A Cyclophane-Based Approach to [*n*]Cycloparaphenylenes and an Allylic Arylation Strategy for Regioselective Triphenylene Synthesis

by

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Abstract

CHAPTER 1 Synthesis of functionalized *p*-terphenyl-containing macrocycles as key intermediates in the synthesis of functionalized [*n*]CPPs

Strategically designed, substituted *para*-terphenyl-containing macrocycles are explored as possible key intermediates in the synthesis of functionalized [*n*]cycloparaphenylenes. These *para*-terphenyl-containing macrocycles are prepared via a streamlined synthesis, proceeding through a macrocyclic 1,4-diketone, that has been previously reported by our group. This strategy does not employ the use of cross-coupling reactions, and is, therefore, tolerant of the incorporation of the functional groups necessary to prepare [*n*]CPPs from these *para*-terphenyl-containing macrocycles.

CHAPTER 2 Toward the Synthesis of [4]Cycloparaphenylene

Synthetic routes towards the next smallest, yet-to-be-synthesized [4]CPP are explored. These strategies aim to employ a macrocyclic 1,4-diketone as a key intermediate. The paracyclophane-based strategy aims to bypass the challenges expected with the macrocyclization of such a highly strained molecule.

CHAPTER 3 Synthesis of regioselectively functionalized triphenylenes via allylic arylation

A series of unsymmetric triphenylene systems are reported. The final two steps of these syntheses are an allylic arylation onto a cyclohex-2-ene-1,4-diol-based system and subsequent aromatization. This synthetic process has been streamlined and applied to both electron rich and electron deficient systems. Selected triphenylenes are explored as substrates for further pi-extension.

Table of Contents

List of Tables

List of Figures

List of Schemes

List of Abbreviations

Ac_2O	Acetic anhydride
AcOH	Acetic acid
Al	Aluminum
Ar	Aryl group
B	Boron
bipy	2,2'-Bipyridine
BORSM	Based on recovered starting material
Bpin	Bis(pinacolato)
Br	Bromine
°C	Degrees celcius
C	Carbon
Cl	Chlorine
cod	1,5-Cyclooctadiene
CNT	Carbon nanotube
CPP	Cycloparaphenylene
Cr	Chromium
Cs	Caesium
Cu	Copper
DavePhos	2-Dicyclohexylphosphino-2'-(*N,N'*-dimethylamino)biphenyl
dba	Dibenzylideneacetone
DDQ	2,3-Dichloro-5,6-dicyano-1,4-benzoquinone
DMA	Dimethylacetamide
DME	Dimethoxyethane
DMF	Dimethylformamide

DMP	Dess-Martin Periodinane
DMSO	Dimethyl sulfoxide
dppf	1,1'-Bis(diphenylphosphino)ferrocene
d.r.	Diastereomeric ratio
EtOAc	Ethyl acetate
Et	Ethyl
Equiv or eq.	Equivalent
F	Fluorine
H	Hydrogen
HG-II	Hoveyda-Grubbs second-generation catalyst
HK	Hydroxy ketone
I	Iodine
*i*Pr	Isopropyl
L	Ligand
LDA	Lithium diisopropylamide
Li	Lithium
Me	Methyl
MeCN	Acetonitrile
MeOH	Methanol
Mg	Magnesium
MOM	Methoxymethyl
MsOH	Methanesulfonic acid
N	Nitrogen
Na	Sodium
NBS	*N*-Bromosuccinimide

n-BuLi	*n*-Butyllithium
Ni	Nickel
NMR	Nuclear magnetic resonance
O	Oxygen
OAc	Acetate
PAH	Polycyclic aromatic hydrocarbon
Pd	Palladium
Ph	Phenyl
PhMe	Toluene
PPh_3	Triphenylphosphine
Pt	Platinum
PTPP	(3,3")*para*-terphenylophane
p-TsOH	*para*-Toluenesulfonic acid
R	General organic structure
RCM	Ring closing metathesis
S	Sulfur
Si	Silicon
Sn	Tin
S-Phos	2-Dicyclohexylphosphino-2',6'-dimethoxybiphenyl
TBAF	Tetra-*n*-butylammonium fluoride
TBAI	Tetra-*n*-butylammonium iodide
TBS	*tert*-Butyldimethylsilyl
Tf	Triflate
THF	Tetrahydrofuran
TES	Triethylsilyl

TMS	Trimethylsilyl
Xe	Xenon
X-Phos	2-Dicyclohexylphosphino-2’,4’,6’-triisopropylbiphenyl
μW	Microwave

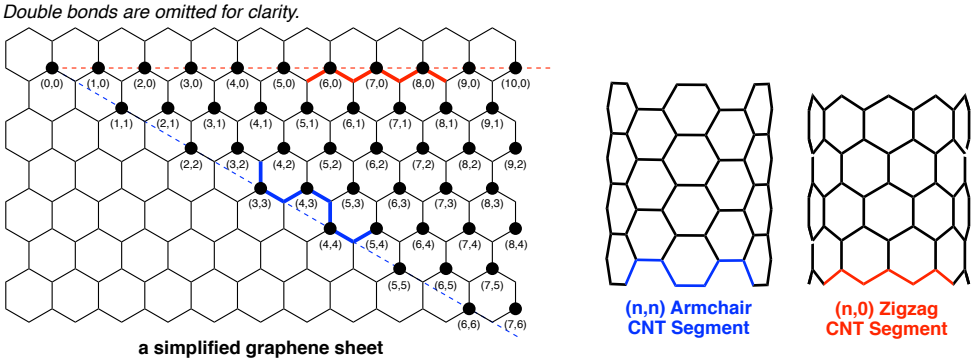
CHAPTER 1 Synthesis of functionalized *p*-terphenyl-containing macrocycles as key intermediates in the synthesis of functionalized [*n*]CPPs

1.1 INTRODUCTION: [*n*]CPPs as key intermediates in the bottom-up synthesis of armchair CNTs

Carbon nanotubes (CNTs) are cylindrical allotropes of sp^2 hybridized carbon atoms that can be viewed as a rolled-up sheet of graphene (Figure 1).[1] CNTs exhibit extraordinary chemical and physical properties that have fascinated researchers across the sciences since they were first reported in 1991.[2] CNTs are predicted to be over eighty times stronger than high tensile strength steel,[3] over ten times more thermally conductive than copper,[4] and can be stretched up to 23% of their original length without breakage.[5] These properties, among others, have led researchers to propose a seemingly infinite number of diverse, potential applications, including their uses in drug delivery systems,[6] device miniaturization,[7] and high efficiency energy storage.[8] However, these properties are dependent upon the specific type of carbon nanotube (*i.e.*, chirality and diameter). In order to fully exploit these potential properties, access to structurally uniform CNTs is required. Current methods for the preparation of carbon nanotubes require high temperatures (some reaching >2000 °C) and pressures (>10 atm).[9] These extreme conditions produce CNTs in complex mixtures that are difficult to purify, making the application of these materials extremely challenging.

Figure 1. Roll vectors of carbon nanotubes and the types of CNTs afforded

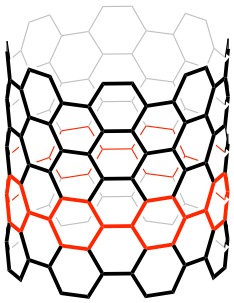
Double bonds are omitted for clarity.



One potential solution to the challenge of preparing homogeneous CNTs, is a bottom-up synthetic approach. In the case of armchair CNTs (**F2.1**, Figure 2), one could imagine constructing the CNT from a macrocyclic template, or hoop-shaped molecule. The smallest possible benzenoid, hoop-shaped fragment that can be traced around the perimeter of an armchair CNT is a cycloparaphenylene (CPP) (red highlighted segment of **F2.1**). [10] [*n*]CPPs are macrocyclic structures composed entirely of *para*-linked (bent) benzene rings, where *n* represents the number of benzene rings contained within the hoop-shaped template. The diameter of the [*n*]CPP corresponds to the diameter of the (n,n)CNT.[11]

1.1.1 Generalized synthetic approach toward cycloparaphenylenes

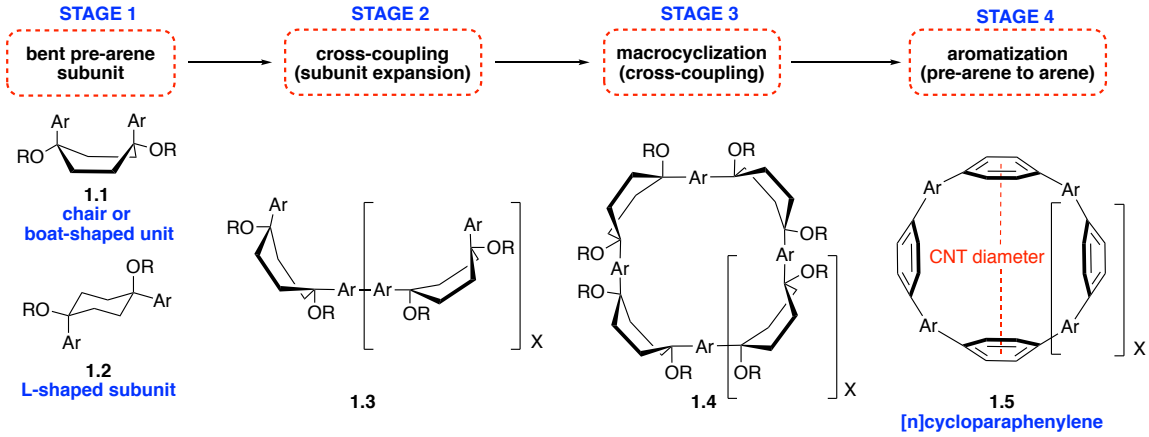
Figure 2. [8]CPP as a fragment of (8,8)CNT



F2.1
(8,8) Armchair CNT
Double bonds are omitted for clarity.

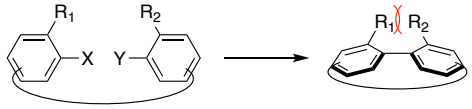
The [*n*]CPPs have been investigated as synthetic targets long before the discovery of the fullerene allotropes of carbon and CNTs.[12] The presence of strained benzene rings contained within a hoop inspired synthetic and physical organic chemists for decades. In 2008, the first syntheses of [*n*]CPPs were reported by Jasti and Bertozzi.[13] After this landmark achievement, the groups of Itami, Yamago and Wang followed with their own approaches to these challenging targets. Virtually all of the reported syntheses of [*n*]CPPs proceed through (a similar) four stage synthetic process.[14] The first stage involves the construction of a bent, pre-arene subunit that contains functionalized aryl groups. The bent, pre-arene portion of these compounds provide the curvature necessary for future macrocyclization reactions to occur and are, most commonly, a cyclohexadiene (boat-shaped, **1.1**, Scheme 1) or cyclohexane (chair or L-shaped, **1.2**). Stage 2 involves the expansion of the pre-arene subunit to a larger, linear oligomer, which is accomplished using a cross-coupling reaction. Once the desired number of "benzene" (arene or pre-arene) units have been incorporated, a macrocyclization reaction to close the oligomer is called upon. This requires the use of cross-coupling or direct arene-arene bond forming reactions, both of which require the use of a transition metal catalyst and an aryl halide (or equivalent). Aromatization of the pre-arene units to benzene rings furnishes the product [*n*]CPP.

Scheme 1. A generalized four-stage synthetic approach to [*n*]CPPs



These generalized approaches have allowed for great advancement in the field of [*n*]CPP synthesis, with [*n*]CPPs ranging from *n* = 5-16, 18, and 21[15] being prepared. Furthermore, gram-scale syntheses of [6]-,[16] [8]-, and [10]CPP[17] have been reported, and [5]- and [12]CPP are both commercially available.[18] However, the reliance upon cross-coupling reactions to furnish synthetic precursors has hindered advancement toward more functionalized [*n*]CPPs. These cross-coupling reactions are not tolerant of halide substituents, particularly those *ortho* to the site of aryl-aryl bond formation (Figure 3). Aryl halides would be the most valuable substituents for future skeletal building reactions and C-C bond formation, but the presence of these functional groups would compete in offsite, intermolecular reactions during stages 2 and 3 of the generalized approach presented above.

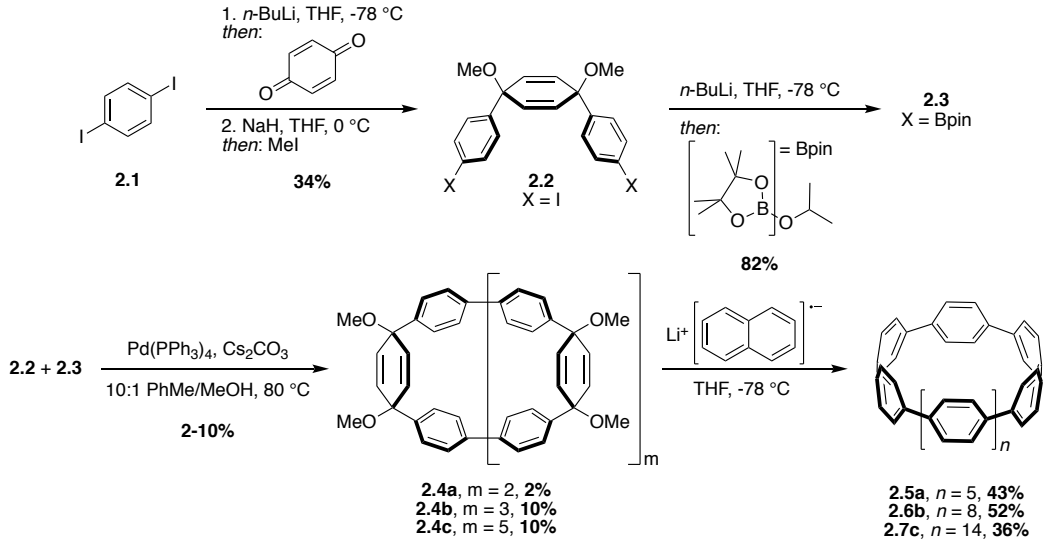
Figure 3. Limitations of cross-coupling in macrocyclization



1.1.2 The first [*n*]CPP syntheses: a 3,6-*syn*-dimethoxy-cyclohexa-1,4-diene-based approach to [9]-, [12]-, and [18]CPP

In 2008, Bertozzi and Jasti reported the synthesis of [9]-, [12]-, and [18CPPs, representing the first report of the successful synthesis of an [*n*]CPP.[8] Their approach began with the preparation of diiodide **2.2** (Scheme 2), which was synthesized by the addition of (4-iodophenyl)lithium (generated from **2.1**) to benzoquinone. Diiodide **2.2** was then borylated by first generating the dilithium species via treatment with *n*-buLi and then the addition of 2-isopropoxy-4,4,5,5-tetramethyl-1,3,2-dioxaborolane, affording **2.3** in an 82% yield. The *syn*-configuration of the 1,4-diol unit present in both **2.2** and **2.3** provided the curvature necessary for successful

Scheme 2. The 2008, Bertozzi and Jasti synthesis of [9]-, [12]-, and [18]CPPs



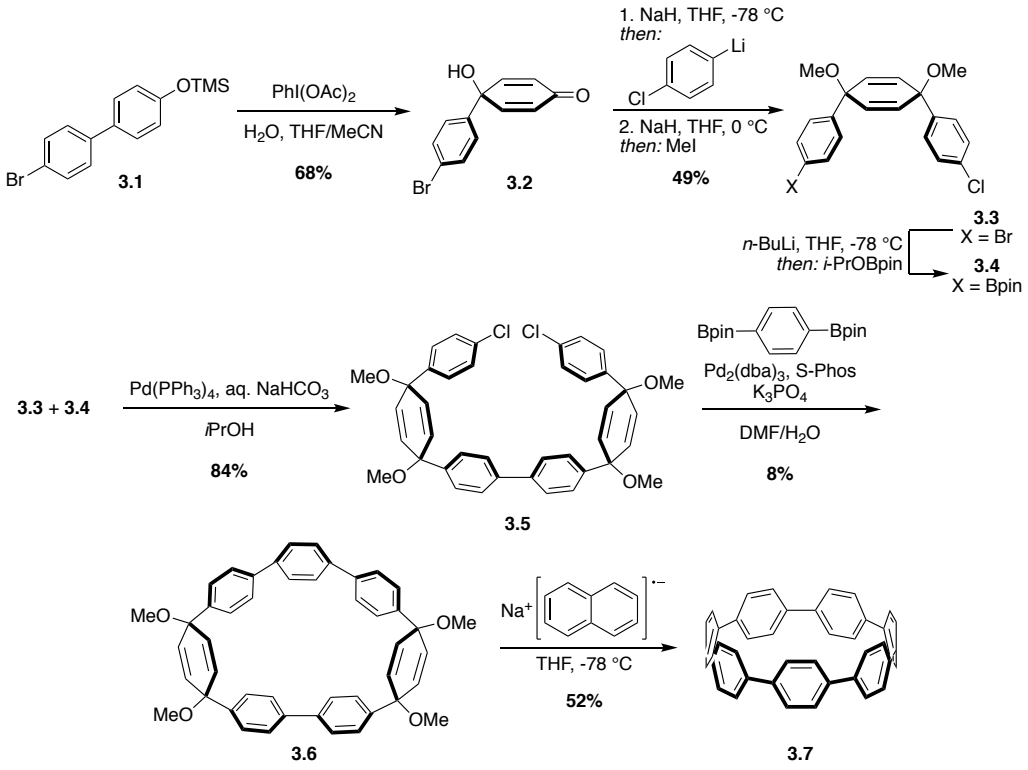
macrocyclization and both could be prepared on a gram-scale. The Suzuki cross-coupling of **2.2** and **2.3** afforded the macrocycles **2.4a**-**c** in 2-10% yield. Subsequent treatment with lithium napthalenide reduced the 3,6-*syn*-dimethoxy-cyclohexa-1,4-diene units, proceeding via two successive single-electron transfers, to give the aromatized products, [*n*]CPPs **2.5a**-**c** in yields of 36-52%. These syntheses were very concise, requiring just 5 synthetic operations to solve a 70-year-old problem in synthetic organic chemistry.

1.1.3 Further applications of cyclohexadiene subunits in [*n*]CPP synthesis

The successful use of a 3,6-*syn*-dimethoxycyclohexa-1,4-diene system as a bent, pre-arene unit led Jasti to utilize the same core structure as key intermediates in the synthesis of several other [*n*]CPPs in his independent career. To implement this cyclohexadiene-based system as the bent, pre-arene subunit in the synthesis of other [*n*]CPPs, the preparation of an unsymmetric analog of **2.2** was required.

In synthesis of [7]CPP (**3.7**, Scheme 3), the unsymmetric cyclohexadiene-based pre-arene subunit **3.4** was prepared as the key intermediate.[20] The first step in this synthesis was the oxidative dearomatization of biphenyl **3.1** to give the ketone **3.2**. Then, (4-Chlorophenyl)lithium was added to a pre-mixed solution of **3.2** and sodium hydride, introducing the final aryl group

Scheme 3. Synthesis of [7]CPP utilizing an unsymmetric cyclohexadiene

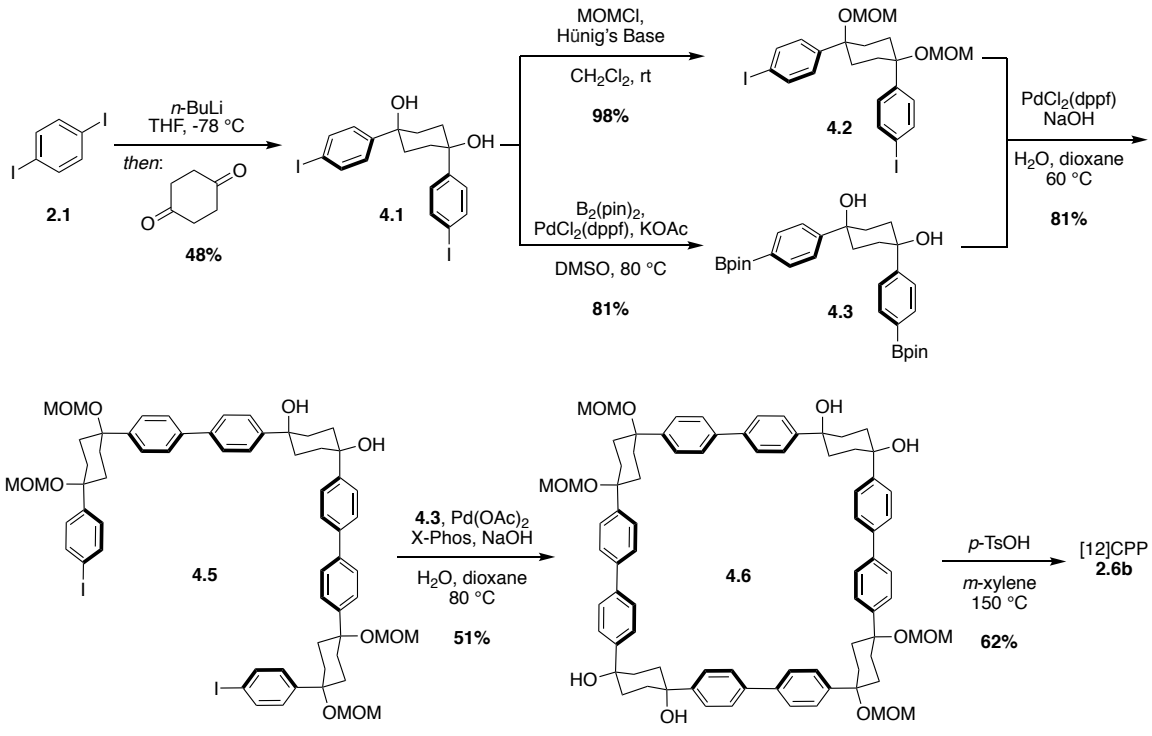


found in the bent, pre-arent unit and subsequent methylation afforded **3.3**, the unsymmetric cyclohexadiene-based unit containing a chlorine and a bromine. This was then borylated using *n*-butyllithium and the isoropoxy-boronic ester to give the unsymmetric cyclohexadiene-based unit **3.4**, containing a chlorine and a boronic ester. Then, **3.3** and **3.4** were coupled together under Suzuki cross-coupling conditions to give the expanded system **3.5**. This was then macrocyclized via another Suzuki cross-coupling with 1,4-phenylenebisboronic acid to give the macrocycle **3.6**. The final, aromatization step was accomplished using sodium napthalenide to afford [7]CPP **3.7**.

1.1.4 Utilizing a 1,4-aryl-substituted cyclohexane as the bent, pre-arene unit in [*n*]CPP synthesis

In 2009, Itami and co-workers reported the first selective synthesis of [12]CPP.[21] This synthesis followed a similar synthetic strategy to that of Jasti and Bertozzi, however the bent pre-arene unit employed was a *syn*-1,4-diarylcyclohexane-1,4-diol as opposed to the 3,6-*syn*-dimethoxycyclohexa-1,4-diene utilized in the former approach. Furthermore, the iterative nature of this approach allowed the authors to selectively prepare [12]CPP without the formation of any other [*n*]CPPs.

Scheme 4. Synthesis of [12]CPP via a cyclohexane-based bent, pre-arene unit



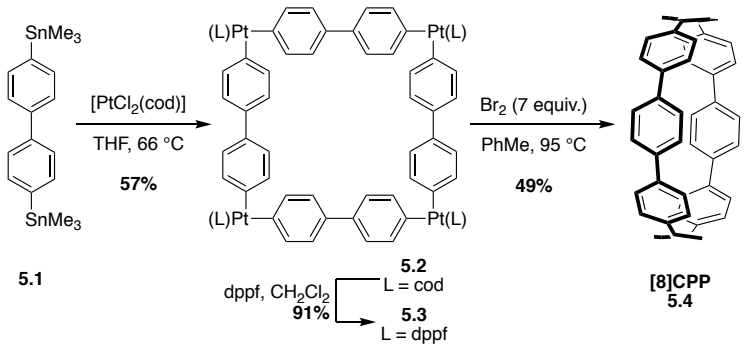
The synthesis of [12]CPP (**2.6b**) began with the bis-addition of (4-iodophenyl)lithium (generated *in situ* from **2.1**) to cyclohexanone, generating *syn*-cyclohexane-1,4-diol **4.1** (Scheme 4). This was then converted to either **4.2** by protecting the tertiary alcohols as the MOM-ether or to **4.3** via borylation. Then, **4.2** and **4.3** (10:1 ratio) were reacted under Suzuki cross-coupling conditions to give the oligomer **4.5**. Macrocyclization was achieved by reacting this with another portion of **4.3** in a second Suzuki reaction, resulting in a 51% yield. **4.6** was then aromatized via an acid-catalyzed deprotection and dehydration of the cyclohexane-based units. Performing the Suzuki reactions sequentially, instead of a shotgun approach, allowed for the selective synthesis of [12]CPP. This stepwise strategy was later applied by the same group in the selective synthesis of [9]CPP[22] and again for [14]-[16]CPP.[23]

1.1.5 Synthesis of [*n*]CPPs via the application of a Square-Shaped Platinum Complex

In 2010, Yamago and co-worked reported the first synthesis of [8]CPP.[24] In contrast to the existing strategies (1.1.2-1.1.4) this synthesis did not make use of a bent, pre-arene subunit to aid in macrocyclization. Instead, a square-shaped macrocycle was constructed by connecting four biphenyl units with square-planar platinum. Because the biphenyl substituents are *cis* to one another, the angle between them is about 90° which provides the L-shape necessary for the preparation of a relatively strain-free macrocycle.

To begin, bis(trimethylstannyl)biphenyl **5.1** (Scheme 5) was treated with $[PtCl_2(cod)]$ to give the macrocyclic, platinum complex **5.2**, followed by a ligand exchange with 1,1'-bis(diphenylphosphino)ferrocene to give **5.3**. This was then subjected to a reductive elimination, forming the aryl-aryl bonds necessary to give [8]CPP (**5.4**) in just three, straightforward steps from **5.1** in an overall yield of 25%.

Scheme 5. Synthesis of [8]CPP via a square-shaped platinum complex

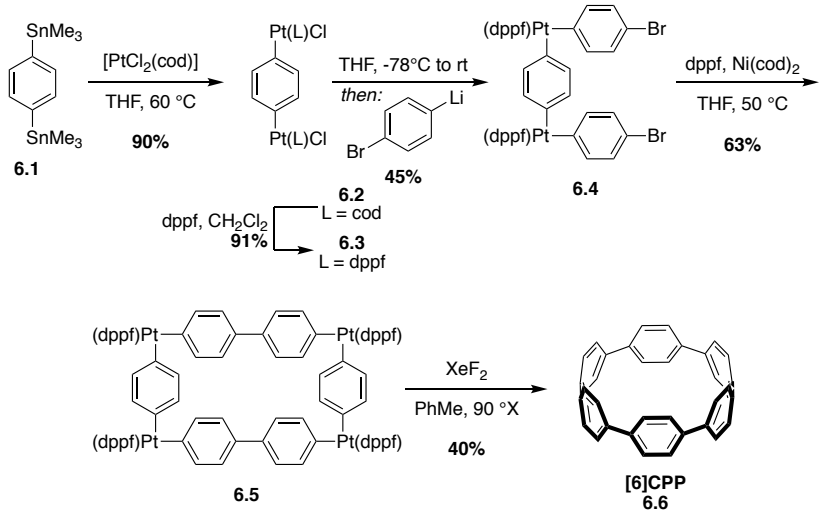


Because of the L-shaped nature of the subunits used in this preparation of [8]CPP, it was originally reported that this method would be most effective in the synthesis of only [4*n*]CPPs.

However, in 2013, Yamago reported the synthesis of [6]CPP which also utilized a square-planar platinum macrocycle.[25] In this, U-shaped subunits were prepared in stepwise manner.

First, 1,4-bis(trimethylstannyl)benzene **6.1** (Scheme 6) was treated with [$PtCl_2$(cod)] to give **6.2**, followed by ligand exchange to give the bis-Pt(dppf) **6.3**. This was then treated with (4-bromophenyl)lithium to give the U-shaped subunit **6.4**. Homocoupling of **6.4** with Ni(cod)$_2$ gave the macrocyclic platinum complex **6.5**, which was then aromatized via reductive elimination with XeF_2.

Scheme 6. Use of the square-shaped platinum complex in the synthesis of [6]CPP



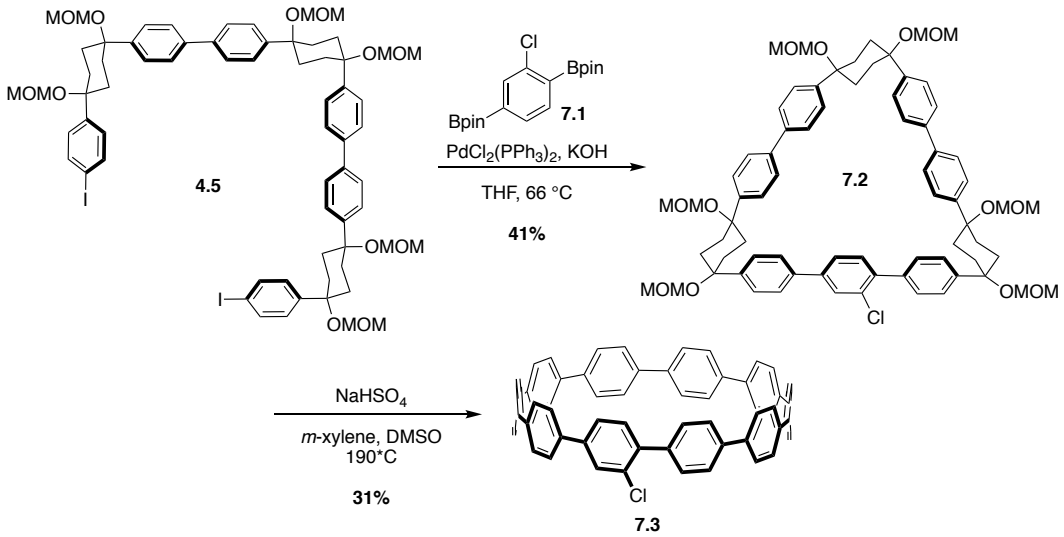
1.2 Selected examples of functionalized [*n*]CPPs

1.2.1 Halogenated [*n*]CPPs

In order to begin to connect [*n*]CPPs and ultimately synthesize armchair CNT segments, functional group handles are necessary. Halogens represent particularly synthetically useful functional groups as they could be used directly in cross-coupling reactions or could be easily converted into other groups.

In 2014, Itami and co-workers reported the first synthesis of a halogenated [*n*]CPP, chloro[10]CPP.[26] This synthesis utilized **4.5**, which was also used in their selective synthesis of [12]CPP (Scheme 4). Macrocyclization was carried out in a 41% yield by coupling **4.5** with the chlorinated 1,4-bisboronic ester **7.1** (Scheme 7) in a Suzuki reaction that preferentially coupled the Bpin groups of **7.1** with the iodine-functionalized termini of **4.5** to afford the macrocycle **7.2**. Other Suzuki conditions led to the formation of the undesired coupling product of the Bpin group of **7.1** with the chlorine present in the same molecule. Then, acid-catalyzed aromatization of **7.2** yielded chloro[10]CPP **7.3** in a 31% yield. The successful dimerization of **7.3** is discussed in the following section.

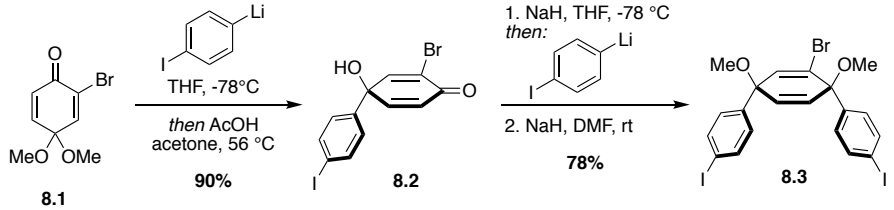
Scheme 7. Synthesis of chloro[10]CPP



1.2.2 Synthesis of [*n*]CPP dimers from halogenated precursors

In 2012, Jasti and co-workers reported the synthesis of an [8]CPP dimer from a brominated macrocyclic intermediate.[27] In contrast to Itami's synthesis of chloro[10]CPP, where the halogen functionality was incorporated at a later stage (the macrocyclization step), here the bromine functionality was introduced at the beginning. This approach began with the construction of a brominated cyclohexadiene **8.3** (Scheme 8). This was achieved by the addition of (4-iodophenyl)lithium to **8.1**, to give the ketone **8.2**. A second addition of (4-iodophenyl)lithium gave the desired brominated cyclohexadiene subunit **8.3** (Scheme 8).

Scheme 8. Preparation of a bromo-substituted cyclohexadiene-based bent, pre-arene unit

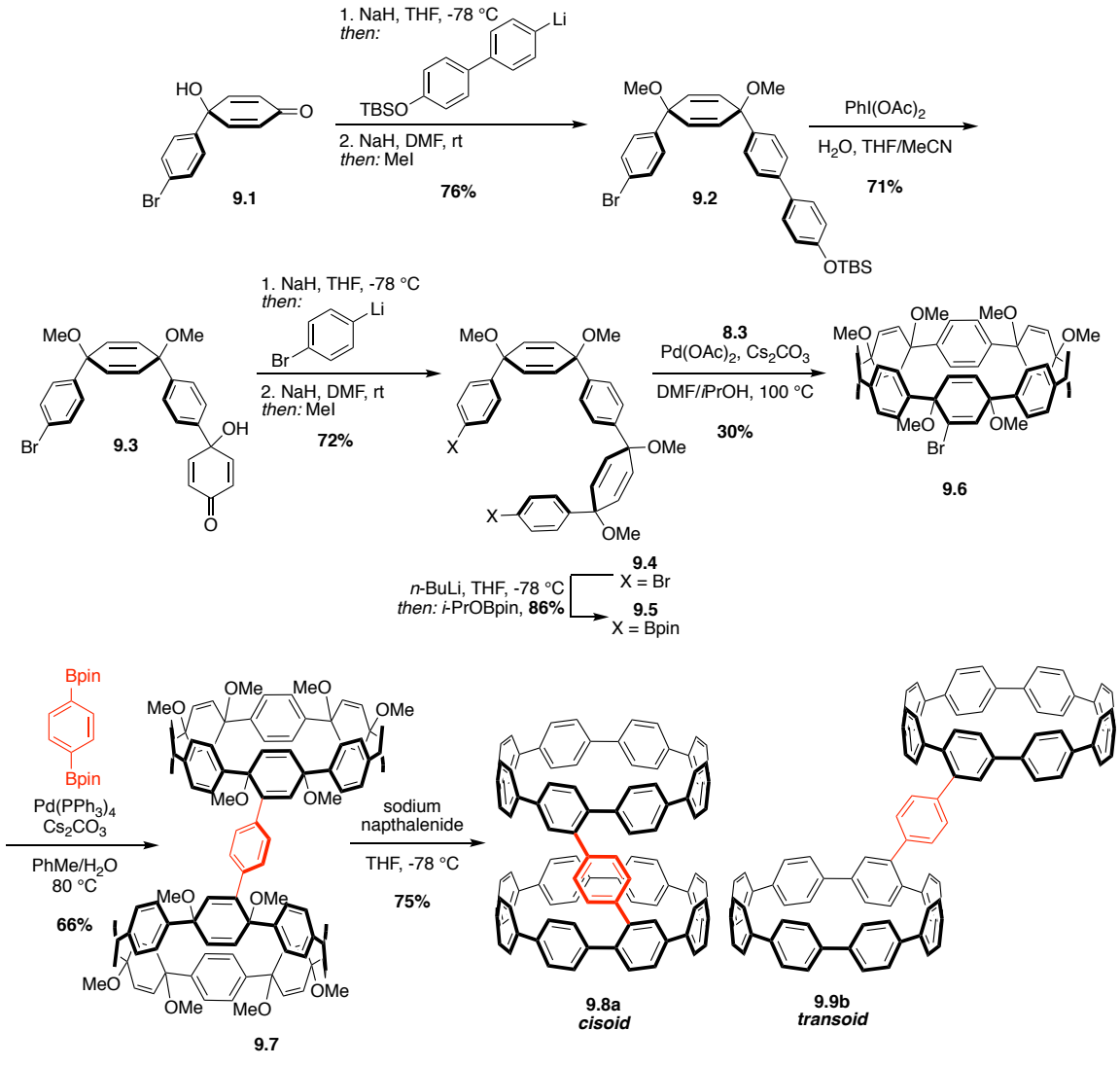


This monobromo cyclohexadiene-based subunit **8.3** was later cross-coupled with bisboronic acid **9.5** (Scheme 9). This bisboronic acid was prepared via iterative aryllithium addition, first, by the addition of biphenyllithium to **9.1** to give **9.2**. Then, dearomatization of the *tert*-butyldimethylsilyl-protected phenol gave **9.3**, which was treated with (4-bromophenyl)lithium and subsequently methylated to give **9.4**. Borylation of the two bromine handles gave the boronic ester **9.5** required for macrocyclization, which proceeded in a 30% yield to give **9.6**.

This system was not aromatized to form the monobromo[8]CPP, but rather dimerization was carried out at this phase. Two equivalents of **9.6** were reacted with the 1,4-benzenediboronic ester to give the dimer **9.7**, which was then treated with sodium napthalenide to give the [8]CPP dimer **9.8a-b**.

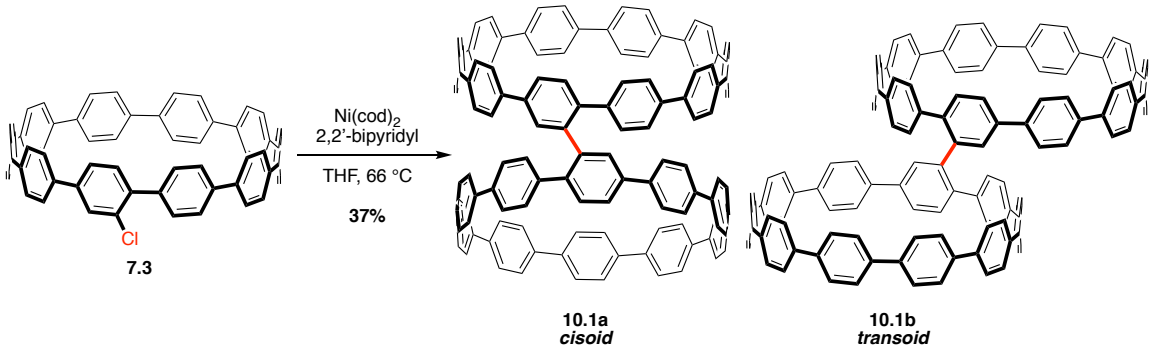
While the authors reported complications in obtaining a crystal structure of these dimers, computational studies were conducted for both the solid and solution phases. In the solid state, the transoid conformation **9.8b** is predicted to be 34 kcal/mol lower in energy than the cisoid conformation **9.8a**. However, in solution phase, the cisoid conformation, that which would be necessary to perform further C-C bond formations (closing in on a nanobelt), was found to be 7 kcal/mol lower in energy.

Scheme 9. Synthesis of an aryl-bridged [8]CPP



The chloro[10]CPP discussed in 1.2.1 has also be used in the synthesis of an [*n*]CPP dimer, **10.1** (Scheme 10). The Yamamoto homocoupling of **7.3** gave the directly linked [10]CPP dimer **10.1** in 1 37% yield. Interestingly, the cisoid conformation (**10.1a**) of this dimer was calculated to have 0 kcal/mol of strain energy, compared to 5.1 kcal/mol of strain energy for the transoid conformation (**10.1b**). There remain 19 C-C bonds that would be closed in order to convert **10.1** into a nanobelt. No further attempts at completing this transformation have been reported by the group.

Scheme 10. Synthesis of a directly linked [10]CPP dimer

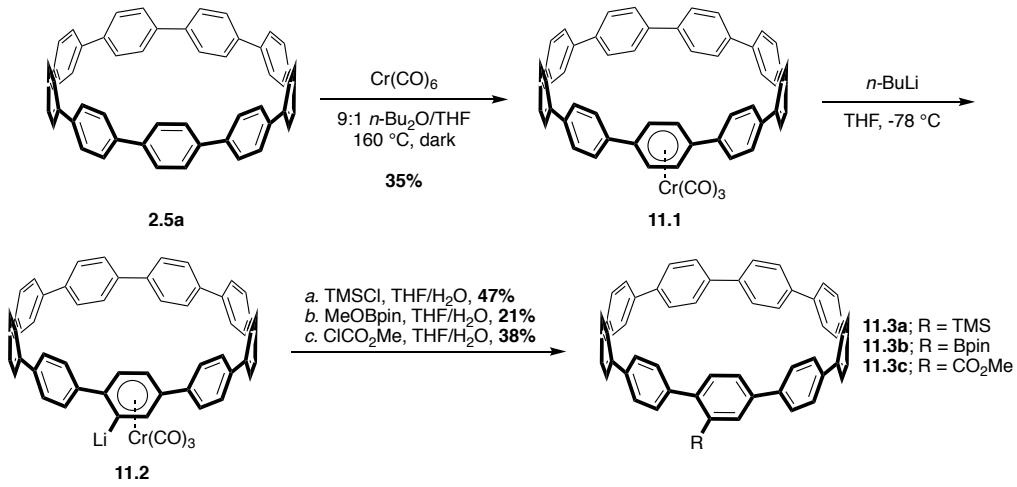


1.2.3 Late-stage functionalization from a chromium complex

In 2015, Itami and co-workers reported the preparation of a [9]CPP-chromium complex. This chromium functionality was introduced to an already formed [9]CPP and then was then converted into three other groups including TMS, Bpin, and a methyl ester.[28] Although no further work has been reported on these systems, these new functional groups could be used in dimerization reactions towards an armchair CNT segment.

The previously synthesized [9]CPP (**2.5a**)[20] was complexed with chromium hexacarbonyl in the dark to form the chromium-complexed [9]CPP **11.1** (Scheme 11). This was then treated with *n*-BuLi to form the lithium-chromium complex **11.2**, which served as the common intermediate in the synthesis of the three different functionalized [9]CPPs. In order to prepare the mono-trimethylsilyl[9]CPP **11.3a**, **11.2** was treated with trimethylsilyl chloride; to prepare the boronic acid-substituted [9]CPP **11.3b**, **11.2** was treated with methoxyboronic acid pinacol ester; and to prepare the methyl ester-substituted [9]CPP **11.3c**, **11.2** was treated with methylchloroformate. All of these subsequent functional group interconversion reactions could be run in ambient light.

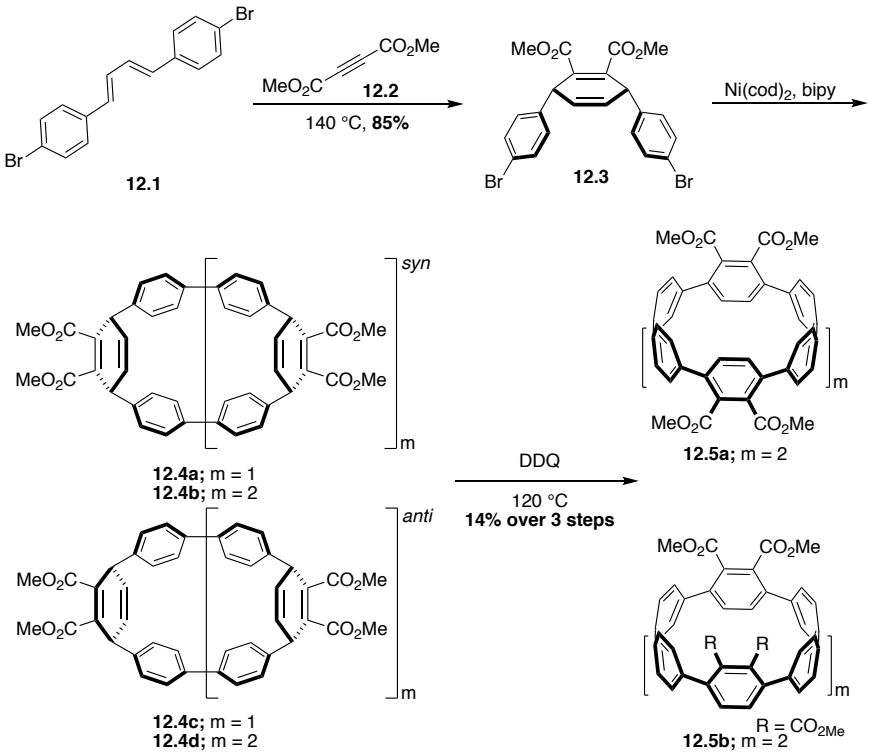
Scheme 11. Synthesis of a chromium-complexed [9]CPP



1.2.4 Cycloadditions in the synthesis of functionalized [*n*]CPPs

Because there can be some functional group intolerance associated with cross-coupling reactions, cycloadditions as a means of incorporating functional group handles into [*n*]CPPs have also been explored.

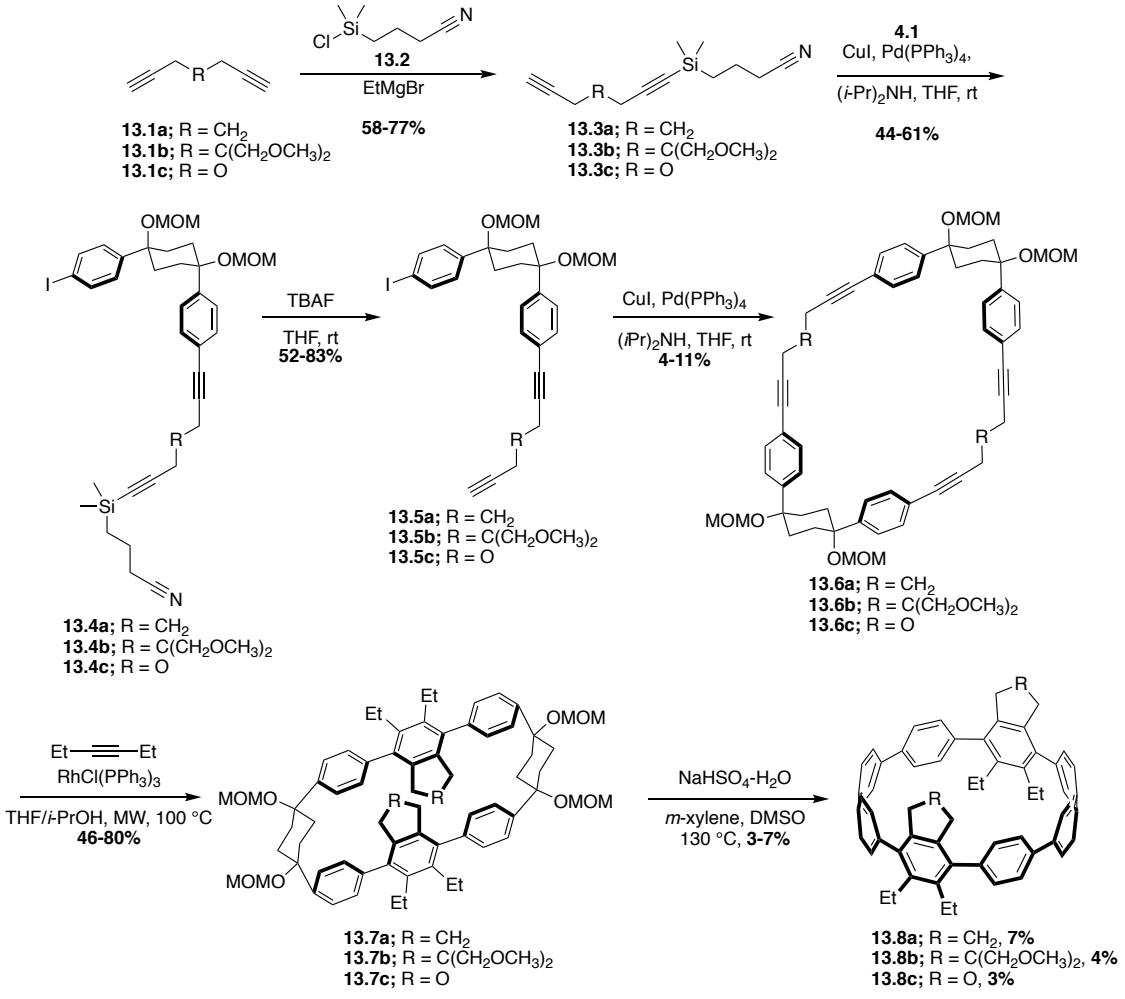
Scheme 12. Wang's Diels-Alder-based approach to a functionalized [9]cycloparaphenylene



In 2016, Wang and co-workers reported the synthesis of a carbomethoxy-substituted [9]CPPs.[29] The introduction of these functional groups was done via the Diels-Alder between **12.1** and **12.2**, which formed the cyclohexadiene-based subunit **12.3** in an 85% overall yield and gave exclusively the *cis*-oriented product (Scheme 12). Treatment with $Ni(cod)_2$ gave a mixture of homocoupling products **12.4a-d**, where both the dimer and trimer were formed and, for each, *syn* and *anti* relative relationships were observed. While the macrocyclic precursors to a functionalized [6]CPP (**12.4a** and **12.4c**) did not undergo aromatization under these conditions, the carbomethoxy-functionalized [9]CPPs **12.5a-b** were successfully prepared in a 14% overall yield.

In 2014, Wegner and co-workers reported the synthesis of a series of functionalized [8]CPPs, where the functionality was introduced during a [2 + 2 + 2] cycloaddition.[30] This synthesis used the same 1,4-diaryl-substituted cyclohexane **4.1** subunit that was employed by

Scheme 13. A [2 + 2 + 2] Cycloaddition strategy in the synthesis of a functionalized [8]CPP

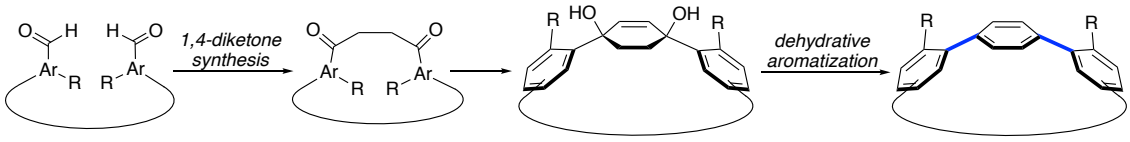


Itami (1.1.4). These cyclohexane subunits were linked by a dialkyne to achieve macrocyclization (Scheme 13). This synthesis began with the preparation of the dialkyne linkers **13.3a-c** by the protection of dialkynes **13.2a-c** with **13.2**. Then, **13.3a-c** was connected to the cyclohexane subunit **4.1** via a Sonagashira reaction to give **13.4a-c**, which was subsequently deprotected with TBAF to give the monomers **13.5a-c**. These were then dimerized via a second Sonagashira reaction to give the macrocycles **13.6a-c**, albeit in low yields (4-11%). At this point, the [2 + 2 + 2] cycloaddition reaction was carried out with 3-hexyne under microwave conditions to give the cycloadducts **13.7a-c** in a 46-80% yield. Finally, deprotection and then aromatization of the cyclohexane units afforded the functionalized [8]CPPs **13.8a-c** in 3-7% yield. The crystal structure of **13.8c** was obtained and the authors found that the functional groups about the [8]CPP were in the *syn*-configuration.

1.3 Incorporation of aromatic bridging groups in *p*-terphenyl-containing macrocycles

Our lab has reported a series of strained, *p*-terphenyl-containing macrocycles **14.4** via an unstrained 1,4-diketone intermediate **14.2** (Scheme 14). This 1,4-diketone is converted into a cyclohex-2-ene-1,4-diol **14.3** via a Grignard reaction with vinylmagnesium chloride followed by ring-closing metathesis. Dehydrative aromatization of **14.3** affords the desired *p*-terphenyl systems **14.4**. Specific conditions are discussed in the following section.

Scheme 14. General strategy for the preparation of *p*-terphenyl-containing macrocycles



14.1 tethered dialdehyde

14.2 1,4-diketo-bridged macrocycle **(unstrained)**

14.3 cyclohex-2-ene-1,4-diol ***bent*** arene precursor

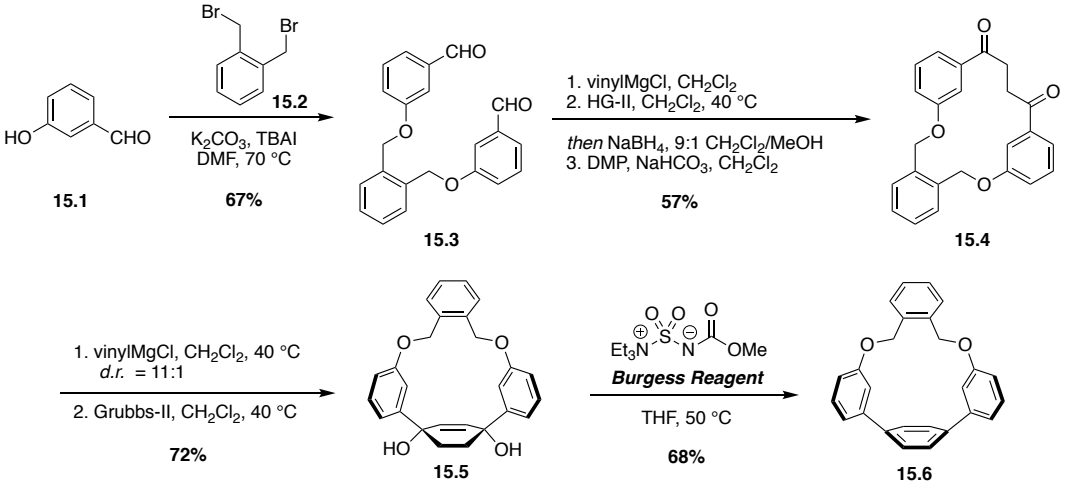
14.4 ***STRAINED*** arene-bridged macrocycle

1.3.1 Synthesis of *ortho*- and *meta*cyclo-*p*-terphenylophanes

Commercially available 3-hydroxybenzaldehyde (**15.1**) was alkylated with *α,α'*-dibromo-*o*-xylene **15.2** to give dialdehyde **15.3** (Scheme 15). This was then converted into macrocyclic diketone **15.4** via a three-step procedure that required a single purification step. A Grignard addition of vinylmagnesium chloride to **15.3** installs the olefins necessary for macrocyclic ring-closing metathesis, which was achieved using the Hoveyda-Grubbs second-generation catalyst. A mixture of olefin and alcohol diastereomers was afforded from this reaction, however, direct hydrogenation of the double bonds present and oxidation of the resulting 1,4-diols, affords 1,4-diktone **15.4** as a single compound on a gram-scale. A diastereoselective Grignard reaction in the presence of vinylmagnesium chloride installs the necessary alkene units for a second ring-closing metathesis, generating the cyclohex-2-ene-1,4-diol-based macrocycle **15.5**. The Grignard reaction of **15.4** produced an inseparable mixture of *syn*- and *anti*-diastereomers (*d.r.* = 11:1), which were separable

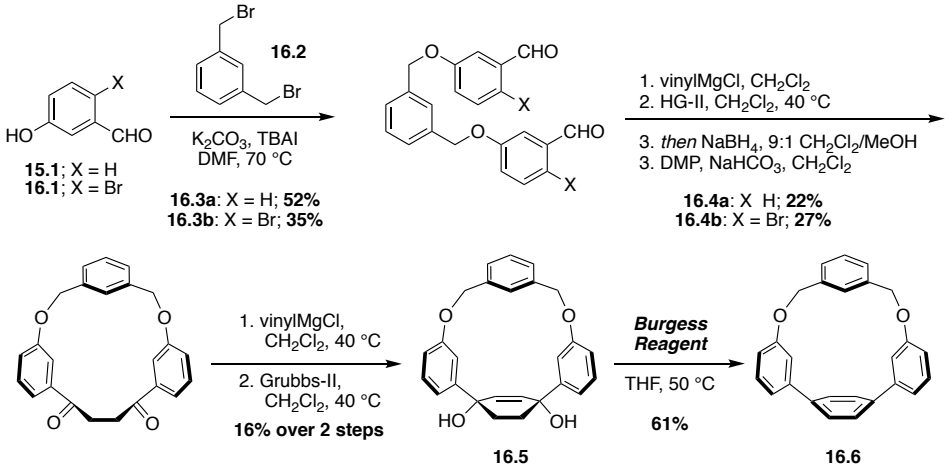
after the RCM. Dehydration and aromatization of **15.5** was achieved using the Burgess Reagent to furnish **15.6** in a 68% yield.

Scheme 15. Synthesis of *orthocyclo-para*-terphenyl-containing macrocycle **15.6**



The same reaction sequence was applied utilizing *α,α'*-dibromo-*m*-xylene **16.2** in the synthesis of *meta*cyclo-*p*-terphenylophane **16.7** (Scheme 16). The diastereoselectivity of the Grignard reaction was found to be 3.6:1. Further studies on the origin of diastereoselectivity in these Grignard additions to macrocyclic 1,4-diketones is underway in our research group. The Burgess reagent-mediated dehydration (and aromatization) of **16.6** proceeded in 61% yield. A survey of various aromatization protocols that have been tested on related *p*-terphenyl-containing macrocycles is presented in section 1.5.

Scheme 16. Synthesis of *metacyclo-p*-terphenyl-containing macrocycle **16.7**



1.3.2 X-Ray crystal structures, optimized geometries, and relevant structural data

The X-ray crystal structure of **15.6** (Figure 5) revealed that the central benzene ring of the *para*-terphenyl system was deviated from planarity. The angle *α* (see Figure 4), that is, the deviation of C-23 and C-24 from the plane defined by C-12, C-13, C-18, and C-19, was found to be (on average) 12.1°. The angle *β*, that is, the deviation of C-22 from the plane defined by C-23, C-13, and C-19 (or of C-25 from C-24, C-12, and C-18) was found to be (on average) 23.4° (Figure 4). The total SE of **15.6** was found to be 39 kcal/mol, with 33 kcal/mol residing on the *p*-terphenyl system and 6 kcal/mol within the bridging benzyloxy group. The vast majority of the SE contained within the *p*-terphenyl nucleus is centralized on the bridging *para*-phenylene ring. At 22.1 kcal/mol, this value exceeds the SE of a single *para*-phenylene ring system in found in [6]CPP (*cf*, 16.3 kcal/mol). In the case of **16.6** (Figure 6), the angle *α* was found to be 10.5° and the angle *β* was found to be 17.5° (Figure 4). The total SE was found to be 28.1 kcal/mol, with 22.2 kcal/mol residing on the *p*-terphenyl system and 5.9 kcal/mol within the bridge.

Figure 4. Angles of deformation in the central benzene ring of the terphenyl system

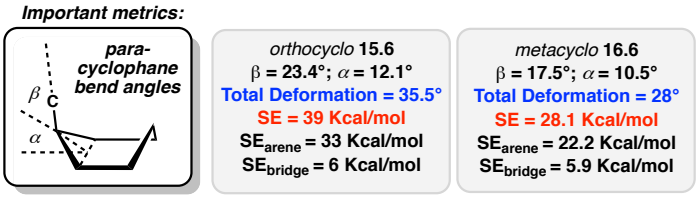


Figure 5. X-Ray crystal structure of *orthocyclo-p*-terphenylophane **15.6**

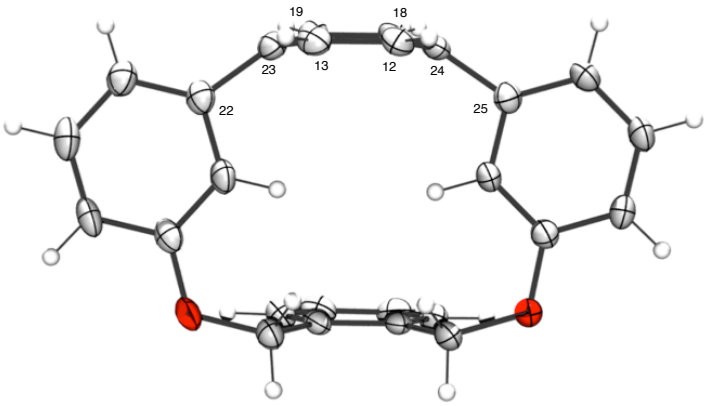
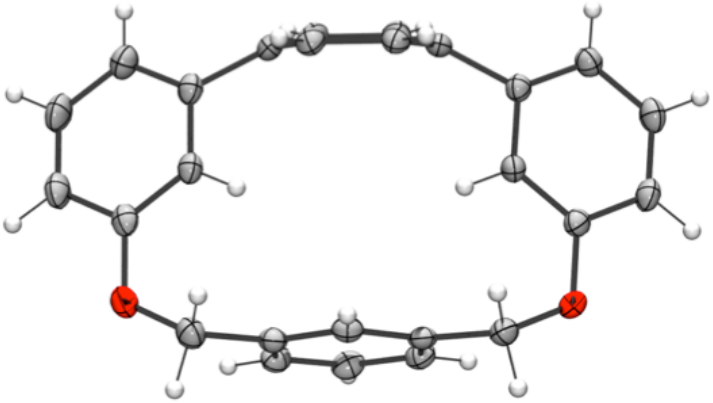


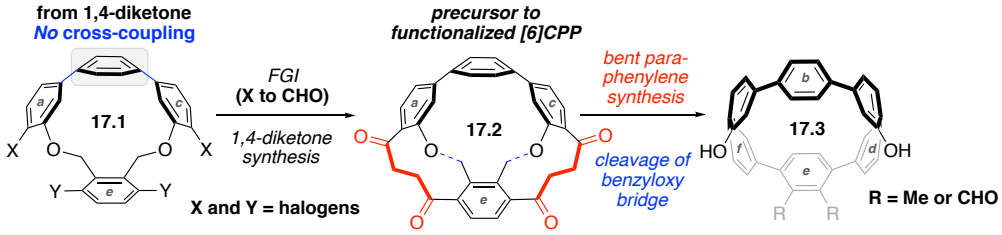
Figure 6. X-Ray crystal structure of *metacyclo-p*-terphenylophane **16.6**



1.3.3 The *orthocyclo-p*-terphenylophane as a starting material for the synthesis of a functionalized [6]CPP

Macrocycle **15.6** could serve as a precursor to a functionalized [6]CPP. This could be prepared if the positions X and Y (**17.1**, Scheme 17) were connected by a *para*-linked benzene ring, which we have demonstrated can be prepared from a 1,4-diketone intermediate akin to that present in **17.2**. Interestingly, the X and Y positions of **15.6** are only 4.34 Å apart, a distance could readily accommodate the envisaged four-atom bridge (1,4-diketone). Once the 1,4-diketone bridges of **17.2** were converted into *para*-linked benzene rings, cleavage of the benzyloxy bridging group would leave behind functional group handles on four of the six rings present in [6]CPP (**17.3**).

Scheme 17. An *orthocyclo-p*-terphenyl system as a precursor to a functionalized [6]CPP



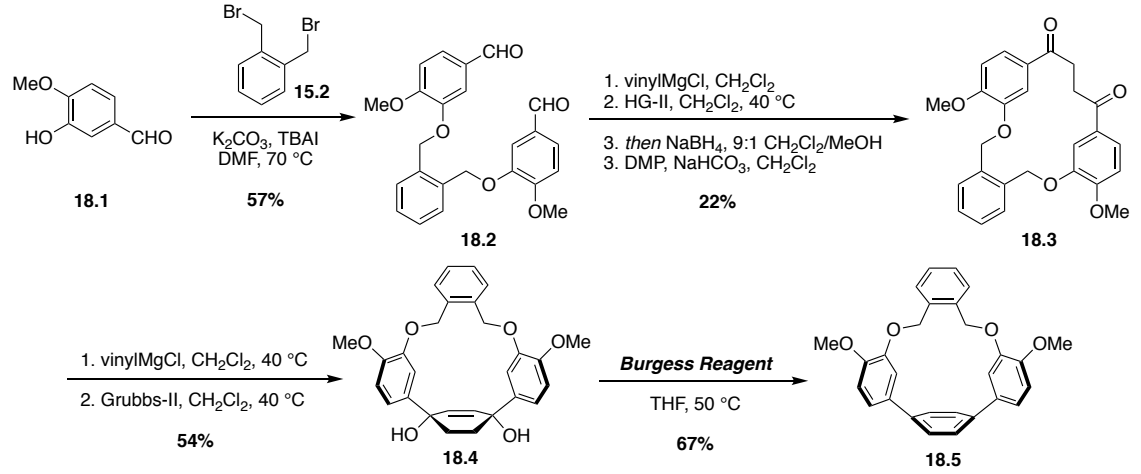
1.4 Introduction of functional group handles into the *orthocyclo-p*-terphenylophane

1.4.1 Synthesis of the methoxy-*ortho*cyclo-*p*-terphenylophane and other functionalization attempts.

The synthesis was then carried out such that a methoxy group was present at the position labeled X (**17.1**, Scheme 17). The purpose of this was to ultimately selectively cleave the methoxy group in the presence of the benzyloxy bridging group. If done at the 1,4-diketone stage, the diketone would stabilize the phenoxide produced. This would allow for the conversion of the methoxy group into other, more useful functional group handles (such as a triflate).

This sequence followed the same previously presented for the *ortho*- and *metacyclo-p*-terphenyl systems. The methoxy-functionality was installed at the beginning, by preparing *orthocyclo*-tethered dialdehyde **18.2** (Scheme 18) via the Williamson ether synthesis between isovanillin (**18.1**) and *α,α'*-dibromo-*o*-xylene **15.2**. The synthesis ultimately successfully afforded *orthocyclo*-methoxy-substituted-*p*-terphenyl system **18.5**.

Scheme 18. Synthesis of a methoxy-substituted *orthocyclo-p*-terphenyl-containing macrocycle

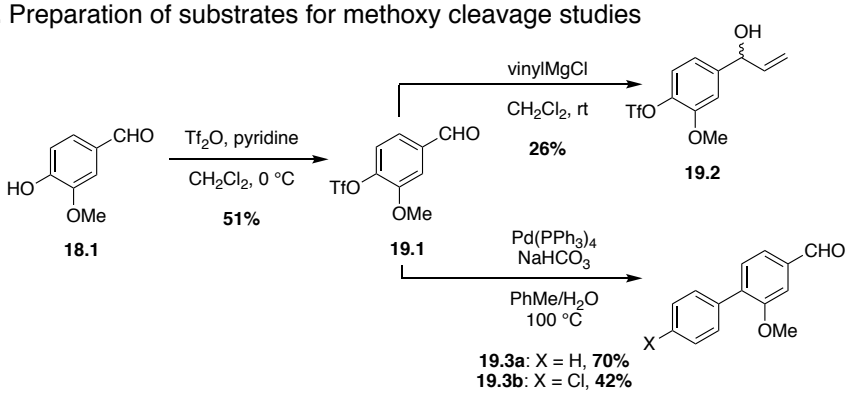


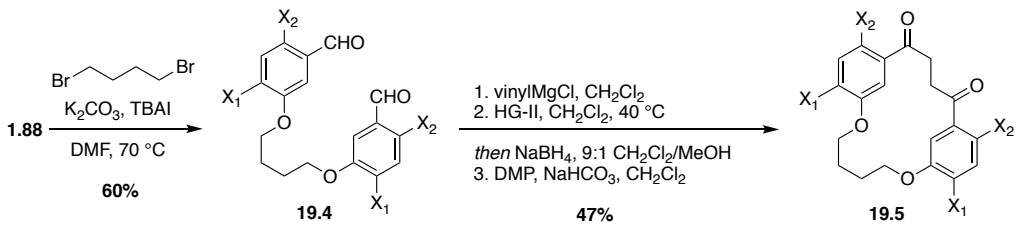
1.4.2 Cleavage of the methoxy group and conversion to a cross-coupling handle

In order to be useful in the formation of a 1,4-diketone bridge (**17.1**, Scheme 17), the methoxy group would need to be cleaved. A few different methoxy-containing systems were prepared to test for the best cleavage conditions.

Vanillin (**18.1**) was treated with triflic anhydride and pyridine to produce the aryl triflate **19.1** (Scheme 19). This was used as a test substrate on its own and also used in the preparation of **19.2** and either **1.93a** or **1.93b**. The first of which was made by simply treating **1.89** with vinylmagnesium chloride to afford the allylic alcohol **1.90**. The latter were prepared via the

Scheme 19. Preparation of substrates for methoxy cleavage studies

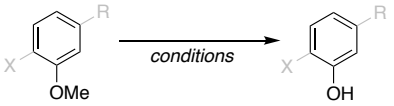




Suzuki cross-coupling with either phenylboronic acid (to yield **19.3a**) or 4-chlorophenylboronic acid (**19.3b**).

Additionally, a methoxy-substituted tethered dialdehyde and diketone not containing the *orthocyclo* bridging group were prepared. First, the Williamson ether synthesis between isovanillin and 1,4-dibromobutane afforded dialdehyde **19.4** in 60% yield. Subjecting this to our streamlined, 4-step protocol afforded the diketone **19.5** in 47% yield.

Table 1. Methoxy cleavage conditions



Entry	Substrate	Conditions	Yield
1	**19.1**	$AlCl_3$, pyridine	0%[a]
2	**19.1**	HBr, AcOH, 120 °C	0%[a]
3	**19.2**	BBr_3, CH_2Cl_2, 0 °C	0%[a]
4	**19.3a**	BBr_3, CH_2Cl_2, 0 °C	0%[b]
5	**19.3a**	HBr, AcOH, 120 °C	partial
6	**19.3b**	HBr, AcOH, 120 °C	63%
7	**19.3b**	EtSNa, DMF, 100 °C	partial
8	**19.3b**	MgI_2 Et_2O, THF, 65 °C??	0%[a]
9	**19.4**	HBr, AcOH, 120 °C	0%
10	**19.4**	NaSEt, DMF, 110 °C	55%
11	**19.5**	BCl_3 (2.4 equiv.), CH_2Cl_2, 0 °C	0%
12	**19.5**	BCl_3 (4.8 equiv.), CH_2Cl_2, 0 °C	0%
13	**19.5**	LiCl, DMF, 100 *C	0%

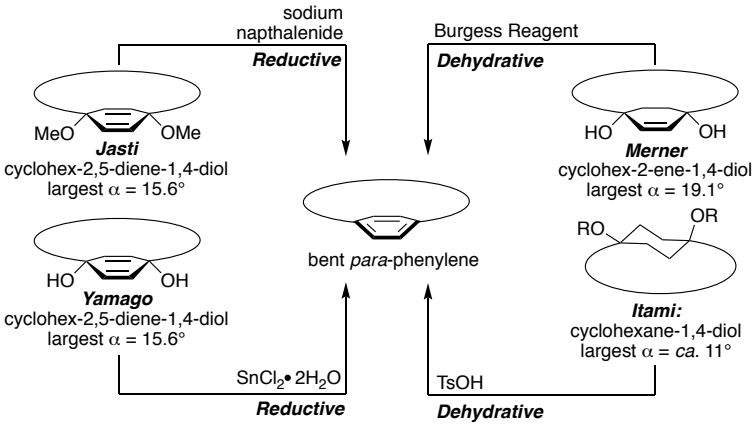
[a] No consumption of starting material. [b] Only bromination product was observed.

Many of the attempted reaction conditions were either unreactive or led to only partial consumption of the starting material (Table 1). Notably, the treatment of biphenyl **19.3a** with boron tribromide led to α-bromination without any cleavage observed. While treatment of **19.3b** with hydrobromic acid and acetic acid did afford the desired alcohol in 63% yield, the production of a complex mixture of byproducts made purification difficult. When treated with sodium ethane thiol, dialdehyde **19.4** gave the desired compound in a 55% yield, without requiring the same arduous chromatography.

1.5 Aromatization strategies for the preparation of *p*-terphenyl-bridged macrocycles

The conditions used in the final, aromatization step of the general synthetic sequence towards [*n*]CPPs (Scheme 1), are dependent upon the specific bent, pre-arene subunit employed, with some aromatization strategies being capable of inducing more strain (preparing smaller systems) than others.

Scheme 20. Various aromatization conditions for the preparation of strained *p*-terphenyl systems



The Jasti group has used a reductive aromatization reaction to convert their cyclohex-2,5-diene-1,4-dimethoxy pre-arene subunits into strained para-phenylene rings (Scheme 20). A similar (reductive aromatization) strategy was employed by Yamago and co-workers and in the synthesis of [5]CPP, which has an α of 15.6° and a strain energy of 23.4 kcal/mol per benzene ring.[32-33] The Itami group has successfully aromatized a cyclohexane-1,4-diol-based pre-arene subunit via a dehydrative protocol to afford [*n*]CPPs as small as [7]CPP, which has an α of 11° and a strain energy of 12.2 kcal/mol per benzene ring.[37] The Merner group has reported the synthesis of a number of *para*-phenylene containing macrocycles, which are aromatized from a cyclohex-2-ene-1,4-diol using the Burgess Reagent.[40] The smallest macrocyclic system to be prepared using this approach had an α of 19.1° and a strain energy of 42.6 kcal/mol in the central benzene ring of the terphenyl system.[36]

Being easy to prepare, the cyclohex-2-ene-1,4-diol systems used by the our research group offer a unique opportunity to directly compare aromatization conditions (Table 2). Thus, a series of cyclohex-2-ene-1,4-diol containing macrocycles (aromatization precursors) were prepared (**15.5**, **16.6**, and **T2a-T2f**) via the previously discussed synthesis of *para*-terphenyl-containing macrocycles (Scheme 15).

The first set of aromatization conditions explored was the use of tosic acid (Condition "A", Table 2, entries 1-9).[14] For the aromatization of the cyclohex-2-ene-1,4-diol-containing systems **T2.1e-T2.1f** (Table 2, entries 1 and 4), where the tether of this system is comprised of 7 and 8 atoms, respectively, these aromatization conditions at 60 °C cleanly afforded the *para*-terphenyl-containing macrocycle **T2.2e-T2.2f** with yields of 74-82%. However, when the temperature is increased to 80 °C, **T2.1e** (7 atom tether, Table 2, entry 5) the yield of the desired, *para*-terphenyl-containing macrocycle **T2.2e** decreases to 38% and the *meta*-rearranged product (**T2.3**) is observed in a 19% yield. This *meta*-rearranged product is thought to form via the protonation of the central (strained) benzene ring of the *para*-terphenyl system (**F7.1**, Figure 8) which then undergoes a strain-induced rearrangement of to afford the *meta*-terphenyl-containing system **F7.4**. As the temperature was increased to 70-80 °C, more highly strained *para*-terphenyl-containing systems **T2.2c-T2.2d** (tether lengths of 5 and 6 atoms, Table 2, entries 8 and 9) afforded exclusively the *meta*-rearranged product.

Figure 7. Strain-relief driven rearrangement of *para*-terphenyl-containing macrocycles

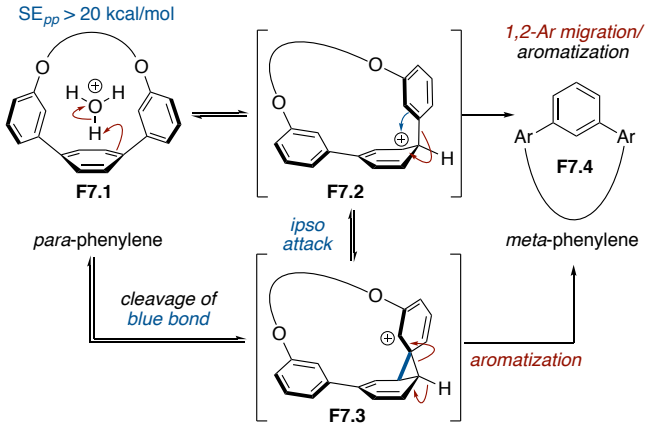
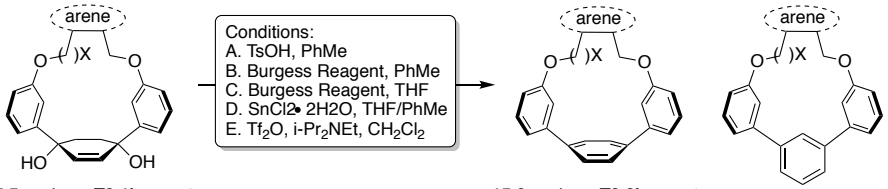


Table 9. Aromatization conditions for the preparation of *para*-terphenyl-containing maxcrocycles



15.5: *ortho* **T2.1b**: x = -1
16.5: *meta* **T2.1c**: x = 0
T2.1a: *para* **T2.1d**: x = 1
T2.1e: x = 2
T2.1f: x = 3

15.6: *ortho* **T2.2b**: x = -1
16.6: *meta* **T2.2c**: x = 0
T2.2a: *para* **T2.2d**: x = 1
T2.2e: x = 2
T2.2f: x = 3

rearranged *m*-terphenyl **T2.3**

Entry	Comp	Conditions	Temp (° C)	Time (h)	Yield (%)
1	**T2.1f**	A	60	2	74
2	**T2.1f**	A	80	0.5	66
3	**T2.1a**	A	55	3	32
4	**T2.1e**	A	60	2	82
5	**T2.1e**	A	90	0.2	38[a]
6	**16.5**	A	80	1.5	74
7	**T2.1d**	A	50-60	5	42
8	**T2.1d**	A	80	4	0[b]
9	**T2.1c**	A	70	3	0[b]
10	**T2.1f**	B	80	0.2	61
11	**T2.1e**	B	80	0.2	66
12	**T2.1d**	B	80	0.5	56
13	**T2.1c**	B	80	0.2	60
14	**T2.1b**	B	80	0.2	<5
15	**T2.1f**	C	50	0.5	64
16	**T2.1a**	C	60	0.2	79
17	**T2.1e**	C	50	0.3	52
18	**16.5**	C	50	0.5	61
19	**T2.1d**	C	50	0.2	75
20	**15.5**	C	50	1	67
21	**T2.1c**	C	50	6	21
22	**T2.1b**	C	50-70	2.5	0(68)[c]
23	**T2.1f**	D	80	48	52
24	**T2.1e**	D	80	25	46
25	**T2.1d**	D	80	4.5	0(62)[c]
26	**T2.1c**	D	80	12	0(78)[c]
27	**T2.1f**	E	0-23	0.2	42
28	**T2.1a**	E	0-23	2	42
29	**T2.1e**	E	0-23	0.5	44
30	**16.5**	E	0-23	24	20
31	**T2.1d**	E	0-23	2	73
32	**15.5**	E	0-23	24	<5
33	**T2.1c**	E	0	0.5	0(16)[d]
34	**T2.1b**	E	0-23	24	0

[a.] 19% of the rearranged [n]MTPP was isolated; [b.] Only the rearranged [n]MTPP isomer was isolated; [c.] Yield of the major, monodehydration product; [d] yield for reaction run on monodehydrated material.

Tin(II) chloride dihydrate has been employed by the Yamago group in the aromatization of a 3,6-*syn*-hydrooxy-cyclohexa-1,4-diene subunit in the synthesis of [5]CPP.[32] However, when the cyclohex-2-ene-1,4-diols **T2.c-T2.f** were subjected to these conditions, the more highly strained systems **T2.2c** (5 atoms, Table 2, entry 26) and **T2.2d** (6 atom tether, Table 2, entry 25) yielded only the monodehydrated product.

Treatment with triflic anhydride did successfully afford the desired *para*-terphenyl-containing macrocycles **T2.2a**, **T2.2d-T2.2f**, and **16.6** (tether lengths of 6-8 atoms, Table 2, entries

27-31), albeit in modest to low yields. On more highly strained systems (**T2.2b-T2.2c**, tethers of 4-5 atoms), however, these conditions fail.

Because of *meta*-rearrangement products observed under protic acid conditions (TsOH), and the low yields of the low yields of the tin(II)chloride dihydrate and triflic anhydride conditions, alternative aromatization conditions were explored. The Burgess Reagent offered a non-acidic dehydrative aromatization that was successful in preparing the desired, *para*-terphenyl-containing maxcrocycles **15.6**, **16.6**, **T2.2a,** and **T2.2c-T2.2f** in yields of up to 79% (Table 2, entries 10-13 and 15-21). Our most highly strained system, **T2.2b** (tether length of 4 atoms, Table 2, entry 22) was the only system that was not able to be prepared using this Burgess reagent mediated aromatization, affording only the monodehydrated product instead.

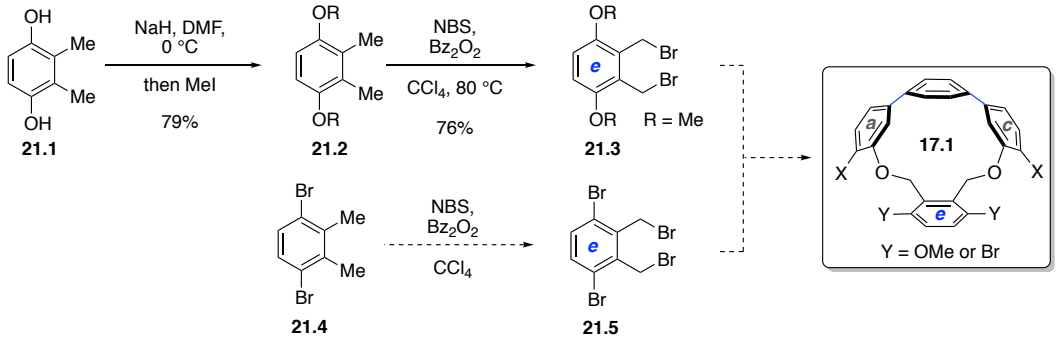
1.6 Conclusions and future directions Introduction of synthetically useful functional groups and proposed strategy

While incorporation of a functional group at the X position of **17.1** (Scheme 17) was successful, a system with functionality in place at the Y position and, ultimately, in both the X and Y positions will be necessary in order to construct a 1,4-diketone bridge.

In the case of substituting the Y position, 2,3-bis(bromomethyl)-1,4-dimethoxy benzene **21.3** is known and has been prepared in our laboratory in 60% overall yield from the commercially available 2,3-dimethyl-1,4-benzenediol **21.1** (Scheme 21). First, by methylating the alcohols of **21.1** and then the NBS bromination of the methyl groups. The success of this route would ultimately be dependent upon the cleavage of these methoxy groups (see Table 1). To circumvent this issue, the alcohols could be converted into a triflate (**21.2**, where R = OTf), which might present a more suitable functional group handle.

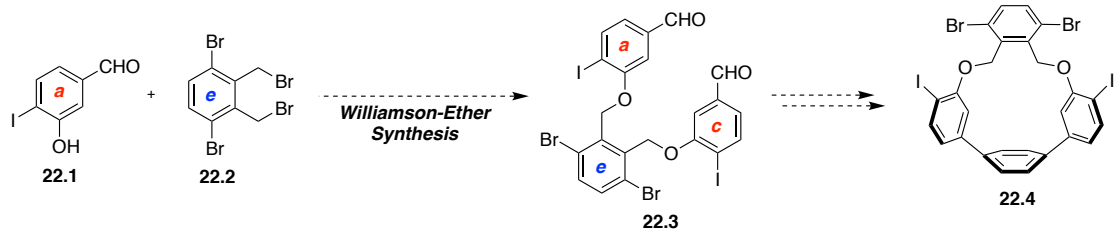
Alternatively, a bridging group could be synthesized that would not require the use of two unnecessary functional group interconversion steps (methylation and demethylation). It is proposed that the tetrabromide **21.5** could be prepared by an analogous NBS bromination of the commercially available 1,4-dibromo-2,3-dimethyl benzene **21.4** (Scheme 21).

Scheme 21. Synthesis of a functionalized *orthocyclo-p*-terphenyl-containing macrocycle



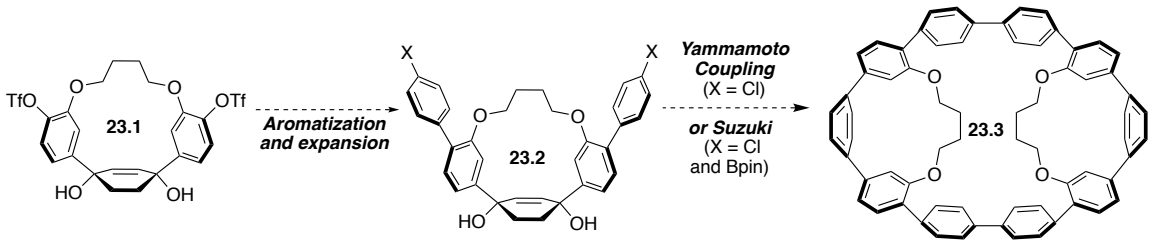
Similarly, functional group interconversion at the Y position could be avoided by using the commercially available 3-hydroxy-4-iodobenzaldehyde **22.1** as the other partner for the initial Williamson ether synthesis (Scheme 22). This approach would install immediately useful halogens at the X and Y positions **17.1** (Scheme 21).

Scheme 22. Preparation of a tetra-halogenated *orthocyclo-p*-terphenyl macrocycle



The synthesis of triflate **23.1** (Scheme 23) could be used as a precursor in the synthesis of even-numbered, functionalized CPPs. Suzuki cross-coupling of ditriflate **23.1** would expand the PTPP unit to **23.2**. Homocoupling at this stage would give an alkoxy bridged [10]CPP **23.3**, which, upon cleavage of the bridging group, would leave behind four functional group handles. This strategy could be employed in the preparation of several even-numbered CPPs, and could be modulated by altering how many aryl groups are added during the extension of **23.1**.

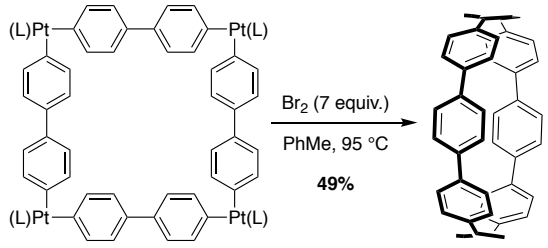
Scheme 23. Coupling of two *p*-terphenyl systems



CHAPTER 2 Attempted Synthesis of [4]Cycloparaphenylene

2.1 A brief survey of the smallest [*n*]CPPs synthesized

Scheme 24. Yamago and co-workers' synthesis of [8]CPP



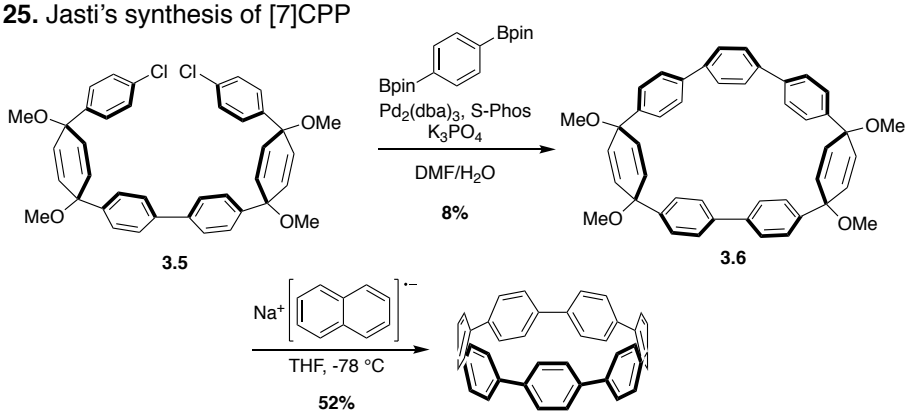
5.3
L = dppf

[8]CPP
5.4

The four smallest [*n*]CPPs that have been reported to date are [5]-, [6]-, [7]-, and [8]CPPs. The first synthesis of [8]CPP (**5.4**) was reported by Yamago and co-workers in 2010, where the key intermediate was a tetraplatinum, square-shaped macrocycle **5.3** (Scheme 24, see section 1.1.5 for discussion).[24] Here, the "curvature" of the macrocycle was created by the square shape geometry of the platinum. The aryl-aryl bonds (leading to **5.4**) were formed as the platinum was lost via reductive elimination with bromine for a yield of 49%.

The next smallest homolog, [7]CPP **3.7**, was reported in 2011 by Jasti and co-workers (see 1.1.3 for discussion).[19] This synthesis featured the use of an unsymmetric version of the 3,6-*syn*-dimethoxy-cyclohexa-1,4-diene that has been used in all of the [*n*]CPP syntheses by this group in order to prepare the dichloride **3.5** (Scheme 25). Macrocyclization was achieved via the Suzuki cross-coupling with 1,4-phenylenebisboronic acid to give **3.6** with a yield of only 8%. Aromatization of **3.6** with sodium napthalenide afforded [7]CPP (**3.7**) in a 52% yield.

Scheme 25. Jasti's synthesis of [7]CPP



3.5

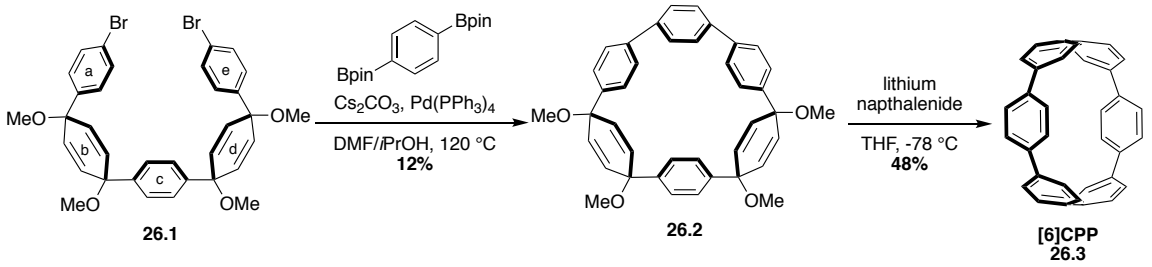
3.6

[7]CPP
3.7

The first synthesis of [6]CPP was reported in 2012 by Jasti co-workers.[31] The key intermediate in this synthesis was the dibromide **26.1** (Scheme 26), which utilizes the same cyclohexadiene-based bent, pre-arene subunit as the other syntheses reported by this group. In a similar strategy to that of the Jasti group's synthesis of [7]CPP, **26.1** was converted to the

macrocycle **26.2** via the Suzuki cross-coupling with 1,4-phenylenebisboronic in a yield of 12%. This macrocycle was then converted to [6]CPP **26.3** via the reductive aromatization utilizing lithium napthalenide for a yield of 48%. The steps of these two challenging transformations remained comparable to those reported in the synthesis of **3.7**.

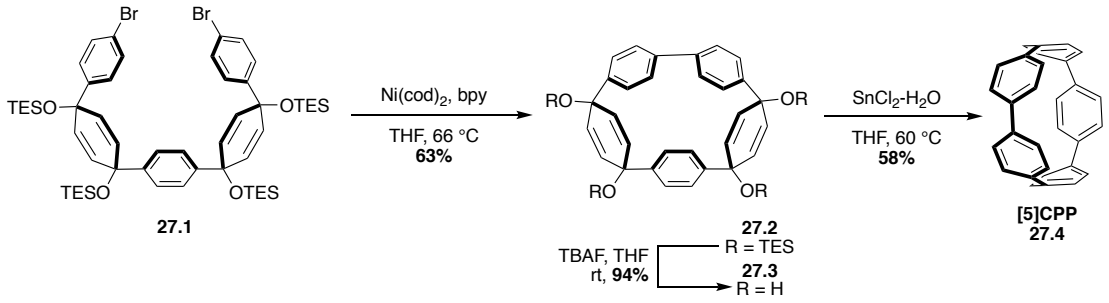
Scheme 26. Jasti's synthesis of [6]CPP



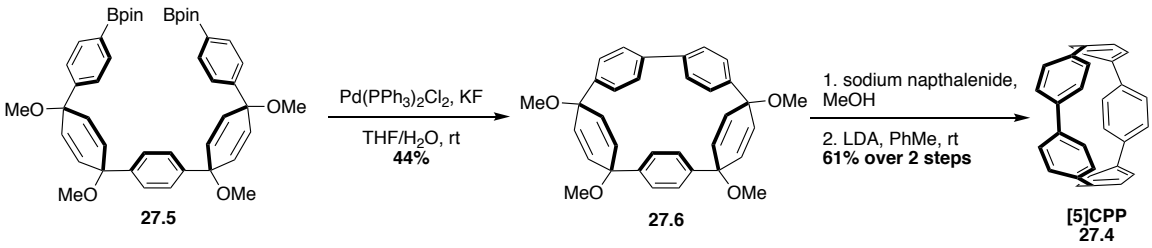
To date, the smallest [*n*]CPP that has been prepared is [5]CPP (**27.4**, Scheme 27), which was reported by both the Yamago[32] (Scheme 27a) and Jasti[33] (Scheme 27b) groups in early 2014. Both syntheses made use of a variation of the cyclohexadiene-based macrocyclization precursor **26.1**, which was also used by the Jasti group in their syntheses of [6]- and [8]CPPs.[31,17] This common intermediate (**2.9** or **2.13**) contains three arene units (a, c, and e rings, Scheme 26) and two bent, pre arene units (b and d rings), where the two terminal arene units (a and e rings) are within proximity to facilitate C-C direct C-C bond formation. The *syn* relationship of the aryl units

Scheme 27. 2014 Syntheses of [5]CPP

a. Yamago:



b. Jasti:



and boat-shape of the cyclohex-2,5-diene-1,4-diol system provide the necessary "kink" for macrocyclization to take place.

In the case of the Yamago synthesis, the two terminal vertices were functionalized with bromine atoms (**27.1**) and macrocyclization was achieved using a nickel-catalyzed coupling reaction to afford the macrocycle **27.2**. Then, the triethylsilyl groups were removed using TBAF to reveal the alcohols present in **27.3**. This was then subjected to reductive aromatization using $SnCl_2 \cdot 2H_2O$ to afford [5]CPP **27.4** in a 58% yield.

In the case of the Jasti synthesis, the two terminal vertices were functionalized with boronic esters (**27.5**), which were used as coupling partners in the palladium catalyzed macrocyclization to afford **27.6**. This was then aromatized to [5]CPP using sodium napthalenide, then lithium diisopropylamide for a 61% yield over these two steps.

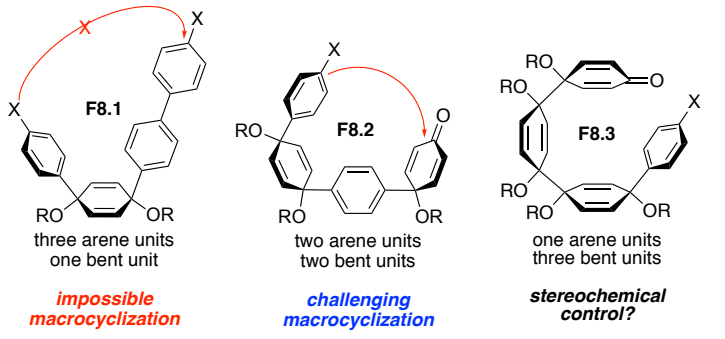
Table 3. Strain energies of the smallest [*n*]CPPs and theoretical values for [4]CPP

n	Diameter (nM)	Strain Energy (kcal/mol)	SE per Benzene (kcal/mol)
4	5.70	144.1	36.0
5	7.05	117.2	23.4
6	8.40	97.23	16.2
7	9.77	85.20	12.2
8	11.13	73.40	9.2

The next target of interest in the [*n*]CPP series is [4]CPP (**F9.1**, Figure 9), which poses significant synthetic challenges. In 2011, Yamago and co-workers published a series of computations in which they calculated the diameter and total strain energies of [*n*]CPPs [4]-[20] (Table 3).[34] In this, the strain energy of [5]CPP was predicted to be 117 kcal/mol total. This value was confirmed when computational data based on Jasti's X-ray crystal structure found the total strain energy to be 119 kcal/mol. The strain energy of [4]CPP is expected to be 144 kcal/mol, or 36 kcal/mol per benzene ring. An aromatization protocol capable of inducing this amount of strain energy would need to be developed.

Another challenge towards the synthesis of [4]CPP lies in the macrocyclization stage. If one considers the common intermediate **26.1** used in the synthesis of [5]CPP, one might envision preparing [4]CPP in a similar way, by simply removing one of the arene or pre-arene units.[36] However, this approach faces a number of obstacles (Figure 8). If one of the bent, pre-arene units is removed, such as in **F8.1** the two terminal vertices are too far apart for macrocyclization to take place. Removal of one of the benzene rings instead to give precursor **F8.2**, places the arene units to be connected closer together, however, this would require a Grignard related

Figure 8. Unlikely strategies toward [4]CPP

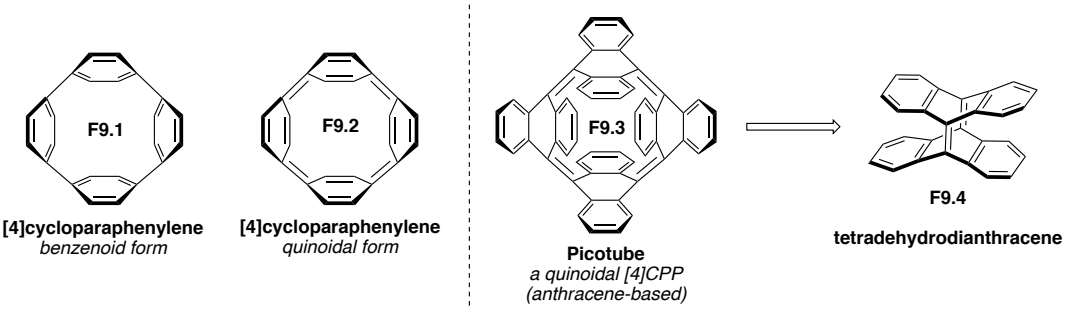


organometallic-mediated reaction. Intermolecular reactions will surely dominate in this instance. Utilizing three bent subunits and only one arene as proposed in **F8.3**, provides the most reasonable macrocyclization precursor, but generating a *syn*-relative stereochemical relationship between the vicinal tertiary diols across the three pre-arene units poses a serious challenge and is, in fact, unprecedented.

2.2 Picotube as a model for the synthesis of [4]CPP

In 1996, Herges and co-workers reported the synthesis of a compound known as picotube (**F9.3**, Figure 8), which is an anthracene-based [4]cycloparaphenylene analog.[35] The synthesis of **F9.3** was achieved via the dimerization of tetradehydrodianthracene **F9.4** and subsequent ring-opening metathesis. The resulting compound (picotube, **F9.3**) was found to be quinoidal as indicated by an X-ray crystal structure, which has led many to believe that the structure of [4]CPP (**F9.1**) and smaller [*n*]CPP homologs would be quinoidal (**F9.2**) in structure as well.

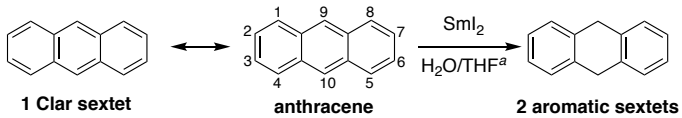
Figure 9. Picotube as a model for [4]CPP



It is noteworthy that [5]CPP was believed to be quinoidal and not benzenoid, however, the chemical synthesis by Jasti and co-workers produced an X-ray crystal structure of **27.4**, proving it is indeed benzenoid.[33] They found that the C-C bond distances within the individual arene units were nearly identical, ranging between 1.38–1.40 Å. This bond distance is indicative of a benzene ring. Furthermore, the biaryl bonds between adjacent benzene rings in the molecule were elongated from what one would expect of a quinoidal geometry (eg., 1.35 Å for the bridging C-C double bond of **28.3**) at 1.49 Å. There is still debate, however, about whether or not [4]CPP will take on a benzenoid (**28.1**) or quinoid (**28.2**) geometry.

However, an anthracene-based system may not be the best model for [4]CPP. In the case of picotube, the 9 and 10 positions are those that were connected (Figure 9). When these positions are functionalized, the favored conformation is the one that results

Figure 10. Substitution of anthracene



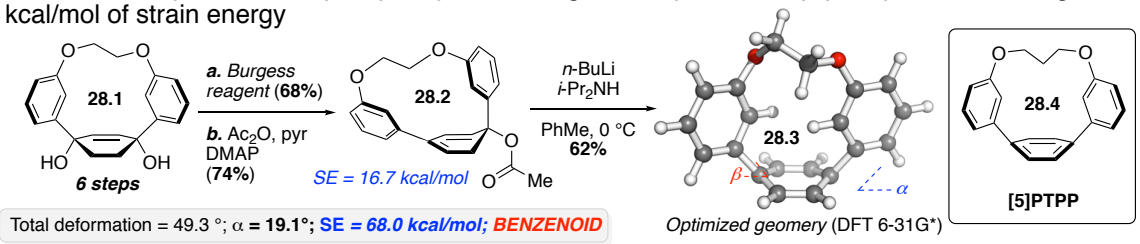
[a] *J. Am. Chem. Soc.* **2015**, *137* (35), 11526.

in the aromatization of the two outer rings, preventing the [4]CPP portion of picotube from being benzenoid.

2.3 Synthesis of a *para*-phenylene monomer unit that is more strained than a monomer unit of [4]CPP

In 2016 our group published the synthesis of a highly strained *para*-terphenylophane **28.3** (Scheme 28).[36] This benzenoid macrocycle contains a central *para*-phenylene ring with 43 kcal/mol of SE, the requisite C_{sp^2}-C_{sp^2} biaryl bonds present in [4]CPP (**F9.1**), and an angle α of 19.1°. This is more strained than the calculated SE for single *para*-phenylene ring of [4]CPP (SE_{TOTAL} = 144 kcal/mol, or SE_{pp} = 36 kcal/mol), making **28.3** a viable model compound of [4]CPP. In particular, the synthesis of **28.3** would address whether a benzenoid(al) or quinoidal geometry is favored for such a highly strained *para*-phenylene ring system. While efforts to produce crystals suitable for X-ray analysis were unsuccessful, an X-ray crystal structure has been obtained for a larger (*n* = *5*) homolog (**28.4**). Experimentally obtained deformation angles of **28.4** were compared using optimized geometries of these compounds, obtained from DFT (B3LYP 6-31-G*) calculations. For example, the deformation angles, *α* and *β* (defined in Scheme 8), were found to be 15.7° and 24.6°, respectively, for the solid-state structure of **28.4**. The computationally derived structure of **28.4** shows excellent agreement with the experimentally determined values, at 15.4° and 24.5°, respectively. Thus, DFT calculations can likely be relied upon in the absence of an X-ray crystal structure for these macrocyclic systems. DFT calculations predict the bond lengths of the central benzene ring of **28.3** to be 1.38-1.40 Å, which is indicative of an aromatic ring. The ^{1}H NMR spectra for the aromatic regions of **28.3** and **28.4** are identical. These data suggest that the central arene unit of **28.3** is benzenoid, which gives optimism that [4]CPP will be benzenoid as well.

Scheme 28. Synthesis of a *p*-terphenyl-containing macrocycle with a *p*-phenylene containing 43 kcal/mol of strain energy

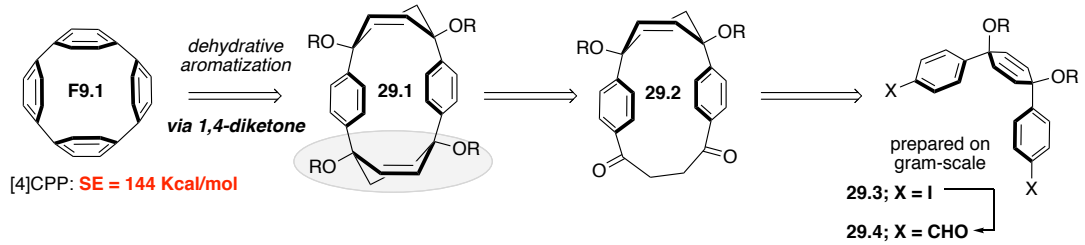


2.4 Utilizing a 3,6-*syn*-dimethoxy-cyclohexa-1,4-diene subunit toward the synthesis of a macrocyclic precursor to [4]CPP

A cyclophane where two arene units are bridged at the *para*-positions by a 1,4-diketone and a boat-shaped pre-arene subunit (eg, **29.2**, Scheme 29) may represent a viable approach to a macrocyclic precursor of [4]CPP, using the strategy for the synthesis of macrocyclic 1,4-diketones that has been developed in our laboratory. Then, this 1,4-diketone could be converted into a cyclohex-2-ene-1,4-

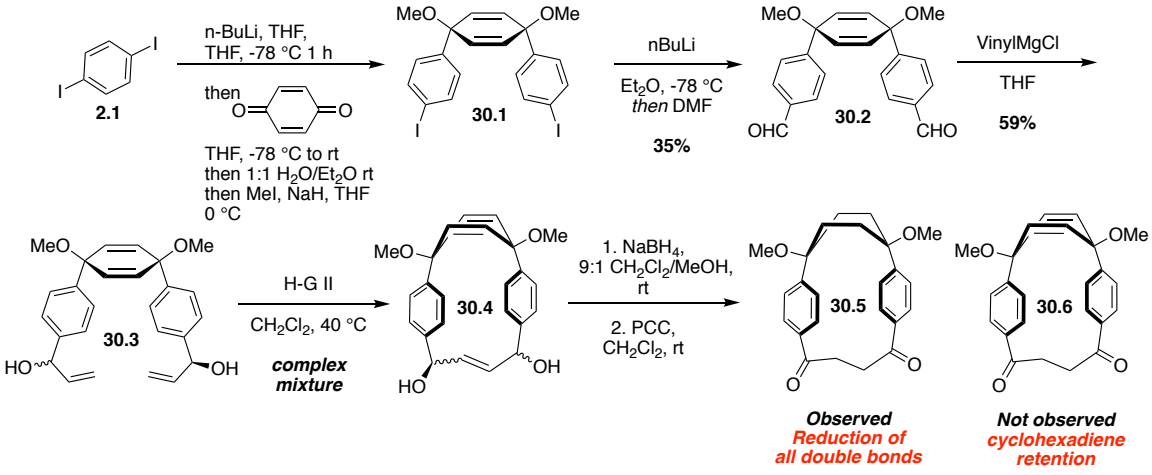
diol, as is present in **29.1**, representing a second bent, pre-arene unit. Aromatization of both bent, pre-arene subunits would afford [4]CPP **F9.1**.

Scheme 29. Synthetic plan for a 1,4-diketone-bridged macrocyclic precursor to [4]CPP



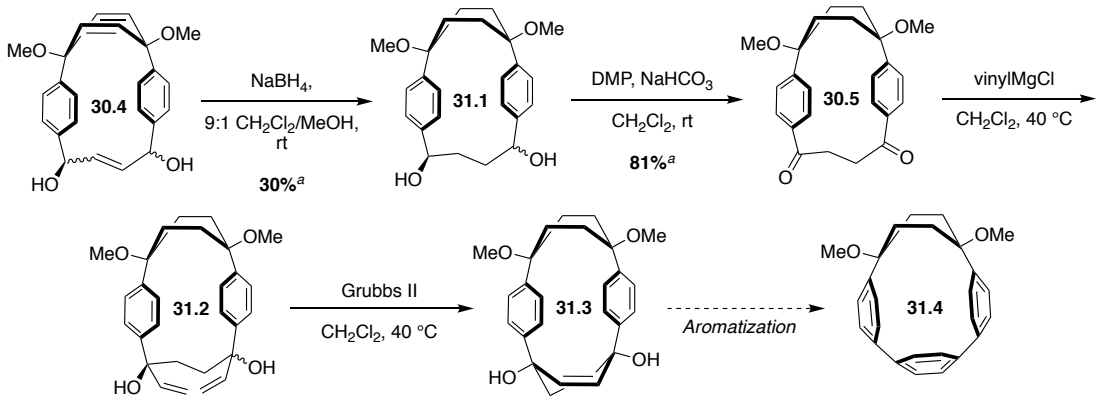
In pursuit of macrocyclic 1,4-diketone precursor **30.6** to [4]CPP (**F9.1**), diiodide **30.1**, which has been utilized by Jasti and co-workers in all their syntheses of [n]CPPs, was prepared according to the literature procedure.[8] This is done by the addition of (4-iodophenyl)lithium (generated *in situ*) to benzoquinone, followed by methylation of the alcohols formed. Diiodide **30.1** was then converted into dialdehyde **30.2** via a halogen-metal exchange with *n*-butyllithium, quenched with dimethyl formamide in a yield of 35%. In an effort to implement the streamlined, 4-step 1,4-diketone synthesis developed by our lab, dialdehyde **30.2** was then treated with vinylmagnesium to yield the allylic diol **30.3** (59%). This was then subjected to a ring-closing metathesis with Hoveyda-Grubbs second generation catalyst to form **30.4**. At this stage in the streamlined synthesis, a transfer hydrogenation reaction (utilizing the same Hoveyda-Grubbs catalyst) and subsequent oxidation is typically performed. On this system, however, it was observed that this sequence of reactions led to the formation of **30.5**, instead of the desired **30.6**, where the olefins present in the cylohexadiene-based subunit had also been reduced.

Scheme 30. Attempted synthesis of a macrocyclic precursor to [4]CPP



While a cyclohexane-1,4-diol subunit such as that present in **30.5** has been employed in the synthesis of [*n*]CPPs by Itami and co-workers, the smallest homolog that has been prepared using this strategy is [7]CPP,[37] for which the *para*-phenylene rings are only strained by 12 kcal/mol. Aromatization conditions for this cyclohexane-based subunit capable of introducing the strain present in a monomer unit of [4]CPP (36 kcal/mol) have not been reported and will likely fail here. However, a macrocycle containing three of the *para*-phenylene rings (**F9.1**) of [4]CPP could be assembled from **30.5** (Scheme 31). To test this, **30.4** was subjected to transfer hydrogenation conditions to give the fully-hydrogenated **31.1**. This was then was then oxidized to afford the 1,4-diketone bridged macrocycle **30.5** in a 24% yield over 2 steps. Subsequent TLC-scale Grignard addition of vinylmagnesium chloride (to form **31.2**) and then ring-closing metathesis gave the cyclohex-2-ene-1,4-diol **31.3**. Future scale-up of this synthesis and test of aromatization conditions will be required.

Scheme 31. Attempted synthesis of a macrocycle containing 3 of the 4 rings present in [4]CPP

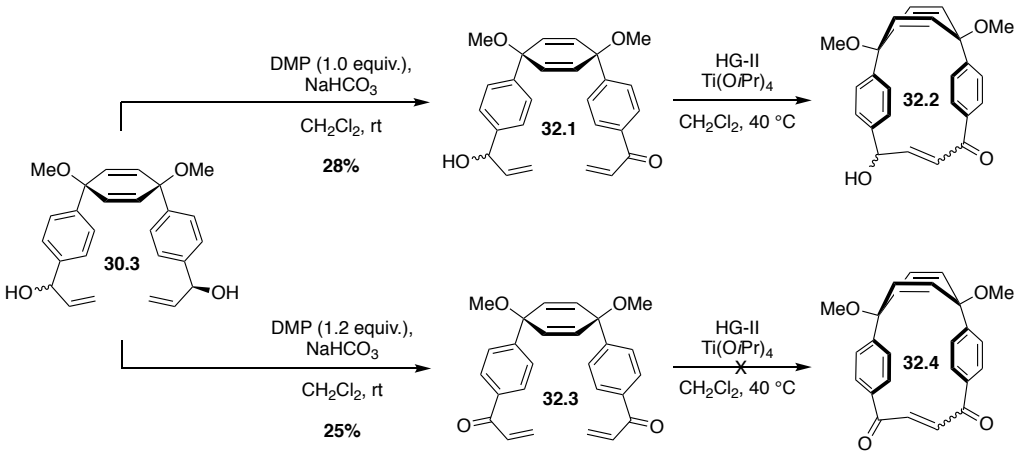


[a] *Yields based on crude mass.*

2.4.1 Alternate macrocyclic ring-closing metathesis substrates

To improve the yield of the macrocyclic RCM step and potentially access more directly helpful macrocyclic precursors, alternate RCM substrates were tested. Allylic diol **30.3** was oxidized to both the mono-ketone **32.1** (Scheme 32) and the diketone **32.3**. While under many conditions, carbonyls will competitively bind with the RCM catalyst, pre-mixing the substrate with titanium isopropoxide (TTiP) had been known to mitigate this via coordination of Ti with the carbonyls. With this in mind, both **32.1** and **32.3** were subjected to RCM conditions in the presence of TTiP, with the mono-oxidized system affording the macrocycle **2.39**.

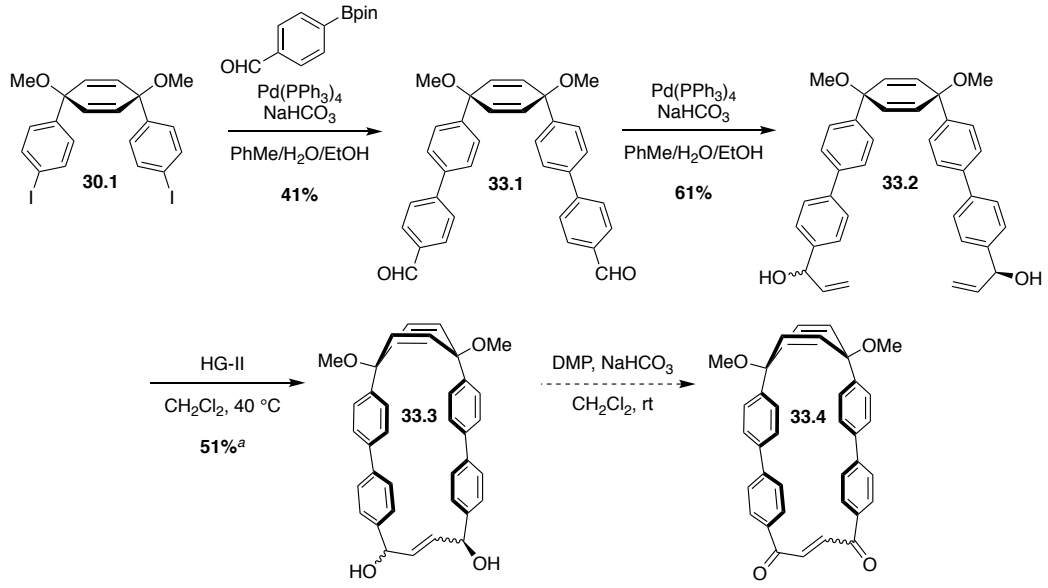
Scheme 32. Alternate macrocyclic RCM substrates



2.4.2 Macrocyclic RCM application to a cyclohexadiene-based [6]CPP precursor

In order to assess whether the challenges with the RCM and oxidation were related to the strain of a [4]CPP precursor and to gain access to a precursor to [6]CPP, **33.3** was prepared (Scheme 33). To begin, the same diiodide used in the preparation of a precursor to [4]CPP, **30.1** was used but, instead, subjected to a Suzuki cross-coupling with 4-formylphenylboronic acid to give the dialdehyde **33.1** in a yield of 41%. This was followed by the the Grignard addition of vinylmagnesium chloride to give **33.2** (61%) and subsequent ring-closing metathesis with afforded the macrocycle **33.3** (51%). Work towards the preparation of the 1,4-diketone and, ultimately, cyclochex-2-ene-1,4-diol will need to be completed.

Scheme 33. Attempted synthesis of a macrocyclic precursor to [6]CPP

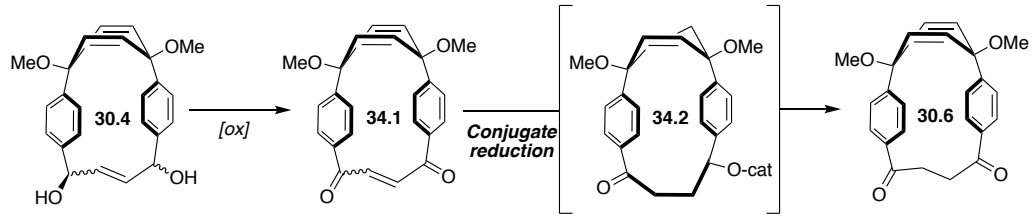


[a]Yield based on crude mass and consumption of starting material.

2.4.3 Alternate approaches to the 1,4-diketone-bridged macrocycle 30.6

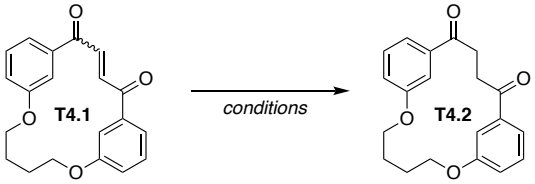
In order to prevent the hydrogenation of the cyclohex-2,5-diene-1,4-dimethoxy subunit, alternate reductive conditions were pursued. One option was to employ the use of a conjugate reduction on the ene-dione **34.1**, which could be prepared via the oxidation of **30.4**. This strategy would avoid reducing the double bonds present in the cyclohexadiene-based subunit because hydrogen is selectively introduced to the double bond of the eneone via a hydride-bearing catalyst that complexes with one of the ketones.

Scheme 34. Alternate routes to the macrocyclic 1,4-diketone **30.6**



Conjugate reduction conditions were explored on a model system of **34.1**, the ene-dione **T4.1** (Table 4). While a number of reduction conditions[38] were attempted most of these reactions afforded only the reduction of the carbonyls present in **T4.1**, giving the ene-diol instead. The use of tri-*n*-butyltin hydride at 80 °C in toluene over 4 h, however, ultimately gave the desired 1,4-diketone in a quantitative yield.

Table 4. Screening of conjugate reduction conditions



Entry	Conditions	Yield
1	$InCl_3$, $NaBH_4$, MeCN	0%
2	TMSOTf, CH_2Cl_2	0%[a]
3	Pd/C, NEt_3, PhMe, 140 °C	0%
4	$LiAlH_4$, THF	0%[b]
5	$LiAlH_4$, CuI, THF, 0 °C	0%[a]
6	Et_3SiH, TFA, rt	0%[a]
7	EtSiH, CuCl, PPh_3, TBAF, DMA, 0 °C	0%[a]
8	Catecholborane, THF, 0 °C	0%[a]
9	nBu_3SnH, PhMe, 80 °C, 1 h	~50%
10	nBu_3SnH, PhMe, 80 °C, 4h	Quant.

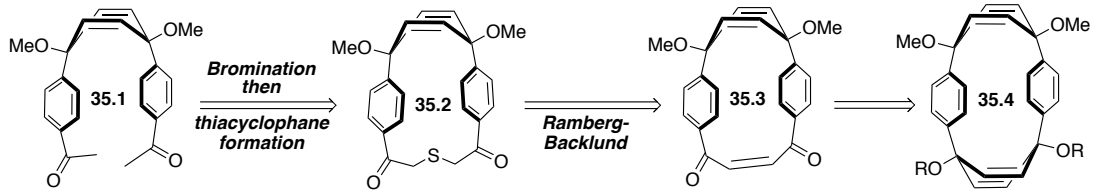
[a] *No consumption of starting material was observed.*
[b] *Only reduction of the carbonyls was observed.*

2.4.4 A thiacyclophane alternative to macrocyclization

Thiacyclophanes have been used in the synthesis of paracyclophanes since the 1970s[41] and have been a valuable tool in the formation of paracyclophanes since being used in the synthesis of systems such as [14][14]metaparacyclophane in 2003[42] and in the synthesis of hirsutellone C[43] in 2009. Thus, a thiacyclophane-based strategy toward macrocyclization may offer the possibility to bypass some of the problems that the RCM-based strategy posed. Methyl ketone **35.1** could be α-halogenated and then converted into the

thiacyclophane **35.2**. This, upon oxidation of the sulfur atom and subsequent Bamberg-Backlund, could selectively afford **35.3** containing an *E*-configured olefin. Because of the *E*-configuration here, reduction of this double bond may not be necessary as the geometry here should still allow for the formation of a six-membered bent, pre-arene unit as in **35.4**.

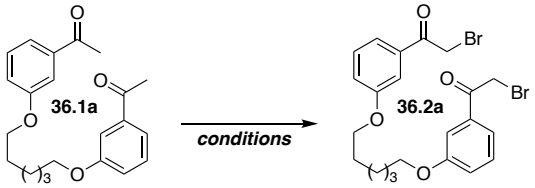
Scheme 35. A thiacyclophane strategy towards the macrocyclic 1,4-diketone precursor to [4]CPP



In order to access the viability of a thiacyclophane-based strategy towards a macrocyclic precursor to [4]CPP, a series of thiacyclophanes **36.3a-d** were prepared. The substrates screened varied in both the length of the tether (either 5 or 8 atom) and the substitution of the aryl groups (either *meta* or *para*).

To begin, the bromination of the methyl ketone was screened on **36.1a** (Table 6). Many of the conditions screened led to either a complex mixture of bromination products or only monobromination, but copper(II) bromide was found to give the desired bisbrominated product **36.2a** in a modest yield. This copper(II) bromide bromination was then applied to the methyl ketones **36.1a-d**, affording the α-brominated systems **36.2a-d** in modest yields of 44-61%. Bromination of a cyclohexadiene-based precursor to [4]CPP **3.51** to afford the dibromide **37.1** (Scheme 37) proceeded with a yield of 33%.

Table 6. Conditions for the α-bromination of acetophenone-based systems

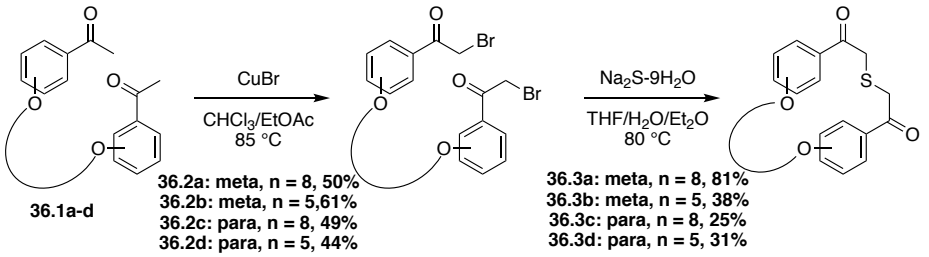


Entry	Conditions	Yield
1	NBS, pTsOH-H_2O, $CHCl_3$, rt	0%[a]
2	NBS, pTsOH-H_2O, $CHCl_3$, -78 °C	0%[b]
3	Br_2, AcOH, rt	0%[a]
4	Br_2, $CHCl_3$	0%[c]
5	Br_2, $AlCl_3$, Et_2O	0%[a]
6	Br_2, $AlCl_3$, 1:1 $Et_2O/CHCl_3$, 0 °C	0%[c]
7	Br_2, $AlCl_3$, -78 °C	0%[a]
8	NBS, AlCl3, CH_2Cl_2, -78 °C	0%[c]
9	$CuBr_2$, 1:1 $CHCl_3$/EtOAc, 85 °C	50%

[a]Inseparable mixture; [b]No consumption of starting material was observed; [c]Only monobromination was observed.

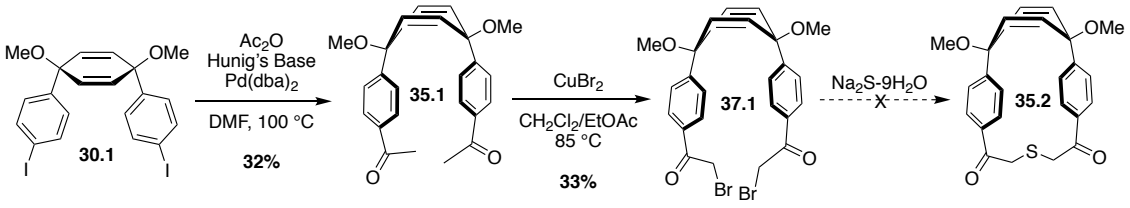
These brominated systems were then treated with sodium sulfide nonahydrate to afford the thiacyclophanes **36.3a-d**, proceeding with yields of 25-81% for these model system. Unfortunately macrocyclization to produce a [4]CPP precursor (**35.2**, Scheme 37) was unsuccessful. Futher, the oxidation of the thiacyclophane is necessary to carry out the Ramberg-

Scheme 36. Synthesis of a series of model thiacyclophane systems



Backlund reaction that was planned, but preliminary oxidation attempts were unsuccessful. Further exploration into this oxidation and alternative thiacyclophane-forming reactions would need to be explored.

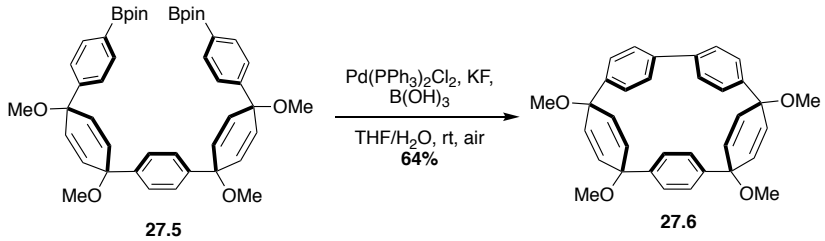
Scheme 37. Application of the thiacyclophane approach on a precursor to [4]CPP



2.4.5 An oxidative boronate coupling as an alternative to macrocyclization

In 2017, Jasti and co-workers reported an oxidative boronate coupling capable of preparing highly strained macrocycles under relatively mild conditions.[39] Among those systems prepared through this method was an update to the macrocyclization stage of their synthesis of [5]CPP (Scheme 38, the original synthesis was originally discussed in 2.1). In this, they were able to increase the yield of this macrocyclization of **27.5** to **27.6** from a 44% to 64% yield, while now running this reaction at room temperature and open to the atmosphere.

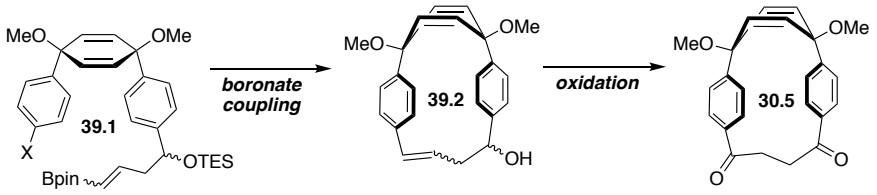
Scheme 38. Jasti's updated macrocyclization conditions towards [5]CPP



It was thought that this reaction might be suitable for the macrocyclization towards a macrocyclic 1,4-diketone precursor (**30.5**) to [4]CPP (Scheme 39). An usymmetric cyclohexadiene-

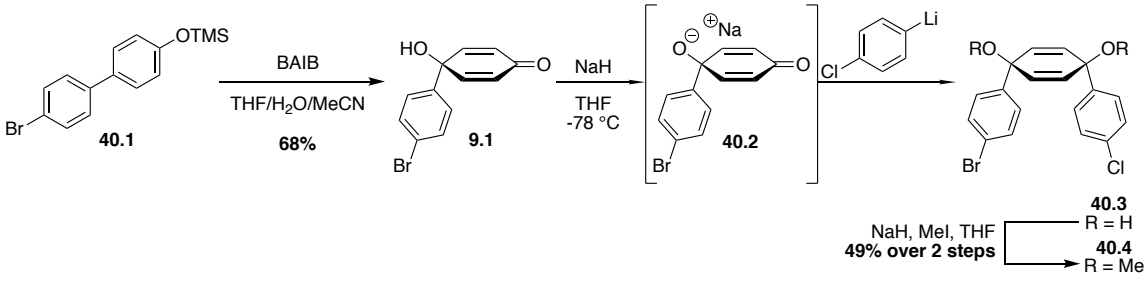
based system such as **39.1** could be subjected these oxidative boronate macrocyclization conditions to give the macrocycle **49.2**. At this stage, **39.2** could be selectively oxidized to afford the macrocyclic 1,4-diketone **30.5** that was a key intermediate in our initial synthetic design toward [4]CPP.

Scheme 39. An oxidative boronate coupling strategy towards **30.5**



This unsymmetric cyclohexadiene unit **39.1** could be prepared using the same methodology as the Jasti group employed in their synthesis of [7]CPP.[19] In this, they prepared the bromochloro cyclohexadiene **40.4** first by the oxidative dearomatization of biphenyl **40.1**, to afford the alcohol **9.1**. This alcohol was deprotonated with sodium hydride and then, with the alkoxide face blocked by the salt formed with the sodium cation, selective addition of 4-chlorophenyllithium afforded the *syn* cyclohexadiene **40.3**. Conversion of the alcohols of **40.3** to methoxy groups afforded the unsymmetric unit **40.4** in a 49% yield from **9.1**.

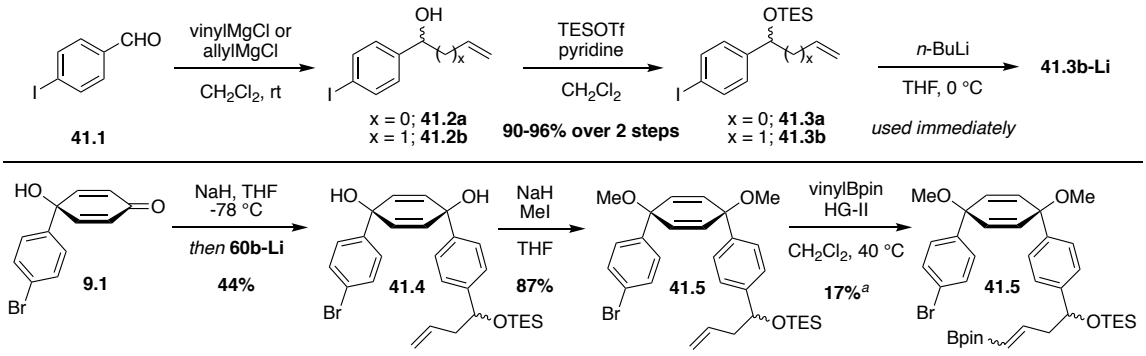
Scheme 40. Synthesis of an unsymmetric cyclohexa-2,5-diene-1,4-diol system



The desired unsymmetric cyclohexadiene **41.5** (Scheme 41) was prepared by using an alternative aryllithium **41.3b-Li**, in this case substituted with a homoallylic alcohol. This was prepared by treating 4-iodobenzaldehyde **41.1** with allylmagnesium chloride to afford the alcohol **41.2b**. The alcohol produced here was then protected with triethylsilyl triflate to give **2.60b** for a yield of 96% over 2 steps from **41.1**.

Then, **2.60b-Li** (generated *in situ*) was added to **9.1**, affording the unsymmetric cyclohexadiene-based subunit **41.4** in a 44% yield, then the alcohols of this subunit were methylated to give **41.5** (87%). In order to install the boronic ester necessary for this macrocyclization reaction, the olefin of **41.5** was subjected to a cross metathesis with vinyl-Bpin in the presence of Hoveyda-Grubbs second generation catalyst to give **41.5** in a 17% yield.

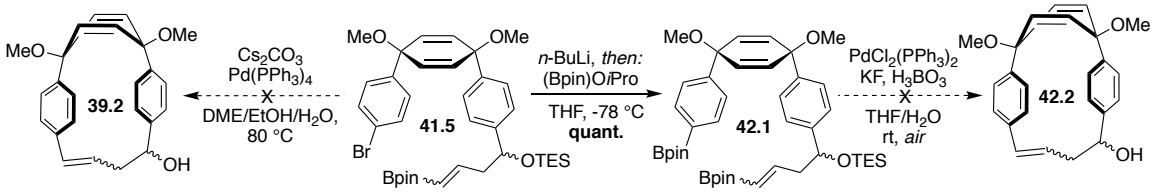
Scheme 41. Planned synthesis of an unymmetric macrocyclization precursor



[a] *Yield based on crude mass*

When subjected to the planned oxidative boronate coupling macrocyclization conditions, **41.5** (with Br and Bpin coupling partners) failed. It was thought that the direct coupling between two boronic esters might instead lead to macrocyclization, and so **41.5** was converted into the bis boronic ester **42.1**. However, the macrocyliozation via this route was also unsuccessful (Scheme 44).

Scheme 42. Oxidative boronate coupling-based macrocyclixation strategy

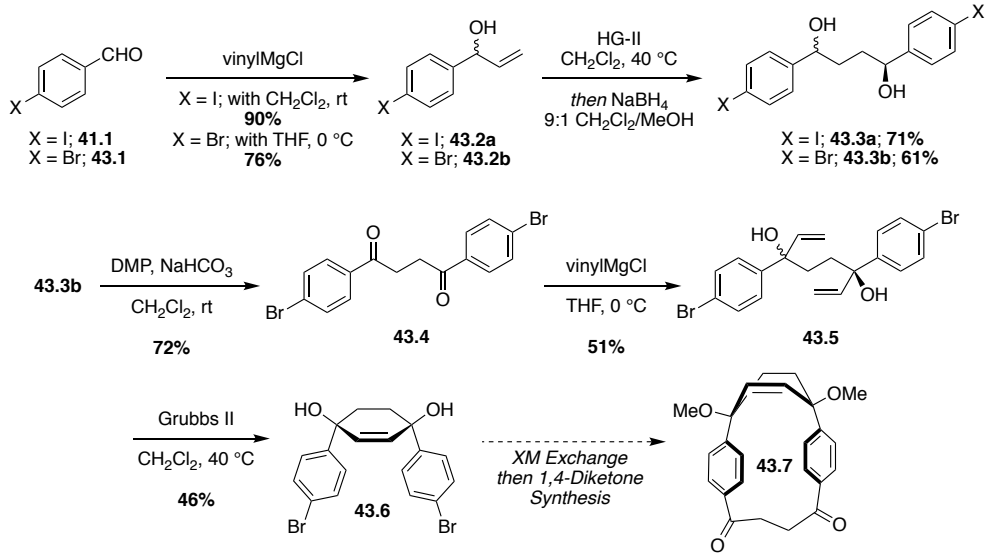


[a] *Yield based on crude mass*

2.4.6 A cyclohex-2-ene-1,4-diol-based macrocycle towards [4]CPP

It was thought that utilizing an alternative bent, pre-arene (instead of the cyclohexa-2,5-diene-1,4-diol-based system) might prevent some of the problems associated with the previously reported syntheses. Instead, an acyclic version of the cyclohex-2-ene-1,4-diol system used by the Merner group was constructed. 4-bromobenzaldehyde **43.1** was treated with vinylmagnesium chloride to give **43.3b** in a yield of 76%. This was then subjected to the same, streamlined 1,4-diketone synthesis utilized in the macrocyclic systems to afford the acyclic 1,4-diketone **43.4** for a yield of 33% from **43.1**. This 1,4-diketone was then treated with a second portion of vinylmagneisum chloride to afford the allyic diol **43.5** (51%), which was then subjected to ring-closing metathesis conditions with Grubbs second-generation catalyst to afford the cyclohex-2-ene-1,4-diol **43.6** in a 46% yield. This represents and alternative starting point to **30.1**, although future macrocyclization strategies will need to be tested on this system.

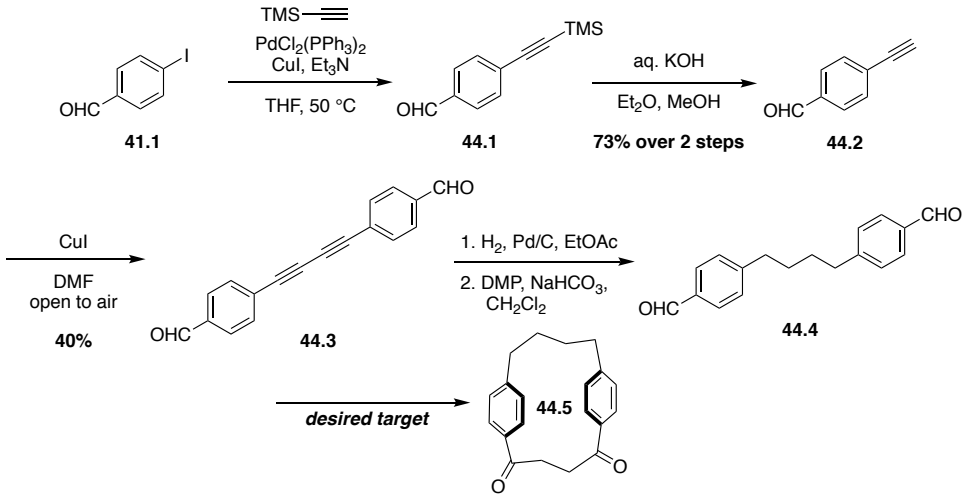
Scheme 43. A cyclohex-2-ene-1,4-diol-containing precursor to [4]CPP



2.4.7 A [4.4]paracyclophane-based strategy towards [4]CPP

Another alternative to **30.1** would be to prepare a [4.4]paracyclophane (such as **44.5**, Scheme 44) instead of utilizing tethered a bent, pre-arene subunit (such as **30.6**). One option for this strategy, would be to make use of a diyne such as **44.3**. The synthesis of this diyne has been previously reported[44] and begins with the Sonagashira coupling of 4-iodobenzaldehyde **41.1** with allyltrimethylsilane to afford **44.1**, followed by the protodesilylation with aqueous potassium hydroxide to give **44.2** in a 73% yield from **41.1**. Then, the copper-mediated Glaser coupling afforded **44.3** in a 40% yield.

Scheme 44. A Glaser strategy toward a [4.4]paracyclophane precursor to [4]CPP

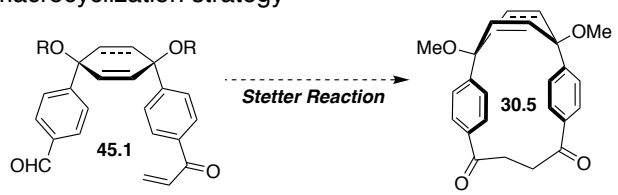


The next steps, hydrogenation of the alkynes of **44.3** also reduced the aldehydes to primary alcohols, although these could be oxidized back to **44.4**. TLC results showed the conversion of **2.75** to the 1,4-diketone containing [4.4]paracyclophane **2.76**, but further optimization of this strategy will be required.

2.5 Future directions

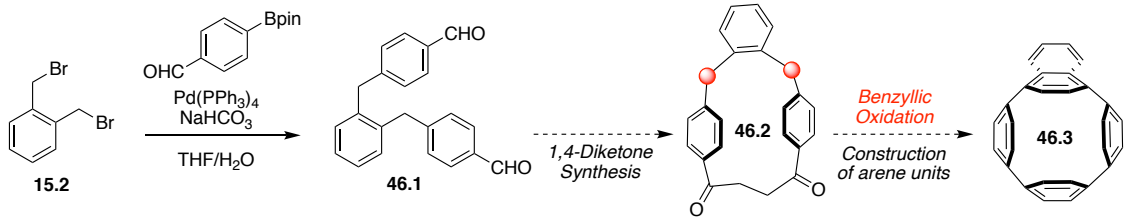
In addition to screening alternative macrocyclic RCM conditions, the Stetter reaction could offer a solution for macrocyclization and also the hydrogenation issues. A system such as **45.1** (Scheme 45), containing an aldehyde and an α,β-unsaturated ketone, should be relatively straightforward to prepare from **30.2**, and could serve as a substrate for the Stetter reaction. A Stetter-based macrocyclization would also bypass the hydrogenation problem (Scheme 30) as the product would be the desired, macrocyclic 1,4-diketone **30.5**.

Scheme 45. Potential use of the Stetter Reaction as a macrocyclization strategy



Another potential solution to the RCM challenges could lie in the use of an alternative bent, pre-arene unit. The use of an *ortho*-bridged tether, as in **46.1**, could put the aldehyde vertices within close enough proximity to one another for RCM to occur, this system would also not pose a problem during the hydrogenation step of the 1,4-diketone synthesis. The benzylic positions of **46.2** (Scheme 50, marked in red) could be oxidized to ketones, allowing for arene formation at that position as well. The product of this synthesis, however, would be a naphthalene-containing [4]CPP, **46.3**.

Scheme 46. Toward a napthalene-containing analog of [4]CPP

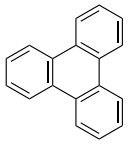


CHAPTER 3 Synthesis of regioselectively functionalized triphenylenes via allylic arylation

3.1 Synthesis and applications of asymmetric triphenylene systems

Triphenylenes (**F11.1**, Figure 11) are a class of polycyclic aromatic hydrocarbons (PAHs) that consists of four fused benzene rings, where the three outer rings are fully aromatic. Triphenylenes have been of synthetic interest since the 1950s[45] for their interesting optical and physical properties,[46] which make them suitable in such applications as electronic displays[47] and solar energy[48]. The properties that make triphenylenes well-suited for these applications can be tuned by either extending the PAH system or by functionalizing the six peripheral positions[49]. Currently, few methods exist that allow for the unsymmetric pi-extension of triphenylenes.

Figure 11. Structure of triphenylene

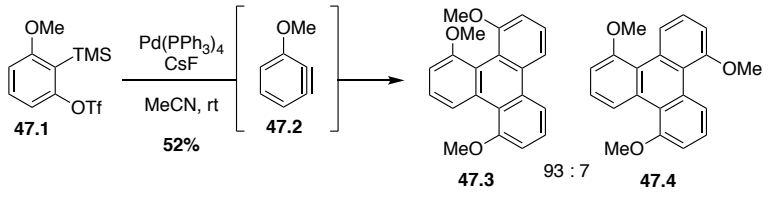


F11.1

3.1.1 Benzyne [2 + 2 + 2] cyclotrimerization in the synthesis of triphenylene systems

In 1998, the group of Pérez and Guitián reported the first metal-catalyzed, benzyne trimerization for the synthesis of an unsymmetric triphenylene.[50] This synthesis of an unsymmetric triphenylene proceeds in a single step and begins with the treatment of the methoxy-substituted **47.1** (Scheme 47) with cesium fluoride, promoting the formation of the benzyne intermediate **47.2**. Then, the palladium(0) catalyst mediates the [2 + 2 + 2] cyclotrimerization of the benzyne **47.2** to give a mixture of the unsymmetric triphenylene **47.3** and triphenylene **47.4** in a 93:7 ratio and a yield of 52%.

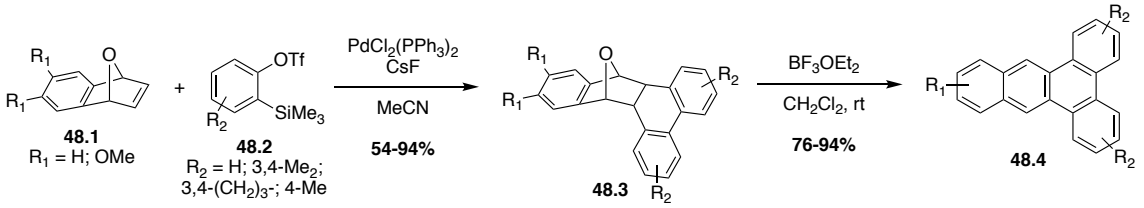
Scheme 47. Palladium-catalyzed [2 + 2 + 2] cyclotrimerization of benzyne



In 2004, Cheng and co-workers reported a [2 + 2 + 2] cyclotrimerization-based approach to unsymmetric triphenylenes where one of the 2-pi, cyclization partners was a bicyclic alkene (**48.1**, Scheme 48), allowing for a pi-extended triphenylene product (**48.4**).[51] In this, **48.2** is treated with cesium fluoride, which generates a benzyne intermediate. This is then treated with the bicyclic alkene unit **48.1** and a palladium(0) catalyst to afford **48.3** in yields of 54-94%. The benzyne-unit **48.2** could be substituted with a few alkyl groups and the bicyclic alkene unit **48.1** with a methoxy group, affording a series of possible functionalization arrangements. Then, **48.3** was treated with

boron trifluoride diethyl etherate to generate a series of pi-extended, unsymmetrically functionalized triphenylenes **48.4** in yields of 76-94%.

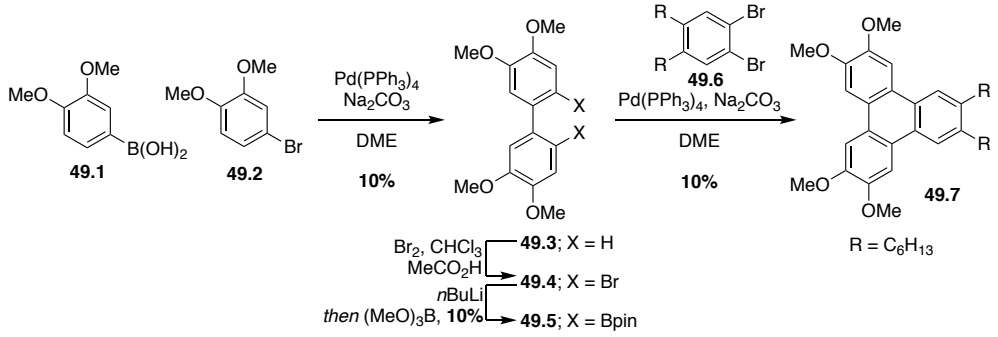
Scheme 48. A [2 + 2 + 2] cyclotrimerization-based strategy towards a pi-extended triphenylene



3.1.2 Preparation of triphenylenes from a biaryl-type precursors

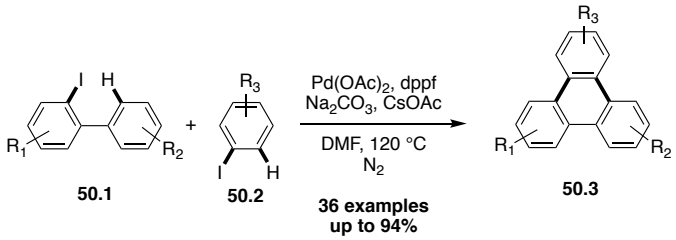
In 1994, Hird and co-workers reported the synthesis of an unsymmetric triphenylene **49.7** (Scheme 48) that was prepared using a Suzuki cross-coupling reaction between the a bisboronic ester biphenyl **49.5** and the *ortho*-dibromide **49.6**.[52] The biphenyl used in this reaction was prepared by first the Suzuki cross-coupling of the arylboronic ester **49.1** and the arylbromide **49.2** to afford **49.3** (X = H). Then, bromination of this biphenyl, followed by borylation gave biphenyl **49.5**, the biphenyl utilized in the key Suzuki step, next. **49.5** was rected with the *ortho*-dibromide **49.6** to afford the unsymmetric triphenylene **49.7**.

Scheme 49. A Suzuki cross-coupling approach to an unsymmetric triphenylene



In 2016, Zhang and co-workers reported the synthesis of a series of unsymmetric triphenylenes **50.3** (Scheme 50) that also made use of a biphenyl precursor, although the new aryl-aryl bonds were formed via iterative C-H activation reactions.[53] This reaction was found to be tolerant of functional group handles on both the biphenyl system **50.1** and the aryl iodide **50.2**, where the functional groups screened included alkyl groups, O-alkyl groups, and halogens on either the biphenyl or aryl iodide system. This reaction represents a method for the preparation of unsymmetric triphenylenes in a single step in yields up to 94%.

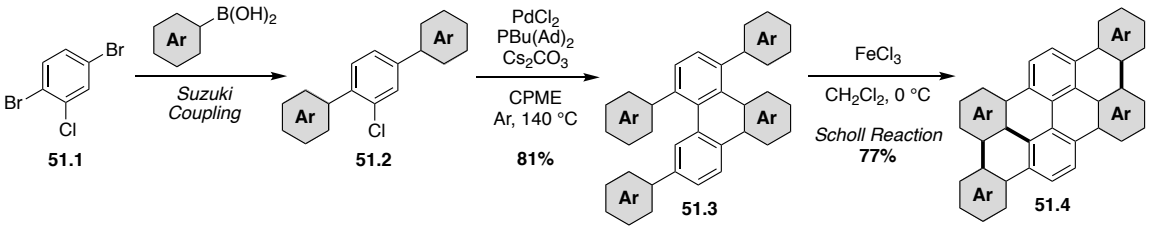
Scheme 50. A C-H activation strategy towards unsymmetric triphenylenes



3.1.3 Examples of APEX chemistry in the synthesis of pi-extended triphenylenes

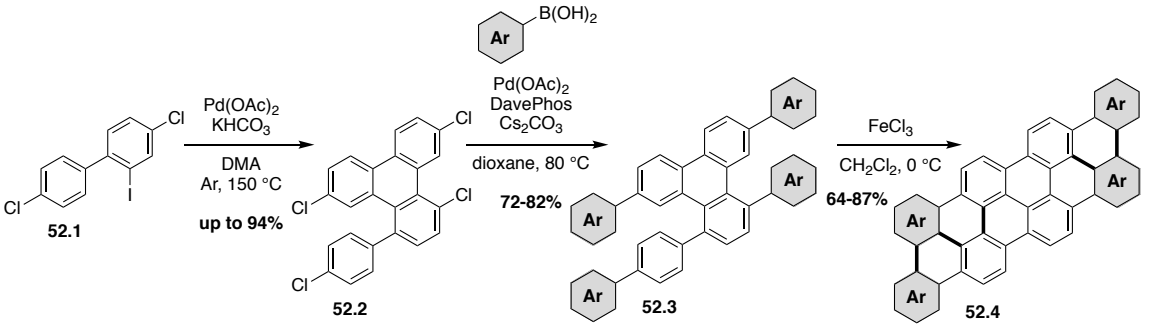
In 2018, the Itami group reported the synthesis of a series of fully fused PAH systems **51.4** (Scheme 51) that were prepared via a triphenylene intermediate.[54] This synthesis began with the extension of **51.1,** to afford the terphenyl **51.2**. Then, the annulative dimerization of **51.2** was catalyzed by palladium(II) chloride to give the unsymmetric triphenylene **51.3** in an 81% yield. This triphenylene system was then used to prepare a fully-fused, extended PAH system **51.4**, which required the formation of three new C-C bonds, via a Scholl reaction, proceeding with a 77% yield. These reaction conditions were also successful on a series of these pi-extended systems.

Scheme 51. Itami's synthesis of a fully-fused PAH segment



Later the same year, Shi and co-wokers reported the synthesis of a similar class of extended PAHs.[55] In this strategy, an asymmetric, tetrachloro triphenylene **52.2** (Scheme 52) was prepared via the annulative dimerization of the biphenyl **52.1** for yields of up to 94%. It was at this, triphenylene, stage that a Suzuki cross-coupling reaction was employed to extend the triphenylene system to **52.3**. Then, as was used in Itami's synthesis (Scheme 50), a Scholl reaction of **52.3** led to the fused PAH **52.4** (64-87%). This synthesis was also successful to prepare other PAHs, including a couple of "butterfly" shaped molecules.

Scheme 52. Another annulative dimerization approach to fully fused PAH systems

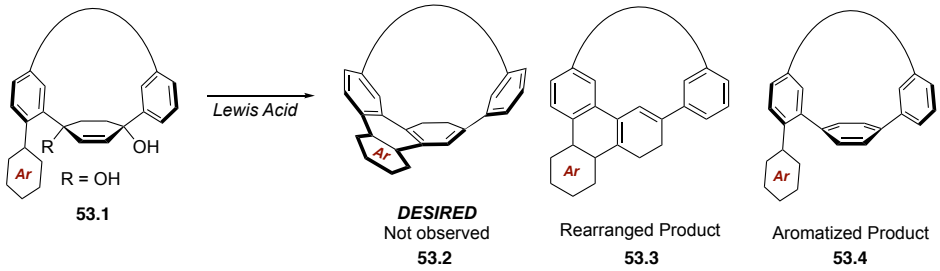


3.2 Preliminary allylic arylation results

Chapter 1 discussed the application of the *para*-terphenyl-containing macrocycles (**53.4**, Scheme 53) reported by our research group in the synthesis of functionalized [*n*]CPPs. Our research group is also interested in exploring the longitudinal pi-extension of [*n*]CPPs, developing methodologies for this also on the *para*-terphenyl-containing macrocycles used by our group.

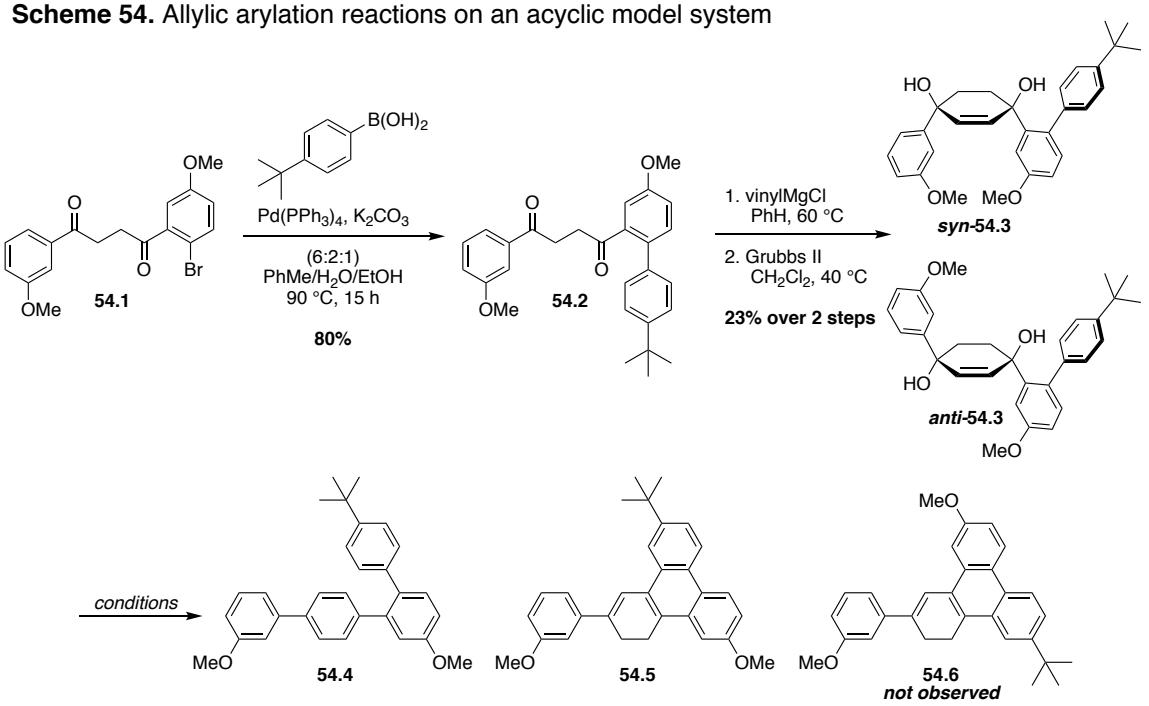
In an effort towards this, our group attempted an allylic arylation on **53.1**, hoping to observe **53.2**. Instead of the desired allylic arylation product, only the rearranged product **53.3** and the aromatized *para*-terphenyl-containing macrocycle **53.4** were observed.

Scheme 53. Attempting the allylic arylation on cyclophane-based systems



In an attempt to better understand these observed results, an acyclic model system **54.3** was prepared. The acyclic monobromo 1,4-diketone **54.1** was subjected to a Suzuki cross-coupling reaction with 4-*tert*-butylphenylboronic acid to give the substituted 1,4-dikeone **54.2** (80% yield). This was then treated with vinylmagnesium chloride and subsequently with Grubbs second-generation catalyst to give a the cyclohex-2-ene-1,4-diol **54.3** as a mixture of the *syn*- and *anti*-isomers.

Scheme 54. Allylic arylation reactions on an acyclic model system



When treated with protic acids, both the *syn*- and *anti*-isomers yielded a mixture of the aromatized product **54.4** and the the allylic arylation product **54.5** (Table 6). Interestingly, the rearranged product **54.5** (which was observed on the cyclic system, **53.3**) was not observed on this acyclic system. Treatment with the Lewis acid iron(III) chloride led to the exclusive formation of the desired, allylic arylation product **54.4**. It was thought that this allylic arylation could be used in the synthesis of unsymmetric triphenylene systems.

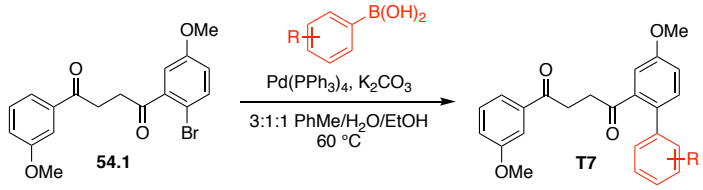
Table 6. Initial allylic arylation results

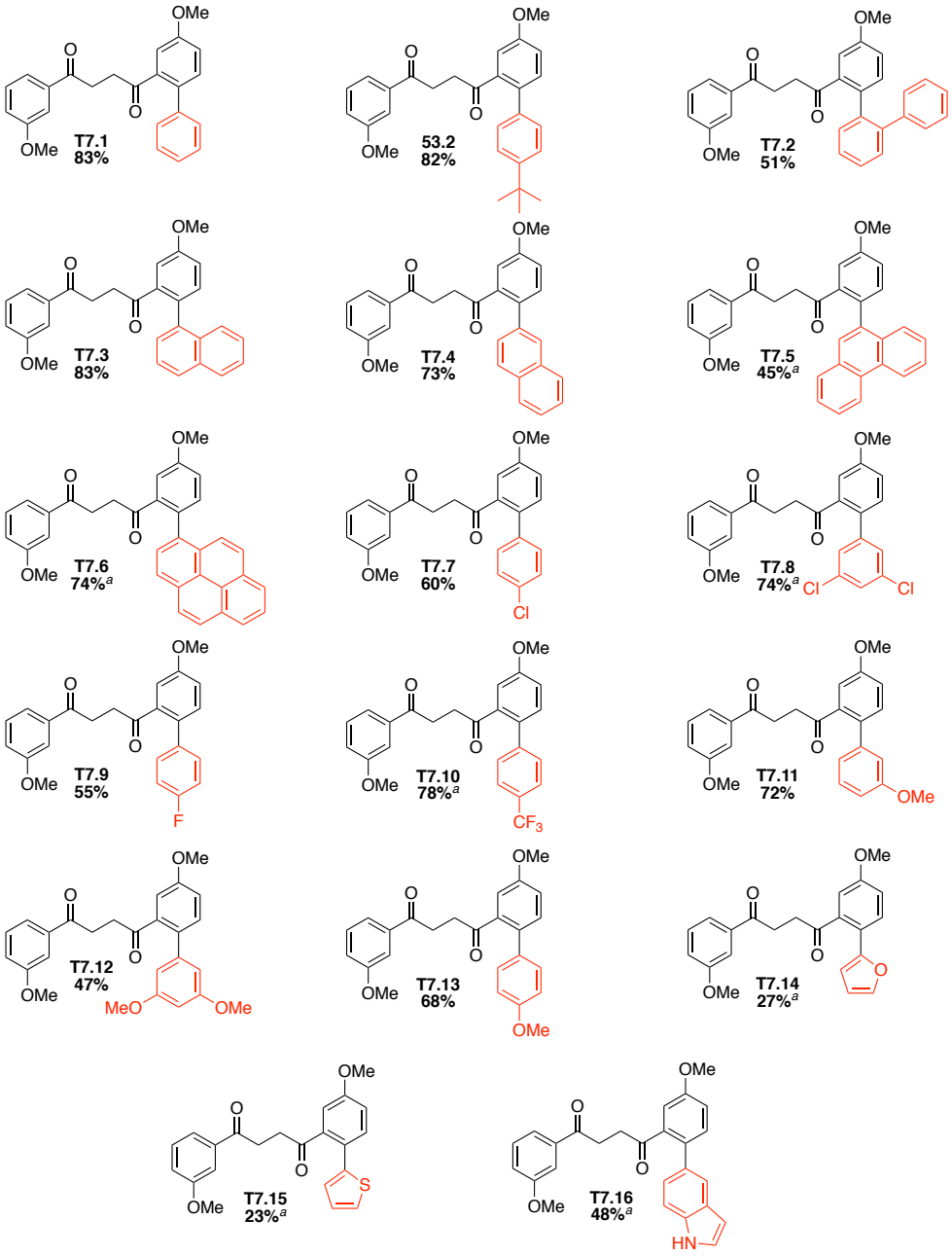
Entry	Substrate	Reagent (equiv.)	solvent	Temp (° C)	54.4	54.5
1	**syn-54.3**	TsOH (6.0)	PhMe	60	50%	50%
2	**anti-54.3**	TsOH (6.0)	PhMe	60	33%	66%
3	**anti-54.3**	MsOH (6.0)	CH_2Cl_2	23	25%	75%
4	**anti-54.3**	$C_6H_5B(OH)_2$ (6.0)	CH_2Cl_2	23	20%	80%
5	**anti-54.3**	$FeCl_3$ (0.2)	CH_2Cl_2	0	0%[a]	95%

3.3 Synthesis of a series of substituted triphenylene systems

The goal of this program was to explore the scope of substituted, unsymmetric triphenylenes accessible via this method. The Suzuki reaction on the key intermediate, the monobromo 1,4-diketone **54.1**, was first explored (Table 8). This cross-coupling was carried out with $Pd(PPh_3)_4$, potassium carbonate, and the corresponding arylboronic acid in a 3:1:1 mixture of tolune, water, and ethanol at 60 °C to afford a series of 17 substituted, 1,4-diketones **T7.1-T7.16** and **53.2** were

Table 8. Scope of the Suzuki reaction



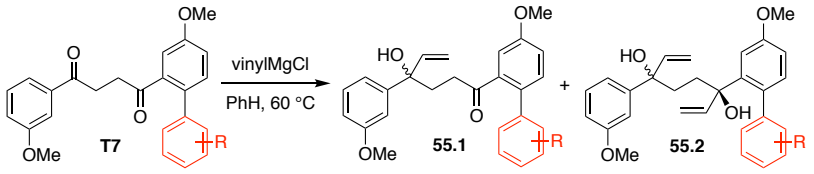


[a] *Yield based on crude mass and crude ^{1}H NMR data.*

successfully prepared including larger PAHs such as naphthalene and pyrene; various methoxy substituted systems; and chlorinated systems, which could be used in future pi-extension reactions. Yields for this reaction ranged from 23-83%.

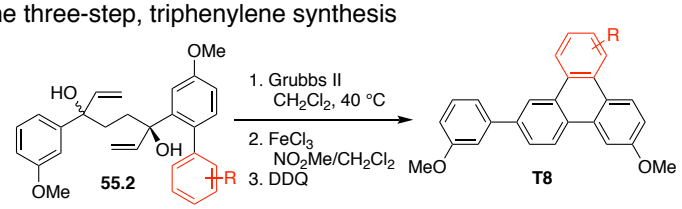
These diketones were then subjected to the Grignard addition of vinylmagnesium chloride. This Grignard reaction, however, represents a limiting step in this synthesis. The formation of the desired, allylic diol **55.2** was sometimes as low as 14% due to the formation of the undesired, hydroxy-ketone **55.1**. Unfortunately, higher Grignard loadings and longer reaction times did not result in the formation of the allylic diol in higher yields. It is believed that the hydroxy ketone may be formed, in part, due to the bulky substituents blocking the neighboring carbonyl. Mechanistic studies into the formation of this unwanted, hydroxy ketone **55.1** are currently underway in our laboratory.

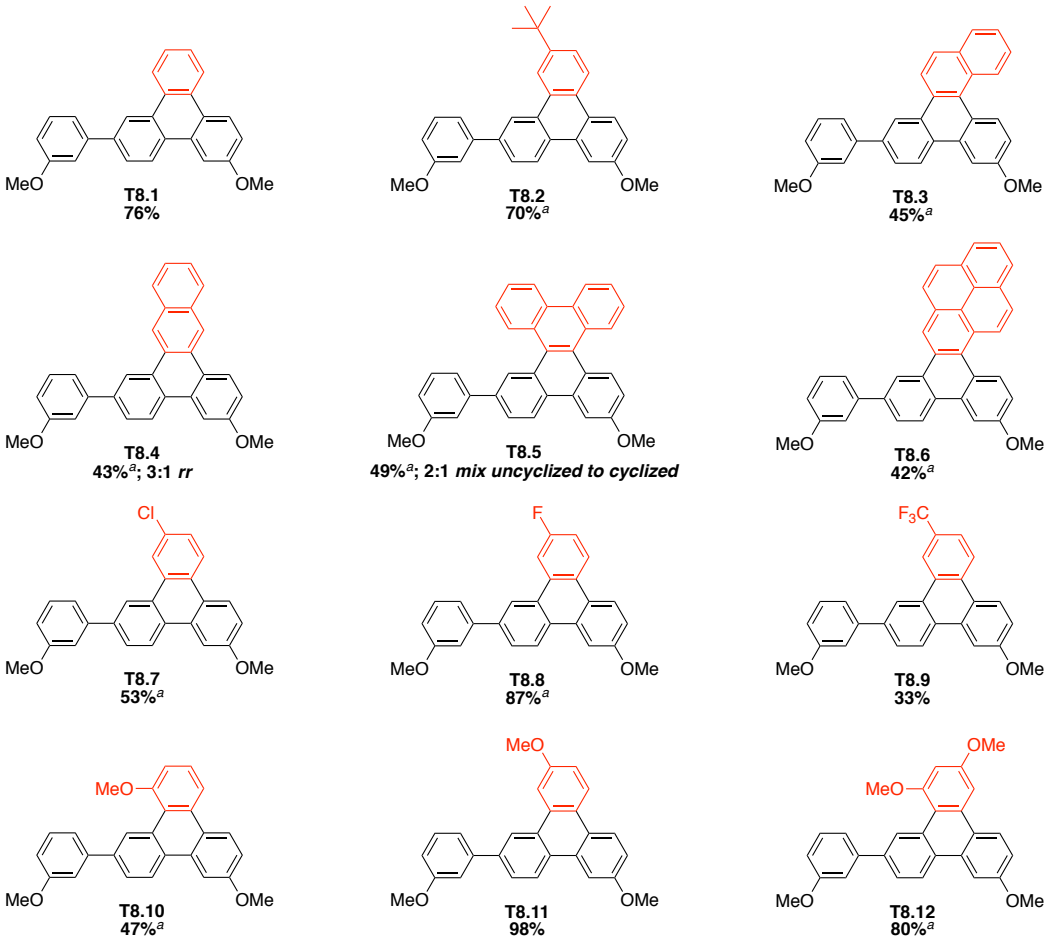
Scheme 55. Grignard addition to the 1,4-diketones **T7**



With allylic diols in hand, these systems were then subjected to a 3-step sequence to prepare the functionalized, unsymmetric triphenylenes **T9.1-12** (Table 8). The first step in this being the ring-closing metathesis of **55.2** with Grubbs second-generation catalyst to form the cyclohex-2-ene-1,4-diol (such as as **54.3** in Scheme 53). Then, the addition of iron(III) chloride in a 9:1 solution of dichloromethane and nitromethane affords the allylic arylation product (such as **54.5**). Finally, treatment with DDQ aromatizes this system to give the unsymmetric triphenylenes **T8.1-T8.12**. This reaction sequence was successful in the preparation of 12 triphenylene systems, including the electron-deficient trifluoromethane-substituted system **T8.9**; larger PAH-containing systems **T8.3-6**; and chlorinated systems such as **T8.7**, which could be used in futher pi-extension of these triphenylenes. Yields for this three-step sequence ranged from 42-98%.

Table 8. Scope of the three-step, triphenylene synthesis



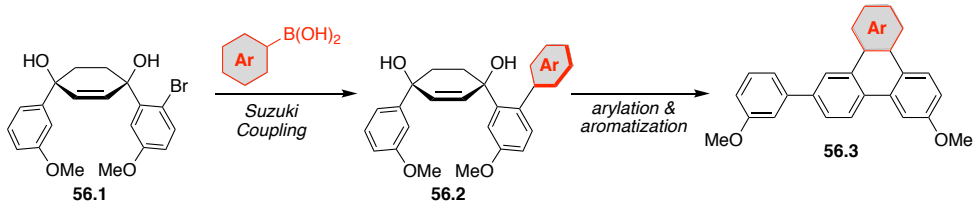


[a] *Yield based on crude mass and crude ^1H NMR data*

3.4 Future directions

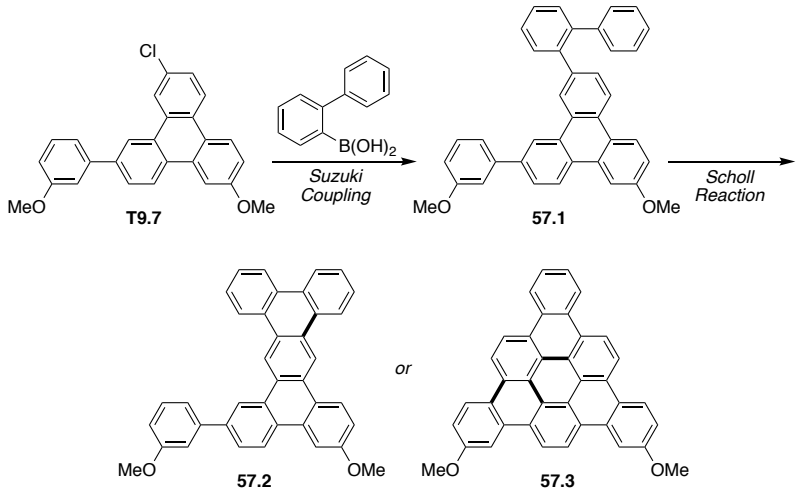
One way to overcome the challenges of the Grignard addition to the 1,4-diketones could be to perform the Suzuki reaction at the later, monobromo cyclohex-2-ene-1,4-diol **56.1** (Scheme 56). If steric hinderance were playing a key role in the low yields of the Grignard addition, this would circumvent that problem.

Scheme 56. Alternative routes to unsymmetric triphenylenes



The ultimate goal of these substituted, unsymmetric tiphenylenes is to use them to prepare larger PAH systems. In the case of the chlorinated **T8.7**, the Suzuki reaction with a system like 2-biphenylboronic acid to afford **57.1** and subsequent Scholl reaction could afford the PAHs **57.2** (1 C-C bond formed) or **57.3** (3 C-C bonds formed).

Scheme 57. Continued pi-extension of the triphenylene systems



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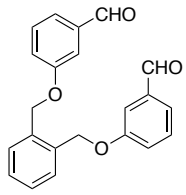
SUPPLEMENTARY INFORMATION

General Experimental Conditions

All reactions were run in flame or oven-dried (120 °C) glassware and under a positive pressure of ultra high pure nitrogen or argon gas. All chemicals were used as received from commercial sources, unless otherwise stated. Anhydrous reaction solvents were purified and dried by passing HPLC grade solvents through activated columns of alumina (Glass Contour SDS). All solvents used for chromatographic separations were HPLC grade (hexanes, ethyl acetate, dichloromethane, chloroform, methanol, and acetone). The degassed solvents used for Suzuki cross-couplings were prepared by bubbling through a constant stream of nitrogen for at least 20 min. Chromatographic separations were preformed using flash chromatography, as originally reported by Still and co-workers, on silica gel 60 (particle size 43-60 μm), and all chromatography conditions have been reported as height × diameter in centimeters. Reaction progress was monitored by thin layer chromatography (TLC), on glass-backed silica gel plates (pH = 7.0). TLC plates were visualized using a handheld UV lamp (254 nm) and stained using an aqueous ceric ammonium molybdate (CAM) solution. Plates were dipped, wiped clean, and heated from the back of the plate. 1H and 13C nuclear magnetic resonance (NMR) spectra were recorded at 400 or 600 MHz, calibrated using residual undeuterated solvent as an internal reference ($CHCl_3$, δ 7.27 and 77.2 ppm), reported in parts per million relative to trimethylsilane (TMS, δ 0.00 ppm), and presented as follows: chemical shift (δ, ppm), multiplicity (s = singlet, br s = broad singlet, d = doublet, dd = doublet of doublets, ddd = doublet of doublet of doublets, dt = doublet of triplets, t = triplet, td = triplet of doublets, m = multiplet, p = pentet), coupling constants (J, Hz). High-resolution mass spectrometric (HRMS) data were obtained using a quadrupole time-of-flight (Q-TOF) spectrometer and electrospray ionization (ESI). Only experimental conditions and spectroscopic data obtained by the author is reported unless otherwise indicated.

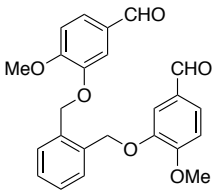
CHAPTER 1 Synthesis of functionalized *p*-terphenyl-containing macrocycles as key intermediates in the synthesis of functionalized [*n*]CPPs

General Procedure A for the formation of tethered dialdehydes:



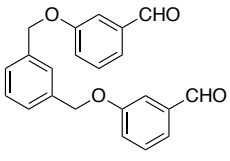
15.3

15.3: α,α'-Dibromo-*o*-xylene (0.503 g, 1.91 mmol) was added to a stirred solution of 3-hydroxybenzaldehyde (0.640 g, 5.24 mmol), K_2CO_3 (0.922 g, 6.67 mmol), and tetrabutylammonium iodide (0.0190 g, 0.0514 mmol) in DMF (12 mL). The reaction was heated at 60 °C for 17 h, at which point the reaction was cooled to room temperature and water (6 mL) and 1 M HCl (6 mL) were added sequentially. The resulting mixture was extracted with ethyl acetate (3 × 10 mL). The organic extracts were combined and washed with a saturated solution of $NaHCO_3$ (15 mL) and brine (15 mL), dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified via flash chromatography (14 × 2.5 cm; dichloromethane) to afford **15.3** as a white powder (0.440 g, 67%): R_f = 0.44 (dichloromethane); ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.95 (s, 2H), 7.54 (dd, *J* = 5.5, 3.5 Hz, 2H), 7.48-7.40 (m, 8H), 7.26-7.22 (m, 2H), 5.25 (s, 4H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 192.0, 159.0, 137.7, 134.6, 130.2, 129.3, 128.8, 124.0, 122.1, 113.0, 68.2; HRMS (ESI) calculated for $C_{22}H_{19}O_4$ ([M+H]$^+$) *m/z* = 347.1283, found 347.1267.



18.2

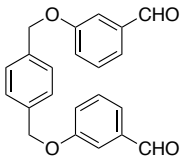
18.2: This compound was prepared using the *general procedure A* with isovanillin (1.15 g, 7.58 mmol), α,α'-dibromo-*o*-xylene (1.00 g, 3.79 mmol), K_2CO_3 (1.83 g, 13.3 mmol), and TBAI (0.035 g, 0.095 mmol) in DMF (16 mL). The residue was purified via flash chromatography (23 × 6 cm, 3% acetone/dichloromethane) to afford the ortho-methoxy-dialdehyde **18.2** as an off-white solid (0.430 g, 28%): R_f = 0.29 (3% acetone/dichloromethane); ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.81 (s, 2H), 7.51 (dd, *J* = 5.5, 3.4 Hz, 2H), 7.45 (d, *J* = 1.9 Hz, 2H), 7.41 (dd, *J* = 8.2, 1.9 Hz, 2H), 7.37 (dd, *J* = 5.6, 3.3 Hz, 2H), 6.90 (d, *J* = 8.2 Hz, 2H), 5.36 (s, 4H), 3.89 (s, 6H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 190.9, 154.9, 148.5, 134.6, 129.8, 129.2, 128.6, 127.1, 110.7, 110.4, 69.6, 56.0; HRMS (ESI) calculated for $C_{24}H_{23}O_6$ ([M + H]$^+$) *m/z* = 407.1495, found = 407.1508.



16.3a

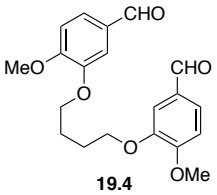
16.3a: This compound was prepared using the *general procedure A* with α,α'-dibromo-*m*-xylene (1.02 g, 2.80 mmol), 3-hydroxybenzaldehyde (1.10 g, 9.01 mmol), K_2CO_3 (1.86 g, 13.5 mmol), and tetrabutylammonium iodide (0.0365 g, 0.0988 mmol) in DMF (17 mL). The residue was purified via flash chromatography (16.5 × 2.5 cm; 4:1 dichlormethane/hexanes to

dichloromethane) to afford **16.3a** as a colorless oil (0.945 g, 72%): R_f = 0.33 (4:1 dichlormethane/hexanes); ^{1}H NMR (600MHz, $CDCl_3$) δ 9.98 (s, 2H), 7.55 (s, 1H), 7.53-7.40 (m, 9H); 7.27-7.25 (m, 2H), 5.16 (s, 4H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 192.0, 159.2, 137.8, 136.9, 130.2, 129.1, 127.3, 126.5, 123.8, 122.2, 113.2, 70.0; HRMS (ESI) calculated for $C_{22}H_{19}O_4$ ([M+H]$^+$) *m/z* = 347.1283, found 347.1287.



SI-1

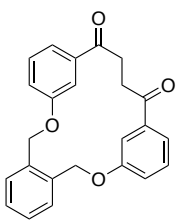
SI-1: This compound was prepared using the *general procedure A* with α,α'-dibromo-*p*-xylene (3.60 g, 13.6 mmol), 3-hydroxybenzaldehyde (5.00 g, 40.9 mmol), K_2CO_3 (6.63 g, 47.7 mmol), and tetrabutylammonium iodide (0.505 g, 1.36 mmol) in DMF (70 mL). The residue was purified via flash chromatography (18 × 5.0 cm; dichloromethane to 1% acetone/dichloromethane) to afford **SI-1** as a white solid (3.13 g, 66%): R_f = = 0.39 (dichloromethane); ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.98 (s, 2H), 7.50- 7.41 (m, 10H), 7.27- 7.20 (m, 2H), 5.14 (s, 4H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 192.1, 159.2, 137.8, 136.3, 130.1, 127.8, 123.8, 122.2, 113.0, 69.8; (ESI) calculated for $C_{22}H_{19}O_4$ ([M+H]$^+$) *m/z* = 347.1283, found 347.1287. *This experiment was conducted by Rolande Meudom.*



19.4

19.4: This compound was prepared using the *general procedure A* with isovanillin (2.0 g, 13 mmol), 1,4-dibromobutane (0.71 mL, 1.3 g, 6.0 mmol), K_2CO_3 (2.9 g, 21 mmol), and TBAI (0.056 g, 0.15 mmol) in DMF (26 mL). The residue was purified via flash chromatography (15 × 2.5 cm, 2:3 EtOAc/hexanes to EtOAc to 10% acetone/EtOAc) to afford the methoxy-dialdehyde **19.4** as a white solid (2.67 g, 57%): R_f = 0.25 (2:3 EtOAc/hexanes); ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.84 (s, 2H), 7.45 (dd, *J* = 8.2, 1.9 Hz, 2H), 7.41 (d, *J* = 1.9 Hz, 2H), 6.97 (d, *J* = 8.2 Hz, 2H), 4.19 (s, 4H), 3.94 (s, 6H), 2.09 (d, *J* = 3.1 Hz, 4H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 191.0, 154.8, 148.9, 130.0, 126.8, 110.5, 110.0, 68.5, 56.1, 25.8; HRMS (ESI) calculated for $C_{20}H_{23}O_6$ ([M + H]$^+$) *m/z* = 359.1495, found = 359.1510.

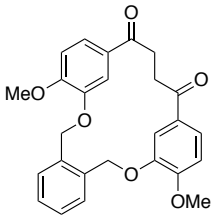
General Procedure B for the formation of macrocyclic 1,4-diketones:



15.4

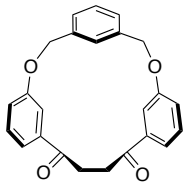
15.4: Vinylmagnesium chloride (1.6 M in THF, 1.7 mL, 2.7 mmol) was added to a stirred solution of **15.3** (0.418 g, 1.21 mmol) in THF (12 mL). After 15 min, the reaction was poured into water (10 mL) and further diluted with 1 M HCl (10 mL). The resulting mixture was extracted with dichloromethane (3 × 10 mL). The combined organic extracts were washed with a saturated solution of $NaHCO_3$ (15 mL) and brine (15 mL), dried over anhydrous $MgSO_4$, filtered, and concentrated

under reduced pressure. The pale yellow residue was dissolved in dichloromethane (80 mL) and was heated to 40 °C, followed by the addition of the Hoveyda-Grubbs second-generation catalyst (0.0383 g, 0.0604 mmol). After 1.5 h, the reaction mixture was concentrated under reduced pressure. The dark brown residue was dissolved in 1:9 methanol/dichloromethane (12 mL), stirred, and sodium borohydride (0.182 g, 4.83 mmol) was added. After 30 min, the reaction was poured into water (6 mL) and further diluted with 1 M HCl (6 mL). The layers were separated and the aqueous phase was extracted with dichloromethane (3 × 10 mL). The combined organic extracts were washed with brine (15 mL), dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The dark brown residue was dissolved in dichloromethane (12 mL), followed by the sequential addition of $NaHCO_3$ (0.203 g, 82.4 mmol) and Dess-Martin periodinane (1.02 g, 2.41 mmol) and the reaction stirred under a glass stopper. After 1.5 h, the reaction was poured into water (15 mL) and stirred 20 min. The layers were separated and the aqueous phase was extracted with dichloromethane (3 × 10 mL). The combined organic extracts were washed with brine (15 mL), dried over anhydrous $MgSO_4$, filtered and concentrated under reduced pressure. The residue was purified via flash chromatography (20 × 2.5 cm; 1:4 EtOAc/hexanes) to afford ortho-1,4-diketone **15.4** as a white solid (0.256 g, 57% from **15.3**): R_f = 0.40 (1:4 EtOAc/hexane); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.66 (ddd, *J* = 7.7, 1.6, 1.0 Hz, 2H), 7.59 (dd, *J* = 5.6, 3.4 Hz, 2H), 7.50 (t, *J* = 7.9 Hz, 2H), 7.45 (dd, *J* = 2.5, 1.6 Hz, 2H), 7.41 (dd, *J* = 5.6, 3.3 Hz, 2H), 7.37 (ddd, *J* = 8.2, 2.5, 1.1 Hz, 2H), 5.34 (s, 4H), 3.07 (s, 4H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 198., 158.8, 137.1, 134.1, 130.6, 128.4, 127.9, 121.7, 121.6, 115.1, 69.8, 36.4; HRMS (ESI) calculated for $C_{24}H_{21}O_4$ ($[M+H]^+$) *m/z* = 373.1440, found 373.1466.



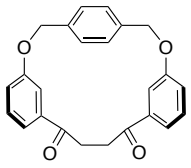
18.3

18.3: This compound was prepared using the *general procedure B* with ortho-methoxy-dialdehyde **18.2** (0.288 g, 0709 mmol) and vinylmagnesium chloride (1.6 M in THF, 3.0 mL, 1.9 mmol) in dichloromethane (8 mL), except that it required chromatography following the first (Grignard) step (23 × 2.5 cm, 2:3 EtOAc/hexanes to EtOAc) to give the allylic diol intermediate as a white solid (0.193 g, 0.416 mmol, 59%). This was used for the remaining steps, along with Hoveyda-Grubbs II (0.0066 g, 0.010 mmol) in dichloromethane (43 mL); $NaBH_4$ (0.064 g, 1.6 mmol) in 1:9 MeOH/dichloromethane (5 mL); and Dess-Martin periodinane (0.36 g, 0.83 mmol) and $NaHCO_3$ (0.075 g, 0.83 mmol) in dichloromethane (4 mL). The residue was purified via flash chromatography (19 × 1.5 cm, 3% acetone/dichloromethane) to afford the ortho-methoxy-diketone **18.3** as a white solid (0.067 g, 37%): R_f = 0.23 (3% acetone/dichloromethane); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.82 (dd, *J* = 8.6, 2.1 Hz, 2H), 7.53-7.47 (m, 4H), 7.35-7.30 (m, 2H), 7.09 (d, *J* = 8.6 Hz, 2H), 5.50 (s, 4H), 4.05 (s, 6H), 2.98 (s, 4H), 1.56 (s, 4H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 197.2, 154.8, 146.6, 133.4, 128.3, 128.2, 127.3, 124.2, 116.3, 112.2, 69.4, 56.2, 36.8; HRMS (ESI) calculated for $C_{26}H_{25}O_6$ ($[M + H]^+$) *m/z* = 433.1651, found = 433.1663.



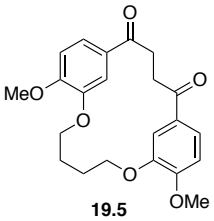
16.4a

16.4a: This compound was prepared using the *general procedure B* with meta-dialdehyde **16.3a** (0.667 g, 1.93 mmol) and vinylmagnesium chloride (1.6 M in THF, 2.7 mL, 4.2 mmol) in THF (20 mL); Hoveyda-Grubbs II (0.0603 g, 0.0963 mmol) in dichloromethane (130 mL); sodium borohydride (0.291 g, 7.70 mmol) in 1:9 methanol/dichloromethane (20 mL); and Dess-Martin periodinane (1.02 g, 3.40 mmol) and $NaHCO_3$ (0.286 g, 3.40 mmol) in dichloromethane (17 mL). The residue was purified via flash chromatography (18 × 1.3 cm; 1:3 EtOAc/hexanes) to afford meta-1,4-diketone **16.4a** as a white solid (0.156 g, 22%): R_f = 0.40 (1:4 EtOAc/hexanes); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35-7.35 (m, 1H), 7.33-7.33 (m, 1H), 7.32-7.30 (m, 1H), 7.29 (d, *J* = 3.0 Hz, 1H), 7.26-7.22 (m, 4H), 7.10 (dd, *J* = 2.6, 1.1 Hz, 1H), 7.08 (dd, *J* = 2.6, 1.1 Hz, 1H), 7.03 (dd, *J* = 2.6, 1.6 Hz, 2H), 5.25 (s, 4H), 3.11 (s, 4H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 199.9, 157.6, 137.9, 137.4, 129.8, 129.3, 126.6, 125.2, 121.6, 120.7, 114.3, 69.5, 35.2; HRMS (ESI) calculated for $C_{24}H_{21}O_4$ ($[M + H]^+$) *m/z* = 373.1440, found 373.1428.



SI-2

SI-2: This compound was prepared using the *general procedure* with para-dialdehyde **SI-1** (0.650 g, 1.40 mmol) and vinylmagnesium chloride (1.6 M in THF, 2.6 mL, 4.1 mmol) in THF (14 mL); Hoveyda-Grubbs II (0.021 g, 0.035 mmol) in dichloromethane (140 mL); sodium borohydride (0.326 g, 8.62 mmol) in 1:9 methanol/dichloromethane (15 mL); and Dess-Martin periodinane (1.19 g, 2.80 mmol) and $NaHCO_3$ (0.236 g, 2.80 mmol) in dichloromethane (18 mL). The residue was purified via flash chromatography (15 × 2.5 cm, 1:3 EtOAc/hexanes) to afford para-1,4-diketone **SI-2** I as a white solid (0.209 g, 40% from **SI-1**): R_f = 0.26 (1:3 EtOAc/hexanes): ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.48 (d, *J* = 7.7 Hz, 2H), 7.40-7.37 (m, 2H), 7.31-7.27 (m, 6H), 6.75-6.70 (m, 2H), 5.28 (s, 4H), 2.98 (s, 4H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 199.1, 157.4, 137.3, 136.5, 129.8, 127.4, 123.5, 120.9, 115.6, 71.1, 34.8; HRMS (ESI) calculated for $C_{24}H_{21}O_4$ ($[M+H]^+$) *m/z* = 373.1440, found 373.1428. *This reaction was conducted by Rolande Meudom.*

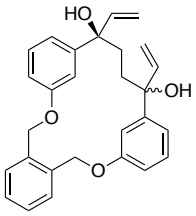


19.5

19.5: This compound was prepared using the *general procedure B* with methoxy-dialdehyde **19.4** (0.460 g, 1.28 mmol) and vinylmagnesium chloride (1.6 M in THF, 2.0 mL, 3.2 mmol) in dichloromethane (12 mL); Hoveyda-Grubbs II (0.020 g, 0.0032 mmol) in dichloromethane (80 mL); $NaBH_4$ (0.20 g, 5.12 mmol) in 1:9 MeOH/dichloromethane (20 mL); and Dess-Martin periodinane (1.2 g, 2.8 mmol) and $NaHCO_3$ (0.24 g, 2.8 mmol) in dichloromethane (15 mL). The residue was purified via flash chromatography (15 × 2.5 cm, 2:3 EtOAc/hexanes to 3:2 EtOAc/hexanes) to afford the methoxy-1,4-diketone **19.5** as a white solid (0.23 g, 47% from **1.92a**): R_f = 0.29 (2:3 EtOAc/hexanes); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.73 (dd, *J* = 8.5, 2.1 Hz, 2H), 7.45

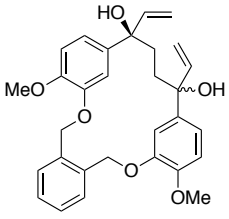
(d, *J* = 2.2 Hz, 2H), 6.99 (d, *J* = 8.6 Hz, 2H), 4.35-4.25 (m, 4H), 3.94 (s, 6H), 3.12 (s, 4H), 1.96-1.89 (m, 4H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 197.8, 155.0, 146.4, 128.8, 123.8, 116.8, 112.0, 69.5, 55.9, 35.8, 25.2; HRMS (ESI) calculated for $C_{22}H_{25}O_6$ ([M + H]$^+$) *m/z* = 385.1627, found = 385.1638.

General Procedure C for the preparation of allylic diols:



SI-3

SI-3: Vinylmagnesium chloride (1.6 M in THF, 0.45 mL, 0.72 mmol) was added to a stirred solution of diketone **15.4** (0.123 g, 0.328 mmol) in dichloromethane (3.5 mL). The slurry was heated at 40 °C for 1 h, at which point the reaction was poured into water (5 mL) and further diluted with 1 M HCl (5 mL). The resulting mixture was extracted with dichloromethane (3 × 10 mL). The combined organic extracts were washed with a saturated solution of $NaHCO_3$ (20 mL) and brine (20 mL), dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified via flash chromatography (17 × 1.3 cm, 3% acetone/dichloromethane) to give the allylic alcohols **SI-3** as a white solid (0.110 g, 79%) as a mixture of diastereomers (dr = 10:1, determined from NMR of the complete mixture): R_f = 0.27 (3% acetone/dichloromethane); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.63 (dd, *J* = 5.6, 3.4 Hz, 2H), 7.45 (dd, *J* = 5.6, 3.3 Hz, 2H), 7.34-7.28 (m, 3H), 7.10-7.05 (m, 2H), 6.99 (dd, *J* = 8.2, 2.5 Hz, 2H), 6.87 (d, *J* = 2.1 Hz, 1H), 6.24 (dd, *J* = 17.2, 10.7 Hz, 2H), 5.37 (dd, *J* = 17.2, 1.2 Hz, 2H), 5.21 (dd, *J* = 10.7, 1.2 Hz, 2H), 5.19-5.13 (m, 4H), 2.42 (s, 2H), 1.89-1.77 (m, 4H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 159.3, 146.1, 143.2, 135.3, 129.4, 128.4, 128.3, 119.2, 114.8, 113.2, 112.5, 76.7, 69.5, 36.6; HRMS calculated for $C_{28}H_{25}O_2$ [(M – 2 H_2O + H)$^+$] *m/z* = 393.1855, found 393.1844.



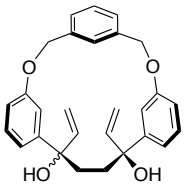
SI-4

SI-4: This compound was prepared using the *general procedure C* with ortho-methoxy-diketone **18.3** (0.019 g, 0.044 mmol) and vinylmagnesium chloride (1.6 M in THF, 0.06 mL, 0.1 mmol) in dichloromethane (0.5 mL). The residue was purified via flash chromatography (10 × 0.5 cm, 3% acetone/dichloromethane to 5% acetone/dichloromethane) to afford the ortho-methoxy-diol as white solid (0. g, 0.019 g, 91%) as a mixture of diastereomers **SI-4** (dr = 3.3:1).

Ortho-methoxy-diol mixture: R_f = 0.20 (3% acetone/dichloromethane); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.64-7.61 (m,, 5H), 7.39-7.37 (m, 5H), 7.21 (dd, *J* = 8.4, 2.2 Hz, 1H), 7.02 (d, *J* = 8.0 Hz, 8H), 6.94 (d, *J* = 8.4 Hz, 1H), 6.87 (d, *J* = 8.1 Hz, 4H), 6.71 (d, *J* = 2.3 Hz, 1H), 6.23-6.15 (m, 4H), 5.97 (dd, *J* = 17.2, 10.6 Hz, 1H), 5.42 (d, *J* = 12.2 Hz, 1H), 5.31 (dd, *J* = 17.2, 1.3 Hz, 5H), 5.26 (d, *J* = 2.0 Hz, 8H), 5.17 (dd, *J* = 10.7, 1.3 Hz, 4H), 5.10 (d, *J* = 12.2 Hz, 1H), 5.02 (dd, *J* = 17.1, 1.0 Hz, 1H), 4.94 (dd, *J* = 10.5, 1.0 Hz, 1H), 3.91 (d, *J* = 14.0 Hz, 15H), 2.32 (d, *J* = 3.6 Hz, 4H), 2.00

(d, *J* = 2.7 Hz, 1H), 1.89-1.73 (m, 10H), 1.66 (s, 1H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 149.5, 148.2, 145.7, 143.5, 137.0, 135.2, 128.6, 128.6, 128.3 , 120.1, 119.4, 113.8, 113.6, 113.0, 112.0, 111.9, 111.7, 76.3, 70.3, 70.2, 55.9, 55.9, 36.4, 34.8; HRMS (ESI) calculated for $C_{30}H_{31}O_5$ ([M – H_2O + H]$^+$) *m/z* = 471.2171, found = 471.2161.

Ortho-methoxy-anti-diol: (Isolated in the ring closing metathesis to make **18.4**) R_f = 0.27 (3% Acetone/dichloromethane): R_f = 0.20 (3% acetone/dichloromethane); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.62 (dd, *J* = 5.6, 3.4 Hz, 2H), 7.38 (dd, *J* = 5.6, 3.3 Hz, 2H), 7.22 (dd, *J* = 8.4, 2.2 Hz, 2H), 6.95 (d, *J* = 8.5 Hz, 2H), 6.72 (d, *J* = 2.3 Hz, 2H), 6.00 (dd, *J* = 17.2, 10.6 Hz, 2H), 5.42 (d, *J* = 12.2 Hz, 2H), 5.16-5.00 (m, 4H), 4.95 (dd, *J* = 10.6, 0.9 Hz, 2H), 3.93 (s, 6H), 1.85 (s, 2H), 1.58 (s, 2H); ^{13}C NMR (101 Hz, $CDCl_3$) δ 149.2, 147.9, 145.6, 136.3, 135.1, 128.5, 128.2, 119.3, 113.6, 112.0, 111.8, 70.3, 55.9, 34.8; HRMS (ESI) calculated for $C_{30}H_{32}O_6Na$ ([M + Na]$^+$) *m/z* = 511.2097, found = 511.2027.



SI-5

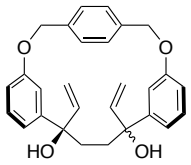
SI-5: This compound was prepared using the *general procedure C* with meta-1,4-diketone **16.4a** (0.146 g, 0.393 mmol) and vinylmagnesium chloride (1.6 M in THF, 0.55 mL, 0.86 mmol) in dichloromethane (4 mL). The residue was purified via flash chromatography (20 × 1.3 cm, 3% acetone/dichloromethane) to give the allylic alcohols as a colorless oil (0.085 g, 51%) as a mixture of diastereomers *meta*-**3** (dr = 3.6:1) and hydroxy-ketone **SI-5** as a colorless oil (0.0550 g, 38%).

Meta-hydroxy-ketone: R_f = 0.53 (3% acetone/dichloromethane); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.48 (d, *J* = 7.6 Hz, 1H), 7.35 -7.27 (m, 6H), 7.25-7.18 (m, 2H), 7.10-7.09 (m, 1H), 6.94 (dd, *J* = 8.2, 2.5 Hz, 1H), 6.83 (t, *J* = 1.9 Hz, 1H), 6.77 (d, *J* = 7.7 Hz, 1H), 6.28 (dd, *J* = 17.4, 10.7 Hz, 1H), 5.42-5.12 (m, 6H), 2.71-2.61 (m, 1H), 2.21-2.06 (m, 2H), 1.63 (s, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 199.3, 157.8, 157.2, 145.4, 144.1, 138.3, 137.9, 137.5, 129.4, 125.6, 124.9, 122.8, 122.4, 119.7, 118.4, 115.6, 113.3, 113.0, 110.5, 70.0, 68.4, 35.8, 32.9; HRMS (ESI) calculated for $C_{26}H_{23}O_3$ [(M – H_2O + H)$^+$] *m/z* = 383.1647, found = 383.1650.

Meta-diol mixture: R_f = 0.27 (3% acetone/dichloromethane); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.30-7.17 (m, 7H), 6.97 (d, *J* = 7.9 Hz, 1H), 6.91 (ddd, *J* = 8.2, 2.5, 1.1 Hz, 2H), 6.82 (dd, *J* = 8.9, 1.9 Hz, 3H), 6.59 (t, *J* = 2.0 Hz, 1H), 5.99 (dd, *J* = 17.2, 10.7 Hz, 2H), 5.34-5.06 (m,8H), 2.73 (s, 2H), 1.76-1.53 (m, 4H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 157.5, 157.5, 147.0, 146.3, 144.1, 143.4, 138.1, 138.0, 129.2, 129.1, 129.1, 125.4, 125.3, 123.6, 118.3, 118.2, 116.0, 115.9, 112.8, 112.5, 110.8, 110.4, 76.2, 69.1, 68.8, 35.0, 34.8; HRMS calculated for $C_{28}H_{25}O_2$ [(M – 2 H_2O + H)$^+$] *m/z* = 393.1855, found 393.1844.

Meta-anti-diol: (Isolated in the ring closing metathesis to make **16.5**) R_f = 0.27 (3% Acetone/dichloromethane); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.30-7.20, (m, 8H), 6.97 (d, *J* = 7.7 Hz, 2H), 6.91 (dd, *J* = 8.2, 2.5 Hz, 2H), 6.60 (dd, *J* = 8.8, 1.9 Hz 2H), 6.00 (dd, *J* = 17.3, 10.7 Hz, 2H), 5.28-5.20 (m, 6H), 5.10 (d, *J* = 10.6 Hz, 2H), 1.70-1.61 (m, 2H), 1.50-1.43 (m, 2H); ^{13}C NMR (101

MHz, $CDCl_3$) δ 157.5, 146.3, 144.1, 138.1, 129.2, 129.0, 125.3, 118.3, 116.0, 112.6, 110.7, 69.1, 34.8; MS calculated for $C_{28}H_{32}NO_4$ [(M + NH_3 + H)$^+$] = 446.2326, found 446.4348.



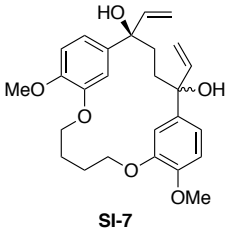
SI-6

SI-6: This compound was prepared using the *general procedure* with para-1,4-diketone **SI-2** (0.101 g, 0.271 mmol) and vinylmagnesium chloride (1.6 M in THF, 0.50 mL, 0.82 mmol) in dichloromethane (3 mL). The solid was purified via flash chromatography (15 × 1.3 cm, 1% acetone/dichloromethane) to give the allylic alcohols **SI-6** as a colorless oil (0.097 g, 84%) as a mixture of diastereomers (dr = 4.9:1) and hydroxy-ketone (0.013g, 12%).

Para-hydroxy-ketone: R_f = 0.55 (1% acetone/dichloromethane); ^{1}H NMR (600 MHz,$CDCl_3$) δ 7.52 (d, *J* = 7.9 Hz, 1H), 7.42 (d, *J* = 7.6 Hz, 1H), 7.40 (m, 2H), 7.34-7.27 (m,1H), 7.22-7.14 (m, 2H), 6.96 (s, 1H), 6.88 (dd, *J* = 8.0, 2.0 Hz, 1H), 6.72-6.66 (m, 2H),6.25 (dd, *J* = 17.3, 10.7 Hz, 1H), 5.40-5.33 (m, 4H), 5.26-5.24 (m, 1H), 5.19 (d, *J* = 10.7Hz, 1H), 5.05 (d, *J* = 14.7 Hz, 1H), 2.60 (ddd, *J* = 19.1, 10.6, 5.2 Hz, 1H), 2.19-2.02 (m, 2H), 1.89 (s, 1H), 1.69-155 (m, 1H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 145.1, 144.7, 138.0, 137.3, 137.2, 129.6, 129.4, 128.3, 127.7, 126.7, 126.0, 123.4, 120.4, 118.5, 116.3, 115.6, 113.0, 111.0, 72.2, 69.3, 35.8, 33.0; HRMS (ESI) calculated for $C_{26}H_{23}O_3$ ([M-(H_2O)+H]$^+$) *m/z* = 383.1647, found 383.1628

Para-diol mixture: R_f = 0.27 (1% acetone/dichloromethane); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.31 (s, 4H), 7.19 (t, *J* = 7.9 Hz, 2H), 6.93-6.87(m, 4H), 6.41-6.40 (m, 2H), 6.03 (dd, *J* = 17.2, 10.6 Hz, 2H), 5.30(d, *J* = 14.2 Hz, 2H), 5.21-5.13 (m, 4H), 5.07 (dd, *J* = 10.6, 0.9 Hz,2H), 1.76 (s, 2H), 1.48-1.44 (m, 2H), 1.18-1.11 (m, 2H); ^{13}C NMR (151 MHz, CDCl3) δ 157.8, 147.1, 143.5, 137.2, 129.3, 127.1, 118.1, 116.5, 113.4, 111.4, 76.7, 69.9, 36.3; HRMS (ESI) calculated for $C_{28}H_{25}O_2$ ([M-(2H_2O)+H]$^+$) *m/z* = 393.1855, found 393.1840.

Para-anti-diol: (Isolated in the ring closing metathesis to make **SI-9**) R_f = 0.27 (3% Acetone/dichloromethane): R_f = 0.27 (1% acetone/dichloromethane); (Isolated in the ring closing metathesis to make 6): R_f = 0.27 (3% Acetone/dichloromethane) ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.31 (s, 4H), 7.19 (m, 2H), 6.94-6.86 (m, 4H), 6.41 (dd, J = 2.6, 1.6 Hz, 2H), 6.03 (dd, J = 17.2, 10.6 Hz, 2H), 5.31 (d, J = 14.3 Hz, 2H), 5.22-5.11 (m, 4H), 5.08 (dd, J = 10.6, 1.0 Hz, 2H), 1.76 (s, 2H), 1.53-1.44 (m, 2H), 1.21-1.11 (m, 2H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 157.4, 146.2, 144.5, 137.2, 129.5, 127.1, 117.4, 116.6, 112.8, 111.4, 76.5, 69.7, 35.5, 29.9; HRMS (ESI) calculated for $C_{28}H_{25}O_2$ ([M-(2H_2O)+H]$^+$) m/z = 393.1855, found 393.1840.



SI-7

SI-7: This compound was prepared using the *general procedure C* with methoxy-diketone **19.5** (0.20 g, 0.52 mmol) and vinylmagnesium chloride (1.6 M in THF, 0.82 mL, 1.3 mmol) in dichloromethane (5.2 mL). The residue was purified via flash chromatography (15 × 2.5 cm, 5% acetone/dichloromethane to 10% acetone/dichloromethane) to afford the methoxy-diol **SI-7** as a white

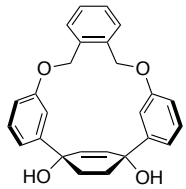
solid (0.10 g, 45%) as a mixture of diastereomers (dr = 7.4:1) and the monoreacted, methoxy-hydroxy-ketone (0.012 g, 6%). *This reaction was performed by Nirmal Mitra.*

Methoxy-hydroxy-ketone: R_f = 0.35 (4% acetone/dichloromethane); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.70 (dd, *J* = 8.5, 2.1 Hz, 1H), 7.13 (d, *J* = 2.2 Hz, 1H), 7.01-6.74 (m, 4H), 6.22 (dd, *J* = 17.3, 10.6 Hz, 1H), 5.30 (d, *J* = 17.3 Hz, 1H), 5.15 (d, *J* = 10.7 Hz, 1H), 4.31 (m, 2H), 4.25-4.03 (m, 3H), 3.90 (d, *J* = 18.8 Hz, 9H), 2.87 (d, *J* = 7.3 Hz, 1H), 2.58-2.38 (m, 2H), 2.27 (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 200.1, 154.6, 149.1, 146.9, 146.5, 144.4, 136.2, 129.6, 123.1, 119.0, 117.5, 113.1, 112.7, 111.9, 111.7, 69.7, 68.5, 55.8, 38.0, 32.7, 25.4, 25.1; HRMS (ESI) calculated for $C_{24}H_{28}O_6Na$ ([M + Na]$^+$) *m/z* = 435.1784, found = 435.1780.

Methoxy-diol mixture: R_f = 0.18 (4% acetone/dichloromethane); ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.90 (dt, *J* = 4.2, 2.1 Hz, 4H), 6.80 (d, *J* = 8.8 Hz, 2H), 6.23 (dd, *J* = 17.2, 10.7 Hz, 2H), 5.32 (d, *J* = 17.2 Hz, 2H), 5.18 (d, *J* = 10.7 Hz, 2H), 4.28-4.06 (m, 5H), 3.86 (d, *J* = 7.9 Hz, 8H), 2.59 (s, 2H), 1.98-1.82 (m, 5H), 1.82-1.65 (m, 5H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 148.9, 147.5, 143.1, 137.4, 118.5, 113.1, 112.4, 111.0, 67.9, 55.7, 36.9, 25.1; HRMS (ESI) calculated for $C_{26}H_{32}O_6Na$ ([M + Na]$^+$) *m/z* = 463.2097, found = 463.2085.

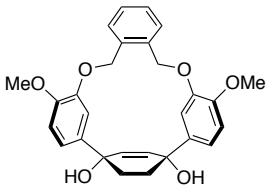
Methoxy-anti-diol: (Isolated in the ring closing metathesis to make meta-cyclohex-2-ene-1,4-diol **SI-10**) R_f = 0.27 (3% Acetone/dichloromethane): R_f = 0.45 (15% acetone/dichloromethane); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.13 (dd, *J* = 8.4, 2.1 Hz, 2H), 6.87 (d, *J* = 8.4 Hz, 2H), 6.49 (d, *J* = 2.1 Hz, 2H), 6.08 (dd, *J* = 17.2, 10.6 Hz, 2H), 5.16-5.07 (m, 2H), 5.06-4.98 (m, 2H), 4.20-4.11 (m, 2H), 4.08-3.99 (m, 2H), 3.88 (s, 8H), 1.90-1.80 (m, 5H), 1.63-1.52 (m, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 148.7, 147.2, 145.3, 136.4, 117.9, 112.2, 112.0, 111.1, 76.3, 67.4, 55.7, 35.5, 24.8; HRMS (ESI) calculated for $C_{26}H_{32}O_6Na$ ([M + Na]$^+$) *m/z* = 463.2097, found = 463.2085.

General Procedure D for the formation of cyclohex-2-ene-1,4-diols:



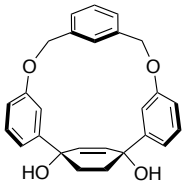
15.5

15.5: Hoveyda-Grubbs second-generation catalyst (0.0056 g, 0.0090 mmol) was added to a stirred solution of *syn*- and *anti*- allylic alcohols **SI-3** (0.152 g, 0.358 mmol) in dichloromethane and the reaction was heated to 40 °C. After 4 h, the mixture was concentrated under reduced pressure and the residue was purified via flash chromatography (20 × 1.3 cm, 1:1 EtOAc/hexanes) to give ortho-cyclohex-2-ene-1,4-diol **15.5** as a white solid (0.0928 g, 65%). R_f = 0.27 (3:7 EtOAc/hexanes); ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.57-7.47 (m, 1H), 7.28-7.17 (m, 4H), 7.16-7.11 (m, 2H), 6.91 (ddd, *J* = 7.9, 2.5, 1.3 Hz, 2H), 6.60-6.47 (m, 2H), 5.83 (s, 2H), 5.27-5.15 (m, 4H), 1.97-1.84 (m, 2H), 1.38 (dt, *J* = 10.3, 6.4 Hz, 2H); ^{13}C NMR (101 MHz, DMSO-d_6) δ 157.7, 150.3, 138.7, 134.0, 129.7, 129.2, 125.7, 125.3, 119.2, 116.2, 112.5, 71.1, 70.1, 36.5. HRMS (ESI) calculated for $C_{26}H_{23}O_3$ ([M – (*H_2O*) + H]$^+$) *m/z* = 383.1647, found 383.1661.



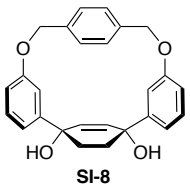
18.4

18.4: This compound was prepared using the *general procedure D* with ortho-methoxy-diol **SI-4** (0.0553 g, 0.113 mmol) and Grubbs II (0.0025 g, 0.0028 mmol) in dichloromethane (2.2 mL). The residue was purified via flash chromatography (15 × 1.3 cm, 8% acetone/dichloromethane to 14% acetone/dichloromethane) to afford methoxy-cyclohex-2-ene-1,4-diol **18.4** as a white solid (0.037 g, 71%): R_f = 0.20 (8% acetone/dichloromethane); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.43 (dd, *J* = 5.7, 3.5 Hz, 2H), 7.31 (dd, *J* = 8.4, 2.2 Hz, 2H), 7.22 (dd, *J* = 5.8, 3.3 Hz, 2H), 6.97 (d, *J* = 8.5 Hz, 2H), 6.71 (d, *J* = 2.2 Hz, 2H), 5.68 (s, 2H), 5.45 (d, *J* = 14.4 Hz, 2H), 5.29 (d, *J* = 14.4 Hz, 2H), 3.97 (s, 6H), 2.10 (d, *J* = 4.2 Hz, 2H), 2.01 (td, *J* = 10.0, 3.3 Hz, 2H), 1.72 (td, *J* = 10.2, 9.7, 2.9 Hz, 2H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 148.8, 146.4, 138.6, 134.4, 133.6, 127.7, 126.6, 117.8, 113.3, 111.9, 72.2, 68.0, 55.9, 36.2; HRMS (ESI) calculated for $C_{28}H_{27}O_5$ ($[M - H_2O + H]^+$) *m/z* = 443.1858, found = 443.1837.



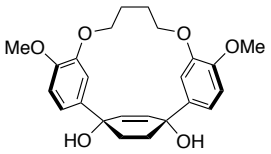
16.5

16.5: This compound was prepared using the *general procedure D* with meta-diol **SI-5** (0.225 g, 0.530 mmol) and Hoveyda-Grubbs II (0.0097g, 0.013 mmol) in dichloromethane (5.3 mL). The residue was purified via flash chromatography (16 × 1 cm, 2:3 EtOAc/hexanes to 3:1 EtOAc/hexanes) to recover the uncyclized *trans*-diol as an off-white oil (0.0452 g, 22%) and to give the cyclized product **16.5** as a white solid (0.118 g, 55%): R_f = 0.20 (2:3 EtOAc/hexanes); ^{1}H NMR (400 MHz, DMSO-D6) δ 6.72 (d, *J* = 1.8 Hz, 1H), 6.47-6.38 (m, 5H), 6.34 (dd, *J* = 7.4, 1.8 Hz, 2H), 6.11 (ddd, *J* = 7.9, 2.5, 1.3 Hz, 2H), 5.74 (dd, *J* = 2.5, 1.5 Hz, 2H), 5.03 (s, 2H), 4.48-4.34 (m, 7H), 1.70 (p, *J* = 1.9 Hz, 2H), 1.16-1.05 (m, 2H), 0.58 (dt, *J* = 10.3, 6.1 Hz, 2H); ^{13}C NMR (101 MHz, DMSO-D6) δ 157.6, 150.1, 138.6, 133.9, 129.6, 129.1, 125.6, 125.2, 119.1, 116.1, 112.4, 71.0, 70.0, 36.3; HRMS calculated for $C_{26}H_{23}O_3$ [$(M - 1\ H_2O + H)^+$] *m/z* = 383.1647, found = 383.1631.



SI-8

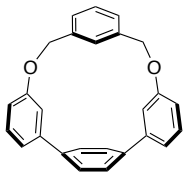
SI-8: This compound was prepared using the *general procedure* with para-diol **SI-6** (0.077 g, 0.18 mmol) and Hoveyda-Grubbs II (0.005 g, 0.0004 mmol) in dichloromethane (2 mL). The residue was purified via flash chromatography (15 × 2.5 cm, 2:3 EtOAc/hexanes) to recover uncyclized *trans*-diol *para*-**7** (0.013 g) and to give the cyclized product **SI-8** as an off-white solid (0.037 g, 51%): R_f = 0.14 (2:3 EtOAc/hexanes); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.33-7.31 (m, 4H), 7.28-7.26 (m, 2H), 7.19-7.19 (m, 2H), 7.01-6.99 (m, 2H), 6.17 (s, 2H), 5.89 (s, 2H), 5.24 (d, *J* = 13.8 Hz, 2H), 5.05 (d, *J* = 13.8 Hz, 2H), 2.10-2.06 (m, 4H), 1.78-1.74 (m, 2H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 158.0, 147.2, 137.5, 134.2, 130.2, 127.6, 127.5, 119.6, 118.5, 114.3, 72.7, 71.9, 35.4; HRMS (ESI) calculated for $C_{26}H_{23}O_3$ ($[M-(H_2O)+H]^+$) *m/z* = 383.1647, found 383.1629. *This reaction was run by Rolande Meudom.*



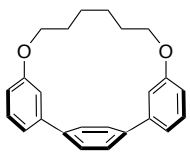
SI-9

SI-9: This compound was prepared using the *general procedure D* with methoxy-diol **SI-7** (0.10 g, 0.22 mmol) and Grubbs II (0.0096 g, 0.011 mmol) in dichloromethane (10 mL). The residue was purified via flash chromatography (15 × 1.3 cm, 3:2 EtOAc/hexanes to 4:1 EtOAc/hexanes) to afford the methoxy-cyclohex-2-ene-1,4-diol **SI-9** as a white solid (0.075 g, 82%): R_f = 0.22 (3:2 EtOAc/hexanes); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.30 (dd, *J* = 8.4, 2.1 Hz, 2H), 6.96 (d, *J* = 2.2 Hz, 2H), 6.91 (d, *J* = 8.5 Hz, 2H), 5.92 (s, 2H), 4.35-4.26 (m, 2H), 4.08 (q, *J* = 5.6 Hz, 2H), 3.85 (s, 6H), 2.58 (s, 2H), 2.17-2.02 (m, 2H), 2.02-1.80 (m, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 149.3, 146.7, 138.6, 134.4, 118.4, 114.7, 112.3, 72.3, 70.4, 55.8, 36.2, 26.0; HRMS (ESI) calculated for $C_{24}H_{27}O_5$ ($[M - H_2O + H]^+$) *m/z* = 395.1858, found = 395.1859.

General Procedure E for the Aromatization via TsOH:

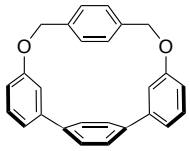

16.6

16.6: (Table 2, Entry 6). *para*-Toluenesulfonic acid monohydrate (0.129 g, 0.677 mmol) was added to a stirred, 80 °C solution of meta-cyclohex-2-ene-1,4-diol **16.5** (0.031 g, 0.075 mmol) in Toluene (1.5 mL). After 1.5 h the reaction was quenched with a saturated solution of $NaHCO_3$ (3 mL). The aqueous layer was extracted with dichloromethane (3 × 3 mL). The combined organic extracts were washed with brine (5 mL), dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified via flash chromatography (15 × 0.5 cm, 1:3 dichloromethane/hexanes to dichloromethane to 2% acetone/dichloromethane) to afford meta-PTPP **16.6** as a white powder (0.022 g, 74%): R_f = 0.47 (3:7 dichloromethane/hexanes); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.35-7.29 (m, 2H), 7.22-7.15 (m, 4H), 7.09-7.07 (m, 2H), 7.05-7.03 (m, 2H), 6.92 (dd, *J* = 8.2, 2.8 Hz, 2H), 5.62 (dd, *J* = 2.7, 1.5 Hz, 2H), 5.17 (s, 4H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 157.3, 144.3, 143.4, 139.0, 129.7, 129.7, 129.0, 124.7, 121.7, 120.2, 116.0, 115.1, 70.7, 29.7; HRMS (ESI) calculated for $C_{26}H_{21}O_2$ ($[M + H]^+$) *m/z* = 365.1542, found 365.1547. *This reaction was run by Nirmal Mitra.*


T2.2f

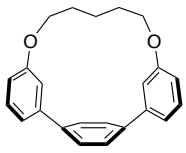
T2.2f: (Table 2, Entry 1). This compound was prepared using the *general procedure E* with previously reported n = 8 cyclohex-2-ene-1,4-diol **T2.1f** (0.184 g, 0.484 mmol) and TsOH•H_2O (0.502 g. 2.92 mmol) in Toluene (20 mL). The residue was purified via flash chromatography (15 × 1.3 cm, 1:1 dichloromethane/hexanes) to afford n = 8 PTPP **T2.2f** as a white solid (0.120 g, 74%). *This reaction was run by Nirmal Mitra.*

T2.2f: (Table 2, Entry 2). This compound was prepared using the *general procedure E* with previously reported n = 8 cyclohex-2-ene-1,4-diol **T2.1f** (0.30 g, 0.79 mmol) and TsOH•H_2O (0.75 g. 3.9 mmol) in Toluene (24 mL). The residue was purified via flash chromatography (15 × 1.3 cm, 1:1 dichloromethane/hexanes) to afford n = 8 PTPP **T2.2f** as a white solid (0.180 g, 66%). *This reaction was run by Nirmal Mitra.*



T2.2a

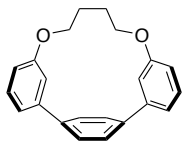
T2.2a: (Table 2, Entry 3). This compound was prepared using the *general procedure E* with para-cyclohex-2-ene-1,4-diol **T2.1s** (0.009 g, 0.02 mmol) and TsOH•H_2O (0.022 g, 0.011 mmol) in Toluene (1 mL). The residue was purified via flash chromatography (10 × 0.5 cm, 5% EtOAc/hexanes to 10% EtOAc/hexanes) to afford para-PTPP **T2.2a** as a white solid (0.0025 g, 32%): R_f = 0.30 (1:4 dichloromethane/hexanes); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.34-7.32 (m, 2H), 7.19 (d, J = 7.3 Hz, 2H), 7.08 (s, 4H), 7.01 (s, 4H), 6.93 (dd, J = 8.3, 2.3 Hz, 2H), 5.41 (s, 2H), 5.15 (s, 4H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 157.5, 144.5, 143.3, 137.4, 129.8, 128.9, 125.7, 121.4, 116.8, 115.8, 71.4; HRMS (ESI) calculated for $C_{26}H_{20}O_2$ ([M+H]$^+$) *m/z* = 364.1463, found 364.1457. *This reaction was run by Rolande Meudom.*



T2.2e

T2.2e: (Table 2, Entry 4). This compound was prepared using the *general procedure E* with previously reported n = 7 cyclohex-2-ene-1,4-diol **T2.1e** (0.390 g, 1.07 mmol) and TsOH•H_2O (1.22 g, 6.39 mmol) in Toluene (50 mL). The residue was purified via flash chromatography (15 × 2.5 cm, 1:19 EtOAc/hexanes) to afford n = 7 PTPP **T2.2e** as a white solid (0.288 g, 82%). *This reaction was run by Nirmal Mitra.*

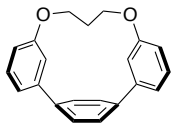
T2.2e: (Table 2, Entry 5). This compound was prepared using the *general procedure E* with previously reported n = 7 cyclohex-2-ene-1,4-diol **T2.1e** (0.012 g, 0.032 mmol) and TsOH•H_2O (0.31 g, 0.19 mmol) in Toluene (1.5 mL). The residue was purified via flash chromatography (10 × 0.5 cm, 1:1 dichloromethane/hexanes) to afford a 2:1 mixture of the desired n = 7 PTPP **T2.2e** (total mass of 0.0061 g, 38%) and the rearranged, n = 7 MTPP (19%). *This reaction was run by Nirmal Mitra.*



T2.2d

T2.2d: (Table 2, Entry 7). This compound was prepared using the *general procedure E* with previously reported n = 6 cyclohex-2-ene-1,4-diol **T2.1d** (0.040 g, 0.11 mmol) and TsOH•H_2O (0.130 g, 0.684 mmol) in Toluene (6 mL). The residue was purified via flash chromatography (15 × 1.3 cm, 1:19 EtOAc/hexanes) to afford n = 6 PTPP **T2.2d** as a white solid (0.015 g, 42%). *This reaction was run by Nirmal Mitra.*

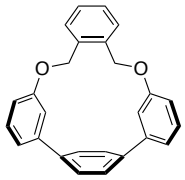
T2.2d: (Table 2, Entry 8). This compound was prepared using the *general procedure E* with previously reported n = 6 cyclohex-2-ene-1,4-diol **T2.1d** (0.015 g, 0.043 mmol) and TsOH•H_2O (0.050 g, 0.26 mmol) in Toluene (5 mL). The residue was purified via flash chromatography (10 × 0.5 cm, 1:1 dichloromethane/hexanes), however the only isolated product was the rearranged, n = 6 MTPP **T2.2d** (0.006 g). *This reaction was run by Nirmal Mitra.*



T2.2c

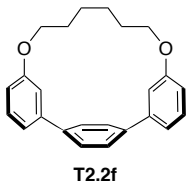
T2.2c: (Table 1A, Entry 9). This compound was prepared using the *general procedure E* with previously reported n = 5 cyclohex-2-ene-1,4-diol **T2.1c** (0.012 g, 0.038 mmol) and TsOH•H_2O (0.060 g, 0.31 mmol) in Toluene (2.5 mL). The residue was purified via flash chromatography (7 × 0.5 cm, 1:1 dichloromethane/hexanes), however the only isolated product was the rearranged, n = 5 MTPP **T2.2c** (0.004 g). *This reaction was run by Nirmal Mitra.*

General Procedure F for the Aromatization via Burgess Reagent in Toluene:



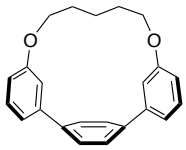
15.6

15.6: Burgess Reagent (0.027 g, 0.11 mmol) was added to a stirred solution of ortho-cyclohex-2-ene-1,4-diol **15.5** (0.0151 g, 0.0375 mmol) in Toluene (1 mL) and the reaction was heated to 80 °C. After 2 h, the reaction mixture was poured into water (5 mL). The resulting mixture was extracted with dichloromethane (3 × 5 mL). The combined organic extracts were dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified via flash chromatography (12.5 × 0.5 cm, 1:1 dichloromethane/hexanes) to give ortho-PTPP **15.6** as a white powder (0.0064 g, 47%). R_f = 0.61 (1:1 dichloromethane/hexanes); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37-7.29 (m, 4H), 7.20 (dt, *J* = 7.4, 1.1 Hz, 2H), 7.16 (dd, *J* = 5.9, 3.4 Hz, 2H), 7.07 (s, 4H), 7.00 (ddd, *J* = 8.3, 2.9, 0.9 Hz, 2H), 4.98 (s, 4H), 4.92 (dd, *J* = 2.9, 1.4 Hz, 2H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 156.0, 144.0, 132.6, 130.2, 129.4, 127.3, 125.4, 119.0, 116.0, 115.7, 65.9; HRMS (EI) calculated for $C_{26}H_{20}O_2$ [M^+] = 364.1463, found 364.1449. HRMS (ESI) calculated for $C_{26}H_{20}O_2$ [M^+] *m/z* = 364.1463, found 364.1449.



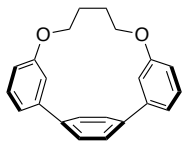
T2.2f

T2.2f (Table 2, Entry 10).This compound was prepared using the *general procedure F* with previously reported n = 8 cyclohex-2-ene-1,4-diol **T2.1f** (0.031 g, 0.081 mmol) and Burgess Reagent (0.062 g, 0.26 mmol) in Toluene (2 mL). The residue was purified via flash chromatography (10 × 0.5 cm, 1:1 dichloromethane/hexanes) to afford n = 8 PTPP **T2.2f** as a white solid (0.017 g, 61%). *This reaction was run by Nirmal Mitra.*



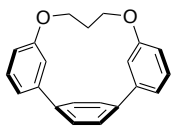
T2.2e

T2.2e: (Table 2, Entry 11).This compound was prepared using the *general procedure F* with previously reported n = 7 cyclohex-2-ene-1,4-diol **T2.1e** (0.026 g, 0.071 mmol) and Burgess Reagent (0.080 g, 0.34 mmol) in Toluene (1.5 mL). The residue was purified via flash chromatography (10 × 0.5 cm, 1:1 dichloromethane/hexanes) to afford n = 7 PTPP **T2.2e** as a white solid (0.016 g, 68%). *This reaction was run by Nirmal Mitra.*



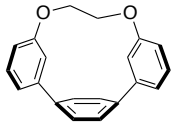
T2.2d

T2.2d: (Table 2, Entry 12). This compound was prepared using the *general procedure F* with previously reported n = 6 cyclohex-2-ene-1,4-diol **T2.1d** (0.010 g, 0.028 mmol) and Burgess Reagent (0.020 g, 0.084 mmol) in Toluene (2 mL). The residue was purified via flash chromatography (10 × 0.5 cm, 2:3 dichloromethane/hexanes) to afford n = 6 PTPP **T2.2d** as a white solid (0.005 g, 56%). *This reaction was run by Nirmal Mitra.*



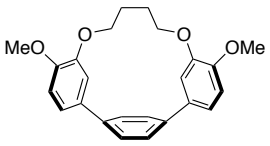
T2.2c

T2.2c: (Table 2, Entry 13). This compound was prepared using the *general procedure F* with previously reported n = 5 cyclohex-2-ene-1,4-diol **T2.1c** (0.008 g, 0.03 mmol) and Burgess Reagent (0.018 g, 0.075 mmol) in Toluene (2.5 mL). The residue was purified via flash chromatography (10 × 0.5 cm, 1:1 dichloromethane/hexanes) to afford n = 5 PTPP **T2.2c** as a white solid (0.0045 g, 60%). *This reaction was run by Nirmal Mitra.*



T2.2b

T2.2b: (Table 2, Entry 14). This compound was prepared using the *general procedure F* with previously reported n = 4 cyclohex-2-ene-1,4-diol **T2.1b** (0.01 g, 0.03 mmol) and Burgess Reagent (0.025 g, 0.11 mmol) in toluene (2 mL). The residue was purified via flash chromatography (10 × 0.5 cm, dichloromethane). This reaction only produced the desired n = 4 PTPP **T2.2b** in trace amounts. *This reaction was run by Nirmal Mitra.*

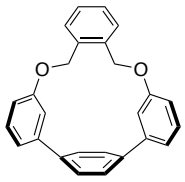


SI-10

SI-10: This compound was prepared using the *General Procedure F* with methoxy-cyclohex-2-ene-1,4-diol **SI-9** (0.040 g, 0.097 mmol) and Burgess Reagent (0.12 g, 0.48 mmol) in toluene (9 mL). The residue was purified via flash chromatography (12 × 1 cm, dichloromethane to 5% acetone/dichloromethane) to afford methoxy-PTPP **SI-10** as a white solid (0.017 g, 47%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34 (s, 4H), 7.19 (dd, *J* = 8.0, 1.9 Hz, 2H), 6.91 (d, *J* = 8.0 Hz, 2H), 5.30 (d, *J* = 1.9 Hz, 2H), 4.00 (s, 4H), 3.91 (s, 6H), 2.19 (s, 1H), 1.61 (s, 1H), 1.45 (q, *J* = 3.8, 3.4 Hz, 4H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 147.6, 145.2, 143.8, 136.1, 118.2, 115.2, 110.8, 67.5, 55.9, 22.3;

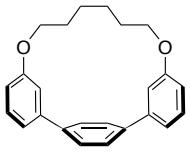
HRMS (ESI) calculated for $C_{24}H_{25}O_4$ ([M + H]$^+$) *m/z* = 377.1753, found = 377.1771. *This reaction was run by Nirmal Mitra.*

General Procedure G for the Aromatization via Burgess Reagent in THF:



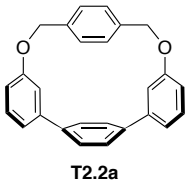
15.6

15.6: (Table 2, Entry 20). Burgess Reagent (0.031 g, 0.13 mmol) was added to a stirred solution of ortho-cyclohex-2-ene-1,4-diol **15.5** (0.023 g, 0.050 mmol) in THF (2 mL) and the reaction was heated to 60 °C. After 4 h, the reaction mixture was poured into water (3 mL). The resulting mixture was extracted with dichloromethane (3 × 3 mL). The combined organic extracts were dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified via flash chromatography (10 × 0.5 cm, 3:7 EtOAc/hexanes to 1:1 EtOAc/hexanes) to give ortho-PTPP **15.6** as a white powder (0.0190 g, 67%).



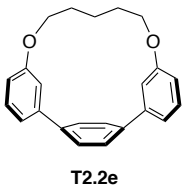
T2.2f

T2.2f: (Table 2, Entry 15).This compound was prepared using the *general procedure G* with previously reported n = 8 cyclohex-2-ene-1,4-diol **T2.1f** (0.024 g, 0.063 mmol) and Burgess Reagent (0.050 g, 0.21 mmol) in THF (3 mL). The residue was purified via flash chromatography (12 × 0.5 cm, 2:3 dichloromethane/hexanes) to afford n = 8 PTPP **T2.2f** as a white solid (0.014 g, 64%). *This reaction was run by Nirmal Mitra.*



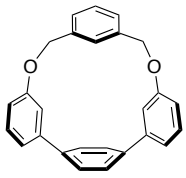
T2.2a

T2.2a: (Table 2, Entry 16). This compound was prepared using the *general procedure G* with para-cyclohex-2-ene-1,4-diol **T2.1a** (0.024 g, 0.060 mmol) and Burgess Reagent (0.036 g, 0.15 mmol) in THF (2.5 mL). The residue was purified by flash chromatography (10 × 0.5 cm, 1:1 dichloromethane/hexanes) to give meta-PTPP **T2.2a** as a white solid (0.015 g, 79%). *This reaction was run by Rolande Meudom.*



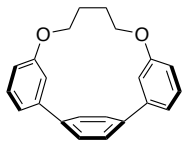
T2.2e

T2.2e: (Table 2, Entry 17). This compound was prepared using the *general procedure G* with previously reported n = 7 cyclohex-2-ene-1,4-diol **T2.1e** (0.025 g, 0.068 mmol) and Burgess Reagent (0.052 g, 0.21 mmol) in THF (2 mL). The residue was purified via flash chromatography (12 × 0.5 cm, 1:1 dichloromethane/hexanes) to afford n = 7 PTPP **T2.2e** as a white solid (0.011 g, 52%). *This reaction was run by Nirmal Mitra.*



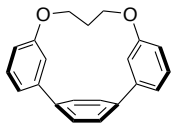
16.6

16.6: (Table 2, Entry 18).This compound was prepared using the *general procedure G* with meta-cyclohex-2-ene-1,4-diol **16.5** (0.024 g, 0.060 mmol) and Burgess Reagent (0.043 g, 0.18 mmol) in THF (3 mL). The residue was purified via flash chromatography (10 × 0.5 cm, 1:1 dichloromethane/hexanes) to give meta-PTPP **16.6** as a white powder (0.013 g, 61%).



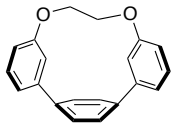
T2.2d

T2.2d: (Table 2, Entry 19). This compound was prepared using the *general procedure G* with previously reported n = 6 cyclohex-2-ene-1,4-diol **T2.1d** (0.060 g, 0.17 mmol) and Burgess Reagent (0.10 g, 0.43 mmol) in THF (1 mL). The residue was purified via flash chromatography (14 × 1.3 cm, 1:19 EtOAc/hexanes) to afford the n = 6 PTPP **T2.2d** as a white solid (0.040 g, 75%). *This reaction was run by Nirmal Mitra.*



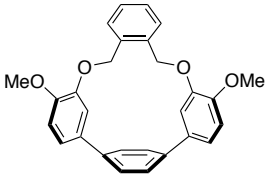
T2.2c

T2.2c: (Table 2, Entry 21). This compound was prepared using the *general procedure G* with previously reported n = 5 cyclohex-2-ene-1,4-diol **T2.1c** (0.008 g, 0.024 mmol) and Burgess Reagent (0.038 g, 0.11 mmol) in THF (2 mL). The residue was purified via flash chromatography (10 × 0.5 cm, 3:7 dichloromethane/hexanes) to afford n = 5 PTPP **T2.2c** as a white solid (0.0015 g, 21%). *This reaction was run by Nirmal Mitra.*



T2.2b

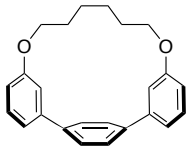
T2.2b: (Table 2, Entry 22). This compound was prepared using the *general procedure G* with previously reported n = 4 cyclohex-2-ene-1,4-diol **T2.1b** (0.010 g, 0.033 mmol) and Burgess Reagent (0.016 g, 0.066 mmol) in THF (2 mL). The residue was purified via flash chromatography (5 × 0.7 cm, dichloromethane to 2% acetone/dichloromethane), however this reaction only produced the monodehydrated product (0.007 g, 68%). *This reaction was run by Nirmal Mitra.*



18.5

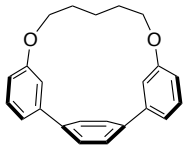
18.5: This compound was prepared using the *general procedure G* with methoxy-cyclohex-2-ene-1,4-diol **18.4** (0.020 g, 0.043 mmol) and Burgess Reagent (0.031 g, 0.13 mmol) in THF (2 mL). The residue was purified via flash chromatography (10 × 0.5 cm, 3:7 EtOAc/hexanes to 1:1 EtOAc/hexanes) to afford the methoxy-PTPP **18.5** as a white solid (0.012 g, 67%): R_f = 0.37 (3:7 EtOAc/hexanes); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.32 (dd, *J* = 5.7, 3.5 Hz, 2H), 7.16 (dd, *J* = 5.9, 3.3 Hz, 2H), 7.12 (dd, *J* = 8.0, 1.9 Hz, 2H), 7.03 (s, 3H), 6.90 (d, *J* = 8.0 Hz, 2H), 5.05 (s, 4H), 4.92 (d, *J* = 2.0 Hz, 2H), 4.00 (s, 6H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 147.7, 145.2, 143.6, 135.6, 132.2, 130.5, 127.4, 125.4, 120.0, 115.7, 110.5, 66.7, 56.1; HRMS (ESI) calculated for $C_{28}H_{25}O_4$ ($[M + H]^+$) *m/z* = 425.1753, found = 425.1753

General Procedure H for the Aromatization via $SnCl_2 \bullet 2H_2O$:



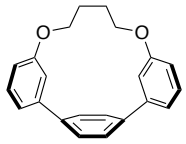
T2.2f

T2.2f: (Table 2, Entry 23). Tin(II) chloride dehydrate (0.12 g, 0.54 mmol) was added to a stirred solution of previously reported n = 8 cyclohex-2-ene-1,4-diol **T2.1f** (0.010 g, 0.027 mmol) in 1:1 THF/Toluene (2 mL) at 80 °C. After 48 h the reaction was cooled to room temperature and was quenched with 3 M NaOH (2 mL) then diluted with dichloromethane (2 mL). The aqueous material was extracted with dichloromethane (3 × 2 mL). The combined organic extracts were washed with brine (5 mL), dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified via flash chromatography (10 × 0.5 cm, 1:1 dichloromethane/hexanes) to afford n = 8 PTPP **T2.2f** as a white solid (0.005 g, 52%). *This reaction was run by NIrmal Mitra.*



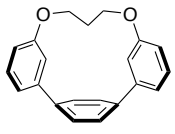
T2.2e

T2.2e: (Table 2, Entry 24).This compound was prepared using the *general procedure H* with previously reported n = 7 cyclohex-2-ene-1,4-diol **T2.1e** (0.010 g, 0.027 mmol) and tin(II) chloride dihydrate (0.13 g, 0.54 mmol) in 1:1 THF/Toluene (3 mL). The reaction was purified via flash chromatography (10 × 0.5 cm, 1:1 dichloromethane/hexanes) to afford n = 7 PTPP **T2.2e** as a white solid (0.0041 g, 46%). *This reaction was run by Nirmal Mitra.*



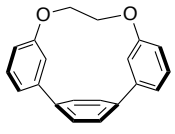
T2.2d

T2.2d: (Table 2, Entry 25). This compound was prepared using the *general procedure H* with previously reported n = 6 cyclohex-2-ene-1,4-diol **T2.1d** (0.010 g, 0.028 mmol) and tin(II) chloride dihydrate (0.064 g, 0.28 mmol) in 1:1 THF/Toluene (2 mL). The residue was purified via flash chromatography (10 × 0.5 cm, 1:9 EtOAc/hexanes), however this reaction only produced the monodehydrated product **T2.2d** (0.006 g, 62%).



T2.2c

T2.2c: (Table 2, Entry 26). This compound was prepared using the *general procedure H* with previously reported n = 5 cyclohex-2-ene-1,4-diol **T2.1c** (0.008 g, 0.02 mmol) and tin(II) chloride dihydrate (0.053 g, 0.23 mmol) in 1:1 THF/Toluene (4 mL). The residue was purified via flash chromatography (4 × 0.7 cm, dichloromethane, 2% acetone/dichloromethane), however this reaction only produced the monodehydrated product **T2.2c** (0.006 g, 78%). *This reaction was run by Nirmal Mitra.*

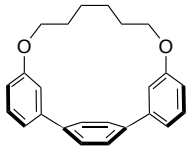


T2.2b

T2.2b: This compound was prepared using the *general procedure H* with previously reported n = 4 cyclohex-2-ene-1,4-diol **T2.1b** (0.040 g, 0.14 mmol) and tin(II) chloride dihydrate (0.625 g, 2.77 mmol) in 1:1 THF/Toluene (6 mL). The

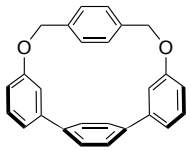
residue was purified via flash chromatography (12 × 1.3 cm, 4% acetone/dichloromethane), however this reaction only produced the monodehydrated product **T2.2b** (0.025 g, 60%). *This reaction was run by Nirmal Mitra.*

General Procedure I for the Aromatization via Tf_2O:



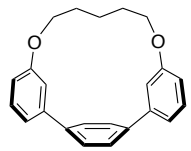
T2.2f

T2.2f: (Table 2, Entry 27).Trifluoromethanesulfonic anhydride (0.024 g, 0.087 mmol) and N,N-diisopropylethylamine (0.070 g, 0.48 mmol) were added to a stirred solution of n = 8 cyclohex-2-ene-1,4-diol **T2.1f** (0.011 g, 0.028 mmol) in dichloromethane (1.5 mL) at 0 °C. After 15 min, the reaction was warmed to room temperature, poured into water (1.5 mL), and further diluted with 1 M HCl (1.5 mL). The aqueous material was extracted with dichloromethane (3 × 3 mL). The combined organic extracts were washed with a saturated solution of $NaHCO_3$ (5 mL) and brine (5 mL), dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified via flash chromatography (10 × 0.5 cm, 1:1 dichloromethane/hexanes) to afford n= 8 PTPP **T2.2f** as a white solid (0.004 g, 42%). *This reaction was run by Rolande Meudom.*



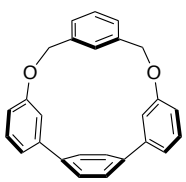
T2.2a

T2.2a: (Table 2, Entry 28). This compound was prepared using the *general procedure I* with para-cyclohex-2-ene-1,4-diol **T2.1a** (0.010 g, 0.025 mmol), Tf_2O (0.022 g, 0.075 mmol), and DIPEA (0.1 mL, 0.07 g, 0.6 mmol) in dichloromethane (2 mL). The residue was purified via flash chromatography (10 × 0.5 cm, 1:1 dichloromethane/hexanes) to afford para-PTPP **T2.2a** as a white solid (0.0038 g, 42%). *This reaction was run by Rolande Meudom.*



T2.2e

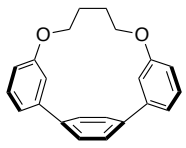
T2.2e: (Table 2, Entry 29). This compound was prepared using the *general procedure I* with previously reported n = 7 cyclohex-2-ene-1,4-diol **T2.1e** (0.010 g, 0.026 mmol), Tf_2O (0.025 g, 0.052 mmol), and DIPEA (0.034 g, 0.026 mmol) in dichloromethane (1.5 mL). The residue was purified via flash chromatography (10 × 0.5 cm, 1:1 dichloromethane/hexanes) to afford n = 8 PTPP **T2.2e** as a white solid (0.004 g, 44%). *This reaction was run by Nirmal Mitra.*



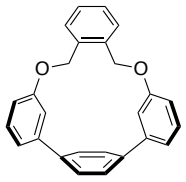
16.6

16.6: (Table 2, Entry 30).This compound was prepared using the *general procedure I* with meta-cyclohex-2-ene-1,4-diol **16.5** (0.018 g, 0.042 mmol), Tf_2O (0.044 g, 0.126 mmol), and DIPEA (0.15 mL, 0.11 g, 0.84 mmol) in dichloromethane (3 mL). The residue was purified via flash chromatography (10

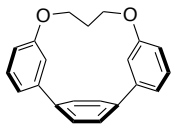
× 0.5 cm, 1:1 dichloromethane/hexanes) to afford meta-PTPP **16.6** as a white solid (0.003 g, 20%).


T2.2d

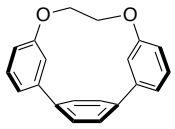
T2.2d: (Table 2, Entry 31). This compound was prepared using the *general procedure I* with previously reported n = 6 cyclohex-2-ene-1,4-diol **T2.1d** (0.010 g, 0.028 mmol), Tf_2O (0.01 mL 0.02 g, 0.09 mmol), and DIPEA (0.01 mL, 0.01 g, 0.09 mmol) in dichloromethane (1 mL). The residue was purified via flash chromatography (10 × 0.5 cm, 3:2 dichloromethane/hexanes) to afford n = 6 PTPP **T2.2d** as a white solid (0.0088 g, 73%). *This reaction was run by NIrmal Mitra.*


15.6

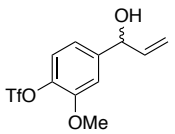
15.6: (Table 2, Entry 32) This compound was prepared using the *general procedure I* with ortho-cyclohex-2-ene-1,4-diol **15.5** (0.010 g, 0.027 mmol), Tf_2O (0.025 g, 0.089 mmol), and DIPEA (0.1 mL, 0.07 g, 0.6 mmol) in dichloromethane (2 mL). This reaction only produced ortho-PTPP **15.6** in trace amount (<5%).


T2.2c

T2.2c: (Table 2, Entry 33). This compound was prepared using the *general procedure I* with previously reported n = 5 monodehydrated material **T2.1c** (0.020 g, 0.062 mmol), Tf_2O (0.088 g, 0.31 mmol), and pyridine (0.5 mL) in dichloromethane (2 mL). The residue was purified via flash chromatography (12 × 0.5 cm, 2:3 dichloromethane/hexanes) to afford n = 5 PTPP **T2.2c** as a white solid (0.003 g, 16%). *This reaction was run by Nirmal Mitra.*


T2.2b

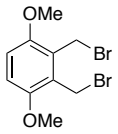
T2.2b: (Table 2, Entry 34). This compound was prepared using the *general procedure I* with previously reported n = 4 monodehydrated material **T2.1b** (0.0015 g, 0.0055 mmol), Tf_2O (0.002 mL, 0.003 g, 0.01 mmol), and DIPEA (0.009 mL, 0.007 g, 0.06 mmol) in dichloromethane (1 mL). The residue was purified via flash chromatography (10 × 0.5 cm, 1:1 dichloromethane/hexanes), however none of the desired, n = 4 PTPP **T2.2b** product was observed. *This reaction was run by Nirmal Mitra.*



19.2

19.2: Vinylmagnesium chloride (0.48 mL, 1.6 M in THF, 0.77 mmol) was added to a stirred, rt solution of **19.1** in dichloromethane (3.6 mL). After 20 min the reaction was quenched with distilled water (15 mL) and 1M HCl (15 mL). The aqueous material was extracted with dichloromethane (3 × 20 mL). The combined organic extracts were washed with a saturated solution of $NaHCO_3$ (25 mL) and brine (25 mL), dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The crude residue was purified via flash chromatography (18 × 1.5 cm; 25% EtOAc/hexanes, 35% EtOAc/hexanes) to afford **19.2** (0.028 g, 26%); R_f = 0.24 (20% EtOAc/hexanes); ^1H NMR (600 MHz, $CDCl_3$) δ 7.19 (d,

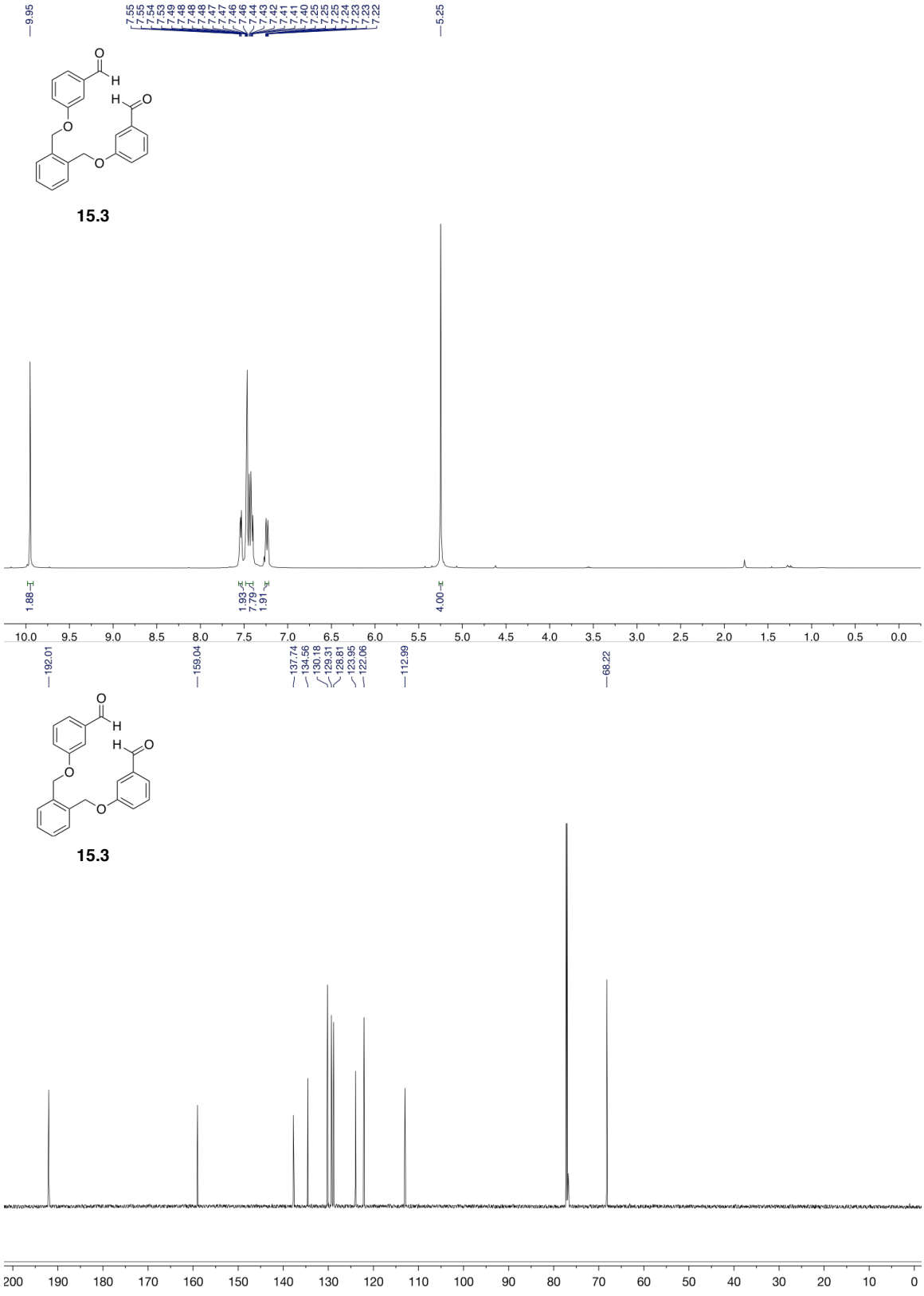
J = 8.4 Hz, 1H), 7.11 (d, *J* = 2.0 Hz, 1H), 6.96 (dd, *J* = 8.3, 2.0 Hz, 1H), 6.01 (ddd, *J* = 16.8, 10.3, 6.3 Hz, 1H), 5.39 (dt, *J* = 17.1, 1.4 Hz, 1H), 5.26 (dt, *J* = 10.2, 1.3 Hz, 1H), 5.22 (d, *J* = 6.3 Hz, 1H), 3.93 (s, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 143.99, 139.49, 137.90, 122.28, 118.52, 116.21, 110.85, 74.75, 56.17.



21.3

21.3: NBS (0.44 g, 2.5 mmol) was added to a stirred, 80 °C solution of **21.2** (0.16 g, 0.99 mmol) and benzoyl peroxide (0.024 g, 0.099 mmol) in CCl_4 (4 mL). The reaction stirred for 4.5 h, at which point it was cooled to room temperature and concentrated under reduced pressure. The crude residue was purified via flash chromatography (18 × 1.5 cm, hexanes, 10% EtOAc/hexanes) to afford **21.3** (0.244 g, 76%); R_f = 0.29 (5% EtOAc/hexanes); ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.85 (s, 2H), 4.75 (s, 4H), 3.87 (s, 7H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 151.66, 126.30, 112.03, 56.17, 23.87.

15.3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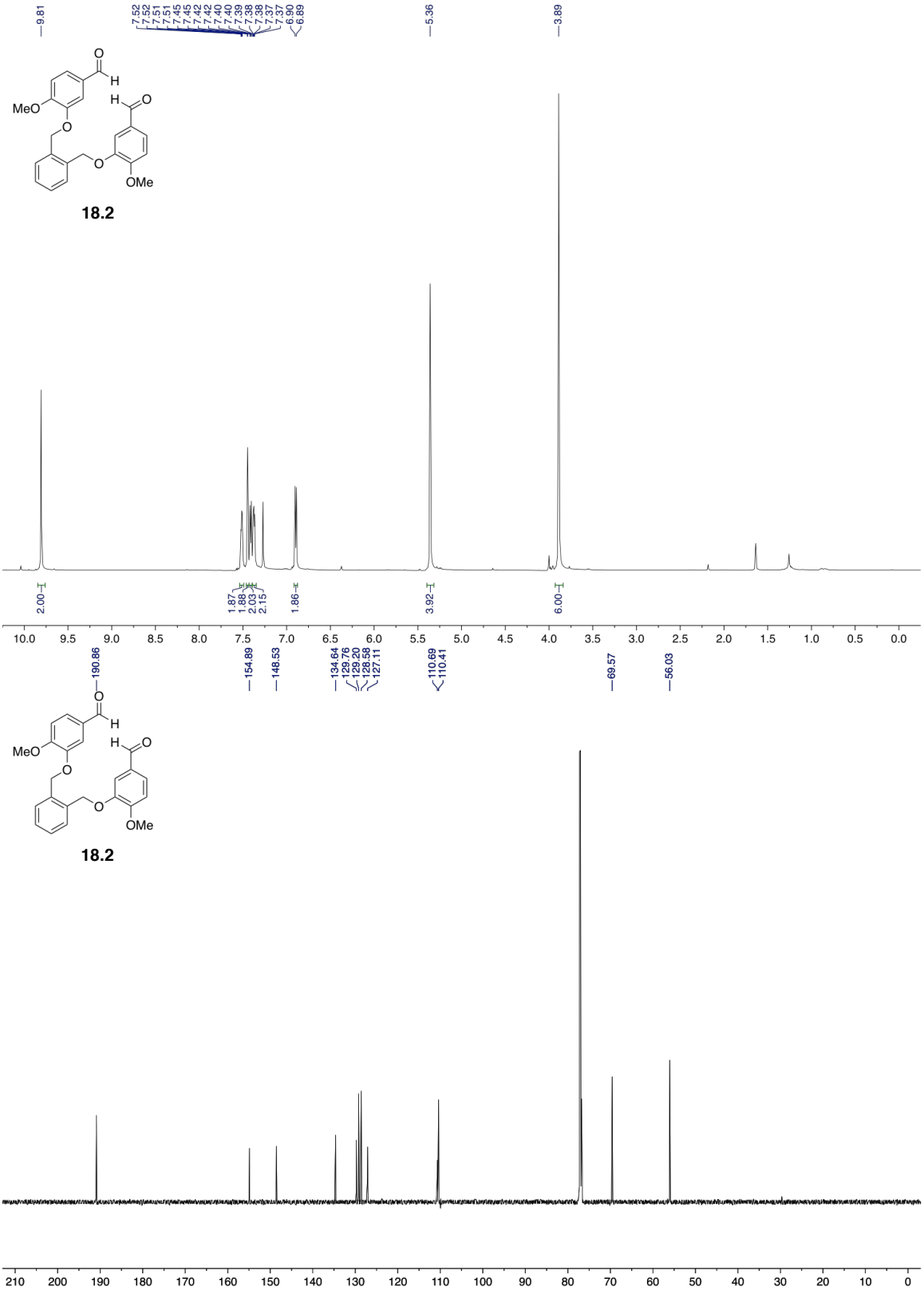
15.3

18.2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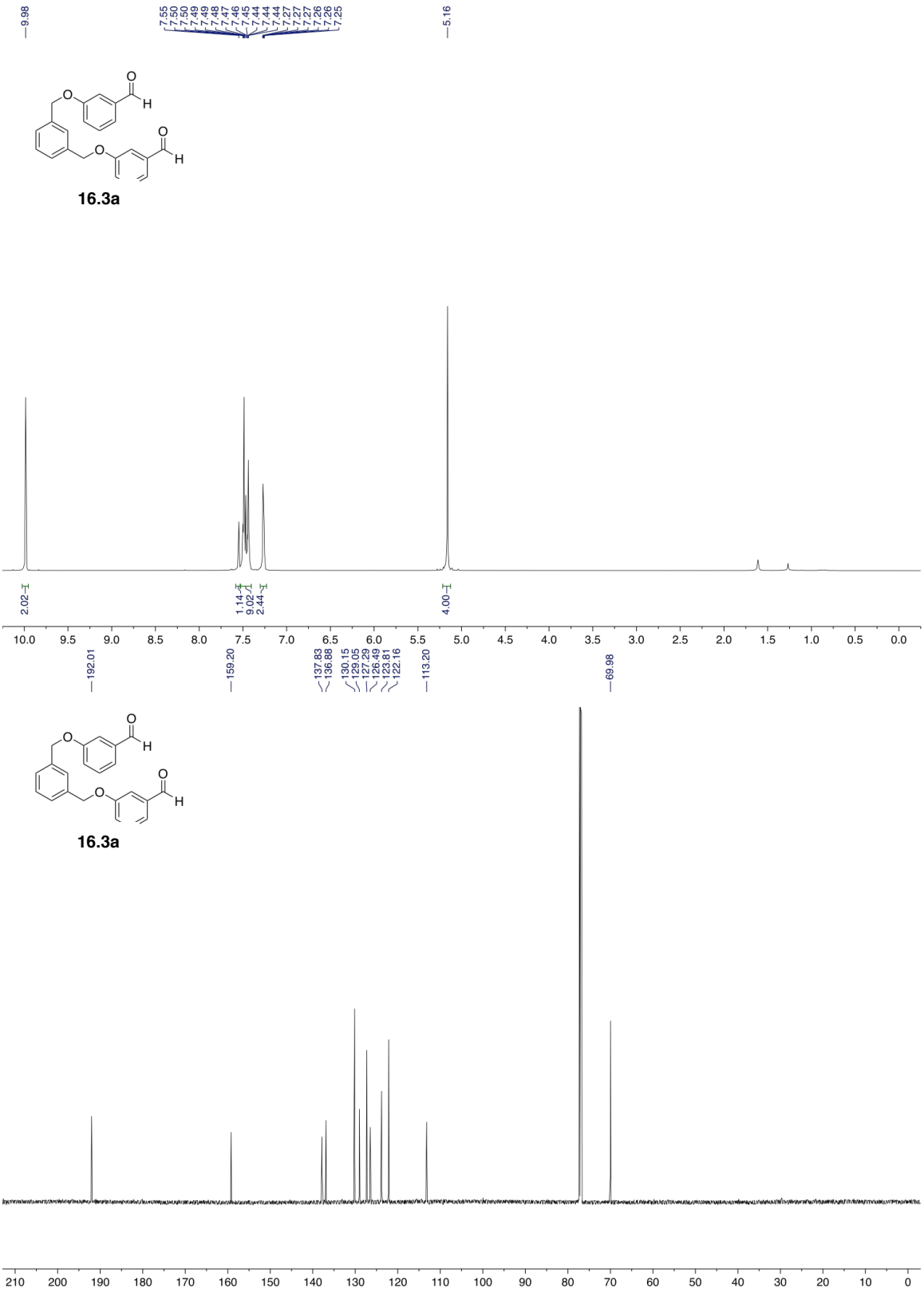
18.2

16.3a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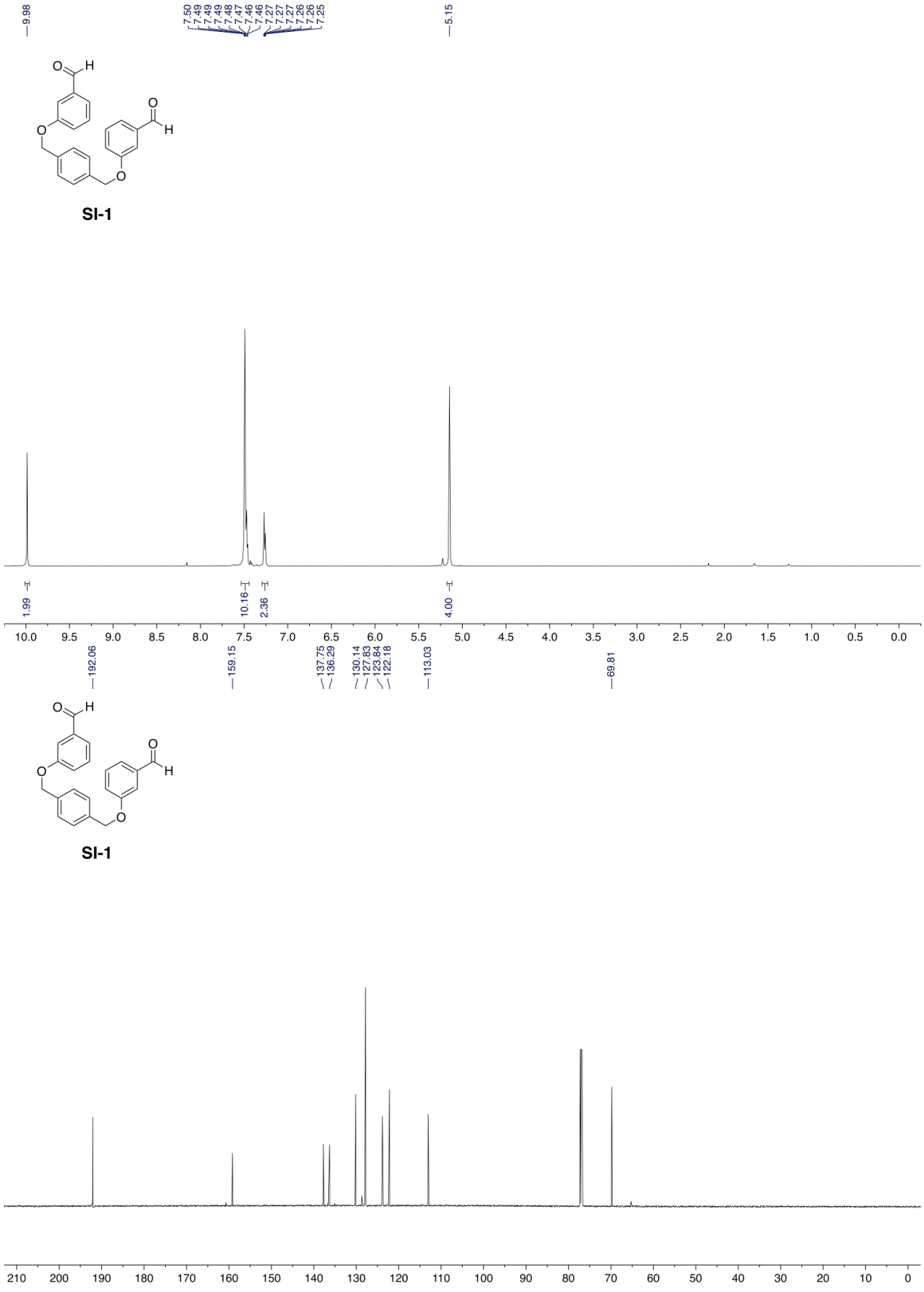
SI-1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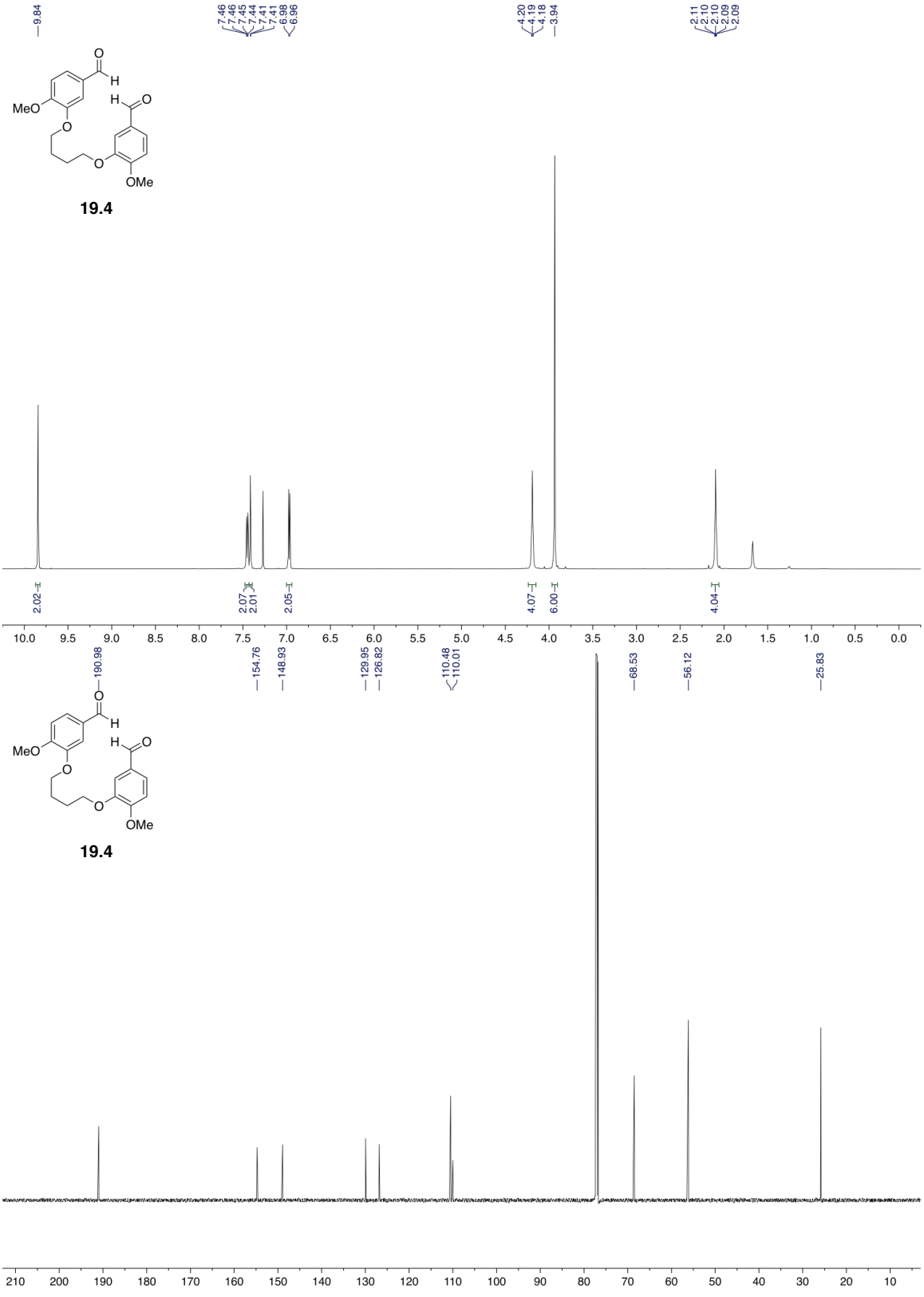
113.03
69.81

SI-1

19.4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19.4

15.4


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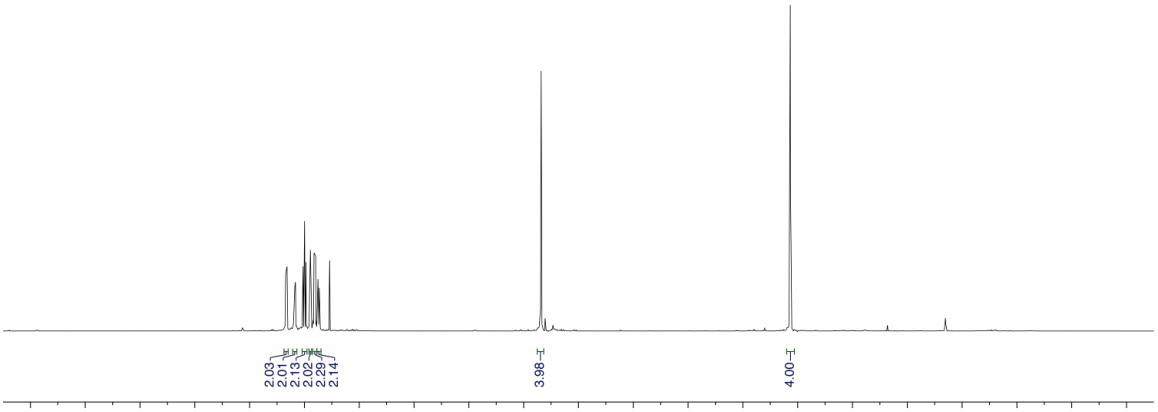
15.4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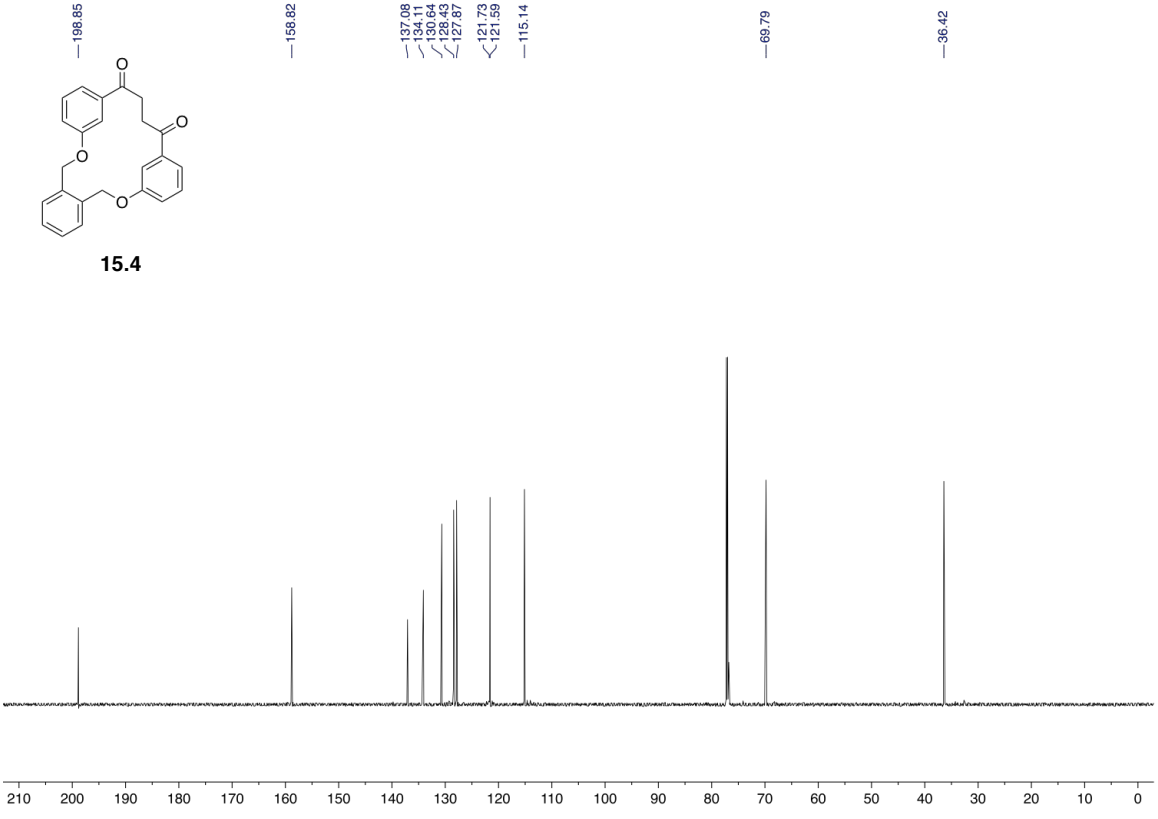
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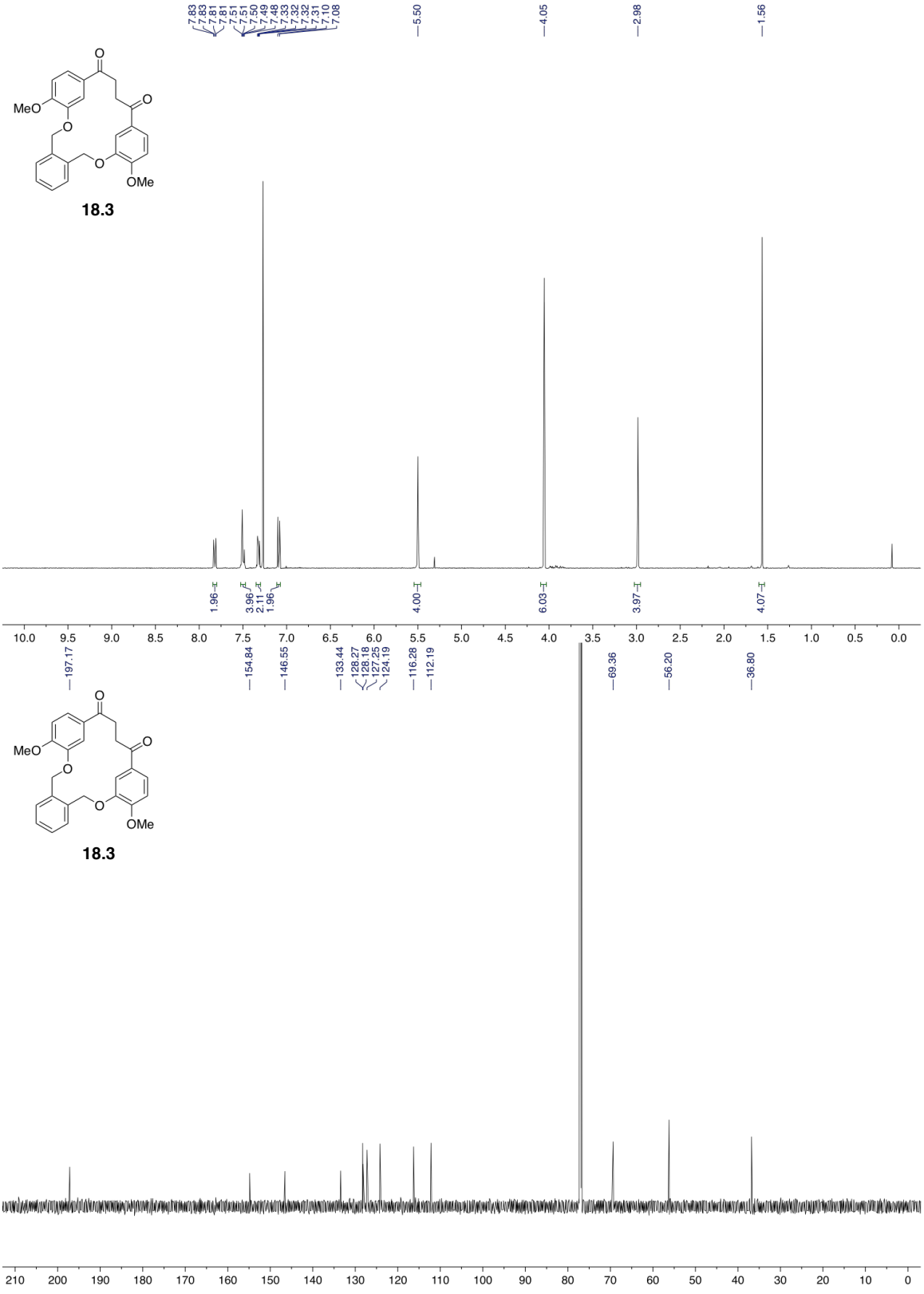
15.4

18.3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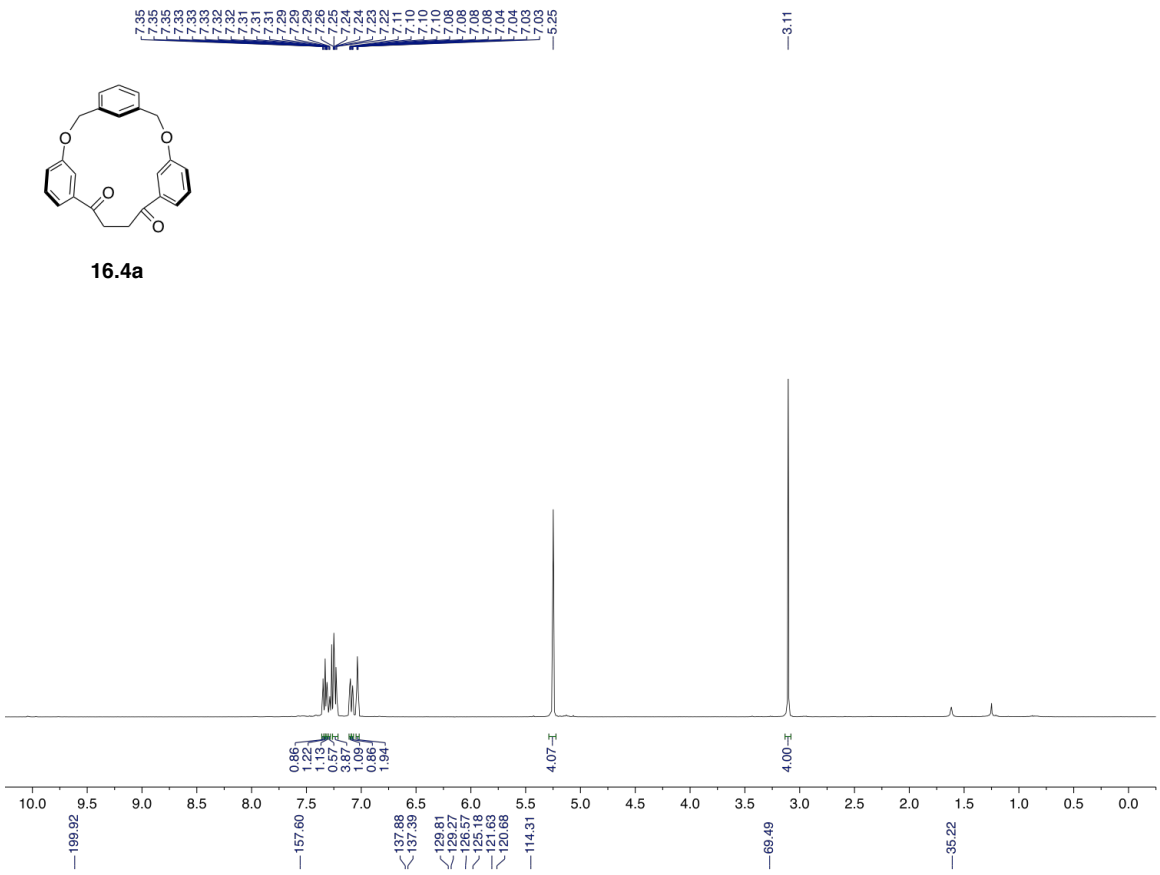
16.4a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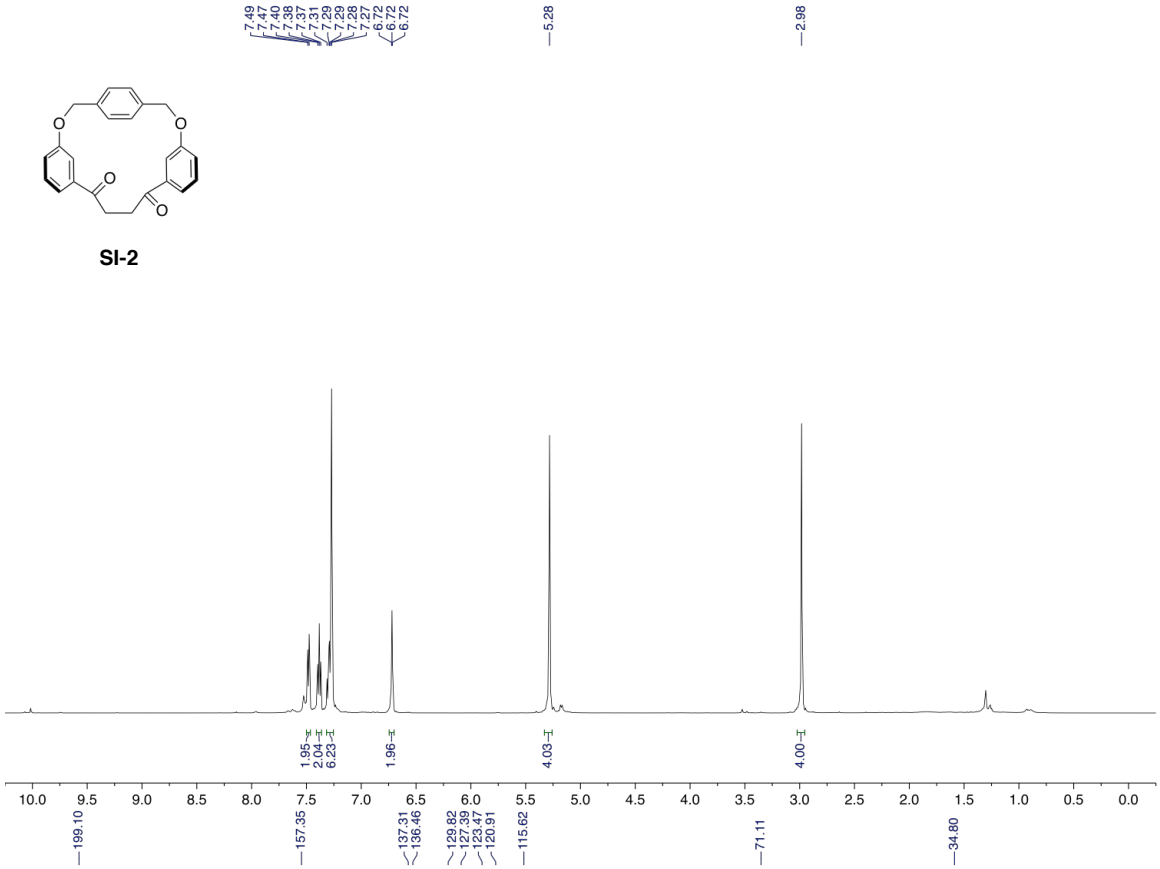
1.22
1.13
0.87
3.87
1.09
0.86
1.94
4.07
4.00
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
199.92
157.60
137.88
137.39
129.81
129.27
126.57
125.18
121.63
120.68
114.31
69.49
35.22
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

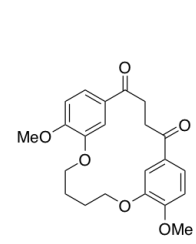
16.4a

SI-2


7.49
7.47
7.40
7.38
7.37
7.31
7.29
7.29
7.28
7.27
6.72
6.72
6.72
5.28
2.98
1.95
2.04
6.23
1.96
4.03
4.00
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
199.10
157.35
137.31
136.46
129.82
127.39
123.47
120.91
115.62
71.11
34.80
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

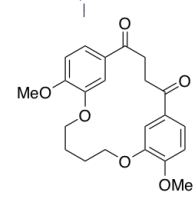
SI-2

19.5



19.5

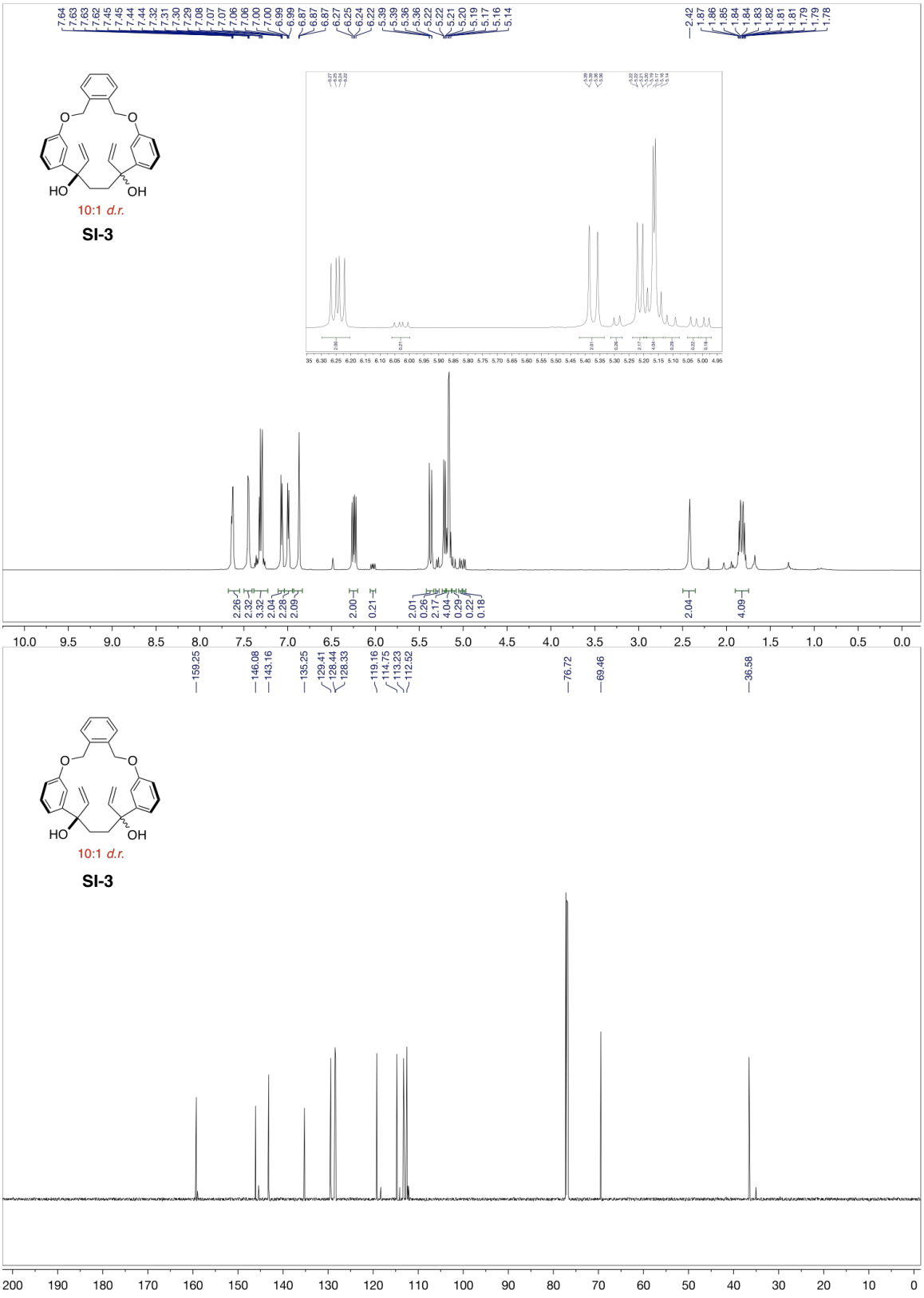
7.75
7.74
7.73
7.72
7.46
7.45
7.00
6.98
4.31
4.30
4.30
4.29
4.28
3.94
3.12
1.94
1.93
1.93
1.92
1.91
1.76
1.76
1.83
3.93
6.00
3.57
3.94
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0



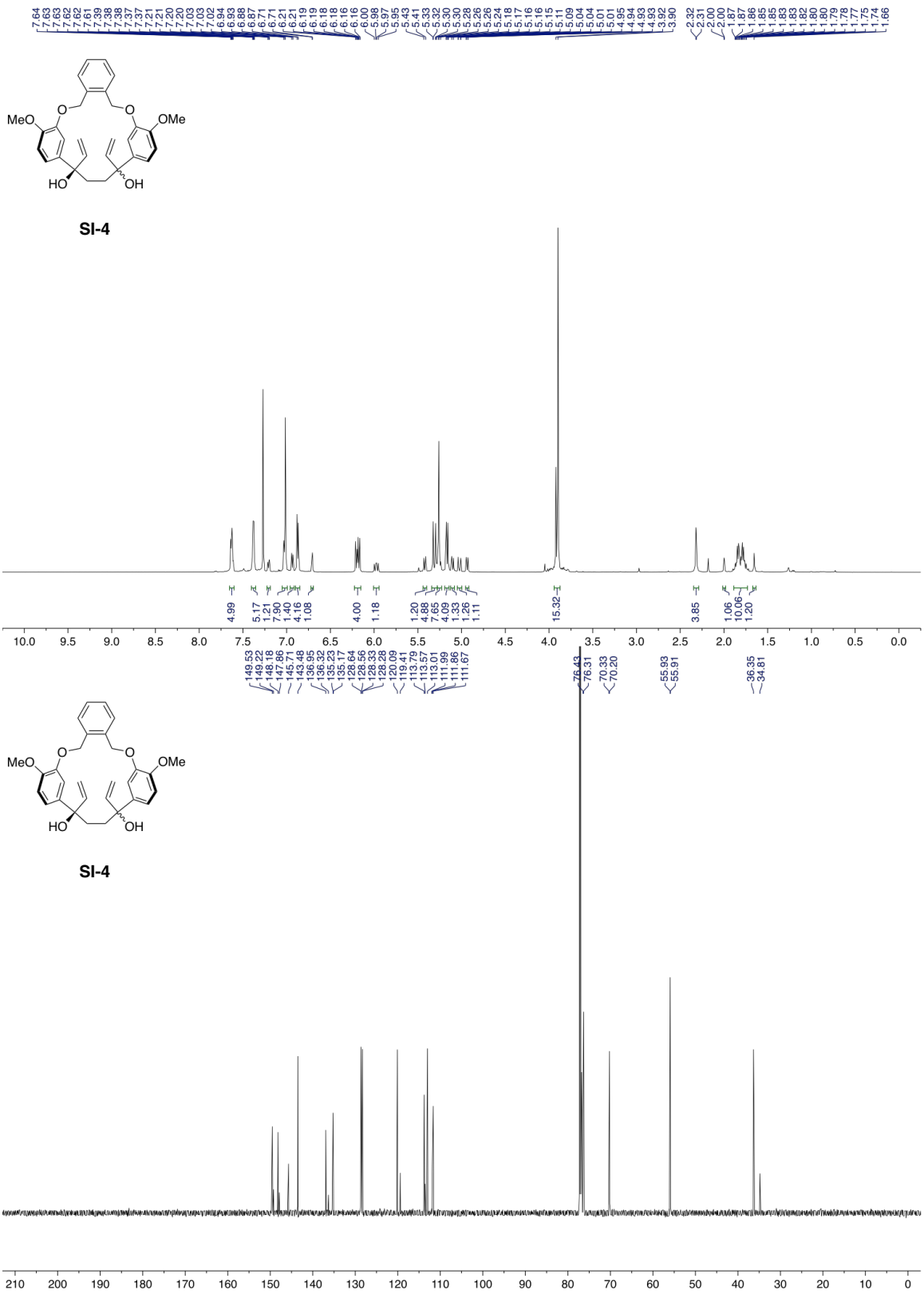
19.5

197.79
154.96
146.44
128.82
123.83
116.82
112.00
69.49
55.89
35.78
25.16
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0

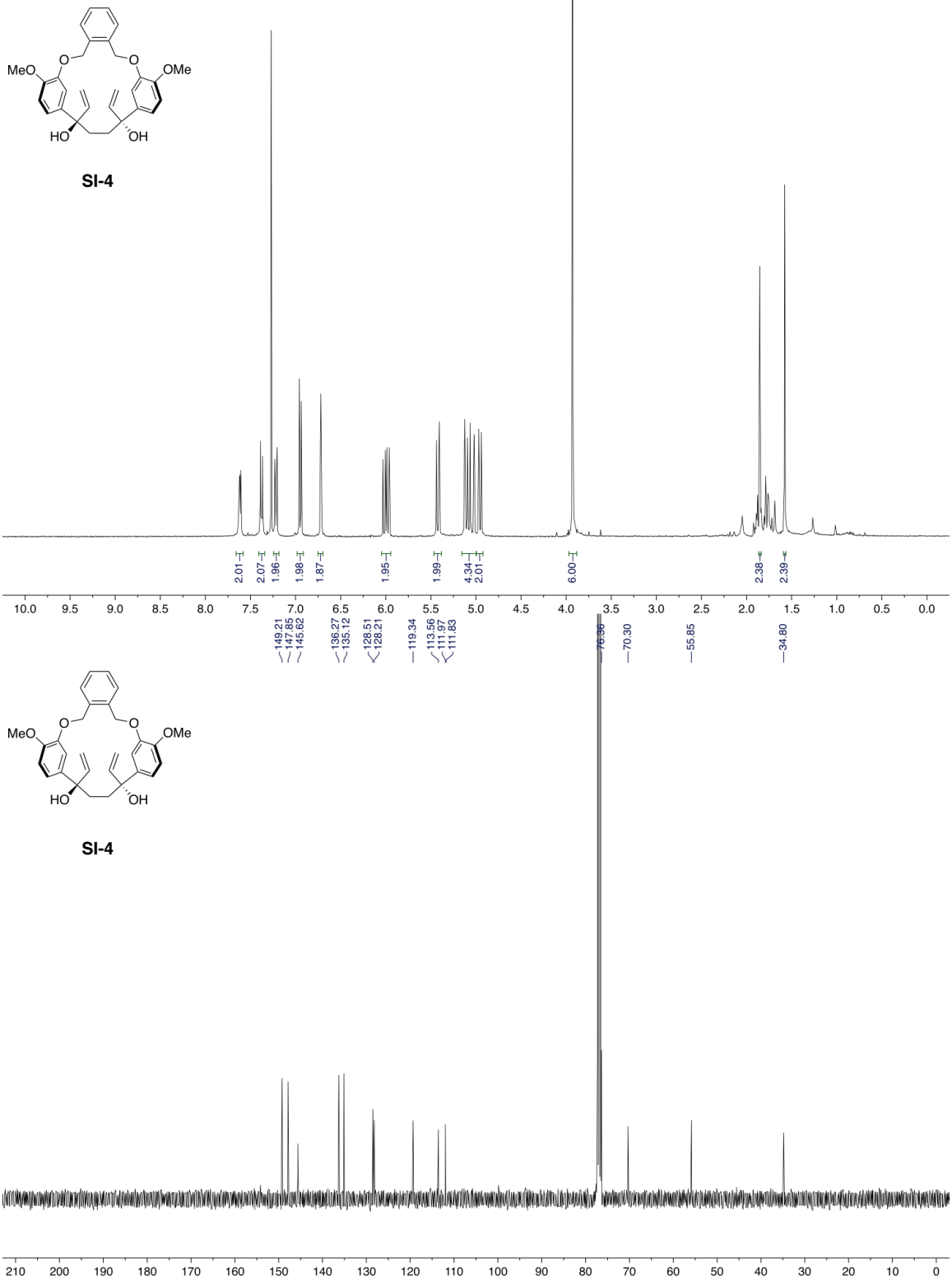
SI-3 mixture



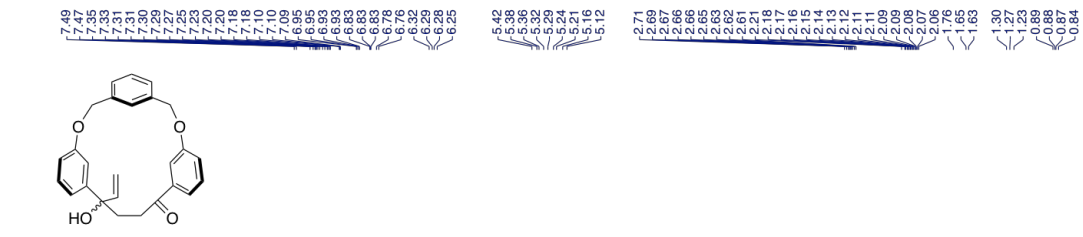
SI-4 mixture



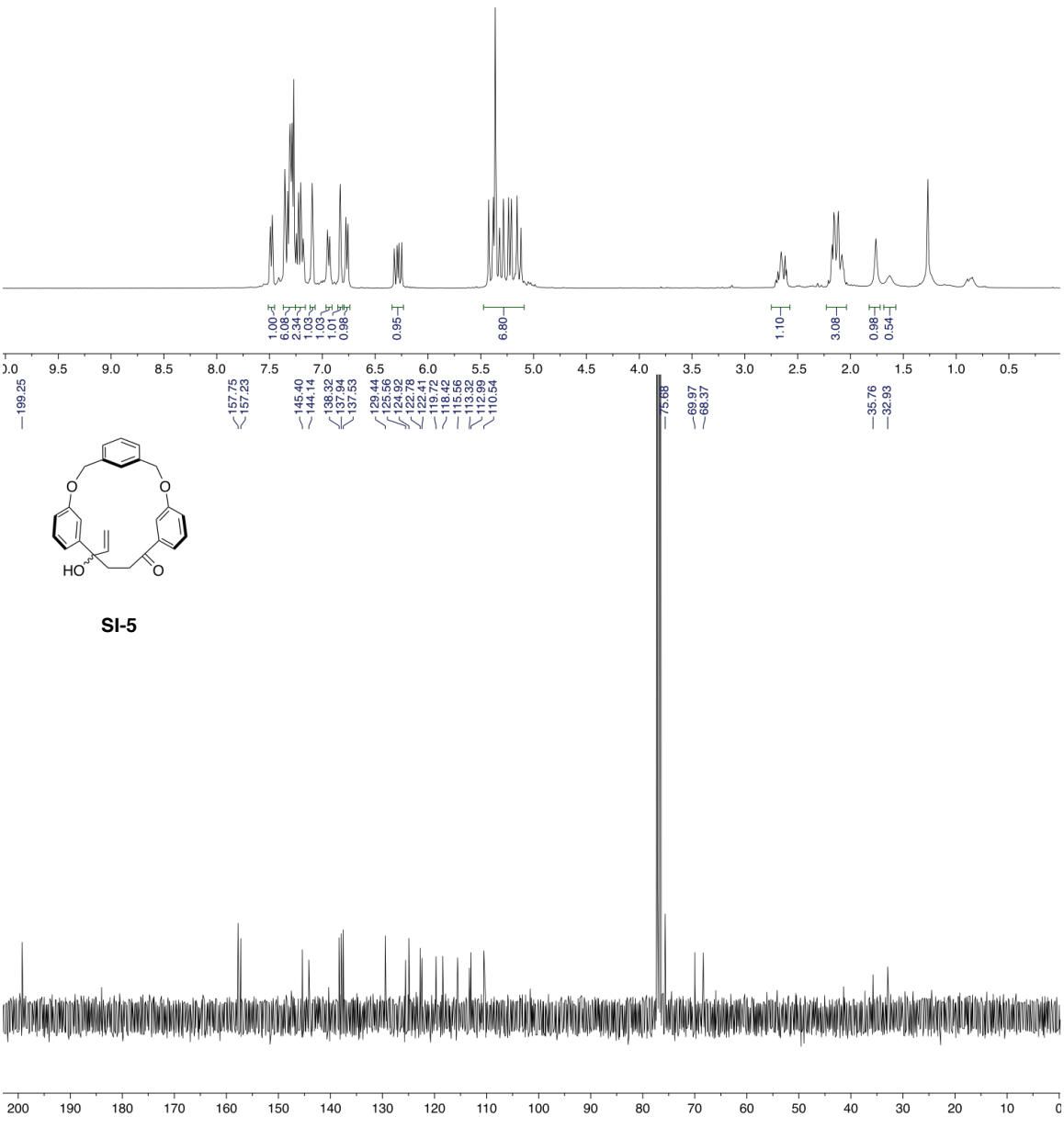
SI-4 anti


MeO
OMe
HO
OH
SI-4
7.63
7.62
7.62
7.61
7.39
7.38
7.37
7.37
7.37
7.23
7.22
7.21
7.20
6.96
6.94
6.72
6.71
6.03
6.00
5.99
5.96
5.44
5.41
5.12
5.09
5.07
5.06
5.02
5.02
4.97
4.97
4.94
4.94
3.93
1.85
1.58
2.01
2.07
1.96
1.98
1.87
1.95
1.99
4.34
2.01
6.00
2.38
2.39
149.21
147.85
145.62
136.27
135.12
128.51
128.21
119.34
113.56
111.97
111.83
76.36
70.30
55.85
34.80

SI-5 hydroxy ketone

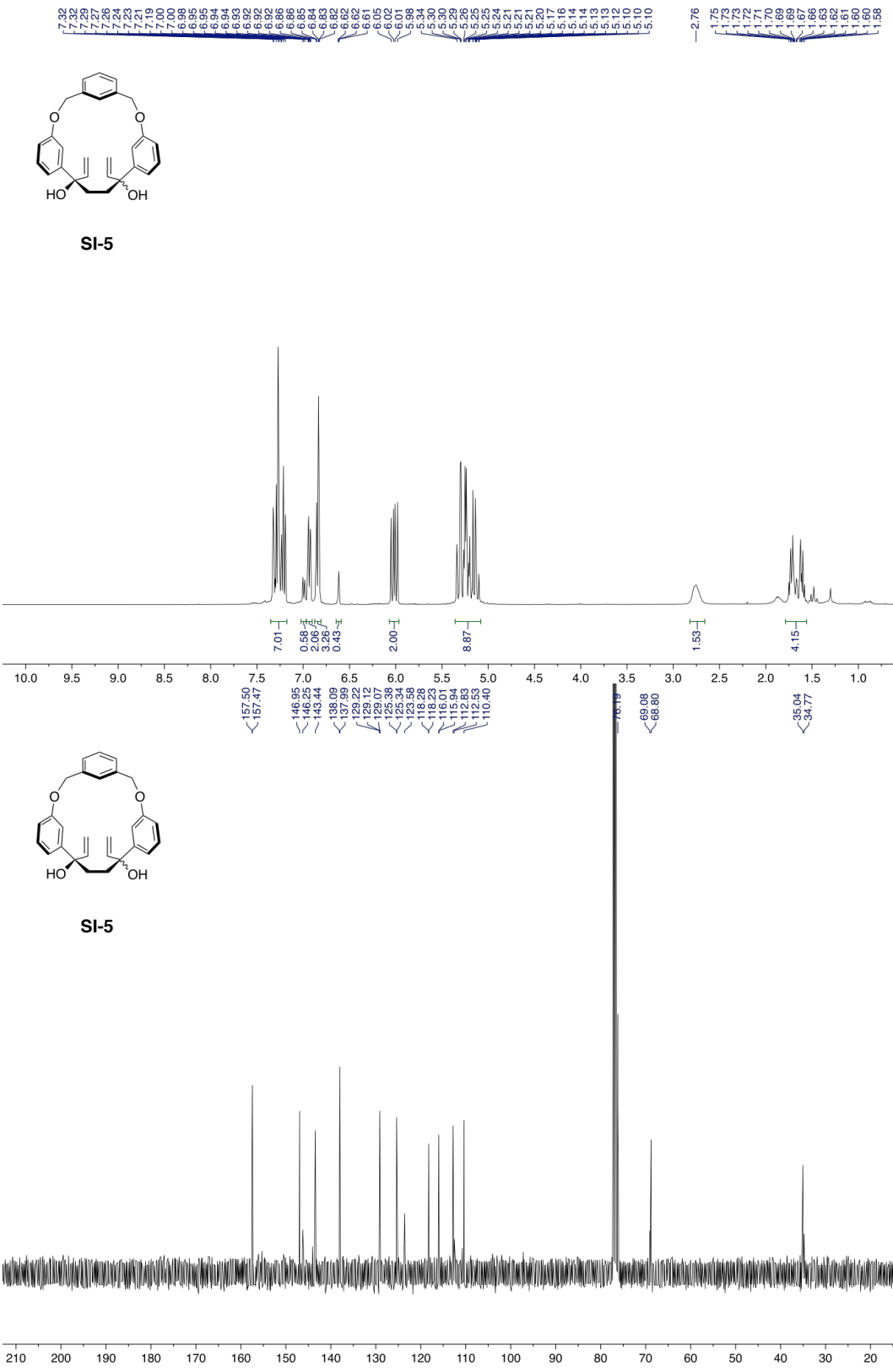


SI-5

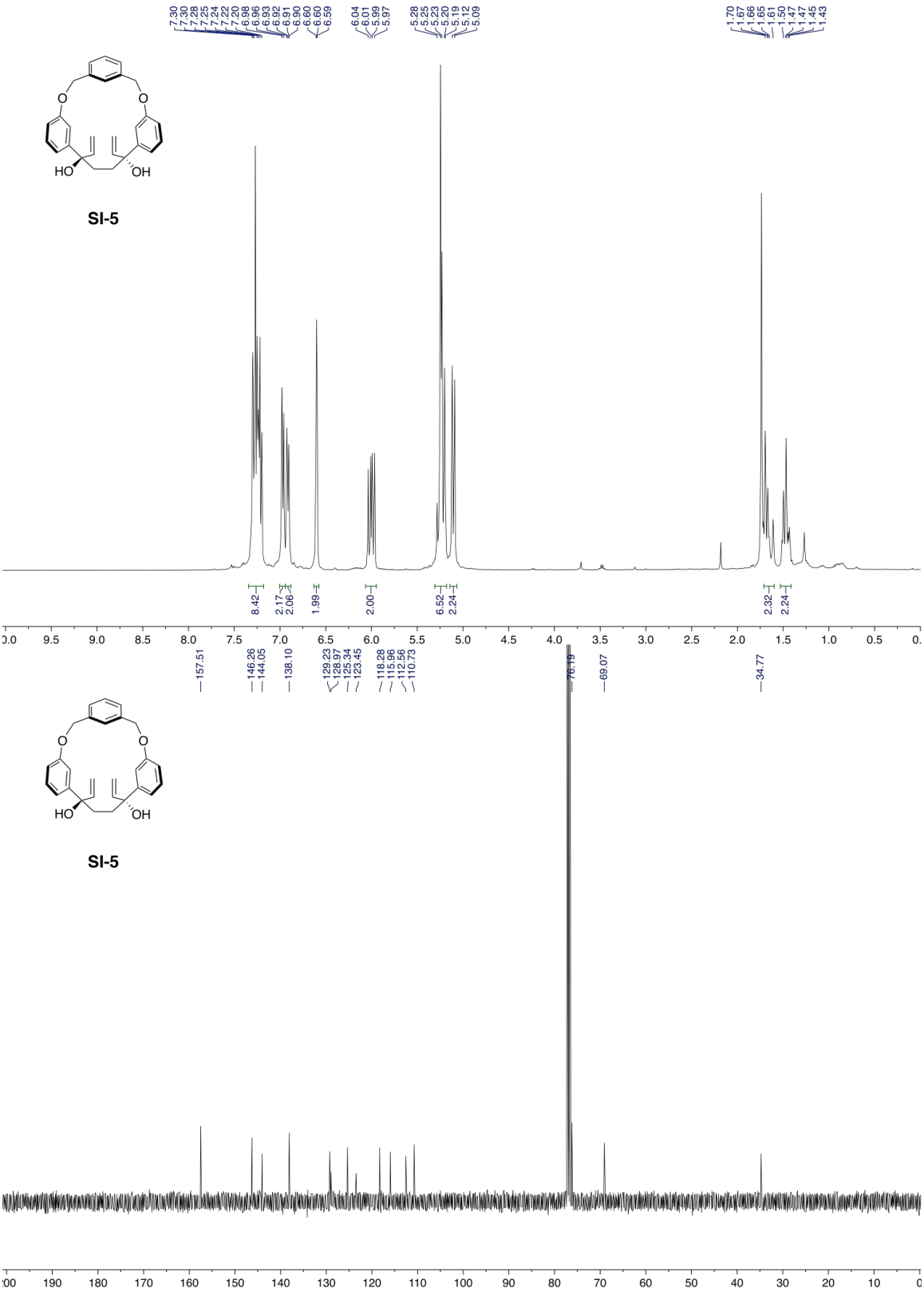


SI-5

SI- 5 mixture


7.32 7.32 7.29 7.27 7.26 7.24 7.23 7.21 7.19 7.19 7.00 6.98 6.95 6.95 6.94 6.94 6.93 6.92 6.92 6.92 6.86 6.85 6.85 6.84 6.83 6.82 6.62 6.62 6.61 6.05 6.02 6.01 5.98 5.94 5.30 5.30 5.29 5.26 5.25 5.25 5.24 5.21 5.21 5.21 5.20 5.17 5.16 5.14 5.14 5.13 5.13 5.12 5.10 5.10 5.10
2.76
1.75 1.73 1.73 1.72 1.71 1.70 1.69 1.69 1.67 1.66 1.63 1.62 1.61 1.61 1.60 1.60 1.58
O O HO OH
SI-5
7.01 0.58 2.06 3.26 0.43 2.00 8.87 1.53 4.15
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
157.50 157.47 146.95 146.25 143.44 138.09 137.99 129.22 129.12 129.07 125.38 125.34 123.58 118.23 116.01 115.94 112.83 112.53 110.40
76.19
69.08 68.80
35.04 34.77
O O HO OH
SI-5
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0

SI-5 anti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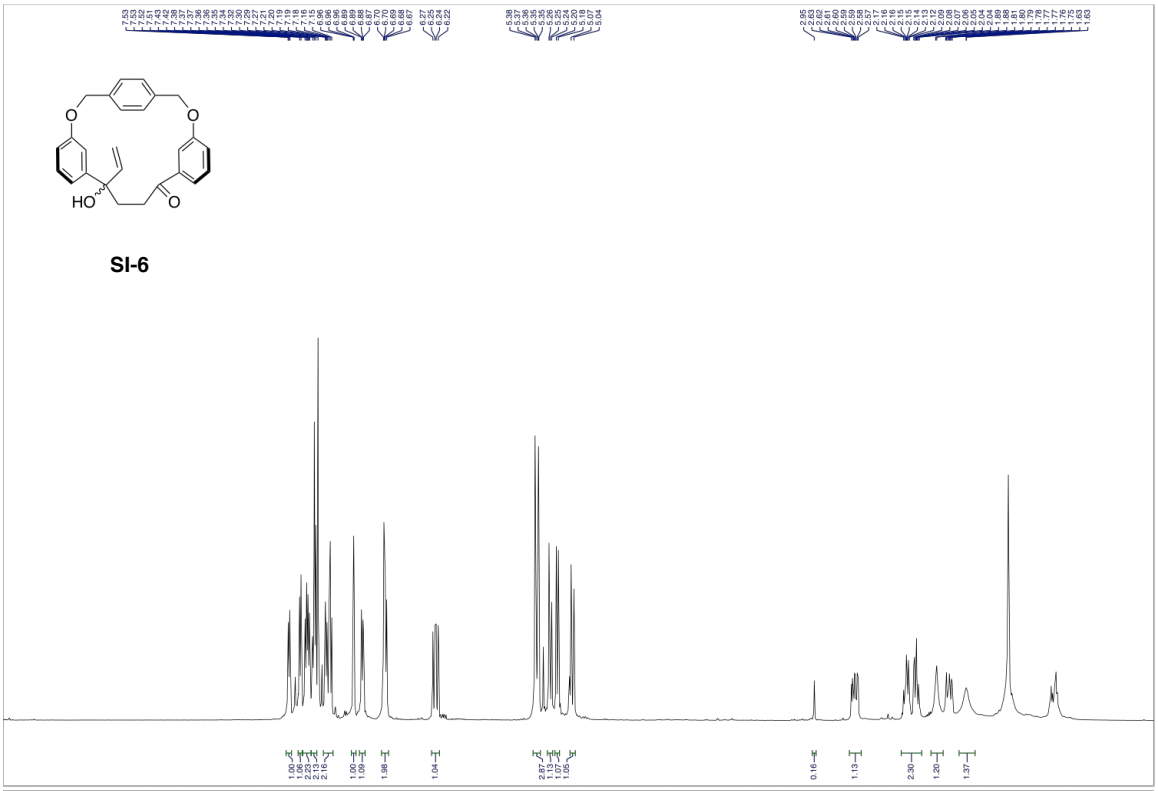
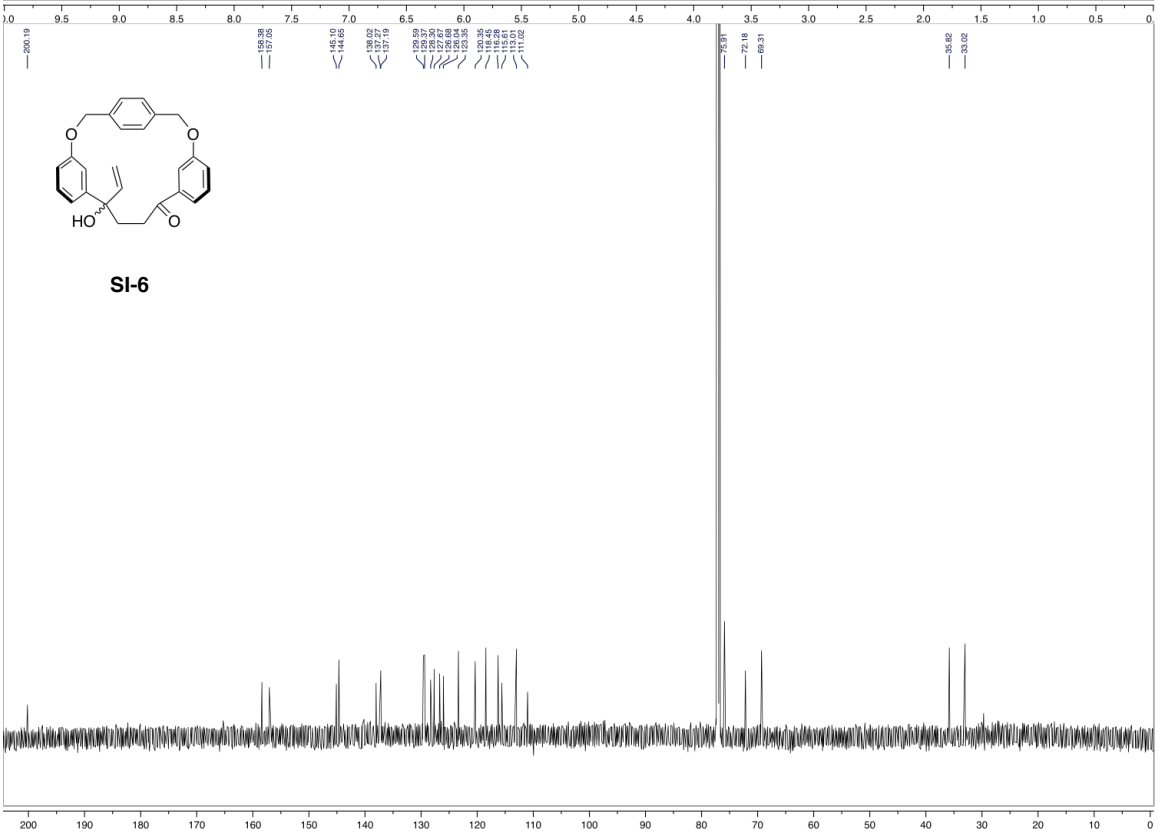
7.30
7.28
7.25
7.24
7.22
7.20
6.98
6.96
6.93
6.92
6.91
6.60
6.60
6.59
6.04
6.01
5.99
5.97
5.28
5.25
5.23
5.20
5.19
5.12
5.09
1.70
1.67
1.66
1.65
1.61
1.50
1.47
1.47
1.45
1.43
HO
OH
SI-5
8.42
2.17
2.06
1.99
2.00
6.52
2.24
2.32
2.24
157.51
146.26
144.05
138.10
129.23
128.97
125.34
123.45
118.28
115.96
112.56
110.73
76.19
69.07
34.77
HO
OH
SI-5

SI-6 hydroxy ketone

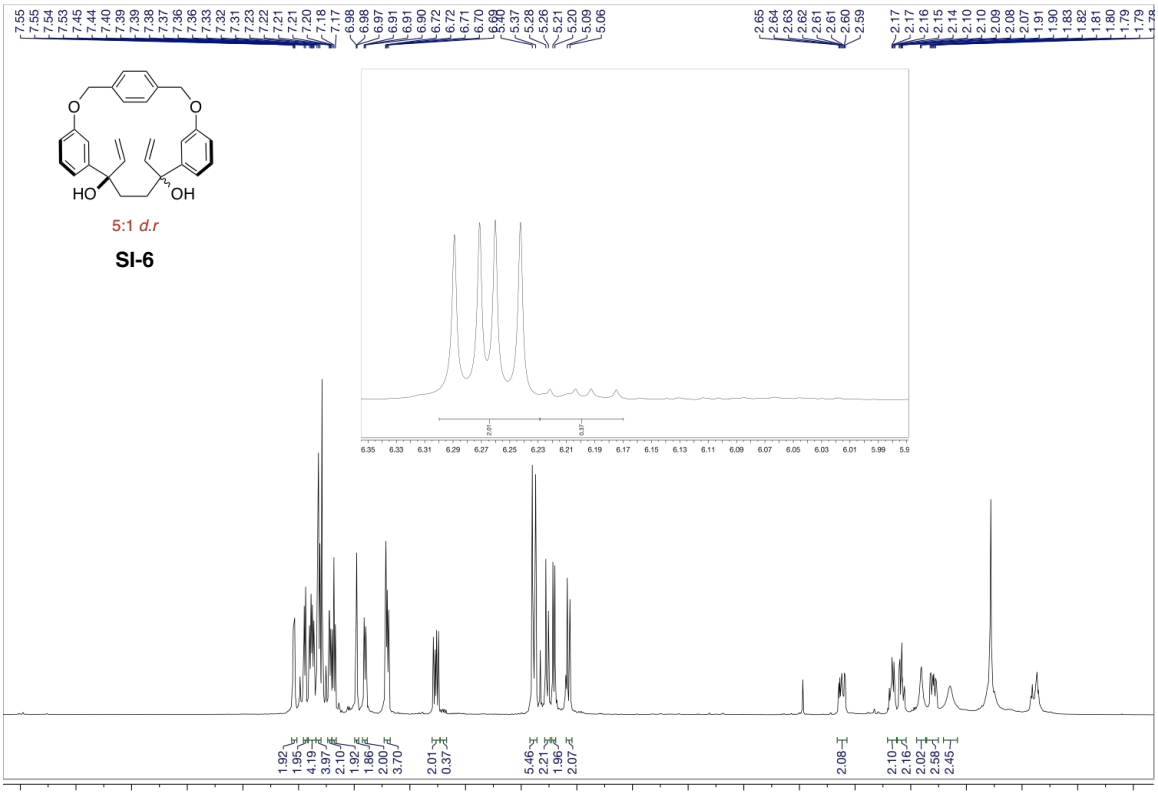


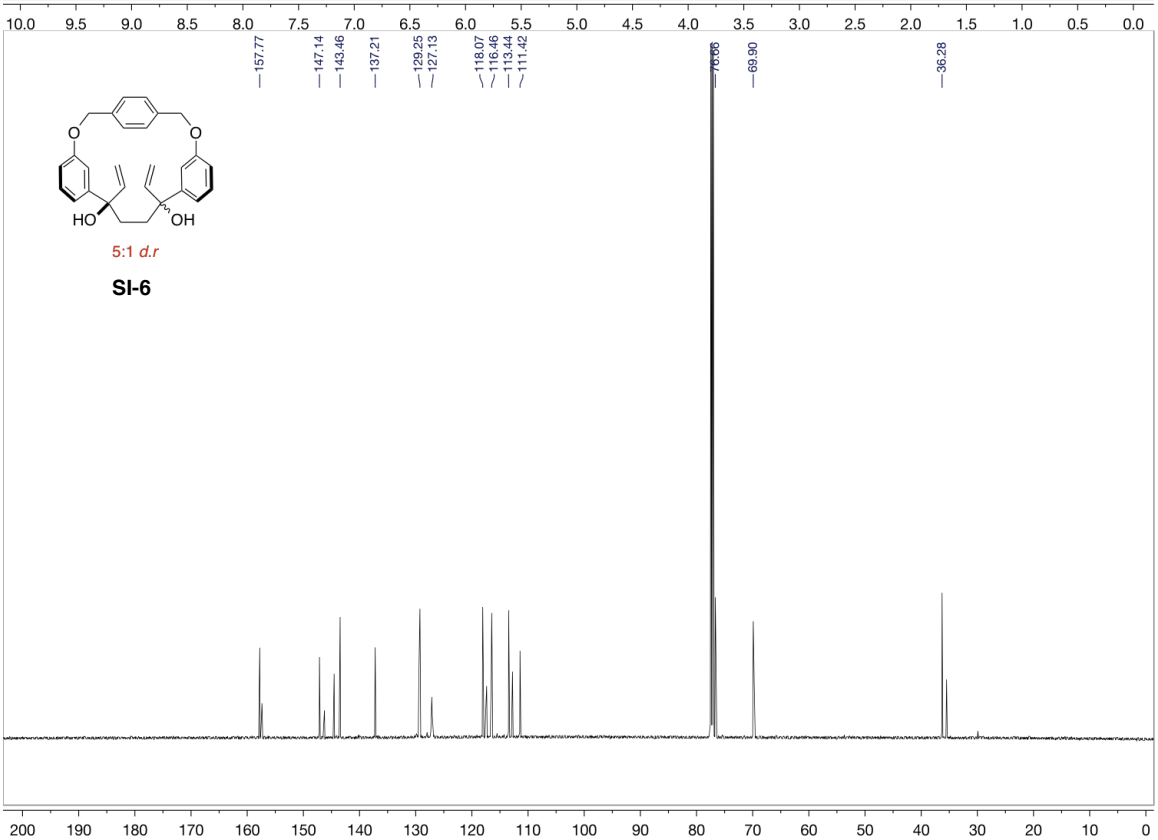
SI-6



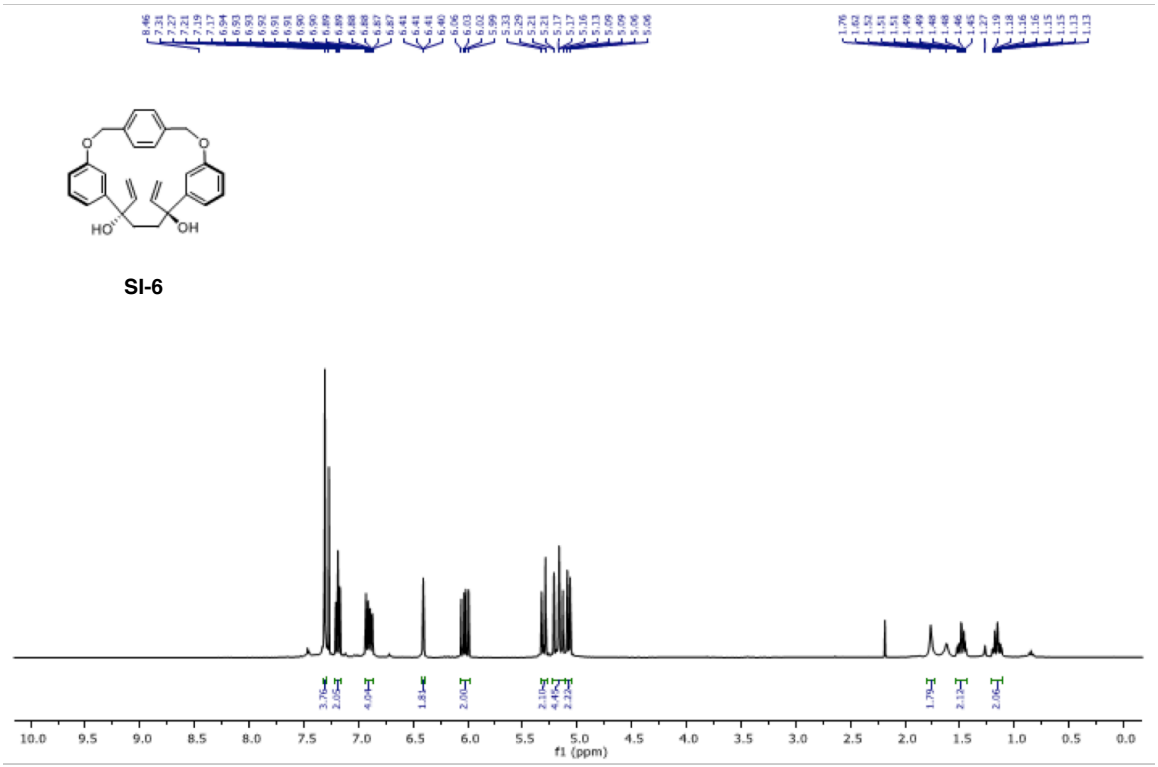
SI-6

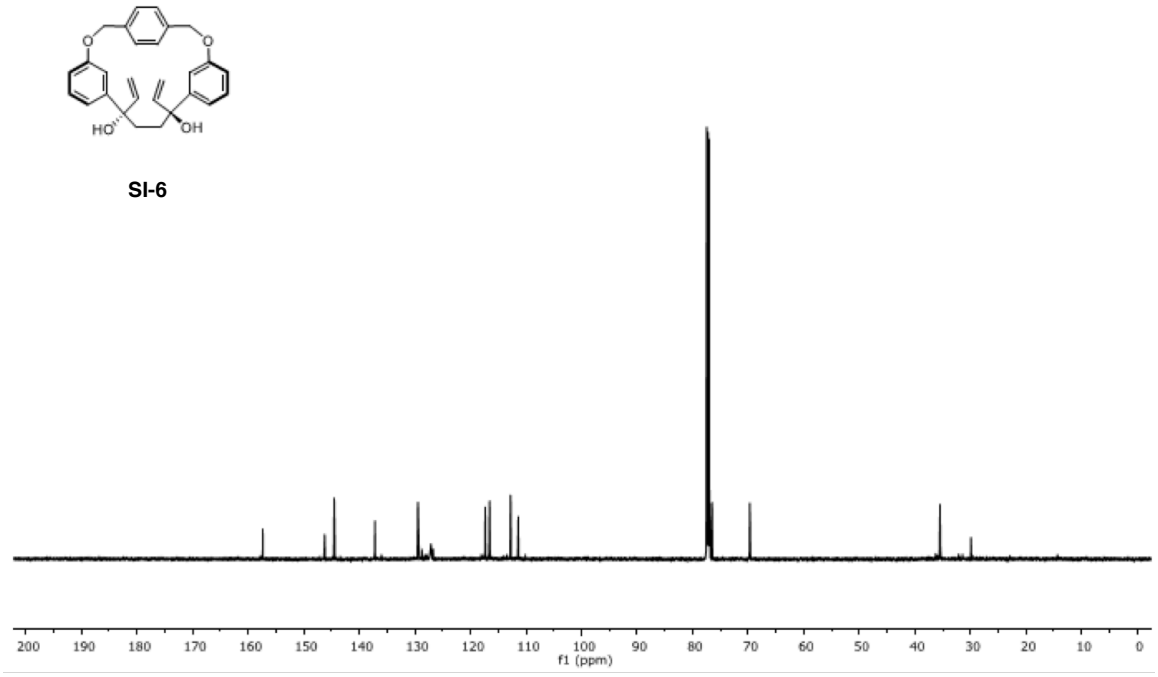
SI-6 mixture



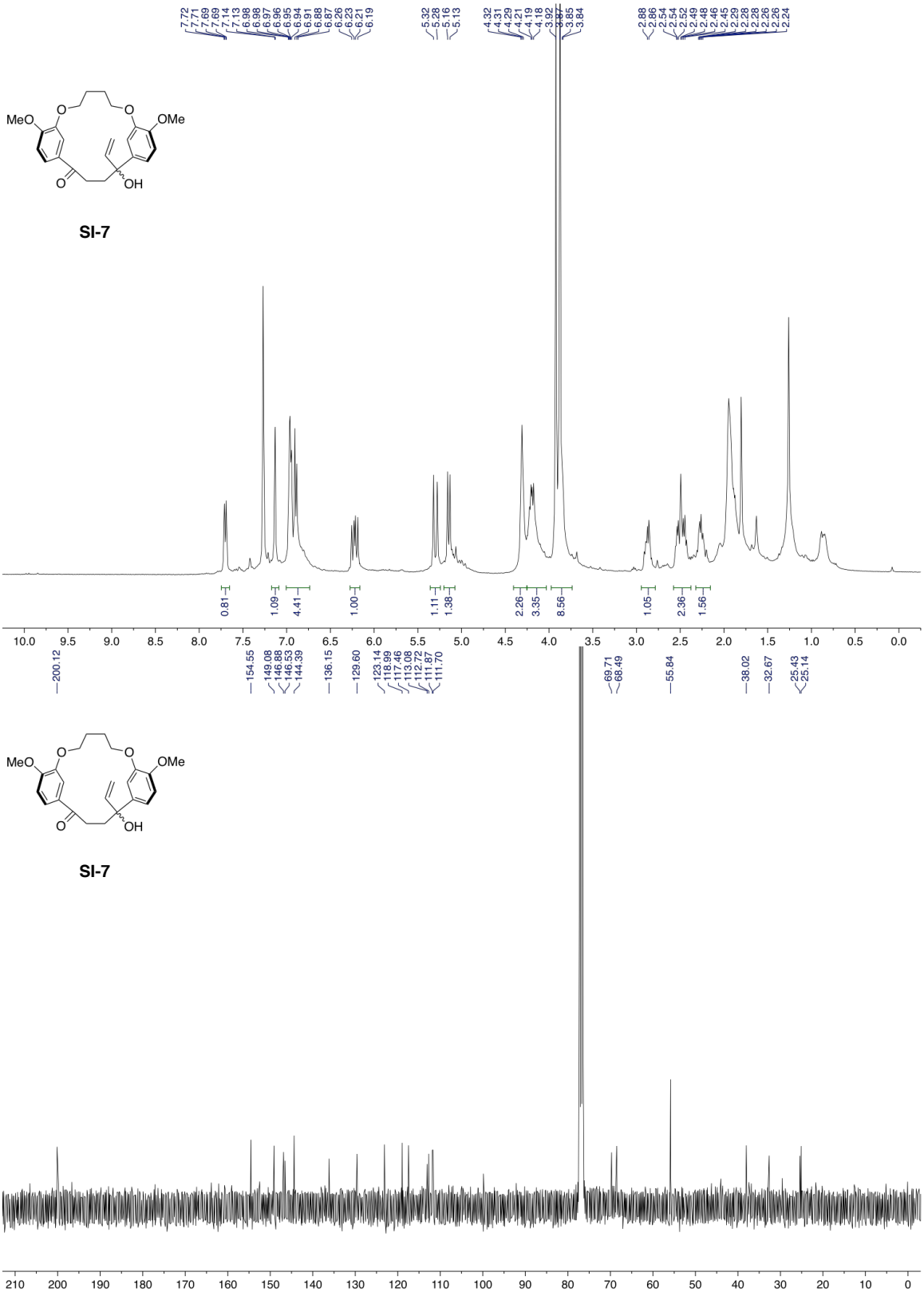


SI-6 anti

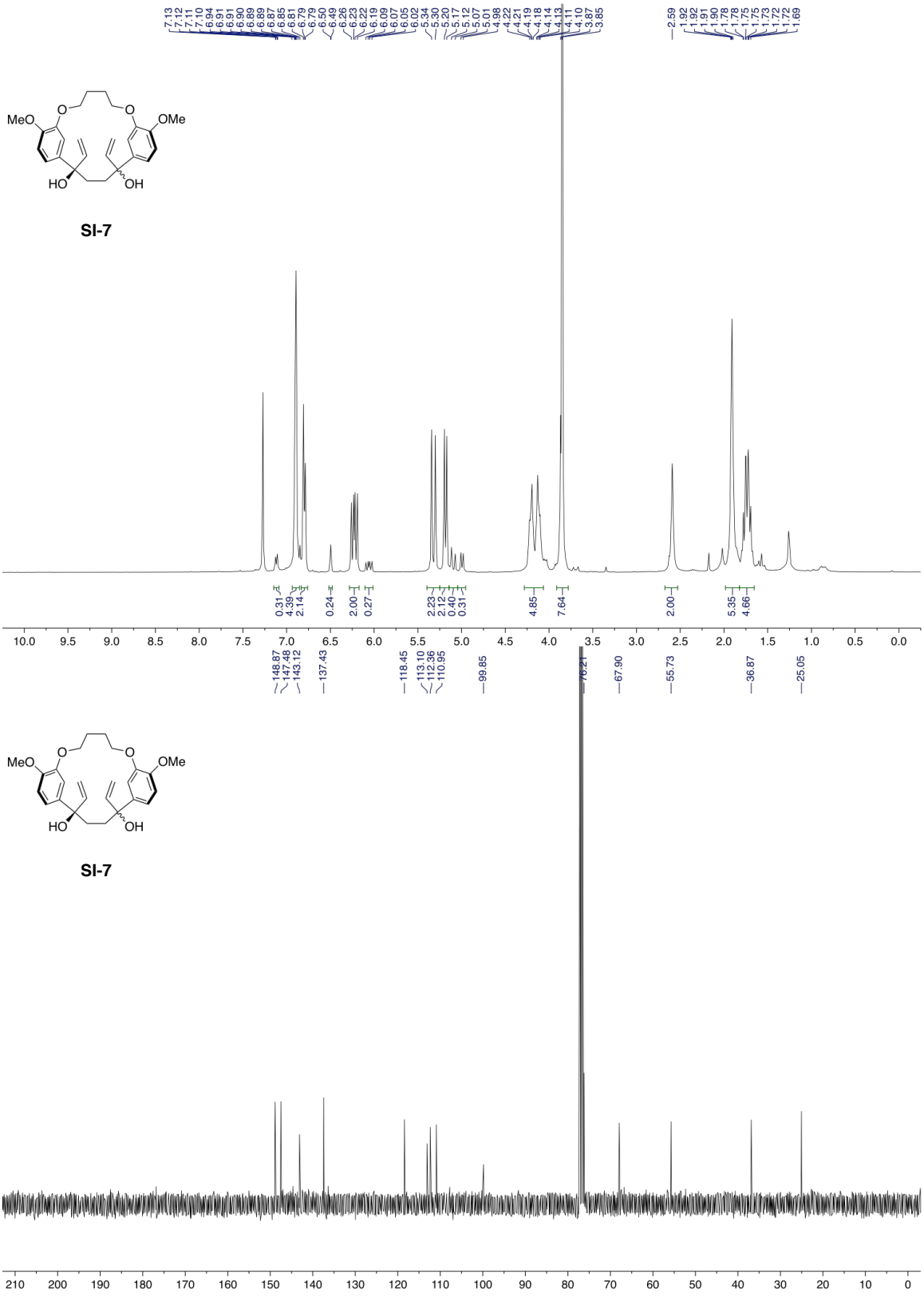




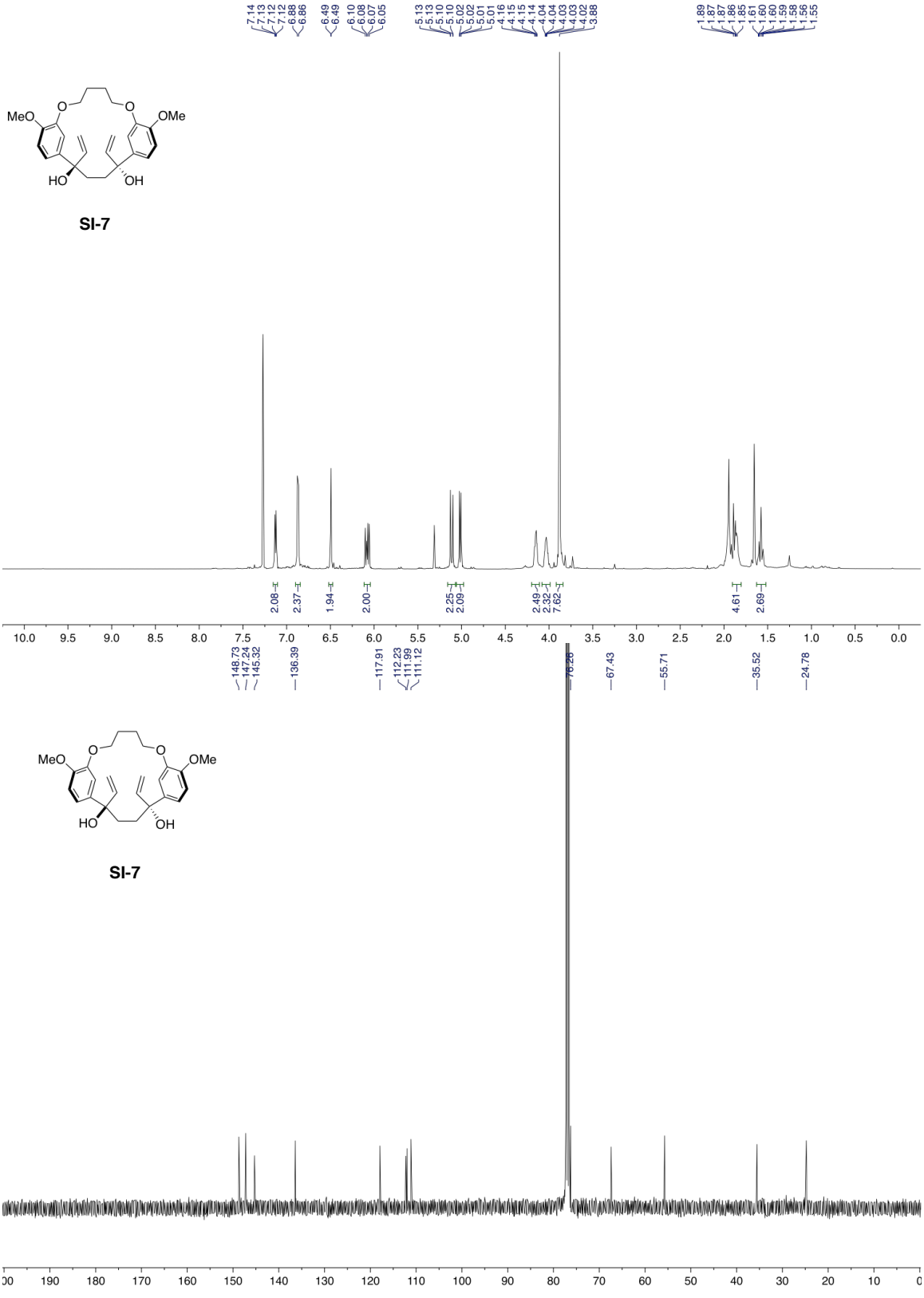
SI-7 hydroxy ketone



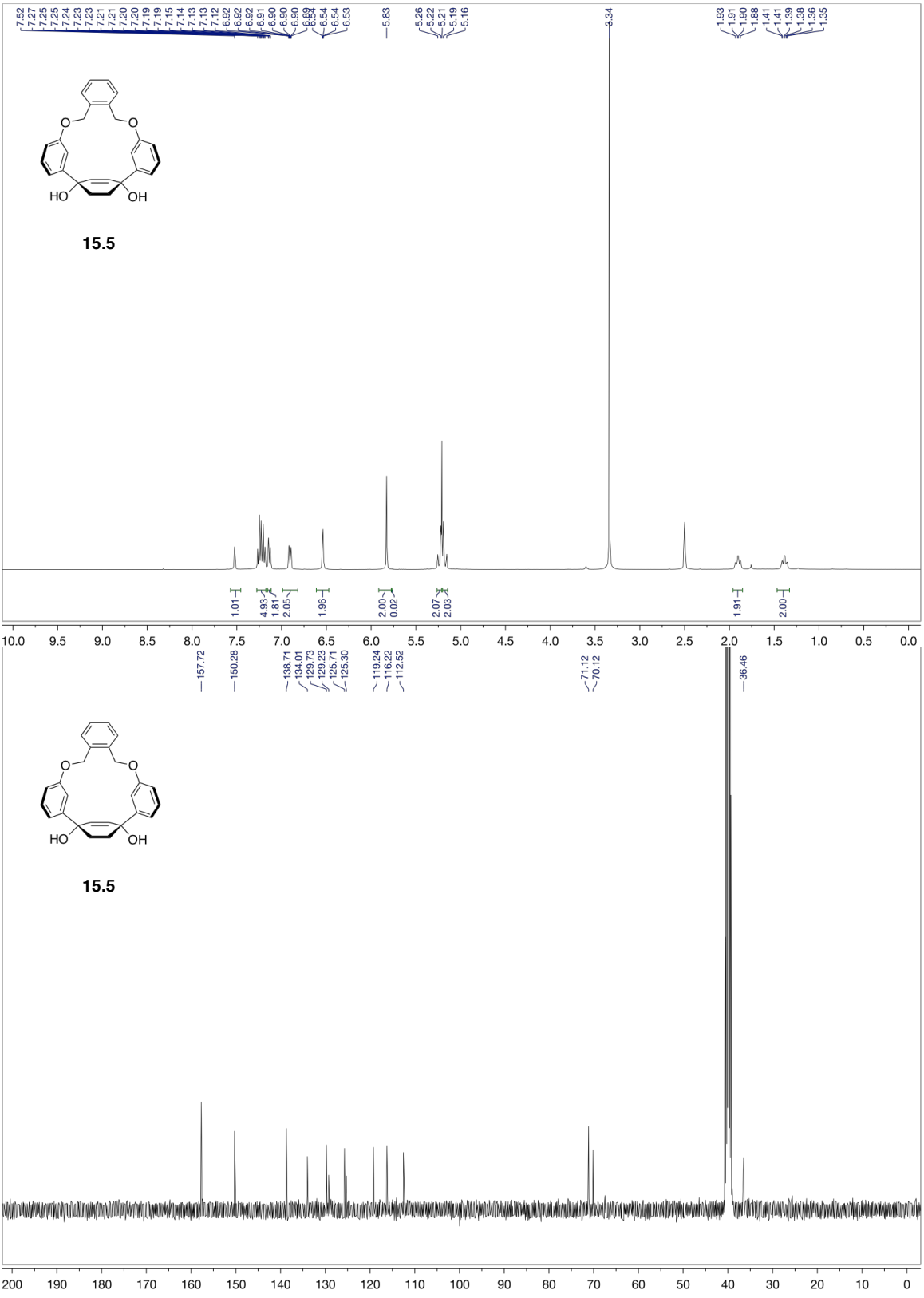
SI-7 mixture



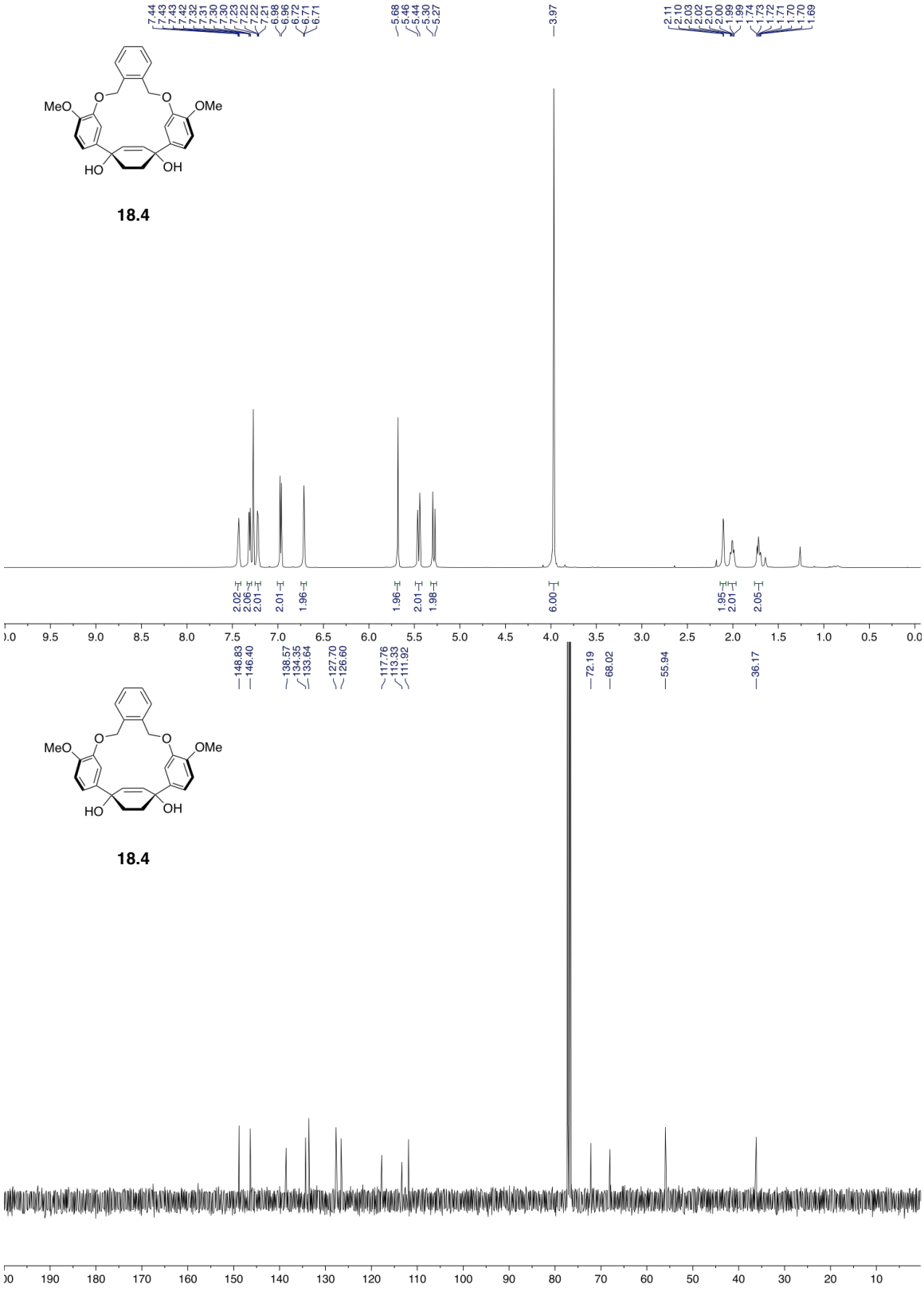
SI-7 anti



15.5



18.4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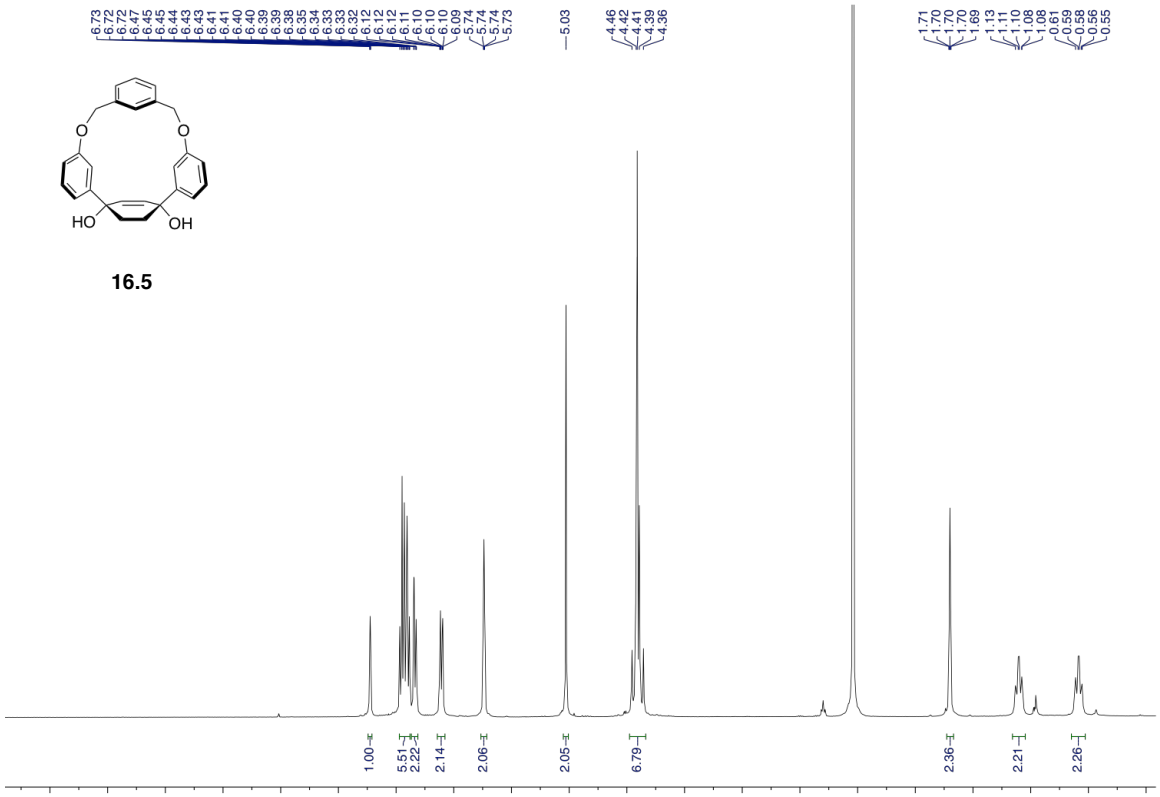
7.43
7.42
7.32
7.31
7.30
7.30
7.23
7.22
7.22
7.21
6.98
6.96
6.72
6.71
6.71
5.68
5.46
5.44
5.30
5.27
3.97
2.11
2.10
2.03
2.02
2.01
2.00
1.99
1.99
1.74
1.73
1.72
1.71
1.70
1.70
1.69
MeO
OMe
HO
OH
2.02
2.06
2.01
2.01
1.96
1.96
2.01
1.98
6.00
1.95
2.01
2.05
148.83
146.40
138.57
134.35
133.64
127.70
126.60
117.76
113.33
111.92
72.19
68.02
55.94
36.17

18.4

16.5


HO
OH

16.5

6.73
6.72
6.72
6.47
6.45
6.45
6.44
6.43
6.41
6.41
6.40
6.40
6.39
6.38
6.35
6.34
6.33
6.33
6.32
6.12
6.12
6.12
6.11
6.10
6.10
6.10
6.09
5.74
5.74
5.73
5.03
4.46
4.42
4.41
4.39
4.36
1.71
1.70
1.70
1.70
1.69
1.13
1.11
1.10
1.08
1.08
0.61
0.59
0.58
0.56
0.55
1.00
5.51
2.22
2.14
2.06
2.05
6.79
2.36
2.21
2.26
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
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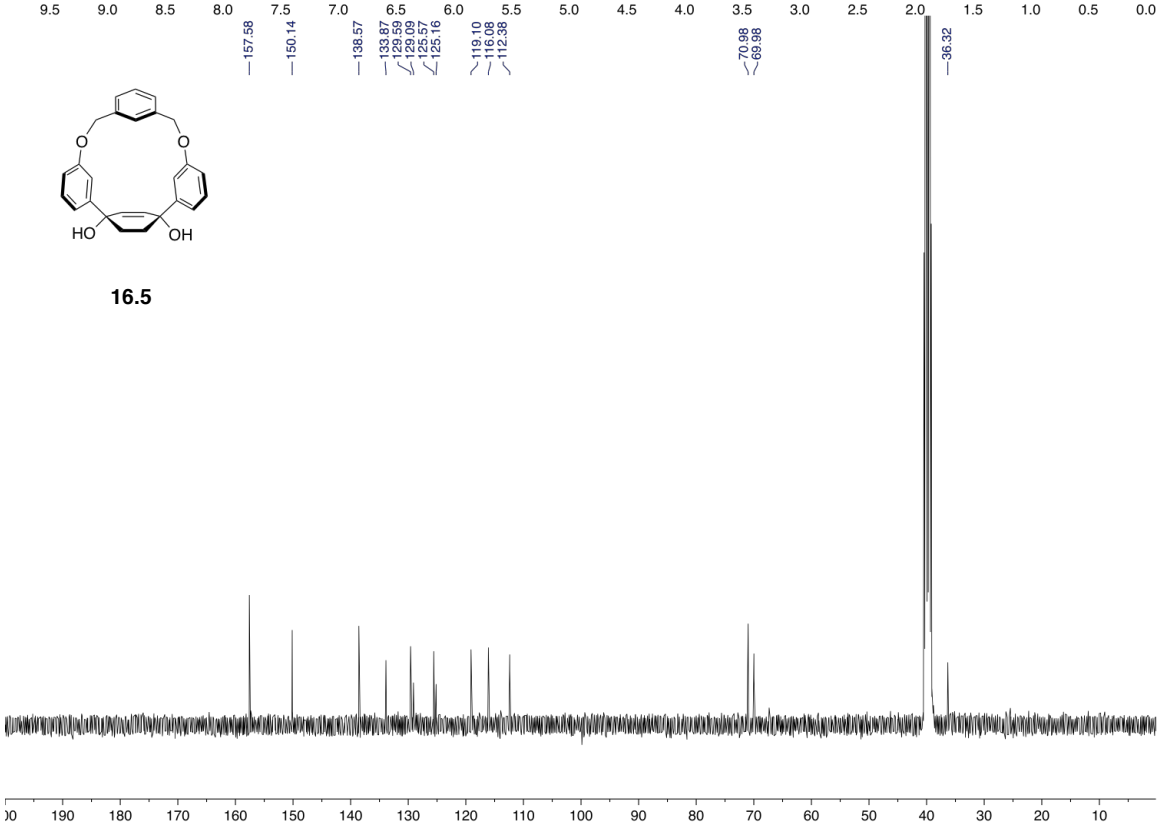
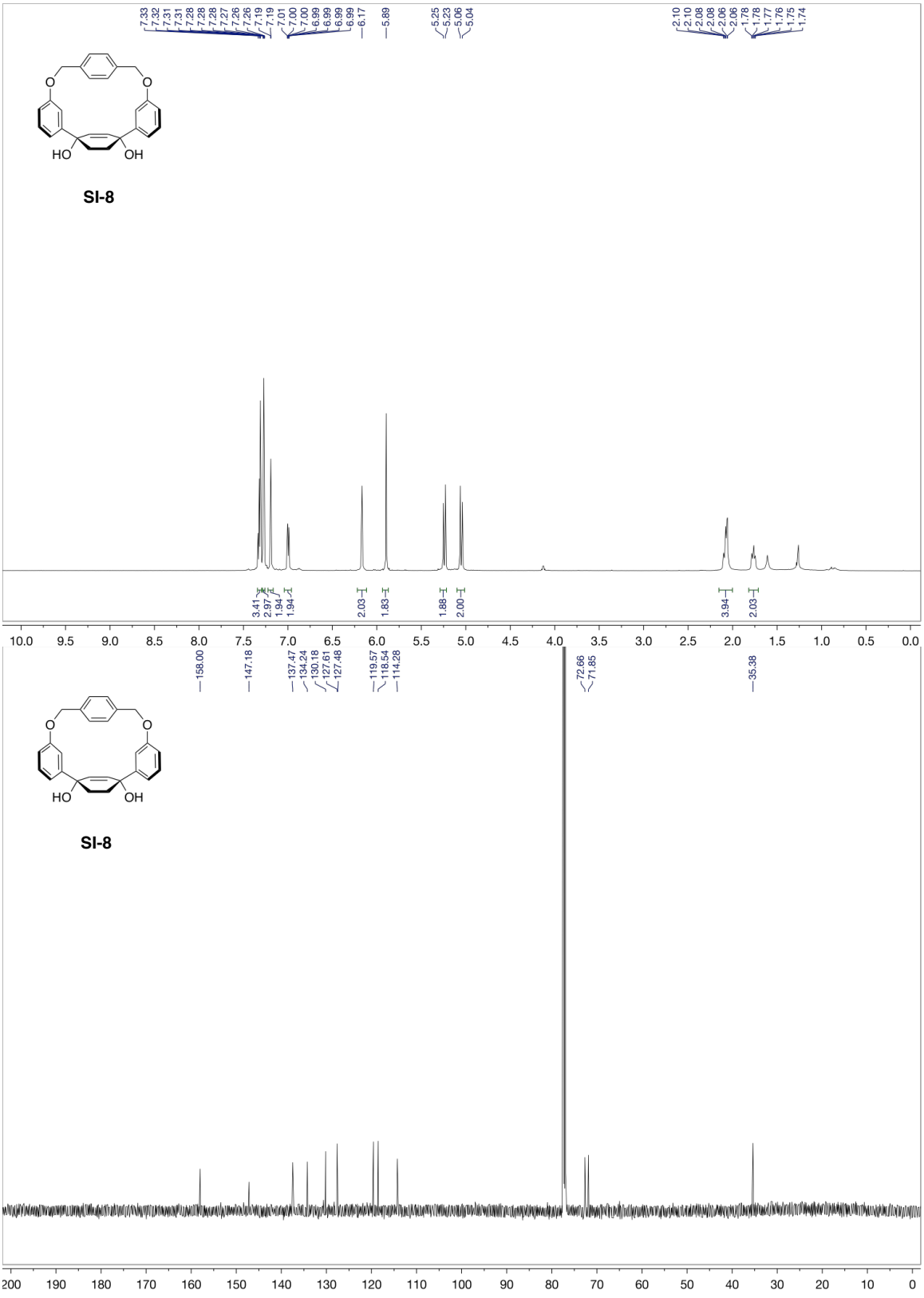
2.0
1.5
1.0
0.5
0.0


157.58
150.14
138.57
133.87
129.59
129.09
125.57
125.16
119.10
116.08
112.38
70.98
69.98
36.32
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10

SI-8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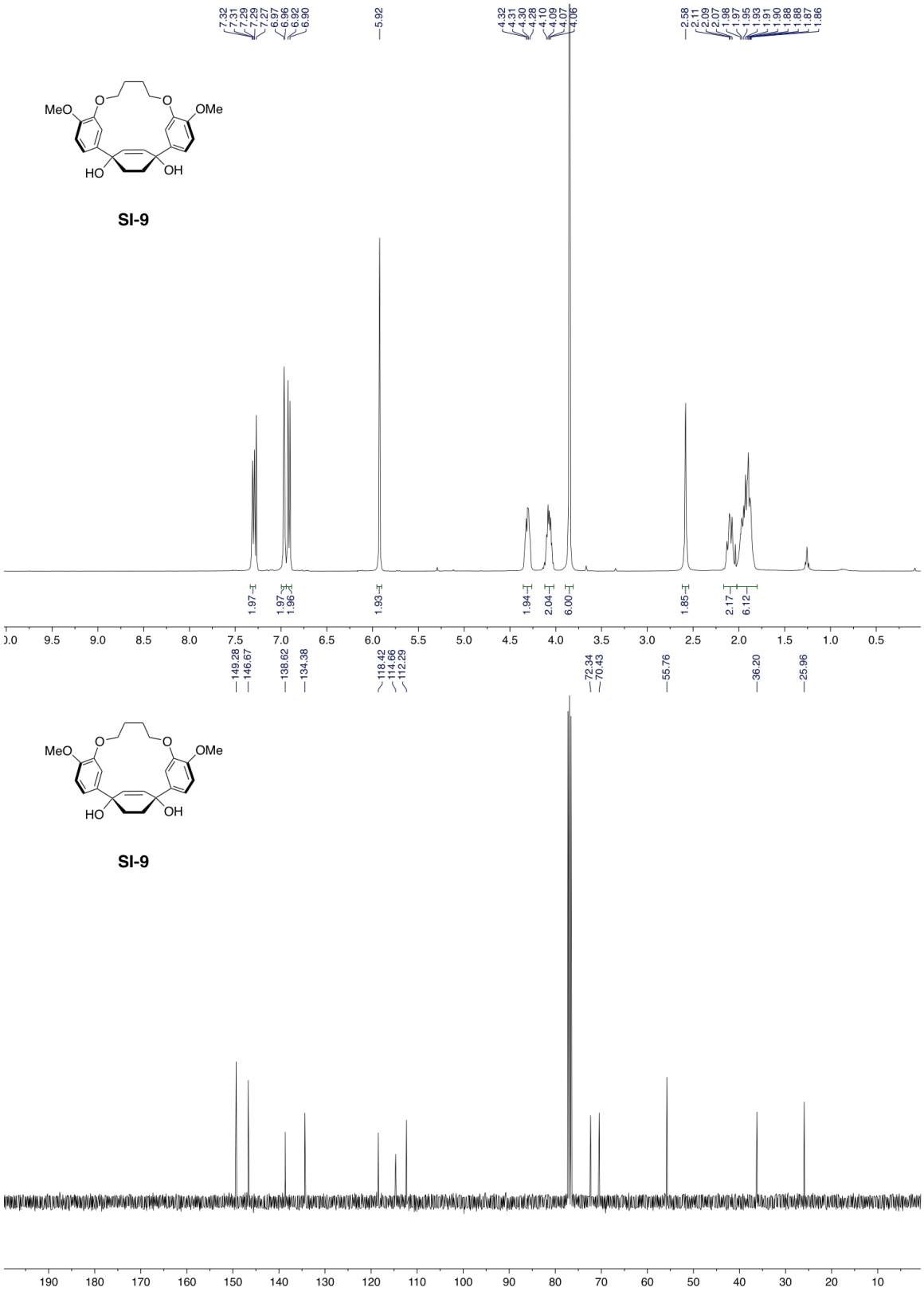
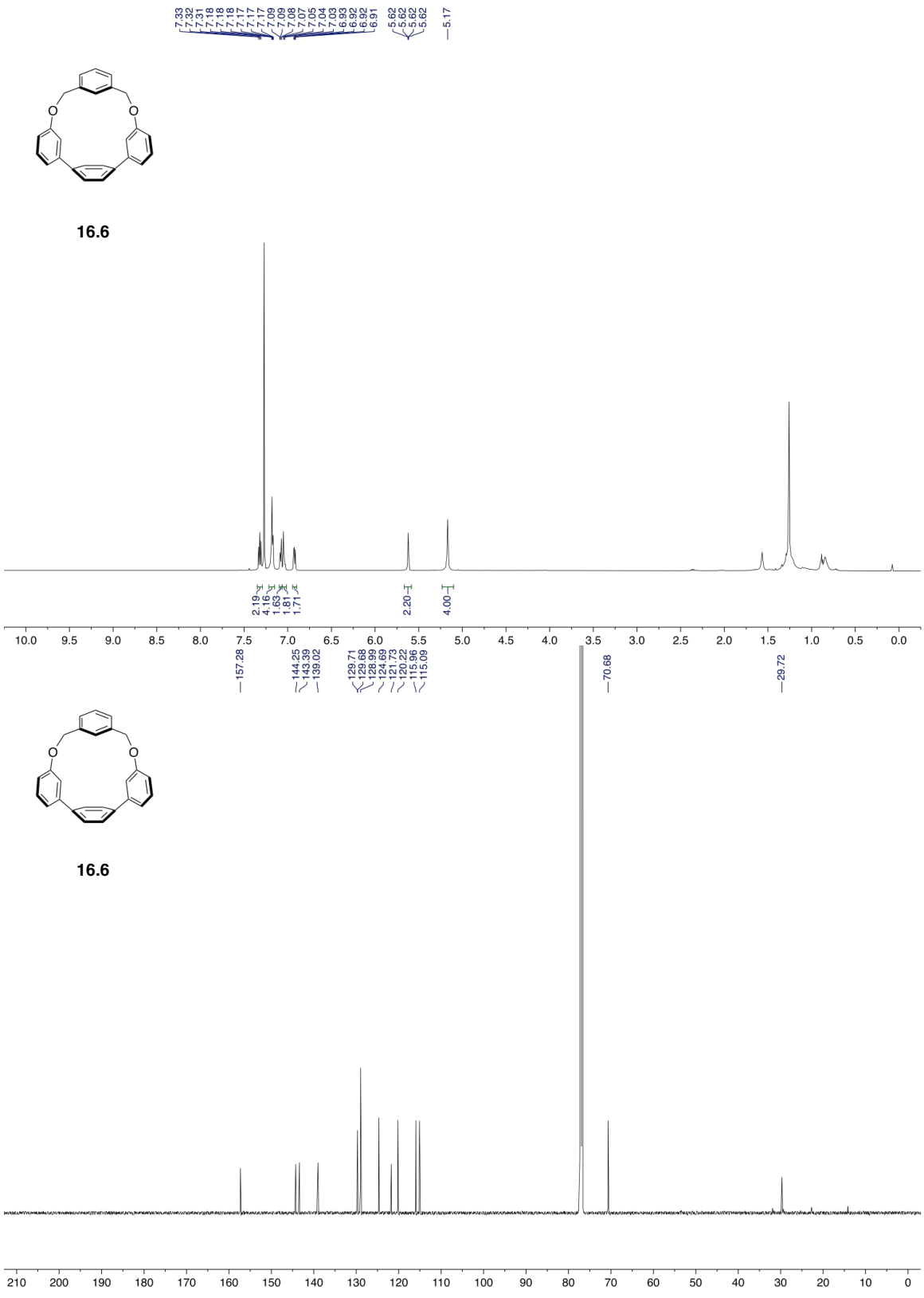
7.32
7.31
7.31
7.28
7.28
7.28
7.27
7.26
7.26
7.19
7.01
7.00
7.00
6.99
6.99
6.99
6.99
6.17
5.89
5.25
5.23
5.06
5.04
2.10
2.10
2.08
2.08
2.06
2.06
1.78
1.78
1.77
1.76
1.75
1.74
O
O
HO
OH
SI-8
3.41
2.97
1.94
1.94
2.03
1.83
1.88
2.00
3.94
2.03
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
158.00
147.18
137.47
134.24
130.18
127.61
127.48
119.57
118.54
114.28
72.66
71.85
35.38
O
O
HO
OH
SI-8
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0

SI-9


MeO
OMe
HO
OH
7.32
7.31
7.29
7.29
7.27
6.97
6.96
6.92
6.90
5.92
4.32
4.31
4.30
4.28
4.10
4.09
4.07
4.06
2.58
2.11
2.09
2.07
1.98
1.97
1.95
1.93
1.91
1.90
1.88
1.88
1.87
1.86
1.97
1.97
1.96
1.93
1.94
2.04
6.00
1.85
2.17
6.12
149.28
146.67
138.62
134.38
118.42
114.66
112.29
72.34
70.43
55.76
36.20
25.96

SI-9

16.6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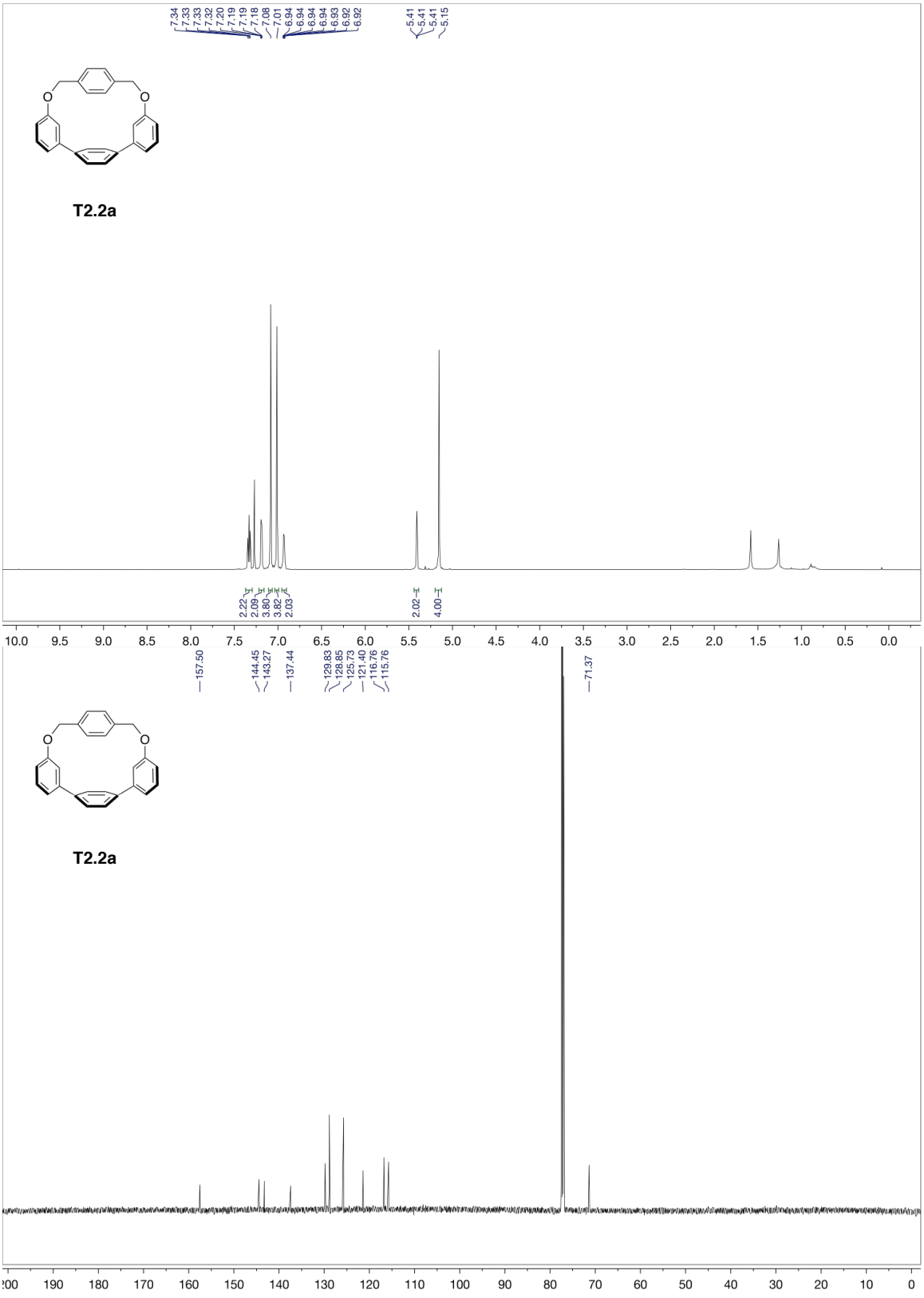
7.32
7.31
7.18
7.18
7.18
7.17
7.17
7.17
7.09
7.09
7.08
7.07
7.05
7.04
7.03
6.93
6.92
6.91
5.62
5.62
5.62
5.62
5.17
O
O
16.6
2.19
4.16
1.83
1.51
1.71
2.20
4.00
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
157.28
144.25
143.39
139.02
129.71
129.68
128.99
124.69
121.73
120.22
115.96
115.09
70.68
29.72
O
O
16.6
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0

T2.2a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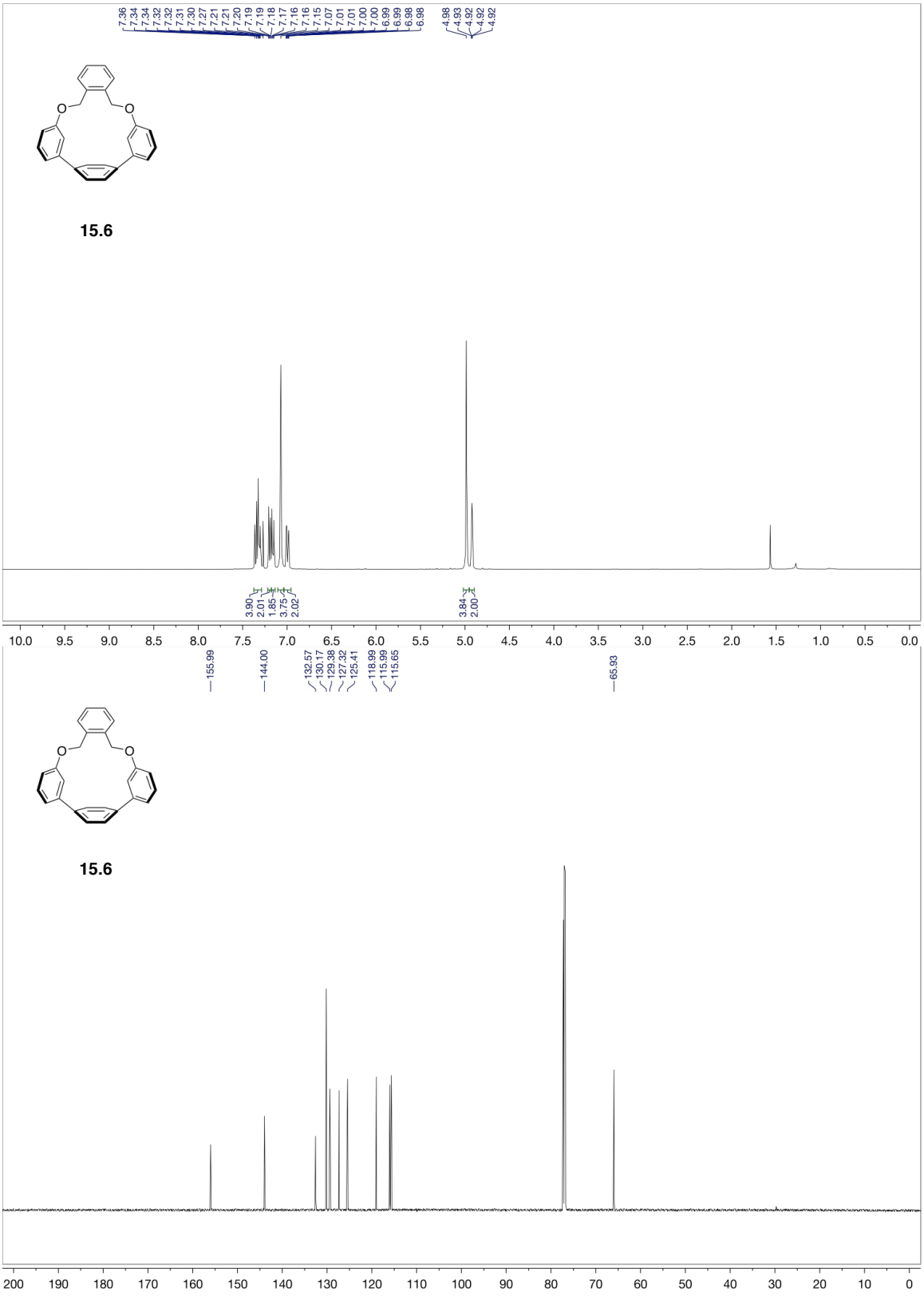
7.33
7.33
7.32
7.20
7.19
7.19
7.18
7.08
7.01
6.94
6.94
6.94
6.93
6.92
6.92
5.41
5.41
5.41
5.15
T2.2a
2.22
2.09
3.80
3.82
2.03
2.02
4.00
157.50
144.45
143.27
137.44
129.83
128.85
125.73
121.40
116.76
115.76
71.37
T2.2a

15.6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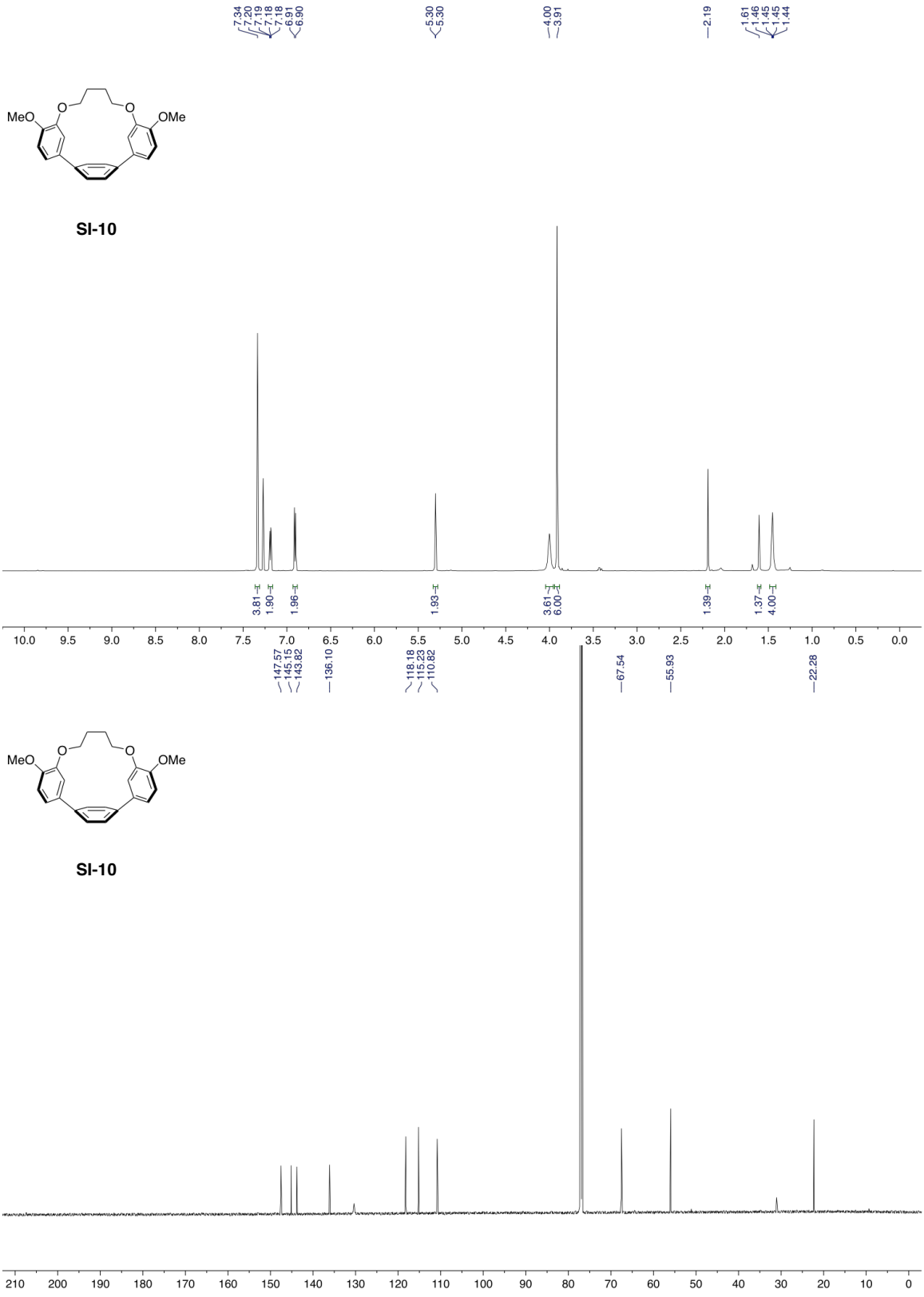
SI-10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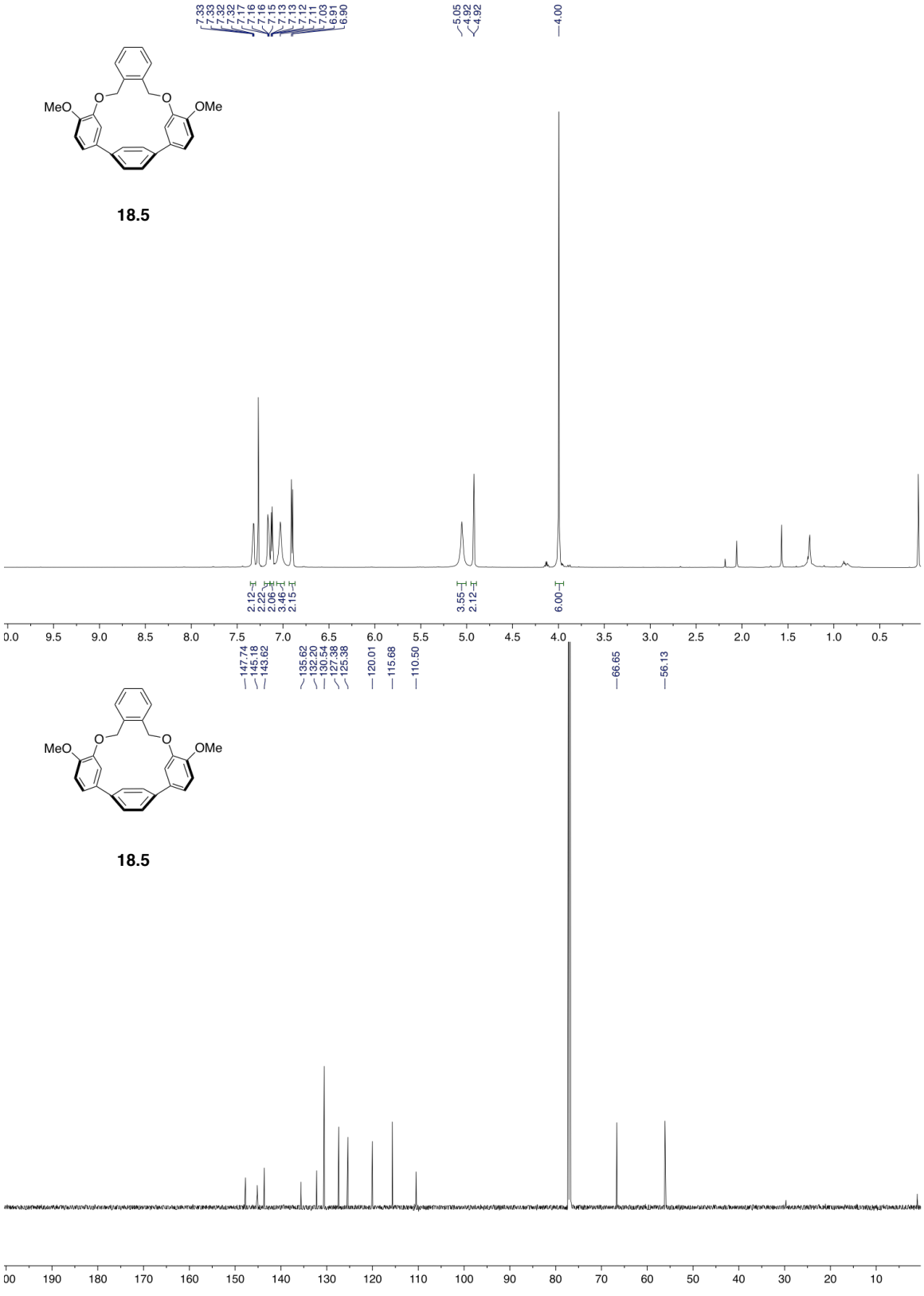
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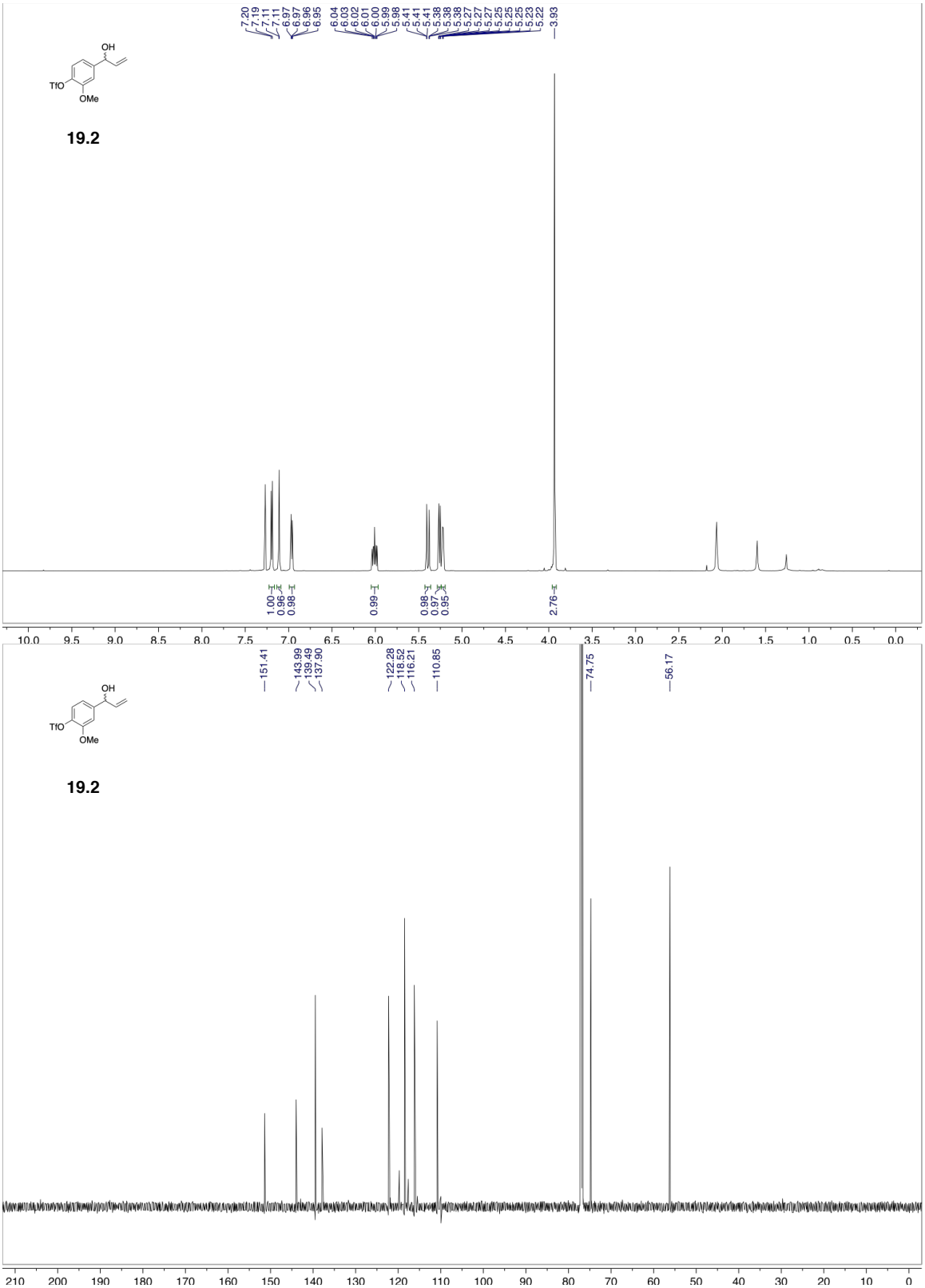
19.2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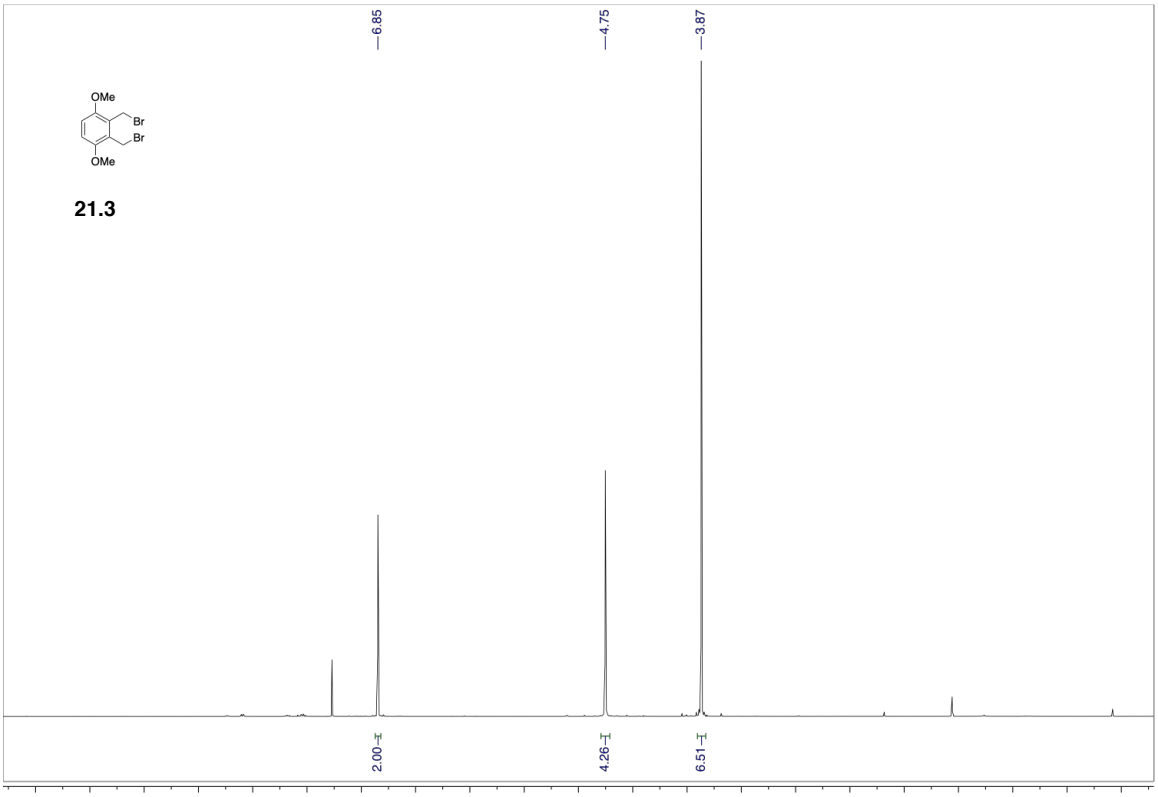
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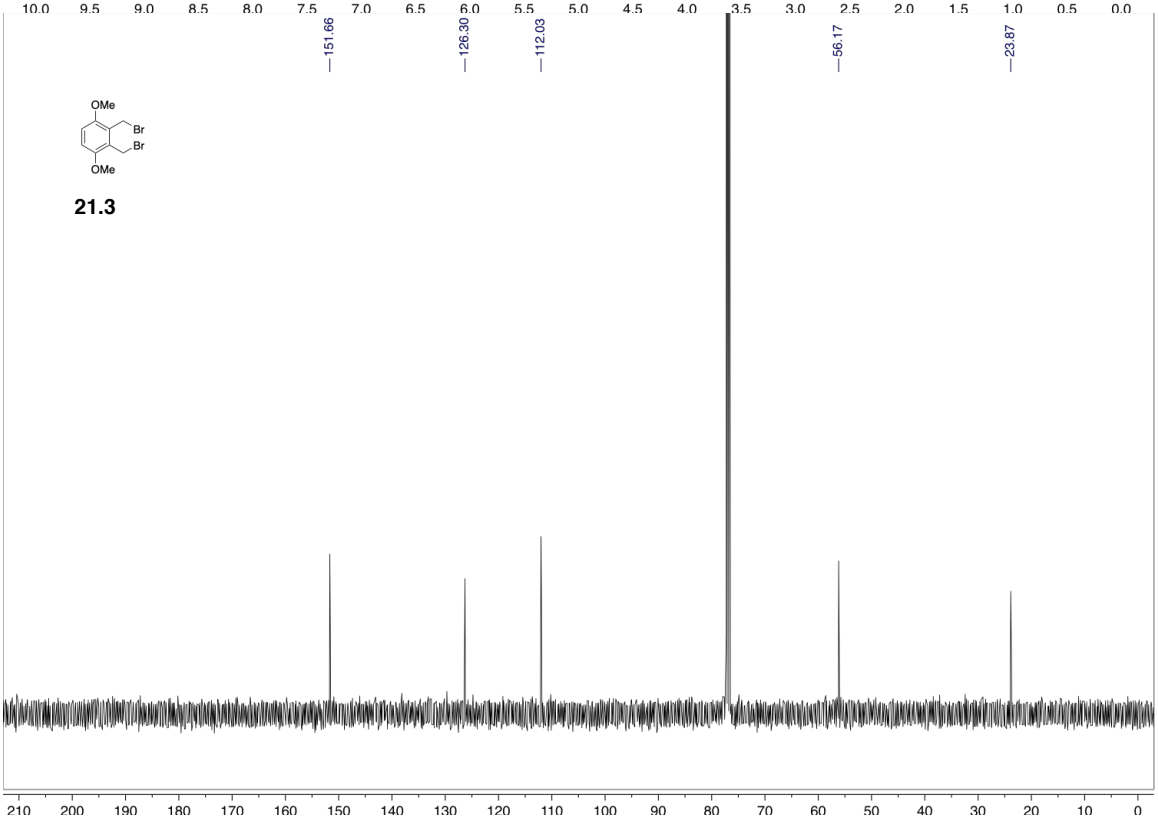
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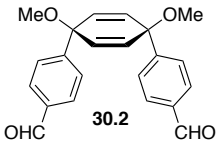
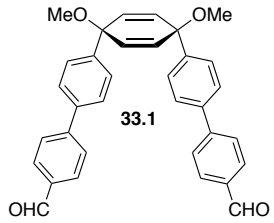


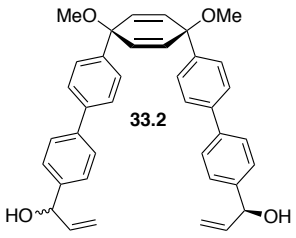
30.2

30.2: *n*BuLi (26 mL, 1.6 M in hexanes, 41 mmol) was added to a stirred, -78 °C solution of diiodide **30.1** (9.7 g, 18 mmol) in diethyl ether (90 mL) over a 7 min period. After 30 min, DMF (14 mL, 13 g, 180 mmol) was added and the reaction was warmed to room temperature. After 3 h, the reaction was quenched with distilled water (100 mL). The aqueous material was extracted with diethyl ether (3 × 100 mL). The combined organic extracts were washed with distilled water (150 mL) and brine (150 mL), dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The crude residue was purified via flash chromatography (19 × 5 cm; 10% EtOAc/hexanes, 30% EtOAc/hexanes) to afford the dialdehyde **30.2** (3.3 g, 53%); R_f = 0.27 (20% EtOAc/hexanes); ^{1}H NMR (600 MHz, $CDCl_3$) δ 10.01 (s, 2H), 7.85 (d, *J* = 8.1 Hz, 4H), 7.57 (d, *J* = 8.1 Hz, 4H), 6.17 (s, 4H), 3.47 (s, 6H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 191.86, 149.59, 135.73, 133.44, 129.93, 126.64, 74.74, 52.17.



33.1

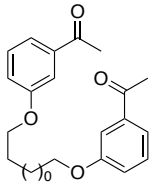
33.1: $Pd(PPh_3)_4$ (0.021 g, 0.018 mmol) was added to a degassed, stirred, 80 °C solution of **30.1** (0.10 g, 0.18 mmol), 4-formylphenylboronic acid (0.059 g, 0.39 mmol), and sodium carbonate (0.098 g, 0.92 mmol) in toluene (12 mL), water (4 mL), and ethanol (2 mL). After 4.5 h the reaction was cooled to room temperature and was quenched with distilled water (10 mL) and diluted with 1M HCl (10 mL). The aqueous material was extracted with dichloromethane (3 × 10 mL). The combined organic extracts were washed with distilled water (20 mL) and brine (20 mL), dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The crude residue was purified via flash chromatography (18 × 1.2 cm; 50% dichloromethane/hexanes, dichloromethane) to afford **33.1** (0.038 g, 41%); R_f = 0.23 (80% dichloromethane/hexanes); ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.06 (s, 1H), 7.95 (d, *J* = 8.1 Hz, 2H), 7.75 (d, *J* = 8.0 Hz, 2H), 7.68-7.50 (m, 4H), 6.20 (s, 2H), 3.50 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 191.76, 146.52, 143.66, 138.88, 135.11, 133.35, 130.15, 127.49, 127.30, 126.58, 51.99.



33.2

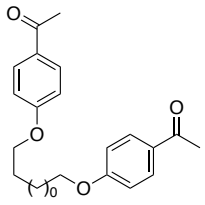
33.2: Vinylmagnesium chloride (0.035 mL, 1.6 M in THF, 0.50 mmol) was added to a stirred, room temperature solution of **33.1** (0.010 g, 0.020 mmol) in dichloromethane (0.5 mL). After 10 min, the reaction was quenched with distilled water (5 mL) and diluted with 1M HCl (3 mL). The aqueous material was extracted with dichloromethane (3 × 5 mL). The combined organic extracts were washed with a saturated solution of sodium bicarbonate (5 mL) and brine (5 mL), dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The crude residue was purified via flash chromatography (10 × 1 cm; 2% acetone/dichloromethane; 4% acetone/dichloromethane) to afford the allylic diol

33.2 (0.0077 g, 69%); R_f = 0.2 (2% acetone/dichloromethane); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.65-7.38 (m, 16H), 6.18 (s, 4H), 6.09 (ddd, *J* = 16.7, 10.3, 6.0 Hz, 2H), 5.40 (dt, *J* = 17.1, 1.5 Hz, 2H), 5.33-5.17 (m, 4H), 3.48 (s, 6H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 142.54, 140.26, 140.13, 140.04, 133.41, 127.28, 127.10, 126.75, 126.47, 115.28, 75.14, 74.74, 52.04.



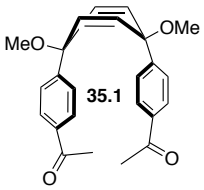
36.1b

36.1b: 1,3-dibromopropane (0.50 mL, 1.0 g, 5.0 mmol) was added to a stirred, 70 °C solution of 3-hydroxybenzaldehyde (1.4 g, 9.9 mmol), potassium carbonate (2.4 g, 17 mmol), and TBAI (0.046 g, 0.12 mmol) in DMF (20 mL). After 3 d, the reaction was cooled to room temperature and quenched with distilled water (15 mL) and diluted with 1M HCl (15 mL). The aqueous material was extracted with dichloromethane (3 × 20 mL). The combined organic extracts were washed with a saturated solution of sodium bicarbonate (30 mL) and brine (30 mL), dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The crude residue was purified via flash chromatography (18 × 2.5 cm; 1% acetone/dichloromethane, 3% acetone/dichloromethane) to afford **36.1b** (0.047 g, 30%); R_f = 0.34 (1% acetone/dichloromethane); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.55 (dd, *J* = 1.6, 1.0 Hz, 2H), 7.53 (dd, *J* = 1.6, 1.0 Hz, 2H), 7.51 (dd, *J* = 2.6, 1.5 Hz, 4H), 7.37 (ddd, *J* = 8.2, 7.6, 0.4 Hz, 4H), 7.14 (dd, *J* = 2.7, 1.0 Hz, 2H), 7.12 (dd, *J* = 2.7, 1.0 Hz, 2H), 4.23 (t, *J* = 6.1 Hz, 8H), 2.60 (s, 12H), 2.31 (p, *J* = 6.0 Hz, 4H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 197.81, 158.90, 138.33, 129.47, 121.07, 119.88, 112.89, 64.33, 29.02, 26.62.



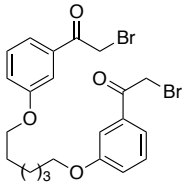
36.1d

36.1d: 1,3-dibromopropane (0.50 mL, 1.0 g, 5.0 mmol) was added to a stirred, 70 °C solution of 4-hydroxybenzaldehyde (1.3 g, 9.9 mmol), potassium carbonate (2.4 g, 17 mmol), and TBAI (0.046 g, 0.12 mmol) in DMF (20 mL). After 7 h, the reaction was cooled to room temperature and quenched with distilled water (15 mL) and diluted with 1M HCl (15 mL). The aqueous material was extracted with dichloromethane (3 × 20 mL). The combined organic extracts were washed with a saturated solution of sodium bicarbonate (30 mL) and brine (30 mL), dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The crude residue was purified via flash chromatography (18 × 2.5 cm; dichloromethane, 3.5% acetone/dichloromethane) to afford **36.1d** (1.2 g, 77%); R_f = 0.58 (2% acetone/dichloromethane); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.94 (d, *J* = 8.9 Hz, 4H), 6.95 (d, *J* = 8.9 Hz, 4H), 4.24 (t, *J* = 6.0 Hz, 4H), 2.56 (s, 6H), 2.36-2.28 (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 196.62, 162.53, 130.49, 130.31, 114.00, 64.29, 26.25.



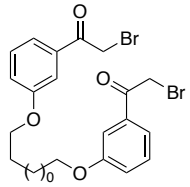
35.1: Acetic anhydride (1.7 mL, 1.9 g, 18 mmol) was added to a 100 °C solution of **30.1** (0.51 g, 1.8 mmol), lithium chloride (0.78 g, 18 mmol), Hünig's base (1.3 mL, 0.95 g, 7.4 mmol), and $Pd_2(dba)_3$ (0.042 g, 0.046 mmol) in DMF (50 mL). After 30 h, the reaction was cooled to room temperature and diluted with diethyl ether (150 mL). The organic layer was washed with distilled water (100 mL), dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The crude residue was purified via flash chromatography (18 × 4 cm; 20% EtOAc/hexanes, 30% EtOAc/hexanes) to afford **35.1** (0.11 g, 32%); R_f = 0.18 (20% EtOAc/hexanes); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.92 (d, *J* = 8.2 Hz, 1H), 7.49 (d, *J* = 8.3 Hz, 1H), 6.15 (s, 1H), 3.46 (s, 2H), 2.61 (s, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 197.65, 148.13, 136.32, 133.28, 128.44, 126.09, 99.87, 52.01, 26.59.

General Procedure J for the preparation of α-bromides:



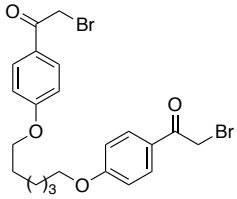
36.2a

36.2a: Copper bromide (0.13 g, 0.56 mmol) was added to a stirred, 85 °C solution of **36.1a** (0.051 g, 0.14 mmol) in a 1:1 mixture of $CHCl_3$/EtOAc (8 mL). The reaction stirred for 5.5 h, at which point the reaction was cooled to room temperature, filtered over a 0.5 cm bed of celite, and concentrated under reduced pressure. The crude residue was purified via flash chromatography (15 cm × 1.3 cm; 90% dichloromethane/hexanes, dichloromethane, 3% acetone/dichloromethane) to afford to dibromide **36.2a** (0.38 g, 45%); R_f = 0.30 (90% dichloromethane/hexanes).



36.2b

36.2b: This compound was prepared using the *general procedure J* using **36.1b** (0.050 g, 0.16 mmol) and copper bromide (0.14 g, 0.64 mmol) in 1:1 EtOAc/$CHCl_3$ (8 mL). The crude residue was purified via flash chromatography (18 × 1.3 cm; 80% dichloromethane/hexanes, dichloromethane, 1% acetone/dichloromethane) to afford **36.2b** (0.046 g, 61%); R_f = 0.43 (dichloromethane); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.61-7.49 (m, 4H), 7.41 (t, *J* = 7.9 Hz, 2H), 7.21-7.12 (m, 2H), 4.46 (s, 4H), 4.24 (t, *J* = 6.0 Hz, 4H), 2.39-2.27 (m, 2H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 191.09, 159.16, 135.21, 129.87, 121.59, 120.91, 113.67, 64.44, 31.03, 29.04.

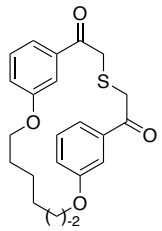


36.2c

36.2c: This compound was prepared using the *general procedure J* using **36.1c** (0.020 g, 0.056 mmol) and copper bromide (0.050 g, 0.023 mmol) in 1:1 EtOAc/$CHCl_3$ (3 mL). The crude residue was purified via flash chromatography (14 × 0.5 cm; dichloromethane, 2% acetone/dichloromethane) to afford **36.2c** (0.014 g, 49%); R_f = 0.34

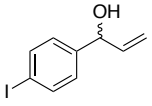
(dichloromethane); ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.05-7.90 (m, 4H), 7.03-6.90 (m, 4H), 4.41 (s, 4H), 4.06 (t, *J* = 6.4 Hz, 4H), 1.87 (dd, *J* = 8.3, 5.1 Hz, 4H), 1.58 (dd, *J* = 7.7, 3.4 Hz, 5H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 163.65, 131.37, 126.71, 114.45, 68.12, 30.71, 29.71, 28.97, 25.76.

General Procedure K for the preparation of thiacyclophanes:



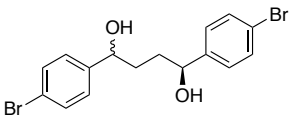
36.3a

36.3b: This compound was prepared using the *general procedure K* using **36.2b** (0.040 g, 0.085 mmol) and sodium sulfide nonahydrate (0.021 g, 0.085 mmol, in 0.5 mL 10% aq. EtOH) in THF (0.5 mL), and ethanol (2.5 mL). The crude residue was purified via flash chromatography (15 × 0.5 cm; 20% EtOAc/hexanes) to afford **36.3b** (0.011 g, 38%); R_f = 0.24 (20% EtOAc/hexanes); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42 (dd, *J* = 2.6, 1.6 Hz, 1H), 7.34-7.17 (m, 2H), 6.99 (ddd, *J* = 8.1, 2.6, 1.1 Hz, 1H), 4.29 (t, *J* = 5.7 Hz, 2H), 3.82 (s, 2H), 2.26-2.15 (m, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 194.63, 158.79, 136.69, 129.58, 120.68, 120.15, 115.12, 63.57, 36.98.



43.2a

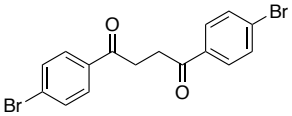
43.2a: Vinylmagnesium chloride (0.81 mL, 1.3 mmol, 1.6 M in THF) was added to a stirred, room temperature solution of 4-iodobenzaldehyde (0.20 g, 0.87 mmol) in dichloromethane (9 mL). After 10 min, the reaction was quenched with distilled water (10 mL) and then diluted with 1M HCl (10 mL). The aqueous material was extracted with dichloromethane (3 × 10 mL). The combined organic extracts were washed with a saturated solution of sodium bicarbonate (10 mL) and brine (10 mL); dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The crude residue was purified via flash chromatography (15 × 1.3 cm; 10% EtOAc/hexanes; 20% EtOAc/hexanes) to afford **43.2a** (0.16 g, 71%); R_f = 0.43 (20% EtOAc/hexanes); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.69-7.60 (m, 1H), 7.12-7.02 (m, 1H), 5.29 (dt, *J* = 17.1, 1.4 Hz, 1H), 5.17 (dt, *J* = 10.3, 1.2 Hz, 1H), 5.08 (dd, *J* = 6.4, 3.1 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 142.27, 139.88, 139.85, 137.67, 128.43, 115.87, 115.86, 115.83, 93.37, 74.87.



43.3b

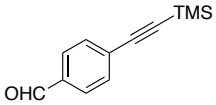
43.3b: Hoveyda-Grubbs II (0.053 g, 0.85 mmol) was added to a stirred, room temperature solution of **43.2b** (1.1 g, 5.4 mmol) in dichloromethane (54 mL). After 2 h, sodium borohydride (0.40 g, 11 mmol) and methanol (6 mL) was added. After 3 h, the reaction was quenched with distilled water (20 mL). The aqueous material was extracted with dichloromethane (3 × 20 mL). The combined organic extracts were washed with a saturated solution of sodium

bicarbonate (15 mL) and brine (15 mL), dried over $MgSO_4$, filtered and concentrated under reduced pressure. The crude residue was purified via flash chromatography (13 × 2.3 cm; 40% EtOAc/hexanes, 50% EtOAc/hexanes) to afford **43.3b** (0.66 g, 61%); R_f = 0.29 (40% EtOAc/hexanes); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40 (d, *J* = 8.3 Hz, 1H), 7.11 (dd, *J* = 8.5, 3.3 Hz, 1H), 4.71-4.45 (m, 1H), 1.74 (ddt, *J* = 18.7, 10.2, 5.2 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 143.60, 143.47, 131.69, 131.68, 127.66, 121.43, 121.38, 74.00, 73.53, 36.05, 34.99.



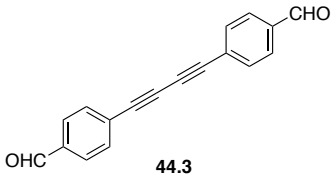
43.4

43.4: Dess-Martin (1.4 g, 3.3 mmol) was added to a stirred, room temperature solution of **43.3b** (0.037 g, 0.92 mmol) and sodium bicarbonate (0.28 g, 3.3 mmol) in dichloromethane (10 mL). After 9 h, the reaction was quenched with distilled water (5 mL) and a $Na_2S_2O_3$ solution (10 mL). The aqueous material was extracted with dichloromethane (3 × 12 mL). The combined organic extracts were washed with brine (10 mL) and a saturated solution of sodium bicarbonate (10 mL), dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The crude residue was purified via flash chromatography (13 × 2.3 cm; 10% EtOAc/hexanes, 80% EtOAc/hexanes) to afford **43.4** (0.26 g, 72%); R_f = 0.65 (40% EtOAc/hexanes); ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.11-7.76 (m, 4H), 7.76-7.57 (m, 4H), 3.42 (s, 4H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 197.72, 135.50, 132.14, 129.84, 128.63, 32.62.



44.1

44.1: TMS acetylene (0.5 mL, 0.3 g, 3 mmol) was added to a stirred, degassed, 45 °C solution of 4-iodobenzaldehyde (0.50 g, 2.2 mmol), copper iodide (0.016 g, 0.086 mmol), and $PdCl_2(PPh_3)_2$ (0.030 g, 0.043 mmol) in Et_3N (0.6 mL) and THF (3 mL). This reaction quickly (within 5 min) progressed from brown to yellow to orange to black. After 30 h, the reaction was cooled to room temperature and concentrated under reduced pressure. The crude residue was then purified via flash chromatography (15 × 1.3 cm; hexanes, 50% chloroform/hexanes, 75% chloroform/hexanes) to afford **44.1** (0.34 g, 78%); R_f = 0.52 (chloroform); ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.00 (s, 1H), 7.87-7.79 (m, 2H), 7.64-7.58 (m, 2H), 0.27 (s, 13H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 191.38, 135.41, 132.35, 129.32, 129.23, 103.69, 98.92.

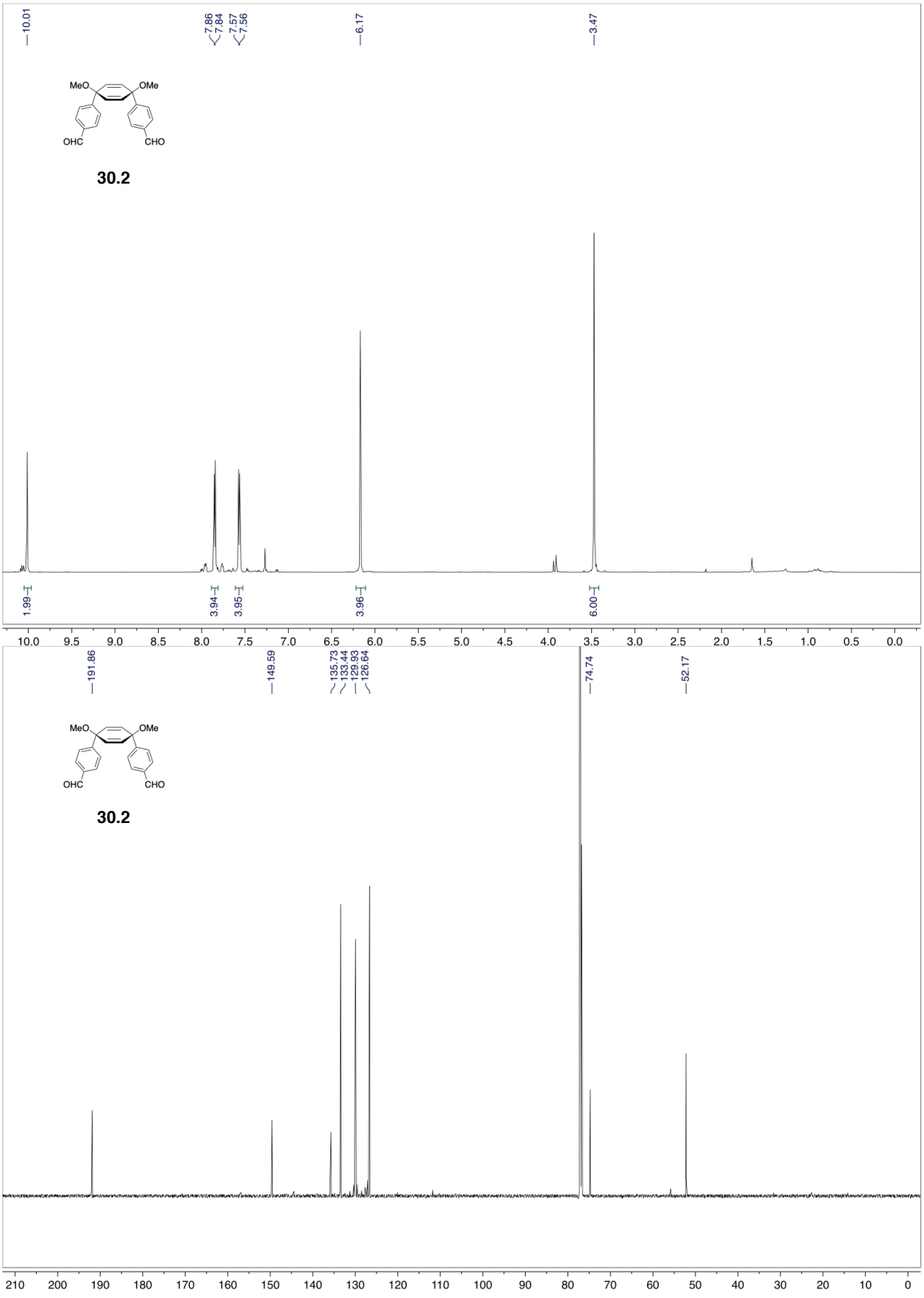


44.3

44.3: Copper iodide (1.6 g, 7.7 mmol) was added to a stirred, 55 °C solution of **44.2** (1.0 g, 7.7 mmol) in DMF (80 mL) open to the air. After 36 h, the reaction was cooled to room temperature and quenched with distilled water (50 mL). The aqueous material was extracted with dichloromethane (3 × 50 mL). The combined organic extracts were washed with distilled water (50 mL), dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. Any residual DMF was removed by blowing a constant stream of N_2 gas over the sample.

The crude residue was purified via flash chromatography (10 × 7 cm; 50% chloroform/hexanes, chloroform, 5% acetone/chloroform) to afford **44.3** (0.40 g, 40%); R_f = 0.13 (50% chloroform/hexanes); ^{1}H NMR (600 MHz, $CDCl_3$) δ 10.04 (d, *J* = 4.1 Hz, 2H), 7.89 (d, *J* = 7.7 Hz, 3H), 7.70 (d, *J* = 7.6 Hz, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 191.36, 136.16, 133.16, 129.65, 82.12.

30.2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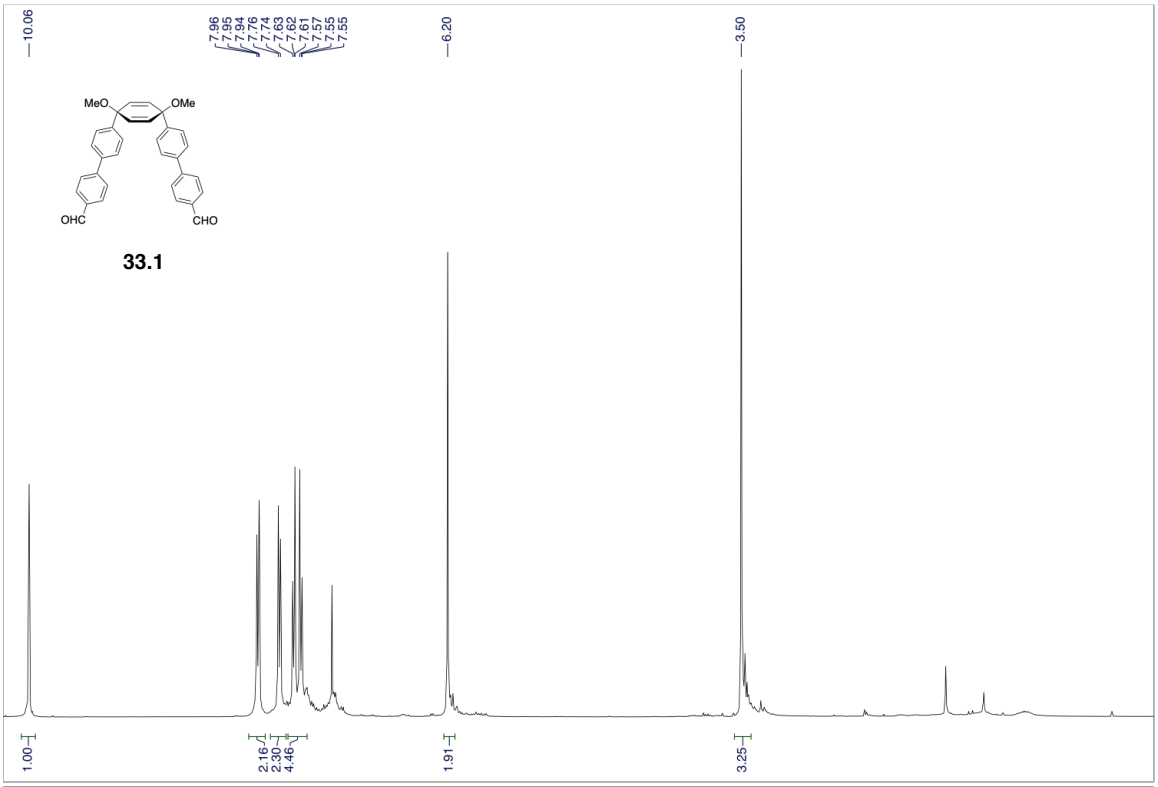
33.1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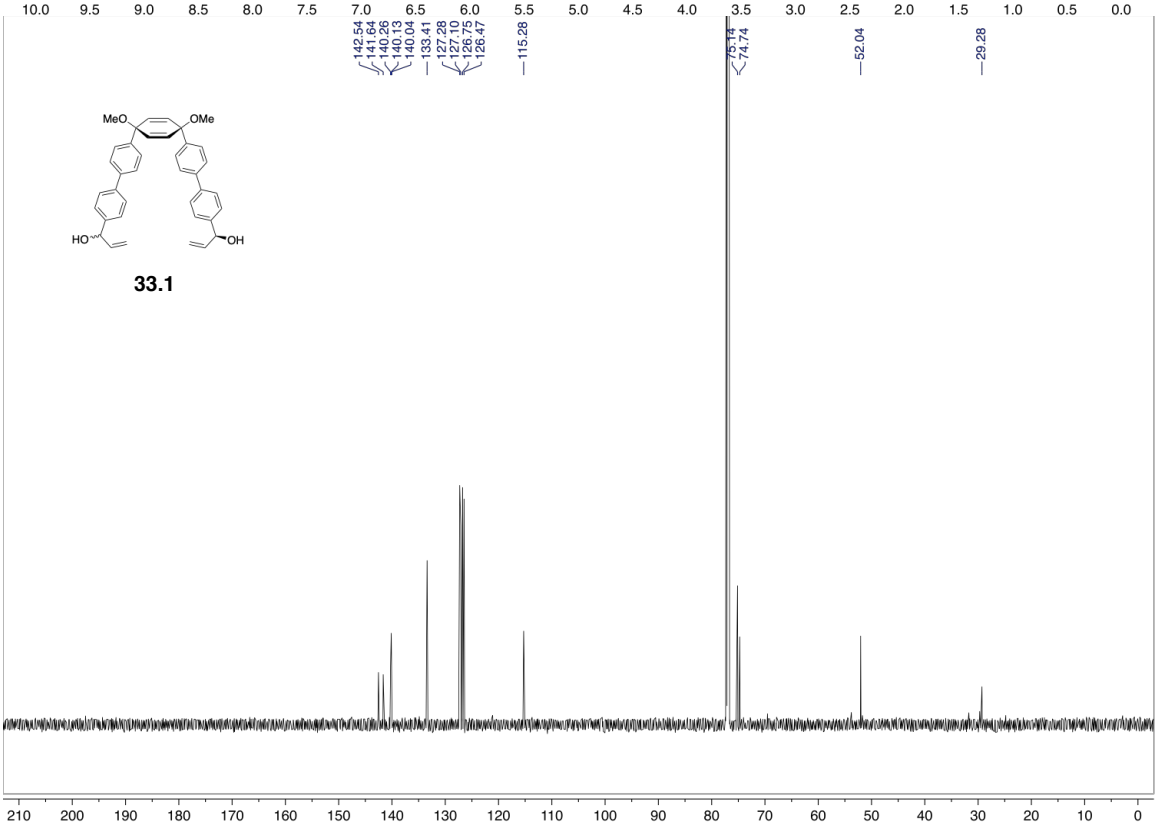
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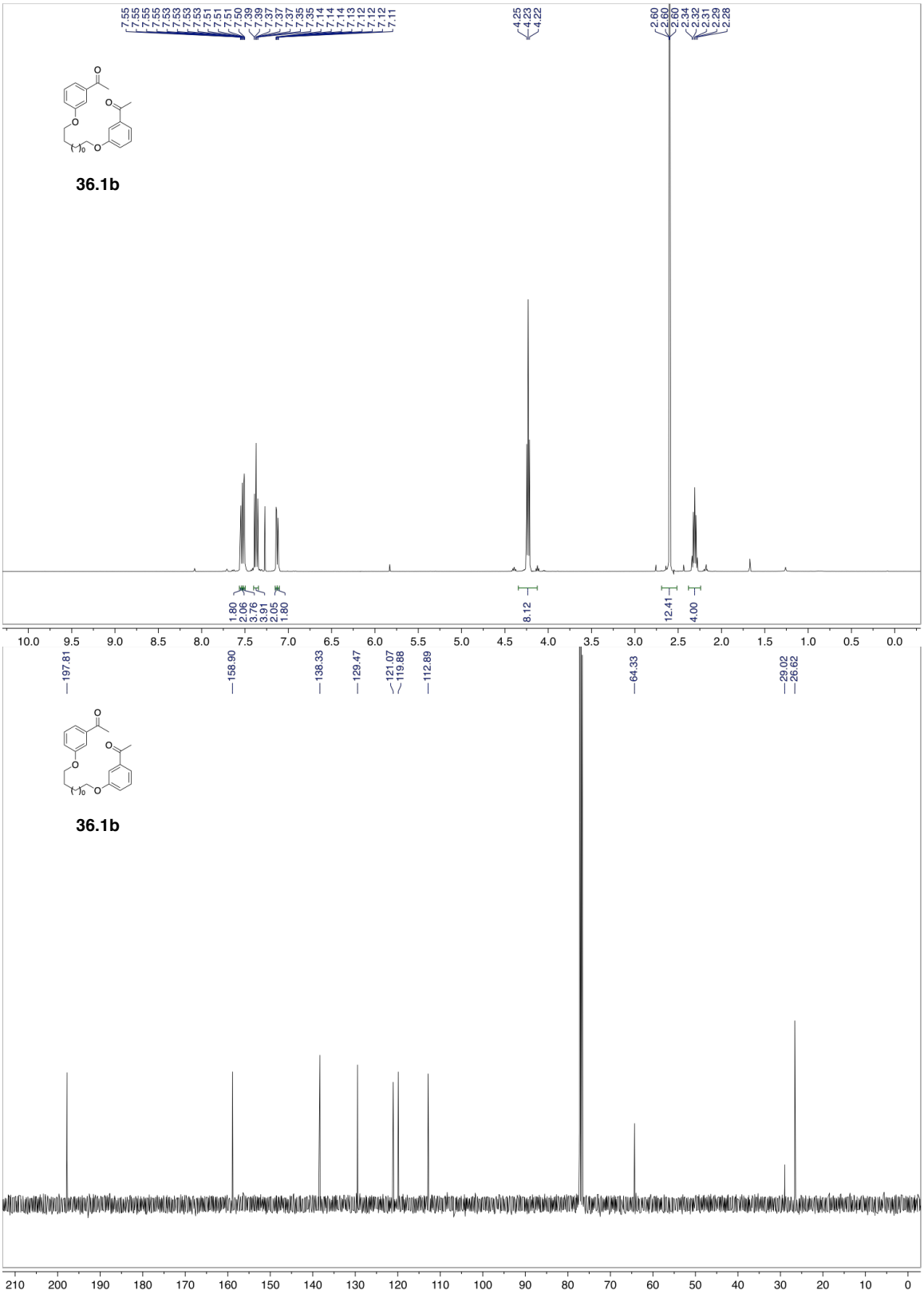
36.1b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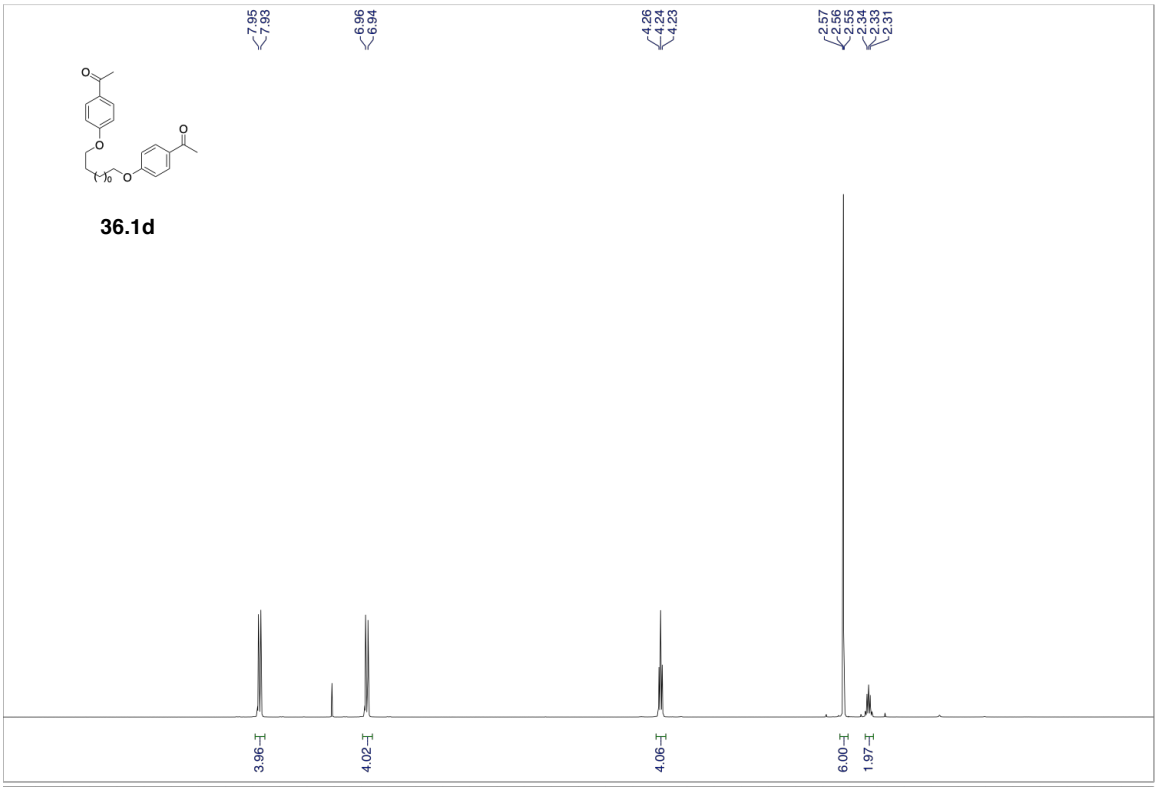
36.1d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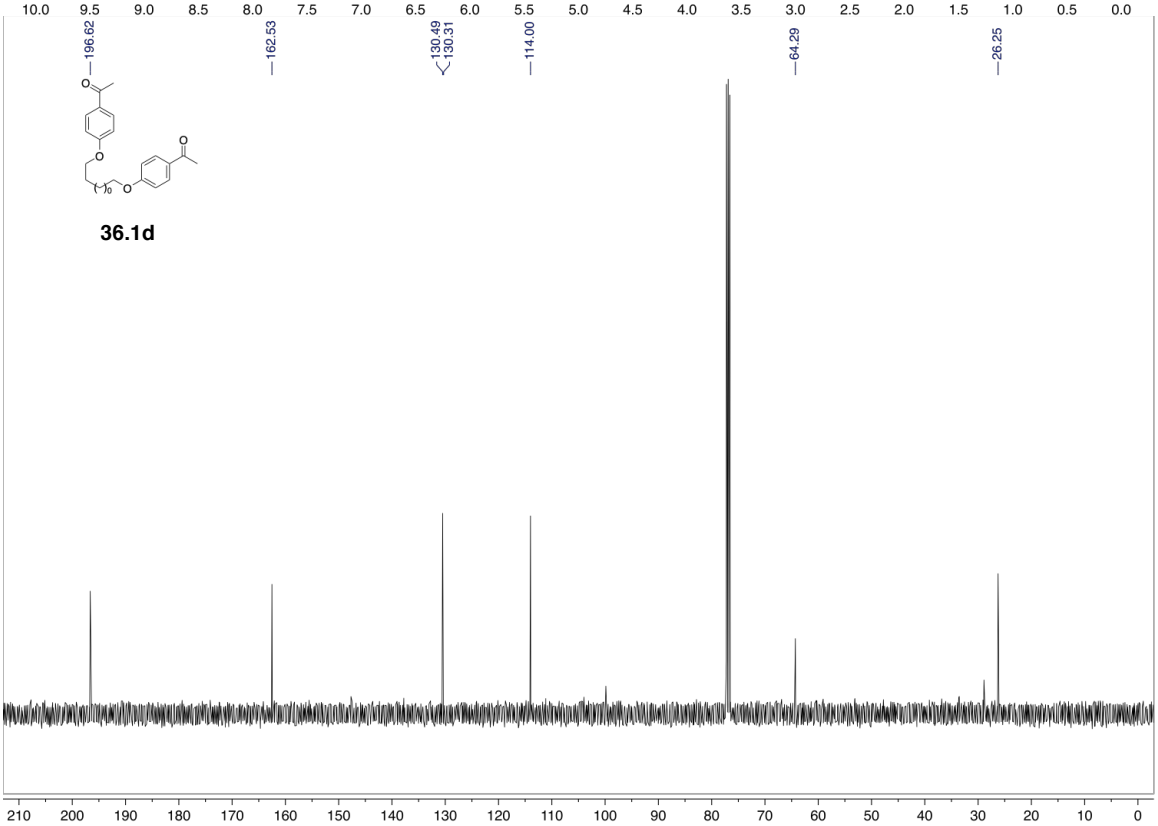
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114.00
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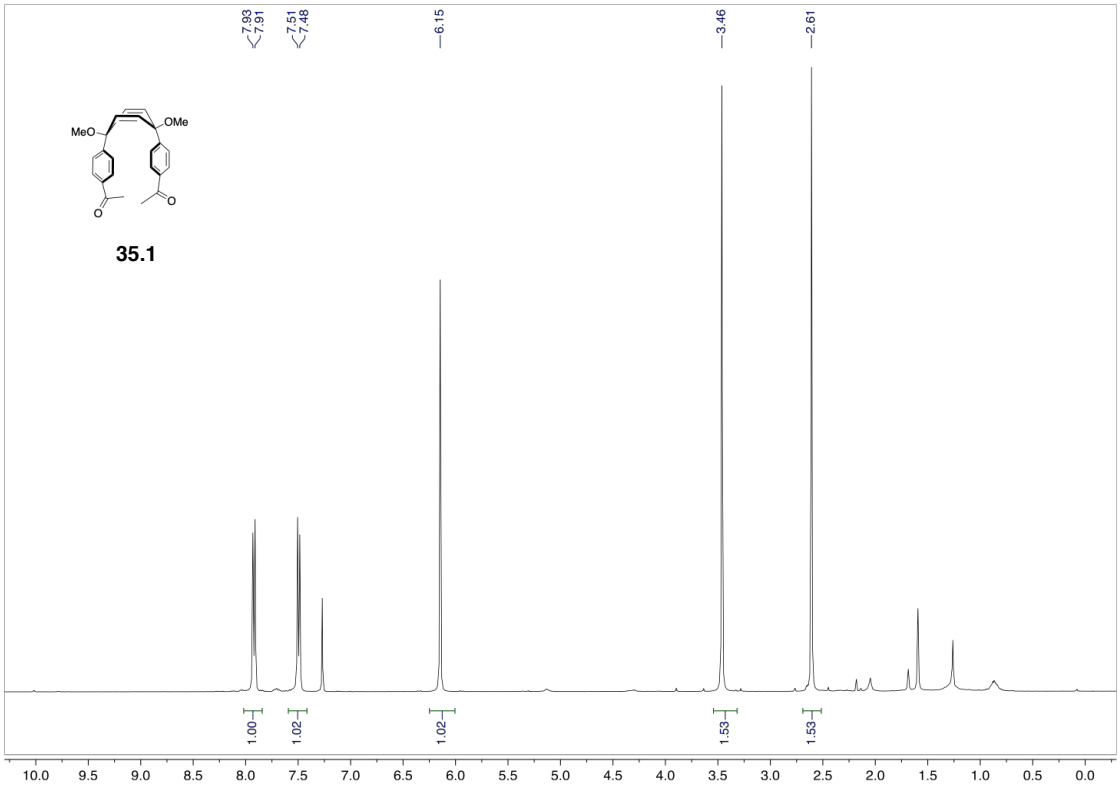
36.1d

35.1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1.53
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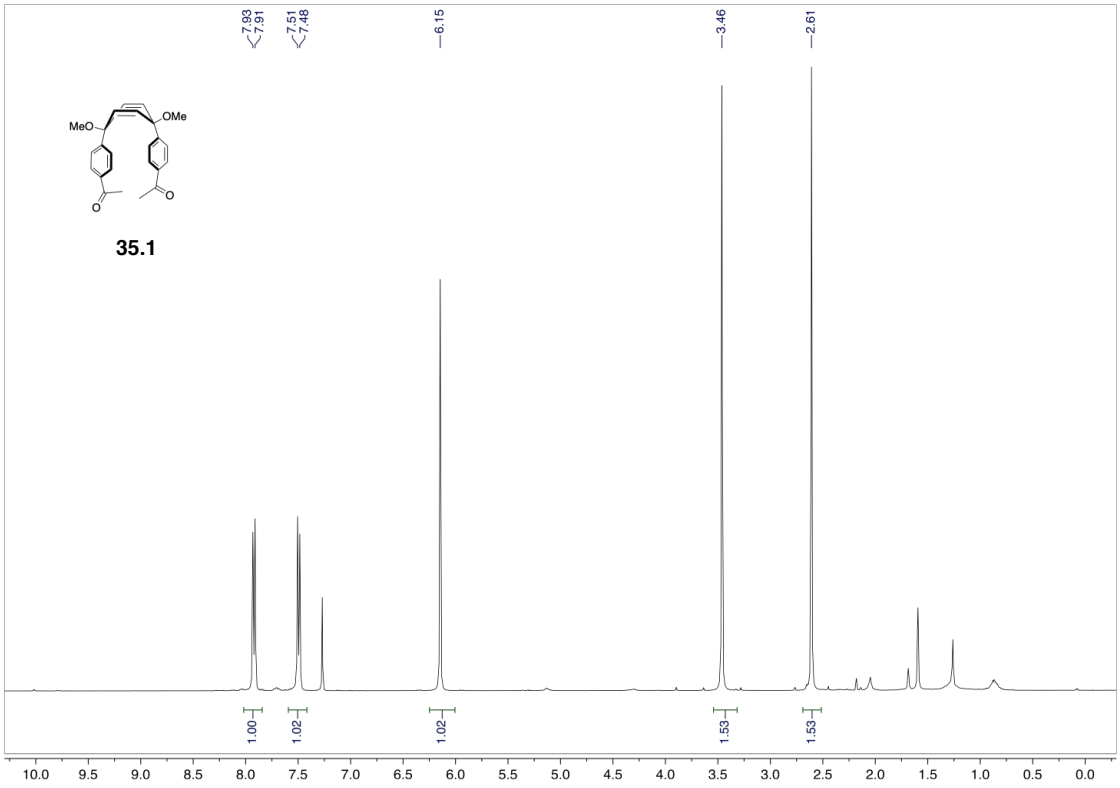
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1.53
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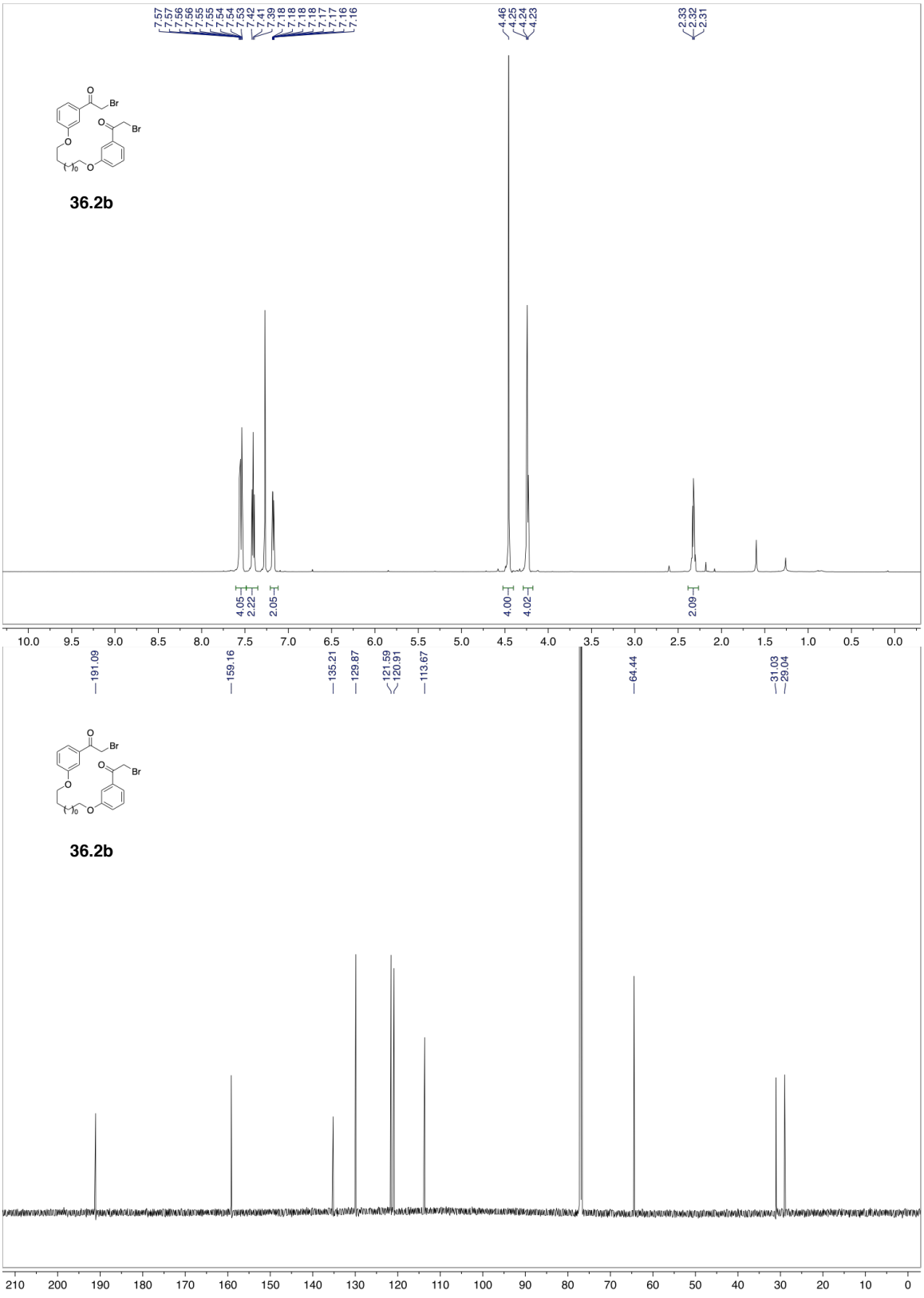
36.2b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2.32
2.31
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Br
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O
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O
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2.05
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4.02
2.09
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135.21
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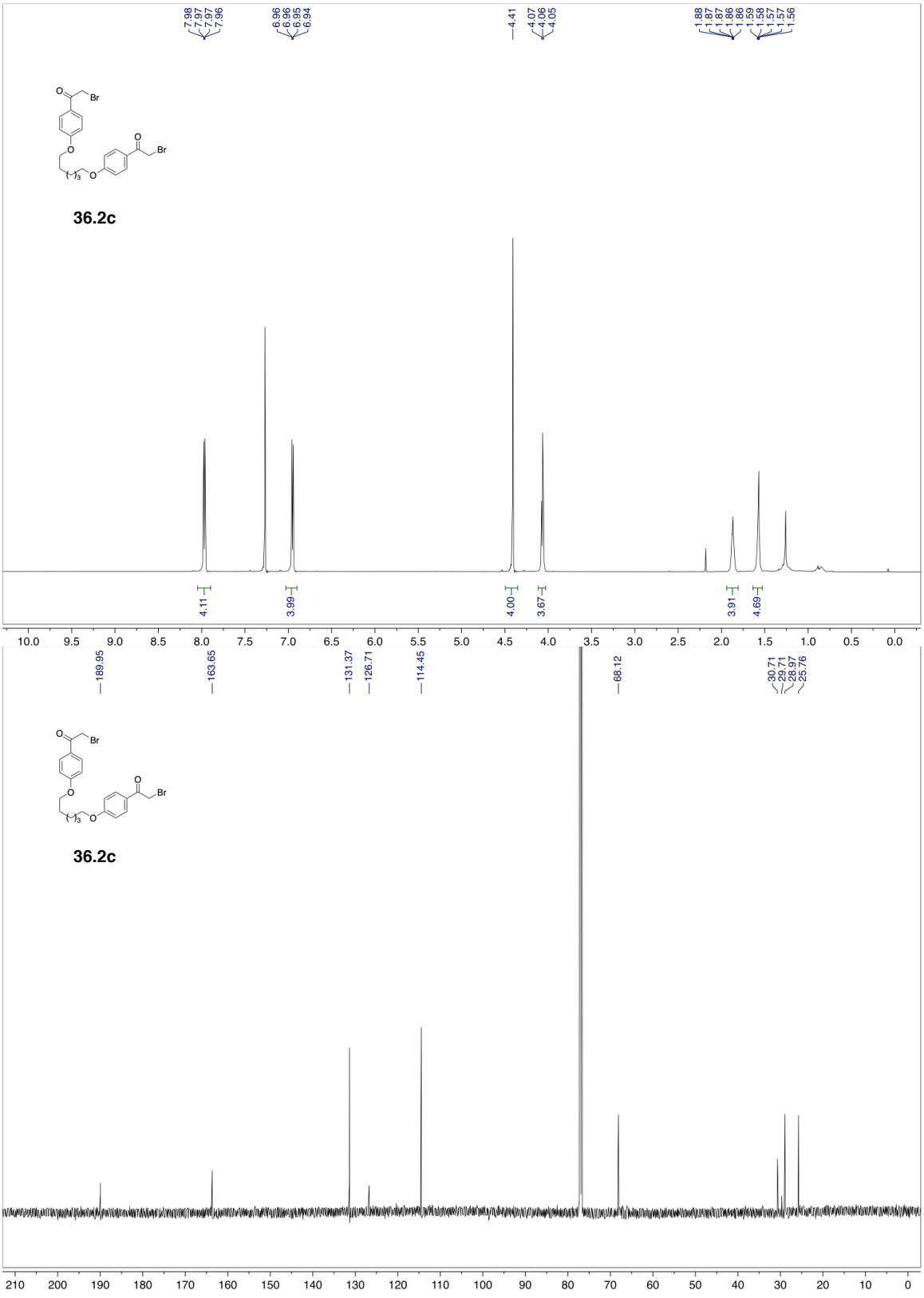
36.2c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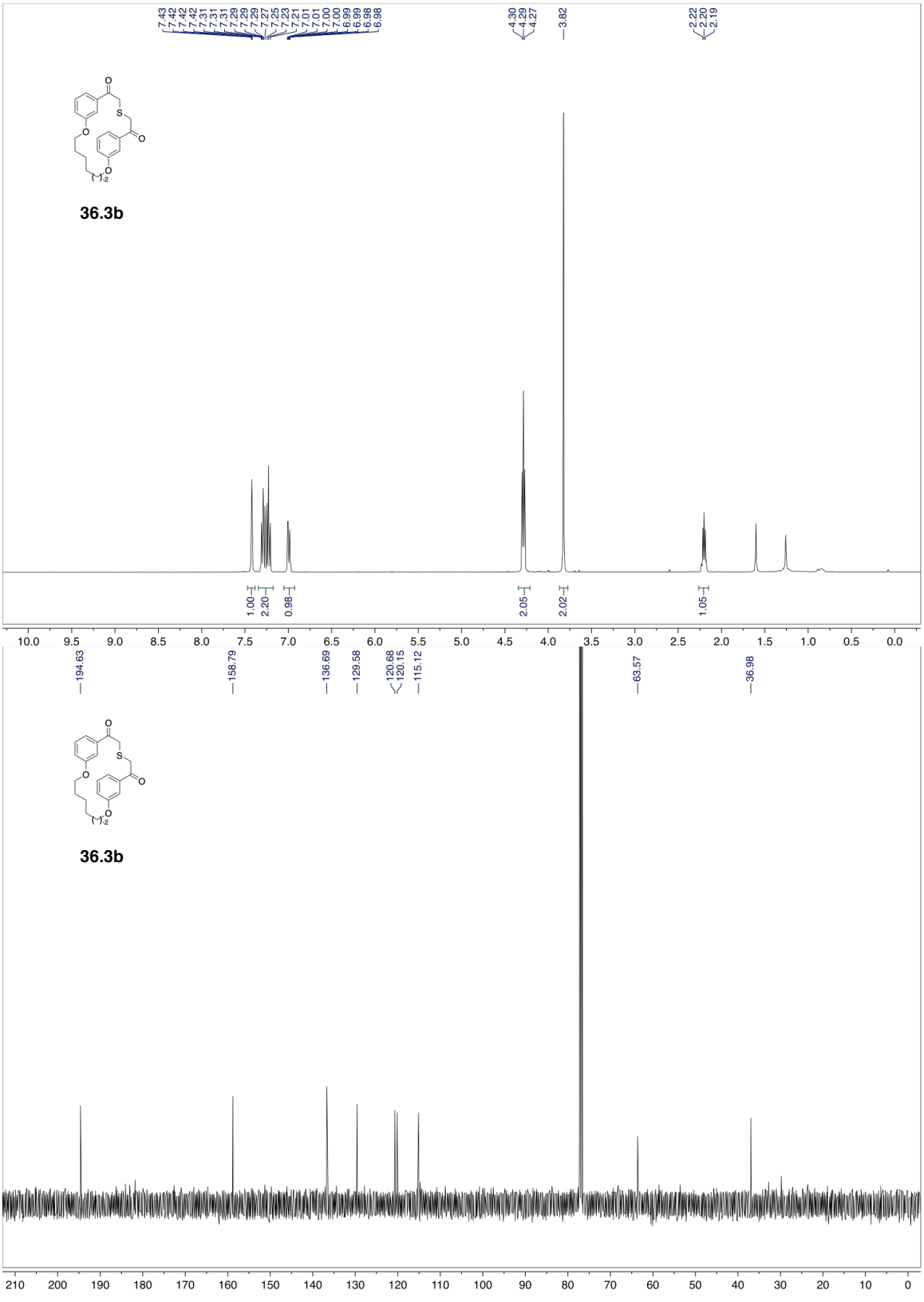
36.3b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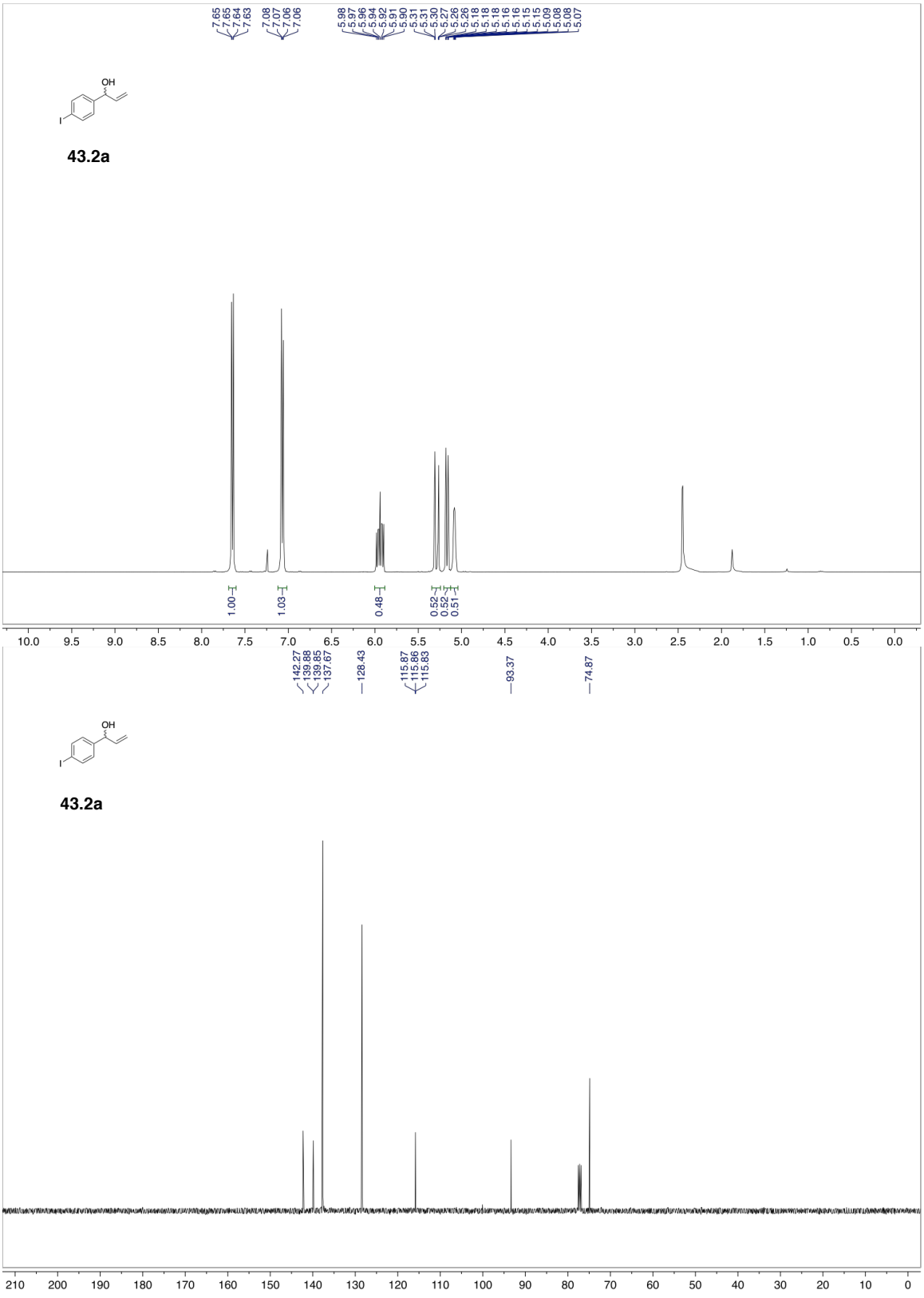
36.3b

43.2a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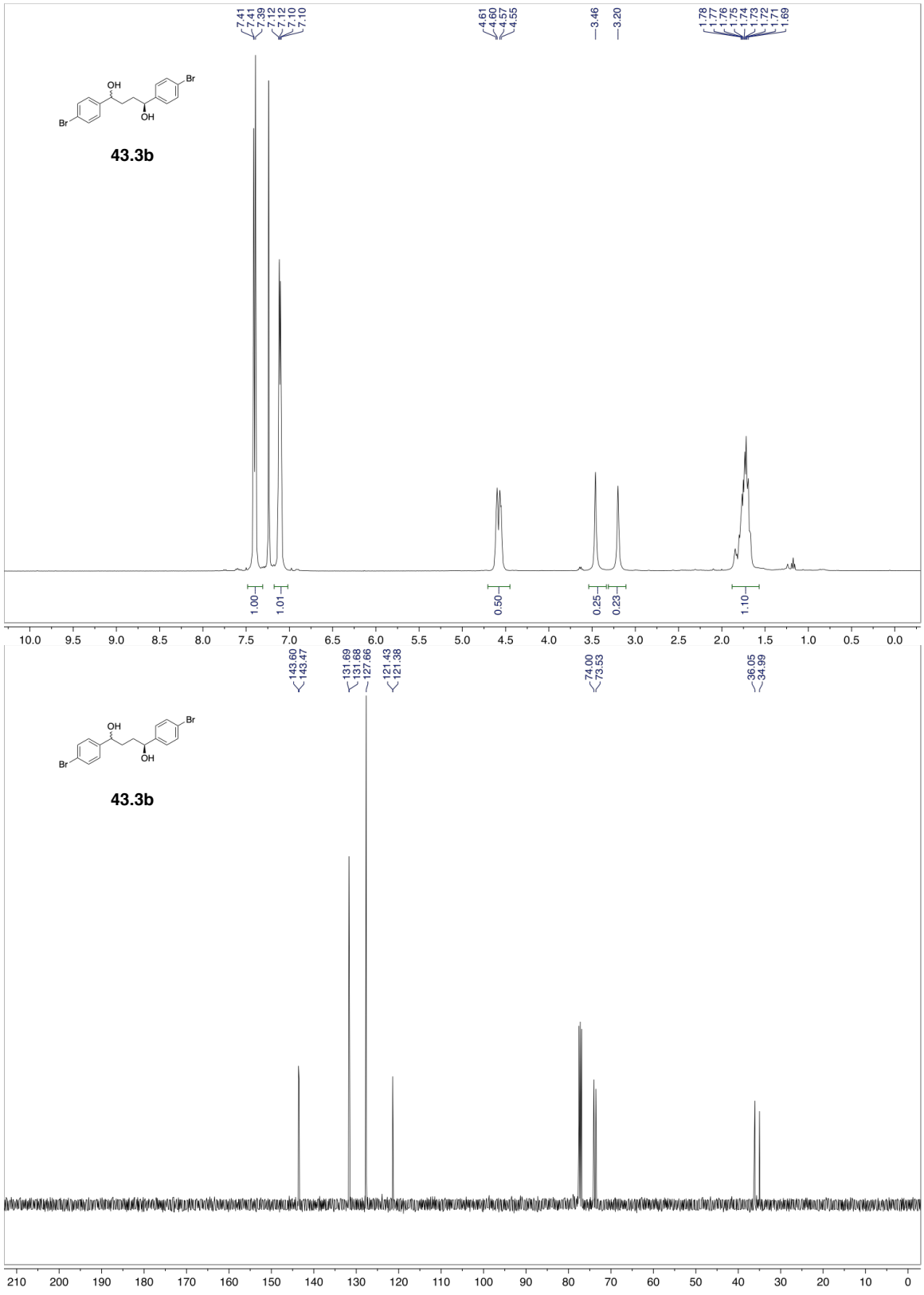
43.3b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OH
Br
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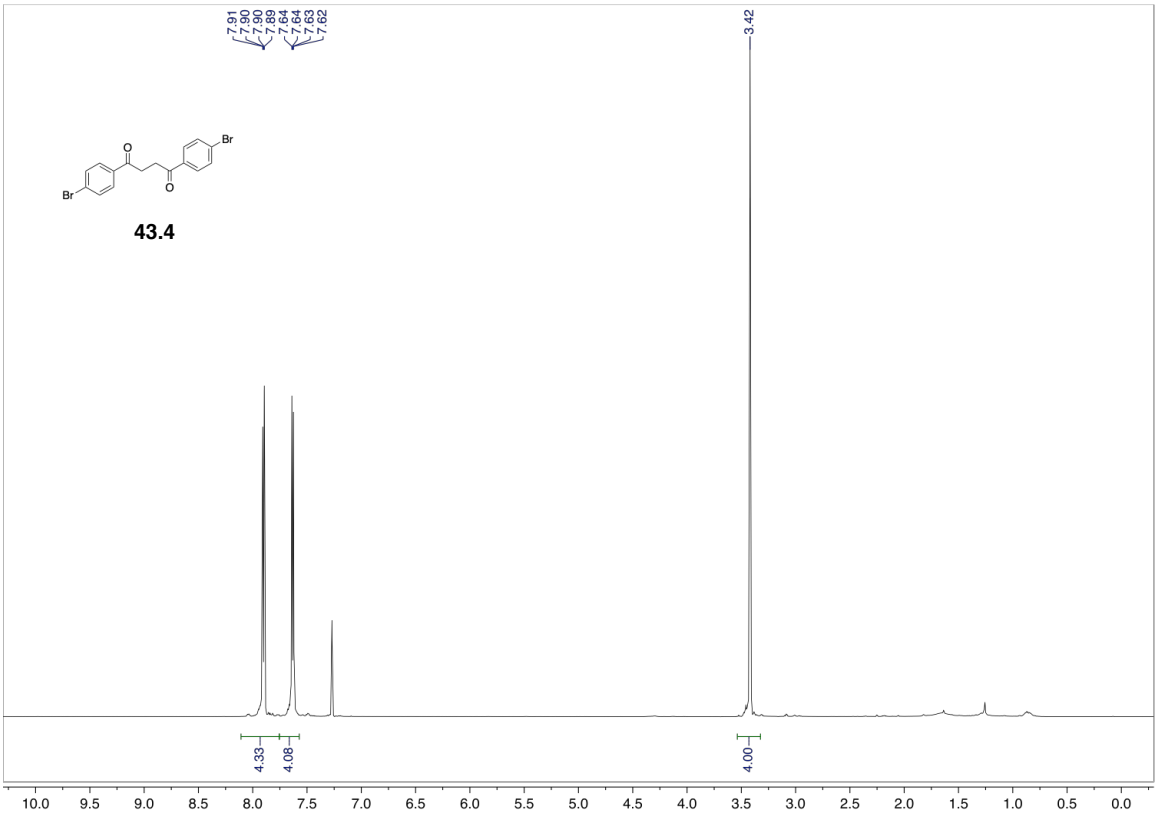
43.4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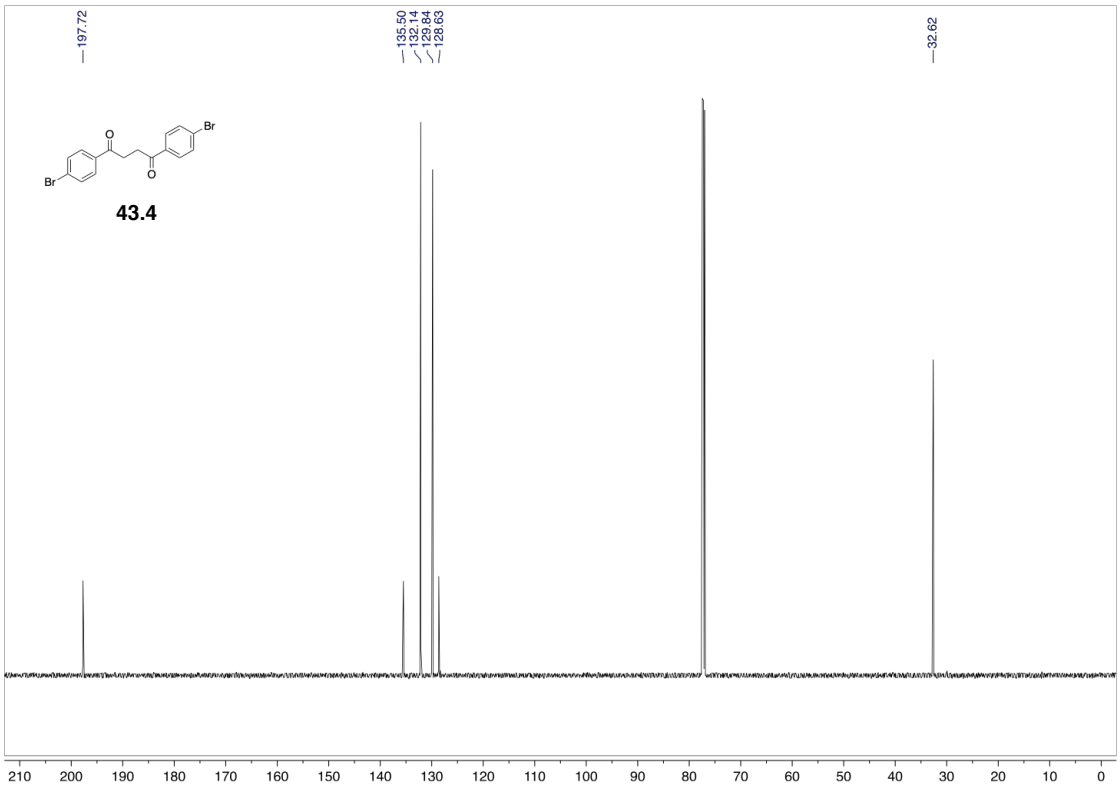
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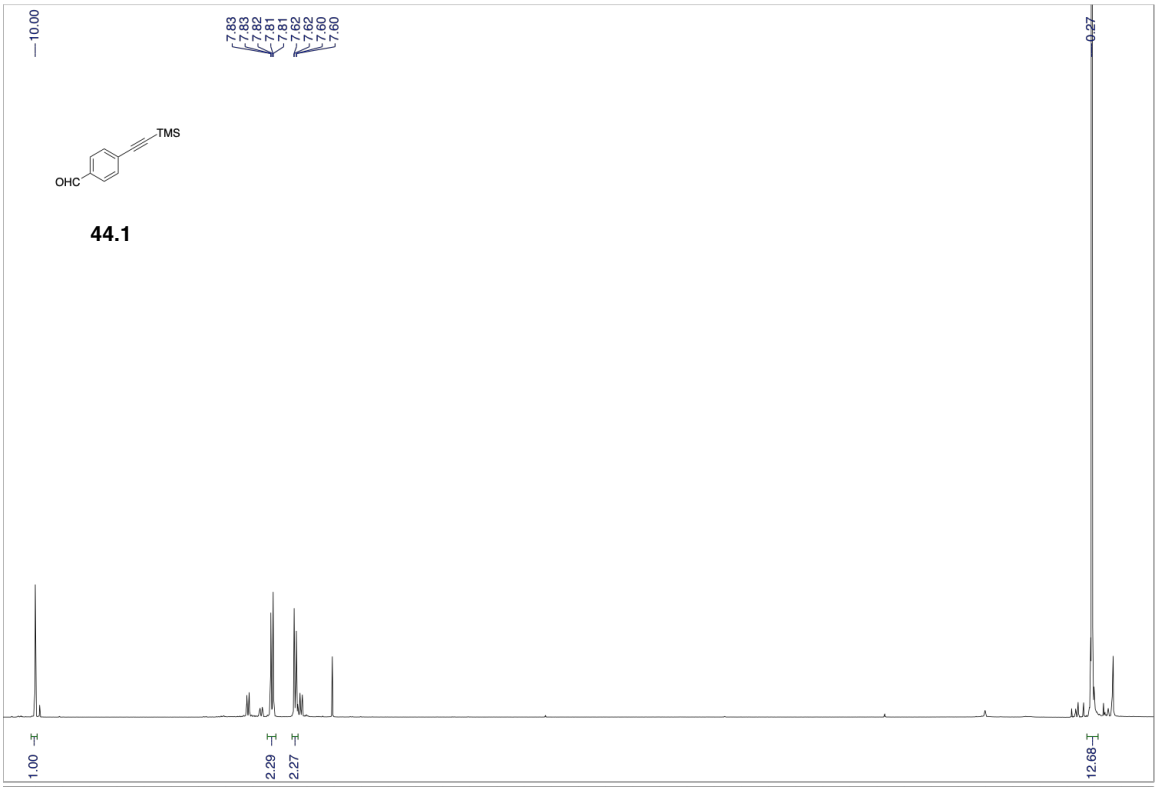
44.1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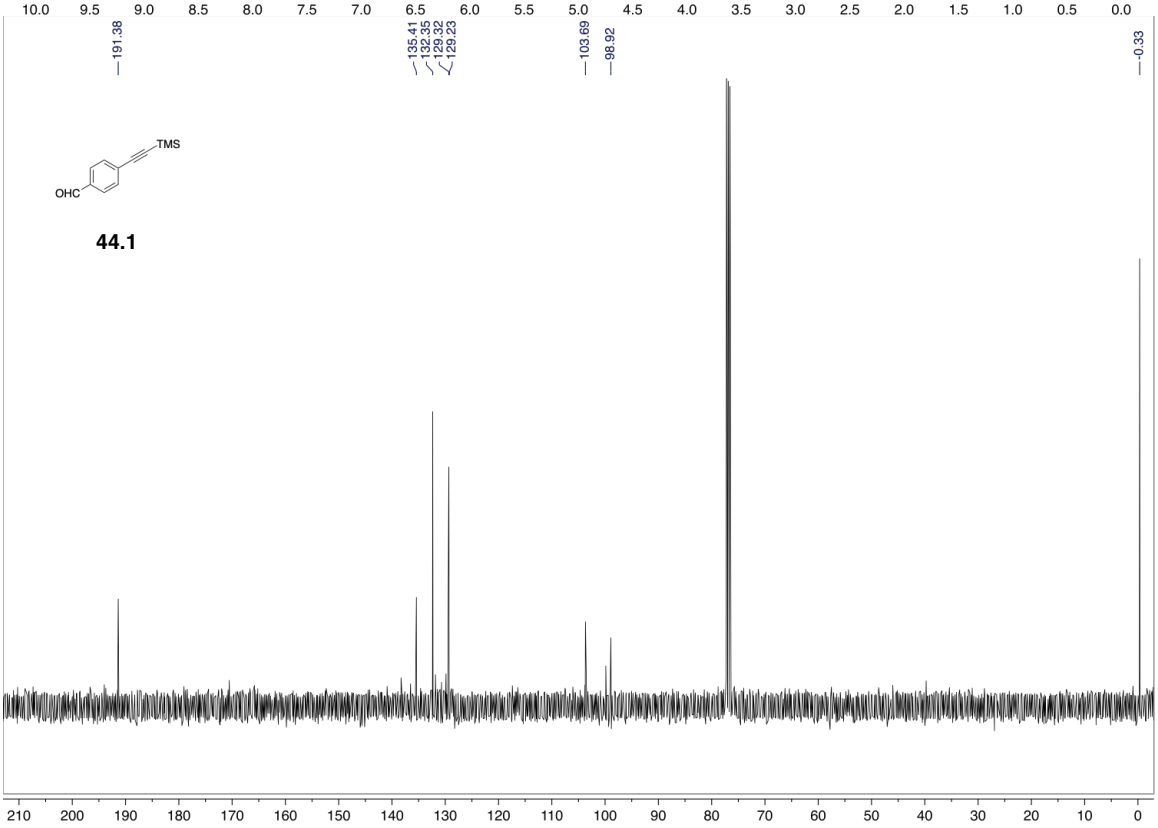
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OHC
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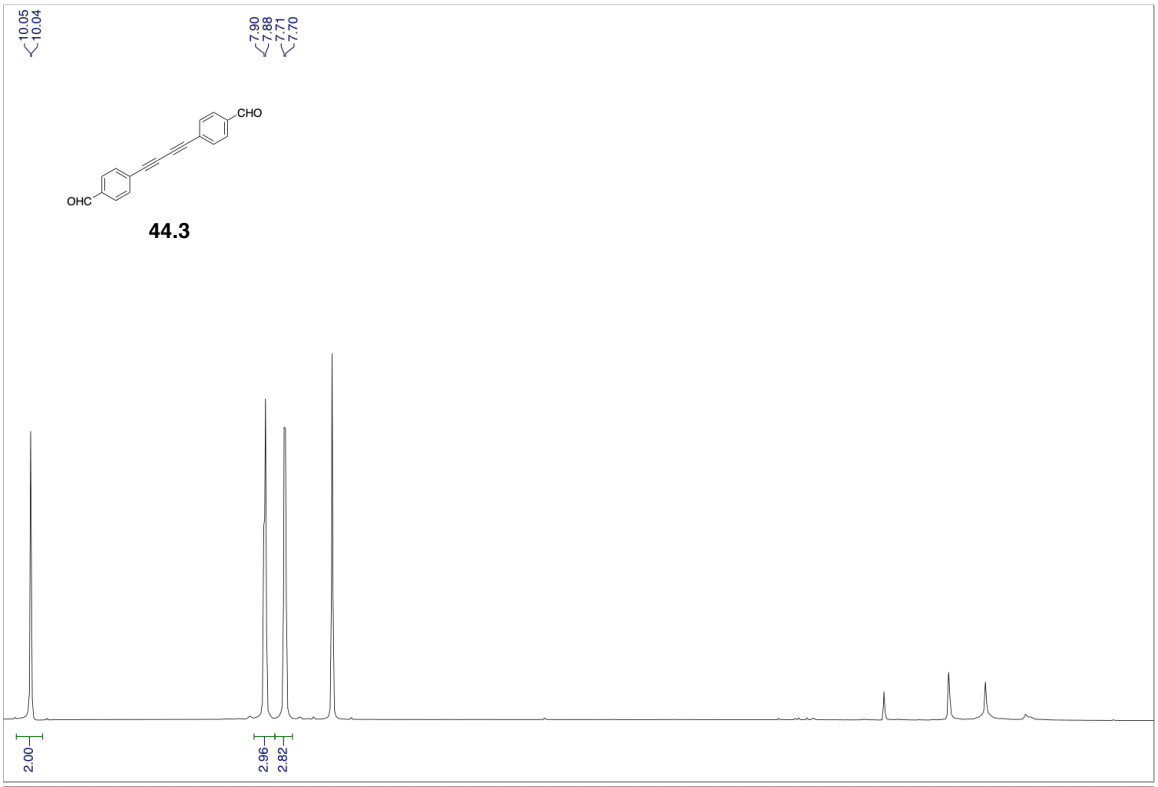
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

44.3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10.04
7.90
7.88
7.71
7.70
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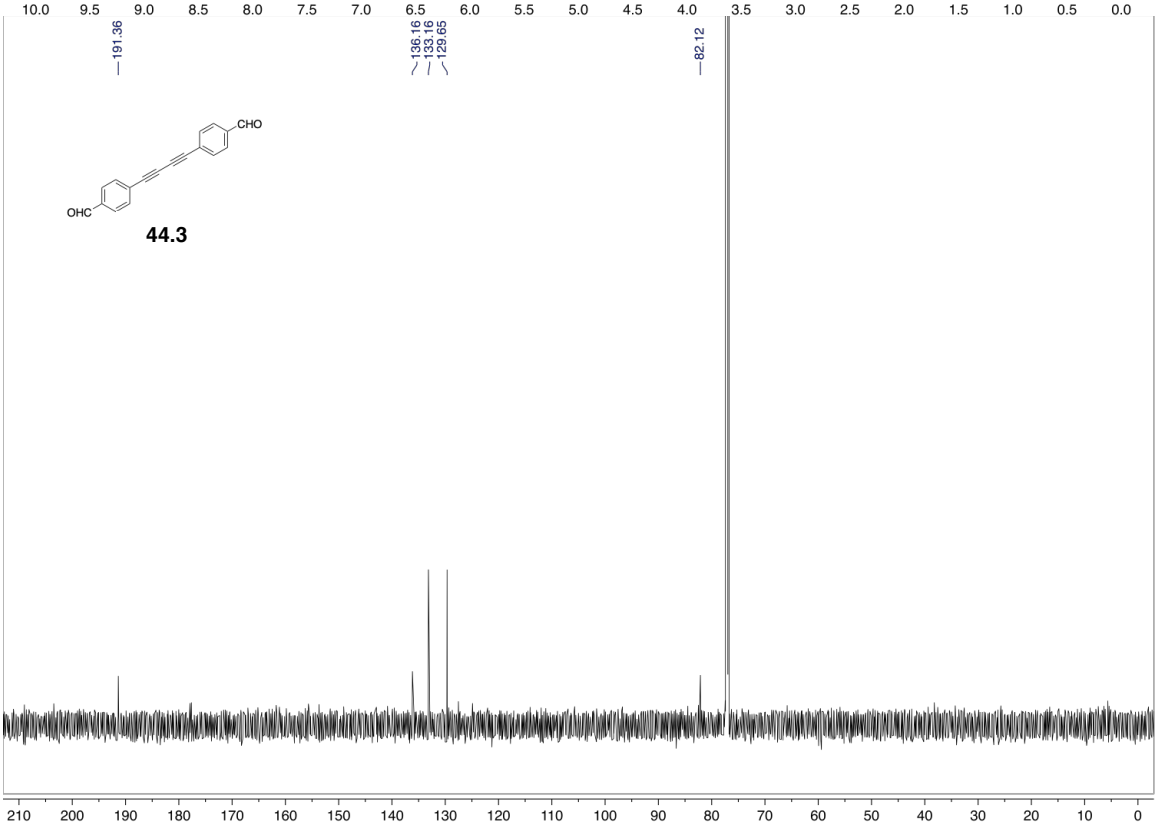
OHC
44.3
2.00
2.96
2.82
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0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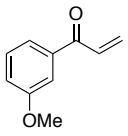
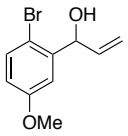
CHO
OHC
44.3
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0



SI-11

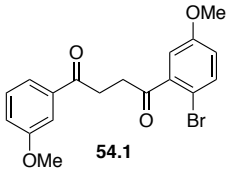
SI-11: Vinylmagnesium chloride (1.6 M, 14 mL, 22 mmol, 1.2 equiv.) was added to a stirred, 0°C solution of 3-methoxybenzaldehyde (2.5 g, 18 mmol, 1.0 equiv.) in dichloromethane (180 mL). After 1 h the reaction was warmed to room temperature and quenched with distilled water (100 mL) and further diluted with 1 M HCl (100 mL). The aqueous material was extracted with dichloromethane (3 × 150 mL). The combined organic extracts were washed with brine (100 mL), dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The crude material was used without further purification. Dess-Martin periodinane (7.82 g, 18.1 mmol, 1.0 equiv.) and $NaHCO_3$ (1.59 g, 18.4 mmol, 1.0 equiv.) was added to a stirred, room temperature solution of the crude material in dichloromethane (220 mL). After 18 h the reaction was quenched with a saturated solution of $Na_2S_2O_3$ (150 mL) and stirred for 3 h at which point the biphasic mixture was separated and the aqueous material extracted with dichloromethane (3 × 100 mL). The combined organic extracts were washed with brine (150 mL), dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The crude residue was purified via flash chromatography (9 × 5 cm; 10% EtOAc/hexanes) to afford the enone **SI-11** as a pale yellow oil (1.55 g, 52%); R_f = 0.36 (10% EtOAc/hexanes); ^{1}H NMR (600 MHz, $CdCl_3$) δ 7.56-7.51 (m, 1H), 7.51-7.47 (m, 1H), 7.40 (t, *J* = 7.9 Hz, 1H), 7.20-7.11 (m, 2H), 6.46 (dd, *J* = 17.1, 1.7 Hz, 1H), 5.95 (dd, *J* = 10.5, 1.7 Hz, 1H), 3.88 (s, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 190.77, 159.74, 138.48, 132.21, 130.43, 129.58, 121.32, 119.67, 112.67, 55.44; HRMS (ESI) calculated for $C_{10}H_{10}O_2$ ($[M]^+$) *m/z* = 162.0681 found 162.0687.



SI-12

SI-12: Methyl iodide (1.4 mL, 3.3 g, 23 mmol, 2.0 equiv.) was added to a stirred solution of 2-bromo-5-methoxybenzaldehyde (2.50 g, 11.6 mmol, 1.0 equiv.), potassium carbonate (2.88 g, 20.9 mmol, 1.8 equiv.), and TBAI (0.19 g, 0.58 mmol, 5 mol %) in DMF (120 mL) and the reaction was heated to 50 °C. After 18 h, the reaction was cooled to room temperature and quenched with distilled water. The aqueous material was extracted with EtOAc (3 × 50 mL). The combined organic extracts were washed with brine (100 mL), dried over anhydrous $MgSO_4$, filtered over a 3 cm plug of silica gel (5% EtOAc/hexanes), and concentrated under reduced pressure. Vinylmagnesium chloride (16 M in THF, 8.0 mL, 13 mmol, 1.1 equiv.) was added to a stirred, 0 °C solution of this crude residue in dichloromethane (100 mL). The reaction ran

for 15 min, at which point it was warmed to room temperature, quenched with distilled water (30 mL) and further diluted with 1 M HCl (30 mL). The aqueous material was extracted with dichloromethane (3 × 50 mL). The combined organic extracts were washed with a saturated solution of $NaHCO_3$ (50 mL), then brine (50 mL), dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The crude residue was purified via flash chromatography (10 × 5 cm; 5% EtOAc/hexanes, 10% EtOAc/hexanes) to afford the enol **SI-12** as a colorless oil (2.26 g, 80%); R_f = 0.19 (10% EtOAc/hexanes); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.42 (d, *J* = 8.7 Hz, 1H), 7.10 (d, *J* = 3.2 Hz, 1H), 6.72 (dd, *J* = 8.8, 3.2 Hz, 1H), 6.01 (ddd, *J* = 16.5, 10.3, 5.4 Hz, 1H), 5.56 (t, *J* = 4.4 Hz, 1H), 5.48-5.38 (m, 1H), 5.28-5.21 (m, 1H), 3.80 (s, 3H), 2.22 (d, *J* = 3.8 Hz, 1H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 159.21, 142.29, 138.01, 133.31, 115.83, 115.19, 112.89, 112.63, 73.48, 55.48; HRMS (ESI) calculated for $C_{10}H_{11}O_2Br$ ($[M]^+$) *m/z* = 241.9942 found 241.9935.

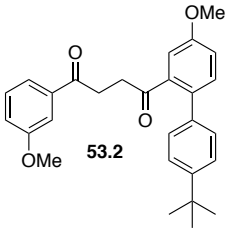


54.1

54.1: Grubbs II (0.842 g, 1.01 mmol, 5 mol%) was added to a stirred solution of enone **SI-11** (8.25 g, 50.7 mmol, 2.5 equiv.) and enol **SI-12** (4.91 g, 20.2 mmol, 1.0 equiv.) in dichloromethane (200 mL) and the reaction was heated to 40 °C. After 2 h, the reaction was cooled to room temperature and concentrated under reduced pressure. The crude residue was immediately purified via flash chromatography (15 × 8 cm; dichloromethane, 5% acetone/dichloromethane) to afford the cross metathesis product as a brown oil (2.24 g, 29%). Then, Hoveyda-Grubbs II (0.193 g, 0.301 mmol, 5 mol%) and $NaBH_4$ (0.453 g, 12.0 mmol, 2.0 equiv.) were added to a stirred, room temperature solution in a 9:1 mixture of dichloromethane/methanol (60 mL). The reaction stirred for 1 h, at which point it was quenched with distilled water (30 mL) and further diluted with 1 M HCl (30 mL). The aqueous material was extracted with dichloromethane (3 × 50 mL). The combined organic extracts were washed with brine, dried over anhydrous $MgSO_4$, filtered, and concentrated. The crude residue was then taken back up in dichloromethane (60 mL) before the addition of Dess-Martin periodinane (3.07 g, 7.22 mmol, 1.2 equiv.) and $NaHCO_3$ (0.62 g, 7.2 mmol, 1.2 equiv.). The reaction stirred for 4 h, at which point it was quenched with a saturated solution of $Na_2S_2O_3$ and stirred for 2 h. The aqueous material was extracted with dichloromethane (3 × 50 mL). The combined organic extracts were washed with a saturated solution of $Na_2S_2O_3$ (2 × 50 mL), then brine (50 mL), dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The crude material was purified via flash chromatography (15 × 5 cm; 70% dichloromethane/hexanes,

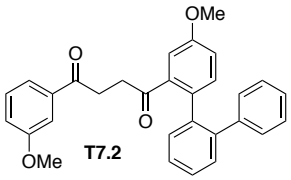
dichloromethane) to afford diketone **54.1** as a colorless oil (0.770 g, 34% over 2 steps); R_f = 31 (80% dichloromethane/hexanes); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.56 (d, *J* = 7.6 Hz, 1H), 7.52-7.47 (m, 1H), 7.45 (d, *J* = 8.9 Hz, 1H), 7.39 (t, *J* = 7.9 Hz, 1H), 7.32 (dd, *J* = 15.4, 1.8 Hz, 1H), 7.15-7.11 (m, 1H), 7.08 (dd, *J* = 10.5, 3.8 Hz, 1H), 6.75 (dd, *J* = 8.8, 3.1 Hz, 1H), 5.86 (td, *J* = 4.1, 1.9 Hz, 1H), 3.86 (s, 3H), 3.79 (s, 3H), 2.54 (d, *J* = 3.8 Hz, 1H), 1.65 (s, 1H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 190.21, 159.71, 159.39, 146.50, 140.83, 138.82, 133.50, 129.58, 124.13, 121.31, 119.71, 115.71, 113.32, 112.60, 112.49, 72.42, 55.53, 55.45; HRMS (ESI) calculated for $C_{18}H_{17}O_4Br$ ([M]$^+$) *m/z* = 376.0310 found 376.0304.

General Procedure L for the preparation of substituted 1,4-diketones



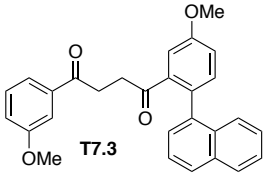
53.2

53.2: Toluene, distilled water, and ethanol were each purged under a constant stream of nitrogen for 30 minutes immediately before use. A round-bottom flask charged with monobromo-diketone **54.1** (0.040 g, 0.11 mmol, 1.0 equiv.), 4-*tert*-butylphenylboronic acid (0.064 g, 0.36 mmol, 2.0 equiv.) and $Pd(PPh_3)_4$ (0.014 g, 0.012 mmol, 5 mol%) was purged with argon for 5 minutes. Then, potassium carbonate (0.040 g, 0.29 mmol, 1.6 equiv.) in 3:1:1 toluene/distilled water/ethanol was added and the reaction was heated to 90 °C. After 15 h, the reaction was cooled to room temperature, quenched with distilled water (10 mL), and further diluted with 1M HCl (10 mL). The aqueous material was extracted with dichloromethane (3 × 10 mL). The combined organic extracts were washed with brine, dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. The crude residue was purified via flash chromatography (15 × 1.3 cm; 15% EtOAc/hexanes) to afford the diketone **53.2** as a white solid (0.080 g, 80%); R_f = 0.43 (15% EtOAc/hexanes); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.51 (dt, *J* = 7.6, 1.2 Hz, 1H), 7.48-7.41 (m, 3H), 7.40-7.32 (m, 2H), 7.29 (s, 2H), 7.11 (dt, *J* = 6.2, 3.0 Hz, 2H), 7.07 (dd, *J* = 8.4, 2.8 Hz, 1H), 3.90 (s, 3H), 3.86 (s, 3H), 3.17 (t, *J* = 6.5 Hz, 2H), 2.73 (t, *J* = 6.5 Hz, 2H), 1.34 (s, 9H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 206.52, 198.26, 159.88, 158.91, 150.65, 141.83, 138.09, 137.53, 132.70, 131.61, 129.67, 128.75, 125.69, 120.83, 119.75, 116.96, 112.47, 112.27, 55.71, 55.57, 36.99, 34.71, 33.69, 31.48. HRMS (APCI) calculated for $C_{28}H_{30}O_4Na$ ([M+H]$^+$+Na) *m/z* = 453.2042, found = 453.2052. *This reaction was performed by Nirmal Mitra.*



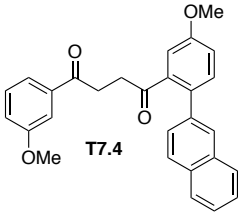
T7.2

T7.2: This compound was prepared using the *General Procedure L* using monobromo-diketone **54.1** (0.100 g, 0.265 mmol, 1.0 equiv.), biphenyl-2-bornic acid (0.106 g, 0.530 mmol, 2.0 equiv.), $Pd(PPh_3)_4$ (0.0155 g, 0.0133 mmol, 5 mol%), and potassium carbonate (0.0723 g, 0.530 mmol, 2.0 equiv.) in 3:1:1 toluene/distilled water/ethanol (10 mL). The crude residue was purified via flash chromatography (10 × 1.2 cm; dichloromethane, 2% acetone/dichloromethane) to afford **T7.2** as a pale yellow oil (0.061 g, 51%); R_f = 0.36 (2% acetone/dichloromethane); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.54 (d, *J* = 7.6 Hz, 1H), 7.48-7.31 (m, 6H), 7.22-7.07 (m, 7H), 6.97 (dd, *J* = 8.4, 2.7 Hz, 1H), 3.85 (d, *J* = 6.4 Hz, 6H), 3.29 ? 3.20 (m, 1H), 3.01 (td, *J* = 19.3, 18.7, 6.1 Hz, 2H), 2.10 (dt, *J* = 21.1, 6.7 Hz, 1H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 202.41, 198.29, 159.60, 158.29, 140.84, 140.48, 140.05, 139.23, 137.87, 133.13, 132.86, 130.68, 130.12, 129.89, 129.50, 127.92, 127.78, 127.55, 126.57, 120.67, 119.63, 116.46, 113.05, 111.92, 55.43, 55.41, 34.56, 33.02.

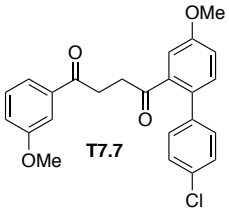


T7.3

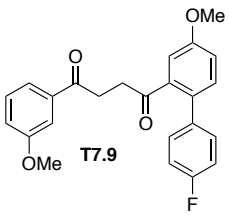
T7.3: This compound was prepared using the *General Procedure L* using monobromo-diketone **54.1** (0.040 g, 0.11 mmol, 1.0 equiv.), naphthalene-1-boronic acid (0.038 g, 0.21 mmol, 2.0 equiv.), $Pd(PPh_3)_4$ (0.0069 g, 0.0054 mmol, 5 mol%), and potassium carbonate (0.031 g, 0.21 mmol, 2.0 equiv.) in 3:1:1 toluene/distilled water/ethanol (5 mL). The crude residue was purified via flash chromatography (10 × 1.2 cm; dichloromethane, 2% acetone/dichloromethane) to afford **T7.3** as an off-white solid (0.038 g, 83%); R_f = 0.39 (2% acetone/dichloromethane); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.89 (dd, *J* = 13.5, 8.3 Hz, 2H), 7.69 (d, *J* = 8.4 Hz, 1H), 7.55-7.47 (m, 2H), 7.44 (td, *J* = 6.7, 3.3 Hz, 1H), 7.41-7.28 (m, 6H), 7.18-7.12 (m, 1H), 7.06 (dd, *J* = 8.2, 2.7 Hz, 1H), 3.95 (d, *J* = 1.9 Hz, 3H), 3.81 (d, *J* = 1.8 Hz, 3H), 2.99-2.85 (m, 2H), 2.49 (t, *J* = 6.3 Hz, 2H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 204.41, 198.08, 159.53, 158.99, 142.08, 138.36, 137.67, 133.50, 132.78, 132.15, 130.87, 129.42, 128.31, 128.08, 127.58, 126.46, 126.01, 125.79, 125.33, 120.62, 119.64, 117.10, 112.60, 111.79, 55.59, 55.36, 35.77, 33.31.



T7.4: This compound was prepared using the *General Procedure L* using monobromo-diketone **54.1** (0.040 g, 0.11 mmol, 1.0 equiv.), naphthalene-2-boronic acid (0.037 g, 0.021 mmol, 2.0 equiv.), $Pd(PPh_3)_4$ (0.0066 g, 0.0084 mmol, 5 mol%), and potassium carbonate (0.031 g, 0.021 mmol, 2.0 equiv.) in 3:1:1 toluene/distilled water/ethanol (5 mL). The crude material was purified via flash chromatography (10 × 1.2 cm; dichloromethane, 2% acetone/dichloromethane) to afford **T7.4** as an off-white solid (0.033 g, 73%); R_f = 0.28 (dichloromethane); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.77 (t, *J* = 8.9 Hz, 1H), 7.45-7.35 (m, 1H), 7.30-7.25 (m, 1H), 7.21-7.14 (m, 1H), 3.81 (d, *J* = 2.0 Hz, 1H), 3.71 (d, *J* = 2.0 Hz, 1H), 3.00 (t, *J* = 6.3 Hz, 1H), 2.64 (t, *J* = 6.3 Hz, 1H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 206.00, 198.12, 159.57, 158.90, 141.64, 137.87, 137.70, 133.27, 132.47, 132.37, 131.86, 129.45, 128.29, 128.03, 127.74, 127.63, 127.14, 126.51, 126.16, 120.66, 119.69, 116.90, 112.53, 111.80, 55.60, 55.37, 36.78, 33.39.

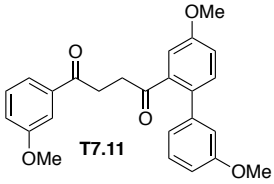


T7.7: This compound was prepared using the *General Procedure L* using diketone **54.1** (0.050 g, 0.13 mmol, 1.0 equiv.), 4-chlorophenylboronic acid (0.042 g, 0.27 mmol, 2.0 equiv.), $Pd(PPh_3)_4$ (0.008 g, 0.007 mmol, 5 mol%), and potassium carbonate (0.037 g, 0.27 mmol, 2.0 equiv.) in 3:1:1 toluene/distilled water/ethanol (5 mL). The crude residue was purified via flash chromatography (14 × 1.3 cm; dichloromethane, 2% acetone/dichloromethane) to afford the diketone **T7.7** as a white solid (0.052 g, 95%). R_f = 0.33 (dichloromethane); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.55-7.49 (m, 1H), 7.48-7.43 (m, 1H), 7.40-7.34 (m, 3H), 7.31-7.24 (m, 4H), 7.15 (d, *J* = 2.7 Hz, 1H), 7.11 (dd, *J* = 8.2, 2.6 Hz, 1H), 7.06 (dd, *J* = 8.4, 2.6 Hz, 1H), 3.90 (d, *J* = 1.9 Hz, 3H), 3.85 (d, *J* = 1.8 Hz, 3H), 3.22 (t, *J* = 6.3 Hz, 2H), 2.82 (t, *J* = 6.3 Hz, 2H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 205.25, 198.07, 159.65, 159.01, 137.73, 133.46, 131.57, 131.30, 130.15, 129.57, 128.74, 120.71, 119.76, 116.76, 112.74, 111.94, 55.59, 55.42, 36.61, 33.21; HRMS (ESI) calculated for $C_{24}H_{22}ClO_4$ ($[M + H]^+$) *m/z* = 409.1207, found = 409.1196.



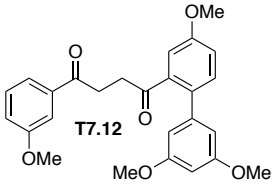
T7.9: This compound was prepared using the *General Procedure L* using monobromo diketone **54.1** (0.100 g, 0.265 mmol, 1.0 equiv.), 4-fluorophenylboronic acid (0.074 g, 0.53 mmol, 2.0 equiv.), $Pd(PPh_3)_4$ (0.015 g, 0.013 mmol, 5 mol%), and potassium carbonate (0.073 g, 0.53 mmol, 2.0 equiv.) in 3:1:1 toluene/distilled water/ethanol (10mL).

The crude residue was purified via flash chromatography (10 × 1.2 cm; dichloromethane, 1% acetone/dichloromethane) to afford **T7.9** as a white solid (0.053 g, 55%); R_f = 0.40 (dichloromethane); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.52 (d, *J* = 7.6 Hz, 1H), 7.45 (s, 1H), 7.37 (d, *J* = 7.9 Hz, 1H), 7.29 (dd, *J* = 8.5, 5.2 Hz, 3H), 7.17-7.04 (m, 5H), 3.88 (dd, *J* = 25.3, 6.5 Hz, 6H), 3.21 (q, *J* = 6.7 Hz, 2H), 2.78 (q, *J* = 6.6 Hz, 2H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 198.06, 159.65, 158.87, 141.31, 137.73, 131.59, 131.49, 130.47, 130.42, 129.55, 120.69, 119.73, 116.77, 115.63, 115.49, 112.54, 111.96, 55.58, 55.42, 36.64, 33.22; HRMS (ESI) calculated for $C_{24}H_{22}O_4F$ ([M + H]$^+$) *m/z* = 393.1502, found = 393.1529.



T7.11

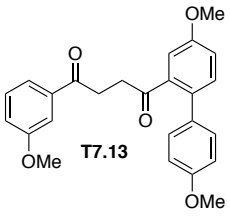
T7.11: This compound was prepared using the *General Procedure L* using monobromo diketone **54.1** (0.040 g, 0.11 mmol, 1.0 equiv.), 3-methoxyphenylboronic acid (0.033 g, 0.21 mmol, 2.0 equiv.), $Pd(PPh_3)_4$ (0.0062 g, 0.0054 mmol, 5 mol%), and potassium carbonate (0.030 g, 0.021 mmol, 2.0 equiv.) in 3:1:1 toluene/distilled water/ethanol. The crude residue was purified via flash chromatography (10 × 1.2 cm; dichloromethane, 2% acetone/dichloromethane) to afford **T7.11** as a white solid (0.031 g, 72%); R_f = 0.43 (2% acetone/dichloromethane); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.50 (d, *J* = 7.7 Hz, 1H), 7.44 (t, *J* = 2.1 Hz, 1H), 7.34 (dq, *J* = 15.6, 7.9 Hz, 3H), 7.13-7.04 (m, 3H), 6.93 ? 6.86 (m, 3H), 3.93-3.81 (m, 9H), 3.17 (t, *J* = 6.4 Hz, 2H), 2.75 (t, *J* = 6.4 Hz, 2H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 206.09, 198.15, 159.62, 159.55, 158.89, 141.51, 132.38, 131.35, 129.63, 129.52, 121.43, 120.70, 119.68, 116.81, 114.20, 113.07, 112.27, 111.94, 55.56, 55.41, 55.25, 36.68, 33.43; HRMS (ESI) calculated for $C_{25}H_{24}O_5Na$ ([M + Na]$^+$) *m/z* = 427.1521, found = 427.1514.



T7.12

T7.12: This compound was prepared according to the *General Procedure L* using diketone **54.1** (0.040 g, 0.11 mmol, 1.0 equiv.), 3,5-dimethoxyphenylboronic acid (0.039 g, 0.21 mmol, 2.0 equiv.), $Pd(PPh_3)_4$ (0.006 g, 0.005 mmol, 5 mol%), and potassium carbonate (0.0029 g, 0.21 mmol, 2.0 equiv.) in 3:1:1 PhMe/distilled water/ethanol (5 mL). The crude residue was purified via flash chromatography (15 × 1.3 cm; 2% acetone/dichloromethane) to afford the diketone **T7.12** (0.022 g, 47%). R_f = 0.40 (dichloromethane); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.54-7.49 (m, 1H), 7.48-7.42 (m, 1H), 7.42-7.30 (m, 2H), 7.15-7.01 (m, 3H), 6.46 (dd, *J* = 15.7, 2.3 Hz, 3H), 6.02 (d, *J* = 1.9 Hz, 1H), 3.88 (s, 3H), 3.85 (s, 3H), 3.80 (s, 6H), 3.75 (s, 2H), 3.19 (t, *J* = 6.2 Hz, 2H), 2.79 (t,

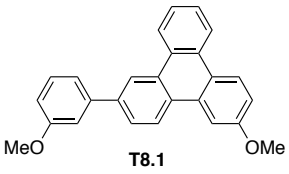
J = 6.3 Hz, 2H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 206.15, 198.20, 160.67, 159.62, 158.95, 142.42, 141.47, 137.77, 132.43, 131.16, 129.52, 120.71, 119.68, 116.80, 112.19, 111.94, 106.96, 99.48, 93.98, 55.56, 55.39, 55.28, 36.65, 33.50; HRMS (ESI) calculated for $C_{26}H_{26}O_6Na$ ([M + Na]$^+$) *m/z* = 457.1627, found = 457.1594.



T7.13

T7.13: This compound was prepared using the *General Procedure L* using monobromo-diketone **54.1** (0.100 g, 0.265 mmol, 1.0 equiv.), 4-methoxyphenylboronic acid (0.083 g, 0.53 mmol, 2.0 equiv.), $Pd(PPh_3)_4$ (0.0148 g, 0.0133 mmol, 5 mol%), and potassium carbonate (0.0717 g, 0.530 mmol, 2.0 equiv.) in 3:1:1 toluene/distilled water/ethanol (10 mL). The crude residue was purified via flash chromatography (10 × 1.2 cm; dichloromethane, 2% acetone/dichloromethane) to afford **T7.13** as white solid (0.073 g, 68%); R*f* = 0.33 (2% acetone/dichloromethane); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.69 (d, *J* = 7.6 Hz, 1H), 7.64 (t, *J* = 2.1 Hz, 1H), 7.55 (s, 1H), 7.49 (d, *J* = 8.4 Hz, 1H), 7.45 (dd, *J* = 8.4, 6.2 Hz, 2H), 7.29 (dd, *J* = 8.5, 2.7 Hz, 1H), 7.24 (dd, *J* = 8.4, 2.7 Hz, 1H), 7.14 (d, *J* = 8.4 Hz, 2H), 4.11-3.99 (m, 9H), 3.37 (t, *J* = 6.4 Hz, 2H), 2.93 (t, *J* = 6.4 Hz, 2H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 206.35, 198.18, 159.60, 158.52, 141.35, 137.76, 132.66, 131.41, 129.94, 129.50, 120.69, 119.66, 116.85, 113.98, 112.15, 111.91, 55.52, 55.38, 55.24, 36.70, 33.38.

General Procedure M for the preparation of triphenylenes:

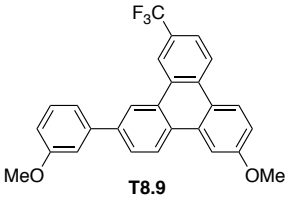


T8.1

T8.1: Vinylmagnesium chloride (0.14 mL, 0.21 mmol, 2.5 equiv.) was added to a stirred, 60 °C solution of diketone **T7.1** in benzene (2 mL). After 30 min the reaction was cooled to room temperature, quenched with distilled water (10 mL) and further diluted with 1 M HCl (10 mL). The aqueous material was extracted with dichloromethane (3 × 10 mL). The combined organic extracts were washed with brine (15 mL), dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The crude residue was purified via flash chromatography (15 × 1.3 cm; 5% acetone/dichloromethane, 10% acetone/dichloromethane) to afford the diol (0.017 g, 19%) and the hydroxy ketone.

Diol: HRMS (ESI) calculated for $C_{24}H_{30}O_4Na$ ([M + Na]$^+$) *m/z* = 453.2042, found = 453.2051.

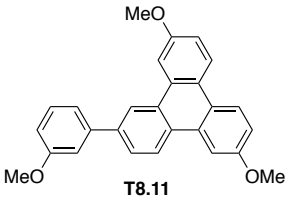
Then, Grubbs second-generation catalyst (0.001 g, 0.001 mmol, 5 mol%) was added to a solution of the diol in dichloromethane (2 mL) and the reaction was heated to 40 °C. After 2 h, the reaction was cooled to room temperature, then 0 °C and a solution of $FeCl_3$ (0.5 mL, 0.005 mmol, 0.006 M in 10:1 dichloromethane/nitromethane, 0.2 equiv.). The reaction turned purple upon addition of the $FeCl_3$ solution. After 15 minutes the reaction was warmed to room temperature and DDQ (0.020 g, 0.092 mmol, 4.0 equiv) was added. The reaction turned green upon addition of DDQ. After 15 min, the reaction was quenched with distilled water (5 mL) and a saturated solution of sodium bicarbonate (5 mL). The aqueous material was extracted with dichloromethane (3 × 5 mL). The combined organic extracts were washed with brine (10 mL), dried over anhydrous $MgSO_4$, filtered over a short pad of silica gel (3 cm), and concentrated under reduced pressure to afford triphenylene **T8.1** as a white solid (0.005 g, 76%). R_f = 0.40 (10% EtOAc/hexanes); ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.85 (d, *J* = 2.1 Hz, 1H), 8.75-8.70 (m, 1H), 8.65 (d, *J* = 8.5 Hz, 1H), 8.59 (dd, *J* = 8.3, 5.4 Hz, 2H), 8.08 (d, *J* = 2.7 Hz, 1H), 7.90 (dd, *J* = 8.2, 1.9 Hz, 1H), 7.71 ? 7.60 (m, 2H), 7.48 (t, *J* = 7.8 Hz, 1H), 7.45 ? 7.39 (m, 1H), 7.37-7.34 (m, 1H), 7.30 (dd, *J* = 9.0, 2.6 Hz, 1H), 7.02-6.96 (m, 1H), 4.06 (s, 3H), 3.95 (s, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 159.95, 158.82, 142.62, 139.72, 130.96, 130.36, 130.06, 129.96, 128.64, 127.40, 126.29, 126.18, 124.98, 123.86, 123.70, 123.27, 122.83, 121.89, 119.91, 115.87, 113.19, 112.67, 105.59, 55.48, 55.41. *This reaction was performed by Nirmal Mitra.*



T8.9

T8.9: This compound was prepared using the *General Procedure M* using diketone **T7.10** (0.043 g, 0.097 mmol, 1.0 equiv.) and vinylmagnesium chloride (0.13 mL, 0.21 mmol, 1.6 M in THF, 2.2 equiv.) in benzene (1 mL). The crude residue was purified via flash chromatography (10 × 1.2 cm; 2% acetone/dichloromethane) to afford the diol as a colorless oil (0.00226 g, 23%) and the hydroxy-ketone as a colorless oil (0.0116 g, 41%). Hydroxy Ketone: HRMS (ESI) calculated for $C_{27}H_{25}O_4F_3Na$ ($[M + Na]^+$) *m/z* = 493.1603, found = 493.1634. Then, using the diol and Grubbs II (0.0041 g, 0.0051 mmol, 10 mol%) in dichloromethane (5 mL); $FeCl_3$ solution (3.4 mL, 0.010 mmol, 0.006 M in 10:1 dichloromethane/nitromethane, 0.4 equiv.); DDQ (0.034 g, 0.015 mmol, 3.0 equiv.). The crude residue was purified via flash chromatography (10 × 1.2 cm; 70% dichloromethane/hexanes) to afford triphenylene **T8.9** as a white solid (0.0072 g, 33%). R_f = 64 (70% dichloromethane/hexanes); ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.92 (s, 1H), 8.80 (d, *J* = 1.9 Hz, 1H), 8.66 (dd, *J* = 8.7, 4.1 Hz, 2H), 8.59 (d, *J* = 9.0 Hz, 1H), 8.07 (d, *J* = 2.5

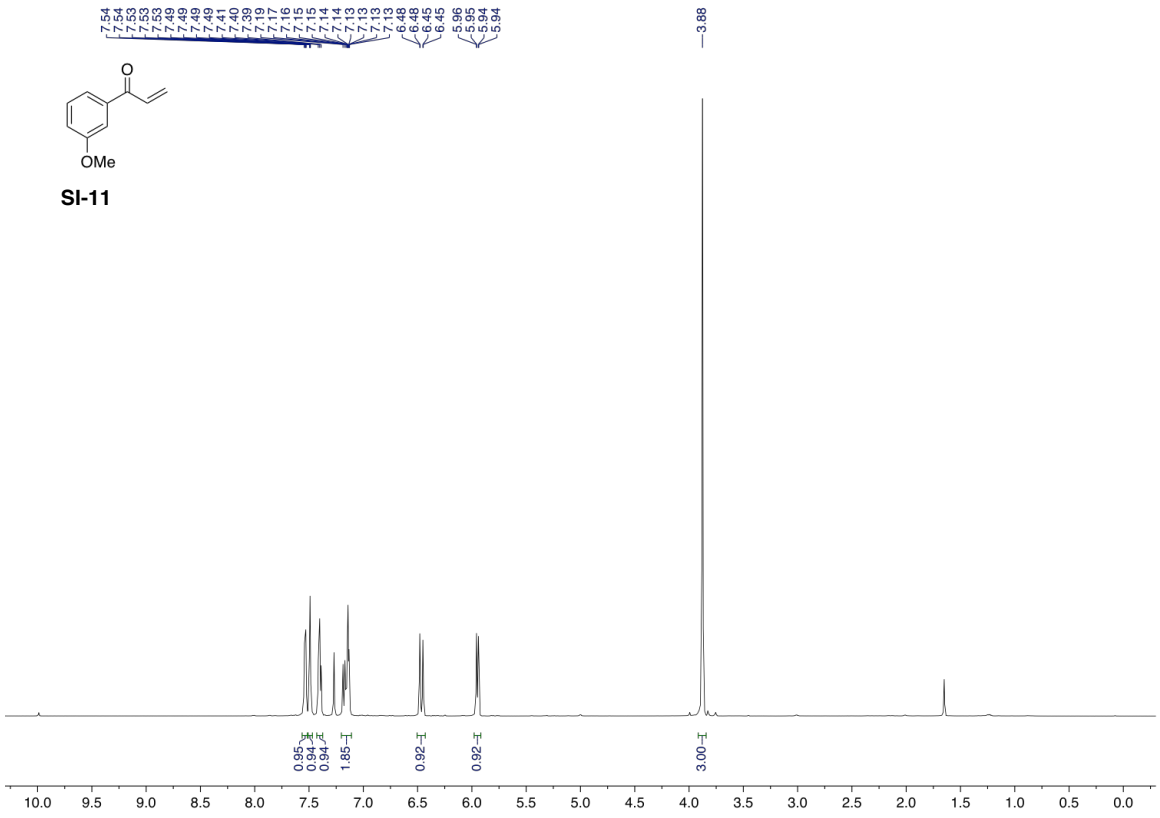
Hz, 1H), 7.93 (dd, *J* = 8.6, 1.9 Hz, 1H), 7.88-7.82 (m, 1H), 7.69-7.64 (m, 2H), 7.57 (d, *J* = 8.8 Hz, 1H), 7.51 (d, *J* = 8.0 Hz, 3H), 7.44-7.36 (m, 2H), 7.36-7.30 (m, 2H), 7.21-7.18 (m, 1H), 7.02 (dd, *J* = 8.1, 2.4 Hz, 1H), 6.93 (dd, *J* = 8.0, 2.6 Hz, 2H), 6.81 (dd, *J* = 9.0, 3.0 Hz, 1H), 4.07 (s, 3H), 3.96 (s, 3H), 3.89 (s, 3H), 3.83 (s, 4H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 159.99, 159.83, 159.65, 158.74, 142.13, 140.32, 140.12, 133.75, 130.08, 129.81, 129.70, 127.07, 126.76, 125.51, 124.01, 123.58, 122.61, 121.87, 119.99, 119.64, 116.54, 116.22, 114.77 , 113.43, 112.81, 112.73 105.70, 55.54, 55.52, 55.45, 55.31.



T8.11

T8.11: This compound was prepared using the *General Procedure M* using diketone **T7.13** (0.013 g, 0.028 mmol, 1.0 equiv.) and vinylmagnesium chloride (0.25 mL, 0.39 mmol, 1.6 M in THF, 2.2 equiv.) in benzene (2 mL). The crude residue was purified via flash chromatography (10 × 1.2 cm; 2% acetone/dichloromethane) to afford the diol as a colorless oil (0.013 g, 16%) and the hydroxy ketone. Then, using the diol and Grubbs II (0.002 g, 0.003 mmol, 10 mol%) in dichloromethane (3 mL); $FeCl_3$ solution (1.8 mL, 0.006 M in 10:1 dichloromethane/nitromethane, 0.4 equiv.); and DDQ (0.021 g, 0.084 mmol, 3.0 equiv.). The crude residue was purified via flash chromatography (10 × 1.2 cm; 80% dichloromethane/hexanes) to afford the Triphenylene **T8.11** as a white solid (0.010 g, 91%); R_f = 0.77 (80% dichloromethane/hexanes); ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.77-8.72 (m, 1H), 8.64 (d, *J* = 8.5 Hz, 1H), 8.50 (dd, *J* = 9.0, 6.1 Hz, 2H), 8.10 (d, *J* = 2.6 Hz, 1H), 8.05 (d, *J* = 2.6 Hz, 1H), 7.88 (dd, *J* = 8.5, 1.9 Hz, 1H), 7.48 (t, *J* = 7.9 Hz, 1H), 7.40 (d, *J* = 7.6 Hz, 1H), 7.34 (t, *J* = 2.1 Hz, 1H), 7.00 (dd, *J* = 8.1, 2.5 Hz, 1H), 4.05 (d, *J* = 4.7 Hz, 6H), 3.95 (s, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 159.94, 158.14, 142.70, 139.65, 130.05, 129.97, 129.83, 126.36, 124.45, 124.40, 123.94, 121.93, 119.98, 115.97, 115.82, 113.33, 112.59, 105.84, 105.58, 55.57, 55.48, 55.43.

SI-11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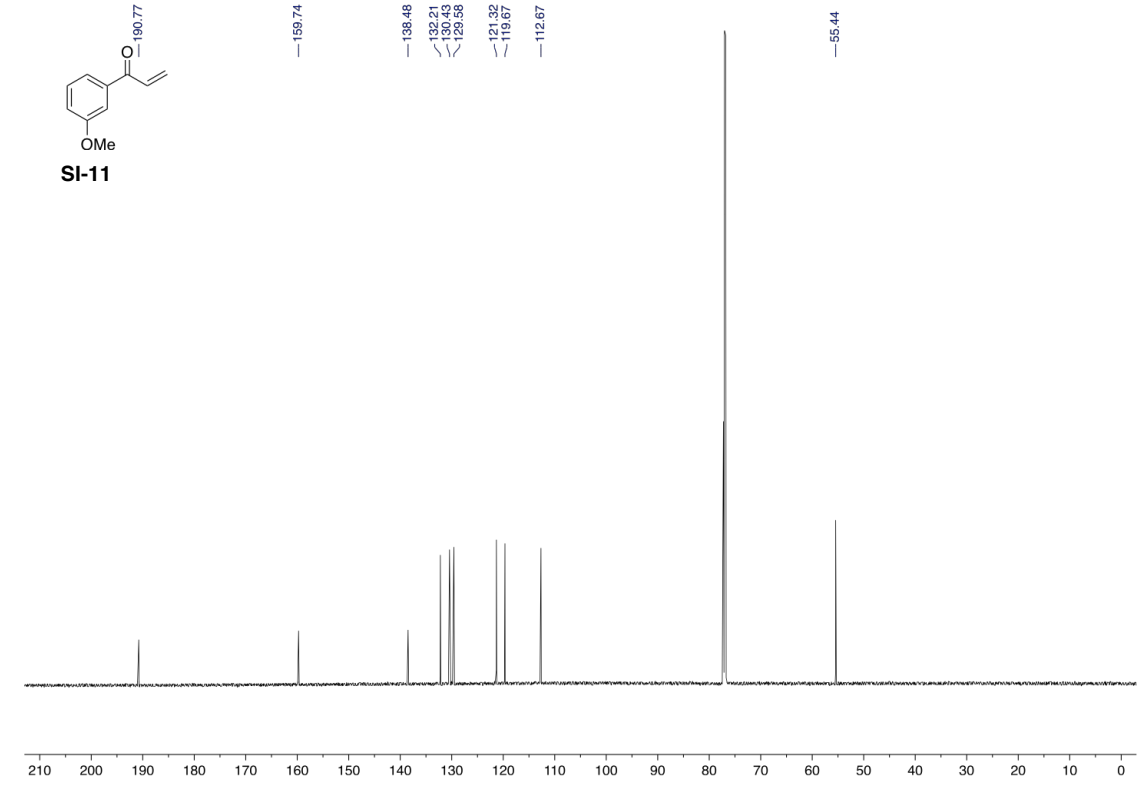
SI-11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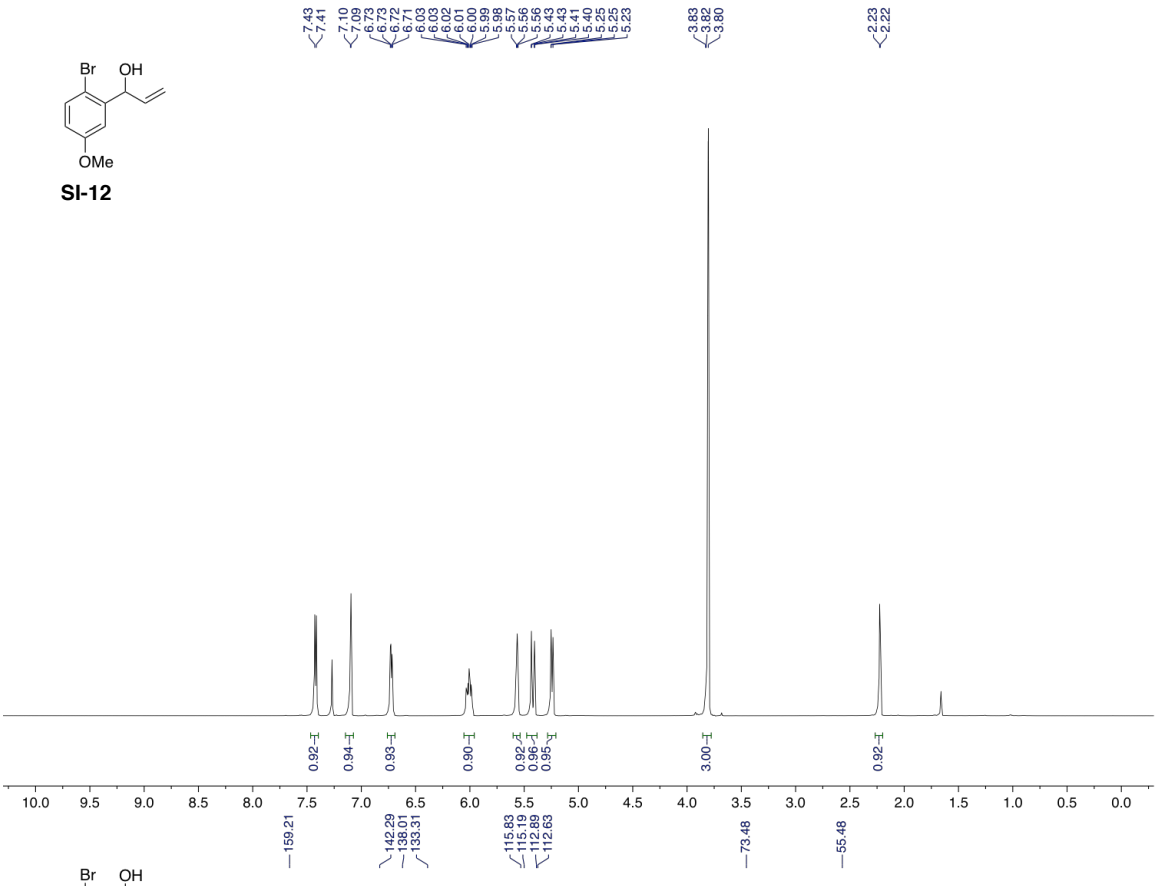
SI-12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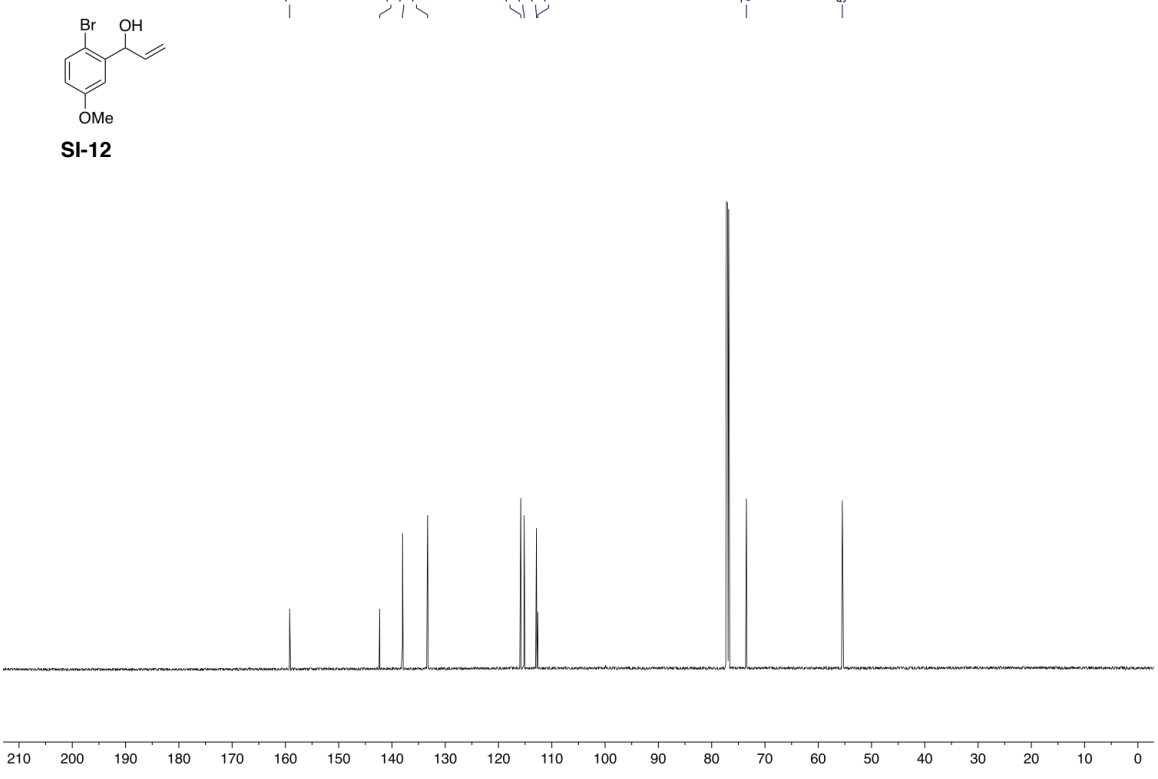
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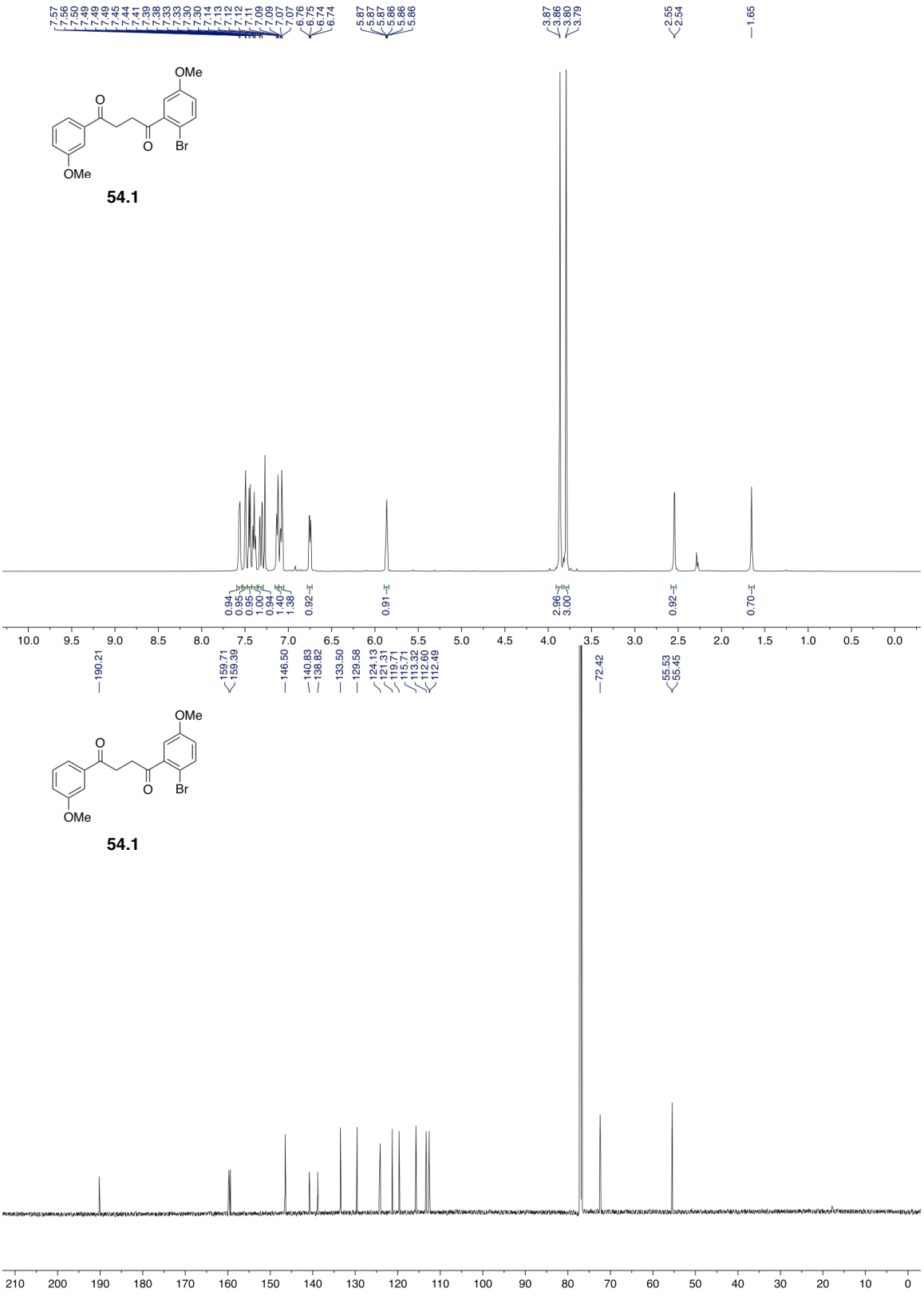
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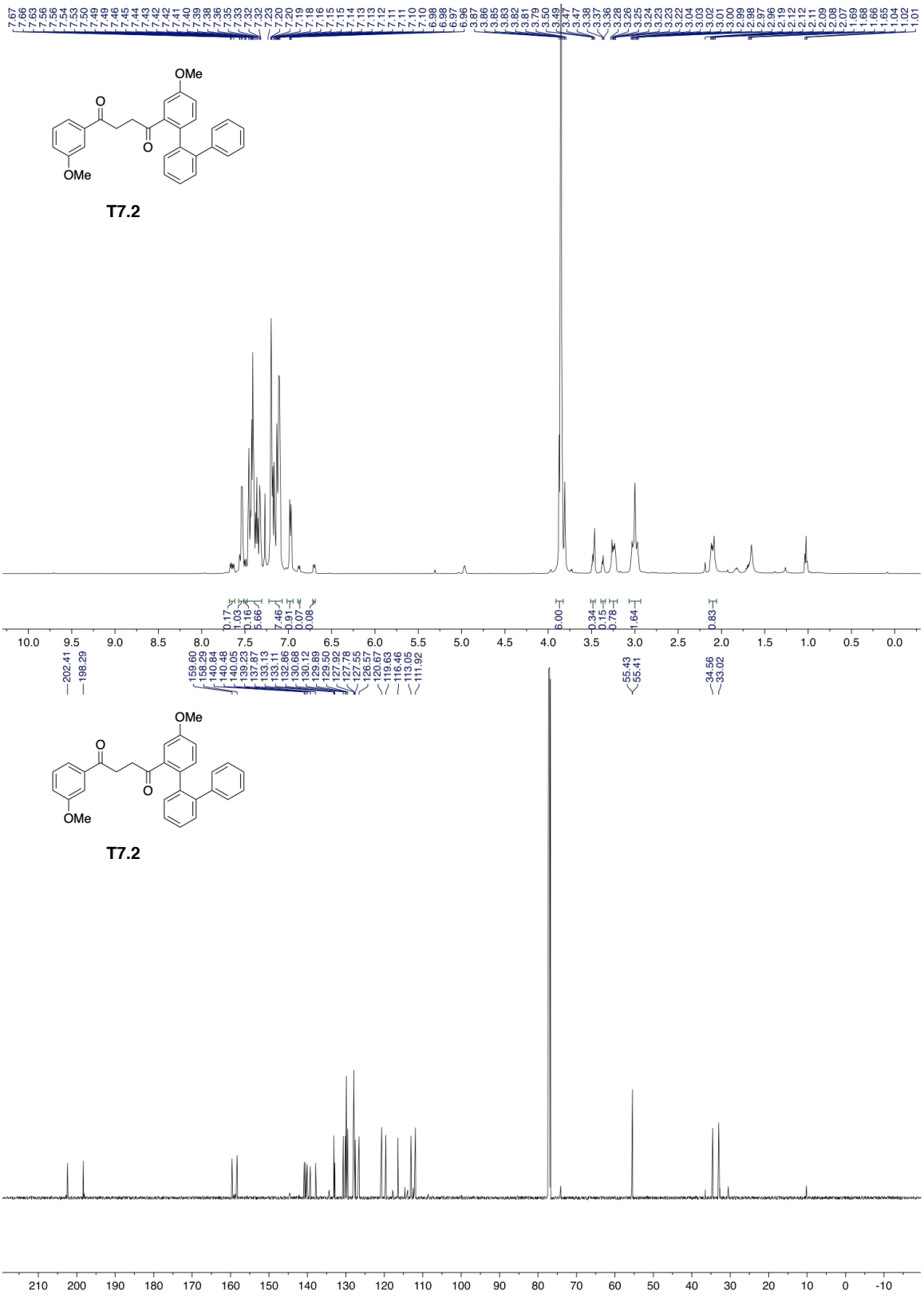

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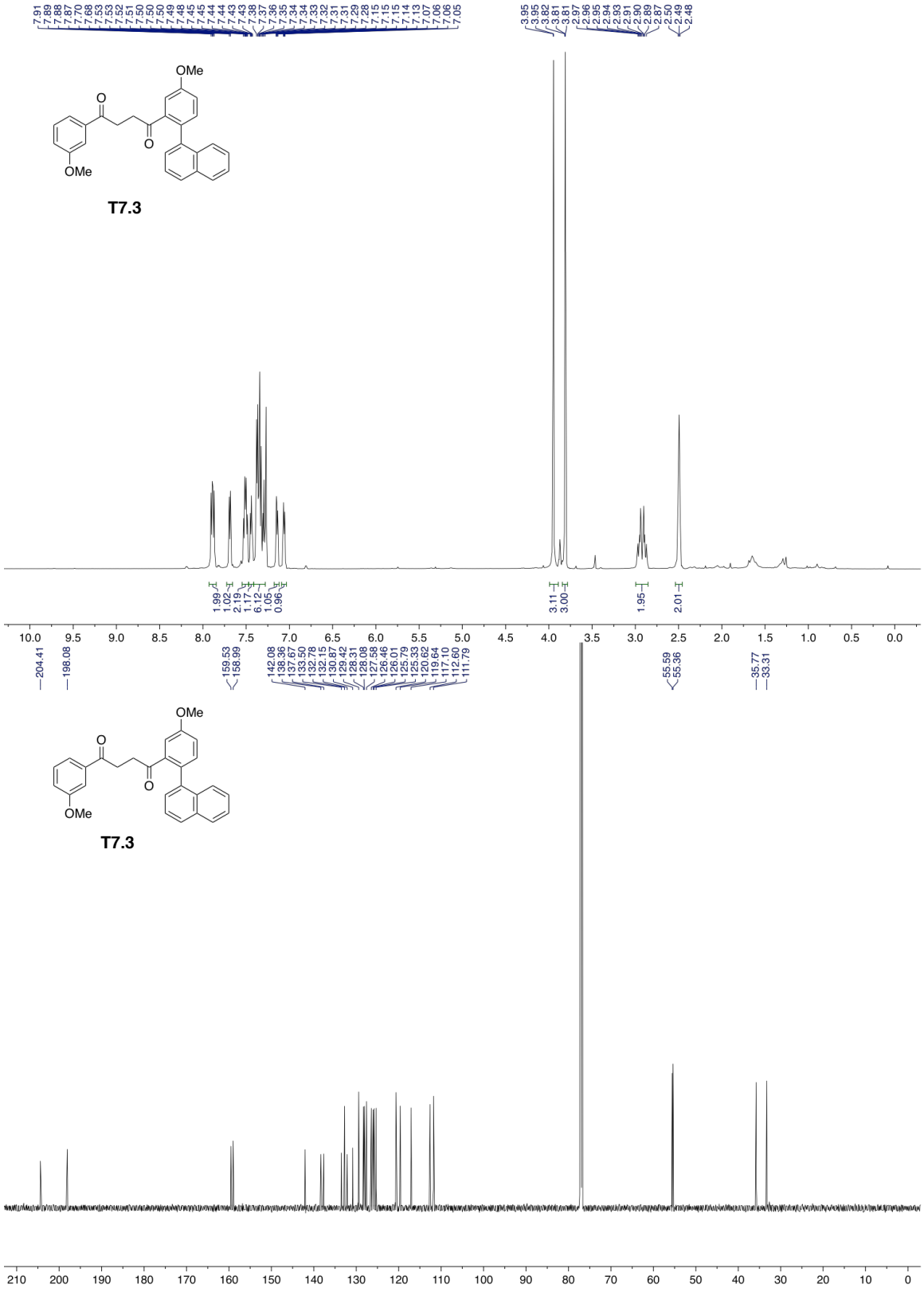
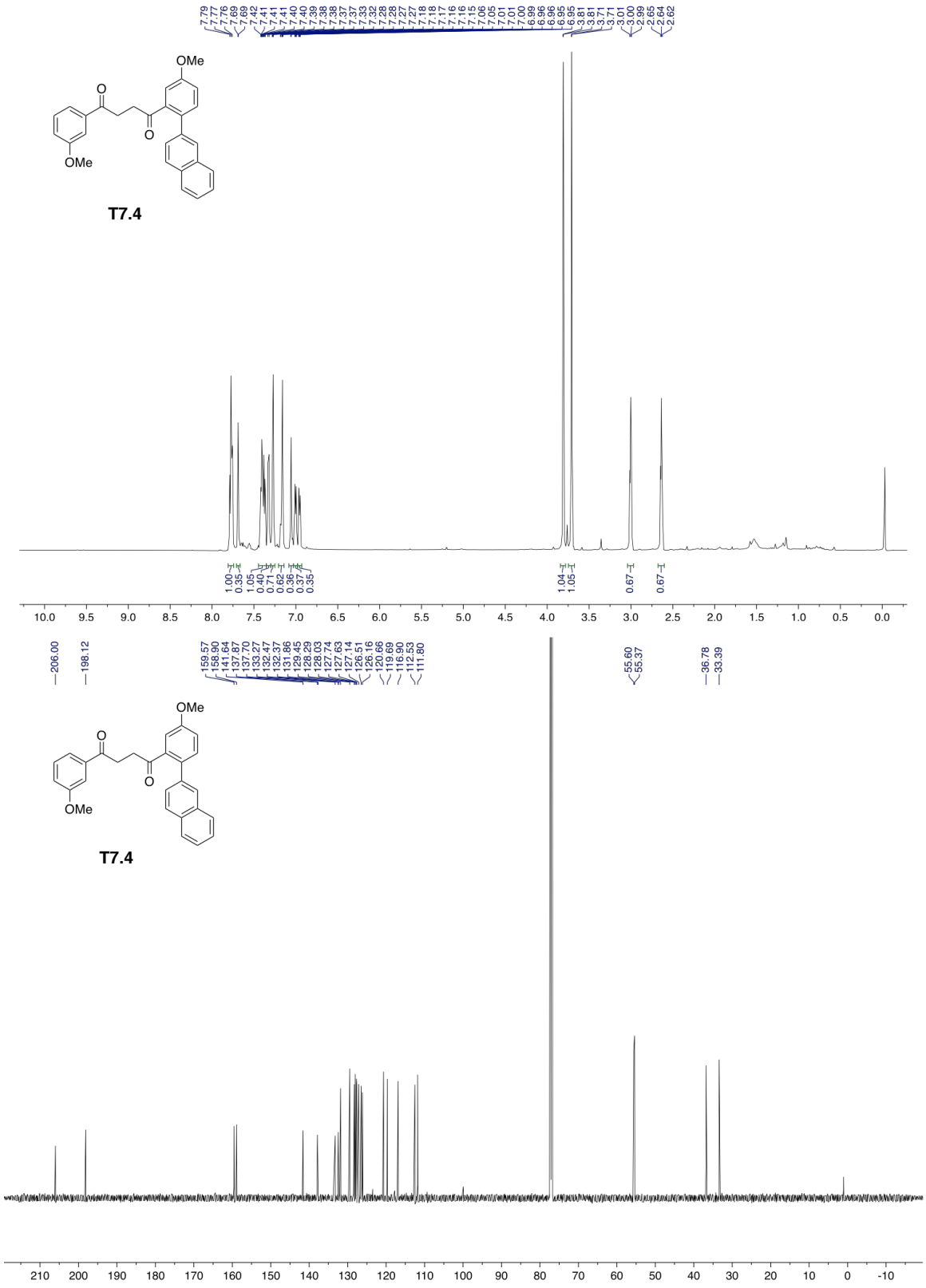
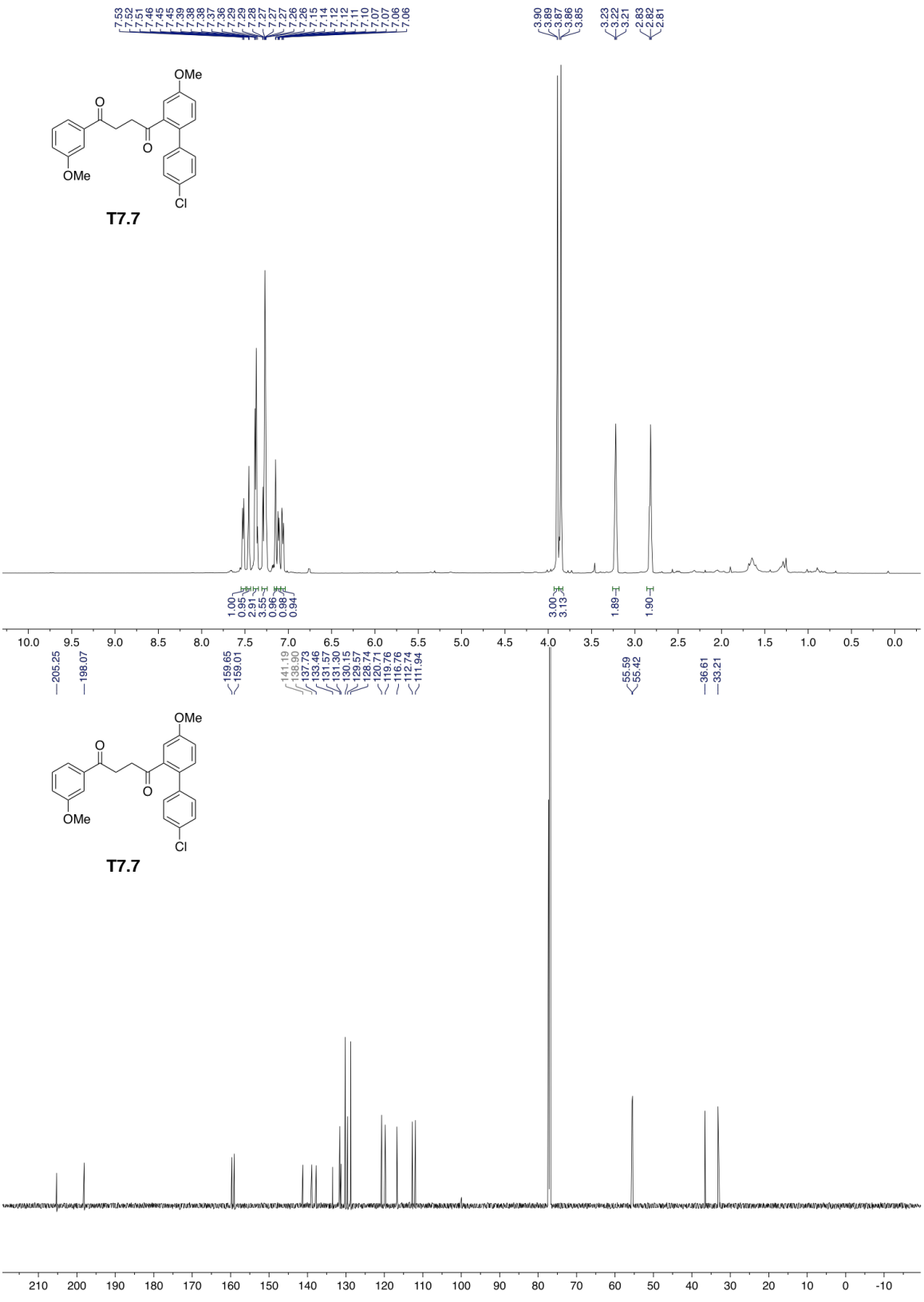


T7.4



T7.7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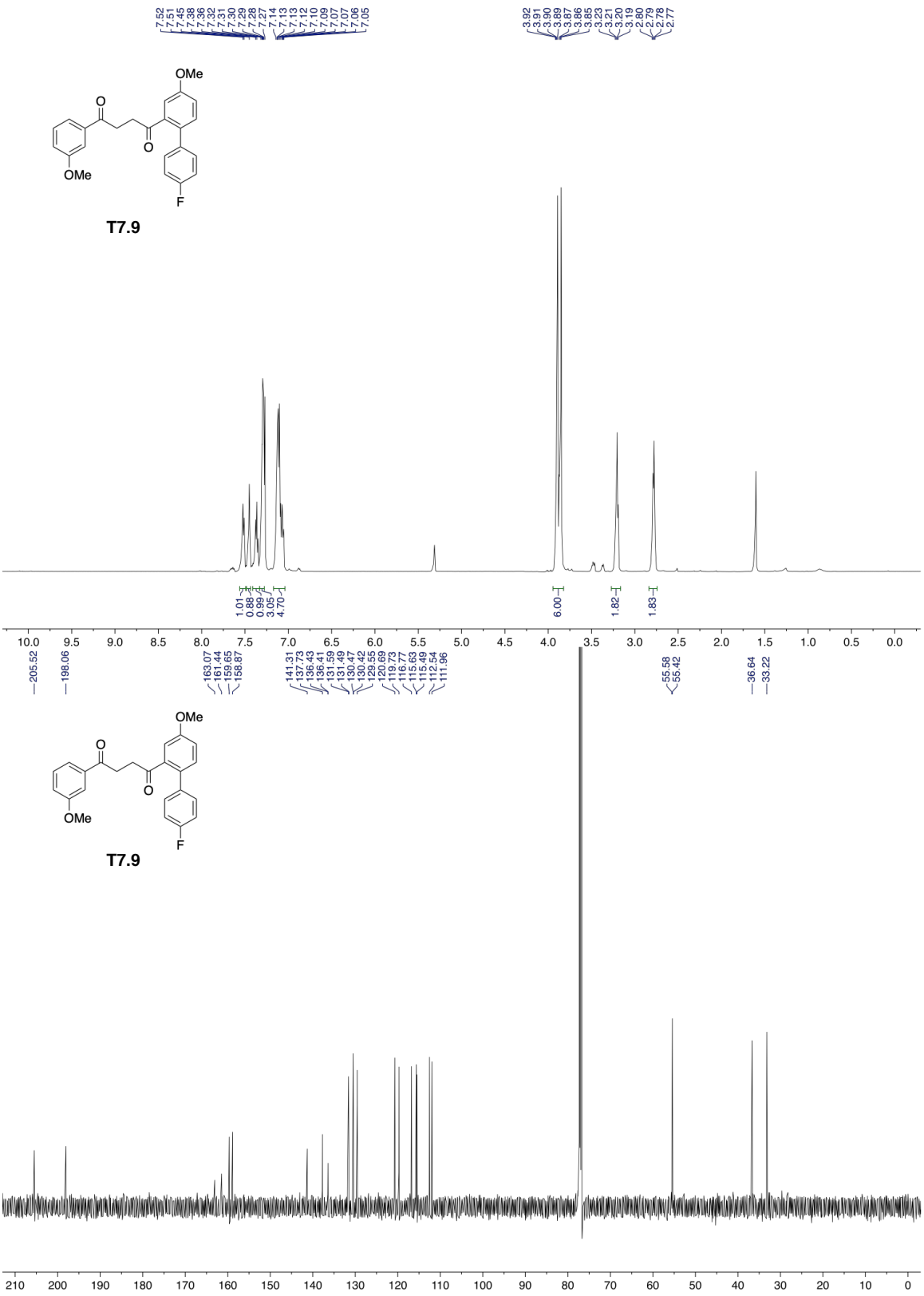
T7.9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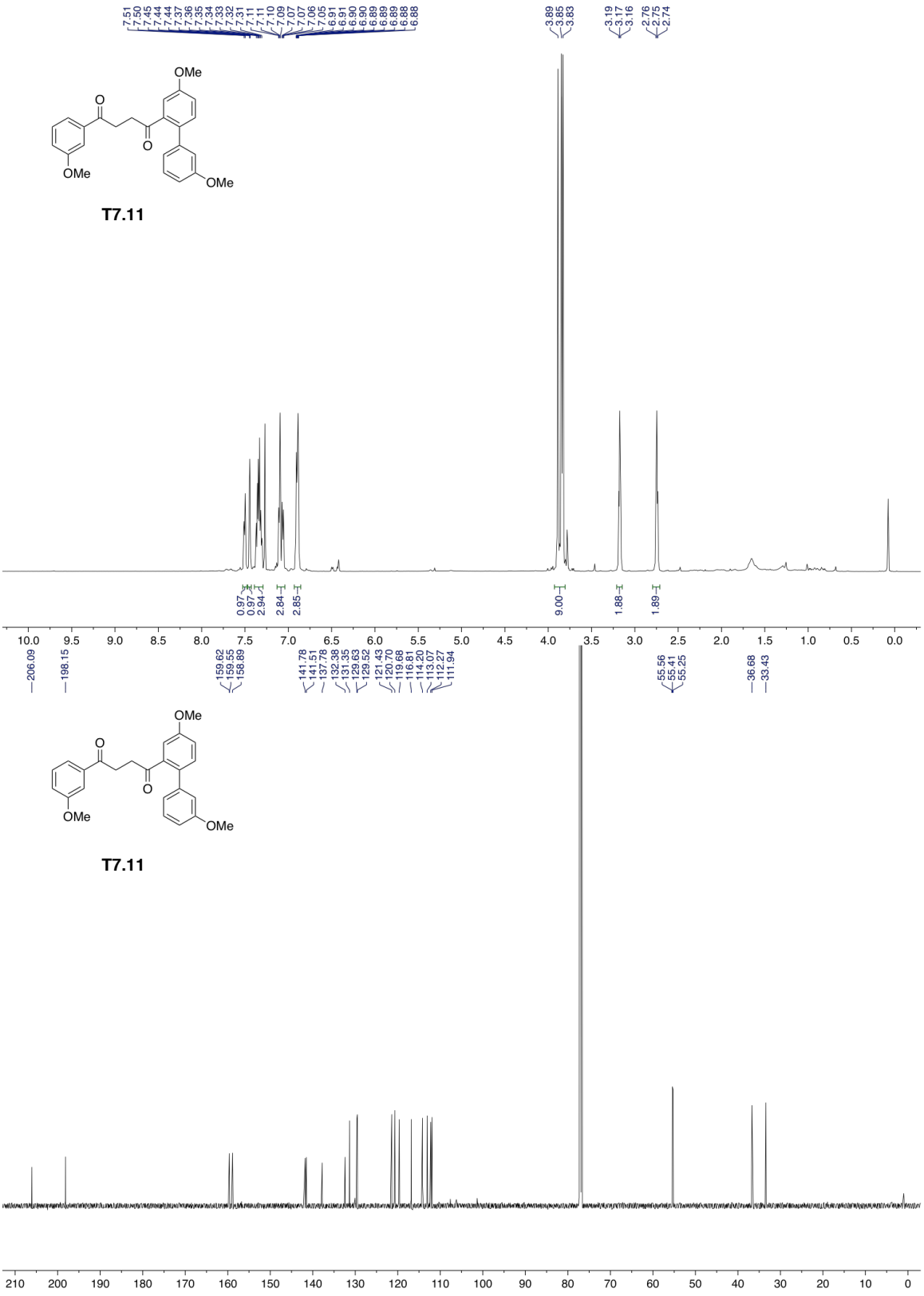
T7.11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OMe
T7.11
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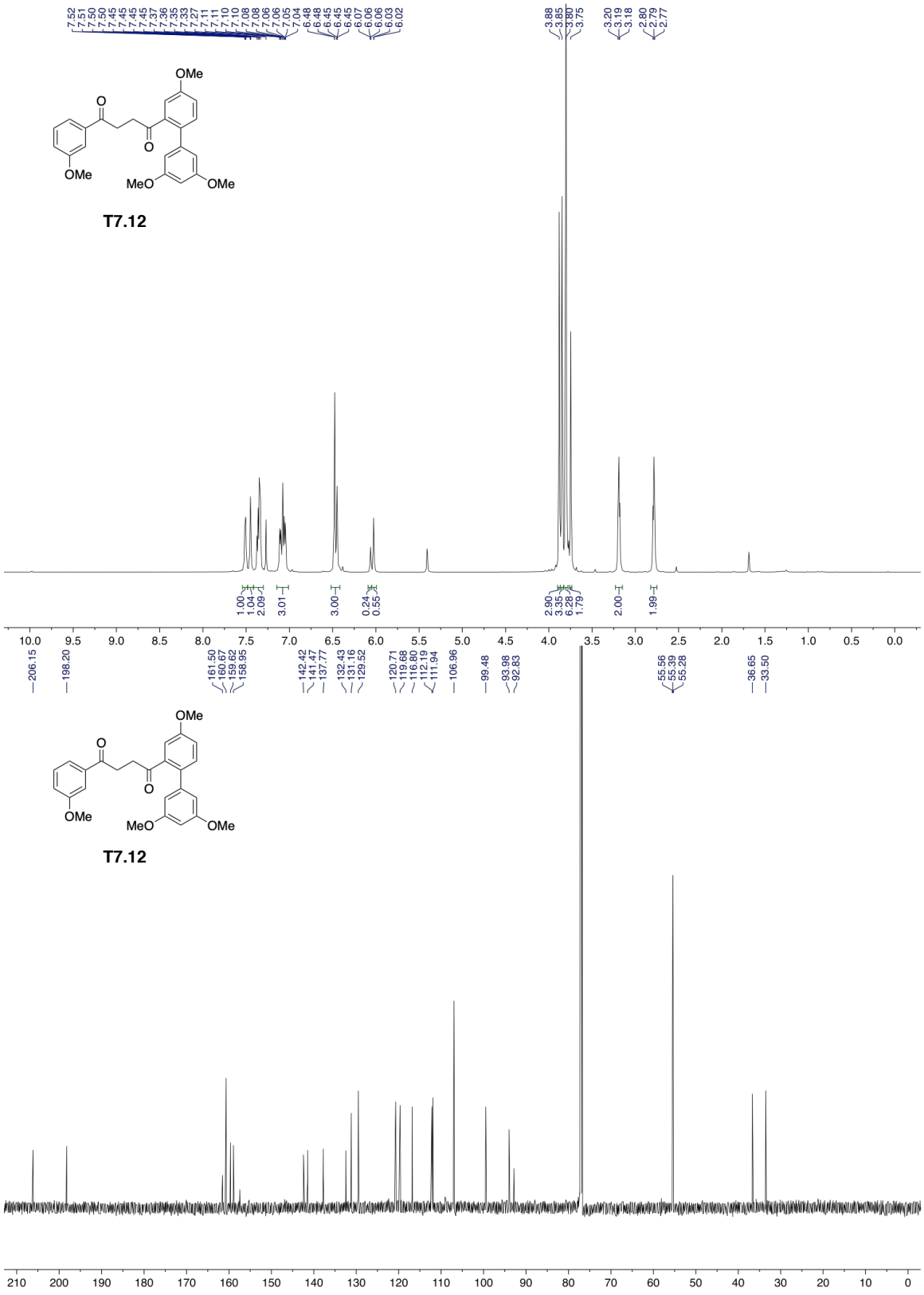

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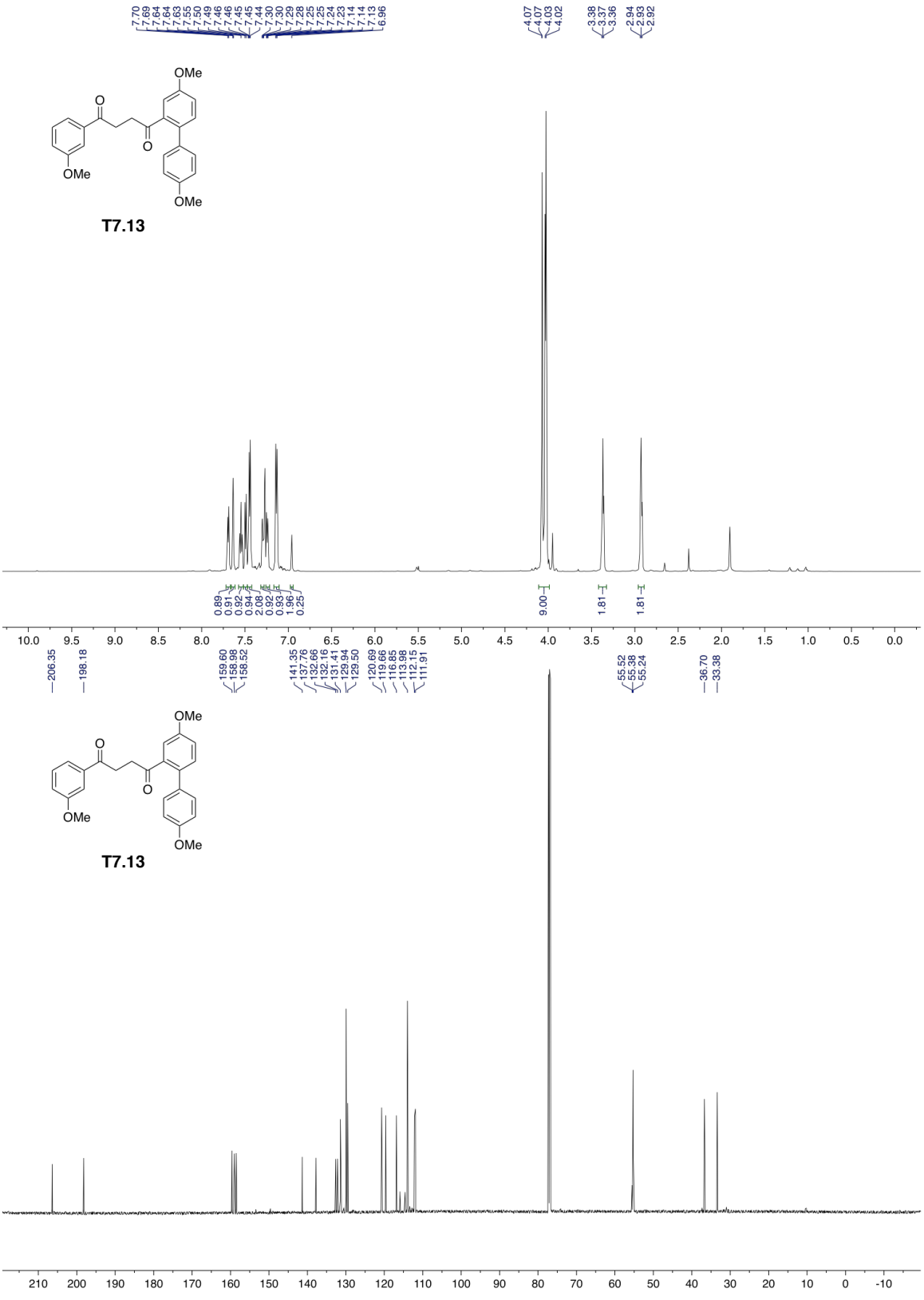
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T7.13
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OMe
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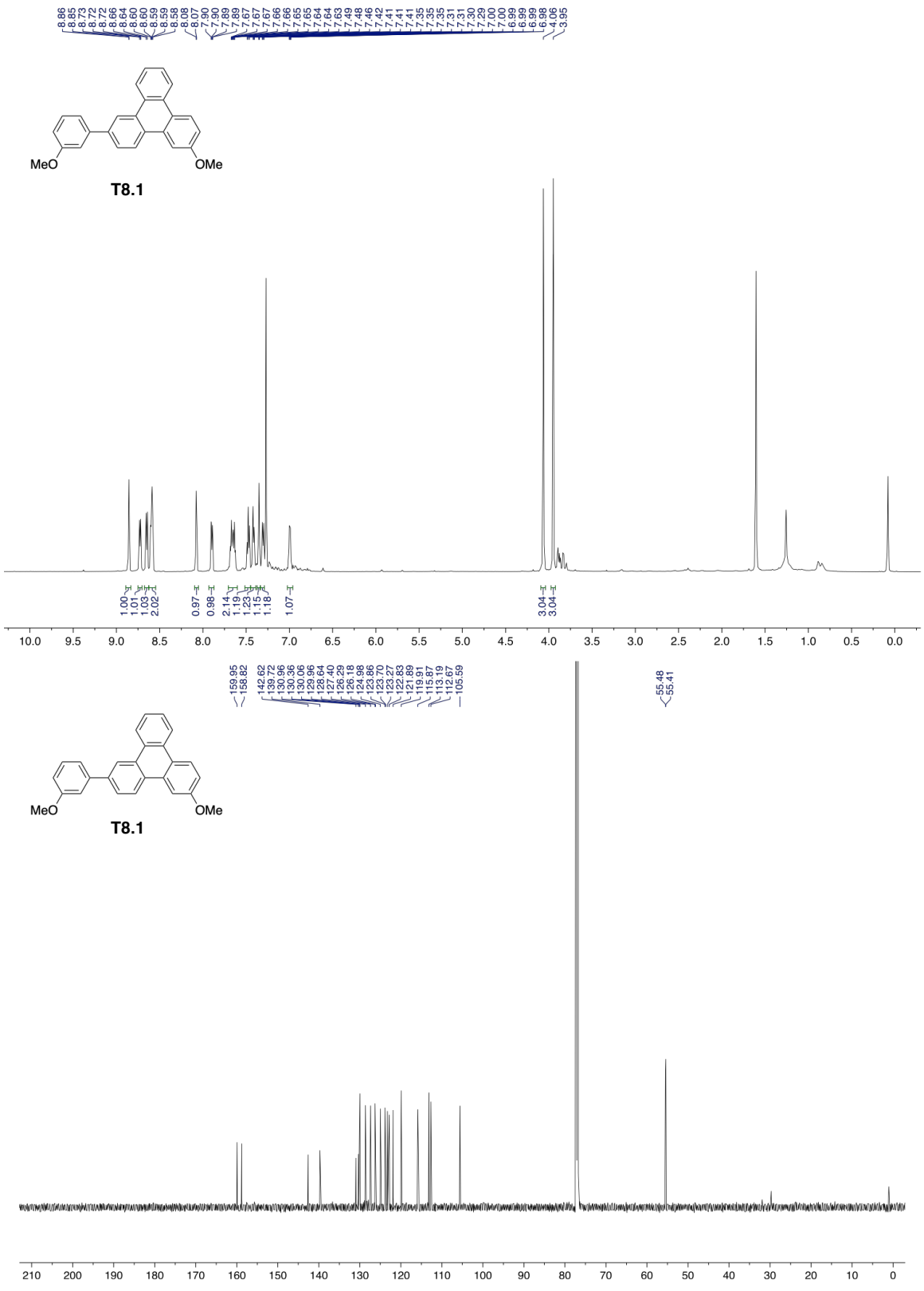
T7.13

T8.1



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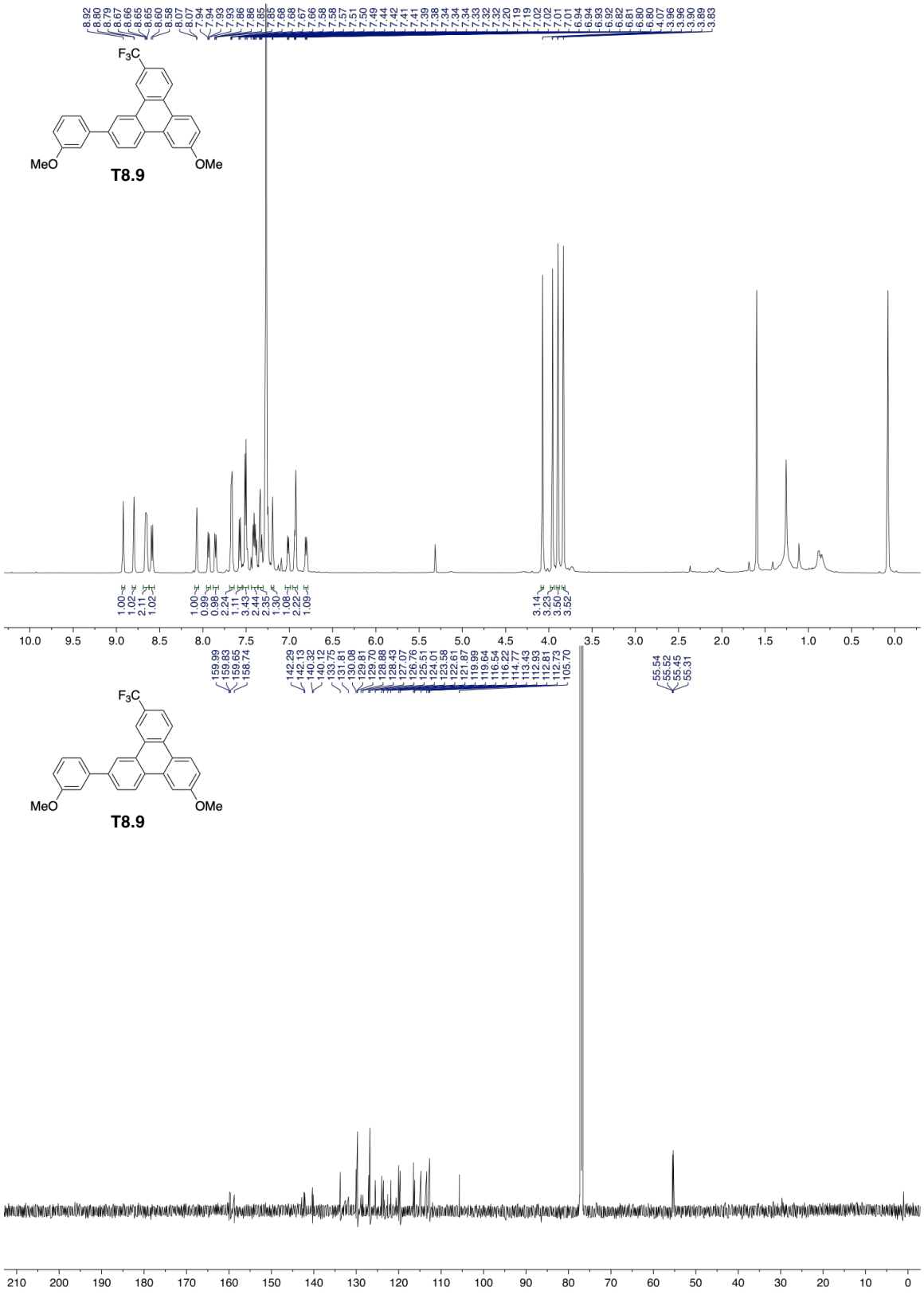

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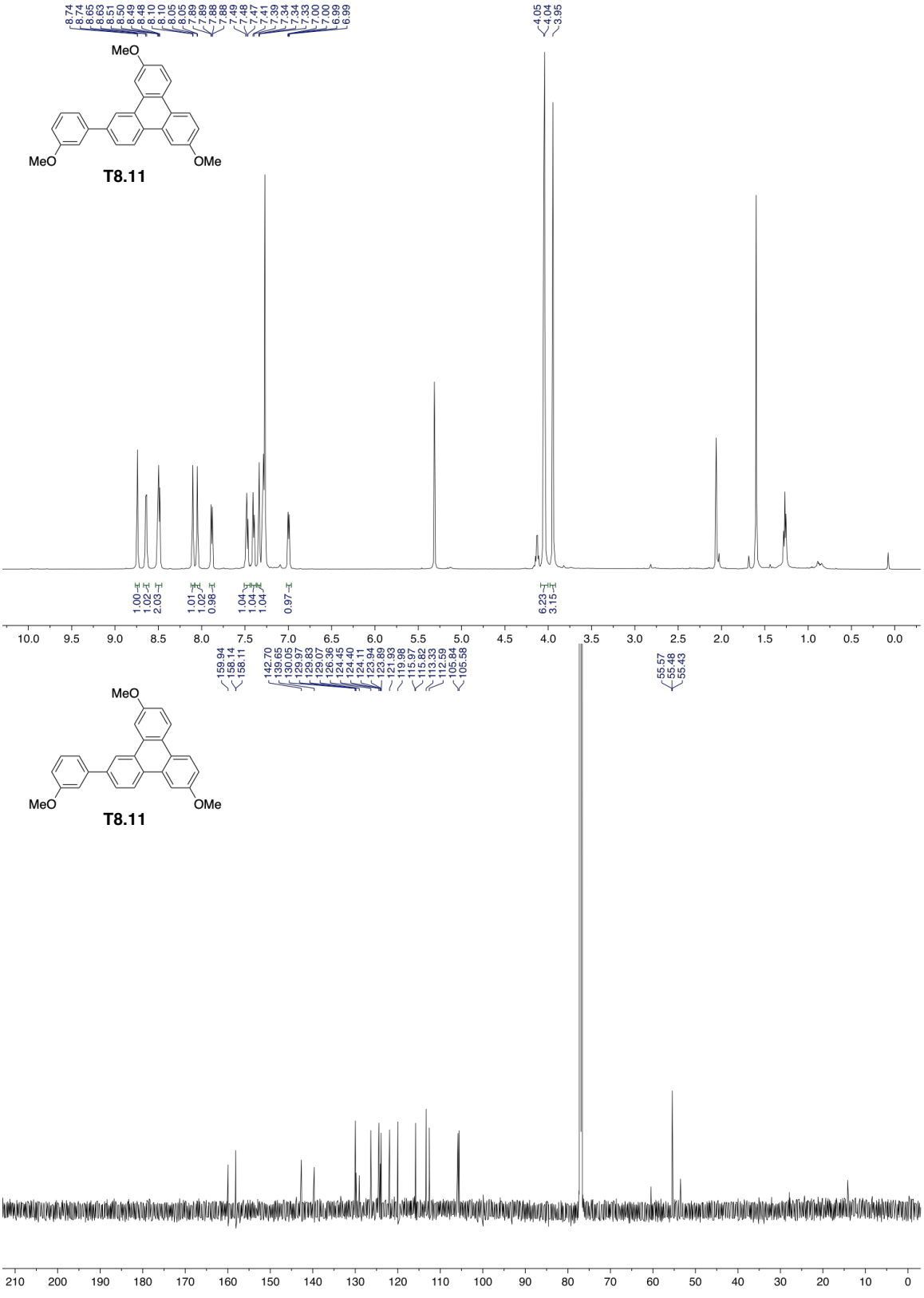
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4.05
4.04
3.95
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MeO
OMe
T8.11
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2.03
1.01
1.02
0.98
1.04
1.04
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0.97
6.23
3.15
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MeO
OMe
T8.11
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