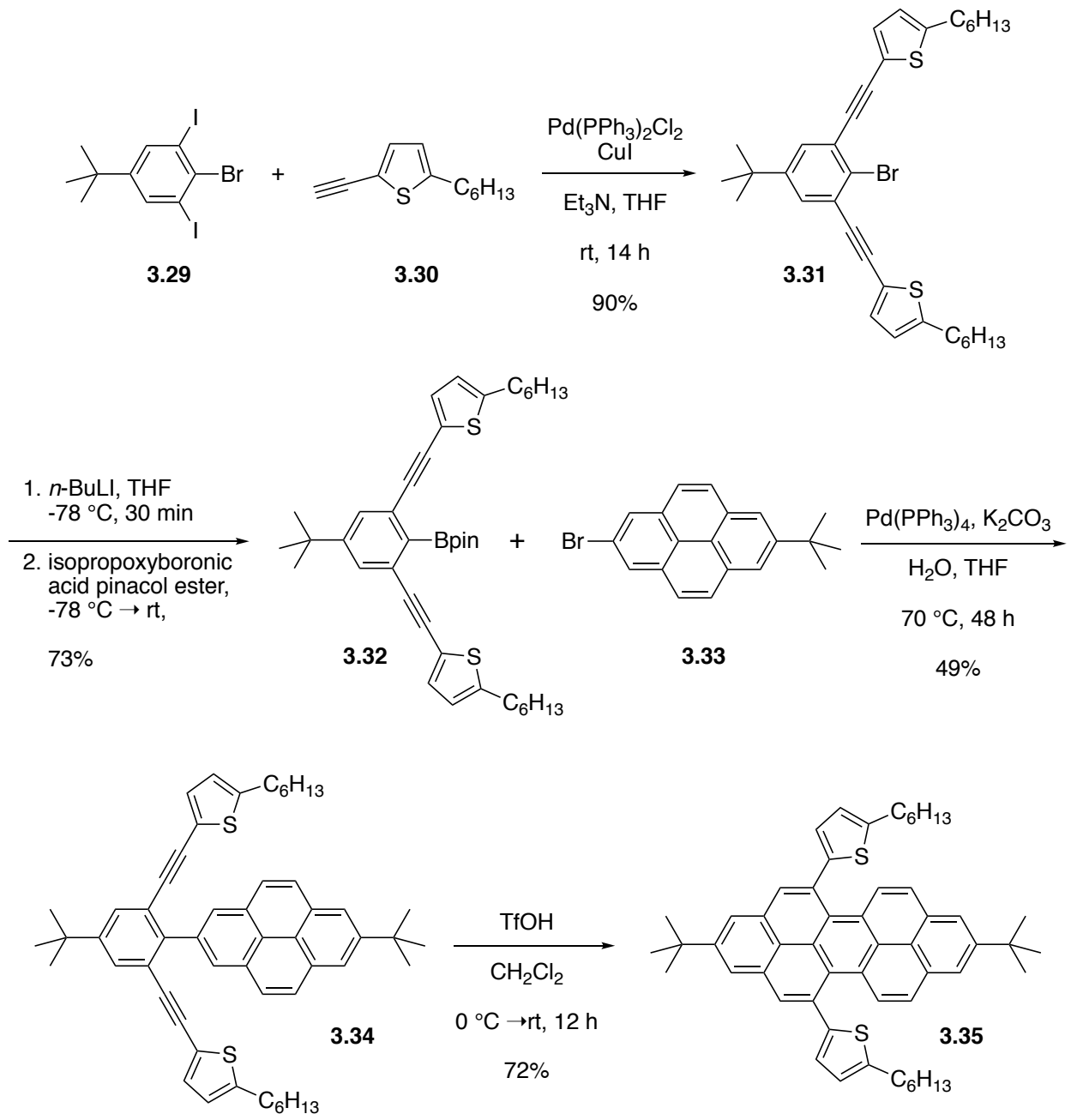


Scheme 3.6 Chalifoux's synthesis of chiral peropyrenes **3.28a**-**d**.

The racemic mixture of peropyrene **2.28b** was successfully separated using HPLC fitted with a chiral stationary phase. With pure enantiomers in hand, the authors investigated the thermal racemization by heating a solution of the second-eluted enantiomer in decalin at 100 °C and monitoring by chiral phase HPLC. Based on this

experiment, the authors determined a value of k_{rac} = 0.0027 min^{-1} (at 100 °C), which means that very little racemization occurs at that temperature.

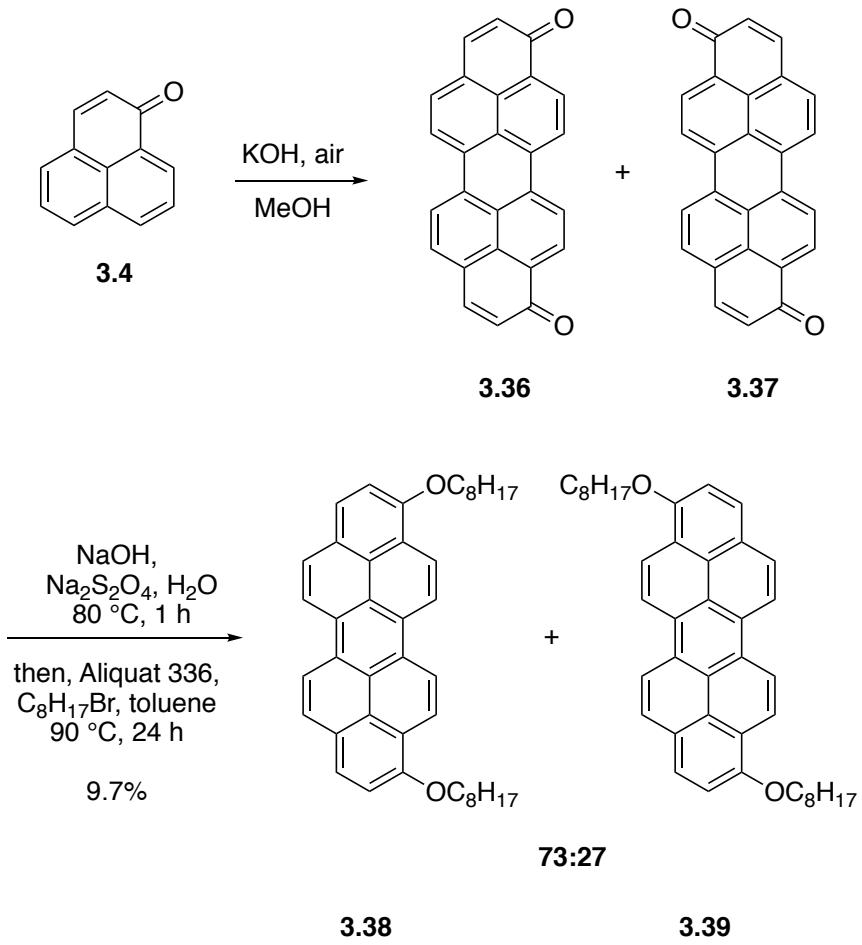
The final contribution to date by Chalifoux *et al*. to the synthesis of peropyrenes involved the same synthetic approach, namely the alkyne-based benzannulation, in the generation of thiophene-functionalized peropyrenes **3.35** (**Scheme 3.7**).[15] Two-fold Sonogashira cross-coupling of diiodoarene **3.39** with alkynylthiophene **3.40** afforded diyne **3.31**, which was subsequently converted into boronate ester **3.32** via lithium-halogen exchange followed by quenching with isopropoxyboronic acid pinacol ester. The boronate ester **3.32** was coupled with 2-bromo-7-*tert*-butylpyrene (**3.33**) under Suzuki-Miyaura cross-coupling conditions to biaryl **3.34** in 49% yield. In their previous examples of alkyne-based benzannulations, the authors performed the first cyclizations with a milder Brønsted acid (TFA) and then used a stronger one (TfOH) to complete the reaction as this was found to give cleaner reactions and higher overall yields. In this work, they found that if a solution of TfOH in CH_2Cl_2 was added slowly via a syringe pump to uncyclized **3.34** the reaction proceeded both cleanly and in good yields (72%, 85% per cyclization) to give peropyrene **3.35**. An X-ray crystal structure determination of thiophene-functionalized peropyrene **3.35** showed that the thiophene groups impart a higher degree of twisting to the peropyrene core then the previously reported phenyl-substituted peropyrene **3.24a** (24° *vs.* 18°).



Scheme 3.7 Chalifoux's synthesis of thiophene-functionalized peropyrene **3.35**.

A more recent synthesis of peropyrene systems was reported by Mateo-Alonso *et al.*, who took inspiration from Clar's initial synthesis of peropyrene (**Scheme 3.8**).[16] Treatment of commercially available perinaphthenone **3.4** with KOH in MeOH produced a mixture of 1,10-(**3.36**) and 1,8-peropyrenoquinones (**3.37**), which could be performed

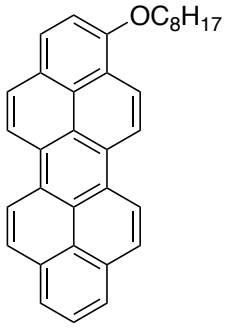
on a multi-gram scale. This mixture was then subjected to reductive alkylation with sodium dithionite and NaOH followed by 1-bromooctane with the aid of a phase-transfer catalyst, Aliquat 336. Successful purification of the two isomeric alkylated products afforded a mixture of 1,10-dioctoxy (**3.38**) and 1,8-dioctoxyperopyrenes (**3.39**) in a 73:27 ratio and 9.7% overall yield. They were surprised at the presence of two isomeric products because there was no mention of different isomers obtained of the peropyrenoquinone **3.4** from Clar's initial report. All efforts to separate the two isomers proved fruitless, although an attempted crystallization did afford one crystal of **3.38**, which was suitable for an X-ray crystal structure determination.



Scheme 3.8 Mateo-Alonso's synthesis of *O*-alkylated peropyrenes **3.38** and **3.39**.

A main motivation for the synthesis of these *O*-alkylated peropreyne derivatives was for use in the fabrication of organic electronic devices, which require a solution processable organic semiconductor. It was found that solutions of peropyrenes **3.38** and **3.39** in either 1-butanol or 1-octanol in the range of 0.6-5% (w/w) spontaneously formed upon cooling and the gels were stable for months.

Mateo-Alonso also reported another *O*-alkylated peropyrene system **3.40** (**Figure 3.4**) which they discovered as an unexpected minor product from the synthesis of peropyrenes **3.39** and **3.40**.[17] This bright orange compound was isolated in 2% yield from the crude reaction mixture and was demonstrated to function as a solution-processable p-type organic semiconductor.

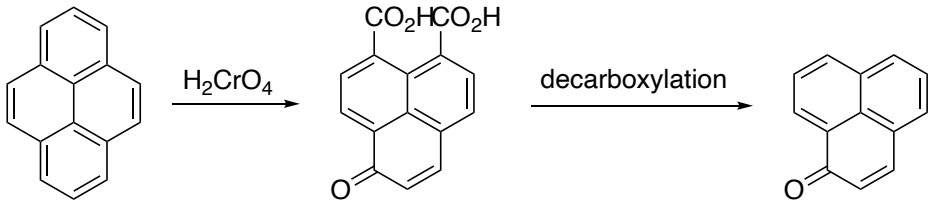


3.40

Figure 3.4 Minor *O*-alkylated peropyrene product.

3.1.3: Phenalene Systems and Their Reactivity

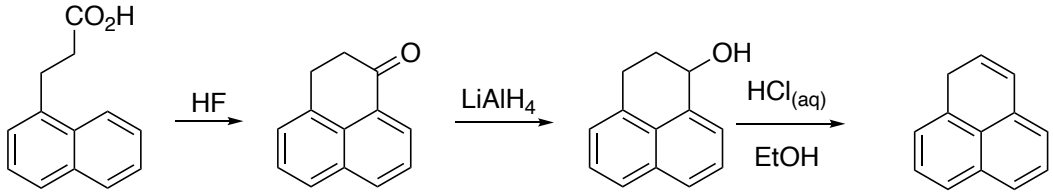
Phenalene (1*H*-phenalene) **3.41** is a C_{15} benzenoid hydrocarbon, which by virtue of its odd number of carbon atoms has one sp^3 hybridized carbon atom in its skeleton. The story of the phenalene system dates back to the 1880s with the isolation of the first phenalene derivative, phenalenone-6,7-dicarboxylic acid (**3.42**), from the oxidation of pyrene (**3.1**) with chromic acid (**Scheme 3.9**).[18] This compound was later decarboxylated to give phenalenone (**3.43)**.



3.1 **3.42** **3.43**

Scheme 3.9 First syntheses of phenalene derivatives.

It was not until 60 years later that a synthesis of the parent phenalene (**3.41**) was reported. All of the synthetic pathways eventually converged on acid **3.44** and the route from this compound to phenalene (**3.41**) has remained essentially unchanged, even if the reagents employed have been updated (**Scheme 3.10**). Originally, acid **3.44** was cyclized by an intramolecular Friedel-Crafts acylation to give 2,3-dihydrophenalen-1-one (**3.45**) by treatment with HF and the resulting ketone **3.45** was then reduced to alcohol **3.46** using $LiAlH_4$. Finally, phenalene (**3.41**) was obtained by dehydration in HCl-EtOH.[19]



3.44 **3.45** **3.46** **3.41**

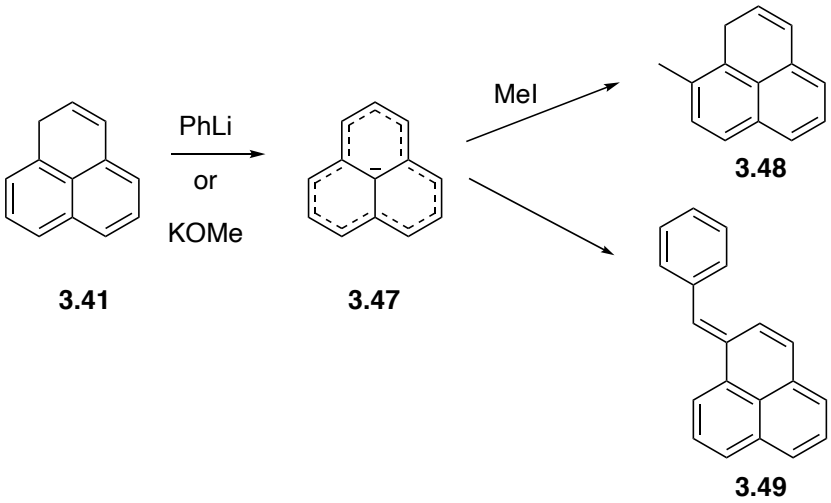
Scheme 3.10 Synthesis of parent phenalene (**3.41**).

3.1.4: Properties of phenalene

Phenalene (**3.41**), when treated with appropriate reagents, can give rise to an anion **3.47**, a cation **3.48**, and a radical **3.49**, which result from the loss of a proton,

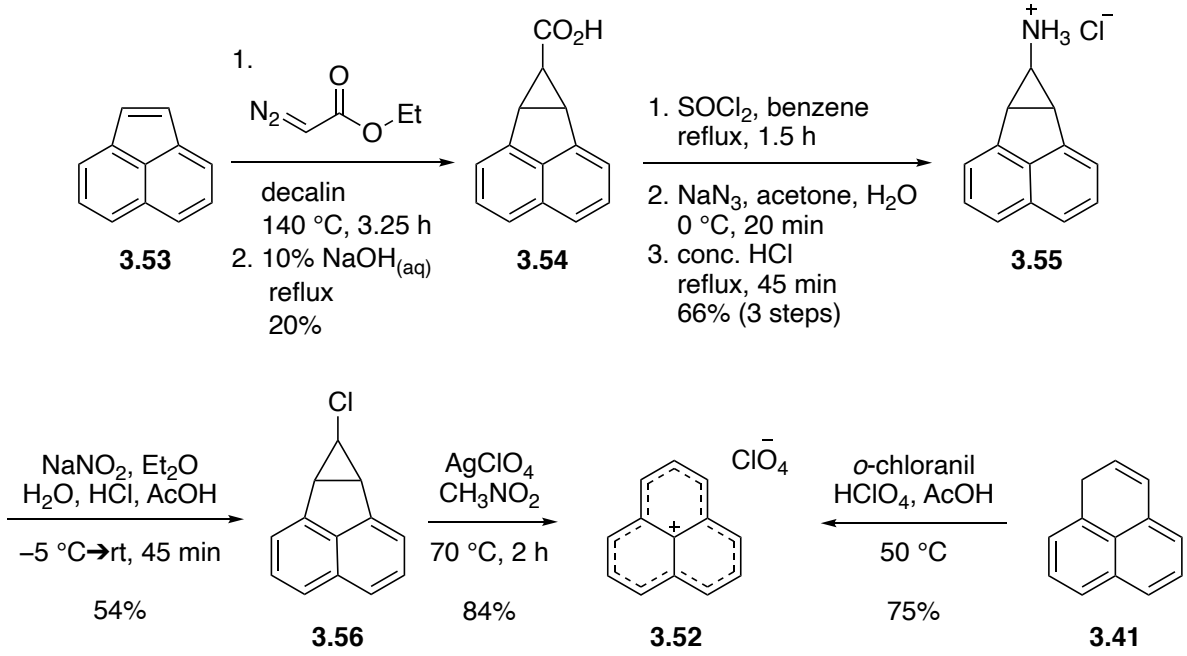
hydride ion and a hydrogen atom, respectively. The resonance stabilization gained from the loss of H, in some form, results in the formation of a relatively stable reactive intermediate, which is more symmetrical (D_{3h}) than the parent phenalene (**3.41**) (C_s).

The phenalenyl anion **3.47** was first prepared by treating phenalene (**3.41**) with either PhLi[19] or KOMe,[20,21] which gave red-coloured solutions (**Scheme 3.11**). The anion could then be trapped by reacting it with either methyl iodide to give 9-methylphenalene (**3.48**) or benzaldehyde to give (after dehydration) the styrene-like molecule **3.49**.[156] Studies performed by Boekelheide showed that when a yellow-orange solution of phenalene (**3.41**) was treated with the triphenylmethyl anion the solution turned to fluorescent olive green from the which triphenylmethane was isolated. This provided evidence that phenalene is more acidic then triphenylmethane pK_a = 30.6 (DMSO). A competition experiment between phenalene (**3.41**) and cyclopentadiene with the triphenylmethyl anion showed no evidence of the phenalene (**3.41**) system acting as a proton donor indicating that it is less acidic then cyclopentadiene pK_a = 18 (DMSO). Later work experimentally determined the pK_a of phenalene to be 18.2 (DMSO).[22]



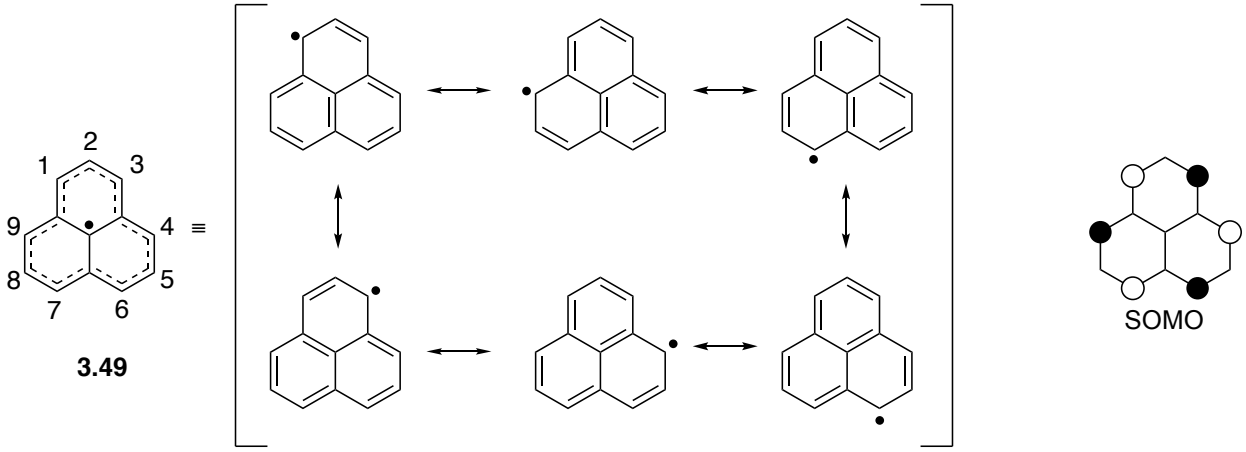
Scheme 3.11 Generation of the phenalenyl anion (**3.47**) and its reactions with methyl iodide and benzaldehyde.

The phenalenyl cation **3.48** was originally produced as its perchlorate salt through a series of reactions (**Scheme 3.12**) by Pettit.[23] Acenaphthylene (**3.53**) was treated with ethyl diazoacetate to form an ester which was hydrolyzed to the corresponding acid **3.54**. The acid was then converted into the corresponding acid chloride with thionyl chloride and this was treated with sodium azide to induce a Curtius rearrangement to give the amine, which was isolated as the hydrochloride salt **3.55** after treatment with HCl. The salt was then dissolved in concentrated HCl, glacial acetic acid and Et_2O to which an aqueous solution of $NaNO_2$ was added dropwise. This afforded chloride **3.56**. To synthesize the perchlorate salt, the chloride **3.56** was dissolved in nitromethane and silver perchlorate was added. After two hours, phenalenium perchlorate (**3.52**) was obtained on a gram scale in 84% yield. Reid also developed a route to phenalenium perchlorate (**3.52**) directly from phenalene (**3.41**) using various quinones, such as *o*-chloranil, in the presence of perchloric acid.[24] Using the direct approach from phenalene, several phenalene cation derivatives have been made bearing alkyl and methoxy groups have been synthesized. The parent phenalene cation perchlorate salt is readily attacked by water, even in moist air, whereas, those cations that bear alkyl or methoxy substituents have shown greater stability.



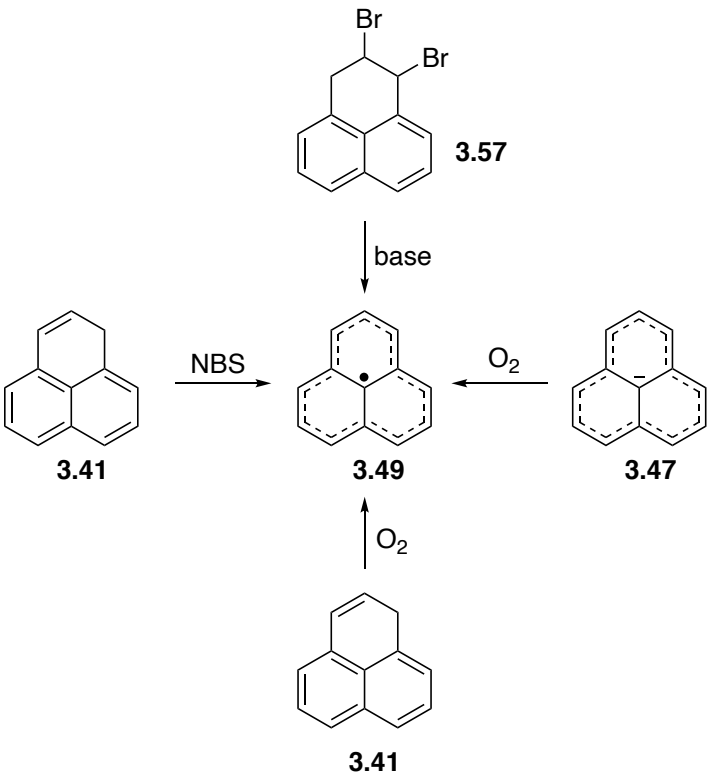
Scheme 3.12 Preparation of phenalenium perchlorate (**3.52**).

The most interesting of the three phenalenyl-type reactive intermediates for the purpose of this thesis is the one that arises from loss of a hydrogen atom (H•), namely the phenalenyl radical **3.49**. This radical is an example of odd-alternant hydrocarbon radical. Odd-alternant hydrocarbons are open-shell systems, which feature a non-bonding singly-occupied molecular orbital (SOMO). The phenalenyl radical **3.49** is thermodynamically stabilized because the unpaired electron density is highly delocalized. In the SOMO, spin density resides on the 1, 3, 4, 6, 7 and, 9 positions (**Scheme 3.13**).[25]



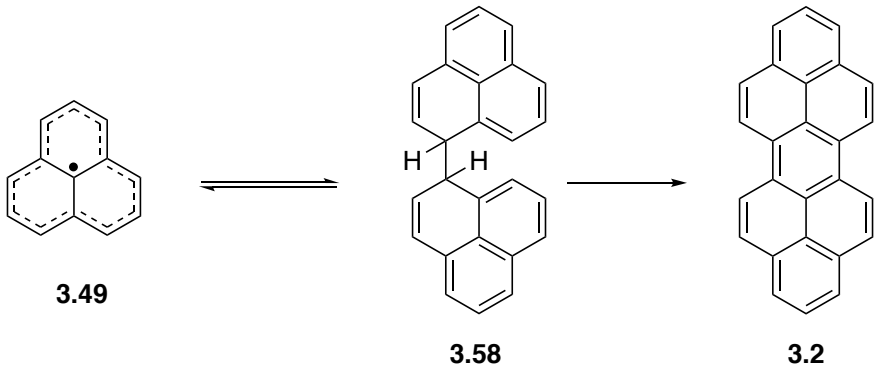
Scheme 3.13 Resonance structures of phenalenyl radical (**3.55**) and its SOMO.

Starting in the 1950s, a number of attempts to isolate the phenalenyl radical **3.49** via various synthetic procedures have been made.[18] Selected examples include the treatment of 1*H*-1,2-dibromodihydrophenalene (**3.57**) with base,[19] treatment of phenalene (**3.41**) with NBS,[19] treatment of the phenalenyl anion **3.47** with molecular oxygen and treatment of phenalene (**3.41**) with molecular oxygen (**Scheme 3.14**). In all cases, the parent radical was never isolated, but evidence of its formation was observed by ESR experiments.



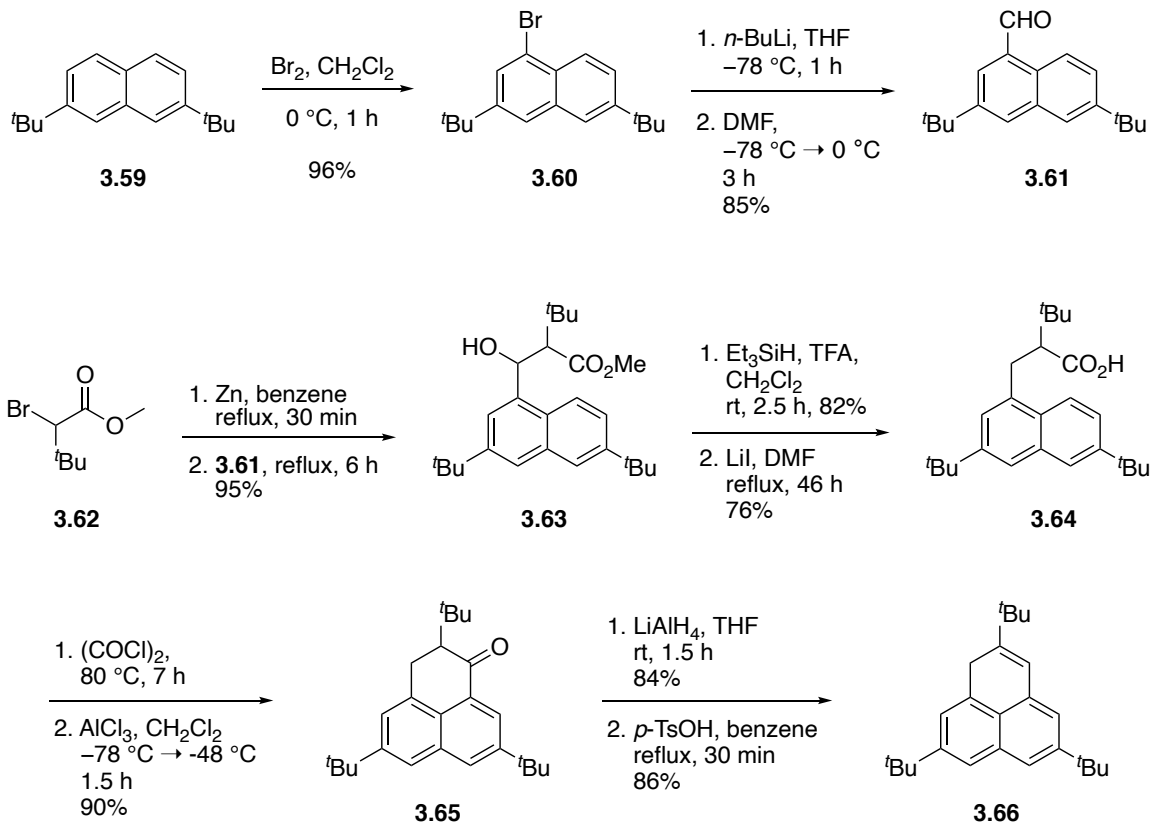
Scheme 3.14 Formation of the phenalenyl radical (**3.55**).

One possible issue with isolation of the radical in pure form is its propensity to undergo further reactions in the presence of oxidizing agents. For example, radical coupling leads to formation of the "σ-dimer" **3.58**. This species has been shown to dehydrogenate, which can be further oxidized to give peropyrene (**3.2**). Indeed, this compound was observed as a side product in the formation of the phenalenyl radical **3.49** (**Scheme 3.15**).[18]



Scheme 3.15 Dimeriation of phenalenyl radical (**3.55**) and its pathway to peropyrene (**3.2**).

In 1999, another dimerization mode of phenalenyl radical derivatives, the "π-dimer", was discovered by Nakasuji *et al.*[26] This discovery was enabled by decorating a phenalene system with *tert*-butyl groups at the 2,5,8-positions. The presence of these bulky substituents served to sterically disfavour formation of the usual σ-dimer. The synthesis commenced with a bromination of 2,7-di-*tert*-butylnapthalene (**3.59**), which occurred regioselectively at the 4-position to give **3.60** (**Scheme 3.16**). This compound was then lithiated with *n*-BuLi and the resulting carbanion was quenched with DMF to give the formylated product **3.61**. A Reformatsky reaction between methyl 2-bromo-3,3'-dimethylbutanoate (**3.62**) and aldehyde **3.61** afforded ester **3.64** as a mixture of diastereomers, which was subsequently reduced and then dealkylated to afford acid **3.64**. The acid was then converted into the corresponding acid chloride with oxalyl chloride then immediately subjected to Friedel-Crafts acylation conditions to afford 2,3-dihydro-2,5,8-tri-*tert*-butylphenalenone (**3.65**). Finally, reduction with $LiAlH_4$ and elimination of water with *p*-TsOH in refluxing benzene gave the trisubstituted phenalene system **3.66**.

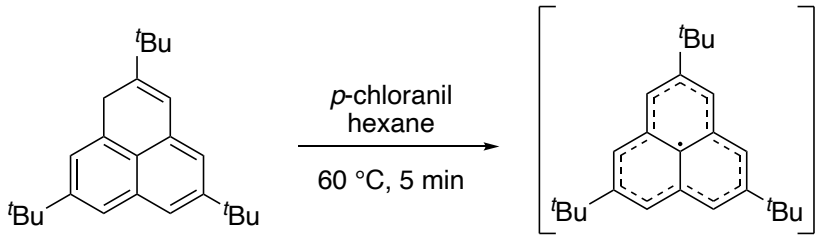


Scheme 3.16 Synthesis of 2,5,8-tri-*tert*-butylphenalene (**3.66**).

Substituted phenalene **3.66** was then oxidized to its corresponding phenalenyl radical **3.67** by treatment with *p*-chloranil in degassed toluene, which resulted in the formation of a blue solution. When the radical was generated in degassed hexane instead of toluene, the product crystallized into needles that were deep blue in colour. These crystals were found to be stable in the absence of air and it took more than a week for them to completely decompose upon exposure to air. The X-ray crystal structure was determined and thus provided the first experimental structural information of an odd-alternant hydrocarbon radical. The phenalenyl ring possesses D_{3h} symmetry. Its C–C bond lengths (1.374-1.421 Å) are comparable to those of naphthalene. The molecule forms a dimeric pair between two phenalenyl molecules in a staggered orientation which can be rationalized two ways. Firstly, this orientation places the *t*-butyl groups the greatest distance apart from each and secondly, effective orbital overlap would be expected in this

orientation between carbon atoms with the largest coefficients in the SOMO. This dimeric structure displays close distances between the pairs between 3.201(8) and 3.323(6) Å. These distances are shorter than what one would expect for two carbon atoms (van der Waals radius = 1.7 Å per carbon), which provides evidence for a bonding interaction. A large absorption band at λ_{max} = 510-700 nm in the solid state is attributed to the intermolecular interaction in the dimer and is not observed in solution.

Further work published a few years later by Kochi *et al.* in 2005 dug deeper into the properties of the π-dimer arising from the oxidative phenalenyl radical generation of the sterically hindered system **3.66**.[27] The authors first unambiguously identified the formation of dimers by monitoring the temperature-dependent disappearance of a phenalenyl radical by diagnostic ESR spectroscopy. The ESR spectrum of the 2,5,8-tri-*t*-butylphenalenyl radical (**3.67**) at 243 K is well-resolved, but almost disappears at 203 K, which provided evidence that dimerization is occurring, although the ESR experiment could not determine which dimer was forming. In order the elucidate the type of dimer formed from radical **3.68**, UV-Vis spectroscopy was used. A solution of radical **3.67** at room temperature displays an absorption band at λ_{max} = 540 nm ($\varepsilon = 10^2$ M^{-1} cm^{-1}) accompanied by a very weak and broad absorption at ~ 600 nm. When the solution is cooled, the band at ~ 600 nm grows in intensity. Along with the ESR and X-ray structural data, this allowed the authors to unambiguously assign that band to the π-dimer. The bond enthalpy of π-dimer **3.67** was found to be 9.5 kcal/mol (CH_2Cl_2) by monitoring changes in the ESR spectrum as a function of temperature, which is in good agreement with the calculated gas-phase dissociation value of 11 kcal/mol.

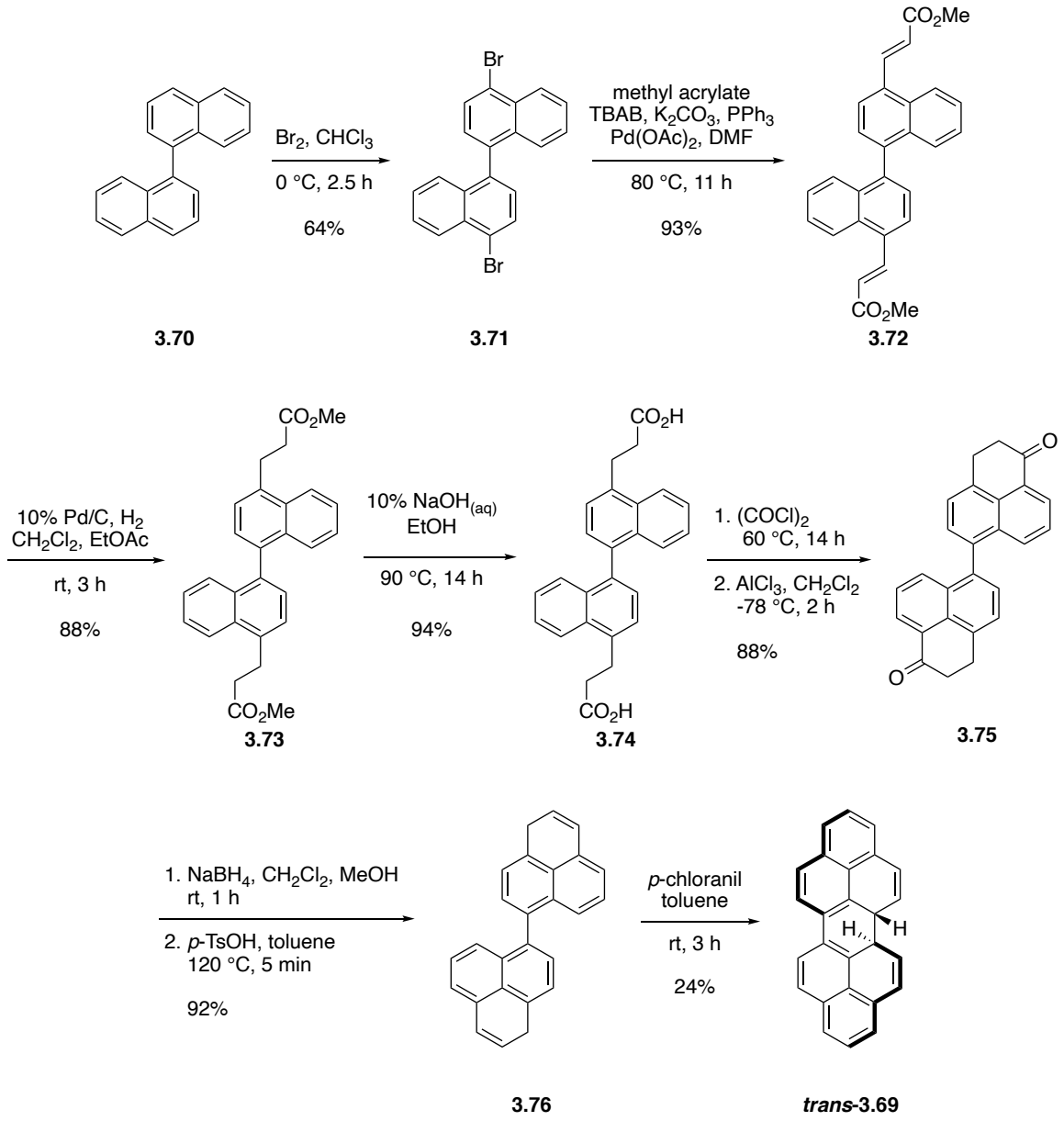


3.66 **3.67**

Scheme 3.17 Generation of tri-*tert*-butylphenalenyl radical **3.67**.

3.2: Dihydroperopyrene and 2,9S-Disubstituted Peropyrenes

In 2016, Kubo *et al*. published work on the fate of the phenalenyl radical (**3.49**) and proposed a mechanism for its conversion to peropyrene (**3.2**).[10] In this work, they were able to detect the presence of biphenalenylidene (**3.68**), which had previously been proposed as an intermediate, but no experimental evidence has been found. In order to probe the existence and nature of **3.69**, the authors first synthesized *trans*-5a,5b-dihydroperopyrene (***trans*-3.69**) (**Scheme 3.18**). 1,1'-Binaphthalene (**3.70**) was doubly brominated with Br_2 to give dibromobinaphthalene **3.71**, which was subjected to a two-fold Heck reaction with methyl acrylate to give unsaturated diester **3.72**. At this point the entire C-skeleton had been introduced and the remainder of the synthesis involved stitching it together. Firstly, the alkenes were hydrogenated to give diester **3.73**, which was then hydrolyzed to afford diacid **3.74**. The diacid **3.74** was then converted into its corresponding bis(acid chloride) and then cyclized under Friedel-Crafts acylation conditions with $AlCl_3$ to furnish biphenalenone **3.75**. Reduction with $NaBH_4$ and elimination of water with catalytic *p*-TsOH in hot toluene gave biphenalene **3.76**. Treatment of biphanelene **3.76** with an equimolar amount of *p*-chloranil resulted in the formation and isolation of ***trans*-3.60** in 24% yield.



Scheme 3.18 Synthesis of ***trans*-3.69**.

This dihydroperopyrene ***trans*-3.69** system can be viewed as a decorated 1,3-cyclohexadiene, which can undergo an electrocyclic ring opening reaction. Based on the Woodward-Hoffman rules, photoirradiation of ***trans*-3.69** should convert it into *Z*-bisphenalenylidene (***Z*-3.68**). A degassed solution of ***trans*-3.69** in CD_2Cl_2 was irradiated with 365 nm light which resulted in drastic changes to the ^1H NMR spectrum and the formation of a single product (NMR measured at 183 K) (**Figure 3.5**). The first spectrum

(**Figure 3.5a**) is that of *trans*-dihydroperopyrene (**trans-3.69**), which clearly shows a single signal for the protons attached to the sp^3 C atoms. The second and third spectra (**Figure 3.5b-c**) show only one product, which was unambiguously characterized by 2D-NMR spectroscopy to actually be *E*-biphenalenylidene (***E*-3.68**). The authors assume that the initial product formed is *Z*-biphenalenylidene (***Z*-3.68**) but that it quickly isomerizes to the more favourable ***E*-3.68**. Upon heating, signal broadening was observed in the spectra of ***E*-3.69** with no complete disappearance of any signal at 253 K. Agranant *et al.* predicted in an earlier study that a biphenalenylidene mixture would exhibit large biradical character which would lead to signal broadening.

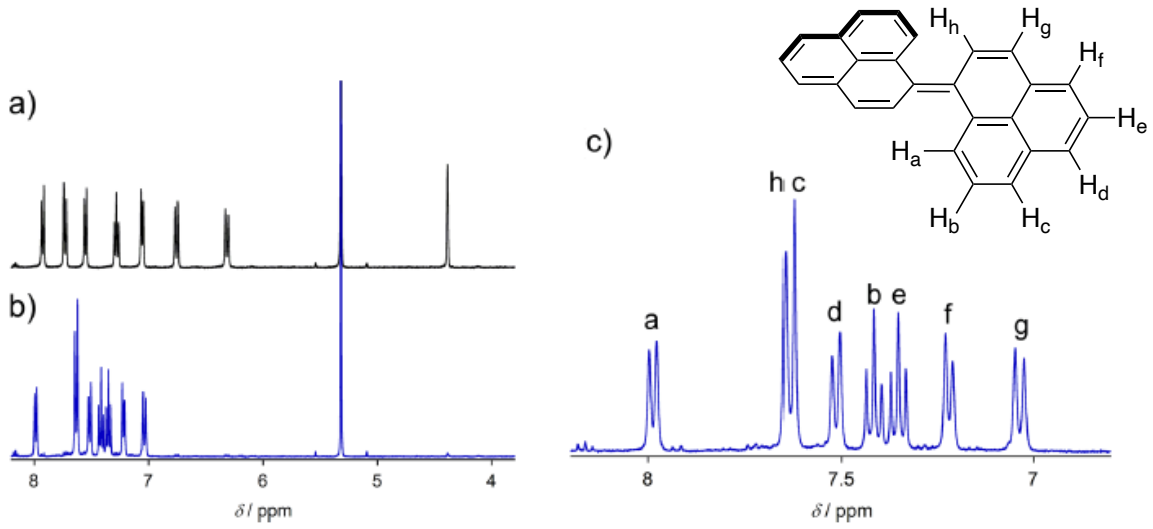


Figure 3.5 ^{1}H NMR spectra measured in CD_2Cl_2 at 183 K (a) ***trans*-3.69** (b) ***E*-3.68** (c) aromatic region of ***E*-3.68.**

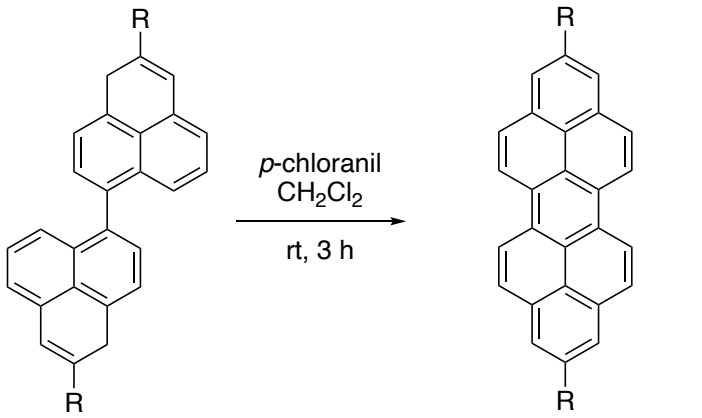
Z-Biphenalenylidene (***Z*-3.68**) was directly observed by suppressing the molecular rotation leading to isomerization. In order to accomplish this the electronic absorption spectrum was measured in glassy 2-methyltetrahydrofuran at 98 K by irradiating ***trans*-3.69** with 355 nm UV light. The result was the appearance of a broad absorption band at 700 nm that was ultimately assignable to ***Z*-3.68**. As the matrix was warmed, the viscosity decreased and isomerization to ***E*-3.68** occurred. This process was monitored by UV-Vis

absorption spectroscopy, which allowed the authors to follow the decay rate as a function of temperature and determine a thermal isomerization barrier of 4.3 ± 0.3 kcal/mol.

The electrocyclic ring closure back to *trans*-dihydroperopyrene (***trans*-3.69**) was also further investigated. Biphenalenylidene ***Z*-3.68** was obtained by photochemically induced electrocyclic ring opening of ***trans*-3.69**, which is allowed by the Woodward-Hoffman rules. The forbidden thermal ring opening reaction did not proceed at all. Surprisingly, based on electronic absorption spectroscopy, ***Z*-3.68** underwent thermal conrotatory electrocyclic ring closing in violation of the Woodward-Hoffman rules. Furthermore, the ring closure of the isomeric biphenalenylidene ***E*-3.68** under thermal conditions was also found to occur. When monitored by electronic absorption and ^{1}H NMR spectroscopy, ***E*-3.68** has completely transformed back into ***trans*-3.69** after 1 h in darkness. The presumption was that ***E*-3.68** underwent a stepwise mechanism that involves initial isomerization to ***Z*-3.68** then cyclization to ***trans*-3.69**. If this transformation occurred directly, it would require a kinetically unfavourable conrotatory ring-closure so it may be that it actually proceeds through a transition state with high diradical character.

When ***trans*-3.69** was stored in air-saturated solution ($CDCl_3$) the ^{1}H NMR spectrum changed drastically with ~50% ***trans*-3.69** being transformed into peropyrene (**3.2**) over two weeks. The half-life of ***trans*-3.69** in the air-saturated solution was estimated at 11 days based on the analysis of changes in the ^{1}H NMR spectrum.

In another report by Kubo *et al.*, a similar synthetic strategy for the synthesis of 2,9-substituted peropyrenes was utilized.[11] Treatment of biphenylenes **3.77a**-**c** with 2 equivalents of *p*-chloranil directly furnished peropyrene **3.78a**-**c** (**Scheme 3.19**).



3.77a R = *n*-Bu
3.77b R = *t*-Bu
4.77c R = Ph

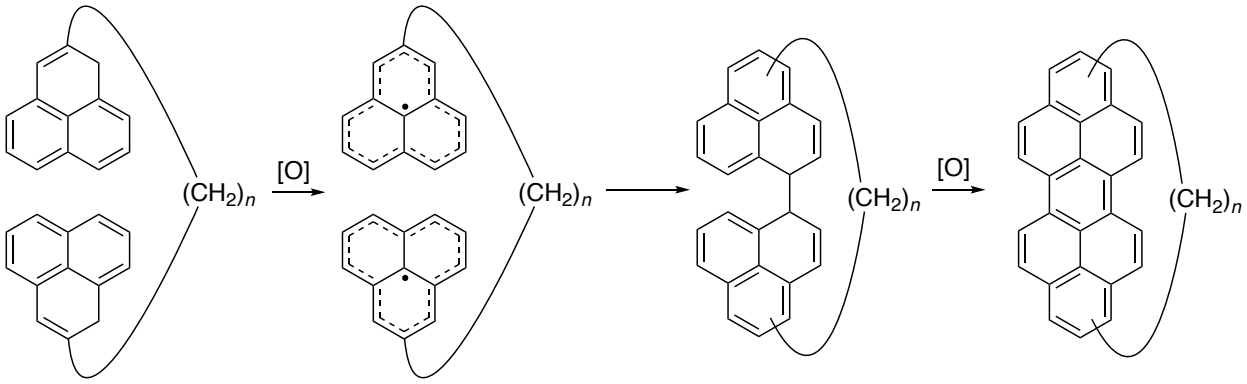
3.78a R = *n*-Bu (70%)
3.78b R = *t*-Bu (20%)
3.78c R = Ph (90%)

Scheme 3.19 Direct synthesis of 2,9-disubtituted peropyrenes **3.78a**-**c**.

These results nicely demonstrated the ease with which phenalenes, especially biphenalenes, can be converted into peropyrenes and provided inspiration for the project that forms the basis of the remainder of this chapter.

3.3: [*n*](*x*,y)Peropyrenophanes

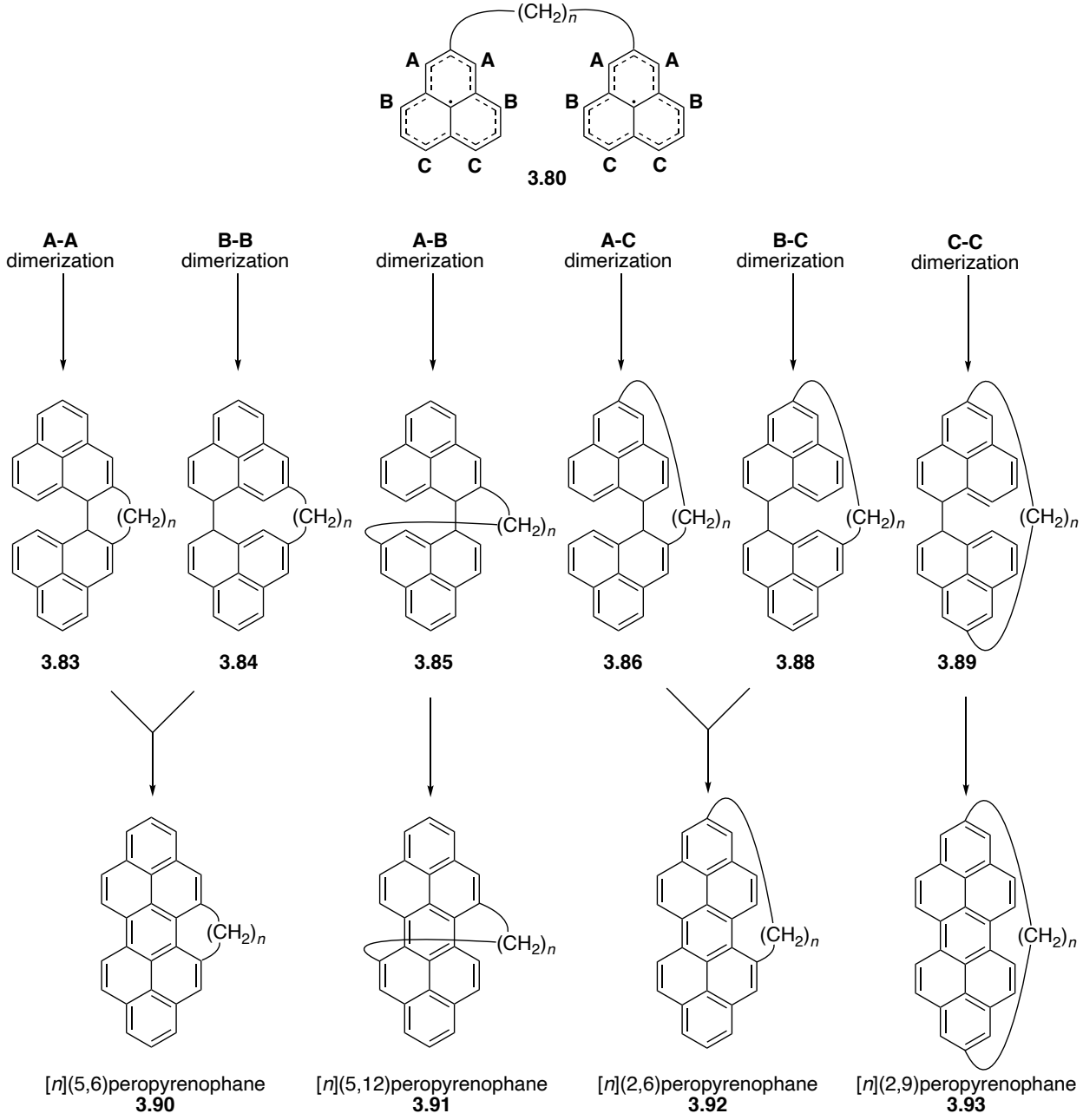
Kubo's successful syntheses of 2,9-disubstituted peropyrenes **3.78a**-**c** provided inspiration for an initiative to exploit their application in the synthesis of peropyrenophanes. If two phenalene units could be tethered together as in **3.79** (**Scheme 3.20**), and then oxidized to a tethered pair of phenalenyl radicals **3.80**, one could envision the tethered radicals finding each other to form a bridged σ-dimer **3.81**. Further oxidation would, as before, then lead to the formation of [*n*](x,y)peropyrenophane **3.82**.



3.79 **3.80** **3.82**

Scheme 3.20 Proposed route to [*n*](x,y)peropyrenophanes **3.82**.

Upon closer inspection, once the diradical system **3.80** is generated there are four possible intramolecularly dimerized products. These arise from the presence of three unique positions of high spin density in the SOMO of each of the phenalenyl radicals, labeled as A, B and C (**Scheme 3.21**), which can combine in six ways **3.83-3.89**. An A-A dimerization gives σ-dimer **3.83** and a B-B dimerization gives σ-dimer **3.84**, both of which ultimately lead to an [*n*](5,6)peropyrenophane (**3.90**). An A-B dimerization gives σ-dimer **3.85** which leads to the formation of an [*n*](5,12)peropyrenophane (**3.91**). An A-C dimerization gives σ-dimer **3.86** and a B-C dimerization gives σ-dimer **3.86**, both of which ultimately lead to an [*n*](2,6)peropyrenophane (**3.92**). The final possible σ-dimer arises from C–C coupling and leads to the formation of an [*n*](2,9)peropyrenophane (**3.93**).



Scheme 3.21 Dimerization modes of diradical **3.80**.

At the outset, the hope was to observe selectively for the C-C dimerization. This was based on the known sensitivity of phenalenyl radicals toward steric effects. Even though a linear alkyl chain does not possess the same steric bulk as a *tert*-butyl group the hope was that it would provide enough steric effect to disfavour dimerization involving

any of the A or B positions of the tethered biradical system. Electronically, no particular dimerization mode would be expected to be favoured over another because all positions (A, B and C) should be relatively equal in the electron spin density in the SOMO.

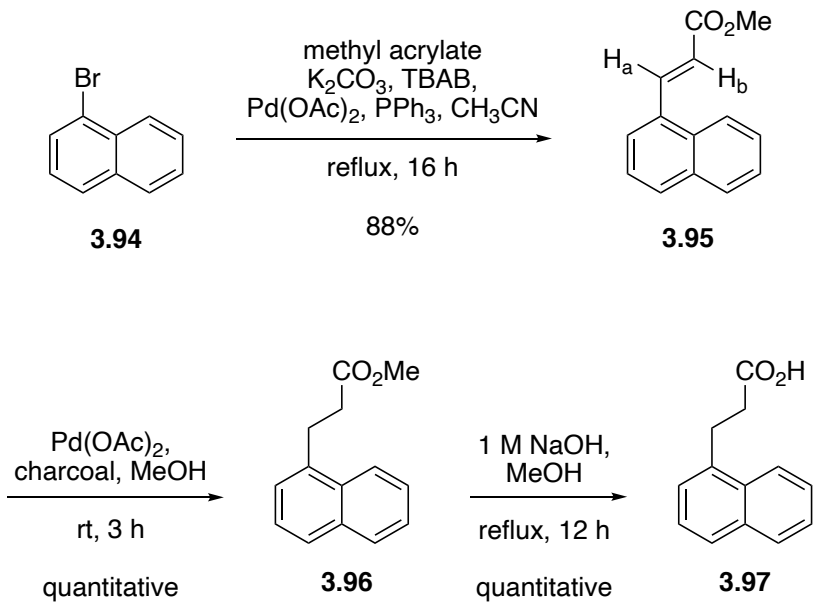
Another factor to consider when thinking about possible product distributions of the [*n*](x,y)peropyrenophanes is the amount of strain in the systems being formed. At the outset, the methodology had only been successfully applied in Kubo's synthesis of planar (unstrained) peropyrenes and it was not known whether the methodology was powerful enough to succeed when called upon to generate strained peropyrenes.

The rest of this Chapter is focused on the exploration of the application of this methodology to the synthesis of[*n*]peropyrenophanes.

3.4: Synthesis of Peropyrenophanes

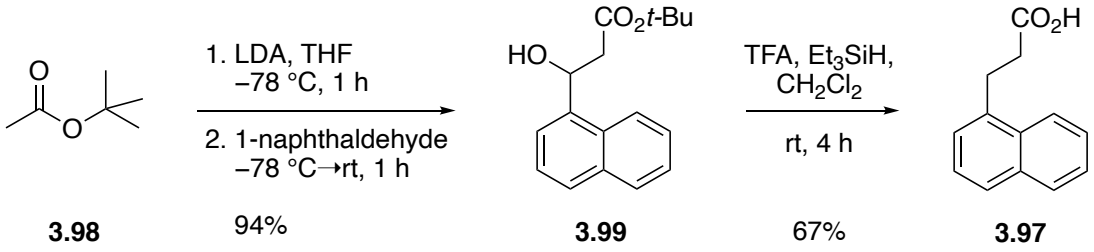
3.4.1: Initial Tethering Approaches

1-Naphthalenepropanoic acid (**3.97**) was identified as a key synthetic intermediate in the synthesis of the targeted peropyrenophane, and a few different ways of accessing it were investigated. The first protocol utilized a Heck reaction between 1-bromonaphthalene (**3.94**) and methyl acrylate, which furnished α,β-unsaturated ester **3.95** in 88% yield (**Scheme 3.22**). This reaction was scalable up to 5.0 grams without any effect on yield. As expected, the Heck reaction afforded the *E*-configured alkene exclusively, as confirmed by coupling constant of H_a and H_b (J = 15.7 Hz). The alkene could then be hydrogenated with an *in situ*-generated catalyst that was generated from $Pd(OAc)_2$ (0.5 mol%) and charcoal (9:1 w/w with $Pd(OAc)_2$) in MeOH.[28] The reaction mixture was then stirred under a H_2 atmosphere and complete conversion was accomplished in 3 h to afford **3.96** quantitatively. The ester was then hydrolyzed using 1 M $NaOH_{(aq)}$ in refluxing MeOH to afford the lynchpin acid **3.97** (quantitative).



Scheme 3.22 Heck coupling approach to 1-naphthalenepropanoic acid (**3.97**).

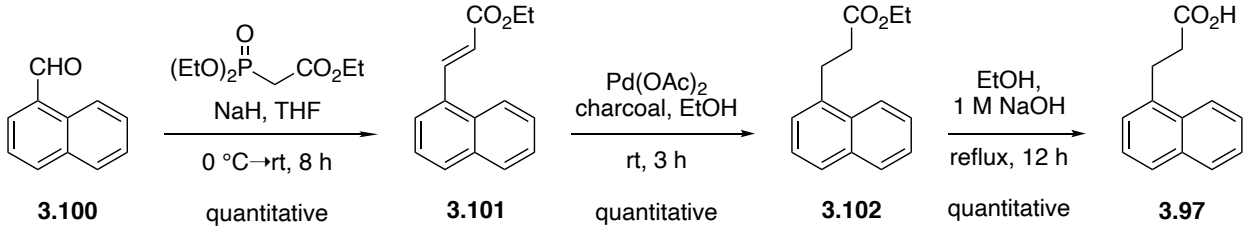
A second protocol for the synthesis of acid **3.97** involved a crossed-aldol reaction between 1-naphthaldehyde (**3.100**) and *tert*-butyl acetate (**3.98**) (**Scheme 3.23**). The enolate of *tert*-butyl acetate was generated by treatment with LDA and its reaction with 1-naphthaldehyde gave β-hydroxyester **3.99** (94%). This product was then simultaneously reduced and de-*tert*-butylated to give acid **3.97** (67%) by treatment with TFA and triethylsilane in CH_2Cl_2.



Scheme 3.23 Crossed-aldol approach to acid **3.97**.

The final sequence employed for the synthesis of acid **3.97** involved a Horner-Wadsworth-Emmons (HWE) reaction between 1-naphthaldehyde (**3.100**) and triethyl

phosphonoacetate (**Scheme 3.24**). The enolate of triethyl phosphonoacetate was produced by treatment with NaH (60% dispersion in mineral oil). Upon complete consumption of NaH, 1-naphthaldehyde (**3.100**) was added, which afforded the alkene **3.101** in quantitative yield. As expected, only the *E*-alkene product **3.101** was obtained. This alkene was hydrogenated in the same fashion as alkene **3.95** with *in situ* generation of the catalyst ($Pd(OAc)_2$ and charcoal). Hydrolysis of the ester using 1 M $NaOH_{(aq)}$ in refluxing EtOH then afforded acid **3.97** quantitatively. This protocol became the preferred procedure for synthesizing synthetically useful quantities of the required acid **3.97** for a couple of reasons. Firstly, all of the reactions were found to be easily scalable. The initial HWE reaction could be comfortably performed on a ~15 g scale with no change in the quantitative yield obtained. Secondly, the products of all three reactions can be used without purification, which, has considerable practical advantages.

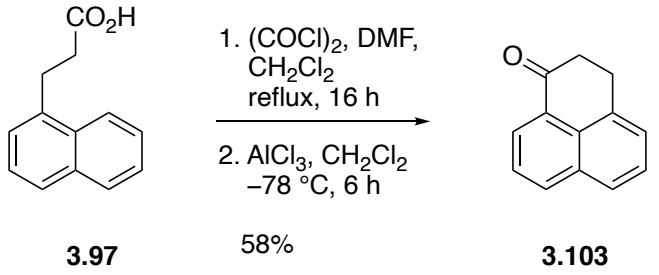


3.100 quantitative **3.101** quantitative **3.102** quantitative **3.97**

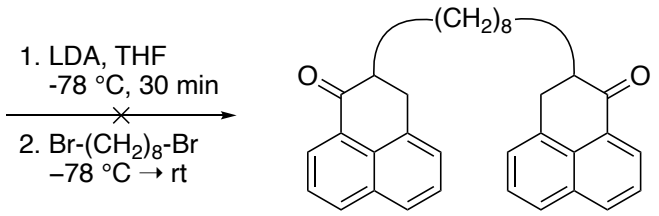
Scheme 3.24 Horner-Wadsworth-Emmons approach to acid **3.97**.

The initial synthetic route involved converting acid **3.97** into the corresponding acid chloride by treatment with oxalyl chloride and then promoting an intramolecular Friedel-Crafts acylation with $AlCl_3$ (**Scheme 3.25**). This two-step procedure furnished 2*H*-2,3-dihydrophenalenone (**3.103**) on a gram scale in 58% yield. The expectation was that treatment of this ketone with LDA would furnish the corresponding enolate, which could then be reacted with a series of α,ω-dihaloalkanes to give a series of tethered bis-phenalenones **3.104** containing all of the carbon atoms necessary for the construction of the targeted [*n*](2,9)peropyrenophanes. However, initial investigations into the feasibility of this approach proved unsuccessful. For *n*=8, none of the desired product was obtained

and only a small amount of the starting phenalenone **3.103** was recovered. It is known that phenalene derivatives are susceptible to oxidation, which may render enolization problematic.[21] In an attempt to determine if oxidation was the issue the reaction was attempted again but exhaustive deoxygenation was undertaken, however, similar results were obtained and different strategies were investigated.



3.97 58% **3.103**

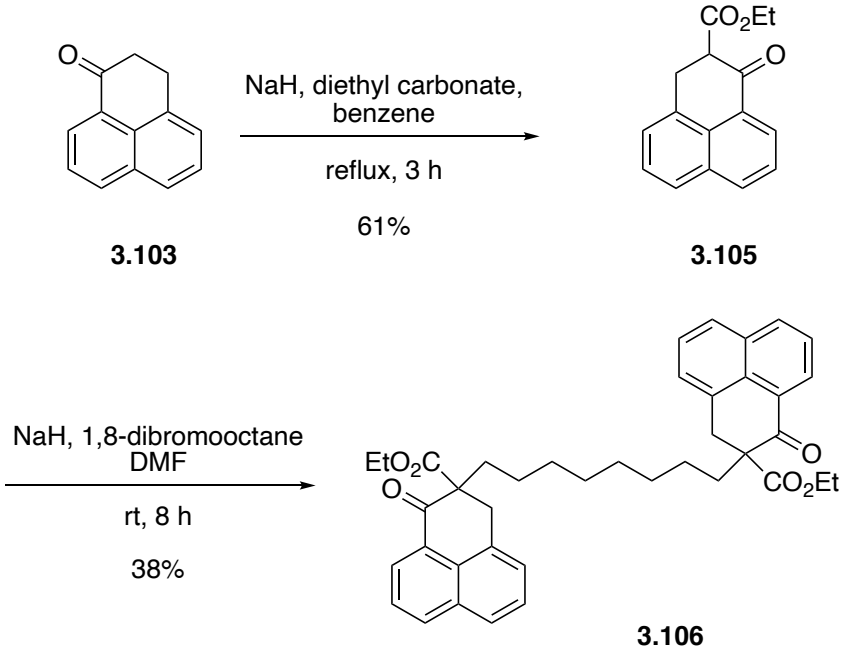


3.104

Scheme 3.25 First approach toward tethering two phenalenone units.

A second attempt to synthesize tethered phenalenone (**3.104**, *n* = 8) involved the reaction of phenalenone (**3.103**), NaH and 1,8-dibromooctane in benzene at reflux. In this case, no reaction was observed and the starting material was recovered. On the other hand, replacement of 1,8-dibromooctane with diethyl carbonate gave β-ketoester **3.105** in 61% yield. The introduction of the ethoxy carbonyl functionality was intended to increase the acidity of the α-hydrogen, the purpose of which was to facilitate alkylation at the α-carbon. The β-ketoester **3.105** was then reacted in DMF with NaH and 1,8-dibromooctane and this did give tethered β-ketoester **3.106**, albeit in modest yield (38%). Of course, the product was obtained as a (1:1) mixture of diastereomers. No TLC conditions were found that showed anything other than a single spot, so no attempt was made to separate the diastereomers. Similar untethered systems have been shown to

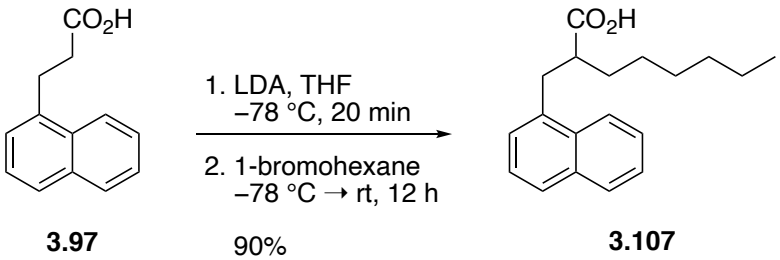
undergo hydrolysis and decarboxylation in boiling ethanolic KOH, but **3.016** failed to do so under these conditions and the tethered β-ketoester **3.105** was recovered. At this point, attention was turned to a different synthetic approach.



Scheme 3.26 Tethering of β-ketoester **3.105** to afford **3.106**.

3.4.2: New Tethering Approach

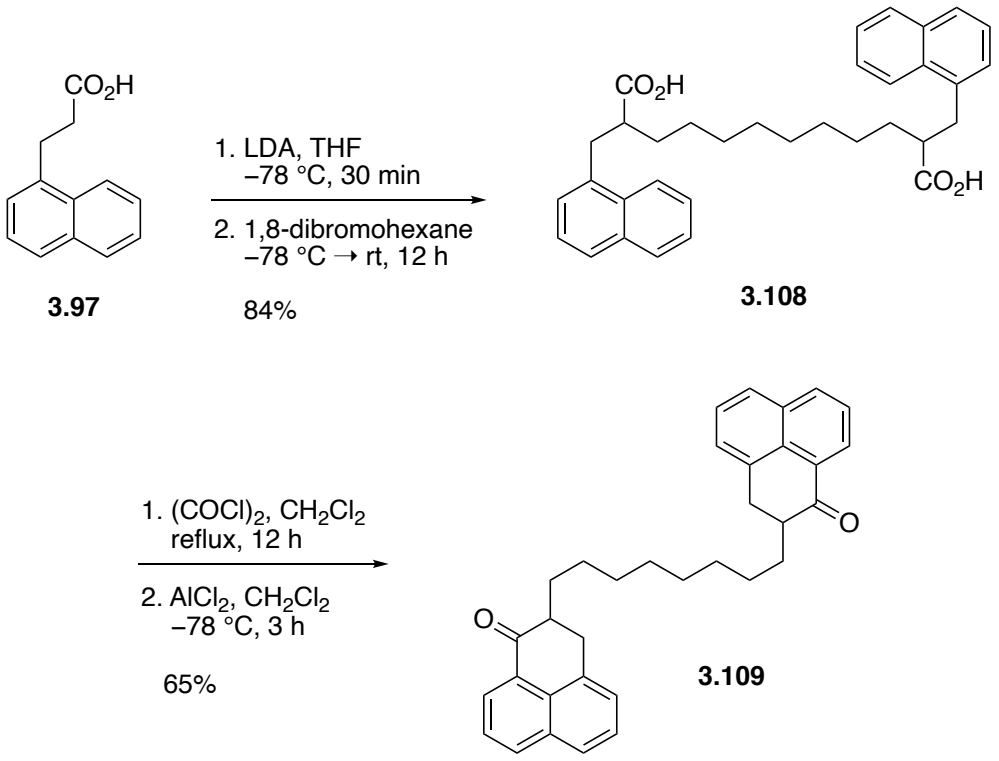
With the difficulty encountered with the direct tethering of phenalenone (**3.103**), it was envisioned that the tethering step could take place prior to the formation of the phenalenone moiety.[29] Acid **3.97** was identified as a suitable system to investigate, and a model reaction was performed by treating acid **3.97** with LDA (2 equiv.) and then allowing the resulting dianionic enolate to react with 1-bromohexane. This cleanly furnished the alkylated product **3.107** in 90% yield.



3.97 90% **3.107**

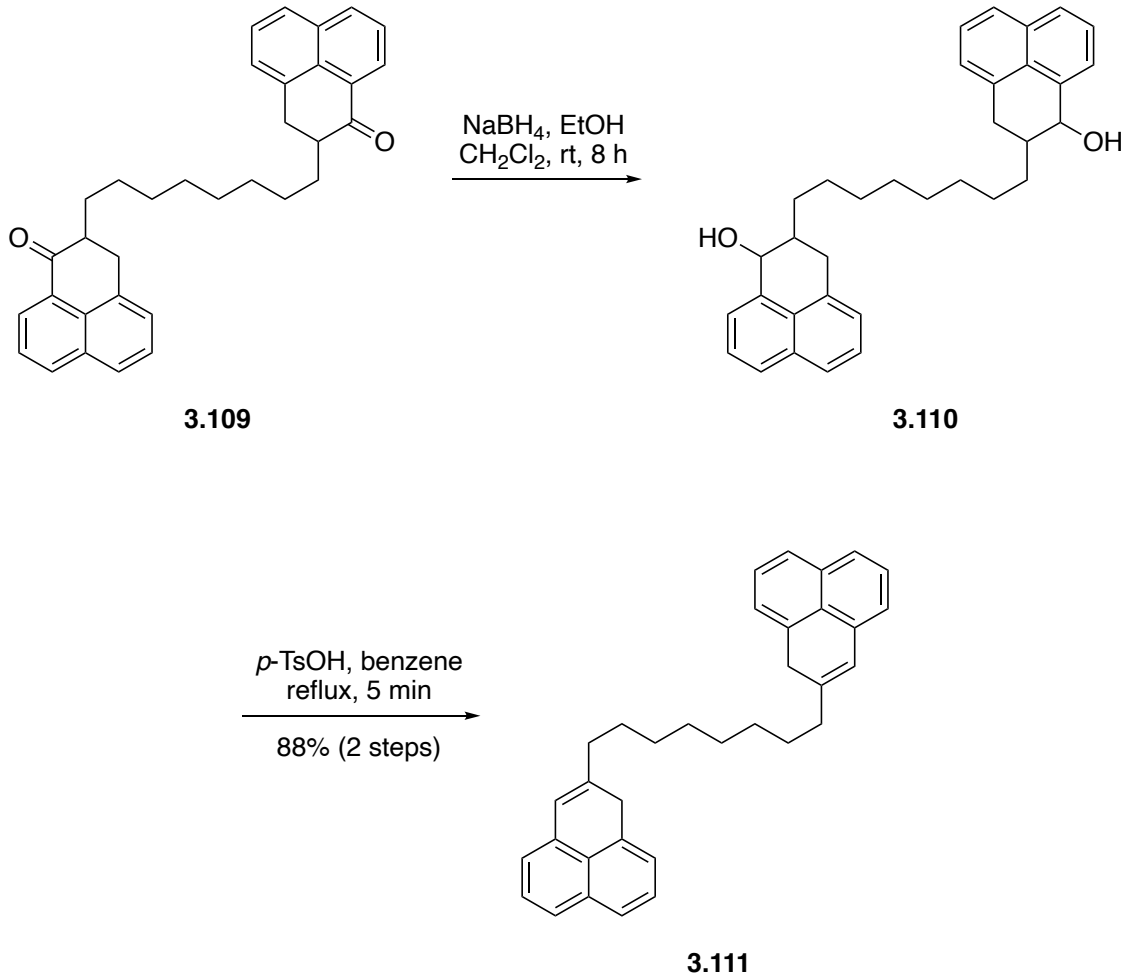
Scheme 3.27 Model alkylation reaction of acid **3.97**.

After the successful model alkylation reaction, tethering of acid **3.97** was undertaken. **3.97** was converted into its corresponding carboxylate enolate with LDA and then 0.5 equivalents of 1,8-dibromooctance was added (**Scheme 3.28**). Gratifyingly, the tethered diacid **3.108** was isolated in 84% yield as a mixture of diastereomers in an approximate ratio of 1:1 (^{1}H NMR analysis). No attempt was made to separate the diastereomers because both stereogenic centers were slated for destruction during the conversion of the phenalenone units into phenalene systems. Diacid **3.108**, was then subjected to reaction with oxalyl chloride in refluxing CH_2Cl_2 to form the corresponding bis(acid chloride). Addition of $AlCl_3$ to a −78 °C solution of the bis(acid chloride) in CH_2Cl_2 led to the formation of tethered phenalenone **3.109** in 65% yield (81% per cyclization).



Scheme 3.28 Synthesis of dione **3.109**.

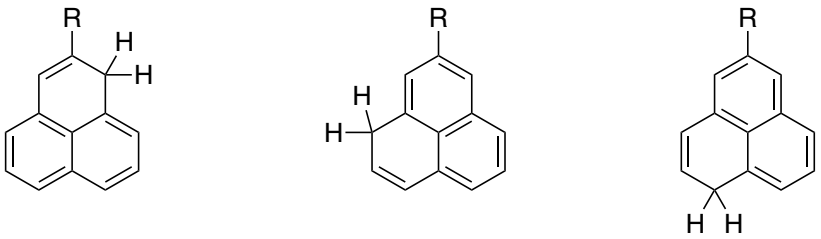
The tethered phenalenone system **3.109** was reduced with sodium borohydride and the crude diol **3.110** was dehydrated with catalytic *p*-toluenesulfonic to give bis(phenalene) **3.111** (**Scheme 3.29**). Based on what is known about the reactivity of phenalene systems and previous work from the Kubo group,[11] the crude reaction mixture was purified by passing it through a small plug of 6% hydrous silica gel with hexane as the eluent. The reason for using hydrated silica gel is to decrease the adsorption strength of the surface silanol systems.[30] It is important for the tethered phenalene system **3.111** to be being quickly passed through silica because of the acidic properties of silica which could degrade the phenalene systems.[31]



3.109 **3.110** **3.111**

Scheme 3.29 Formation of bis(phenalene) **3.111**.

The isolated product from this procedure is in fact a mixture of isomeric tethered phenalenes (**Scheme 3.30**), in which the sp^3-hybridized carbon atom can reside at any *peri* position carbon atom. The three unique phenalene isomers possible can lead to the formation of 6 possible bis(phenalene) products. The ^{1}H NMR spectrum of compound **3.111** is quite messy indicating that the product is a mixture of isomers from rearrangements of the 1H-phenalene core (**Figure 3.6**). This product was carried forward without any further attempts a purification or characterization.



3.112 **3.113** **3.114**

Figure 3.6 Isomers of substituted 1H-phenalenes.

3.5: Phenalenyl Radical Reaction Setup

The generation of phenalenyl radicals using *p*-chloranil requires strict oxygen-free reaction conditions, which can lead to practical difficulty in the running of these experiments. To address this challenge, the Kubo group created specialized glassware (herein named an H-pump tube), which allowed the dissolved radical precursor and *p*-chloranil to be housed unmixed in separate compartments while providing the opportunity for evacuation and degassing of the entire system (**Figure 3.7)**. After satisfactory degassing the system can then be flame-sealed and the radical precursor and oxidant can then be combined, by tipping the apparatus, to initiate the reaction. The H-pump tube is very useful for small-scale reactions as well as somewhat larger scale reactions that can be performed under more concentrated conditions.

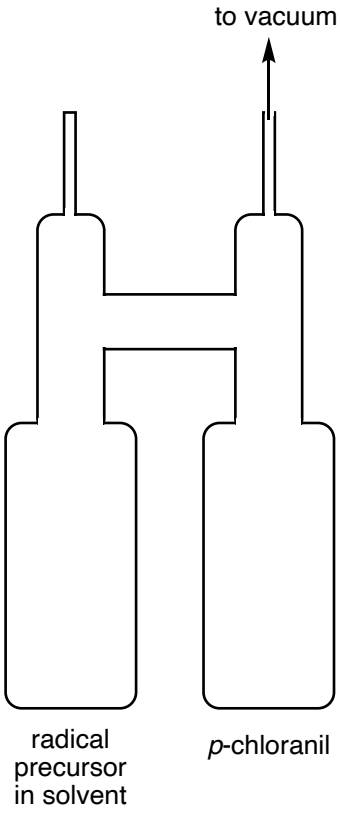


Figure 3.7 H-pump tube for phenalenyl radical generation.

For larger-scale reaction or reactions requiring higher dilution a similar setup could be assembled from a three-necked round-bottomed flask, a curved arm attachment, a glass stopper and a vacuum joint (**Figure 3.8**). The radical precursor is dissolved in a solvent in the round-bottomed flask and solid *p*-chloranil is placed in the curved arm, which prevent the solid from falling into the solution until the arm is turned. The system is then degassed, and the arm is turned dropping the *p*-choranil into the solution.

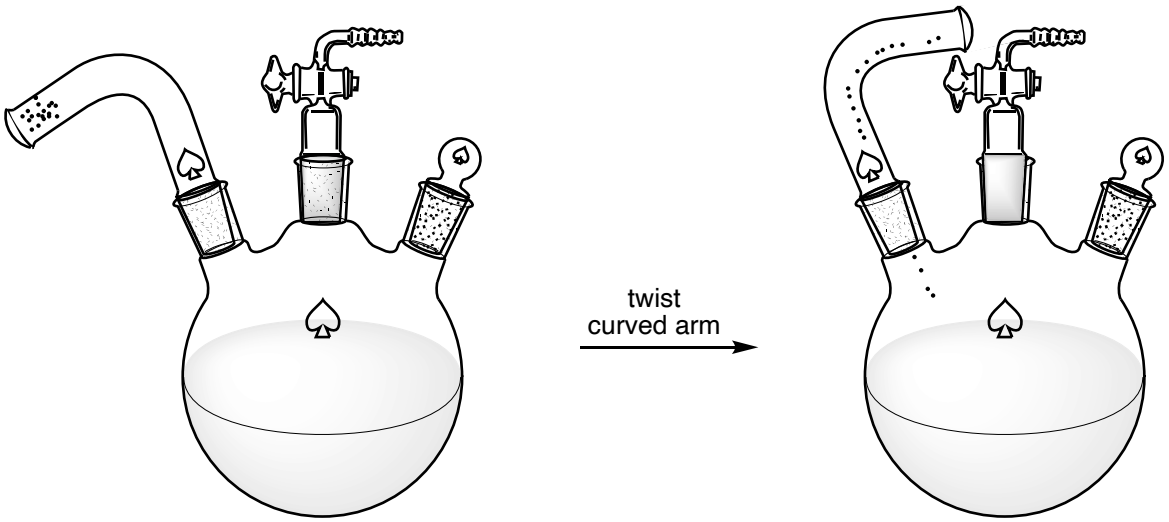
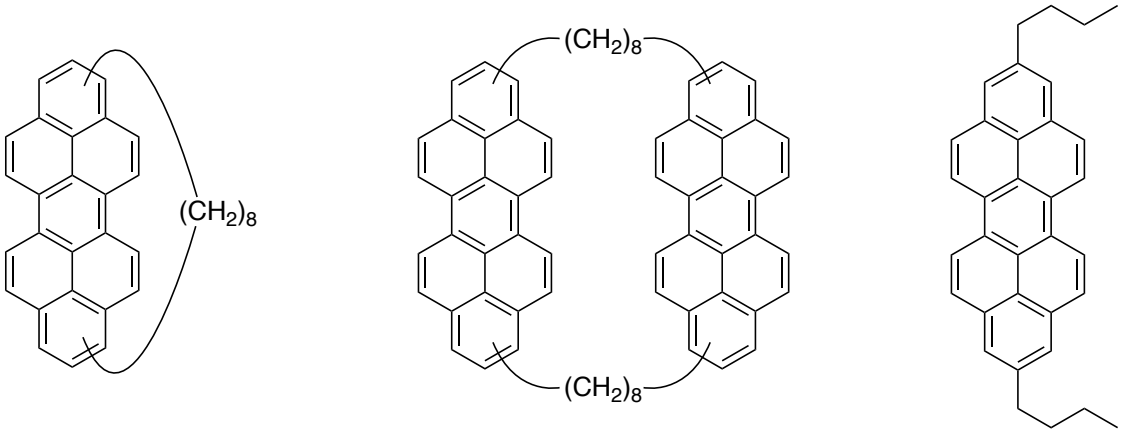


Figure 3.8 Glassware for larger-scale phenalenyl radical generation.

3.6: Initial Results of Phenalenyl Radical Formation

The first experiment performed in an attempt to synthesize a peropyrenophane was undertaken on the 8-carbon tethered bis(phenalene) **3.111** using an H-pump tube on a 25 mg scale with a concentration of approximately 4.0×10^{-3} M using chlorobenzene as the solvent. The reaction system was heated at 60 °C under high vacuum overnight. Mass spectrometric analysis of the crude reaction mixture suggested the presence of one or more [8](x,y)peropyrenophane (**3.115**) (*m/z* = 436.3193) as well as dimeric peropyrenophane(s) (**3.116**) (*m/z* = 872.4382) (**Figure 3.9**). This initial result was encouraging, but the reaction did not yield enough crude product to obtain an NMR spectrum. The UV/Vis absorbance of the crude reaction mixture was measured and the observation of three absorbance peaks at 405, 430 and 452 nm, provided strong evidence for the presence of a peropyrene system (**Figure 3.10**). By comparison, 2,9-dibutylperopyrene (**3.117**) exhibits an absorption maximum at 447 nm with similar spectral shape. To the naked eye, a solution of the crude reaction mixture appeared highly fluorescent, which is expected for a peropyrene system.



3.115 **3.116** **3.117**

Scheme 3.9 Results of small-scale reaction of **3.111** and the structure of 2,9-dibtuylperopyrene.

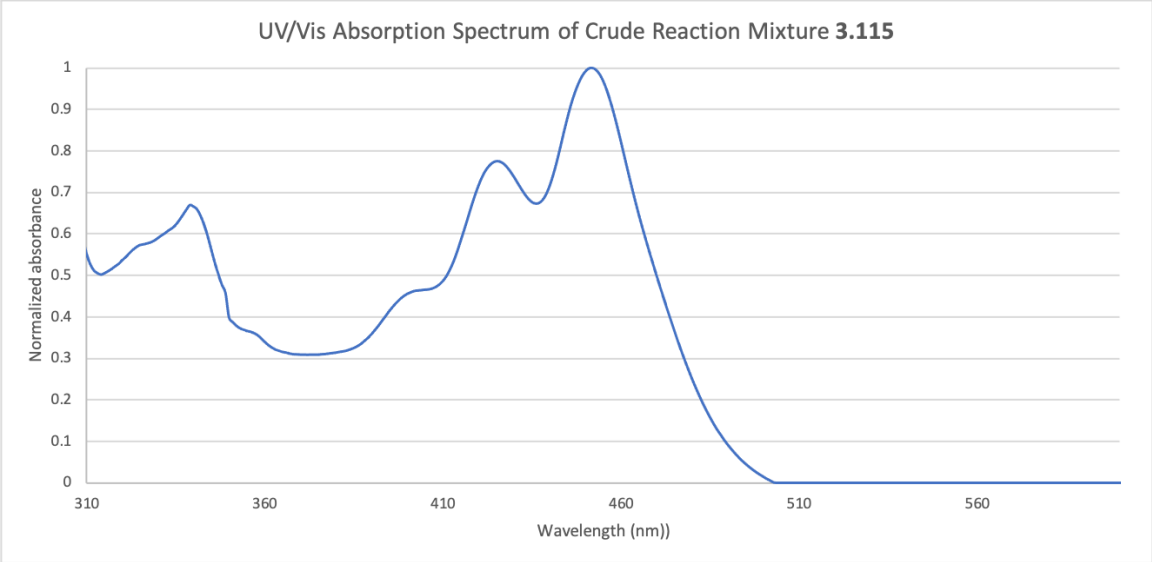


Figure 3.10 UV/Vis absorption of attempted peropyrenophane (**3.115**) synthesis.

In order to probe the reaction further, the progress was monitored by following changes in the UV/Vis spectrum over time. This was accomplished using a modified H-pump tube, where one compartment of the apparatus is replaced with a cuvette. After thoroughly mixing the two components to generate phenalenyl radicals, some reaction mixture was tipped into the cuvette which was placed in the spectrometer. The moment at which *p*-chloranil and bis(phenalene) **3.111** first comes into contact (t = 0 min) an

absorption peak centred at 683 nm was observed (**Figure 4**). Absorption at this wavelength has been shown to correspond to *Z*-bisphenalenylidene systems, which are expected intermediates *en route* to the [8](x,y)peropyrenophanes (**3.115**). Additionally, at t = 0 min there is little evidence to suggest the presence of any peropyrene system due to lack of structured absorption bands between 400 and 500 nm. At t = 15 min. the peak at 683 nm had grown slightly and some structured absorption had begun to appear in the 400-500 nm region. As more time passed, the peak assigned to *Z*-bisphenalenylidene systems continued to decrease and eventually disappeared completely after about t = 2 h, while the bands assigned to peropyrene systems became more intense.

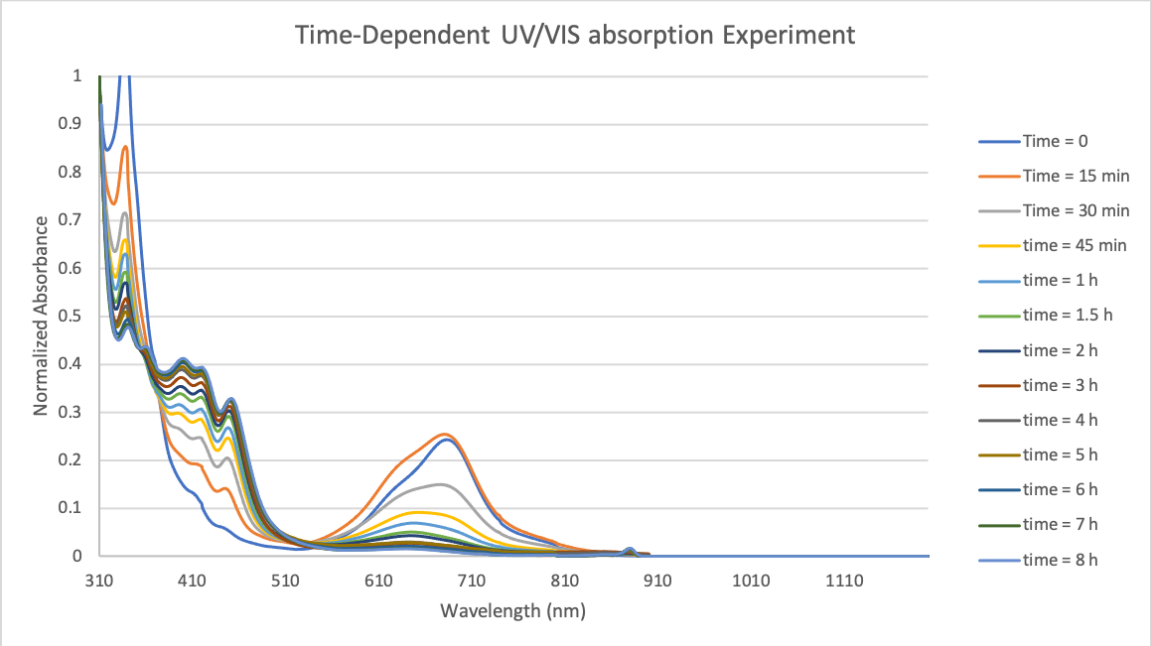


Figure 3.11 Time-dependent UV/Vis experiment.

In an attempt to isolate enough product to determine which peropyrenophane isomer(s) was(were) formed, the experiment was repeated on a larger scale (70 mg). In addition to increasing the scale of the reaction, it was also performed under higher dilution. To accommodate the higher volume of the solvent, the reaction was run using the apparatus described in **Figure 3.8**. This reaction yielded 29 mg of a pale yellow-green solid, which consisted of at least three compounds according to TLC analysis (20% CH_2Cl_2/hexanes). When subjected to column chromatography (20% CH_2Cl_2/hexanes) four

fractions were isolated: fraction 1 (5 mg), fraction 2 (6 mg), fraction 3 (6 mg) and fraction 4 (column flush with EtOAc) (6 mg). The UV/Vis spectra of all four fractions suggested the presence of peropyrene systems (**Figure 3.12**).

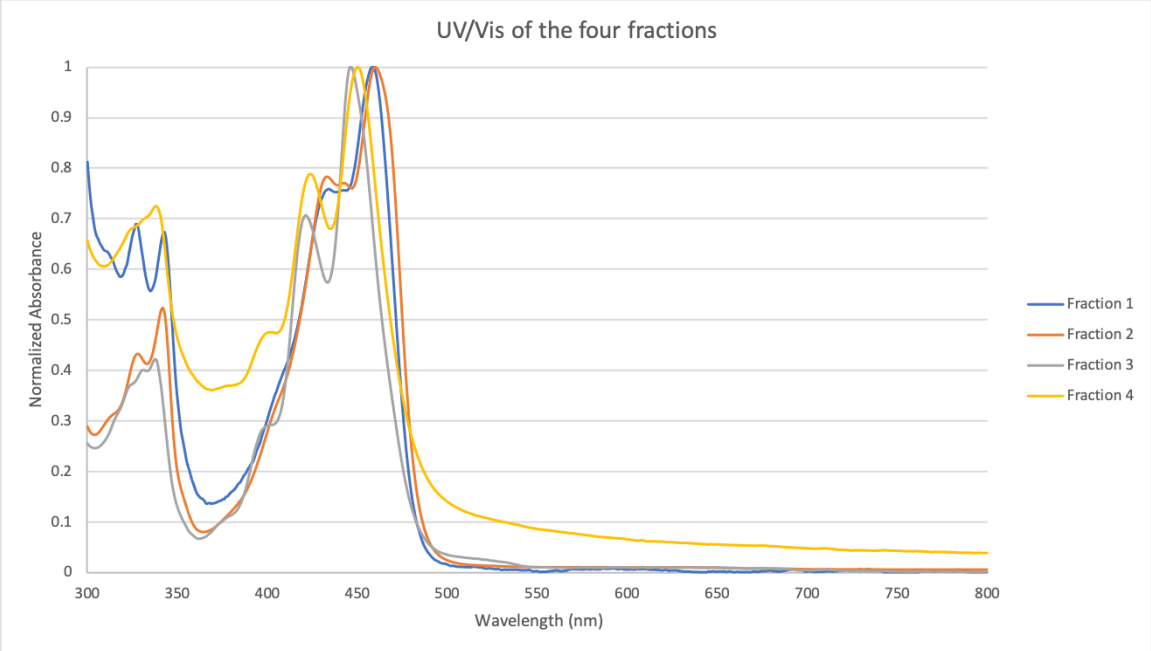


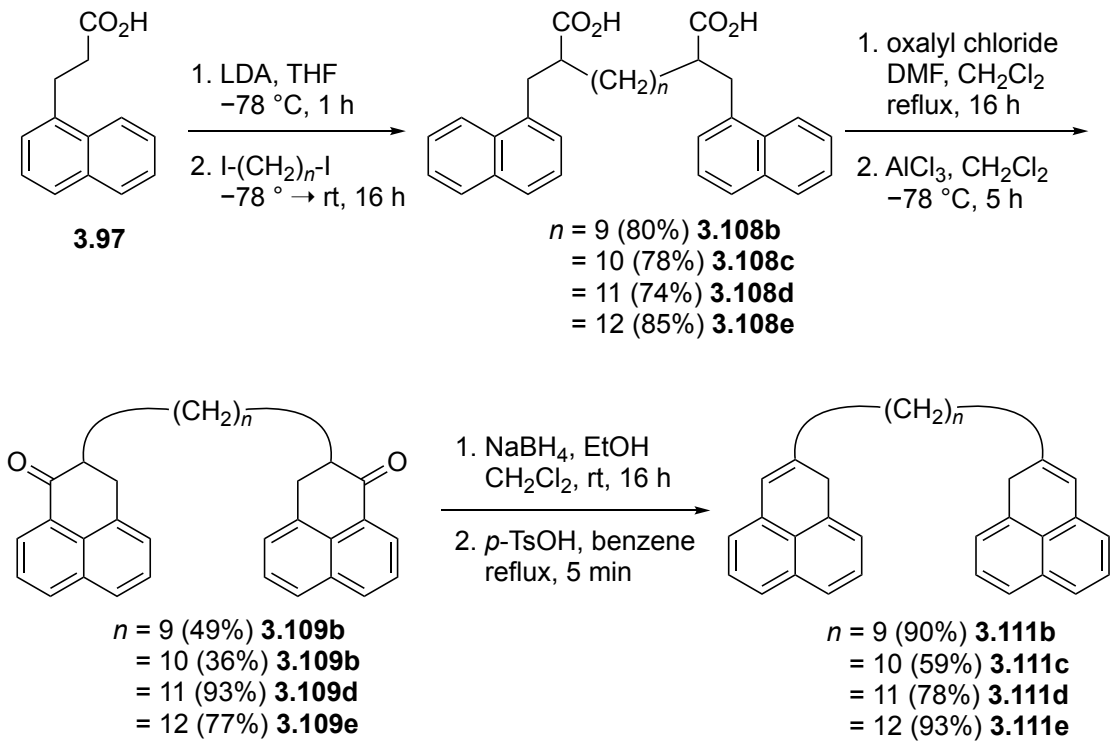
Figure 3.12 UV/Vis of the four isolated fractions from reaction of **3.111.**

Unexpectedly, the ^{1}H NMR spectra of the solids obtained from the four fractions were completely uninterpretable due to the very large number of small and poorly resolved signals spanning a broad range. This very puzzling result made it impossible to make any conclusions about the structure of the products. All attempts to grow crystals were also unsuccessful. At this point attention was turned to systems with longer alkyl chain, but with the clear intention to revisit the C_8-tethered system.

3.7: Synthesis of Larger Tethered Phenalene Systems

The cause for the inconclusive results concerning the structure of the products obtained from the 8-carbon tethered system was puzzling. It was speculated that it may have its origin in the degree of distortion in the peropyrene system of the products, which

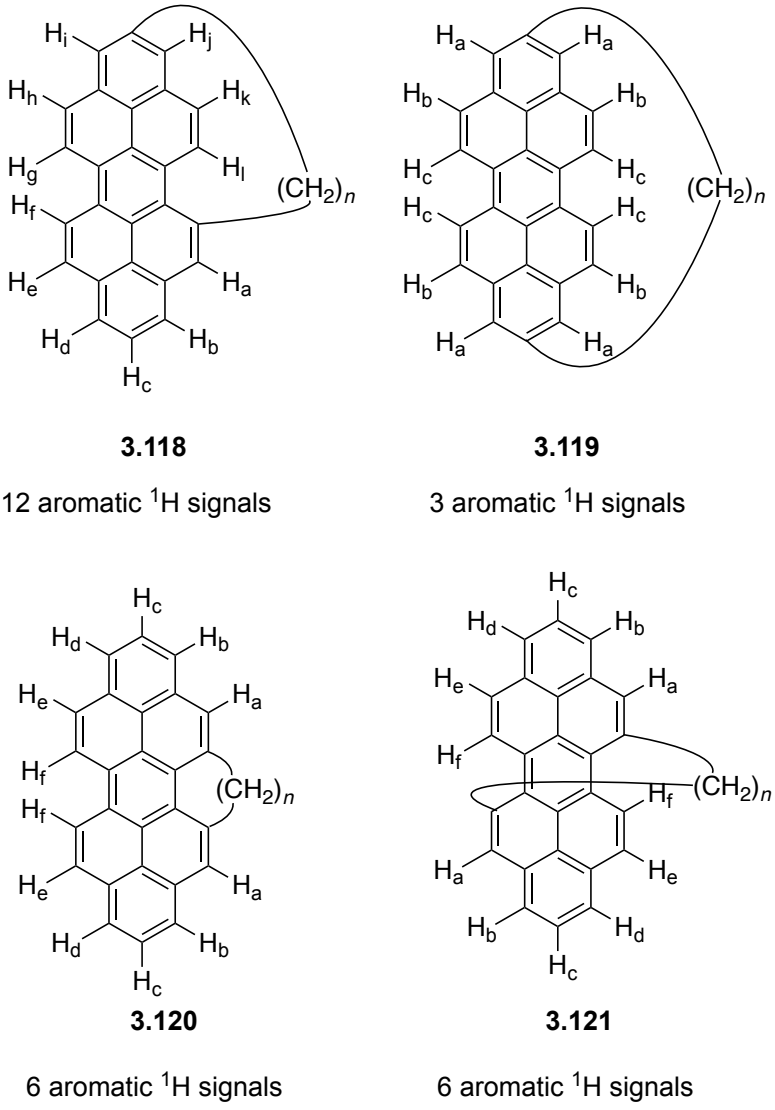
arises from an 8-carbon tether. To probe this, the synthesis of bis(phenalenyl) systems (**3.111b-e)** with tether lengths from 9-12 carbon atoms were undertaken (**Scheme 3.30**). Carboxylic acid **3.79** served as a common starting point. As before, it was converted into its enolate by treatment with LDA (2 equiv.) and then reacted with a series of diiodoalkanes to afford tethered diacids **3.108b-e**, which were carried forward as mixtures of diastereomers. The use of diiodides, which were easily synthesized from the commercial dibromides via the Finkelstein reaction (experimental section), was found to give more consistent results than dibromides. The diacids **3.108b-e** were converted into their corresponding bis(acid chlorides) by treatment with oxalyl chloride and a catalytic amount of DMF in refluxing CH_2Cl_2, and then immediately treated with $AlCl_3$ to bring about intramolecular Friedel-Crafts acylation. This sequence of transformations produced the desired phenalenones **3.109b-e** in modest to good yields (36%-93%), again as a mixture of diastereomers. The phenalenones **3.109b-e** were then reduced with $NaBH_4$ and dehydrated with catalytic *p*-TsOH in refluxing benzene afford tethered bis(phenalenes) **3.111b-e**. As was the case with the 8-carbon tethered system, scrambling of the positions of the sp^3-hybridized carbon atom in the phenalene system onto any of the *peri*-positions resulted in the formation of a mixture of constitutional isomers. While this complicated the characterization (especially by NMR), it was ultimately of no consequence because all isomers led to the same diradical species upon oxidation.



Scheme 3.30 Synthesis of various length tethered phenalenes **3.111b-e**.

Using the apparatus for the larger scale / higher dilution reaction conditions (**Figure 3.8**), tethered bis(phenalene)s **3.111b-e** were reacted with *p*-chloranil in chlorobenzene at 80 °C under closed reaction conditions lacking atmosphere. With no convenient way to monitor the progress of these reactions, a rather long reaction time (2 d) was chosen in an effort to ensure completion of the reaction.

Of the four possible isomeric peropyrenophane products (**Scheme 3.21**), two should be easily distinguishable by ^{1}H NMR (**Figure 3.13**). The (2,6)peropyrenophanes **3.118** would be expected to have 12 aromatic signals due to their low symmetry (C_1). In contrast, the more highly-symmetric (2,9)peropyrenophanes **3.119** (C_{2v}) would be expected to have just 3 signals in the aromatic region. Both the (5,6)peropyrenophane **3.120** (C_s when planar, but C_2 when the two bay region alkyl groups cause the peropyrene system to twist) and (5,12)peropyrenophane **3.121** (C_2) would be expected to give 6 aromatic signals and would therefore be more challenging to distinguish by NMR.



3.118

12 aromatic ^{1}H signals

3.119

3 aromatic ^{1}H signals

3.120

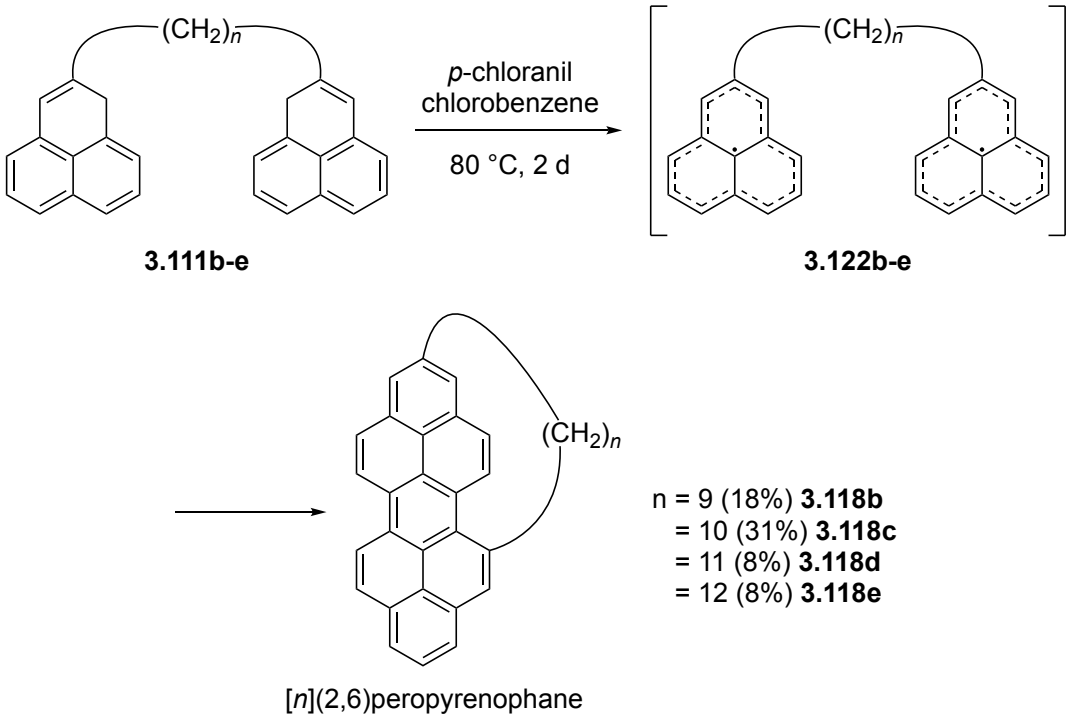
6 aromatic ^{1}H signals

3.121

6 aromatic ^{1}H signals

Figure 3.13 Possible peropyrenophanes and their expected aromatic ^{1}H NMR signals.

In the case of the 9-12 carbon tethered systems one product was isolated after purification in each case (8-31% yields). For all four systems, the ^{1}N NMR spectra clearly revealed which peropyrenophane systems were formed in each case, the [*n*](2,6)peropyrenophanes.



Scheme 3.31 Formation of [*n*](2,6)peropyrenophanes **3.118b-e**.

3.8: Characterization of [*n*](2,6)Peropyrenophanes (3.118b-e)

3.8.1: ^{1}H NMR Characterization of [*n*](2,6)Peropyrenophanes (3.118b-e)

The [*n*](2,6)peropyrenophanes are chiral by virtue of their C_1 symmetry. As a result, the protons of the aliphatic methylene groups are diastereotopic (**Figure 3.14**). In the case of [9](2,6)peropyrenophane **3.118b**, protons H_1 and H_2 have been assigned to the 1H doublet of doublet of doublets (ddd) that appear at 2.91-2.97 ppm (J_1 = 13.1 Hz, J_2 = 9.1 Hz, J_3 = 4.2 Hz) and 3.25-3.30 ppm (J_1 = 12.6 Hz, J_2 = 7.2 Hz, J_3 = 5.2 Hz). These two signals show a COSY cross peak. Proton H_3, which is the proton situated in the bay region pointing toward H_I, has been assigned to the 1H doublet of doublet of doublets (ddd) at 4.28-4.34 ppm (J_1 = 14.0 Hz, J_2 = 5.7 Hz, J_3 = 5.7 Hz), which is much further downfield (~ 1 ppm) than the other benzylic protons (presumably due to steric

deshielding). Its diastereotopic partner H_4 has been assigned to the 1H doublet of doublet of doublets at 3.10-3.16 ppm (J_1 = 14.5 Hz, J_2 = 7.7 Hz, J_3 = 7.4 Hz). A COSY cross peak is observed for these two signals.

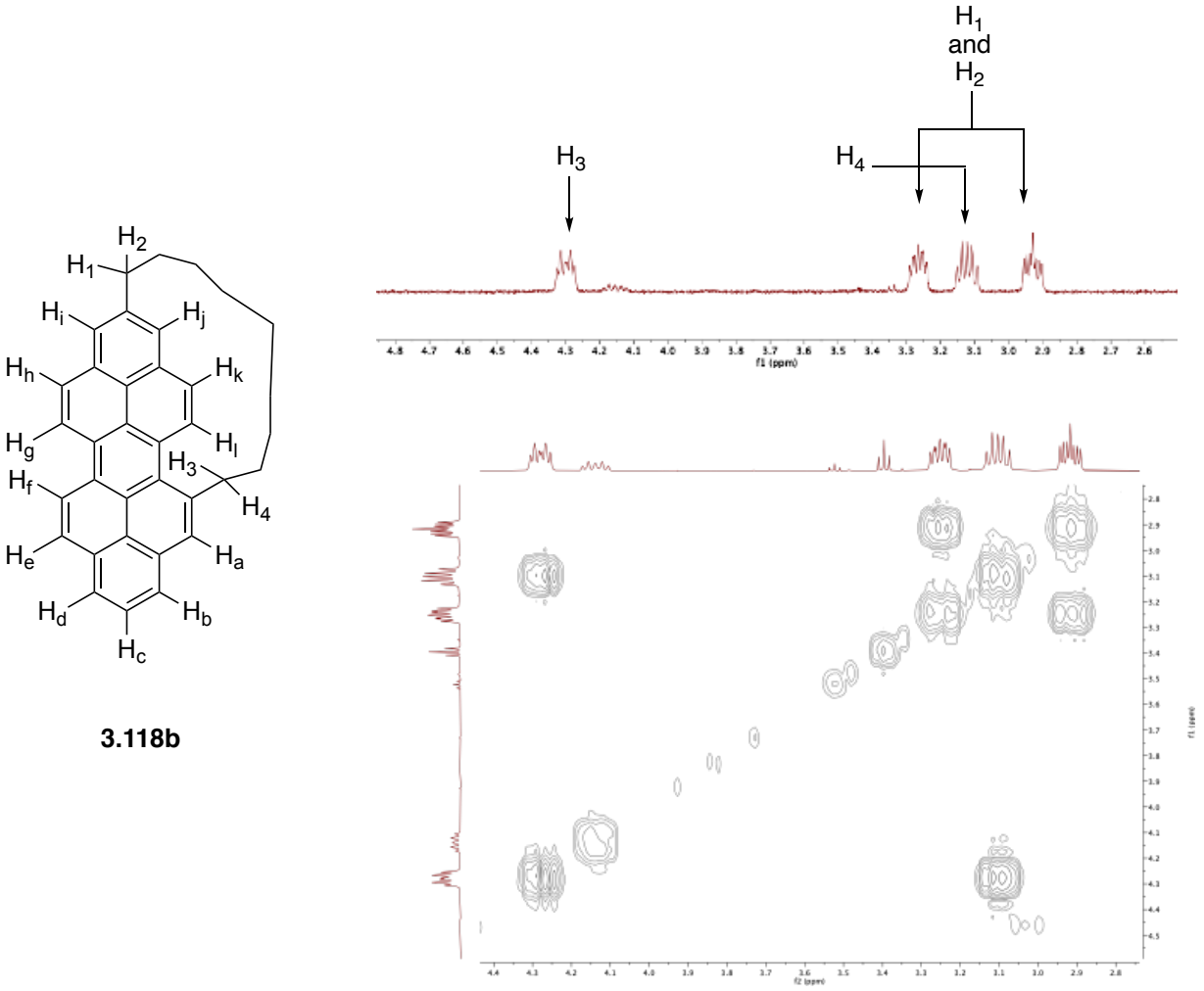
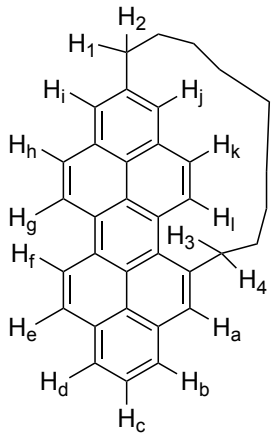
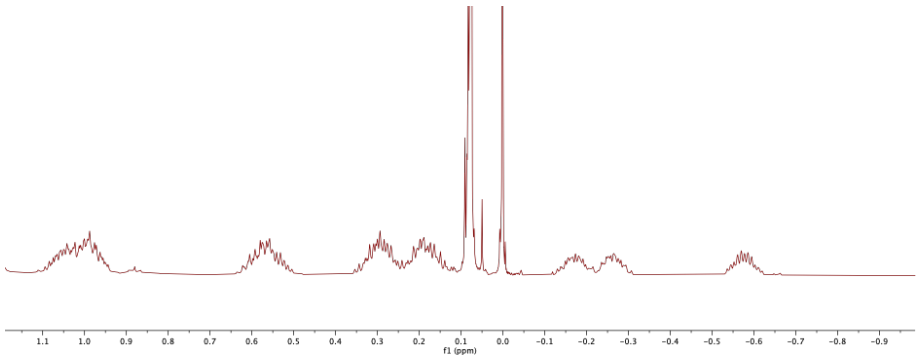


Figure 3.14 Labelled [9](2,6)peropyrenophane (**3.118b**) and benzylic protons.

The 9-carbon methylene bridge sits, at least partially, under the aromatic core as evidenced by the upfield chemical shifts of 1H-signals at –0.12- –0.18 ppm (1H), –0.22- –0.28 ppm (1H) and –0.52- –0.60 ppm (1H) (**Figure 3.15**). These signals suggest that in the middle of bridge the diastereotopic protons are in different environments with one proton angled into the shielding cone of peropyrene system and the others are pointing away and are therefore less shielded.



3.118b



Scheme 3.15 Shielded bridge methylene protons of **3.118b**.

The aromatic region of [9](2,6)peropyrenophane's (**3.118b**) ^{1}H NMR spectrum is shown in **Figure 3.16** along with the ^{1}H,^{1}H-COSY spectrum. The signal corresponding to H_a (7.98 ppm, singlet) can be assigned to the most upfield signal in the aromatic region based on a NOESY cross peaks to H_4. Three *K*-regions are present in the aromatic core. The first includes protons H_l (8.89 ppm, doublet, J = 9.2 Hz) (based of NOESY cross peak to H_3) coupled to H_k (8.14 ppm, doublet, J = 9.2 Hz) (COSY cross peak). The signal corresponding to H_j (8.02 ppm, singlet) was assigned by its NOESY cross peak to H_k, which allowed, based on process of elimination, H_i (8.19 ppm, singlet) to be assigned as the remaining singlet. Based on the assignment of H_i, another *K*-region containing protons H_h (8.29 ppm, doublet, J = 9.2 Hz, overlaps with another signal) (NOESY cross peak to H_i) coupled with H_g (9.02 ppm, doublet, J = 9.2 Hz) (COSY cross peak) can be assigned. The assignment of the penultimate *K*-region allowed for the assignment of the final *K*-region containing protons H_f (9.12 ppm, doublet, J = 9.1 Hz) (NOESY cross peak to H_g) coupled to H_e (8.33 ppm, doublet, J = 9.1 Hz) (COSY cross peak). The only expected triplet arising from the aromatic core was assigned to H_c (8.05 ppm, triplet, overlaps with H_i) which allowed the assignment of H_b (8.28 ppm, doublet, J = 7.6 Hz,

overlapping with H_g) and H_d (8.22 ppm, doublet) based on the observed COSY cross peaks.

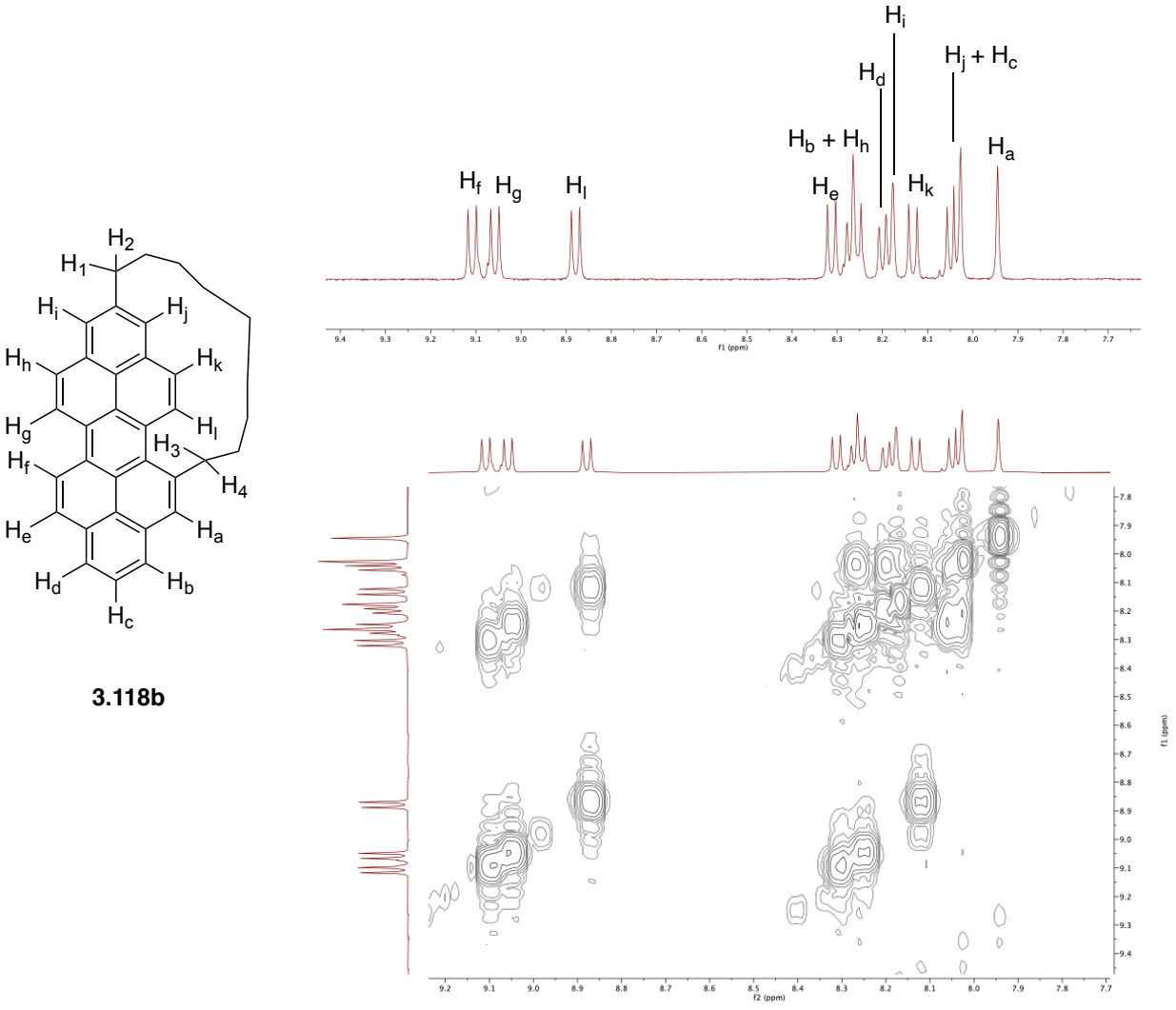


Figure 3.16 Aromatic ^{1}H NMR assignments for [9](2,6)peropyrenophane (**3.118b**).

In the case of [10](2,6)peropyrenophane **3.118c**, proton H_3, which is the proton situated in the bay region pointing toward H_l, has been assigned to the 1H doublet of doublet of doublets (ddd) at 4.45-4.50 ppm (J_1 = 14.1 Hz, J_2 = 8.5 Hz, J_3 = 5.3 Hz), which is again much further downfield (~ 1 ppm) than the other benzylic protons. Its diastereotopic partner H_4 has been assigned (COSY cross peak) to the 1H doublet of doublet of doublets (ddd) at 3.11-3.17 ppm (J_1 = 14.7 Hz, J_2 =8.5 Hz, J_3 = 6.6 Hz) (**Figure**

3.17). Protons H_1 and H_2 have been assigned as the doublet of doublet of doublets (ddd) at 3.00-3.06 ppm (J_1 = 12.4 Hz, J_2 = 4.7 Hz, J_3 = 4.7 Hz) and 3.32-3.37 ppm (J_1 = 13.0 Hz, J_2 = 4.3 Hz, J_3 = 4.3 Hz). A COSY cross peak is observed for these two signals.

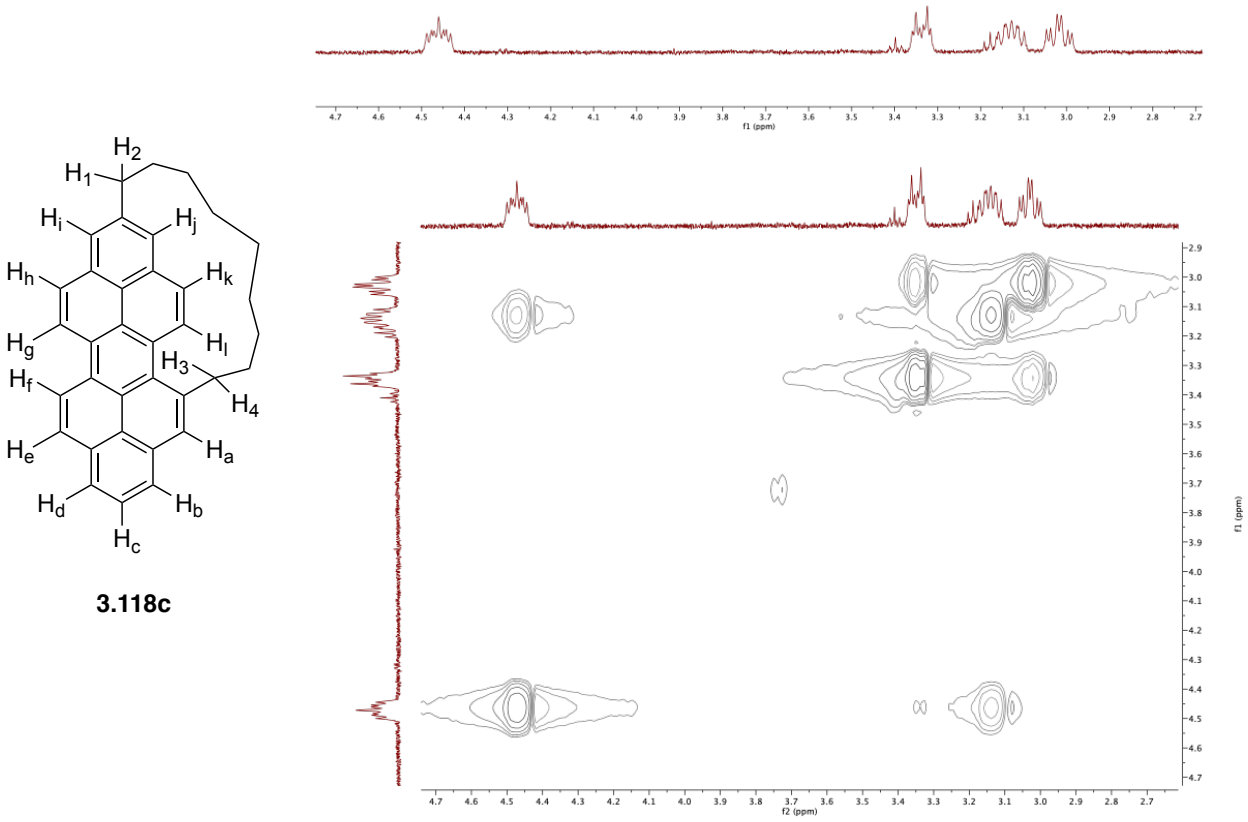
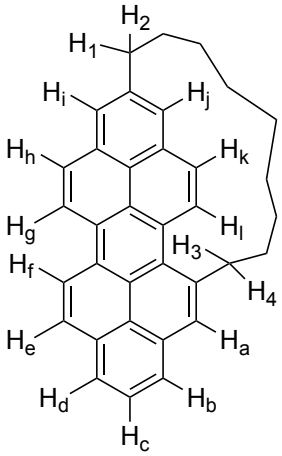


Figure 3.17 Labelled [10](2,6)peropyrenophane **3.118c** and benzylic protons.

The 10-carbon methylene bridge sits, at least partially, under the aromatic core as evidenced by the upfield chemical shifts of some of the methylene protons (**Figure 3.18**). Two 1H multiplets are observed, centered at δ –0.48 and –1.14 ppm.



3.118c

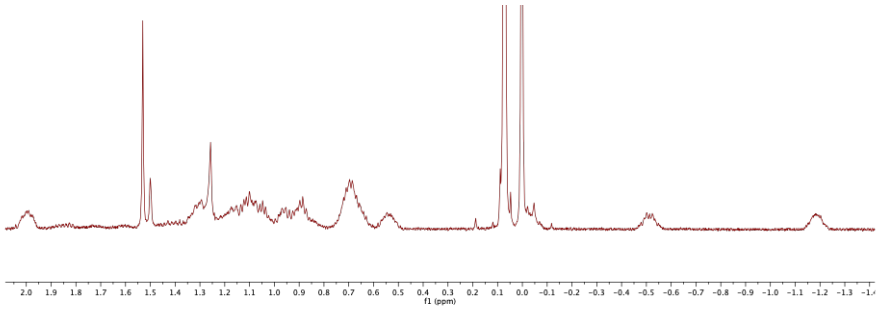
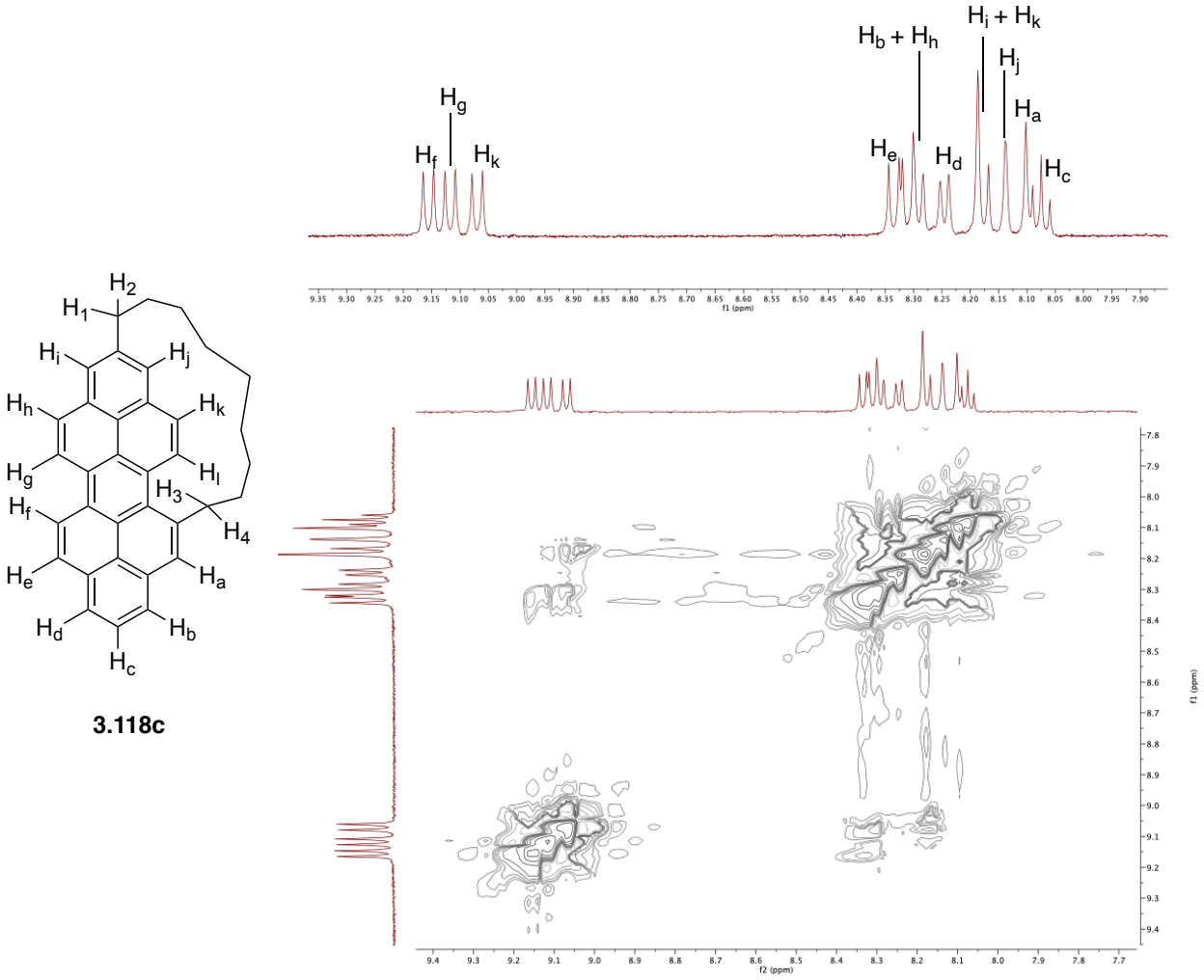


Figure 3.18 Shielded bridge methylene protons of **3.118c**.

The aromatic region of [10](2,6)peropyrenophane's (**3.118c**) ^{1}H NMR spectrum is shown in **Figure 3.19** along with the ^{1}H,^{1}H-COSY spectrum. The signal corresponding to H_a (8.10 ppm, singlet) can be assigned based of the NOESY cross peak with H_4. Three *K*-regions are present in the aromatic core. The first includes protons H_l (9.07 ppm, doublet, J = 9.1 Hz) (NOESY cross peak with H_3) coupled with H_k (8.17 ppm, doublet, J = 9.2 Hz) (COSY cross peak). The signal corresponding to H_j (8.14 ppm, singlet,) was assigned by its NOESY cross peak to H_k, which allowed, based on a process of elimination, H_i (8.18 ppm, singlet, overlapping) to be assigned as the remaining singlet. Based on the assignment of H_i, another *K*-region containing set of protons H_h (8.31 ppm, doublet, J = 9.2 Hz) (NOESY cross peak with H_i) coupled with H_g (9.12 ppm, doublet, J = 9.2 Hz) (COSY cross peak) can be assigned. The assignment of the penultimate *K*-region allowed for the assignment of the final *K*-region containing protons H_f (9.15 ppm, doublet, J = 9.1 Hz) (NOESY cross peak to H_g) coupled to H_e (8.33 ppm, doublet, J = 9.1 Hz) (COSY cross peak). The only expected triplet arising from the aromatic core was assigned to H_c (8.07 ppm, triplet, J = 7.6 Hz) which allowed the assignment of H_b (8.29 ppm, doublet) (overlapping with H_e) and H_d (8.24 ppm, doublet, J = 7.6 Hz) based on the observed COSY cross peaks.



Scheme 3.19 Aromatic ^{1}H NMR assignments for [10](2,6)peropyrenophane (**3.118c**).

As mentioned above, the [*n*](2,6)peropyrenophanes are chiral. The two enantiomers differ in which of the enantiotopic faces of the 2,6-disubstituted peropyrene the aliphatic bridge sits over. The interconversion of the two enantiomers thus can occur via a skipping rope movement. The effect of such a conformational change is that the diastereotopic protons on each of the CH_2 group in the bridge exchange their environments. Therefore, the observation of well-resolved signals for each of the benzylic protons demonstrates that the bridge flip occurs slowly on the NMR timescale at room temperature for **3.118b** and **3.119c**. To obtain information about the bridge flipping process, VT NMR experiments were conducted using a toluene-d_8 solution of **3.118c**.

Spectra were measured at 10 K intervals from 298 K to 368 K (**Figure 3.20**). The aliphatic region is shown, since the expectation is that coalescence would be most easily shown by the diastereotopic benzylic protons. No appreciable change was observed in the spectrum of [10](2,6)peropyrenophane (**3.118c**), indicating that the coalescence temperature (T_c) must be much higher. With a conservative estimate of T_c = 450 K, then a lower limit for the barriers to racemization can be calculated at 21.5 kcal/mol

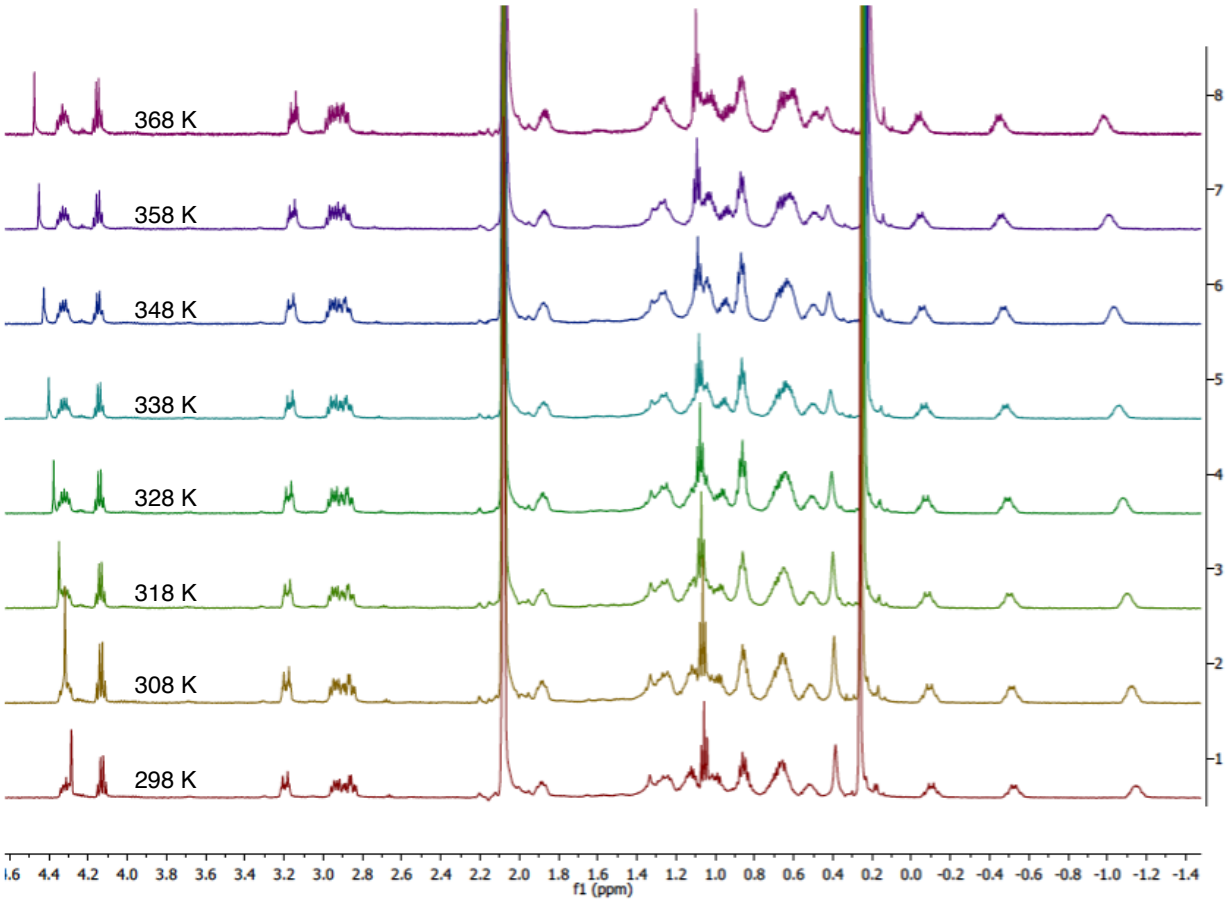


Figure 3.20 VT NMR of the aliphatic region of [10](2.6)peropyrenophane (**3.118c**).

The ^{1}H NMR spectrum of [11](2,6)peropyrenophane (**3.118d**) is quite similar to those of its lower homologue **3.118b** and **3.118c**. Of the benzylic protons, H_1, H_2, and H_3 overlap to form a multiplet between 3.12-3.26 ppm, which integrates for 3H. The proton corresponding to H_4 is, like in the other peropyrenophanes, is a doublet of doublet of

doublets shifted further downfield (4.37-4.42 ppm, J_1 =14.2 Hz, J_2 = 8.9 Hz, J_3 = 4.8 Hz, ddd).

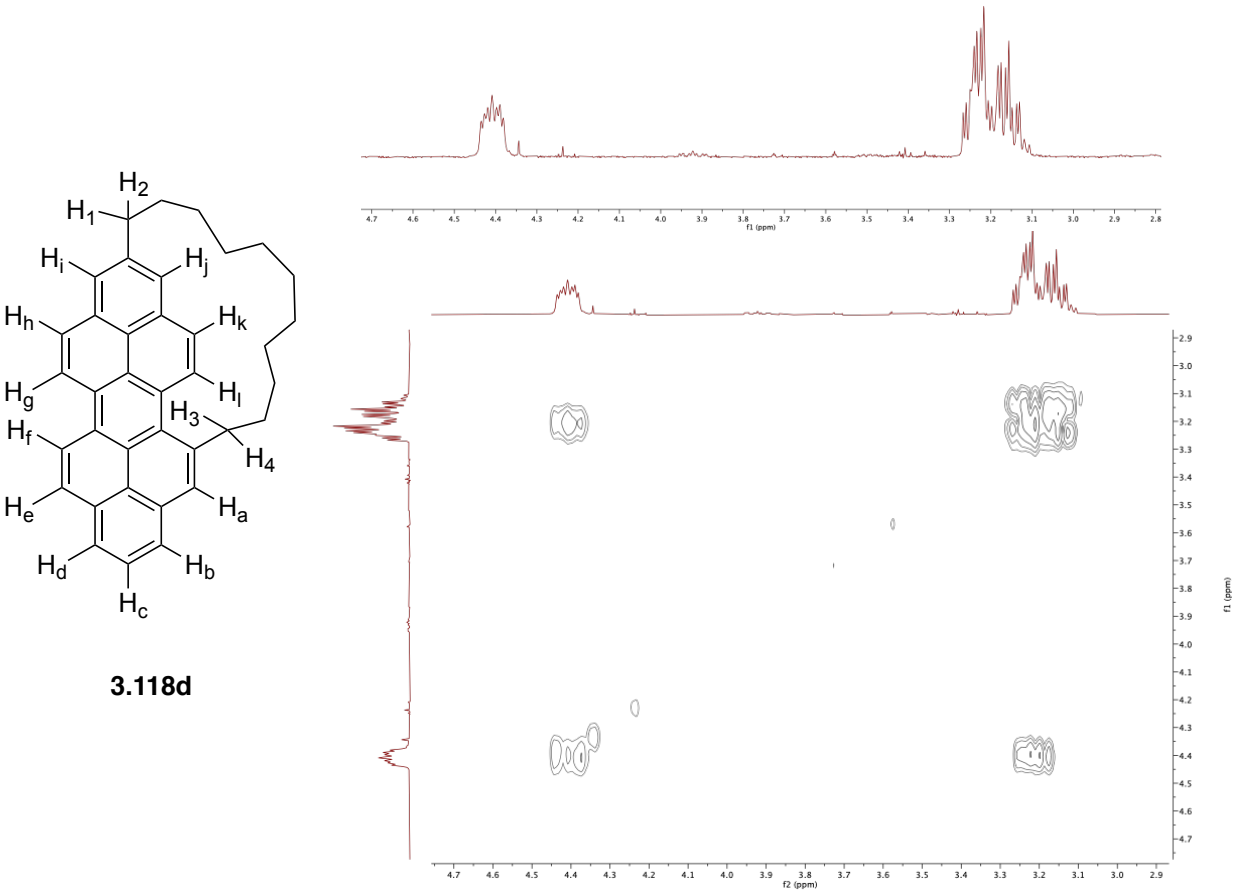
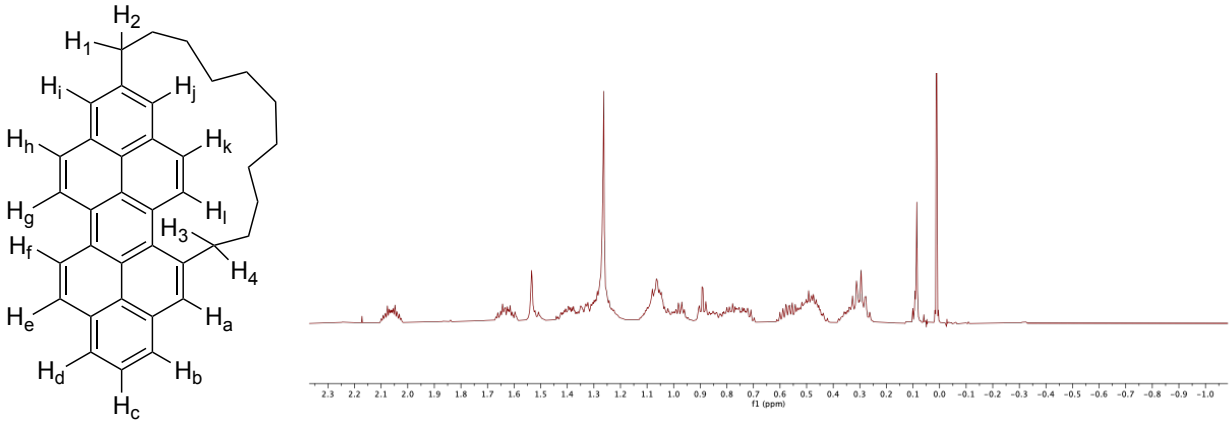


Figure 3.21 Labelled [11](2,6)peropyrenophane **3.118d** and benzylic protons.

Based on the chemical shifts of the remaining bridge protons, the bridge is situated within the shielding cone (*i.e.* underneath the aromatic core) to a lesser extent than observed in [9](2,6)peropyrenophane (**3.118b**) and [10](2,6)peropyrneophane (**3.118c**) (**Figure 3.22**).



3.118d

Figure 3.22 Shielded bridge methylene protons of **3.118d**.

The aromatic region of [11](2,6)peropyrenophane's (**3.118d**) ^{1}H NMR spectrum is shown in **Figure 3.23** along with the 1H,1H-COSY spectrum. Three *K*-region are present in the aromatic core. The first includes protons H_l (9.11 ppm, doublet, *J* = 9.2 Hz) (NOESY cross peak with H_3) coupled with H_k (8.17 ppm, doublet, *J* = 9.2 Hz) (COSY cross peak). The signal corresponding to H_j (8.13 ppm, narrow doublet, *J* = 1.1 Hz) was assigned by its NOESY cross peak to H_k, which allowed, based on process of elimination, H_i (8.20, narrow doublet, *J* = 1.1 Hz) to be assigned as the other narrow doublet based on the coupling constant (no COSY cross peak was easily observable). Based on the assignment of H_i, another *K*-region containing protons H_h (8.31 ppm, doublet, *J* = 9.2 Hz) (NOESY cross peak to H_i) couple with H_g (9.12 ppm, doublet, *J* = 9.2 Hz) (COSY cross peak) could be assigned. The assignment of the penultimate *K*-region allowed for the assignment of the final *K*-region containing protons H_f (9.15 ppm, doublet, *J* = 9.2 Hz) (NOESY cross peak with H_g) coupled with H_e (8.32 ppm, doublet, *J* = 9.2 Hz) (COSY cross peak). The only expected triplet arising from the aromatic core was assigned to H_c (8.07 ppm, triplet, *J* = 7.5 Hz) which allowed the assignment of H_b (8.29 ppm, doublet, overlapping with H_e) and H_d (8.24 ppm, doublet, *J* = 7.6 Hz) based on the observed COSY cross peaks.

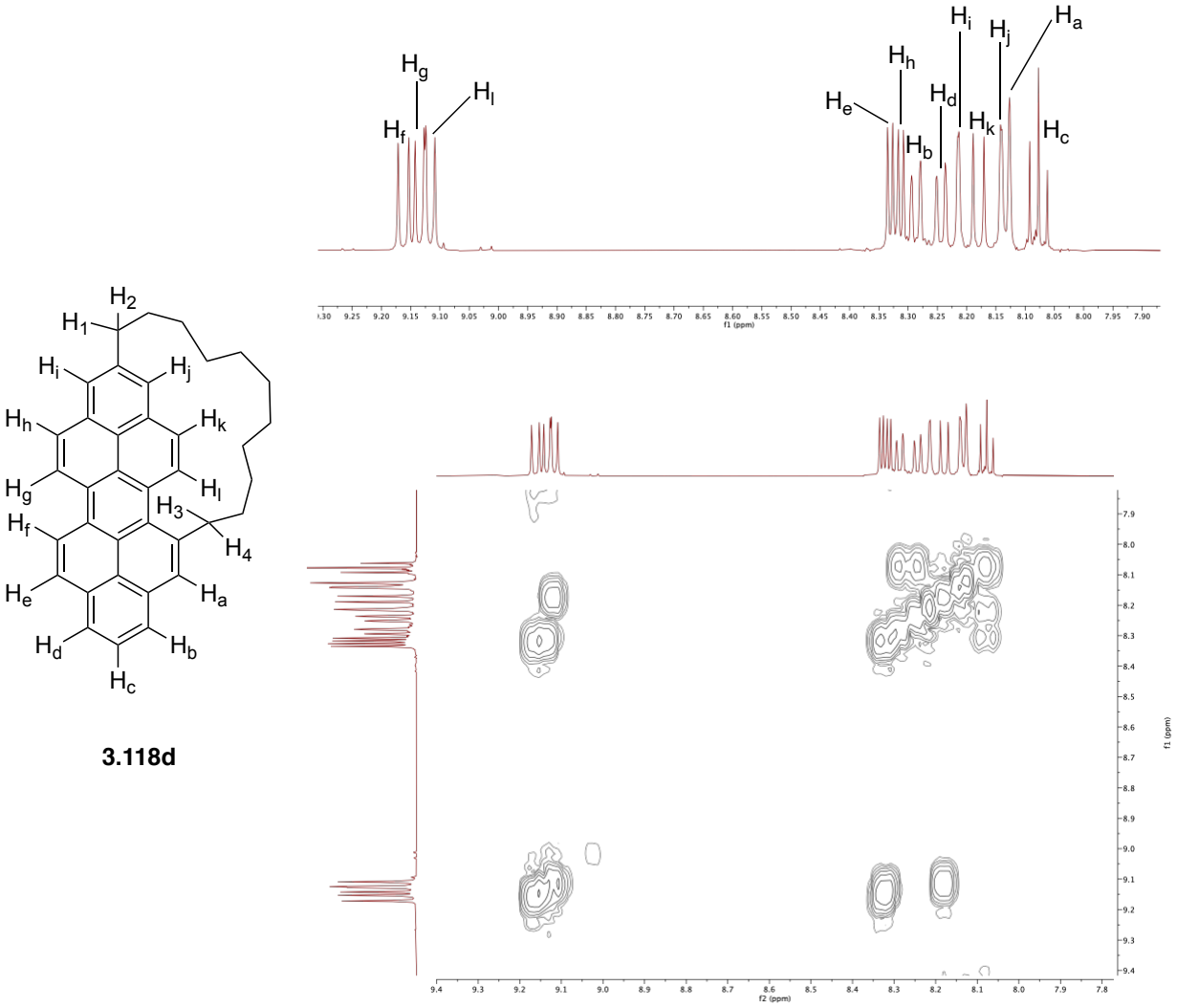


Figure 3.23 Aromatic ^{1}H NMR assignments for [11](2,6)peropyrenophane (**3.118d**).

To discover whether the bridge could flip on the ^{1}H NMR time scale VT NMR experiments were conducted in toluene-d_8. Spectra were measured at 10 K intervals from 298 K to 368 K (**Figure 3.24**). The aliphatic region is shown, since the expectation is that coalescence would be most easily shown by the diastereotopic benzylic protons. There is only slight broadening and overlapping of 3 benzylic protons of [11](2,6)peropyrenophane (**3.118d**) as the temperature is increased, but the system is still

far from coalescence. The observation of some slight broadening did provide some evidence that the barrier to racemization is lower in **3.118d** than it is in **3.118c**.

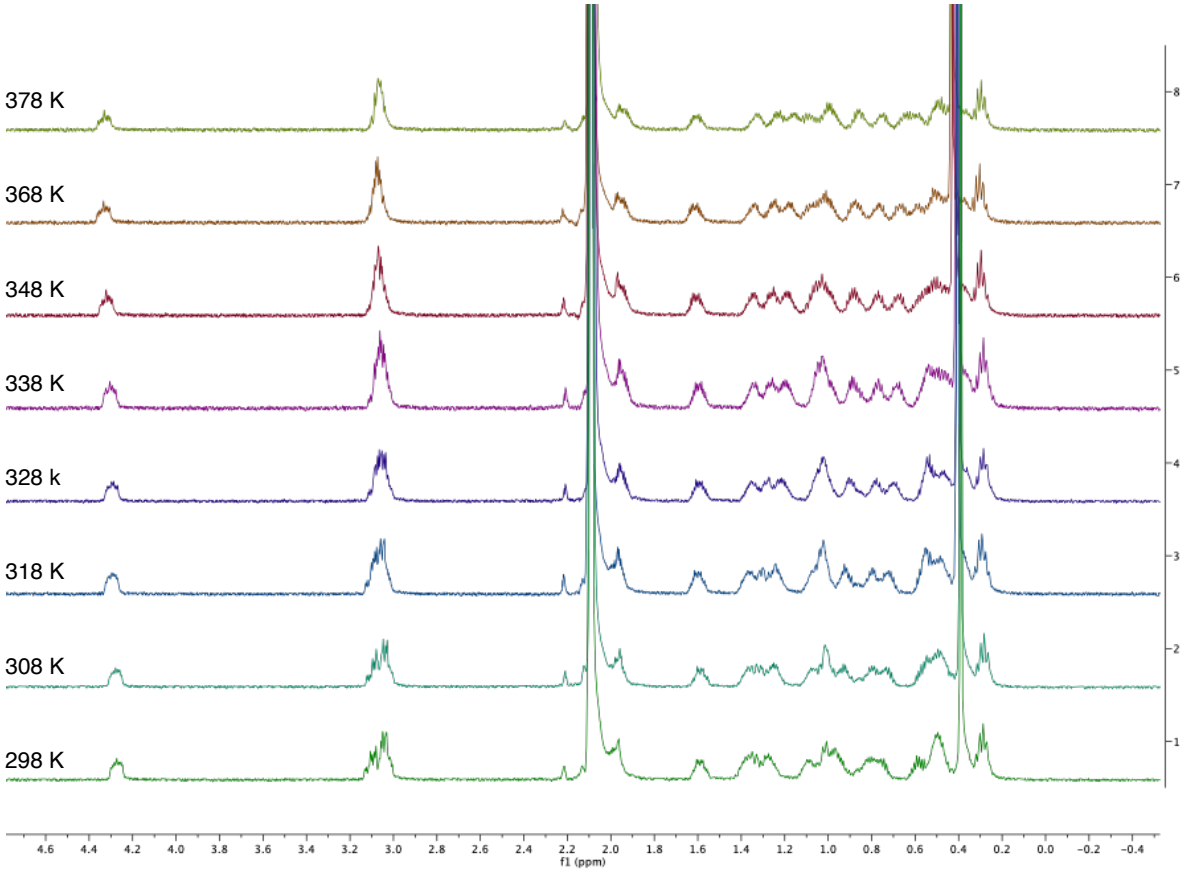


Figure 3.24 VT NMR of the aliphatic region of [11](2.6)peropyrenophane (**3.118d**).

The aliphatic region of the ^{1}H NMR spectrum of [12](2,6)peropyrenophane (**3.118e**) is quite different from the other [*n*](2,6)peropyrenophanes (**3.118b-d**). The broadening of the signals associated with the benzylic protons H_1 + H_2 and H_3 + H_4 (**Figure 3.25**) implies that the 12-carbon bridge is freely flipping in the NMR timescale. The 1H,1H-COSY spectrum still shows cross peaks associated with the resolved diastereotopic proton peaks.

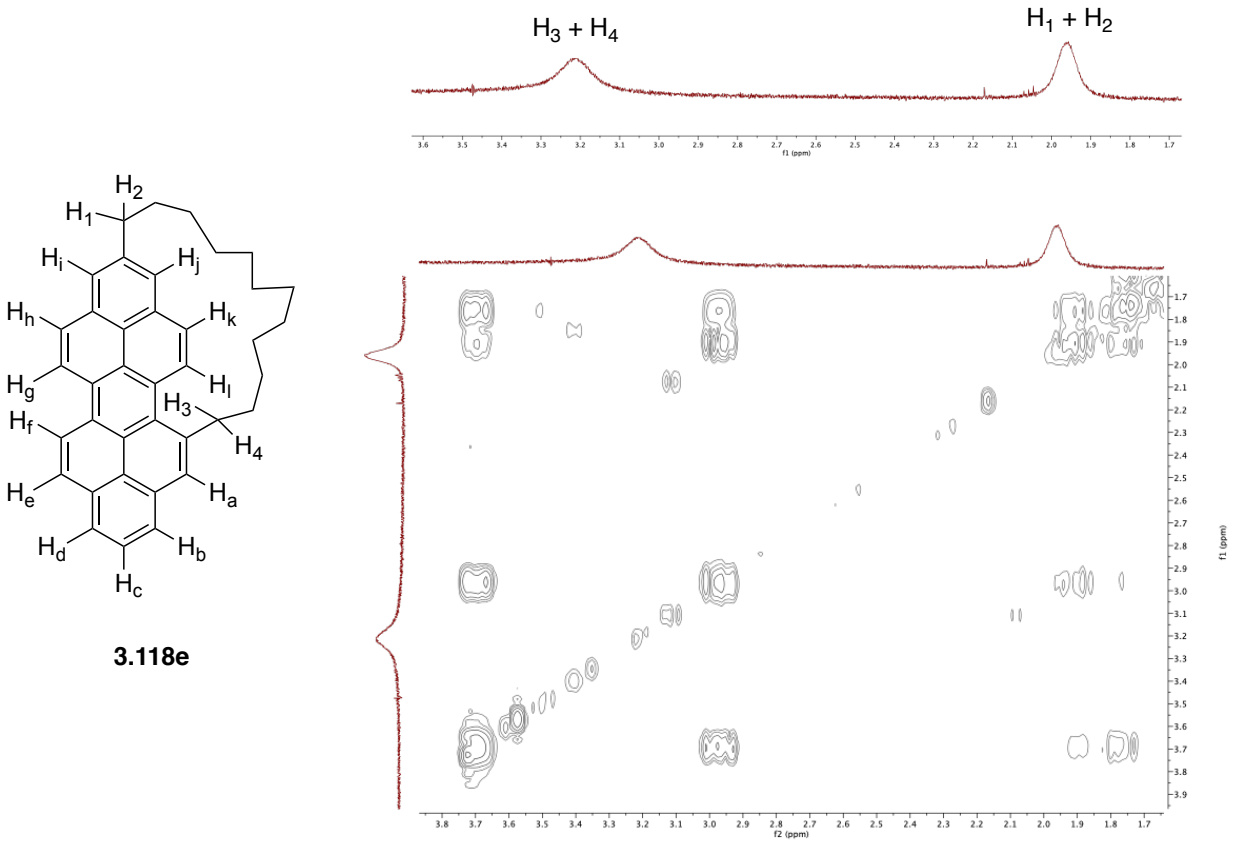
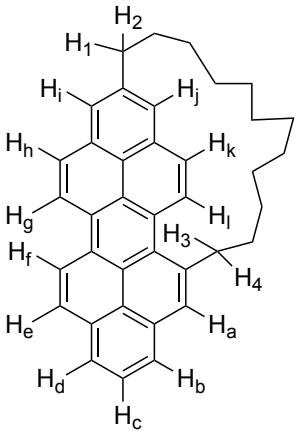


Figure 3.25 Labelled [12](2,6)peropyrenophane **3.118e** and benzylic protons.

The signals corresponding to the other methylene protons are also broadened (**Figure 3.26**). Additionally, none of the signals appear to be especially shielded suggesting that the bridge lies primarily beside the aromatic system instead of underneath it.



3.118e

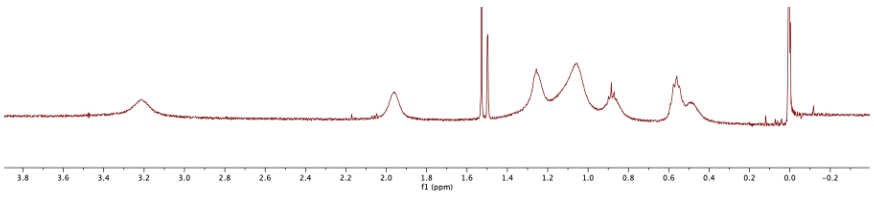


Figure 3.26 Bridge methylene protons of **3.188e**.

The aromatic region of [12](2,6)peropyrenophane (**3.118e**) is similar to that of the other [*n*](2,6)peropyrenophanes (**3.118b-d**) (**Figure 3.27**). Three *K*-region are present in the aromatic core. The first includes protons H_l (9.24 ppm, doublet, *J* = 9.4 Hz) (NOESY cross peak with H_3) coupled with H_k (8.20 ppm, doublet, *J* = 9.1 Hz) (COSY cross peak). The signal corresponding to H_j (8.14 ppm, narrow doublet, *J* = 1.0 Hz) was assigned by its NOESY cross peak to H_k, which allowed, based on process of elimination, H_i (8.20, narrow doublet, overlapped with H_k) to be assigned as the other narrow doublet based. The assignment of the other two *K*-region was not determined ambiguously, since the signals corresponding the protons H_e and H_f are perfectly overlapped (8.34 ppm, doublet, *J* = 9.2 Hz) and are coupled to both H_f and H_g by COSY cross peaks (9.20 ppm, doublet, *J* = 9.4 Hz and 9.18 ppm, doublet, *J* = 9.4 Hz) without the ability to further determine which signals corresponds to which proton. The only expected triplet arising from the aromatic core was assigned to H_c (8.08 ppm, triplet, *J* = 7.5 Hz) which allowed the assignment of H_b (8.29 ppm, doublet, *J* = 7.4 Hz) (NOESY cross peak to H_a) and H_d (8.24 ppm, doublet, *J* = 7.4 Hz) based on the observed COSY cross peaks.

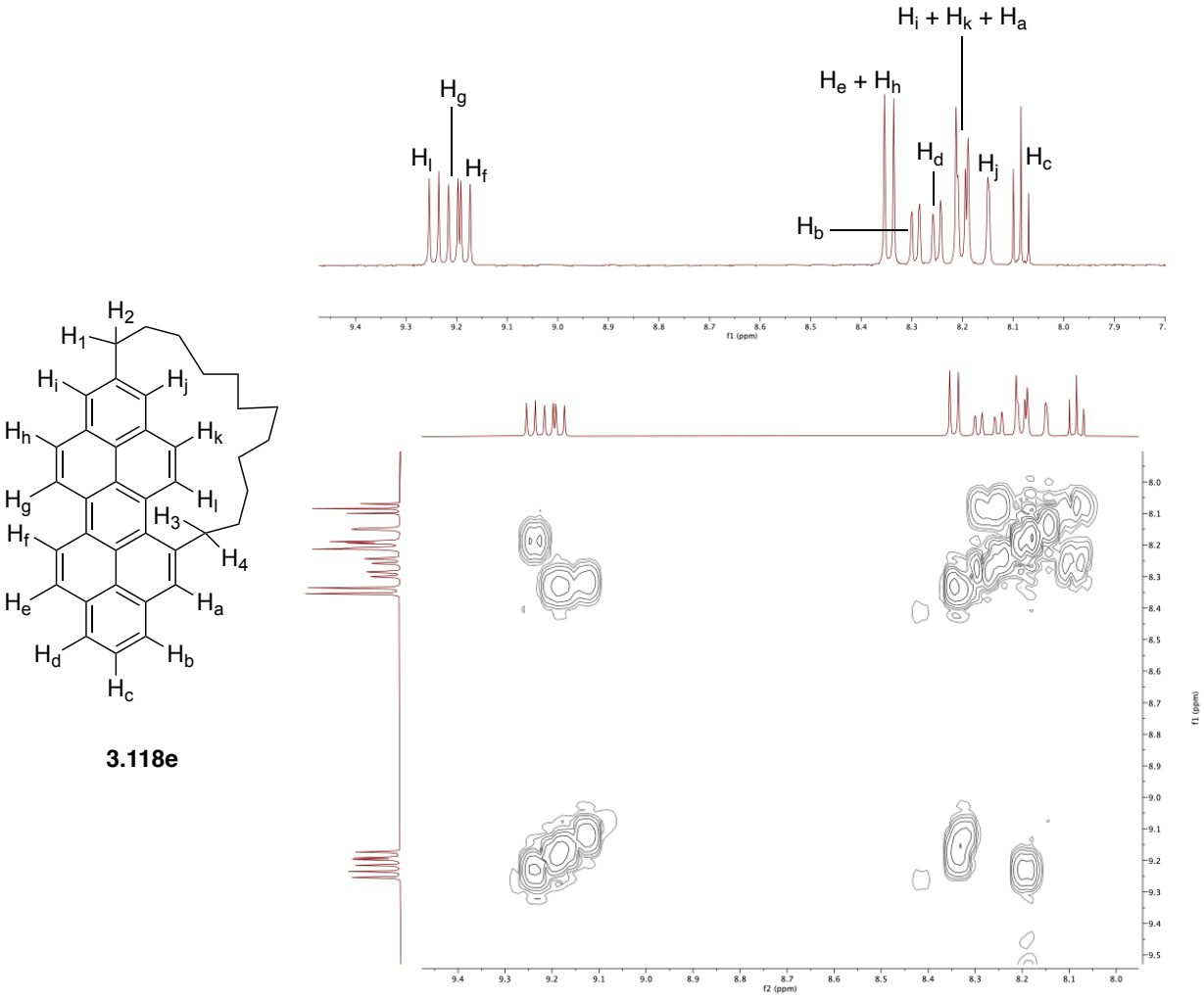


Figure 3.27 Aromatic ^{1}H NMR assignments for [12](2,6)peropyrenophane (**3.118e**).

Variable temperature ^{1}H NMR experiments were performed in tolune-d_8, both heating above 298 K to 338 K and cooling to 233 K (**Figure 3.28**). In toluene-d_8 all four benzylic protons appear as a broad singlet (3.08 ppm, integration 4H) at **298** K. Upon heating to 348 K it appears to split into two broad singlets (3.74 ppm and 3.08 ppm), which roughly integrate for 2H each. Upon cooling to 233 K four separate signals are observable each integrating for 1H either as a broad singlet or multiplet (4.32, 3.27, 3.01 and 2.92

ppm). The coalescence temperature of 273±10 K corresponds to an activation barrier for the bridge-flipping process of $\Delta G^{\ddagger}$ = 12.7±0.5 kcal/mol.

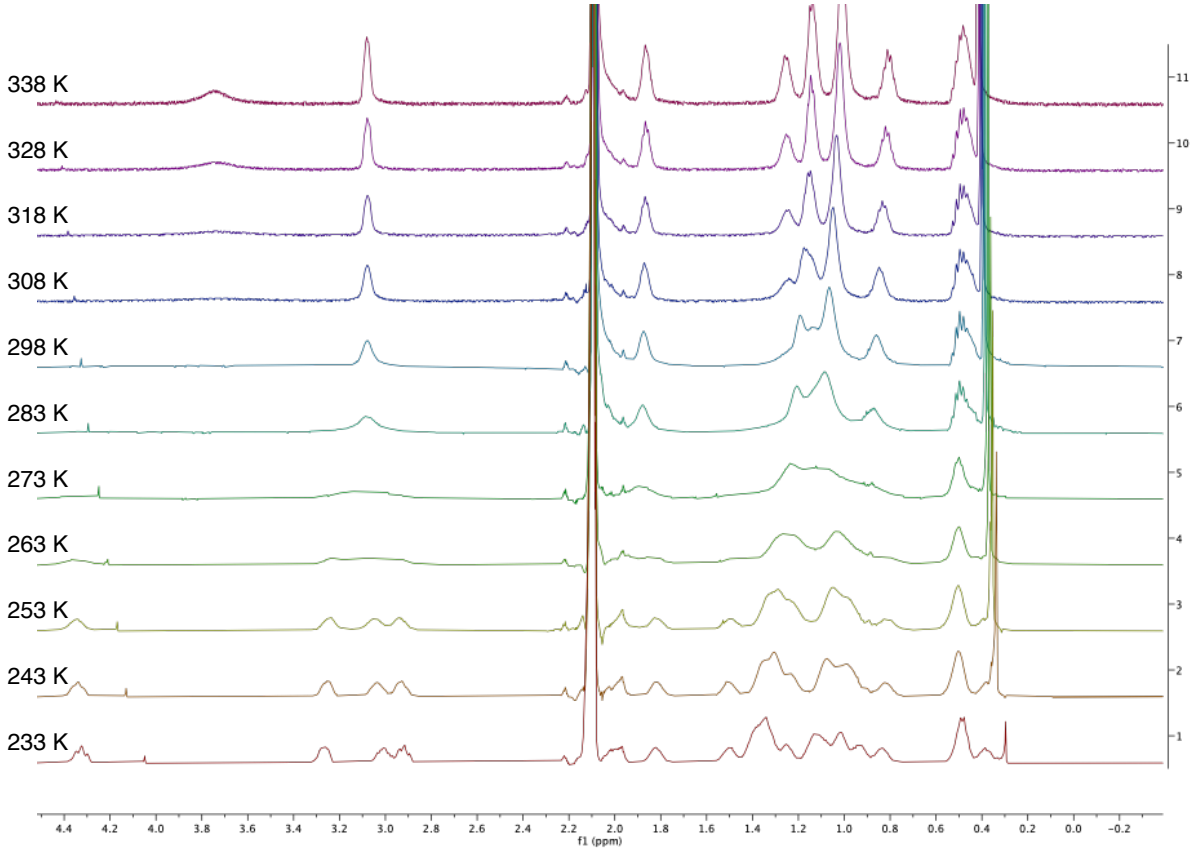


Figure 3.28 VT NMR of the aliphatic region of [12](2.6)peropyrenophane (**3.118e**).

It is interesting that the presence of only one additional methylene to the bridge in going from **3.118d** to **3.118e** has such substantial effect on the energy barrier to bridge mobility from being slow on the NMR time-scale at 378 K for [11](2,6)peropyrenophane (**3.118d**) to rapid bridge flipping at 298 K for [12](2,6)peropyrenophane (**3.118e**).

3.8.2: UV/Vis and Emission Spectroscopy of [*n*](2,6)Peropyrenophanes

The UV/Vis absorption spectra of the [*n*](2,6)peropyrenophane (**3.118b-e**) were measured in $CHCl_3$ (10^{-5} M). There is a very slight blue shift in the λ_{max} as the bridge is

lengthed (**Figure 3.29** and **Table 3.1**). The λ_{max} values for the peropyrenophanes are slight red-shifted in comparison to those of peropyrenene (444 nm) and 2,7-dialkylperopyrenes (447 nm), albeit these were measured in chlorobenzene.

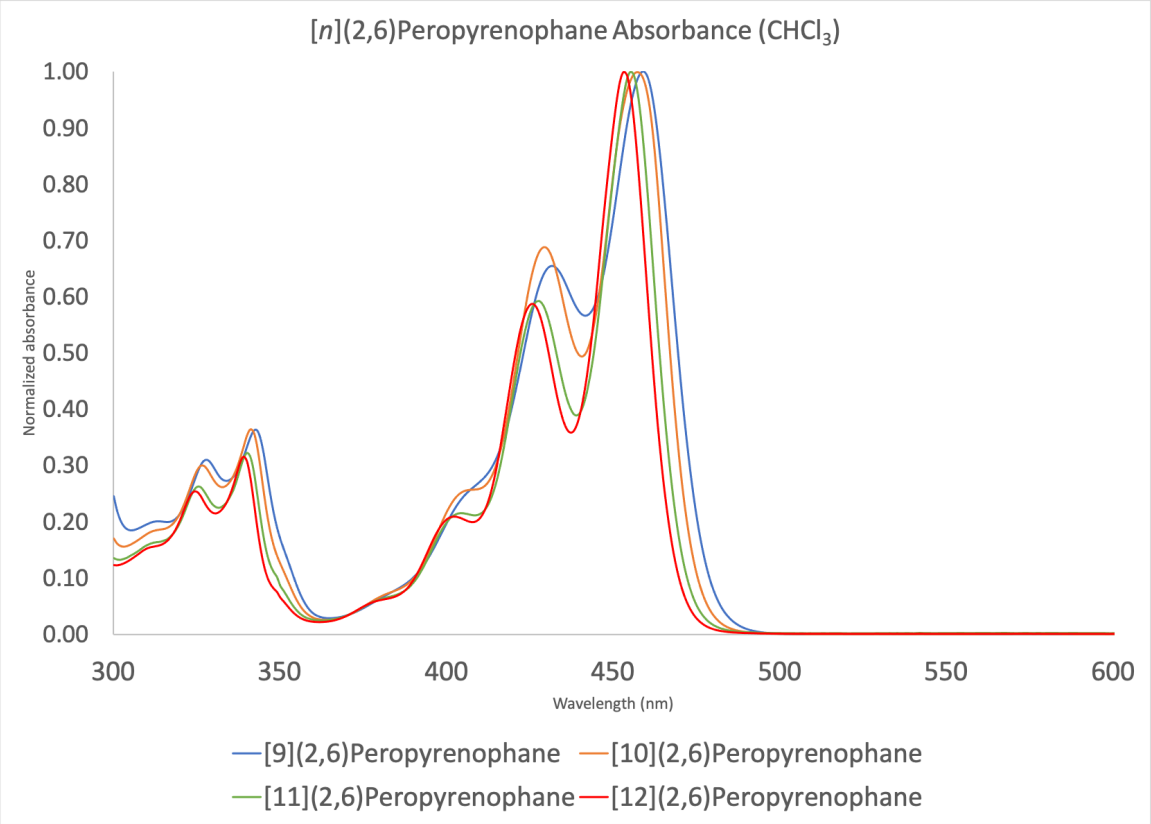


Figure 3.29 UV/Vis absorption spectra of [*n*](2,6)peropyrenophane **3.118b-e**.

The emission spectra of [*n*](2,6)peropyrenophanes (**3.118b-e**), measured in $CHCl_3$, are less structured then those observed for peropyrene and 2,7-dialkylperopyrenes, which are near-perfect mirror images the absorption spectra. An interesting trend is observed going from 9- (482 nm), to 10- (480 nm), to 11-atom bridged systems (473 nm) whereby a blue shift of the emission maximum is oberserved, whereas the 12-atom bridged system (486 nm) is red-shifted in relation to all other peropyrenophanes (**Figure 3.30**). This phenomenon results in variable Stokes shifts (**Table 3.1**)

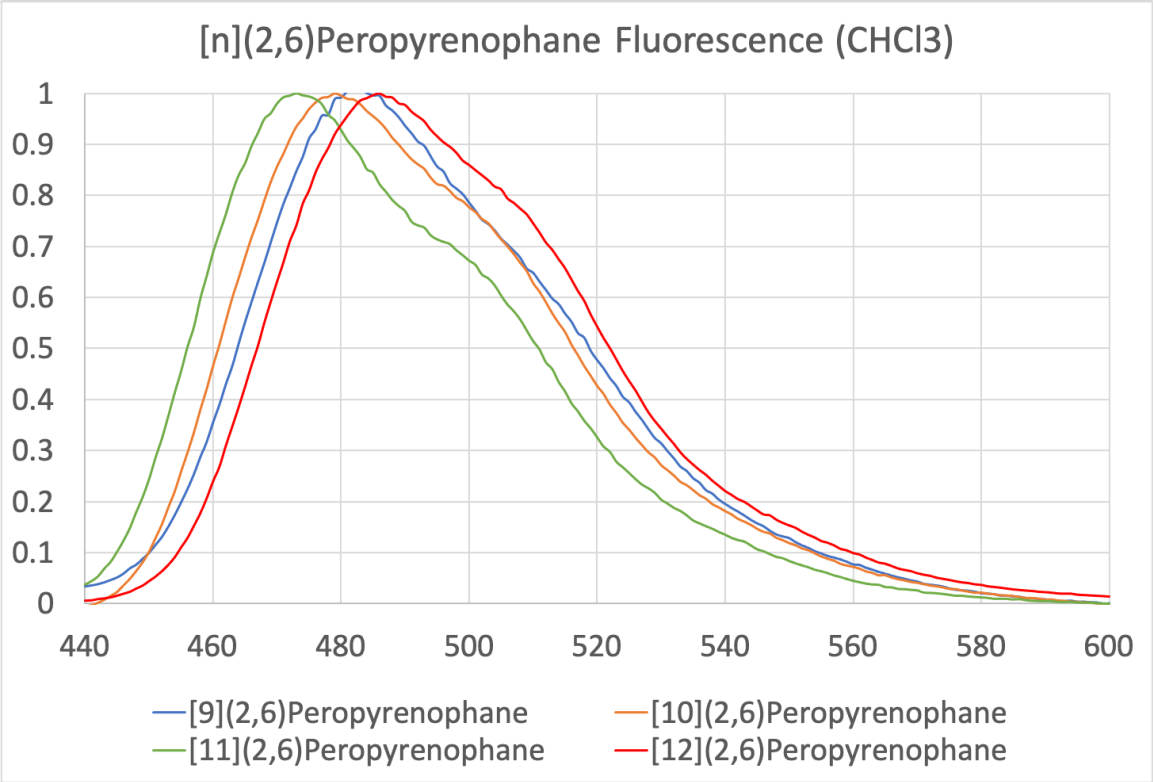


Figure 3.30 Fluorescence spectra of [*n*](2,6)peropyrenophane **3.118b-e**.

	λ_{max} (absorption) ($CHCl_3$)	**λ_{max} (emission) (excitation 400 nm) ($CHCl_3$)**	**Stokes shift (cm^{-1})**
[9](2,6)Peropyrenophane	459 nm 433 nm (second max)	482 nm	1040
[10](2,6)Peropyrenophane	458 nm 430 (second peak)	480 nm	1001
[11](2,6)Peropyrenophane	456 nm 428 nm (second peak)	473 nm	788

[12](2,6)Peropyrenophane	454 nm 427 (second peak)	486 nm	1450

Table 3.1 Tabulated absorption and emission data of [*n*](2,6)peropyrenophanes (**3.118b-e**).

A hope at the beginning of this work was that any peropyrenophanes synthesized would be potential singlet fission materials. Alkyl group functionalization at the 2- and 7-positions did little to perturb the HOMO-LUMO energies from the parent peropyrene based on Kubo's work. Unfortunately, based on calculations performed by the Kubo group in collaboration (and outside the scope of this thesis) our systems do not appear to exhibit singlet fission.

3.8.3: X-Ray Crystal Structures of [9](2,6)Peropyrenophane and [10](2,6)Peropyrenophane

Crystals suitable for X-ray diffraction (XRD) analysis of [9](2,6)peropyrenophane (**3.118b**) and [10](2,6)peropyrenophane (**3.118c**) were grown from slow evaporation of heptane solutions. The asymmetric unit of [9](2,6)peropyrenophane (**3.118b**) consists of a single molecule (**Figure 3.31a**), in which the peropyrene unit displays an end-to-end twist of 27.1° based on the angle between the planes created by the two phenalene units. The torsion angles around the central ring system are tabulated (**Table 3.2**). The distortion around the central ring is larger on the side closest to the bridgehead and less pronounced on the other side. The torsional angles are similar those reported by Chalifoux (18°) mentioned previously (**Scheme 3.5**). The C-C bond lengths are not significantly different from those of 2,9-dibutylperopyrene (**3.78a**) based on an analysis of bond types and their averages (**Table 3.4**).[9] The packed unit cell (**Figure 3.31d**) contains four molecule, two of each configuration. Close C(sp^2)-H$\cdots\pi$ contacts are observed

between molecule of the same configuration and π···π interactions are observed between molecule of opposite configuration.

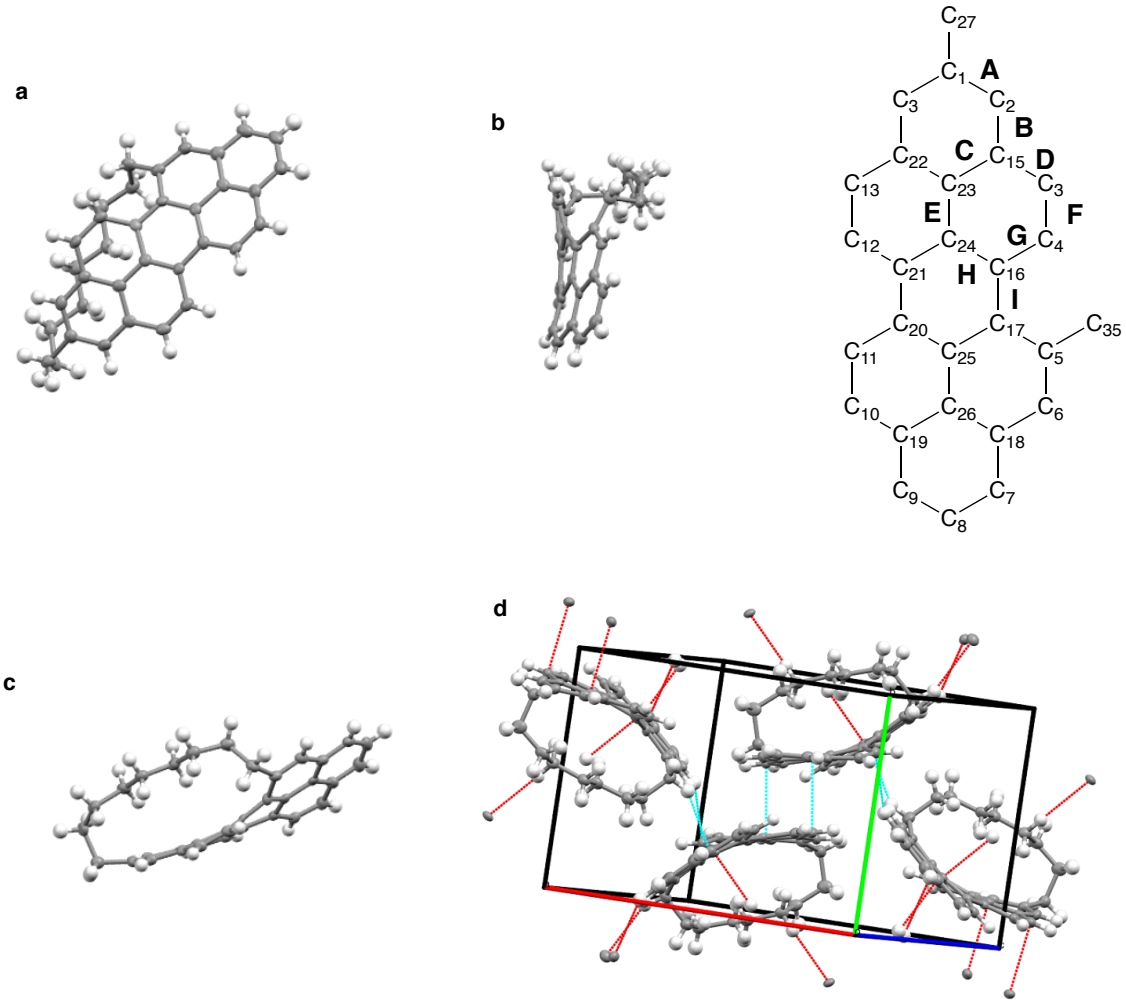
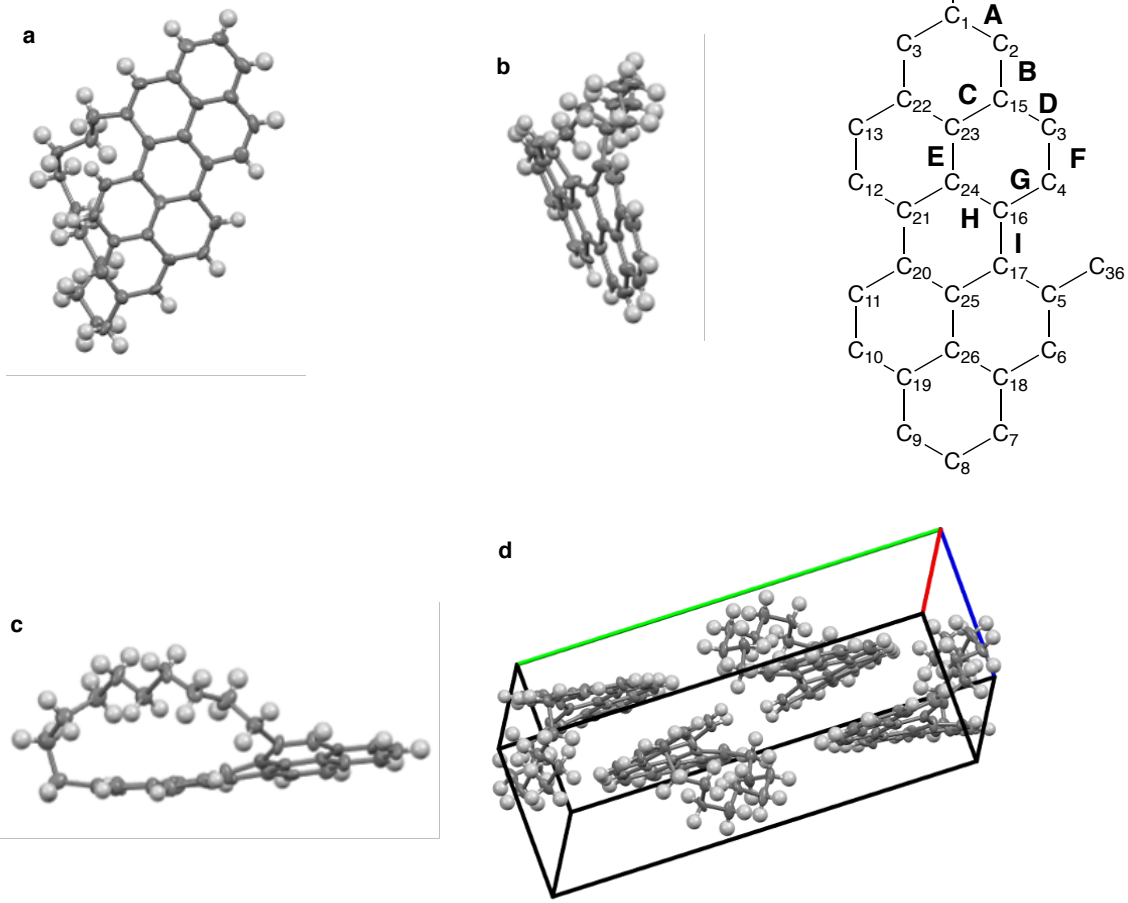


Figure 3.31 X-ray crystal structure of [9](2,6)peropyrenophane (**3.118b**).

Unit	Torsion Angle (°)
C_{11}-C_{20}-C_{21}-C_{12}	16.16
C_{25}-C_{20}-C_{21}-C_{24}	15.71
C_{25}-C_{17}-C_{16}-C_{24}	21.39
C_5-C_{17}-C_{16}-C_4	28.48

Table 3.2 Torsional angles of the central ring in [9](2,6)peropyrenophane (**3.118b**).

The asymmetric unit of [10](2,6)peropyrenophane (**3.118c**) consists of a single molecule (**Figure 3.32a**) in which the peropyrene unit displays an end-to-end twist of 12.8° based on the angle between the planes created by the two phenalene units. The torsion angles around the central ring system are tabulated (**Table 3.3**). The distortion around the central ring is larger on the side closest to the bridgehead and less pronounced on the other side. The C-C bonds lengths (**Table 3.4**) are in general longer than what was observed for [9](2,6)peropyrenophane (**3.118b**), however, this likely a consequence of lower quality data as a result of the poorly diffracting crystal. The packed unit cell (**Figure 3.32d**) contains four molecule, two of each configuration. Close C(sp^2)-H···π contacts are



observed between molecule of the same configuration and π···π interactions are observed between molecule of opposite configuration.

Figure 3.32 X-ray crystal structure of [10](2,6)peropyrenophane (**3.118c**).

Unit	Torsion Angle (°)
C_{11}-C_{20}-C_{21}-C_{12}	7.75
C_{25}-C_{20}-C_{21}-C_{24}	5.00
C_{25}-C_{17}-C_{16}-C_{24}	19.23
C_5-C_{17}-C_{16}-C_4	16.40

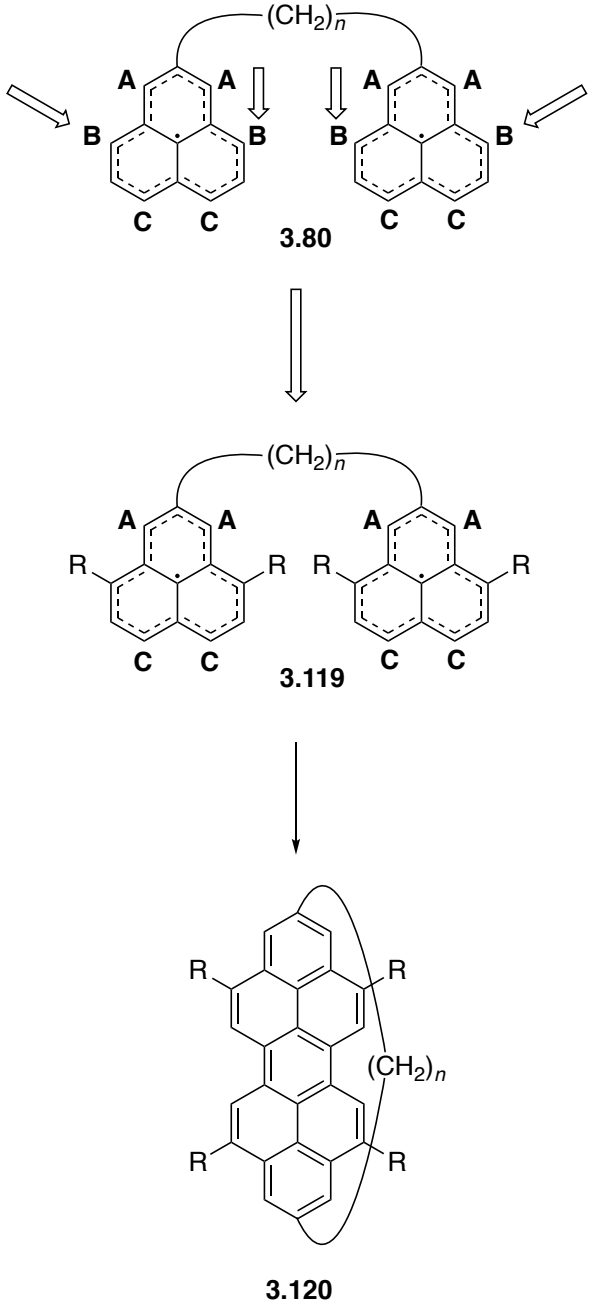
Table 3.3 Torsional angles of the central ring in [10](2,6)peropyrenophane (**3.118c**).

Bond type	Bond length range (average) (Å)		
	[9](2,6)peropyrenophane (**3.118b**)	[10](2,6)peropyrenophane (**3.118c**)	2,9-dibutylperopyrene (**3.21a**)
A	1.363-1.394 (1.380)	1.426-1.448 (1.437)	1.388-1.391 (1.390)
B	1.383-1.402 (1.394)	1.408-1.419 (1.415)	1.398-1.401 (1.400)
C	1.404-1.442 (1.422)	1.444-1.460 (1.451)	1.419-1.421 (1.420)
D	1.403-1.437 (1.425)	1.449-1.476 (1.462)	1.431-1.433 (1.432)
E	1.432-1.445 (1.439)	1.454-1.459 (1.457)	1.432 (1.432)
F	1.342-1.360 (1.353)	1.367-1.395 (1.380)	1.351-1.353 (1.352)
G	1.432-1.461 (1.444)	1.463-1.512 (1.472)	1.438 (1.438)
H	1.401-1.447 (1.415)	1.464-1.506 (1.483)	1.425-1.427 (1.426)
I	1.415-1.415 (1.415)	1.437-1.442 (1.440)	1.421 (1.421)

Table 3.4 Bond lengths in [9](2,6)peropyrenophane (**3.118b**), [10](2,6)peropyrenophane (**3.118c**) and 2,9-dibutylperopyrene (**3.21a**).

3.9: Progress Towards an [*n*](2,9)Peropyrenophane

At the outset, our goal was to create a series of [*n*](2,9)peropyrenophanes, which is one of the possible outcomes outlined in **Scheme 3.21**. When oxidative phenalene homofusion reactions were performed, only [*n*](2,6)peropyrenophanes were isolated. Still desiring access to peropyrenophanes with a 2,9-substitution pattern, it was theorized that blocking the "**b**" sites of tethered phenalenyl radical **3.80** with appropriate substituents, as in **3.119**, would block every other type of dimerization and thereby force the system to ultimately funnel towards the [*n*](2,9)peropyrenophane motif (**3.120**) (**Scheme 3.35**).

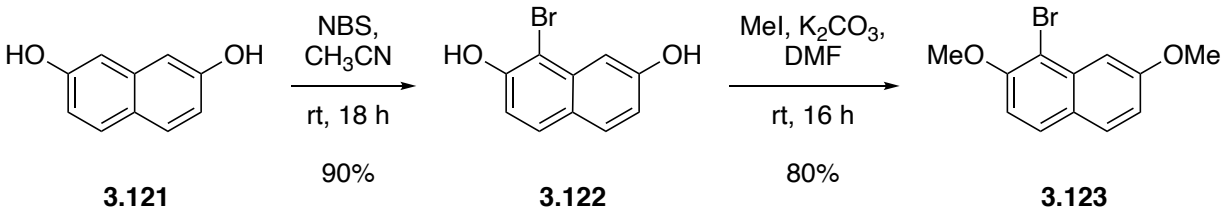


Scheme 3.35 Blocking approach to [*n*](2,9)peropyrenophane **3.120**.

The choice of blocking group was reliant on two factors: the ease with which it could be introduced synthetically their influence on the stability of the phenalenyl radicals that would be generated. Three options were considered, i.e. R = Me, Br, and OMe. The

latter was chosen due to its ability to stabilize radicals and (unlike Me and Br) its inertness in the presence of radicals.[8]

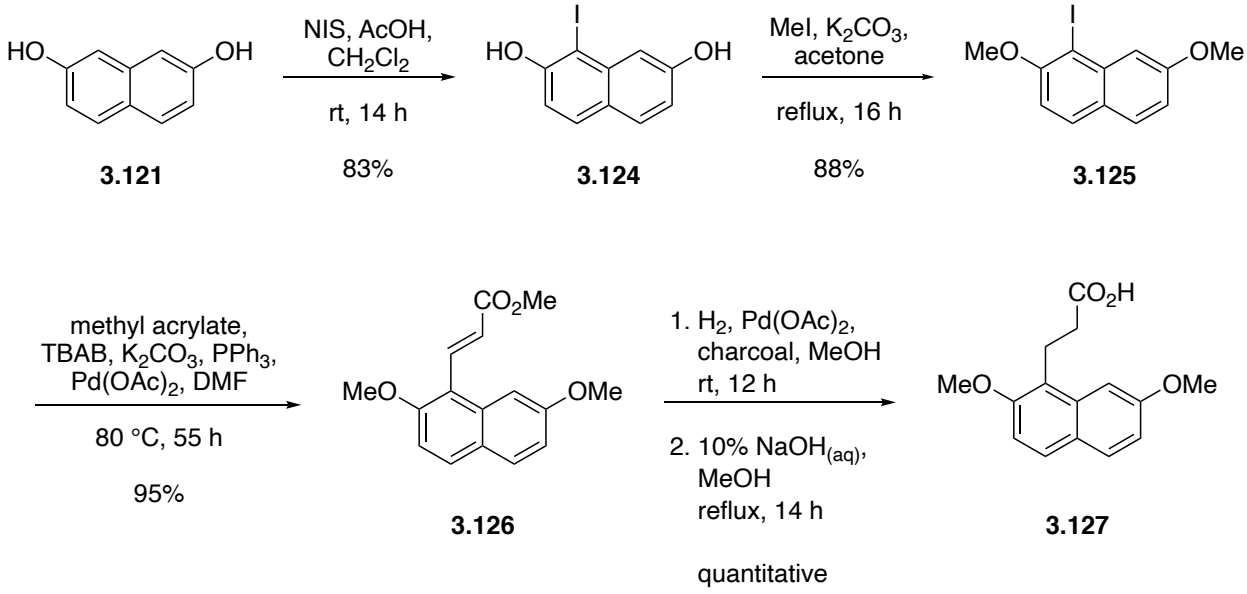
Synthetic access to methoxy substituted systems began with 2,7-dihydroxynaphthtalene (**2.121**), which was readily brominated at the 1-position to give 1-bromo-2,7-dihydroxynaphthalene (**2.122**) in 90% yield (**Scheme 3.36**). This bromide was then methylated to give 1-bromo-2,7-dimethoxynaphthalene (**2.123**) in 80% yield.



3.121 **3.122** **3.123**

Scheme 3.36 Synthesis of **3.123**.

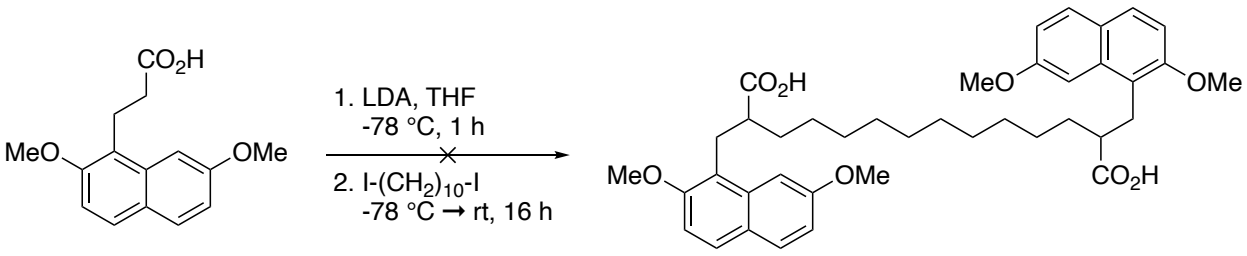
Following a synthetic pathway similar to the one outlined in **Scheme 3.22** above, a Heck coupling of bromide **3.123** with methyl acrylate was attempted, but with no success. Only unreacted starting material was recovered from the reaction mixture. Replacing the bromide with an iodide was accomplished by the reaction of diol **3.121** with NIS using a procedure similar to the previous one using NBS. This afforded iodide **3.124** in 83% yield (**Scheme 3.37**). *O*-Methylation then furnished iodide **3.125** in 88% yields. This system successfully underwent Heck coupling with methyl acrylate under strict oxygen-free conditions to give α,β-unsaturated ester **3.126** in 95% yield. The olefin was hydrogenated under the previously discussed *in situ* generation of Pd/C and then converted to the corresponding acid **3.127** by saponification in quantitative yield over two steps.



3.121 **3.124** **3.125** **3.126** **3.127**

Scheme 3.37 Synthesis of acid **3.127**.

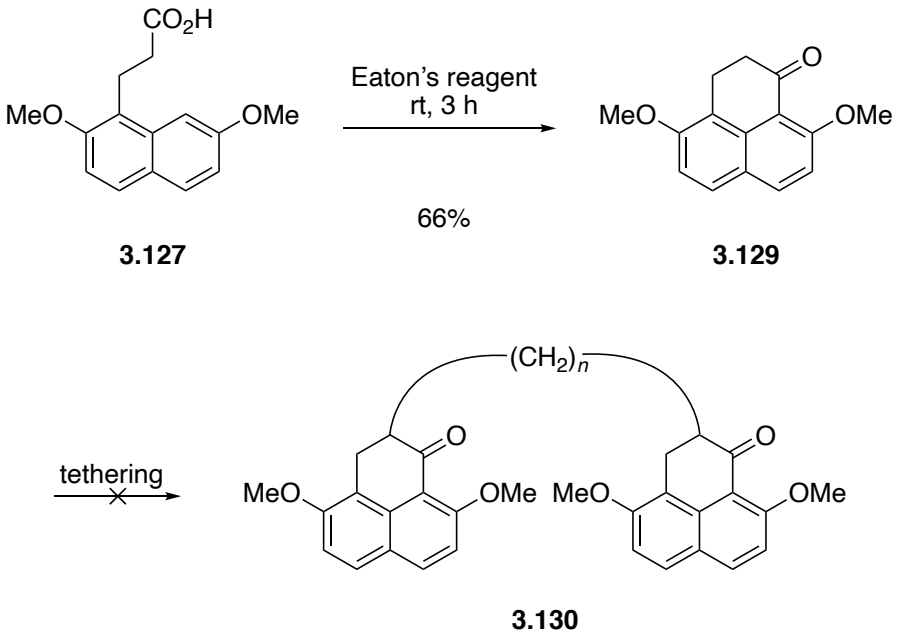
Attempts at tethering acid **3.127** using the same strategy as the parent system, namely enolization and alkylation, was unsuccessful in this case with only recovery of unreacted starting material (**Scheme 3.38**). Even when an excess of LDA was employed (3 equiv.) no product was obtained.



3.127 **3.128**

Scheme 3.38 Failed tethering of acid **3.127.**

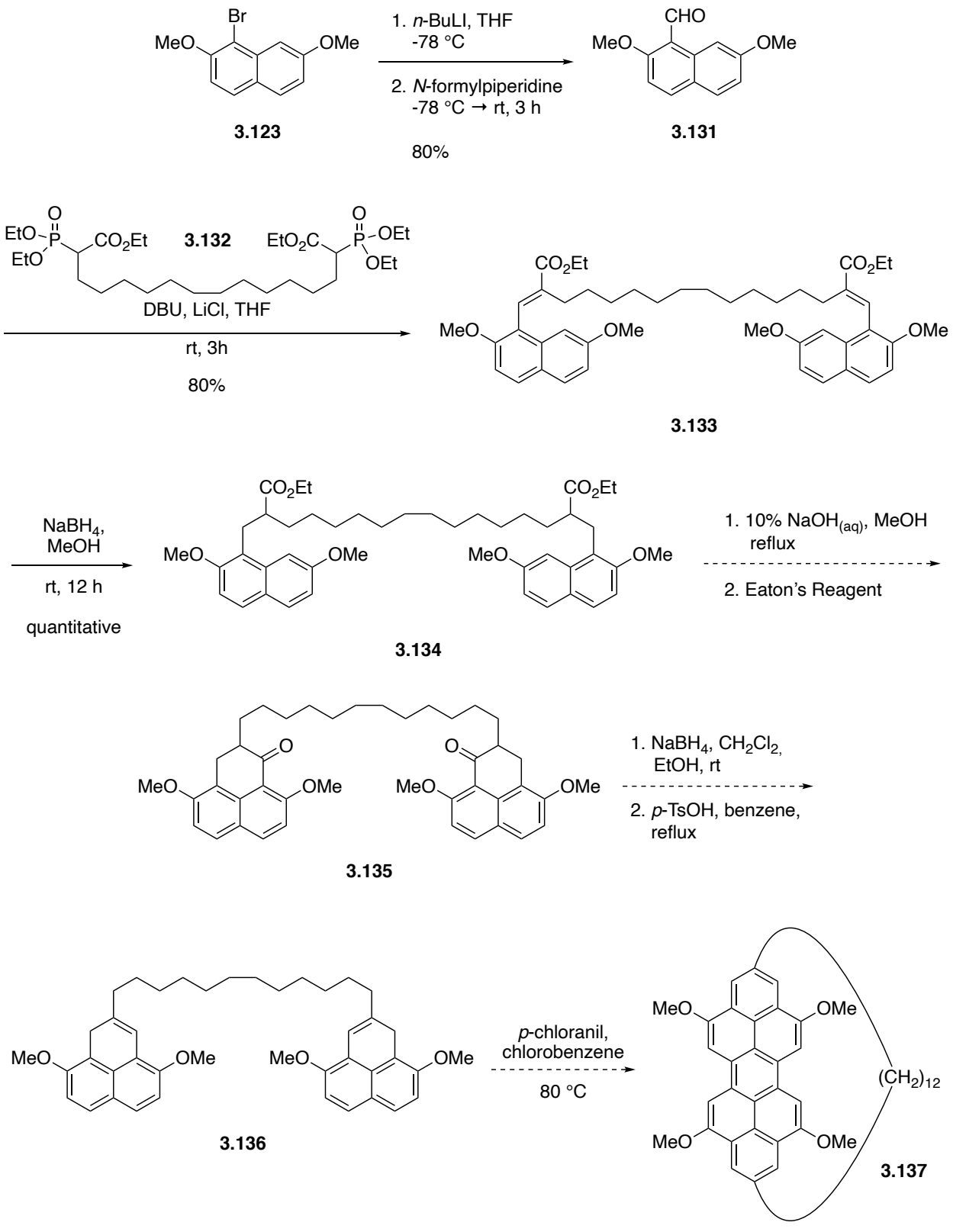
An attempt to convert acid **3.127** into phenalenone **3.129** via the corresponding acid chloride failed. The starting material was consumed, but only intractable material was formed. Replacement of $AlCl_3$ with the powerfully dehydrating Eaton's reagent (7.7 wt% P_2O_5 in methansulfonic acid) promoted cyclization to give phenalenone derivative **3.130** in 66% yield (**Scheme 3.39**). Attempts to tether phenalenone **3.129** by treatment with LDA then diiodoalkanes failed to produce any of the desired tethered diphenalenone **3.130**. This attempt was, admittedly, a longshot form the outset.



Scheme 3.39 Cyclization of acid **3.127** and failed tethering reaction.

It became quickly obvious that a different route would need to be investigated en route to a 2,9-substituted peropyrenophane. A different tethering strategy utilizing Horner-Wadsworth-Emmons chemistry, was therefore investigated. The previously synthesized 1-bromo-2,7-dimethoxynaphthalelene (**3.123**) was converted into the corresponding aldehyde **3.131** by lithium-halogen exchange followed by quenching with *N*-formylpiperidine in 80% yield (**Scheme 3.40**). Two equivalents of aldehyde **3.131** were reacted with 12-carbon tethered bis(triethylphosphonoacetate) **3.132** under Masamune-

Roush conditions to afford the tethered bis(α,β-unsaturated ester) **3.133** in 80% yield.[32] The most effective strategy for reduction of the olefins was by conjugate reduction with $NaBH_4$, which gave hydrogenated diester **3.134** quatitatively. This is the final stage that was completed during this program, however, the required transformations are also outline in **Scheme 3.40**. Firstly, saponification of the ester to the corresponding acids followed by cyclization with Eaton's reagent, based on what was learned during the cyclization of the untethered system. With the phenalenone system **3.135**, the next steps would be performed in the same fashion as the parent system above. Reduction of the ketone functionalities to alcohols followed by *p*-TsOH catalyzed dehydration to give phenalene system **3.136.** Subjection of this compound to the oxidative phenalene homofusion reaction would then hopefully afford (2,9)peropyrenophane **3.137**.



Scheme 3.40 Progress towards a 2,9-substituted peropyrenophane.

A potential added benefit to synthesizing a functionalized [*n*](2,9)peropyrenophane is the possibility of manipulating the functional groups in such a way as to enable the pi extension of the pereopyrene system.

3.10: Conclusions

A series of [*n*](2,6)peropyrenophanes (**3.118b-e**) was successfully synthesized and characterized. In an effort to gain access to [*n*](2,9)peropyrenophanes, progress was made towards the synthesis of fourfold functionalized (2,9)peropyrenophanes.

3.11: References

(1) Unikela, K. S.; Merner, B. L.; Ghasemabadi, P. G.; Warford, C. C.; Qiu, C. S.; Dawe, L. N.; Zhao, Y.; Bodwell, G. J. The Development of Synthetic Routes to 1,1,n,n-Tetramethyl[n](2,11)teropyrenophanes. *Eur. J. Org. Chem.* **2019**, 4546–4560.

(2) Clar, E. Aromatic hydrocarbons and their derivatives. XXXIX. Investigations of the fine structure of anthanthrene and its benzologs by the anellation process. *Ber. Dtsch. Chem. Ges.* **1943**, 328-333.

(3) Wenzel, U.; Löhmannsröben, H.-G. Photophysical and fluorescence quenching properties of peropyrene in solution. *J. Photochem. Photobiol. A* **1996**, *96*, 13–18.

(4) Nichols, V. M.; Rodriguez, M. T.; Piland, G. B.; Tham, P.; Nesterov, V. N.; Youngblood, W. J.; Bardeen, C. J. Assessing the Potential of Peropyrene as a Singlet Fission Material: Photophysical Properties in Solution and the Solid State. *J. Phys. Chem. C* **2013**, *117*, 16802–16810.

(5) Smith, M. B.; Michl, J. Singlet Fission. *Chem. Rev.* **2010**, *110*, 6891–6936.

(6) Rao, A.; Friend, R. H. Harnessing singlet exciton fission to break the Shockley–Queisser limit. *Nat. Rev. Mater.* **2017**, 17063.

(7) Pogodin, S.; Agranat, I. Large PAHs by Reductive *Peri-Peri* "Dimerization" of Phenalenones. *Org. Lett.* **1999**, *31*, 1387-1390.

(8) Umemoto, T.; Kawashima, T.; Sakata, Y.; Misumi, S. Layered Compounds. XXV. Peropyrene and Teropyrene - A New Synthetic Route of Pyrene-like Polynuclear Aromatic Hydrocarbons. *Tetrahedron Lett.* **1975**, *12*, 1005–1006.

(9) Beer, L.; Mandal, S. K.; Reed, R. W.; Oakley, R. T; Tham, F. S.; Donnadieu, B.; Haddon, R. C. The First Electronically Stabilized Phenalenyl Radical: Effect of Substituents on Solution Chemistry and Solid-State Structure. *Cryst. Growth. Des.* **2007**, *7*, 802–809.

(10) Uchida, K.; Ito, S.; Nakano, M., Abe, M.; Kubo, T. Biphenalenylidene: Isolation and Characterization of the Reactive Intermediate on the Decomposition Pathway of Phenalenyl Radical. *J. Am. Chem. Soc.* **2016**, *138*, 2399–2410.

(11) Uchida, K.; Kubo, T.; Yamanaka, D.; Furube, A.; Matsuzaki, H.; Nishii, R.; Sakagami, Y.; Abulikemu, A.; Kamada, K. Synthesis, crystal structure, and photophysical properties of 2,9-disubstituted peropyrene derivatives. *Can. J. Chem.* **2017**, *95*, 432–444.

(12) Yang, W.; Monteiro, J. H. S. K.; de Bettencourt-Dias, A.; Catalano, V. J.; Chalifoux, W. A. Pyrenes, Peropyrenes, and Teropyrenes: Synthesis, Structures, and Photophysical Properties. *Angew. Chem. Int. Ed.* **2016**, *55*, 10427–10430.

(13) Yang, W.; Longhi, G.; Abbate, S.; Lucotti, A.; Tommasini, M.; Villani, C.; Catalano, V. J.; Lykhin, S. A.; Varganov, S. A.; Chalifoux, W. A. Chiral Peropyrene: Synthesis, Structure, and Properties. *J. Am. Chem. Soc.* **2017,** *139*, 13102–13109.

(14) Yang, W.; Monteiro, J. H. S. K.; de Bettencourt-Dias, A.; Chalifoux, W. A. New thiophene-functionalized pyrene, peropyrene, and teropyrene via a two- or four-fold alkyne annulation and their photophysical properties. *Can. J. Chem.* **2017**, *95*, 341–345.

(15) Yang, W.; Kazemi, R. R.; Karunathilake, N.; Catalano, V. J.; Alpuche-Aviles, M. A.; Chalifoux, W. A. Expanding the scope of peropyrenes and teropyrenes through a facile $InCl_3$-catalyzed multifold alkyne benzannulation. *Org. Chem. Front.* **2018**, *5*, 2288–2295.

(16) Martínez-Abadía, M.; Antonicelli, G.; Saeki, A.; Mateo-Alonso, A. Readily Processable Hole-Transporting Peropyrene Gels. *Angew. Chem. Int. Ed.* **2018**, *57*, 8209–8213.

(17) Martínez-Abadía, M.; Antonicelli, G., Saeki, A.; Melle-Franco, M.; Mateo-Alonso, A. Isolation and Characterization of the Unexpected 1-n-Octyloxyperopyrene: A Solution-Processable p-Type Organic Semiconductor. *J. Org. Chem.* **2019**, *84*, 3270–3274.

(18) Reid, D. H. The chemistry of the phenalenes. *Q. Rev. Chem. Soc.* **1965**, *19*, 274-302.

(19) Boekelheide, V.; Larrabee, C. E. An Investigation of the Preparation and Some Properties of Perinaphthene. *J. Am. Chem. Soc.* **1950**, *72*, 1245–1249.

(20) Stafford, W. Condensation of β-dicarbonyl compounds with *o*-phenylenediamine. *Chem. Ind.* **1956**, 765–766.

(21) Reid, D. H. Stable π-electron systems and new aromatic structures. *Tetrahedron* **1958**, *3*, 339–352.

(22) Bausch, M. J.; Guadalupe-Fasano, C.; Jirka, G.; Peterson, B.; Selmarten, D. Examinations of Dimethyl Sulfoxide-Phase Equilibrium Acidities of Selected Polycyclic Aromatic Compounds. *Polycycl. Aromat. Cmpd.* **2006**, *2*, 19–27.

(23) Pettit, R. Synthesis of the perinaphthindenylium cation. *Chem. Ind.* **1956**, 1306–1307.

(24) Reid, D. H.; Sutherland, R. G. 613. Hydride ions in organic reactions. Part II. Preparation of phenalenium salts by the reaction of phenalenes with quinones in the presence of acids. *J. Chem. Soc.* **1963**, 3295-3308.

(25) O'Connor, G. D.; Troy, T. P.; Roberts, D. A.; Chalayavi, N; Fückel, B. Spectroscopy of the Free Phenalenyl Radical. *J. Am. Chem. Soc.* **2011**, *133*, 14554–14557.

(26) Goto, K.; Kubo, T.; Yamamoto, K.; Nakasuji, K.; Sato, K. A Stable Neutral Hydrocarbon Radical: Synthesis, Crystal Structure, and Physical Properties of 2,5,8-Tri-tert-butyl-phenalenyl. *J. Am. Chem. Soc.* **1999**, *121*, 1619–1620.

(27) Zaitsev, V., Rosokha, S. V., Head-Gordon, M.; Kochi, J. K. Steric Modulations in the Reversible Dimerizations of Phenalenyl Radicals via Unusually Weak Carbon-Centered π- and σ-Bonds. *J. Org. Chem.* **2006**, *71*, 520–526.

(28) Felpin, F. X.; Fouquet, E. A Useful, Reliable and Safer Protocol for Hydrogenation and the Hydrogenolysis of *O*-Benzyl Groups: The In Situ Preparation of an Active Pd^0/C Catalyst with Well-Defined Properties. *Chem. Eur. J.* **2010,** *16*, 12440-12445.

(29) Hempenius, M. A.; Heinen, W.; Mulder, P. P. J.; Erkelens, C.; Zuilhof, H.; Lugtenburg, J.; Cornelisse, J. Spectrometry and Reactivity of Phenalenyl Anions. *J. Phys. Org. Chem.* **1994,** *7*, 296-302.

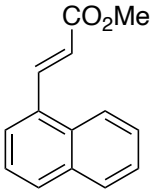
(30) Scott, R. P. W. The Silica-Gel Surface and its Interactions with Solvent and Solute in Liquid Chromatography. *Faraday Symp. Chem. Soc.* **1980,** *15*, 49-68.

(31) Boudjouk, P.; Johnson, P. D. Improved Routes to Phenalene and Phenalanone. Alane, Borane, and Silane Reductions of Phenalenone. *J. Org. Chem.* **1978,** *43*, 3979-3980.

(31) Blanchette, M. A.; Choy, W.; Davis, J. T.; Essenfeld, A. P.; Masamune, S.; Roush, W. R.; Sakai, T. Horner-Wadsworth-Emmons Reaction: Use of Lithium Chloride and An Amine For Base-Sensitive Compounds. *Tetrahedron Lett.* **1984,** *25*, 2183-2186.

3.12: Experimental Procedures and Characterization Data

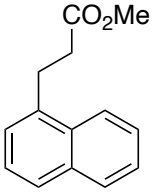
(*2E*)-3-(1-Naphthalenyl)-2-propenoic acid methyl ester (3.95)



3.95

A mixture of 1-bromonaphthalene (**3.95**) (3.40 mL, 5.00 g, 24.4 mmol), K_2CO_3 (6.80 g, 48.9 mmol), TBAB (19.7 g, 61.1 mmol), methyl acrylate (10.4 g, 10.9 mL, 121 mmol) and CH_3CN (100 mL) was purged with N_2 for 5 min. PPh_3 (989 mg, 4.89 mmol) and $Pd(OAc)_2$ (550 mg, 2.45) were then added and the resulting reaction mixture was heated at reflux under a N_2 atmosphere for 16 h. The reaction mixture was cooled to rt and concentrated under reduced pressure. The resulting residue was subjected to column chromatography (20% CH_2Cl_2/hexanes) to yield (*2E*)-3-(1-naphthalenyl)-2-propenoic acid methyl ester (**3.95**) (4.60 g, 88%) as a clear, colourless oil. R_f = 0.23 (20% CH_2Cl_2/hexanes) ^{1}H NMR (500 MHz, $CDCl_3$) δ8.53 (d, *J* = 15.7 Hz, 1H), 8.19 (d, *J* = 8.0 Hz, 1H), 7.85-7.90 (m, 2H), 7.74 (d, *J* = 7.2 Hz, 1H), 7.45-7.59 (m, 3H), 6.52 (d, *J* = 15.7 Hz, 1H), 3.85 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ167.30, 141.89, 133.66, 131.74, 131.40, 130.53, 128.72, 126.87, 126.23, 125.45, 125.01, 123.37, 120.45, 51.78; HRMS (LC-APPIMS) calculated for $C_{14}H_{12}O_2$ (M^+) 212.0873, found 212.0840.

3-(1-Naphthalenyl)propanoic acid methyl ester (3.96)

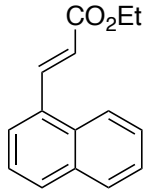


3.96

(*2E*)-3-(1-Naphthalenyl)-2-propenoic acid methyl ester (**3.95**) (4.60 g, 21.7 mmol), $Pd(OAc)_2$ (24 mg, 0.11 mmol) and charcoal (220 mg) were slurried in MeOH (100 mL) in a Schlenk flask. The atmosphere within the flask was evacuated and back-filled with H_2 three times. The resulting mixture was stirred for 3 h at rt. The reaction mixture was filtered through Celite and concentrated under reduced pressure to afford 3-(1-naphthalenyl)propionic acid methyl acid (**3.96**) (4.60 g, quantitative) as a clear, colourless oil that was used without further purification.

R_f = 0.23 (20% CH_2Cl_2/hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ8.02 (d, J = 8.1 Hz, 1H), 7.88 (d, J = 7.7 Hz, 1H), 7.72 (d, J = 7.9 Hz, 1H), 7.44- 7.55 (m, 2H), 7.32-7.41 (m, 2H), 3.69 (s, 3H), 3.42 (t, J = 8.0 Hz, 2H), 2.76 (t, J = 8.0 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ173.52, 136.53, 133.94, 131.65, 128.95, 127.21, 126.14, 125.97, 125.66, 125.63, 123.42, 51.73, 35.05, 28.18.

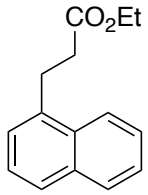
(2*E*)-3-(1-naphthalenyl)-2-propenoic acid ethyl ester (3.101)



3.101

NaH (2.82 g, 60% in paraffin oil, 70.4 mmol) was slurried in THF (200 mL) and cooled to 0 °C under a N_2 atmosphere. Triethyl phosphonoacetate (17.2 g, 15.3 mL, 76.8 mmol) was added dropwise to the cooled slurry outfitted with an outlet needle for the evolution of H_2 gas. 1-naphthaldehyde (10.9 g, 9.48 mL, 69.8 mmol) (**3.110**) was added dropwise via syringe. After complete addition the reaction was allowed to gradually warm to rt and stirred for 8 h under N_2. The reaction mixture was quenched with saturated $NH_4Cl_{(aq)}$ (100 mL) and extracted with EtOAc (3 × 75 mL). The combined organic extracts were washed with H_2O (75 mL) and brine (75 mL) then dried ($MgSO_4$), filtered and concentrated under reduced pressure. The resulting residue was subjected to column chromatography (20% CH_2Cl_2/hexanes) to yield (2*E*)-3-(1-naphthalenyl)-2-propenoic acid ethyl ester (**3.101**) (14.08 g, 99%) as a pale yellow oil. R_f = 0.25 (20% CH_2Cl_2/hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ8.52 (d, J = 15.8 Hz, 1H), 8.18 (d, J = 8.1 Hz, 1H), 7.79-7.84 (m, 2H), 7.74 (d, J = 7.1 Hz, 1H), 7.57-7.47 (m, 3H), 6.52 (d, J = 15.7 Hz, 1H), 4.32 (q, J = 7.2 Hz, 2H), 1.37 (t, J = 7.2 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 173.08, 136.63, 133.95, 131.70, 128.94, 127.17, 126.11, 126.00, 125.64, 125.62, 123.48, 60.54, 35.20, 28.20, 14.29; LCMS-Trap (HRMS) (ESI) calculated for $C_{15}H_{14}O_2$ M^+ 226.0994, found 226.0932.

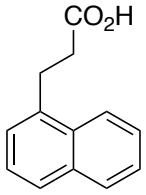
Ethyl 1-naphthalenepropanoate (3.102)



3.102

(2*E*)-3-(1-Naphthalenyl)-2-propenoic acid ethyl ester (**3.101**) (1.13 g, 5.00 mmol) was dissolved in MeOH (6.5 mL) in a 20 mL microwave vial. Cyclohexene (2.5 g, 3.0 mL, 30 mmol) was added via syringe then $Pd(OAc)_2$ (6 mg, 0.025 mmol) and charcoal (94 mg, 9:1 by mass to $Pd(OAc)_2$) were added. The reaction mixture was heated at 130 °C for 30 min under microwave irradiation. The reaction mixture was filtered and concentrated under reduced pressure to afford ethyl 1-naphthalenepropanoate (**3.102**) (1.14 g, 99%) as a pale yellow oil. R_f = 0.25 (20 % CH_2Cl_2/hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.98 (d, *J* = 8.4 Hz, 1H), 7.78 (d, *J* = 7.4 Hz, 1H), 7.66 (d, *J* = 8.1 Hz, 1H), 7.47-7.41 (m, 2H), 7.34-7.28 (m, 2H), 4.11 (q, *J* = 7.2 Hz, 2H), 3.37 (t, *J* = 8.0 Hz, 2H), 2.70 (t, *J* = 8.0 Hz, 2H), 1.18 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 173.08, 136.63, 133.95, 131.70, 128.94, 127.17, 126.11, 126.00, 125.64, 125.62, 123.48, 60.54, 35.30, 28.30, 14.29.

3-(1-Naphthalenyl)propionic acid (3.97)

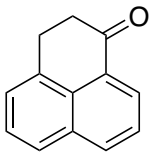


3.97

A mixture of 3-(1-naphthalenyl)propionic acid methyl ester (**3.95**) (4.60 g, 21.5 mmol), MeOH (50 mL) and 1 M $NaOH_{(aq)}$ (50 mL) were heated at reflux for 12 h. The reaction mixture was cooled to rt and the volume was reduced to *ca.* 50 mL under reduced pressure. The resulting slurry was acidified with 1 M $HCl_{(aq)}$ (100 mL) and the resulting mixture was extracted with diethyl ether (3 × 50 mL). The combined organic layers were washed with brine, dried ($MgSO_4$), filtered and concentrated under reduced pressure to yield 3-(1-naphthalenyl)propionic acid (**3.97**) (4.08 g, 95%) as an off-white solid that was used without further purification. R_f = 0.35 (30% ethyl acetate/hexanes); m.p. 144-145 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.03 (d, *J* = 8.4 Hz, 1H), 7.87 (d, *J* = 8.0 Hz, 1H), 7.75 (d, *J* = 8.0 Hz, 1H), 7.56-7.48 (m, 2H), 7.42-7.36 (m, 2H), 3.45 (t, *J* = 8.0 Hz, 2H), 2.84 (t, *J* = 8.0 Hz, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ

178.09, 136.10, 133.90, 131.55, 128.94, 127.28, 126.18, 125.92, 125.67, 125.58, 123.28, 34.70, 27.81. HRMS (LC-ESIMS) calculated for $C_{13}H_{12}O_2$ $(M-H)^-$ 199.083, found 199.0754.

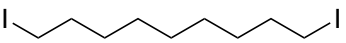
1*H*-Phenalen-1-one (3.103)



3.103

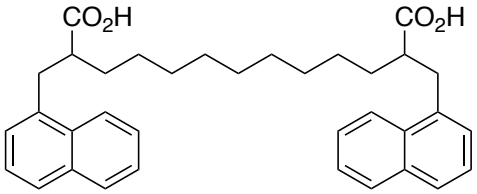
3-(1-Naphthalenyl)propionic acid (**3.97**) (2.00 g, 10.1 mmol) was dissolved in CH_2Cl_2 (100 mL) to which DMF (1 mL) was added via syringe. Oxalyl chloride (2.56 g, 1.73 mL, 20.2 mmol) was added slowly to the reaction mixture via syringe. The reaction mixture was stirred at reflux under a N_2 atmosphere for 16 h. The volatiles were removed *in vacuo* and then immediately dissolved in CH_2Cl_2 (100 mL) and cooled to –78 °C under a N_2 atmosphere. $AlCl_3$ (1.48 g, 11.1 mmol) was added and the reaction was stirred at –78 °C for 6 h. The reaction mixture was warmed to rt and quenched with 1M $HCl_{(aq)}$ (50 mL) then extracted with CH_2Cl_2 (3 × 50 mL). The combined organic extracts were dried ($MgSO_4$), filtered and concentrated under reduced pressure. The resulting residue was subjected to column chromatography (CH_2Cl_2) to afford 1*H*-phenalen-1-one (**3.103**) (1.07 g, 58%) as a white solid. R_f = 0.55 (CH_2Cl_2); m.p 84-86 °C (EtOH); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.20 (dd, *J* = 1.3 Hz, 7.2 Hz, 1H), 8.09 (dd, *J* = 1.1 Hz, 8.2 Hz, 1H), 7.80 (dd, *J* = 1.6 Hz, 7.5 Hz, 1H), 7.60 (dd, *J* = 7.2 Hz, 8.2 Hz, 1H), 7.45-7.51 (m, 2H), 3.44 (t, *J* = 7.1 Hz, 2H), 2.99 (t, *J* = 7.1 Hz, 2H); HRMS (LC-ESIMS) calculated for $C_{13}H_{13}O$ (M+1) 183.0732, found 183.0800.

1,9-Diiodononane

1,9-Dibromononane (5.00 g, 3.55 mL, 17.5 mmol) was  dissolved in acetone (100 mL) to which NaI (13.1 g, 87.4 mmol) was added. The reaction mixture heated to reflux under a N_2 atmosphere for 24 h. The reaction mixture was cooled and filtered through a plug of celite. The resulting residue was purified by

column chromatography (CH_2Cl_2) to yield 1,9-diiodononane (6.14 g, 95%) as a pale yellow oil. R_f = 0.70 (CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.19 (t, J = 7.1 Hz, 4H), 1.79-1.85 (m, 4H), 1.37-1.40 (m, 4H), 1.30 (broad s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 33.51, 30.45, 29.20, 28.44, 7.33.

(±) and meso-1,9-Bis(2-(3-(1-naphthalenyl)propionic acid))nonane (3.108b)

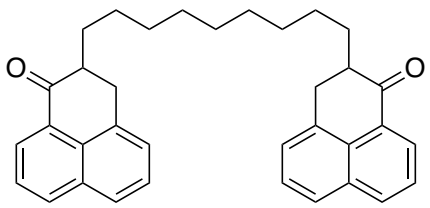


3.108b

^{i}Pr$_2$NH (3.1 mL, 2.2 g 22.0 mmol) was dissolved in THF (40 mL) and cooled to -78 °C under a N_2 atmosphere. *n*-BuLi (8.4 mL, 2.5 M in hexanes, 21 mmol) was added dropwise to the cooled solution then stirred while maintaining cooling for an additional 15 min. A solution of 3-(1-naphthalenyl)propionic acid (**3.97**) (2.00 g, 9.98 mmol) in THF (40 mL) was added dropwise to the cooled LDA solution *via* cannula. The resulting solution was stirred for 1 h while maintaining cooling. A solution of 1,9-diiodononane (1.71 g, 4.49 mmol) in THF (20 mL) was added dropwise to the reaction mixture. The reaction mixture was allowed to gradually warm to rt then stirred for 16 h then quenched with saturated $NH_4Cl_{(aq)}$ (75 mL) and the volume was reduced to *ca.* 75 mL under reduced pressure. The residue was dissolved in diethyl ether (200 mL) and washed with 10% $HCl_{(aq)}$ (100 mL) then brine (100 mL). The organic layer was dried ($MgSO_4$), filtered and concentrated under reduced pressure. The resulting residue was subjected to column chromatography (30% ethyl acetate/hexanes) to yield (±) and *meso* 1,9-bis(2-(3-(1-naphthalenyl)propionic acid))nonane (**3.108b**) (1.88 g, 80%) as a white foamy solid as a mixture of diastereomers. R_f = 0.25 (30% ethyl acetate/hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.00 (d, J = 8.1 Hz, 2H), 7.85 (d, J = 7.6 Hz, 2H), 7.73 (d, J = 7.6 Hz, 2H), 7.54-7.45 (m, 4H), 7.40-7.31 (m, 4H), 3.50-3.43 (m, 2H), 3.20-3.12 (m, 2H), 2.88 (m, 2H), 1.72-1.68 (m, 2H), 1.59-1.54 (m, 2H), 1.28-1.22 (m, 16H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 182.01, 135.07, 135.03, 133.93, 131.80, 128.90, 127.32, 127.07, 126.07, 125.56, 125.39, 123.49,

46.61, 46.44, 35.32, 35.19, 32.20, 28.94, 28.79, 28.77, 28.59, 26.82, 26.75; HRMS (LC-ESIMS) calculated for $C_{35}H_{40}O_4$ (M^+) 524.2927, found 524.2947.

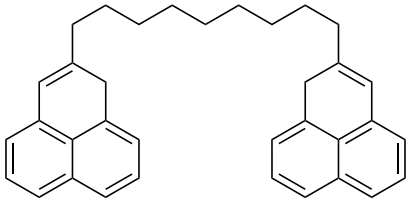
(±) and *meso*-1,9-bis(2-(2,3-dihydro-1H-phenalen-1-one))nonane (3.109b)



3.109b

To a solution og (±) and *meso* 1,9-bis(2-(3-(1-naphthalenyl)propionic acid))nonane (**3.108b**) (1.78 g, 3.40 mmol) in CH_2Cl_2 (50 mL) was added DMF (1 mL). Oxalyl chloride (0.88 mL, 1.3g, 10 mmol) was added dropwise via syringe over the course of 10 minutes. The reaction mixture was heated at reflux under a N_2 atmosphere for 16 h then cooled to rt and the volatiles were removed under reduced pressure. The residue was immediately dissolved in CH_2Cl_2 (50 mL) and cooled to -78 °C under a N_2 atmosphere. $AlCl_3$ (1.81 g, 13.6 mmol) was added and the reaction mixture was stirred at −78 °C for 5 h. The reaction mixture was quenched by slow addition of a 10% $HCl_{(aq)}$ (50 mL) and extracted with CH_2Cl_2 (3 × 50 mL). The combined organic layers were washed with H_2O (50mL), brine (50 mL) then dried ($MgSO_4$), filtered and concentrated under reduced pressure. The resulting residue was subjected to column chromatography (CH_2Cl_2) to yield (±) and *meso* 1,9-bis(2-(2,3-dihydro-1H-phenalen-1-one))nonane (**3.109b**) (818 mg, 49%) as a light brown oil. R_f = 0.40 (CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$) δ8.16 (dd, *J* = 1.3 Hz, 7.2 Hz, 2H), 8.06 (dd, *J* = 1.3 Hz, 8.3 Hz, 2H), 7.78 (dd, *J* = 1.5 Hz, 7.8 Hz), 7.59 (dd, *J* = 7.2 Hz, 8.2 Hz, 2H), 7.43-7.51 (m, 2H), 3.50 (dd, *J* = 5.6 Hz, 15.8 Hz, 2H), 3.18 (dd, *J* = 8.9 Hz, 15.9 Hz, 2H), 2.85-2.94 (m, 2H), 1.85-1.91 (m, 2H), 1.43-1.50 (m, 2H), 1.20-1.33 (m, 14H); ^{13}C NMR (75 MHz, $CDCl_3$) δ201.04, 133.67, 133.15, 132.94, 131.22, 129.75, 126.31, 126.12, 125.85, 125.79, 125.28, 47.45, 34.20, 30.05, 29.60, 29.50, 29.46, 27.12; HRMS (LC-dual-ESIMS) calculated for $C_{35}H_{36}O_2$ $(M+H)^+$ 489.2715, found 289.2773.

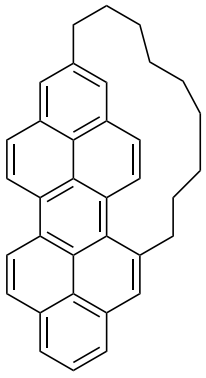
1,9-bis(2-(1H-Phenalene)nonane (3.111b)



3.111b

To a solution of (±) and *meso* 1,9-bis(2-(2,3-dihydro-1H-phenalen-1-one))nonane (**3.109b**) (780 mg, 1.59 mmol) in CH_2Cl_2 (25 mL) and EtOH (25 mL) was added $NaBH_4$ (483 mg, 12.77 mmol). The reaction mixture was stirred for under a N_2 atmosphere at rt for 16 h. The reaction mixture was quenched with saturated $NH_4Cl_{(aq)}$ (50 mL) and extracted with CH_2Cl_2 (3 × 50 mL). The combined organic layers were dried ($MgSO_4$), filtered and concentrated under reduced pressure to obtain yellow oily solid (727 mg) which was used without further purification. This crude residue was dissolved in benzene (20 mL) and heated to reflux under a N_2 atmosphere. *p*-TsOH (30 mg, 0.16 mmol) was added and the reaction mixture was stirred for 5 minutes with heating then cooled to rt, diluted with hexanes (20 mL) and subjected directly to column chromatography (20% CH_2Cl_2) packed with 6% hydrous silica gel to yield as a yellow solid 1,9-bis(2-(1H-phenalene)nonane (**3.111b**) (657 mg, 90%) as mixture of isomers, a small sample of which was recrystallized from heptane. R_f = 0.67 (20% CH_2Cl_2/hexanes); HRMS (LC-dual-ESIMS) calculated for (M^+) $C_{35}H_{36}$ 456.2827, found 456.2808.

[9](2,6)Peropyrenophane (3.118b)

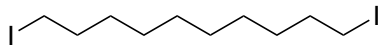


3.118b

1,9-Bis(2-(1H-phenalene)nonane (**3.111b**) (255 mg, 0.560 mmol) was dissolved in chlorobenzene (200 mL) in a 500 mL three-necked round-bottom flask. *p*-Chloranil (576 mg, 2.34 mmol) was placed into a sidearm connected to the three-necked flask. The reaction system was degassed *via* freeze-pump-thaw cycles. The sidearm was turned, dropping the *p*-chloranil into the reaction mixture. The flask was lowered into an oil bath at 80 °C and stirred for 2 days devoid of atmosphere. The reaction mixture

was cooled to rt and filtered through a plug of alumina (CH_2Cl_2) and concentrated under reduced pressure. The resulting residue was subjected to column chromatography (10% CH_2Cl_2/hexanes) to yield [9](2,6)peropyrenophane (**3.118b**) (46 mg, 18%) as an orange solid that was recrystallized from heptane. R_f = 0.51 (20% CH_2Cl_2/hexanes); m.p. decomposition >200 °C (heptane); ^{1}H NMR (500 MHz, $CDCl_3$) δ9.12 (d, *J* = 9.1 Hz, 1H), 9.07 (d, *J* = 9.2 Hz, 1H), 8.89 (d, *J* = 9.2 Hz, 1H), 8.32 (d, *J* = 9.1 Hz), 8.26-8.29 (m, 2H), 8.19-8.22 (m, 2H), 8.14 (d, *J* = 9.2 Hz, 1H), 8.04-8.07 (m, 2H), 7.96 (s, 1H), 4.27-4.33 (m, 1H), 3.24-3.29 (m, 1H), 3.09-3.15 (m, 1H), 2.90-2.96 (m, 1H), 1.68-1.73 (m, 1H), 1.50-1.56 (m, 1H), 0.96-1.11 (m, 3H), 0.53-0.64 (m, 2H), 0.15-0.36 (m, 4H), -0.12- -0.18 (m, 1H), -0.22- -0.26 (m, 1H), -0.52- -0.60 (m, 1H);) HRMS (LC-dual-ESIMS) calculated for $C_{35}H_{30}$ (M^+) 451.2348, found 451.2429.

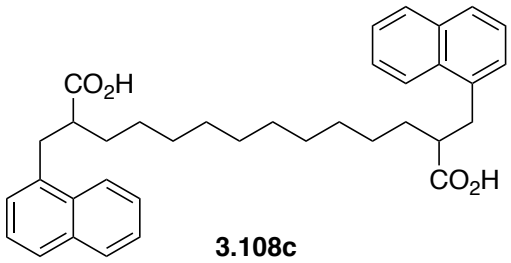
1,10-Diiododecane



1,10-Dibromodecane (5.00 g, 16.7 mmol) was dissolved in acetone (100 mL) to which NaI (9.99 g, 66.7 mmol) was added. The reaction mixture was heated at reflux for 6 h then cooled to rt and filtered through a plug of celite. The reaction mixture was concentrated under reduced pressure and the resulting residue was purified by column chromatography (CH_2Cl_2) to yield 1,10-diiododecane (6.24 g, 95%) as a white solid. R_f = 0.80 (CH_2Cl_2); m.p. 29-32 °C (CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$) δ3.19 (t, *J* = 7.0 Hz, 4H), 1.79-1.85 (m, 4H), 1.37-1.40 (m, 4H), 1.29 (broad s, 8H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 35.55, 30.49, 29.32, 28.50, 7.40.

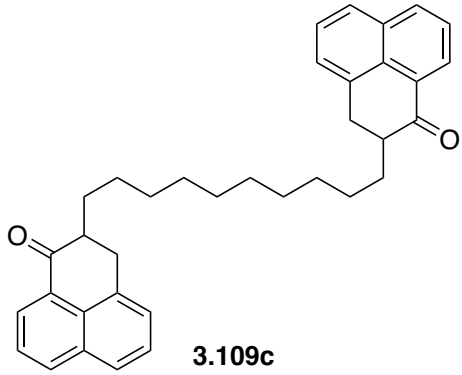
(±) and *meso* 1,10-Bis(2-(3-(1-naphthalenyl)propionic acid))decane (3.108c)

$^{i}Pr_2NH$ (3.1 mL, 2.2 g 22.0 mmol) was dissolved in THF (30 mL) and cooled to −78 °C under a N_2 atmosphere to which *n*-BuLi (8.4 mL, 2.5 M in hexanes, 21 mmol) was added dropwise then stirred for 15 min. A solution of 3-(1-naphthalenyl)propionic acid (**3.97**) (2.00 g, 9.98 mmol) in THF (50 mL) was added dropwise to the cooled LDA solution via cannula then was stirred for 1 h with cooling maintained. A solution of 1,10-diiododecane (1.77 g, 4.49 mmol) in THF (20 mL) was then added dropwise to the reaction mixture then gradually warmed to rt then stirred for 14 h. The reaction mixture was quenched with a saturated $NH_4Cl_{(aq)}$ (75 mL) and the volume was reduced to *ca.* 75 mL under reduced pressure. The residue was dissolved in diethyl ether (150 mL) and washed with a 10% $HCl_{(aq)}$ (75 mL) and brine (50 mL). The organic layer was dried ($MgSO_4$), filtered and concentrated under reduced pressure. The resulting residue was subjected to column chromatography (20% ethyl acetate/hexanes) to yield (±) and *meso* 1,10-bis(2-(3-(1-naphthalenyl)propionic acid))decane (**3.108c**) (1.89 g, 78%) as a white solid as a mixture of diastereomers. R_f = 0.32 (30% ethyl acetate/hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.00 (d, *J* = 8.2 Hz, 2H), 7.86 (d, *J* = 7.9 Hz, 2H), 7.74 (d, *J* = 7.7 Hz), 7.45-7.55 (m, 4H), 7.34-7.44 (m, 4H), 3.41-3.52 (m, 2H), 3.13-3.19 (m, 2H), 2.82-2.91 (m, 2H), 1.65-1.8 (m, 4H) 1.20-1.28 (m, 16H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 182.34, 135.02, 133.94, 131.81, 128.91, 127.33, 127.10, 126.08, 125.56, 125.40, 123.50, 46.69, 46.55, 35.34, 35.38, 32.40, 32.16, 28.64, 28.61, 28.18, 28.05, 27.89, 27.64, 26.38; HRMS (LC-dual-ESIMS) calculated for $C_{36}H_{42}O_4$ (M^+) 538.3083, found 538.3106.



3.108c

(±) and *meso* 1,10-Bis(2-(2,3-dihydro-1H-phenalen-1-one))decane (3.109c)

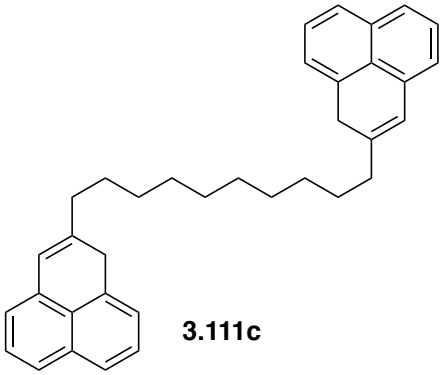


3.109c

To (±) and *meso* 1,9-bis(2-(3-(1-naphthalenyl)propionic acid))nonane (**3.108c**) (2.41 g, 4.47 mmol) in CH_2Cl_2 (50 mL) was added DMF (1 mL). Oxalyl chloride (3.1 mL, 4.53 g, 35.8 mmol) was then added dropwise via syringe over the course of 10 minutes. The reaction mixture was heated a reflux under a N_2 atmosphere for 18 h then cooled to rt. The volatiles were removed under reduced pressure and the resulting residue was immediately dissolved in CH_2Cl_2 (100 mL) and cooled to -78 °C under a N_2 atmosphere. $AlCl_3$ (2.38 g, 17.9 mmol) was added and the reaction mixture was stirred at −78 °C for 5.5 h. The reaction mixture was quenched by slow addition of a 10% $HCl_{(aq)}$ (50 mL) and extracted with CH_2Cl_2 (3 × 50 mL). The combined organic layers were washed with H_2O (50mL), brine (50 mL) then dried ($MgSO_4$), filtered and concentrated under reduced pressure. The resulting residue was subjected to column chromatography (70% CH_2Cl_2/hexanes) to yield (±) and *meso* 1,10-bis(2-(2,3-dihydro-1H-phenalen-1-one))decane (**3.109c**) (809mg, 36%) as a brown waxy solid. R_f = 0.35 (30% ethyl acetate/hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ8.16 (dd, *J* = 1.2 Hz, 7.2 Hz, 2H), 8.06 (dd, *J* = 1.2 Hz, 8.2 Hz, 2H), 7.78 (dd, *J* = 0.7 Hz, 8.0 Hz, 2H), 7.59 (t. *J* = 7.6 Hz, 2H), 7.44-7.50 (m, 4H), 3.50 (dd, *J* = 5.6 Hz, 15.8 Hz, 2H), 3.18 (dd, *J* = 8.9 Hz, 15.7 Hz, 2H), 2.88-2.92 (m, 2H), 1.85-1.92 (m, 2H), 1.46-1.50 (m, 4H), 1.19-1.27 (m, 14H); ^{13}C NMR (75 MHz, $CDCl_3$) δ201.06, 133.66, 133.16, 132.95, 131.23, 129.76, 126.30, 126.12, 125.85, 125.78, 125.28, 447.46, 34.21, 30.06, 29.62, 29.55, 29.49, 27.14; HRMS (LC-dual-ESIMS)calculated for $C_{36}H_{38}O_2$ (M+) 502.2872, found 502.2862.

1,10-Bis(2-(1H-phenalene)decane (3.111c)

1,10-Bis(2*H*-dihydrophenalenone)decane (**3.109c)** (809 mg, 1.61 mmol) was dissolved in CH_2Cl_2 (50 mL) and EtOH (50 mL) to which $NaBH_4$ (487 mg, 12.9 mmol) was added. The reaction was stirred at rt under a nitrogen atmosphere for 24 h then the reaction was quenched with saturated $NH_4Cl_{(aq)}$ (100 mL) and extracted with CH_2Cl_2 (3 × 40 mL). The combined organic extracts were washed with brine (50 mL) then dried ($MgSO_4$), filtered and concentrated under reduced pressure to yield the corresponding diol (555 mg), which was used without further purification. 1,10-Bis(2*H*-dihydrophenalenol)decane (555 mg, 1.09 mmol) was dissolved in benzene (50 mL) and heated to reflux to which *p*-TsOH (41 mg, 0.22 mmol) was added and stirred for 5 min. The reaction mixture was diluted with hexane (20 mL) and loaded immediately onto a column packed with 6% hydrous silica gel (eluent 20% CH_2Cl_2/hexanes) to yield 1,10-bis(phenalenyl)decane (450 mg, 59%) as an off-white solid as a mixture of isomers. HRMS (LC-dual-ESIMS) calculated for $(M)^+$ $C_{36}H_{38}$ 470.2974, found 470.2940.

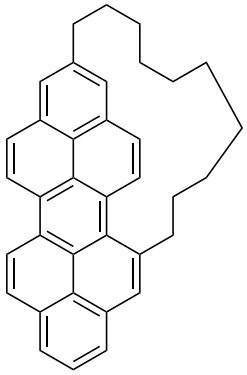


3.111c

[10](2,6)Peropyrenophane (3.118c)

1,10-Bis(2-(1H-phenalene)decane (**3.111c**) (250 mg, 0.530 mmol) was dissolved in chlorobenzene (200 mL) in a 500 mL three-necked round-bottom flask.

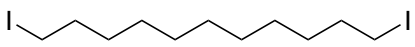
p-Chloranil (522 mg, 2.12 mol) was placed in a sidearm connected to the three-necked flask. The reaction system was degassed *via* freeze-pump-thaw cycles. The sidearm was turned, dropping the *p*-chloranil into the reaction solution. The flask was lowered into an oil bath at 80 °C and stirred for 2 days devoid of atmosphere. The reaction mixture



3.118c

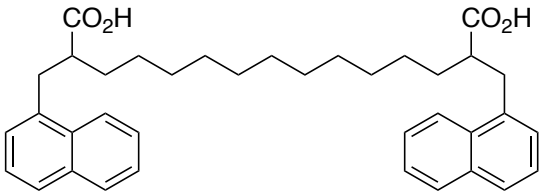
was cooled to rt and filtered through a plug of alumina (CH_2Cl_2) then concentrated under reduced pressure. The resulting residue was subjected to column chromatography (10% CH_2Cl_2/hexanes) to yield [10](2,6)peropyrenophanes (**12**) (76 mg, 31%) as a bright orange-yellow solid, as small portion of which was recrystallized from heptane. R_f = 0.46 (20% CH_2Cl_2/hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ9.18 (d, *J* = 9.1 Hz, 1H), 9.14 (d, *J* = 9.2 Hz, 1H), 9.10 (d, *J* = 9.2 Hz, 1H), 8.36 (d, *J* = 9.1 Hz, 1H), 8.31-8.35 (m, 2H), 8.27 (d, *J* = 7.6 Hz, 1H), 8.16 (m, 3H), 8.13 (s, 1H), 8.10 (t, *J* = 7.5 Hz, 1H), 4.47-4.52 (m, 1H), 3.35-3.40 (m, 1H), 3.13-3.19 (m, 1H), 3.01-3.08 (m, 1H), 2.00- 2.04 (m, 1H), 1.32-1.42 (m ,1H), 0.89-1.23 (m, 6H), 0.65-0.76 (m, 4H), 0.54-0.61 (m, 1H), -0.01—0.05 (m, 1H), -0.44 - -0.52 (m, 1H), -1.12 - -1.17 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ140.27, 139.73, 131.69, 131.49, 131.09, 128.57, 126.99, 126.79, 126.20, 126.03, 125.50, 125.45, 124.88, 124.85, 124.77, 124.67, 124.59, 123.96, 122.96, 122.85, 37.37, 36.88, 30.60, 30.46, 30.03, 29.84, 29.38, 28.94, 28.44, 27.12 (34 of 35 observed); HRMS (LC-dual-ESIMS) calculated for (M^+) $C_{36}H_{32}$ 464.2504, found 464.2510.

1,11-diiodoundecane



1,11-Dibromoundecane (5.00 g, 15.9 mmol) was dissolved in acetone (100 mL) to which NaI (9.53 g, 63.6 mmol) was added. The reaction mixture was heated at reflux for 5 h then cooled to rt and filtered through a plug of celite. The reaction mixture was concentrated under reduced and the resulting residue was purified quickly by column chromatography (CH_2Cl_2) to yield 1,11-diodoundecane (6.22 g, 96%) as a light yellow solid. R_f = 0.75 (CH_2Cl_2); m.p. 31-33 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ3.19 (t, *J* = 7.0 Hz, 4H), 1.87-1.77 (m, 4H), 1.41-1.28 (m, 14H); ^{13}C NMR (75 MHz, $CDCl_3$) δ33.56, 30.51, 29.43, 29.37, 28.53, 7.41.

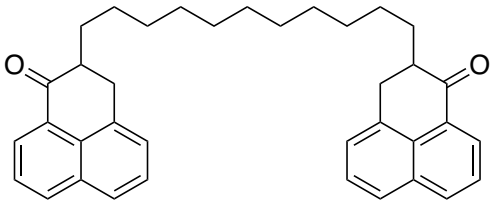
(±) and meso-1,11-Bis(2-(3-(1-naphthalenyl)propionic acid))undecane (3.108d)



3.108d

$^{i}Pr_2NH$ (3.1 mL, 2.2 g, 22 mmol) was dissolved in THF (40 mL) and cooled to -78 °C under a N_2 atmosphere to which *n*-BuLi (8.4 mL, 2.5 M in hexanes, 21 mmol) was added dropwise then stirred for 15 mins. 3-(1-Naphthalenyl)propanoic acid (**3.97**) (2.0 g, 10 mmol) in dissolved THF (50 mL) was added dropwise via cannula to the cooled LDA solution and stirred for an additional 1 h. 1,11-Dibromoundecane (1.5 g, 4.8 mmol) dissolved in THF (10 mL) was added dropwise to the cooled solution and the reaction was warmed to rt and stirred for 18 h. The reaction mixture was quenched with saturated $NH_4Cl_{(aq)}$ (50 mL) and the volume was reduced to *ca.* 75 mL under reduced pressure. The residue was dissolved in diethyl ether (200 mL) and washed with 10% $HCl_{(aq)}$ (100 mL) then brine (100 mL). The organic layer was dried ($MgSO_4$), filtered and concentrated under reduced pressure and the resulting residue was subjected to column chromatography (30% ethyl acetate/hexanes) to yield (±) and meso-1,11-bis(2-(3-(1-naphthalenyl)propionic acid))undecane (**3.108d**) (1.97 g, 74%) as a white oily solid as a mixture of diastereomers. R_f = 0.30 (30% ethyl acetate/hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ8.02 (m, 2H), 7.84-7.87 (m, 2H), 7.73 (m, 2H), 7.45-7.50 (m, 4H), 7.31-7.40 (m, 4H), 3.40-3.51 (m, 2H), 3.14-3.21 (m, 2H), 2.79-2.90 (m, 2H) 1.70-1.74 (m, 2H), 1.54-1.60 (m, 2H), 1.22-1.38 (m, 18H); ^{13}C NMR (75 MHz, $CDCl_3$) δ182.21, 182.17, 135.06, 135.03, 133.94, 131.81, 128.90, 127.33, 127.10, 126.07, 125.56, 125.39, 123.50, 46.62, 46.40, 35.42, 35.31, 32.11, 32.08, 30.93, 28.99, 28.87, 28.79, 26.98, 26.89.

(±) and *meso* 1,11-Bis(2-(2,3-dihydro-1H-phenalen-1-one))undecane (3.109d)

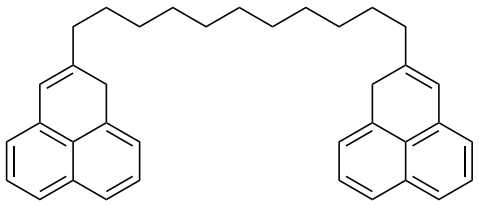


3.109d

To (±) and *meso* 1,11-bis(2-(3-(1-naphthalenyl)propionic acid))undecane (**3.108d**) (1.94 g, 3.51 mmol) dissolved in CH_2Cl_2 (50 mL) was added DMF (1 mL). Oxalyl chloride (2.4 mL, 3.6 g, 28 mmol) was added dropwise via syringe over the course of 10 min then the reaction mixture was heated to reflux under a N_2 atmosphere for 18 h. The reaction mixture was cooled to rt and the volatiles were removed under reduced pressure and he resulting residue was immediately dissolved in CH_2Cl_2 (100 mL) and cooled to -78 °C under a N_2 atmosphere. $AlCl_3$ (3.74 g, 28.1 mmol) was added and the reaction mixture was stirred at −78 °C for 3.5 h. The reaction mixture was quenched by slow addition of a 10% $HCl_{(aq)}$ (50 mL) and extracted with CH_2Cl_2 (3 × 50 mL). The combined organic layers were washed with H_2O (50mL), brine (50 mL) then dried ($MgSO_4$), filtered and concentrated under reduced pressure. The resulting residue was subjected to column chromatography (CH_2Cl_2) to yield (±) and *meso* 1,11-bis(2-(2,3-dihydro-1H-phenalen-1-one))undecane (**3.109d**) (1.68 g, 93%) as a yellow solid as a mixture of diastereomers. R_f = 0.35 (CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$) δ8.16 (dd, *J* = 1.2 Hz, 7.2 Hz, 2H), 8.04 (dd, *J* = 1.2 Hz, 8.2 Hz, 2H), 7.77 (dd, *J* = 0.6 Hz, 8.0 Hz, 2H), 7.58 (dd, *J* = 7.2 Hz, 8.2 Hz, 2H) 7.42-7.19 (m, 4H), 3.48 (dd, *J* = 5.6 Hz, 15.8 Hz, 2H), 3.16 (dd, *J* = 9.0 Hz, 15.8 Hz, 2H), 2.86-2.92 (m, 2H), 1.85-1.92 (m, 2H), 1.45-1.50 (m, 4H), 1.19-1.27 (m, 16H); ^{13}C NMR (75 MHz, $CDCl_3$) δ201.02, 133.67, 133.17, 132.96, 131.24, 129.77, 126.31, 126.13, 125.85, 125.79, 125.27, 47.46, 34.22, 30.08, 29.66, 29.62, 29.59, 29.53, 27.16; HRMS (LC-dual-ESIMS)calculated for $C_{37}H_{40}O_2$ (M^+) 516.3028, found 516.3022.

1,11-Bis(2-(1H-phenalene)undecane (3.111d)

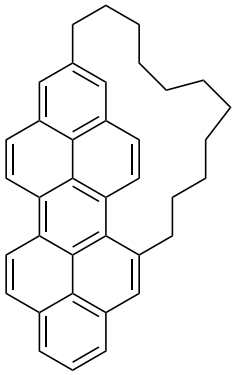
To a solution of (±) and *meso* 1,11-bis(2-(2,3-dihydro-1H-phenalen-1-one))undecane (**3.109d**) (1.20 g, 2.37 mmol) in CH_2Cl_2 (40 mL) and EtOH (40 mL) was added $NaBH_4$ (360 mg, 9.47 mmol). The reaction mixture was stirred under a N_2 atmosphere at rt for 19 h. The reaction mixture was quenched with saturated $NH_4Cl_{(aq)}$ (50 mL) and extracted with CH_2Cl_2 (3 × 50 mL). The combined organic layers were dried ($MgSO_4$), filtered and concentrated under reduced pressure to obtain yellow oily solid which was used without further purification (727 mg). The crude residue was dissolved in benzene (20 mL) and heated to reflux under a N_2 atmosphere to which *p*-TsOH (85 mg, 0.57 mmol) was added then stirred for 5 min. The reaction mixture was cooled to rt, diluted with hexanes (20 mL) and subjected directly to column chromatography (20% CH_2Cl_2/hexanes) packed with 6% hydrous silica gel to yield as a yellow solid 1,11-bis(2-(1H-phenalene)undecane (**3.111d**) (897 g, 78%) as mixture of isomers, a small sample of which was recrystallized from heptane. HRMS (LC-dual-ESIMS) calculated for $C_{37}H_{40}$ (M^+) 484.3130, found 484.3064.



3.111d

[11](2,6)Peropyrenophane (3.118d)

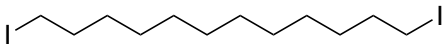
1,11-Bis(2-(1H-Phenalene)undecane (**3.111d**)
(333 mg, 0.69 mmol) was dissolved in chlorobenzene (200 mL) in a 500 mL three-necked round-bottom flask.
p-Chloranil (693 mg, 2.81 mmol) was placed in a sidearm connected to the three-necked flask. The reaction system was degassed via freeze-pump-thaw cycles. The sidearm was turned, dropping the *p*-chloranil into the reaction solution. The flask was lowered into an oil bath at 80 °C and stirred for 2 days devoid of atmosphere. The reaction mixture was cooled to rt and filtered through a plug of alumina (CH_2Cl_2) concentrated under reduced pressure.



3.118d

The resulting residue was subjected to column chromatography (10% CH_2Cl_2/hexanes) to yield [11](2,6)peropyrenophane (**3.118d**) (12 mg, 4%) as a bright orange-yellow solid, a small portion of which was recrystallized from heptane. R_f = 0.18 (20% CH_2Cl_2/hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ9.15 (d, *J* = 9.2 Hz, 1H), 9.12 (d, *J* = 9.2 Hz, 1H), 9.11 (d, *J* = 9.2 Hz, 1H), 8.32 (d, *J* = 9.2 Hz, 1H), 8.31 (d, *J* = 9.2 Hz, 1H), 8.28 (d, *J* = 7.5 Hz, 1H), 8.24 (d, *J* = 7.5 Hz, 1H), 8.20 (d, *J* = 1.1 Hz, 1H), 8.17 (d, *J* = 9.3 Hz, 1H), 8.13 (d, *J* = 1.1 Hz, 1H), 8.12 (s, 1H), 8.07 (t, *J* = 7.5 Hz, 1H), 4.37-4.42 (m, 1H), 3.12-3.26 (m, 3H), 2.02-2.08 (m, 1H), 1.59-1.65 (m, 1H), 1.31-1.41 (m, 2H), 0.90-1.07 (m, 2H), 0.70-0.79 (m, 3H), 0.43-0.59 (m, 4H), 0.25-0.35 (m, 3H) ; ^{13}C NMR (75 MHz, $CDCl_3$) δ141.09, 139.03, 131.50, 131.36, 131.07, 130.39, 129.10, 127.17, 126.99, 126.58, 126.24, 126.04, 125.95, 125.54, 125.23, 124.88, 124.86, 124.78, 124.60, 124.14, 124.11, 123.24, 123.13, 123.02, 122.81, 39.82, 37.35, 30.06, 29.95, 29.71, 29.66, 29.54, 29.30, 29.21, 28.82, 28.20; HRMS (LC-dual-ESIMS) calculated for (M^+) $C_{36}H_{32}$ 464.2504, found 464.2510.

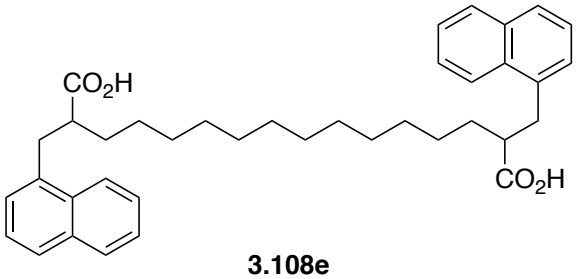
1,12-Diiododododecane



1,12-dibromododecane (5.00 g, 15.2 mmol) and NaI (5.71g, 38.1 mmol) were dissolved in acetone (100 mL) was heated to reflux for 24 h. The reaction mixture was cooled to rt and filtered through a plug of celite and concentrated under reduced pressure. The resulting residue was subjected to column chromatography (CH_2Cl_2) to yield 1,12-diiododododecane (6.11 g, 95%) as a yellow solid. R_f = 0.82 (CH_2Cl_2); m.p. 38-40 °C (CH_2Cl_2); ^{1}H NMR (300 MHz, $CDCl_3$) δ3.19 (t, *J* = 7 Hz, 4H), 1.87-1.77 (m, 4H), 1.41-1.27 (m, 16H); ^{13}C NMR (75 MHz, $CDCl_3$) δ33.57, 30.51, 29.48, 29.39, 28.53, 7.35.

(±) and meso-1,12-Bis(2-(3-(1-naphthalenyl)propionic acid))dodecane (3.108e)

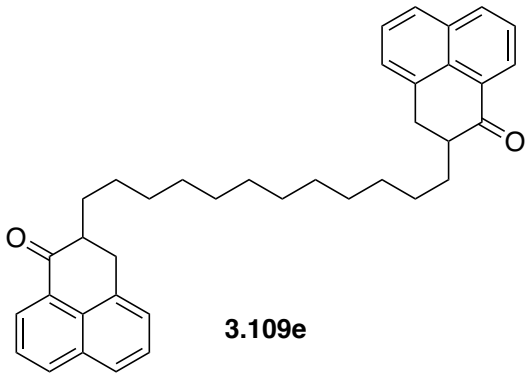
$^{i}Pr_2NH$ (3.1 mL, 2.2 g, 22 mmol) was dissolved in THF (40 mL) and cooled to -78 °C under a N_2 atmosphere to which *n*-BuLi (8.4 mL, 2.5 M in hexanes, 21 mmol) was added then stirred for 15 min. 3-(1-Naphthalenyl)propanoic acid (**3.97**) (2.0 g, 10 mmol) dissolved in THF (50 mL) was added dropwise via cannula to the cooled LDA solution and stirred for 1 h. 1,12-diiododododecane (2.0 g, 4.8 mmol) dissolved in THF (10 mL) was added dropwise to the cooled solution then warmed to rt and stirred for 16 h. The reaction mixture was quenched with saturated $NH_4Cl_{(aq)}$ (50 mL) and the volume was reduced to *ca.* 75 mL under reduced pressure. The residue was dissolved in diethyl ether (200 mL) and washed with 10% $HCl_{(aq)}$ (100 mL) then brine (100 mL). The organic layer was dried ($MgSO_4$), filtered and concentrated under reduced pressure. The residue was subjected to column chromatography (30% ethyl acetate/hexanes) to yield (±) and meso-1,12-bis(2-(3-(1-naphthalenyl)propionic acid))dodecane (**3.108e**) (2.31 g, 85%) as a yellow oily solid as a mixture of diastereomers. R_f = 0.28 (30% ethyl acetate/hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ8.02 (d, *J* = 8.3 Hz, 2H), 7.84-7.86 (m, 2H), 7.74 (d, *J* = 8.1 Hz, 2H), 7.45-7.53 (m, 4H), 7.36-7.39 (m, 2H), 7.32-7.34 (m, 2H), 3.45-3.51 (m, 2H), 3.13-3.19 (m, 2H), 2.84-2.91 (m, 2H), 1.68-1.73 (m, 2H), 1.53-1.58 (m, 2H), 1.21-1.41 (m, 20H); ^{13}C NMR (75 MHz, $CDCl_3$) δ182.55, 182.38, 135.03, 133.94, 131.81, 128.90, 127.33, 127.10, 126.07, 125.56, 125.39, 123.50,



3.108e

(±) and *meso*-1,12-Bis(2-(2,3-dihydro-1H-phenalen-1-one))dodecane (3.109e)

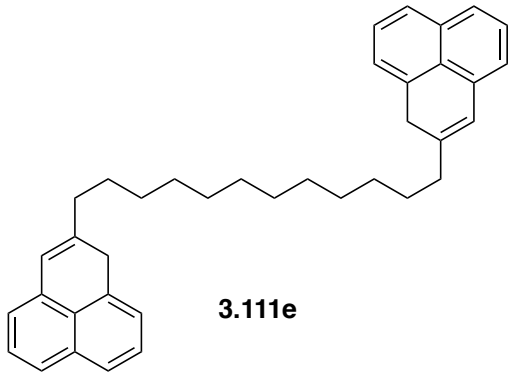
To (±) and *meso*-1,12-bis(2-(3-(1-naphthalenyl)propionic acid))dodecane (**3.108e**) (2.31 g, 4.07 mmol) dissolved in CH_2Cl_2 (50 mL) was added DMF (1 mL). Oxalyl chloride (2.8 mL, 4.1 g, 33 mmol) was added dropwise via syringe over 10 min. The reaction mixture was heated at reflux under a N_2 atmosphere for 18 h then cooled to rt and the volatiles were removed under reduced pressure. The residue was immediately dissolved in CH_2Cl_2 (50 mL) and cooled to −78 °C under a N_2 atmosphere. $AlCl_3$ (4.33 g, 32.6 mmol) was added and the reaction mixture was stirred with cooling for 5.5 h. The reaction mixture was quenched by slow addition of 10% $HCl_{(aq)}$ (50 mL) and extracted with CH_2Cl_2 (3 × 50 mL). The combined organic layers were washed with H_2O (50 mL), brine (50 mL), then dried ($MgSO_4$), filtered and concentrated under reduced pressure. The residue was subjected to column chromatography (CH_2Cl_2) to yield (±) and *meso*-1,12-bis(2-(2,3-dihydro-1H-phenalen-1-one))dodecane (**3.109e**) (1.62 g, 77%) as a yellow solid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.16 (dd, *J* = 1.3, 7.2 Hz, 2H), 8.06 (dd, *J* = 1.3, 8.2 Hz, 2H), 7.77-7.80 (m, 2H), 7.57-7.62 (m, 2H), 7.43-7.51 (m, 4H), 3.42-5.52 (m, 2H), 3.14-3.22 (m, 2H), 2.97-2.99 (m, 2H), 1.84-1.93 (m, 2H), 1.44-1.51 (m, 2H), 1.20-1.25 (m, 20H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 201.06, 134.08, 133.66, 133.16, 132.96, 129.76, 126.30, 126.12, 125.85, 125.78, 125.28, 47.46, 38.52, 34.21, 30.07, 29.64, 29.61, 29.59, 29.51, 27.15 (20 signals observed, 19 expected)



3.109e

1,12-Bis(2-(1H-phenalene)dodecane (3.111e)

To a solution of (±) and *meso* 1,12-bis(2-(2,3-dihydro-1H-phenalen-1-one))dodecane (**3.109e**) (1.62 g, 3.13 mmol) in CH_2Cl_2 (50 mL) and EtOH (50 mL) was added $NaBH_4$ (950 mg, 25.1 mmol). The reaction mixture was stirred under a N_2 atmosphere at rt for 24 h. The reaction mixture was quenched with saturated $NH_4Cl_{(aq)}$ (50 mL) and extracted with CH_2Cl_2 (3 × 50 mL).

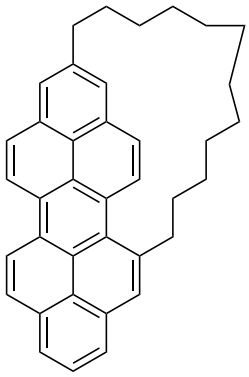


3.111e

The combined organic layers were dried ($MgSO_4$), filtered and concentrated under reduced pressure to obtain yellow oily solid which was used without further purification (727 mg). The crude residue was dissolved in benzene (20 mL) and heated to 80 °C under a N_2 atmosphere. *p*-TsOH (110 mg, 0.63 mmol) was added and the reaction mixture was stirred for 5 min with heating. The reaction mixture was cooled to rt, diluted with hexane (20 mL) and subjected directly to column chromatography (20% CH_2Cl_2) packed with 6% hydrous silica gel to yield as a yellow solid 1,12-bis(2-(1H-phenalene)dodecane (**3.111e**) (1.45 g, 93%) as mixture of isomers, a small sample of which was recrystallized from heptane. HRMS (LC-dual-ESIMS) calculated for $C_{38}H_{42}$ (M^+) 498.3287, found 498.3301.

[12](2,6)Peropyrenophane (3.118e)

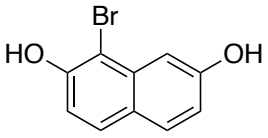
1,12-Bis(2-(1H-phenalene)undecane (400 mg, 0.800 mmol) (**3.111e**) was dissolved in chlorobenzene (200 mL) in a 500 mL three-necked round-bottom flask. *p*-Chloranil (808 mg, 3.29 mol) was placed in a sidearm connected to the three-necked flask. The reaction system was vigorously degassed via freeze-pump-thaw cycles. The sidearm was turned, dropping the *p*-chloranil into the reaction solution. The flask was lowered into an oil bath at 80 °C and



3.118e

stirred for 2 days devoid of atmosphere. The reaction mixture was cooled to rt and filtered through a plug of alumina (CH_2Cl_2) and concentrated under reduced pressure. The resulting residue was subjected to column chromatography (10% CH_2Cl_2/hexanes) to yield 52 mg of an orange-yellow solid which appears to be a mixture of [12]peropyrenophane isomers. This mixture was crystallized from heptane to afford [12](2,6)peropyrenophanes (32 mg, 8%) as a bright yellow solid. R_f = 0.48 (20% CH_2Cl_2/hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ9.24 (d, *J* = 9.4 Hz, 1H), 9.20 (d, *J* = 9.4 Hz, 1H), 9.18 (d, *J* = 9.4 Hz, 1H), 8.34 (d, *J* = 9.1 Hz, 2H), 8.28 (d, *J* = 7.5 Hz, 1H), 8.24 (d, *J* = 7.0 Hz, 1H), 8.18-8.21 (m, 3H), 8.14 (d, *J* = 1.1 Hz, 1H), 8.08 (t, *J* = 7.5 Hz, 1H), 3.20 (broad s, 2H), 1.95 (broad s, 2H), 1.25 (broad s, 5H), 1.05 (broad s, 8H), 0.86 (broad s, 3H), 0.48-0.55 (m, 4H);^{13}C NMR (75 MHz, $CDCl_3$) δ; HRMS (LC-dual-ESIMS) calculated for $C_{38}H_{36}$ (M^+) 492.2817, found 492.2836.

1-Bromo-2,7-dihydroxynaphthalene (3.122)

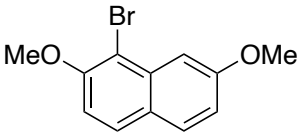


3.122

2,7-dihydroxynaphthalene (5.00 g, 31.2 mmol) (**3.121**) was dissolved in CH_3CN (50 mL) and cooled to 0 °C under a N_2 atmosphere in a 250-mL round-bottom flask equipped with a dropping funnel. *N*-Bromosuccinimide (5.55 g, 31.2 mmol) was dissolved CH_3CN (50 mL) and added to the dropping funnel and then added dropwise to the cooled solution. After complete addition, the reaction was warmed to rt and stirred for 16 h. The reaction mixture was quenched with H_2O (100 mL) and extracted with EtOAc (3 × 50 mL). The combined organic extracts were washed with brine then dried ($MgSO_4$), filtered and concentrated under reduced pressure. The resulting residue was subjected to column chromatography (CH_2Cl_2) to yield 1-bromo-2,7-dihydroxynaphthalene (**3.122**) (6.69 g, 90%) as a white solid. R_f = 0.35 (CH_2Cl_2); m.p. 137-140 °C (CH_2Cl_2); ^{1}H NMR ($CDCl_3$, 500 MHz) δ7.69 (d, *J* = 8.7 Hz, 1H), 7.66 (d, *J* = 8.8 Hz, 1H), 7.35 (d, *J* = 2.5 Hz, 1H), 7.11 (d, *J* = 8.8 Hz, 1H), 6.99 (dd, *J* = 8.7 Hz, 2.5 Hz, 1H), 5.87 (s, 1H), 5.08 (s, 1H) ppm; ^{13}C NMR

($CDCl_3$, 75 MHz) δ155.34, 151.26, 133.90, 130.48, 129.19, 124.98, 115.66, 114.75, 108.00, 104.63 ppm; HRMS (LC-APPIMS) calculated for $C_{10}H_7O_2Br$ (M^+) 239.0680, found 239.0698.

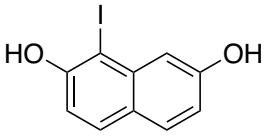
1-Bromo-2,7-dimethoxynaphthalene (3.123)



3.123

1-Bromo-2,7-dihydroxynaphthalene (**3.122**) (6.69 g, 28.0 mmol) was dissolved in DMF (100 mL) to which K_2CO_3 (9.67 g, 67.0 mmol) was added and the reaction was stirred at rt under a N_2 atmosphere for 5 min. MeI (9.93 g, 4.35 mL, 67.0 mmol) was added via syringe and the reaction was stirred at rt for 18 h. The reaction mixture was poured into H_2O (500 mL) and extracted with CH_2Cl_2 (3 × 100 mL). The combined organic extracts were washed with brine then dried ($MgSO_4$), filtered and concentrated under reduced pressure. The resulting residue was subjected to column chromatography (20% ethyl acetate/hexanes) to obtain 1-bromo-2,7-dimethoxynaphthalene (**3.123**) (5.94 g, 80%) as an off-white solid. R_f = 0.40 (20% ethyl acetate/hexanes); m.p. 76-78 °C (CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$) δ7.73 (d, *J* = 8.9 Hz, 1H), 7.67 (d, *J* = 8.9 Hz, 1H), 7.49 (d, *J* = 2.5 Hz, 1H), 7.11 (d, *J* = 8.9 Hz, 1H), 7.04 (dd, *J* = 8.9 Hz, 2.5 Hz, 1H), 4.02 (s, 3H), 3.98 (s, 3H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ159.38, 154.30, 134.57, 129.74, 128.59, 125.18, 117.26, 110.78, 107.48, 104.45, 56.90, 55.35; HRMS (LC-APPIMS) calculated for $C_{12}H_{11}O_2Br$ (M^+) 265.9942, found 266.0009.

2,7-Dihydroxy-1-iodonaphthalene (3.124)

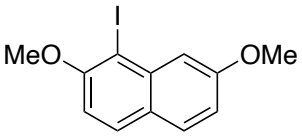


3.124

2,7-Dihydroxynaphthalene (**3.121**) (1.67 g, 7.28 mmol) was dissolved in CH_2Cl_2 (25 mL) and AcOH (25 mL). *N*-Iodosuccinimide (1.72 g, 7.66 mmol) was added in one portion and the reaction mixture was stirred at room temperature under a N_2 atmosphere for 14 h. The reaction mixture was poured in

H_2O (50 mL) and extracted with CH_2Cl_2 (3 × 50 mL). The combined organic extracts were washed with saturated aqueous $NaHCO_3$ (50 mL), H_2O (50 mL) and brine (50 mL) then dried ($MgSO_4$), filtered and concentrated under reduced pressure. The resulting residue was purified by column chromatography (CH_2Cl_2) to yield 2,7-dihydroxy-1-iodonapthalene (**3.124**) (1.73 g, 83%) as an off-white solid. R_f = 0.32 (CH_2Cl_2); m.p. 178-180 °C (CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$) δ7.66 (d, J = 4.8 Hz, 1H), 7.64 (d, J = 4.8 Hz, 1H), 7.29 (d, J = 2.4 Hz, 1H), 7.10 (d, J = 8.7 Hz, 1H), 6.97 (dd, J = 8.7 Hz, 2.4 Hz, 1H), 5.73 (s, 1H), 5.09 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ155.63, 154.38, 136.52, 130.60, 130.47, 124.85, 115.60, 114.12, 113.04, 84.42 ppm; HRMS (LC-APPIMS) calculated for $C_{10}H_7O_2I$ (M^+) 285.9491, found 285.0482.

1-Iodo-2,7-dimethoxynaphthalene (3.125)

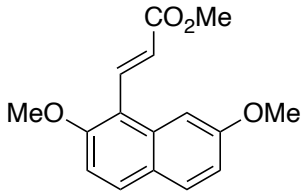


3.125

2,7-Dihydroxy-1-iodonaphthalene (**3.124**) (3.80 g, 13.3 mmol) was dissolved in acetone (100 mL) to which K_2CO_3 (4.59 g, 33.2 mmol) was added. The reaction mixture was stirred at room temperature under a N_2 atmosphere, to which MeI (4.72 g, 2.10 mL, 33.2 mmol) was added via syringe. The reaction mixture was heated to reflux for 16 h, then cooled to room temperature and quenched with saturated $NH_4Cl_{(aq)}$ (10 mL) and volatiles were removed under reduced pressure. The resulting residue was dissolved in CH_2Cl_2 (75 mL) and washed with saturated aqueous NH_4Cl (50 mL), H_2O (50 mL), and brine (50 mL). The organic layer was dried ($MgSO_4$), filtered and concentrated under reduced pressure. The crude residue was subjected to column chromatography (20% ethyl acetate/hexanes) to yield 1-iodo-2,7-dimethoxynaphthalene (**3.125**) (3.68 g, 88%) as a white solid. R_f = 0.45 (20% ethyl acetate/hexanes); m.p. 145-147 °C (CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$) δ7.75 (d, J = 8.9 Hz, 1H), 7.65 (d, J = 8.9 Hz, 1H), 7.47 (d, J = 2.4 Hz, 1H), 7.07 (d, J = 8.9 Hz, 1H), 7.03 (dd, J = 8.9 Hz, 2.5 Hz, 1H), 4.02 (s, 3H), 3.99 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ159.76,

157.12, 137.21, 130.00, 129.95, 125.22, 117.18, 110.20, 109.88, 86.50, 57.08, 55.40; HRMS (LC-APPIMS) calculated for $C_{12}H_{11}O_2I$ (M^+) 313.9804, found 313.9813.

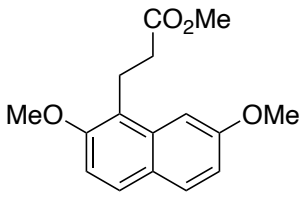
(*E*)-Methyl-3-(2,7-dimethoxynaphthalen-1-yl)acrylate (3.126)



3.126

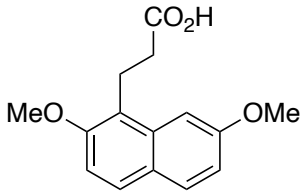
1-Iodo-2,7-dimethoxynaphthaele (**3.125**) (5.06 g, 16.1 mmol), K_2CO_3 (4.45 g, 32.2 mmol) and TBAB (13.0 g, 40.3 mmol) were dissolved in degassed DMF (100 mL). $Pd(OAc)_2$ (722 mg, 3.22 mmol) and PPh_3 (1.30 mg, 6.44 mmol) were added followed by methyl acrylate (6.93 g, 7.3 mL, 80.5 mmol). The reaction mixture was heated at 80 °C under a N_2 atmosphere for 55 h and then cooled to room temperature. The reaction mixture was poured into a large amount of H_2O (500 mL) and extracted with CH_2Cl_2 (3 × 50 mL). The combined organic extracts were washed with H_2O (100 mL) and brine (50 mL), then dried ($MgSO_4$), filtered and concentrated under reduced pressure. The resulting residue was subjected to column chromatography (20% ethyl acetate/hexanes) to yield (*E*)-methyl-3-(2,7-dimethoxynaphthalen-2-yl)acrylate (**3.126**) (4.18 g, 95%) as a yellow oil. R_f = 0.25 (20% ethyl acetate/hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ8.28 (d, *J* = 16.1 Hz, 1H), 7.74 (d, *J* = 9.0 Hz, 1H), 7.66 (d, *J* = 9.0 Hz, 1H), 7.41 (d, *J* = 2.5 Hz, 1H), 7.09 (d, *J* = 9.0 Hz, 1H), 7.02 (dd, *J* = 8.9 Hz, 2.4Hz, 1H), 6.78 (d, *J* = 16.1 Hz, 1H), 3.96 (s, 3H), 3.92 (s, 3H), 3.84 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ168.53, 159.08, 157.47, 138.19, 134.30, 131.41, 130.23, 124.40, 122.20, 116.38, 115.54, 109.99, 102.07, 56.07, 55.38, 51.67; HRMS (LC-APPIMS) calculated for $C_{16}H_{16}O_4$ (M^+) 272.1049, found 272.1063.

Methyl-3-(2,7-dimethoxynaphthalen-1-yl)propanoate



(*E*)-Methyl-3-(2,7-dimethoxynaphthalen-1-yl)acrylate (**3.126**) (2.87 g, 10.5 mmol) was dissolved in EtOAc (50 mL) and CH_2Cl_2 (50 mL) to which 10% Pd/C (300 mg) was added. The atmosphere within the flask was evacuated and refilled with H_2, then stirred at rt overnight. The reaction mixture was filtered through a plug of celite and washed with CH_2Cl_2 (3 × 30 mL), then concentrated under reduced pressure to obtain methyl-3-(2,7-dimethoxynaphthalen-1-yl)propanoate (2.88 g, quant.) as a brown oil which was used without further purification. R_f = 0.25 (20% ethyl acetate/hexanes); ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.68 (d, *J* = 8.5 Hz, 1H), 7.66 (d, *J* = 7.6 Hz, 1H), 7.22 (d, *J* = 2.3 Hz, 1H), 7.11 (d, *J* = 9.0 Hz, 1H), 7.02 (d, *J* = 2.4 Hz, 1H), 7.00 (d, *J* = 2.4 Hz, 1H), 3.94, (s, 3H), 3.93 (s, 3H), 3.70, (s, 3H), 3.38-3.35 (m, 2H), 2.62-2.59 (m, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 174.13, 158.43, 155.08, 133.96, 130.19, 127.86, 124.64, 120.33, 115.87, 110.39, 101.37, 56.20, 55.31, 51.63, 33.69, 20.84; HRMS (LC-APPIMS) calculated for $C_{16}H1_8O_4$ (M^+) 274.1205, found 274.1219.

2,7-Dimethoxy-1-propionic acid naphthalene (3.127)

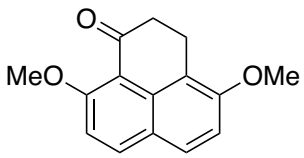


3.127

Methyl-3-(2,7-dimethoxynaphthalen-1-yl)propanoate (2.00 g, 7.30 mmol) was dissolved in THF (50 mL) to which 1M $NaOH_{(aq)}$ (50 mL) was added. The reaction mixture was heated at reflux for 16 h then cooled to rt. The volatiles were removed under reduced pressure then redissolved in EtOAc (100 mL). The organic layer was washed with 10% $HCl_{(aq)}$ (3 × 100 mL), H_2O (50 mL), and brine (50 mL). The organic layer was dried ($MgSO_4$), filtered and concentrated under reduced to afford 2,7-dimethoxy-1-propionic acid naphthalene (**3.127**) (1.90 g, 99%) as a light-yellow solid which was used without further purification. A small sample was recrystallized from heptane for characterization. R_f = 0.35 (40 % ethyl acetate/hexanes); m.p. 212-215 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.70 (d, *J* = 4.8 Hz,

1H), 7.68 (d, *J* = 4.8 Hz, 1H), 7.24 (d, *J* = 2.3 Hz, 1H), 7.12 (d, *J* = 8.9 Hz, 1H), 7.02 (dd, *J* = 2.4, 8.9 Hz, 1H), 3.94 (s, 6H), 3.39 (t, *J* = 8.2 Hz, 2H), 2.67 (t, *J* = 8.2 Hz, 2H); ^{13}C (75 MHz, $CDCl_3$) δ 178.77, 158.46, 155.12, 133.94, 130.22, 127.96, 124.65, 120.12, 115.91, 110.39, 101.34, 56.20, 55.30, 33.72, 20.71; HRMS (LC-APPIMS) calculated for $C_{15}H_{16}O_4$ (M^+) 260.1049, found 260.1066.

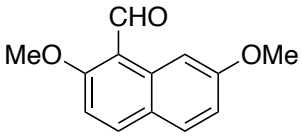
4,9-Dimethoxy-2*H*-2,3-dihydrophenalen-1-one (3.129)



3.129

2,7-Dimethoxy-1-propionic acid naphthalene (**3.127**) (1.00 g, 3.84 mmol) was dissolved in Eaton's Reagent (25 mL) and stirred at rt under a N_2 atmosphere for 3 h. The reaction mixture was cooled to 0 °C and quenched by slow addition of H_2O then extracted with CH_2Cl_2 (3 × 50 mL). The combined organic extracts were dried ($MgSO_4$), filtered and concentrated under reduced pressure. The resulting residue was subjected to column chromatography (50 % ethyl acetate/hexanes) to afford 4,9-dimethoxy-2*H*-2,3-dihydrophenalen-1-one (613 mg, 66%) as a yellow solid. R_f = 0.20 (20% ethyl acetate/hexanes); m.p. 124-127 °C (CH_2Cl_2); ^{1}H NMR (500 MHz, C_6D_6) δ 7.58 Hz (d, *J* = 9.1 Hz, 1H), 7.44 (d, *J* = 9.0 Hz, 1H), 6.76 (d, *J* = 9.0 Hz, 1H), 6.72 (d, *J* = 9.1 Hz, 1H), 3.50 (s, 3H), 3.35 (s, 3H), 3.18 (t, *J* = 7.5 Hz, 2H), 2.68 (t, *J* = 7.5 Hz, 2H); ^{13}C NMR (C_6D_6, 75 MHz) δ 195.44, 158.35, 155.12, 135.43, 134.66, 123.96, 117.95, 116.24, 112.25, 110.72, 56.24, 55.37, 39.77, 22.64; HRMS (LC-APPIMS) calculated for $C_{15}H_{14}O_3$ (M^+) 242.0943, found 242.0966.

2,7-Dimethoxynaphthaldehyde (3.131)



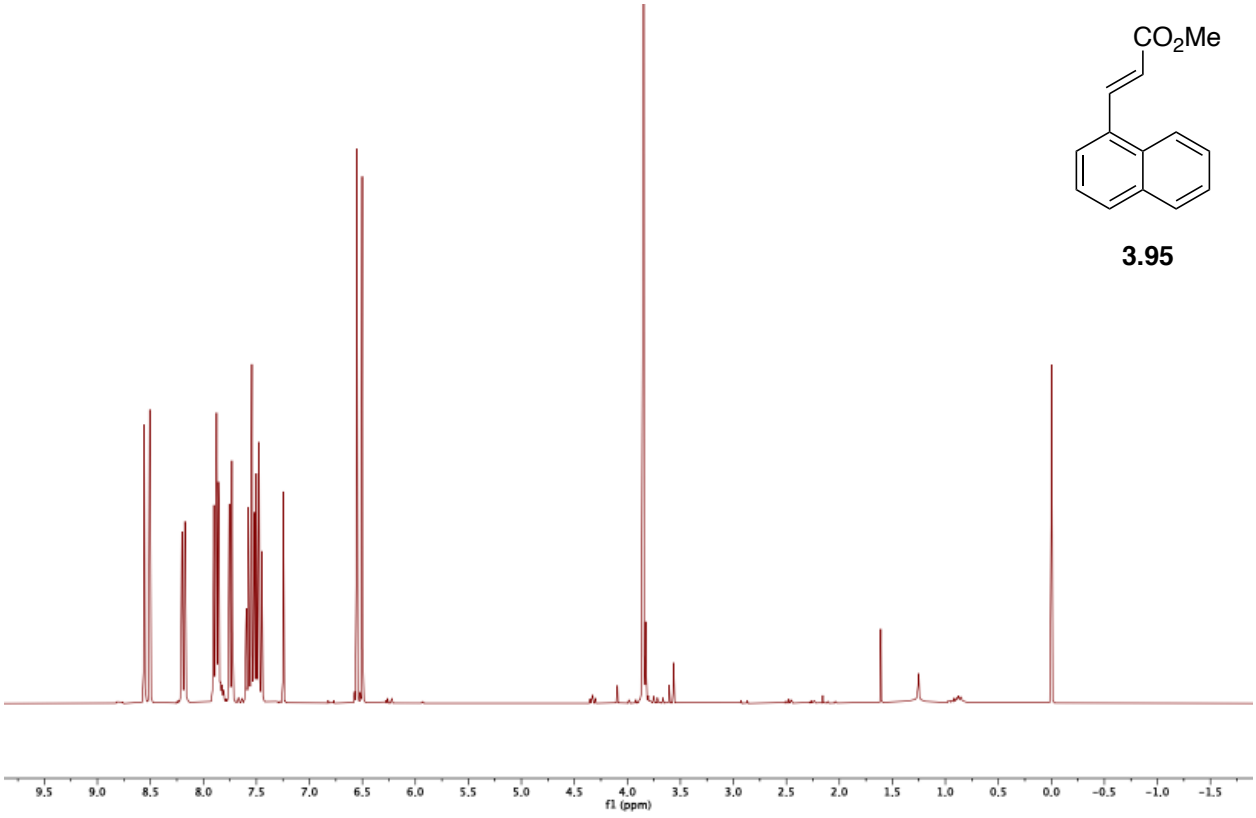
3.131

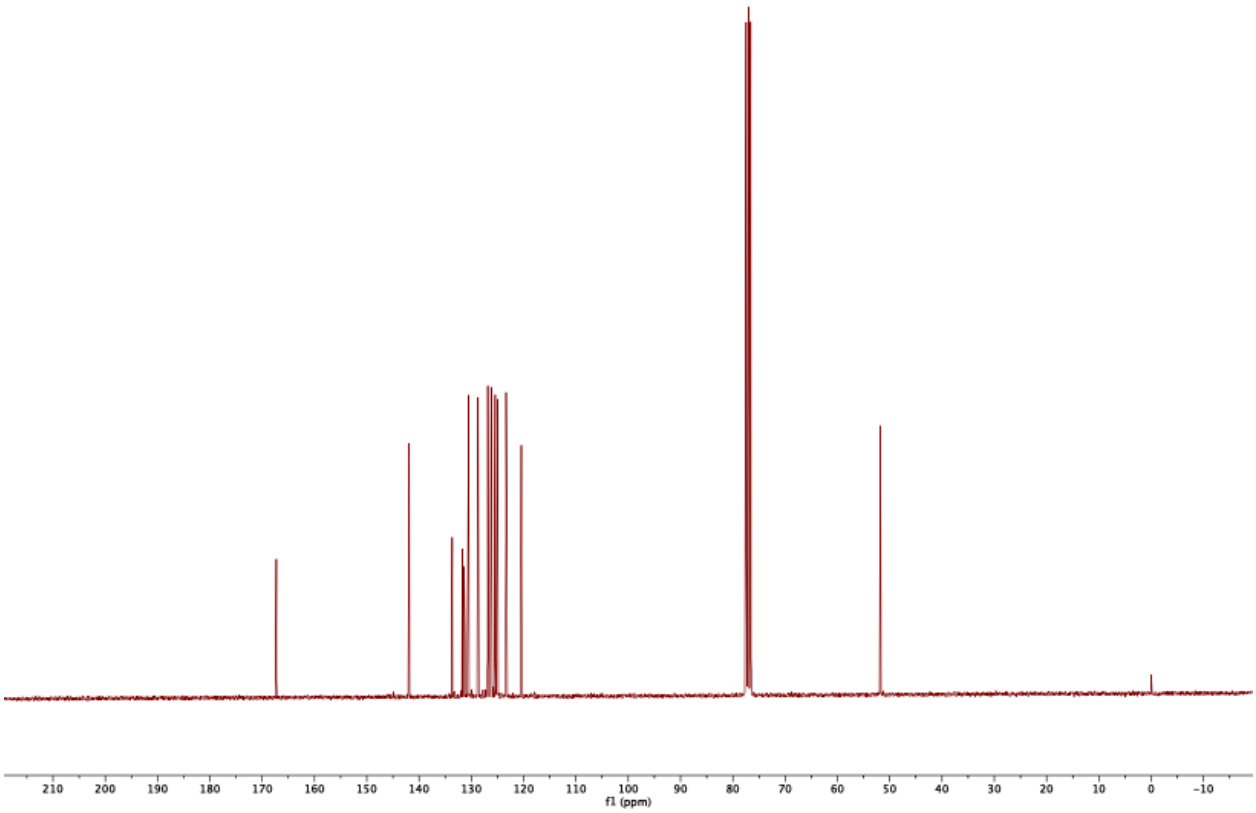
1-Bromo-2,7-dimethoxynaphthalene (**3.123**) (1.00 g, 3.74 mmol) was dissolved in THF (60 mL) and cooled to −78 °C under a N_2 atmosphere. *n*-BuLi (10.5 mL, 1.07 M, 11.23 mmol) was added

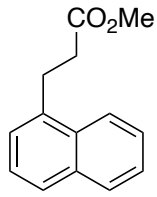
dropwise via syringe over several minutes and upon complete addition the reaction was allowed to stir with cooling for 20 min. *N*-Formylpiperidine (2.11 g, 2.10 mL, 18.7 mmol) was added via syringe and the reaction was warmed to rt then stirred for an additional 3 h, after which the reaction mixture was quenched by addition of 10% $HCl_{(aq)}$ (50 mL). The volatiles were removed in vacuo and then extracted with CH_2Cl_2 (3 × 50 mL). The combined organic extracts were washed with H_2O (50 mL) and (50 mL) brine, then dried ($MgSO_4$), filtered and concentrated under reduced pressure. The resulting residue was subjected to column chromatography (20% EtOAc/hexane) to yield 2,7-dimethoxy-1-naphthaldehyde (**3.131**) (643 mg, 80%) as an off-white solid. R_f = 0.40 (20% ethyl acetate/hexanes); m.p. 145-147 °C (CH_2Cl_2); ^{1}H NMR ($CDCl_3$, 500 MHz) δ10.89 (s, 1H), 8.84 (d, *J* = 2.5 Hz, 1H), 7.97 (d, *J* = 9.0 Hz, 1H), 7.65 (d, *J* = 8.9 Hz, 1H), 7.11 (d, *J* = 9.0 Hz, 1H), 7.06 (dd, *J* = 8.9 Hz, 2.5 Hz, 1H) ppm ; ^{13}C NMR ($CDCl_3$, 75 MHz) δ192.10, 164.90, 161.51, 137.37, 133.53, 129.74, 124.01, 117.46, 115.75, 109.46, 103.45, 56.43, 55.45 ppm; ; HRMS (LC-APPIMS) calculated for $C_{13}H_{12}O_3$ (M^+) 216.0786, found 216.0792.

Appendix 2:

Selected ^{1}H and ^{13}C NMR Spectra for Chapter 3

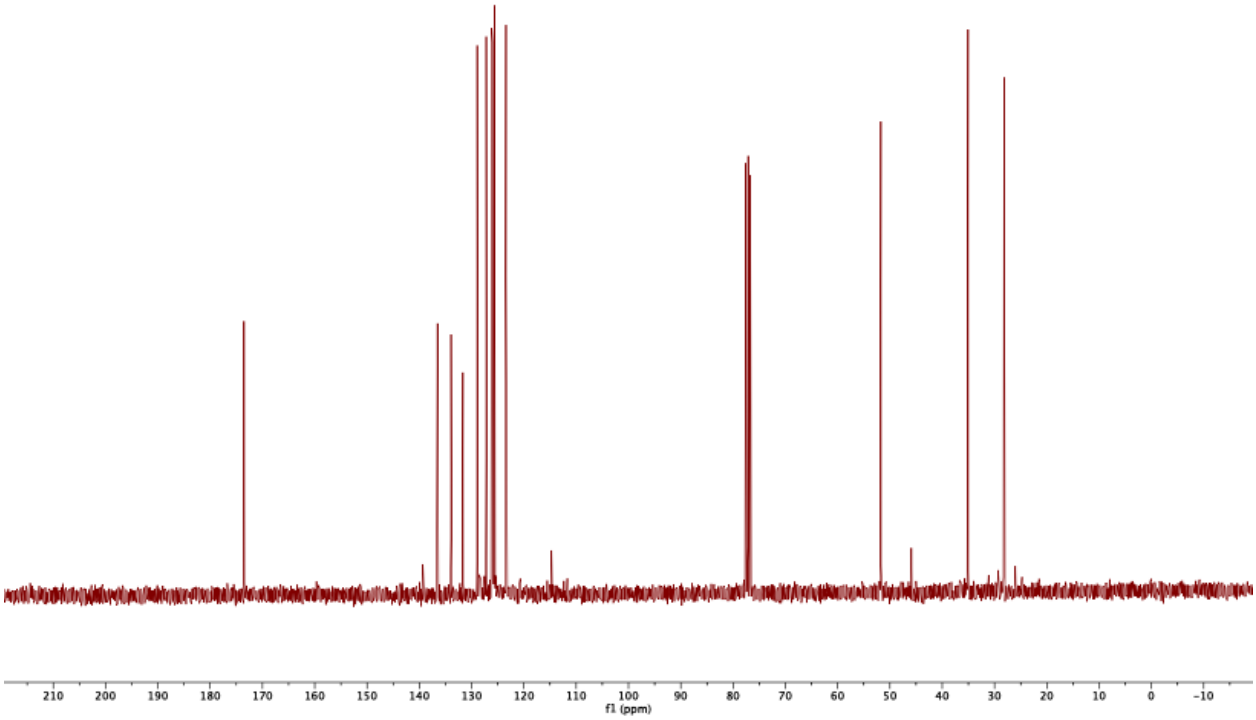

CO2Me
3.95
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1.0
-1.5
f1 (ppm)

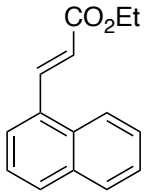

210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


CO2Me

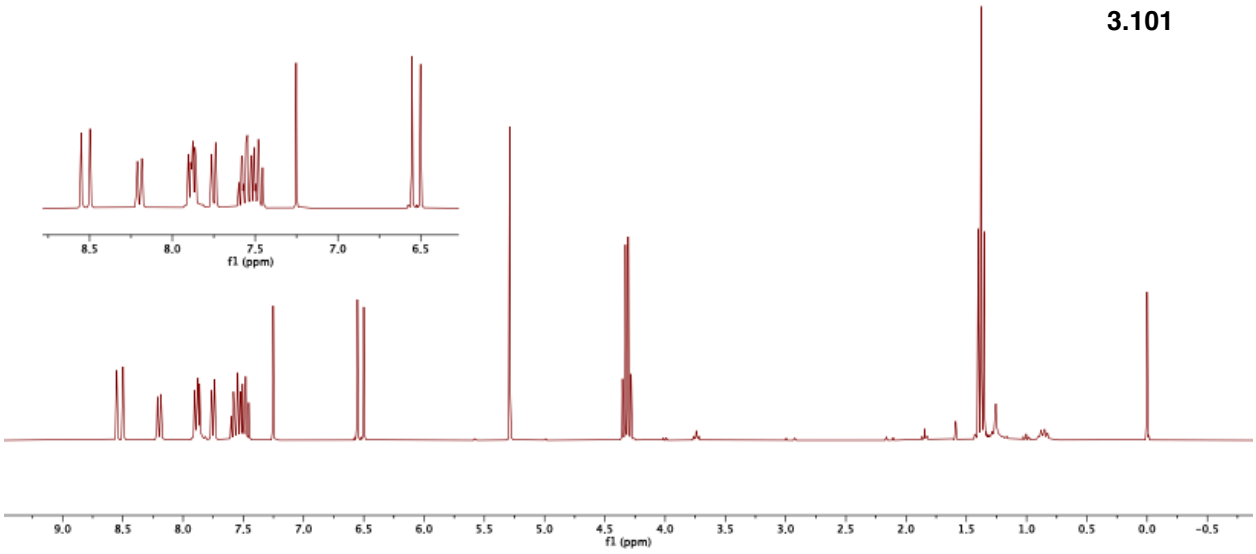
3.96

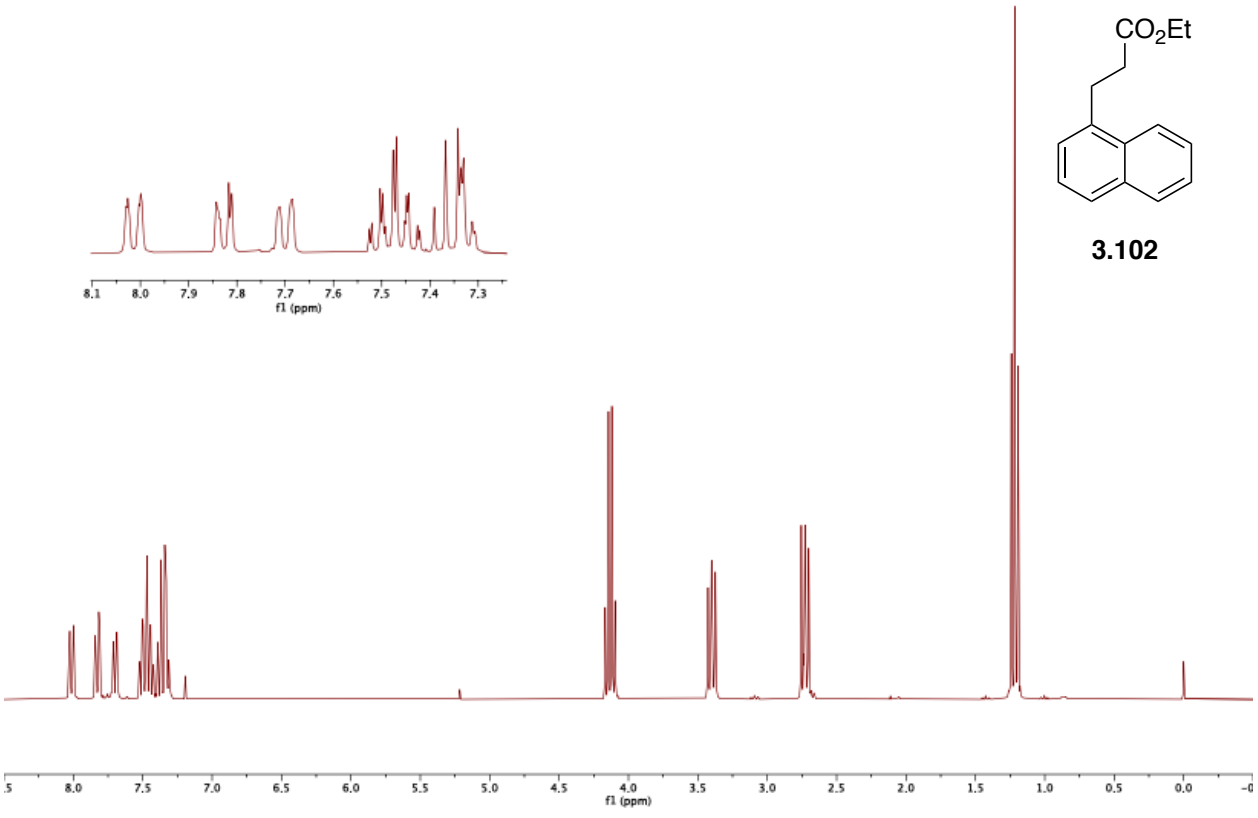
8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

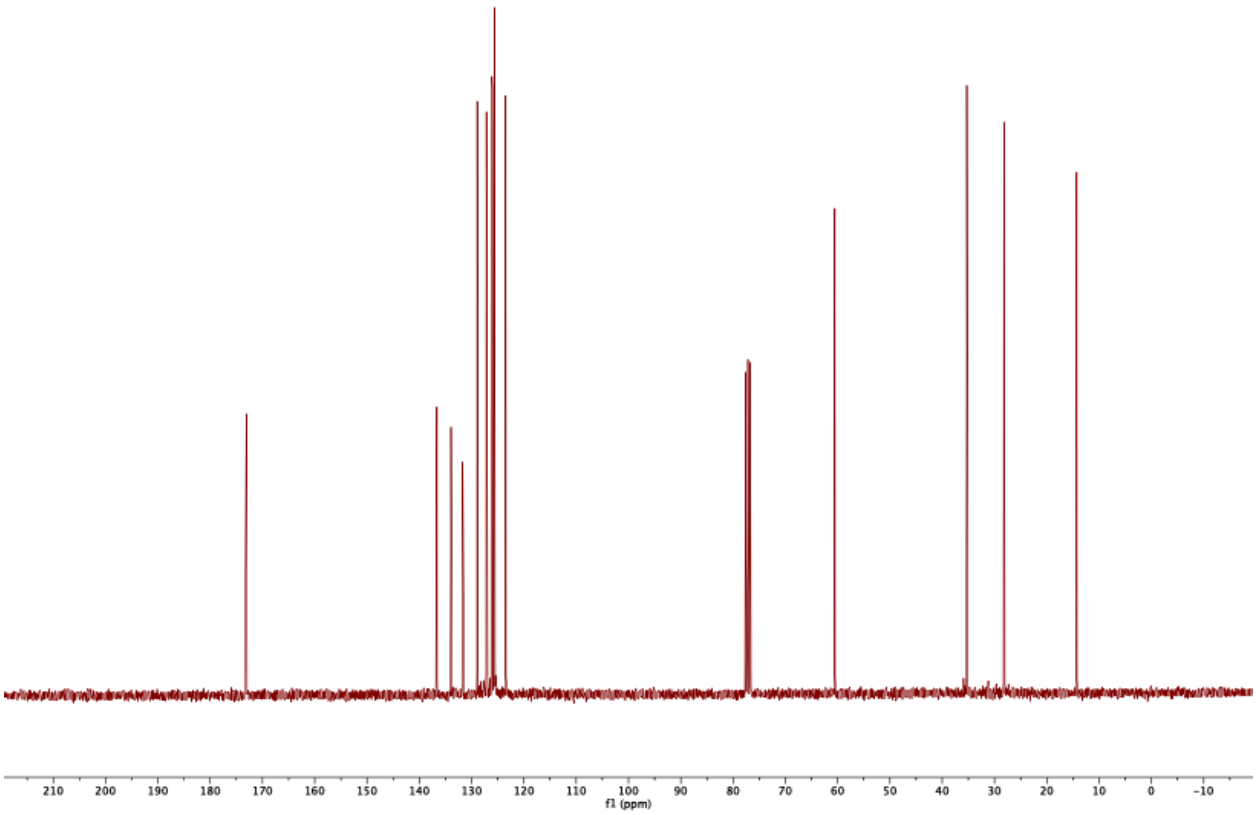

210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

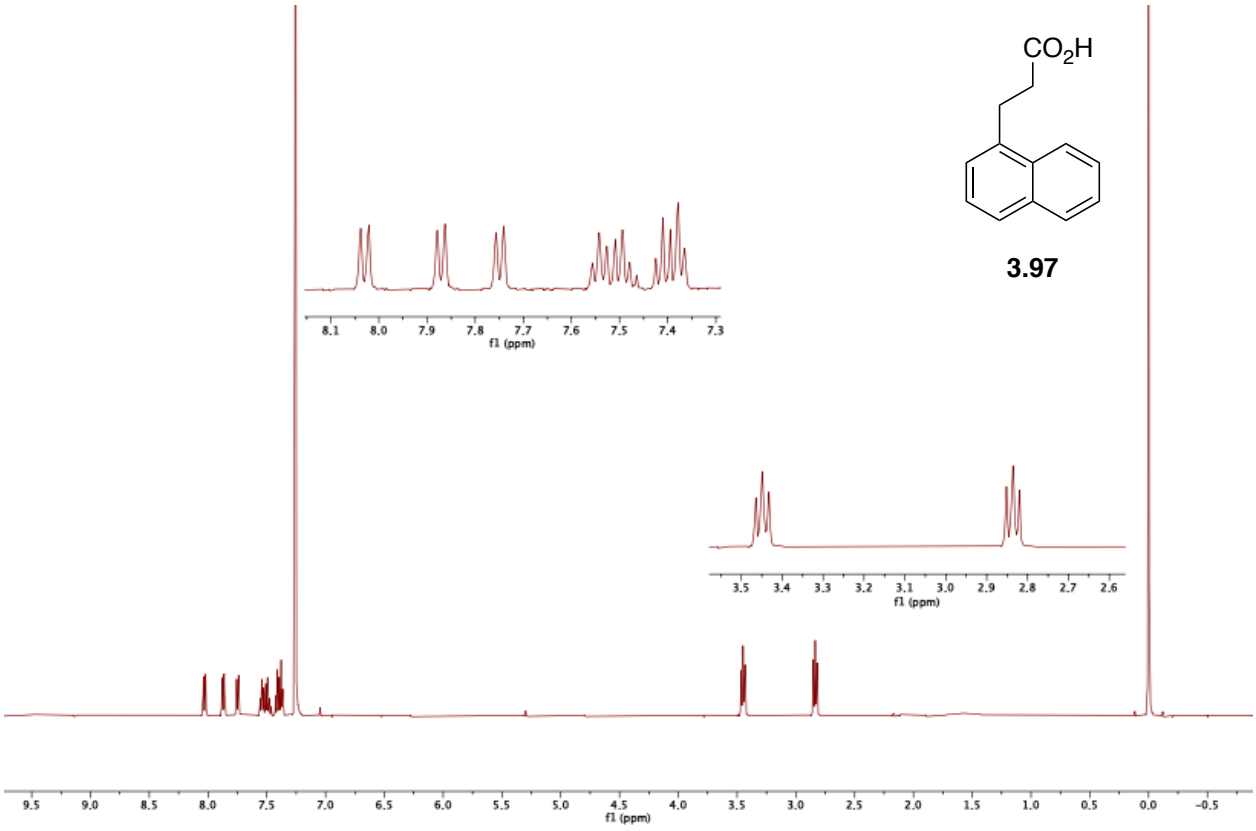

CO2Et

3.101

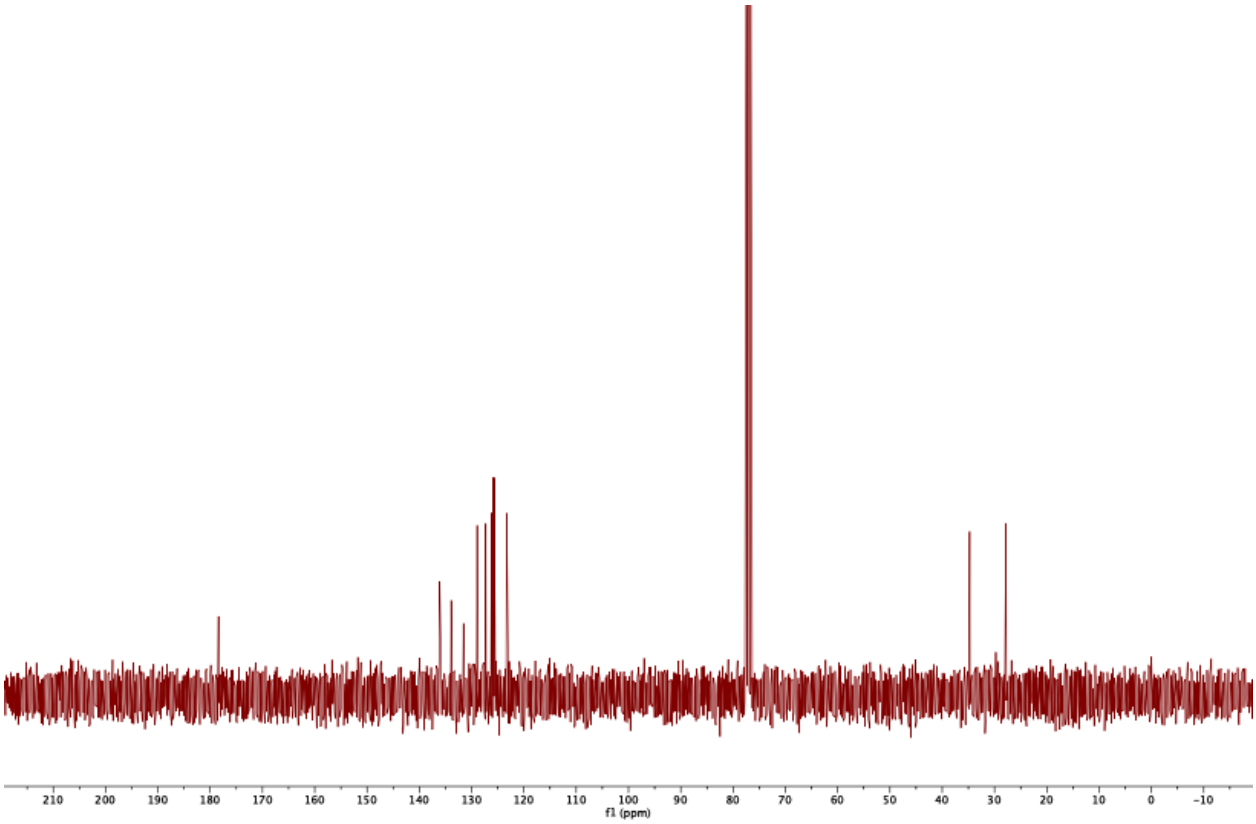

8.5 8.0 7.5 7.0 6.5
f1 (ppm)
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

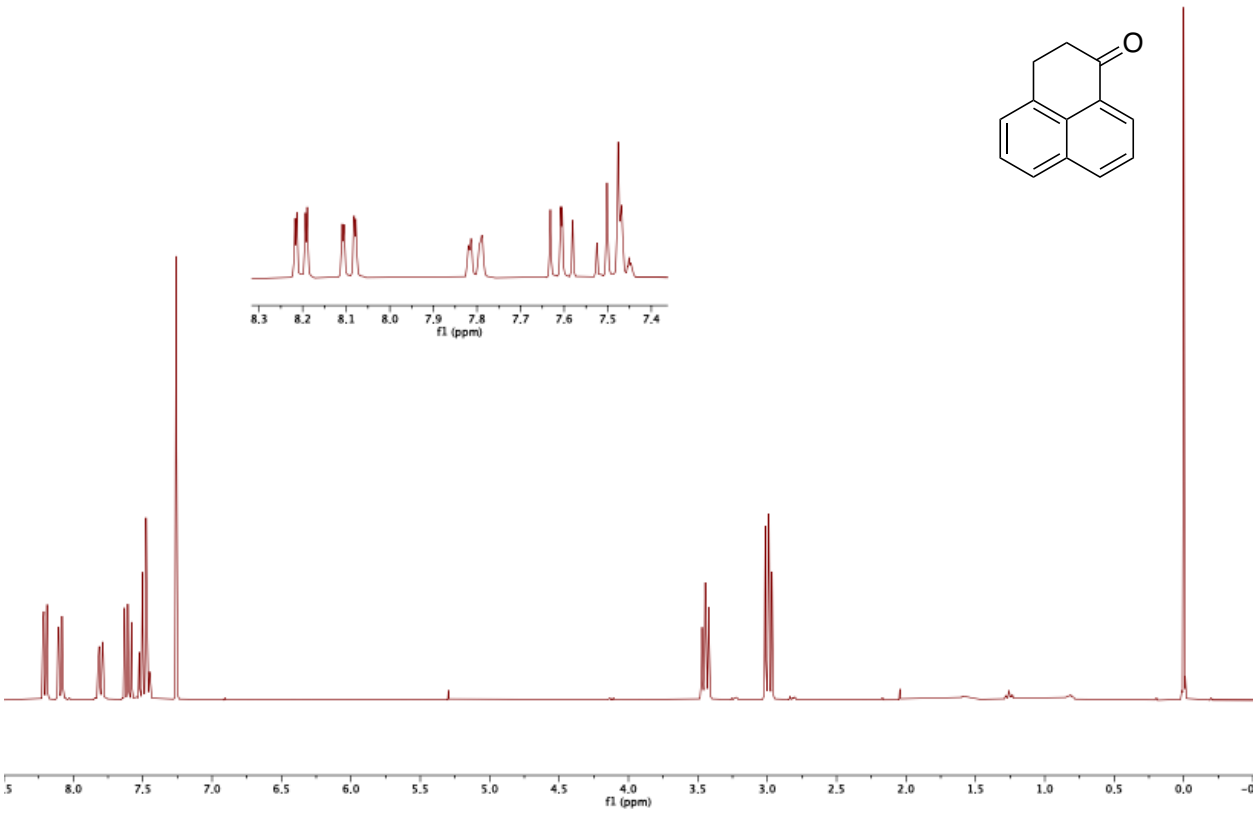

CO2Et
3.102
8.1
8.0
7.9
7.8
7.7
7.6
7.5
7.4
7.3
f1 (ppm)
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

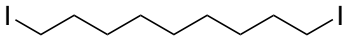

210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

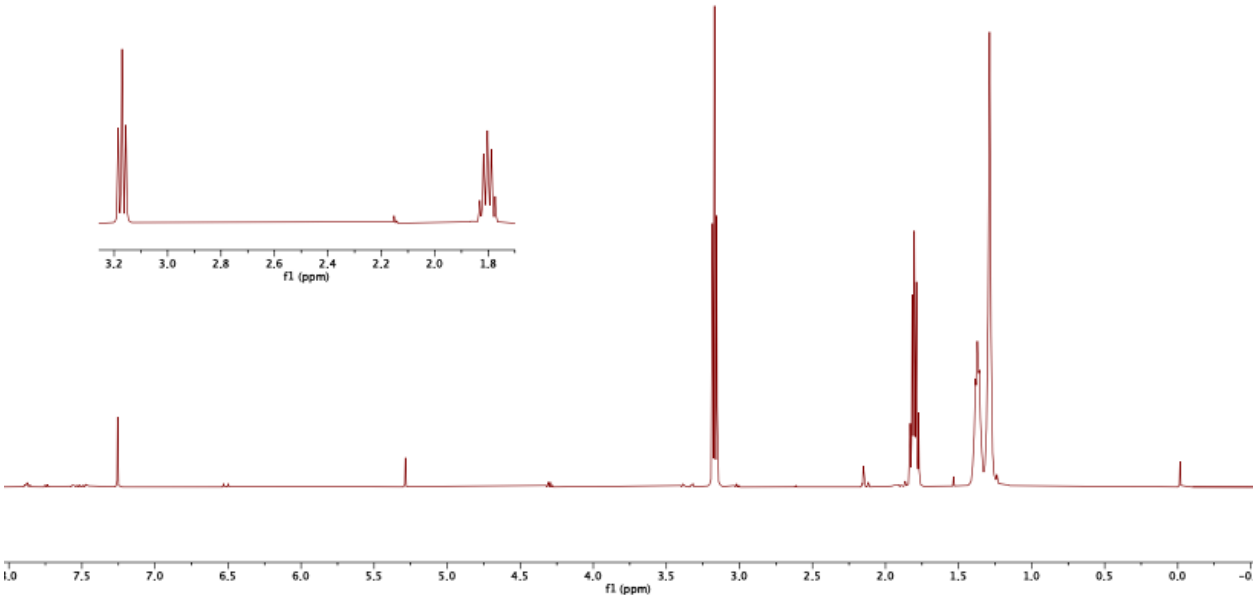

CO2H
8.1 8.0 7.9 7.8 7.7 7.6 7.5 7.4 7.3
f1 (ppm)
3.5 3.4 3.3 3.2 3.1 3.0 2.9 2.8 2.7 2.6
f1 (ppm)
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

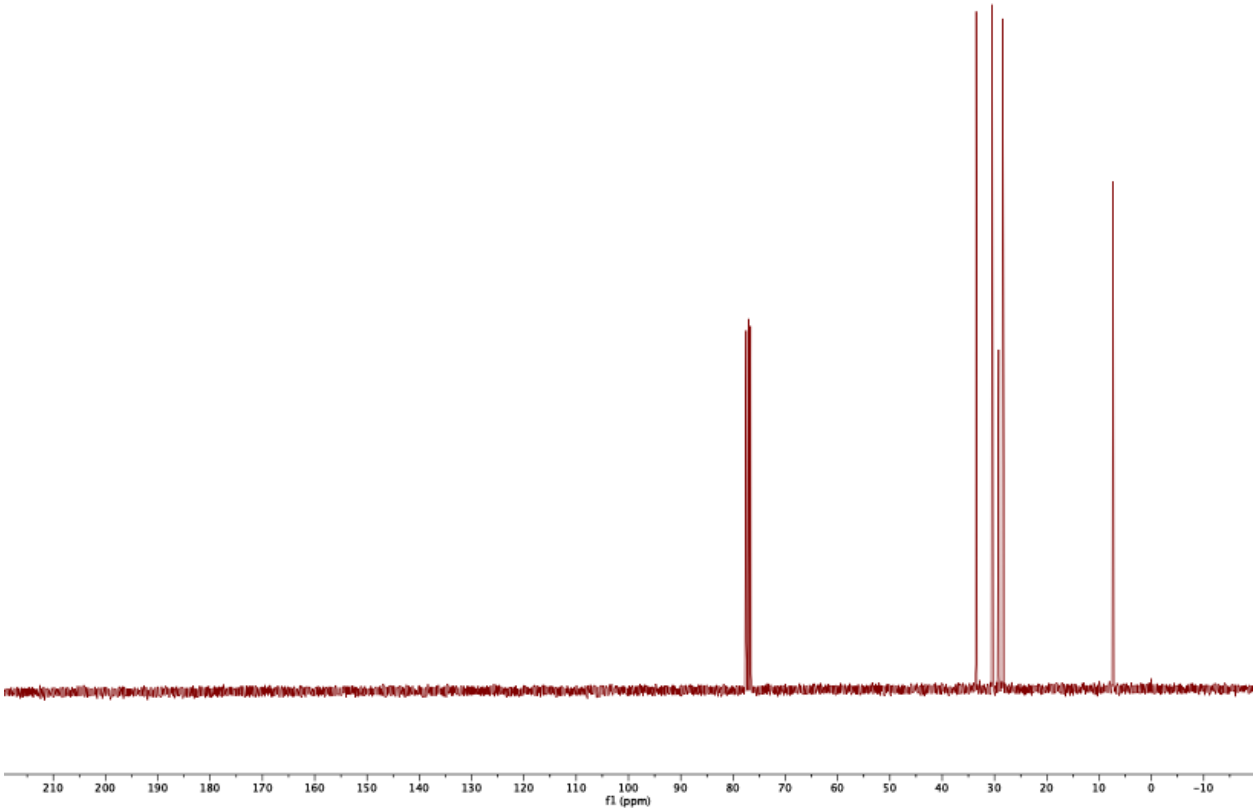
3.97

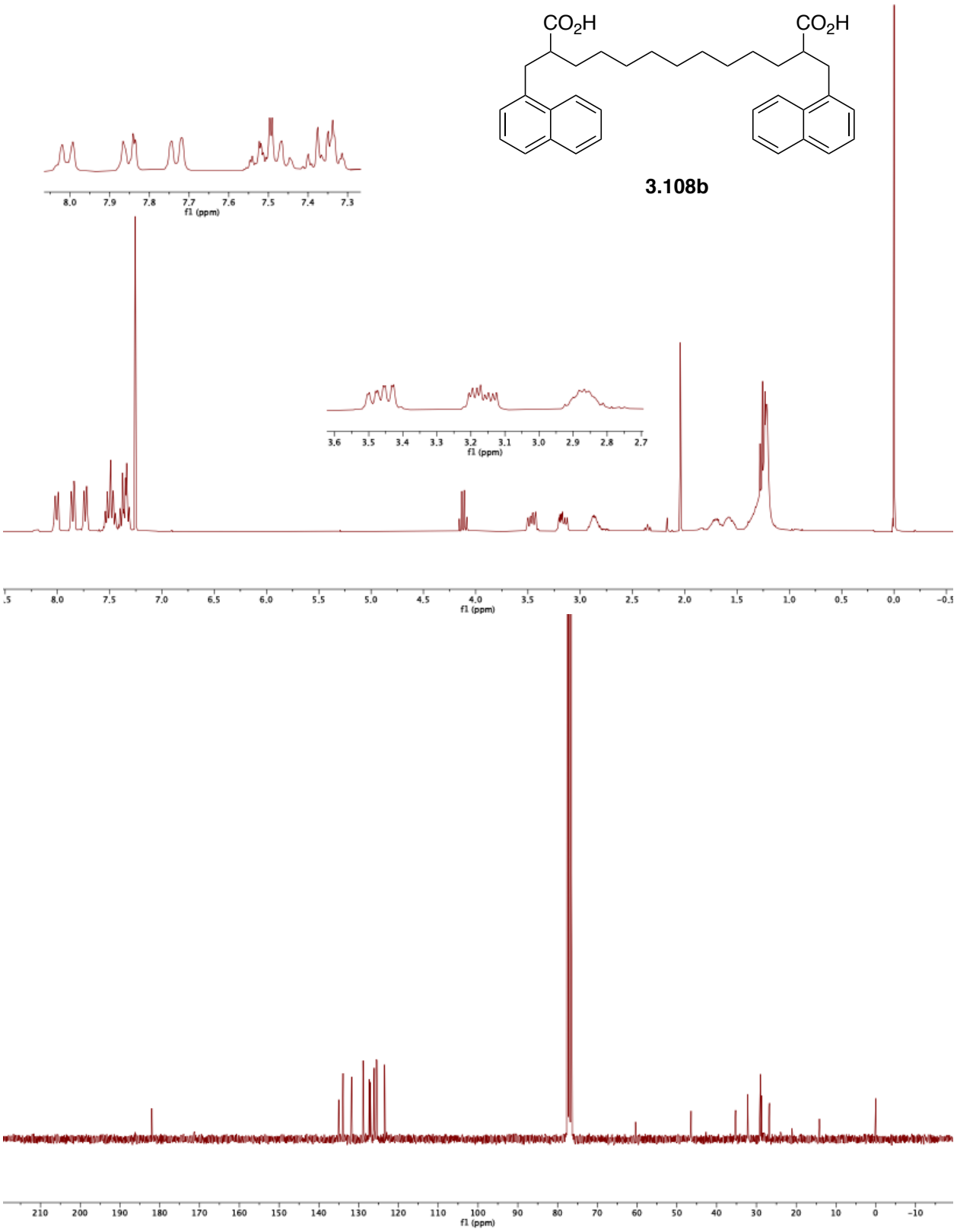

210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
−10
f1 (ppm)

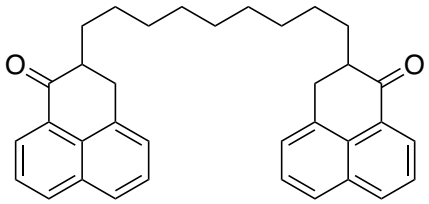

O
8.3 8.2 8.1 8.0 7.9 7.8 7.7 7.6 7.5 7.4
f1 (ppm)
8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)



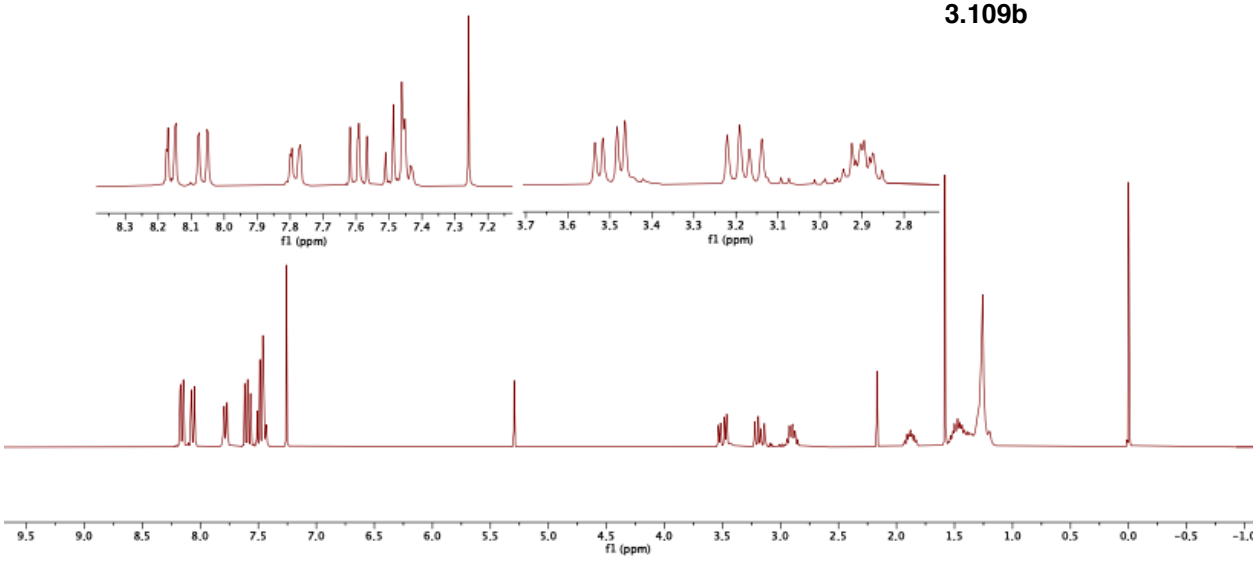

3.2
3.0
2.8
2.6
2.4
2.2
2.0
1.8
f1 (ppm)
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

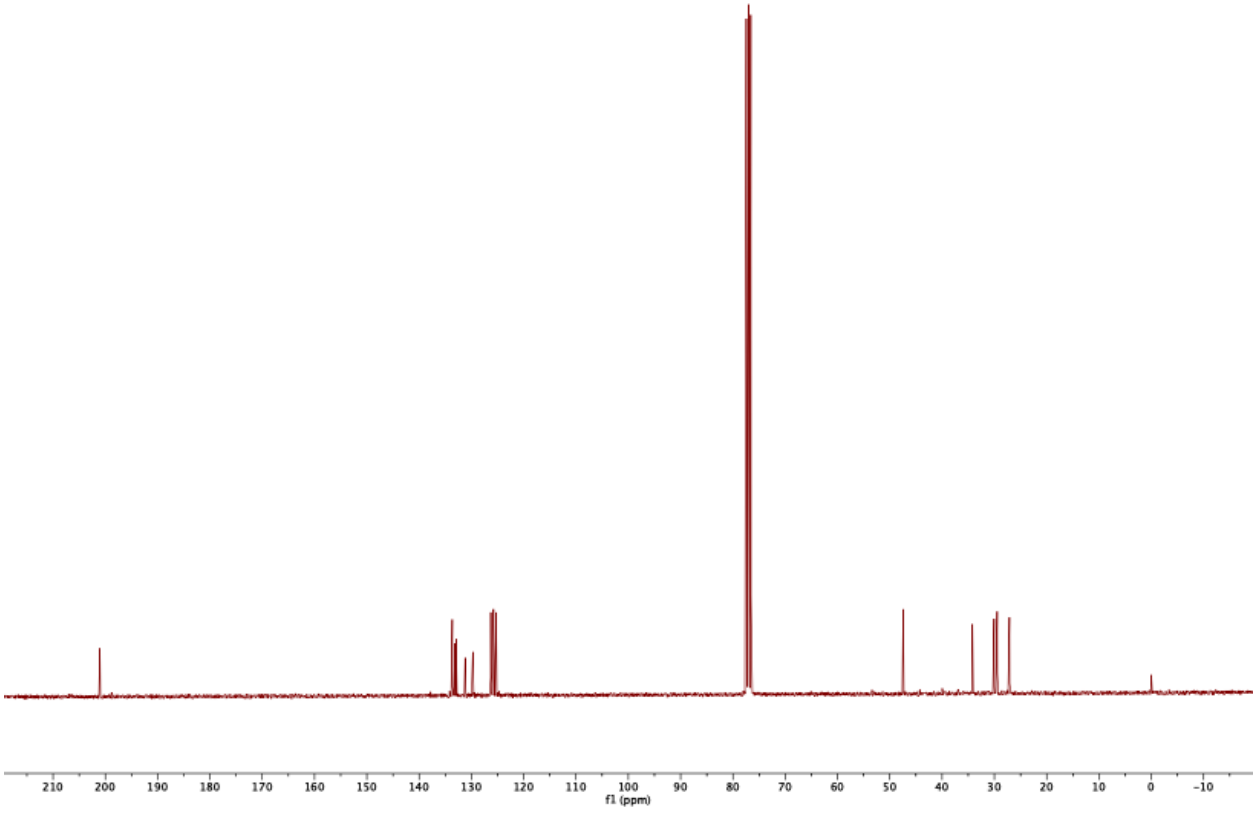

210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

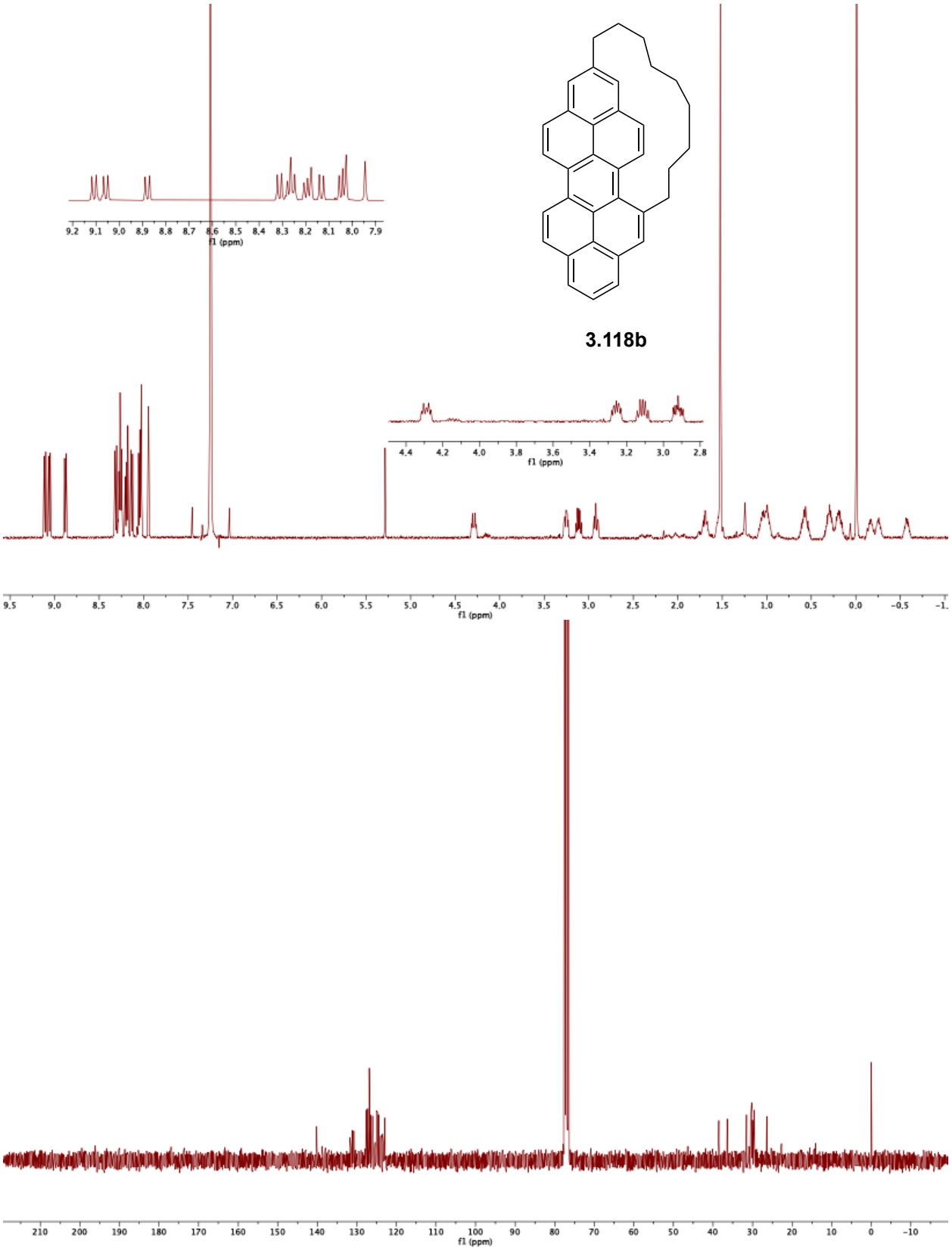

CO2H
CO2H
3.108b
f1 (ppm)

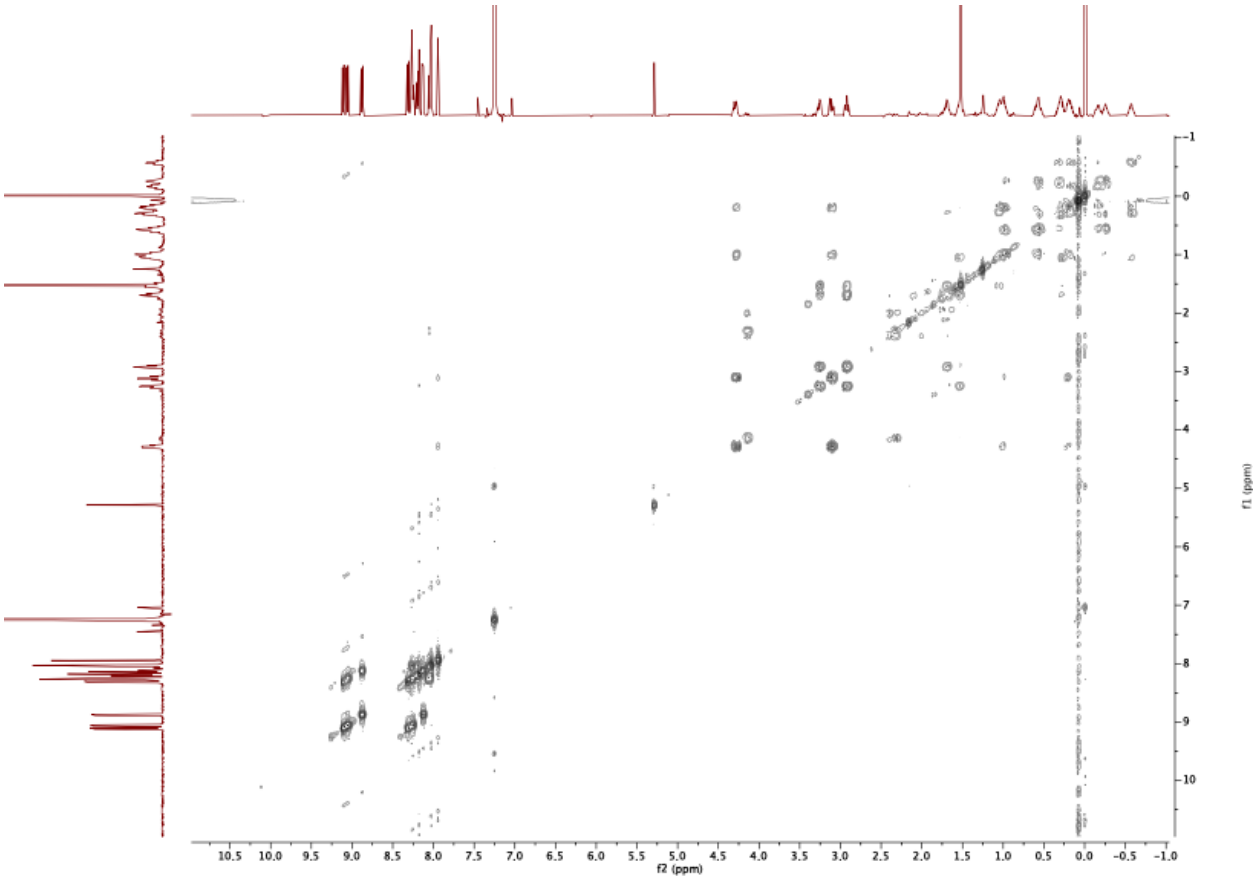

O
O

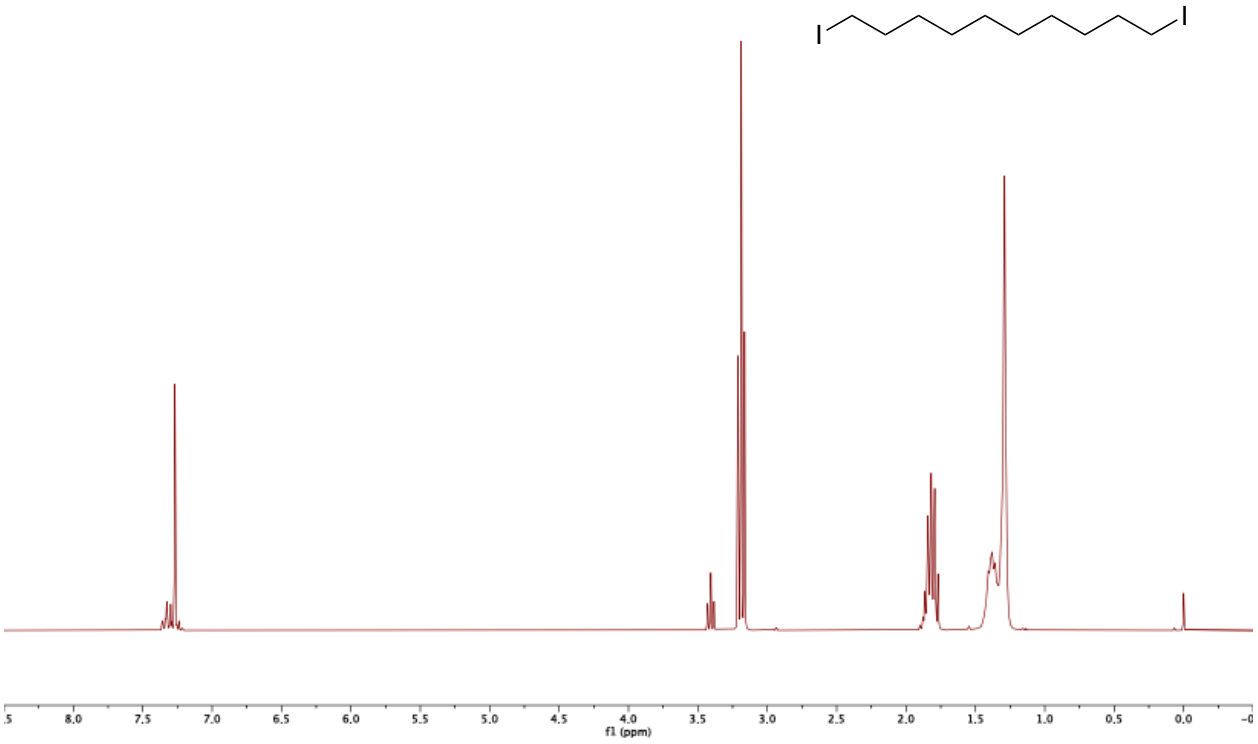
3.109b

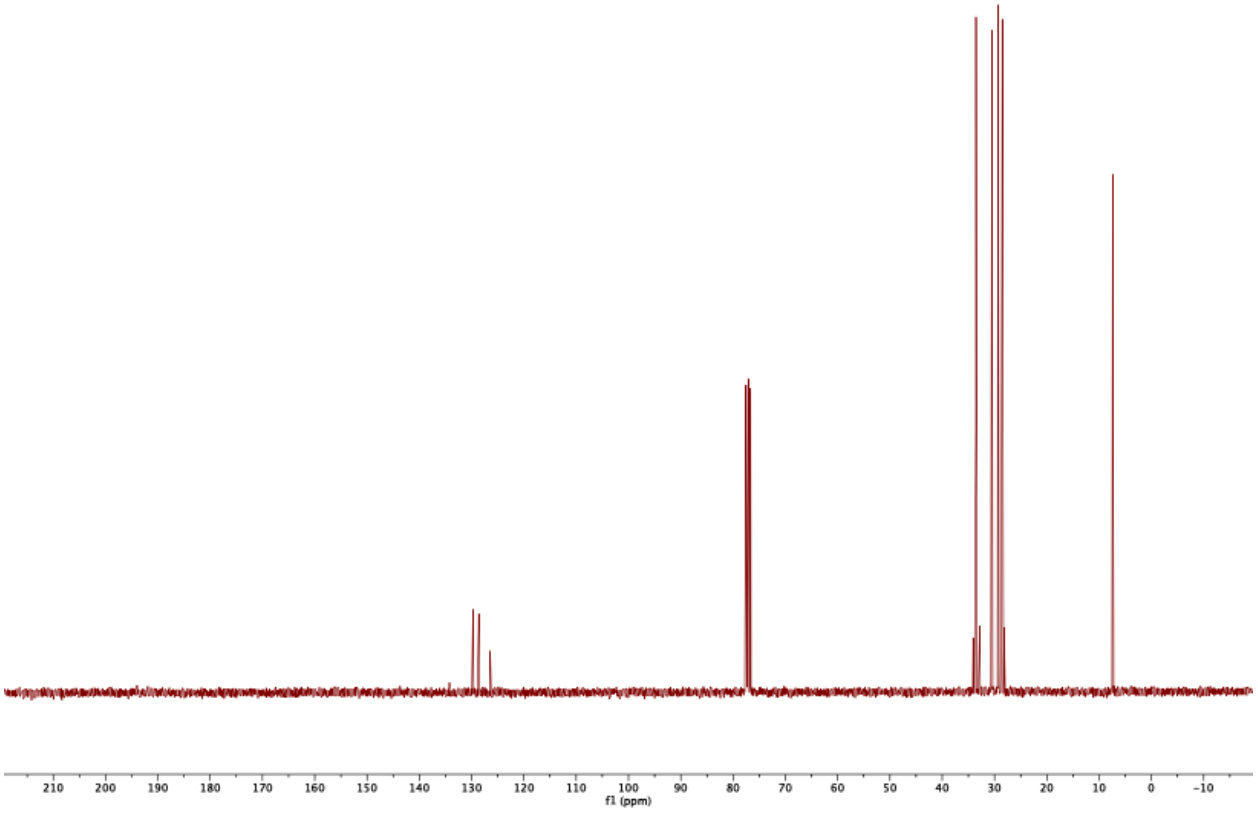

8.3 8.2 8.1 8.0 7.9 7.8 7.7 7.6 7.5 7.4 7.3 7.2
f1 (ppm)
3.7 3.6 3.5 3.4 3.3 3.2 3.1 3.0 2.9 2.8
f1 (ppm)
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

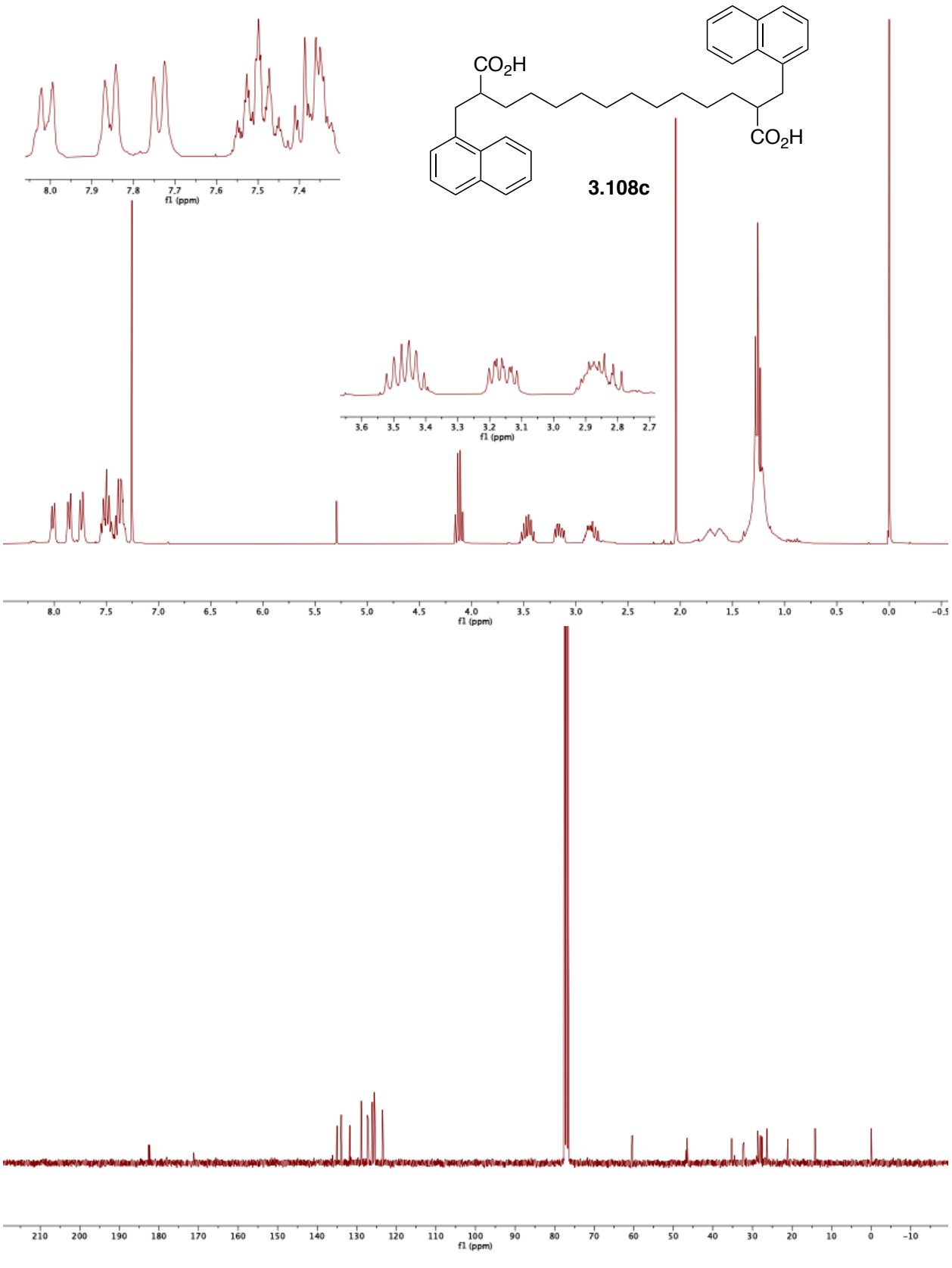

210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

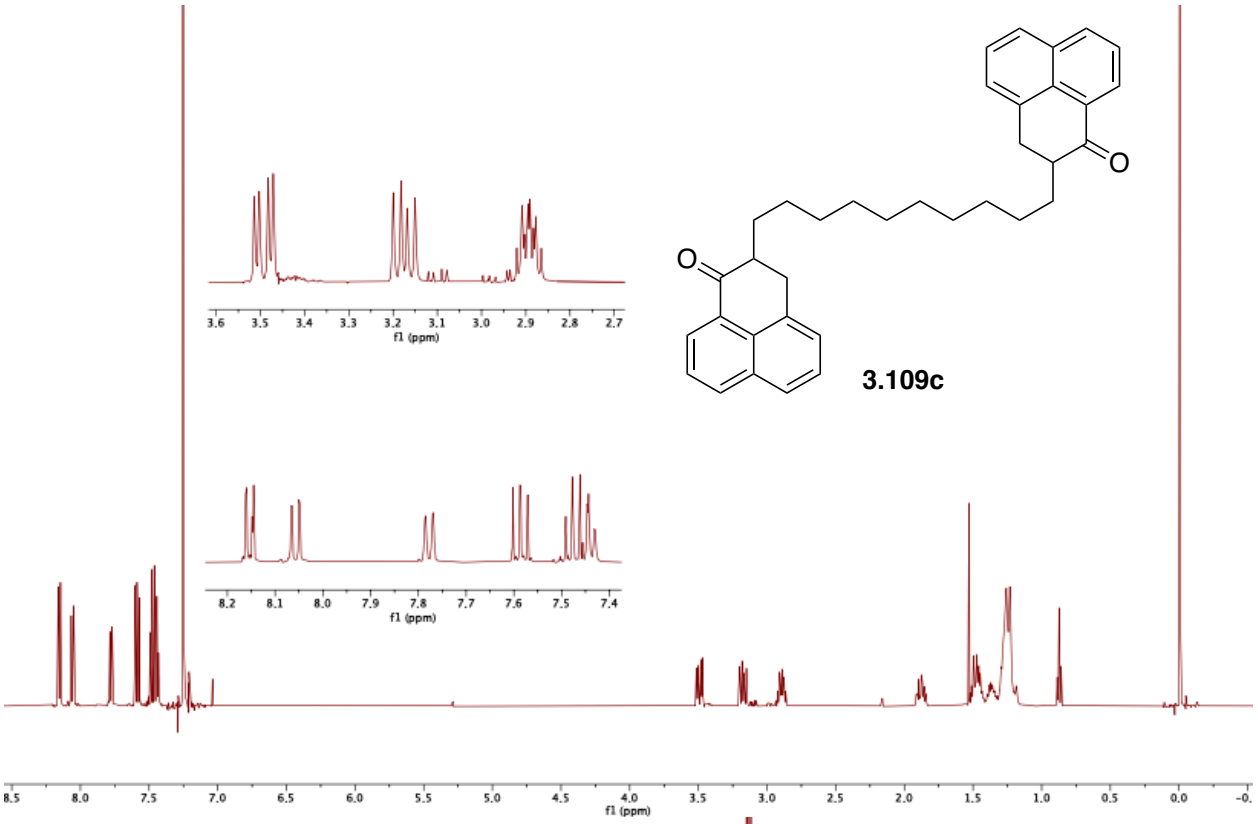

f1 (ppm)
3.118b

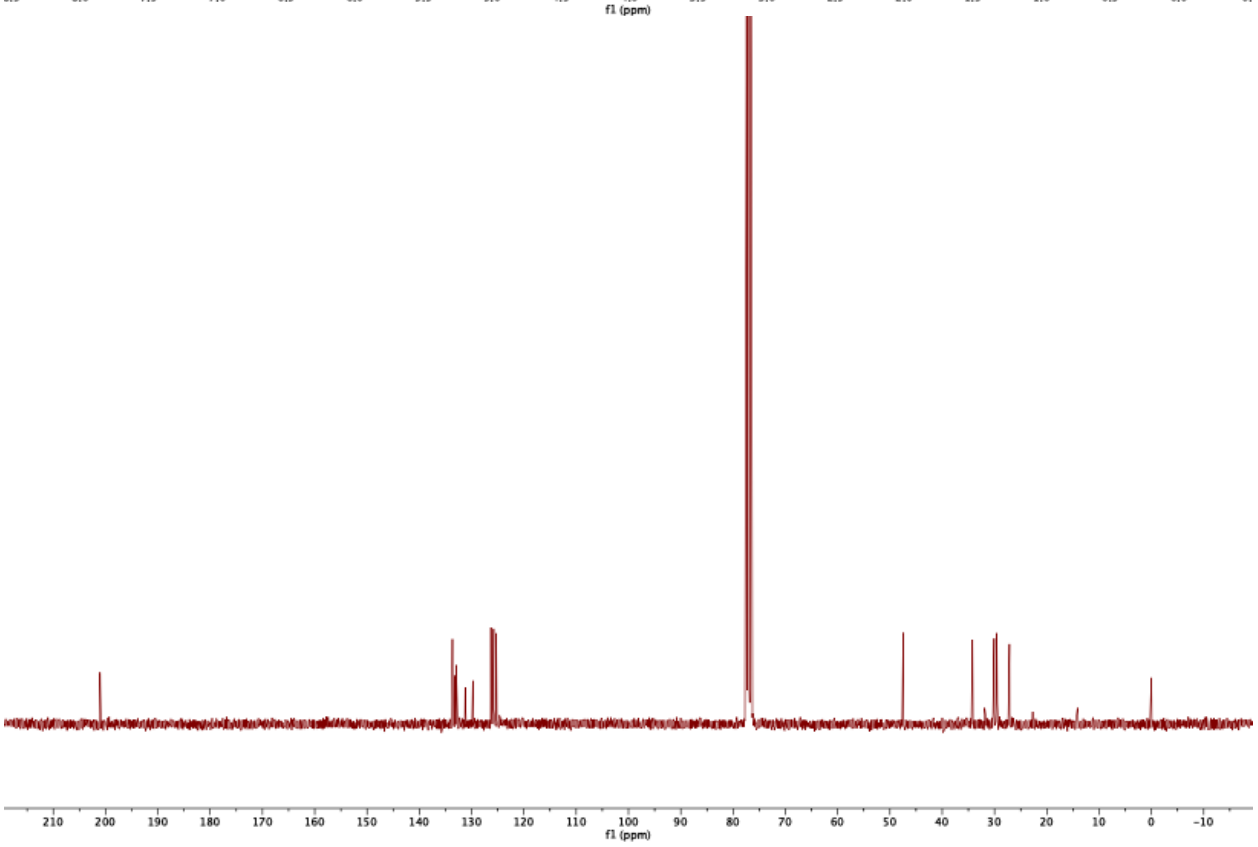

10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.0
f2 (ppm)
-1 0 1 2 3 4 5 6 7 8 9 10
f1 (ppm)

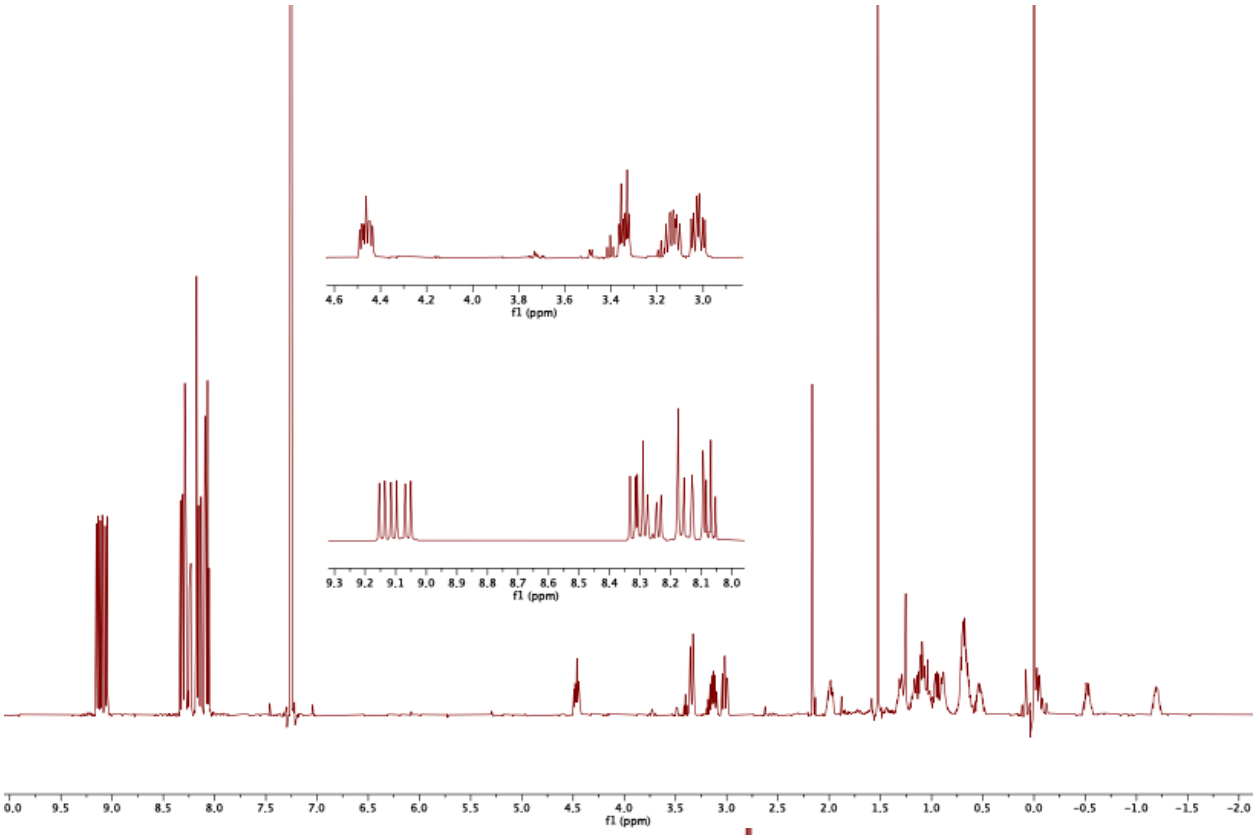

I
I
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

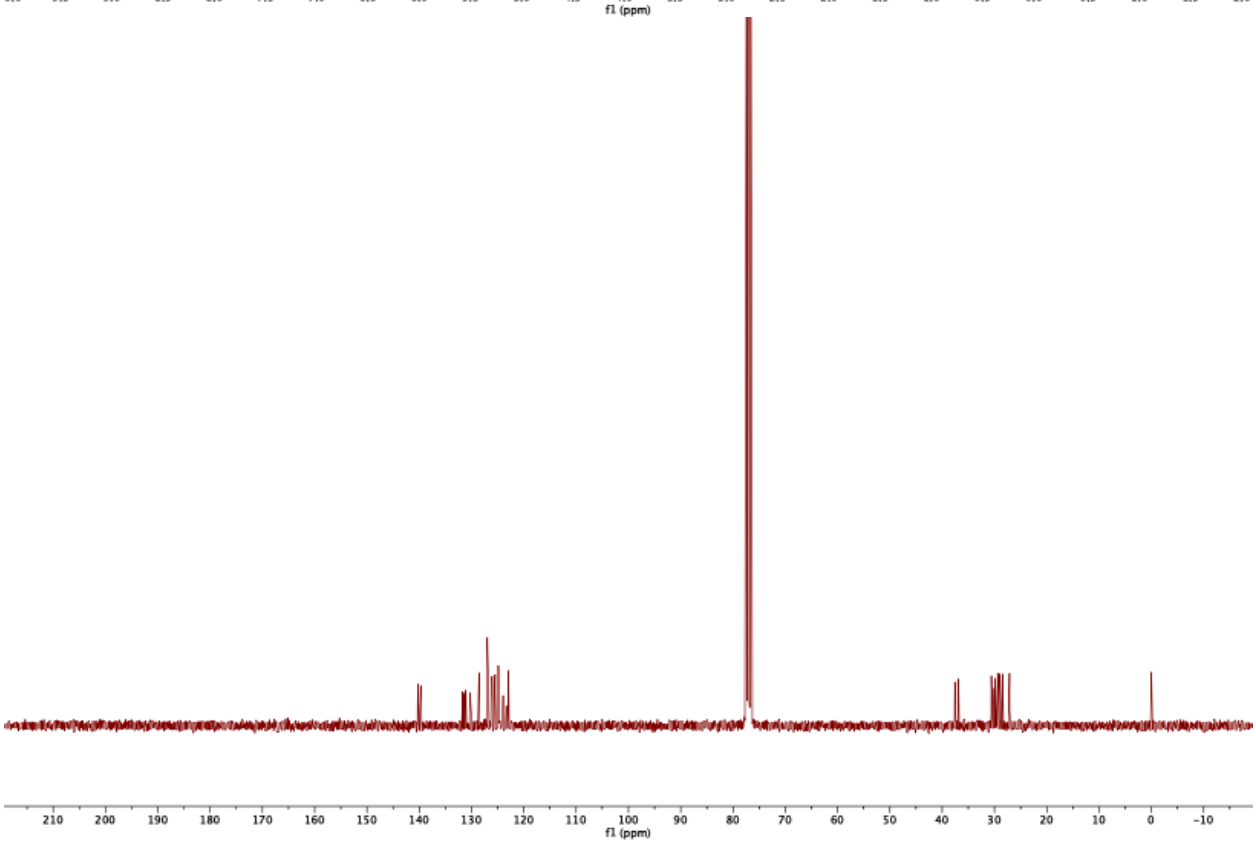

210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

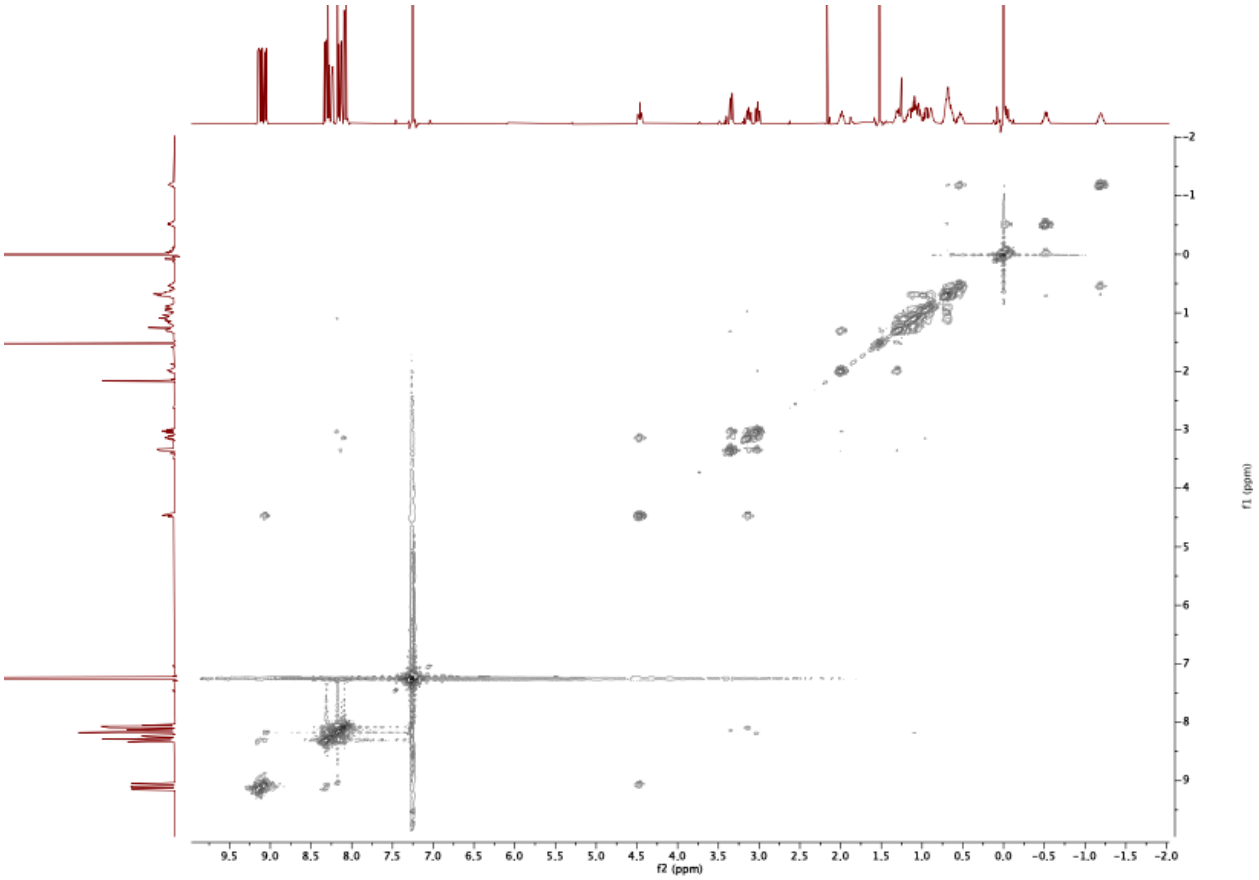

CO2H
CO2H
3.108c
f1 (ppm)

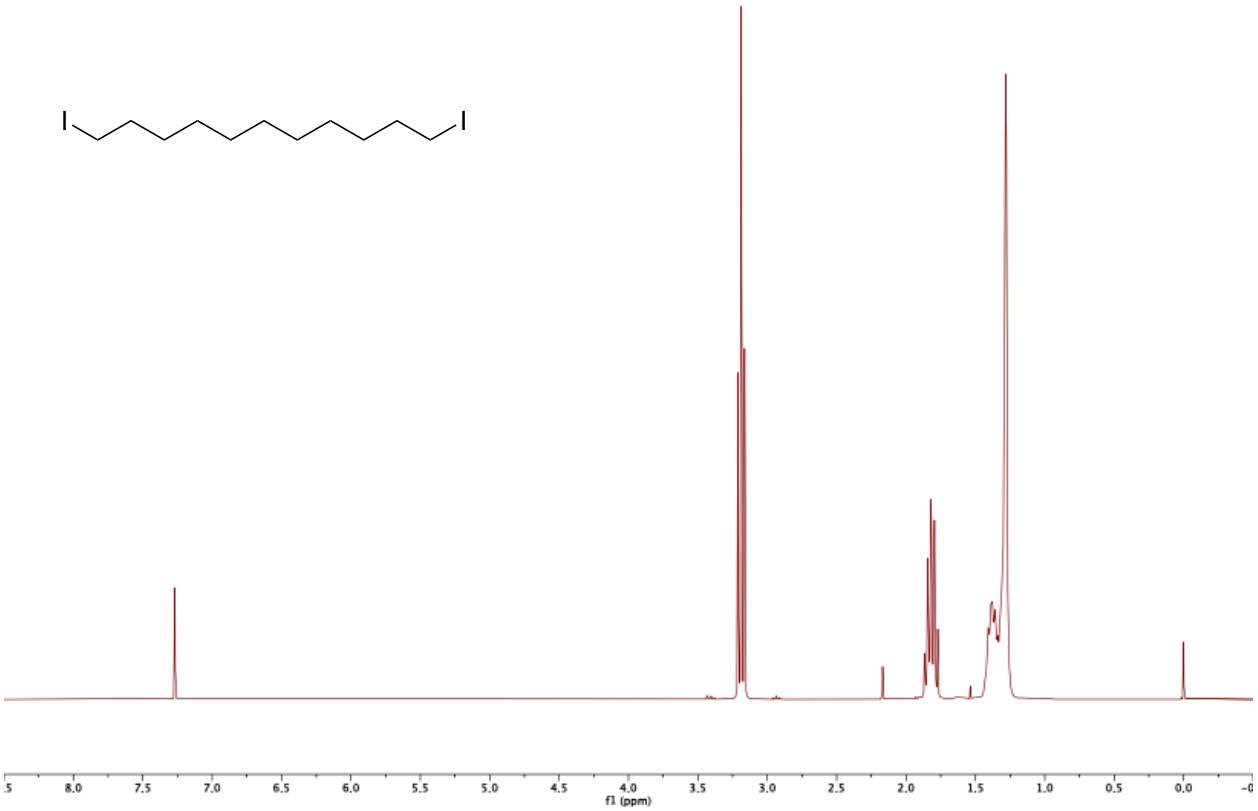

O
O
3.109c
f1 (ppm)
f1 (ppm)
f1 (ppm)

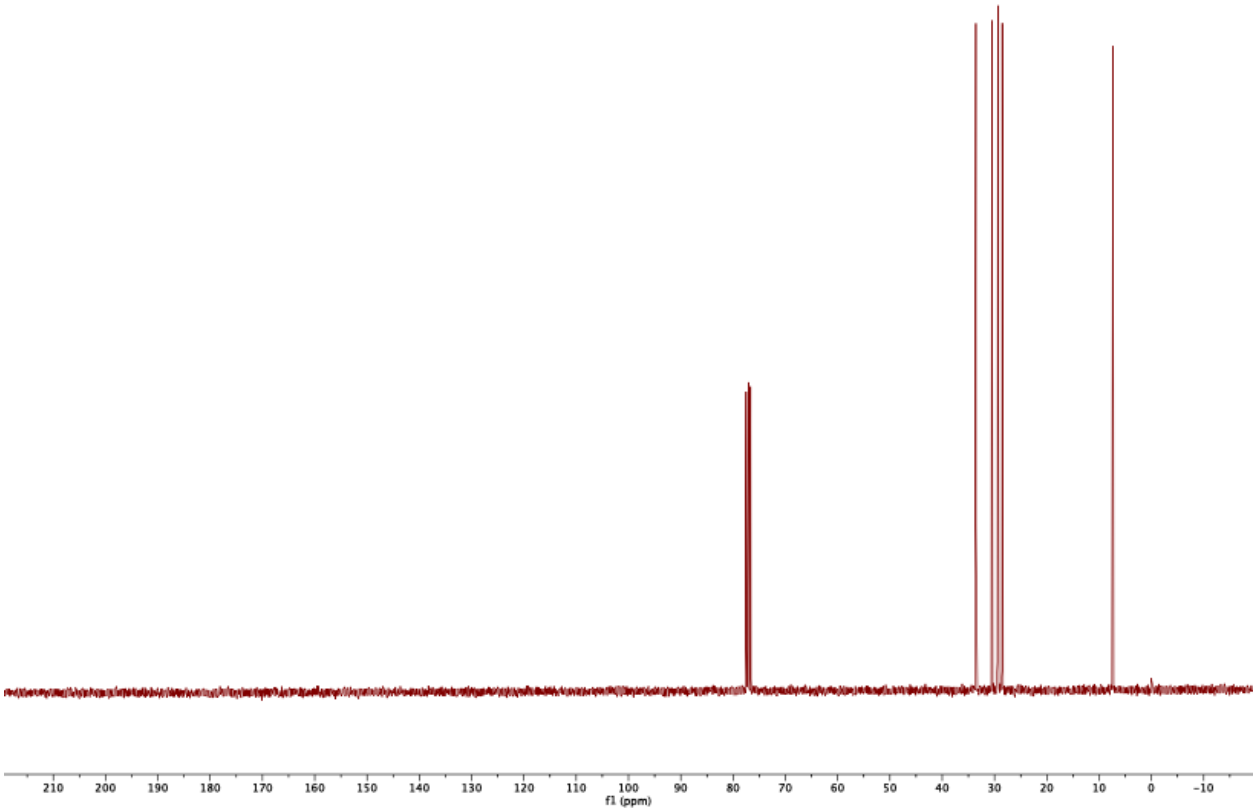

f1 (ppm)

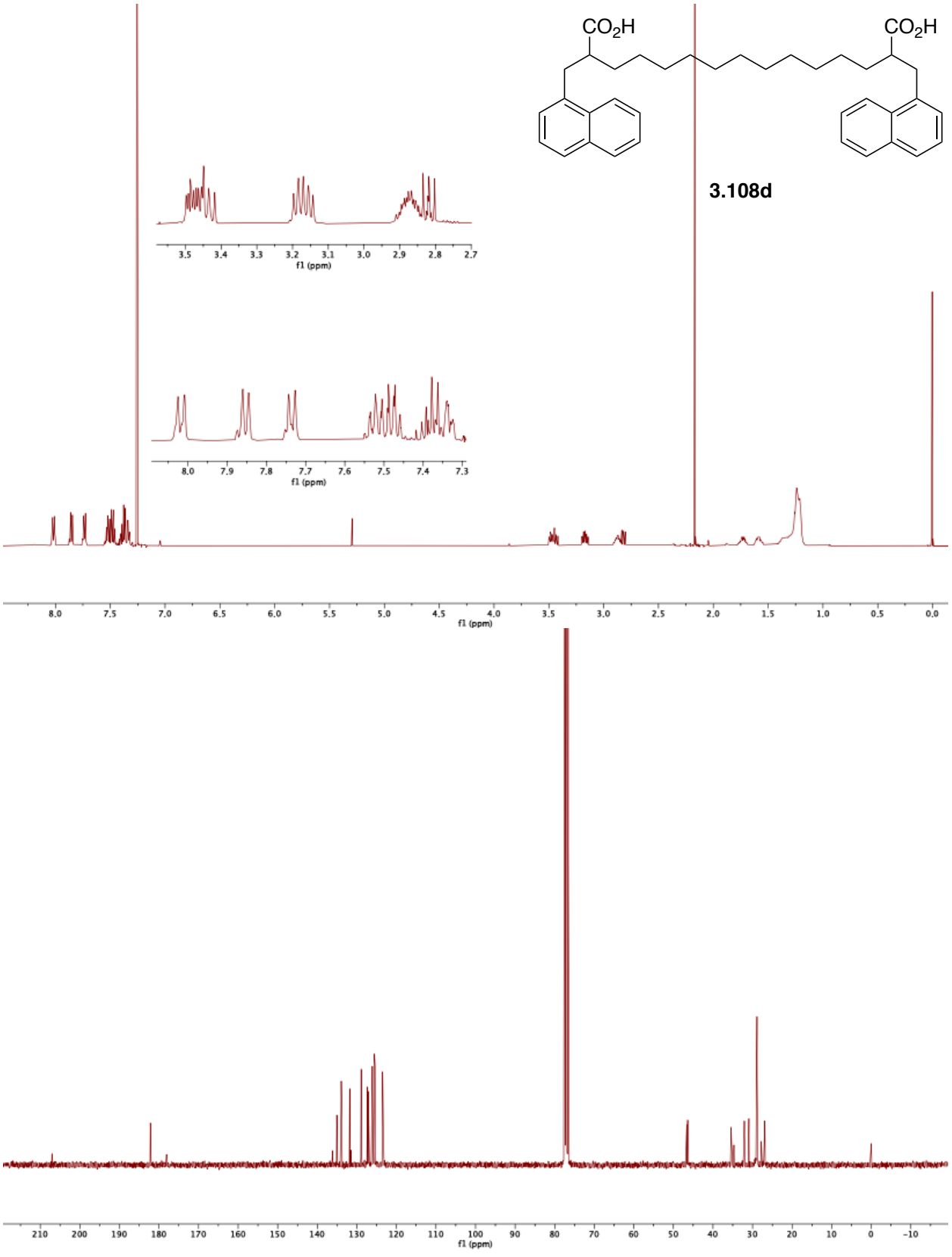

4.6 4.4 4.2 4.0 3.8 3.6 3.4 3.2 3.0
f1 (ppm)
9.3 9.2 9.1 9.0 8.9 8.8 8.7 8.6 8.5 8.4 8.3 8.2 8.1 8.0
f1 (ppm)
0.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.0 -1.5 -2.0
f1 (ppm)

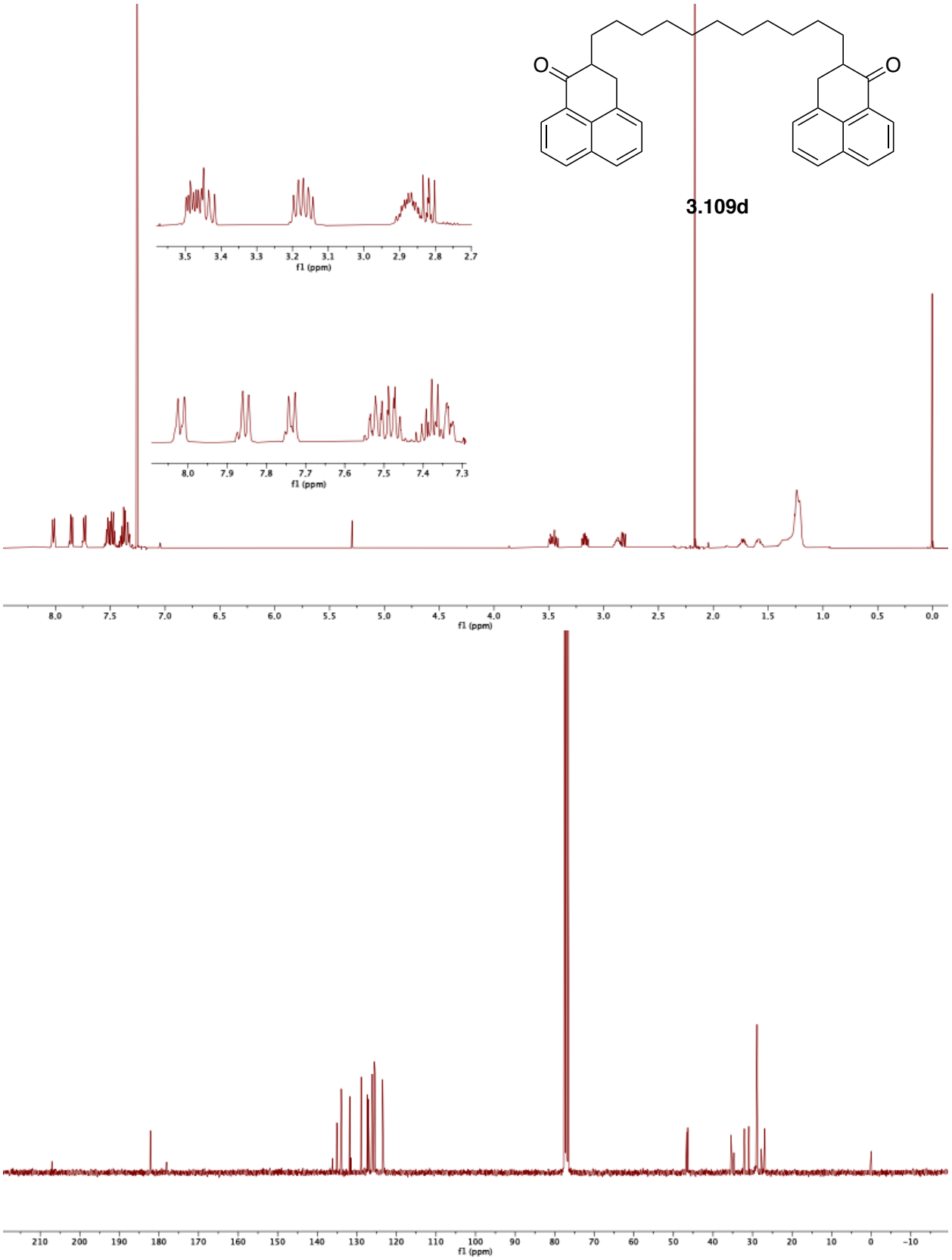

210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

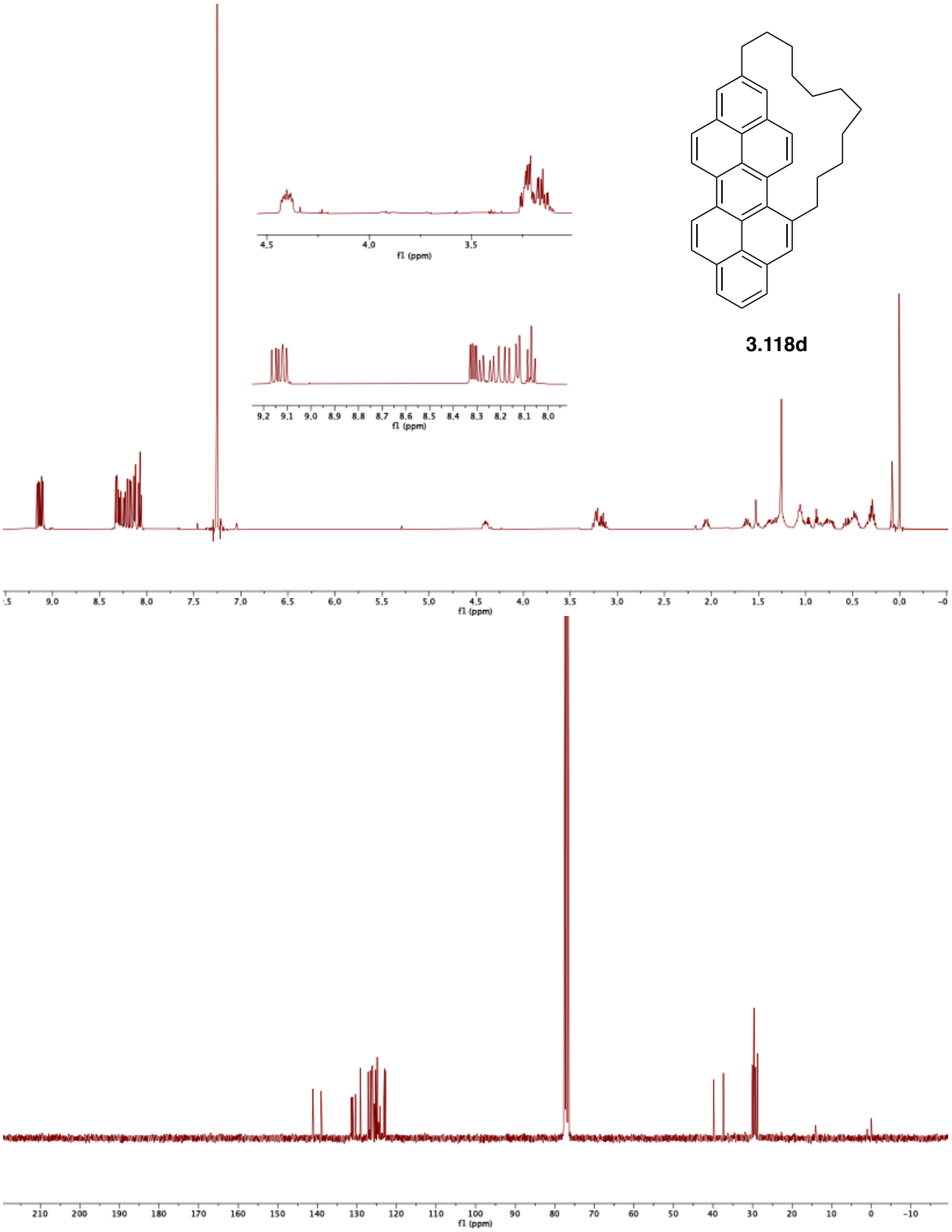

f2 (ppm)
f1 (ppm)

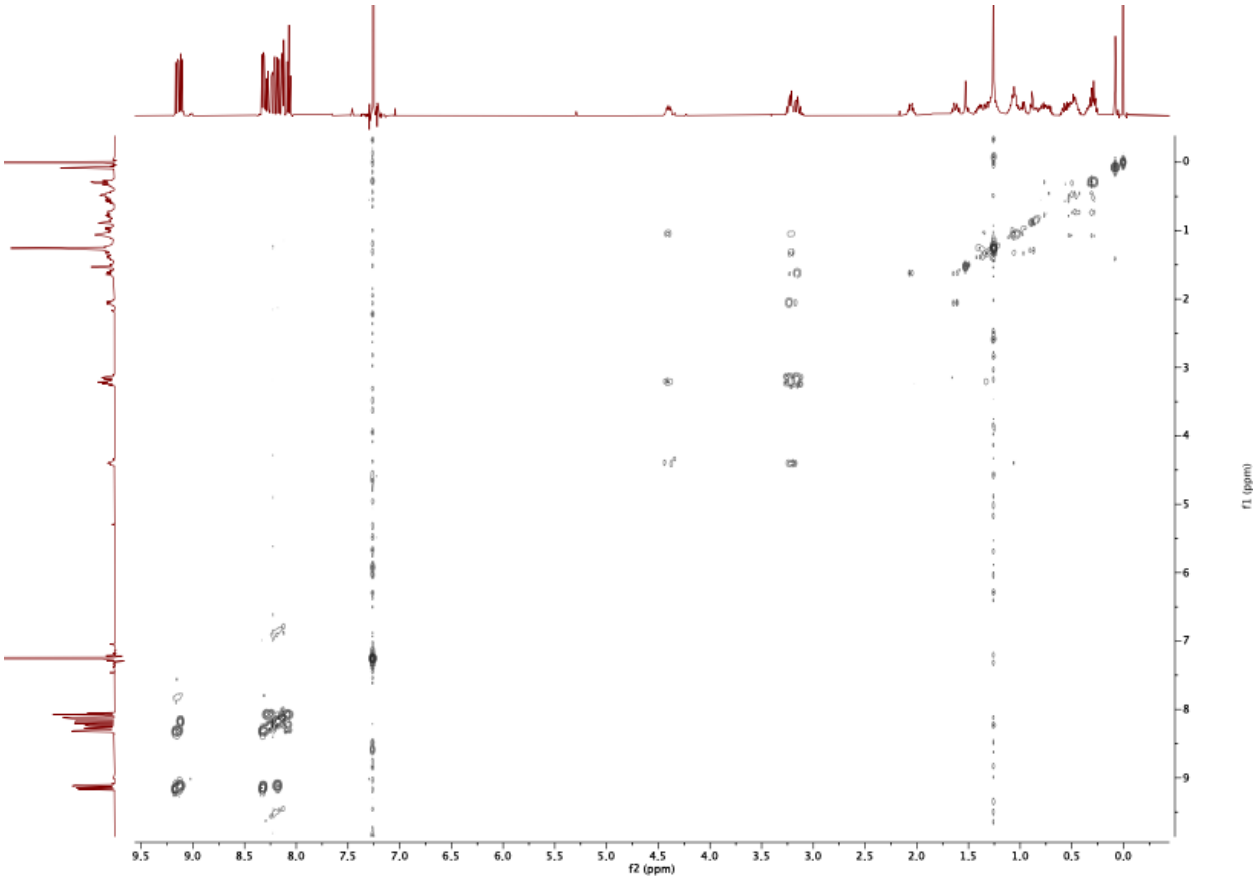

I
I
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

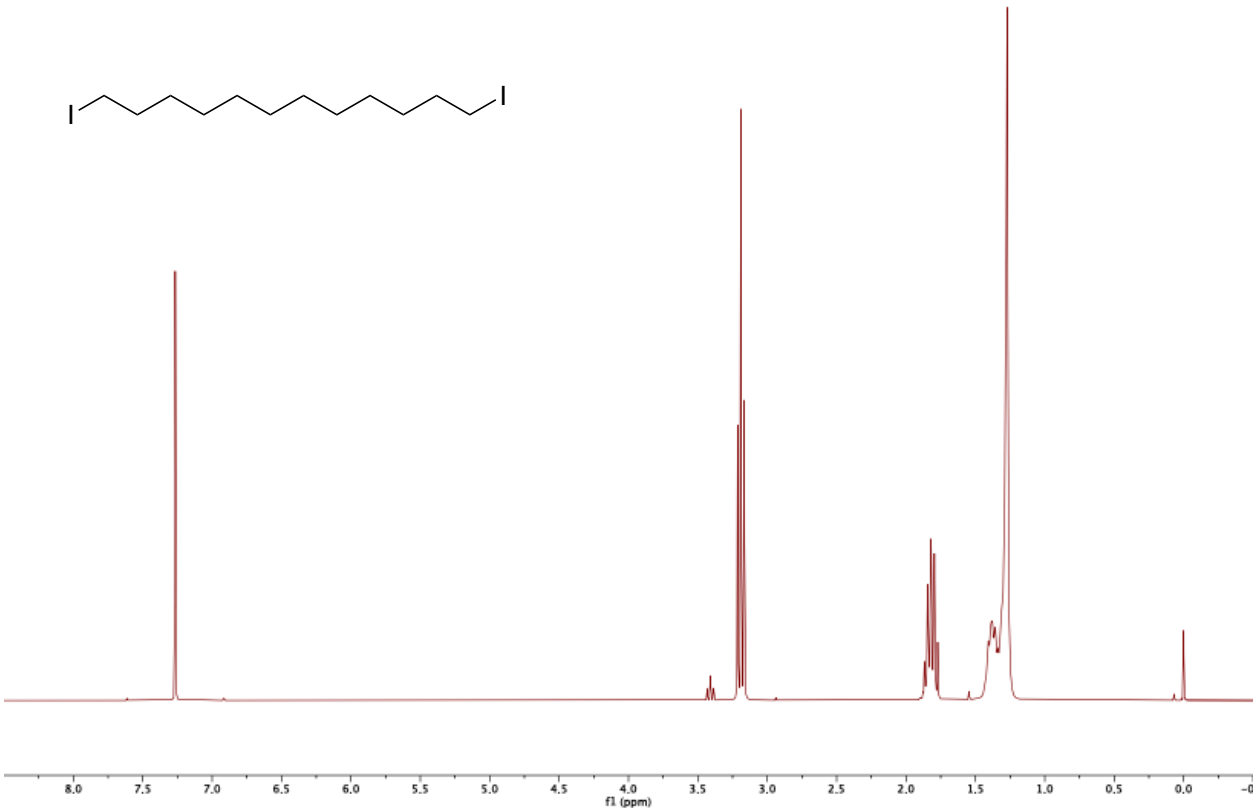

210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

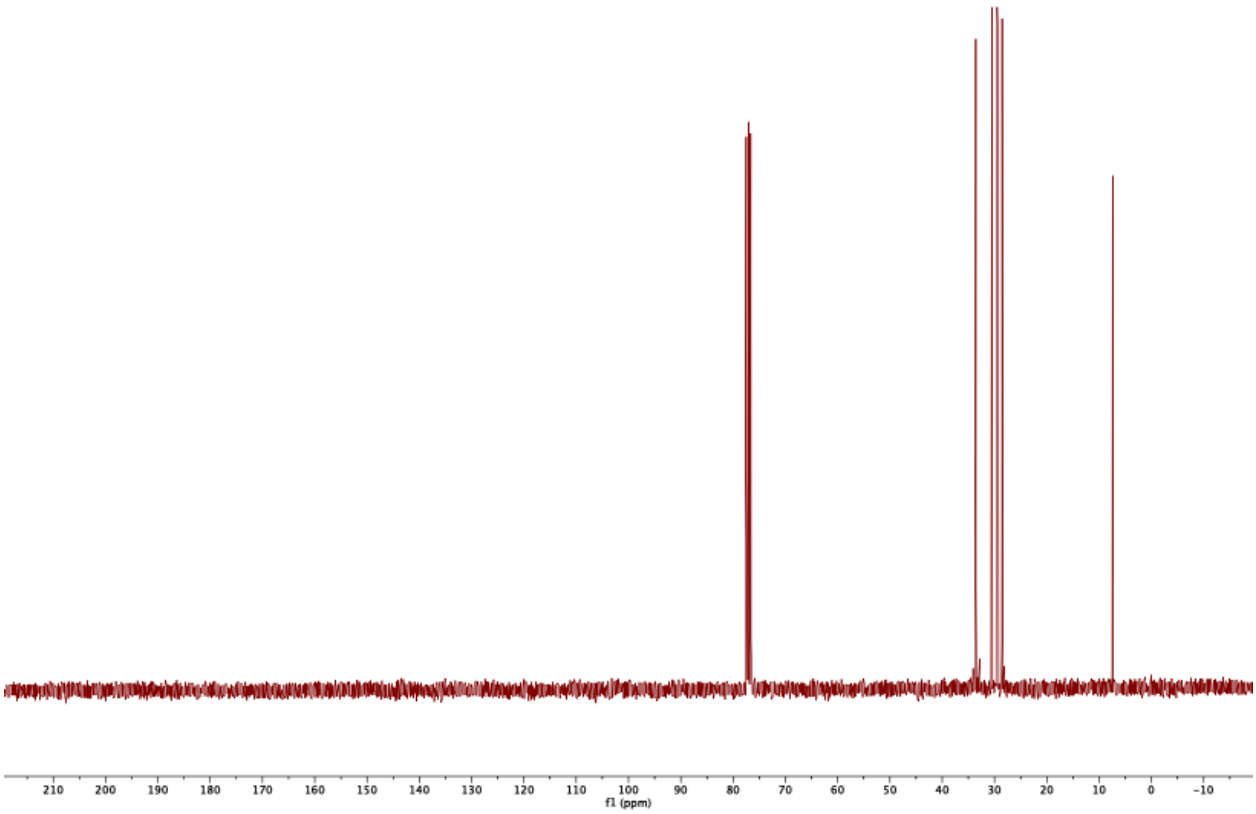

CO2H
CO2H
3.108d
f1 (ppm)
f1 (ppm)
f1 (ppm)

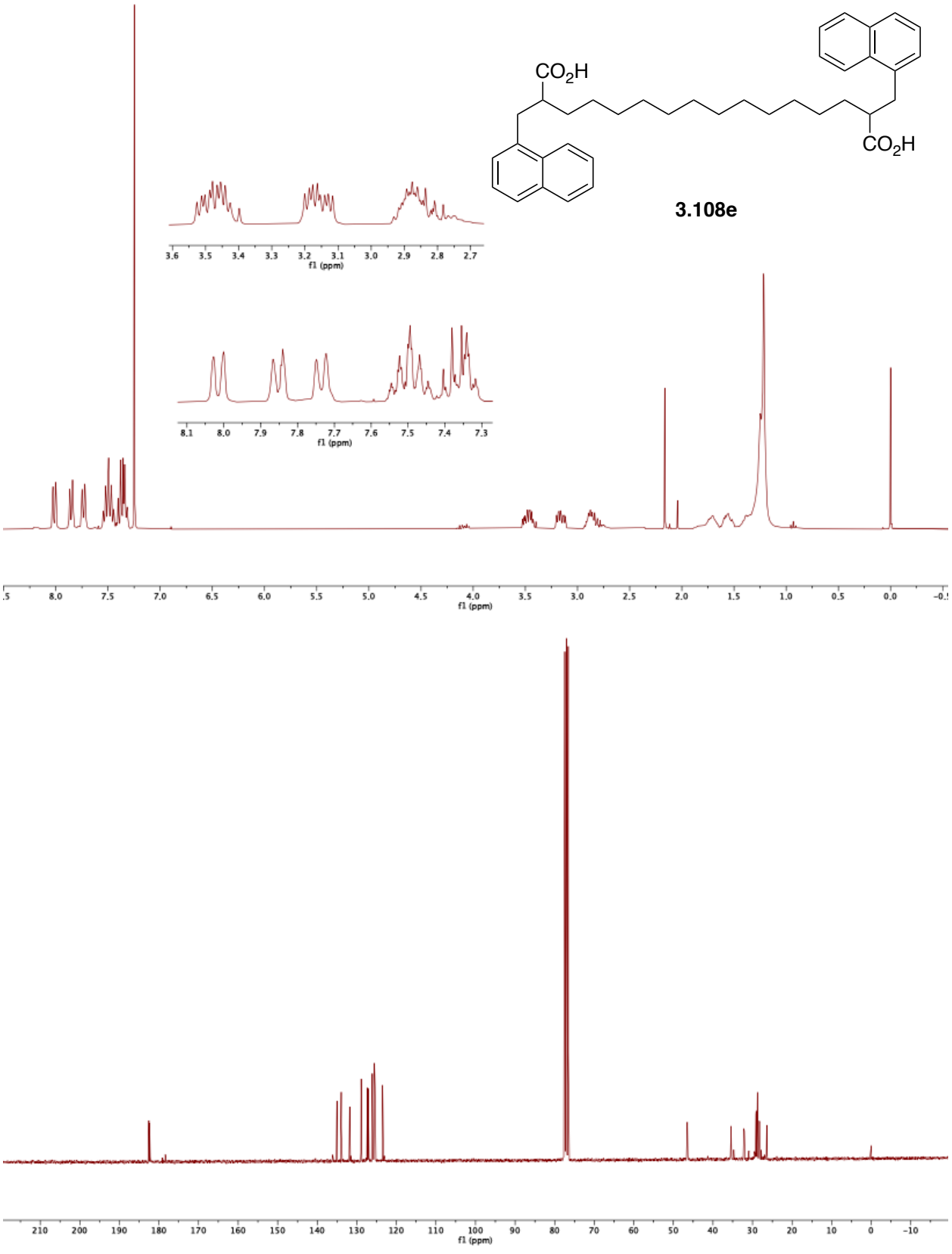

O
O
3.109d
f1 (ppm)
f1 (ppm)
f1 (ppm)
f1 (ppm)

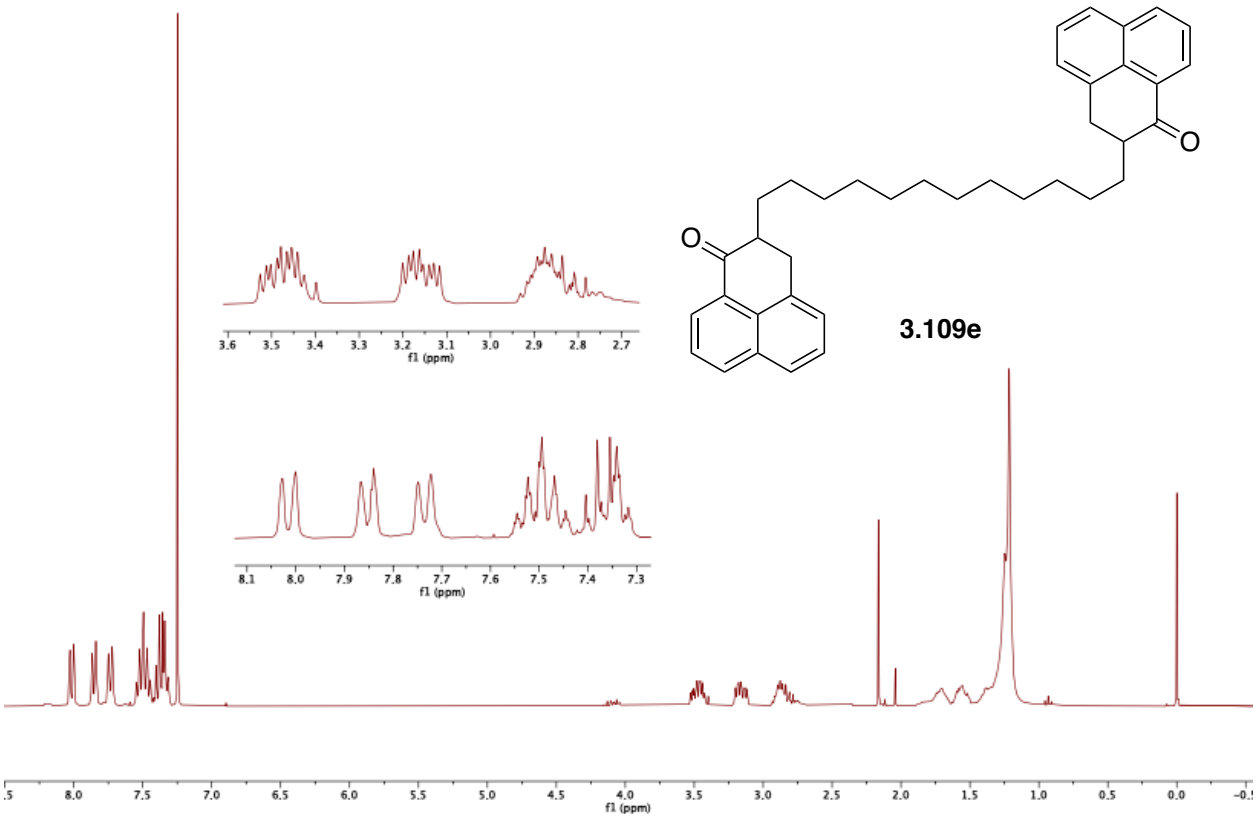

4.5
4.0
3.5
f1 (ppm)
9.2 9.1 9.0 8.9 8.8 8.7 8.6 8.5 8.4 8.3 8.2 8.1 8.0
f1 (ppm)
3.118d
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

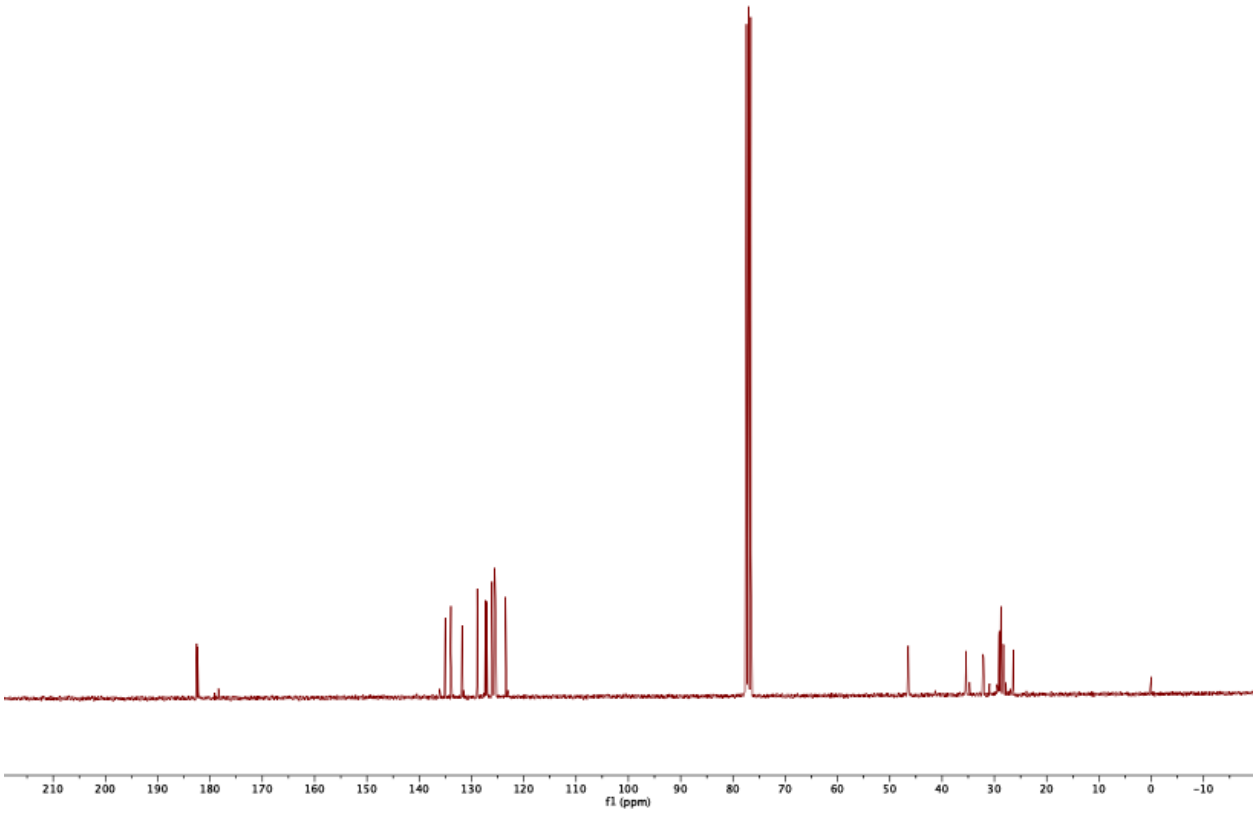

9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f2 (ppm)
0
1
2
3
4
5
6
7
8
9
f1 (ppm)

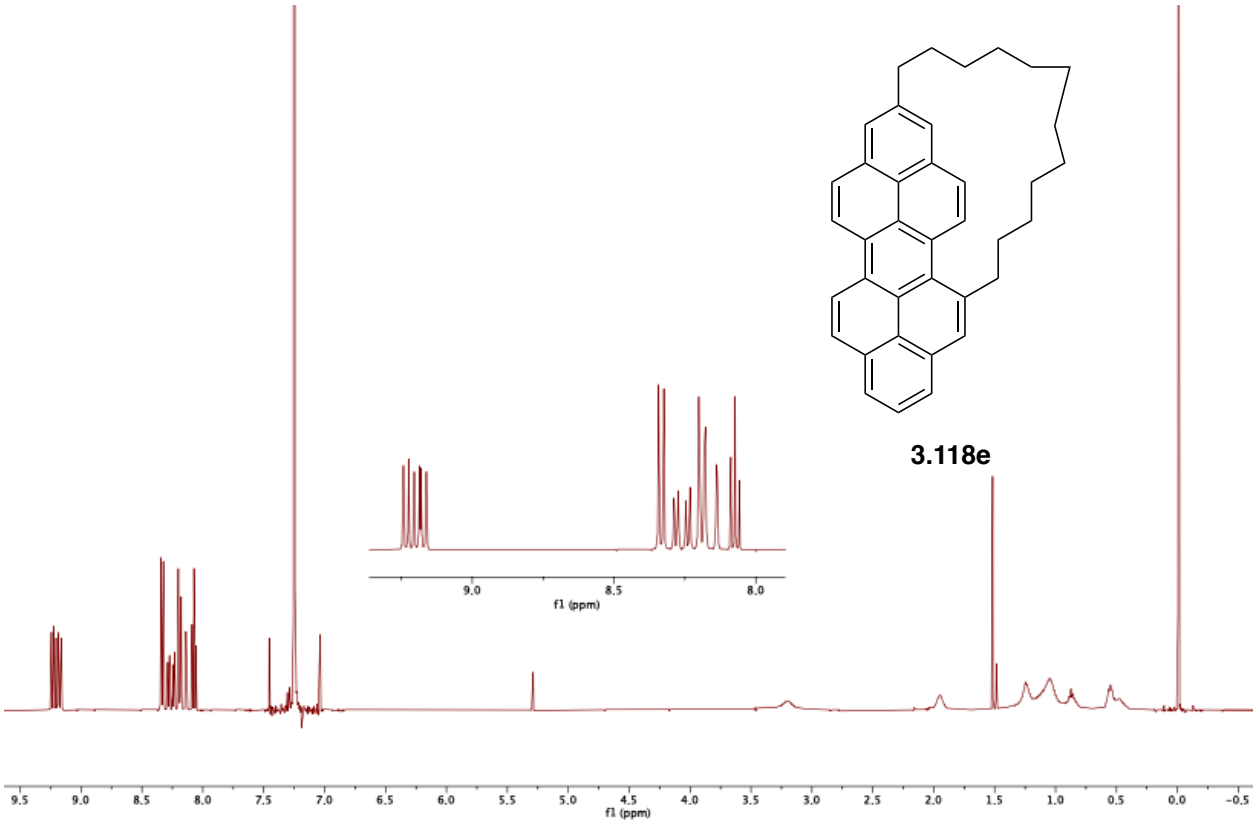

I
I
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

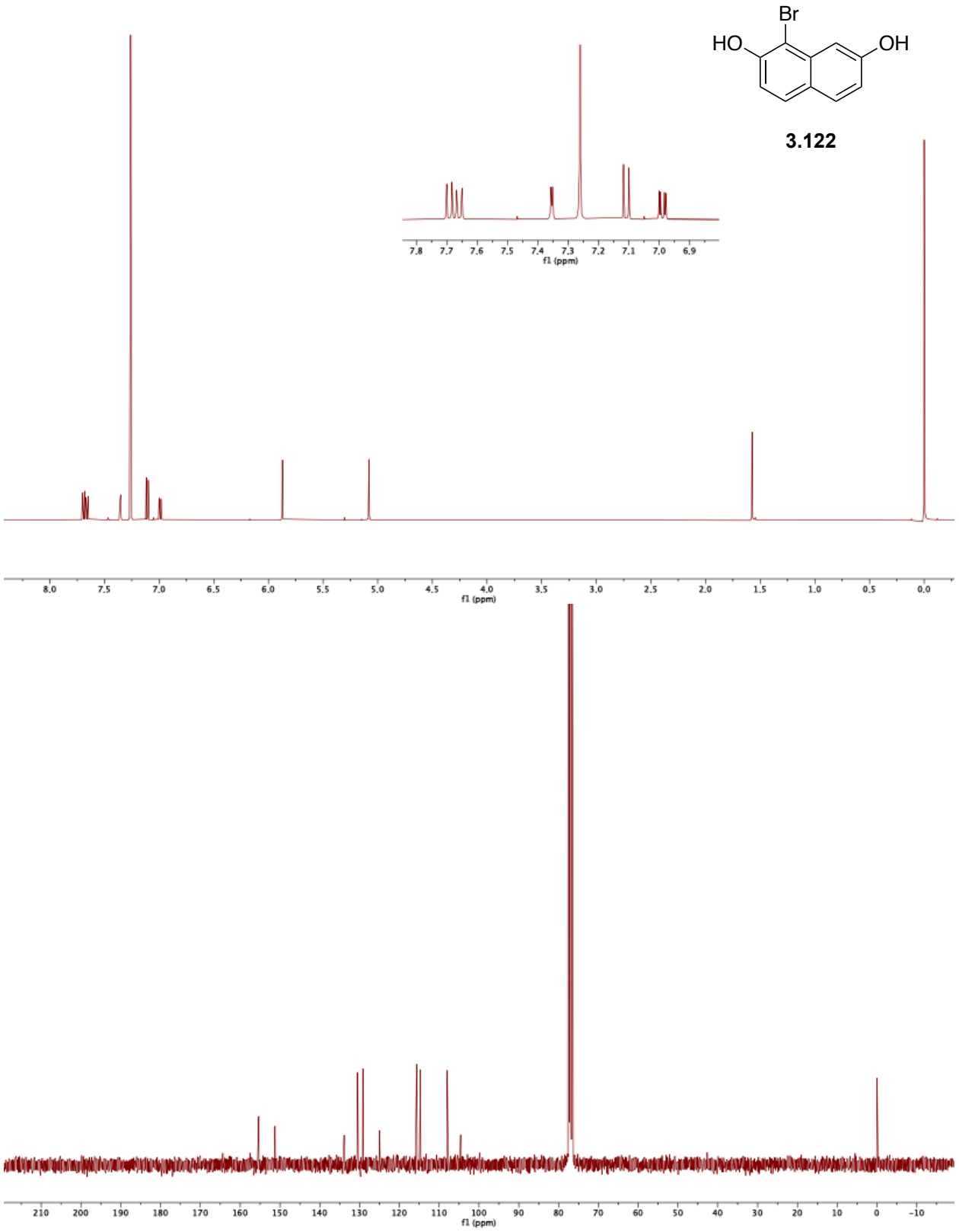

210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

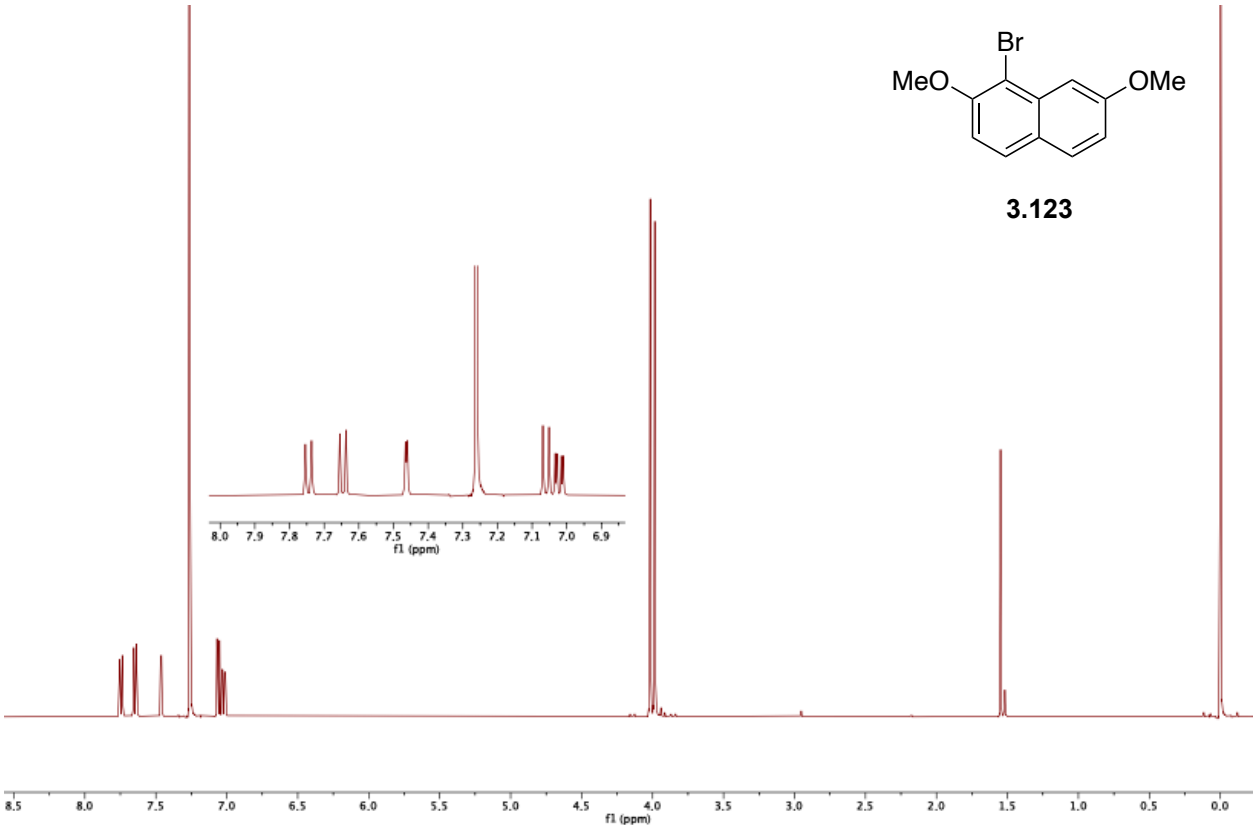

CO2H
CO2H
3.108e
f1 (ppm)
f1 (ppm)
f1 (ppm)
f1 (ppm)


O
O
3.109e
f1 (ppm)
f1 (ppm)
f1 (ppm)

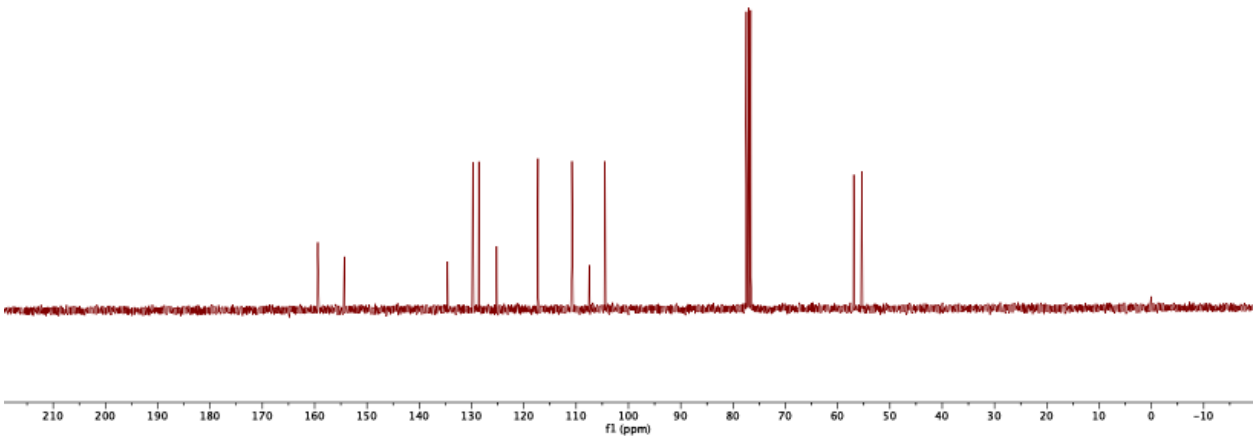

f1 (ppm)

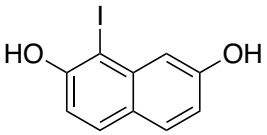

3.118e
9.0
8.5
8.0
f1 (ppm)
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)


Br
HO
OH
3.122
f1 (ppm)


Br
MeO
OMe
8.0 7.9 7.8 7.7 7.6 7.5 7.4 7.3 7.2 7.1 7.0 6.9
f1 (ppm)
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

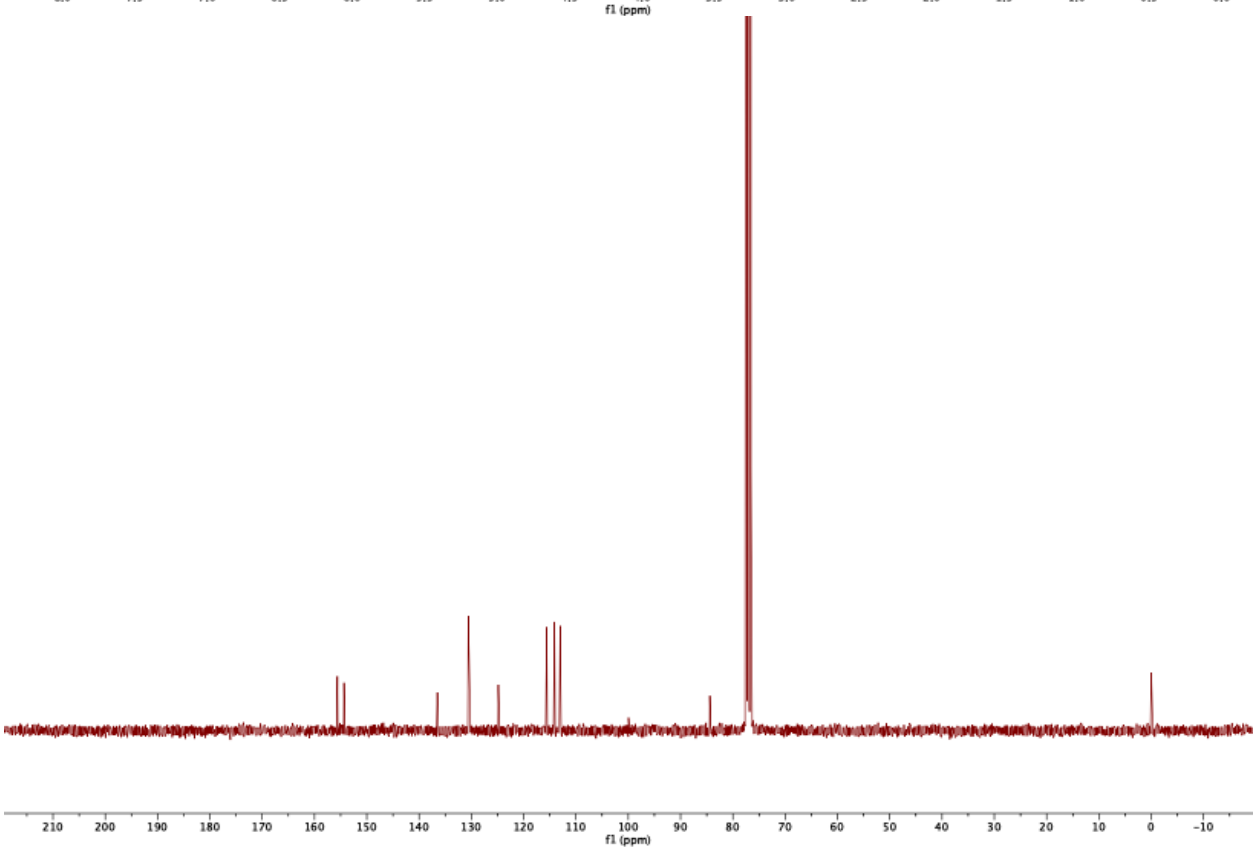
3.123

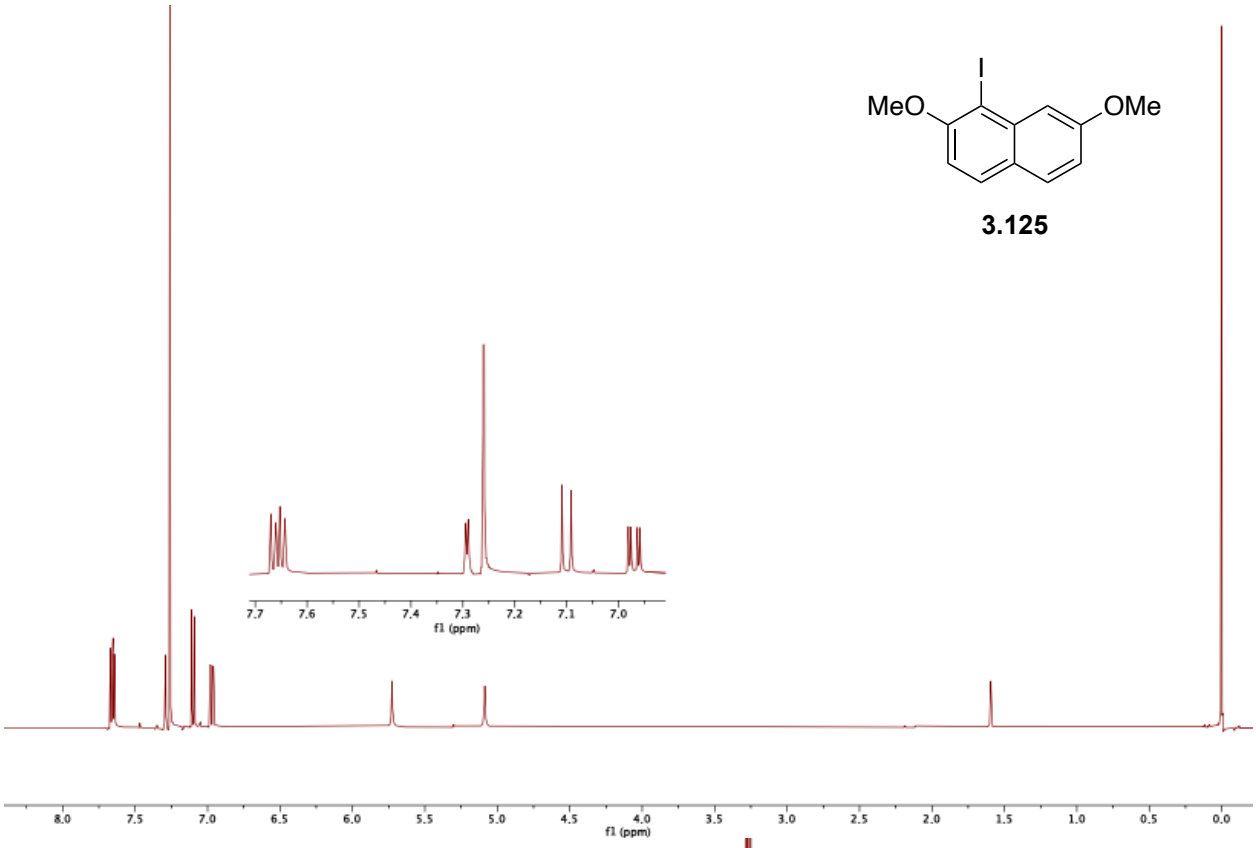

210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


HO
I
OH

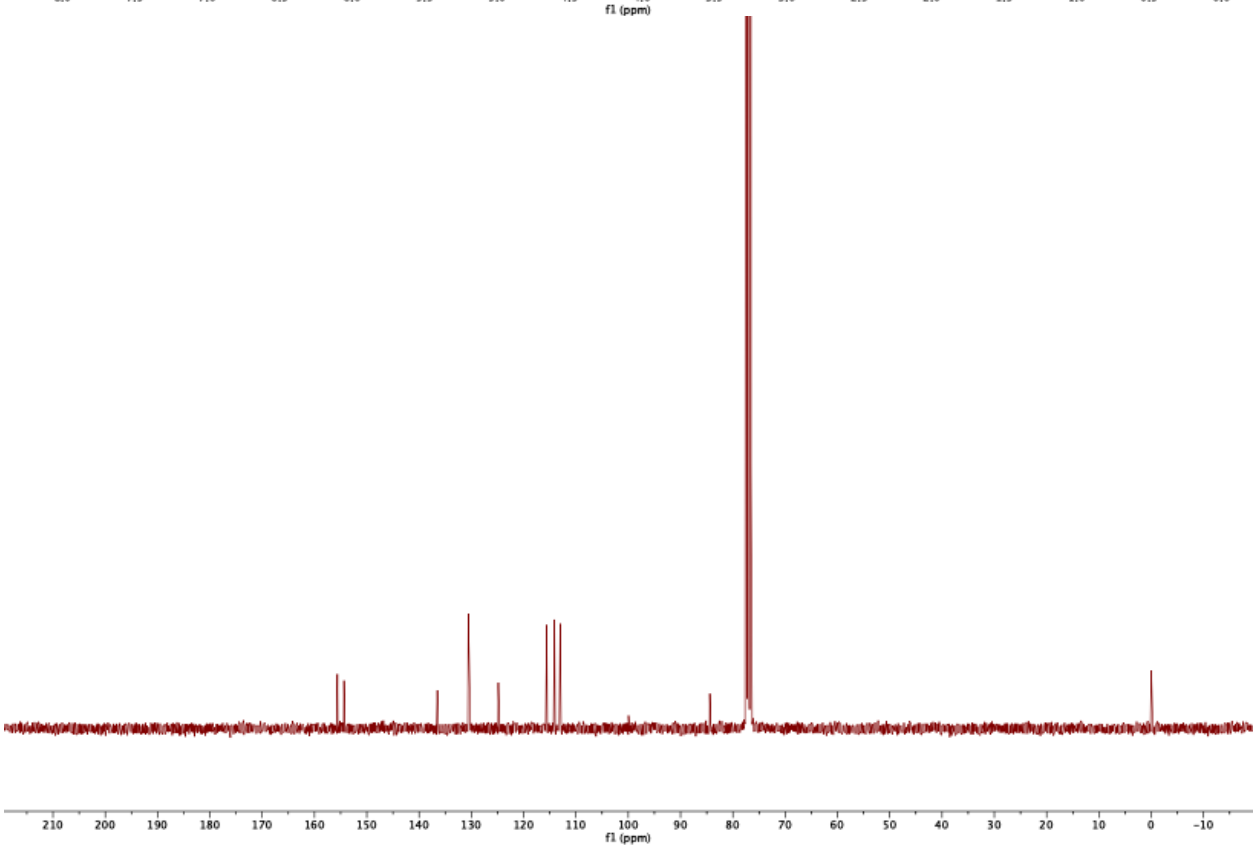
3.124

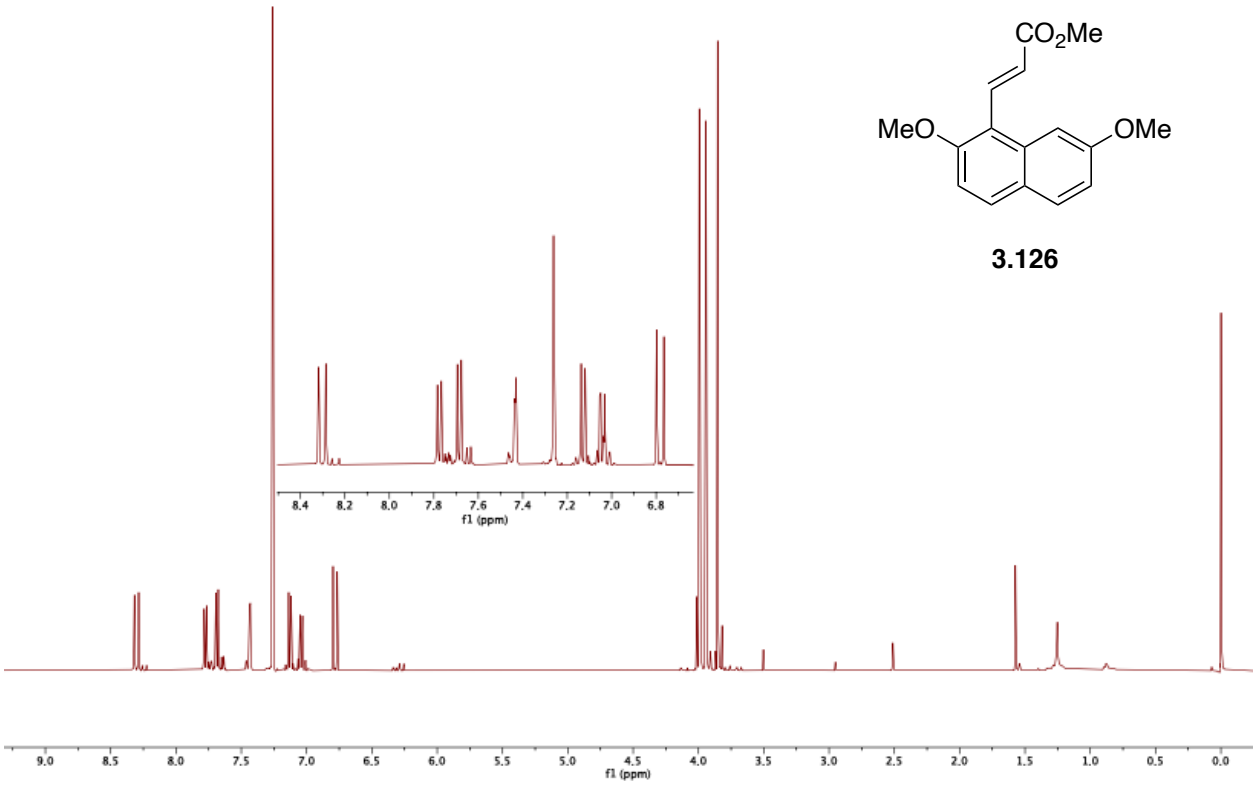
7.7
7.6
7.5
7.4
7.3
7.2
7.1
7.0
f1 (ppm)
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

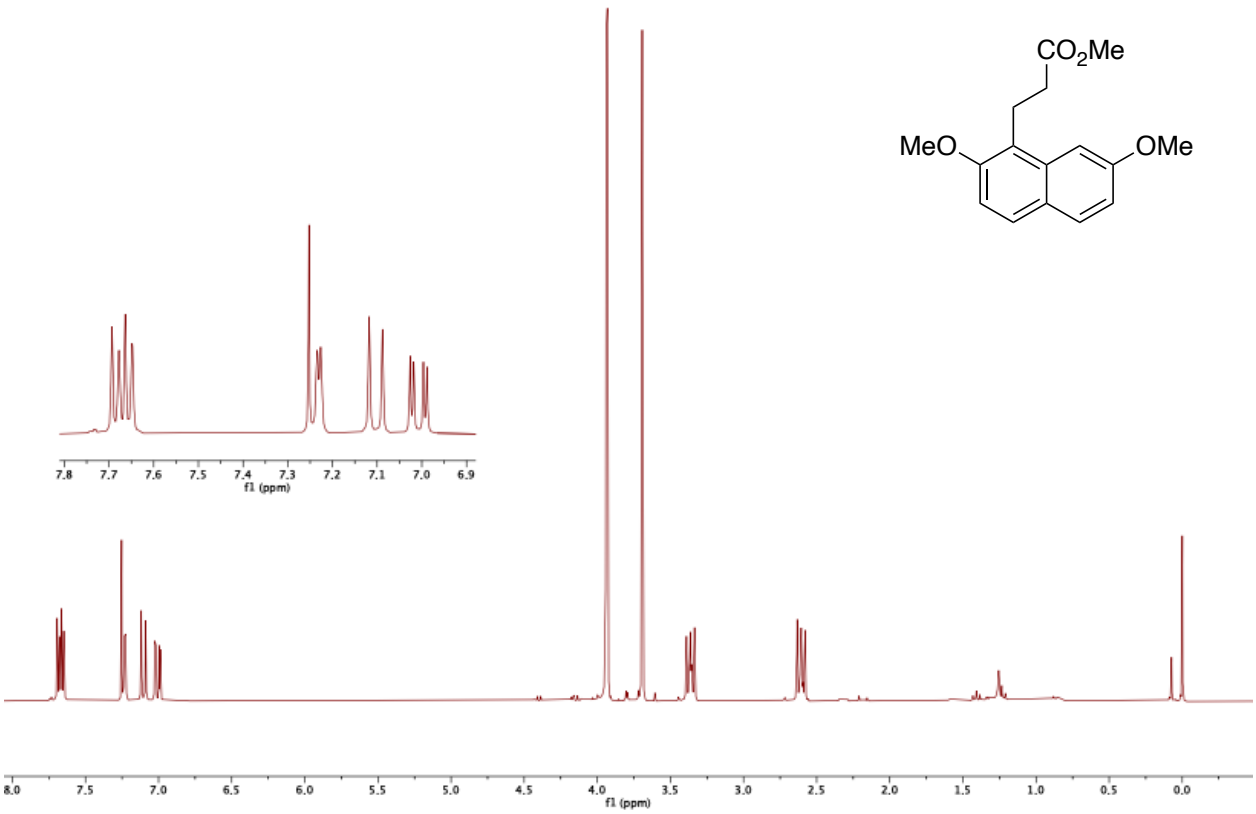

I
MeO
OMe
7.7
7.6
7.5
7.4
7.3
7.2
7.1
7.0
f1 (ppm)
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

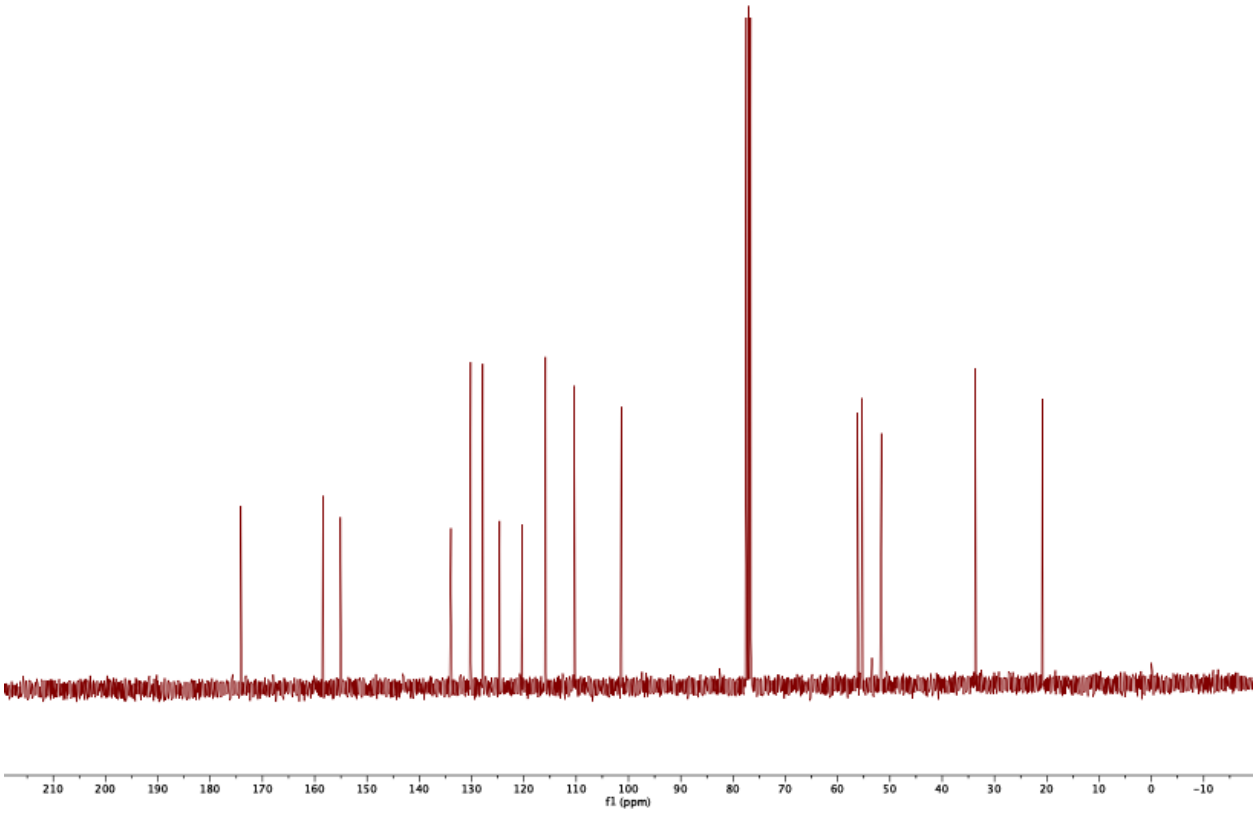
3.125


210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)


CO2Me
MeO
OMe
8.4
8.2
8.0
7.8
7.6
7.4
7.2
7.0
6.8
f1 (ppm)
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

3.126


CO2Me
MeO
OMe
7.8 7.7 7.6 7.5 7.4 7.3 7.2 7.1 7.0 6.9
f1 (ppm)
8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)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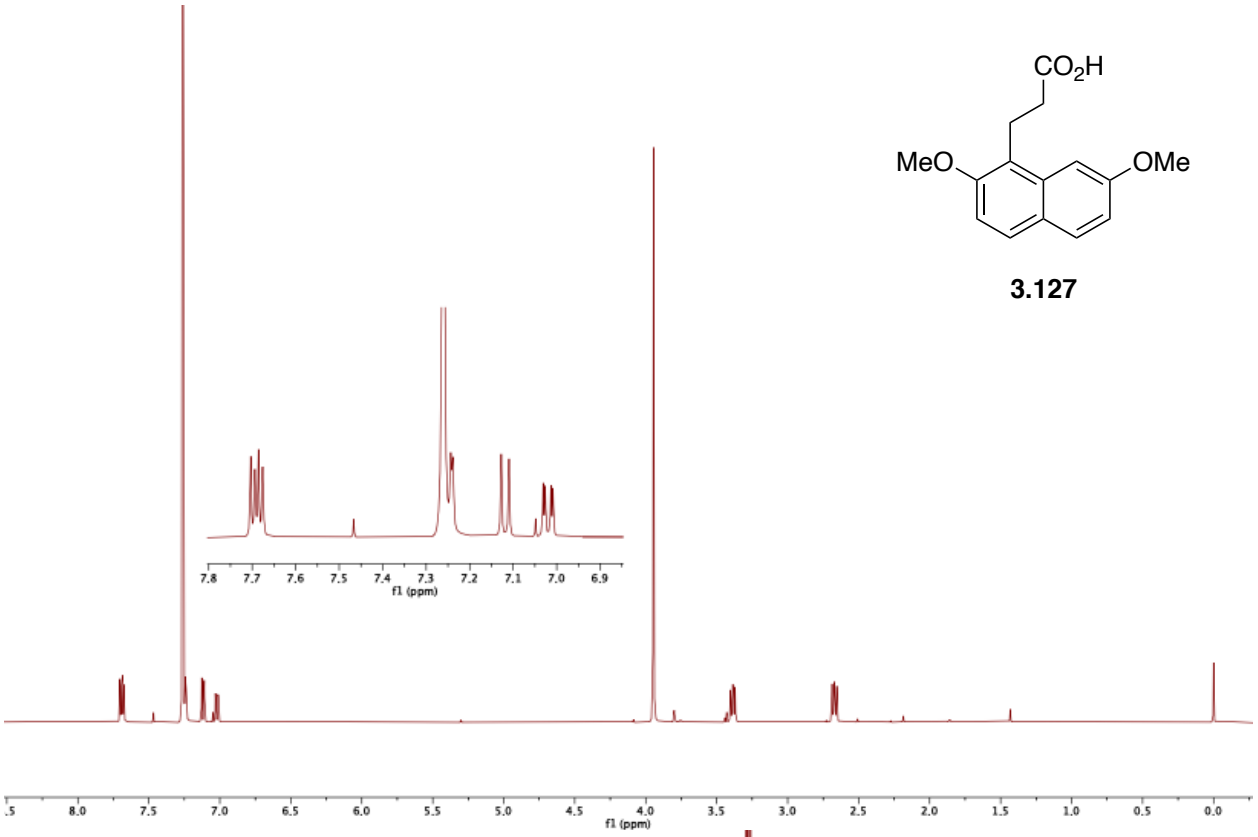
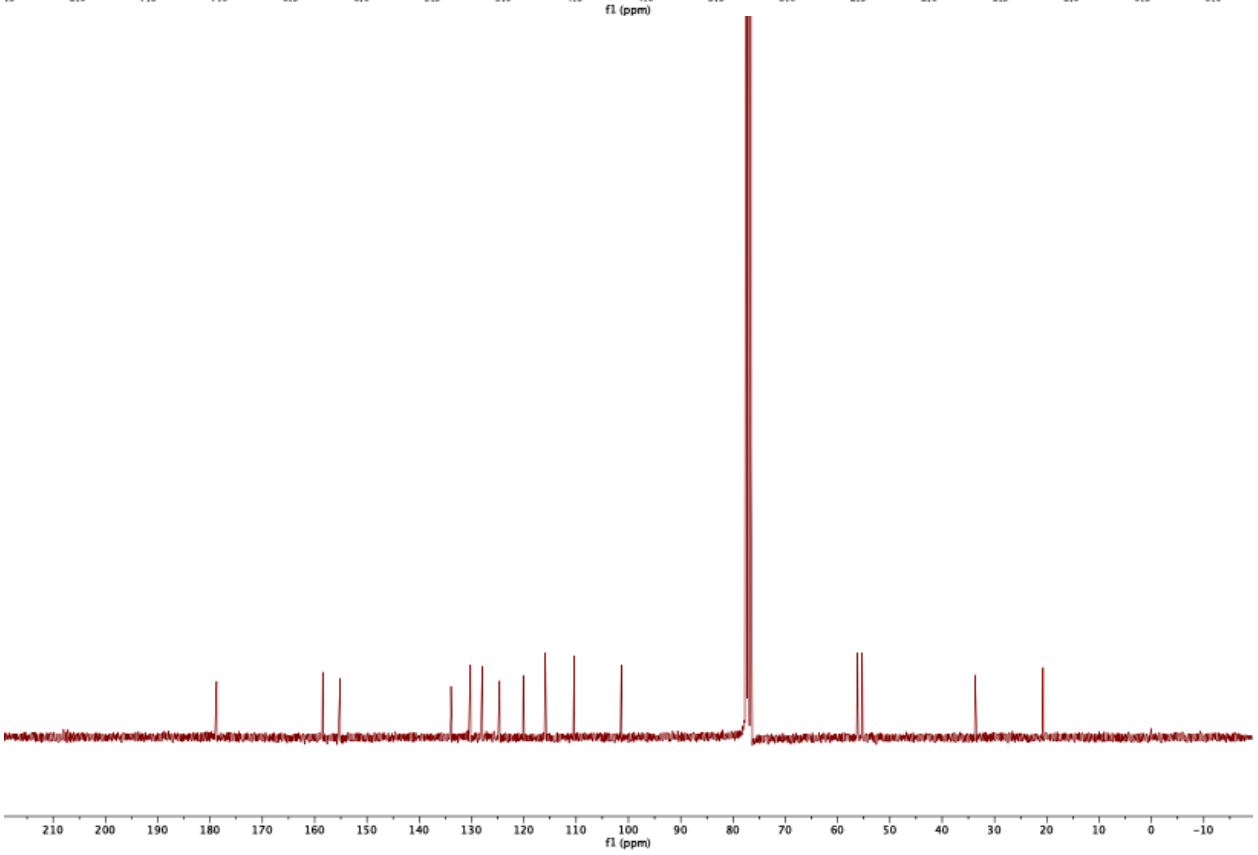
f1 (ppm)


CO2H
MeO
OMe
7.8 7.7 7.6 7.5 7.4 7.3 7.2 7.1 7.0 6.9
f1 (ppm)
8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

3.127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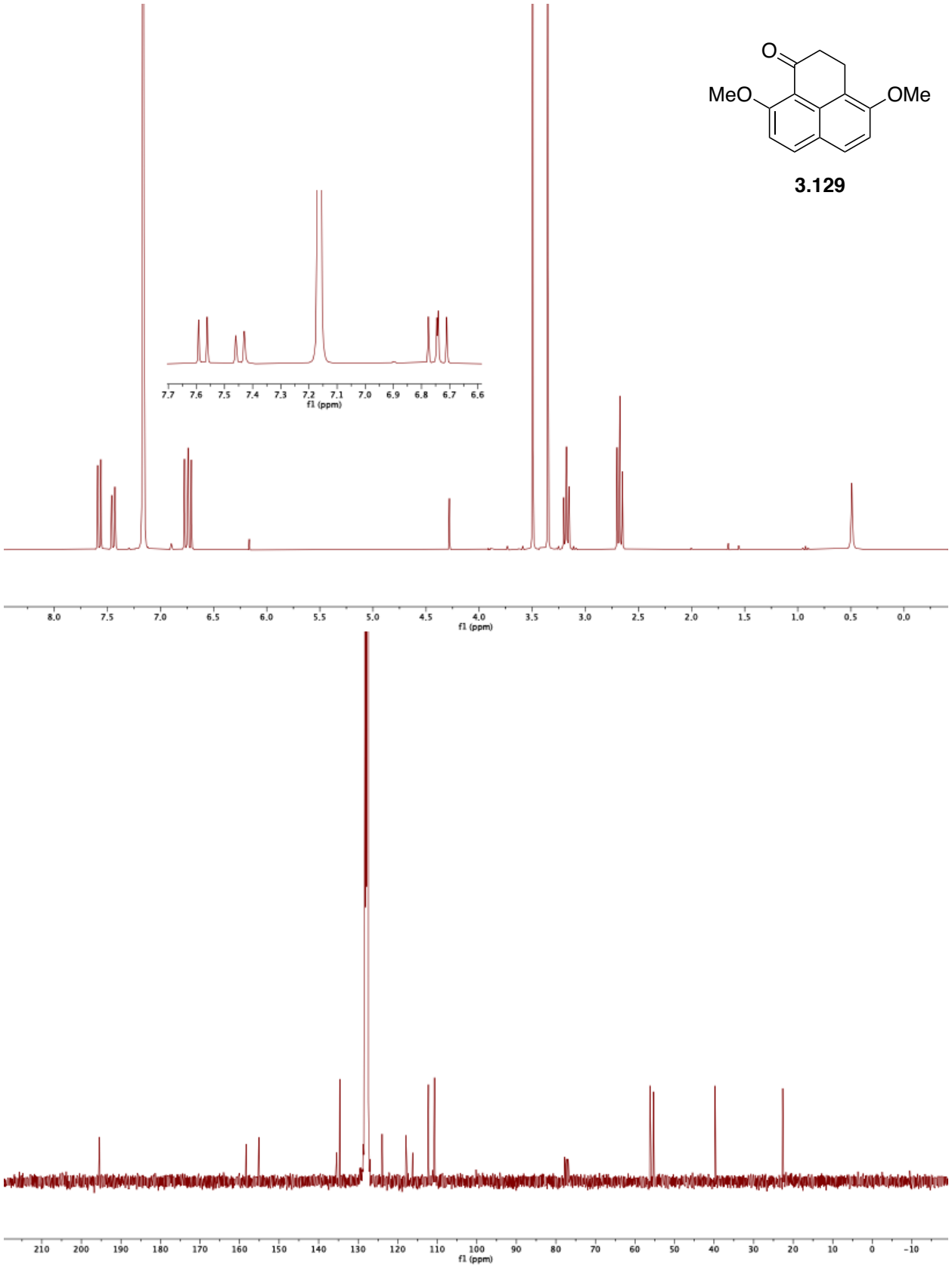
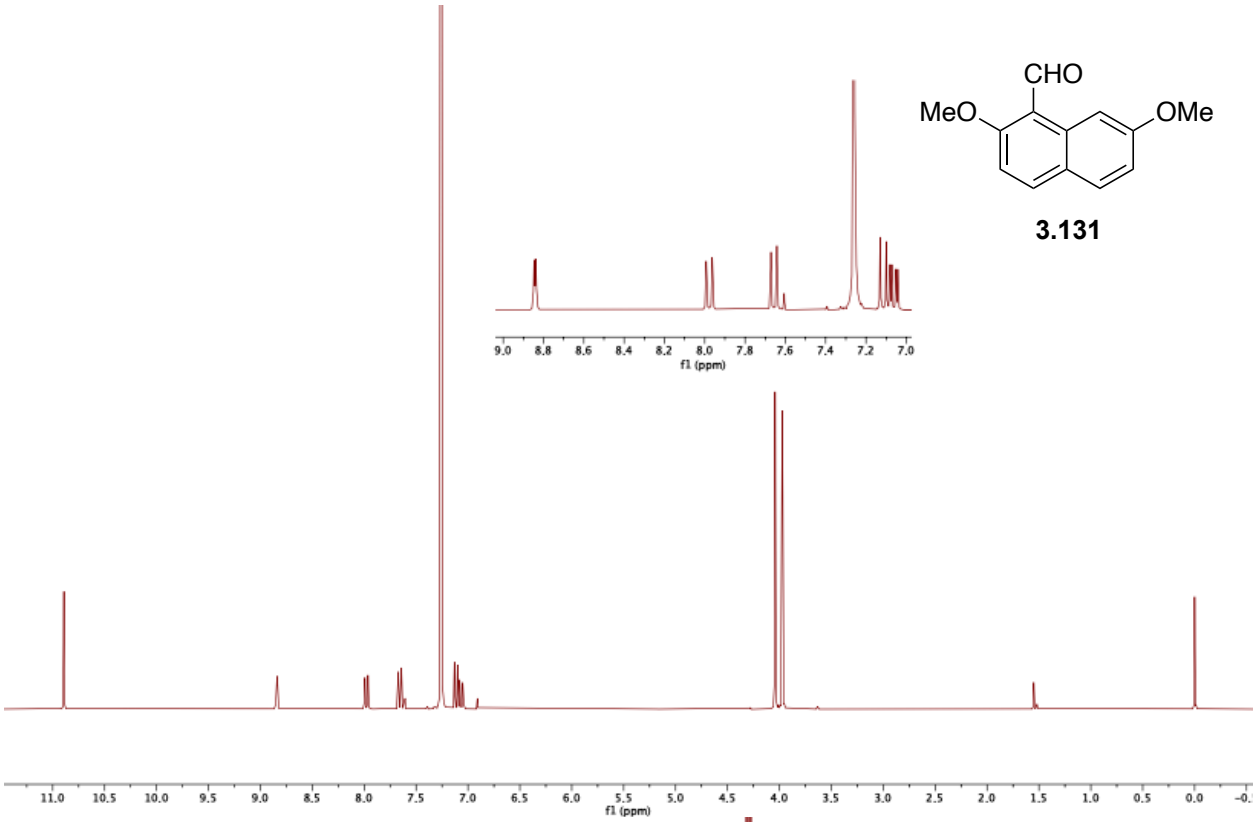
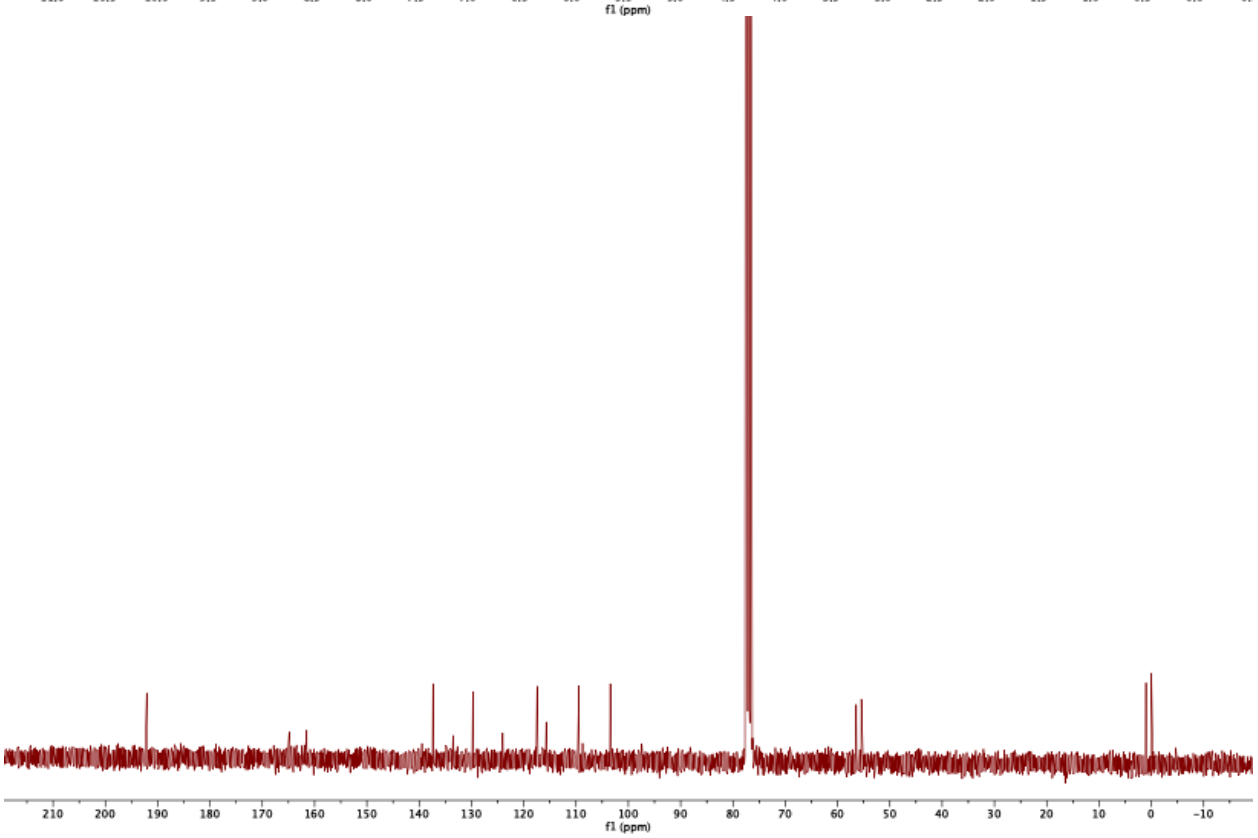

O
MeO
OMe
7.7 7.6 7.5 7.4 7.3 7.2 7.1 7.0 6.9 6.8 6.7 6.6
f1 (ppm)
8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

3.129


CHO
MeO
OMe
3.131
f1 (ppm)


f1 (ppm)

Chapter 4: Conclusions and Perspectives

4.1: Conclusions

This thesis began by introducing nonplanar polycyclic aromatic hydrocarbons and why chemists are interested in synthesizing and studying these systems. The three strategies employed to incorporate nonplanarity (embedding non-6-membered rings, steric crowding and bridging) are briefly introduced, which a focus placed in the bridging in cyclophanes containing one aromatic system and one bridge.

The goal of this thesis was twofold:

1. To demonstrate improved synthetic methods in the synthesis of various [*n*](2,7)pyrenophanes.
2. Explore new methodology for the synthesis of a new class of [*n*]peropyrenopyrenophanes.

In order to place the improved synthesis of various [*n*](2,7)pyrenophanes within the context of cyclophane chemistry, an in depth and roughly chronological review of cyclophanes containing pyrene system was undertaken. In this review of the literature, pyrenophanes of all breeds are described along with their varied syntheses. Included in these are a number of examples, spanning two decades, from the Bodwell group using common transformations from a series of [3.3]dithiacyclophanes. This familiar series of transformations for those in the research group include, in order, (1) methylation of the thioethers with Borch reagent, (2) thia-Stevens rearrangement, (3) methylation of the resulting exocyclic thioethers with Borch reagent, (4) Hofmann elimination, and finally (5) valence-isomerization dehydrogenation.

This work included improvements, both in yield, efficiency and cost savings to the synthetic sequences of 1,*n*-dioxa[*n*](2,7)pyrenophanes and [*n*](2,7)pyrenophanes. These improvements have allowed for the preparation of larger amounts of materials to aid in the further exploration of these systems. One of the major improvements across both systems of pyrenophanes presented within was the synthesis of [3.3]dithiacyclophanes from the corresponding tethered tetrabromides. Traditionally, these transformations were accomplished using Al_2O_3 impregnated with Na_2S (Na_2S/Al_2O_3) as the reagent and has been used in a plethora of different synthetic sequences. While this reagent is successful in accomplishing the transformation, the yields vary from poor to good. In the search for a more reliably high yielding reagent, focus was placed on the replacement of Al_2O_3 with another solid support. The only replacement explored to date was coal fly ash (CFA), which is a product of coal combustion produced in massive quantities worldwide. Efforts towards mitigating the buildup of static stockpiles of material have been underway for many years with most efforts focused its utilization as a construction material. To a lesser degree, CFA has been explored as a solid support material for catalysts in chemical synthesis. For the first time, work in this thesis looked at CFA as a solid support for a reagent to promising results.

The improvements to the formation of [3.3]ditihiacyclophanes ultimately enabled the synthesis of larger quantities of the 1,*n*-dioxa[*n*](2,7)pyrenophanes and [*n*](2,7)pyrenophanes which allowed for a brief exploration into their reactivity towards formylation. In the case of the 1,*n*-dioxa[*n*](2,7)pyrenophanes, classic Rieche formylation proved too harsh, even at −78 °C, and led to bridge rupture. Modified conditions replacing $TiCl_4$ with AgOTf allowed for 1,10-dioxa[10](2,7)pyrenophane to be successfully formylated at 0 °C, however, 1,9-dioxa[9](2,7)pyrenophanes did not formylate under these milder conditions and once again led to a bridge ruptured product. Therefore, it seems clear that these systems are not the best suited for further synthetic modification due to the lability of the bridge. The [*n*](2,7)pyrenophanes

proved to be more robust to Rieche formylation conditions, at least in the case of the least strained [9](2,7)pyrenophane and [10](2,7)pyrenophane systems. The introduction of a synthetic handle to the pyrene core will allow for future work to continue on these systems, opening the gateway to cyclphanes with extended pi systems.

Perhaps the most enduring aspect from Chapter 2 of this thesis is the discovered utility of coal fly ash (CFA) as a solid support the synthesis. Not only have we demonstrated that it is a superior solid support for Na_2S, but preliminary results in the lab have also provided some evidence to its usefulness as a solid support in other reactions.

In Chapter 3, only the second example ever of cyclophane systems containing peropyrene aromatic units were discussed. In order to get access to these systems a new cyclophane forming strategy was required that relied on the dimerization of phenalenyl radicals followed by a known oxidative pathway to peropyrene systems. The successful synthesis of [*n*](2,6)peropyrenophanes (where *n* = 9-12) were completed and characterized. Additionally, preliminary studies into the photophysical properties were undertaken.

Hopeufully in the future, this cyclophane forming strategy can be used for the synthesis of the desired [*n*](2,9)peropyrenophanes to align with the previously reported (2,7)pyrenophanes and (2,11)teropyrenophanes. This would allow for direct comparisons to be made between the systems.

4.2: Perspectives

I would like to finish off this dissertation by passing on some lessons learned during my time in graduate school. Firstly, on a personal level I would suggest that you prioritize self-care at the same level with your research work and studies. Your research will suffer if you do not take time away from lab and take of both your mental and physical health. In that same vein, take advantage of all the resources available to you as a student including, but not limited to, the Student Health Services, Counselling Services, The Writing Centre, The Field House and whichever services would be useful to you.

As for strategies to succeed in the lab itself, the biggest piece of advice I can give is to characterize all of your compounds at the earliest possible moment. You will save yourself lots of time and headache when it comes to compiling your data and starting to write-up your thesis. Another piece of advice I can give is always try that reaction that no one thinks is going to work, especially if you have some downtime in the middle of your day. You never know what you might discover. Finally, I would suggest that you read literature that is outside of your different field of expertise, for example, if you are focused on cyclophanes or organic materials take some time and read some total synthesis literature, you will always learn a lot and get new ideas for your own project.