# SYNTHESIS OF $C_2$-SYMMETRIC PYRENOPHANES AND AROMATIC BELT PRECURSORS

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by

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## Abstract

The research described in this thesis mainly dealt with methodology development, design, synthesis as well as the study of the physical properties of new pyrenophanes and aromatic belt precursors cyclophanetetraene 4.16. The valence isomerization/dehydrogenation (VID) methodology was employed in all of the projects, to the synthesis of pyrenophanes with extended aromatic surfaces as well as ultimate goal: fully aromatic "Vögtle" type belts.

Over the past several years, Bodwell's group has exploited a valence isomerization/dehydrogenation (VID) reaction, which can accomplish the formation of [*n*](2,7)pyrenophane with nonplanar pyrene units. In all these cases, the pyrenophane is achiral. In Chapter 2, a $C_2$-symmetric, chiral pyrenophane, [10](1,6)pyrenophane was successfully synthesized using the VID reaction along with [10](1,8)pyrenophane.

In addition, toward the synthesis of aromatic belt precursor cyclophanetetraene, two molecular boards were prepared in Chapter 3. One large scaled (8 g) molecular board **3.11** which was obtained from *m*-xylene in 12 steps (6%). Another molecular board, which was not the intended target, was synthesized in 9 steps from 4-hydroxyisophthalic acid (14%) and this synthetic route could possibly be used to synthesize larger sized molecular boards.

In Chapter 4, the large scaled molecular board **3.11** was used to covert to aromatic belt precursors. A straightforward synthetic plan for the synthesis of aromatic belts also is described in this Chapter.

## Acknowledgements

Firstly, I would like to thank my supervisor Dr. Graham J. Bodwell for his support and encouragement over the past two years. He is very patient to every student even like me with very less chemistry knowledge. His support and encouragement pushed me to study more and more. I am not only learned his understanding about chemistry but also the good attitude towards science or even life.

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**Chapter 3 Synthesis of Molecular boards**

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# List of Schemes

## List of Symbols, Abbreviations and Acronyms

| | |
|---|---|
| Δ | Heat |
| δ | (in NMR) Chemical shift |
| ε | Extinction Coefficient |
| λ | Wavelength |
| χ | Mole fraction |
| ∅ | Quantum yield |
| θ | Bend angle (in pyrenophanes) |
| Å | Angstroms |
| Ac | Acetyl, $CH_3C(O)$- |
| APCI | Atmosphere pressure chemical ionization |
| ASE | Aromatic stabilization energy |
| *β* | "Beta" band (in aromatic UV spectrum) |
| Borch reagent | Dimethoxycarbonium tetrafluoroborate |
| $BTMAICl_2$ | Benzyltrimethylammonium dichloroiodate |
| br | Broad band (in NMR) |
| BuLi | *n*-Butylithium |
| Cat. | Catalyst |
| CPP | Cycloparaphenylene |
| CPPA | Cycloparaphenylene ethynylene |
| COD | Cyclooctadiene |
| conc. | Concentrated |

| | |
|---|---|
| *d* | Deuterium (in NMR solvent, *e.g.* THF-$d_8$) |
| d | Doublet (in NMR) |
| dd | Doublet of doublet (in NMR) |
| DBU | 1,8-Diazabicyclo[5.4.0]undec-7-ene |
| DDQ | 1,2-Dichloro-5,6-dicyanobenzoquinone |
| DIBAl-H | Diisobutylaluminum hydride |
| DMA | *N*,*N*-Dimethylacetamide |
| DME | 1,2-Dimethoxyethane |
| DMF | Dimethylformamide |
| DMSO | Dimethylsulfoxide |
| dtbpy | 4,4'-Di-*tert*-butyl-2,2'-dipyridyl |
| eq. | Equivalents |
| Et. | Ethyl, $C_2H_5$- |
| $Et_3N$ | Triethylamine |
| FGI | Functional group interconversion |
| HOMA | Harmonic Oscillator Model of Aromaticity |
| HOMO | Highest Occupied Molecular Orbital |
| h | Hour |
| HPLC | High pressure liquid chromatography |
| *hv* | Light |
| Hz | Hertz |
| IBX | 2-Iodoxybenzoic acid |

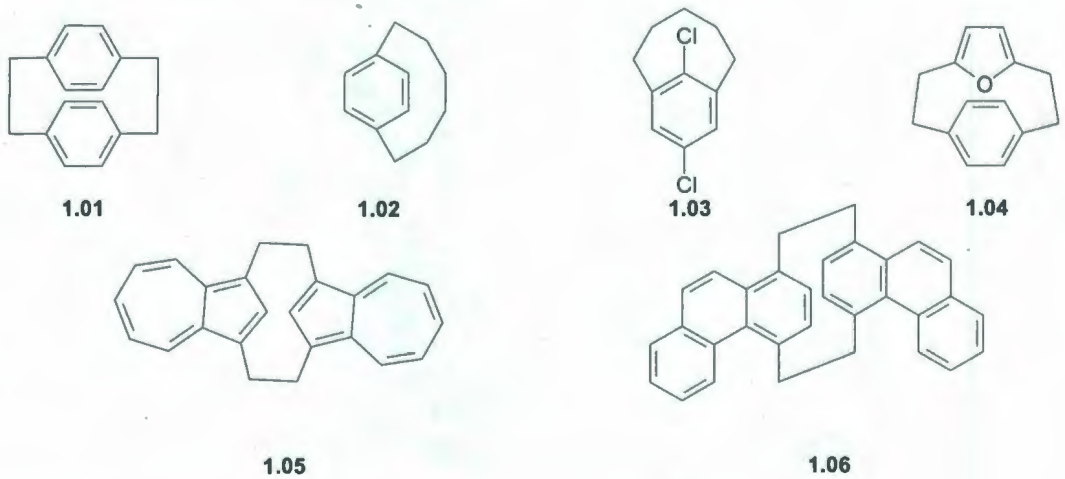
| | |
|---|---|
| IR | Infrared |
| J | (in NMR) Coupling constant (Hz) |
| K | Kelvin |
| kJ | Kilojoule |
| $LiAlH_4$ | Lithium aluminum hydride |
| m | Multriplet (in NMR) |
| $M^+$ | Mass peak |
| MCPBA | *meta*-Chloroperoxybenzoic acid |
| Me | Methyl, $CH_3$- |
| MHz | megahertz |
| min | Minute |
| mM | Millimolar |
| mp | Melting point |
| NBS | *N*-bromosuccinimide |
| nm | Nanometer |
| NMR | Nuclear magnetic resonance |
| *p* | "Para" band (in aromatic UV spectrum) |
| pin | pinacolato |
| Ph | Pheny, $C_6H_5$- |
| ppm | Parts per million |
| PTAD | 4-Phenyl-1,2,4-triazoline-3,5-dione |
| q | Quartet (in NMR) |

| | |
|---|---|
| $R_f$ | Retention factor (in TLC) |
| rt | Room temperature |
| s | Singlet (in NMR) |
| s | Strong |
| SWCNT | Single walled carbon nanotube |
| t | Triplet (in NMR) |
| TBAI | Tetrabutylammonium iodide |
| *t*Bu | *tert*-Butyl, $(CH_3)_3C$- |
| *t*BuOK | Potassium *tert*-butoxide, $(CH_3)_3COK$ |
| TCNE | Tetracyanoethylene |
| Tf | Trifluoromethanesulfonyl, $CF_3SO_2$- |
| TFA | Trifluoroacetic acid |
| THF | Tetrahydrofuran |
| TLC | Thin layer chromatography |
| TMS | Tetramethylsilane (in NMR), trimethylsilane (in structures) |
| Ts | *p*-Toluenesulfonyl |
| UV | Ultraviolet |
| Vis | Visble (light) |
| VID | Valence isomerization-dehydrogenation |
| vs | Very strong (in IR) |
| w | Weak (in IR) |

# Chapter One
# Introduction

## 1.1 Cyclophanes

Cyclophanes first entered chemists' sights in 1949 when Brown and Farthing reported the accidental discovery of [2.2]paracyclophane **1.01** (Figure 1.1). This discovery triggered a huge amount of interest in this area which started with Cram's rational synthesis of [2.2]paracyclophane in 1951.[1] Strain, symmetry, synthetic challenge of unusual structures (*e.g.* nonplanar aromatic systems) and unusual properties (chemical and physical) are the reasons why this developed into one of the more actively investigated fields in modern chemistry.[2]




**1.01** **1.02** **1.03** **1.04**

**1.05** **1.06**

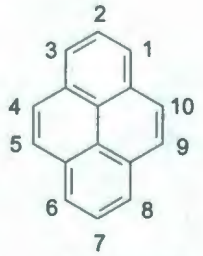
**Figure 1.1** Structures of several simple cyclophanes.

The simplest cyclophanes consist of an aromatic system in which two nonadjacent atoms on this system are connected by a bridge, which can be any series of atoms. When the aromatic system is benzene, the prefixes *para*- and *meta*- are used to indicate the

relationship of the carbons that are bridged. The number of atoms in the bridge is placed in brackets. Thus compounds **1.02** and **1.03** (Figure 1.1) are named [6]paracyclophane and 8,11-dichloro[5]metacyclophane.[3,4] Cyclophanes can have any number of aromatic systems and as many bridges as permitted by the aromatic units. Accordingly, a detailed system of nomenclature has been developed.[9] In the case of compound **1.01**,[1,5] [2.2] means there are two bridges connecting the two aromatic systems, and each bridge is two carbon atoms in length. *Para*- again indicates that the bridgehead carbons of the aromatic rings are *para*-related. In addition to simple benzenoid systems, the aromatic units could also be heterocyclic (*e.g.* **1.04**[6]), non-benzenoid (*e.g.* **1.05**[7]) or polycyclic (*e.g.* **1.06**[8]). When the aromatic system is pyrene, the cyclophane is called a pyrenophane. In this thesis, the focus will be mainly on pyrenophanes, which are compounds of major interest in the Bodwell group.

## 1.2 Pyrenophanes

### 1.2.1 Pyrene

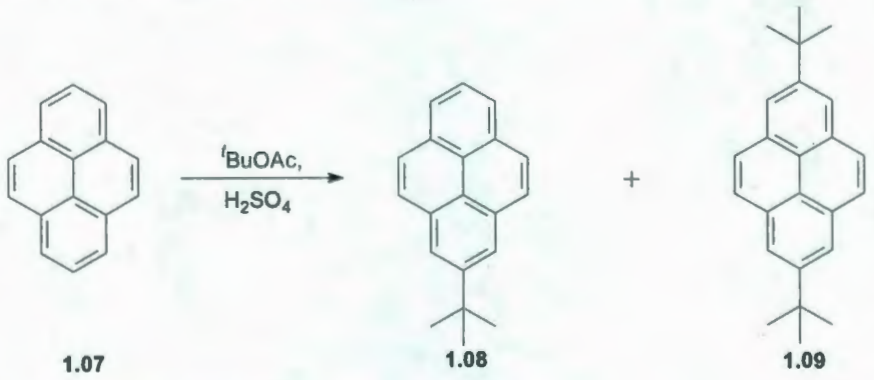



pyrene (**1.07**)

**Figure 1.2** Structure and numbering scheme for pyrene.

Pyrene was first isolated from coal tar in 1871.[10] It is the smallest peri-fused

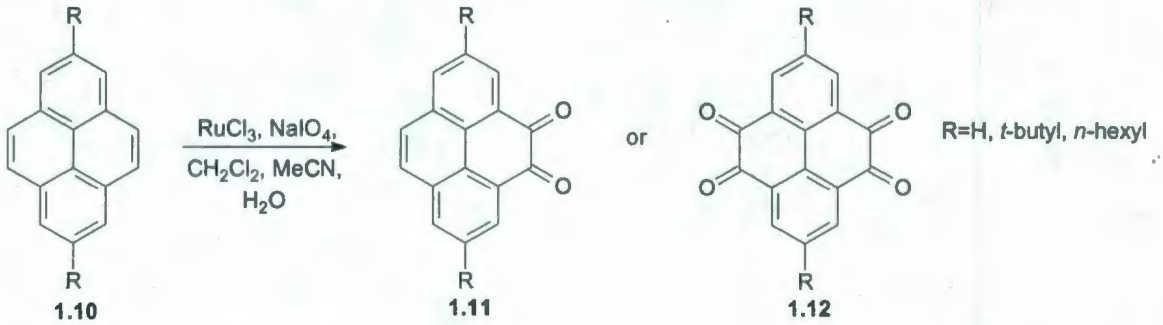
polycyclic aromatic hydrocarbon and has very useful photophysical and photochemical properties. For example, its first singlet excited state $S_1$ is quite long-lived (410 ns in ethanol at 293 K) and has a different structure than the ground state $S_0$.[11] Pyrene has a high fluorescence quantum yield ($\Phi_{em}$ = 0.65) and easily forms excimers. Both the fluorescence quantum yield and the excimer formation are very sensitive to its environment. For these reasons, derivatives of pyrene have found application in areas such as plastics, dyes, pesticides, pharmaceuticals and electroluminescent devices.[12]




**Scheme 1.1** Friedel-Crafts *t*-butylation of pyrene.

The chemistry of pyrene is limited compared to that of benzene. Pyrene is electron-rich and thus relatively reactive in electrophilic aromatic substitution reactions. The HOMO has very large orbital coefficients at the 1,3,6 and 8 positions and this accounts for the typically high selectivity for electrophilic aromatic substitution at these positions (Figure 1.2).[13] One big exception is Friedel-Crafts *t*-butylation, which occurs only at the 2,7-positions (Scheme 1.1). The reason for this feature is steric hindrance. Only the 2,7-positions are not sterically hindered peri-positions.[14] Pyrene can also be

oxidized to afford the 4,5-diketone **1.11** or 4,5,9,10-tetraketone **1.12** (Scheme 1.2).[15]




**Scheme 1.2** Oxidation of pyrene.

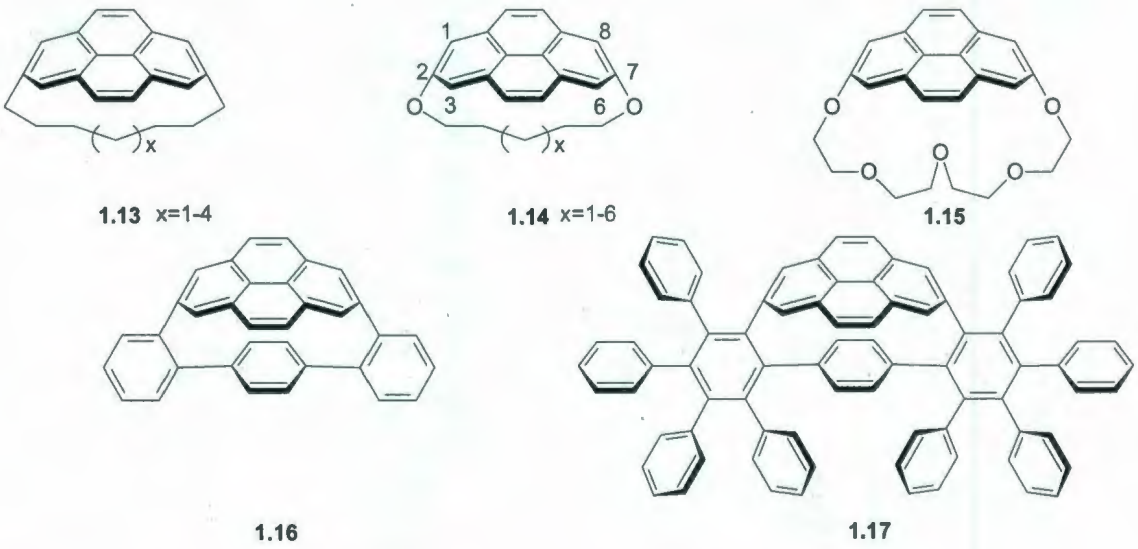
### 1.2.2 Known bridging motif of pyrenophanes

There are 13 unique pairs of nonadjacent carbon atoms in pyrene that could serve as bridgeheads in a cylcophane, *i.e.* (1,3), (1,4), (1,5), (1,6), (1,7), (1,8), (1,9), (2,4), (2,5), (2,6), (2,7), (4,9) and (4,10) (Figure 1.2). Only the (1,3), (1,6), (1,8), (2,4), (2,7) and (4,9) bridging motifs have been discovered.[12] This fact is probably due to the difficulty in synthesizing the appropriately substituted pyrenes required for several of the possible bridging motifs.

### 1.2.3 Synthesis of [*n*](2,7)pyrenophanes in the Bodwell group

Several [*n*](2,7)pyrenophanes have been synthesized in the Bodwell group (Figure 1.3) using a common synthetic strategy. In this strategy, a valence isomerization/dehydrogenation (VID) reaction of a tethered [2.2]metacyclophane-1,9-diene was used as the key reaction that generates the pyrene system. When the length of the bridge is short enough, the geometry of the pyrene part will be bent and the degree of bend will increase as the bridge becomes shorter.[16] The

nonplanarity of pyrene can be quantified by the bend angle $\theta$, which is the smallest angle between the C1-C2-C3 and C6-C7-C8 planes. The bend angle $\theta$ for planar pyrene is 0°. The largest $\theta$ angle measured for a pyrenophane is 109.2° for 1,7-dioxa[7](2,7)pyrenophane **1.14** (x=1).[2] According to DFT-calculations, the bend angle $\theta$ of pyrene units of compounds **1.16** and **1.17** are 93.6° and 95.8°, respectively.[17]



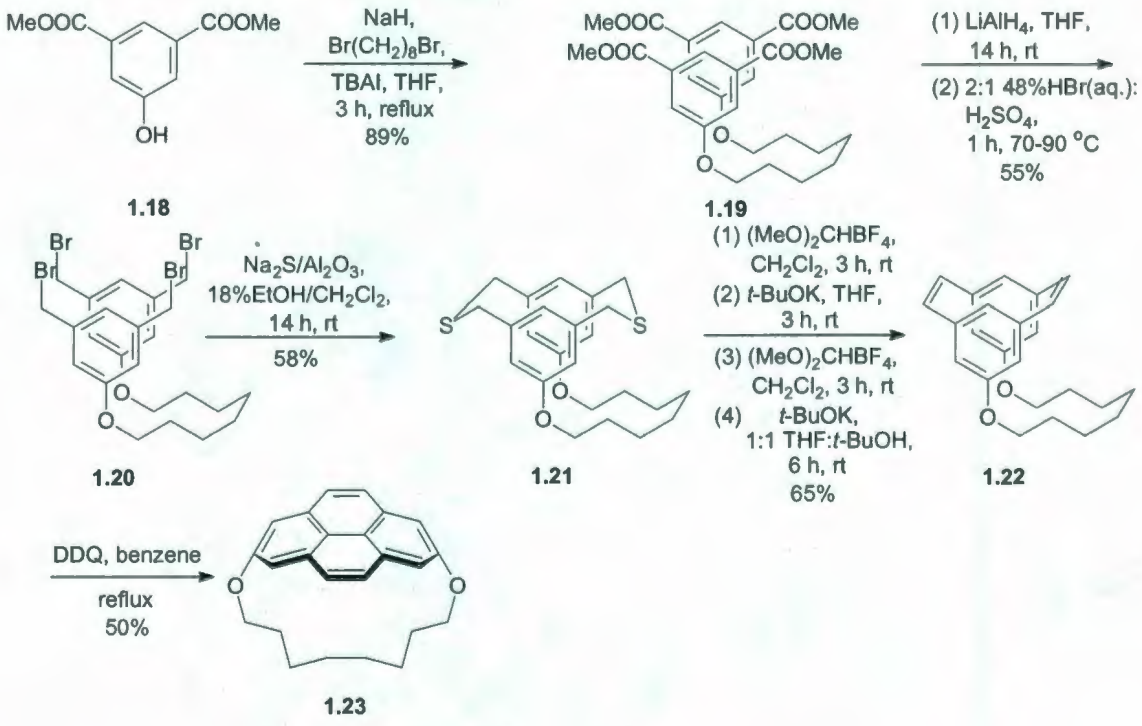

**1.13** x=1-4 **1.14** x=1-6 **1.15**

**1.16** **1.17**

**Figure 1.3** Several [*n*](2,7)pyrenophanes synthesized in the Bodwell group.

The synthetic route can be exemplified by the syntheses of the 1,10-dioxa[10](2,7)pyrenophane **1.23** (Scheme 1.3).[18] A Williamson ether synthesis between diester **1.18** and 1,8-dibromooctane afforded tetraester **1.19**. Tetrabromide **1.20** was then prepared in 55% yield by reduction of the four ester groups with $LiAlH_4$ followed by treatment of the crude product with $HBr/H_2SO_4$. The two benzene rings were then joined together upon reaction of **1.20** with $Na_2S/Al_2O_3$ to afford dithiacyclophane **1.21**. *S*-Methylation of dithiacyclophane **1.21** by $(MeO)_2CHBF_4$ (Borch reagent),

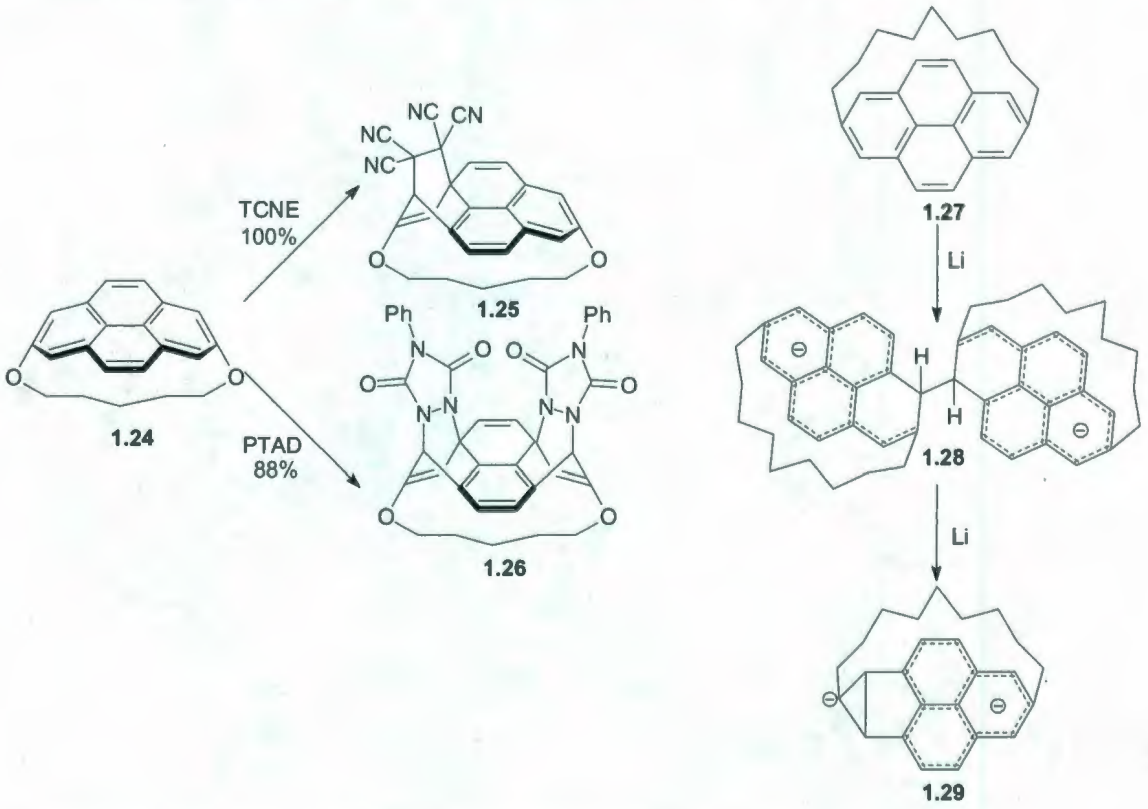
followed by Stevens rearrangement gave a mixture of ring-contracted isomers, which could not be separated. A second *S*-methylation followed by Hofmann elimination formed the key *syn*-[2.2]metacyclophanediene **1.22**, in an overall yield of 65% from **1.21**. The $^1$H NMR showed that about half of the *syn*-[2.2]metacyclophanediene **1.22** had been converted to product **1.23**. Another less symmetrical product, which has not been indentified unequivocally is also formed in this reaction. However, compounds **1.22**, and **1.23** could not be separated and the mixture was treated with DDQ to give the pyrenophane **1.23**. The VID reaction has proved to be a very powerful reaction for the formation of nonplanar pyrenes. Details of the mechanism are discussed in Chapter 2.




**Scheme 1.3** Synthesis of the 1,10-dioxa[10](2,7)pyrenophane **1.23**.

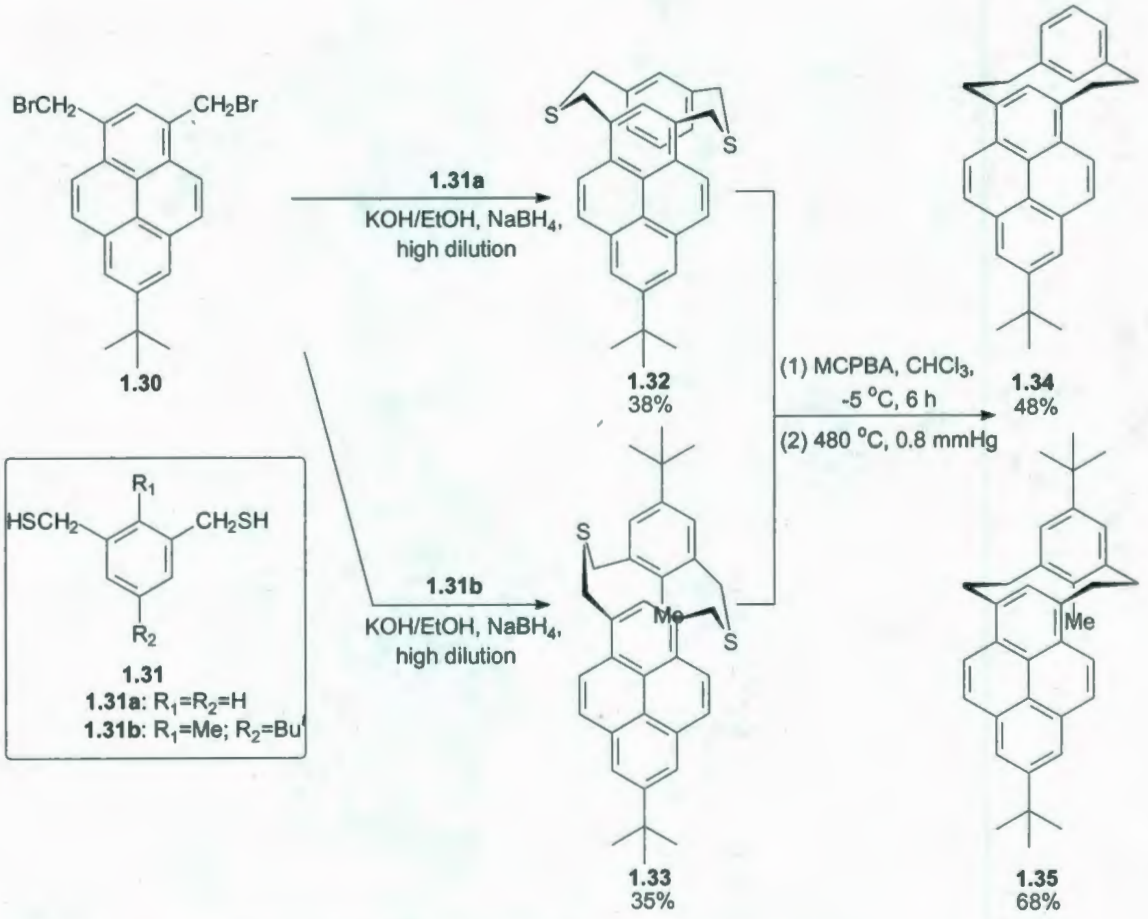
The more highly strained a pyrenophane becomes, the more reactive the pyrene

system within it becomes. For example, compound **1.24** reacted with tetracyanoethene (TCNE) in benzene at room temperature to give compound **1.25** in 100% yield. Although reaction between **1.24** and 4-phenyl-1,2,4-triazoline-3,5-dione (PTAD) was much slower than TCNE, a 2:1 adduct was obtained.[19,20] Reduction of strained pyrenophane **1.27** with lithium gave dimeric dianion **1.28**, and further reduction with lithium led to the formation of monomeric dianion **1.29** (Scheme 1.4).[21] These unusual reactions, which do not occur in less strained higher homologs, are presumably driven by the relief of strain.




**Scheme 1.4** Some unusual reactions of strained pyrenophanes.

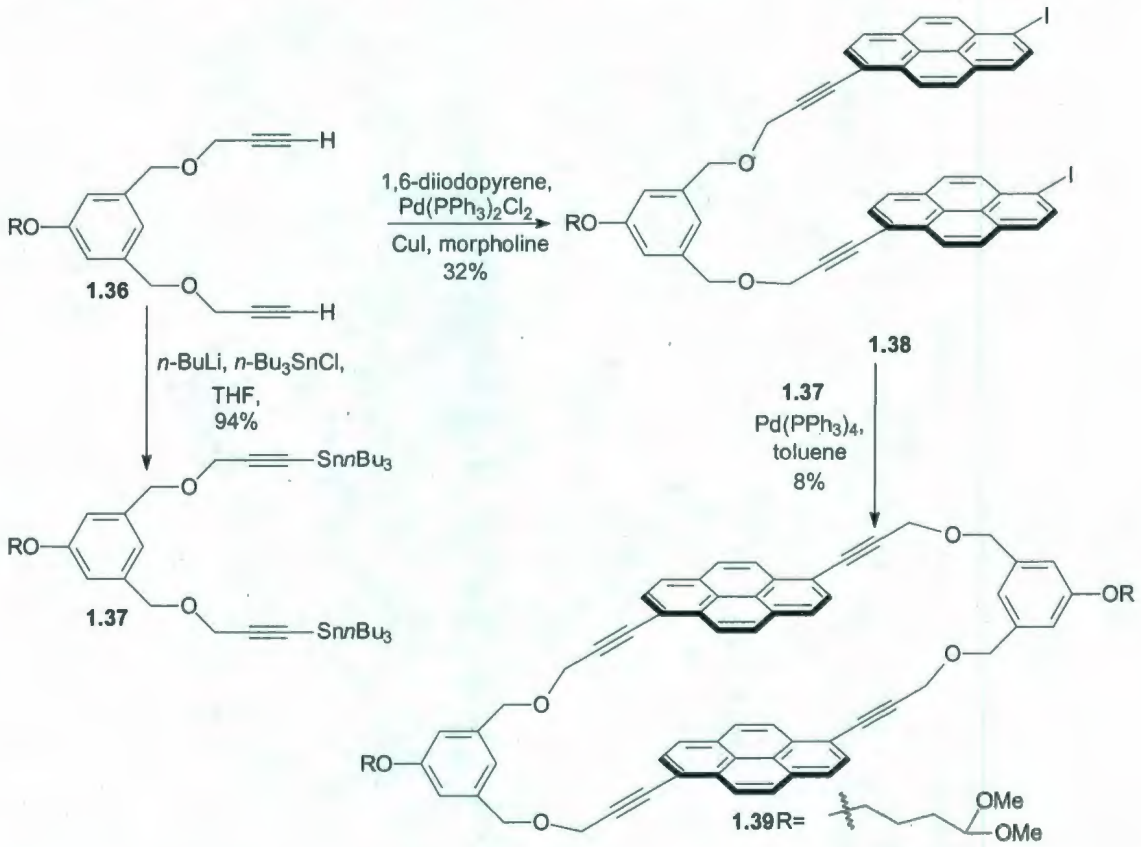
### 1.2.4 Synthesis of pyrenophanes by other groups




**Scheme 1.5** Synthesis of 8-substituted [2]metacyclo[2]pyrenophanes.

Several (1,3)pyrenophanes also have been reported.[13,22] Yamato and co-workers reported the synthesis of some (1,3)pyrenophanes in 1993.[13] 1,3-Disubstituted pyrene **1.30** (Scheme 1.5) was easy to prepare because the *t*-Bu group at the 7 position prevented substitution at the 6 and 8 positions. Coupling of dibromide **1.30** and dithiol **1.31a** under high dilution condition afforded (1,3)pyrenophane **1.32**. Interestingly, when **1.30** was coupled with **1.31b**, which has a methyl group at the "internal" position, only the *anti*-conformer of **1.33** was obtained. The conformation didn't change after oxidation of sulfides **1.32** and **1.33** to the corresponding sulfones. However, after carrying out

pyrolysis under high vacuum, both of the oxidation products, (1,3)pyrenophanes **1.34** and **1.35**, were obtained as *anti*-conformers. The conformations of all of these pyrenophanes were evidenced by the chemical shift of the proton at the 2 position of pyrene ($\delta_{syn\mathbf{1.32}}$=6.85, $\delta_{anti\mathbf{1.33}}$=5.85, $\delta_{anti\mathbf{1.34}}$=5.09, $\delta_{anti\mathbf{1.35}}$=4.53).

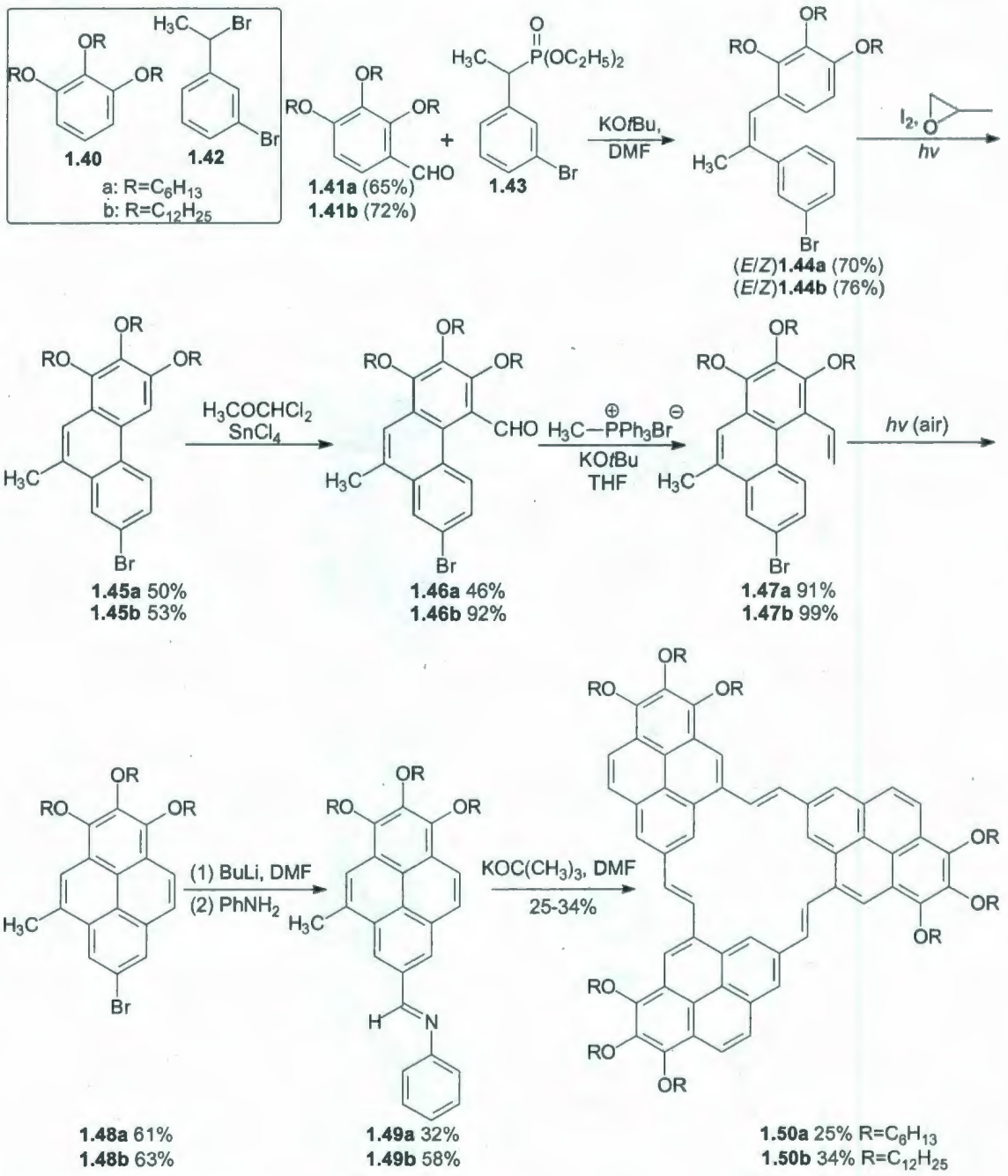



**Scheme 1.6** Synthesis of (1,6)pyrenophane with polycationic or amphiphilic functionality.

A series of large (1,6)pyrenophanes with polycationic or amphiphilic functionality was synthesized by the Inouye group,[23] mainly using cross-coupling chemistry. Sonogashira coupling of diacetylenes **1.36** with 1,6-diiodopyrene gave diiodide **1.38**. This intermediate was subjected to Stille coupling with distannane **1.37** (which was

synthesized from **1.36**) to form (1,6)pyrenophane **1.39**. Various R groups (*e.g.* an $\omega$-acetal) were incorporated to increase the solubility of the macrocycle, as well as to serve as handles for further functionalization (Scheme 1.6). In addition to these (1,6)pyreneophanes, Misumi also reported the synthesis of [2.2](1,6)pyrenophane and [2.2](1,6)(2,7)pyrenophane in 1978.[24]

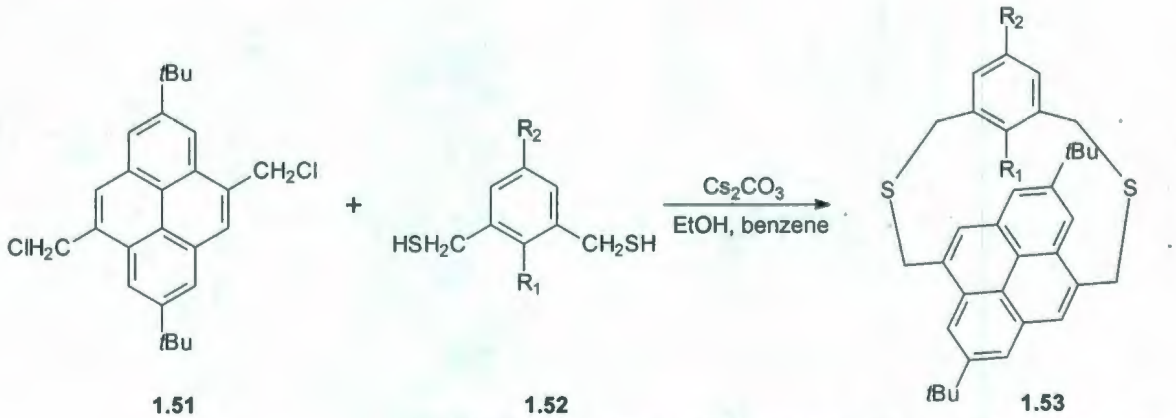
Meier *et al.* synthesized a tripyreno[2,3,4-*abc*:2,3,4-*ghi*:2,3,4-*mno*][18]annulenes **1.50**, which can also be viewed as (2,4)pyrenophanes.[25] Interestingly, Meier's synthesis did not start with an intact pyrene system. Two building blocks **1.41** and **1.43**, which were synthesized from **1.40** and **1.42**, were joined via a Horner-Wadsworth-Emmons reaction to afford (*E/Z*) **1.44**. Photochemical cyclodehydrogenation afforded phenanthrene derivative **1.45**. A vinyl group was then introduced by a formylation-Wittig sequence. A second cyclodehydrogenation gave the full pyrene skeleton **1.48**. The bromide functional groups were converted into *N*-phenylimines in two steps, and the desired (2,4)pyrenophanes **1.50** were then obtained by a threefold, highly (*E*)-selective Siegrist reaction.[26] Although an [18]annulene skeleton can be identified in **1.50**, these compounds behaved like assemblies of three bridged pyrene systems, *i.e.* as pyrenophanes (Scheme 1.7). To date, Meier's (2,4)motifs are the only known (2,4)pyrenophanes, to have been reported.




**Scheme 1.7** Synthesis of (2,4)pyrenophanes **1.50**.

A (4,9)pyrenophane was successfully obtained by the Tsuge group using classical cyclophane chemistry. This compound is the only known (4,9)pyrenophane.[27] Bis(chloromethyl)pyrene **1.51** reacted with bis(mercaptomethyl)benzene **1.52** in the

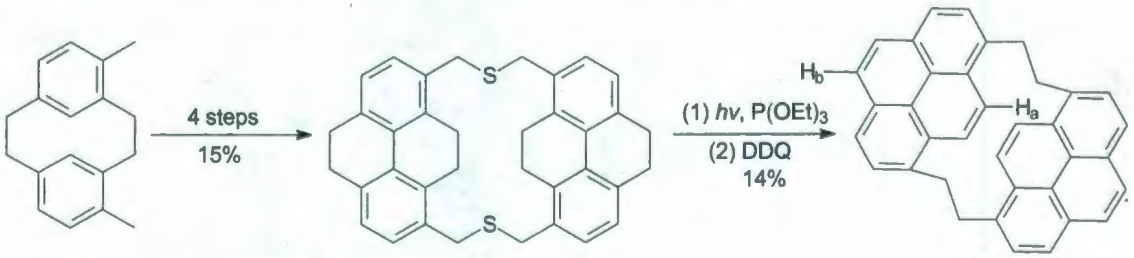
presence of $Cs_2CO_3$ under high dilution conditions to afford the corresponding dithiapyrenophane **1.53**. Reduction of the nitro- group on the benzene ring afforded an amine, which was used to study the NH-π interaction between the internal amino group and the pyrene ring (Scheme 1.8).




**1.51** **1.52** **1.53**

**1.53a** $R_1$=H, $R_2$=$CH_3$ **1.53c** $R_1$=$OCH_3$, $R_2$=H **1.53e** $R_1$=$NO_2$, $R_2$=H
**1.53b** $R_1$=H, $R_2$=$OCH_3$ **1.53d** $R_1$=H, $R_2$=$NO_2$ **1.53f** $R_1$=F, $R_2$=H
**1.53g** $R_1$=H, $R_2$=H

**Scheme 1.8** Synthesis of (4,9)benzeopyrenophanes **1.53**.




**1.54** **1.55** **1.56**

**Scheme 1.9** Synthesis of (1,8)pyrenophanes **1.56**.

The only known (1,8)pyrenophanes were synthesized using the same synthetic approach as **1.53**. Dithiacyclophane **1.55** (a tetrahydropyrenophane) was synthesized in four steps from **1.54** and the sulfur groups were extended with $P(OEt)_3$. Dehydrogenation with DDQ afforded *anti*-**1.56**. The *anti* conformation was proved by the upfield chemical

shift of $H_a$ relative to $H_b$ ($\delta_{Ha}$=6.55, $\delta_{Hb}$=8.03) (Scheme 1.9).[24]

### 1.2.5 Applications

As discussed earlier, the photophysical properties of pyrene have been used in various ways. For example, fluorescent probes have been designed that take advantage of excimer/monomer emission and long fluorescence lifetime.[28] Furthermore, some molecular assemblies containing pyrene have recognition properties. For example, triazole tethered ferrocene-pyrene dyad **1.57** is able to selectively recognize the pyrophosphate anion (Figure 1.4).[29] As far as pyrenophanes are concerned, relatively few applications have been reported. Water-soluble pyrenophane **1.39** (see Section 1.2.4), which has a cavity size of 0.46 × 0.95 × 1.31 Å also shows molecular recognition abilities.[30] This size of the cavity allows **1.39** to recognize anionic arenes as well as nucleotides (Figure 1.4).[23] It seems likely that further applications of pyrenophanes will be discovered, which rely upon the special characteristics of the pyrene units(s) (*i.e.*photophysical properties and π-π interactions) or the pyrenophane as a whole (*i.e.* size and shape of the cavity).

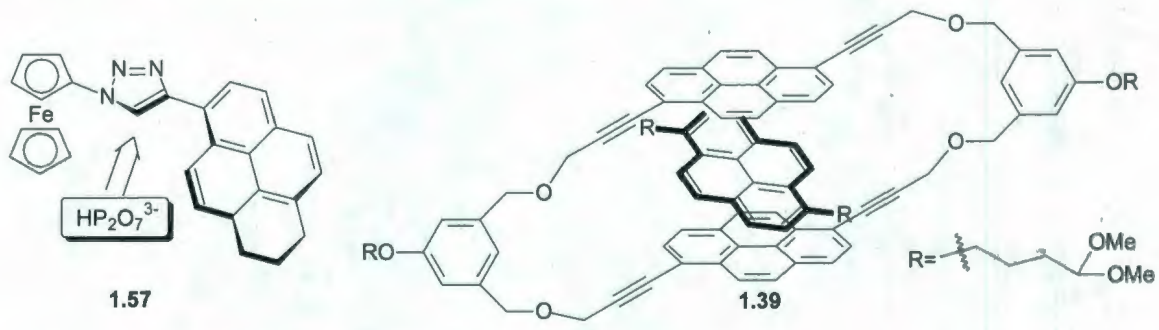



**Figure 1.4** Recognition systems of **1.57** and **1.39**.

## 1.3 Aromatic belts

### 1.3.1 General introduction

**1.58**
a generic belt

**1.59**
[10]cyclacene
subunit of a zig-zag SWCNT

**1.60**
[10]cyclophenacene
subunit of a armchair SWCNT

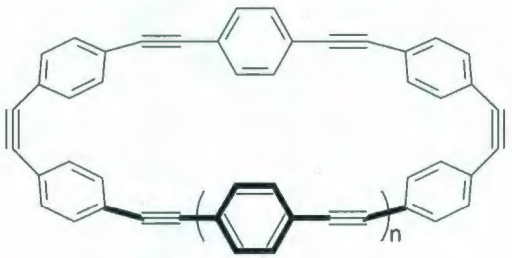
**Figure 1.5** Aromatic belt motifs.

A belt has two continuous, nonintersecting edges and a width that is smaller than its circumference, as depicted in structure **1.58** (Figure 1.5).[16] Belt-like molecules have been attracting both synthetic and theoretical interest for many years, even before the advent of fullerenes and carbon nanotubes.[31] When the surface of a molecular belt consists entirely of a polycyclic aromatic framework, it is called an aromatic belt. Interestingly, aromatic belts are subunits of single-walled carbon nanotubes (SWCNTs). As such there is a direct homology between the roll-up motif (chirality) of SWCNTs and different types of aromatic belts. [*n*]Cyclacenes, *e.g.* [10]cyclacene **1.59**, correspond to zigzag SWCNTs and [*n*]cyclophenacenes, *e.g.* [10]cyclophenacene **1.60**, correspond to armchair SWCNTs (Figure 1.5). SWCNTs are currently the subjects of very broad interest from the general scientific community because of their potential for use in applications that exploit their optical, electronic and mechanical properties. SWCNTs are produced under very harsh

conditions and are obtained as complex mixtures that vary in the lengths, diameters, and chiralities. Thus, the synthesis of a particular aromatic belt would be an important first step toward the production of single chirality SWCNTs.[32]

### 1.3.2 From rings to belts to aromatic belts

Free-standing (*i.e.* not embedded within other structures) aromatic belts (cyclacenes, cyclophenacenes and related structures) have not yet been successfully synthesized, but great progress in this direction has been made over the past two decades.



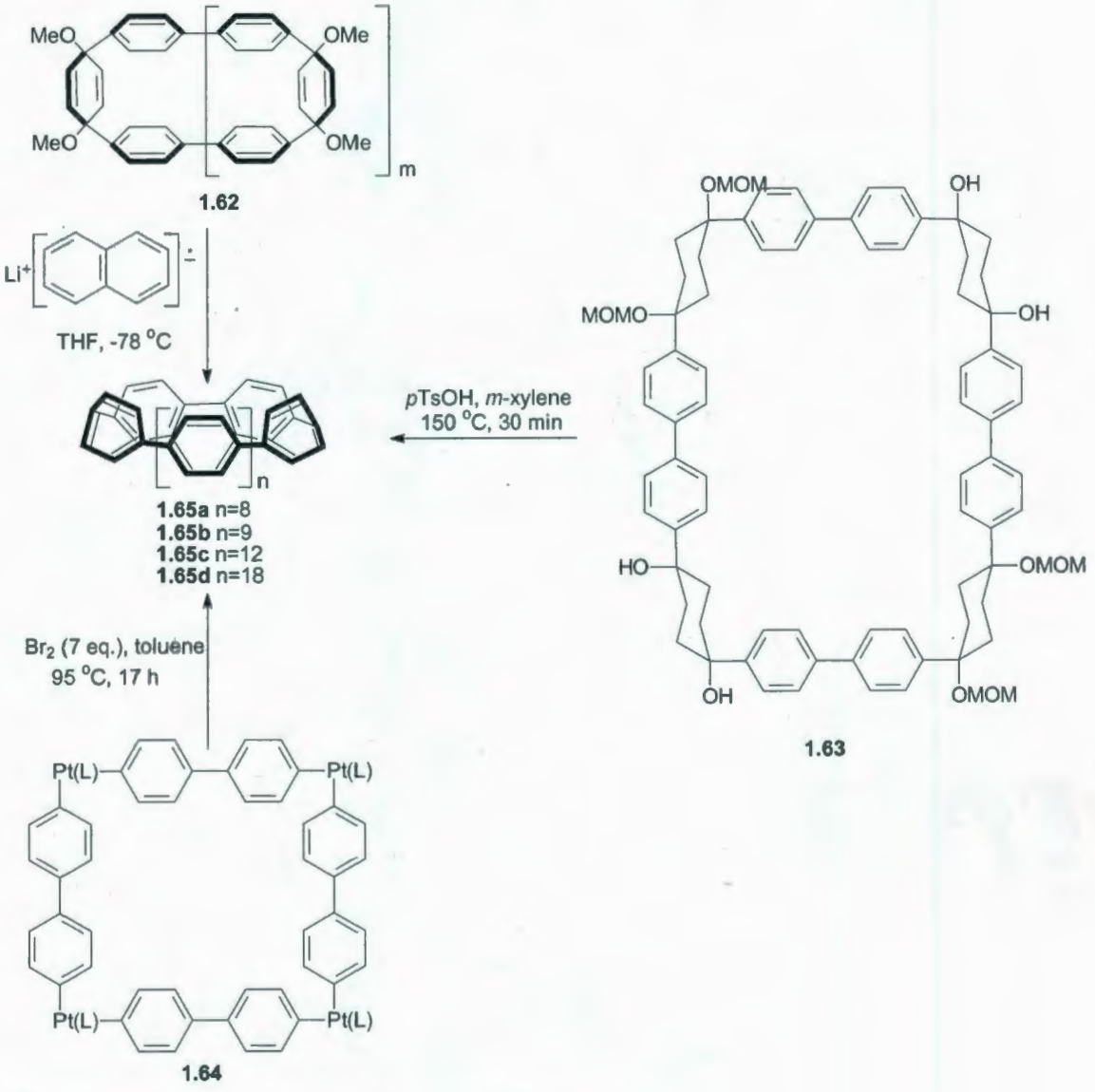

**1.61a** n=1
**1.61b** n=2
**1.61c** n=3
**1.61d** n=4

**Figure 1.6** Cycloparaphenylene ethynylenes **1.61**.

The cyclioparaphenylene ethynylenes (CPPAs) **1.61** are important compounds in this area (Figure 1.6). They are not aromatic belts because their two edges intersect repeatedly, but they were the first cyclic system with radially oriented *p* orbitals to be synthesized.[33,34]

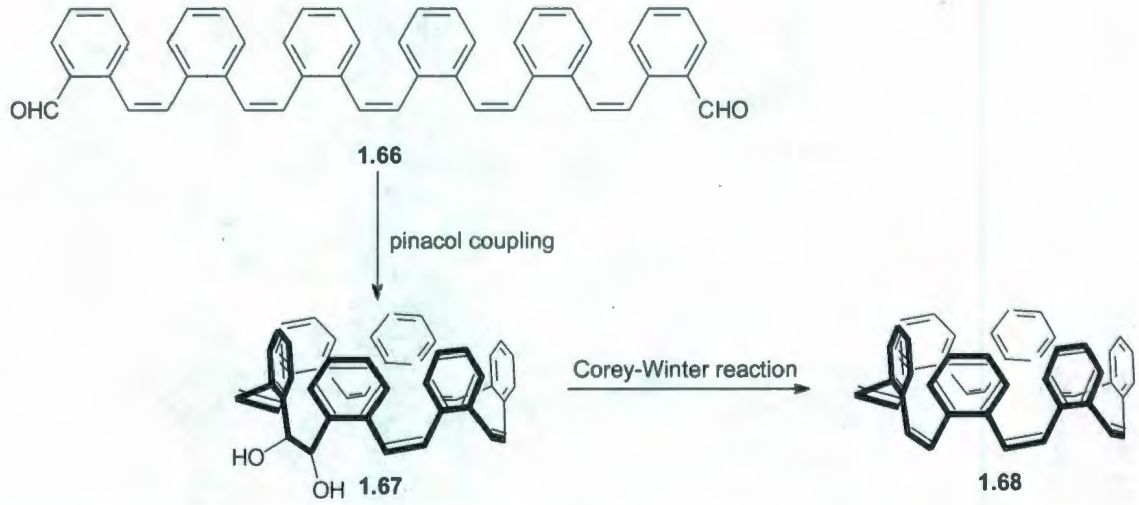
The cycloparaphenylenes (CPPs) **1.65** are also not belts due to the repeated intersection of the two edges, but they do map onto SWCNTs. The synthesis of various CPPs was recently accomplished by three different research groups. Bertozzi *et al.* prepared [9]-, [12]- and [18]cycloparaphenylenes **1.65b**, **1.65c**, **1.65d** in 2008[35], using

*syn*-3,6-dimethoxycyclohexa-1,4-diene units as aromatic ring precursors in the macrocyclic intermediate **1.62**. The increase in strain that came from aromatization of these rings was counterbalanced by the gain in aromatic stabilization energy (ASE).[36,37] The chemistry was also noteworthy because the reaction of **1.62** with lithium naphthalenide is an example of a *reductive* aromatization.




**Scheme 1.10** Synthesis of [*n*]cycloparaphenylenes **1.65**.

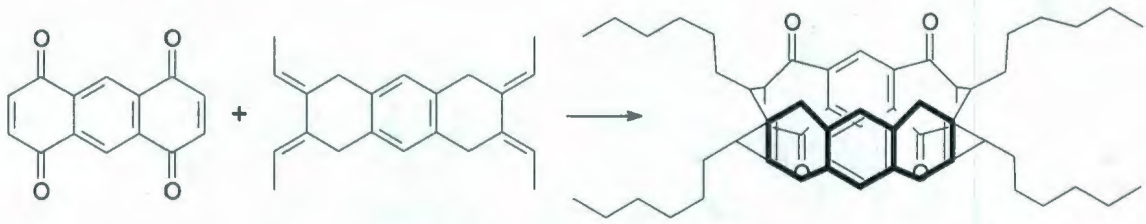
The Itami group in Japan synthesized [12]cycloparaphenylene **1.65c** using *syn*-3,6-dialkoxycyclohexane units as nonplanar benzene precursors.[38] Most recently, Yamago synthesized [8]cycloparaphenylene **1.65a** using a fourfold reductive elimination of macrocyclic Pt complex **1.64**.[39] In this case the energy obtained from the C-C bond-forming reaction is a major factor in counteracting the developing strain energy (Scheme 1.10).




**Scheme 1.11** The strategy to synthesis of (*all-Z*)-hexabenzo[24]annulene **1.68**.

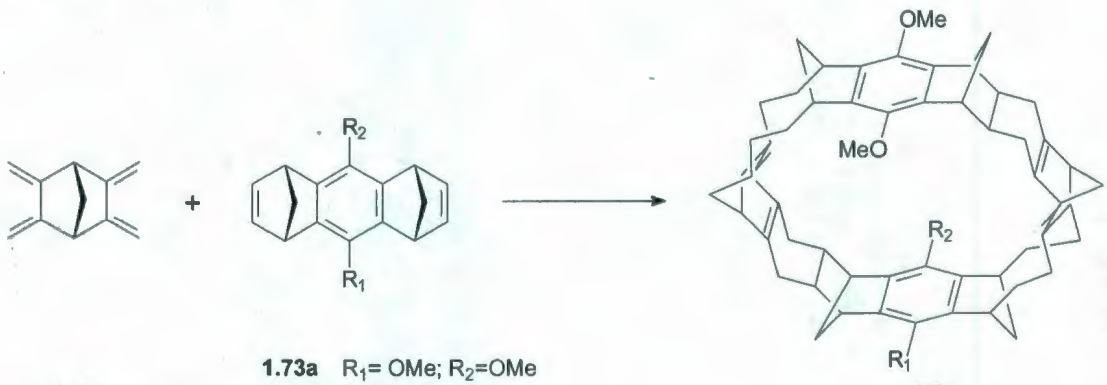
In moving to aromatic belts (systems with nonintersecting edges), similar success has not yet been achieved. In an attempt to synthesis [12]cyclophenacene, Kuwatani used a McMurry reaction to convert linear dialdehyde **1.66** to diol ring **1.67**, which was then converted into (*all-Z*)-hexabenzo[24]annulene (**1.68**). As with the cycloparaphenylenes **1.65, 1.68** is not a belt, but maps onto armchair SWCNTs. Moreover, **1.68** could possibly be transformed into a belt via a sixfold cyclodehydrogenation reaction. There has been no

report of any attempt to do this reaction. It is likely that all attempts failed (Scheme 1.11).[40]



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

**Scheme 1.12** Cory's belt.

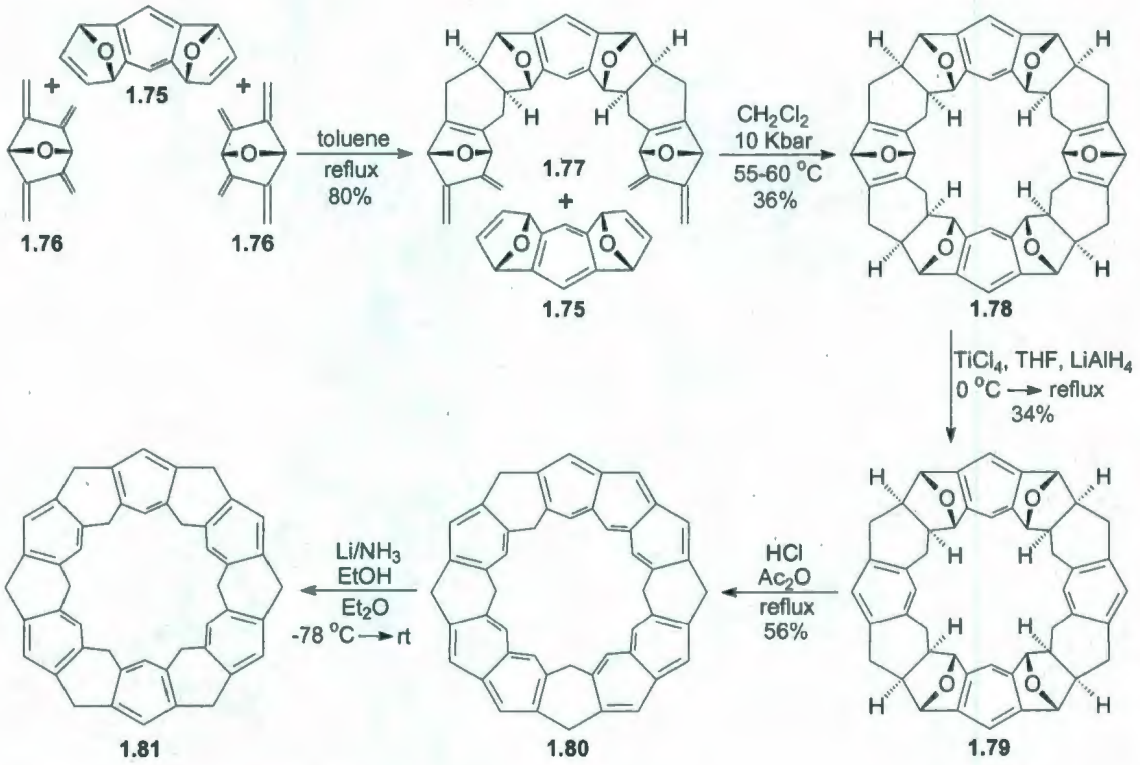



**1.72** **1.73a** $R_1$= OMe; $R_2$=OMe **1.73b** $R_1$=Me; $R_2$=OH **1.74**

**Scheme 1.13** Klärner's belt.

Several *molecular* belts have been synthesized as possible precursors to cyclacene-type aromatic belts. Various strategies have been used by different groups, the most common of which is a Diels-Alder-based approach. Cory used a double Diels-Alder cycloaddition to afford a belt-like macrocyclic cyclophane **1.71** (Scheme 1.12).[41] The Klärner group also synthesized a molecular belt by a series of Diels-Alder reactions of compounds **1.72** and **1.73**. These Diels-Alder reactions required high pressure (8 Kbar) and high temperature (125 °C) to afford the desired products (Scheme 1.13).[42] The

presence of six methano bridges effectively ruled out the conversion of **1.74** into an aromatic belt.

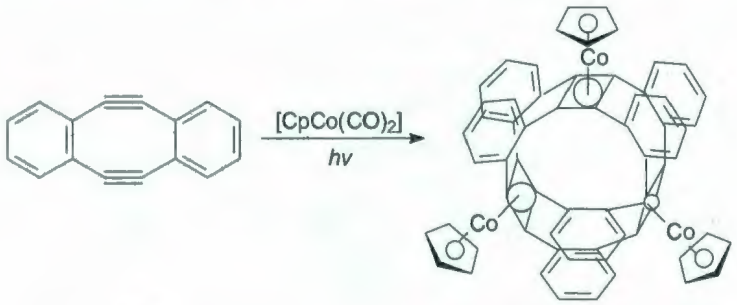



**Scheme 1.14** Stoddart's belt.

On the other hand, Stoddart used a similar Diels-Alder strategy to synthesize a related belt **1.81**.[43] The key difference in Stoddart's work was the replacement of that Klärner's methano bridges were replaced with oxa bridges, which were intended to be used in elimination reactions that would aromatize the belt. Unfortunately, only partially aromatized belts were obtained. Again, the final cycloadditions required both high temperature and high pressure (Scheme 1.14).

In 2004, Gleiter synthesized a (Cp)Co-stabilized beltene **1.83**, which can be viewed

as a cyclacene composed of eight-membered rings and four-membered rings instead of just six-membered rings. Highly strained cyclic diyne **1.82** reacted with [$CpCo(CO)_2$] to give "[4.8]$_3$cyclacene" **1.83** in a single synthetic operation. Later study showed that a Rh-based reagent could also afford this product.[44,45] Unlike four- and six-membered rings, eight-membered rings consisting only of $sp^2$-hybridized carbon atoms are not innately planar. This is very important in the case of **1.83**, because the natural tub conformation allows for a relatively unstrained belt to form (Scheme 1.15).

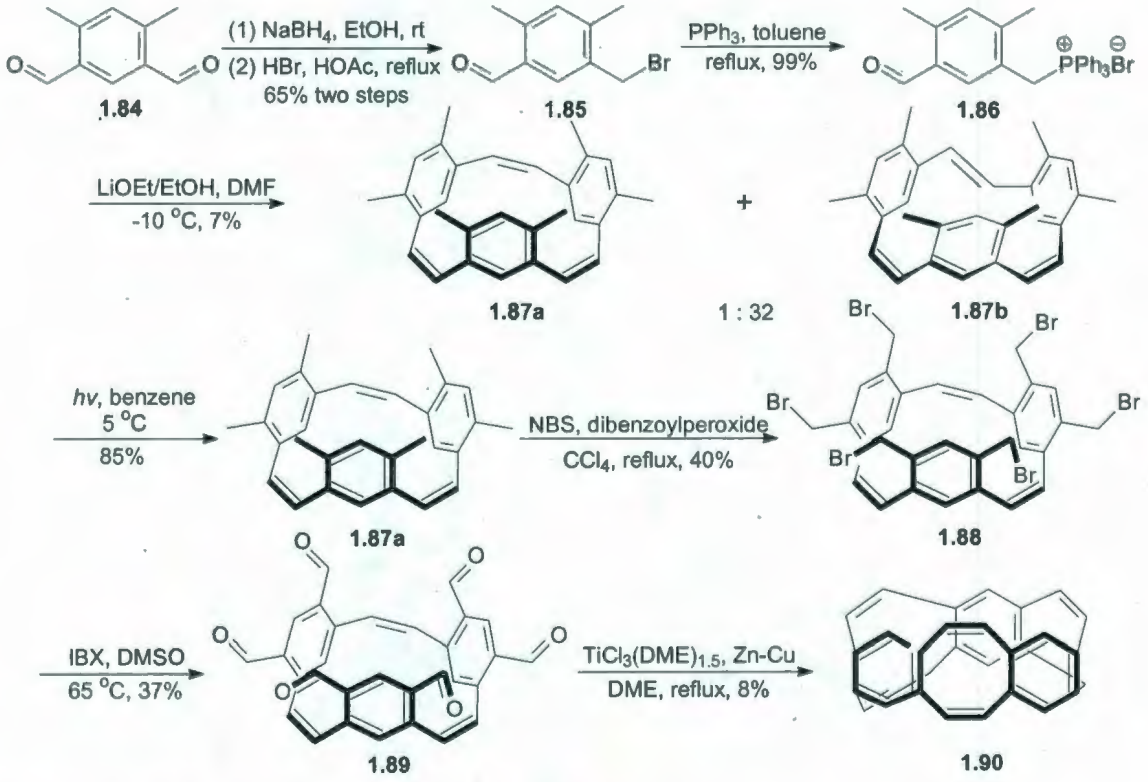



**1.82** **1.83**

**Scheme 1.15** Preparation of beltene **1.83**.

Based on the idea that eight-membered rings could be used to avoid strain, [6.8]$_3$cyclacene **1.90** was designed to be the first purely hydrocarbon cyclacene and a model for a new type of carbon nanotube.[46] The synthesis started from readily available dialdehyde **1.84**. Partial reduction afforded a monoalcohol, which was converted into benzylic bromide **1.85** by HBr in HOAc. Phosphonium salt **1.86** was formed by refluxing **1.85** with $PPh_3$ (99%). Self-Wittig reaction of **1.86** occurred to give a 1:32 mixture of (*Z,Z,Z*)- and (*E,Z,Z*)-hexamethyl[2]$_3$-metacyclophanetrienes **1.87a** and **1.87b**. The major

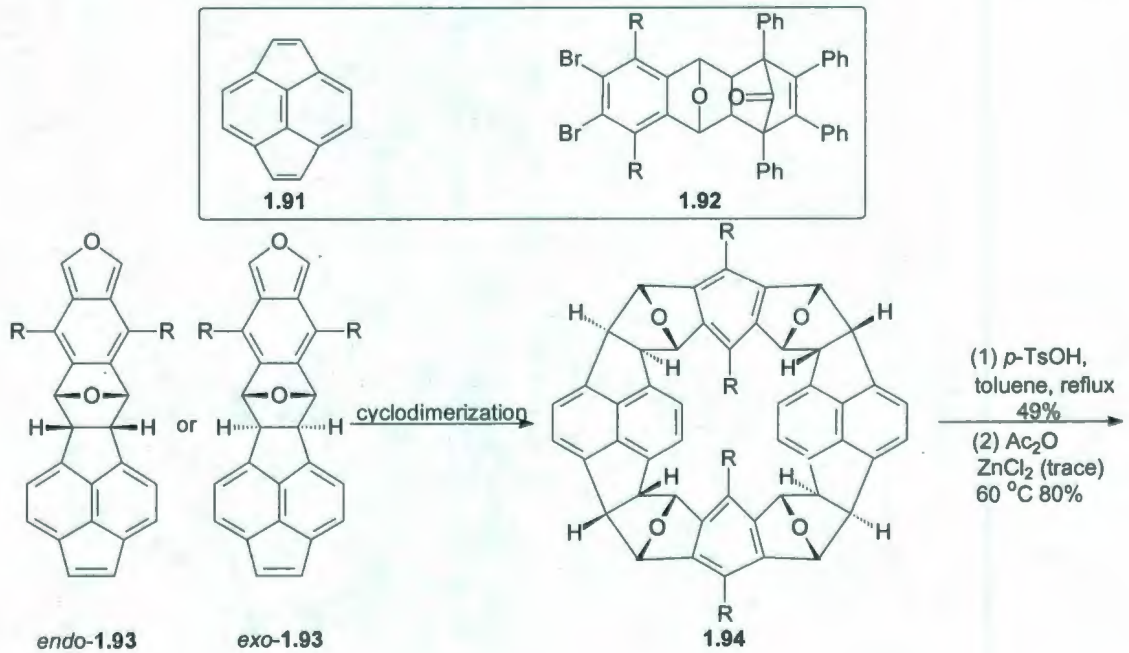
cyclization product **1.87b** could be converted into the (*Z,Z,Z*) isomer **1.87a** by irradiation in benzene with a high pressure mercury lamp. Sixfold benzylic bromination of **1.87a** was carried out using NBS to afford hexabromide **1.88**. IBX oxidation of **1.88** gave hexaaldehyde **1.89**. [6.8]$_3$Cyclacene **1.90** was then synthesized by a threefold intramolecular McMurry coupling using $TiCl_3$-DME complex (Scheme 1.16).

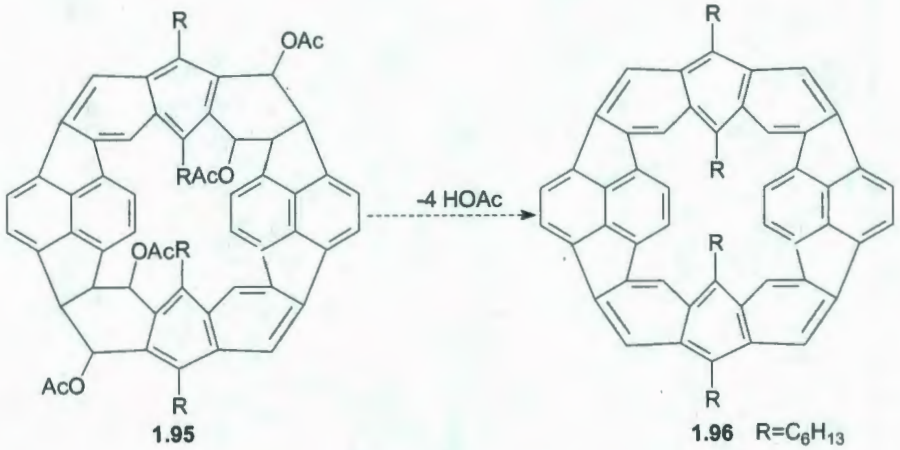



**Scheme 1.16** Synthesis of [6.8]$_3$cyclacene **1.90**.

Schlüter has also contributed greatly to the area of fully aromatic belts. However, his main target is the belt region of $D_2$-$C_{84}$, which contains four five-membered rings. Again, the strategy is Diels-Alder-based. It relies on the self-reaction of molecules that have a diene at one end and a dienophile at the other. In such cases, Schlüter suggested there is a

ring-chain equilibrium between ladder polymers and cyclic oligomers. When the conformation of linear oligomers matches the geometrical requirements of facile ring closure, cyclization will become the main reaction.[47] *Endo*-**1.93** and *exo*-**1.93** were prepared in five steps from **1.91** and **1.92**. Both isomers of **1.93** underwent cyclodimerization to afford the same isomer of macrocycle **1.94**.[48] Numerous attempts to aromatize **1.94** (formally a fourfold dehydration) proved to be unsuccessful. Calculations suggested that the large increase in strain associated with this conversion far outweighed any gains in ASE. In the mass spectrum, tetraacetate **1.95** showed the loss of four HOAc molecules to give a species with the mass of the desired belt. However, as Schlüter pointed out, this could be an isomer of **1.96** with one or more exocyclic double bonds (Scheme 1.17).[49]

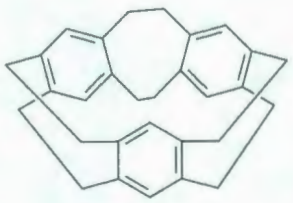





**1.95** **1.96** R=$C_6H_{13}$

**Scheme 1.17** Schlüter's approach to the $D_2$-$C_{84}$ of belt region.

Cory, Stoddart and Schlüter targeted cyclacenes and were all unsuccessful in their attempts because their targets have high strain and low ASE.[49,50] Gleiter circumvented this problem by incorporating innately nonplanar (and also nonaromatic!) eight-membered rings. This strategy also had the effect of leaving three isolated aromatic systems (benzene or CpCo-cyclobutadieyl). In fact, Gleiter's cyclacenes can be viewed (like Meier's pyrenophane **1.50**) as assemblies of three bridged aromatic systems, *i.e.* as cyclophanes.

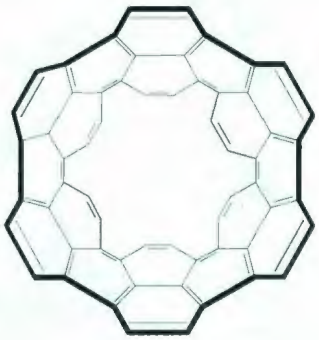


**1.97**

**Figure 1.7** Structure of Boekelheide's deltaphane.

The very close similarity between "cyclacene" **1.90** and Boekelheide's "deltaphane" **1.97** emphasizes this point (Figure 1.7).[51] The synthesis and isolation of cyclacenes and

related species comprised of only innately planar rings (4,5,6-membered) therefore remains a big challenge.



**1.98**

**Figure 1.8** Structure of a Vögtle belt.

Returning to cyclophenacene-type belts, which have been calculated to be considerably more stable than cyclacenes,[46] Vögtle proposed a family of pyrenoid aromatic belts, *e.g.* **1.98**, but all attempts to synthesize members of this family failed (Figure 1.8).[52] In fact, it is worth repeating that, to date, no aromatic belts have been rationally synthesized by assembling small building blocks.


**1.99** **1.100**

**Scheme 1.18** Synthesis of capped [10]cyclophenacene **1.100**.

However, Nakamura's group successfully *revealed* the [10]cyclophenacene system

present in [60]fullerene **1.99** by performing two sets of fivefold additions to the two polar caps. Capped [10]cyclophenacene **1.100** is a stable compound that exhibits bright yellow fluorescence ($\lambda$=620 nm) (Scheme 1.18).[53]

### 1.3.3 Potential applications of aromatic belts

Based on the special structures of aromatic belts, they might be expected to have applications in various areas. Their cavities could incorporate some small-sized molecules; their noncovalent interactions could enable them to participate in molecular recognition; the unique π-systems may have electronic and photophysical properties that could be useful in optoelectronic devices.[42,43,54]

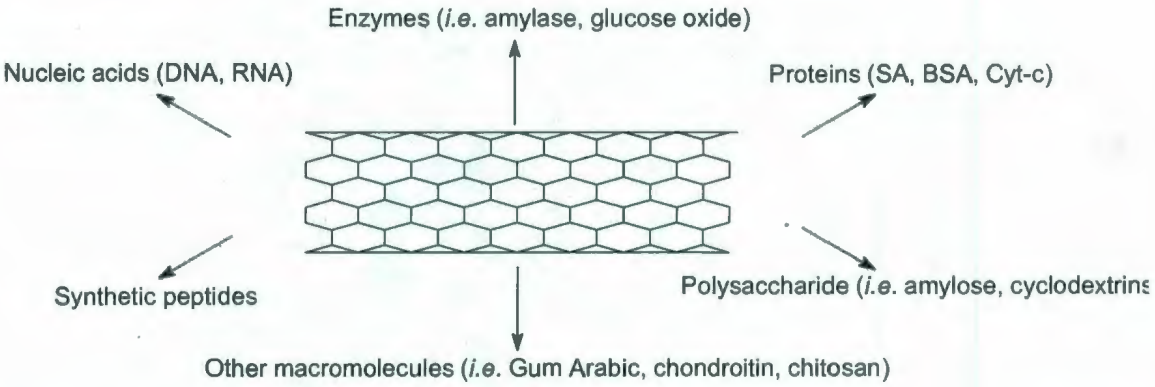



**Figure 1.9** Examples of noncovalent functionalisation of carbon nanotubes with different biomolecules.[55]

Single-walled carbon nanotubes are currently being studied for their potential applications in various areas including biology and medicinal chemistry. A major problem in this regard is that SWCNTs come as complex mixtures that are very difficult to work with and characterize. Aromatic belts, when they became available, will be

monodisperse SWCNT segments, which will likely allow for easier manipulation and characterization, while hopefully retaining usable properties.

Through noncovalent interactions, SWCNTs have been functionalized with biomacromolecules such as enzymes, peptides, proteins and polysaccharides (Figure 1.9). Although aromatic belts will not likely interact with such macromolecules in the same way, they may still be useful in delivering small molecules such as the platinum-based chemotherapeutic agents Cisplatin **1.101**, Carboplatin **1.102**, and Oxaliplatin **1.103**, which have been put into nanotubes.[56] This kind of chemicals will probably require functionalization similar to Pantarotto's functionalized SWCNT **1.104** (Figure 1.10).[57]

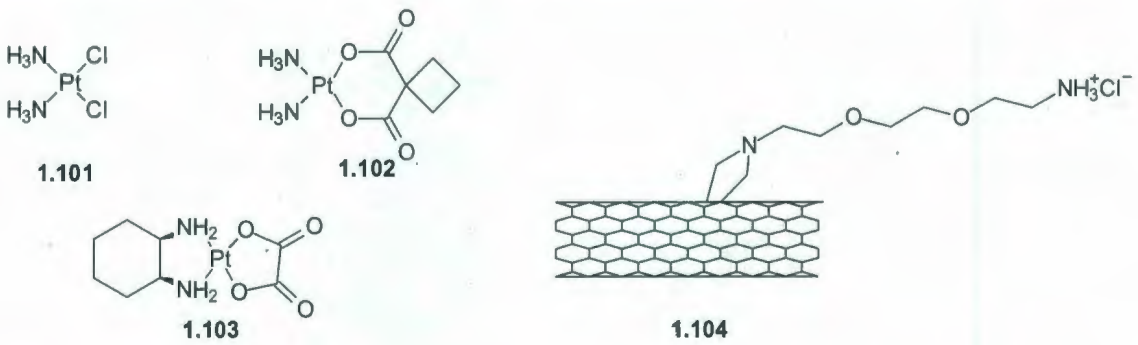



**Figure 1.10** The platinum-based chemotherapeutic agents and Pantarotto's functionalized SWCNT **1.104**.

Some polymer/SWCNT assemblies (*e.g.* SWCNT/poly(3-octylthiophene) composites) have optical and photovoltaic properties because, under irradiation with visible light, the photo-excited polymer can transfer electrons efficiently to the SWCNTs. The study of analogous polymer/aromatic belt assemblies would be worthwhile.[58]

Functionalized aromatic belts also have potential properties as biosensors. Some studies have shown that modified SWCNTs can function as glucose biosensors.[59] Other potential areas of application for aromatic belts include hydrogen storage, molecular imaging and catalysis.[55]

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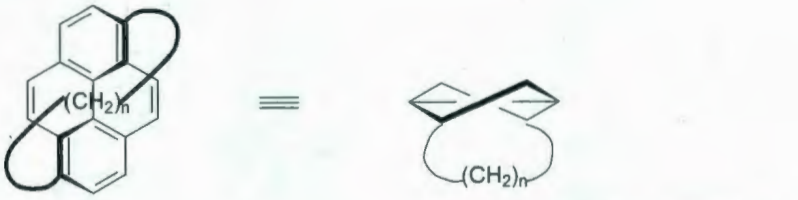
# Chapter Two
# Synthesis of $C_2$-symmetric pyrenophanes

## 2.1 Introduction



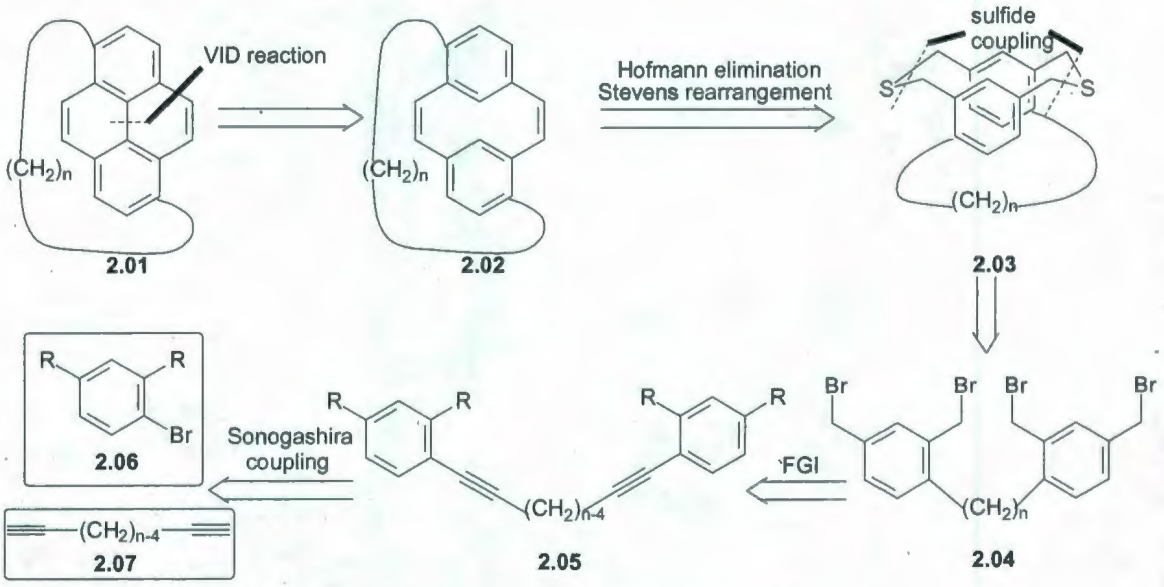

**2.01** side view (stylized representation)

**Figure 2.1** View of [*n*](1,6)pyrenophanes.

The Bodwell group has synthesized a series of about 20 different pyrenophanes (Figure 1.3). All of them have a (2,7) bridging motif and are achiral, most of them being (on average) $C_{2v}$-symmetric.[1,2,3] Changing the bridging motif from (2,7) to (1,6) would lower the (average) symmetry of the [*n*]pyrenophanes to $C_2$ and thus render them chiral. Instead of just an end-to-end bend, which is observed in the (2,7)pyrenophanes, the bridge of the [*n*](1,6)pyrenophanes would be expected to impose a longitudinal twist, or torsion, around the long axis of the pyrene system (Figure 2.1). If the enantiomers of such a pyrenophane could be separated, this would allow the chiroptical and photophysical properties of an inherently chiral pyrene system to be studied. In fact, this was a project started by a former Ph.D. student in the Bodwell group, Michael Mannion.[4] He attempted to synthesize [9](1,6)pyrenophane (**2.01**; *n*=9) towards the end of his Ph.D. studies, using a synthetic approach similar to the one used for the parent [*n*](2,7)pyrenophanes **1.12**. Ultimately, he produced a small quantity (26 mg) of a

mixture of compounds that appeared to contain some of the desired (1,6)pyrenophane. However, this compound could not be isolated. The objective of the work described in this Chapter was to revisit Mannion's (1,6)pyrenophane project and to obtain the target pyrenophanes in enantiomerically pure form.

## 2.2 Retrosynthetic analysis



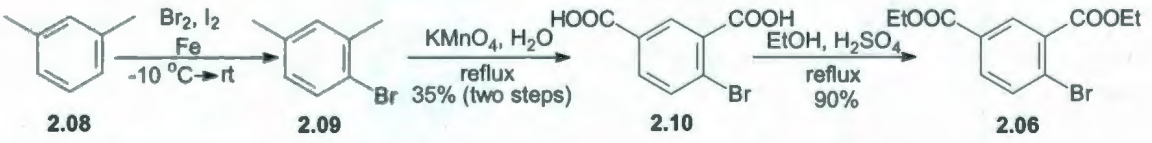

**Scheme 2.1** Retrosynthetic analysis of [*n*](1,6)pyrenophanes **2.01**.

The retrosynthetic analysis of [*n*](1,6)pyrenophanes **2.01** (Scheme 2.1) is analogous to that of the [*n*](2,7)pyrenophanes. The valence isomerization/dehydrogenation (VID) approach was developed to accomplish the formation of nonplanar pyrene systems, so **2.01** can be taken back to cyclophanediene **2.02** according to this reaction. Hofmann elimination and Stevens rearrangement transforms lead back to dithiacyclophane **2.03**, which could be obtained from tetrabromide **2.04** using sulfide coupling. Functional group interconversion (FGI) affords diynetetraester **2.05** (R=$CO_2Et$), which is the expected

product of Sonogashira cross-coupling of bromodiester **2.06** (R=$CO_2Et$) and diyne **2.07**.

## 2.3 Results and Discussion

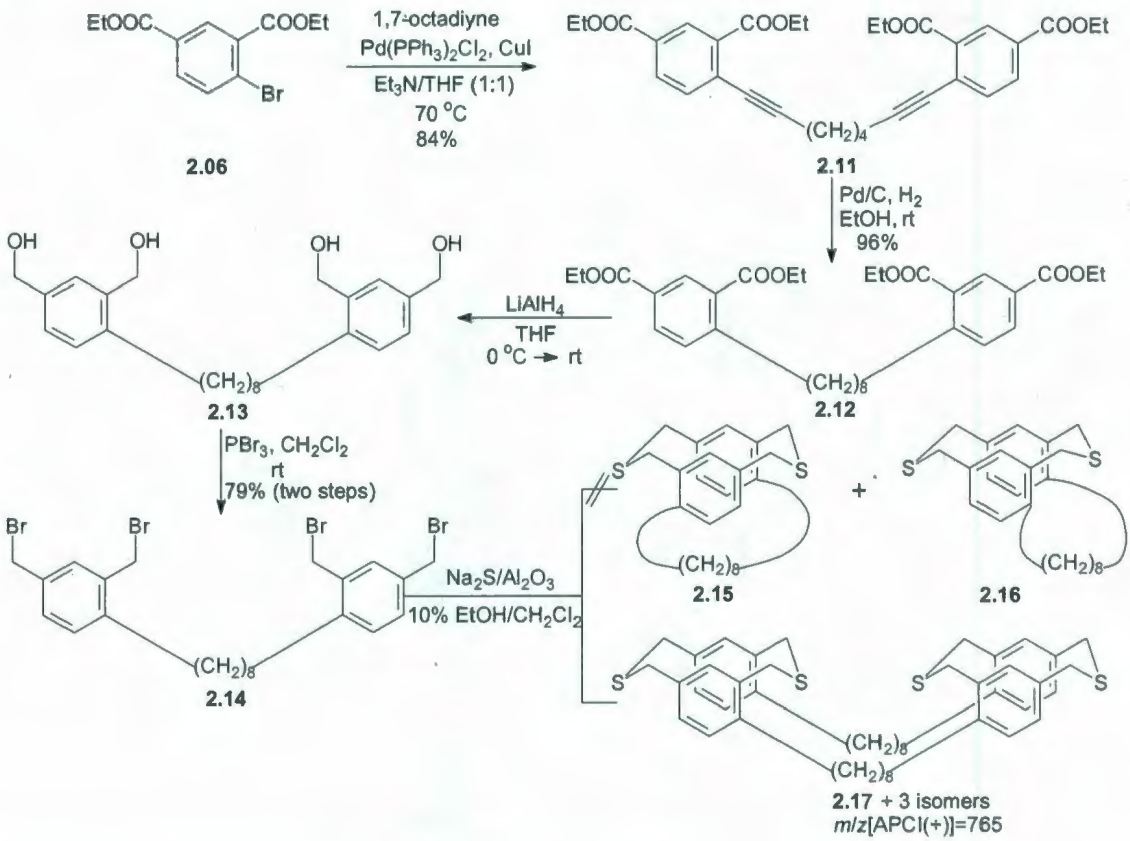
Several congeners of building block **2.07** (*n*=3-6) are commercially-available compounds. The other building block **2.06** was synthesized previously in the Bodwell group from commercially available *m*-xylene (**2.08**) and this synthesis was repeated (Scheme 2.2).[5] Electrophilic bromination of *m*-xylene gave 4-bromo-*m*-xylene (**2.09**), the crude product of which was oxidized to 4-bromoisophthalic acid (**2.10**) using $KMnO_4$ (35%, two steps). Fischer esterfication of **2.10** then gave diethyl 4-bromoisophthalate (**2.06**) in 90% yield. The yields are comparable to those obtained previously.




**Scheme 2.2** Synthesis of building block **2.06**.

The first target to be chosen was [8](1,6)pyrenophane (**2.01**, *n*=8). An eight-carbon bridge was chosen because it was expected to impart significant, but not excessive twist to the pyrene system. The required diyne **2.07** (*n*=8) was also immediately available. The reaction of tetrabromide **2.14** with $Na_2S/Al_2O_3$ was expected to give a mixture of constitutionally isomeric dithiacyclophanes **2.15** and **2.16**. Two isomers are formed because the two prochiral benzene rings can be connected in a face-to-face or face-to-back fashion. Obtaining a mixture at this point was expected to be unavoidable (this is what Mannion obtained with a nine-carbon tether) and separation at this stage or

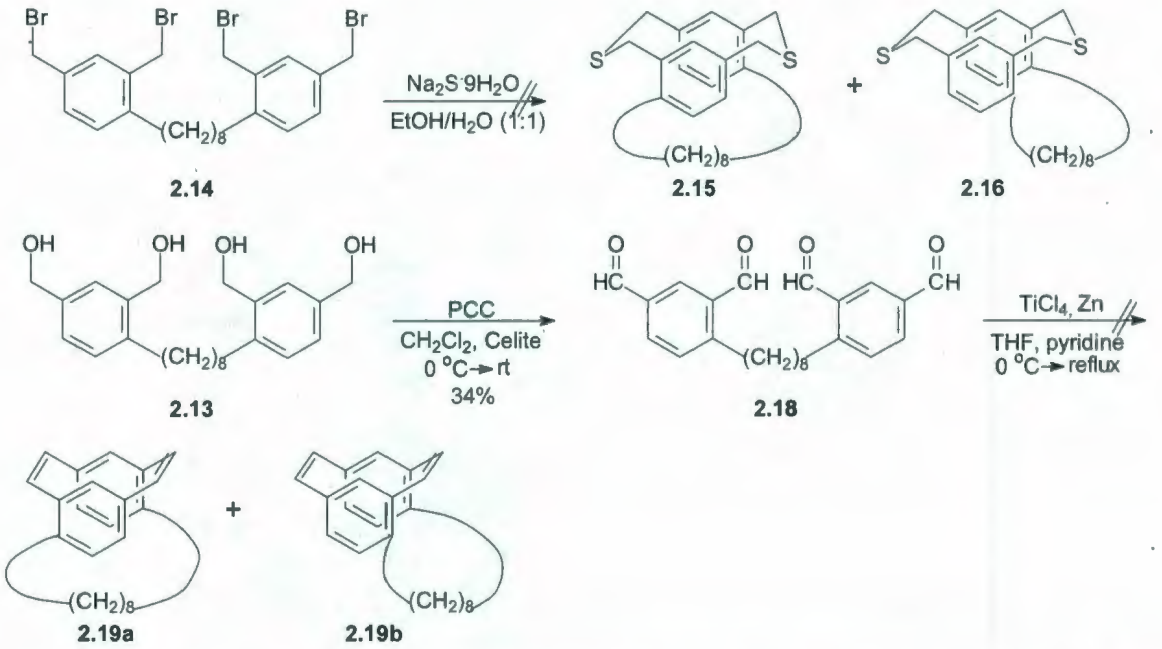
later in the synthesis was part of the plan.




**Scheme 2.3** Attempted synthesis of [8](1,6)pyrenophane **2.01** (*n*=8).

However, the reaction of tetrabromide **2.14** with $Na_2S/Al_2O_3$ gave little or none of the desired dithiacyclophanes **2.15** and **2.16**. It is unclear why this reaction fails to give the desired products. The $^1H$ NMR spectrum of the crude product was too complicated to interpret. However, the mass spectrum (APCI, positive) showed a base peak at *m/z*=765, which corresponds to products resulting from the coupling of two tetrabromide molecules, *e.g.* **2.17**. Only a small mass peak was observed corresponding to **2.15** and **2.16** (*m/z*=382, 6%). However, the possibility that this peak arises from a fragment of the base peak

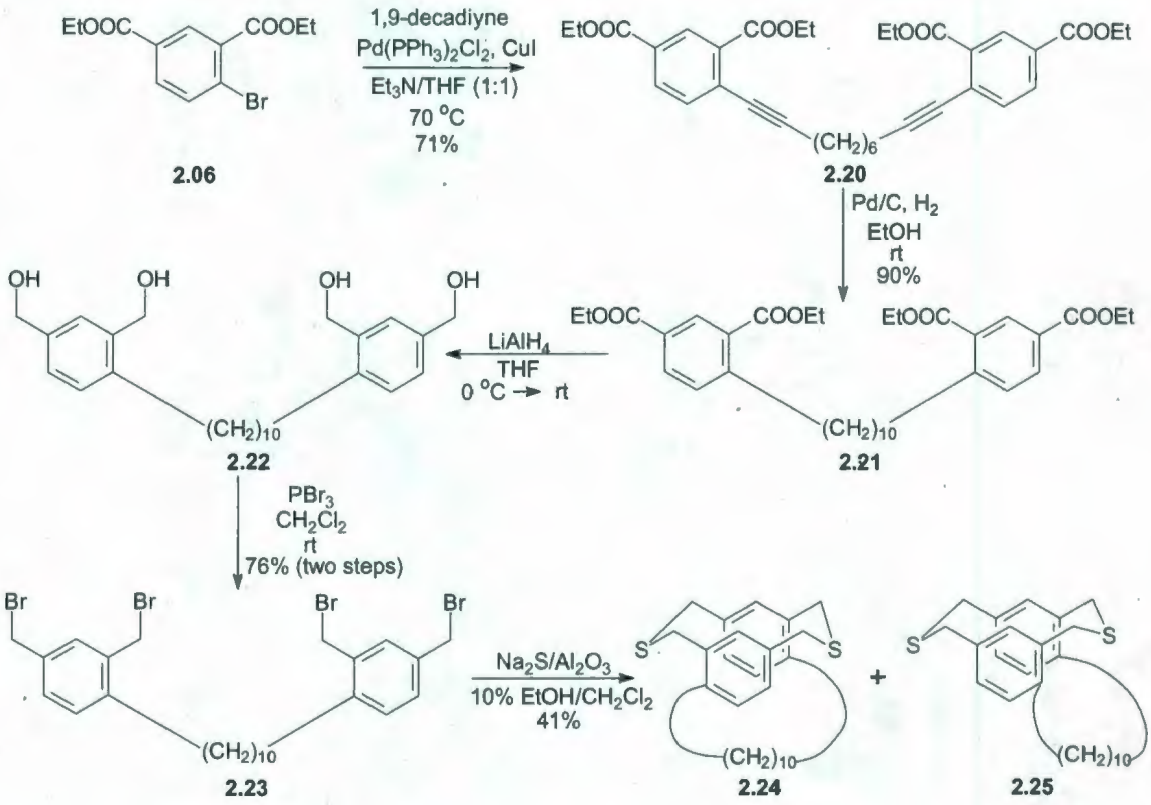
cannot be ruled out. There are four possible isomers of **2.17**, only one of which is shown in Scheme 2.3. The other possible structures are shown in Appendix 1.




**Scheme 2.4** Attempted use of other approaches to afford target cyclophanedienes **2.19a** and **1.29b**.

The use of $Na_2S·9H_2O$ instead of $Na_2S/Al_2O_3$ was investigated briefly, but no reaction with **2.14** in $EtOH/H_2O$ was observed (Scheme 2.4). Only the starting material was recovered, which is probably due to its insolubility in the reaction medium. In an attempt to avoid the sulfide coupling, a twofold intramolecular McMurry reaction was then investigated. This idea was inspired by the recent successful use of an intramolecular McMurry reaction by a former Bodwell group member in the synthesis of 1,1,8,8-tetramethyl[8](2,11)teropyrenophane.[6] Tetraalcohol **2.13** was oxidized to tetraaldhyde **2.18** (34%), which was then subjected to McMurry reaction conditions. If

this reaction had been successful, it would have directly afforded cyclophanedienes **2.19a** and **2.19b**, and shortened the synthesis by 3 steps. However, although tetraaldehyde **2.18** was fully consumed, no mobile products were observed by tlc analysis. Only a baseline spot was present, even when using a relatively polar eluent such as EtOAc. At this point, work on the eight-carbon bridge was halted. Considering, the problems Mike Mannion had with the nine-carbon bridge, [10](1,6)pyrenophane **2.01** ($n$=10) was chosen as the next target.



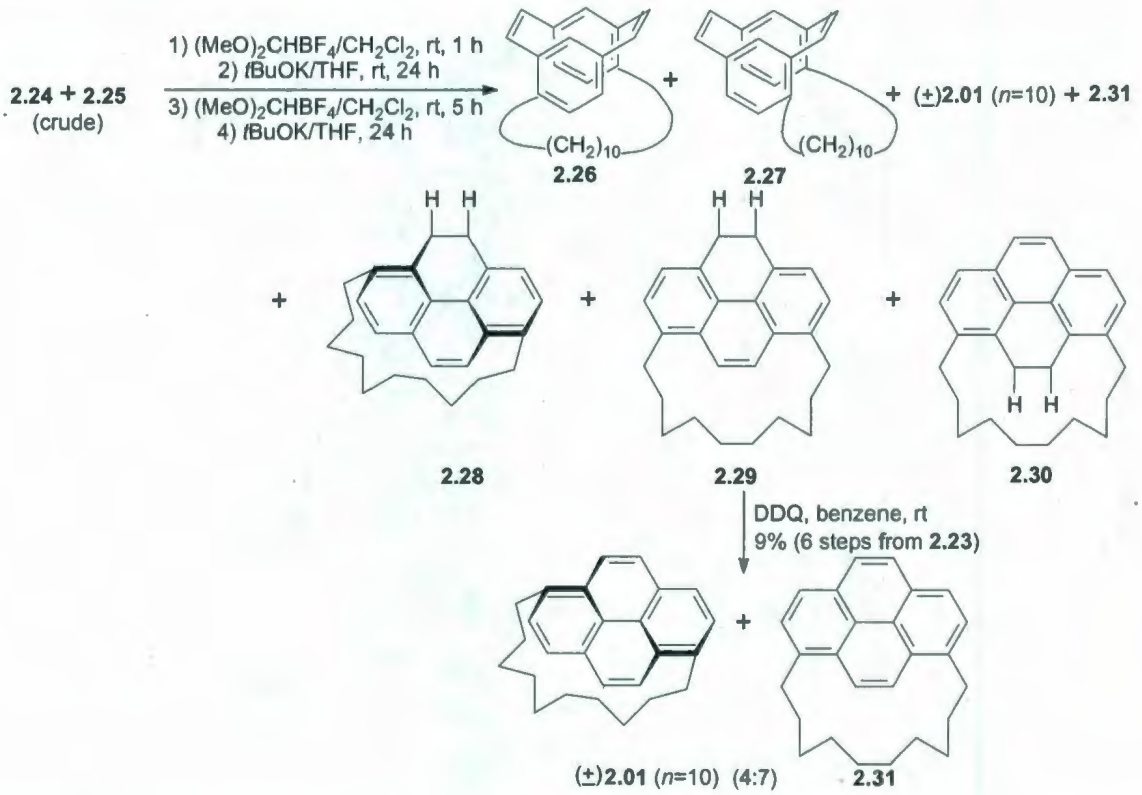

**Scheme 2.5** Synthesis of dithiacyclophanes **2.24** and **2.25**.

Tetrabromide **2.23**, which has a ten-carbon tether, was synthesized in exactly the same way as tetrabromide **2.14** except that commercially available 1,9-decadiyne **2.07**

($n$=10) was used in the Sonogashira reaction with **2.06** instead of 1,7-octadiyne (Scheme 2.5). The reaction yields throughout the synthesis were similar in each case. However, the outcome of the reaction of tetrabromide **2.23** with $Na_2S/Al_2O_3$ was different than that observed with **2.14**. The APCI (positive) mass spectrum of the crude reaction mixture showed peaks at $m/z$=411 and $m/z$=821 (the corresponding peaks of $[M+ H_2O]^+$ were also observed, see Appendix 1), indicating the purely intramolecular reaction had occurred in this case. After column chromatography, **2.24** and **2.25** were obtained in a combined 41% yield (purity≈ 90% by $^1$H NMR analysis). The $^1$H NMR spectrum is consistent with only those two isomers (ratio≈ 2:1), despite the overlap of several signals. It was not possible to assign which peaks belong to which isomer. Because **2.24** and **2.25** are unstable to column chromatography or even to storage under ambient conditions, it was found to be practical to filter the reaction mixture through a plug of Celite to remove most of the inorganic chemicals and use the crude material (yield≈ 90%, no estimation of purity) directly in the next step.

The crude mixture of **2.24** and **2.25** was then subjected to an *S*-methylation/Stevens rearrangement/*S*-methylation/Hofmann elimination sequence of reactions with the intention of forming cyclophanedienes **2.26** and **2.27** (Scheme 2.6). However, the $^1$H NMR spectrum of the crude reaction mixture showed that the reaction gave mainly the target pyrenophanes **2.01** ($n$=10) and **2.31**. The APCI mass spectrum suggested the presence of one or more species two mass units heavier than **2.26** and **2.27**. These could

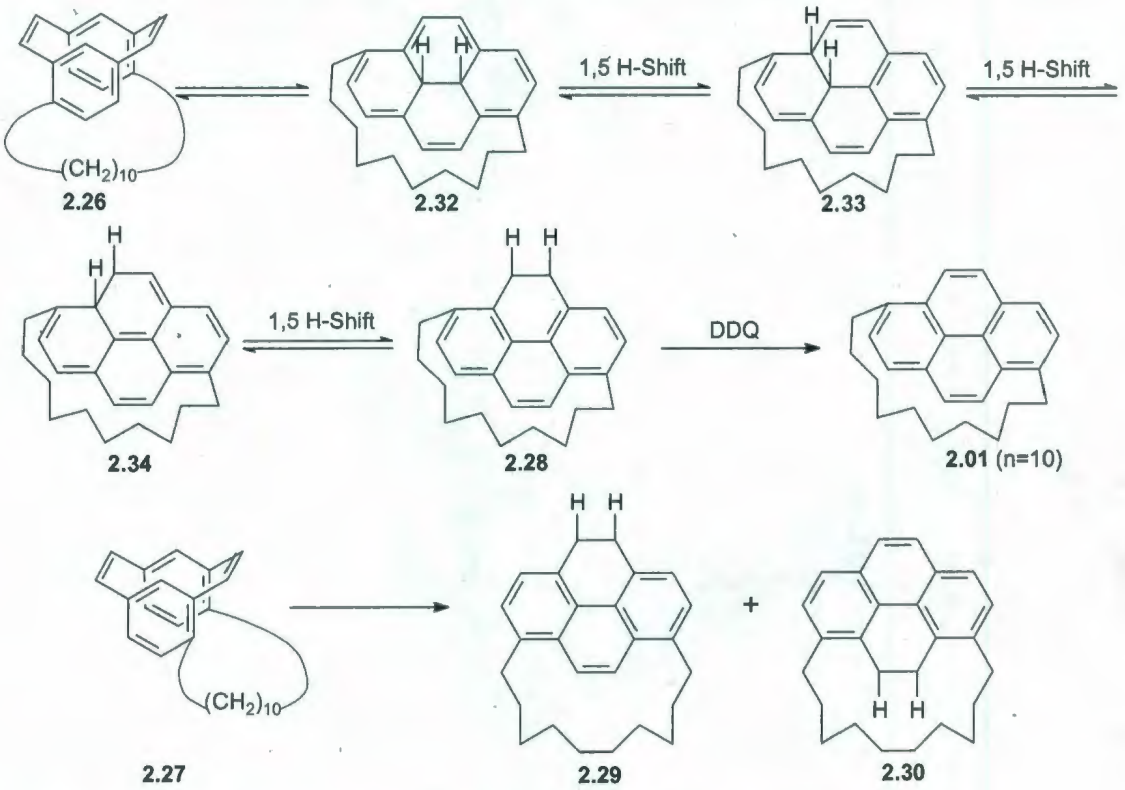
be dihydropyrenophanes **2.28**, **2.29** and **2.30** or the cyclophanedienes **2.26** and **2.27**. The formation of pyrenophanes and/or dihydropyrenophanes during Hofmann elimination reactions leading to cyclophanedienes has been observed several times previously, especially when the pyrenophane is not very strained.[7]




**Scheme 2.6** Synthesis of [10](1,6)pyrenophane **2.01** (*n*=10) and [10](1,8)pyrenophane **2.31**.

The explanation for the formation of a dihydropyrenophane is valence isomerization of the cyclophanedienes under the conditions of its formation followed by a series of three [1,5]-H shifts (Scheme 2.7).[7] In the case of **2.26**, this leads to 4,5-dihydropyrene **2.28**. This isomer presumably accumulates because the ASE of the phenanthrene system (66.6 kcal/mol)[8] is greater than that of the other dihydropyrenophane isomers **2.32**

([14]annulene, $E_{aroma}$=33 kcal/mol)[9], **2.33** (benzene, 29.3 kcal/mol)[8] and **2.34** (no aromatic system, 0 kcal/mol). Due to symmetry, cyclophanediene **2.26** can only give one dihydropyrenophane **2.28**, but cyclophane **2.27** can give two dihydropyrenophanes **2.29** and **2.30**. Upon examination of the minor peaks in the aromatic region of the $^1$H NMR spectrum, it was not possible to draw any firm conclusions about the structure of the minor product(s). Whatever the nature of the minor product(s), treatment of the mixture with DDQ at room temperature converted any cyclophanedienes and any dihydropyrenophanes into a mixture of [10](1,6)pyrenophane (±)-**2.01** ($n$=10) and [10](1,8)pyrenophane **2.31** (9% over 6 steps from tetrabromide **2.23**).




**Scheme 2.7** Possible reactions of cyclophanedienes **2.26** and **2.27**.

The ratio of [10](1,6)pyrenophane **2.01** ($n$=10) to [10](1,8)pyrenophane **2.31** was determined to be 4:7 by $^1$H NMR spectrum analysis, especially in the aromatic region. The $C_2$-symmetric [10](1,6)pyrenophane **2.01** ($n$=10) should show two AB systems (four doublets) in this region. These signals are labeled in red in Figure 2.2. On the other hand, [10](1,8)pyrenophane **2.31**, which has a plane of symmetry running through the middle of the pyrene system, should display one AB system (two doublets) and two singlets. These signals are labeled in purple in Figure 2.2. An important structural feature of **2.01** ($n$=10), which has a (1,6) bridging motif, is that the bridge is necessarily situated across one face of the pyrene system. As a result, some of the aliphatic proton signals are observed at very high field. For example, two 2H multiplets appear at -1.95 ppm and -2.65 ppm.

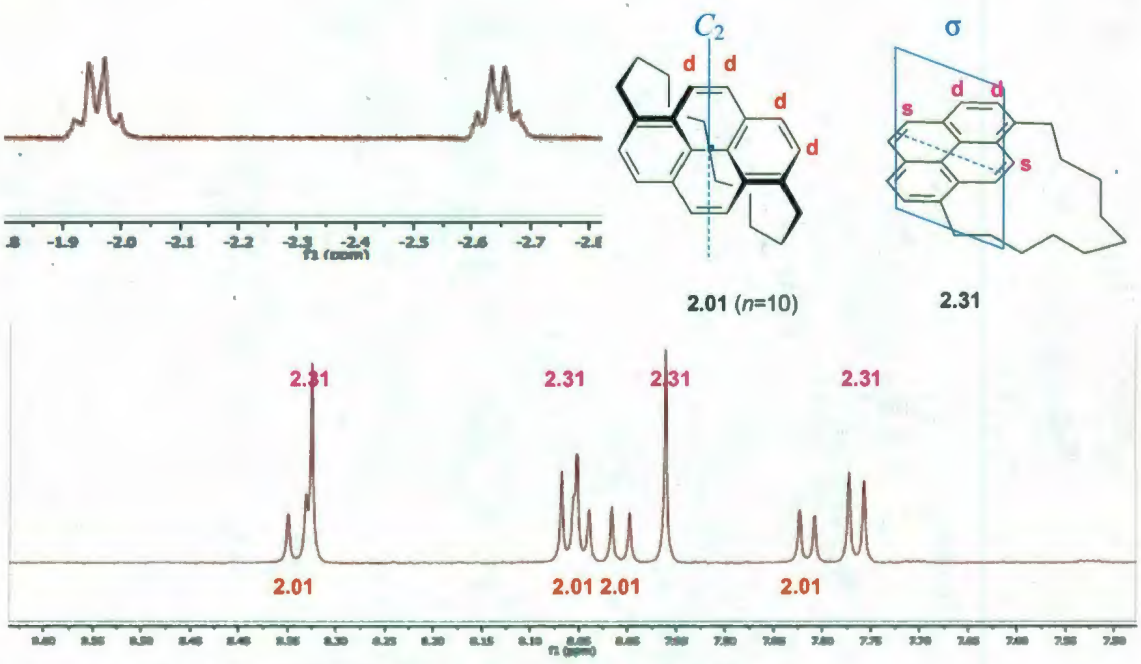



**Figure 2.2** $^1$H NMR spectrum of **2.01** ($n$=10) and **2.31** in $CDCl_3$.

The UV-vis spectrum of pyrene (**1.07**) exhibits a β' band at 242 nm, two β bands at 273 nm and p bands at 306, 320 and 336 nm.[8,10] The UV-vis spectrum of the mixture of **2.01** (*n*=10) and **2.31** was as expected for simple pyrene derivatives, in that all of the bands were slightly red shifted (Figure 2.3). The β' band was observed at 245 nm, two β bands at 277 and 284 nm and the p bands at 323, 340 and 359 nm. (β, β', p are related to electronic transitions with different energies. β is referred as the transition from $^1A_{1g}$ ground state to excited singlet states $^1B_{1u}$ and p is referred as the transition from $^1A_{1g}$ to $^1E_{1u}$.)[11] The magnitude of red shifts (11-23 nm) is likely due primarily to alkyl substitution rather than any effect arising from the twist of the pyrene system, especially in [10](1,6)pyrenophane **2.01** (*n*=10). More concrete discussion will have to await the separation of **2.01** (*n*=10) and **2.31**. The fluorescence spectrum of the mixture of **2.01** (*n*=10) and **2.31** showed three bands at 388, 409 and 429 nm.[12]

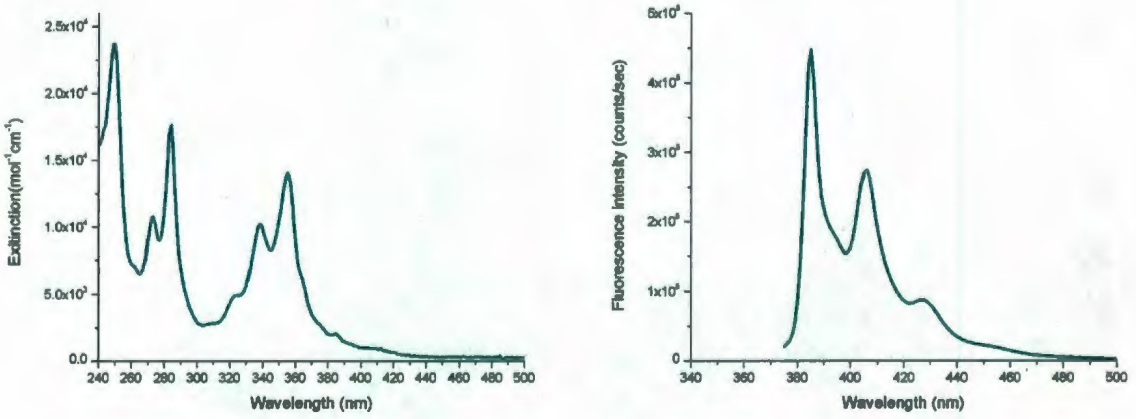
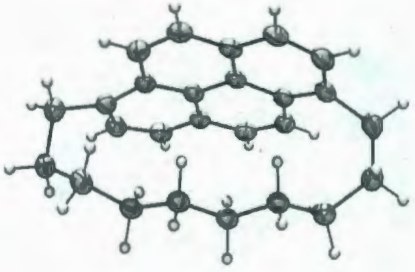


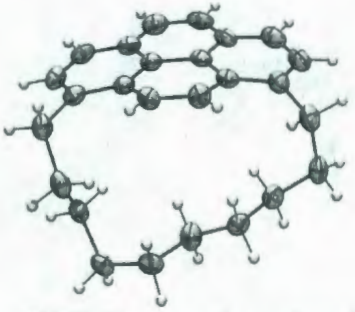

**Figure 2.3** Absorption and emission spectrum of **2.01** (*n*=10) and **2.31** in $CHCl_3$.

As stated earlier, [10](1,6)pyrenophane **2.01** (*n*=10) and [10](1,8)pyrenophane **2.31**

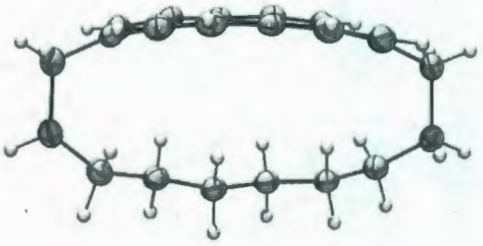
could not be separated either by recrystalization, column chromatography or HPLC. Luckily, during one recrystalization, two types of crystals were obtained: Plates and needles. One of the plates and one of the needles were selected by Dr. L. Dawe, who determined crystal structures using X-ray crystallography. The plate was found to be [10](1,6)pyrenophane **2.01** and the needle was found to be [10](1,8)pyrenophane **2.31** (Figure 2.4).



[10](1,6)pyrenophane (plates)



[10](1,8)pyrenophane (needles)



[10](1,6)pyrenophane (side view)

**Figure 2.4** X-ray structures of **2.01** ($n$=10) and **2.31**.

Interestingly, in the crystal structure of **2.01** ($n$=10), some close intermolecular CH-π contacts were observed. In particular, three protons $H_{(3b)}$, $H_{(4a)}$ and $H_{(5b)}$ in one molecule point directly toward the centers of three benzene rings in an adjacent molecule. The H-centroid distances are 2.76, 2.66 and 2.64 Å, respectively (Figure 2.5). Such

interactions have never been noticed in other (2,7)pyrenophanes synthesized in the Bodwell group. It would be interesting to revisit the structures to see if such interactions are general in [*n*]pyrenophanes.

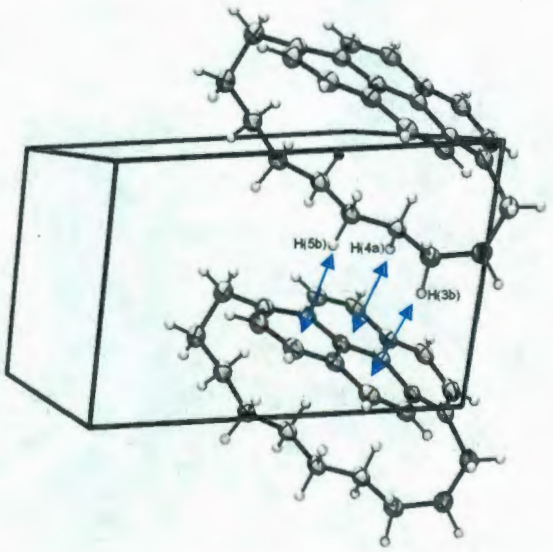



**Figure 2.5** The CH-$\pi$ interactions between [10](1,6)pyrenophane molecules in the unit cell.

## 2.4 Conclusion

In summary, the first chiral [*n*]pyrenophane [10](1,6)pyrenophane **2.29**, has been successfully synthesized, albeit as the minor component in a mixture with [10](1,8)-pyrenophane **2.30**. Although the [10](1,6)pyrenophane and [10](1,8)pyrenophane could not be separated by column chromatography, recrystalization and HPLC, single crystal X-ray structures were obtained by manual separation of two different crystal types.

## 2.5 Experimental section

All chemicals mentioned in this chapter were used as received from commercial

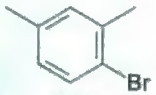
sources (Aldrich, TCI and Alfa Aesar) without further purification. All reactions were performed under the protection of nitrogen gas unless otherwise indicated. THF was freshly distilled from sodium benzophenone ketyl. Dichloromethane was freshly distilled from calcium hydride. Hexanes were distilled before use for column chromatography. Organic solvents were evaporated under reduced pressure using a rotary evaporator. Flash chromatography was performed using Silicycle silica gel 60, particle size 40–63 μm. Compounds on tlc plates were visualized under UV light (254 and 365 nm).

**Instrumentation:**

Melting points were measured on a Fisher-Johns apparatus and are uncorrected and the solvents for recrystallization were given in the brackets. $^{1}H$ NMR (500.13 MHz) and $^{13}C$ NMR (125.76 MHz) were recorded on a Bruker AVANCE instrument ($CDCl_3$, unless otherwise indicated). Chemical shifts are reported relative to internal standards: $Me_4Si$ (δ 0.00 ppm) and $CDCl_3$ (δ 77.23 ppm). $^{1}H$ NMR data are presented as follows: chemical shift, multiplicity (s=singlet, d=doublet, t=triplet, q=quartet, m=multiplet, br s=broad singlet, dd=doublet of doublets), coupling constant (*J* in Hz), integration (Number of H). IR spectra were obtained on a Bruker TENSOR 27 infrared spectrometer. Low-resolution mass spectrometric data (MS) were determined on an Agilent 1100 series LC/MSD instrument. High-resolution mass spectra (HRMS) of compounds were obtained using a Waters Micromass GCT Premier™ instrument. MS data are presented as follows: *m/z* (relative intensity), assignment (when appropriate), calculated mass for corresponding

formula. UV-vis and fluorescence spectra were recorded using an Agilent 8453 spectrometer and a Photon Technology International machines. X-ray crystallography was performed by Dr. Louise Dawe using an AFC8-Saturn 70 single crystal X-ray diffractometer from Rigaku/MSC, equipped with an X-stream 2000 low temperature system.

**4-Bromo-*m*-xylene (2.09)**[5]

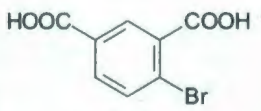



**2.09**

*m*-Xylene (200.0 g, 1.873 mol), iron filings (4.801 g, 85.73 mmol), and $I_2$ (several crystals) were added to a 500 mL three-necked round-bottomed flask, which was fitted with a dropping funnel, a magnetic stir bar, a condenser and a thermometer (the bulb extended beneath the surface of the *m*-xylene). The top of the condenser was connected to a gas absorption trap. The mixture was stirred and cooled in a dry ice/acetone bath. $Br_2$ (264.0 g, 1.652 mol) was added dropwise over a 3 h period and the internal temperature was maintained at $\leq$ 10 °C. The mixture was then allowed to warm to room temperature and stirred for a further 18 h under air. The solution was quenched by the addition of a saturated aqueous $NaHSO_3$ solution (100 mL). The layers were separated and the organic layer was washed with water (200 mL), washed with brine (150 mL) and dried over $MgSO_4$. Unreacted *m*-xylene was removed under reduced pressure to yield product **2.09** as a clear colorless oil (273.1 g, 1.471 mol, 90%): $R_f$ (20:80 $CH_2Cl_2$/hexanes): 0.74; $^1H$

NMR (500 MHz, $CDCl_3$): δ 7.29 (d, *J*=8.2 Hz, 1H), 6.91 (br s, 1H), 6.72 (dd, *J*=8.1, 1.6Hz, 1H), 2.27 (s, 3H), 2.17 (s, 3H).

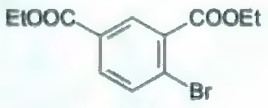
**4-Bromoisophthalic acid (2.10)**[5]




**2.10**

A mixture of 4-bromo-*m*-xylene (**2.09**) (40.00 g, 0.2154 mol) and $KMnO_4$ (160.0 g, 1.013 mol) in $H_2O$ (1 L) in a 2 L round-bottomed flask was mechanically stirred at reflux overnight under air. The precipitate was removed by suction filtration and the filtrate was acidified by adding HCl (conc.) slowly to pH=1. The precipitate was collected by suction filtration and dried in the air for 2 d to afford product **2.10** as a white solid (34.11 g, 0.1392 mol, 64%): $^1$H NMR (500 MHz, acetone-$d_6$): δ 8.47 (d, *J*=2.1 Hz 1H), 8.05 (dd, *J*=8.3, 2.2 Hz, 1H), 7.91 (d, *J*=8.3 Hz, 1H).

**Diethyl 4-bromoisophthalate (2.06)**[5]

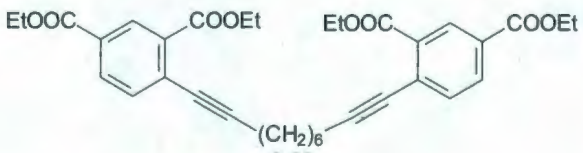



**2.06**

A mixture of diacid **2.10** (30.00 g, 0.1224 mol) $H_2SO_4$ (8 mL) and EtOH (200 mL) was heated at reflux overnight in a 500 mL round-bottomed flask equipped with a reflux condenser under air. After cooling to room temperature, the reaction mixture was concentrated under reduced pressure and the residue was dissolved in EtOAc (100 mL). The resulting organic solution was washed with $H_2O$ (100 mL), washed with brine (70

mL), dried over $MgSO_4$ and concentrated under reduced pressure. The residue was subjected to column chromatography (50:50 $CH_2Cl_2$/hexanes) to afford **2.06** as a colorless oil (31.85 g, 0.1057 mol, 87%): $R_f$ (50:50 $CH_2Cl_2$/hexanes): 0.33; $^1$H NMR (500 MHz, $CDCl_3$): 8.63 (d, $J$=1.8 Hz, 1H), 8.15 (dd, $J$=8.1, 1.8 Hz, 1H), 7.71 (d, $J$=8.1 Hz, 1H), 4.46 (q, $J$=7.1 Hz, 2H), 4.42 (q, $J$=7.1 Hz, 2H), 1.43 (t, $J$=7.1 Hz, 3H), 1.42 (t, $J$=7.1 Hz, 3H).

**1,10-Bis(2,4-bis(ethoxycarbonyl)phenyl)deca-1,9-diyne (2.20)**

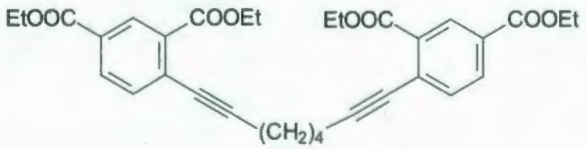



**2.20**

To a degassed mixture of diethyl 4-bromoisophthalate (**2.06**) (1.003 g, 3.331 mmol), $Pd(PPh_3)Cl_2$ (47 mg, 0.067 mmol), and CuI (13 mg, 0.067 mol) and 1:1 degassed THF/$Et_3N$ (40 mL) in a 100 mL round-bottomed flask was added 1,9-decadiyne (268 mg, 2.00 mmol) in one portion. The reaction was stirred at 80 °C for 18 h. The precipitate was removed by suction filtration and the filter cake was washed with EtOAc (50 mL). The filtrate was washed with saturated aqueous $NH_4Cl$ solution (25 mL), washed with $H_2O$ (30 mL) and washed with brine (25 mL). The organic layer was dried over $MgSO_4$ and concentrated under reduced pressure. The residue was subjected to column chromatography (20:80 EtOAc/hexanes) to afford **2.20** as a colorless oil (1.352 g, 2.354 mmol, 71%): $R_f$(20:80 EtOAc/hexanes); 0.21; IR (neat) ν: 2955 (m), 1716 (s), 1366 (w),

1285 (m), 1173 (s), 1071 (s), 762 (m) $cm^{-1}$; $^1H$ NMR (500 MHz, $CDCl_3$): δ 8.53 (d, *J*=1.4 Hz, 2H), 8.05 (dd, *J*=8.1, 1.6 Hz, 2H), 7,57 (d, *J*=8.1 Hz, 2H), 4.42 (q, *J*=7.2 Hz, 4H), 4.39 (q, *J*=7.2 Hz, 4H), 2.53 (t, *J*=7.1 Hz, 4H), 1.71-1.68 (m, 4H), 1.57-1.54 (m, 4H), 1.42 (t, *J*=6.9 Hz, 6H), 1.40 (t, *J*=7.0 Hz, 6H); $^{13}C$ NMR (125 MHz, $CDCl_3$): δ 166.1, 165.8, 134.7, 132.8, 132.2, 132.6, 129.4, 129.1, 99.8, 79.6, 61.72, 61.69, 28.8, 28.7, 20.3, 14.7 (2C); LCMS [APCl(+)] *m/z* (%): 575 ($[M+H]^+$, 100), 529 (6); UV/Vis ($CHCl_3$) $\lambda_{max}$ (log ε) 277 nm (16342); HRMS [CI(+)] calcd for $C_{34}H_{38}O_8$: 575.2645, found: 575.2643.

**1,8-Bis(2,4-bis(ethoxycarbonyl)phenyl)octa-1,7-diyne (2.11)**

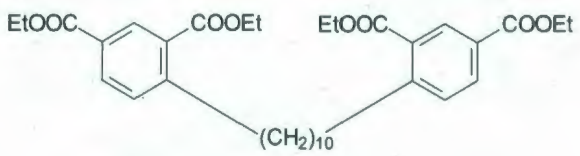



**2.11**

This compound was prepared analogously to **2.20**, above, using 4-bromodiester **2.06** (12.00 g, 39.96 mmol), $Pd(PPh_3)_2Cl_2$ (560 mg, 0.803 mmol), CuI (152 mg, 0.802 mmol), diyne (2.545 g, 23.97 mmol) and (1:1) THF/$Et_3N$ (200 mL) to yield product **2.11** as light yellow needles (7.331 g, 13.45 mmol, 69%): $R_f$(20:80 EtOAc/hexanes): 0.27; mp (EtOH): 73.0-74.0 °C; IR (neat) ν: 2976 (w), 1718 (s), 1368 (m), 1298 (s), 1259 (s), 1147 (m), 1109 (s), 1009 (s), 764 (s) $cm^{-1}$; $^1H$ NMR (500 MHz, $CDCl_3$): δ 8.53 (d, *J*=1.4 Hz, 2H), 8.06 (dd, *J*=8.1, 1.6 Hz, 2H), 7.57 (d, *J*=8.1 Hz, 2H), 4.40 (q, *J*=7.1 Hz, 4H), 4.39 (q, *J*=7.1 Hz, 4H), 2.59-2.57 (m, 4H), 1.87-1.86 (m, 4H), 1.41 (t, *J*=7.1 Hz, 6H), 1.40 (t, *J*=7.1 Hz, 6H); $^{13}C$ NMR (125 MHz, $CDCl_3$): δ 166.1, 165.7, 134.7, 132.9, 132.2, 132.6,

129.5, 128.9, 99.2, 79.8, 61.71, 61.69, 28.0, 19.9, 14.67, 14.66; LCMS [APCl(+)] *m/z* (%): 547 ($[M+H]^+$, 100), 519 (10); UV/Vis ($CHCl_3$) $\lambda_{max}$ (log ε) 279 nm (30439); HRMS [EI(+)] calcd for $C_{32}H_{34}O_8$: 546.2254, found: 546.2245.

**1,10-Bis(2,4-bis(ethoxycarbonyl)phenyl)decane (2.21)**

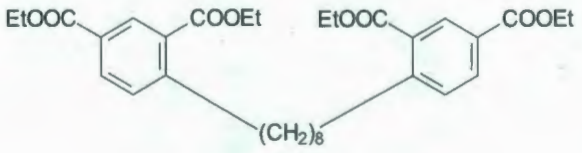



**2.21**

To a well-stirred mixture of diynetetraester **2.20** (9.461 g, 16.47 mmol) and EtOH (250 mL) in a 500 mL round-bottomed flask with EtOH (250 mL) was added 10% Pd/C (3.740 g). This mixture was stirred under $H_2$ (balloon), and the reaction was monitored by $^1H$ NMR. After the reaction was completed for 18 h, the mixture was concentrated under reduced pressure. The residue was dissolved in $CH_2Cl_2$ (200 mL) and the black precipitate was removed by suction filtration. The filtrate was concentrated under reduced pressure and recrystalization of this residue from EtOH afforded **2.21** as a white solid (8.614 g, 14.77 mmol, 90%): $R_f$ (20:80 EtOAc/hexanes): 0.21; mp (EtOH): 77.0-78.0 °C; IR (neat) ν: 2925 (w), 1722 (m), 1289 (w), 1238 (m), 1096 (w), 1071 (w), 1026 (w), 762 (w) $cm^{-1}$; $^1H$ NMR (500 MHz, $CDCl_3$): δ 8.49 (d, *J*=1.4 Hz, 2H), 8.05 (dd, *J*=8.0, 1.6Hz, 2H), 7,34 (d, *J*=18.4 Hz, 2H), 4.39 (q, *J*=7.1 Hz, 4H), 4.38 (q, *J*=7.1 Hz, 4H), 2.98 (t, *J*=7.7 Hz, 4H), 1.62-1.56 (m, 4H), 1.41 (t, *J*=7.0 Hz, 6H), 1.40 (t, *J*=7.0 Hz, 6H), 1.36-1.34 (m, 4H), 1.27-1.25 (m, 8H); $^{13}C$ NMR (125 MHz, $CDCl_3$): δ 167.6, 166.3,

149.9, 132.7, 132.1, 131.4, 130.7, 128.6, 61.51, 61.48, 34.9, 32.0, 30.1, 30.0, 29.9, 14.74, 14.70; LCMS [APCl(+)] *m/z* (%): 583 ($[M+H]^+$, 100), 537 (71); UV/Vis ($CHCl_3$) $\lambda_{max}$ (log ε) 283 nm (1876); HRMS [CI(+)] calcd for $C_{34}H_{46}O_8$: 583.3271, found: 583.3264.

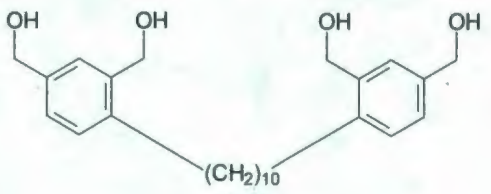
**1,8-Bis(2,4-bis(ethoxycarbonyl)phenyl)octane (2.12)**




**2.12**

This compound was prepared analogously to **2.21,** above, using starting material **2.11** (14.68 g, 27.67 mmol), 10% Pd/C (3.122 g) and EtOH (200 mL) to yield tetraester **2.12** as a white solid (14.37 g, 26.58 mmol, 96%): $R_f$ ($CH_2Cl_2$): 0.14; mp (EtOH): 96.0-96.5 °C; IR (neat) ν: 2935 (w), 1719 (s), 1364 (w), 1297 (s), 1219 (m), 1130 (m), 1067 (m), 1024 (m), 764 (m) $cm^{-1}$; $^1H$ NMR (500 MHz, $CDCl_3$): δ 8.51 (d, *J*=1.6 Hz, 2H), 8.07 (dd, *J*=6.6, 1.4Hz, 2H), 7.33 (d, *J*=8.0 Hz, 2H), 4.41 (q, *J*=7.2 Hz, 4H), 4.40 (q, *J*=7.2 Hz, 4H), 3.00 (t, *J*=7.7 Hz, 4H), 1.64-1.58 (m, 4H), 1.43 (t, *J*=7.2 Hz, 6H), 1.42 (t, *J*=7.2 Hz, 6H), 1.38-1.30 (m, 8H); $^{13}C$ NMR (125 MHz, $CDCl_3$): δ 167.5, 166.3, 149.9, 132.7, 132.1, 131.4, 130.6, 128.6, 61.51, 61.48, 34.9, 32.0, 30.1, 29.8, 14.74, 14.70; LCMS [APCl(+)] *m/z* (%): 555 ($[M+H]^+$, 100), 541 (20), 527 (7), 509 (46), 495 (9); UV/Vis ($CHCl_3$) $\lambda_{max}$ (log ε) 284 nm (1746); HRMS [EI(+)] calcd for $C_{32}H_{42}O_8$: 554.2880, found:554.2883.

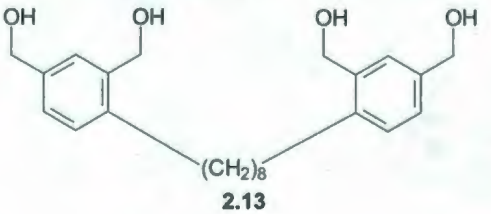
**1,10-Bis(2,4-bis(hydroxymethyl)phenyl)decane (2.22)**




**2.22**

To a 0 °C solution of tetraester **2.21** (8.300 g, 14.23 mmol) in THF (250 mL) in a 500 mL round-bottomed flask in ice bath was added dropwise a slurry of $LiAlH_4$ (2.970 g, 78.26 mmol) in dry THF (20 mL). The resulting mixture was stirred at room temperature overnight. Then reaction was quenched by careful addition of EtOAc (50 mL) and then EtOH (25 mL). The resulting mixuter was poured into a 1 M aqueous HCl solution (100 mL), extracted with EtOAc (200 mL). The organic layer was washed with brine (150 mL) and concentrated under reduced pressure to afford crude **2.22** as a white solid (5.889 g): this compound was not purified, but used directly in the next step. IR (neat) ν: 3311 (w), 2920 (m), 1465 (w), 1233 (w), 1041 (s), 985 (m), 924 (w), 822 (m), 705 (m) $cm^{-1}$; $^1H$ NMR (500 MHz, DMSO-$d_6$): δ 7.33 (s, 2H), 7.10-7.06 (m, 4H), 5.08-5.03 (m, 4H), 4.51 (s, 4H), 4.45 (s, 4H), 2.56 (t, $J$=7.8 Hz, 4H), 1.50 (br m, 4H), 1.29-1.18 (m, 12H); $^{13}C$ NMR (125 MHz, DMSO-$d_6$): δ140.4, 140.1, 138.8, 129.3, 126.6, 125.8, 63.8, 61.5, 32.1, 31.4, 29.93, 29.90, 29.8.

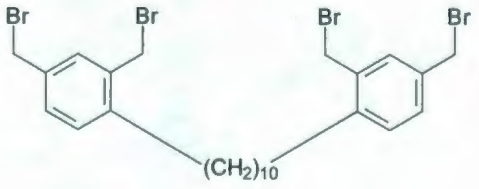
**1,8-Bis(2,4-bis(hydroxymethyl)phenyl)octane (2.13)**




**2.13**

This compound was prepared analogously to **2.22**, above, using tetraester **2.12** (5.000 g, 9.020 mmol) and $LiAlH_4$ (1.931 g, 50.88 mmol) and THF (200 mL) to yield crude tetraalcohol **2.13** as a white solid (3.370 g): This compound was not purified, but used directly in the next step. IR (neat) ν: 3301 (m), 2922 (m), 1467 (w), 1224 (w), 1157 (m), 1049 (s), 1021 (s), 889 (m), 828 (m), 724 (m) $cm^{-1}$; $^1H$ NMR (500 MHz, DMSO-$d_6$): δ 7.32 (s, 2H), 7.11-7.05 (m, 4H), 5.12 (t, *J*=5.7 Hz, 2H), 5.08 (t, *J*=5.4 Hz, 2H), 4.50 (d, *J*=5.3 Hz, 4H), 4.44 (d, *J*=5.6 Hz, 4H), 2.54 (t, *J*=7.5 Hz, 4H), 1.49 (br m, 4H), 1.30 (br s, 8H); $^{13}C$ NMR (125 MHz, DMSO-$d_6$): δ 140.4, 140.2, 138.8, 129.3, 126.7, 125.8, 63.8, 61.5, 32.1, 31.4, 29.9, 29.8.

**1,10-Bis(2,4-bis(bromomethyl)phenyl)decane (2.23)**

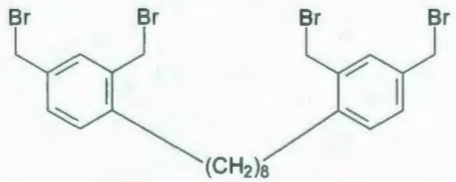



**2.23**

To a well-stirred mixture of tetraalcohol **2.22** (3.000 g, 7.300 mmol) in $CH_2Cl_2$ (100 mL) was added $PBr_3$ (7.844 g, 29.00 mmol) at room temperature under $N_2$. This mixture was stirred for 18 h and then quenched with $H_2O$ (100 mL). The layers were separated and the organic layer was washed with saturated aqueous $NaHSO_4$ solution (50 mL), washed with brine (100 mL), dried over $MgSO_4$ and concentrated under reduced pressure. The residue was subjected to column chromatography (50:50 $CH_2Cl_2$/hexanes) to give **2.23** as a white solid (3.665 g, 5.534 mmol, 76%): $R_f$ (50:50 $CH_2Cl_2$/hexanes): 0.57; mp:

111.0-113.0 °C; IR (neat) ν: 2926 (m), 2849 (m), 1503 (w), 1465 (m), 1210 (s), 1162 (w), 904 (w), 864 (m), 737 (m) $cm^{-1}$; $^1H$ NMR (500 MHz, $CDCl_3$): δ 7.35 (d, *J*=1.3 Hz, 2H), 7.27 (dd, *J*=7.9, 1.4 Hz, 2H), 7.17 (d, *J*=7.9 Hz, 2H), 4.51 (s, 4H), 4.46 (s, 4H), 2.70 (t, *J*=7.8 Hz, 4H), 1.66-1.60 (m, 4H), 1.41-1.33 (m, 12H); $^{13}C$ NMR (125 MHz, $CDCl_3$): δ 142.6, 136.22, 136.18, 131.4, 130.7, 129.9, 33.4, 32.5, 31.5, 31.2, 30.1, 29.91, 29.86.

**1,8-Bis(2,4-bis(bromomethyl)phenyl)octane (2.14)**




**2.14**

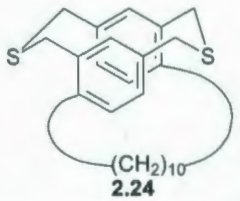
This compound was prepared analogously to **2.23**, above, using tetraalcohol **2.13** (1.000 g, 2.611 mmol) and $PBr_3$ (2.888 g, 10.67 mmol) to yield tetrabromide **2.14** as a white solid (0.773 g, 1.219 mmol, 79%): $R_f$ (20:80 $CH_2Cl_2$/hexanes): 0.20; mp: 142.0-143.0 °C; IR (neat) ν: 2929 (w), 2851 (w), 1464 (w), 1209 (m), 904 (w), 827 (w), 737 (w) $cm^{-1}$; $^1H$ NMR (500 MHz, $CDCl_3$): δ 7.35 (d, *J*=1.6 Hz, 2H), 7.27 (dd, *J*=7.9, 1.8 Hz, 2H), 7.17 (d, *J*=7.9 Hz, 2H), 4.51 (s, 4H), 4.48 (s, 4H), 2.70 (t, *J*=7.8 Hz, 4H), 1.67-1.61 (m, 4H), 1.41-1.37 (m, 8H); $^{13}C$ NMR (125 MHz, $CDCl_3$): δ 142.5, 136.23, 136.21, 131.4, 130.7, 129.9, 33.4, 32.5, 31.5, 31.2, 30.1, 29.8.

**Preparation of $Na_2S/Al_2O_3$**[13]

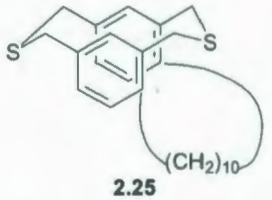
$Na_2S{\cdot}9H_2O$ (10.730 g, 44.708 mmol) was dissolved in deionized $H_2O$ (400 mL) and suction filtered onto basic alumina (basic 5016A, 10.490 g). The water was removed by

reduced pressure and the resulting pink solid was dried in vacuum. This $Na_2S/Al_2O_3$ was stored under $N_2$ in the fridge.

**(± )-$C_2$-18,27-Dithia[10.3.3](1,2,4)cyclophane (2.24) and $C_s$-18,26-dithia[10.3.3](1,2,4) cyclophane (2.25)**



**2.24**



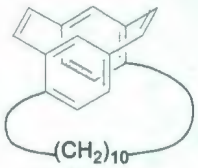
**2.25**

To a solution of tetrabromide **2.23** (1.000 g, 1.510 mmol) in 10% EtOH (anhydrous)/$CH_2Cl_2$ (250 mL) was added $Na_2S/Al_2O_3$ (2.332 g, 29.90 mmol of $Na_2S$). The mixture was then stirred overnight. The precipitate was removed by suction filtration and the filtrate was concentrated under reduced pressure. The residue was subjected to column chromatography (50:50 $CH_2Cl_2$/hexanes) to yield a mixture of **2.24** and **2.25** as white solid (254 mg, 0.620 mmol, 41%): $R_f$ (50:50 $CH_2Cl_2$/hexanes): 0.43; $^1$H NMR (500 MHz, $CDCl_3$): δ 7.26 (s, 2H), 6.87-6.81 (m, 4H), 4.05 (d, $J$=14.8 Hz, 2H), 3.89-3.78 (m, 6H), 2.79-2.66 (m, 2H), 2.31-2.20 (m, 2H). 1.74-1.67 (m, 2H), 1.55-1.51 (m, 2H), 1.51-1.47 (m, 2H), 1.36-1.25 (m, 10H); $^{13}$C NMR (125 MHz, $CDCl_3$): δ 139.2, 138.1, 135.4, 134.7, 132.9, 132.5, 128.8, 128.5, 127.7, 127.5, 39.1, 39.0, 31.3, 30.2, 28.8, 28.1, 27.9, 27.54, 27.47, 27.2, 27.1, 27.1 (four signals fewer than expected); LCMS [APCl(+)] *m/z* (%): 411 ($[M+H]^+$, 39), 377 (7).

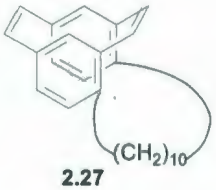
**Preparation of Borch reagent**[13]

A solution of $BF_3{\cdot}Et_2O$ (36.5 mL) in $CH_2Cl_2$ (30 mL) was slowly added in to a 250 mL round-bottomed flask containing a well-stirred sample of $(CH_3O)_3CH$ (27.5 mL) at -30 °C under $N_2$. After this addition, the mixture was warmed to 0 °C and stirred for 20 min. The upper layer was removed by syringe. The bottom layer was washed with $CH_2Cl_2$ (4× 50 mL), and dried under high vacuum at -20 °C for 6 h.

**(± )-*C*$_2$-[10.2.2]Cyclophane-16,25-diene (2.26) and *C*$_s$-[10.2.2]cyclophane-16,25-diene (2.27)**




**2.26**

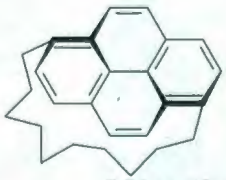



**2.27**

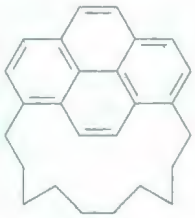
To a solution of thiacyclophane **2.24** and **2.25** (254 mg, 0.620 mmol) in $CH_2Cl_2$ (10 mL) was added Borch reagent (457 mg, 2.74 mmol) slowly over 5 min by syringe. The mixture was stirred for 1 h and the solvent was removed under reduced pressure. To the resulting residue was added EtOAc (6 mL) and this mixture was stirred vigorously for 5 min. Stirring was discontinued and the supernatant was decanted and the residue was dried in vacuum. To a suspension of the residue in THF (15 mL) was added *t*BuOK (352 mg, 3.12 mmol) in one portion and the reaction was stirred overnight. This mixture was quenched with saturated aqueous $NH_4Cl$ solution (1 mL) and concentrated under reduced pressure. The residue was filtered through a plug of Celite ($CH_2Cl_2$) to afford a yellow oil (253 mg, 0.620 mmol). To a solution of this yellow oil (253 mg, 0.620 mmol) in $CH_2Cl_2$

(10 mL) was added Borch reagent (269 mg, 1.61 mmol) and the resulting mixture was stirred for 4 h. The solvent was removed under reduced pressure and the residue was suspended in THF (15 mL). To this mixture was added *t*BuOK (253 mg, 2.23 mmol) in one portion and the resulting mixture was sonicated (Fisher Scientific FS-14) for 1 h. Then the mixture was removed from the sonicator and stirred at room temperature overnight. The solvent was removed under reduced pressure and the residue was immediately loaded onto a column for column chromatography (25:75 $CH_2Cl_2$/hexanes) to yield a mixture of compounds consisting mainly of pyrenophanes **2.01** ($n$=10) and **2.31** and possibly some cyclophanedienes **2.26** and **2.27** and dihydropyrenophanes **2.28**, **2.29** and **2.30** as colorless oil (85 mg, 0.25 mmol, 40%): $R_f$ (20:80 $CH_2Cl_2$/hexanes): 0.50; LCMS [APCl(+)] *m/z* (%): 343 ($[M+H]^+$, 36), 342 (25), 341 (78), 340 (65).

**[10](1,6)Pyrenophane (2.01, *n*=10) and [10](1,8)pyrenophane (2.31)**



**2.01** ($n$=10)



**2.31**

To a well-stirred solution of the product mixture from the previous reaction in degassed benzene (8 mL) was added a solution of DDQ (227 mg, 0.714 mmol) in degassed benzene (2 mL). The reaction mixture turned green, then orange, then dark red within 10 min. The mixture was stirred overnight at room temperature and then

concentrated under vacuum. The resulting residue was purified by column chromatography (10:90 $CH_2Cl_2$/hexanes) to afford pyrenophanes **2.01** ($n$=10) and **2.31** as white needles (43 mg, 0.16 mmol, 9%, 6 steps from tetrabromide **2.23**): $R_f$ (10:90 $CH_2Cl_2$/hexanes): 0.14; mp: 140.0-143.5 °C; $^1$H NMR (500 MHz, $CDCl_3$): δ 8.34 (d, $J$=9.3 Hz, 2H), 8.33 (s, 2H), 8.06 (d, $J$=7.7 Hz, 2H), 8.04 (d, $J$=6.0 Hz, 2H), 8.01 (d, $J$=9.2 Hz, 2H), 7.96 (s, 2H), 7.82 (d, $J$=7.8 Hz, 2H), 7.76 (d, $J$=7.7 Hz, 2H), 3.73-3.67 (m, 2H), 3.16 (t, $J$=4.4 Hz, 2H), 3.13(t, $J$=4.4 Hz, 2H), 1.97-1.92 (m, 2H), 1.15-1.09 (m, 10H), 1.06-1.01 (m, 12H), 0.58-0.51 (m, 2H), 0.80--0.12 (m, 4H), -1.94--2.00 (m, 2H), -2.61--2.68 (m, 2H); $^{13}$C NMR (125 MHz, $CDCl_3$): δ 138.1, 137.0, 130.4, 129.92, 129.87, 129.2, 127.7, 126.8, 126.5, 126.3, 125.5, 125.1, 124.9, 124.2, 123.7, 33.5, 31.52, 31.47, 30.7, 30.4, 30.1, 29.81, 29.80 28.3, 28.0, 25.9 (one signal fewer than expected); LCMS [APCl(+)] *m/z* (%): 341 ([M+H]$^+$, 100), 340 (29); HRMS [CI(+)] calcd for $C_{26}H_{28}$: 341.2269, found: 341.2263.

**Crystallographic Data for 2.01 ($n$=10) and 2.31**

X-ray crystallographic analysis for compounds **2.25a** and **2.25b** was performed by Dr. Louise N. Dawe, Memorial University. The text and data given below were taken from the reports provided by Dr. Dawe.

**[10](1,6)Pyrenophane (2.01 ($n$=10)) (plates)**

A colorless prism crystal of $C_{26}H_{28}$ having approximate dimensions of 0.20 × 0.20 × 0.20 mm was mounted on a low temperature diffraction loop. All

measurements were made on a Rigaku Saturn CCD area detector with a SHINE optic and Mo-K radiation.

Indexing was performed from 360 images that were exposed for 30 seconds. The crystal-to-detector distance was 40.15 mm.

Cell constants and an orientation matrix for data collection corresponded to a primitive triclinic cell with dimensions:

a=7.3519(19) Å □ α =73.766(16)°

b=10.560(3) Å □ β =73.458(17)°

c=12.901(3) Å □ γ =80.230(20)°

V=917.4(4) $Å^3$

For Z=2 and F.W.=340.51, the calculated density is 1.233 $g/cm^3$. Based on a statistical analysis of intensity distribution, and the successful solution and refinement of the structure, the space group was determined to be:

P-1 (#2)

The data were collected at a temperature of -120 ± 1 °C to a maximum 2 value of 61.4°. A total of 680 oscillation images were collected. A sweep of data was done using scans from -75.0 to 105.0° in 0.5° step, at χ=45.0° and Ø=90.0°. The exposure rate was 60.0 [sec./°]. The detector swing angle was 15.05°. A second sweep was performed using scans from -75.0 to 25.0° in 0.5° step, at χ=45.0° and Ø= 180.0°. The exposure rate was 60.0 [sec./°]. The detector swing angle was 15.05°. Another sweep was performed

using scans from -60.0 to 0.0° in 0.5° step, at $\chi$=0.0° and Ø=90.0°. The exposure rate was 60.0 [sec./°]. The detector swing angle was 15.05°. The crystal-to-detector distance was 40.15 mm. Readout was performed in the 0.137 mm pixel mode.

**[10](1,8)Pyrenophane (2.31) (needles)**

A colorless prism crystal of $C_{26}H_{28}$ having approximate dimensions of 0.40 × 0.09 × 0.08 mm was mounted on a low temperature diffraction loop. All measurements were made on a Rigaku Saturn CCD area detector with a SHINE optic and Mo-K radiation.

Indexing was performed from 300 images that were exposed for 25 seconds. The crystal-to-detector distance was 39.96 mm. Cell constants and an orientation matrix for data collection corresponded to a primitive monoclinic cell with dimensions:

a=9.800(5) Å

b=34.783(16) Å □ β =124.708(12)°

c=13.065(7) Å

V=3661(3) Å$^3$

For Z=8 and F.W.=340.51, the calculated density is 1.236 g/cm$^3$. The systematic absences of:

h0l: l ± 2n

0k0: k ± 2n

Uniquely determine the space group to be:

$P2_1/c$ (#14)

The data were collected at a temperature of -120 ± 1 °C to a maximum 2 value of 62.0°. A total of 918 oscillation images were collected. A sweep of data was done using scans from -75.0 to 75.0° in 0.5° step, at $\chi$=0.0° and $\emptyset$=180.0°. The exposure rate was 50.0 [sec./°]. The detector swing angle was 15.24°. A second sweep was performed using scans from -75.0 to 99.0° in 0.5° step, at $\chi$=45.0° and $\emptyset$=180.0°. The exposure rate was 50.0 [sec./°]. The detector swing angle was 15.24°. Another sweep was performed using scans from -75.0 to 60.0° in 0.5° step, at $\chi$=0.0° and $\emptyset$=0.0°. The exposure rate was 50.0 [sec./°]. The detector swing angle was 15.24°. The crystal-to-detector distance was 39.96 mm. Readout was performed in the 0.137 mm pixel mode.

**2.6 References**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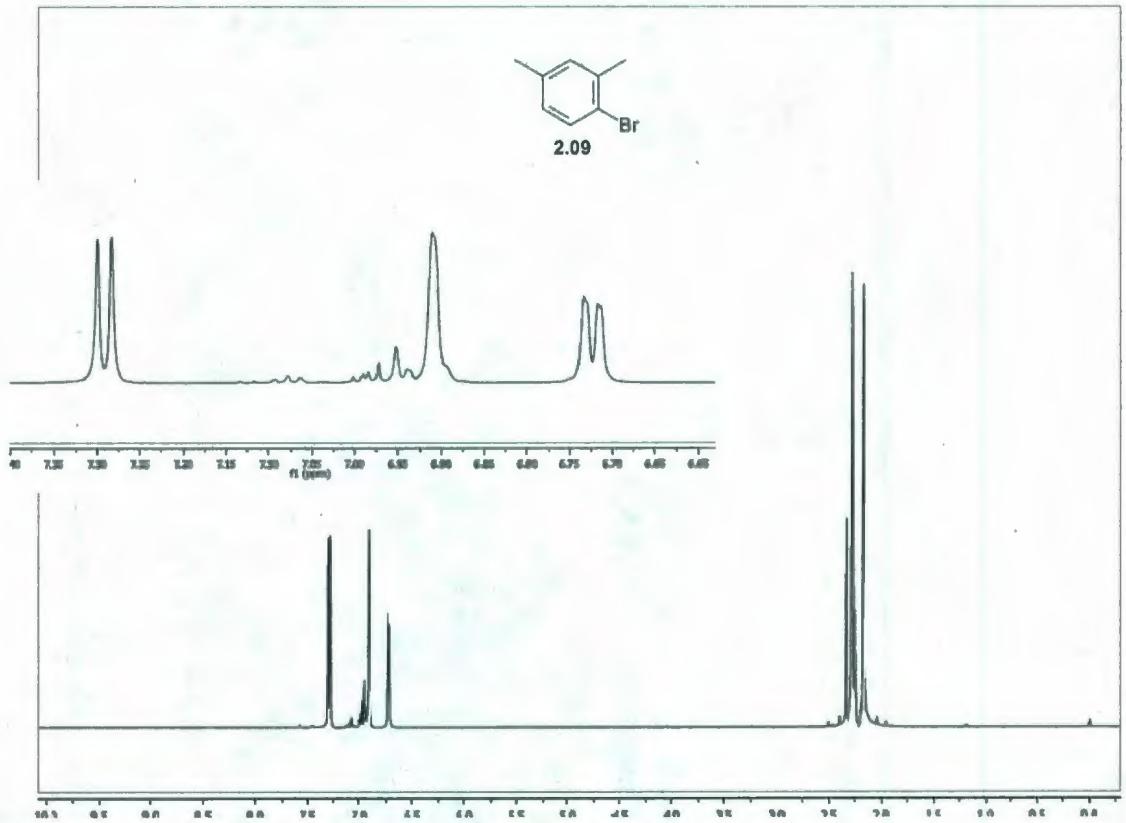
12. Zhang, B. *Ph.D. dissertation* **2007**, Memorial Univeristy.

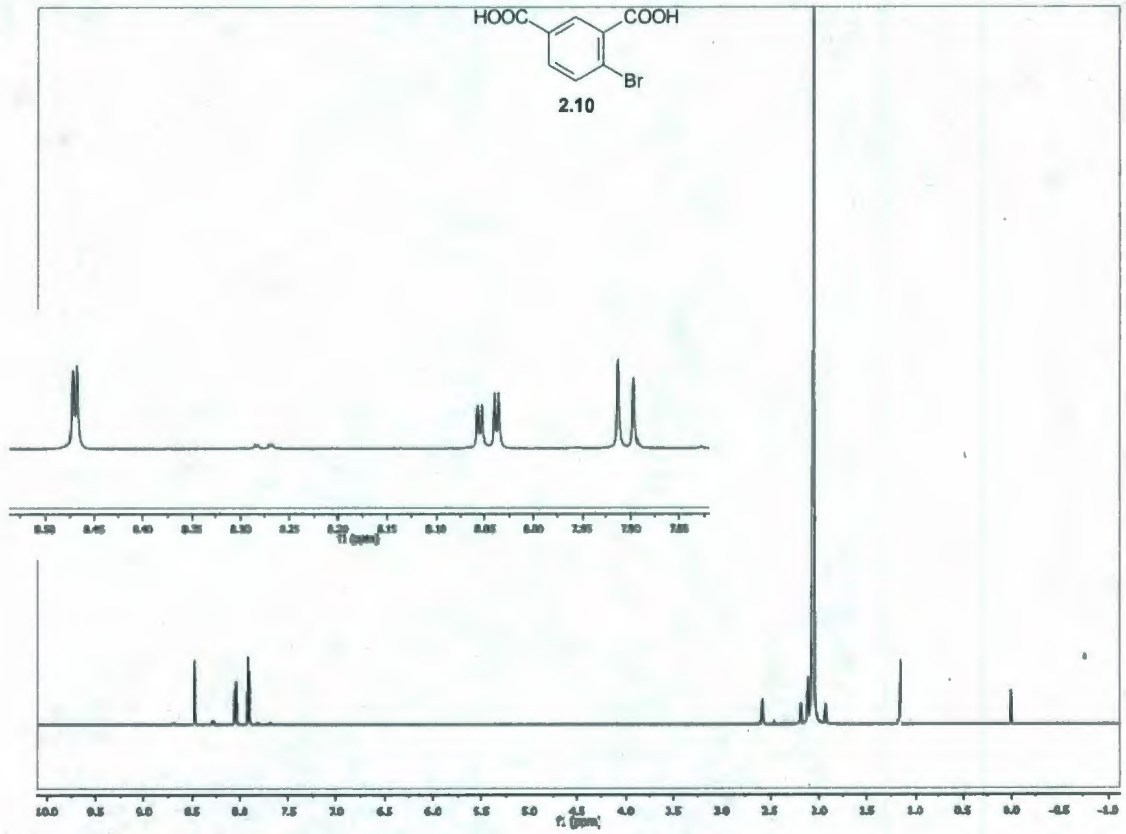
13. Yao, T. *Ph. D. dissertation* **2009**, Memorial University.

# Appendix 1

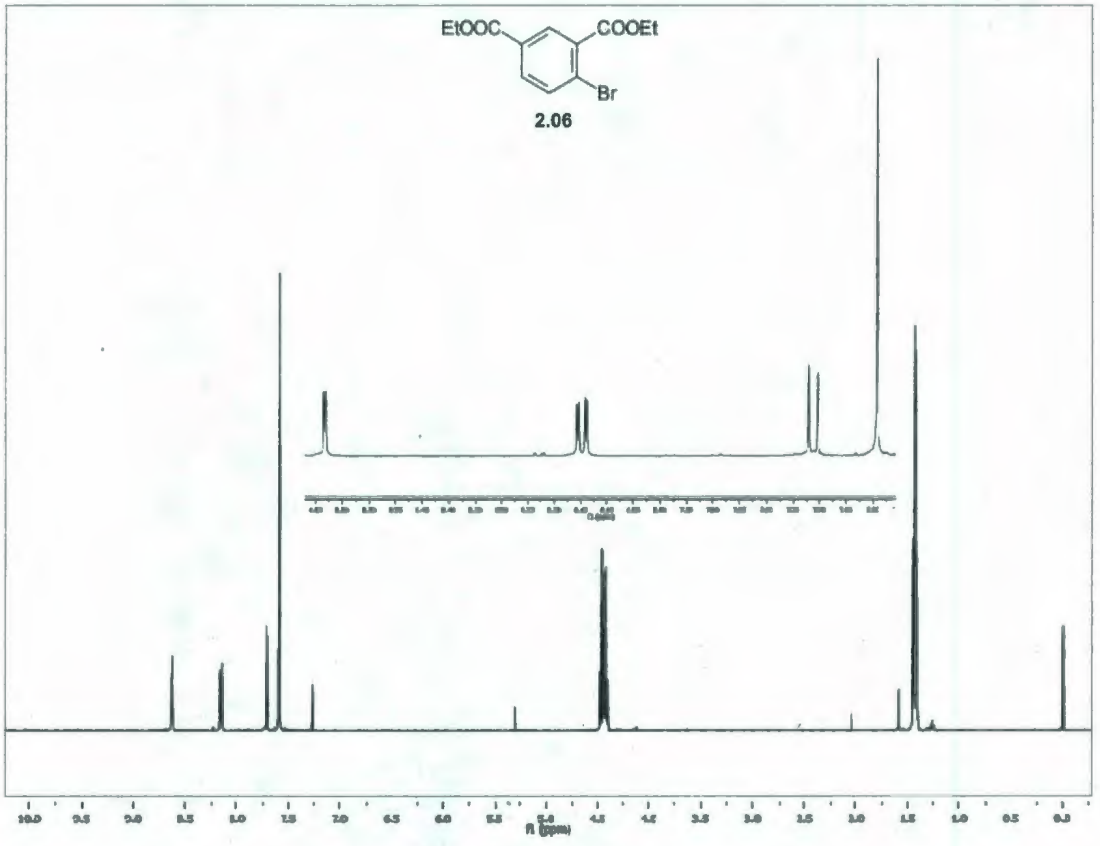
## Selected Spectra of Synthesized Compounds




2.09




2.10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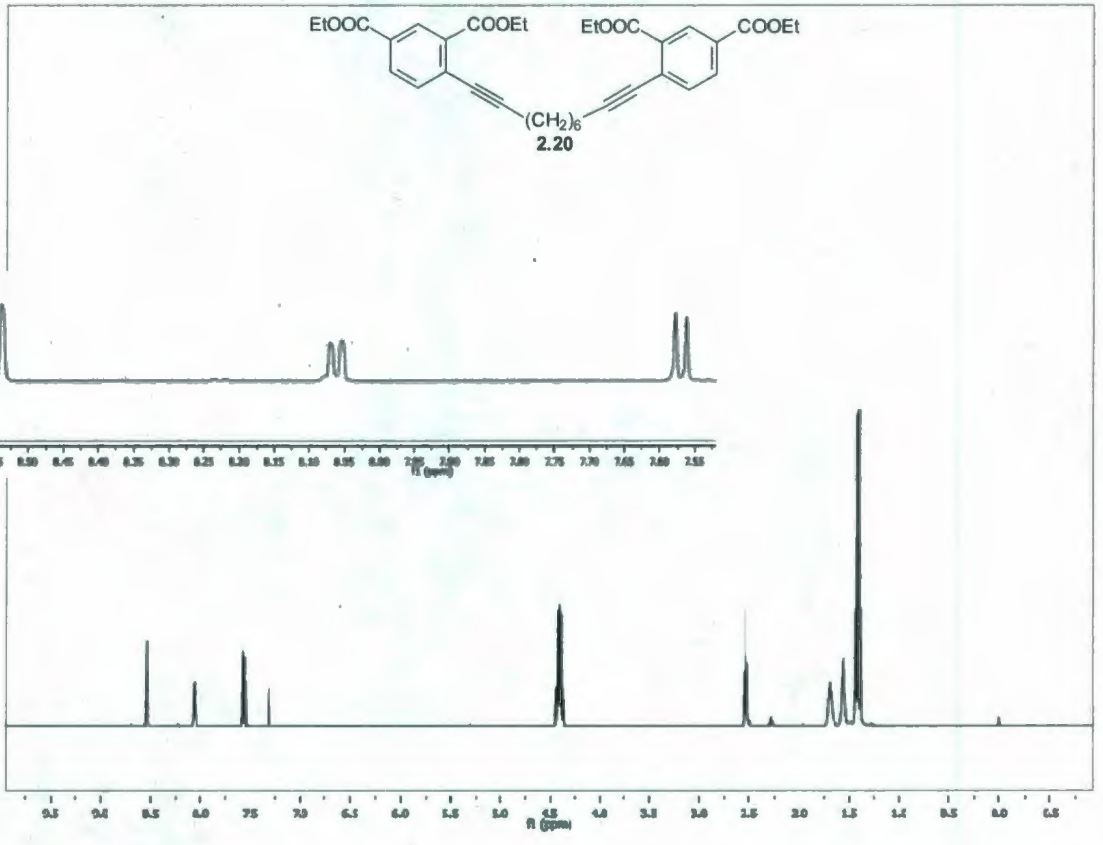
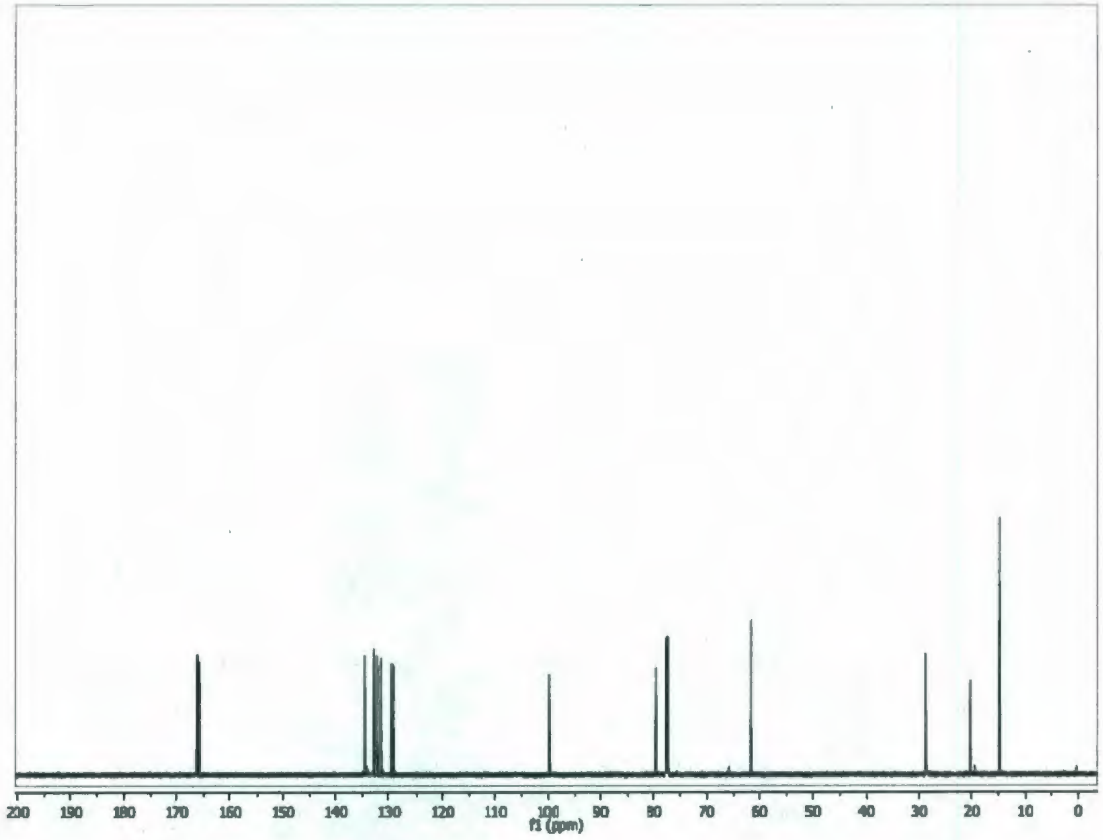
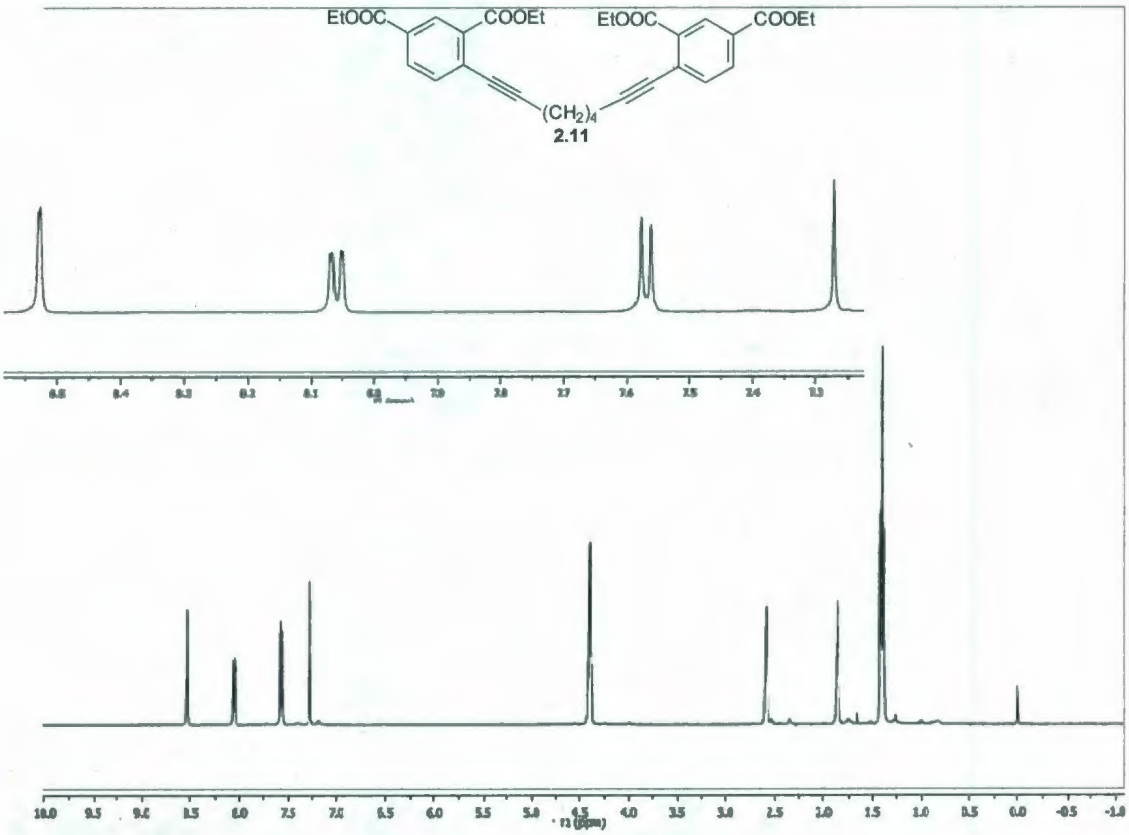
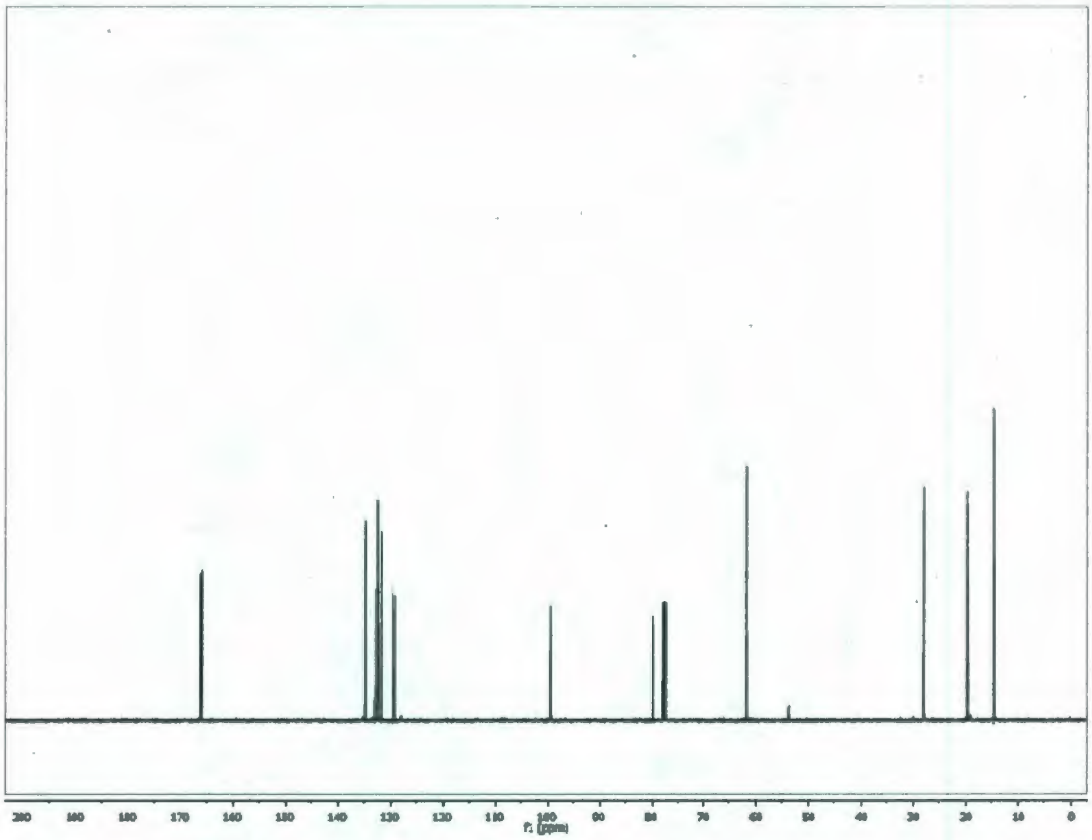
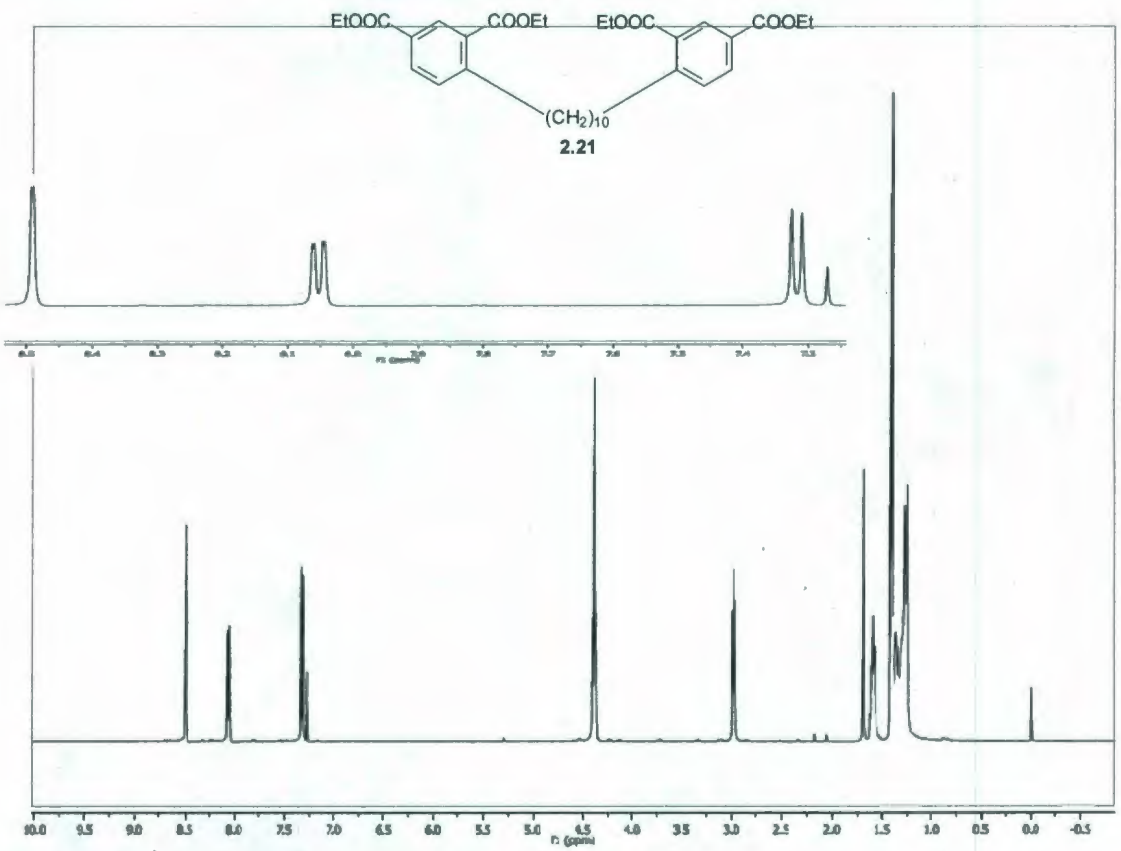
COOEt
Br
2.06


EtOOC
COOEt
EtOOC
COOEt
(CH2)6
2.20

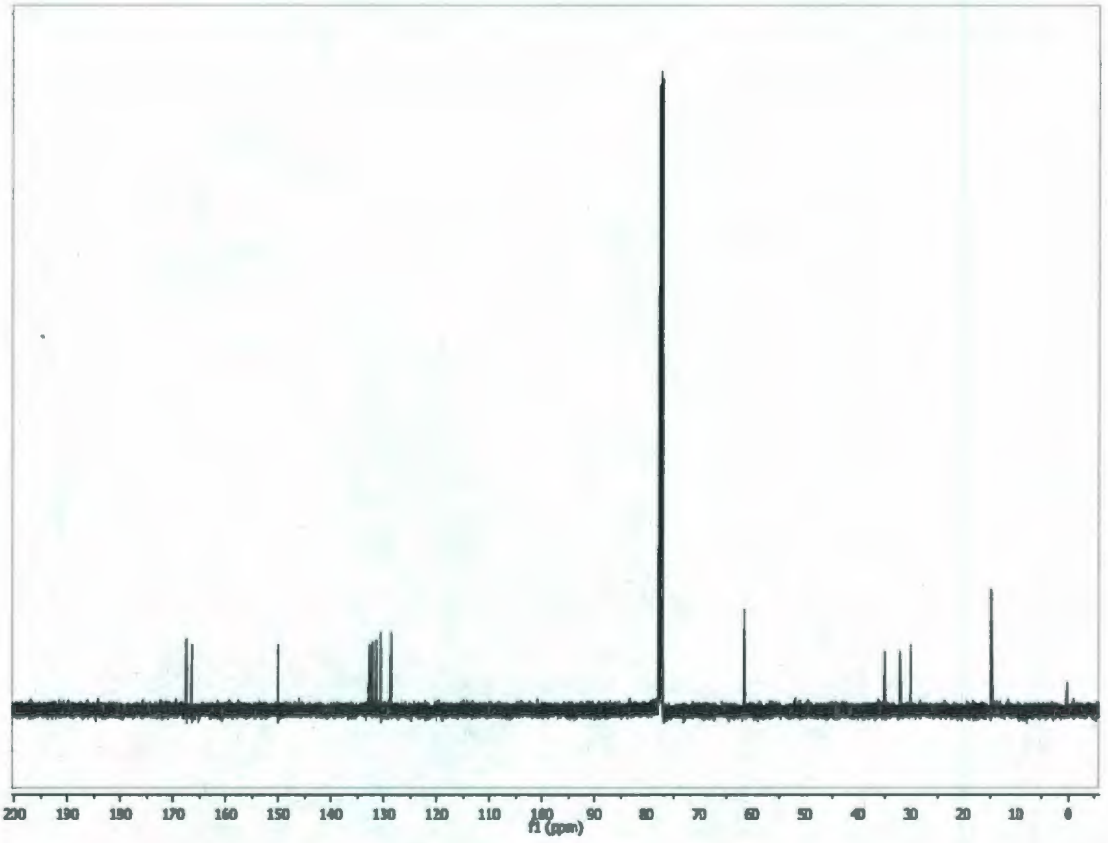

200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

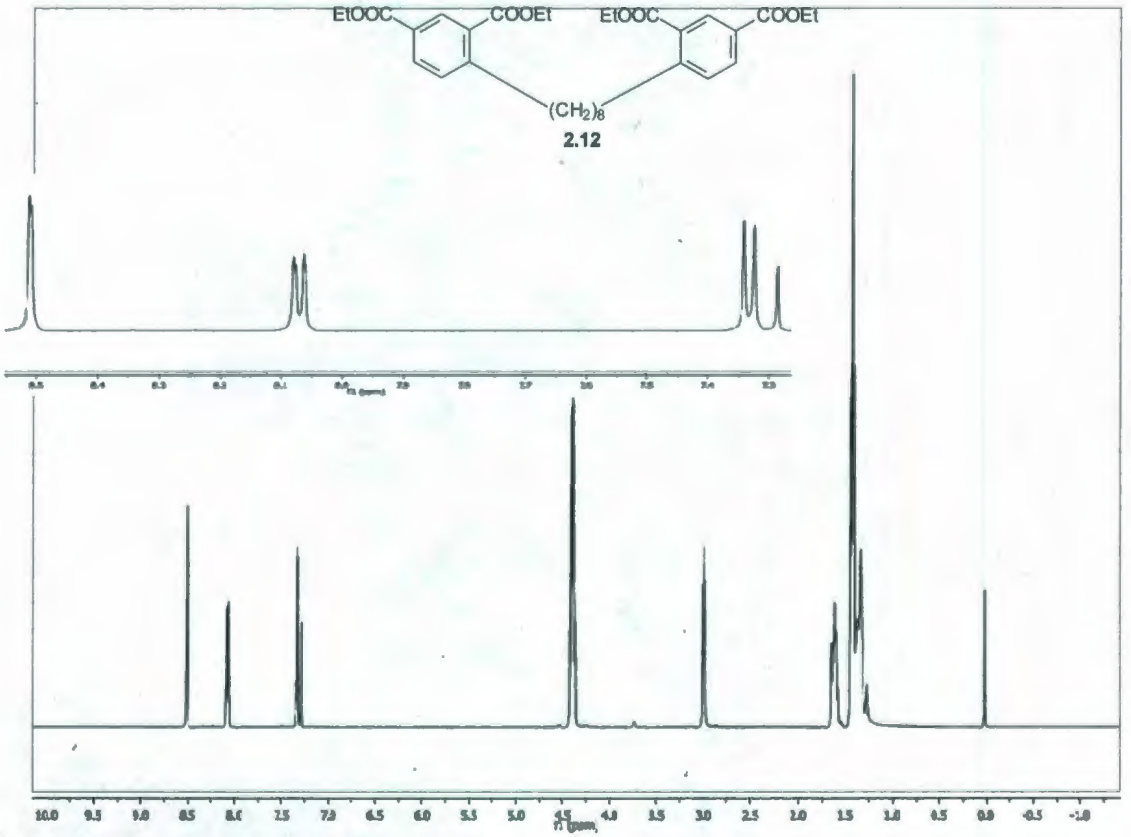

EtOOC
COOEt
EtOOC
COOEt
(CH2)4
2.11
18.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.0
f1 (ppm)



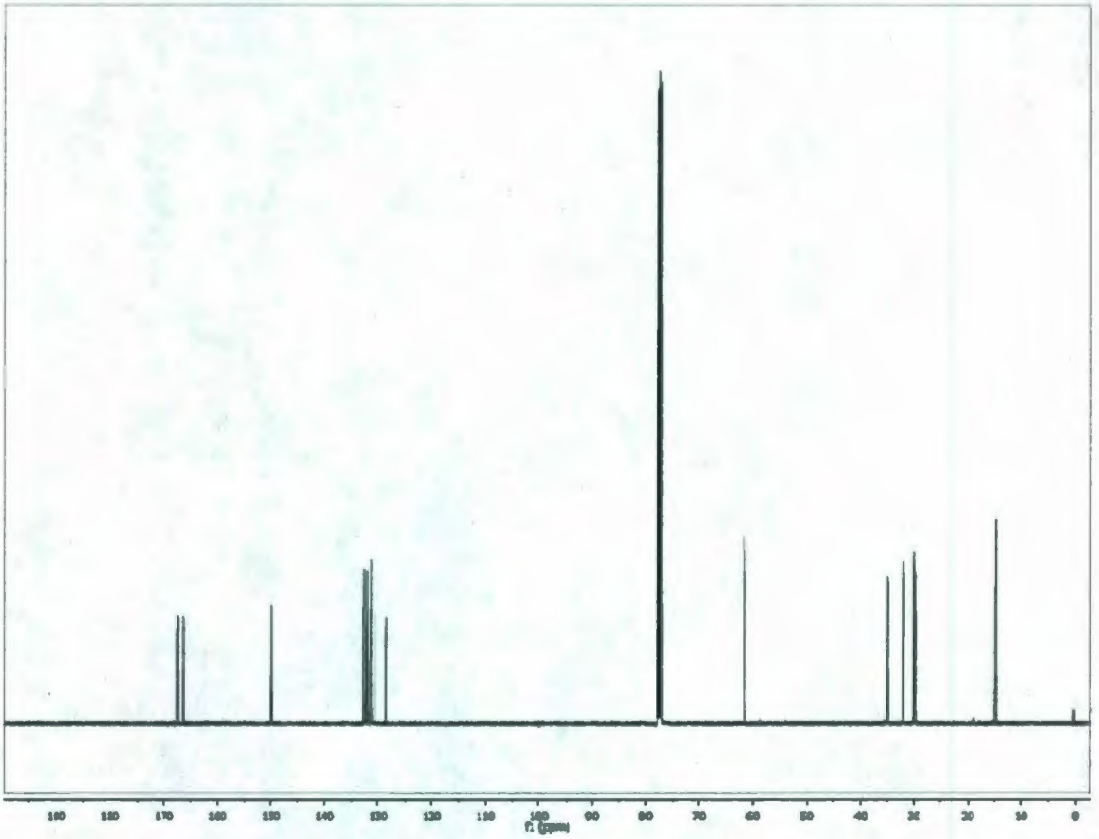


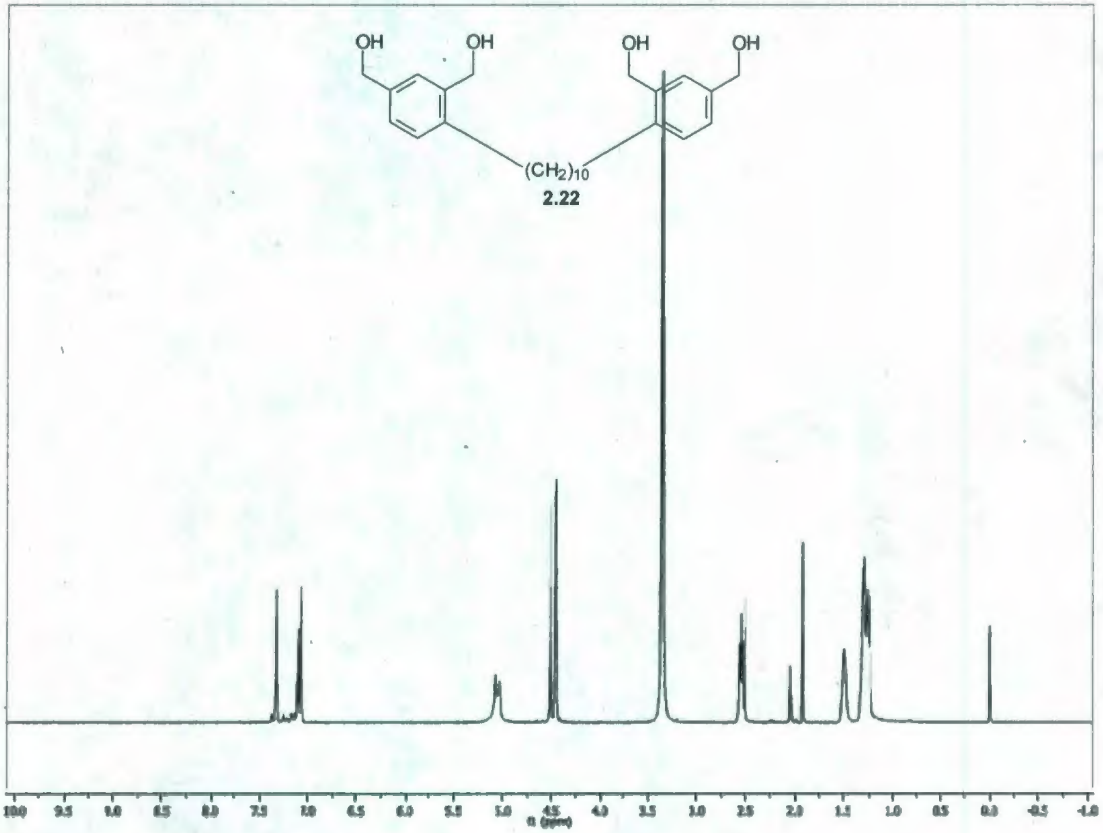

**2.21**


220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


EtOOC
COOEt
EtOOC
COOEt
(CH2)8
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
f1 (ppm)

**2.12**



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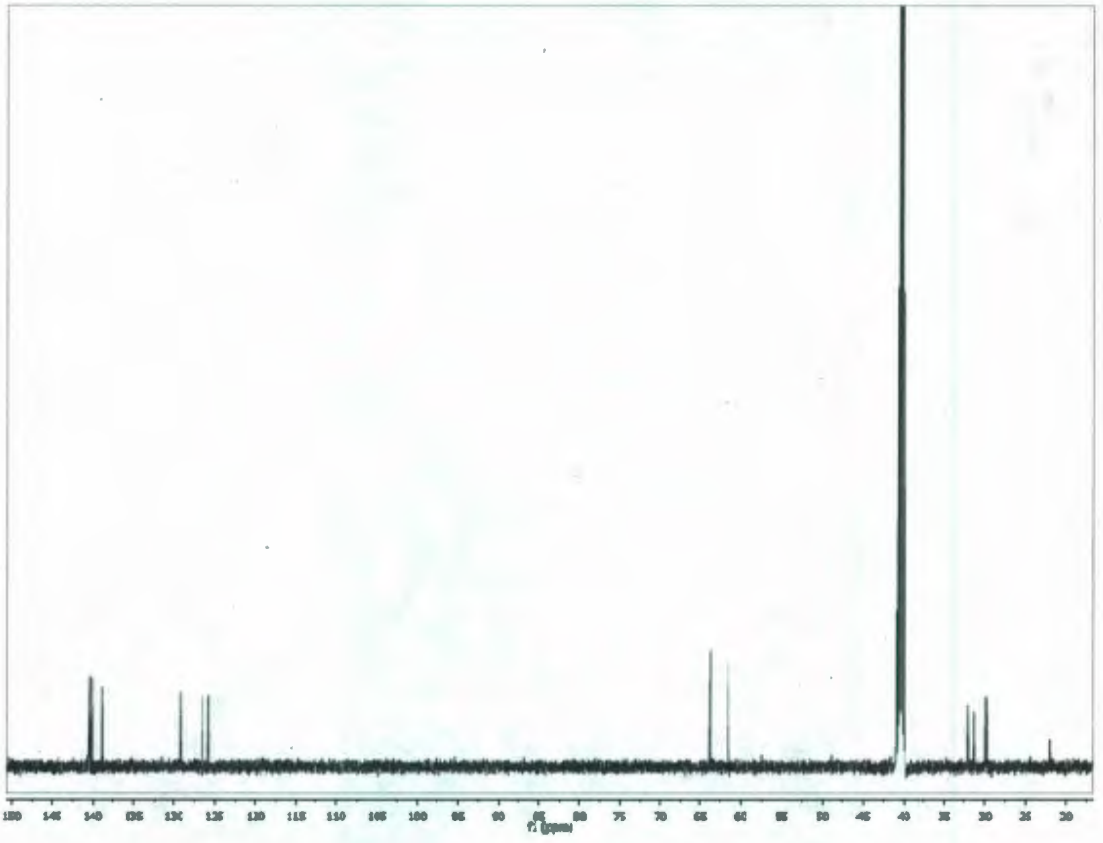
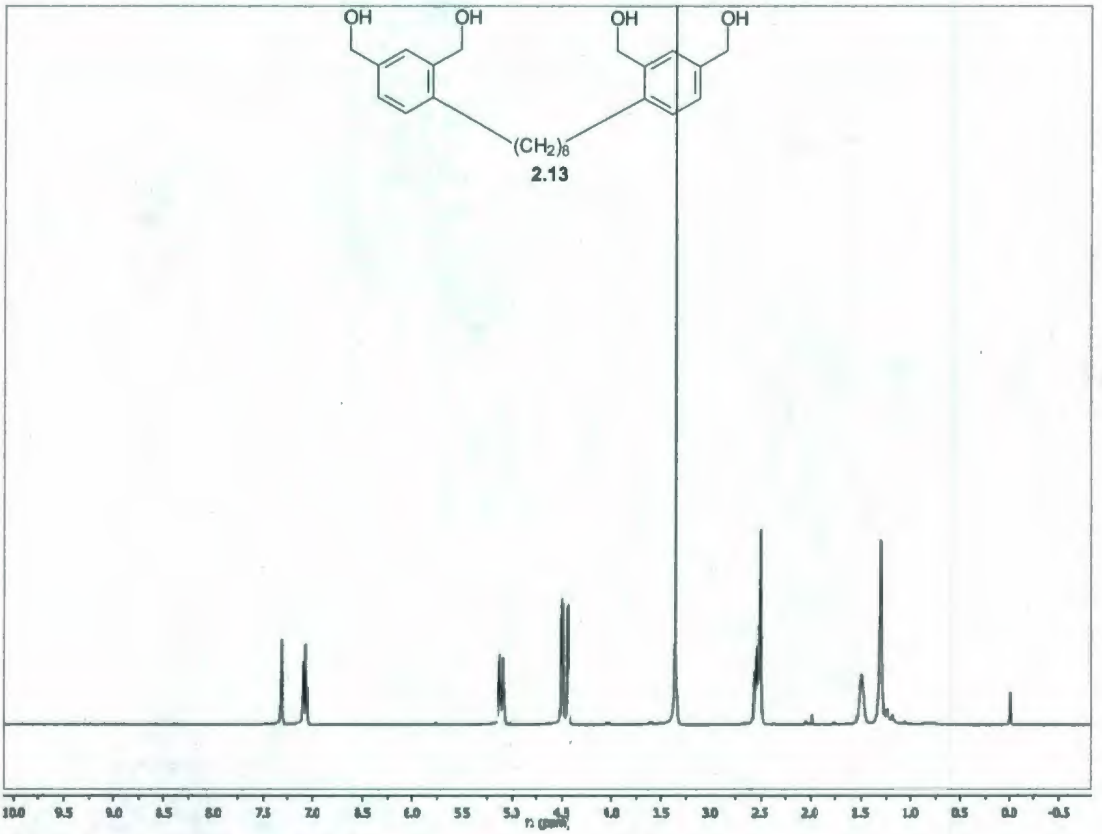
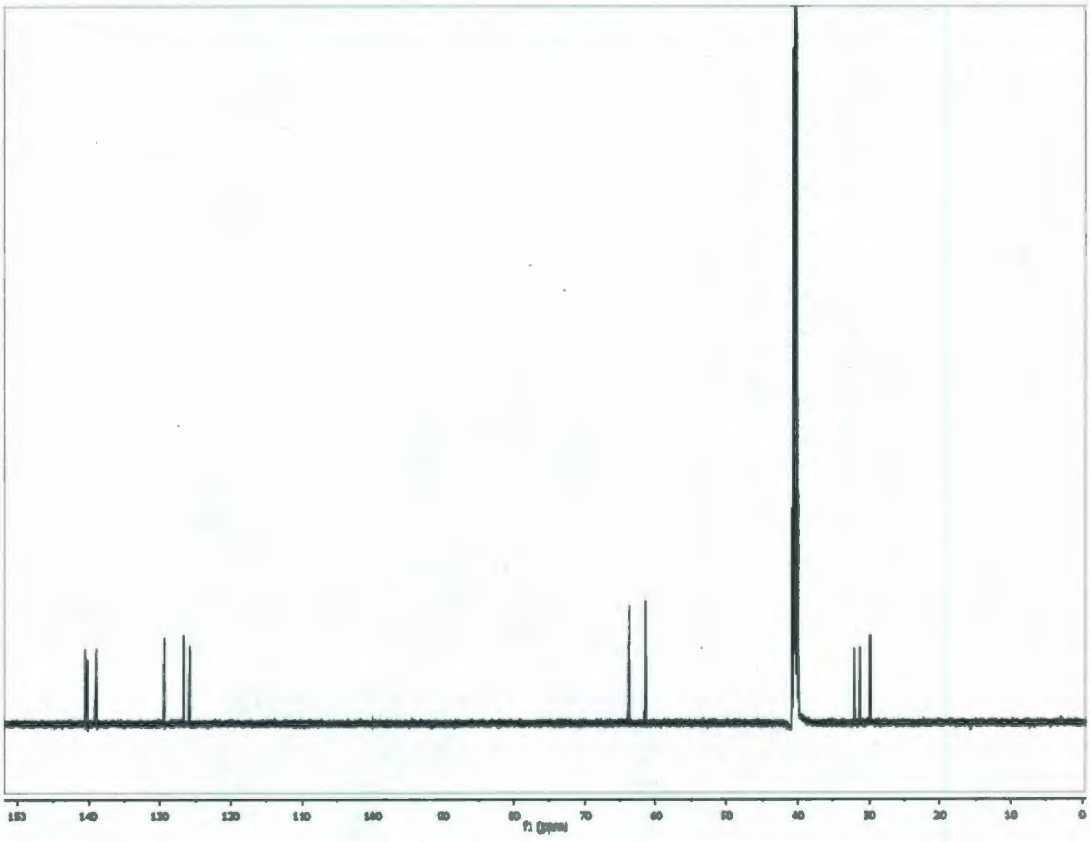
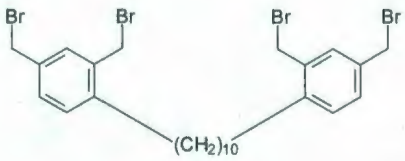


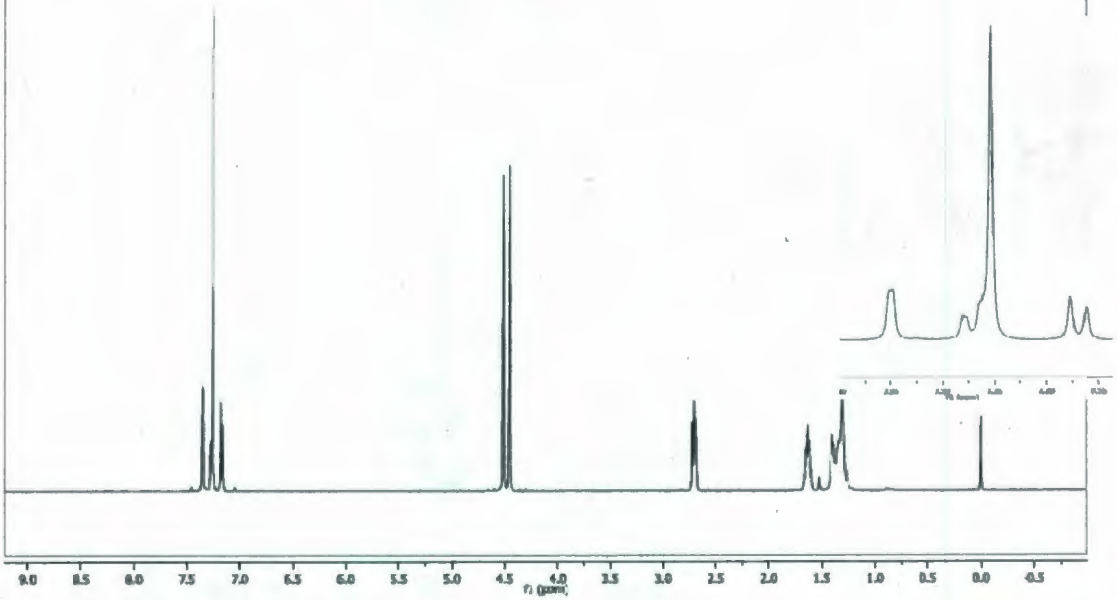


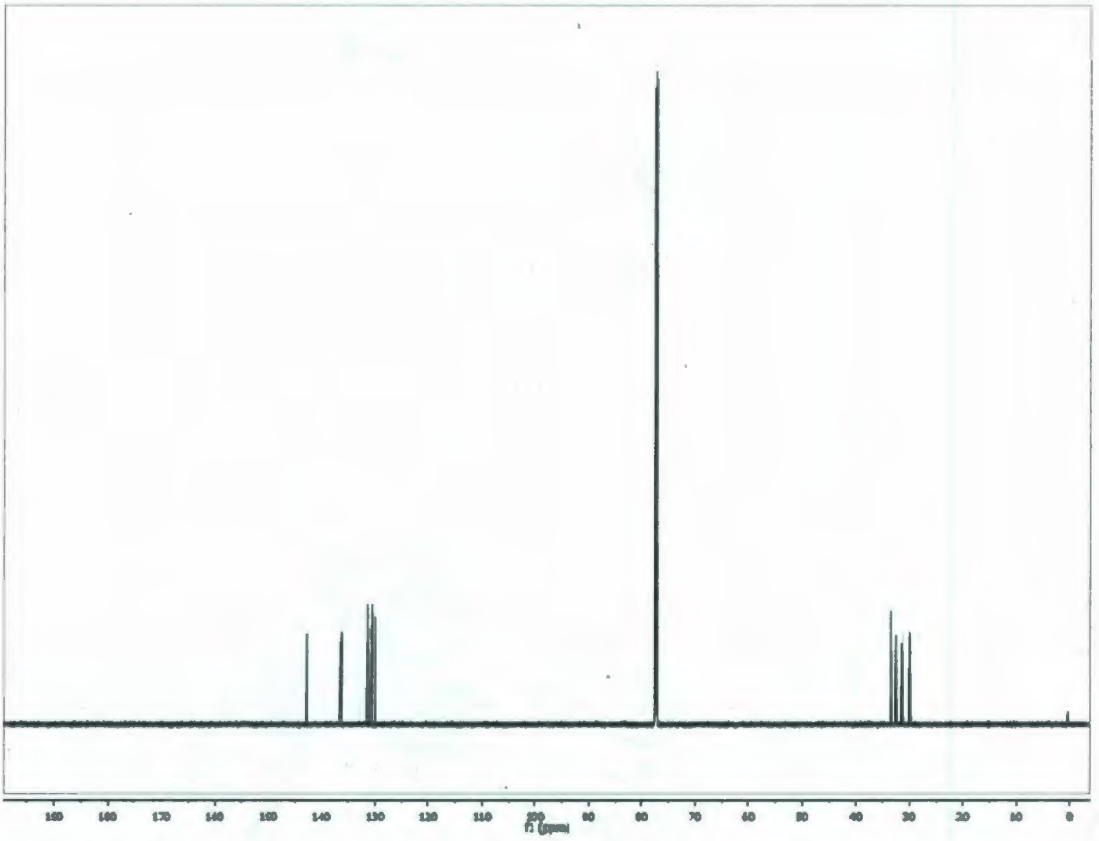

**2.13**

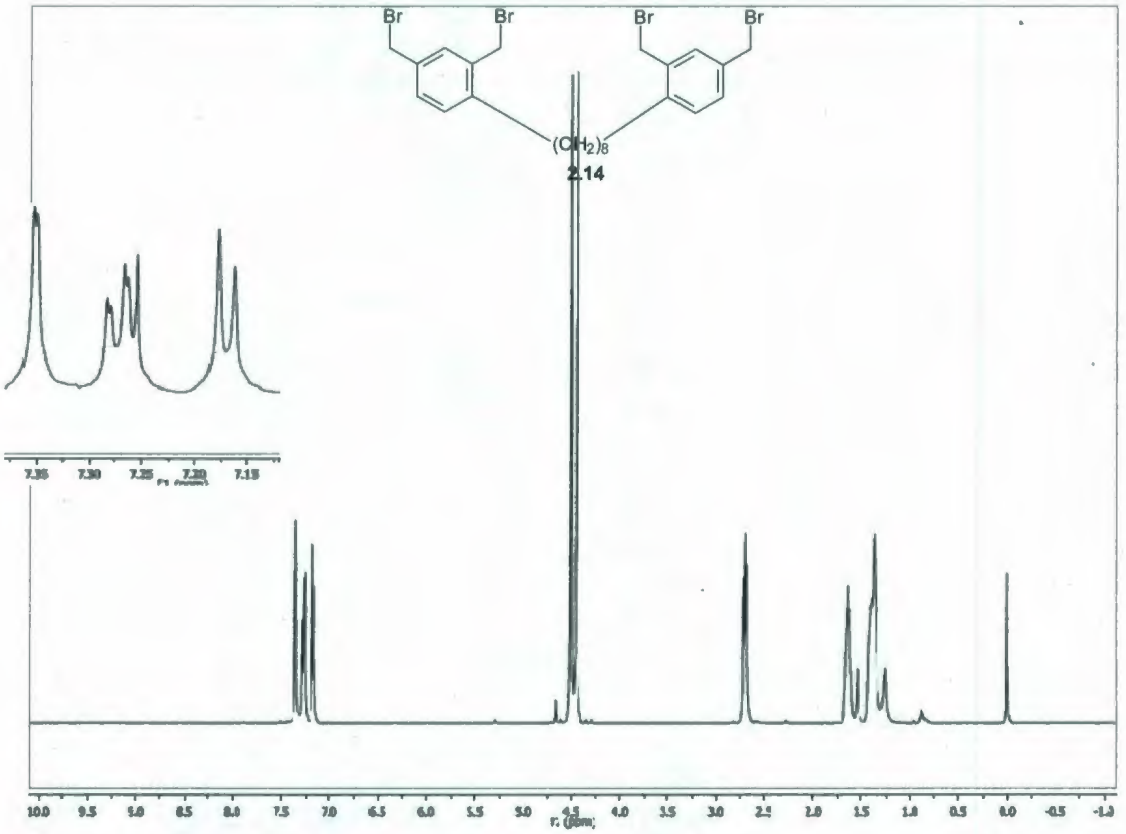




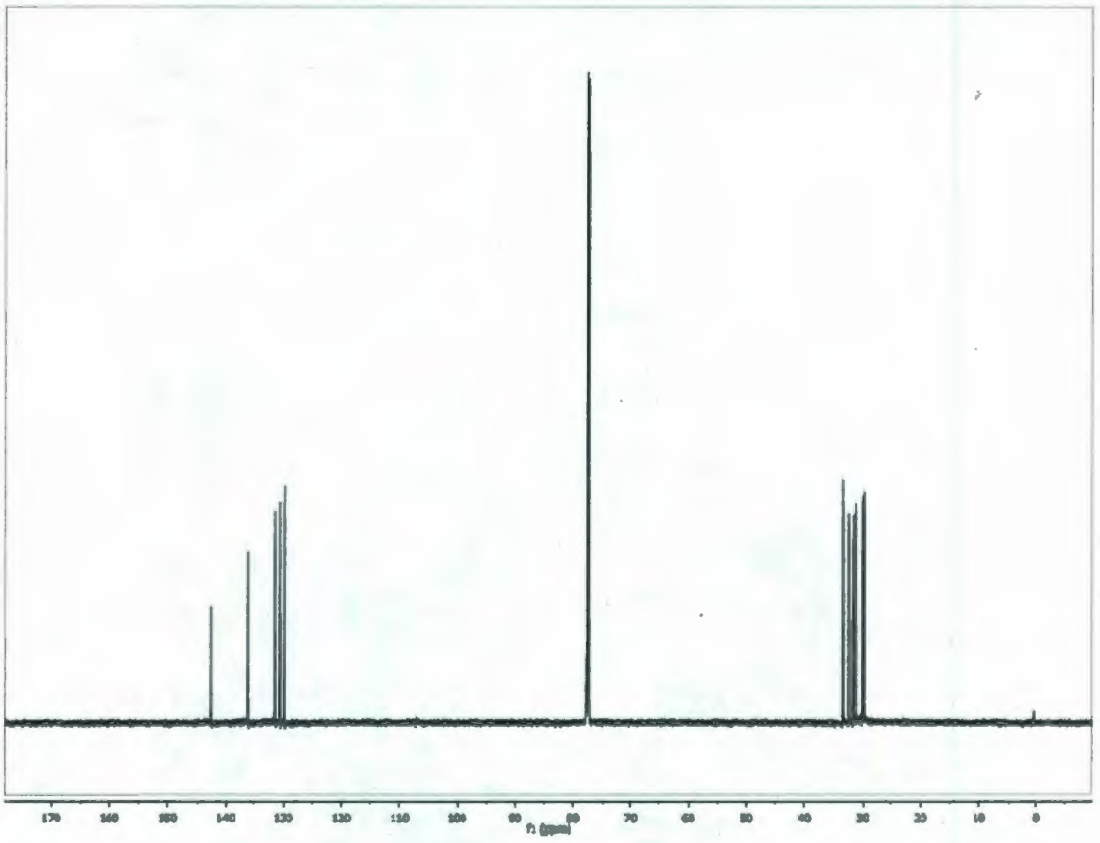

**2.23**

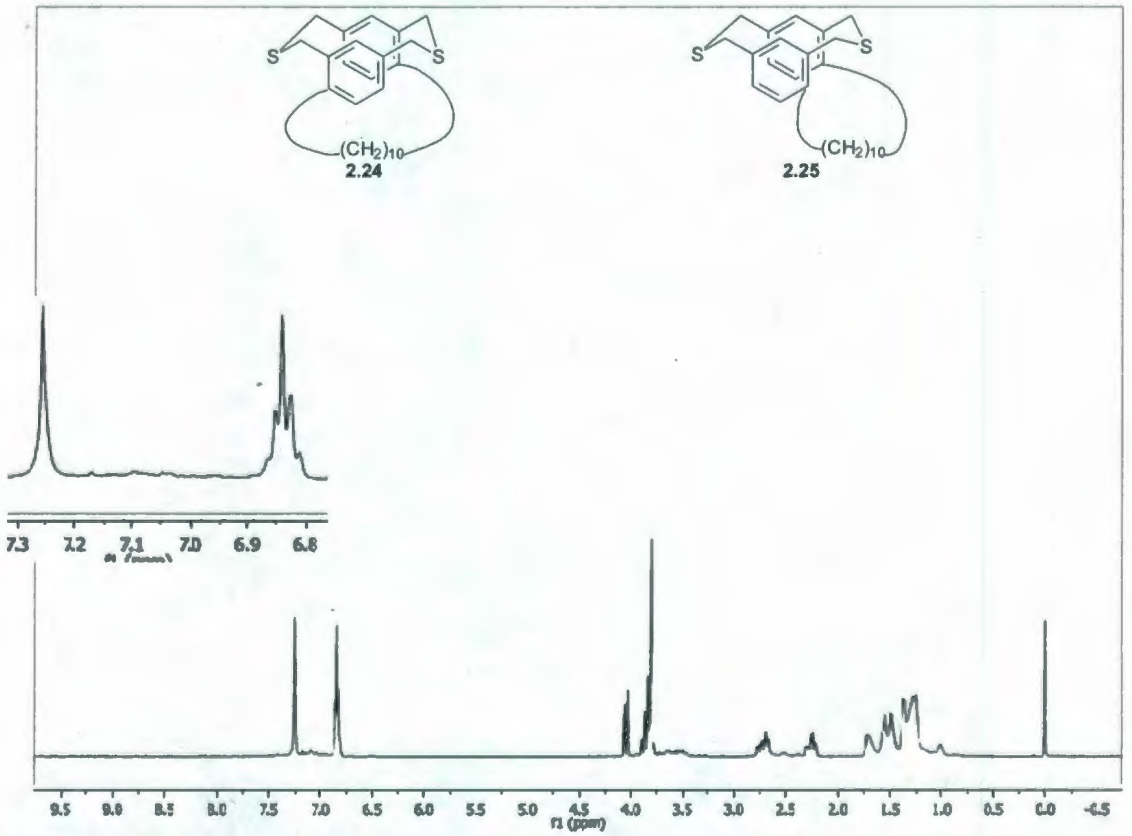


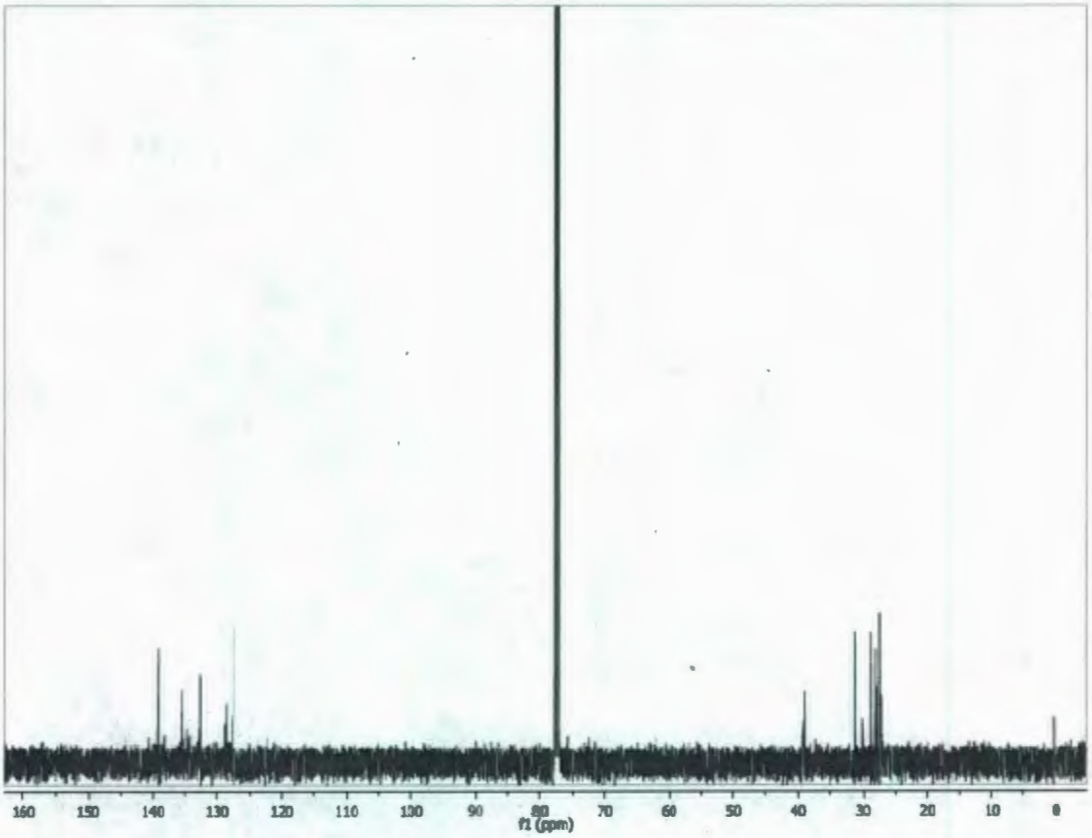





2.14




S
S
(CH2)10
2.24
S
S
(CH2)10
2.25
7.3
7.2
7.1
7.0
6.9
6.8
f1 (ppm)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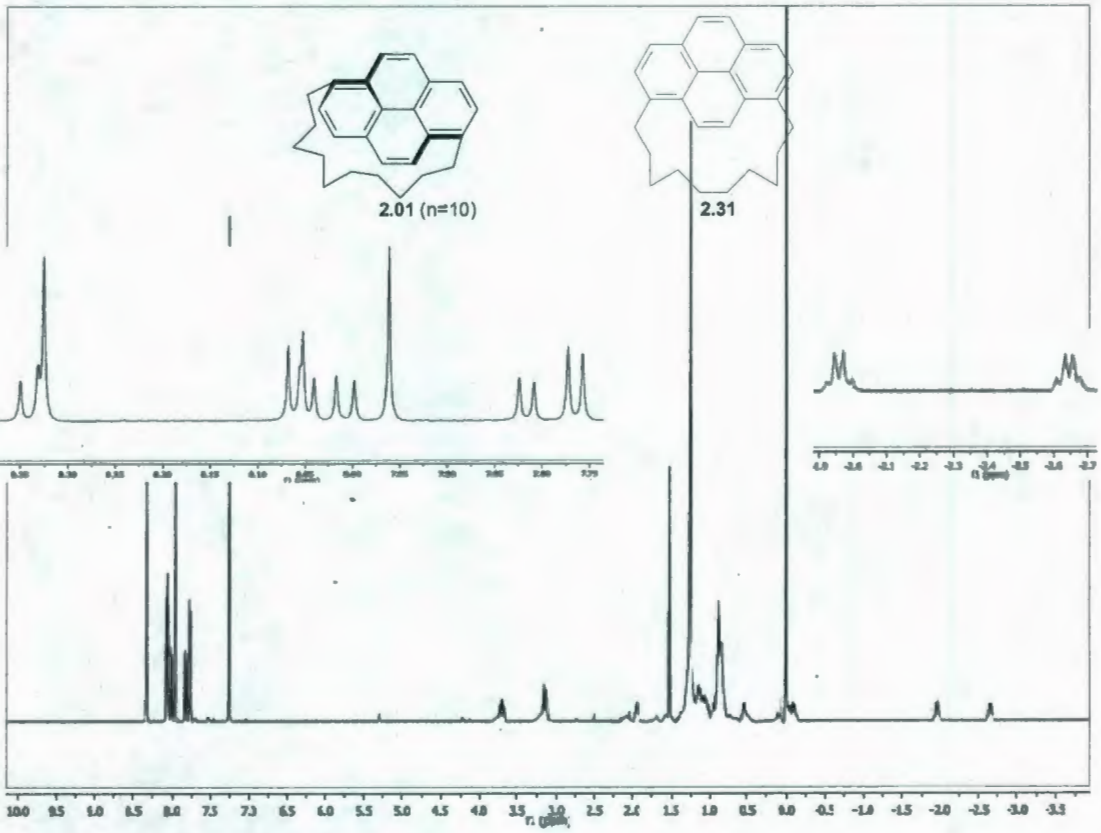
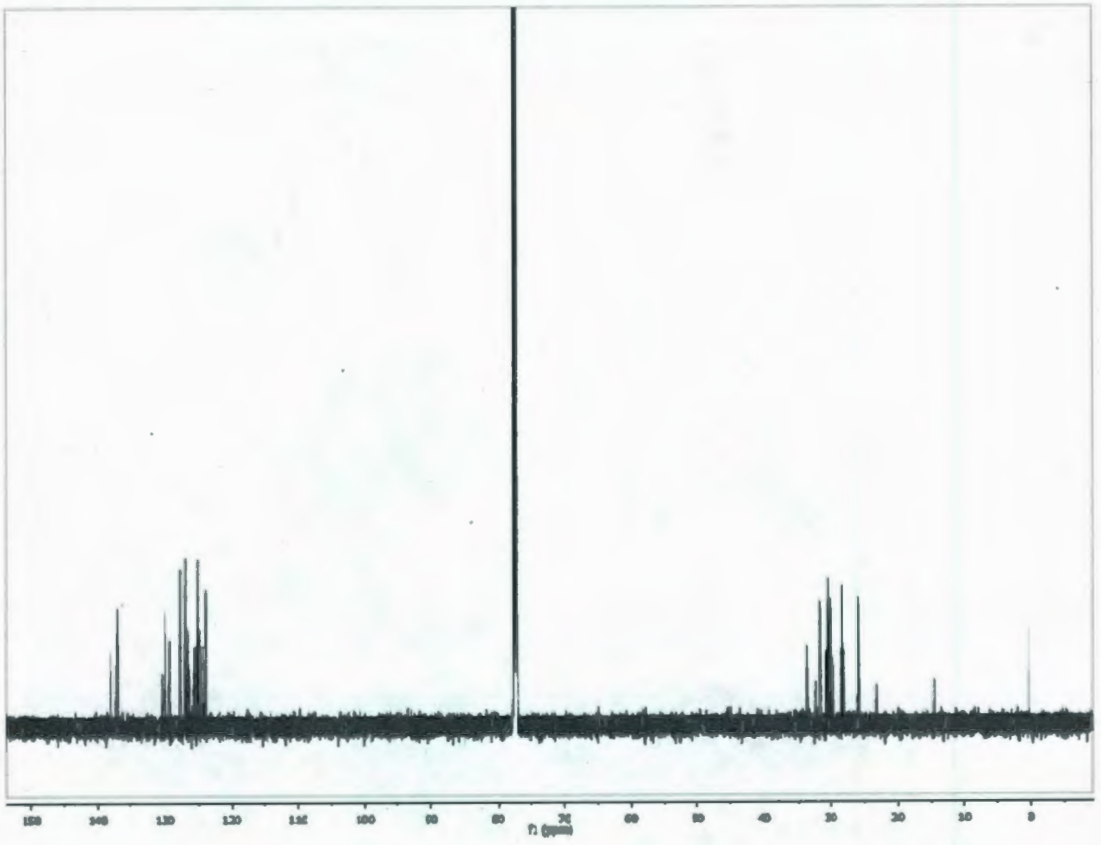
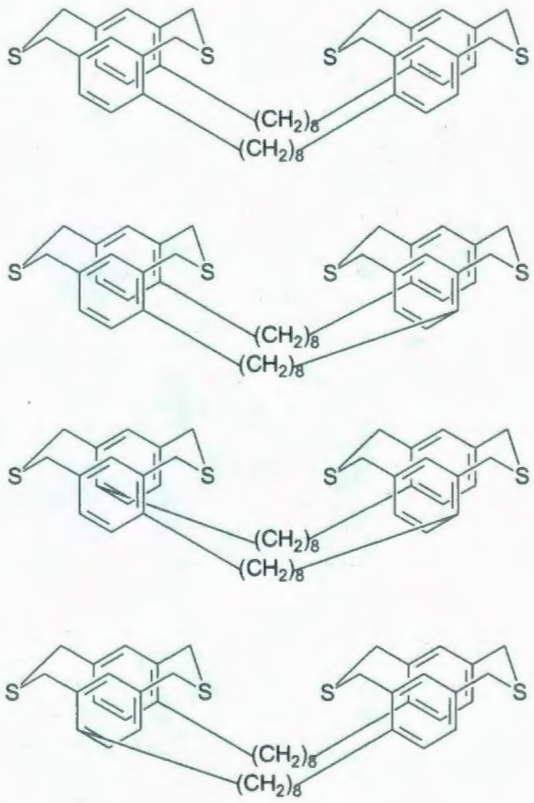
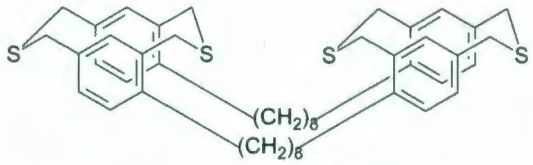
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


2.01 (n=10)
2.31
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
-1.5
-2.0
-2.5
-3.0
-3.5

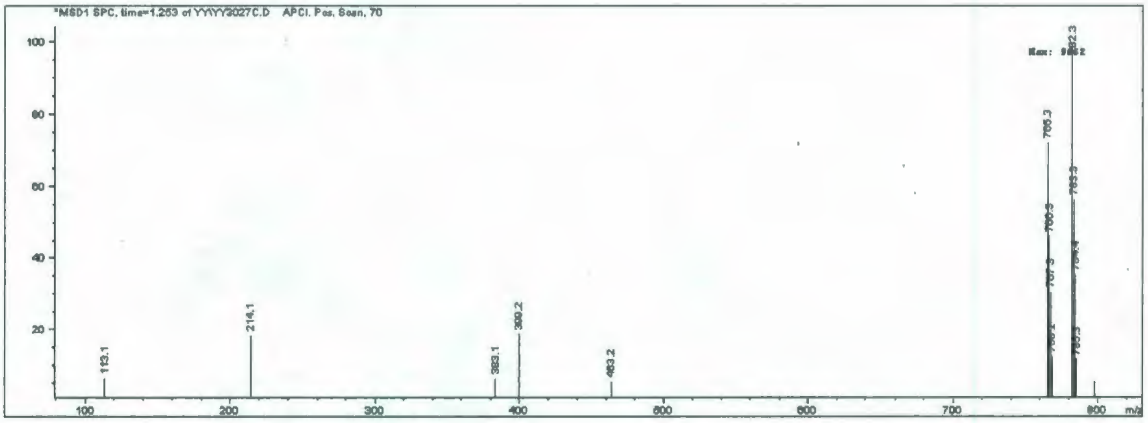


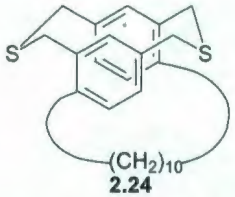
Four possible structures of compound **2.17**.



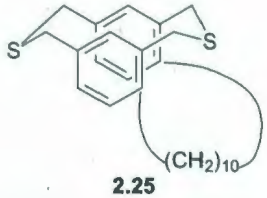



**2.17** + 3 isomers

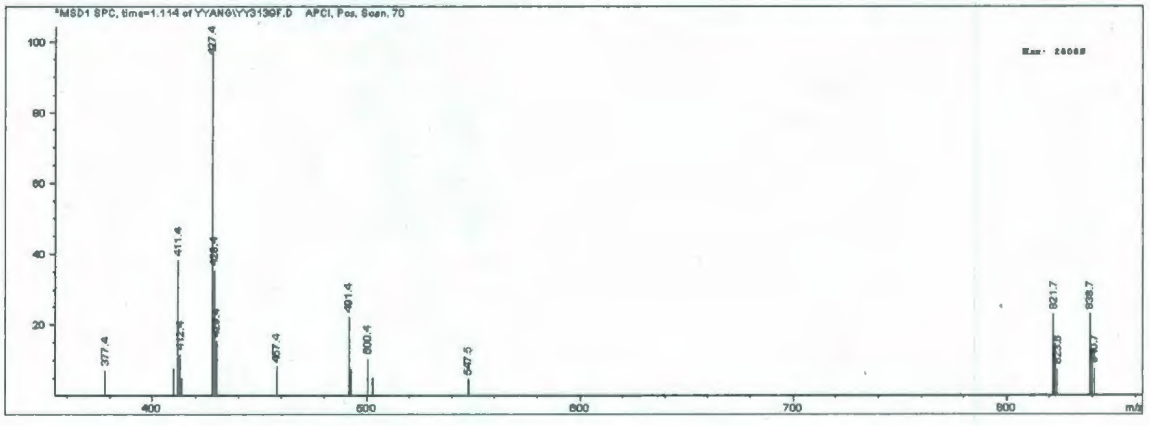



**2.24**

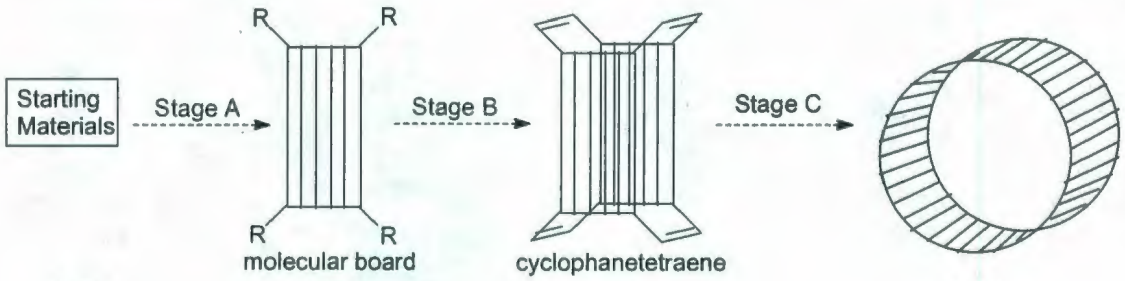



**2.25**



# Chapter Three
# Synthesis of Molecular Boards

## 3.1 Introduction



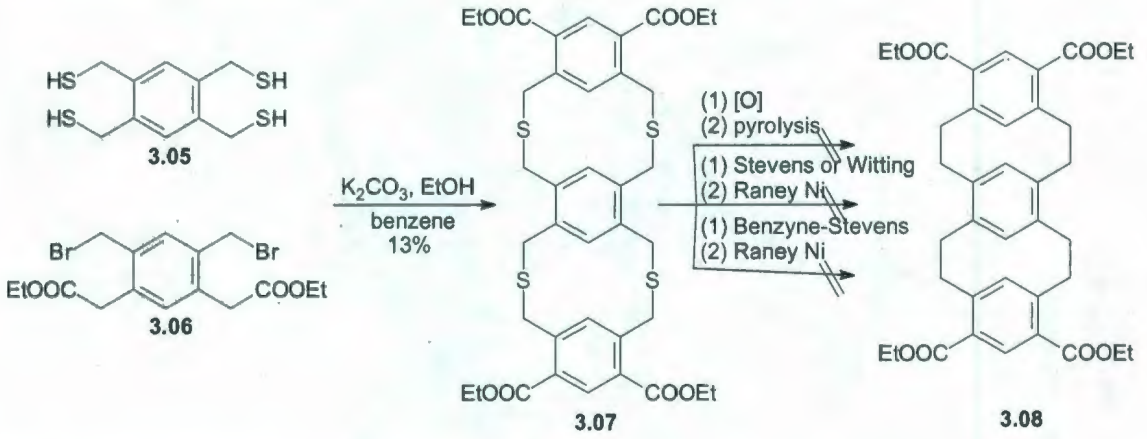

**Scheme 3.1** A strategy for the synthesis of aromatic belts.

A general approach to the synthesis of Vögtle type belts is being investigated in the Bodwell group (Scheme 3.1). This approach involves three stages. In Stage A, an appropriately substituted molecular board **3.02** is synthesized from commercially available starting materials **3.01**. The key feature of the molecular boards **3.02** is a set of *meta*-related substituents at each end of the board. These substituents are to be used in Stage B, in which the two boards are joined via unsaturated 2-C bridges. The resulting cyclophanetetraene **3.03** is than poised to undergo a twofold VID reaction to afford an aromatic belt **3.04** (Stage C). The work described in this chapter was aimed at finding new and/or improved solutions to Stage A of the general strategy. An attempt to complete Stage B and C is described in Chapter 4.

Several factors should be considered when designing a suitable molecular board. These include size (both the length and the width of the molecular board), solubility (a

molecular board should have a good solubility, which may require the inclusion of some solubilizing side chains), full *vs.* partial aromaticity (has implications for solubility), symmetry (has implications in Stage B, which are discussed in Chapter 4) and the distance between functional groups and side chains (the side chains should not adversely affect the reactivity of the functional groups sterically or electronically).

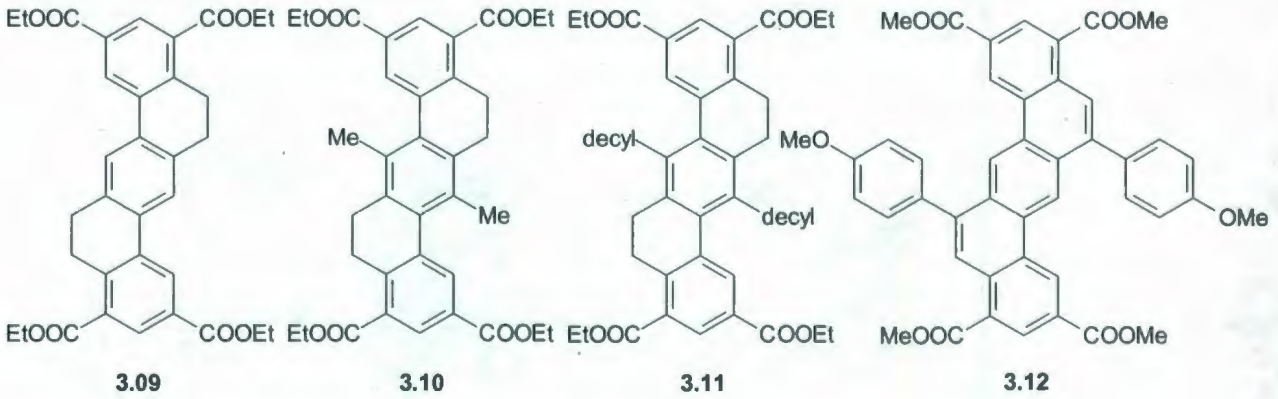
Vermeij, a doctoral student in the Bodwell group, first attempted to synthesize the molecular board **3.08**. In his work, tetrathiacylophane **3.07** was prepared from tetrathiol **3.05** and dibromide **3.06**, but the next step of the ring construction failed to give metacylophane **3.08** under a variety of conditions (Scheme 3.2).[2]




**Scheme 3.2** Vermeij's approach to molecular board **3.08**.

To simplify the synthesis, the Bodwell group then focused on the synthesis of dibenzo[*a*,*h*]anthracene-based boards. Two molecular boards **3.09** and **3.10** were synthesized by Hao Yu, a masters student in the Bodwell group, and Tieguang Yao, a doctoral student in the Bodwell group, respectively. Unfortunately, neither of these

boards could be carried on through Stage B because of their poor solubility (Figure 3.1).[3] Tieguang Yao solved this problem by replacing the methyl side chains with decyl groups in his synthesis of another molecular board, **3.11**.[4]




**3.09** **3.10** **3.11** **3.12**

**Figure 3.1** Dibenzo[*a*,*h*]anthracene-based boards prepared in the Bodwell group.

In this Chapter, a large scale synthesis of molecular board **3.11** is described, the objective being to use Yao's 12-step route and improve it where possible (Figure 3.1). The second molecular board **3.12**, which has aryl instead of alkyl solubilizing groups and different points of attachment, required the development of a new synthetic route.

## 3.2 Synthesis of molecular board 3.11

### 3.2.1 Retrosynthetic analysis

The intramolecular direct arylation, which was popularized by Fagnou[5], was identified as a key reaction for the closure of two six-membered rings (blue disconnection) (Figure 3.2). Sonogashira reactions were slated to be used to connect the three benzene rings (red disconnection) and attach the solubilizing side chains (purple disconnection). Application of these disconnections leads back to starting materials **2.06**,

**3.13** and **3.14**.

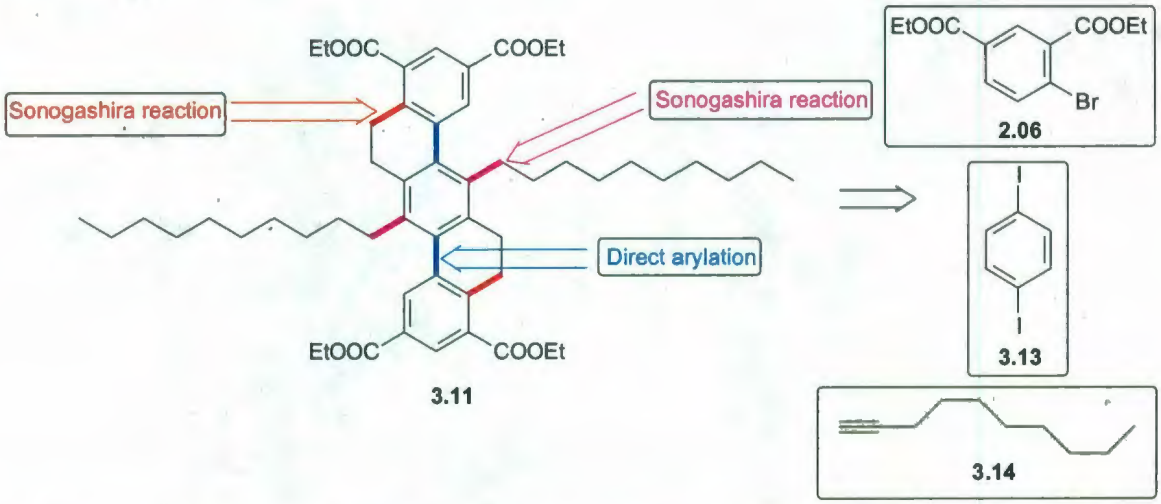
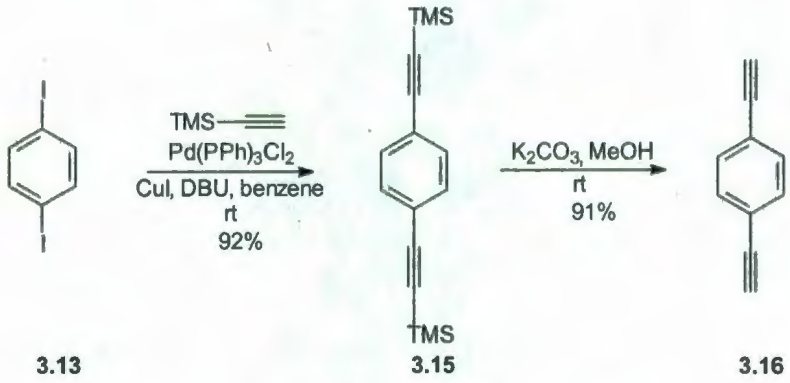


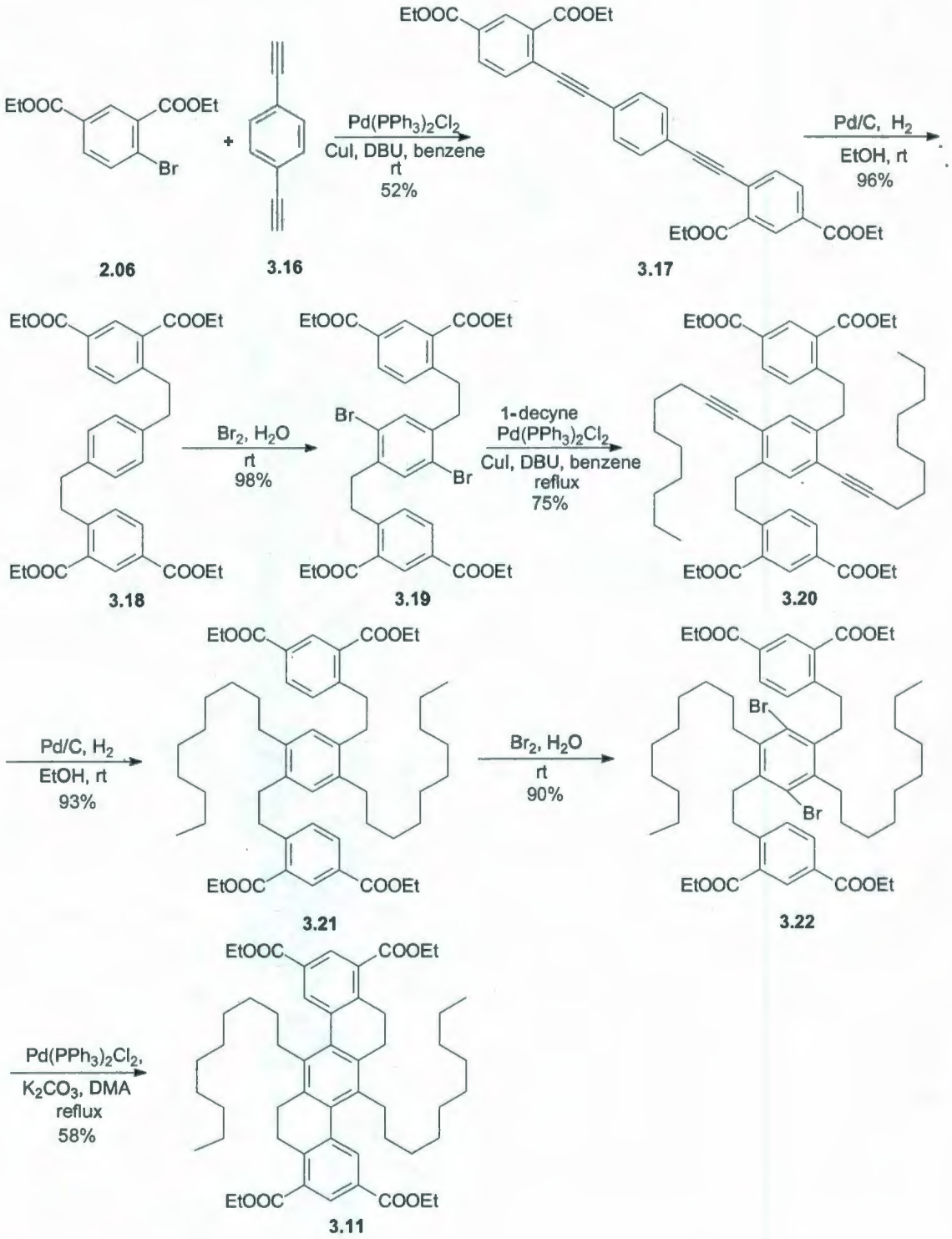

**Figure 3.2** Structures of molecular board **3.11** and key disconnections.

### 3.2.2 Results and Discussion




**Scheme 3.3** Synthesis of 1,4-diethynylbenzene (**3.16**).

The synthesis started with the union of two of the building blocks, diethyl 4-bromoisophthalate (**2.06**), the synthesis of which was discussed in Chapter 2 and 1,4-diethynylbenzene (**3.16**), which was obtained in good yield from 1,4-diiodobenzene (**3.13**) by Sonogashira reaction with trimethylsilylacetylene followed by protiodesilylaiton (Scheme 3.3).




**Scheme 3.4** Synthesis of molecular board **3.11**.

A Sonogashira cross-coupling reaction between diester **2.06** and diyne **3.16** afforded

diynetetraester **3.17** in 52% yield (Scheme 3.4). The alkyne functional groups were no longer needed, so they were saturated by using catalytic hydrogenation to afford tetraester **3.18**. Bromination of **3.18** then occurred with complete selectivity on the electron-rich central ring to give dibromotetraester **3.19**. Dibromotetraester **3.19** was then reacted with 1-decyne in a Sonogashira reaction to give **3.20**, in which all of the carbon atoms of molecular board **3.11** are present. Catalytic hydrogenation of the triple bonds afforded **3.21**. Another bromination of the electron-rich central ring afforded dibromide **3.22** and the molecular board **3.11** was generated using a double direct arylation reaction. The yield of last step (54-58%) was lower than that of Yao's synthesis (90%), but a total of 8 g this molecular board **3.11** was prepared from 4 separate reactions (4× 2 g of **3.22** each).

## 3.3 Synthesis of molecular board 3.12

### 3.3.1 Retrosynthetic analysis

Compared to **3.11**, molecular board **3.12** was designed to be a fully aromatic molecular board, *i.e.* all six-membered rings were to be aromatic (Figure 3.3). The solubilizing groups were also changed to aryl groups and their position of attachment was also changed. A twofold 2-ethynylbiphenyl cyclization reaction was planned to close two six-membered rings and generate the fully aromatic board (purple disconnection). A twofold Sonogashira reaction was to be used to attach the side chain precursors (red disconnection) and a twofold Suzuki reaction (blue disconnection) was identified as a

key reaction for connecting the three benzene units, which constitute the backbone of board **3.12**. These disconnections led back to three building blocks **3.23**, **3.24** and **3.25**. The main challenges in this approach were expected to be the synthesis of **3.23** and the achievement of chemoselectivity in its reactions with **3.24** and **3.25**. More specifically, building block **3.23** has two different functional groups –X and –Y (halides or pseudohalides), which must be able to react selectively with building block **3.24** (Suzuki reaction) and building block **3.25** (Sonogashira reaction).

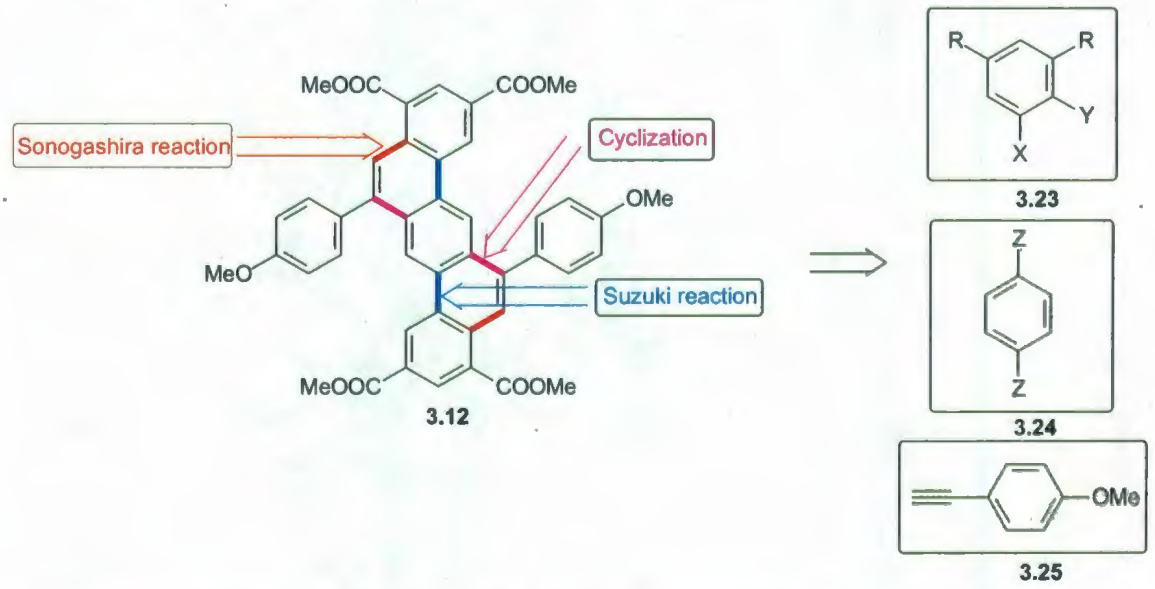
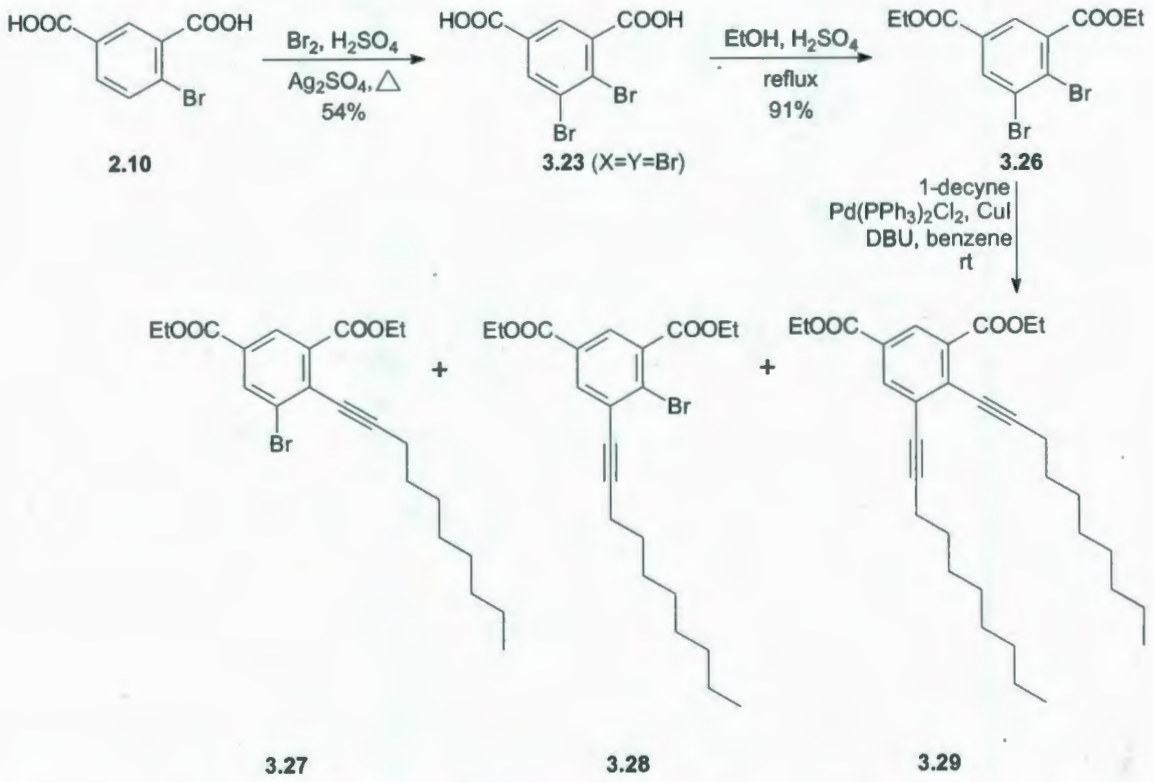



**Figure 3.3** Structures of molecular boards **3.12** and key disconnections.

### 3.3.2 Results and discussion

Chemoselectivity in the cross coupling reactions of building block **3.23** was expected to come from known reactivities of aryl halides (and pseudohalides) in various palladium-catalyzed coupling reactions: –I > –OTf > –Br > –Cl.[6] It is also known that the reactivity of a given halide can be influenced by its position relative to the other

functional groups on the same aromatic ring.[7] As such, the possibility of having X=Y in building block **3.23** was investigated first.




**Scheme 3.5** Selectivity studies of **3.23** (X=Y=Br) by palladium-catalyzed coupling reactions.

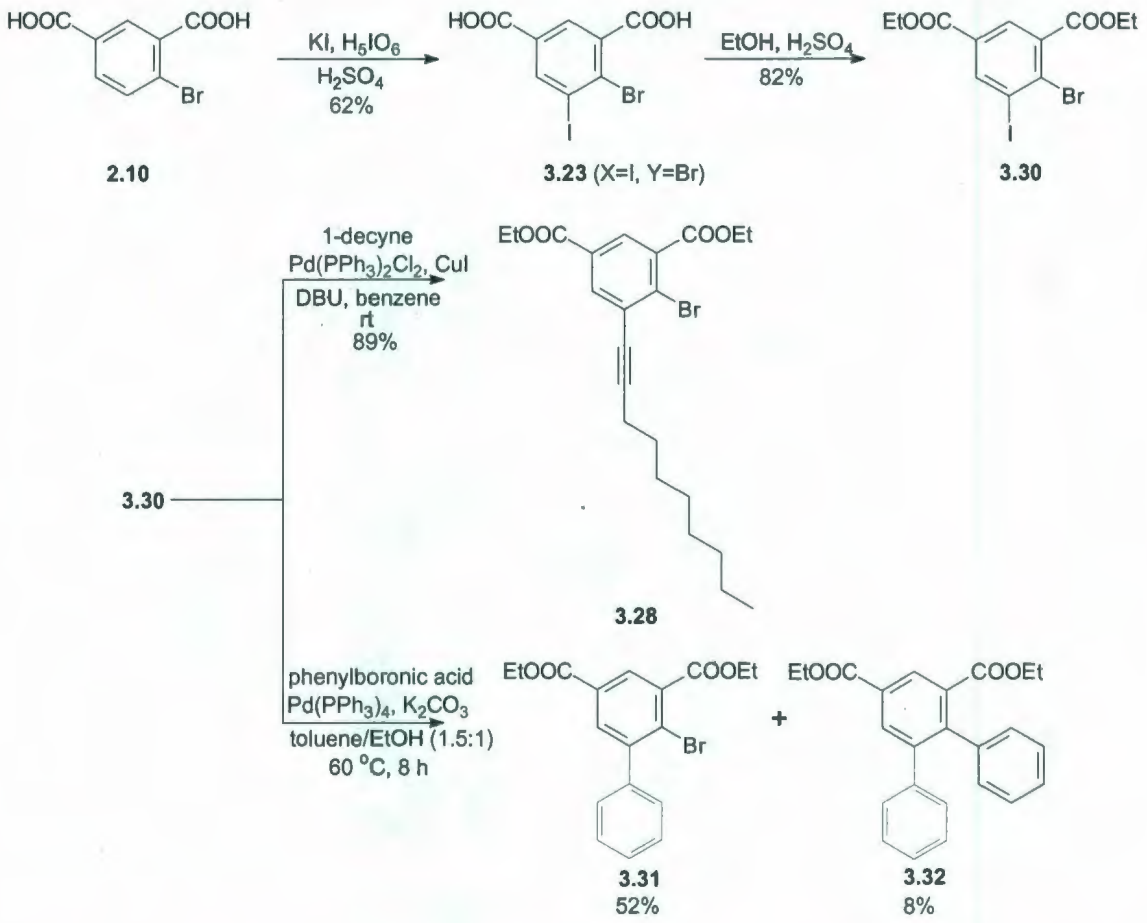
The synthesis of **3.23** (X=Y=Br) started with the bromination of 4-bromoisophthalic acid (**2.10**) (Scheme 3.5). The directing effects of the three substituents in **3.23** (X=Y=Br) (-COOH is *meta*-directing, -Br is *ortho*-, *para*-directing) work cooperatively to cause bromination to occur exclusively at the 5 position, thereby giving 4,5-dibromoisophthalic acid **3.23** (X=Y=Br). Esterfication of **3.23** (X=Y=Br) then gave diester **3.26** (91%). Because of their different relationships to the two ester groups, the two –Br groups in **3.26** were expected to exhibit different reactivity. A Small-scale Sonogashira reaction of

**3.26** with 1-decyne at room temperature gave a mixture of products. Mass spectrometric analysis of the crude reaction mixture indicated the presence of starting dibromide **3.26**, a monoyne (either **3.27** or **3.28**) and diyne **3.29**.

Column chromatography afforded a small amount (6%) of monoyne **3.28**. The aromatic region of the $^1$H NMR spectrum of the monoyne consisted of a nearly degenerate AB system ($\delta_A$=8.143, $\delta_B$=8.139 ppm, $J$=2.2 Hz). By comparison, the aromatic region of the $^1$H NMR spectrum of starting dibromide **3.26** contains an AX system ($\delta_A$=8.35, $\delta_B$=8.17 ppm, $J$=1.8 Hz). The ~0.2 ppm change in chemical shift of one of the aromatic protons in going from 8.35 to 8.17 ppm suggests that the Sonogashira reaction occurred adjacent to one of the aromatic H atoms, *i.e.* the monoyne is **3.28** not **3.27**. This tentative assignment was confirmed later by the synthesis of **3.28** via a different route. The observation of selective Sonogashira reaction at the 5-Br substituent indicates that steric effects outweigh electronic effects in **3.26**.[8] Despite the promising selectivity, the yield of **3.28** was low and its isolation was nontrivial. As such, a different version of building block **3.23** in which X≠ Y was targeted.

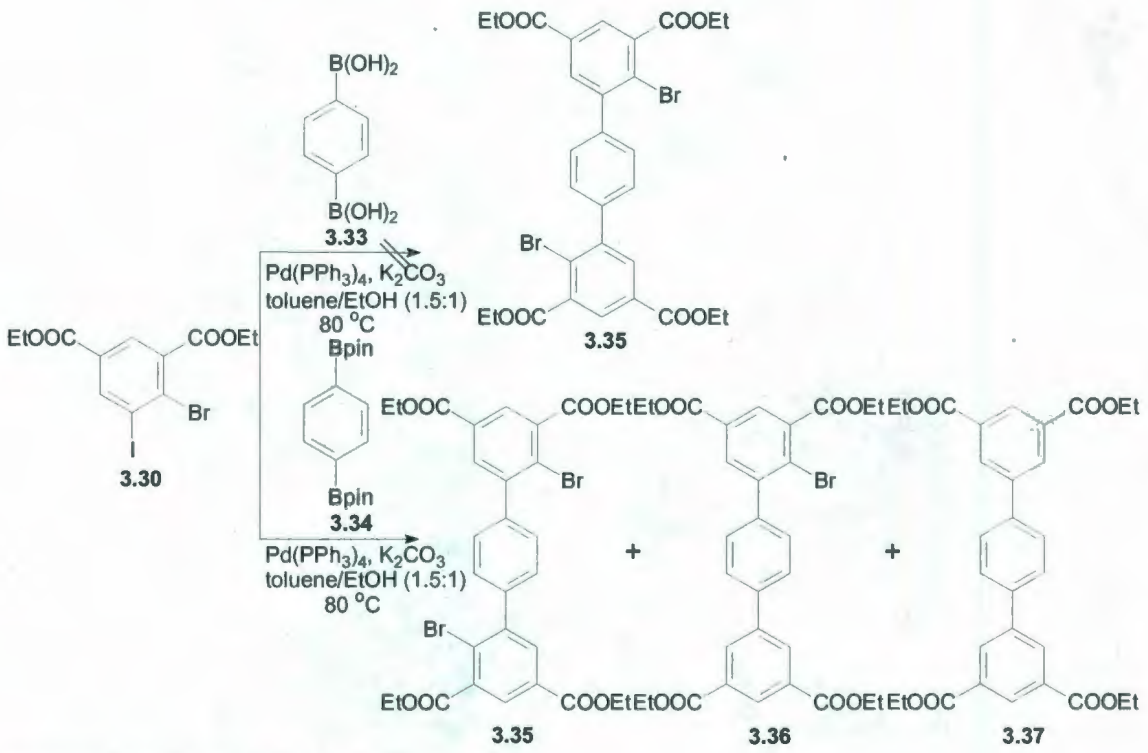
Iodination of **2.10** afforded the 4-bromo-5-iodoisophthalic acid (**3.23**) (X=I, Y=Br) in 62% yield.[9] In this case, the Sonogashira reaction was expected to occur with excellent selectivity at the 5-iodo substituent. Indeed, Sonogashira reaction between **3.30** and 1-decyne at room temperature again afforded **3.28** (*m/z*=436) in 89%. The Suzuki reaction between **3.30** and phenylboronic acid at 60 °C was also selective, giving the

mono-coupling product **3.31** in 52% yield along with bis-coupling byproduct **3.32** in 8% yield (Scheme 3.6).



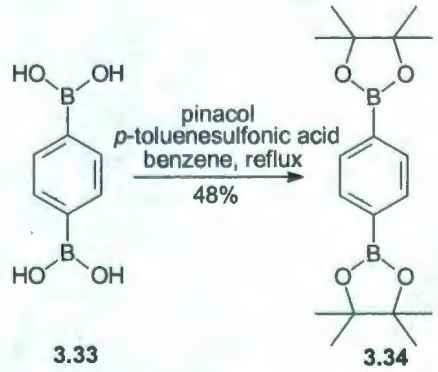

**Scheme 3.6** Selectivity studies of **3.23** (X=I, Y=Br) by palladium-catalyzed coupling reactions.

Unfortunately, the double Suzuki reaction between **3.30** and 1,4-phenylenebis(boronic acid) (**3.33**) under the same conditions did not give dibromide **3.35** (Scheme 3.7). The starting material **3.30** was completely consumed, but no new mobile spots were observed by tlc analysis.




**Scheme 3.7** Double Suzuki reaction of **3.30**.

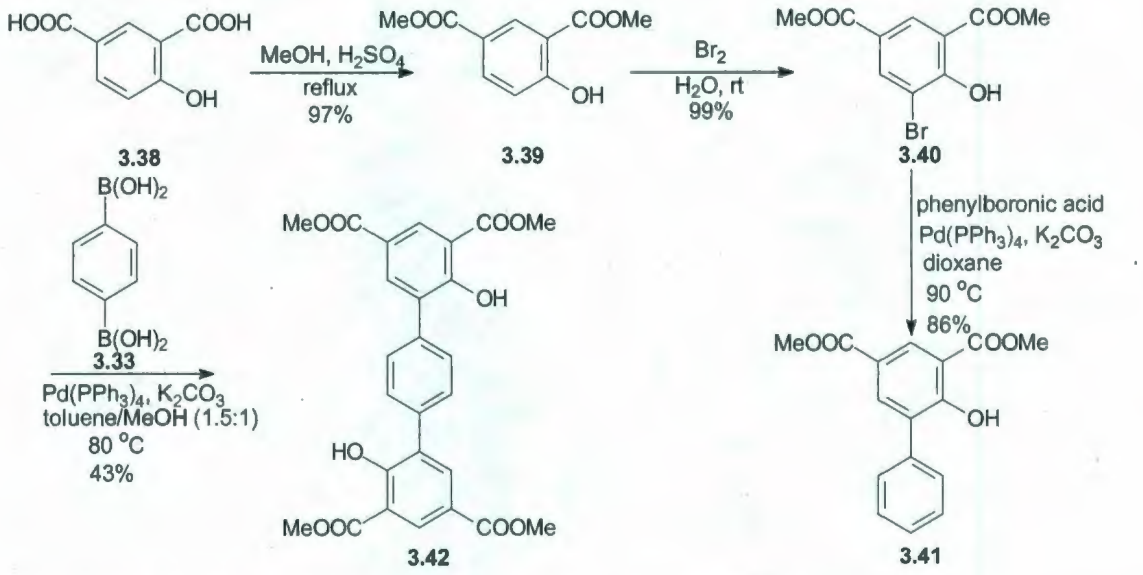
The less reactive 1,4-phenylenebis(boronate pinacol ester) (**3.34**) was synthesized from bis(boronic acid) **3.33** using *p*-toluenesulfonic acid-catalyzed esterfication (Scheme 3.8).[10]




**Scheme 3.8** Pinacol esterfication of 1,4-phenylenebis(boronic acid) **3.33**.

Suzuki reaction of **3.34** with **3.30** also resulted in complete consumption of **3.30**, but gave a mixture of **3.35**, **3.36** and **3.37** according to $^1$H NMR and mass spectrometric

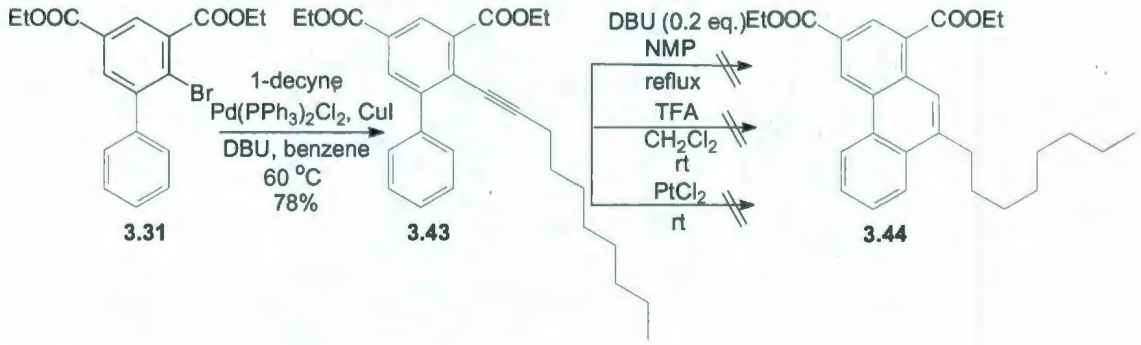
analysis (Scheme 3.7). A partial separation of the doubly protodebrominated product **3.37** was achieved by column chromatography, but no pure sample of the desired dibromide **3.35** could be obtained.




**Scheme 3.9** Synthesis of double Suzuki reaction product **3.42**.

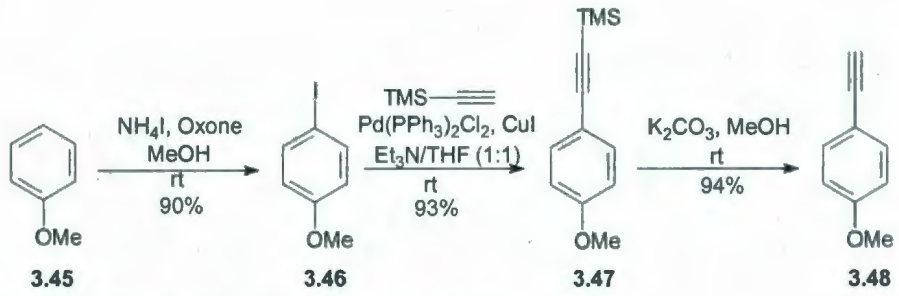
Another synthetic route was designed, which started from commercially available 4-hydroxyisophthalic acid (**3.38**) (Scheme 3.9). Dimethyl-5-bromo-4-hydroxy isophthalate (**3.40**) was obtained using an esterfication/bromination sequence (96%, 2 steps). This route had several advantages. First, the –OH group is strongly activating, which enabled the completely regioselective bromination of **3.39** to process virtually quantitatively at room temperature. Second, the –OH group does not participate in Pd-catalyzed cross-coupling reactions, which removes any chemoselectivity problems. Furthermore, the –OH group can be converted into a triflate group when required. In fact, the –OH group did not need to be protected. Suzuki reaction between **3.40** and

phenyleneboronic acid afforded **3.41** in 86% yield. In many Suzuki reactions, $H_2O$ is used as a co-solvent to improve the solubility of the base. However, in this case, the reaction was performed under anhydrous conditions to prevent hydrolysis of the ester groups. Attention was then turned to the double Suzuki reaction between **3.33** and **3.40** to afford **3.42**. After some experimentation, it was found that 0.6 eq. of bis(boronic acid) **3.33**, 10 mol% $Pd(PPh_3)_4$, 10 eq. of $K_2CO_3$ and toluene/MeOH (1.5:1) as the solvent gave **3.42** in the best yield (43%).



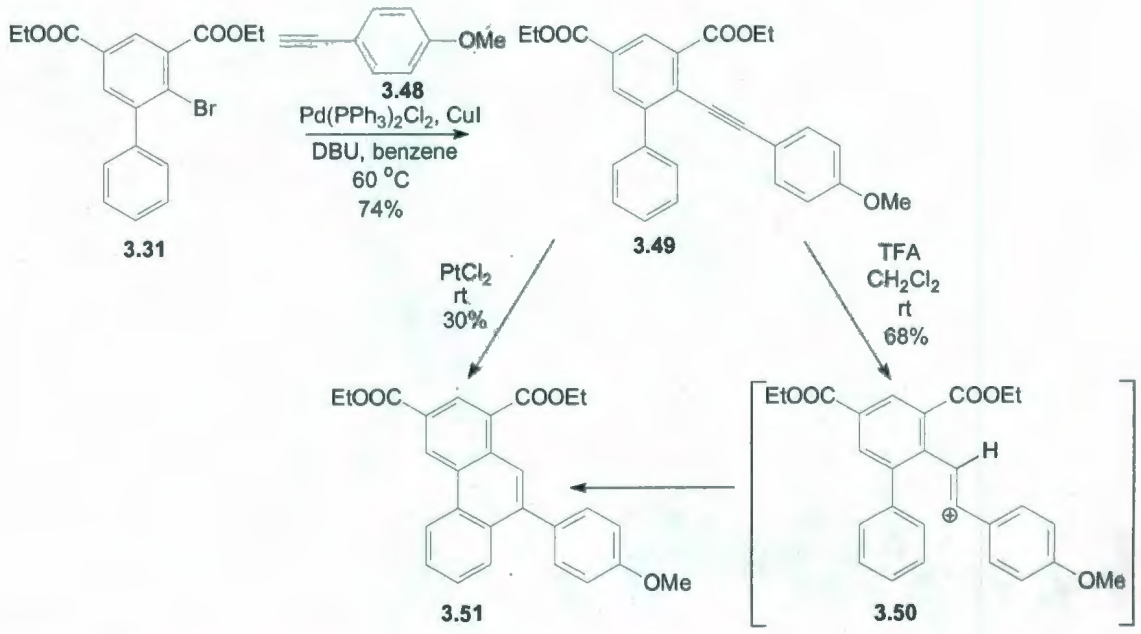

**Scheme 3.10** Cyclization through decynyl side chain.

To test the viability of a decynyl side chain as a cyclization precursor, a Sonogashira reaction of **3.31** (Scheme 3.6) with 1-decyne was then performed. This gave **3.43** in 78% yield (Scheme 3.10). However, three different cyclization conditions: base-catalyzed cyclization using DBU,[11] acid-catalyzed cyclization using TFA[12] and metal-catalyzed cyclization[13] all failed to afford ring-closed compound **3.44**. Either intractable material (DBU) or recovered starting material (TFA or $PtCl_2$) was obtained.




**Scheme 3.11** Synthesis of compound **3.48**.

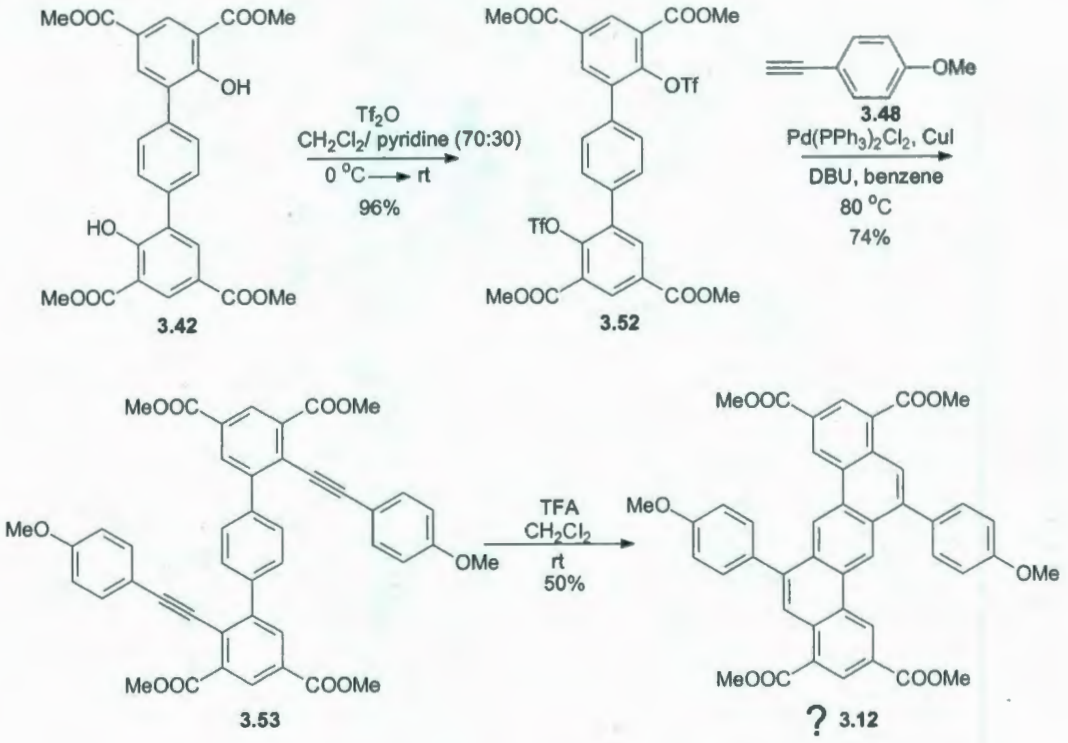
The use of an aryl side chain was then investigated. The required alkyne **3.48** for Sonagashira reaction with **3.31** was synthesized from methoxybenzene (**3.45**) (Scheme 3.11). Iodination of **3.45** gave **3.46** (90%)[14] and **3.46** reacted with TMS-acetylene under Sonogashira conditions to afford **3.47**. The desired alkyne **3.48** was then obtained by removal of the TMS group.




**Scheme 3.12** Cyclization of 3.49 to afford "half board" **3.51** with an aryl side chain.

A Sonogashira reaction between **3.31** and **3.48** afforded **3.49** (74%), which easily underwent TFA-catalyzed cyclization to afford phenanthrene **3.51** in 68% yield (Scheme

3.12).[12] In this case, the methoxy group presumably helps the cyclization by stabilizing developing positive charge on the benzylic carbon atom indicated in structure **3.50**. Whether or not a full carbocation actually forms is debatable, but the mechanism is likely an intramolecular electrophilic aromatic substitution. $PtCl_2$-catalyzed cyclization also afforded **3.51**, but the yield (30%) was considerably lower than the electrophilic cyclization using TFA.




**Scheme 3.13** Synthesis of molecular board **3.12**.

After the successful synthesis of a "half molecular board" **3.51**, the same method was used to synthesize molecular board **3.12** (Scheme 3.13). The two –OH groups in **3.42** were converted to triflate groups using triflic anhydride in $CH_2Cl_2$/pyridine (70:30) (96%).[15] Double Sonogashira coupling between **3.48** and **3.52** gave diyne **3.53** in 74%

yield and **3.53** reacted with TFA to afford a fluorescent compound with the correct mass (*m/z*=722) for molecular board **3.12** (50%).

The $^1$H NMR spectrum of the product was as expected, expect for the aromatic signals of the 4-methoxyphenyl substituent. Instead of the expected well-resolved AA'BB' (or AA'XX') system, four very broad singlets were observed at δ 6.85, 6.69, 6.51 and 6.39 ppm. Suspecting that the product was conformationally mobile, a variable temperature NMR experiment was performed (Figure 3.4). Upon cooling to 5 °C, four somewhat broad doublets emerged.

The roofing of the signals suggested that the protons responsible for the signals at δ 6.87 and 6.70 ppm were coupled, as were those responsible for the signals at δ 6.52 and 6.39 ppm. Apparently, for each methoxyphenyl group, all four protons are in different environments, but the two protons *ortho* to the methoxy group exchange their environments as do the two protons *meta* to the methoxy group. This means that the signals at δ 6.87 and 6.70 ppm (midpoint δ 6.79 ppm) should coalesce and the signals at δ 6.52 and 6.39 ppm (midpoint δ 6.50 ppm) should coalesce to give an AA'BB' spectrum at high temperature. The observation of a broad singlet at δ 6.60 ppm at 55 °C is entirely consistent with this expectation. A crude estimate of the energy barrier of the observed processes in $\Delta G = 15.8 \pm 0.5$ kcal/mol (Appendix 2).[16] A reasonable explanation of these observation is that the TFA-catalyzed cyclization of **3.53** did not afford dibenzo[*a*,*h*]anthracene derivative **3.12**, but rather the unexpected isomeric picene

derivative **3.54**.

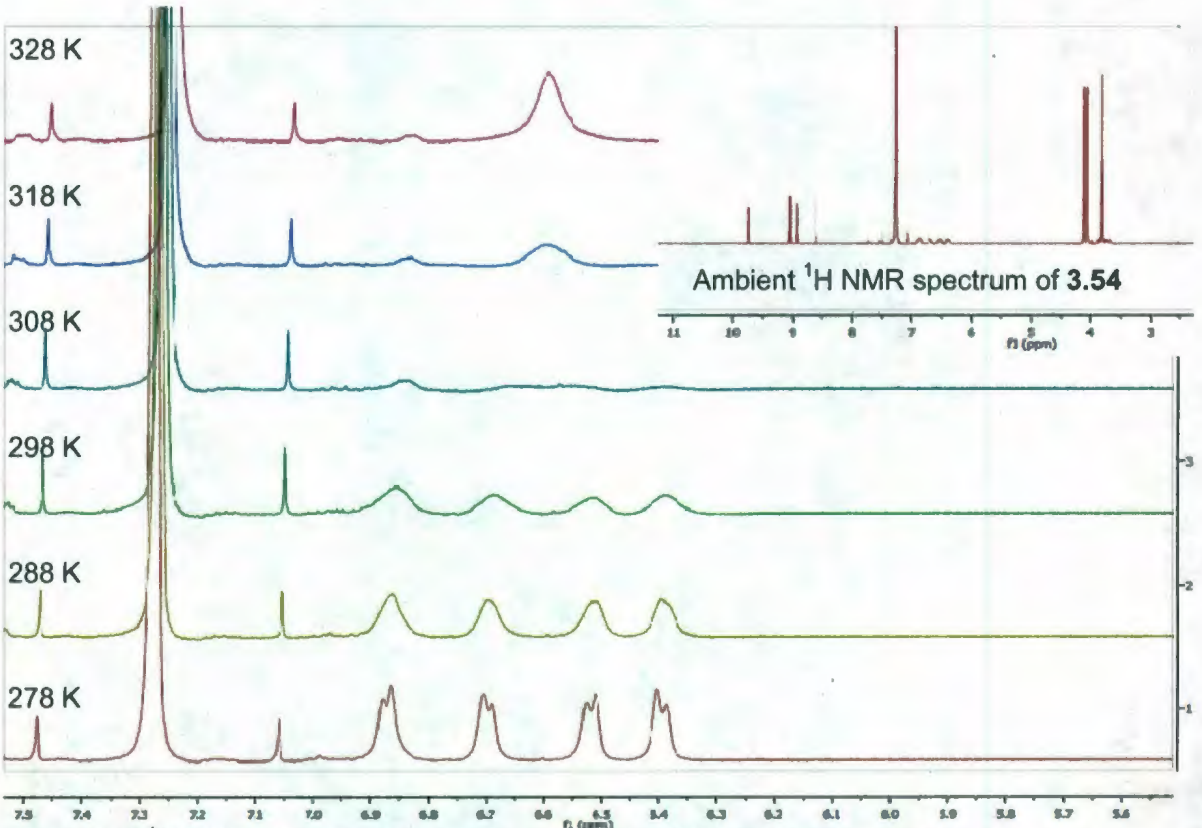
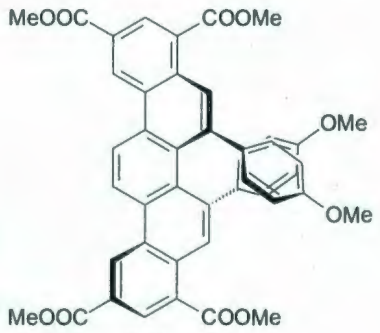



**Figure 3.4** $^1$H NMR study on molecular board **3.54** at different temperatures.

To avoid occupying the same space, the two 4-methoxyphenyl groups cause the picene system to twist out of planarity, which lowers the molecular symmetry $C_2$ from $C_{2v}$. The exchange process can either be rotations of the 4-methoxyphenyl groups around their respective biaryl bonds or degenerate twisting of the picene system from one enantiomeric form to the other (Figure 3.5). AM1 calculations predict picene derivative **3.54** to be 14.8 kcal/mol higher in energy than dibenzo[*a*,*h*]anthracene derivative **3.12**. Selection of the pathway leading to **3.54** must occur before the very unfavorable steric interaction in **3.56** developed.

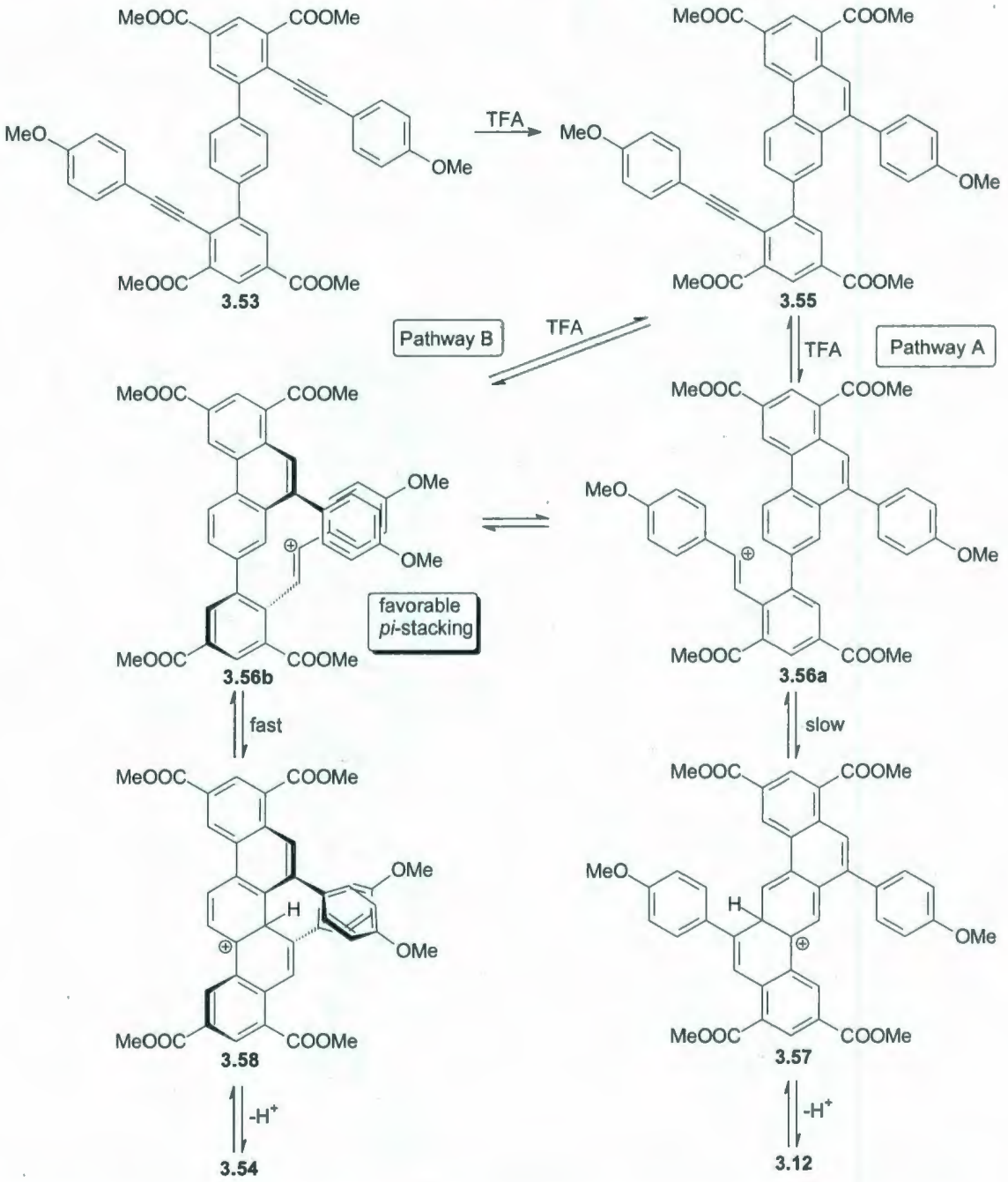



**3.54**

**Figure 3.5** Structure of picene derivative **3.54**.

An explation of the unexpected outcome of this reaction comes out of a step-by-step consideration of the assumed reaction mechanism (Scheme 3.14). The first cyclization event (from **3.53** to **3.55**) is common to both reaction pathways. Protonation of **3.55** affords a carbocation **3.56**, which can potentially cyclize at either of two positions, one of which ultimately leads to **3.12** and the other to **3.54**. Examination of molecular models revealed that carbocation **3.56** can adopt a seemingly unstrained conformation in which the electron-rich 4-methoxyphenyl group attached to the phenanthrene system sits over the other 4-methoxyphenyl group, which bears a significant portion of the positive charge of the benzylic carbocation. Thus, it would appear that π-stacking between the two pendant aryl groups of complementary electronic nature predisposes the molecule to cyclize exclusively to give carbocation **3.56b** and not **3.56a**. The presence of an $sp^3$-hybridized carbon atom in **3.58** imports a twisted structure to the pentacyclic system, which appears to allow the π-stacking between the 4-methoxyphenyl groups to be maintained. When **3.58** undergoes deprotonation to give **3.54**, the pentacyclic system now prefers a planar structure and only at this late stage do the unfavorable steric

interactions between the 4-methoxyphenyl groups emerge in earnest.

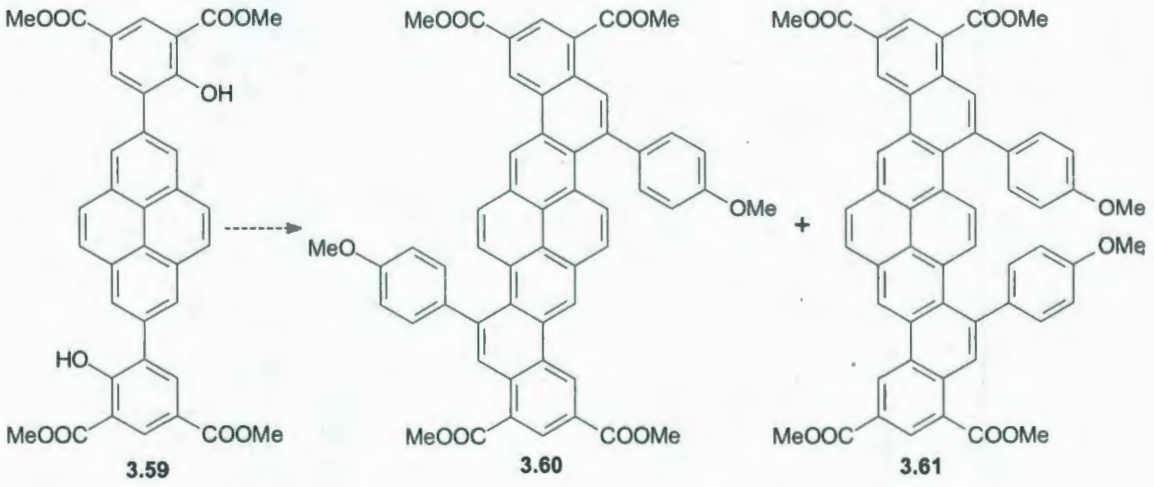



**Scheme 3.14** The assumed reaction mechanism for a double TFA-catalyzed cyclization.

The formation of picene derivative **3.54** is interesting, but it is an unwelcome result.

The strategy for the synthesis of aromatic belts requires planar or nearly planar boards. However **3.54** is considerably twisted and has aryl groups situated above and below the average plane of the picene system. These features would not only be expected to hinder the union of two boards, but also to inhibit the bending of the two boards during the VID reaction at the end of the synthesis. For these reasons, this approach to board **3.12** was concluded.

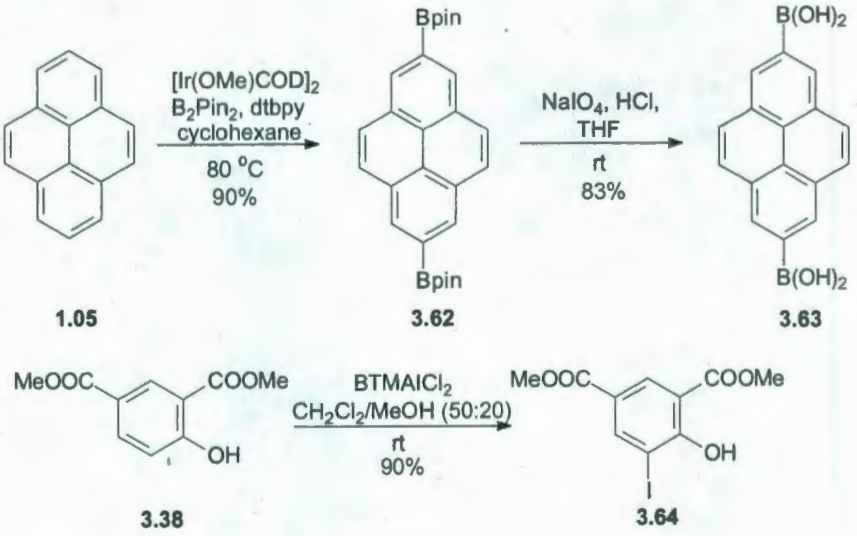
### 3.4 Future works




**Scheme 3.15** Preparation of a larger sized molecular board **3.60** and its isomer **3.61**.

Considering that problems in the attempted synthesis of **3.12** arose from the proximity of the 4-methoxyphenyl groups, it would be worthwhile to move them apart by using a 2,7-pyrenylene spacer instead of a 1,4-phenylene spacer, *i.e.* **3.59** (Scheme 3.15). Not only will this action spread out the two aryl substituents, but it will also give larger sized molecular boards **3.60** and **3.61**. The disadvantage of this approach will be the generation of two isomeric boards, which will probably be hard to separate. Synthetically,

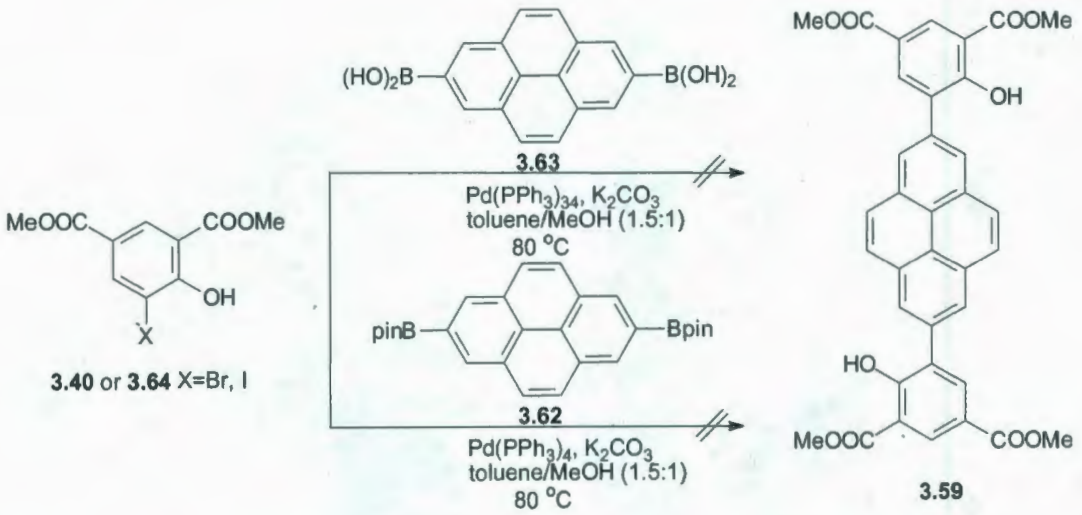
the approach will be the same as the synthesis of molecular board **3.12**, except that bis(boronate ester) **3.62** or bis(boronic acid) **3.63** will be used in place of 1,4-phenylene bis(boronic acid).




**Scheme 3.16** Synthesis of two new building blocks.

Preliminary work in this direction was initiated. The central building block, bis(boronate pinacol ester) **3.62**, was synthesized using iridium-catalyzed boronation of pyrene (80%),[17] and the more reactive bis(boronic acid) **3.63** was generated upon hydrolysis of **3.62**.[18]

Unfortunately, initial Suzuki reaction between **3.62** or **3.63** and bromide **3.40** or the corresponding iodide **3.64**[19] (synthesized in 90% yield from **3.38**, Scheme 3.16) did not afford **3.59** (Scheme 3.17). However, there is still plenty of room to optimize the conditions of these reactions, which are still under investigation in the Bodwell group.




**Scheme 3.17** Attempt to synthesize molecular board **3.60** using the Suzuki reaction.

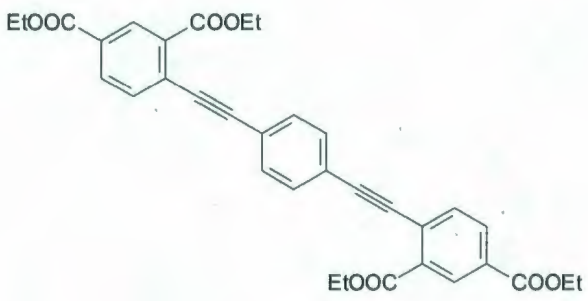
### 3.5 Conclusion

Two soluble molecular boards **3.11** and **3.54** have been synthesized. The synthesis of molecular board **3.11** from *m*-xylene required 12 steps and the overall yield was 6%. A total of 8 g of this compound was produced and it was used to synthesize aromatic belt precursors (see Chapter 4). Another molecular board **3.54**, which was not the intended target, was synthesized in 9 steps from 4-hydroxyisophthalic acid and overall yield is 14%. The twisted structure of **3.54** makes it a poor candidate for subsequent conversion into an aromatic belt. However, the synthetic route by which it was synthesized could possibly be used to synthesize larger sized molecular board *e.g.* **3.60** and **3.61**.

### 3.6 Experimental section

**General**: For general procedures, please refer to the experimental section in Chapter 3.

**1,4-Bis(2,4-bis(ethoxycarbonyl)phenylethynyl)benzene (3.17)**

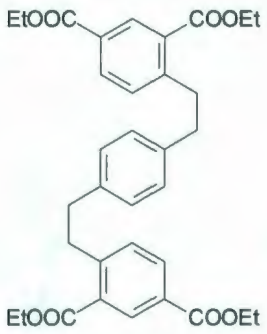



**3.17**

To a solution of diethyl 4-bromoisophthalate (**2.06**) (18.00 g, 59.77 mmol) in degassed benzene (250 mL) were added $Pd(PPh_3)_2Cl_2$ (628 mg, 0.901 mmol) and CuI (291 mg, 1.52 mmol). After 5 min a solution of DBU (17.96 g, 118.0 mmol) and 1,4-diethynylbenzene (**3.16**) (6.030 g, 47.80 mmol) in degassed benzene (50 mL) was added dropwise through a dropping funnel. The reaction mixture was stirred at room temperature for 18 h. The precipitate was removed by suction filtration. The resulting residue was concentrated under reduced pressure and dissolved in EtOAc (300 mL). The organic layer was washed with saturated aqueous $NH_4Cl$ solution (150 mL), washed with $H_2O$ (150 mL) and washed with brine (100 mL). The organic layer was dried over $MgSO_4$ and concentrated under reduced pressure. The residue was subjected to column chromatography (30:70 EtOAc/hexanes) to afford **3.17** as a colorless oil (8.861 g, 15.65 mmol, 52%): $R_f(CH_2Cl_2)$: 0.25; $^1$H NMR (500 MHz, $CDCl_3$): δ 8.63 (d, *J*=1.8 Hz, 2H), 8.15 (dd, *J*=10.1, 1.8Hz, 2H), 7.71 (d, *J*=11.9 Hz, 2H), 7.59 (s, 4H), 4.46 (q, *J*=7.1 Hz, 4H), 4.35 (q, *J*=7.1 Hz, 4H), 1.432 (t, *J*=7.1 Hz, 6H), 1.425 (t, *J*=7.1 Hz, 6H); $^{13}$C NMR (125 MHz, $CDCl_3$): δ 165.8, 165.7, 134.5, 132.8, 132.5, 132.2, 132.0, 130.4, 128.0, 123.8,

97.2, 90.4, 61.96, 61.91, 14.8, 14.7; LCMS [APCl(+)] *m/z* (%): 567 ($[M+H]^+$, 100); HRMS [EI(+)] calcd for $C_{34}H_{30}O_8$: 566.1941, found: 566.1960.

**1,4-Bis(2-(2,4-bis(ethoxycarbonyl)phenyl)phenyl)ethyl)benzene (3.18)**

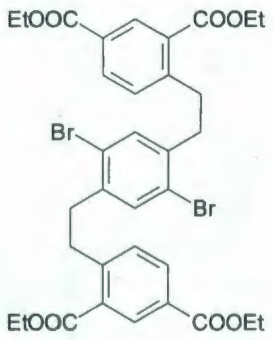



**3.18**

To a solution of tetraesterdiyne **3.17** (15.40 g, 27.18 mmol) in EtOH (250 mL) was added 10% Pd/C (6.160 g). The reaction mixture was stirred at room temperature under $H_2$ (balloon) and the reaction was monitored by $^1$H NMR. After the reaction was completed (18 h), this mixture was concentrated under reduced pressure. The residue was dissolved in $CH_2Cl_2$ (250 mL) and the catalyst was removed by suction filtration. The filtrate was concentrated under reduced pressure and recrystallization of this residue from EtOH gave **3.18** as an off-white solid (15.00 g, 26.09 mmol, 96%): $R_f$($CH_2Cl_2$): 0.24; mp (EtOH): 101.0-103.0 °C; IR (neat) ν: 2919 (w), 1720 (s), 1291 (m), 1224 (s), 1118 (m), 1073 (m), 1023 (m), 763 (m), 709 (m) $cm^{-1}$; $^1$H NMR (500 MHz, $CDCl_3$): δ 8.54 (d, *J*=1.9 Hz, 2H), 8.04 (dd, *J*=8.0, 1.9 Hz, 2H), 7.25 (d, *J*=8.1 Hz, 2H), 7.11 (s, 4H), 4.42 (q, *J*=7.1 Hz, 4H), 4.41 (q, *J*=7.1 Hz, 4H), 3.30 (t, *J*=7.9 Hz, 4H), 2.88 (t, *J*=8.3 Hz, 4H), 1.43 (t, *J*=7.1 Hz, 6H), 1.42 (t, *J*=7.1 Hz, 6H); $^{13}$C NMR (125 MHz, $CDCl_3$): δ 167.3,

166.3, 148.8, 139.5, 132.8, 132.3, 131.8, 130.6, 128.91, 128.90, 61.60, 61.55, 37.8, 37.1, 14.8, 14.7; LCMS [APCI(+)] *m/z* (%): 575 ($[M+H]^+$, 80), 529 (63), 515 (12), 483 (12); HRMS [EI(+)] calcd for $C_{34}H_{38}O_8$: 574.2567, found: 574.2571.

**1,4-Dibromo-2,5-bis(2-(2,4-bis(ethoxycarbonyl)phenyl)ethyl)benzene (3.19)**

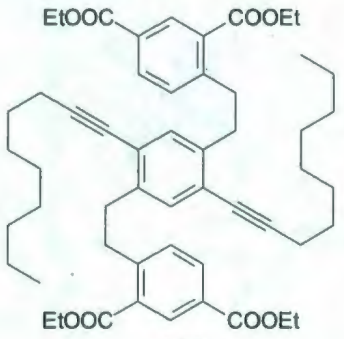



**3.19**

To a mixture of tetraester **3.18** (8.492 g, 14.79 mmol) in $H_2O$ (250 mL) was added $Br_2$ (23.60 g, 14.77 mmol) by syringe. This reaction was stirred for 48 h at room temperature. The excess $Br_2$ was quenched by the addition of a saturated aqueous $NaHSO_3$ solution (25 mL). The resulting mixture was extracted with $CH_2Cl_2$ (200 mL) and the organic layer was washed with $H_2O$ (200 mL), washed with brine (150 mL), dried over $MgSO_4$ and concentrated under reduced pressure. The residue was subjected to column chromatography ($CH_2Cl_2$) to give **3.19** as a white solid (10.64 g, 14.50 mmol, 98%): $R_f$($CH_2Cl_2$): 0.21; mp: 142.5-144.0 °C; IR (neat) ν: 2926 (w), 1717 (s), 1390 (w), 1303 (m), 1225 (s), 1137 (m), 1107 (m), 1054 (m), 758 (s), 713 (s) $cm^{-1}$; $^1H$ NMR (500 MHz, $CDCl_3$): δ 8.56 (d, *J*=1.8 Hz, 2H), 8.07 (dd, *J*=8.0, 1.9 Hz, 2H), 7.40 (s, 2H), 7.31 (d, *J*=8.0 Hz, 2H), 4.41 (q, *J*=7.1 Hz, 4H), 4.40 (q, *J*=7.1 Hz, 4H), 3.28 (t, *J*=7.8 Hz, 4H),

2.99 (t, *J*=8.3 Hz, 4H), 1.43 (t, *J*=7.1 Hz, 6H), 1.41 (t, *J*=7.2 Hz, 6H); $^{13}$C NMR (125 MHz, $CDCl_3$): δ 167.1, 166.2, 148.0, 140.8, 134.5, 133.0, 132.4, 131.8, 130.6, 129.2, 123.6, 61.7, 61.6, 37.4, 35.0, 14.8, 14.7; LCMS [APCl(+)] *m/z* (%): 735 ([M+H]$^+$, $^{81}Br^{81}Br$, 25), 733 ([M+H]$^+$, $^{79}Br^{81}Br$, 67), 731 ([M+H]$^+$, $^{79}Br^{79}Br$, 33), 704 (8), 689 (11); HRMS [EI(+)] calcd for $C_{34}H_{36}O_8Br_2$($^{79}Br^{81}Br$): 732.0781, found: 730.0767.

**1,4-Didecynyl-2,5-bis(2-(2,4-bis(ethoxycarbonyl)phenyl)ethyl)benzene (3.20)**

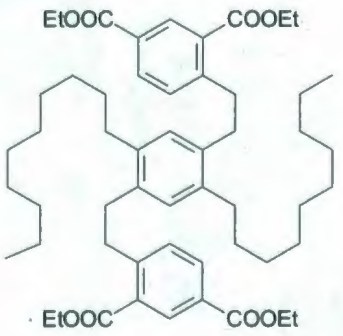



**3.20**

To a mixture of dibromide **3.19** (10.86 g, 14.82 mmol) and degassed benzene (200 mL) in a 500 mL round-bottomed flask was added $Pd(PPh_3)_2Cl_2$ (519 mg, 0.742 mmol) and CuI (282 mg, 1.48 mmol). After this mixture had been stirred for 5 min, DBU (6.762 g, 44.42 mmol) and 1-decyne (5.120 g, 37.11 mmol) were added to the solution and the resulting mixture was stirred at room temperature for 10 min and then heated at reflux overnight. The mixture was cooled to room temperature and the precipitate was removed by suction filtration. The filtrate was washed with saturated aqueous $NH_4Cl$ solution (70 mL), washed with $H_2O$ (150 mL), washed with brine (100 mL), dried over $MgSO_4$ and concentrated under reduced pressure. The residue was subjected to column

chromatography (30:70 $CH_2Cl_2$/hexanes→$CH_2Cl_2$) to give **3.20** as a tan solid (9.405 g, 11.11 mmol, 75%): $R_f$($CH_2Cl_2$): 0.52; mp: 73.0-75.0 °C; IR (neat) ν: 2923 (w), 1718 (m), 1221 (m), 1111 (m), 758 (s) $cm^{-1}$; $^1H$ NMR (500 MHz, $CDCl_3$): δ 8.56 (d, *J*=1.6 Hz, 2H), 8.05 (dd, *J*=8.0, 1.7 Hz, 2H), 7.28 (d, *J*=8.1 Hz, 2H), 7.22 (s, 2H), 4.42 (q, *J*=7.1 Hz, 4H), 4.40 (q, *J*=7.1 Hz, 4H), 3.32 (t, *J*=7.4 Hz, 4H), 3.03 (t, *J*=8.3 Hz, 4H), 2.44 (t, *J*=7.8 Hz, 4H), 1.63-1.59 (m, 4H), 1.43 (t, *J*=7.1 Hz, 6H), 1.41 (t, *J*=7.1 Hz, 6H), 1.30-1.26 (m, 20H), 0.87 (t, *J*=6.6 Hz, 6H); $^{13}C$ NMR (125 MHz, $CDCl_3$): δ 167.1, 166.2, 148.9, 141.0, 132.8, 132.7, 132.2, 131.7, 130.6, 128.8, 123.2, 95.3, 79.5, 61.5, 61.4, 35.9, 35.7, 32.2, 29.6, 29.5, 29.4, 29.2, 23.0, 20.1, 14.7, 14.5 (one signal less than expected); LCMS [APCl(+)] *m/z* (%): 847 ([M+H]$^+$, 100); HRMS [EI(+)] calcd for $C_{54}H_{70}O_8$: 846.5071, found: 846.5051.

**1,4-Didecyl-2,5-bis(2-(2,4-bis(ethoxycarbonyl)phenyl)ethyl)benzene (3.21)**

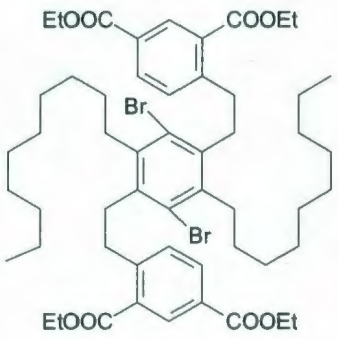



**3.21**

To a solution of tetraesterdiyne **3.20** (7.650 g, 9.037 mmol) in EtOH (200 mL) was added 10% Pd/C (2.311 g). The reaction mixture was stirred at room temperature under $H_2$ (balloon) and monitored by $^1H$ NMR. After the reaction was complete (1 d), this

mixture was concentrated under reduced pressure. The residue was dissolved in $CH_2Cl_2$ (150 mL), and the catalyst was removed by suction filtration. The filtrate was concentrated under reduced pressure and the residue was subjected to column chromatography ($CH_2Cl_2$) to give **3.21** as a white solid (7.182 g, 8.404 mmol, 93%): $R_f$ ($CH_2Cl_2$): 0.66; mp: 68.0-70.5 °C; IR (neat) ν: 2924 (w), 1723 (s), 1284 (w), 1226 (s), 1134 (w), 1110 (w), 1078 (m), 1029 (w), 758 (s) $cm^{-1}$; $^1H$ NMR (500 MHz, $CDCl_3$): δ 8.53 (d, *J*=1.9 Hz, 2H), 8.04 (dd, *J*=8.0, 1.9 Hz, 2H), 7.24 (d, *J*=8.0 Hz, 2H), 6.90 (s, 2H), 4.25 (q, *J*=7.1 Hz, 4H), 4.21 (q, *J*=7.1 Hz, 4H), 3.26 (t, *J*=7.8 Hz, 4H), 2.86 (t, *J*=8.3 Hz, 4H), 2.52 (t, *J*=7.9 Hz, 4H), 1.42 (t, *J*=7.1 Hz, 6H), 1.41 (t, *J*=7.1 Hz, 6H), 1.29-1.26 (m, 32H), 0.87 (t, *J*=6.8 Hz, 6H); $^{13}C$ NMR (125 MHz, $CDCl_3$): δ 167.3, 166.3, 149.1, 138.5, 137.0, 132.7, 132.2, 131.8, 130.7, 130.6, 128.8, 61.6, 61.5, 34.5, 32.7, 32.3, 32.0, 30.3, 30.10, 30.06, 30.01, 29.8, 23.1, 14.8, 14.7, 14.5 (one signal less than expect); LCMS [APCl(+)] *m/z* (%): 855 ($[M+H]^+$, 21), 827 (16), 809 (45), 795 (9); HRMS [EI(+)] calcd for $C_{54}H_{78}O_8$: 854.5697, found: 854.5662.

**1,4-Dibromo-2,5-didecyl-3,6-bis(2-(2,4-bis(ethoxycarbonyl)phenyl)ethyl)benzene (3.22)**

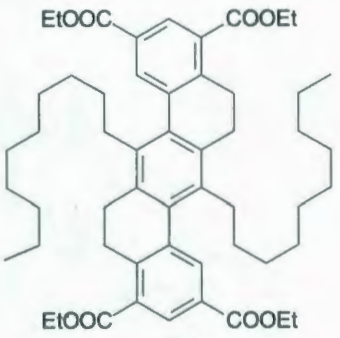



**3.22**

To a mixture of tetraester **3.21** (7.963 g, 9.318 mmol) and $H_2O$ (200 mL) was added $Br_2$ (14.87 g, 93.05 mmol) by syringe. This reaction was stirred for 48 h at room temperature. The excess $Br_2$ was quenched with saturated aqueous $NaHSO_3$ solution (30 mL) and extracted with $CH_2Cl_2$ (200 mL). The organic layer was washed with $H_2O$ (200 mL), washed with brine (150 mL), dried over $MgSO_4$ and concentrated under reduced pressure. The residue was subjected to column chromatography ($CH_2Cl_2$) to give **3.22** as a white solid (8.487 g, 8.400 mmol, 90%): $R_f$($CH_2Cl_2$): 0.39; mp: 116.5-118.0 °C; IR (neat) ν: 2922 (w), 1719 (s), 1456 (w), 1300 (w), 1222 (m), 1131 (m), 1109 (m), 1072 (m), 1030 (w), 765 (s) $cm^{-1}$; $^1H$ NMR (500 MHz, $CDCl_3$): δ 8.57 (d, *J*=1.8 Hz, 2H), 8.12 (dd, *J*=8.0 Hz, 1.9 Hz, 2H), 7.51 (d, *J*=8.0 Hz 2H), 4.43 (q, *J*=7.1 Hz, 4H), 4.43 (q, *J*=7.1 Hz, 4H), 3.32-3.29 (m, 4H), 3.23-3.20 (m, 4H), 2.99 (t, *J*=7.2 Hz, 4H), 1.50-1.47 (br m, 6H), 1.46 (t, *J*=7.1 Hz, 6H), 1.44 (t, *J*=7.1 Hz, 6H), 1.32-1.28 (br m, 26H), 0.90 (t, *J*=6.8 Hz, 6H); $^{13}C$ NMR (125 MHz, $CDCl_3$): δ 167.1, 166.3, 148.7, 141.1, 139.1, 132.9, 132.1, 131.7, 130.6, 129.1, 129.0, 61.60, 61.58, 36.9, 35.2, 34.1, 32.3, 30.34, 30.25, 30.1, 30.0, 29.82, 29.77, 23.08, 14.8, 14.7, 14.5; LCMS [APCl(+)] *m/z* (%): 1015 ($[M+H]^+$, $^{81}Br^{81}Br$,

12), 1013 ([M+H]$^+$, $^{79}Br^{81}Br$, 16), 1011 ([M+H]$^+$, $^{79}Br^{79}Br$, 9), 984 (14); HRMS [EI(+)] calcd for $C_{54}H_{76}O_8Br_2$ ($^{79}Br^{81}Br$): 1012.3852, found: 1012.3862.

**7,14-Didecyl-5,6,12,13-tetrahydrodibenz[*a*,*h*]anthracene-2,4,9,11-tetracarboxylic acid tetraethyl ester (3.11)**

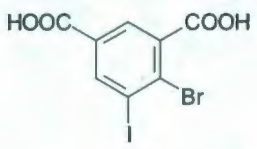



**3.11**

To a mixture of dibromide **3.22** (500 mg, 0.495 mmol), $K_2CO_3$ (409 mg, 2.96 mmol) and DMA (50 mL) in a 100 mL round-bottomed flask was added $Pd(PPh_3)_2Cl_2$ (37 mg, 0.05 mmol). The reaction was stirred at room temperature for 5 min. The flask was then plunged into an oil bath preheated to 180 °C and the reaction mixture was stirred for 3 h. The reaction mixture was cooled to room temperature and the black solid were removed by suction filtration. The filtrate was extracted with EtOAc (50 mL), washed with $H_2O$ (100 mL× 3), washed with brine (50 mL), dried over $MgSO_4$ and concentrated under reduced pressure. The residue was subjected to column chromatography (50:50 $CH_2Cl_2$/hexanes→$CH_2Cl_2$) to give the product as a white solid (243 mg, 0.286 mmol, 58%): $R_f$($CH_2Cl_2$): 0.34; mp: 95.0-96.5 °C; IR (neat) ν: 2922 (w), 1716 (m), 1458 (w), 1365 (w), 1314 (w), 1248 (m), 1149 (w), 1132 (w), 1077 (w), 1033 (w), 765 (s) cm$^{-1}$; $^1$H

NMR (500 MHz, $CDCl_3$): δ 8.48 (d, *J*=1.6 Hz, 2H), 8.27 (d, *J*=1.4 Hz, 2H), 4.44 (q, *J*=7.1 Hz, 4H), 4.41 (q, *J*=7.1 Hz, 4H), 2.81-2.78 (m, 8H), 1.78-1.68 (m, 4H), 1.45 (t, *J*=7.1 Hz, 6H), 1.39 (t, *J*=7.1 Hz, 6H), 1.30-1.20 (m, 32H), 0.89 (t, *J*=6.8, 6H); $^{13}C$ NMR (125 MHz, $CDCl_3$): δ 167.7, 166.4, 147.1, 138.2, 137.7, 134.8, 134.2, 133.0, 130.00, 129.95, 127.9, 61.7, 61.5, 32.3, 31.7, 31.2, 30.3, 30.1, 30.0, 29.8, 29.7, 27.4, 26.6, 23.1, 14.77, 14.76, 14.5; LCMS [APCl(+)] *m/z* (%): 851 ($[M+H]^+$, 100), 840 (20), 822 (17), 805 (14), 750 (16); HRMS [EI(+)] calcd for $C_{54}H_{74}O_8$: 850.5384, found: 850.5382.

**4-Bromo-5-iodoisophthalic acid (3.23) (X=I, Y=Br)**[9]

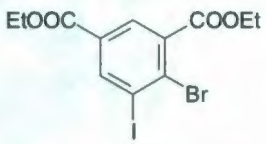



**3.23** (X=I, Y=Br)

To a stirred solution of periodic acid (9.121 g, 39.99 mmol) in $H_2SO_4$ (100 mL) at 0 °C was added potassium iodide (20.32 g, 0.1224 mol) and 4-bromoisophthalic acid (**2.10**) (10.00 g, 40.81 mmol). The resulting black mixture was stirred at room temperature for 24 h and then carefully poured onto crushed ice (500 mL). The precipitate was collected by suction filtration washed with water and then dissolved in saturated aqueous $NaHCO_3$ solution (200 mL). This solution was acidified by the slow addition of concentrated HCl to afford a white solid (9.090 g, 24.58 mmol, 62%): mp: >300 °C; IR (neat) ν: 2861 (br, w), 1688 (s), 1234 (m), 910 (m), 758 (s), 689 (s) $cm^{-1}$; $^1H$ NMR (500 MHz, acetone-$d_6$) δ: 8.62 (d, *J*=2.0 Hz, 1H), 8.27 (d, *J*=2.0 Hz, 1H); $^{13}C$ NMR (125 MHz, acetone-$d_6$) δ:

171.6, 169.8, 148.3, 142.0, 137.4, 136.6, 135.8, 109.8; LCMS [APCl(-)] *m/z* (%): 371 ([M-H]$^-$, $^{81}$Br, 41), 369 ([M-H]$^-$, $^{79}$Br, 38), 325 (8), 307 (17); HRMS [EI(+)] calcd for $C_8H_4O_4IBr(^{81}Br)$: 371.8318, found: 371.8320; HRMS [EI(+)] calcd for $C_8H_4O_4IBr(^{79}Br)$: 369.8338, found: 369.8336.

**Diethyl 4-bromo-5-iodoisophthalate (3.30)**

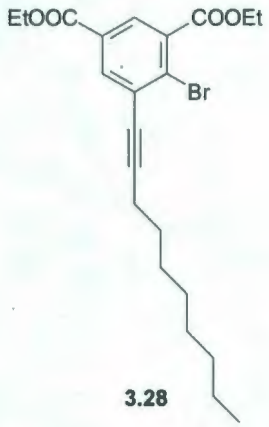



**3.30**

A solution of 4-bromo-5-iodoisophthalic acid (**3.23**) (X=I, Y=Br) (7.932 g, 21.44 mmol) and $H_2SO_4$ (1 mL) in EtOH (200 mL) was heated at refluxe for 24 h. After cooling to room temperature, the reaction mixture was concentrated under reduced pressure. The residue was dissolved in EtOAc (40 mL). The organic layer was washed with $H_2O$ (30 mL), washed with saturated aqueous NaCl solution (30 mL), dried over $MgSO_4$ and concentrated under reduced pressure. The residue was subjected to column chromatography ($CH_2Cl_2$) to afford the product as a white solid (7.511 g, 17.63 mmol, 82%): $R_f$($CH_2Cl_2$): 0.45; mp (EtOH): 88.0-89.0 °C; IR (neat) ν: 1712 (m), 1391 (w), 1237 (s), 1020 (m), 755 (m) cm$^{-1}$; $^1$H NMR (500 MHz, $CDCl_3$): δ 8.59 (d, *J*=2.0 Hz, 1H), 8.18 (d, *J*=2.1 Hz, 1H), 4.43 (q, *J*=7.1 Hz, 2H), 4.40 (q, *J*=7.1 Hz, 2H), 1.42 (t, *J*=7.1 Hz, 3H), 1.40 (t, *J*=7.1 Hz, 3H); $^{13}$C NMR (125 MHz, $CDCl_3$): δ 166.1, 164.2, 143.1, 136.1, 133.1, 130.9, 130.6, 104.7, 62.8, 62.3, 14.7, 14.5; LCMS [APCl(-)] *m/z* (%): 399 ([M-Et]$^-$,

$^{81}$Br, 98), 397 ([M-Et]$^{-}$, $^{79}$Br, 100), 363 (19), 355 (36), 353 (49), 319 (11), 289 (10), 130 (10), 127 (16) (no molecular ion was observed); HRMS [EI(+)] calcd for $C_{12}H_{12}O_4I^{81}Br$: 427.8934, found: 427.8941; HRMS [EI(+)] calcd for $C_{12}H_{12}O_4I^{79}Br$: 425.8964, found: 425.8965.

**Diethyl 4-bromo-5-decynl-isophthalate (3.28)**

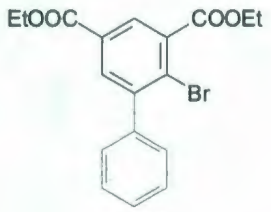



**3.28**

To a solution of diethyl-4-bromo-5-iodoisophthalate (**3.30**) (500 mg, 1.17 mmol), $Pd(PPh_3)_2Cl_2$ (10 mg, 0.014 mmol) and CuI (5 mg, 0.03 mmol) in benzene (12 mL) were added DBU (225 mg, 1.47 mmol) and 1-decyne (160 mg, 1.16 mmol). The mixture was stirred at room temperature for 24 h. The precipitate was removed by suction filtration and the filtrate was washed with saturated aqueous $NH_4Cl$ solution (20 mL), washed with $H_2O$ (25 mL), washed with saturated aqueous NaCl solution (15 mL), dried over $MgSO_4$ and concentrated under reduced pressure. The residue was subject to column chromatography (50:50 $CH_2Cl_2$/hexanes) to afford the product as a brown oil (425 mg, 0.974 mmol, 89%): $R_f$($CH_2Cl_2$): 0.49; IR (neat) 1724 (s), 1587 (w), 1368 (m), 1296 (s),

1021(s) $cm^{-1}$; $^1H$ NMR (500 MHz, $CDCl_3$): δ 8.14-8.13 (m, 2H), 4.42 (q, *J*=7.1 Hz, 2H), 4.39 (q, *J*=7.1 Hz, 2H), 2.48 (t, *J*=7.0 Hz, 2H), 1.67-1.61 (m, 2H), 1.52-1.46 (m, 2H), 1.42 (t, *J*=7.1 Hz, 3H), 1.40 (t, *J*=7.1 Hz, 3H), 1.33-1.29 (m, 8H), 0.88 (t, *J*=7.0 Hz, 3H); $^{13}C$ NMR (125 MHz, $CDCl_3$): δ 166.3, 165.1, 136.0, 135.1, 129.8, 129.7, 129.07, 129.05, 98.2, 79.2, 62.4, 62.0, 32.2, 29.6, 29.5, 29.3, 28.8, 23.0, 20.0, 14.6, 14.5, 14.5; LCMS [APCl(-)] *m/z* (%): 409 ([M-Et]$^-$, $^{81}Br$, 92), 407 ([M-Et]$^-$, $^{79}Br$, 100), 280 (21), 149 (10) (no molecular ion was observed); HRMS [EI(+)] calcd for $C_{22}H_{29}O_4{}^{81}Br$: 438.1230; found: 438.1238; HRMS [EI(+)] calcd for $C_{22}H_{29}O_4{}^{79}Br$: 436.1249; found: 436.1253.

**Diethyl 4-bromo-5-phenylisophthalate (3.31)**

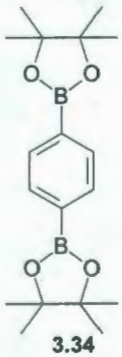



**3.31**

To a degassed mixture of diethyl 4-bromo-5-iodoisophthalate (**3.30**) (1.000 g, 2.293 mmol), phenylboronic acid (299 mg, 2.45 mmol), $K_2CO_3$ (800 mg, 5.80 mmol) in toluene/EtOH (1.5:1) (20 mL) was degassed in acetone/dry ice 10 min was added $Pd(PPh_3)_4$ (27 mg, 0.023 mmol) and the mixture was degassed again. The reaction mixture was warmed up to room temperature and heated to 60 °C for 8 h. After cooling to room temperature, $H_2O$ (20 mL) was added and the resulting mixture was extracted with $CH_2Cl_2$ (50 mL). The organic layer was washed with saturated aqueous NaCl solution (20 mL) and dried over $MgSO_4$. The solvent was concentrated under reduced pressure

and the residue was subjected to column chromatography (50:50 $CH_2Cl_2$/hexanes) to afford **3.31** as a colorless oil (449 mg, 1.19 mmol, 52%); $R_f(CH_2Cl_2)$: 0.52; IR (neat): 2981 (w), 1720 (vs), 1590 (w), 1368 (m), 1331 (m), 1235 (vs), 1182 (s), 1095 (s), 1020 (vs), 759 (s), 722 (s) $cm^{-1}$; $^1H$ NMR (500 MHz, $CDCl_3$): δ 8.21 (d, *J*=2.1 Hz, 1H), 8.04 (d, *J*=2.1 Hz, 1H), 7.48-7.43 (m, 3H), 7.38-7.36 (m, 2H), 4.45 (q, *J*=7.2 Hz, 2H), 4.39 (q, *J*=7.1 Hz, 2H), 1.43 (t, *J*=7.1 Hz, 3H), 1.39 (t, *J*=7.1 Hz, 3H); $^{13}C$ NMR (125 MHz, $CDCl_3$): δ 167.1, 165.5, 145.2, 140.7, 136.0, 133.9, 130.0, 129.9, 129.7, 128.6, 126.3, 62.6, 62.0, 14.7, 14.6 (one signal less than expected); LCMS [APCl(-)] *m/z* (%):349 ([M-Et]$^-$, $^{81}Br$, 83), 347 ([M-Et]$^-$, $^{79}Br$, 100), 303 (10) (no molecular ion was observed); HRMS [EI(+)] calcd for $C_{18}H_{17}O_4{}^{81}Br$: 378.0317, found: 378.0302; HRMS [EI(+)] calcd for $C_{18}H_{17}O_4{}^{79}Br$: 376.0310, found: 376.0314.

**1,4-Benzenediboronic acid bis(pinacol) ester (3.34)**[10]

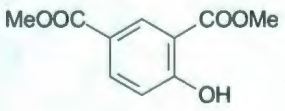


**3.34**

To a refluxing solution of 1,4-phenylenebisboronic acid (**3.33**) (500 mg, 3.01 mmol) in benzene (80 mL) was added pinacol (1.070 g, 9.052 mmol) and a catalytic amount of *p*-toluenesulfonic acid (5 mg, 0.03 mmol). Water was removed using a Dean-Stark

apparatus over 24 h. After cooling to room temperature, the benzene was removed under reduced pressure and the resulting residue was dissolved in $CH_2Cl_2$ (30 mL), washed with saturated aqueous $NaHCO_3$ solution (20 mL), washed with saturated aqueous NaCl solution (20 mL), dried over $MgSO_4$ and concentrated under reduced pressure. The residue was subjected to column chromatography (50:50 $CH_2Cl_2$/hexanes) to afford **3.34** as a white solid (476 mg, 1.44 mmol, 48%): $R_f$($CH_2Cl_2$): 0.36; mp: 243.0-245.0 °C (lit.[20] mp: 235-236 °C); $^1$H NMR (500 MHz, $CDCl_3$): δ 7.80 (s, 4H), 1.35 (s, 24H); $^{13}$C NMR (125 MHz, $CDCl_3$) δ 134.3, 84.2, 25.3 (one signal less than expected).

**Dimethyl 4-hydroxyisophthalate (3.39)**[3]

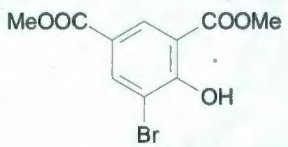



**3.39**

To a solution of diacid **3.38** (5.000 g, 27.45 mmol) in MeOH (100 mL) in a 250 mL round-bottomed flask equipped with a reflux condenser was added $H_2SO_4$ (3 mL) and the resulting mixture was heated at refulx overnight. After cooling to room temperature, the mixture was concentrated under reduced pressure, and then dissolved in EtOAc (100 mL). The organic layer was washed with $H_2O$ (100 mL), washed with brine (70 mL), dried over $MgSO_4$ and concentrated under reduced pressure. The residue was subjected to column chromatography (50:50 $CH_2Cl_2$/hexanes) to afford **3.39** as a white solid (5.596 g, 26.63 mmol, 97%): $R_f$($CH_2Cl_2$): 0.32; mp: 102.5-104 °C (lit.[21] mp: 94-95 °C); $^1$H NMR (500 MHz, $CDCl_3$): 11.16 (s, 1H), 8.49 (d, $J$=2.2 Hz, 1H), 8.07 (dd, $J$=8.8, 2.2 Hz, 1H),

6.97 (d, *J*=8.8 Hz, 1H), 3.97 (s, 3H), 3.90 (s, 3H); $^{13}$C NMR (125 HMz, $CDCl_3$): δ 170.4, 166.2, 165.4, 136.8, 132.7, 121.7, 118.0, 112.4, 52.9, 52.3; LCMS [APCl(-)] *m/z* (%): 209 ([M-H]$^-$, 100), 195 (11).

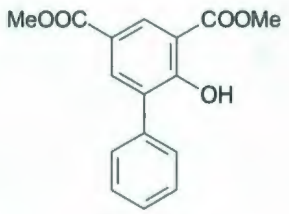
**Dimethyl 5-bromo-4-hydroxyisophthalate (3.40)**[4]




**3.40**

To a mixture of dimethyl 4-hydroxyisophthalate (**3.39**) (5.000 g, 23.81 mmol) in $H_2O$ (100 mL) was added $Br_2$ (15.20 g, 95.13 mmol). The mixture was stirred at room temperature for 24 h, and quenched by the addition of a saturated aqueous $NaHSO_3$ solution (20 mL). The mixture was extracted with $CH_2Cl_2$ (20 mL). The combined organic layer was washed with $H_2O$ (50 mL), washed with saturated aqueous NaCl solution (25 mL), dried over $MgSO_4$ and concentrated under reduced pressure to afford a white solid (6.853 g, 23.80 mmol, 99%), which was used without purification in the next step: $R_f$ ($CH_2Cl_2$): 0.43; mp: 142.5-143.0 °C; IR (neat): 1727 (m), 1433 (m), 1291 (s), 1238 (s), 759 (s) cm$^{-1}$; $^1$H NMR (500 MHz, $CDCl_3$): δ 11.90 (s, 1H), 8.52 (d, *J*=2.1 Hz, 1H), 8.40 (d, *J*=2.0 Hz, 1H), 4.01 (s, 3H), 3.92 (s, 3H); $^{13}$C NMR (125 HMz, $CDCl_3$): δ 170.2, 165.3, 162.1, 140.1, 131.7, 122.7, 113.4, 111.8, 53.5, 52.8; LCMS [APCl(-)] *m/z* (%): 289 ([M-H]$^-$, $^{81}$Br, 98), 287 ([M-H]$^-$, $^{79}$Br, 100).

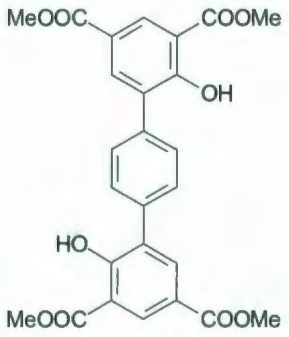
**Dimethyl 4-hydroxy-5-phenylisophthalate (3.41)**




**3.41**

To a degassed mixture of dimethyl 5-bromo-4-hydroxyisophthalate (**3.40**) (107 mg, 0.372 mmol), phenylboronic acid (50 mg, 0.41 mmol), $K_2CO_3$ (77 mg, 0.56 mmol) in dioxane (20 ml) was added $Pd(PPh_3)_4$ (22 mg, 0.019 mmol). This mixture was degassed again and the reaction mixture was heated to 90 °C for 24 h. After cooling to room temperature, $H_2O$ (20 mL) was added and the resulting mixture was extracted with $CH_2Cl_2$ (50 mL). The organic layer was washed with saturated aqueous NaCl solution (50 mL), dried over $MgSO_4$ and concentrated under reduced pressure. The residue was subjected to column chromatography (10:90 EtOAc/hexanes) to afford **3.41** as a white solid (92 mg, 0.32 mmol, 86%); $R_f$(20:80 EtOAc/hexanes): 0.37; mp: 130.0-131.5 °C; $^1$H NMR (500 MHz, $CDCl_3$): δ 11.77 (s, 1H), 8.61 (d, *J*=2.2 Hz, 2H), 8.24 (d, *J*=2.0 Hz, 2H), 7.63-7.61 (m, 2H), 7.38 (t, *J*=7.3 Hz, 2H), 7.42-7.40 (m, 1H), 4.04 (s, 3H), 3.95 (s, 3H); $^{13}$C NMR (125 MHz, $CDCl_3$): δ 171.0, 166.5, 162.9, 137.7, 136.6, 131.9, 131.2, 129.7, 128.7, 128.3, 121.6, 112.9, 53.2, 52.6; LCMS [APCl(-)] *m/z* (%): 285 ($[M-H]^-$, 100).

**1,4-Bis(2-hydroxy-3,5-bis(methoxycarbonyl)phenyl)benzene (3.42)**

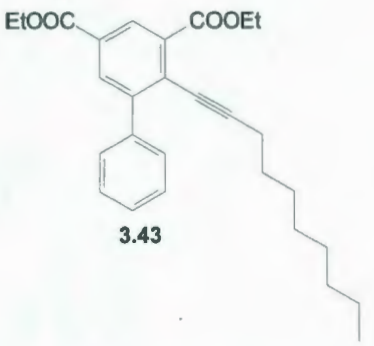



**3.42**

To a mixture of dimethyl 5-bromo-4-hydroxyisophthalate (**3.40**) (1.000 g, 3.474 mmol), 1,4-phenylenebisboronic acid (**3.33**) (374 mg, 2.26 mmol), $K_2CO_3$ (4.795 g, 34.69 mmol) in toluene/MeOH (1.5:1) (50 mL) was added $Pd(PPh_3)_4$ (401 mg, 0.347 mmol). The resulting mixture was degassed again and the reaction mixture was heated to 80 °C for 24 h. After cooling to room temperature, $H_2O$ (20 mL) was added and the resulting mixture was extracted with $CH_2Cl_2$ (70 mL). The organic layer was washed with saturated aqueous NaCl solution (50 mL), dried over $MgSO_4$ and concentrated under reduced pressure. The residue was subjected to column chromatography (50:50 $CH_2Cl_2$/hexanes→$CH_2Cl_2$) to afford **3.42** as a white solid (738 mg, 1.49 mmol, 43%); $R_f$ (30:70 EtOAc/hexanes): 0.40; mp (EtOAc): 273.0-274.0 °C; IR (neat): 2956 (w), 1720 (m), 1678 (m), 1445 (m), 1352 (m), 1238 (s), 1199 (m), 1087 (w), 1001 (s), 807 (w), 757 (s), 692 (m) $cm^{-1}$; $^1H$ NMR (500 MHz, $CDCl_3$): δ 11.79 (s, 2H), 8.60 (d, *J*=2.2 Hz, 2H), 8.27 (d, *J*=2.0 Hz, 2H), 7.70 (s, 4H), 4.03 (s, 6H), 3.93 (s, 6H); $^{13}C$ NMR (125 MHz, $CDCl_3$): δ 171.0, 166.5, 162.9, 137.7, 136.1, 132.0, 130.7, 130.2, 129.6, 127.4, 121.7, 112.9, 53.2, 52.6; LCMS [APCI(-)] *m/z* (%): 493 ($[M-H]^-$, 100); HRMS [EI(+)] calcd for

$C_{26}H_{22}O_{10}$: 494.1213, found: 494.1206.

**Diethyl 4-decynl-5-phenylisophthalate (3.43)**

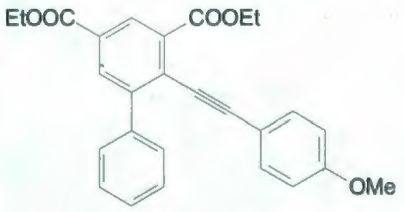



**3.43**

To a solution of diethyl 4-bromo-5-phenylisophthalate (**3.31**) (100 mg, 0.27 mmol), $Pd(PPh_3)_2Cl_2$ (5 mg, 0.007 mmol) and CuI (3mg, 0.01mmol) in benzene (25 mL) was added DBU (121 mg, 0.802 mmol) and 1-decyne (55 mg, 0.40 mmol). The mixture was stirred at room temperature for 10 min and then heated at 60 °C 24 h. After cooling to room temperature, the precipitate was removed by suction filtration and the filtrate was washed with saturated aqueous $NH_4Cl$ solution (20 mL), washed with $H_2O$ (25 mL), washed with saturated aqueous NaCl solution (20 mL), dried over $MgSO_4$ and concentrated under reduced pressure. The residue was subjected to column chromatography (50% $CH_2Cl_2$/hexanes) to afford **3.43** as a red oil (89 mg, 0.21 mmol, 78%): $R_f$ ($CH_2Cl_2$): 0.40; $^1$H NMR (500 MHz, $CDCl_3$): δ 8.40 (d, *J*=1.8 Hz, 1H), 8.10 (d, *J*=1.8 Hz, 1H), 7.52-7.51 (m, 2H), 7.43-7.36 (m, 3H), 4.42 (q, *J*=7.2 Hz, 2H), 4.39 (q, *J*=7.2 Hz, 2H), 2.29 (t, *J*=7.0 Hz, 2H), 1.42 (t, *J*=7.2 Hz, 3H), 1.40 (t, *J*=7.2 Hz, 3H), 1.36-1.26 (m, 12H), 0.89 (t, *J*=7.0 Hz, 3H); $^{13}$C NMR (125 MHz, $CDCl_3$): δ 167.1, 165.9,

146.5, 140.3, 135.0, 133.2, 129.8, 129.6, 129.1, 128.3, 128.1, 126.8, 103.6, 61.9, 61.8, 32.3, 29.54, 29.53, 29.2, 28.4, 20.3, 14.71, 14.70, 14.5 (two signal less than expected); LCMS [APCl(-)] *m/z* (%): 405 ([M-Et]$^-$, 100), 391 (11), 377 (47); HRMS [EI(+)] calcd for $C_{28}H_{34}O_4$: 434.2448, found: 434.2457.

**Diethyl 4-(4-methoxyphenylethynl)-5-phenylisophthalate (3.49)**

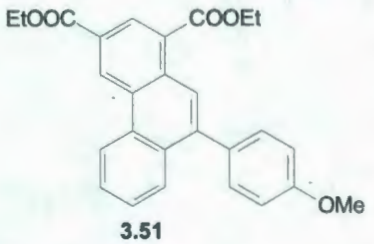



**3.49**

To a degassed solution of diethyl 4-bromo-5-phenylisophthalate (**3.31**) (100 mg, 0.27 mmol), $Pd(PPh_3)_2Cl_2$ (6 mg, 0.009 mmol) and CuI (5 mg, 0.03 mmol) in benzene (25 mL) were added DBU (64 mg, 0.33 mmol) and 4-methoxyphenylethyne (42 mg, 0.32 mmol). The mixture was stirred at room temperature and then heated at 60 °C for 24 h. After cooling to room temperature, the precipitate was removed by suction filtration and the filtrate was washed with saturated aqueous $NH_4Cl$ solution (20 mL), washed with $H_2O$ (25 mL), washed with saturated aqueous NaCl solution (20 mL), dried over $MgSO_4$ and concentrated under reduced pressure. The residue was subject to column chromatography (50:50 $CH_2Cl_2$/hexanes) to afford **3.49** as a red oil (84 mg, 0.20 mmol, 74%): $R_f$ ($CH_2Cl_2$): 0.31; IR (neat): 2926 (w), 1712 (s), 1597 (m), 1567 (s), 1369 (s), 1240 (vs), 1175 (m), 1025 (s), 831 (m), 763 (s), 702 (m) cm$^{-1}$; $^1$H NMR (500 MHz, $CDCl_3$): δ 8.52 (d, *J*=1.6 Hz, 1H), 8.17 (d, *J*=1.6 Hz, 1H), 7.60-7.59 (m, 2H), 7.49-7.42

(m, 3H), 7.18-7.16 (m, 2H), 6.80-6.79 (m, 2H), 4.48 (q, *J*=7.1 Hz, 2H), 4.41 (q, *J*=7.1 Hz, 2H), 3.78 (s, 3H), 1.44 (t, *J*=7.2 Hz, 3H), 1.41 (t, *J*=7.1 Hz, 3H); $^{13}$C NMR (125 MHz, $CDCl_3$): δ 166.7, 165.8, 160.6, 146.3, 140.2, 133.9, 133.6, 133.4, 130.2, 130.0, 128.3, 128.33, 128.31, 126.6, 115.4, 114.4, 101.8, 86.8, 62.0, 61.9, 55.7, 14.8, 14.7; LCMS [APCl(+)] *m/z* (%): 429 ($[M+H]^+$, 100); HRMS [CI(+)] calcd for $C_{27}H_{24}O_5$: 429.1702, found: 429.1701.

**9-(4-Methoxyphenyl)phenathrene-1,3-dicarboxylic acid diethyl ester (3.51)**

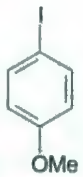



**3.51**

To a solution of diethyl 4-(4-methoxyphenylethynl)-5-phenylisophthalate (**3.49**) (65 mg, 0.15 mmol) and $CH_2Cl_2$ (25 mL) in a 50 mL round-bottomed flask was added TFA (621 mg, 5.45 mmol) in one portion at room temperature. The solution was stirred overnight. The mixture was washed with 10% $NaHCO_3$ solution (3× 20 mL), washed with $H_2O$ (2× 30 mL), dried over $MgSO_4$ and concentrated under reduced pressure. The residue was subjected to column chromatography ($CH_2Cl_2$) to give the product as a light yellow solid (44 mg, 0.10 mmol, 68%): $R_f$ (30:70 EtOAc/hexanes): 0.49; mp: 107.0-108.0 °C; $^1$H NMR (500 MHz, $CDCl_3$): δ 9.62 (s, 1H), 8.87 (d, *J*=8.2 Hz, 1H), 8.79 (d, *J*=1.6 Hz, 1H), 8.71 (d, *J*=1.6 Hz, 1H), 8.00 (d, *J*=8.1 Hz, 1H), 7.74 (t, *J*=7.0 Hz, 1H), 7.62 (t, *J*=7.1 Hz, 1H), 7.51-7.50 (m, 2H), 7.07-7.05 (m, 2H), 4.53 (q, *J*=7.1 Hz,

2H), 4.49 (q, *J*=7.1 Hz, 2H), 3.91 (s, 3H), 1.51 (t, *J*=7.2 Hz, 3H), 1.47 (t, *J*=7.2 Hz, 3H); $^{13}$C NMR (125 MHz, $CDCl_3$): δ 167.8, 166.6, 159.8, 143.0, 133.2, 133.2, 131.5, 131.5, 131.2, 130.5, 130.1, 129.2, 128.9, 127.8, 127.7, 127.6, 127.1, 124.5, 123.7, 61.90, 61.88, 55.8, 14.9, 14.8 (one signal less than expected); LCMS [APCl(+)] *m/z* (%): 429 ($[M+H]^+$, 100), 383 (28), 279 (8); HRMS [CI(+)] calcd for $C_{27}H_{24}O_5$: 429.1702, found: 429.1707.

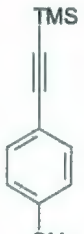
**4-Iodomethoxybenzene (3.46)**[14]




**3.46**

To a solution of methoxybenzene (3.391 g, 31.36 mmol) and $NH_4I$ (5.000 g, 34.50 mmol) in methanol (200 mL) was added Oxone (21.21g, 34.50mmol) at room temperature. The reaction was monitored by TLC. After consumption of the starting material, the reaction mixture was filtered and the solvent was removed under reduced pressure. Recrystallization of residue from EtOH/$H_2O$ gave **3.46** as a white solid (6.614 g, 28.26 mmol, 90%): $R_f$ (50:50 $CH_2Cl_2$/hexanes): 0.55; mp (EtOH/$H_2O$) 46.0-47.5 °C (lit.[22] mp: 51-53 °C); $^1$H NMR (500 MHz, $CDCl_3$): δ 7.56-7.53 (m, 2H), 6.67-6.65 (m, 2H), 3.76 (s, 3H); $^{13}$C NMR (125 MHz, $CDCl_3$): δ 159.9, 138.7, 116.8, 83.1, 55.7; LCMS [APCl(+)] *m/z* (%): 235 ($[M+H]^+$, 100), 214 (67), 164 (44).

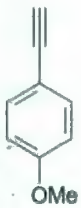
**4-Methoxy(trimethylsilylethynyl)benzene (3.47)**[4]




**3.47**

To a solution of 4-iodomethoxybenzene (**3.46**) (100 mg, 0.43 mmol), $Pd(PPh_3)_2Cl_2$ (5 mg, 0.009 mmol), CuI (3 mg, 0.02 mmol) in THF/$Et_3N$ (1:1) (50 mL) was added trimethylsilylacetylene (46 mg, 0.47 mmol). This mixture was stirred at room temperature overnight. The precipitate was removed by suction filtration. The filtrate was washed with saturated aqueous $NH_4Cl$ solution (50 mL), washed with $H_2O$ (50 mL) and washed with brine (40 mL). The organic layer was dried over $MgSO_4$ and concentrated under reduce pressure. The residue was subjected to column chromatography (50:50 $CH_2Cl_2$/hexanes) to yield **3.47** as a light red oil (82 mg, 0.40 mmol, 93%): $R_f$ (50:50 $CH_2Cl_2$/hexanes): 0.43; $^1$H NMR (500 MHz, $CDCl_3$): δ 7.41-7.39 (m, 2H), 6.82-6.80 (m, 2H), 3.79 (s, 3H), 0.24 (s, 9H).

**4-Methoxy-ethynylbenzene (3.48)**[4]

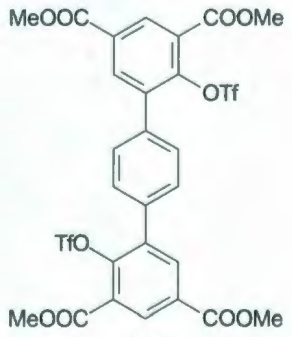



**3.48**

To a mixture of 4-methoxy(trimethylsilylethynyl)benzene (**3.47**) (7.571 g, 37.05 mmol) in MeOH (120 mL) was added $K_2CO_3$ (7.681 g, 55.57 mmol) at room temperature.

The reaction mixture was stirred for 1 h and $K_2CO_3$ was removed by suction filtration. The filtrate was concentrated under reduced pressure. The residue was dissolved in $CH_2Cl_2$ (100 mL) and washed with $H_2O$ (100 mL), washed with brine (80 mL) and dried over $MgSO_4$. The solvent was removed under reduced pressure to yield **3.48** as a red oil (4.608 g, 34.87 mmol, 94%): $R_f$ (50:50 $CH_2Cl_2$/hexanes): 0.44; $^1$H NMR (500 MHz, $CDCl_3$): δ 7.44-7.41 (m, 2H), 6.85-6.82 (m, 2H), 3.80 (s, 3H), 3.00 (s, 1H); $^{13}$C NMR (125 MHz, $CDCl_3$): δ 160.3, 134.0, 114.6, 114.3, 84.1, 76.2, 55.7; LCMS [APCl(+)] *m/z* (%): 133 ($[M+H]^+$, 100).

**1,4-Bis(2-trifluromethylsulfonyloxy-3,5-bis(methoxycarbonyl)phenyl)benzene (3.52)**

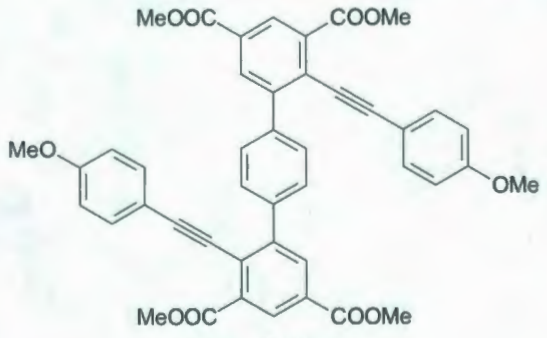



**3.52**

To a solution of **3.42** (250 mg, 0.51 mmol) in a mixture of pyridine/$CH_2Cl_2$ (30/70, 100 ml) at 0 °C was slowly added triflic anhydride (428 mg, 1.52 mmol). The reaction mixture was allowed to warm to room temperature and was stirred for 1 h. This solution was then washed with 5% aqueous HCl solution (300 mL). The organic layer was washed with saturated aqueous $NaHCO_3$ solution (100 mL), washed with $H_2O$ (200 mL), washed with saturated aqueous NaCl solution (100 mL), dried over $MgSO_4$ and

concentrated under reduced pressure. The residue was recrystallized from MeOH to afford **3.52** as a white solid (368 mg, 0.496 mmol, 96%): $R_f(CH_2Cl_2)$: 0.21; mp (MeOH): 221.0-222.0 °C; IR (neat): 1730 (s), 1422 (s), 1340 (w), 1257 (m), 1147 (s), 1131 (s), 1075 (m), 996 (m), 865 (s), 846 (s), 829 (m), 754 (m) $cm^{-1}$; $^1H$ NMR (500 MHz, $CDCl_3$): δ 8.69 (d, *J*=2.2 Hz, 2H), 8.49 (d, *J*=2.1 Hz, 2H), 7.64 (s, 4H), 4.00 (s, 6H), 3.98 (s, 6H); $^{13}C$ NMR (500 MHz, $CDCl_3$): δ 165.1, 164.6, 148.1, 137.2, 136.7, 135.9, 133.2, 130.6, 130.5, 127.7, 126.9, 53.5, 53.3 (expected q at ~118 ppm for $\underline{C}F_3$ not observed); LCMS [APCl(+)] *m/z* (%): 758 ($[M+H]^+$, 100), 732 (20), 704 (6), 626 (57). Acceptable HRMS could not be obtained.

**1,4-Bis(4-(2-methoxyphenylethynl)-3,5-bis(methoxycarbonyl)phenyl)benzene (3.53)**

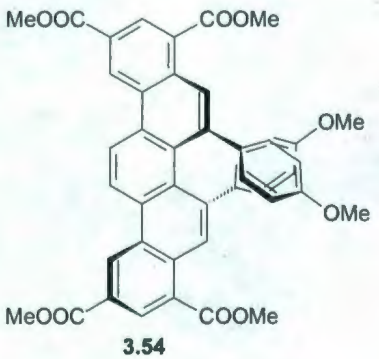



**3.53**

To a degassed solution of ditriflate (**3.52**) (100 mg, 0.13 mmol), $Pd(PPh_3)_2Cl_2$ (5 mg, 0.007 mmol) and CuI (3 mg, 0.01 mmol) in benzene (20 mL) was added DBU (100 mg, 0.66 mmol) and 4-methoxyphenylethyne (44 mg, 0.33 mmol). The mixture was stirred at room temperature for 10 min and then heated to 80 °C for 24 h. After cooling to room temperature, the precipitate was removed by suction filtration and the filtrate was

washed with saturated aqueous $NH_4Cl$ solution (20 mL), washed with $H_2O$ (25 mL), washed with saturated aqueous NaCl solution (20 mL), dried over $MgSO_4$ and concentrated under reduced pressure. The residue was subjected to column chromatography (30:80 EtOAc/hexanes) to afford **3.53** as a white solid (70 mg, 0.097 mmol, 74%): $R_f$ (50:50 EtOAc/hexanes): 0.31; mp: 228.0-230.0 °C; IR (neat): 2926 (w), 1712 (s), 1597 (m), 1567 (s), 1369 (s), 1240 (vs), 1175 (m), 1025 (s), 831 (m), 763 (s), 702 (m) $cm^{-1}$; $^1H$ NMR (500 MHz, $CDCl_3$): δ 8.58 (d, *J*=1.7 Hz, 2H), 8.25 (d, *J*=1.7 Hz, 2H), 7.72 (s, 4H), 7.17-7.15 (m, 4H), 6.71-6.70 (m, 4H), 4.03 (s, 6H), 3.98 (s, 6H), 3.73 (s, 6H); $^{13}C$ NMR (125 MHz, $CDCl_3$): δ 166.9, 166.2, 160.6, 145.9, 139.9, 133.8, 133.6, 133.6, 130.6, 129.6, 128.9, 127.1, 115.1, 114.4, 102.7, 86.7, 55.6, 52.9 (one signal less than expected); LCMS [APCl(+)] *m/z* (%): 723 ($[M+H]^+$, 100). Acceptable HRMS could not be obtained.

**6,7-Bis(4-methoxyphenyl)picene-2,4,9,11-tetracarboxylic acid tetramethyl ester (3.54)**

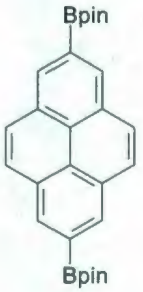



**3.54**

To a solution of 1,4-bis(4-(2-methoxyphenylethynl)-3,5-bis(methoxycarbonyl)

benzene (**3.53**) (280 mg, 0.392 mmol) in $CH_2Cl_2$ (50 mL) in a 100 mL round-bottomed flask with was added TFA (1.590 g, 13.95 mmol) in one portion at room temperature. The solution was stirred overnight. The mixture was washed with 10% $NaHCO_3$ solution (40 mL), washed with $H_2O$ (50 mL) dried over $MgSO_4$ and concentrated under reduced pressure. The residue was subjected to column chromatography (30:70 EtOAc/hexanes) to give **3.54** as a light yellow oil (137 mg, 0.19 mmol, 50%): $R_f$ (50:50 EtOAc/hexanes): 0.38; $^1$H NMR (500 MHz, $CDCl_3$): δ 9.73 (s, 2H), 9.05 (s, 2H), 8.92 (s, 2H), 8.60 (s, 2H), 6.87 (br s, 2H), 6.70 (br s, 2H), 6.52 (br s, 2H), 6.39 (br s, 2H), 4.11 (s, 6H), 4.04 (s, 6H), 3.82 (s, 6H); $^{13}$C NMR (125 MHz, $CDCl_3$): δ 167.7, 167.0, 159.3, 143.7, 136.2, 134.0, 132.0, 130.9, 130.1, 129.7, 128.2, 127.8, 126.8, 126.1, 123.1, 55.8, 53.0, 52.8 (two signals less than expected); LCMS [APCl(+)] *m/z* (%): 723 ($[M+H]^+$, 13), 615 (14), 554 (21), 458 (100), 441 (18), 414 (8). Acceptable HRMS could not be obtained.

**2,7-Pyrene bisboronate pinacol esters (3.62)**[17]

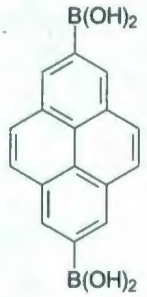



**3.62**

To a mixture of pyrene (2.000 g, 9.891 mmol), $B_2pin_2$ (7.533 g, 29.66 mmol) and dtbpy (265 mg, 0.993 mmol) in cyclohexane (125 mL) was added $[Ir(OMe)COD]_2$ (328 mg, 0.49 mmol). The reaction mixture was stirred vigorously for 5 min and then heated

at reflux at overnight. The solvent was removed under reduced pressure and the residue was subjected to column chromatography (20:80 $CH_2Cl_2$/hexanes) to give **3.62** as a white solid (4.042 g, 8.904 mmol, 90%): $R_f$ (50:50 $CH_2Cl_2$/hexanes): 0.30; mp: > 300.0 °C (lit.[23] mp: 332-334 °C); $^1$H NMR (500 MHz, $CDCl_3$): 8.63 (s, 4H), 8.07 (s, 4H), 1.40 (s, 24H); $^{13}$C NMR (125 MHz, $CDCl_3$): δ 131.7, 131.3, 128.1, 126.8, 84.6, 25.4 (one signal less than expected); LCMS [APCl(+)] *m/z* (%): 455 ($[M+H]^+$, 100).

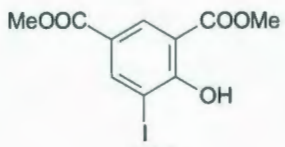
**2,7-Pyrene bisboronic acid (3.63)**[18]




**3.63**

To a solution of bisboronic acid pinacol ester **3.62** (1.000 g, 2.202 mmol) in THF/$H_2O$ (4:1) (100 mL) was added sodium periodate (2.824 g, 13.20 mmol). After stirring for 30 min at room temperature, 1 M aqueous HCl solution (4 mL) was added. This mixture was stirred for 17 h and then diluted with $H_2O$, extracted with EtOAc (100 mL), washed with brine (80 mL), dried over $MgSO_4$ and concentrated under reduced pressure. The residue was washed with a small portion of hexane to give an off-white solid product (532 mg, 1.83 mmol, 83%): mp (hexanes): > 300.0 °C; $^1$H NMR (500 MHz, DMSO-$d_6$): 8.67 (s, 4H), 8.40 (s, 4H), 8.15 (s, 4H).

**Dimethyl 4-hydroxy-5-iodoisophthalate (3.64)**[19]




**3.64**

To a solution of 4-hydroxyisophthalate **3.38** (1.000 g, 4.765 mmol) in $CH_2Cl_2$/MeOH (50:20) (50 mL) was added $BTMAICl_2$ (1.739 g, 4.992 mmol) and $NaHCO_3$ (2.398 g, 28.54 mmol). The mixture was stirred for 3 h at room temperature, during which time the yellow color of the solution gradually changed to light brown. The excess $NaHCO_3$ was removed by suction filtration and the filtrate was concentrated under reduced pressure. A saturated aqueous $NaHCO_3$ solution (30 mL) was added to the residue and the mixture was extracted with $CH_2Cl_2$ (50 mL). The organic layer was dried over $MgSO_4$ and concentrated under reduced pressure. The residue was subjected to column chromatography (50:50 $CH_2Cl_2$/hexanes) to give the product as white crystals (1.434 g, 4.273 mmol, 90%): $R_f$ ($CH_2Cl_2$): 0.66; mp: 143.0-144.0 °C; IR (neat): 2953 (w), 2360 (w), 1704 (s), 1672 (s), 1413 (m), 1335 (m), 1287 (m), 1239 (s), 1169 (s), 963 (s), 801 (m), 761 (s), 718 (s) $cm^{-1}$; $^1H$ NMR (500 MHz, $CDCl_3$): δ 12.07 (s, 1H), 8.60 (d, *J*=2.0 Hz, 1H), 8.55 (d, *J*=2.1 Hz, 1H), 4.01 (s, 3H), 3.91 (s, 3H); $^{13}C$ NMR (125 MHz, $CDCl_3$): δ 170.1, 165.1, 164.1, 146.3, 132.7, 123.4, 112.4, 85.4, 53.5, 52.8; LCMS [APCl(-)] *m/z* (%): 335 ([M-H]$^-$, 100); HRMS [CI(+)] calcd for $C_{10}H_9O_5I$: 335.9495, found: 335.9502.

### 3.7 References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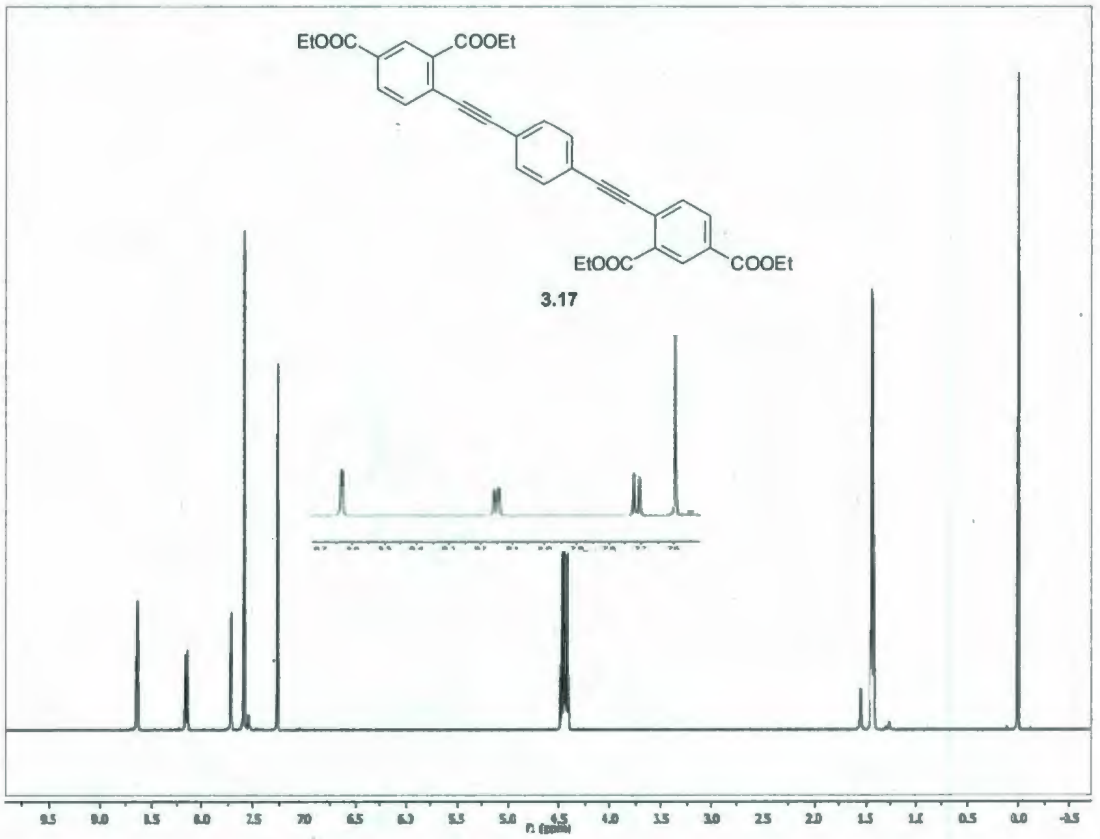
# Appendix 2

## Selected Spectra of Synthesized Compounds

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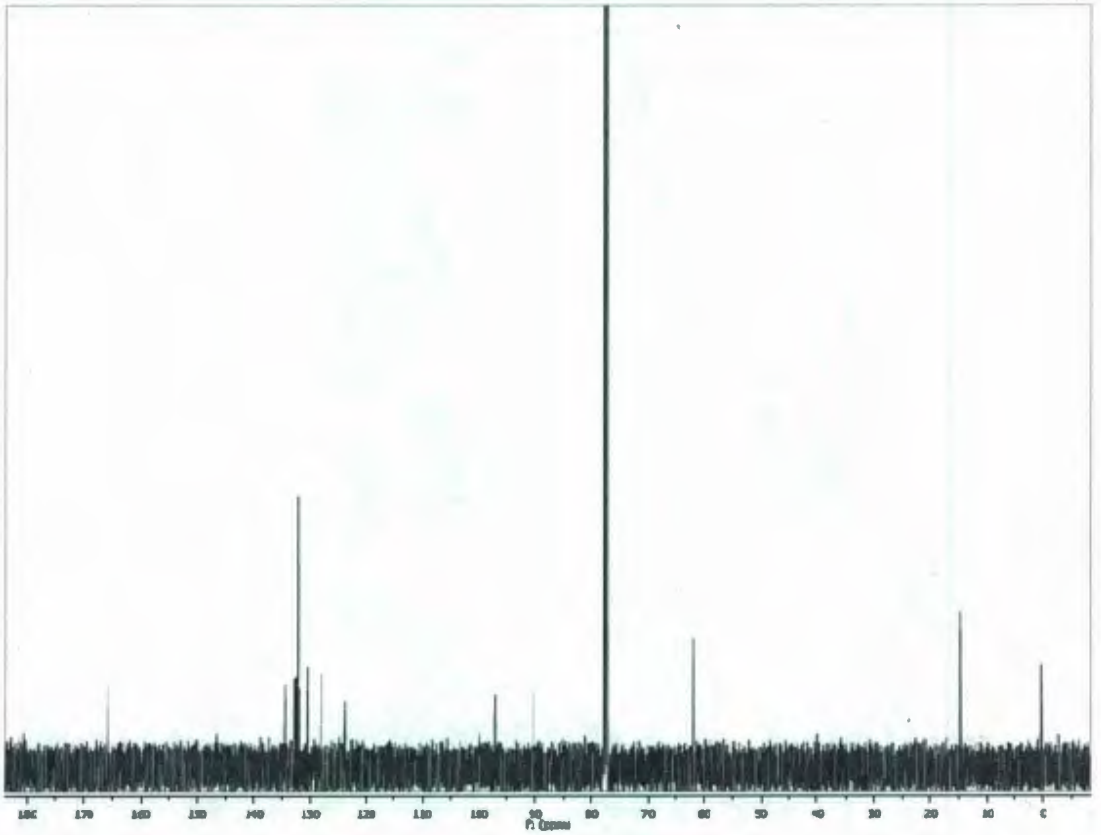
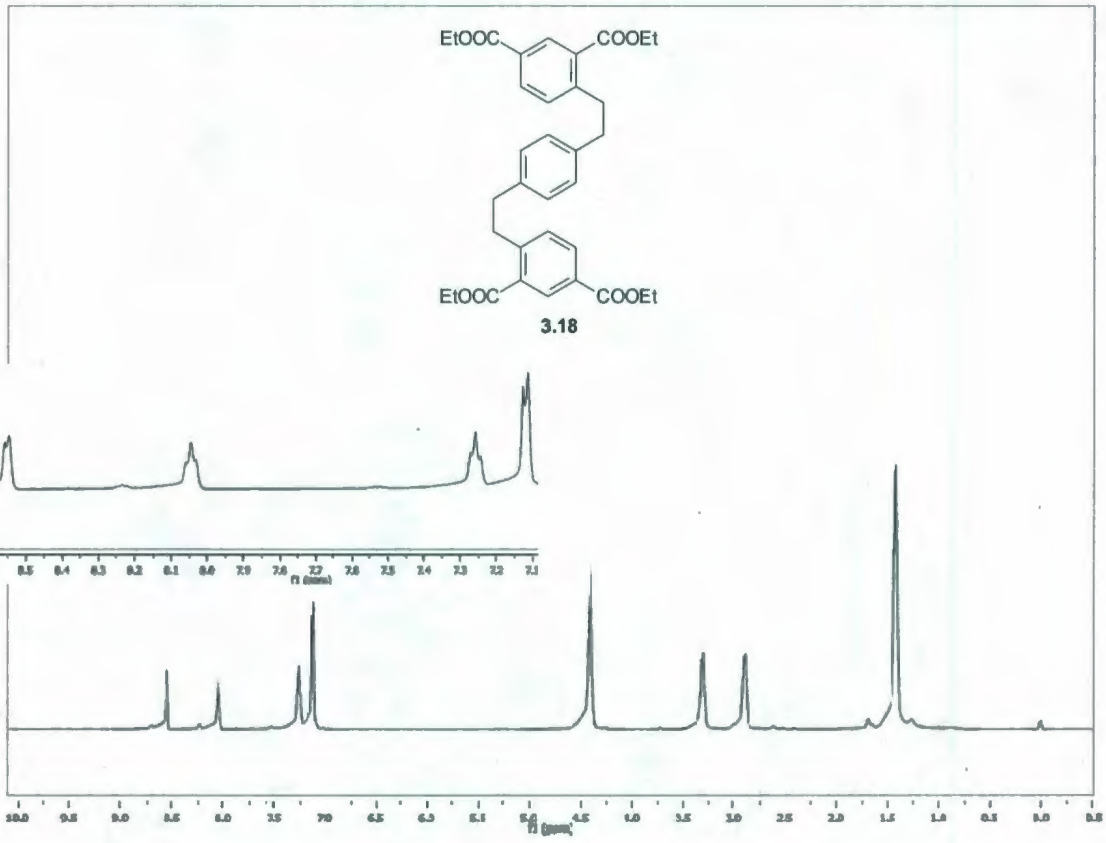
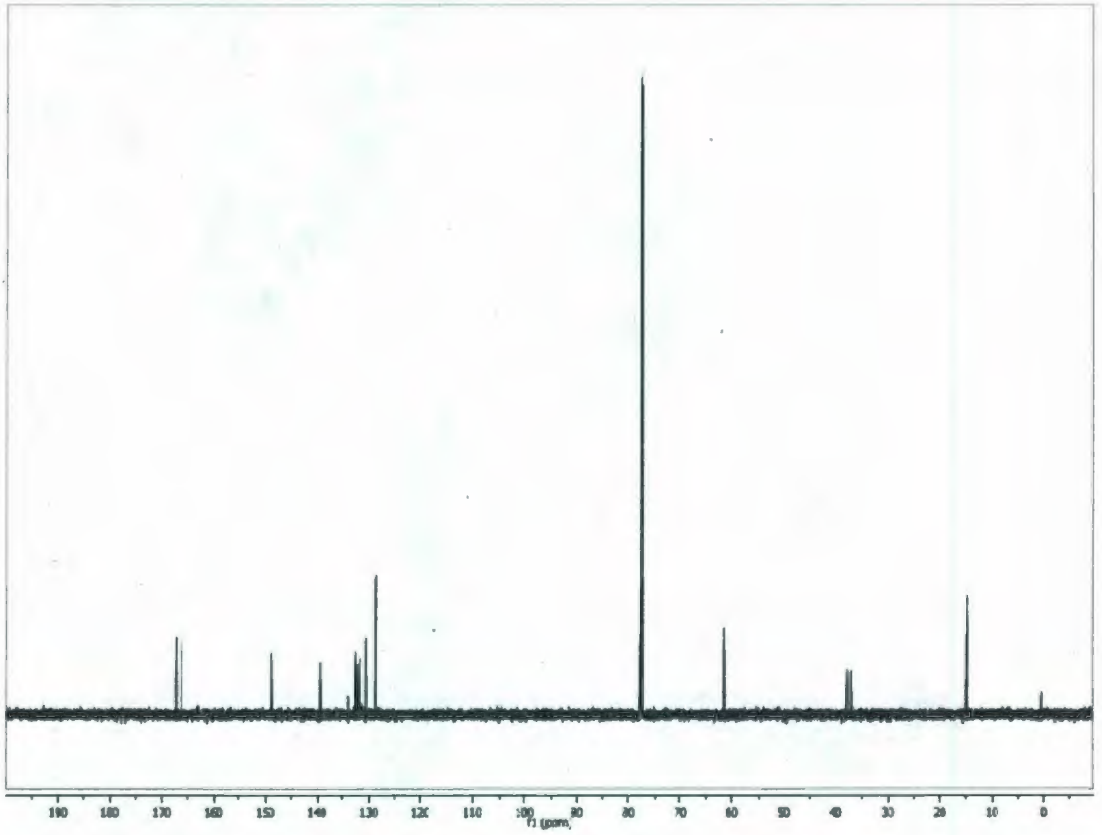
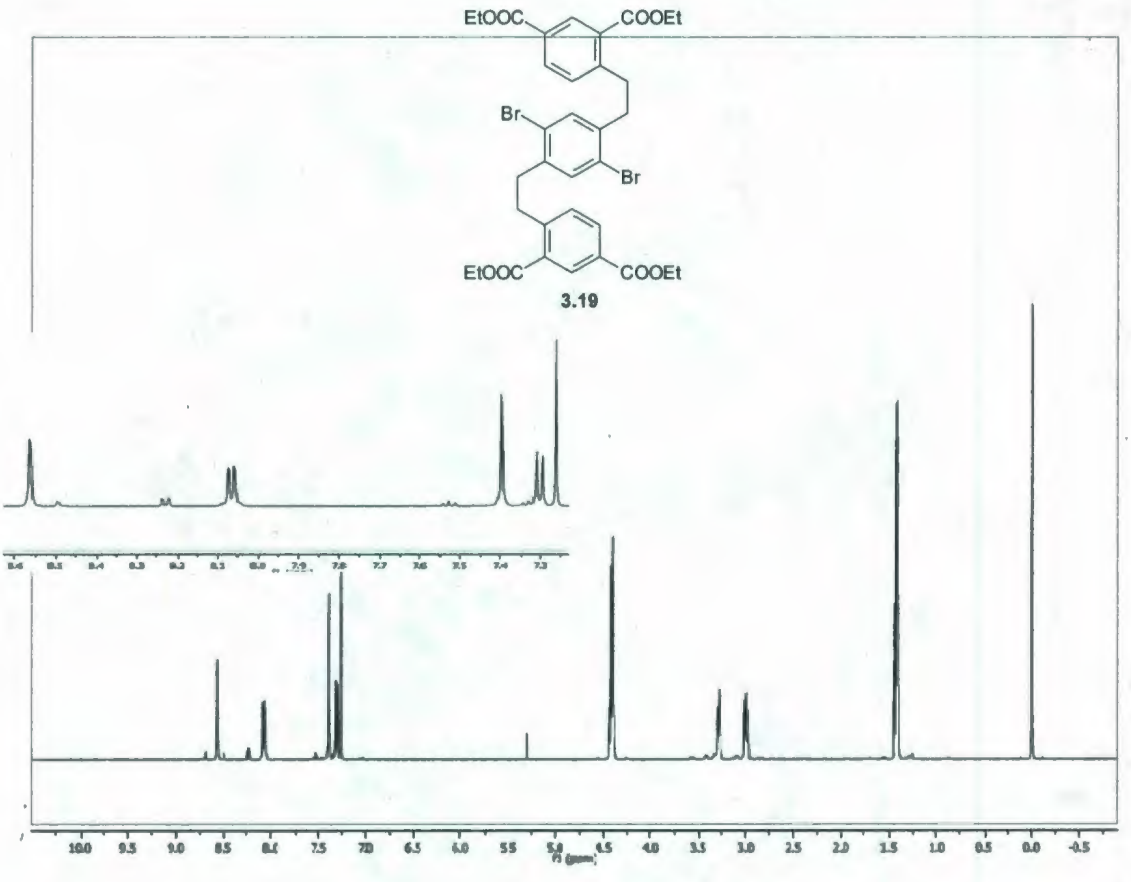





3.18





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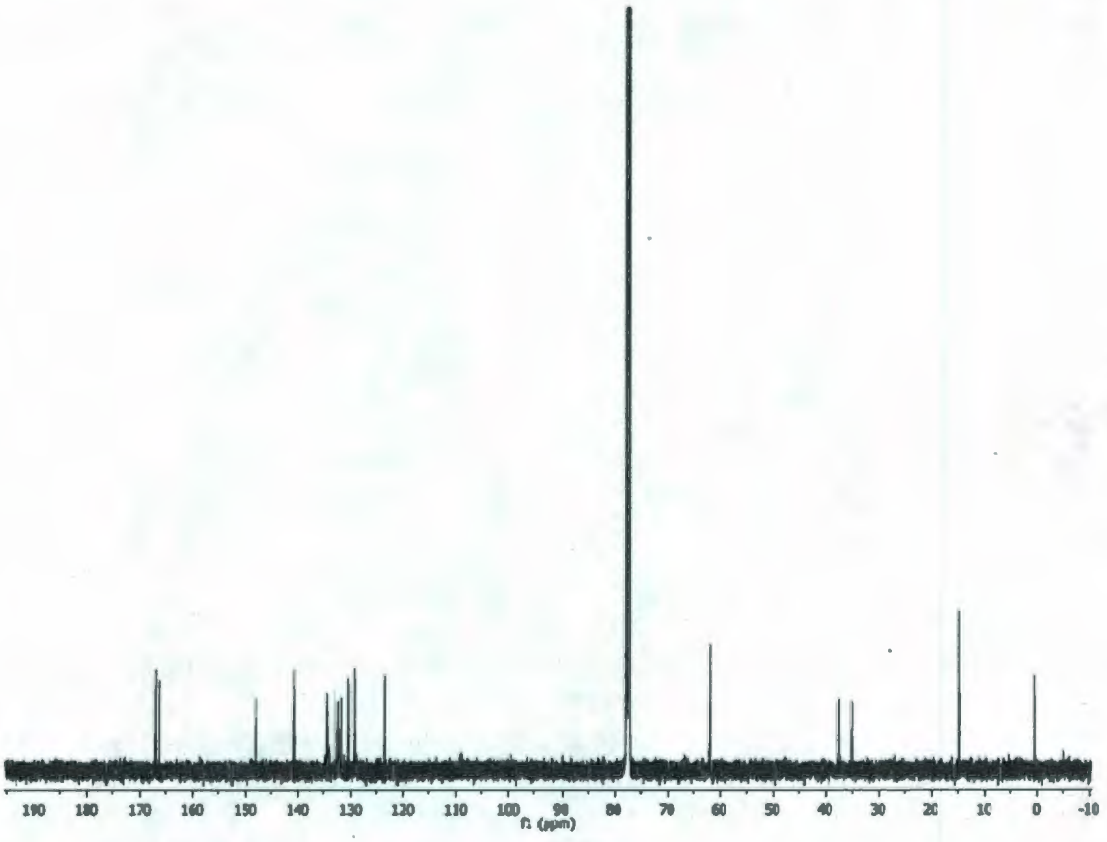

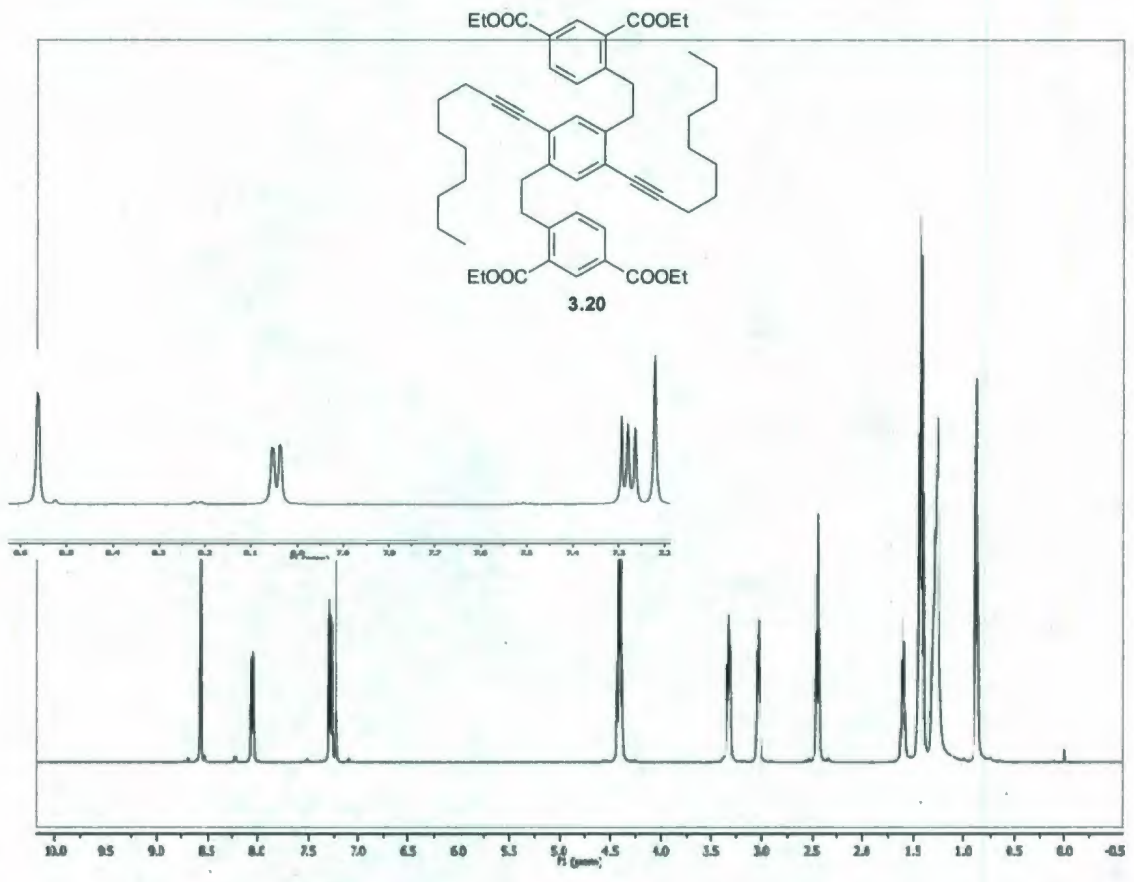


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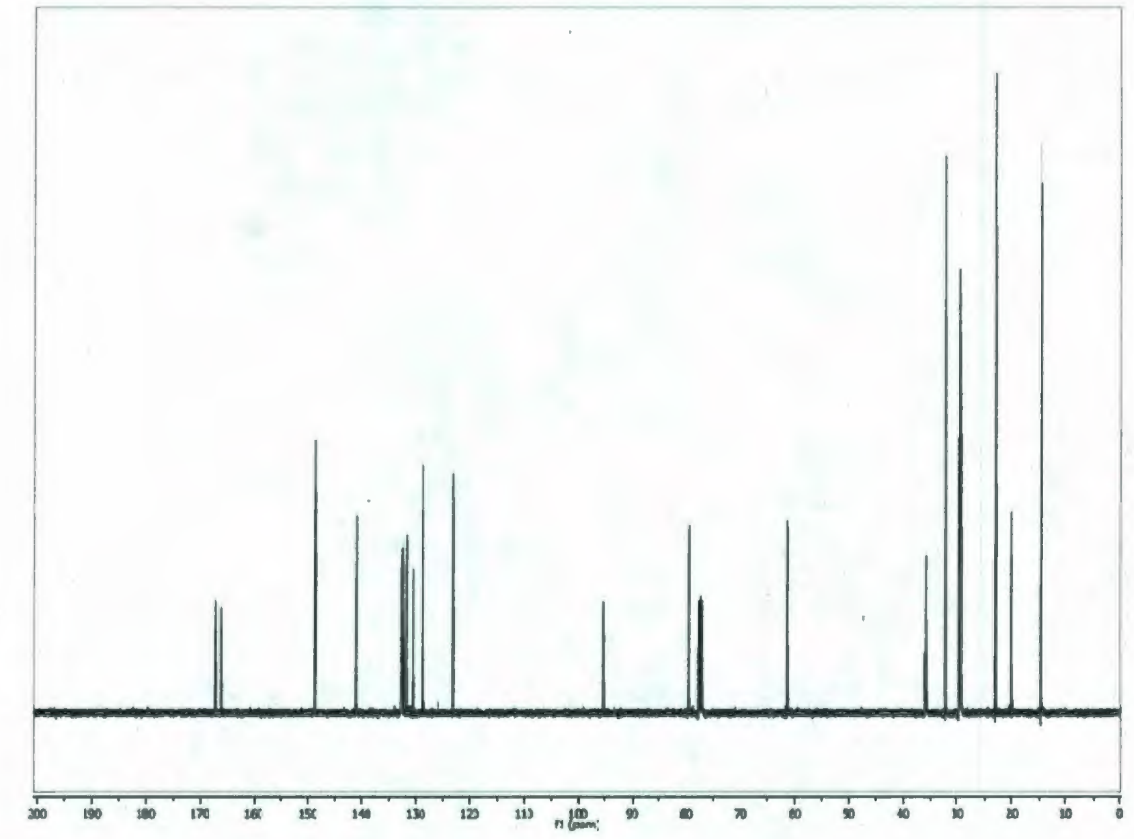

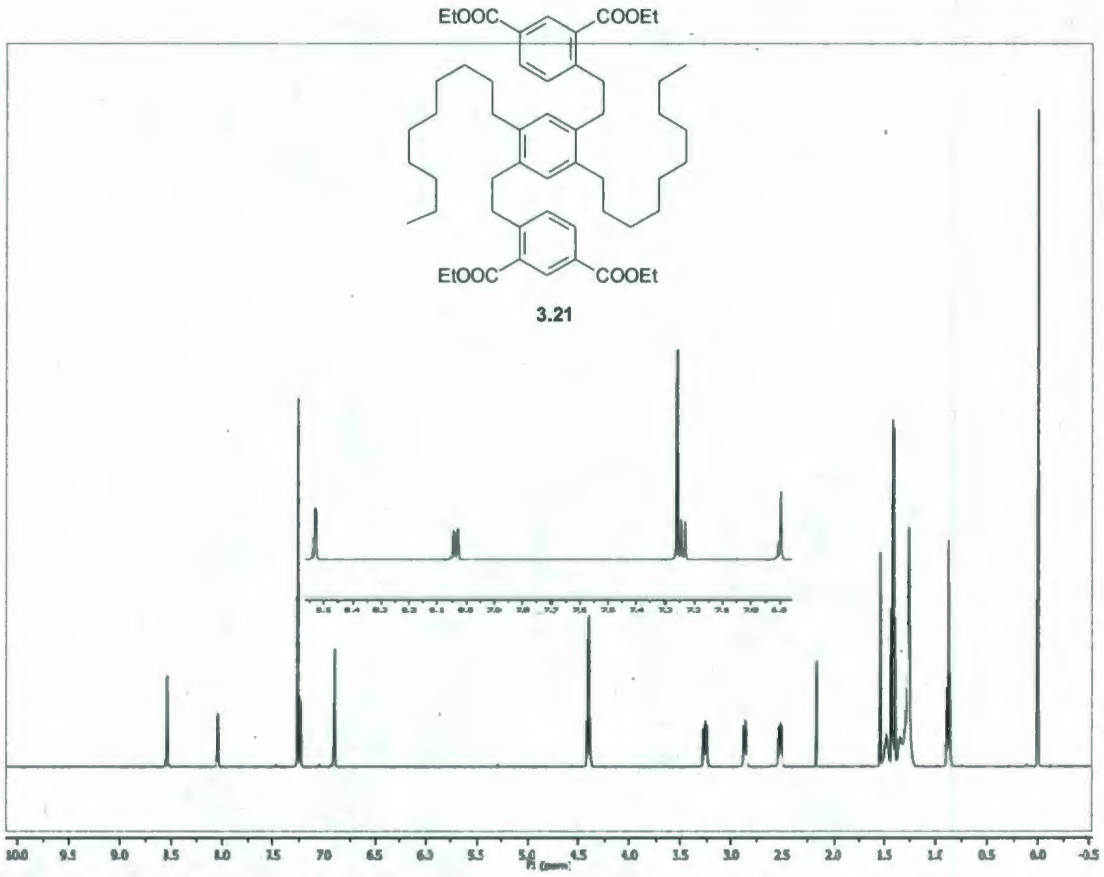


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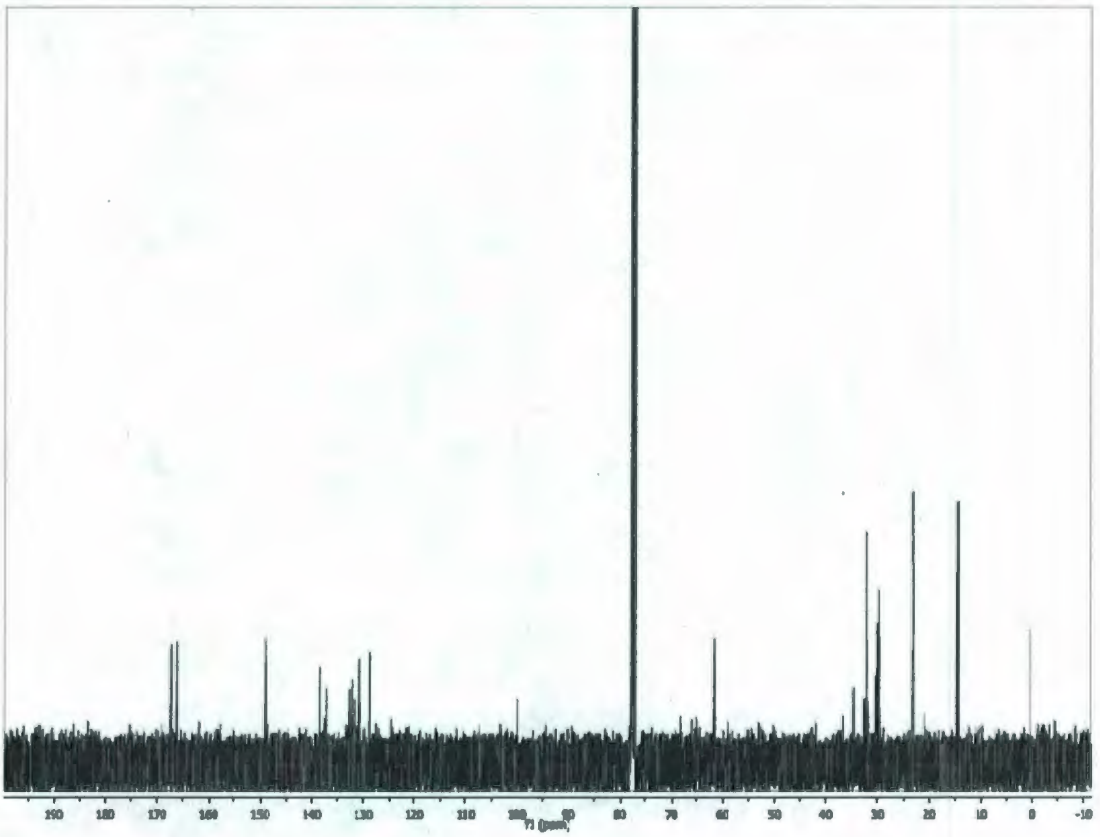

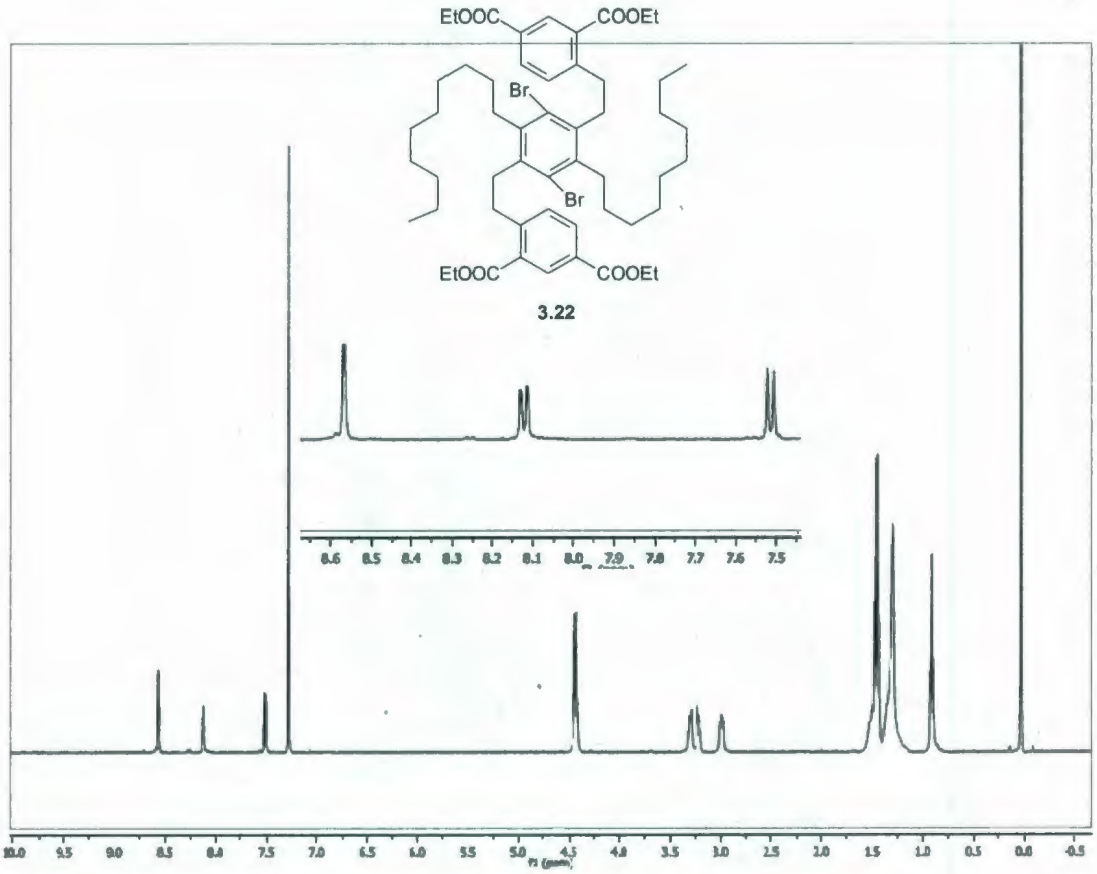
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Br
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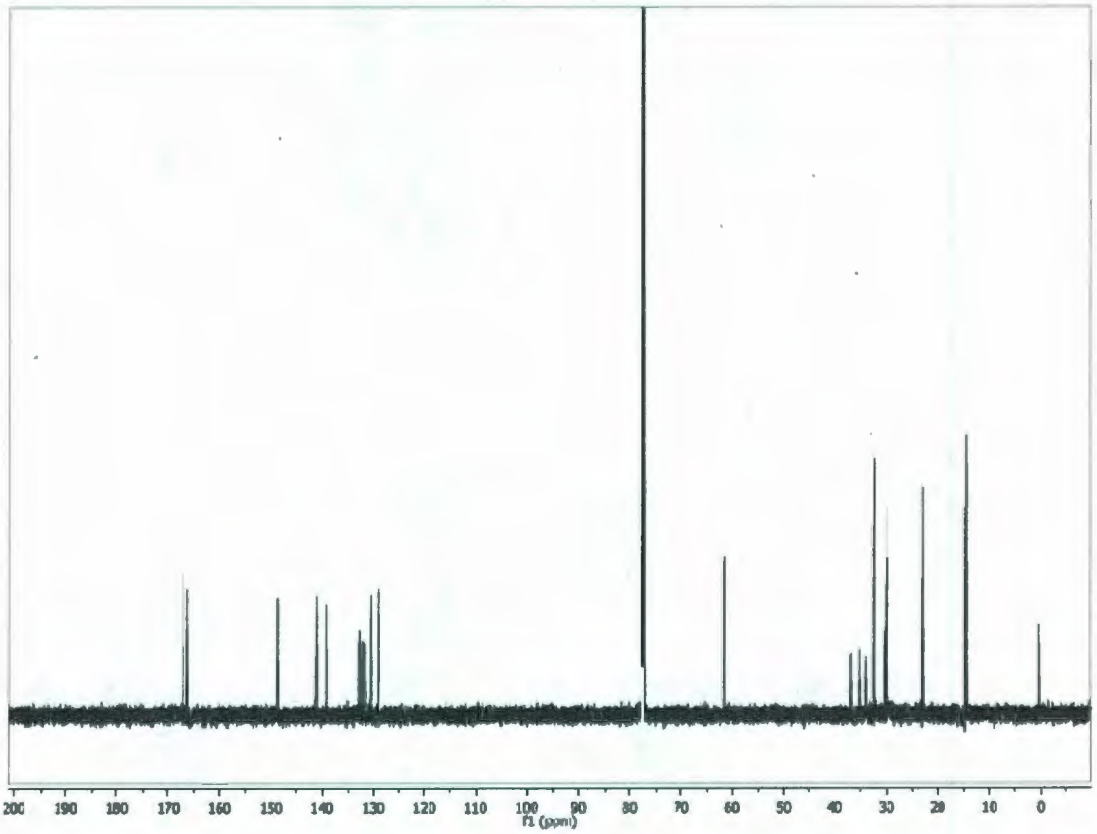

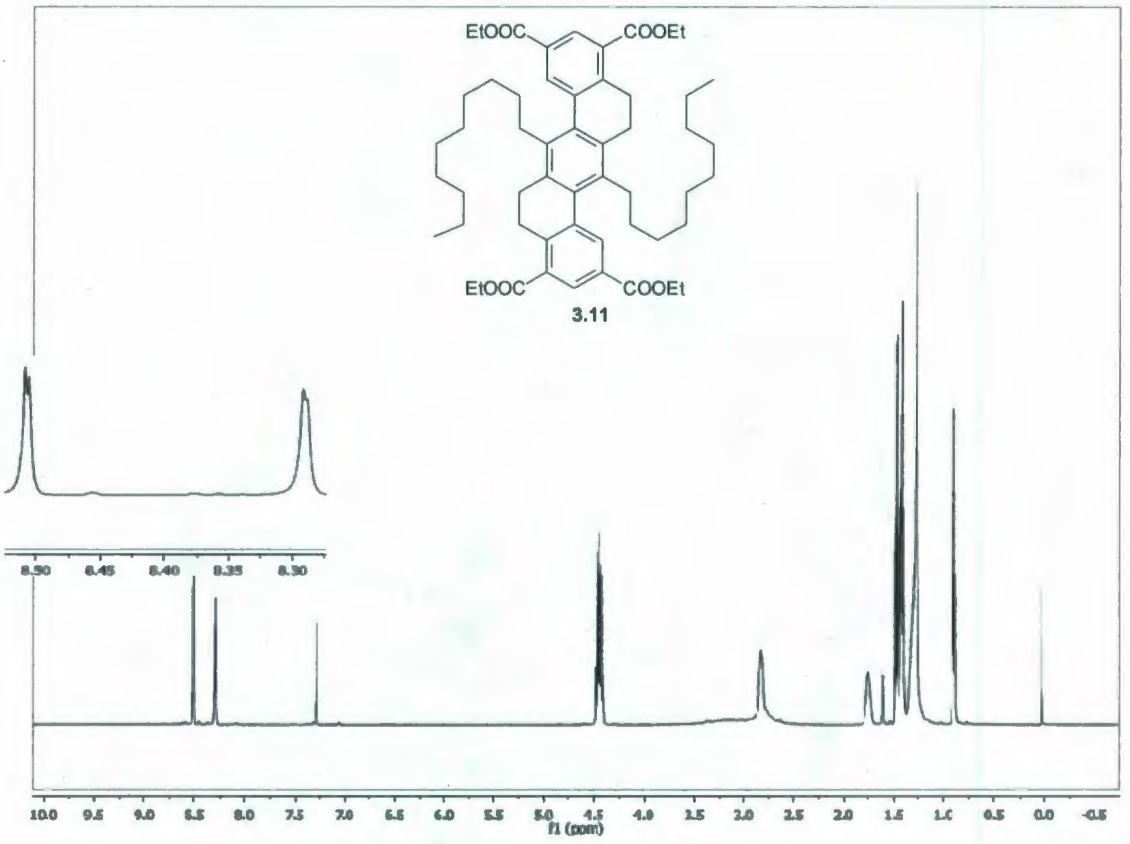
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9.0
8.5
8.0
7.5
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5.0
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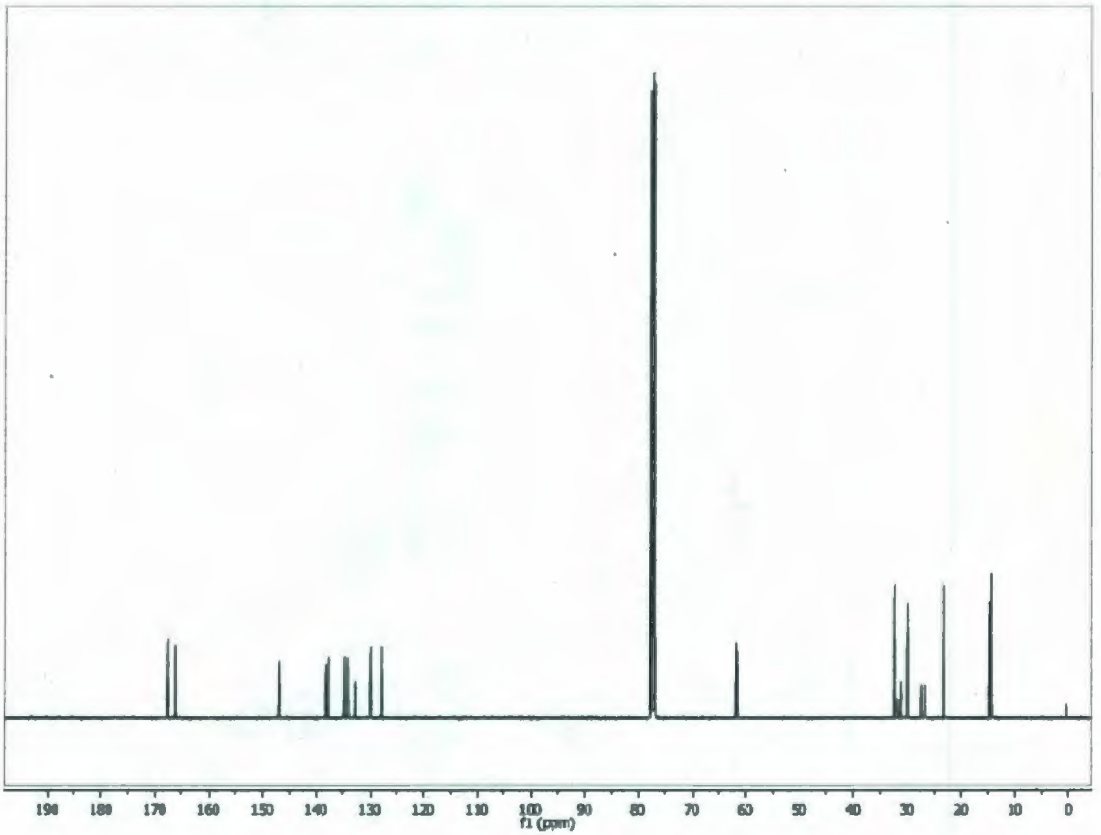
f1 (ppm)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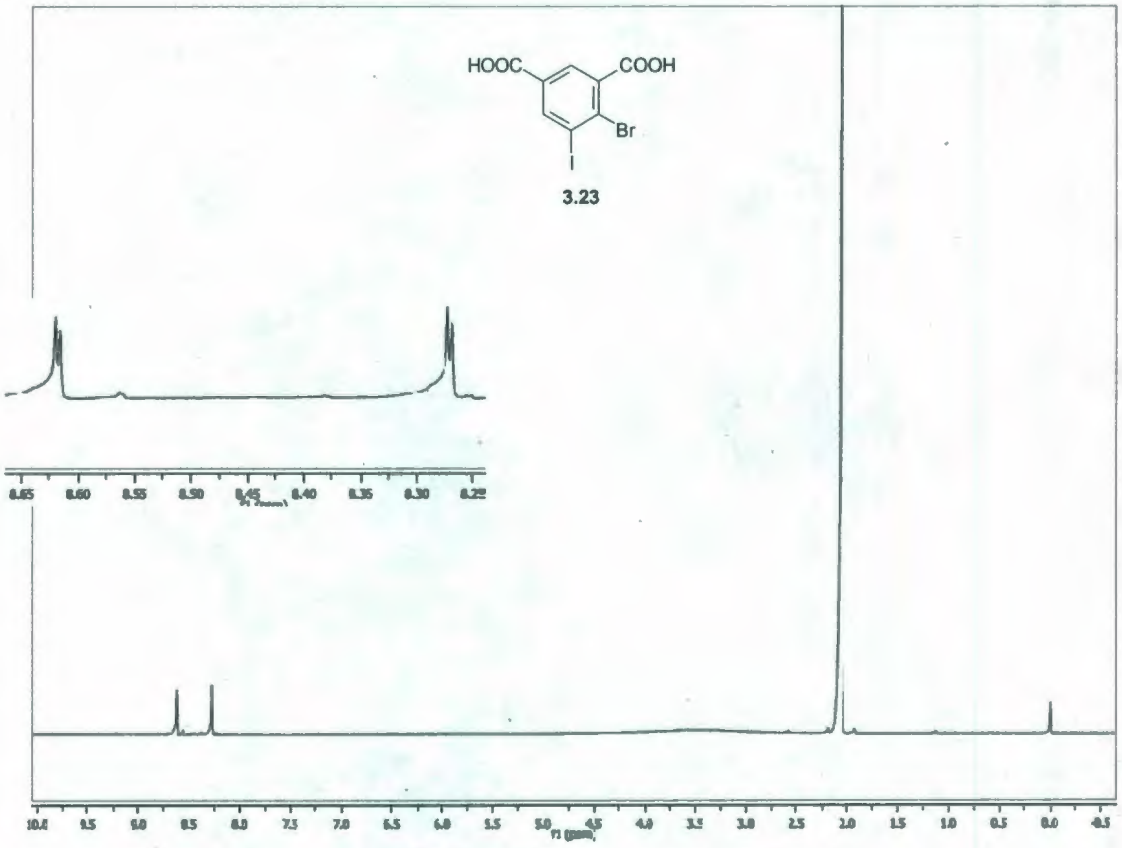


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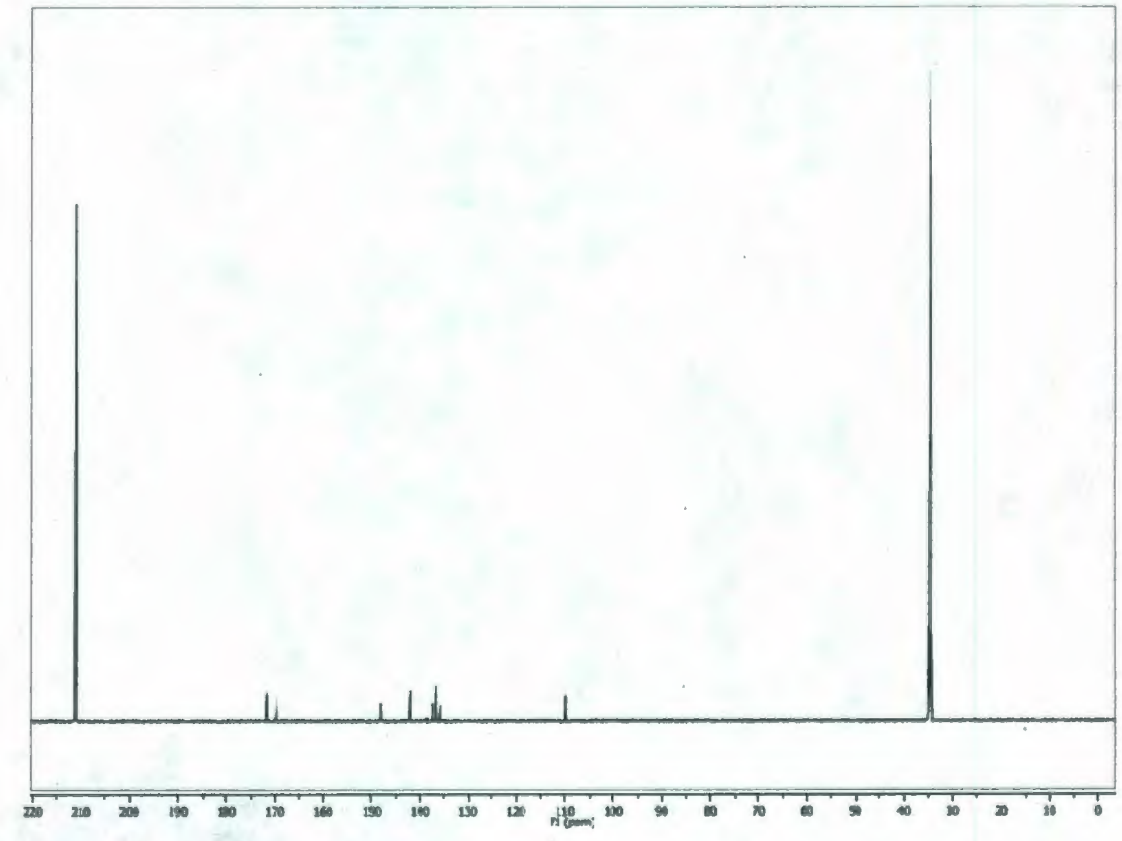

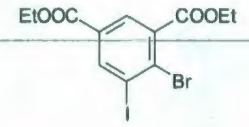


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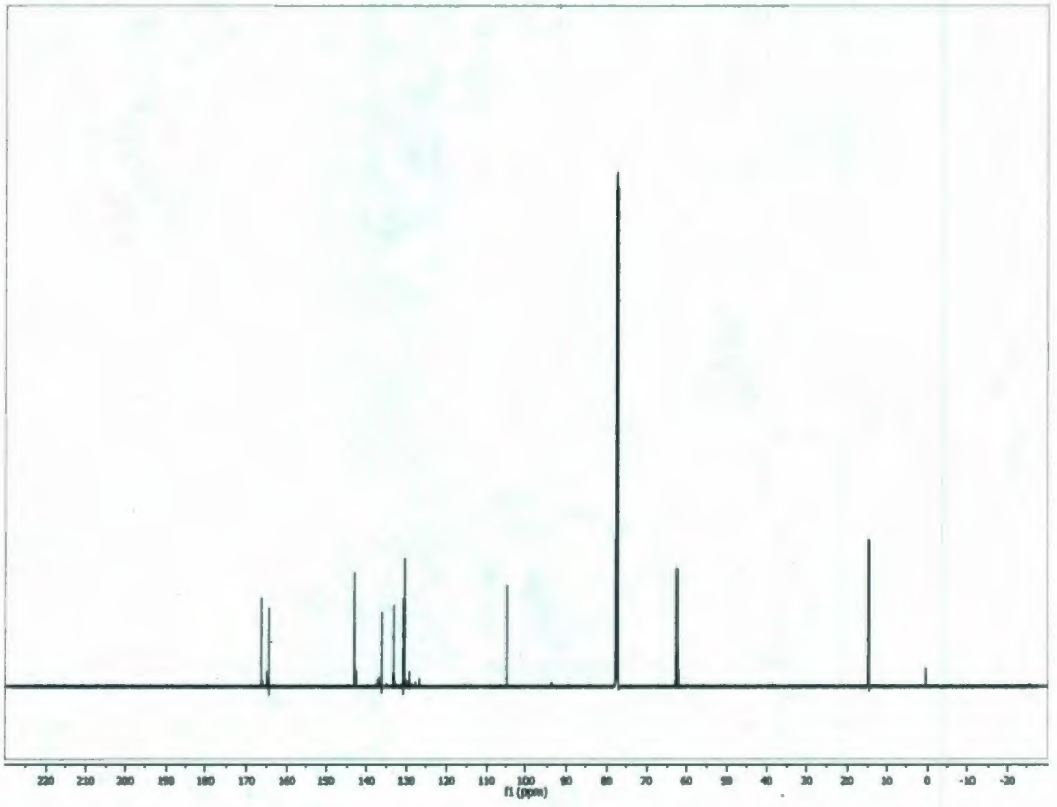
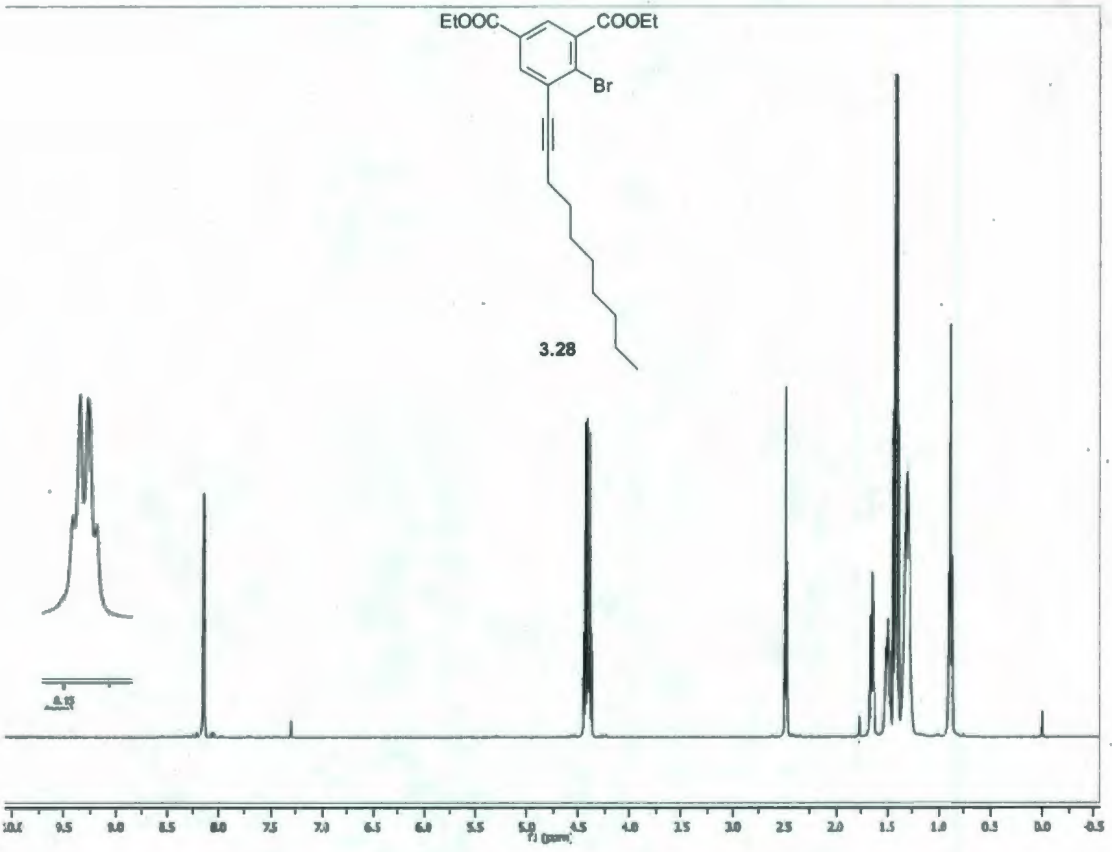
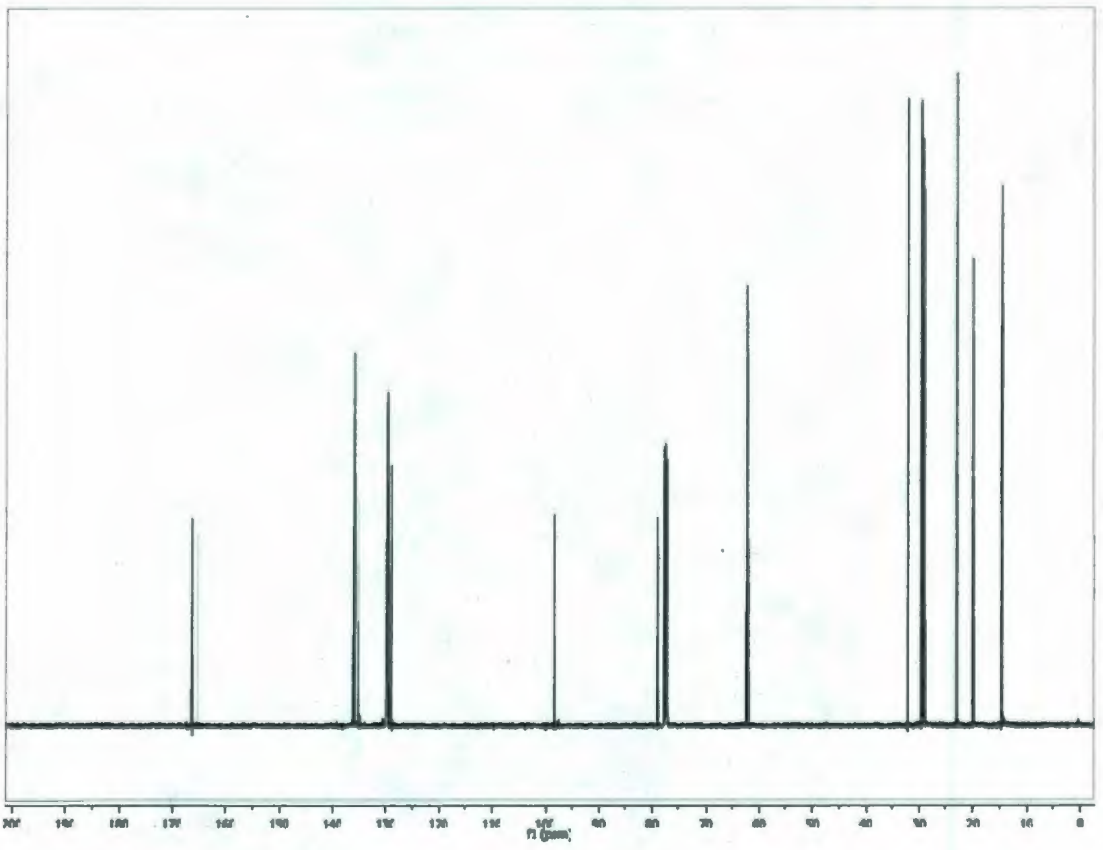
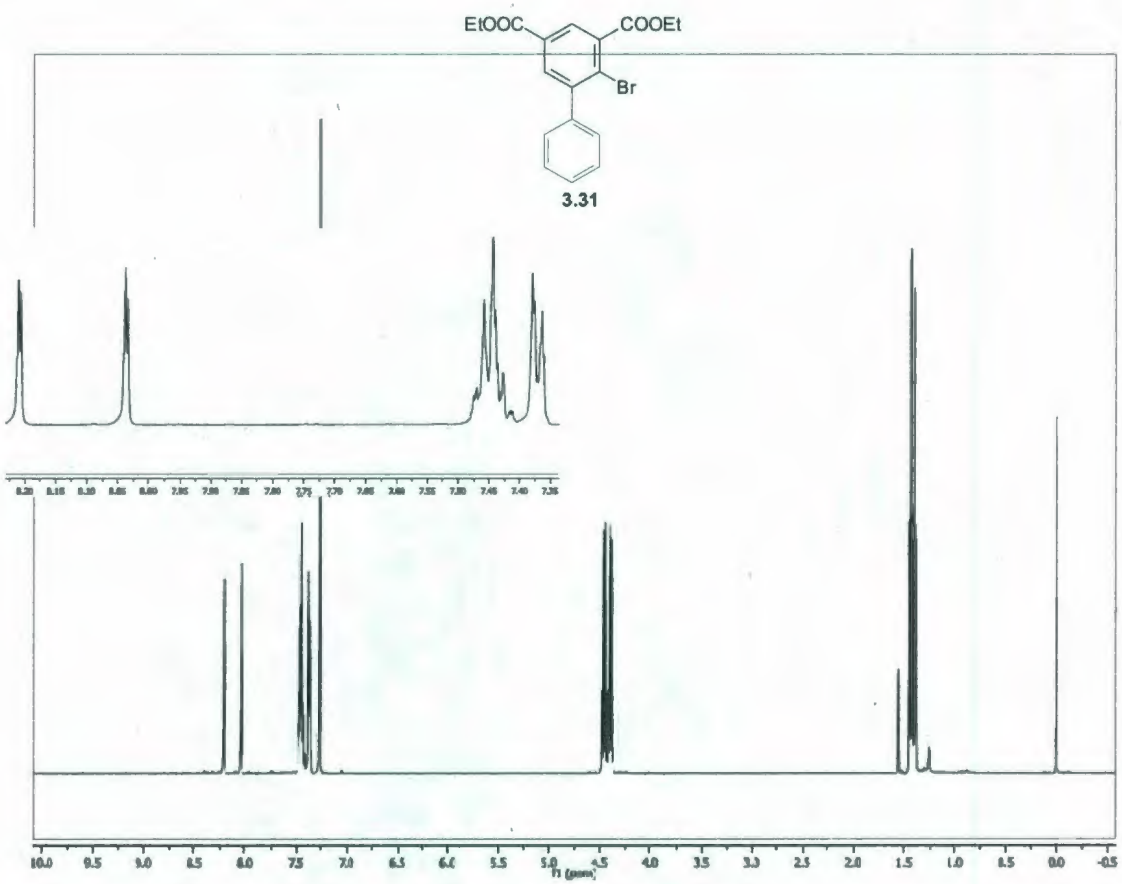





3.28



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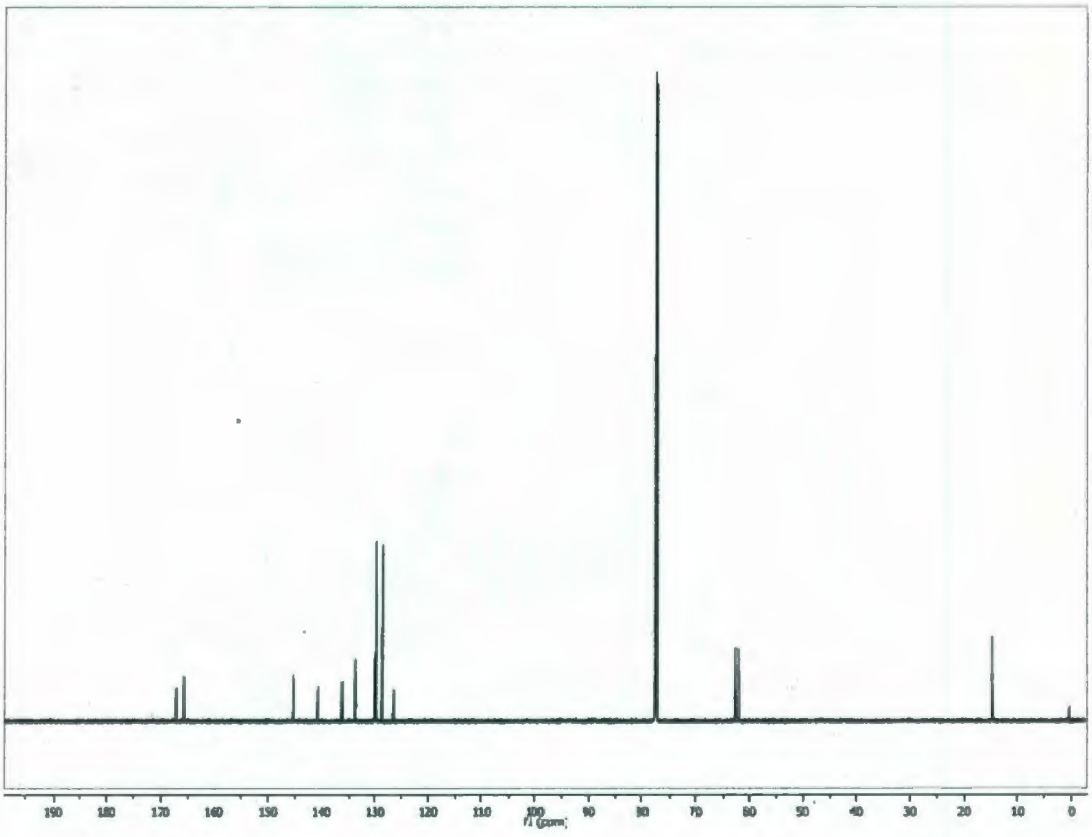

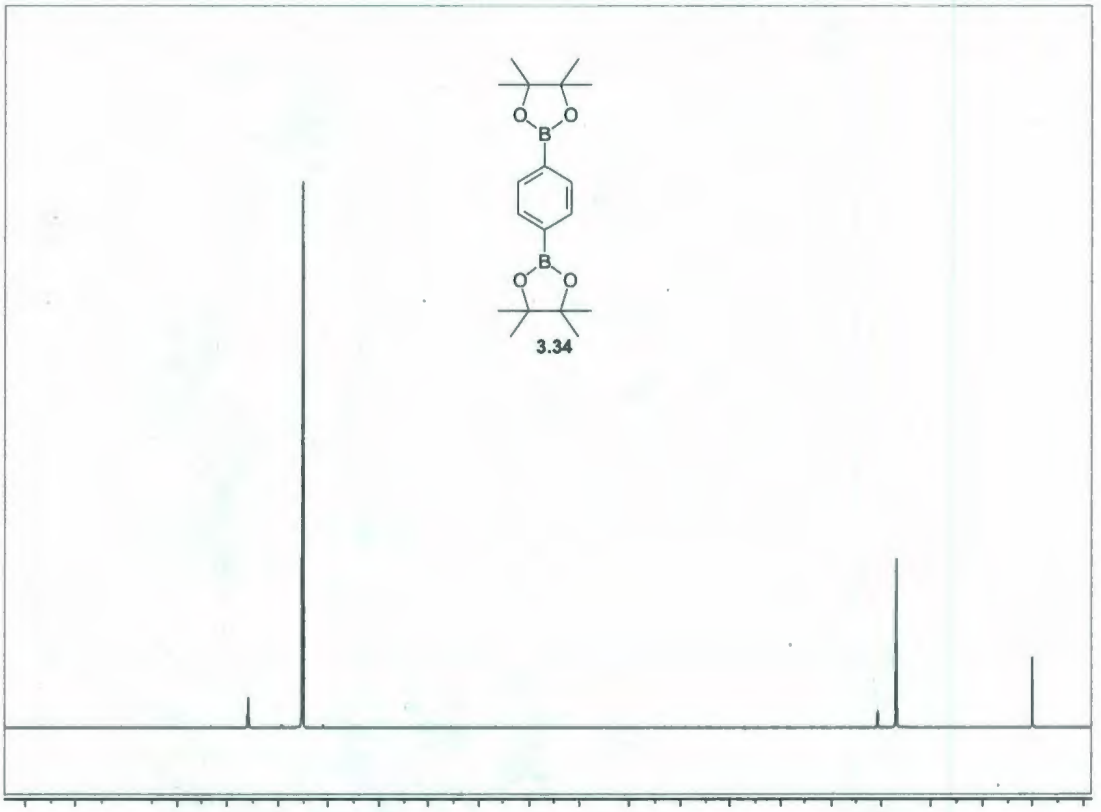


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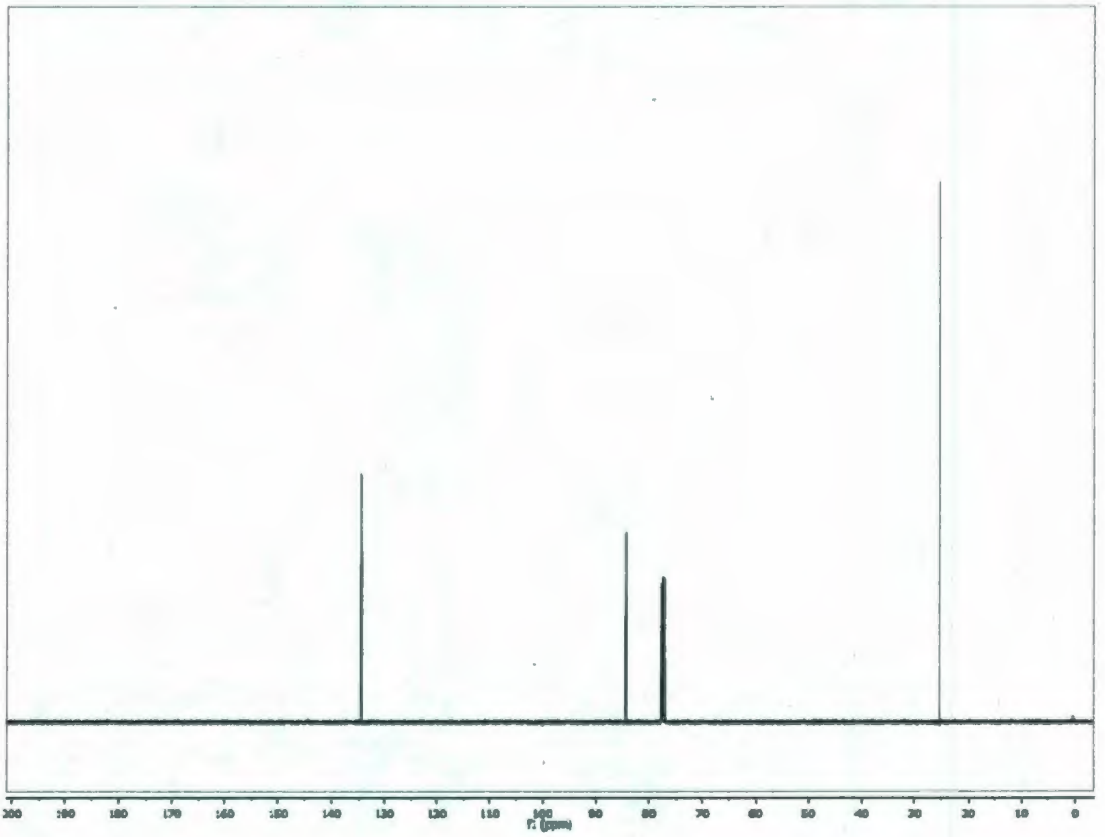

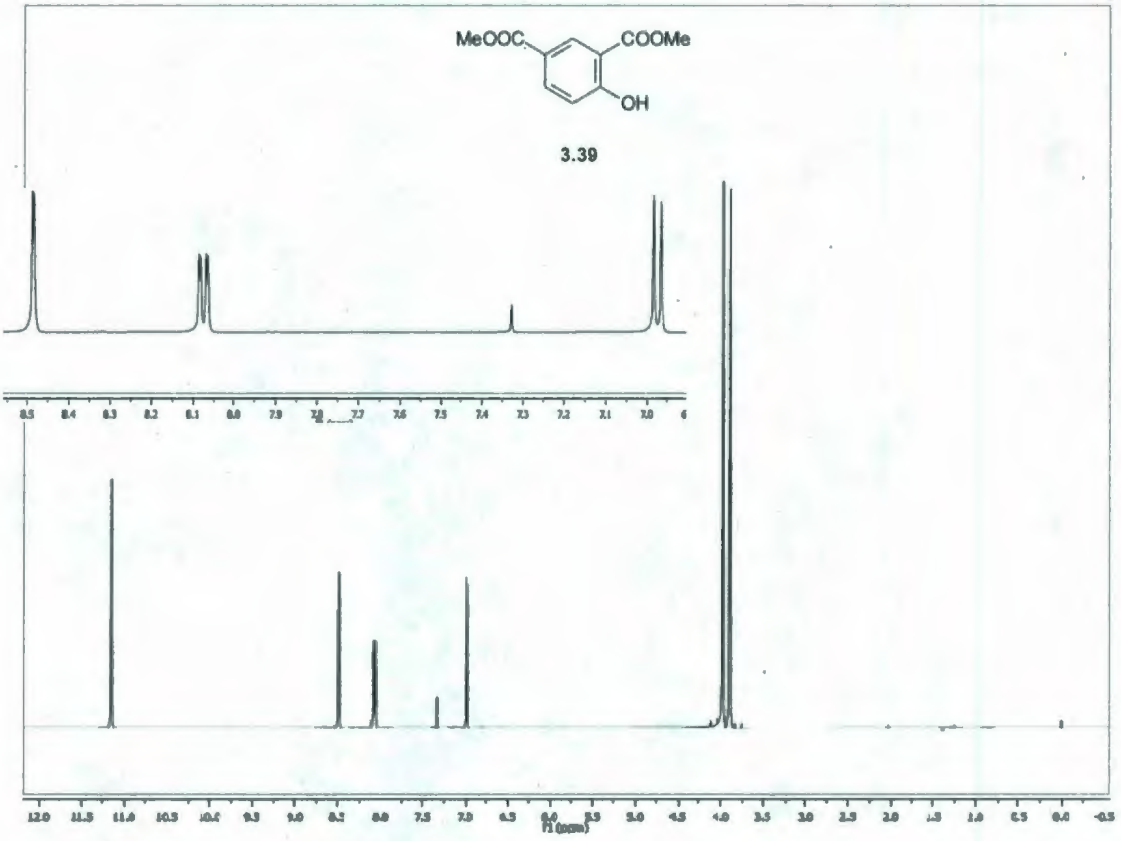


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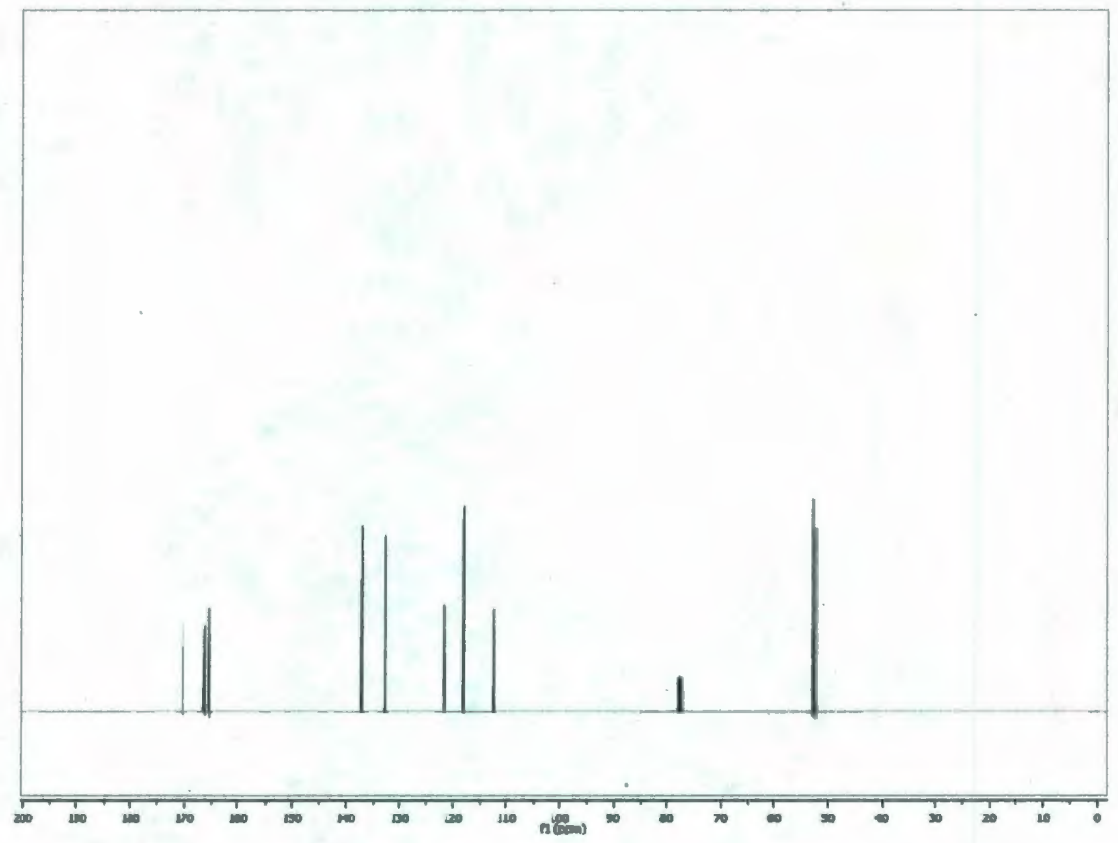

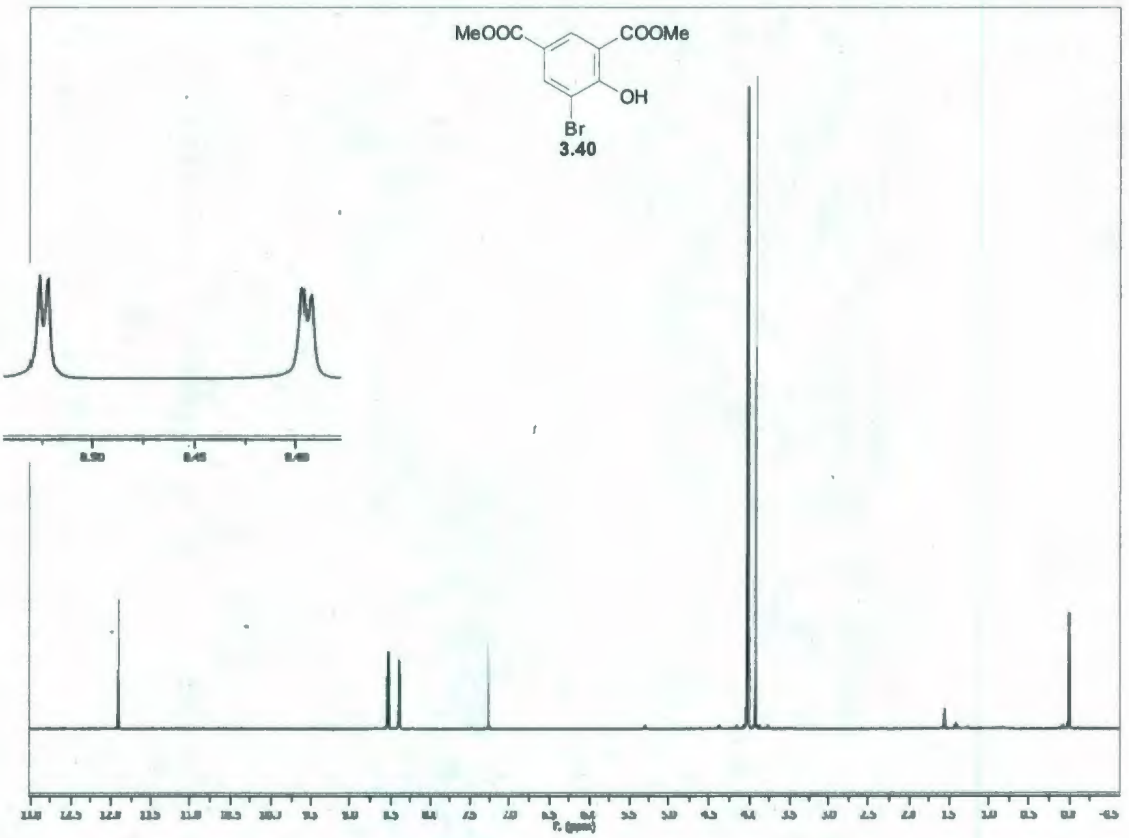
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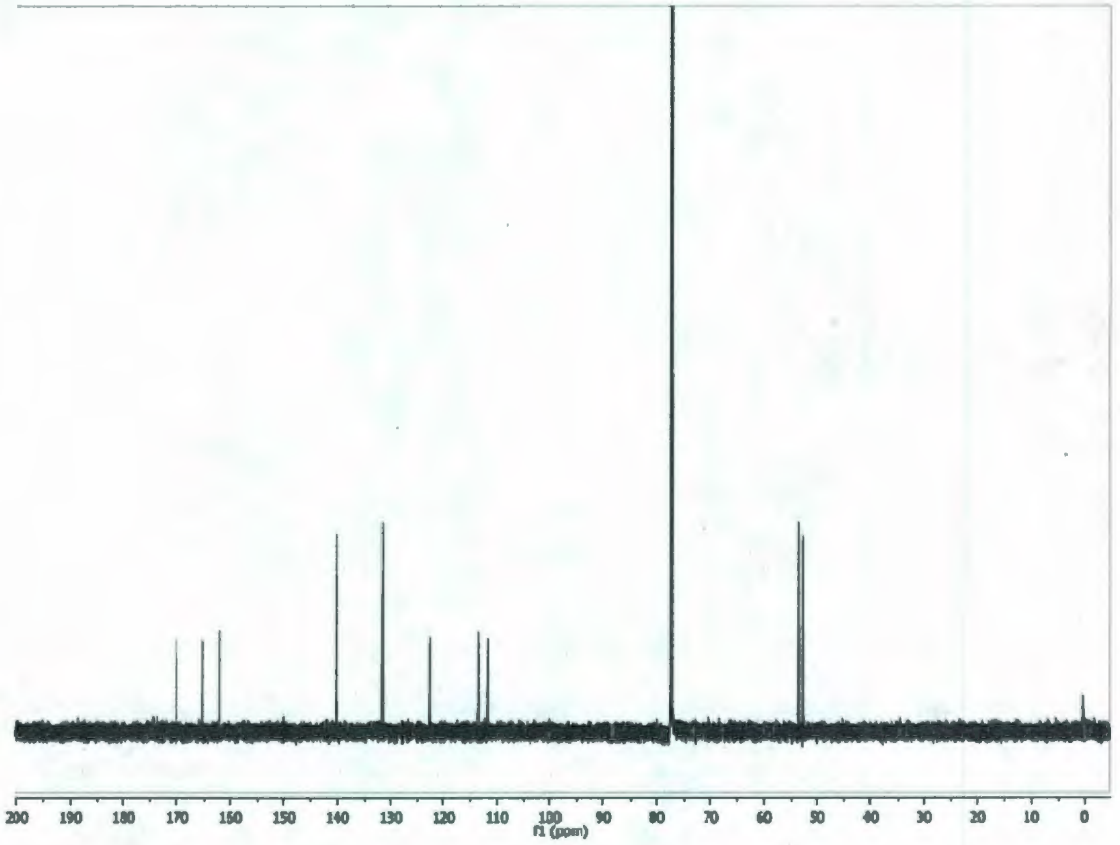
COOMe
OH
Br
3.40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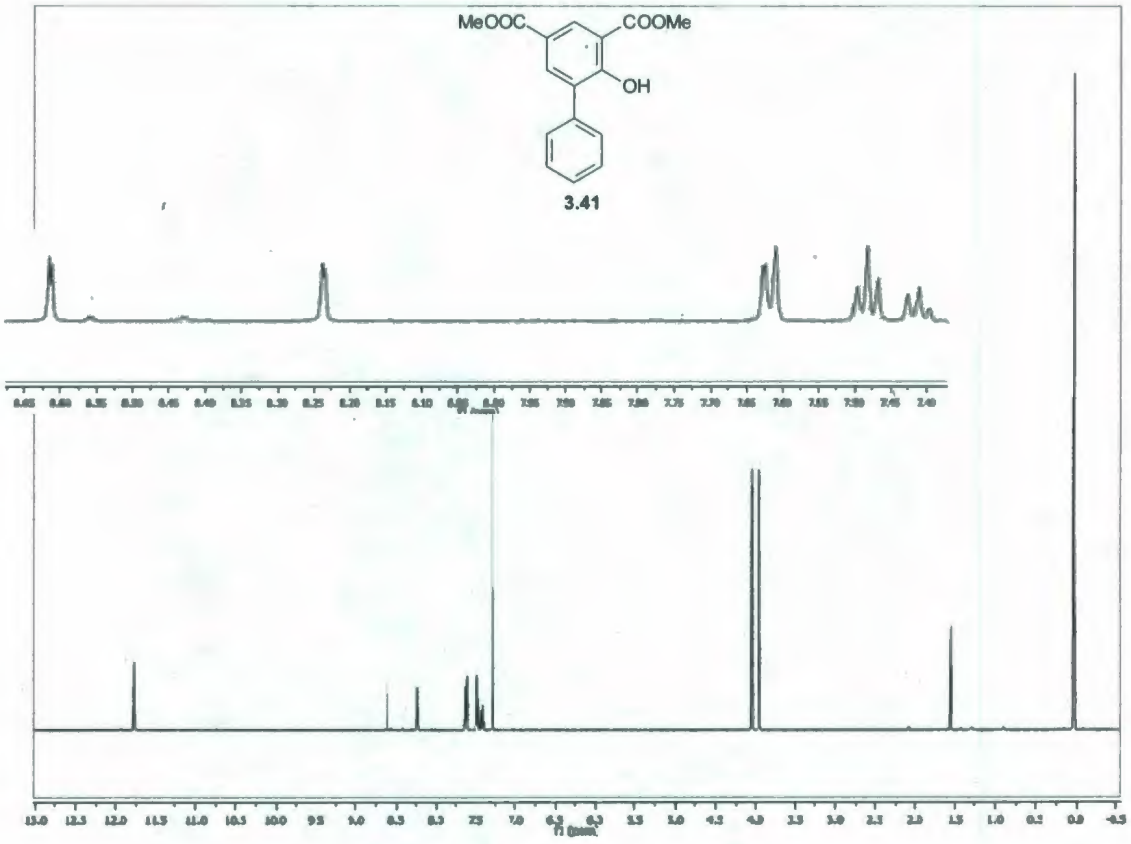
f1 (ppm)

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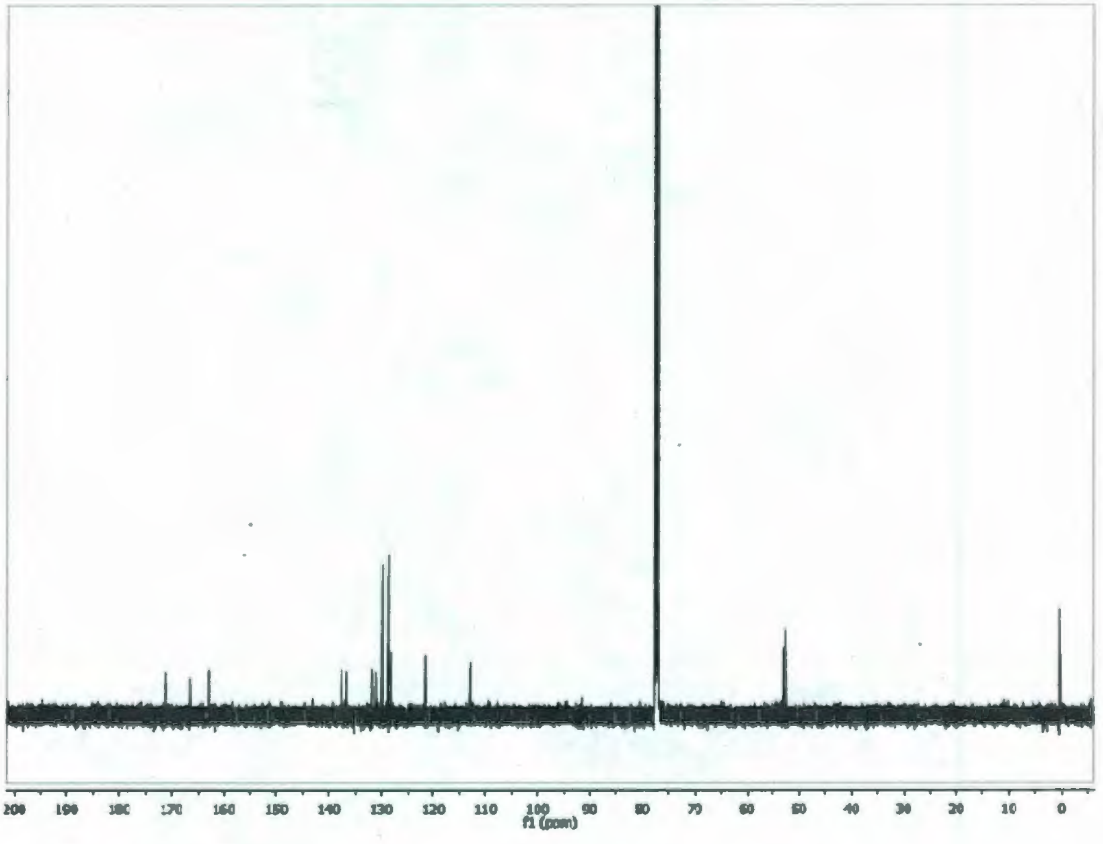

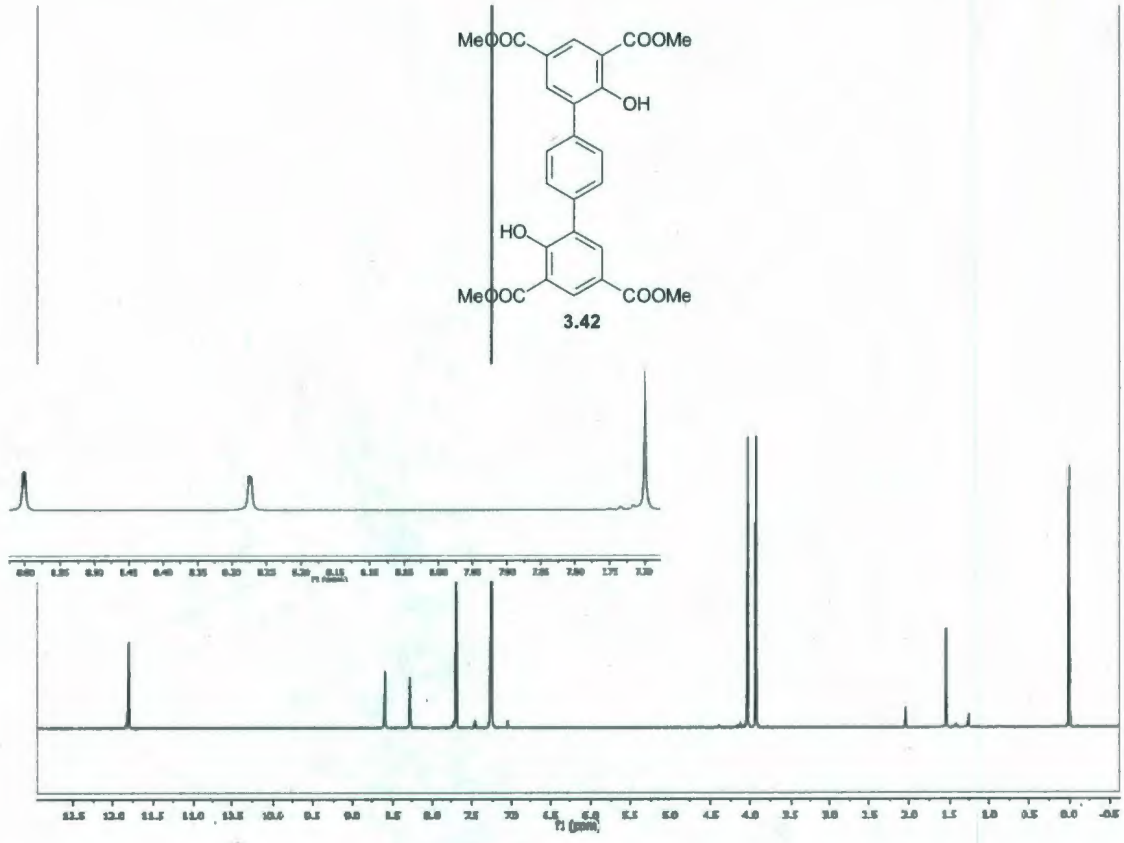


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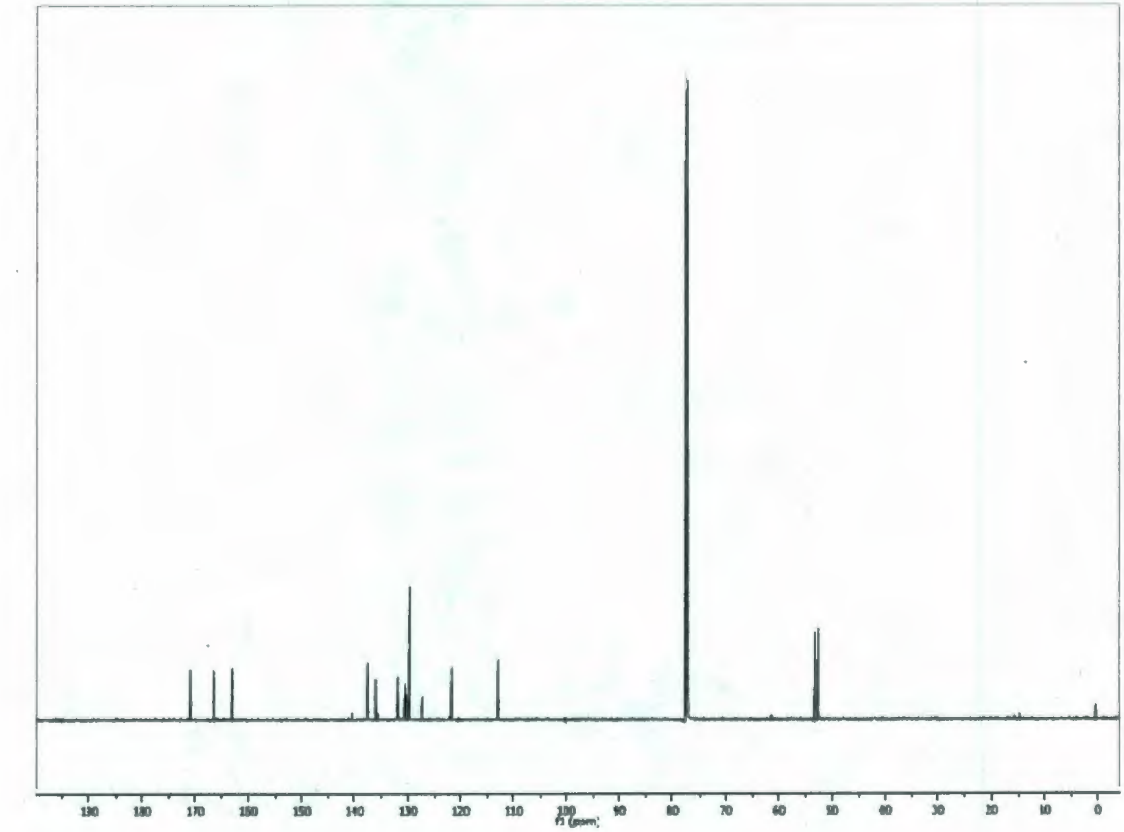

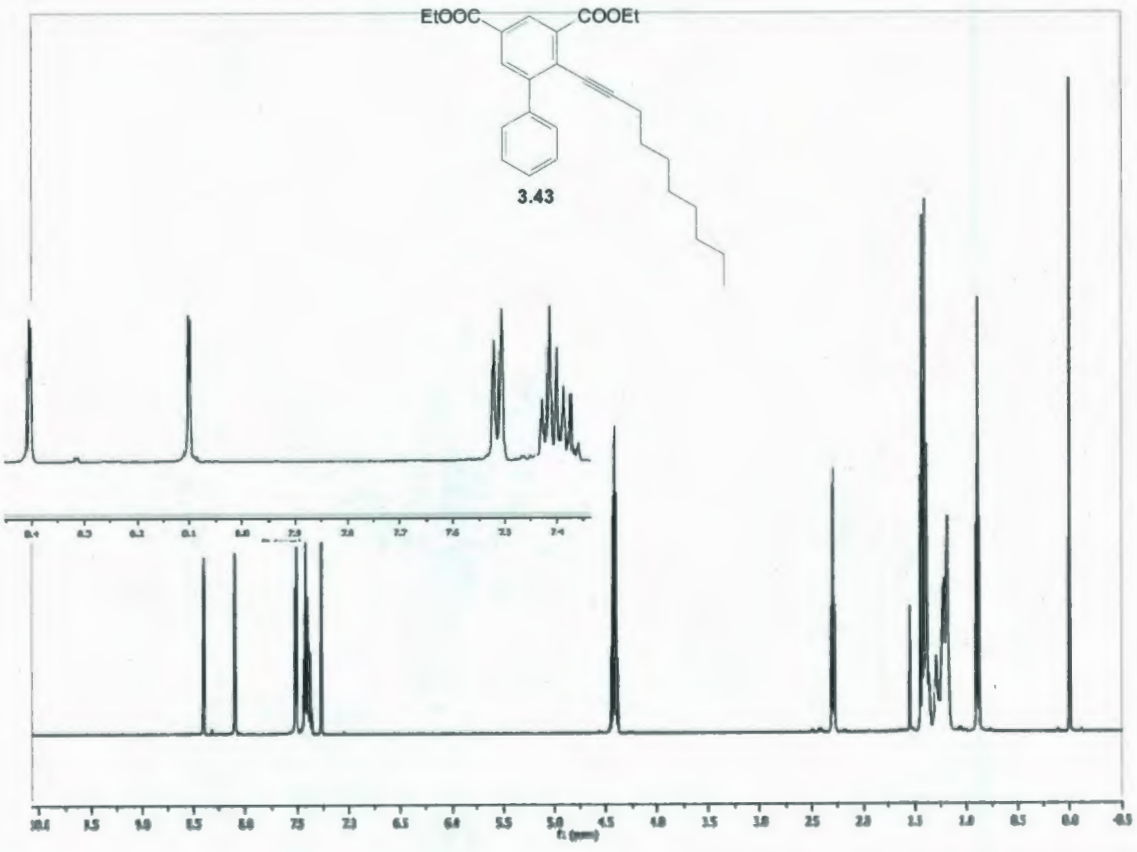


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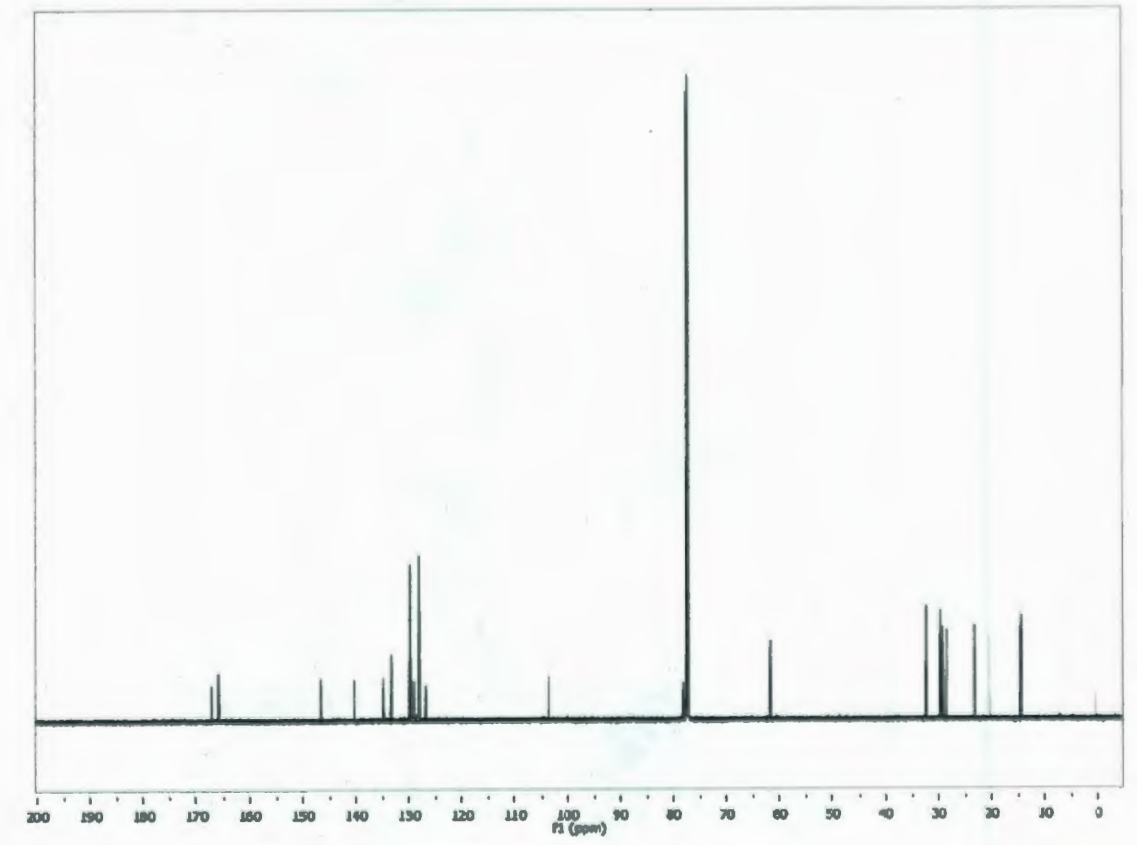

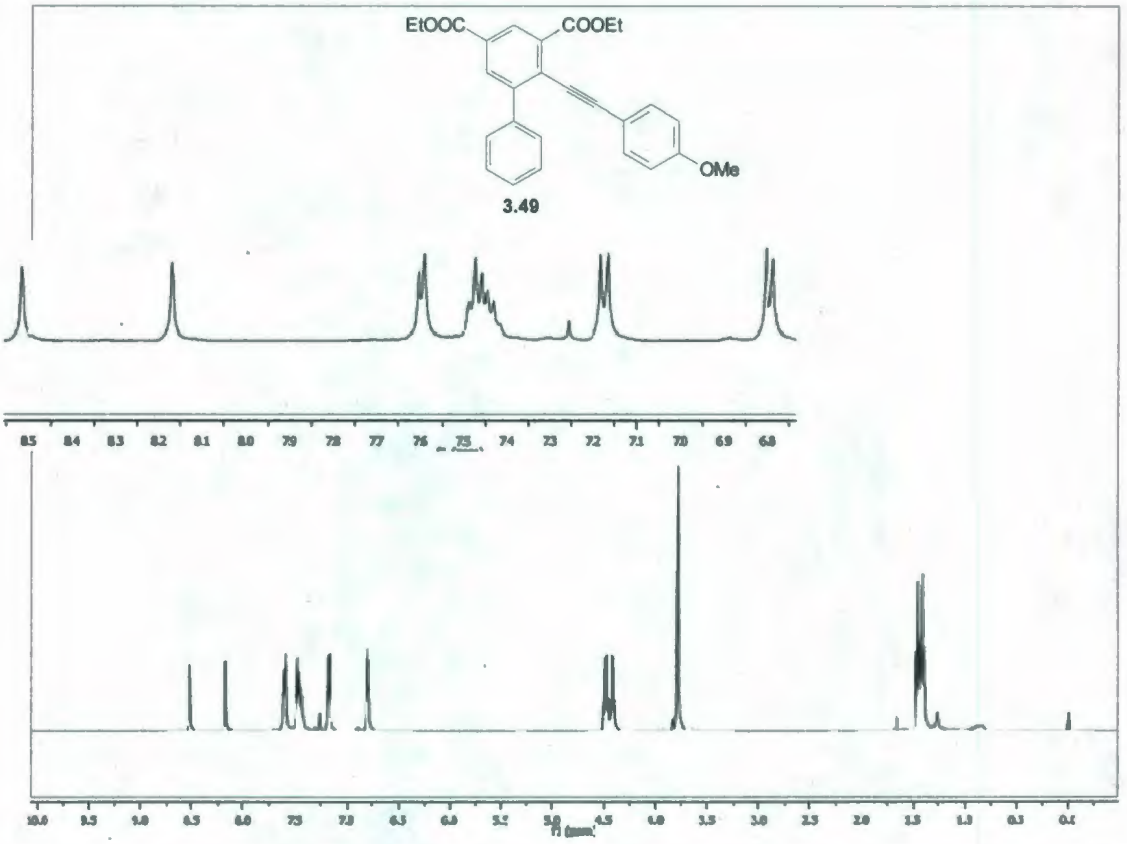


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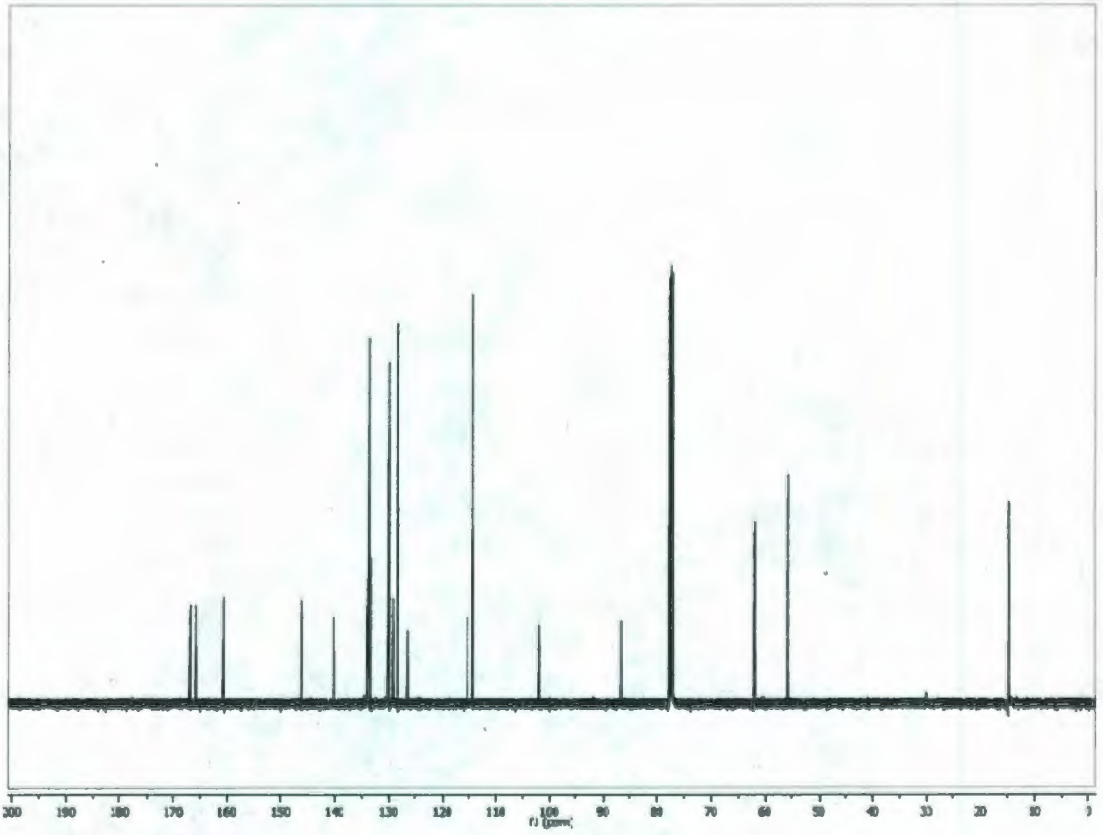

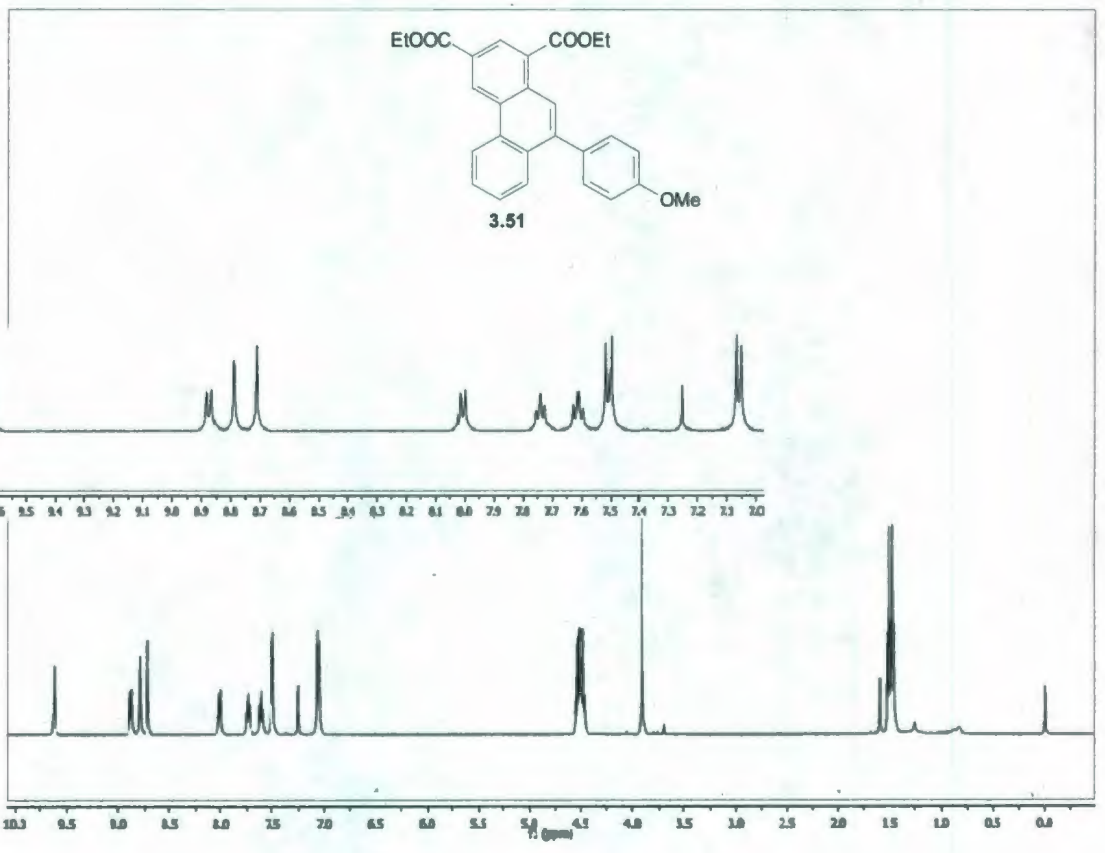


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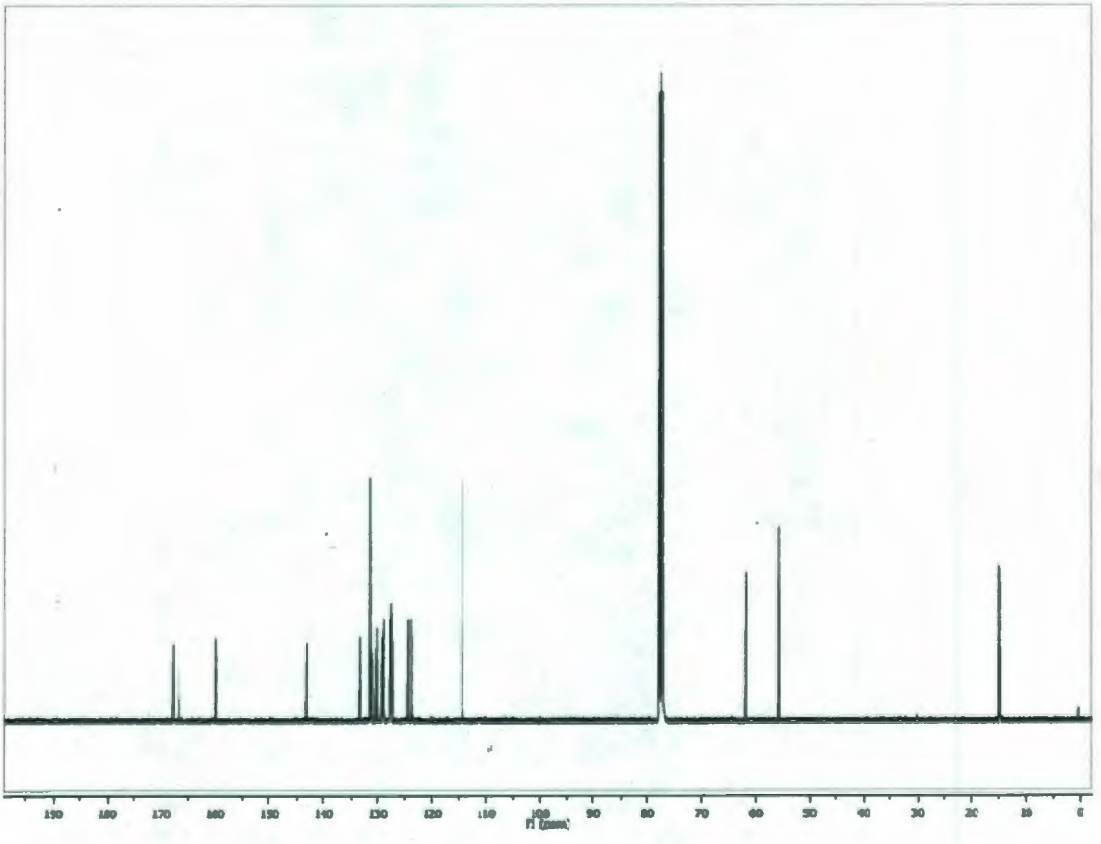
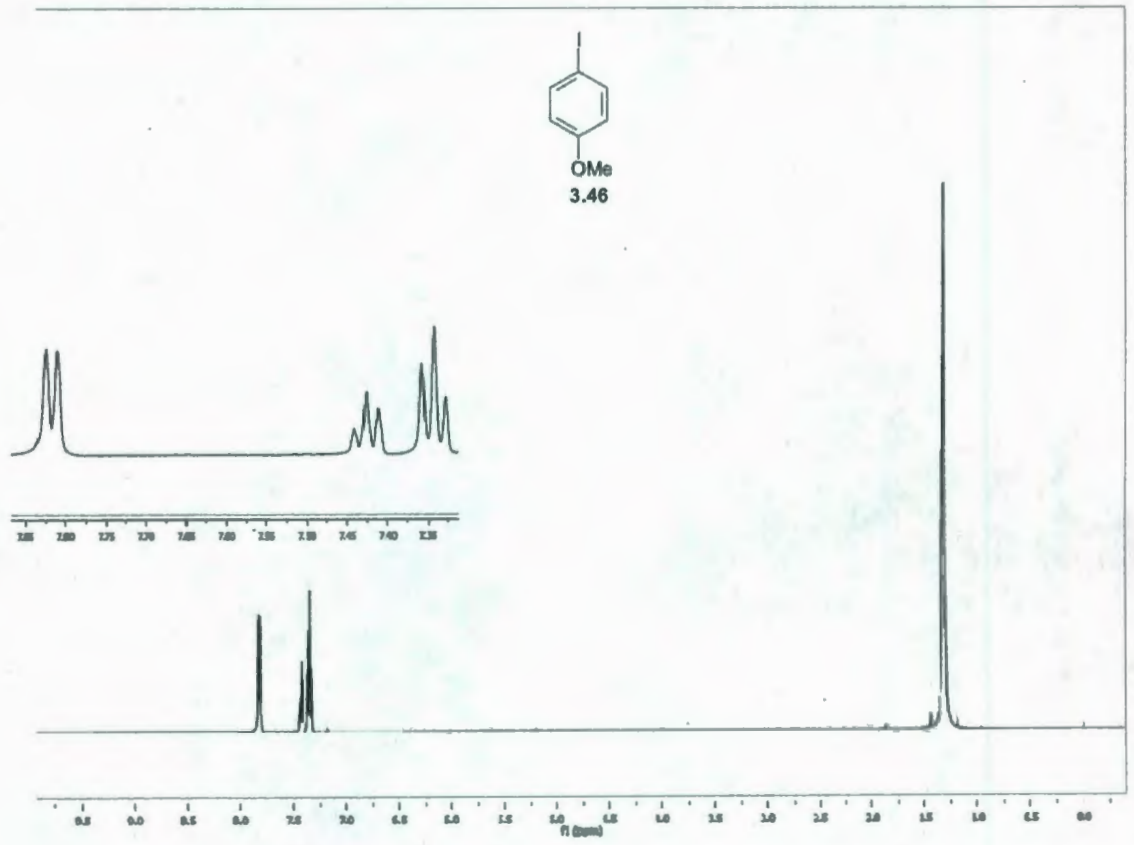
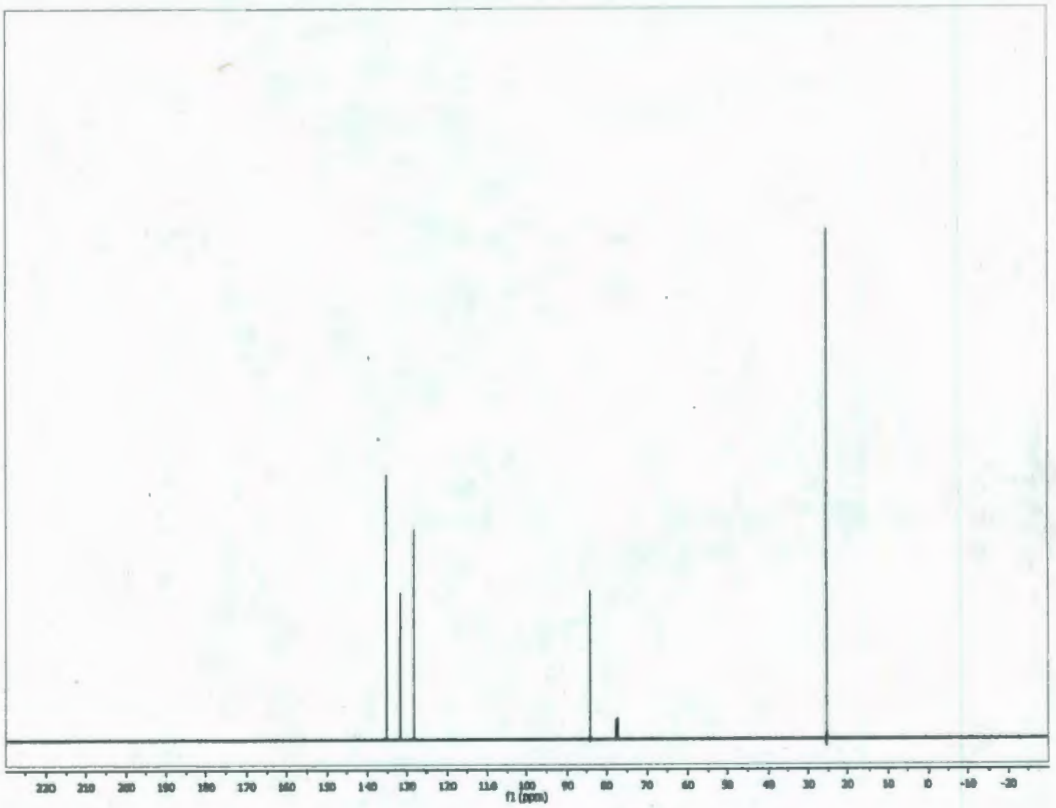
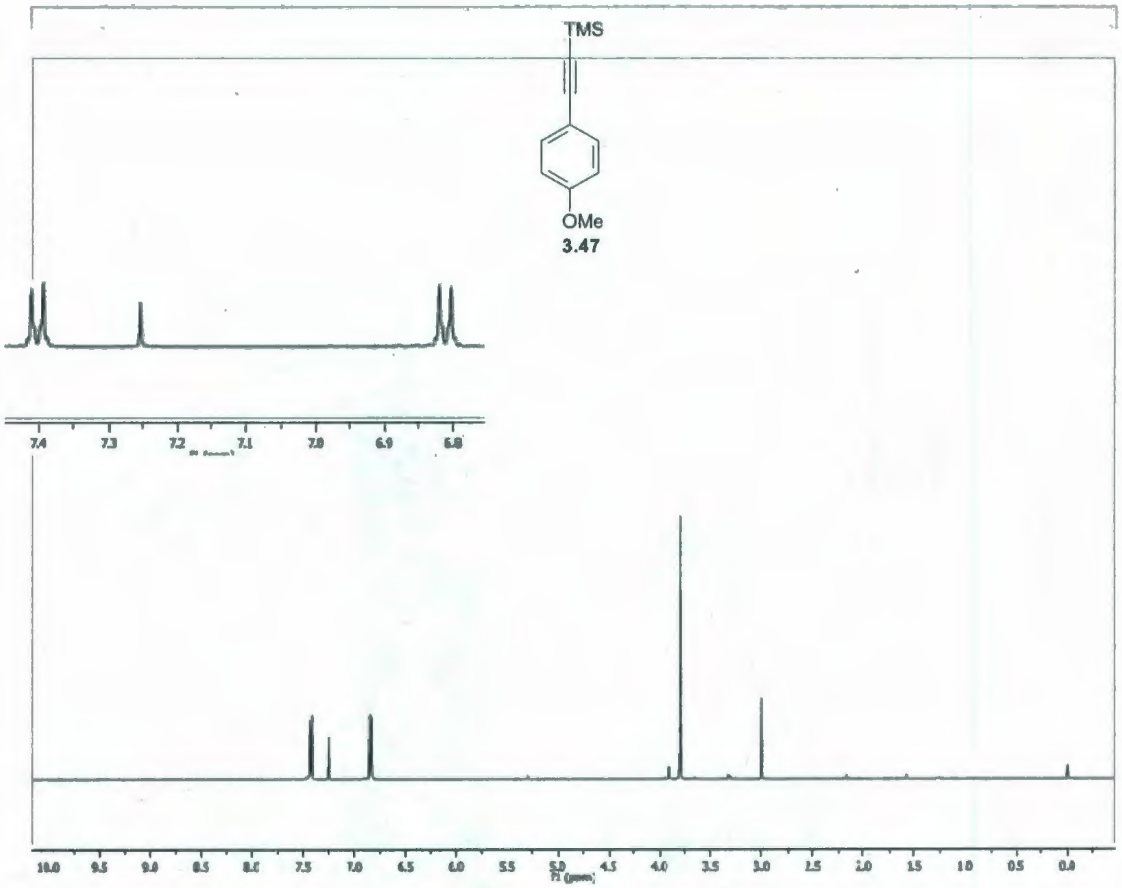
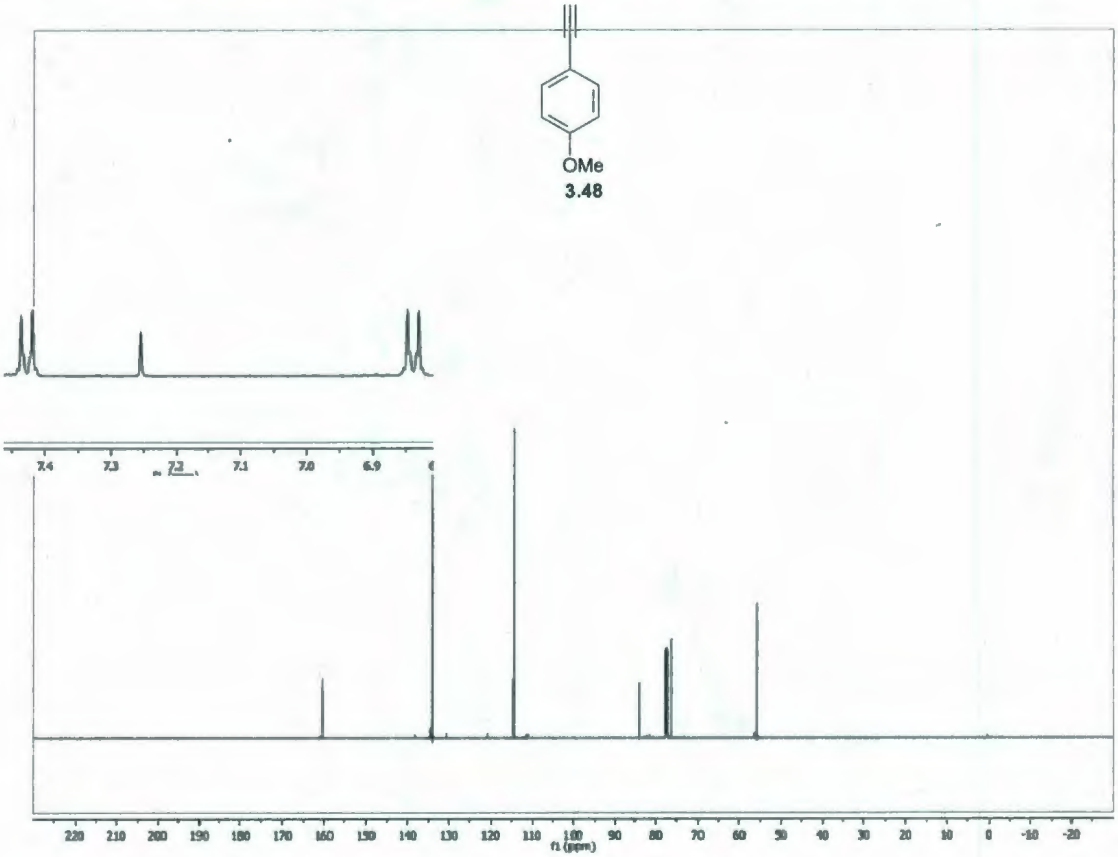
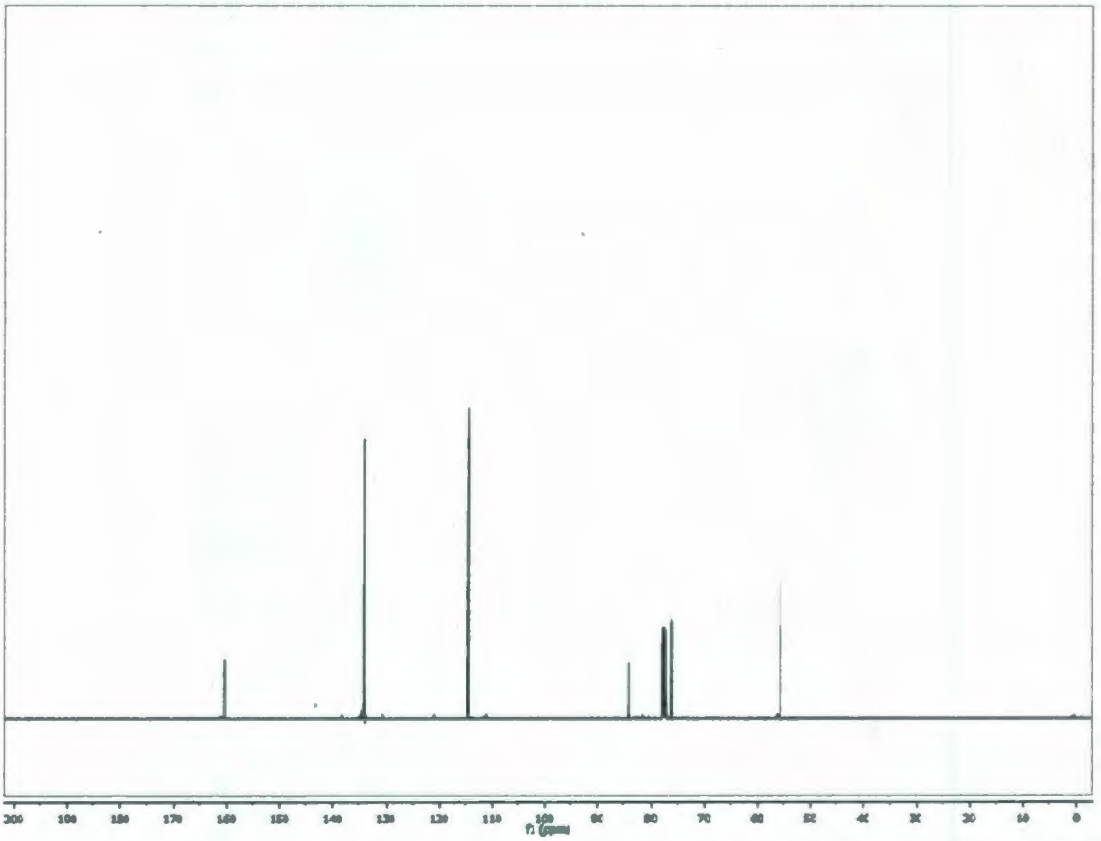


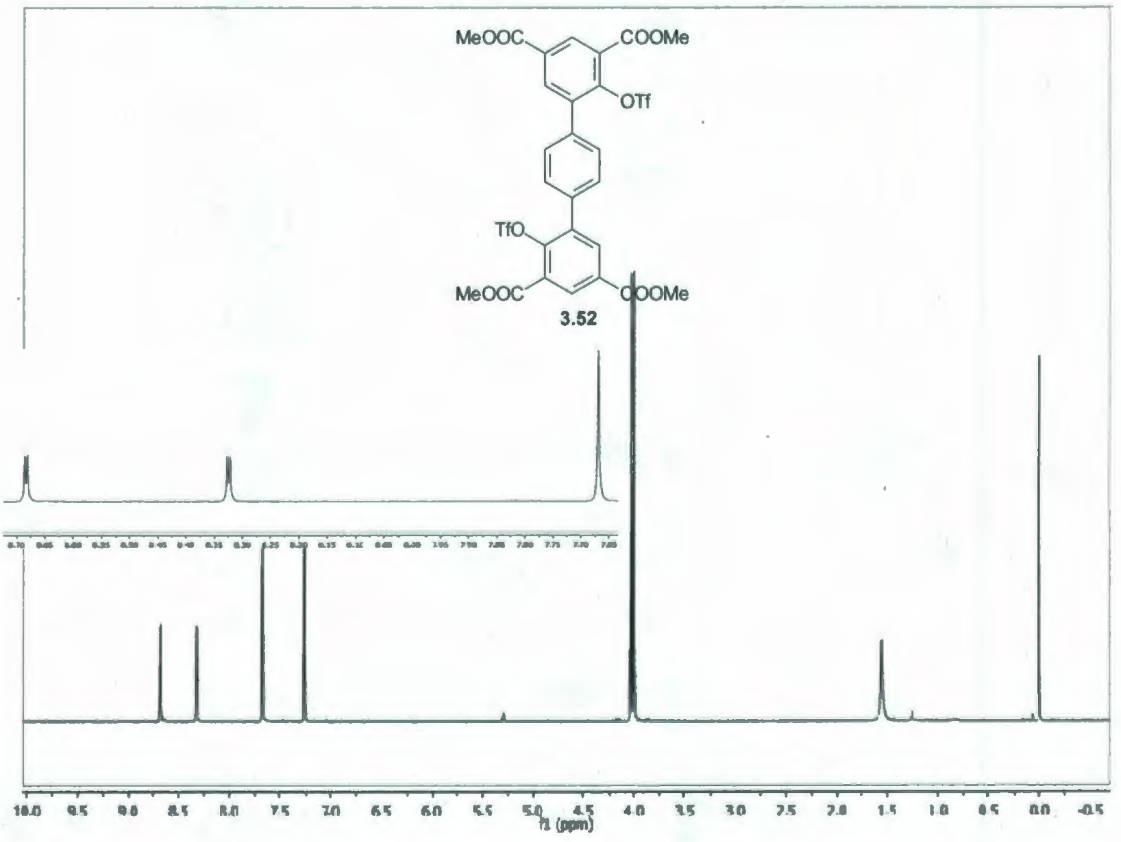

OMe
3.46
f1 (ppm)


f1 (ppm)


TMS
OMe
3.47


OMe
3.48



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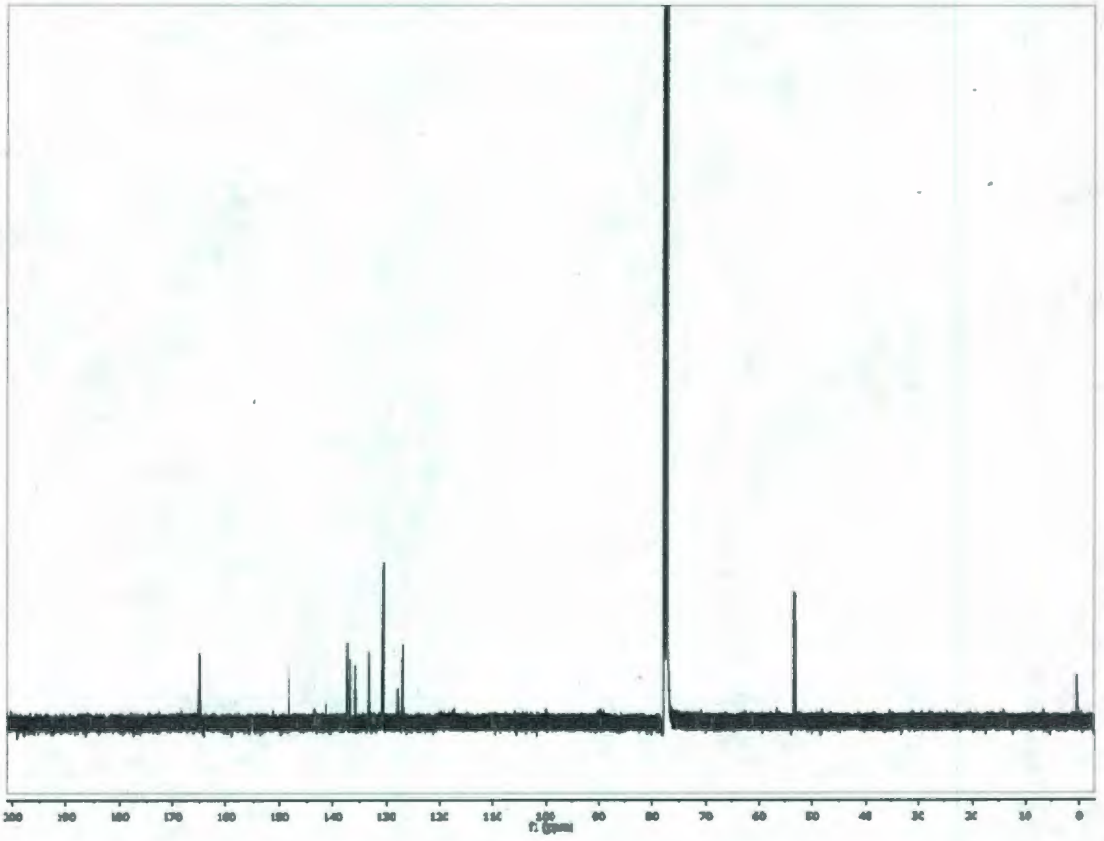
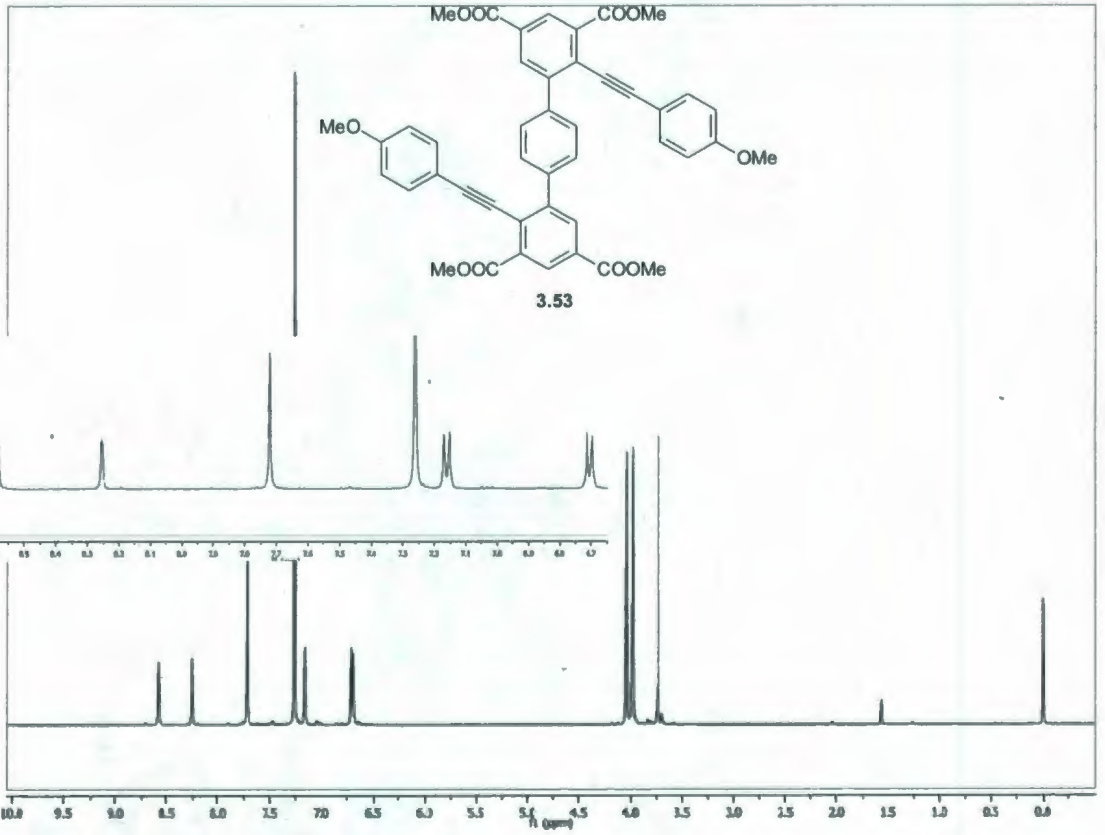
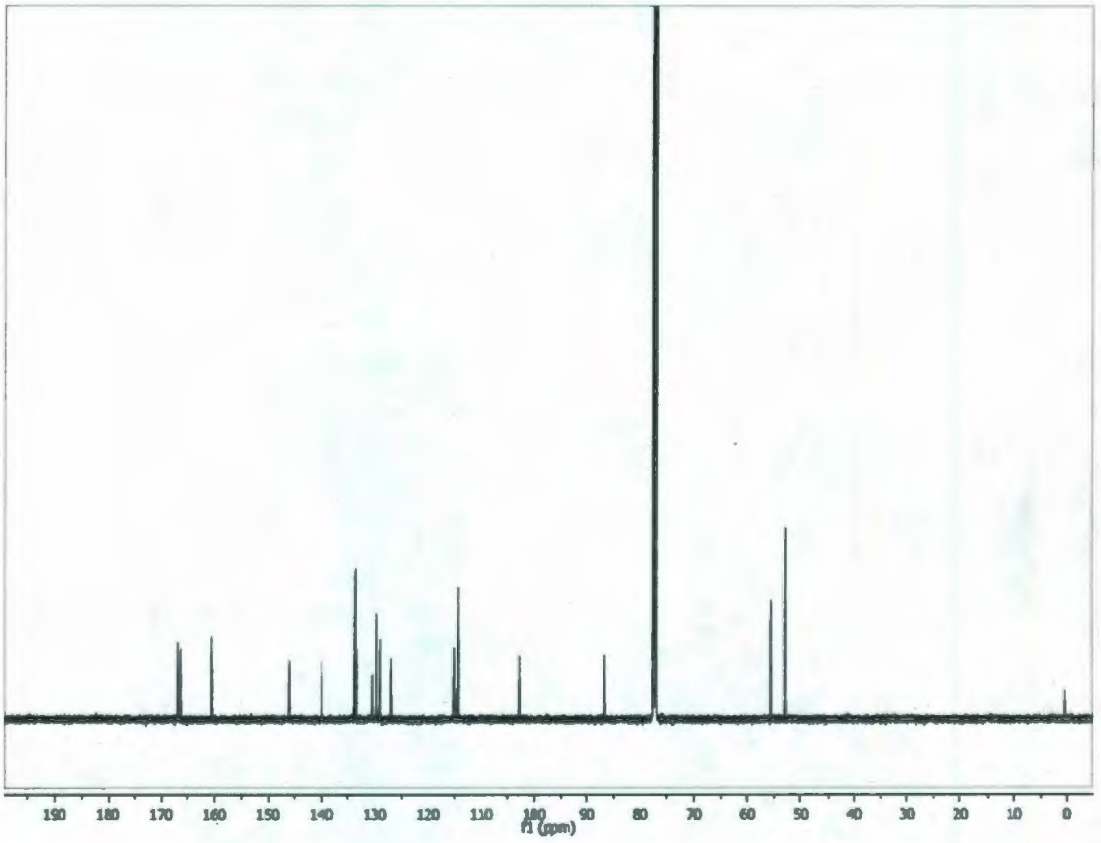





3.53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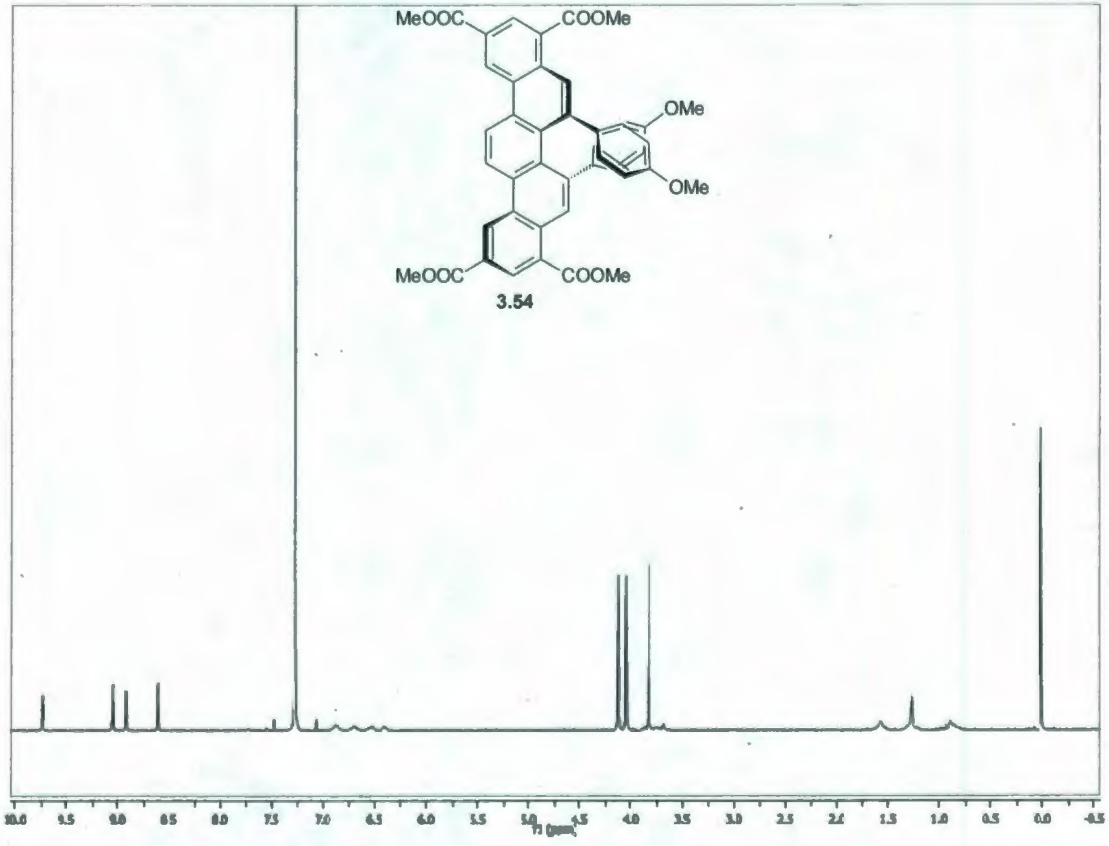
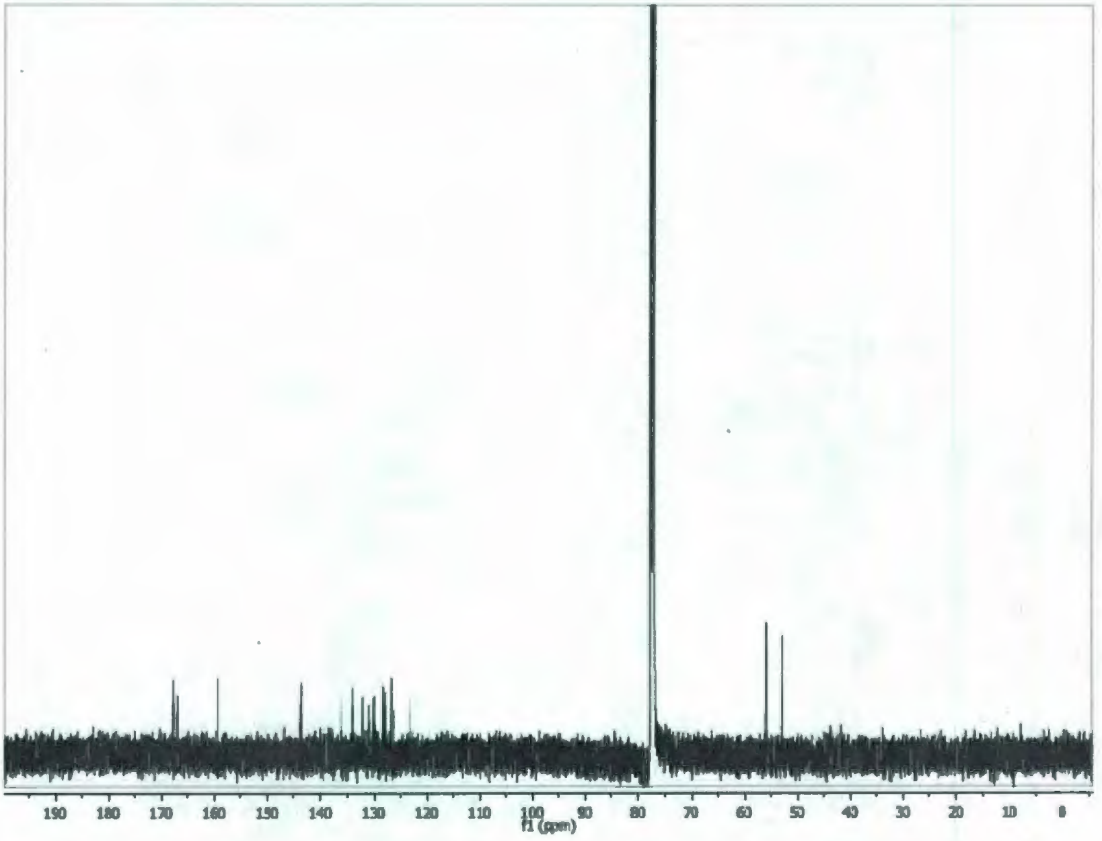
f1 (ppm)


MeOOC
COOMe
OMe
OMe
MeOOC
COOMe
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
f1 (ppm)

3.54


190
180
170
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140
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120
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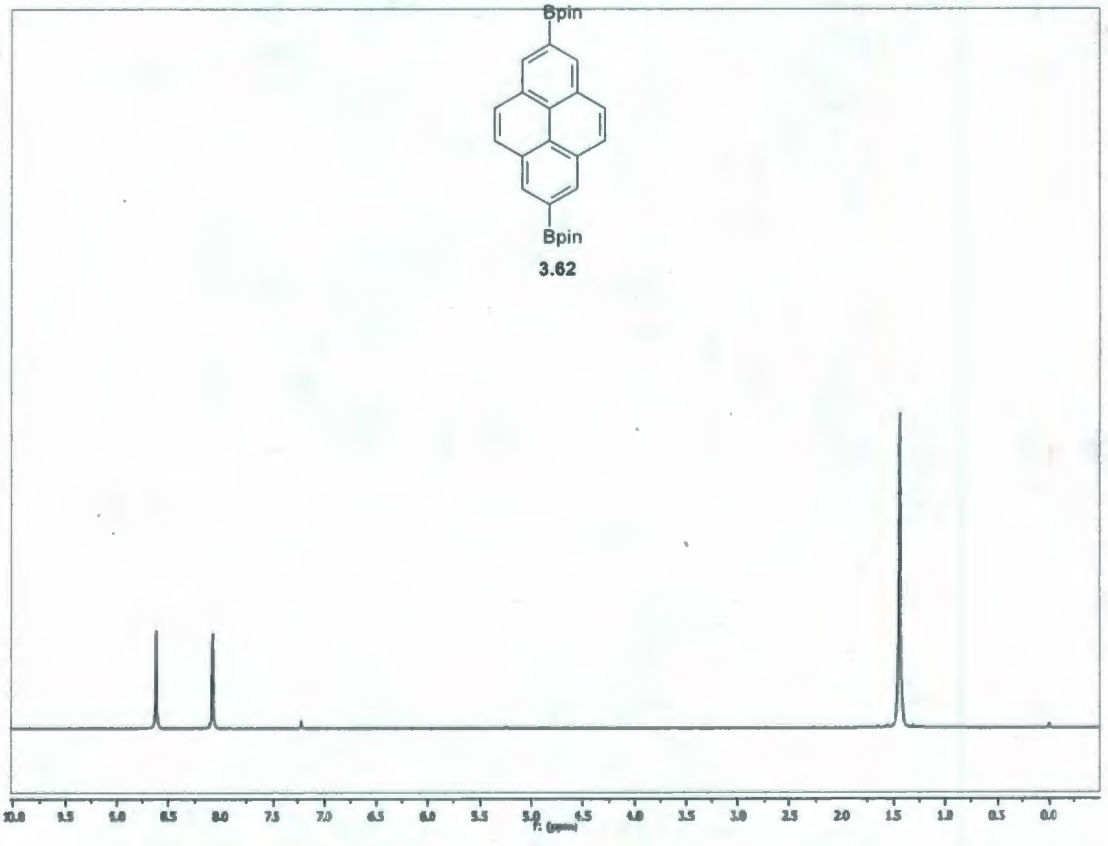
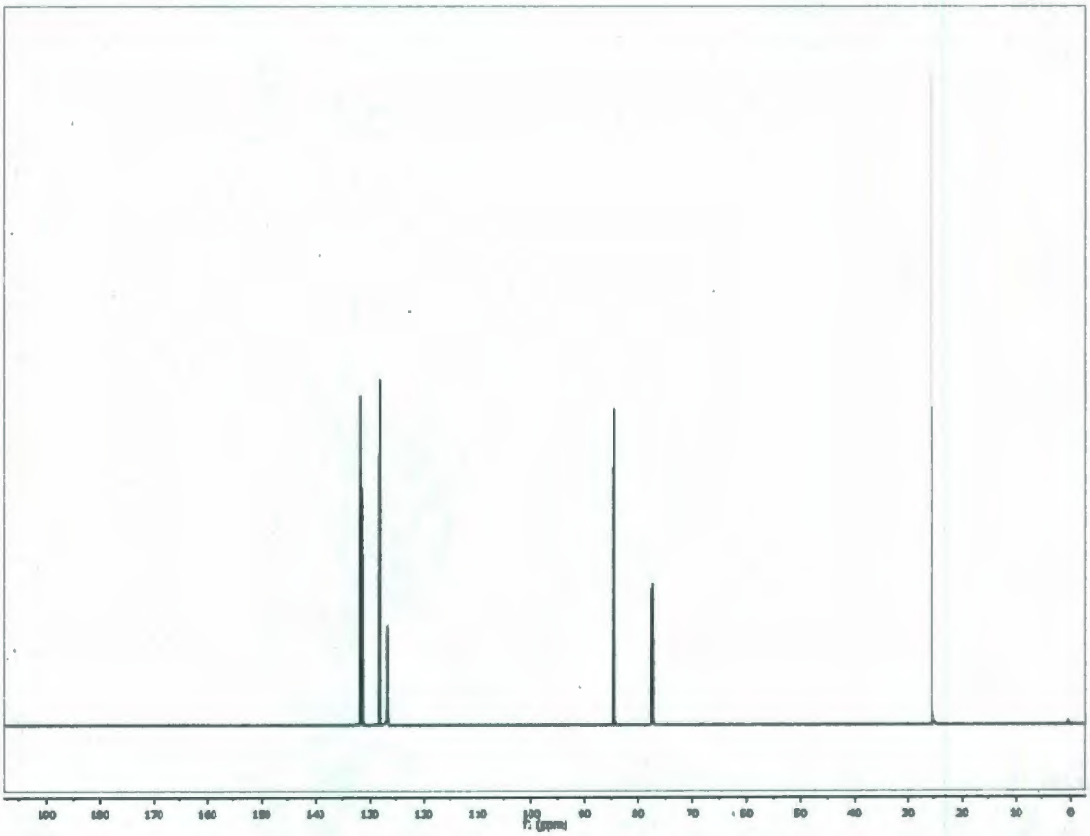
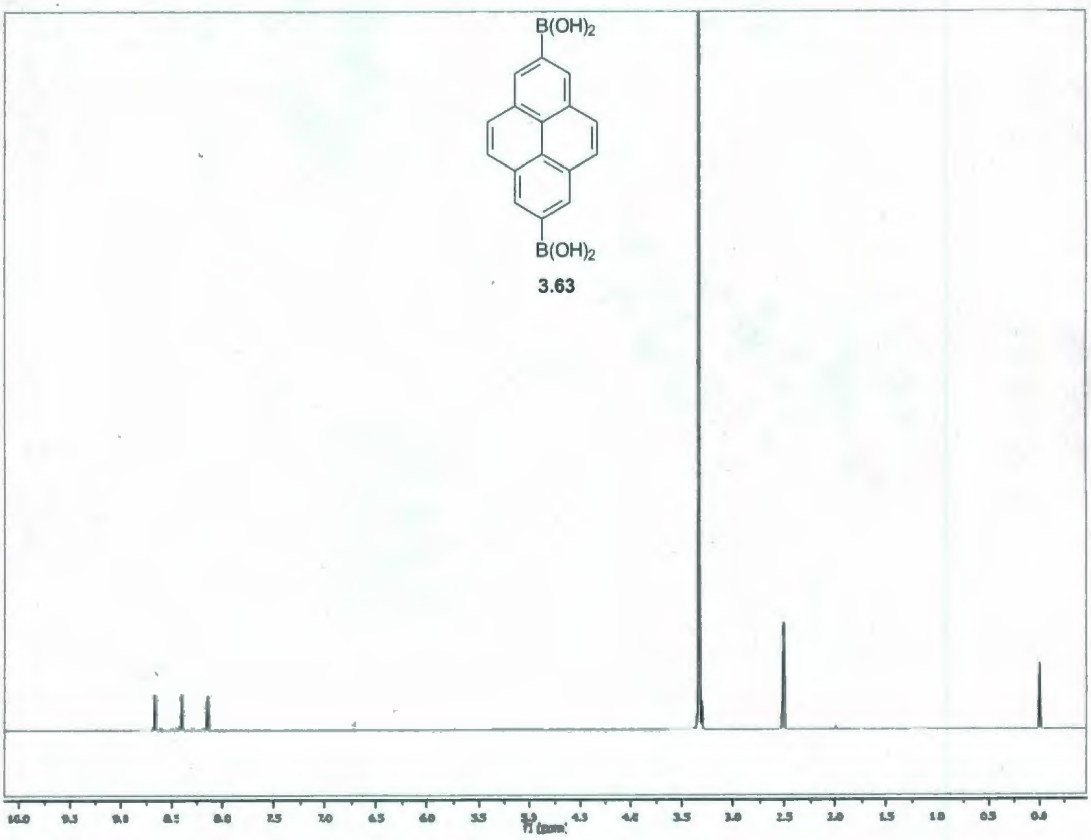
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

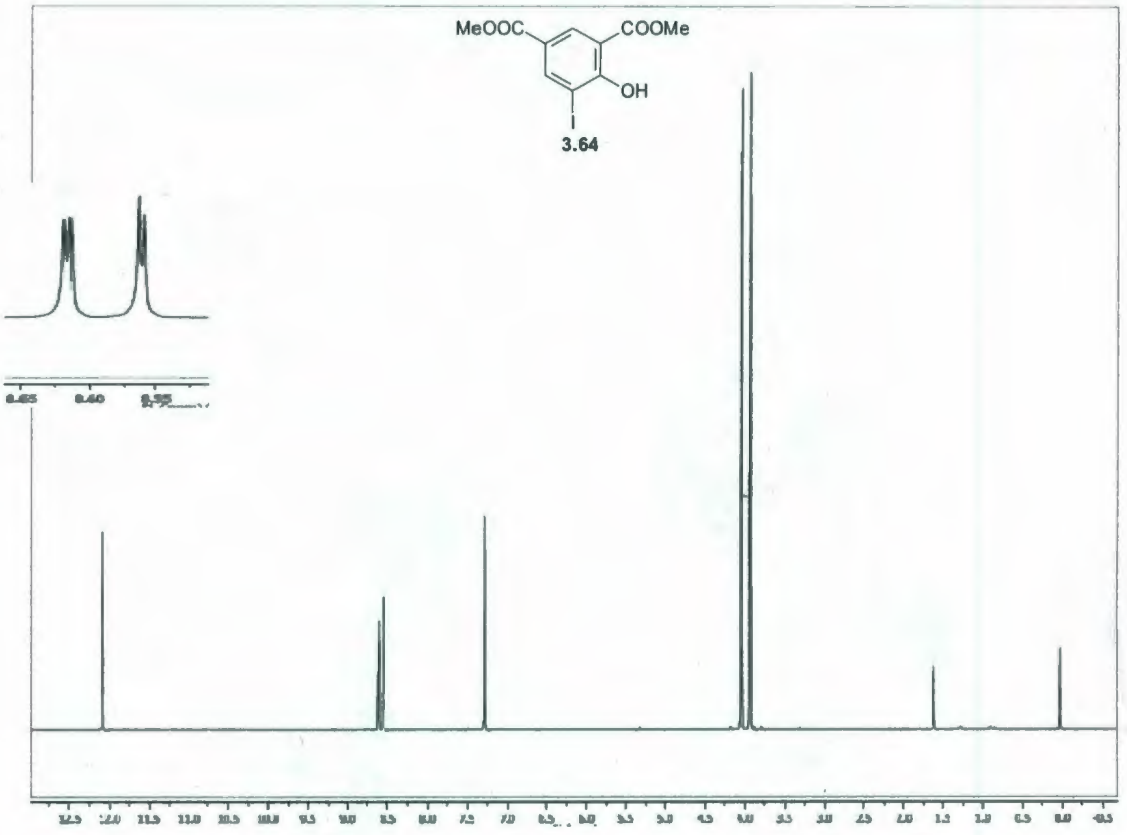

Bpin
Bpin
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

**3.62**






**3.63**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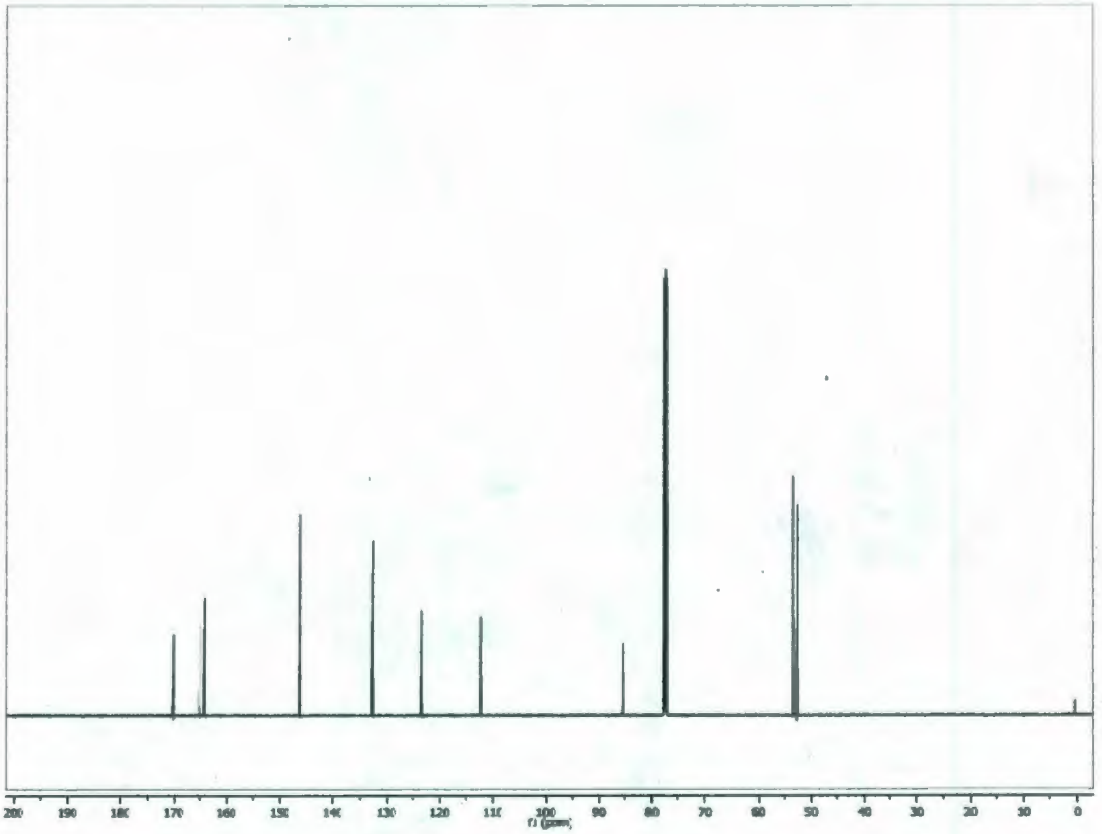
COOMe
OH
3.64



Calculation of energy barrier of molecular board **3.54**.

(1) $k^1=\pi\Delta\upsilon/\sqrt{2}$

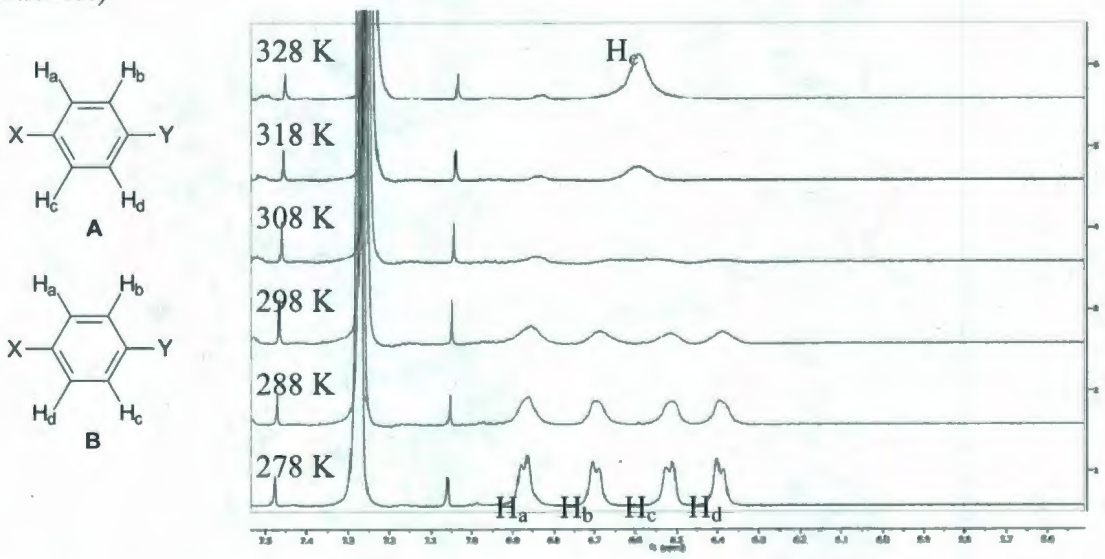
(2) $\Delta G=2.303RT_c(10.319-\log_{10}k_1+\log_{10}T_c)$

The rate of exchange $k_1$ at the temperature of coalescence $T_c$ (308 K) was calculated by the method of Gutowsky and Holm from equation (1).[16]

$\Delta\upsilon$ is the frequency separation of the resolved signals at low temperature.

$\Delta G$ was derived from the Eyring equation (2).

(The error of the measured temperature is ± 10 °C, so the error of the $\Delta G$ is ± 0.5 kcal/mol)




$\delta_{Ha}$=6.87151 ppm, $\delta_{Hb}$=6.69862 ppm, $\delta_{Hc}$=6.51802 ppm $\delta_{Hd}$=6.39496 ppm

$\delta_{He}$=6.59959 ppm.

Signals should coalesce in two different ways (**A** or **B**).

**A** : if $H_a \leftrightarrow H_c$

$\Delta\upsilon_1$=47.58 Hz, $k_1$=105.68

$\Delta\upsilon_2$=26.40 Hz, $k_2$=58.62

$\Delta G_1$=15.20 kcal/mol

$\Delta G_2$=15.56 kcal/mol

$\Delta G_{ave(A)}$=15.38 kcal/mol

**B**: if $H_a \leftrightarrow H_d$

$\Delta\upsilon_1$=16.82 Hz, $k_1$=37.35

$\Delta\upsilon_2$=4.37 Hz, $k_2$=9.69

$\Delta G_1$=15.83 kcal/mol

$\Delta G_2$=16.66 kcal/mol

$\Delta G_{ave(B)}$=16.24 kcal/mol

$\Delta G$=15.8± 0.5 kcal/mol

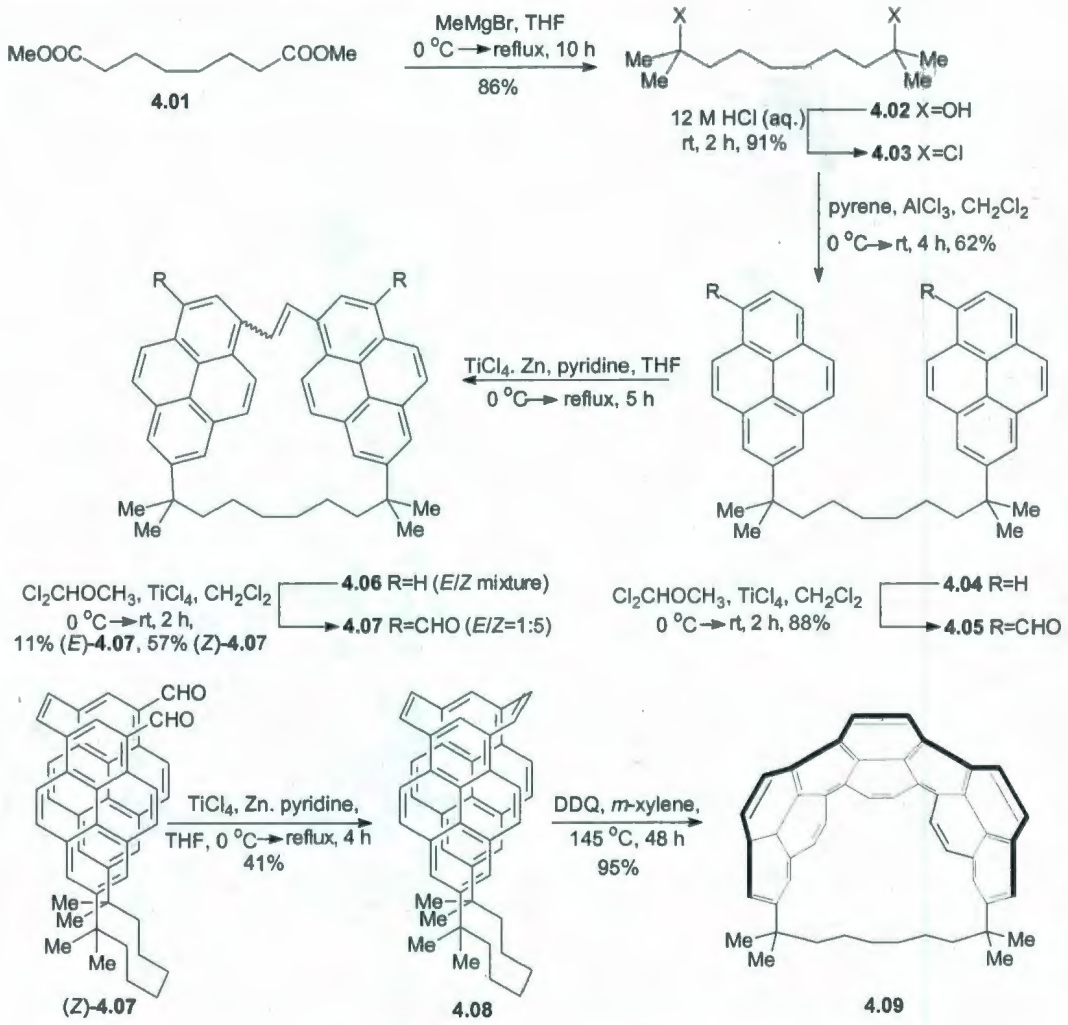
# Chapter Four
# Synthesis of Aromatic Belt Precursors

## 4.1 Introduction

As discussed in Chapter 1, aromatic belts have received a great deal of attention over the past quarter century. Cyclophenacene-type belts are predicted to be more reasonable synthetic targets than cyclacenes because of their greater stablility.[1] In 1983, Vögtle proposed a family of pyrenoid aromatic belts, *e.g.* **1.98** (Figure 1.8, Page 12).[2] Although his efforts to synthesize these synthetically challenging systems ultimately failed, the $D_{6h}$-symmetric Vögtle belt **1.98** later became very interesting to the Bodwell group. Synthetic work aimed at **1.98** was started by a Ph.D. student, Rolf Vermeij,[3] but his route failed at an early stage, *i.e.* the construction of an appropriately substituted molecular board.

Another doctoral student in the Bodwell group, Bradley Merner, successfully synthesized 1,1,8,8-tetramethyl[8](2,11)teropyrenophane, which can be viewed as half of a Vögtle-type aromatic belt and a segment of an (8,8)single-walled carbon nanotube (Scheme 4.1).[4] Two pyrenes systems were tethered using a regioselective twofold Friedel-Crafts alkylation. Formylation of each pyrene system was followed by an intramolecular McMurry reaction, which afforded an inseparable mixture of (*E*)-**4.06** and (*Z*)-**4.06**. Formylation of this mixture gave a chromatographically separable mixture of (*E*)-**4.07** (11%) and (*Z*)-**4.07** (57%). Surprisingly, intramolecular McMurry reaction of (*Z*)-**4.07** gave cyclophanediene **4.08** in 41% yield. The VID reaction of

**4.08** to afford half belt **4.09** occurred essentially quantitatively in *m*-xylene at reflux. The success of this VID reaction is cause for cautious optimism that Vögtle-type aromatic belts will be accessible using this methodology.




**Scheme 4.1** Synthesis of 1,1,8,8-tetramethyl[8](2,11)teropyrenophane **4.09**.

Another Ph.D. student, Tieguang Yao, worked on the synthesis of two isomeric aromatic belts: $C_{2h}$-**4.10a** and $D_2$-**4.10b** (Figure 4.1), which are Vögtle belts that are missing some benzene rings. The synthetic strategy for the synthesis of these two belts followed the general strategy shown in Scheme 3.1 (Page 78): (1) synthesis of an

appropriately functionalized molecular board; (2) the connection of two units of molecular boards to give a tetrathiacylophane; (3) the preparation of the corresponding cylophanetetraenes; (4)VID reaction to afford a belt.[5]

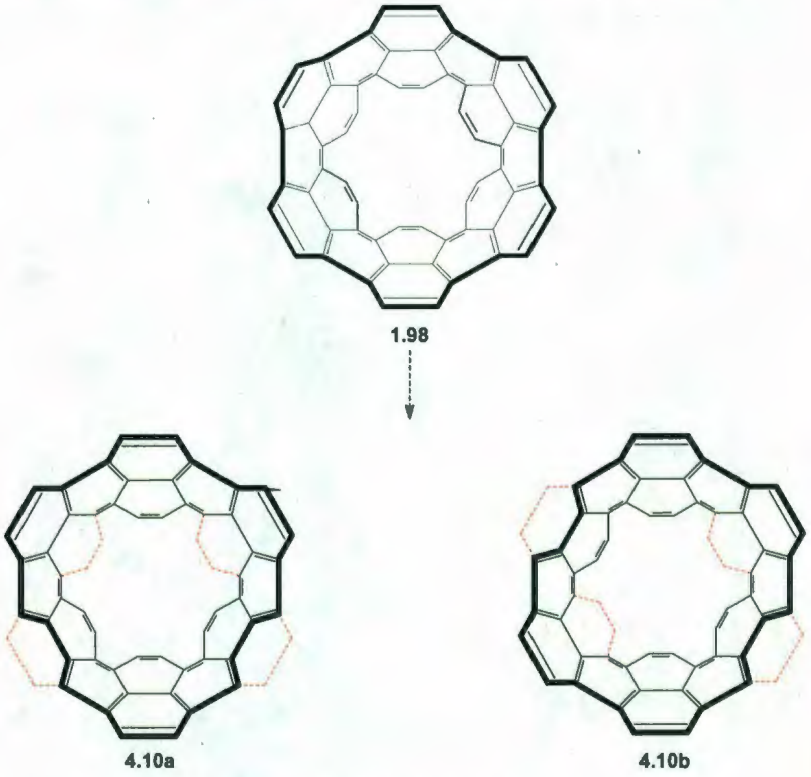


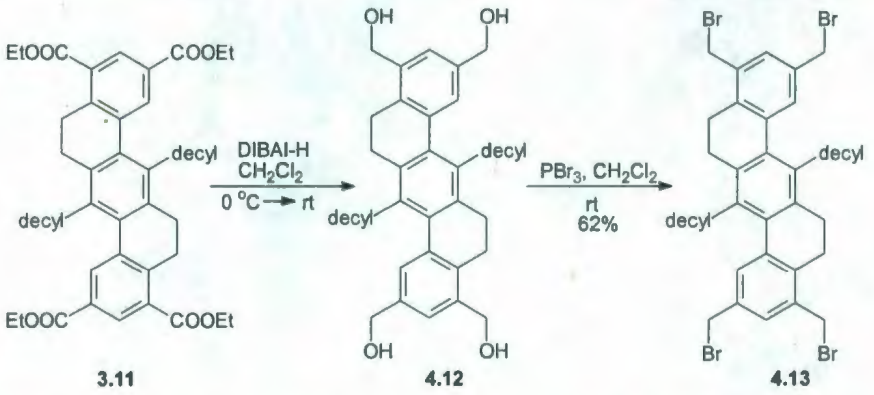

**Figure 4.1** Structure of synthetic targets Vögtle belts.

During Yao's doctoral studies, he obtained small quantities (> 2 mg) of the cyclophanetetraene precursors to **4.10a** and **4.10b**, but his attempts to form aromatic belts were inconclusive.[6] The mass spectrum of these reaction products showed that dehydrogenation was occurring, but that mixtures of products were being formed. Signals corresponding to the desired belts were observed among others, but this could also be due to isomers of the target belts. The very small scale of these VID reactions made analysis of the product mixtures difficult. The object of the work described in

this Chapter is to use the same synthetic route to produce greater amounts of Yao's aromatic belt precursors and attempt to convert them into aromatic belts $C_{2h}$-**4.10a** and $D_2$-**4.10b**.

## 4.2 Results and Discussion

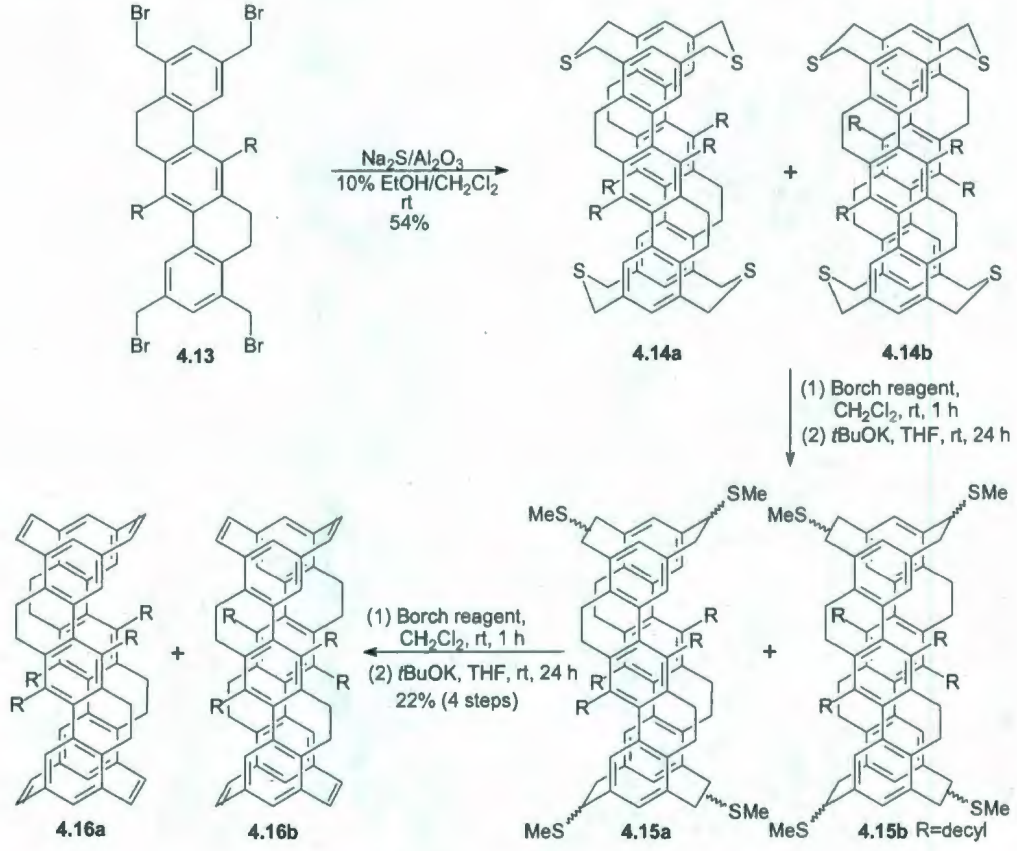
As discussed in Chapter 3, molecular board **3.11** was prepared on a 8 gram scale. The functionalized tetrabromide **4.13** was obtained from **3.11** using reduction with DIBAL and bromination of the resulting diol **4.12** with $PBr_3$ (62%) (Scheme 4.2).




**Scheme 4.2** Conversion of tetraeaster to functionalized tetrabromide **4.13**.

Two units of tetrabromide **4.13** were joined by treatment with $Na_2S/Al_2O_3$, which gave two tetrathiacyclophanes **4.14a** and **4.14b** (54%). These tetrathiacyclophanes were somewhat unstable, so the mixture was quickly filtered through a plug of Celite and the crude material was used directly in next step. Accordingly, the crude mixture of **4.14a** and **4.14b** was subjected to an *S*-methylation/Stevens rearrangement sequence to afford methylthio-substituded metacyclophanes **4.15a** and **4.15b**. Yao calculated that up to 148 isomers can possibly by produced in this step, so no further purification was attempted. The crude mixture was treated with Borch reagent

(*S*-methylation) and *t*BuOK (Hofmann elimination) to give aromatic belt precursors, cyclophanetetraenes **4.16a** and **4.16b** (22%). In total, 50 mg of **4.16a** and **4.16b** were synthesized.




**Scheme 4.3** Synthesis of cyclophanetetraenes **4.16a** and **4.16b**.

In his original work on this synthetic route, Yao found that $^1$H NMR was not useful for the identification of reaction products starting with tetrathiacyclophanes **4.14a** and **4.14b**. The reasons for this are that the molecules from this point onward are mixtures of isomers, each of which has several highly coupled protons. Further complication could arise from conformational mobility in the tetrahydrodibenzo[*a*,*h*]anthracene systems.

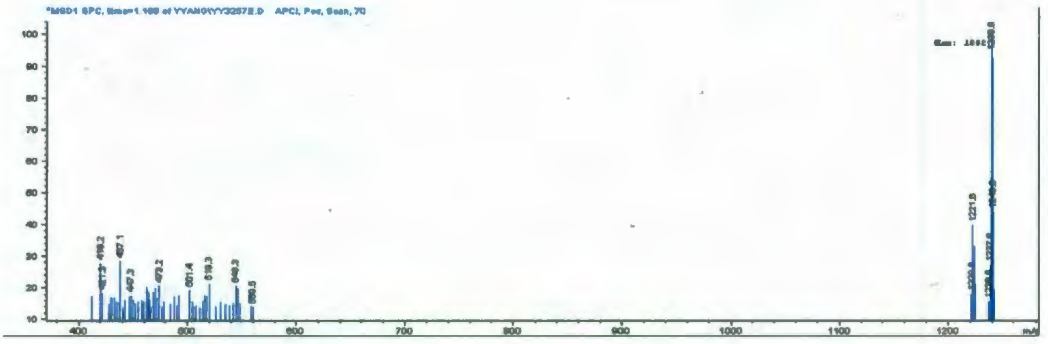


**Figure 4.2** Mass Spectrum of **4.16a** and **4.16b**.

The same difficulty with $^1$H NMR was experienced in this work and mass spectrometry was the only method that could provide evidence for the formation of cyclophanetetraenes **4.16a** and **4.16b** (*m/z*=1220) (Figure 4.2).

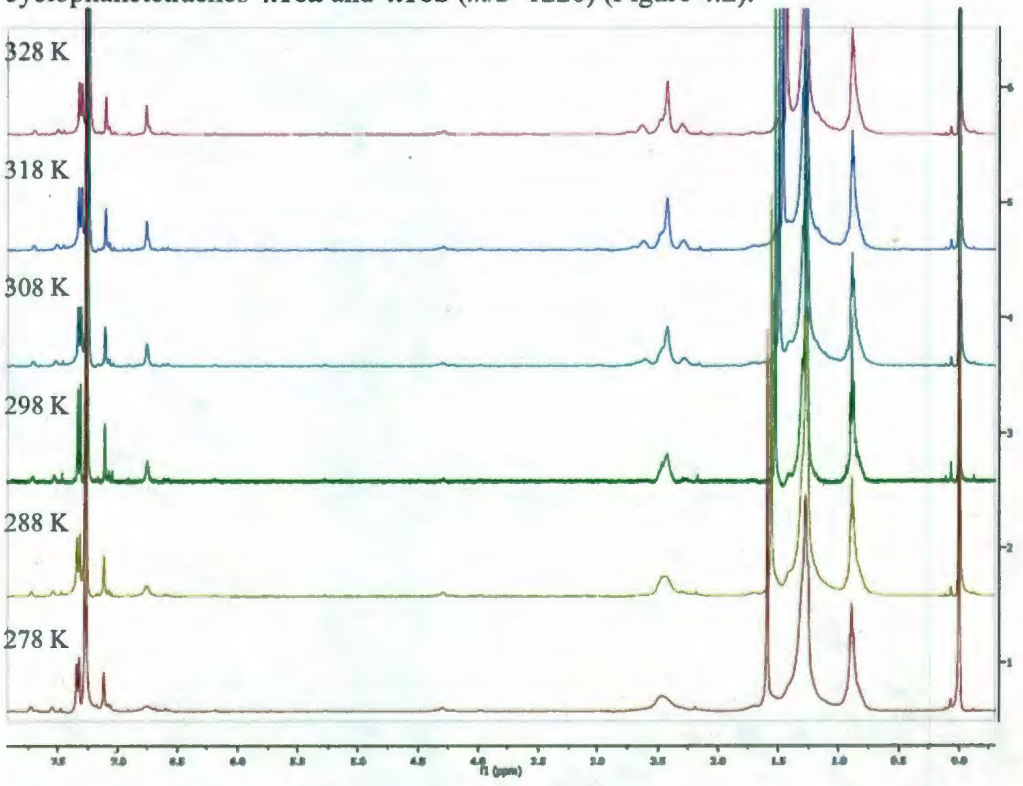
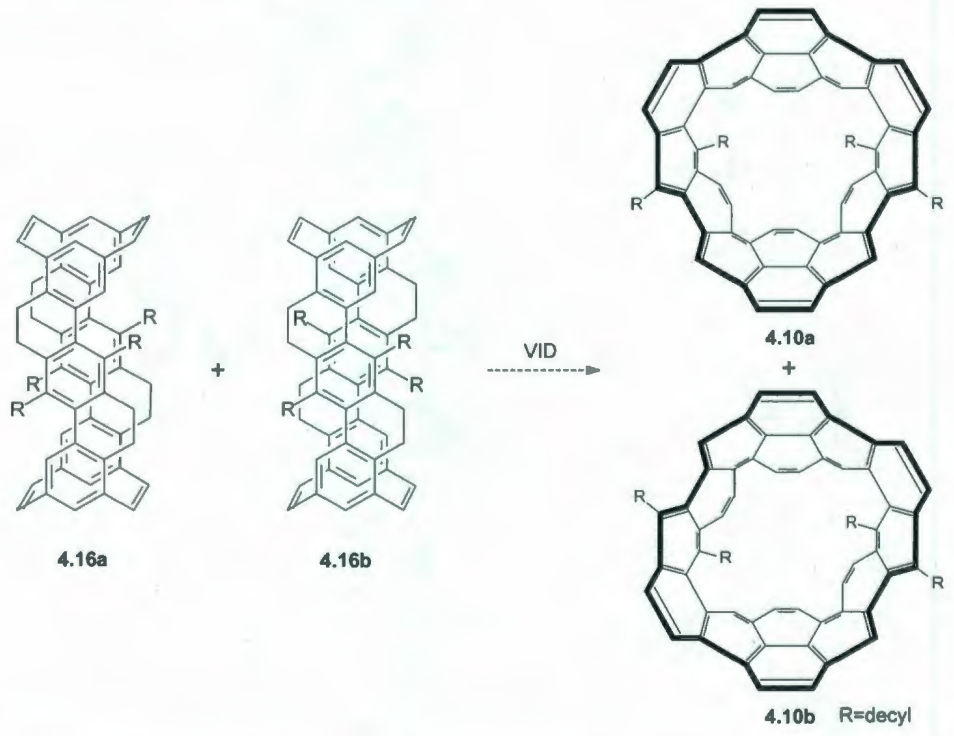



**Figure 4.3** $^1$H NMR of cyclophanetetraenes **4.16a** and **4.16b** at different temperatures.

To investigate whether conformational mobility in **4.16a** and **4.16b** was contributing to the broad features of the $^1$H NMR spectrum, a variable temperature $^1$H

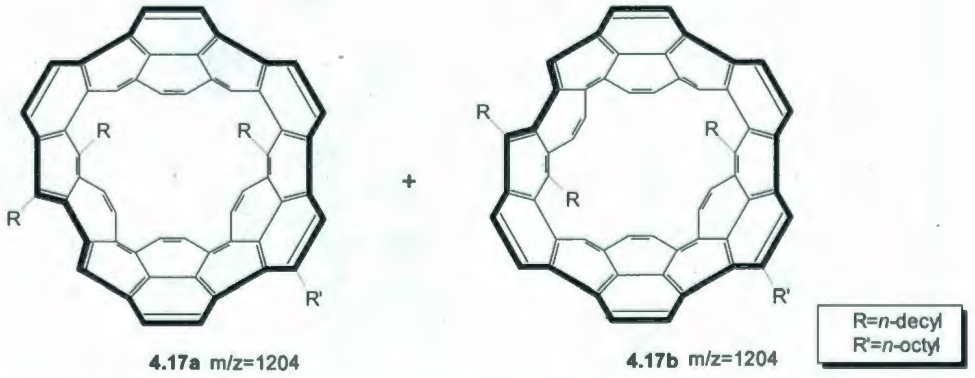
NMR experiment was performed. Tetraenes **4.16a** and **4.16b** should each exhibit three signals in the aromatic region (two aromatic+one alkene signal), but the spectra of the two compounds might be expected to be very close to one another. At 278 K, three singlets were observed in the aromatic region (δ 7.34, 7.32, 7.12 ppm). Upon warming the solution of **4.16a** and **4.16b**, a very broad hump at δ 6.74 ppm grew steadily into a relatively sharp singlet. At the same time a very broad featureless signal at δ 2.47 ppm developed into at least three distinct signals (δ 2.63, 2.42, 2.30 ppm), the outer two of which appeared to be symmetrical. Although nothing concrete could be concluded from this experiment, it was certainly consistent with conformational mobility in either **4.16a, 4.16b** or both (Figure 4.3).




**Scheme 4.4** Attempted synthesis of aromatic belts.

With about 50 mg of a mixture of **4.16a** and **4.16b** in hand, attention was turned

to converting it into aromatic belts **4.10a** and **4.10b** (Scheme 4.4). A 10 mg-scale reaction with DDQ in benzene at reflux resulted in the consumption of the starting material after 1.5 h and the formation of a yellow-fluorescent new compound (tlc analysis). Column chromatography afforded 5 mg of this material. However, its $^1$H NMR spectrum contained only very weak peaks ascribable to impurities or contaminants, with the exception of a broad singlet at δ 7.02 ppm. Both **4.10a** and **4.10b** are expected to exhibit three AB systems and a singlet in the aromatic regions of their $^1$H NMR spectra, so it is hard to imagine that seven signals of both compounds would accidentally have the same chemical shift, let alone at such high field for a polycyclic aromatic hydrocarbon.




**4.17a** m/z=1204 **4.17b** m/z=1204

**Figure 4.4** Structures of compound **4.17a** and **4.17b**.

The APCI(+) mass spectrum showed a signal at *m/z*=1205.8, which presumably arises from a species with a monoisotopic molar mass of 1204. This is four mass units below that of **4.10a** and **4.10b**. Yao also obtained this result. Compound **4.17a** and **4.17b** (Figure 4.4) would have the correct mass, but they would only arise through a side-chain dehydrogenation/valence isomerization/dehydrogenation sequence of

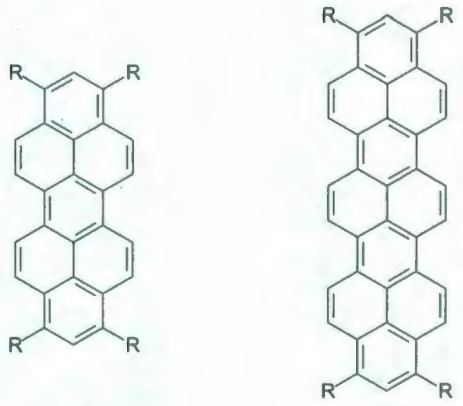
reactions. The initial side-chain dehydrogenation does have some precedent (indan→indene),[7] but it is not clear why this would only occur once, when there are four available side-chains. Thus, the outcome of the reaction remains unclear.

A second 10 mg-scale reaction under exactly the same conditions gave a slightly different result. The tlc analysis and $^1$H NMR spectrum were essentially unchanged, but the APCI(+) mass spectrum contained no signal above *m/z*=1000. The highest mass signals were observed at *m/z*=922.3 and 923.4, which correspond closely to the loss of two decyl groups form the *m/z*=1205.8 signals. In fact, a signal at *m/z*=923.7 was the base peak in the APCI(+) mass spectrum of the previous reaction. Again, the result was inconclusive.

Finally, a 30 mg-scale reaction was conducted with the objective of producing a more workable quantity of the yellow fluorescent material. However, this reaction gave only 7 mg of a product that, by tlc analysis, contained only a trace amount of the yellow fluorescent material along with a series of other new compounds. The APCI(+) mass spectrum of the product obtained from a filter column was unlike those of the previous two experiments. The highest mass peak was observed at *m/z*=1024 and numerous other signals were obtained down to *m/z*=600.

Although the starting tetraenes are being consumed in benzene at reflux, the outcome of the reaction has not been easy to determine. There is some evidence (mass peak at *m/z*=1205.8) to suggest that the desired belts **4.10a** and **4.10b** may have formed, but that they reacted further under the conditions of their formation.

## 4.3 Future Work and Conclusion




**4.18** **4.19**

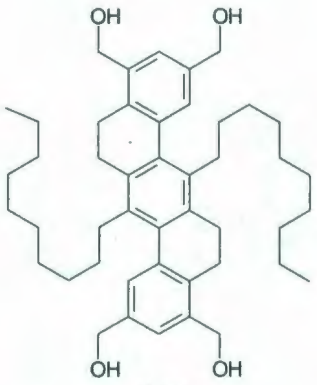
**Figure 4.5** More highly symmetrical boards **4.18** and **4.19**.

About 50 mg of cyclophanetetraenes **4.16a** and **4.16b**, the precursors to the aromatic belts, were successfully synthesized. However, attempts to prepared aromatic belts **4.10a** and **4.10b** using the VID reaction were, at best, inconclusive and, at worst, unsuccessful. The main problems with this approach to aromatic belts were the mixtures of isomers and the VID reaction. Future work in this area should be focused on the synthesis of more highly symmetrical boards, *e.g.* based on **4.18**, which will only give a single isomer when two of them are joined. Longer boards, e.g. base on **4.19** should also be targeted because they should lead to less strained and consequently more stable belts.

## 4.4 Experimental section

**General**: For general procedures, please refer to the experimental section in Chapter 4.

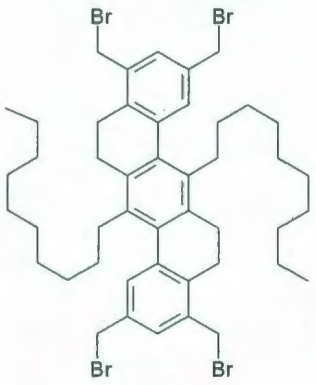
**7,14-Didecyl-2,4,9,11-tetrakis(hydroxymethyl)-5,6,12,13-tetrahydrodibenz[*a*,*h*]-anthracene (4.12)**




**4.12**

To a solution of molecular board tetraester **3.11** (1.412 g, 1.665 mmol) in $CH_2Cl_2$ (20 mL) at 0 °C was added 1 M DIBAL-H (26.5 mL, 26.5 mmol) dropwise. The reaction mixture was allowed to warm to room temperature slowly and stirred overnight. Then it was quenched by adding $H_2O$ dropwise at 0 °C, and the precipitate was collected by suction filtration to give the crude product as a white solid (1.132 g): mp: 166.0-167.5 °C; IR (neat) ν: 3356 (w), 2921 (w), 1772 (w), 1653 (w), 1458 (w), 1027 (w), 764 (m) $cm^{-1}$; $^1H$ NMR (500 MHz, DMSO-$d_6$): δ 7.29 (s, 2H), 7.26 (s, 2H), 5.10 (br s, 4H), 4.61 (s, 4H), 4.51 (s, 4H), 2.81-1.78 (br m, 4H), 2.69-2.58 (br m, 4H), 1.62-1.58 (br m, 4H), 1.39-1.33 (br m, 4H), 1.33-1.15 (br m, 32H), 0.85 (t, *J*=6.6 Hz, 6H); $^{13}C$ NMR (125 MHz, DMSO-$d_6$): δ 139.6, 138.5, 137.8, 136.9, 135.8, 135.5, 133.9, 126.2, 125.3, 64.1, 62.4, 32.2, 31.5, 31.0, 30.0, 29.9, 29.6, 27.0, 25.0, 23.0, 14.8 (two signal less than expected).

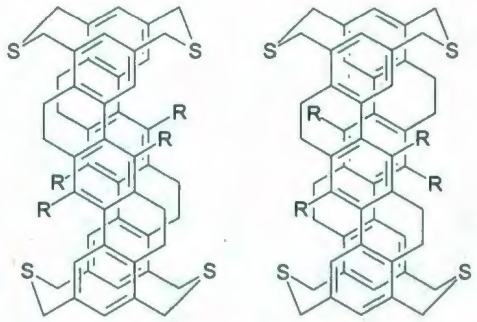
**7,14-Didecyl-2,4,9,11-tetrakis(bromomethyl)-5,6,12,13-tetrahydrodibenz[*a*,*h*]-anthracene (4.13)**




**4.13**

To a mixture of tetraalcohol **4.12** (1.132 g, 1.653 mmol) in $CH_2Cl_2$ (100 mL) was added $PBr_3$ (1.785 g, 6.591 mmol) by syringe at room temperature. This mixture was stirred overnight and then quenched by the addition $H_2O$ (20 mL). The organic layer was washed with brine (100 mL), dried over $MgSO_4$ and concentrated under reduced pressure. The residue was subjected to column chromatography (25:75 $CH_2Cl_2$/hexanes→$CH_2Cl_2$) to yield **4.13** as a white solid (954 mg, 1.02 mmol, 62%): $R_f$(50:50 $CH_2Cl_2$/hexanes): 0.59; mp: 159.0-161.5 °C; IR (neat) ν: 2922 (w), 1772 (w), 1652 (w), 1465 (w), 1202 (w), 1071 (w), 773 (s) $cm^{-1}$; $^1H$ NMR (500 MHz, $CDCl_3$): δ 7.45 (s, 2H), 7.31 (d, *J*=1.5 Hz, 2H), 4.61 (s, 4H), 4.50 (s, 4H), 2.84-2.81 (m, 8H), 1.71-1.68 (br m, 4H), 1.44-1.42 (br m, 4H), 1.31-1.26 (br m, 28H), 0.88 (t, *J*=6.7 Hz, 6H); $^{13}C$ NMR (125 MHz, $CDCl_3$): δ 140.2, 137.9, 137.8, 135.3, 135.2, 134.5, 134.3, 130.4, 129.0, 33.8, 32.3, 32.2, 31.7, 31.2, 30.3, 30.1, 30.0, 29.9, 29.8, 26.5, 25.5, 23.1, 14.5.

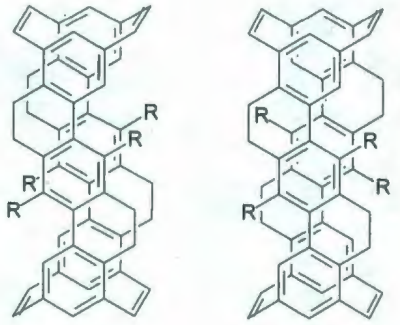
**Thiacyclophane (4.14a) and (4.14b)**



**4.14a** **4.14b** R=decyl

To a solution of tetrabromide **4.13** (100 mg, 0.11 mmol) in EtOH/$CH_2Cl_2$ (10:90) (20 mL) was added $Na_2S/Al_2O_3$ (660 mg, 8.46 mmol of $Na_2S$) in 4 rough equal portions. This reaction mixture was stirred at room temperature 2 d. The solvent was removed under reduced pressure and residue was dissolved in $CH_2Cl_2$ (20 mL). The precipitate was removed by suction filtration through a plug of Celite, and the filtrate was concentrated under reduced pressure to give a crude mixture of thiacyclophane **4.14a** and **4.14b** (72 mg): $R_f$(10:90 EtOAc/hexanes): 0.17; LCMS [APCl(+)] *m/z* (%): 1057 ($[M+H]^+$, 96), 727 (100).

**6,7,13,14,20,21,27,28-Octahydro-5,12,22,29-tetradecyl-(1Z,17Z,33Z,35Z)-[2$_4$](2,4, 9,11)dibenzo[*a,h*]anthracenophane-1,17,33,35-tetraene ($C_{2h}$-4.15a) and 6,7,13,14,22,23,29,30-Octahydro-5,12,21,28-tetradecyl-(1Z,17Z,33Z,35Z)-[2$_4$](2,4, 9,11)dibenzo[*a,h*]anthracenophane-1,17,33,35-tetraene ($D_2$-4.15b)**



4.16a 4.16b

To a solution of tetrathiacyclophane (539 mg, 0.401 mmol) in $CH_2Cl_2$ (30mL) was added Borch reagent (642 mg, 3.97 mmol) slowly over 5 min by syringe. The mixture was stirred at room temperature for 3 h. The solvent was removed under reduced pressure. To the resulting residue was added EtOAc (10 mL) and this mixture was stirred vigorously for 5 min. Stirring was discontinued, the supernatant was decanted and the residue was dried under vacuum. To a suspension of the resulting residue in THF (20 mL) was added *t*BuOK (2.230 g, 2.694 mmol) in one portion and the reaction was stirred overnight. This mixture was quenched by the addition of saturated aqueous $NH_4Cl$ solution (2 mL) and concentrated under reduced pressure. The residue was subjected to column chromatography ($CH_2Cl_2$) to afford a yellow oil (125 mg, 0.088 mmol). To a solution of this yellow oil (125 mg, 0.088 mmol) in $CH_2Cl_2$ (20 mL) was added Borch reagent (142 mg, 0.882 mmol) and the resulting mixture was stirred for 4 h. The solvent was removed under reduced pressure and the residue was suspended in THF (15 mL). To this mixture was added *t*BuOK (494 mg, 4.40 mmol) in one portion and the resulting mixture was sonicated (Fisher Scientific FS-14) for 1 h. Then the mixture was removed from the sonicator and stirred at room

temperature overnight. The solvent was removed under reduced pressure and the residue was immediately loaded onto a column for column chromatography (10:90 $CH_2Cl_2$/hexanes) to yield a mixture of **4.15a** and **4.15b** as yellow oil (23 mg, 0.019 mmol, 22%): $R_f$ (15:85 $CH_2Cl_2$/hexanes): 0.36; $^1$H NMR (500 MHz, $CDCl_3$): δ 7.34 (s, 4H), 7.31 (s, 4H), 7.11 (s, 4H), 6.76-6.74 (br, m, 4H), 2.43-2.41 (br, m, 16H), 1.28-1.26 (br, m, 72H), 0.89 (t, *J*=6.2 Hz, 12H); LCMS [APCl(+)] *m/z* (%): 1225 (16), 1224 (26), 1223 (29), 1222 (40), 1221 ($[M+H]^+$, 24), 1220 (21).

**4.5 References**

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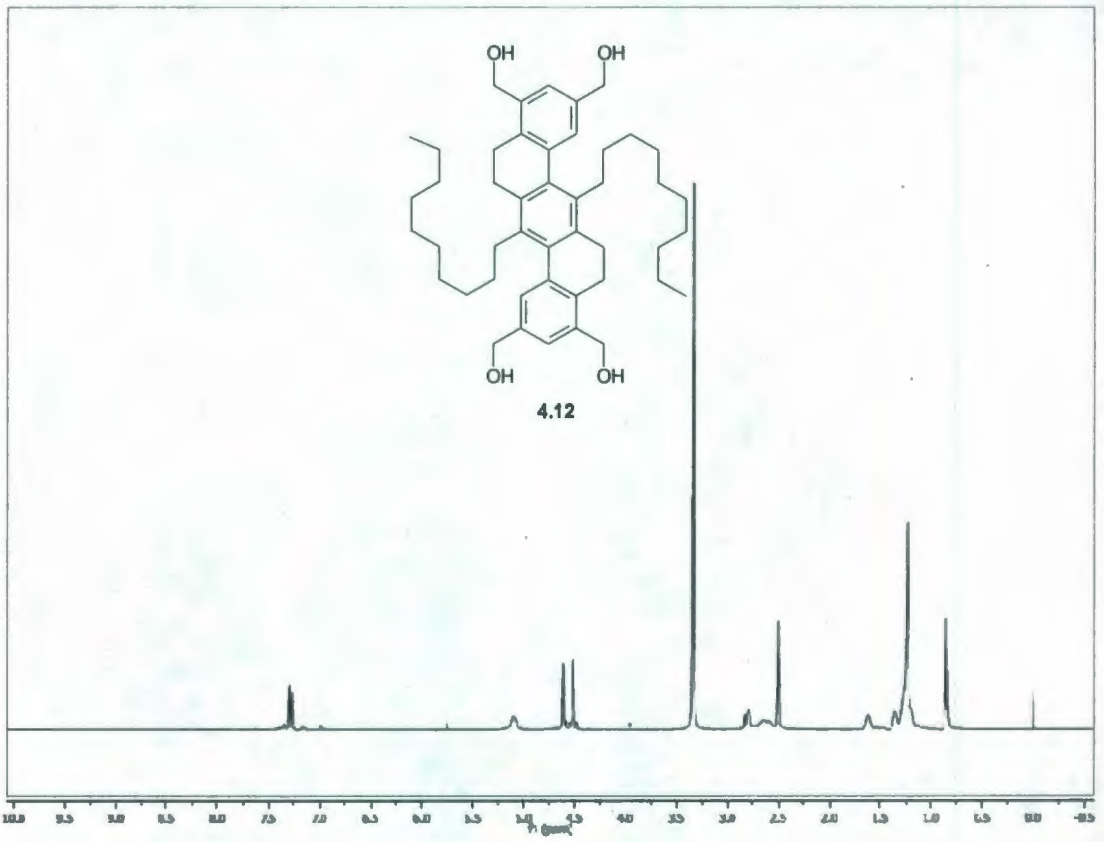
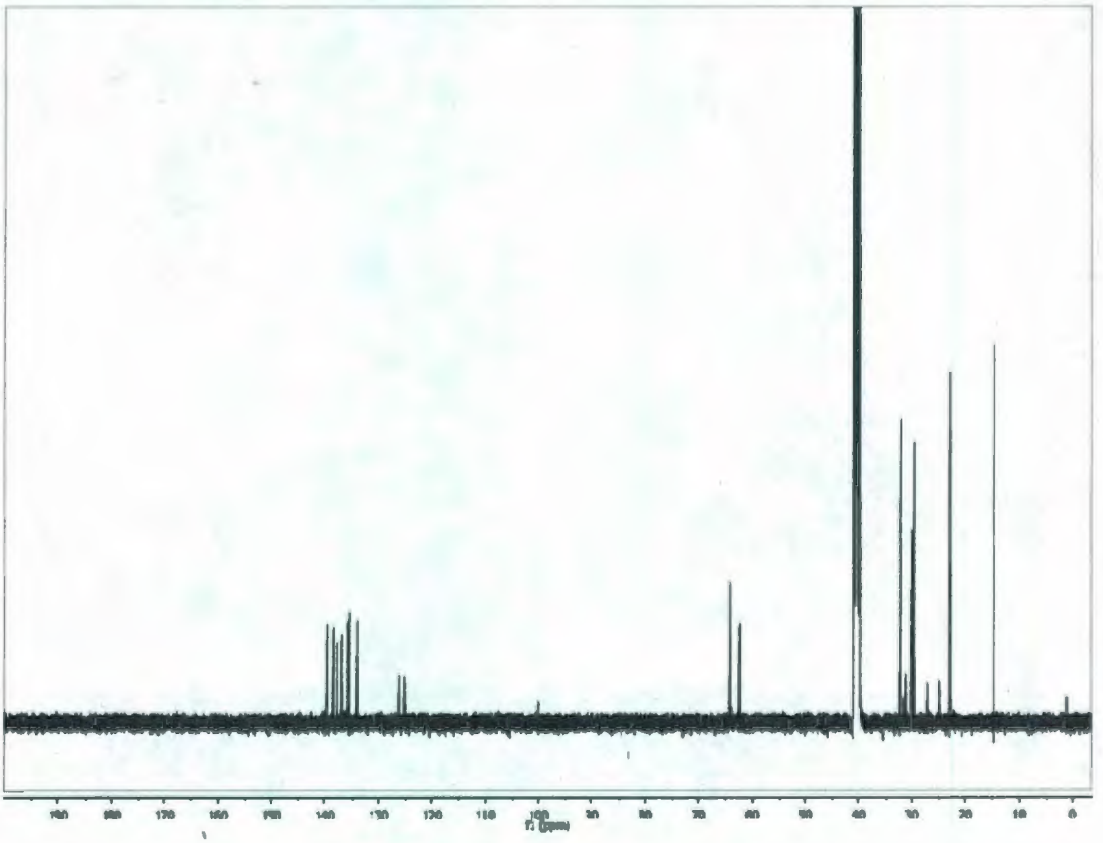
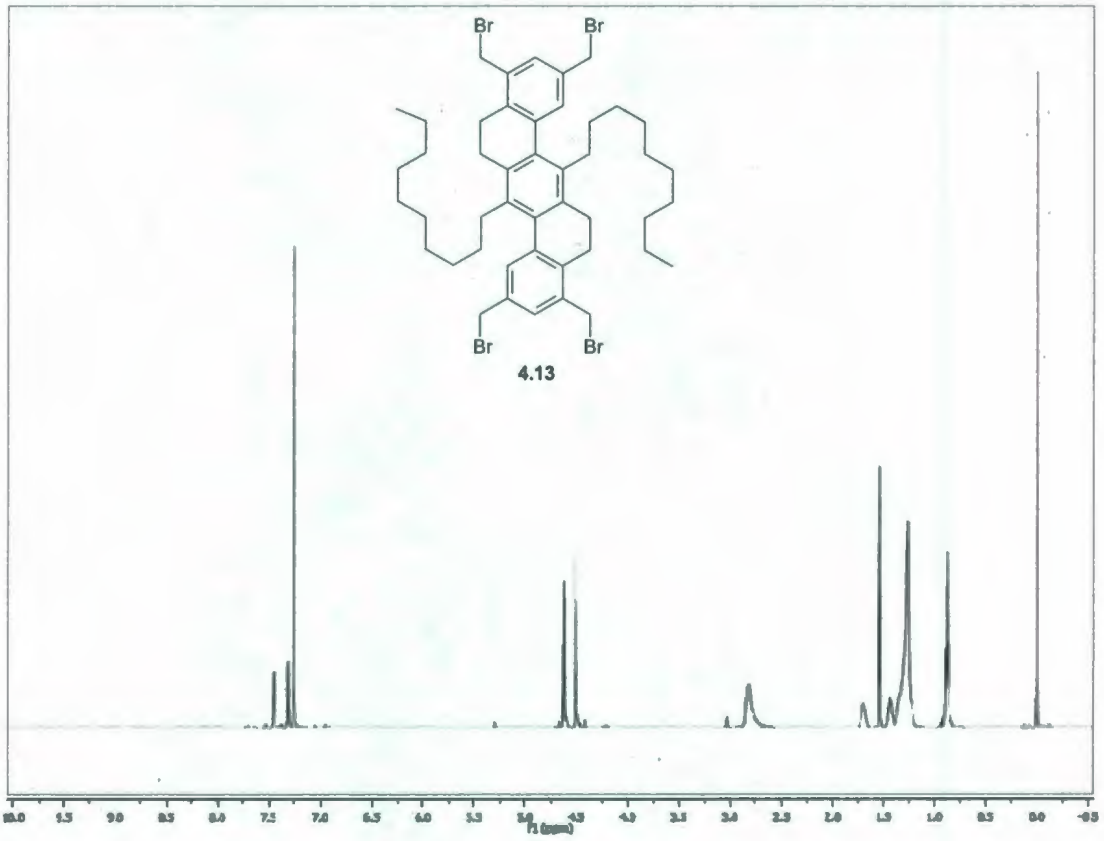
# Appendix 3

## Selected Spectra of Synthesized Compounds

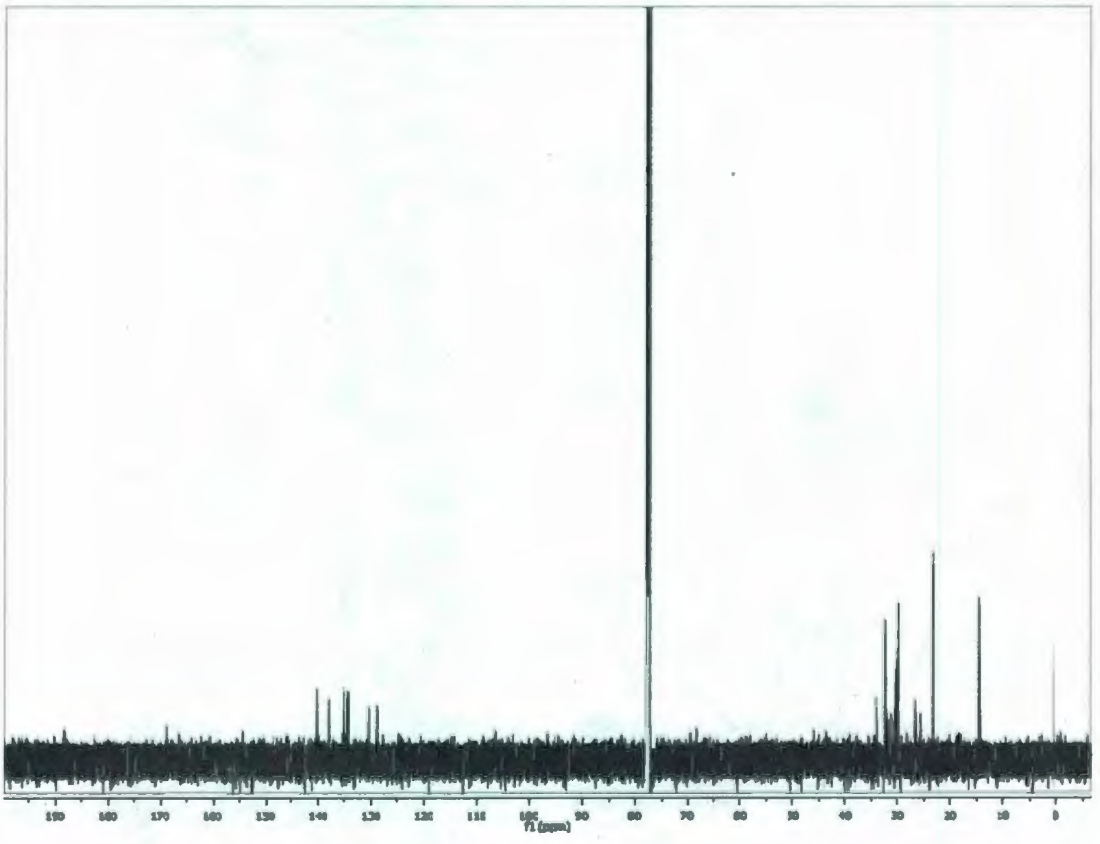


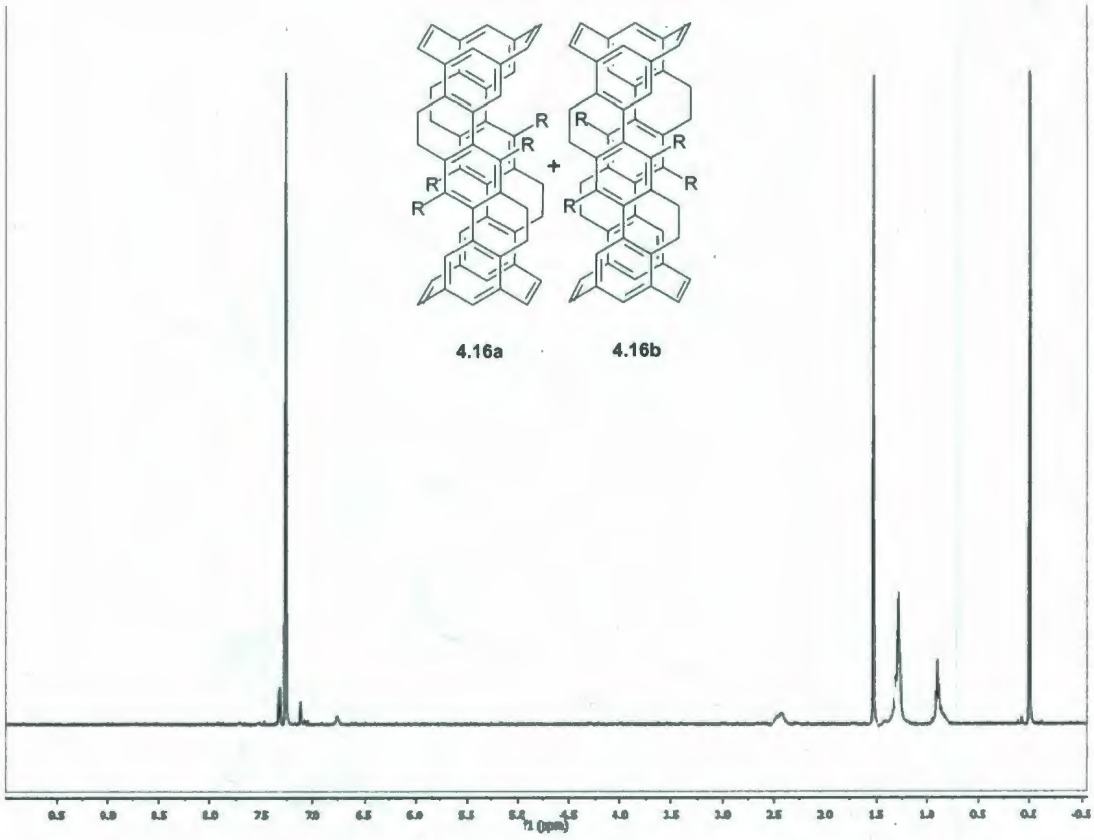

4.12

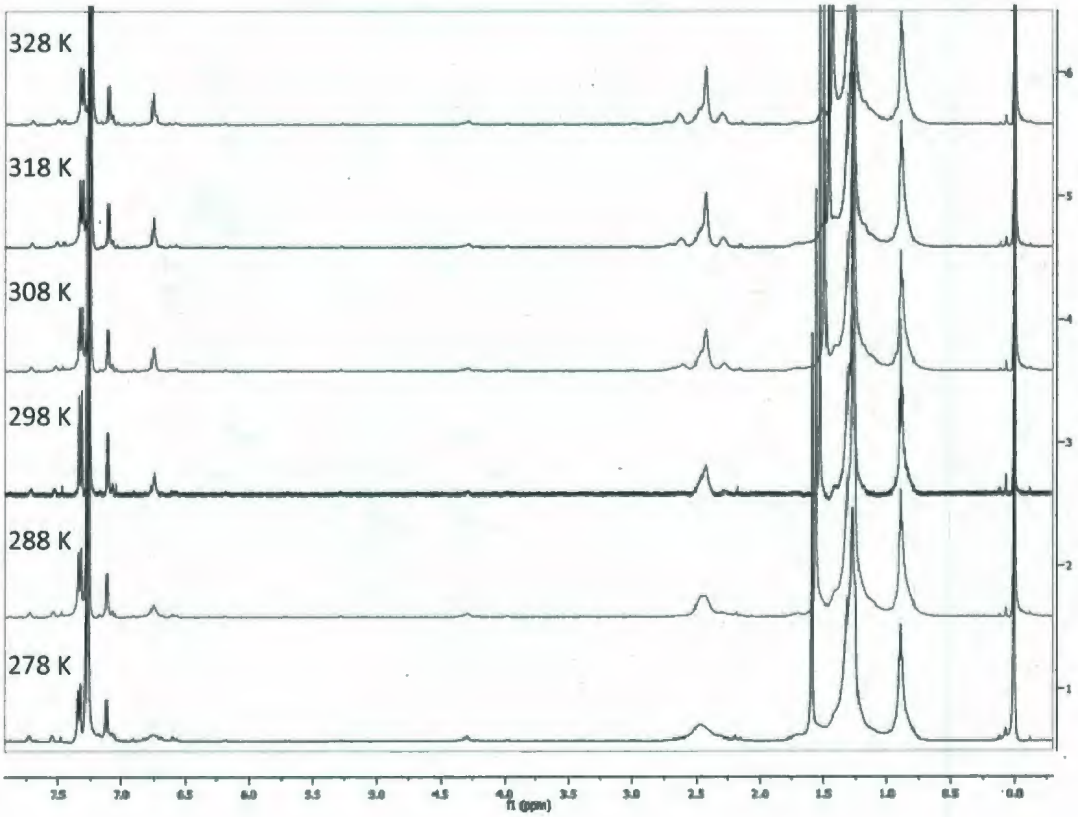





4.13




4.16a
4.16b
f1 (ppm)


328 K
318 K
308 K
298 K
288 K
278 K
f1 (ppm)