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Synthesis of Helical and Bowl-Shaped Polycyclic Aromatic Compounds via Benzannulated Enyne-Allenenes

Bo Wen
West Virginia University

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**Synthesis of Helical and Bowl-Shaped Polycyclic Aromatic Compounds
via Benzannulated Enyne-Allenenes**

Bo Wen

**Dissertation submitted to the Eberly College of Arts and Sciences
at West Virginia University
in partial fulfillment of the requirements
for the degree of**

**Doctor of Philosophy
in
Organic Chemistry**

Approved by

Kung K. Wang, Ph. D., Chair

Jeffrey L. Petersen, Ph. D.

Björn C. Söderberg, Ph. D.

Peter M. Gannett, Ph. D.

Xiaodong Shi, Ph. D.

**C. Eugene Bennett Department of Chemistry
Morgantown, West Virginia
2010**

**Keywords: Enyne-Allene, Schmitt Cyclization, 4,5-Diheteroarylphenanthrene
1,4-Naphthoquinone Methide, Buckybowl**

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ABSTRACT

Synthesis of Helical and Bowl-shaped Polycyclic Aromatic Compounds via Benzannulated Enyne-Allenenes

BO WEN

The cascade radical cyclization of the benzannulated enyne-allenes provides an efficient synthetic pathway to a variety of polycyclic aromatic hydrocarbons. Three indeno-fused 4,5-diheteroarylphenanthrenes were synthesized by thermolysis of corresponding benzannulated enyne-allenes. Its X-ray structure shows that the substituents at C4 and C5 positions of the phenanthryl system are essentially parallel to each other and cause severe helical twist of the structures. The presence of two terpyridyl units in **2.2c** allowed it to be used as a ligand for the synthesis of dinuclear ruthenium(II) bis(terpyridine) complexes possessing severe helical twists.

Several 1,4-naphthoquinone methides were synthesized via an unusual acid-catalyzed cascade cyclization sequence followed by two-carbon ring expansion of benzannulated enediynyl alcohols. The simplicity of the synthetic sequence and the mildness of the reaction condition make this pathway especially attractive.

A new synthetic route to a bowl-shaped aromatic hydrocarbon **4.87** was developed. The key steps of this efficient pathway include a cascade cyclization of the corresponding enyne-allene and subsequent palladium-catalyzed intramolecular arylation reactions of the aromatic dibromides. Several attempts were made to synthesize a precursor of buckybowl **4.54**. The suitable precursor will bear a framework of **4.54** and could be fully aromatized to form **4.54**. Further exploration is required to overcome difficulties encountered toward the synthesis of buckybowl **4.54**.

DEDICATED TO

**My wife, Ting Zhao, My daughter, Hannah
and My Parents**

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TABLE OF CONTENTS

Title Page.....	i
Abstract.....	ii
Dedication.....	iii
Acknowledgement.....	iv
Table of Contents.....	v
List of Figures.....	viii
List of ^1H and ^{13}C NMR Spectra.....	ix

CHAPTER 1 PRELUDE 1

1. Introduction.....	1
2. The thermal cyclization of enediynes and enyne-allenes.....	1
3. The synthetic methodologies for the preparation of benzannulated enyne-allenes	5
3.1. Prototropic rearrangement of alkynes	5
3.2. Palladium-catalyzed cross-coupling reactions	6
3.3. Rearrangement of propargylic alcohol derivatives.....	7
4. Construction of novel polycyclic aromatic hydrocarbons via the Schmittel cyclization reactions of enyne-allenes	11
5. References.....	13

CHAPTER 2 SYNTHESIS OF 4,5-DIHETEROARYLPHENANTHRENES AND THEIR DINUCLEAR RU(II) BIS(2,2':6',2''-TERPYRIDINE) COMPLEXES POSSESSING SEVERE HELICAL TWISTS..... 16

1. Synthesis and structure characterization of 4,5-diheteroaryl-phenanthrenes compounds that possess sever helical twists	16
1.1. Introduction	16
1.2. Results and discussion	17
2. Synthesis and structure analysis of dinuclear ruthenium(II) bis(terpyridine) complexes	21
2.1. Introduction	21
2.2. Results and discussion	22
3. Synthesis of pyridine, bipyridine, terpyridine ligands used in the helical twist compounds.	26
4. Conclusions	27
5. Reference	28

CHAPTER 3 SYNTHESIS OF 1,4-NAPHTHOQUINONE METHIDES VIA ACID-CATALYZED CASCADE CYCLIZATIONS OF THE BENZANNULATED ENEDIYNYL ALCOHOLS

1. Introduction	30
1.1. Parent Quinone Methides	30
1.2. Properties and Synthetic Applications of Quinone Methides	31
1.3. Synthetic method used to generate quinone methides	33
2. Results and Discussion	35
2.1. The synthesis of 1,4-naphthoquinone methides	35
2.2. The properties of 1,4-naphthoquinone methides	39
2.3. The synthesis of requisite fragments	41

3. Conclusion	42
4. Reference	43
CHAPTER 4. SYNTHESIS OF BOWL-SHAPED FULLERENE FRAGMENTS WITH CURVED SURFACES: BUCKYBOWLS	45
1. Introduction	45
2. Literature survey for the synthesis of buckybowls	47
2.1. Synthesis of buckybowls in solution chemsitry	47
2.2. Synthesis of buckybowls by flash vacuum pyrolysis	51
3. Research objective	53
4. Result and Discussion	56
4.1. Retrosynthetic Analysis for Buckybowl 4.54	56
4.2. Initial Approach	57
4.3. Second Approach	61
4.4. Third Approach	63
4.4. Fourth Approach	64
5. Conclusions	67
6. References	69
CHAPTER 5. EXPERIMENT SECTION	74
Experimental Methods	75
Appendix	120
Publications & Presentations	280

LIST OF FIGURES

Figure 1.1 Structures of 1.1 , 1.2 , and 1.3	1
Figure 1.2 Molecular structures of 1.56a and 1.56b	9
Figure 2.1 Structures of 4,5-disubstituted phenanthrenes	17
Figure 2.2 ¹ H NMR spectrum of the 4,5-di(4-pyridyl)phenanthrene 2.2a	19
Figure 2.3 ORTEP drawings of the crystal structures of 2.2a and 2.2c	20
Figure 2.4 (a) UV-vis absorption spectra and (b) luminescence spectra of 2.2a (black), 2.2b (red), and 2.2c (blue) in dichloromethane at room temperature.	21
Figure 2.5 X-ray crystal structure of [Ru(tpy) ₂]	22
Figure 2.6 NMR spectra of 2.10	24
Figure 2.7 UV-vis absorption spectra of 2.13 (black), 2.14 (red), and [Ru(4'-EtOtpy) ₂](PF ₆) ₂ (blue) in acetonitrile at room temperature.	25
Figure 3.1 The structures of parent quinone methides.	30
Figure 3.2 Structures of stabilized <i>p</i> -QMs.	35
Figure 3.3 The scope and limitation of the new synthetic pathway for QMs	37
Figure 3.4 ORTEP drawing of the crystal structure of 3.49 and 3.54	39
Figure 3.5 UV-vis absorption spectra of 3.49 , 3.50 , 3.54 , and 3.57 in CH ₃ CN.	40
Figure 3.6 Luminescence spectra of 3.49 and 3.50 in CH ₃ CN.	40
Figure 3.7 UV-vis absorption spectra of 3.49 in CH ₃ CN with varying H ₂ SO ₄ concentration.	40
Figure 3.8 UV-vis absorption spectra of 3.49 , 3.50 , 3.54 , and 3.57 in CH ₃ CN with acid	40
Figure 4.1 Model of fullerenes	45
Figure 4.2 Bowl-shaped polycyclic aromatic hydrocarbons.	46
Figure 4.3 ORTEP drawing of the crystal structure of 4.53	55
Figure 4.4 MM2-optimized structure of 4.54	55

Figure 4.5 POAV angles of fullerene and buckybowl.....	55
Figure 4.6 Proposed application of buckybowl 4.54	56
Figure 4.7 Retrosynthetic analysis for buckybowl 4.54	57
Figure 4.8 MM2-optimized structure and NOE of 4.78	59
Figure 5.1 ORTEP drawings of the crystal structures of two diastereomers of 2.8a	118
Figure 5.2 ORTEP drawings of the crystal structures of 3.66	119
Figure 5.3 ORTEP drawings of the crystal structures of 4.97	119

LIST OF ¹H AND ¹³C NMR SPECTRA

¹ H and ¹³ C NMR Spectra of compound 2.5	120–121
¹ H and ¹³ C NMR Spectra of compound 2.6	122–123
¹ H and ¹³ C NMR Spectra of compound 2.8a	124–127
¹ H and ¹³ C NMR Spectra of compound 2.2a	128–129
¹ H and ¹³ C NMR Spectra of compound 2.8b	130–131
¹ H and ¹³ C NMR Spectra of compound 2.2b	132–133
¹ H and ¹³ C NMR Spectra of compound 2.8c	134–135
¹ H and ¹³ C NMR Spectra of compound 2.2c	136–137
¹ H NMR Spectra of compound 2.10	138
¹ H and ¹³ C NMR Spectra of compound 2.13	139–140
¹ H NMR Spectra of compound 2.14	141
¹ H and ¹³ C NMR Spectra of compound 3.75	142–143
¹ H and ¹³ C NMR Spectra of compound 3.43	144–145
¹ H and ¹³ C NMR Spectra of compound 3.76	146–147
¹ H and ¹³ C NMR Spectra of compound 3.44	148–149
¹ H and ¹³ C NMR Spectra of compound 3.46	150–151
¹ H and ¹³ C NMR Spectra of compound 3.47	152–153

^1H and ^{13}C NMR Spectra of compound 3.48	154–155
^1H and ^{13}C NMR Spectra of compound 3.49	156–159
^1H and ^{13}C NMR Spectra of compound 3.50	160–163
^1H and ^{13}C NMR Spectra of compound 3.53	164–165
^1H and ^{13}C NMR Spectra of compound 3.54	166–168
^1H and ^{13}C NMR Spectra of compound 3.81	169–170
^1H and ^{13}C NMR Spectra of compound 3.55	171–172
^1H and ^{13}C NMR Spectra of compound 3.56	173–174
^1H and ^{13}C NMR Spectra of compound 3.57	175–176
^1H and ^{13}C NMR Spectra of compound 3.59	177–178
^1H NMR Spectra of compound 3.60	179
^1H and ^{13}C NMR Spectra of compound 3.62	180–181
^1H NMR Spectra of compound 3.63	182
^1H and ^{13}C NMR Spectra of compound 3.65	183–184
^1H and ^{13}C NMR Spectra of compound 3.66	185–186
^1H and ^{13}C NMR Spectra of compound 3.68	187–188
^1H and ^{13}C NMR Spectra of compound 3.70	189–190
^1H and ^{13}C NMR Spectra of compound 3.71	191–192
^1H and ^{13}C NMR Spectra of compound 4.67	193–194
^1H and ^{13}C NMR Spectra of compound 4.68	195–196
^1H and ^{13}C NMR Spectra of compound 4.71	197–198
^1H and ^{13}C NMR Spectra of compound 4.73	199–201
^1H and ^{13}C NMR Spectra of compound 4.74	202–203
^1H and ^{13}C NMR Spectra of compound 4.76	204–205
^1H and ^{13}C NMR Spectra of compound 4.77	206–207
^1H and ^{13}C NMR Spectra of compound 4.78	208–209
gCoty and ^1H NMR Spectra of compound 4.78	210–211

^1H and ^{13}C NMR Spectra of compound 4.82	212–215
^1H and ^{13}C NMR Spectra of compound 4.83	216–217
^1H and ^{13}C NMR Spectra of compound 4.84	218–219
^1H and ^{13}C NMR Spectra of compound 4.85	220–221
^1H and ^{13}C NMR Spectra of compound 4.86	222–223
^1H NMR Spectra of compound 4.87 and 4.88	224
1 D NOESY NMR Spectra of compound 4.87 and 4.88	225–226
1 D TOCSY NMR Spectra of compound 4.87 and 4.88	227–228
Seldecoupled ^1H NMR Spectra of compound 4.87	229–232
^1H and ^{13}C NMR Spectra of compound 4.93	233–234
^1H and ^{13}C NMR Spectra of compound 4.94	235–238
^1H and ^{13}C NMR Spectra of compound 4.95	239–240
^1H and ^{13}C NMR Spectra of compound 4.96	241–242
^1H and ^{13}C NMR Spectra of compound 4.97	243–244
^1H and ^{13}C NMR Spectra of compound 4.98	245–246
^1H and ^{13}C NMR Spectra of compound 4.99	247–248
^1H and ^{13}C NMR Spectra of compound 4.100	249–250
^1H and ^{13}C NMR Spectra of compound 4.101	251–252
^1H and ^{13}C NMR Spectra of compound 4.103	253–254
^1H and ^{13}C NMR Spectra of compound 4.104	255–256
^1H and ^{13}C NMR Spectra of compound 4.105	257–258
^1H and ^{13}C NMR Spectra of compound 4.106	259–260
^1H and ^{13}C NMR Spectra of compound 4.107	261–262
^1H and ^{13}C NMR Spectra of compound 4.108	263–264
^1H and ^{13}C NMR Spectra of compound 4.121	265–266
^1H and ^{13}C NMR Spectra of compound 4.122	267–268
^1H and ^{13}C NMR Spectra of compound 4.123	269–270

^1H and ^{13}C NMR Spectra of compound 4.124	271–272
^1H and ^{13}C NMR Spectra of compound 4.126	273–274
^1H and ^{13}C NMR Spectra of compound 4.129	275–276
^1H and ^{13}C NMR Spectra of compound 4.130	277–278
^1H NMR Spectra of compound 4.137	279

CHAPTER 1

Prelude

1. Introduction

Allenes have been known for more than 100 years to organic chemists. The correct core structure of allenes was predicted in 1874 by Jacobus H. Van'tHoff,¹ the first Nobel laureate in chemistry. Interestingly, the aim in the first documented synthesis of an allene was to prove the non-existence of this class of “highly unstable” organic compounds.^{2,3} The cumulated diene system of allenes has been described as consisting of two double bonds with two π -orbitals perpendicular to each other. Over the past 20 years, the chemistry of allenes has developed rapidly because of their unusual properties, such as the axial chirality of the elongated tetrahedron and the various functionality. With multi-reactivity, an allene can serve as a powerful candidate for synthetic manipulations. Hence, allenes hold great potential for the discovery of new and exciting organic reactions for a variety of chemical transformations.⁴⁻¹⁰

The focus of this dissertation is the preparation of benzannulated enyne-allenes as precursors for use in the synthesis of helical polycyclic aromatic hydrocarbons **1.1**, bowl-shaped fullerene fragments **1.2**, and 1,4-naphthoquinone methides **1.3** (Figure 1.1).

Figure 1.1 Structures of 1.1, 1.2, and 1.3

2. The thermal cyclization of enediynes and enyne-allenes

Because allenes have a hybrid character of an olefin and an acetylene, most of the reactions that simple alkenes and alkynes undergo are also available to the allenes. The reactive diradical intermediates **1.5** and **1.8** were formed in the thermal cyclizations of enediynes **1.4** (Bergman, C¹-C⁶)¹¹⁻¹³ and enyne-allenes **1.7** (Myers-Saito, C²-C⁷)¹⁴⁻¹⁷ (Scheme 1.1).

Scheme 1.1. Thermal cyclization of enediynes and enyne-allenes

Both of the intermediates were of great interest for organic chemist and they also could be used to simulate antitumor antibiotics for natural enediynes in biology.¹⁸ The biological activity of the enediynes is attributed to their ability to cleave DNA irreversibly. For example, a thermal C²-C⁷ cyclization was proposed to be a key step for the DNA damage action of neocarzinostatin A by Myers (Scheme 1.2).¹⁹

Scheme 1.2. Mechanism of DNA cleavage by **1.10**

In Scheme 1.2, stereospecific nucleophilic attack at C12 initiated the DNA damage. Subsequently, the ring skeleton was rearranged with epoxide opening and a cumulene was formed in a labile intermediate **1.11**. Afterward, biradical **1.12** was formed by a rapid Myers-Saito cyclization, which extracted two hydrogen atoms from the sugar-phosphate backbone of DNA, leading to the formation of **1.13** and DNA cleavage. The occurrence of the Myers-Saito cyclization to form highly reactive intermediates is due in part to the aromaticity gained on cyclization.

The thermal C^1-C^5 diradial cyclization of parent enediyne **1.4** (Scheme 1.1), a variant of the Bergman cyclization, is unlikely because the high energy barrier for cyclization (41.0 vs 25.2 kcal/mol at the BLYP/6-31G(d) level of theory).²⁰⁻²² In 2008, Robert A. Pascal reported that benzannulated enediyne **1.14** with the 2,4,6-trichlorophenyl group at both alkyne termini gave indene derivatives **1.15** and **1.16** (Scheme 1.3) in 19% and 50% isolated yields, respectively.²³ The pathway switch from C^1-C^6 to C^1-C^5 is attributed to the increased steric conflict between substituents on the alkyne termini in the Bergman TS and the stabilization of the diradical intermediate in the C^1-C^5 pathway.

Scheme 1.3. Thermal C^1-C^5 cyclization of enediyne **1.14**

Similar studies of the thermal C^2-C^6 cyclizaion of enyne-allenes **1.7** were reported by Schmittle in 1995 (Scheme 1.1).²⁴⁻²⁸ The aromaticity was not gained in this cyclization, but it is still promoted by the formation of a strong sp^2-sp^2 σ bond from sp -hybridized carbons. Since then, this second reaction motif for enyne-allenes has proven valuable in synthesis and has been studied mechanistically and theoretically.^{21,22,29-31} Through theoretical studies, the C^2-C^7 cyclization of the parent (Z)-1,2,4-heptatrien-6-yne is

predicted to be favored over C^2-C^6 by about 10 kcal/mol.³² However, substantial evidence showed that two competing thermal reaction modes of enyne-allenes can be most conveniently controlled through the proper choice of substituents at the alkyne terminus (Scheme 1.4). The C^2-C^6 cyclization of **1.17** is favored by radical stabilizing groups or bulky groups at C^7 . Whereas, the C^2-C^7 reaction mode is observed with $R^1 = H$ or an n-alkyl group.

Scheme 1.4. A switch from C^2-C^7 cyclization to C^2-C^6 cyclization

The C^2-C^6 cyclization can proceed through a stepwise diradical mechanism or a concerted pericyclic pathway (Scheme 1.5).³³ Some mechanistic and theoretical evidence showed this reaction involves a fulvenyl diradical intermediates. However, a formal ene reaction was used to explain the overall conversation when the substituent is an alkyl group at C^1 .^{34,35} Due to multiple bonding changes and the wide variation of substituents tolerated in the Schmittel cyclization, there may be a changeover from the stepwise to the

Scheme 1.5. Possible mechanism of the C^2-C^6 cyclization

concerted pathway. The considerations of both kinetic isotope effects and dynamic effects, even for complex reactions in solution, are necessary to understand the mechanism.

3. The synthetic methodologies for the preparation of benzannulated enyne-allenes

As mentioned in the introduction, the cyclization reactions of benzannulated enyne-allenes can be used to construct polycyclic ring systems. Several synthetic methods were developed to prepare benzannulated enyne-allenes with diverse structural features.

3.1. Prototropic rearrangement of alkynes

The 1,3-Prototropic rearrangement of alkynes is the most important isomerization reaction used for preparation of allenes. Depending on the substituted substrates of the alkyne, the reaction can provide a good yield when the migrating π -bond moves into conjugation with a neighboring alkene or arene. The prototype of this reaction leading to allene **1.26** and **1.28** has been described (Scheme 1.6).³⁶⁻³⁸ The isomerizations have also been successfully used in the synthesis of a series of 1,3-diarylallenes, which even tolerate other functional groups.

Scheme 1.6. 1,3-Prototropic rearrangement of alkynes to allenes

Recently, our research group reported a convenient pathway to prepare the benzannulated enyne-allene **1.33** in situ by a prototropic rearrangement of the

benzannulated enediyne **1.32** (Scheme 1.7).^{39,40} This method involves the condensation of **1.29** and the lithium acetylide **1.30**, followed by protonation to produce the propargylic alcohol **1.31**. Reduction of **1.31** with triethylsilane in the presence of trifluoroacetic acid provides the benzannulated enediyne **1.32**. 1,3-Prototropic rearrangement, promoted by potassium *tert*-butoxide in refluxing toluene at 110 °C, produces the benzannulated enyne–allene **1.33** in situ. It undergoes the cascade cyclization sequence via biradical **1.34**, derived from C²-C⁶cyclizaion, followed by a prototropic rearrangement to regain aromaticity to produce 5-aryl-11*H*-benzo[*b*] fluorenyl derivative **1.35** in excellent yield.

Scheme 1.7. Synthesis of benzannulated enyne-allene.

3.2. Palladium-catalyzed cross-coupling reactions

The palladium-catalyzed cross-coupling reactions have been developed and used for the construction of a wide range of simple and complex molecules. A series of preparations of substituted allenes were reported by cross coupling of allenes with suitable halogen or metal substituents at one of the sp²-hybridized carbons. Two examples are outlined in Scheme 1.8.

Scheme 1.8. Palladium catalyzed cross coupling reactions to benzannulated enyne-allene.

(a) *n*-BuLi, THF, -90°C, 10 min; ZnCl₂, -90°C to -20°C; (b) *n*-BuLi, THF, -90°C, 10 min; B(OCH₃)₃, -90°C to 0°C; Ag₂O, H₂O; (c) coupling of **1.37a**: Pd(PPh₃)₄ (5mol%), AsPh₃ (40mol%), THF, rt; (d) coupling of **1.37b**: Pd₂(dba)₃CHCl₃ (5mol%), AsPh₃ (40mol%), THF, rt; (e) 1,4-CHD, 70°C, 3h

Gillmann and his co-workers described an efficient Negishi coupling reaction between haloallene carboxylates **1.38** and arylzinc halide **1.37a**, generated from the corresponding aryl bromides **1.36**, which led to the construction of benzannulated enyne-allene ester **1.39**.⁴¹ Saalfrank's group reported a second method to prepare **1.39** by a Suzuki coupling of allenyl bromide **1.38** with boronic acid **1.37b**.⁴² When **1.39** was heated in the presence of 1,4-CHD at 70 °C for 3 h, 1*H*-cyclobut[*a*]indene **1.40** was produced by the Schmittel cyclization reaction.

3.3. Rearrangement of propargylic alcohol derivatives

One of the most useful methods for the asymmetric synthesis of allenes was the rearrangement of propargylic precursors from the corresponding propargylic alcohols. Treatment of the chiral propargylic alcohol **1.41** with thionyl bromide gave a 9:1 mixture of **1.43** and **1.44**.⁴³ A rearrangement reaction from **1.42** was proposed to be responsible for the formation of **1.43** (Scheme 1.9).

Scheme 1.9. Rearrangement of propargyl alcohol derivatives

Our group developed a new synthetic pathway to generate the chlorinated benzoenyne–allene system **1.48** in situ by the S_Ni' reaction of the corresponding benzannulated propargylic alcohol **1.46** with thionyl chloride (Scheme 1.10).^{39,44} The subsequent rapid cascade radical cyclization sequence leads to the chlorinated benzofluorenyl derivative **1.50**. The hydrolysis of **1.50**, on exposure to water/silica gel, furnishes alcohol **1.51** in 74% overall yield from **1.46**. A minor amount of **1.52**, derived from the intramolecular [2 + 2] cycloaddition reaction of **1.48**, is also produced in 12% yield.

Scheme 1.10. Treatment of a propargylic alcohol with thionyl chloride to form an enyne-allene.

Interestingly, the intramolecular [2 + 2] cycloaddition reaction of the chlorinated benzoenyne–allene intermediates occurred preferentially in certain cases to form 1*H*-cyclobut[*a*]indenes (Scheme 1.11). Condensation between benzannulated enediynes

Scheme 1.11. Intramolecular [2 + 2] cycloaddition reaction

(**1.30** or **1.53**) and pivalophenone (**1.29**) as reported previously furnished the corresponding benzannulated enediynyl propargylic alcohol **1.54**. Treatment of **1.54** with thionyl chloride gave the [2 + 2] cycloaddition adduct **1.56** predominately. The competition between [4 + 2] and [2 + 2] cycloaddition may be attributed to the emergence of the nonbonded steric interactions between the chloro substituent and the *tert*-butyl group.

Figure 1.2 Molecular structures of **1.56a** and **1.56b**.

Selected bond lengths (Å) and angles (deg): **1.56a** C(1)-C(2), 1.594(4); C(1)-C(11), 1.543(4); C(2)-C(3), 1.363(4); C(3)-C(11), 1.430(4); C(11)-C(1)-C(2), 81.7(2); C(1)-C(2)-C(3), 92.1(2);

C(2)-C(3)-C(11), 94.5(2); C(3)-C(11)-C(1) 91.7(2). **1.56b** C(9)-C(10), 1.619(5); C(10)-C(11), 1.563(5); C(8)-C(9), 1.356(6); C(8)-C(11), 1.458(5); C(11)-C(10)-C(9), 81.1(3); C(8)-C(9)-C(10), 92.8(3); C(9)-C(8)-C(11), 94.6(3); C(8)-C(11)-C(10), 91.4(3).

Single crystals of **1.56a** and **1.56b** were isolated by crystallization from a hexanes-ether mixture, from which the solid-state structure of the compounds were determined by X-ray diffraction (Figure 1.2). From the X-ray analysis of the four membered ring compounds obtained by the [2 + 2] cycloaddition reaction of the chlorinated benzoenyne-allene intermediates, it is apparent that one of the C(sp³)-C(sp²) bond distance in the cyclobutene ring of **1.56a** (1.594 Å) and **1.56b** (1.619 Å) is significantly longer than the 1.50 Å expected for a normal C(sp³)-C(sp²) single bond. The existence of the longer C-C bond most likely is due to the steric repulsion between the bulky substituents on the four member ring. Comparison of these two cyclobutene compounds, **1.56b** with a more bulky dibromide benzene substituent gave a longer C-C bond than **1.56a** with a benzene substituent on the four member ring. The longer C-C bond distance will result in lower bond dissociation energy.

The activation of carbon-carbon bonds for cleavage has long been an area of great interest to synthetic chemists. To facilitate selective C-C bond cleavage, the potential for the relief of ring strain in substrates has been employed as a driving force.^{45,46} Recently, we found that thermolysis of **1.56a** and **1.56b** at 150-210 °C in the high boiling point solvents led to a homolytic carbon-carbon bond cleavage in the cyclobutene ring (Scheme 1.12). Instead of undergoing ring-opening polymerization, the products resulting from the thermolysis of **1.56a** and **1.56b** were the more stable [4 + 2] adducts **1.59a** and **1.59b**, which furnished **1.57a** and **1.57b** after hydrolysis on exposure to water/silica gel. Both results may be explained by the formation of the diradical intermediates **1.58a** and **1.58b**, which are the reverse reactions of the [2 + 2] cycloaddition reactions. The corresponding **1.58b** underwent thermal homolytic C-C bond cleavage more readily, consistent with a higher degree of ring strain.

Scheme 1.12. Thermal opening of cyclobutene ring

4. Construction of novel polycyclic aromatic hydrocarbons via the Schmitt cyclization reactions of enyne-allenes

A new synthetic pathway was developed by our group to generate a $C_{44}H_{26}$ hydrocarbon **1.68** bearing a 44-carbon framework of C_{60} (Scheme 1.13).⁴⁴ The key steps in this route included two Schmitt cyclizations of chlorosubstituted benzanulated enyne-allenes. Condensation of mono-ketal **1.60** with lithium acetylide **1.30** followed by cyclization with thionyl chloride and reduction with sodium borohydride produced **1.63**.

Scheme 1.13. Synthesis of a 44-carbon framework of C_{60}

Hydrolysis of the ketal group in **1.63** led to **1.64** having a carbonyl group to allow a repeat of the condensation, cascade cyclization, and reduction sequence. In all, the polycyclic aromatic hydrocarbon **1.68** was synthesized in 8 steps with a 12.8% overall yield.

Several helical 4,5-diaryldiindenophenanthrenes have been prepared in our group (Scheme 1.14).^{40,47,48} The synthetic sequence started with the condensation of the *p*-dipivaloylbenzene **1.69** with 2 equiv of the lithium acetylide, derived from **1.30** and was followed by reduction of the resulting propargylic alcohol **1.70** to give the requisite benzannulated enediyne **1.71** for subsequent cascade cyclization reactions. Treatment of **1.71** with potassium *tert*-butoxide in refluxing toluene at 110 °C produced benzofluorene **1.72**. Interestingly, the final products have twisted aromatic frameworks because of the nonbonded steric interactions between the two substituents at the C4 and C5 positions, which cause them to bend away from the mean plane of the aromatic system.

Scheme 1.14. Synthesis of helical polycyclic aromatic hydrocarbon

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CHAPTER 2

Synthesis of 4,5-Diheteroarylphenanthrenes and Their Dinuclear Ru(II) Bis(2,2':6',2''-terpyridine) Complexes Possessing Severe Helical Twists

1. Synthesis and structure characterization of 4,5-diheteroaryl-phenanthrenes compounds that possess severe helical twists.

1.1. Introduction

The 4,5-disubstituted phenanthrenes are nonplanar and possess a helical twist.¹⁻⁴ The X-ray crystallographic structure of 4,5-dimethylphenanthrene (**2.1**) shows a 27.9° twist between the mean planes of the two outer benzene rings.² Such a structural distortion was caused by the nonbonded steric interactions between the two substituents at the C4 and C5 positions. Several synthetic methods for 4,5-dimethylphenanthrene and related compounds have been reported, including ozonolysis of pyrene,⁵ intramolecular cyclization of 2,2'-bis(halomethyl)-6,6'-dimethylbiphenyls,^{6,7} and photochemically induced dehydrocyclization of stilbenes.^{8,9} Photocyclization of 1-(8-phenyl-2-naphthyl)-4-phenyl-1-buten-3-yne was reported to produce 4,5-diphenylphenanthrenes in 65% yield.^{10,11} We recently reported a new synthetic pathway leading to the diindeno-fused 4,5-diarylphenanthrenes **2.2** (Ar = phenyl, 3,5-dimethylphenyl, or 4-biphenyl) via cascade cyclization reactions of the corresponding benzannulated enyne-allenes.³ The twist angle of the outer benzene rings (rings A and C) of the phenanthryl system in **2.2** (Ar = phenyl) is a more pronounced 46.1°. Our continued interest in nonplanar polycyclic aromatic compounds led us to apply this synthetic sequence to construct several

4,5-diheteroarylphenanthrene compounds. We now have used a modified and efficient pathway for the synthesis of 4,5-diheteroarylphenanthrenes **2.2a**, **2.2b**, and **2.2c** bearing pyridyl, 2,2'-bipyridyl, and 2,2':6',2''-terpyridyl substituents, respectively. The distorted structures of **2.2a** and **2.2c** were established by X-ray structure analyses. The presence of two units of pyridyl, bipyridyl, or terpyridyl substituents allows them to serve as potential building blocks for complex formation with transition metals to produce supramolecular systems.¹²⁻¹⁴

Figure 2.1 Structures of 4,5-disubstituted phenanthrenes

1.2. Results and discussion

Synthesis of 4,5-diheteroarylphenanthrenes possessing severe helical twists. The synthetic sequence outlined in Scheme 2.1 for **2.2a**, **2.2b**, and **2.2c** involved initial condensations between 2 equiv of the lithium acetylide derived from **2.3**¹⁵ and diketone **2.4**³ to give the corresponding propargylic alcohol **2.5** as an essentially 1:1 mixture of two diastereomers. Reduction of **2.5** with triethylsilane in the presence of trifluoroacetic acid furnished **2.6** also as an essentially 1:1 mixture of diastereomers. The subsequent Sonogashira reactions^{16,17} with 4-ethynylpyridine (**2.7a**)^{18,19} produced **2.8a**. The structures of the two diastereomers of **2.8a** were established by X-ray structure analyses. Similarly, **2.8b** and **2.8c** were synthesized by coupling with 5-ethynyl-2,2'-bipyridine (**2.7b**)^{20,21} and 4'-ethynyl-2,2':6',2''-terpyridine (**2.7c**)^{20,22-24} respectively. Treatment of

2.8a with potassium *tert*-butoxide in refluxing toluene produced 4,5-diheteroarylphenanthrene **2.2a** bearing a helical twist in a single operation. Presumably, the transformation from **2.8a** to **2.2a** proceeded through a cascade sequence of reactions involving two prototropic rearrangements to form the corresponding benzannulated enyne–allene units in **2.9**.³ The subsequent Schmitt cyclization reactions^{25,26} generate the corresponding biradicals followed by the intramolecular radical–radical couplings and two prototropic rearrangements to regain aromaticity then gave **2.2a** as reported previously.³ Because the relative reaction rates of the steps of the cascade sequence have not been determined, it is also possible that the first benzannulated enediyne unit in **2.8a** could undergo the cascade transformation before the second unit would begin its cyclization sequence. Similarly, **2.2b** and **2.2c** were obtained from **2.8b** and **2.8c**, respectively.

Scheme 2.1

The ^1H NMR spectrum of **2.2a** show a set of AB quartet signals at δ 4.42 and δ 4.20 ($J = 21.0$ Hz) from the diastereotopic methylene hydrogens on the five-membered rings, manifesting the presence of a helical twist (Figure 2.2). Such an AB pattern was also observed for **2.2b** and **2.2c**. Indeed, the X-ray crystallographic structures of **2.2a** and **2.2c** (Figure 2.3) reveal severe structural distortion due to nonbonded steric interactions between the two heteroaromatic substituents. The two heteroaromatic substituents are bent away from each other, causing a pronounced 45.1° helical twist between the mean planes of rings A and C of **2.2a** and a 55.8° twist of that of **2.2c**. As observed in the case of **2.2** (Ar = phenyl), the two heteroaromatic substituents are oriented in essentially twisted parallel positions, but are at a 55.8° angle from the mean plane of either ring A or C of **2.2a** and at a 47.0° angle from those of **2.2c**. The orientations of the heteroaromatic substituents also place several aromatic hydrogens in the magnetic shielding regions of the aromatic ring currents, causing significant upfield shifts. In the crystal structures, the perpendicular distance between the planes of the two heteroaromatic substituents is ca. $2.80 \text{ \AA}$ for **2.2a** and ca. $3.03 \text{ \AA}$ for **2.2c**, much shorter than the usual π system van der Waals contact distance of ca. $3.4 \text{ \AA}$ between parallel aromatic hydrocarbons in crystals¹⁰ and the graphite layer distance of $3.35 \text{ \AA}$.

Figure 2.2 ^1H NMR spectrum of the 4,5-di(4-pyridyl)phenanthrene **2.2a**

At 28 °C, the ^1H NMR spectrum of **2.2c** exhibits broad humps for the aromatic hydrogens on the terpyridyl substituents. At 60 °C, these signals are less broad and a singlet at δ 7.91 attributable to the four hydrogens at the 3' and 5' positions of the two central pyridyl rings could be clearly discerned. At -20 °C, multiple signals of the terpyridyl substituents start to appear. These observations suggest restricted rotations around the carbon-carbon single bonds connecting the terpyridyl substituents to the C4

Figure 2.3 ORTEP drawings of the crystal structures of **2.2a** and **2.2c**.

or the C5 position of the central phenanthryl system. Similarly, at 28 °C broad signals in the aromatic region attributable to the hydrogens on the bipyridyl substituents of **2.2b** were also observed. The rates of racemization of **2.2a–c** can be expected to be slow as observed previously for **2.2** (Ar = phenyl).³

The UV–vis absorption spectra of **2.2a**, **2.2b**, and **2.2c**, recorded in dichloromethane, show absorption bands in the near-UV region from ca. 235 to 305 nm and less intense bands in the visible region with maxima at ca. 405 nm (Figure 2.4). The dichloromethane solutions of **2.2a–c** show bright yellow color. Upon excitation at 360 nm, they exhibit blue emission with maxima at ca. 460 nm.

Figure 2.4 (a) UV-vis absorption spectra and (b) luminescence spectra of **2.2a** (black), **2.2b** (red), and **2.2c** (blue) in dichloromethane at room temperature.

2. Synthesis and structure analysis of dinuclear ruthenium(II) bis(terpyridine) complexes.

2.1. Introduction

Because metal-ligand coordination has been applied extensively in supramolecular chemistry, there is an increasing interest in developing chelating ligands and their

transition metal complexes.¹² For instance, 2,2',6',2''-terpyridine and its 4'-substituted derivatives are common ligands that can coordinate to many different transition metal ions and form metal complexes. The resultant metal complexes have linear or rod-like structures, which have potential applications in the fields of macromolecular chemistry, nanoscience, and photophysics.²⁷ A wide variety of ruthenium-terpyridine complexes have been reported, which exhibit interesting photophysical, photochemical, and electrochemical properties. Ruthenium-bis(terpyridine) complexes of the type $[\text{Ru}(\text{tpy})_2\text{X}_2]$ ($\text{X} = \text{e.g. Cl}^-, \text{ClO}_4^-, \text{PF}_6^-$) has been well-known for the strength of their metal-ligand bond, arising from the strong metal-ligand ($\text{d}-\pi^*$) back donation. Arrangement of the ligands around the ruthenium atom contributes to a distorted octahedral geometry of the formed bis(terpyridine) Ru complexes, determined by a single crystal X-ray structure analysis of $[\text{Ru}(\text{tpy})_2]$, shown in Figure 2.5.²⁸ Herein, two dinuclear ruthenium(II) bis(terpyridine) complexes of **2.2c** possessing severe helical twists were successfully synthesized.

Figure 2.5 X-ray crystal structure of $[\text{Ru}(\text{tpy})_2]$

2.2. Results and discussion

Synthesis of dinuclear ruthenium(II) bis(terpyridine) complexes The presence of two terpyridyl substituents in **2.2c** provides opportunities for the formation of dinuclear ruthenium(II) bis(terpyridine) complexes possessing helical twists. A reported procedure for the synthesis of Ru(II) bis(terpyridine) complexes¹¹ was adopted by first treating **2.2c**

with ruthenium trichloride to form the Ru(III) trichloride complex **2.10** (Scheme 2.2). Treatment of **2.10** with 4'-ethoxy-2,2':6',2''-terpyridine (**2.11**) or 4'-chloro-2,2':6',2''-terpyridine (**2.12**) followed by the addition of a large excess of NH_4PF_6 then formed the brown precipitates of $[(4'\text{-EtOtpy})\text{Ru}(\mathbf{2.2c})\text{Ru}(4'\text{-EtOtpy})](\text{PF}_6)_4$ (**2.13**) or $[(4'\text{-Cltpy})\text{Ru}(\mathbf{2.2c})\text{Ru}(4'\text{-Cltpy})](\text{PF}_6)_4$ (**2.14**), respectively. ^1H NMR studies of the CD_3CN solutions of the heteroleptic species **2.13** and **2.14** show the presence of minor amounts of the homoleptic species $[\text{Ru}(4'\text{-EtOtpy})_2](\text{PF}_6)_2$ and $[\text{Ru}(4'\text{-Cltpy})_2](\text{PF}_6)_2$, respectively, as observed previously in the synthesis of other heteroleptic ruthenium complexes.²⁹

Scheme 2.2

Because of the presence of an unpaired electron in the t_{2g} orbital of the low-spin d^5 Ru(III) ions, the ^1H NMR signals of **2.10** are broadened and shifted dramatically (Figure 2.6).^{30,31} Several signals are shifted upfield or downfield to very large extents. The signals

at δ -32.35 and -35.56 can be attributed to the hydrogens at the 6 and 6'' positions of the terpyridyl system, where they are closest to the paramagnetic Ru(III) ions. The presence of these two distinct signals also indicates a relatively slow rate of rotation on the NMR time scale around the carbon-carbon single bonds attaching the terpyridyl units to the C4 or the C5 position of the central phenanthryl system. The AB quartet signals of **2.10** appear at δ 7.75 ($J = 21.0$ Hz) and 4.83 ($J = 21.0$ Hz). For **2.13** without the presence of paramagnetic ruthenium ions, the AB quartet signals appear at δ 4.46 ($J = 21.6$ Hz) and 4.30 ($J = 21.6$ Hz). The ^1H NMR signals of the ethoxyl groups and the hydrogens on the diindeno-fused phenanthryl system are sharp with well-defined splitting patterns. Similarly, for **2.14** the AB quartet signals appear at δ 4.46 ($J = 21.6$ Hz) and 4.30 ($J = 21.6$ Hz). Again, due to slow rate of rotation around the carbon-carbon single bonds attaching the terpyridyl units to the C4 or the C5 position of the central phenanthryl system, the signals of the aromatic hydrogens on the terpyridyl groups of **2.13** and **2.14** are broad.

Figure 2.6 NMR spectra of **2.10**

Figure 2.7 UV-vis absorption spectra of **2.13** (black), **2.14** (red), and $[\text{Ru}(4'\text{-EtOtpy})_2](\text{PF}_6)_2$ (blue) in acetonitrile at room temperature.

The UV-vis absorption spectra of **2.13** and **2.14**, recorded in acetonitrile, show intense ligand-centered $\pi\text{-}\pi^*$ transition bands of the aromatic terpyridyl structures in the near-UV region (Figure 4).³² The less intense broad bands in the visible region, which is responsible for the deep red color, can be attributed to the spin-allowed metal-to-ligand charge-transfer (MLCT) transitions involving promotion of an electron from the metal t_{2g} orbital to a π^* antibonding orbital of the ligand with absorption maxima at ca. 495 to 505 nm. Compared to the parent $[\text{Ru}(\text{tpy})_2](\text{PF}_6)_2$ complex, which exhibits an absorption maximum at 474 nm, these MLCT bands undergo a red shift. Such a red shift is reminiscent of what was observed in the cases of $[\text{Ru}(4'\text{-EtOtpy})_2](\text{PF}_6)_2$ complex ($\lambda = 485$ nm) bearing electron donating ethoxyl groups, $[\text{Ru}(4'\text{-Cltpy})_2](\text{PF}_6)_2$ complex ($\lambda = 480$ nm) bearing chloro substituents, and $[\text{Ru}(4'\text{-Phtpy})_2](\text{PF}_6)_2$ complex ($\lambda = 487$ nm) bearing phenyl groups. Luminescence was not observed for **2.13** and **2.14** at room temperature.

3. Synthesis of pyridine, bipyridine, terpyridine ligands used in the helical twist compounds.

4-ethynylpyridine (**2.7a**)^{18,19}, 5-ethynyl-2,2'-bipyridine (**2.7b**)^{20,21}, 4'-ethynyl-2,2':6',2''-terpyridine (**2.7c**)^{20,22-24}, 4'-ethoxy-2,2':6',2''-terpyridine (**2.11**)²⁴ and 4'-chloro-2,2':6',2''-terpyridine (**2.12**)²⁴ were prepared according to the reported procedures. The synthetic procedures for these compounds were summarized in Scheme 2.3.

Scheme 2.3. Synthesis of bipyridine, terpyridine ligands.

4. Conclusions

Three 4,5-diheteroarylphenanthrenes **2.2a**, **2.2b**, and **2.2c** were synthesized via cascade cyclization reactions of the corresponding benzannulated enyne–allenes. The nonbonded steric interactions of the substituents at the C4 and C5 positions of the phenanthryl system cause severe helical twist of the structures. The structures of **2.2a** and **2.2c** were established by X-ray structure analyses, permitting direct measurements of the extent of the structural distortion. The presence of two terpyridyl units in **2.2c** allowed it to be used as a ligand for the synthesis of dinuclear ruthenium(II) bis(terpyridine) complexes possessing severe helical twists. The two ruthenium(II) bis(terpyridine) units are in close proximity to each other, making it possible for electronic interactions between the two heteroaromatic π systems.

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Chapter 3

Syntheses of 1,4-Naphthoquinone Methides via Acid-Catalyzed Cascade Cyclizations of the Benzannulated Enediynyl Alcohols

1. Introduction

Quinone methides (QMs) contain a cyclohexadiene core, to which a carbonyl group and a methylene unit are attached. In terms of structure, QMs are related to benzoquinones and quinone dimethides. However, QMs are highly polarized and quite reactive unlike benzoquinones because QMs have two different function groups. Many QMs are believed to be major intermediates in many different biochemical transformations. Significantly, QMs can serve as ultimate cytotoxins, contributing to the drug efficacy of antitumor drugs, antibiotics, and DNA alkylators.¹⁻³

1.1. Parent Quinone Methides

In the areas of chemistry and biology, parent *ortho* (**3.1**) and *para* (**3.2**) quinone methides (QMs) are the most often encountered isomers. *Meta*-QMs (**3.3**) are drawn as zwitterionic (**3.3a**) or biradical (**3.3b**) structures because they have non-Kekulé structures (Figure 3.1).⁴

Figure 3.1 The structures of parent quinone methides.

For simple QMs without substituents on the exocyclic methylene group, the QMs molecules are often too reactive to be isolated in pure form because polymerization occurs upon concentrating the dilute solutions.⁵ QMs belong to the antiaromatic Hückel pseudo $4n$ π -electron system. However, the reactivity of QMs can be directly measured at a low temperature with the aid of matrix isolation techniques.^{6,7}

1.2. Properties and Synthetic Applications of Quinone Methides

Both *ortho*- and *para*-quinone methides have zwitterionic resonance structures. Therefore, these molecules have both cationic and anionic centers and they can react with both nucleophiles and electrophiles (Scheme 3.1). When nucleophilics attack on a quinone methide, an aromatic phenol ring is usually generated. The quinone methide reactivity is enhanced by the aromatization of the ring. Additionally, rearomatization of the ring can occur when chroman derivatives are produced by formal [4+2] cycloaddition reactions of *ortho*-quinone methides with electron-rich dienenophiles.⁸

Scheme 3.1. Reactions of *ortho*- and *para*-quinone methides.

QMs have been reported to be important intermediates in a variety of chemical synthesis and biological processes. *o*-QMs have often been employed in intramolecular or intermolecular [4+2] cycloaddition, dimerization, and electrocyclization reactions (Scheme 3.2). For example, tanzanene **3.8** was prepared by a diastereoselective cycloaddition reaction between the exocyclic olefin of alloaromadendrene **3.7** and the

parent *o*-QM.⁹ Pettila reported that Margaspidin **3.11** could be prepared from C-alkylation of a phenol **3.9** with its corresponding *o*-QM **3.10**.¹⁰ A one-pot synthesis of precocene **3.18** was achieved through a chelation controlled regioselective addition of aldehyde **3.13** *ortho* to the hydroxyl group in phenol **3.12** and an electrocyclization of *Z* *o*-QM **3.17** which is in equilibrium with its *E* isomer **3.16**.¹¹ Moore proposed that the formation of an *o*-QM species in vivo upon bio-reductive activation accounted for the anticancer efficacy of several quinone nature products.¹²

Scheme 3.2. Synthetic application of *ortho*-quinone methid.

para-Quinone methides have also been used in synthetic chemistry. Generally, *p*-QMs are easily reduced to the corresponding *p*-alkyl phenols. Aromatization of *p*-QMs can occur by nucleophilic 1,6 addition.^{13,14} Angle reported that *p*-QMs could either undergo intramolecular cyclization to produce a variety of *p*-hydroxyphenyl- substituted ring systems or react with an alkene to give indanes through a formal [3+2] cycloaddition

(Scheme 3.3).¹⁵⁻¹⁷ In the biosynthesis, *p*-QMs are considered to be crucial intermediates and subsequent chemistry of lignin.¹⁸ Additionally, *p*-QMs were reported to have useful applications in a variety of areas, such as serving as cationic dyes and pH-sensitive indicators.¹⁹⁻²²

Scheme 3.3. Synthetic application of *para*-quinone methid.

1.3. Synthetic method used to generate quinone methides

Due to the wide applications of quinone methides as intermediates in organic synthesis, many different methods have been developed for their preparation. The synthetic methods include (a) tautomerization, (b) oxidation, (c) thermolysis, (d) photolysis, (e) acid promotion, (f) base facilitation and (g) the olefination of quinones.

Jurd firstly demonstrated that tautomerization of benzoquinone **3.25** to an *o*-QM could initiate a subsequent reaction (Scheme 3.4).^{23,24} Waters found that a combination of silver(I) oxide with **3.27** generated the *o*-QM **3.28** that underwent immediate self-condensation to form a spirodimer.²⁵ Many precursors have been selected in the generation of *o*-QM by thermolysis. For example, 1-azobenzofuran **3.29** was heated to expel N₂ and form an intermediate nitrene, which underwent further rearrangement to afford the nitrile *o*-QM **3.30**.²⁶ However, only the thermally unstable precursors of *o*-QMs

can be used in the thermal generation techniques. For the thermally stable QM precursors that possess poor leaving groups such as the hydroxy or alkoxy group, photochemical methods are employed. The best-studied photochemical *o*-QM precursors are *o*-hydroxybenzyl and ethers as depicted in **3.31**. These compounds could form the corresponding *o*-QM **3.32** easily at room temperature after photolysis at 254 nm.²⁷⁻²⁹

Scheme 3.4. Synthetic methods for *ortho*-quinone methid.

Because *para*-quinone methides are less polarized and more stable than their corresponding *o*-QMs, *p*-QMs are formed more readily than *o*-QMs. The most often used synthetic methods for *p*-QMs involved the preparation of triarylmethyl precursors for subsequent transformations. The synthesis of diphenylmethylene-substituted *p*-quinone (**3.34**) by the *O*-demethylation of methoxyphenyl trityl alcohol **3.33** under acidic condition or the photodehydration of *para*-hydroxytriphenylmethanol **3.35** was reported

Scheme 3.5. Synthetic methods for *para*-quinone methid.

many years ago.³⁰⁻³⁴ The use of the Wittig reaction for condensation with *p*-benzoquinones¹³ and 1,4-naphthoquinones³⁵ has also been reported (Scheme 3.5).

To stabilize the reactive π -electron system of *p*-QMs and then isolate the pure products, various experiment approaches have been proposed.³⁶⁻³⁸ Figure 3.2 shows the examples for the most successful approach, including (a) introduction of bulky *tert*-butyl substituents in the *ortho* positions to the carbonyl group (**3.39**); (b) replacement of exocyclic methylene hydrogen by an electron-donating group (**3.40**); (c) annelation of an aromatic π -electron system to the six membered quinonoid ring (**3.41**); (d) coordination of a metal to the exocyclic methylene group of simple *p*-QMs (**3.42**).

Figure 3.2 Structures of stabilized *p*-QMs.

2. Results and Discussion

2.1. The synthesis of 1,4-naphthoquinone methides

In our investigations of the cascade cyclization reactions of benzannulated enediynyl alcohols,³⁹ a serendipitous discovery led to the development of a new synthetic pathway to 1,4-naphthoquinone methides bearing two aryl substituents at the *exo*-cyclic methylene group under a mild acidic condition at room temperature.

Treatment of the benzannulated enediyne **3.42** with lithium diisopropylamide (LDA) to form the corresponding lithium acetylide followed by condensation with 1-indanone **3.45** produced the benzannulated enediynyl alcohol **3.46** after aqueous workup (Scheme 3.6). On exposure to trifluoroacetic acid at room temperature for 10 min, **3.46** was

smoothly transformed to 1,4-naphthoquinone methide **3.49** in 92% isolated yield. Similarly, **3.50** was obtained from **3.43** and **3.45**. However, no quinone methide **3.51** was formed from the corresponding **3.48**. Several other examples of using different combinations of benzannulated enediynes and aryl ketones to form 1,4-naphthoquinone methides are shown in Figure 3.3. The transformations from **3.53** to **3.54** and from **3.56** to **3.57** occurred within 20 min at room temperature. In the cases of **3.60** and **3.63**, the reaction mixtures were stirred at room temperature for 60 min. Unexpected, ketone **3.66** was formed under this reaction conditions. The transformation to 1,4-naphthoquinone methides by this method is particularly efficient for cyclic aromatic ketones bearing a methoxyl group at the position *para* to the keto group and involves an unusual two-carbon ring expansion. It is also worth noting that unlike other reported methods, this new synthetic pathway involves the formation of the *p*-quinone methide ring system from an acyclic precursor.

Scheme 3.6. Synthesis of 1,4-naphthoquinone methides.

Using the transformation from **3.46** to **3.49** as an example, a proposed reaction mechanism is outlined in Scheme 3.7. The acid-catalyzed transformation of the propargylic alcohol moiety in **3.46** through cationic intermediates **3.46a** and **3.46b** could produce the α,β -unsaturated ketone system in **3.46c**. A subsequent carbon–carbon bond formation between one of the acetylenic carbons and the β -carbon of the enone system to form a new six-membered ring could lead to **3.46d**. The carbocationic center in **3.46d** could be captured by an electron-rich π bond of the methoxyl-substituted benzene system

entry	ketones	alcohols	t[min]	QMs
1	3.52	3.53 , 94%	20	3.54 , 90%
2	3.55	3.56 , 95%	20	3.57 , 92%
3	3.58	3.59 , 92%	60	3.60 , 23%
4	3.61	3.62 , 98%	20	3.63 , 25%
5	3.64	3.65 , 95%	360	3.66 , 45%
6	3.67	3.68 , 90%	360	3.69 , 0%

Figure 3.3 The scope and limitation of the new synthetic pathway for QMs to form **3.46e** having a strained cyclobutenyl ring. A subsequent carbon–carbon bond cleavage with the relief of the ring strain could then lead to 1,4-naphthoquinone methide

3.49 with an unusual two-carbon ring expansion.

Scheme 3.7. Proposed mechanism from **3.46** to **3.49**.

The proposed reaction mechanism is supported by the observation that on exposure to trifluoroacetic acid, the benzannulated enediynyl alcohol **3.70** produced the α,β -unsaturated ketone **3.71** with the second acetylenic group being hydrated to form a keto group (Scheme 3.8). Apparently, in this case the rate of hydration of the second acetylenic group bearing a 4-methoxyphenyl substituent is faster than that of attacking the β -carbon of the enone system as shown in **3.46c**. The presence of a methoxyl group in **3.46** is crucial to the success of the reaction. Without the methoxyl group, a complex mixture of products was observed. Presumably, the presence of a *para*-methoxyl group in **3.46a** further stabilizes this carbocationic species and may also facilitate the capture of the carbocationic center in **3.46d**. In addition, without the α,α -dimethyl group in **3.46** simple dehydration occurred to form an indene derivative.

Scheme 3.8. The formation of ketone **3.71**.

2.2. The properties of 1,4-naphthoquinone methides

The X-ray crystal structures of **3.49** and **3.54** indicate that the phenyl substituents are oriented essentially perpendicular to the exocyclic carbon–carbon double bond of the *p*-quinone methide system (Figure 3.4). In the case of **3.54**, the eight-membered ring adopts a tub-like conformation, causing the benzene ring of the *p*-methoxyphenyl group also to orient essentially perpendicular to the exocyclic carbon–carbon double bond. For **3.49**, the ^1H NMR signals of the aliphatic *gem*-dimethyl and methylene hydrogens and the aromatic hydrogens on the phenyl substituent are broad at room temperature, indicating a relatively slow rate of ring inversion of the 7-membered ring and a slow rate of rotation of the phenyl substituent on the NMR time scales. At $-20\text{ }^\circ\text{C}$, however, two singlets from the *gem*-dimethyl group and a distinct AB coupling pattern of the methylene hydrogens could be clearly discerned. A similar dynamic NMR phenomenon was also observed for **3.54**. In addition, the tub-like conformation of the eight-membered ring in **3.54** causes one of the methyls of the *gem*-dimethyl group to be located in the magnetically shielding region of the *p*-methoxyphenyl group. As a result, its ^1H NMR signal exhibits a significant upfield shift, appearing at $\delta = 0.43$.

Figure 3. 4 ORTEP drawing of the crystal structure of **3.49** and **3.54**

The UV-vis absorption spectra of **3.49** and **3.54**, recorded in CH₃CN (5.0×10^{-5} M), reveal absorption bands in the visible region with maxima at 397 and 402 nm, respectively (Figure 3.5). This is similar to what was observed for the 1,4-naphthoquinone methide having two phenyl substituents on the *exo*-cyclic methylene group, which exhibits an absorption maximum at 400 nm.⁴ Bathochromic shifts were observed for **3.50** ($\lambda_{\text{max}} = 410$ nm) bearing an additional *p*-methoxyl substituent and **3.57** ($\lambda_{\text{max}} = 413$ nm) having an additional *o*-alkoxyl substituent. Fluorescence spectra of **3.49** and **3.50** were shown in Figure 3.6. On exposure of **3.49** to increasing concentration of sulfuric acid, an absorption band with maximum at 559 nm emerges with increasing intensity, which is attributable to the formation of the corresponding triarylmethyl cation (Figure 3.7).⁴⁰

Figure 3.5 UV-vis absorption spectra of **3.49**, **3.50**, **3.54**, and **3.57** (5.0×10^{-5} M) in CH₃CN.

Figure 3.6 Luminescence spectra of **3.49** and **3.50** (5.0×10^{-5} M) in CH₃CN.

Figure 3.7 UV-vis absorption spectra of **3.49** (5.0×10^{-5} M) in CH₃CN with varying H₂SO₄ concentration.

Figure 3.8 UV-vis absorption spectra of **3.49**, **3.50**, **3.54**, and **3.57** with acid..

Similar absorption bands were observed for **3.50** ($\lambda_{\text{max}} = 570 \text{ nm}$), **3.54** ($\lambda_{\text{max}} = 615 \text{ nm}$), and **3.57** ($\lambda_{\text{max}} = 609 \text{ nm}$) on exposure to sulfuric acid with pronounced bathochromic shifts for the cases of **3.54** and **3.57** bearing an eight-membered ring (Figure 3.8). As a result, the color of the solution turns red in the cases of **3.49** and **3.50** and turns green in the cases of **3.54** and **3.57**.

2.3. The synthesis of requisite fragments

Ketones **3.80** and **3.85** were prepared according to the reported procedures. The synthetic procedures for benzannulated enediyne **3.43** and **3.44**, ketone **3.82** and **3.86** were summarized in Scheme 3.9.

Scheme 3.9. synthesis of benzannulated enediynes and ketones

3. Conclusion

In conclusion, a new acid-catalyzed cascade cyclization pathway to transform benzannulated enediynyl alcohols to 1,4-naphthoquinone methides was discovered. For cyclic alcohols, the transformation involved an unusual two-carbon ring expansion. In addition, the *p*-quinone methide ring system was constructed from an acyclic precursor. Compared to the Schmittel cyclization reaction of the enyne–allene systems, derived from benzannulated enediynyl alcohols, leading to benzofluorenyl systems via biradical intermediates, the current process proceeds through cationic intermediates, leading to 1,4-naphthoquinone methides.

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CHAPTER 4

Synthesis of bowl-shaped fullerene fragments with curved surfaces: Buckybowls

1. Introduction

Research in carbon cages has attracted considerable attention in the field of physics, chemistry, and material science since the discovery of the spherical fullerenes and carbon nanotubes (a new form of element carbon).¹ Fullerenes are cage-like, extremely stable forms of carbon (Figure 4.1). Buckminsterfullerene (or buckyball) have a molecular formula of C_{60} . The three dimensional structure of buckyball consists of twenty six-membered aromatic rings surrounding twelve five-membered rings. Robert Curl, Harold Kroto, and Richard Smalley won the 1996 Nobel Prize in Chemistry for discovering the first fullerene in 1985.² In 1991, Iijima Sumio of Japan introduced the elongated cousins of buckyballs, carbon nanotubes.³ Carbon nanotubes have three dimensional structures like cylinders and each cylinder wall consists of a sheet of

Figure 4.1 Model of fullerenes

hexagonal rings arranged by the carbon atoms. The structures of cylinders usually have closed-off ends, ranging from 2 to 10 micrometers in length and from 5 to 40 nanometers in diameter. Generally, the ends of carbon nanotubes were capped by fullerene substructure with the existence of pentagonal rings (necessary for closure of the tubes).

Interesting electronic and magnetic behaviors have been observed for buckyballs and carbon nanotubes. These properties allow them to find useful application in structural materials and medicine. The presence of multiple aromatic rings and the superaromaticity might account for their unusual electronic and magnetic properties.⁴

Inspired by the discovery and applications of fullerenes, bowl-shaped polyaromatic hydrocarbons (PAHs) with molecular networks that can be mapped on the surface of buckyball (C_{60}) are now also considered to be a group of important materials in the science of nonplanar π -conjugated carbon systems (Figure 4.2).⁵⁻⁷ These open geodesic polyarenes have commonly been referred to as “fullerene fragments” or “buckybowls”. In the past 20 years, synthesis, structural characterization, and properties of buckybowls, such as corannulene (**4.1**), sumanene (**4.2**), and tetrabenzopyracylene (**4.3**), have been actively investigated. All of them are characterized by both concave and convex π -surfaces as well as by a high degree of strain energy resulting from the pyramidalization of interior trigonal carbon atoms. Corannulene and sumanene possess

Figure 4.2 Bowl-shaped polycyclic aromatic hydrocarbons.

five- and three-fold symmetry, respectively representing the fundamental structure motifs of buckminsterfullerene.

The synthesis and study of buckybowls are of interest for several reasons. First, appropriate buckybowls can serve as potential substrate for the total synthesis of fullerenes and nanotubes.⁸⁻¹¹ Second, studies of *exo* vs. *endo* preferences of reactivity including metal complex formation can be performed on accessible convex and concave faces of buckybowls.¹²⁻¹⁹ Third, possessing curved carbon surfaces, buckybowls could be used as scaffolds for molecular systems host/guest chemistry. Fourth, buckybowls could be used as model compounds of fullerenes as well as possible synthetic intermediates for artificially designed fullerene derivatives.²⁰

2. Literature survey for the synthesis of buckybowls

Since curved buckybowls have strain energy caused by pyramidalization of interior sp^2 -hybridized carbon atoms, a successful method for buckybowls synthesis must be able to overcome the high degree of the strain energy.²¹ Only limited approaches can be utilized for buckybowl synthesis. Until now, most of the strained fullerene fragments have been successfully synthesized using flash vacuum pyrolysis (FVP) of appropriate precursors at high temperature.^{7,22} In solution phase, the bulkybowls were prepared by constructing the complete bowl-shaped carbon framework with multiple tetrahedral sp^3 -hybridized carbons as the precursor, followed by dehydrogenating the bowl precursors in the last step.^{5,23} Recently, the transition metal catalyzed intramolecular coupling of aryl, benzyl, or benzyldiene halides has been applied to synthesize the curved buckybowls.²⁴

2.1. Synthesis of buckybowls in solution chemistry

In 1966, Barth and Lawton reported the first total synthesis of corannulene from

acenaphthene (**4.8**) in 17 steps (Scheme 4.1).^{25,26} They constructed the three-dimensional framework **4.10** using tetrahedral sp^3 carbons and subsequent aromatization to synthesize the target compound. Not surprisingly, additional studies of corannulene were stopped in the 1970s because of the length of the synthesis and quite low overall yield (< 1%). Until the discovery of C_{60} at 1985, corannulene was known as the only bowl-shaped polynuclear aromatic hydrocarbon.²⁷

Scheme 4.1. Synthesis of corannulene by Bath and Lawton

Several synthetic groups attempted to synthesize corannulene using alternative synthetic routes, in which fluoranthene derivatives were served as potential starting materials.^{28,29} However, all of these attempts failed until Siegel reported a successful solution synthesis of methylcorannulene **4.13** from tetrabromide **4.11** in 1996 (Scheme 4.2).³⁰ The ring closures of **4.11** were completed by low-valent titanium coupling, and then dehydrogenation were achieved by DDQ oxidation.

Scheme 4.2. Synthesis of methylcorannulene by Siegel.

In 1999, a methodology similar to Siegel's approach was employed by Rabideau's group. They discovered that the employment of dibromomethyl groups in **4.15** and the low-valent vanadium coupling led to a single step formation of corannulene in an impressive yield of 70-75% (Scheme 4.3).³¹

Scheme 4.3. Synthesis of corannulene by Rabideau

Later, Rabideau's group further improved their synthesis using an alternative method to prepare 1,2,5,6-tetrabromocorannulene **4.17** and a 83% yield was achieved (Scheme 4.4).³² The approach is simpler and less expensive compared to the low-valent metal methods. The parent corannulene can be prepared by debromination of **4.17** under refluxing with KI and Zn powder in EtOH. In addition, corannulene derivatives can be obtained from the compound **4.17** by standard coupling procedures.^{33,34}

Scheme 4.4. Improved synthesis of corannulene.

Sumanene, the C_{3v} symmetric subunit of fullerene, was recognized as a potential synthon for the synthesis of fullerene fragment some time ago.³⁵ Recently, Hirao's research group successfully synthesized this compound (Scheme 4.5).³⁶ In their synthesis, the Ru-catalyzed tandem ring-opening and ring-closing metathesis reaction of syn-benzotris(norbornadiene) **4.19a** leading to hexahydrosumanene **4.20** were the key steps. The required π -conjugated structure of sumanene was achieved by DDQ oxidative aromatization of **4.20** at the last step. Variable-temperature NMR revealed a higher inversion energy barrier of sumanene (19.6 kcal/mol) than corannulene. This result indicates that sumanene is much more rigid than corannulene and the bowl to bowl inversion of sumanene is slower than corannulene at room temperature.

Scheme 4.5. Synthesis of Sumanene by ROM and RCM.

A similar stepwise conversion synthetic rout for sumanene was utilized to synthesize a C_3 symmetric chiral buckybowl **4.22** from chiral halonorbornene derivative (1*S*,4*S*)-**4.21**.³⁷ The final stage of the synthesis was the aromatization step, where the sp^3 chirality of the bowl-shaped intermediate **4.22** was converted to the bowl chirality of **4.23** (Scheme 4.6).

Scheme 4.6. Synthesis of chiral buckybowl

Since 2000, a few strained bowl-shaped polycyclic aromatic hydrocarbons have been synthesized by palladium-catalyzed intramolecular arylation reactions from relatively simple PAH derivatives (Scheme 4.7). The first successful attempt was achieved by Scott research group in their synthesis of dibenzo[*a,g*]corannulene **4.25**.³⁸ In their research, various palladium catalysts, bases, and reaction conditions were tested to optimize conditions. Later, synthesis of buckybowl **4.27** and **4.29** were completed by two other research groups.^{24,39} More recently, this method has also successfully employed in the preparation of several indeno-fused corannulenes, including pentaindenocorannulene

4.31.^{40,41}

Scheme 4.7. Synthesis of buckybowl by palladium coupling reaction.

2.2. Synthesis of buckybowl by flash vacuum pyrolysis

In 1977, Brown reported that vinylidene **4.33**, which was generated thermally from terminal acetylenes **4.32** in gas phase, could be trapped intramolecularly, thereby constructing both five- and six-membered rings (Scheme 4.8).⁴²

Scheme 4.8 Cyclization of terminal acetylene under FVP condition

Inspired by Brown's work, Scott's group successfully synthesized corannulene by flash vacuum pyrolysis of diethynylfluoranthene **4.37** which was prepared in six steps from acenaphthenquinone **4.34**.⁴³ Two more rings were formed under FVP condition from two vinylidene moieties, trapped by insertion into nearby C-H bonds. Corannulene was also synthesized by another improved three-step route, in which commercially available chemicals were used as starting materials and a 35-40% overall yield was achieved in the final FVP step.⁴⁴ In the improved method, the bis(1-chlorovinyl) fluoranthene **4.38** could be easily sublimed cleanly without polymerization because it is more stable than **4.37** at elevated temperatures. **4.38** loses 2 mol of HCl in the hot zone to generate **4.37** in situ, which then cyclizes twice (Scheme 4.9).

Scheme 4.9. Synthesis of corannulene via FVP condition.

The success of FVP is attributed to two reasons: (1) in pyrolysis, enough thermal energy can be delivered to the molecules to overcome the high energy barriers during intramolecular ring closures; (2) competing intermolecular reactions are avoided by performing the reaction in gas phase.

Since the major breakthrough for the synthesis of corannulene by FVP,⁴⁵⁻⁴⁹ several research groups have reported many other FVP based procedures leading to buckybowl from various precursors (Scheme 4.10).⁵⁰⁻⁵³ The culminating achievement was the use of FVP of $C_{60}H_{27}Cl_3$ reported by Scott, de Meijere and coworkers to produce C_{60} with an

estimated yield of 0.1-1.0%.⁵⁴ This work also proved that fullerene could be formed by rational synthetic methods instead of by empirical experiments.

Scheme 4.10 Various buckybowls prepared by FVP.

Although a number of curved molecules have been synthesized by FVP, the FVP method is problematic due to the following limitations: (1) minimum functional group tolerance arising from high temperature applied in FVP, (2) the yield drops dramatically with the increase of the size for buckbowls, (3) scale-up is difficult since FVP is a gas-phase process, and (4) the potential for thermal rearrangement of molecular framework at the high temperatures normally employed (1000-1100°C).²⁴

3. Research objective

Our group has reported a simple and efficient pathway recently to synthesize bowl-shaped polycyclic aromatic hydrocarbons via palladium-catalyzed intramolecular

arylation reactions.⁵⁵ This synthetic sequence was outlined in Scheme 4.11, involving cascade cyclization reactions of a benzannulated enyne-allene **4.48** formed from the corresponding benzannulated enediyne **4.47**. The presence of two properly situated bromo substituents in **4.49** allowed the application of the palladium-catalyzed intramolecular arylation reactions for additional carbon-carbon bond formation. Similarly, dibromides **4.52**, readily prepared by the condensation between aryl ketones **4.51** and **4.45**, were used to synthesize the corresponding bowl-shaped PAH **4.53**. X-ray structural analysis of **4.50** and **4.53** indicates the presence of significant curvatures in their structures (Figure 4.3)

Scheme 4.11 Synthesis of bowl-shaped polycyclic aromatic hydrocarbons via palladium-catalyzed intramolecular arylation reactions.

Figure 4.3 ORTEP drawing of the crystal structure of **4.53**.

We were interested in further exploring the use of similar strategy to prepare a new bowl-shaped π -conjugated hydrocarbon **4.54** which has a carbon framework represented on the surface of C_{60} (Figure 4.4). It is worth noting that the structure of buckybowl **4.54** contains an additional five-membered ring compared to tetrabenzopyracylene (**4.3**). By comparison with sumanene (**4.2**), the structure of **4.54** has two additional fused benzene rings.

Figure 4.4 MM2-optimized structure of **4.54**

Based on the geometry obtained from the X-ray analysis, one of the central ethylene carbon atoms in **4.53** has a pyramidalization angle of 10.3° , defined as $\Theta_{\sigma\pi} - 90^\circ$ using the π -orbital axis vector analysis (POAV), which is larger than those of tetrabenzopyracylene (**4.3**). Apparently, the presence of an additional five-membered ring in **4.53** causes its structure to be more strained and creates a more pronounced curvature (Figure 4.5).

Figure 4.5 POAV angles of fullerene and buckybowls.

Compared to **4.53**, we can predict that the buckybowl **4.54** will exhibit a larger local curvature because one more fused benzene ring is involved in its carbon framework. This deeper π -bowl will have some advantages over corannulene and sumanene, including the properties more similar to fullerenes and the presence of a benzylic position that should permit further functionalization to make new bowl-shaped species or dimerization to create a large buckybowl **4.56** having 54 carbons (90 % of C_{60}).

Figure 4. 6 Proposed application of buckybowl **4.54**.

4. Result and Discussion

4.1. Retrosynthetic Analysis for Buckybowl **4.54**.

In our retrosynthetic analysis, buckybowl **4.54** can be synthesized from the precursor dibromide hydrocarbon **4.62**. The two broken carbon-carbon bond in the northwestern corner in **4.54** could be constructed by palladium-catalyzed intramolecular arylation reactions of **4.62**. Further analysis showed the benzene ring in the southeastern corner of **4.54** could be formed from alkyl iodide **4.61** via an intramolecular alkylation reaction followed by aromatization. Alkyl iodide **4.61** could be obtained from deprotection of methyl ether **4.60** followed by iodination. The methyl ether **4.60** could be produced from propargylic alcohol **4.59** via reduction and cascade Schmitt cyclization. Propargylic alcohol **4.59** could be synthesized from condensation of lithium acetylide **4.58** and the α,α -disubstituted indanone **4.57** (Figure 4.7).

15% yield of the monoalkylation product was achieved when LDA was displaced by sodium hydride.

Scheme 4.13

To increase the yield, an alternative approach (Scheme 4.14) was used for preparing **4.71**. In this approach, 1-indanone was converted to the corresponding TMS silyl enol ethers **4.69** and alkylated with methyl iodide under mild conditions in the presence of cesium fluoride. In addition to **4.70**, the rest of the product mixture consisted of dimethylated material (5-10%) and hydrolyzed starting material. Subsequently, the alkylated indanone **4.70** was alkylated by refluxing with NaH and 1-iodo-2-methoxyethane (**4.65**). A 68% yield was achieved in the second alkylation to produce disubstituted indanone **4.71**.

Scheme 4.14

With the alkylation product in hand, condensation of **4.71** and lithium acetylide **4.72**, obtained by lithiation of 1-(2-ethynylphenyl)-2-phenylethyne, afforded enediynyl propargylic alcohol **4.73** as a 1:1 diastereomeric pairs (Scheme 4.15). Reduction of **4.73** with triethylsilane in the presence of trifluoroacetic acid then produced **4.74**. On exposure to potassium *tert*-butoxide in refluxing toluene for 6 h, a sequence of cascade reactions occurred, including an initial prototropic rearrangement to form the benzannulated enyne-allene **4.75**. A subsequent Schmitt cyclization reaction to generate biradical followed by an intramolecular radical-radical coupling and a prototropic

Scheme 4.15

rearrangement to regain aromaticity then led to **4.76**. Cleavage of the methyl ether in **4.76** with Me_3SiI produced iodide **4.77**.^{57,58} In the presence of potassium *tert*-butoxide, **4.77** was smoothly converted to the desired hydrocarbon **4.78** in THF at 40 °C by an intramolecular alkylation reaction. The structure of **4.78** was confirmed by ^1H and ^{13}C NMR spectroscopy. The stereochemistry of **4.78** was confirmed by NOESY experiments (Figure 4.7).

Figure 4. 8 MM2-optimized structure and NOE of **4.78**.

Encouraged by the success in obtaining **4.53** and **4.78**, we slightly modified the synthetic Scheme 4.15 to allow for the incorporation of the bromo substituents to give **4.86** (Scheme 4.16). The requisite (2,6-dibromophenyl)ethyne (**4.79**) was prepared by the Sonogashira coupling reaction between 1,3-dibromo-2-iodobenzene and (trimethylsilyl)-

Scheme 4.16

ethyne, followed by desilylation as reported previously.⁵⁹ A second Sonogashira reaction between **4.79** and 1-(2-iodophenyl)-2-(trimethylsilyl)ethyne (**4.80**) then led to **4.81**, which was readily desilylated to afford the benzannulated enediyne **4.58**.

It is worth noting that compared to **4.53** the subsequent Pd-catalyzed intramolecular arylation reactions were more efficient in producing **4.87** in 30% yield (Scheme 4.17). Simultaneously, the monocyclized adducts **4.88** and **4.89** were also produced in 3% and 28% yields, respectively. Compared to **4.53**, the benzofluorene substructure **4.86** is already strained and contains a significant curvature. Apparently, the strain in **4.86** is responsible for the higher efficiency. The strategy of using existing strain in the precursor to promote carbon-carbon bond formation was employed previously to prepare strained compounds.⁶⁰ Unfortunately, attempts for final fully aromatization step to buckybowl **4.54** were unsuccessful by using DDQ for oxidation.

Scheme 4.17

4.3. Second Approach

In the second synthetic strategy, the methyl group was displaced with a group that could be removed for the final aromatization step. It was hypothesized that hydrocarbon **4.90** could undergo retro-ene reaction under high temperature, and form buckybowl **4.54** (Scheme 4.18). To proceed with this proposed route, substituted indanone **4.93** was prepared by allylation and alkylation.

Scheme 4.18

With ketone **4.93** in hand, the synthetic sequence outlined in Scheme 4.19 was adopted for the preparation of hydrocarbon **4.90**. From the ketone **4.93**, the propargylic alcohol **4.94** was reduced to form **4.95**, which in turn were converted to **4.96** by a cascade cyclization sequence. It is worth mentioning that the cleavage of the methyl ether in **4.96**

with Me₃SiI is unsuccessful without the 2,6-bis(1,1-dimethylethyl)-4-methyl -pyridine. An intramolecular cyclization reaction led to the major product **4.97**. The structure of **4.97** was confirmed by X-ray analysis. The observed reaction is most likely due to the presence of catalytic amounts of HI in trimethylsilyl iodide. However, alcohol **4.98** was obtained when 2,6-bis(1,1-dimethylethyl)-4-methyl- pyridine was added to the reaction mixture, which trapped the trace amount of HI.

Scheme 4.19

Iodide **4.100** can be conveniently synthesized in two steps from alcohol **4.98** (Scheme 4.20). In the presence of potassium *tert*-butoxide and iodine, iodide **4.100** was transformed into alkene **4.101**. Apparently, an intramolecular cyclization of **4.100** occurred initially. The carbon-carbone double bond then was formed by producing the benzofluorenyl anion followed by iodination and dehydroiodination.

The retro-ene reaction of **4.101** was performed under high temperature. Unfortunately, this reaction was unsuccessful and ¹H NMR spectrum of the crude reaction mixture showed broad peaks in the aromatic region.

Scheme 4.20

4.4. Third Approach

Our third synthetic route to prepare buckybowl **4.54** relied on a similar strategy, except that we decided to displace the methyl group with a proton. However, the alkylation reaction in Scheme 4.13 did not afford monoalkylation product **4.67** in high yield. In an effort to improve the poor yield in this initial route, we investigated the possibility of forming ketone **4.67** from hydrazone **4.103** (Scheme 4.21). 1-Indanone was converted into its hydrazone derivative **4.103** in quantitative yield by treatment with *N,N*-dimethylhydrazine in the presence of a catalytic amount of acetic acid.^{61,62} Alkylation with LDA and 1-iodo-2-methoxyethane (**4.65**) gave product **4.67** in a 61% yield.

Scheme 4.21

Due to the possibility of producing the dehydration product during the reduction of propargylic alcohol, an alternative route was undertaken (Scheme 4.22). The Wittig olefination of **4.67** afforded **4.104** as a mixture of the *E* and *Z* isomers,⁶³

p-Toluenesulfonic acid was used to hydrolyze the enol ether **4.104**, thus providing indane aldehyde **4.105** in good yield.⁶⁴ Acetylene **4.106** was prepared by condensation between **4.105** and the Ohira-Bestmann reagent, which was synthesized in two steps.⁶⁵ Bezannulated enediyne **4.107** was accessed through the Sonogashira coupling reaction between acetylene **4.106** and 1,3-dibromo-2-[(2-iodophenyl)ethynyl]benzene. However, when **4.107** was treated with potassium *tert*-butoxide at 80 °C, only 10% of the Schmittel cyclization product **4.108** was obtained as a minor product along with many other unexpected byproducts. The synthetic route was not further investigated because of the low yield in the cyclization step.

Scheme 4.22

4.4. Fourth Approach

With the failure of the previous three routes for the synthesis of buckybowl **4.54**, we quickly switched to an alternative approach by starting from ketone **4.123**. After literature survey, the synthesis of ketone **4.123** could be achieved from the acid catalyzed ring expansion of allenylcyclobutanbenzen-1-ol **4.118** by a Wagner-Meerwein shift (Scheme 4.24).⁶⁶⁻⁶⁹ To proceed with this planned route, benzocyclobutenone **4.113** and allene **4.117** were prepared from commercial available starting materials based on the reported procedures (Scheme 4.23).^{70,71}

Scheme 4.23

It is important to note that allene **4.117** is thermally very unstable and prone to decomposition. This compound decomposed within a matter of hours when refrigerated, results in decomposition. It must be used as soon as it is prepared. The subsequent condensation between benzocyclobutenone **4.113** and allene **4.117** was investigated at -78°C . 1-lithio-1-benzyloxyallene was added to benzocyclobutenone to give **4.118** as an intermediate. It is interesting to note that allenyl adduct **4.118** on treatment with trifluoroacetic acid and water at lower or room temperature can provide two totally different products. The production of compound **4.121** is due to the [4+2] cycloaddition of allene-diene **4.119**,⁷² which was obtained by the benzocyclobutene ring opening at room temperature.

Scheme 4.24

The hydrolysis-ring-expansion reaction of **4.118** was performed under -78°C with acid and water, and led to 2-hydroxy-2-vinyl-2,3-dihydro-1*H*-inden-1-one (**4.122**) in good isolated yield (92%).

With the hydroxyketone **4.122** in hand, our next step was to convert **4.122** into its methyl ether **4.123** by treatment of **4.122** with NaH and iodomethane (Scheme 4.25). Condensation between **4.123** and lithium acetylide **4.72** afforded enediynyl propargylic alcohol **4.124** as a single diastereoisomer. However, the following Schmitt cyclization with thionyl chloride was unsuccessful. Alternatively, attempts were made to reduce the propargylic alcohol **4.124** initially to benzannulated enndiyne **4.126**. However, the next cyclization triggered by potassium *tert*-butoxide also failed because the methoxy group could serve as a leaving group in this reaction.

Scheme 4.25

In an attempt to form the Schmitt cyclization product, an alternative synthetic pathway outlined in Scheme 4.26 was pursued. Condensation of ketone **4.123** and lithium trimethylsilylacetylide produced propargylic alcohol **4.128**. Deprotection of trimethylsilyl acetylene was achieved by using a catalytic amount of silver triflate under mild conditions, and afforded **4.129** in a good yield.⁷³ Treatment of **4.129** with thionyl bromide produced allenic bromide **4.130** as a diastereomeric pairs.⁷⁴ In the next step, we tried to make the benzannulated enyne-allene **4.133** with a palladium-catalyzed coupling reaction between **4.130** and arylzinc chloride **4.132**.⁷⁵ Interestingly, instead of lithium iodine exchange in compound **4.131**, lithium bromine exchange occurred at low temperature. Thus, the palladium-coupling reaction between **4.130** and arylzinc chloride **4.135** led to

the benzannulated enyne-allene **4.136**, which was transformed to the corresponding cyclization product **4.137** through the Schmitt cyclization reaction. The ^1H NMR showed that compound **4.137** exists as two atropisomers due to the slow rate of rotation of the iodophenyl substitute in **4.137** on the NMR time scale. All attempts to avoid the lithium bromine exchange were unsuccessful. Based on the unexpected results, this synthetic pathway was not investigated further after the hydroboration step.

Scheme 4.26

5. Conclusions

A bowl-shaped polycyclic aromatic hydrocarbon **4.87**, bearing a framework of sumanene, was successfully synthesized from a polycyclic aromatic dibromide. This simple and efficient pathway employed the Schmitt cyclization reaction and palladium-catalyzed intramolecular arylation reactions as key steps. This overall synthetic strategy

has found success in producing curved hydrocarbons. Several attempts were made to synthesize the precursor of buckybowl **4.54** by using different combination of benzoenediynes and substituted indanones. Further exploration is required to overcome difficulties encountered toward the synthesis of buckybowl **4.54**.

6. References

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Chapter 5

Experiment Section

General Experimental Methods. All reactions were conducted in oven-dried (120 °C) glassware under a nitrogen atmosphere. Diethyl ether and tetrahydrofuran (THF) were distilled from benzophenone ketyl prior to use. Commercially available chemicals were of reagent grade and were used as received without further purification. Purification by column chromatography was performed using 32-63 μm silica gel. Melting points were uncorrected. High resolution mass spectra were obtained on a hybrid linear ion trap Fourier transform mass spectrometer system equipped with an ion source. UV-vis spectra of 2.5×10^{-5} M solutions of **2.2a–c** in dichloromethane and 1.0×10^{-5} M solutions of **2.13**, **2.14**, and $[\text{Ru}(4'\text{-EtOtpy})_2](\text{PF}_6)_2$ in acetonitrile were recorded at room temperature. Emission spectra of 1.0×10^{-7} M solutions of **2.2a–c** in dichloromethane were recorded at room temperature upon excitation at 360 nm. UV-vis spectra of 5.0×10^{-5} M solutions of **3.49**, **3.50**, **3.54**, and **3.57** in acetonitrile were recorded at room temperature. Spectrophotometer cells with an optical path length of 10 mm were used in recording UV-vis spectra. Emission spectra of 5.0×10^{-5} M solutions of **3.49** and **3.50** in acetonitrile were recorded at room temperature upon excitation at 350 and 400 nm, respectively.

Propargylic Alcohol 2.5. To 6.00 g (26.3 mmol) of 1-ethynyl-2-iodobenzene (**2.3**) in 50 mL of THF under a nitrogen atmosphere at 0 °C was added 23.3 mL of a 1.2 M solution of LDA (28.0 mmol) in hexanes. After 30 min of stirring, a solution of 3.23 g of diketone **2.4** (13.1 mmol) in 40 mL of THF was introduced via cannula, and the reaction mixture was allowed to warm to room temperature. After an additional 2 h, 50 mL of water was introduced, and the reaction mixture was extracted with diethyl ether. The combined organic extracts were washed with brine and water, dried over sodium sulfate, and concentrated. The residue was purified by flash column chromatography (silica gel/20% THF in hexanes, R_f = 0.33) to produce 8.73 g (12.5 mmol, 95%, 1:1 mixture of the *meso* and *rac* isomers) of **2.5** as a white solid: mp 227–228 °C; IR 3559, 757 cm^{-1} ; ^1H NMR (mixture of the *meso* and *rac* isomers, CDCl_3 , 600 MHz) δ 7.85 (2 H, dd, J = 7.8, 1.2 Hz), 7.71 (4 H, s), 7.48 (2 H, dd, J = 7.8, 1.2 Hz), 7.30 (2 H, td, J = 7.5, 1.2 Hz), 7.01 (2 H, td, J = 8.1, 1.8 Hz), 2.45 (2 H, br), 1.12 (18 H, s); ^{13}C NMR (mixture of the *meso* and *rac* isomers, CDCl_3 , 150 MHz) δ 141.0, 138.8, 133.2, 129.52, 129.49, 127.7, 126.7, 100.4, 96.1, 87.6, 79.5, 40.0, 25.7; HRMS m/z calcd for $\text{C}_{32}\text{H}_{32}\text{I}_2\text{O}_2\text{Na}$ (MNa^+) 725.0384, found 725.0385.

Diiodide 2.6. To a mixture of **2.5** (8.4 g, 11.96 mmol) and triethylsilane (4.17 g, 35.9 mmol) in 200 mL of dichloromethane was added 1.09 g of trifluoroacetic acid (95.6 mmol). After 1 h of stirring at room temperature, 5.1 g (48.1 mmol) of sodium carbonate was added followed by 50 mL of water. The organic layer was separated, washed with brine and water, dried over sodium sulfate, and evaporated under reduced pressure. The residue was purified by flash column chromatography (silica gel/10% diethyl ether in hexanes, R_f = 0.57) to provide 7.69 g (11.5 mmol, 96%, 1:1 mixture of the *meso* and *rac* isomers) of **2.6** as a white solid: mp 182–183 °C; IR 2219, 1462, 750 cm^{-1} ; ^1H NMR (mixture of the *meso* and *rac* isomers, CDCl_3 , 600 MHz) δ 7.83 (2 H, dd, J = 8.1, 1.2 Hz), 7.43 (2 H, dd, J = 7.8, 1.8 Hz), 7.38 (4 H, s), 7.26 (2 H, td, J = 7.5, 1.2 Hz), 6.96 (2 H, td,

$J = 7.8, 1.8$ Hz), 3.68 (2 H, s), 1.08 (18 H, s); ^{13}C NMR (mixture of the *meso* and *rac* isomers, CDCl_3 , 150 MHz) δ 138.6, 137.4, 133.0, 130.6, 129.1, 128.8, 127.6, 100.6, 95.7, 85.6, 50.3, 35.7, 27.9; HRMS m/z calcd for $\text{C}_{32}\text{H}_{33}\text{I}_2$ (MH^+) 671.0666, found 671.0665.

Tetraacetylene 2.8a. The following procedure for **2.8a** is representative for the preparation of tetraacetylenes **2.8a–c**. To a mixture of **2.6** (0.90 g, 1.34 mmol), $\text{Pd}(\text{PPh}_3)_2\text{Cl}_2$ (0.047 g, 0.067 mmol), and CuI (0.0064 g, 0.034 mmol) in 40 mL of triethylamine under a nitrogen atmosphere was added via cannula a solution of **2.7a** (0.29 g, 2.81 mmol) in 20 mL of triethylamine. The resulting mixture was heated to reflux for 24 h before it was allowed to cool to room temperature. The mixture was concentrated in vacuo. The black residue was dissolved in 100 mL of dichloromethane and then washed with brine and water. The organic layer was separated, dried over sodium sulfate, and concentrated. Purification by flash column chromatography (silica gel/ CH_2Cl_2 :MeOH = 19:1, $R_f = 0.45$) provided 0.75 g (1.2 mmol, 90%, 1:1 mixture of the *meso* and *rac* isomers) of **2.8a** as a yellow solid with some fractions contained only the *meso* or the *rac* isomer: mp 183–185 °C; IR 2218, 1590, 1235, 821, 764 cm^{-1} ; *meso*-**2.8a**: ^1H NMR (CDCl_3 , 600 MHz) δ 8.55 (4 H, br s), 7.56 (2 H, dd, $J = 7.8, 1.2$ Hz), 7.53 (2 H, dd, $J = 7.8, 1.2$ Hz), 7.35 (2 H, td, $J = 7.8, 1.2$ Hz), 7.30 (2 H, td, $J = 7.8, 1.2$ Hz), 7.297–7.28 (8 H, m), 3.66 (2 H, s), 1.02 (18 H, s); ^{13}C NMR (CDCl_3 , 150 MHz) δ 148.0, 137.6, 133.2, 132.5, 132.4, 129.3, 129.0, 127.6, 126.8, 126.1, 124.0, 96.4, 95.1, 89.4, 82.2, 50.2, 35.5, 27.8. *rac*-**2.8a**: ^1H NMR (CDCl_3 , 600 MHz) δ 8.50 (4 H, br s), 7.52 (2 H, d, $J = 7.8$ Hz), 7.46 (2 H, d, $J = 6.6$ Hz), 7.30–7.24 (12 H, m), 3.67 (2 H, s), 1.01 (18 H, s); ^{13}C NMR (CDCl_3 , 150 MHz) δ 149.4, 137.5, 132.3, 132.2, 131.6, 128.9, 128.8, 127.4, 126.7, 125.6, 124.3, 96.3, 93.3, 89.7, 82.1, 50.2, 35.5, 27.7; MS m/z 621 (MH^+), 254; HRMS m/z calcd for $\text{C}_{46}\text{H}_{41}\text{N}_2$ (MH^+) 621.3264, found 621.3261. Recrystallization of the separated *meso*-**2.8a** and *rac*-**2.8a** from CH_2Cl_2 /MeOH produced crystals suitable for X-ray structure analyses.

Tetraacetylene 2.8b. The same procedure was repeated as described for **2.8a** except that 0.27 g (1.5 mmol) of **2.7b** was treated with a mixture of **2.6** (0.50 g, 0.75 mmol), Pd(PPh₃)₂Cl₂ (0.028 g, 0.040 mmol), and CuI (0.0043 g, 0.023 mmol) in 50 mL of triethylamine. Purification by flash column chromatography (silica gel/CH₂Cl₂:MeOH = 19:1, *R_f* = 0.52) furnished 0.49 g of **2.8b** (0.65 mmol, 86%, 1:1 mixture of the *meso* and *rac* isomers) as a yellow solid: mp 189–192 °C; IR 2210, 1739, 1217, 752 cm⁻¹; ¹H NMR (mixture of the *meso* and *rac* isomers, CDCl₃, 600 MHz) δ 8.76–8.66 (4 H, m), 8.50–8.43 (4 H, m), 7.89 (1 H, t, *J* = 7.2 Hz), 7.83 (1 H, t, *J* = 7.2 Hz), 7.81–7.77 (2 H, m), 7.54–7.51 (3 H, m), 7.48–7.46 (1 H, m), 7.39–7.34 (2 H, m), 7.32 and 7.31 (4 H, two singlets), 7.28–7.24 (4 H, m), 3.71 and 3.66 (2 H, two singlets), 1.01 (18 H, s); ¹³C NMR (mixture of the *meso* and *rac* isomers, CDCl₃, 150 MHz) δ 154.3, 152.9, 151.7, 151.6, 147.9, 139.74, 139.72, 138.3, 137.54, 137.46, 132.29, 132.23, 132.19, 132.15, 128.99, 128.97, 128.53, 128.47, 127.4, 126.64, 126.59, 124.71, 124.67, 124.2, 122.1, 121.0, 96.29, 96.27, 93.38, 93.33, 89.3, 82.3, 82.1, 50.2, 35.51, 35.50, 27.8; MS *m/z* 775 (MH⁺), 718; HRMS *m/z* calcd for C₅₆H₄₇N₄ (MH⁺) 775.3795, found 775.3789.

Tetraacetylene 2.8c. The same procedure was repeated as described for **2.8a** except that 0.26 g (1.0 mmol) of **2.7c** was treated with a mixture of **2.6** (0.32 g, 0.48 mmol), Pd(PPh₃)₂Cl₂ (0.015 g, 0.021 mmol), and CuI (0.005 g, 0.026 mmol) in 50 mL of triethylamine. Purification by flash column chromatography (silica gel/CH₂Cl₂:MeOH = 9:1, *R_f* = 0.43) furnished 0.34 g of **2.8c** (0.37 mmol, 77%, 1:1 mixture of the *meso* and *rac* isomers) as a yellow solid: mp 251–253 °C; IR 2220, 1738, 1583, 1390, 788 cm⁻¹; ¹H NMR (mixture of the *meso* and *rac* isomers, CDCl₃, 600 MHz) δ 8.72 (4 H, d, *J* = 3.6 Hz), 8.60 (4 H, d, *J* = 8.4 Hz), 8.59 (4 H, s), 7.86 (4 H, t, *J* = 7.8 Hz), 7.54 (2 H, m), 7.43 (2 H, m), 7.34 (4 H, t, *J* = 6.3 Hz), 7.32 (4 H, s), 7.27–7.22 (4 H, m), 3.64 (2 H, s), 1.01 (18 H, s); ¹³C NMR (mixture of the *meso* and *rac* isomers, CDCl₃, 150 MHz) δ 155.3, 155.2, 148.9, 137.3, 137.2, 133.4, 132.4, 132.2, 129.0, 128.6, 127.3, 126.8, 124.7, 124.0,

123.2, 121.4, 96.5, 93.2, 90.6, 82.1, 50.2, 35.5, 27.7; MS m/z 929 (MH^+), 872, 815; HRMS m/z calcd for $C_{66}H_{53}N_6$ (MH^+) 929.4326, found 929.4319.

4,5-Diheteroarylphenanthrene 2.2a. To 0.28 g (0.45 mmol) of **2.8a** in 30 mL of anhydrous toluene under a nitrogen atmosphere was added 1.0 mL of a 1.0 M solution of potassium *tert*-butoxide (1.0 mmol) in 2-methyl-2-propanol. The reaction mixture was then heated under reflux for 6 h. After the reaction mixture was allowed to cool to room temperature, 10 mL of water and 120 mL of dichloromethane were introduced, and the organic layer was separated, dried over sodium sulfate, and concentrated. Flash column chromatograph (silica gel/ CH_2Cl_2 :MeOH =19:1, R_f = 0.33) provided 0.16 g (0.26 mmol, 58%) of **2.2a** as a yellow solid: mp >350 °C; IR 1594, 830, 741 cm^{-1} ; 1H NMR ($CDCl_3$, 600 MHz) δ 8.33 (4 H, d, J = 5.4 Hz), 7.89 (2 H, s), 7.45 (2 H, d, J = 7.8 Hz), 7.13 (2 H, t, J = 7.5 Hz), 6.80 (2 H, t, J = 7.5 Hz), 6.63 (4 H, d, J = 6.0 Hz), 6.30 (2 H, d, J = 8.4 Hz), 4.45 (2 H, d, J = 21.0 Hz), 4.19 (2 H, d, J = 21.0 Hz), 1.83 (18 H, s); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 149.2, 147.3, 144.4, 141.4, 140.2, 139.8, 136.8, 132.1, 131.8, 130.2, 127.4 (br), 127.0, 125.7, 124.1, 122.6, 122.3, 39.7, 38.0, 33.3; HRMS m/z calcd for $C_{46}H_{41}N_2$ (MH^+) 621.3264, found 621.3263. Recrystallization of **2.2a** from CH_2Cl_2 /MeOH produced a crystal suitable for X-ray structure analysis.

4,5-Diheteroarylphenanthrene 2.2b. To 0.26 g (0.33 mmol) of **2.8b** in 30 mL of anhydrous toluene under a nitrogen atmosphere was added 0.7 mL of a 1.0 M solution of potassium *tert*-butoxide (0.7 mmol) in 2-methyl-2-propanol. The reaction mixture was then heated under reflux for 6 h. After the reaction mixture was allowed to cool to room temperature, 10 mL of water and 120 mL of dichloromethane were introduced, and the organic layer was separated, dried over sodium sulfate, and concentrated. Flash column chromatograph (silica gel/ CH_2Cl_2 :MeOH =19:1, R_f = 0.4) provided 0.14 g (0.17 mmol, 53%) of **2.2b** as a yellow solid: mp > 350 °C; IR 1707, 1458, 746 cm^{-1} ; 1H NMR

(CDCl₃, 600 MHz) δ 8.70 (2 H, d, J = 3.6 Hz), 8.47 (2 H, br s), 8.20 (2 H, br s), 7.93 (2 H, s), 7.89 (4 H, br s), 7.40 (2 H, d, J = 7.2 Hz), 7.35 (2 H, t, J = 5.4 Hz), 7.06–7.02 (4 H, m), 6.72 (2 H, t, J = 7.8 Hz), 6.29 (2 H, d, J = 7.8 Hz), 4.43 (2 H, d, J = 21.0 Hz), 4.19 (2 H, d, J = 21.0 Hz), 1.85 (18 H, s); ¹³C NMR (CDCl₃, 150 MHz) δ 155.6, 148.6, 144.4, 141.1, 140.2, 137.8, 137.5, 135.7, 132.2, 131.0, 130.3, 126.7, 125.9, 124.1, 123.8, 122.5, 122.4, 122.0, 121.2, 39.9, 38.0, 33.4; MS m/z 775 (MH⁺), 760; HRMS m/z calcd for C₅₆H₄₇N₄ (MH⁺) 775.3795, found 775.3788.

4,5-Diheteroarylphenanthrene 2.2c. To 0.32 g (0.34 mmol) of **2.8c** in 30 mL of anhydrous toluene under a nitrogen atmosphere was added 0.7 mL of a 1.0 M solution of potassium *tert*-butoxide (0.7 mmol) in 2-methyl-2-propanol. The reaction mixture was then heated under reflux for 6 h. After the reaction mixture was allowed to cool to room temperature, 10 mL of water and 120 mL of dichloromethane were introduced, and the organic layer was separated, dried over sodium sulfate, and concentrated. Flash column chromatograph (silica gel/CH₂Cl₂:MeOH = 9:1, R_f = 0.32) provided 0.15 g (0.16 mmol, 48%) of **2.2c** as a yellow solid: mp >350 °C; IR 1583, 1565, 1466, 793, 735 cm⁻¹; ¹H NMR (CDCl₃, 60 °C, 600 MHz) δ 8.44 (4 H, br), 8.40 (4 H, br), 7.91 (4 H, br), 7.90 (2 H, s), 7.68 (4 H, br), 7.32 (2 H, d, J = 7.2 Hz), 7.10 (4 H, br), 6.97 (2 H, t, J = 7.2 Hz), 6.70 (2 H, d, J = 7.8 Hz), 6.59 (2 H, t, J = 7.5 Hz), 4.18 (2 H, d, J = 21.0 Hz), 4.13 (2 H, d, J = 21.0 Hz), 1.88 (18 H, s); ¹³C NMR (CDCl₃, 150 MHz) δ 155 (very br), 148.4 (br), 148.2 (br), 144.4, 141.0 (br), 140.0, 137 (very br), 136.5, 132.5 (very br), 132.0, 126.6, 126.0 (br), 125.8, 123.9, 123.3 (br), 122.3, 122.2, 121.1 (br), 39.6, 38.1, 33.3; HRMS m/z calcd for C₆₆H₅₃N₆ (MH⁺) 929.4325, found 929.4319. Recrystallization of **2.2c** from CH₂Cl₂/MeOH produced a crystal suitable for X-ray structure analysis.

[Cl₃Ru(2c)RuCl₃] (2.10). To a suspension of 0.066 g of RuCl₃·3H₂O (0.25 mmol) and 15 mL of ethanol was added 0.110 g of **2c** (0.118 mmol). The reaction mixture was heated to reflux for 16 h before it was allowed to cool to room temperature. The dark brown

precipitate was collected by filtration, washed thoroughly with methanol, water, and diethyl ether, and dried in vacuo to yield 0.146 g of **2.10** (92%) as a dark brown solid: mp >350 °C; IR 1599, 1469, 790, 752 cm⁻¹; ¹H NMR (CDCl₃, 600 MHz) δ 14.40 (2 H, s), 14.28 (2 H, s), 13.82 (2 H, s), 10.17 (2 H, s), 7.75 (2 H, d, *J* = 21.0 Hz), 7.26 (2 H, s), 4.83 (2 H, d, *J* = 21.0 Hz), 4.51 (2 H, s), 1.24 (2 H, s), 0.59 (18 H, s), -1.53 (2 H, s), -2.75 (2 H, s), -3.64 (2 H, s), -7.02 (2 H, s), -9.35 (2 H, s), -9.80 (2 H, s), -32.35 (2 H, s), -35.56 (2 H, s); HRMS *m/z* calcd for C₆₆H₅₂Cl₆N₆Ru₂ (M⁺) 1342.0471, found 1342.0531.

[(4'-EtOtpy)Ru(2c)Ru(4'-EtOtpy)](PF₆)₄ (2.13**).** A mixture of **2.10** (0.084 g, 0.062 mmol), 4'-EtOtpy (0.035 g, 0.126 mmol), and *N*-ethylmorpholine (0.043 g, 0.37 mmol) in 7 mL of methanol was heated under reflux for 1 h before it was allowed to cool to room temperature. The mixture was filtered and the filtrate was treated with an excess of NH₄PF₆ (0.10 g, 0.62 mmol) in 10 mL of methanol to give a brown precipitate. The brown precipitate was collected by filtration, washed with water, methanol, and diethyl ether, and dried in vacuo to produce 0.102 g (0.045 mmol, 73%) of **2.13** as a brown solid. The ¹H NMR spectrum of the brown solid showed the presence of a small amount of the homoleptic species [Ru(4'-EtOtpy)₂](PF₆)₂. The brown solid was further purified by flash column chromatography (silica gel/acetonitrile:saturated aqueous potassium nitrate:water = 7:1:0.5, *R_f* = 0.48). The main brown band was collected followed by the addition of excess NH₄PF₆. The solution was further concentrated in *vacuo* to induce precipitation. The precipitate was collected and washed with a small amount of methanol, dried in *vacuo*, to produce a more homogenous sample of **2.13** as a light brown solid: mp >350 °C; IR 1615, 1213, 826, 787 cm⁻¹; ¹H NMR (CD₃CN, 600 MHz) δ 8.48 (4 H, br s), 8.33 (2 H, s), 8.31 (4 H, s), 7.82 (4 H, br s), 7.64 (2 H, d, *J* = 7.2 Hz), 7.39 (2 H, td, *J* = 7.2, 1.2 Hz), 7.33 (2 H, d, *J* = 8.4 Hz), 7.15 (4 H, br s), 7.02 (2 H, t, *J* = 7.8 Hz), 4.61 (4 H, q, *J* = 7.2 Hz), 4.46 (2 H, d, *J* = 21.6 Hz), 4.30 (2 H, d, *J* = 21.6 Hz), 1.97 (18 H, s), 1.64 (6 H, t, *J* =

7.2 Hz); ^{13}C NMR (CD_3CN , 150 MHz) δ 167.7, 156.6, 153.9, 147.2, 145.9, 144.3, 142.8, 139.3, 138.9, 137.5, 134.3, 133.8, 131.3, 129.4, 128.9, 127.9, 126.6, 124.6, 122.6, 112.3, 67.2, 40.4, 39.3, 33.9, 14.8; HRMS m/z calcd for $\text{C}_{100}\text{H}_{82}\text{F}_{24}\text{N}_{12}\text{O}_2\text{P}_4\text{Ru}_2$ (M^+) 2266.3338, found 2266.3423.

[(4'-Cltpy)Ru(2c)Ru(4'-Cltpy)](PF₆)₄ (2.14). A mixture of **2.10** (0.025 g, 0.019 mmol), 4'-Cltpy (**2.12**) (0.010 g, 0.038 mmol), and *N*-ethylmorpholine (0.014 g, 0.12 mmol) in 5 mL of methanol was heated under reflux for 1 h before it was allowed to cool to room temperature. The mixture was filtered and the filtrate was treated with an excess of NH_4PF_6 (0.033 g, 0.20 mmol) in 10 mL of methanol to give a brown precipitate. The brown precipitate was collected by filtration, washed with water, methanol, and diethyl ether, and dried in vacuo to produce 0.028 g (0.013 mmol, 68%) of **2.14** as a brown solid: ^1H NMR (CD_3CN , 600 MHz) δ 8.87 (4 H, s), 8.50 (4 H, m), 8.34 (2 H, s), 7.9–7.85 (4 H, br), 7.65 (2 H, d, J = 7.8 Hz), 7.40 (2 H, t, J = 6.6 Hz), 7.36 (2 H, d, J = 8.4 Hz), 7.19 (4 H, t, J = 6.0 Hz), 7.04 (2 H, t, J = 7.2 Hz), 4.46 (2 H, d, J = 21.6 Hz), 4.30 (2 H, d, J = 21.6 Hz), 1.96 (18 H, s); HRMS m/z calcd for $\text{C}_9\text{H}_7\text{Cl}_2\text{N}_{12}\text{Ru}_2$ ($\text{M} - 4 \text{PF}_6$)⁺ 1666.3467, found 1666.3552. The ^1H NMR spectrum showed that the sample contains minor amount of the homoleptic species $[\text{Ru}(4'\text{-Cltpy})_2](\text{PF}_6)_2$.

1-Ethynyl-2-[2-(4-methoxyphenyl)ethynyl]benzene (3.43). To 0.600 g of 1-[2-(4-methoxyphenyl)ethynyl]-2-[2-(trimethylsilyl)ethynyl]benzene (1.97 mmol) in 90 mL of methanol was added 1.37 g of potassium carbonate (9.91 mmol). After 3 h at room temperature, the mixture was filtered to remove solid particles. Then 20 mL of a 2 M HCl solution was added slowly to the filtrate. The reaction mixture was extracted with diethyl ether (3 $\times$ 30 mL). The combined organic extracts were washed with brine and water, dried over sodium sulfate, and concentrated. Flash column chromatography (silica gel/2% diethyl ether in hexanes) provided 0.441 g of **3.43** (1.90 mmol, 96% yield) as a white

solid: mp 133–134 °C; IR 3299, 2216, 1509, 1247 cm^{-1} ; ^1H NMR (CDCl_3 , 600 MHz) δ 7.54–7.50 (4 H, m), 7.32 (1 H, td, $J = 7.8, 1.8$ Hz), 7.26 (1 H, td, $J = 7.8, 1.2$ Hz), 6.89 (2 H, d, $J = 9.0$ Hz), 3.83 (3 H, s), 3.36 (1 H, s); ^{13}C NMR (CDCl_3 , 150 MHz) δ 159.8, 133.2, 132.5, 131.5, 128.5, 127.5, 126.7, 124.4, 115.3, 114.0, 93.7, 86.7, 82.3, 80.9, 55.3; HRMS m/z calcd for $\text{C}_{17}\text{H}_{12}\text{ONa}$ (MNa^+) 255.0780, found 255.0784.

4-[(2-ethynylphenyl)ethynyl]-N,N-dimethylaniline (3.44). To 0.510 g of 4-(2-((trimethylsilyl)ethynyl)phenyl)ethynyl-N,N-dimethyl-aniline (1.61 mmol) in 70 mL of methanol was added 0.8 g of potassium carbonate (6.90 mmol). After 3 h at room temperature, the mixture was filtered to remove solid particles. Then 20 mL of a 2 M HCl solution was added slowly to the filtrate. The reaction mixture was extracted with diethyl ether (3×30 mL). The combined organic extracts were washed with brine and water, dried over sodium sulfate, and concentrated. Flash column chromatography (silica gel/20% diethyl ether in hexanes) provided 0.355 g of **3.44** (1.45 mmol, 90% yield) as a yellow solid: ^1H NMR (CDCl_3 , 600 MHz) δ 7.53–7.51 (2 H, m), 7.47–7.44 (2 H, m), 7.30 (1 H, td, $J = 7.8, 1.2$ Hz), 7.23 (1 H, td, $J = 7.8, 1.2$ Hz), 6.67 (2 H, d, $J = 8.4$ Hz), 3.36 (1 H, s), 2.99 (6 H, s); ^{13}C NMR (CDCl_3 , 150 MHz) δ 150.2, 132.9, 132.4, 131.3, 128.4, 127.2, 127.0, 124.0, 111.8, 109.9, 95.2, 86.1, 82.5, 80.7, 40.1.

Propargylic Alcohol 3.46. The following procedure is representative for the preparation of propargylic alcohols. To 0.222 g (1.10 mmol) of **3.42** in 20 mL of THF under a nitrogen atmosphere at -78 °C was added 0.638 mL of a 1.8 M solution of lithium diisopropylamide (LDA, 1.15 mmol) in hexanes. After 30 min of stirring, a solution of 0.190 g of **3.45** (1.00 mmol) in 10 mL of THF was introduced via cannula, and the reaction mixture was allowed to warm to room temperature. After an additional 1 h, 30 mL of water was introduced, and the reaction mixture was extracted with diethyl ether (3×30 mL). The combined organic extracts were washed with brine and water, dried over

sodium sulfate, and concentrated. Flash column chromatography (silica gel/20% diethyl ether in hexanes) provided 0.372 g of **3.46** (0.95 mmol, 95% yield) as a yellow oil: IR 3465, 2201, 755 cm^{-1} ; ^1H NMR (CDCl_3 , 600 MHz) δ 7.56–7.52 (3 H, m), 7.45–7.43 (2 H, m), 7.32–7.27 (5 H, m), 6.76 (1 H, d, J = 1.8 Hz), 6.64 (1 H, dd, J = 8.4, 2.4 Hz), 3.78 (3 H, s), 3.00 (1 H, d, J = 15.6 Hz), 2.63 (1 H, d, J = 15.0 Hz), 2.16 (1 H, s), 1.31 (3 H, s), 1.20 (3 H, s); ^{13}C NMR (CDCl_3 , 150 MHz) δ 160.5, 144.4, 138.1, 132.2, 132.0, 131.8, 128.3, 128.2, 128.1, 127.9, 125.9, 125.2, 125.1, 123.1, 112.4, 110.8, 93.2, 93.0, 88.2, 85.3, 81.4, 55.4, 49.3, 44.6, 26.5, 21.5; HRMS m/z calcd for $\text{C}_{28}\text{H}_{25}\text{O}_2$ (MH^+) 393.1849, found 393.1856.

1,4-Naphthoquinone Methide 3.49. The following procedure is representative for the preparation of the 1,4-naphthoquinone methides. Propargylic alcohol **3.46** (0.350 g, 0.893 mmol) in 20 mL of dichloromethane was treated with trifluoroacetic acid (0.305 g, 2.67 mmol). After 10 min of stirring, the reaction mixture was treated with 10 mL of a saturated NaHCO_3 solution and extracted with dichloromethane (3×20 mL). The combined organic extracts were washed with brine and water, dried over sodium sulfate, and concentrated. Flash column chromatography (silica gel/30% diethyl ether in hexanes) provided 0.322 g of **3.49** (0.820 mmol, 92% yield) as a yellow solid: mp 152–153 $^\circ\text{C}$; IR 1643, 1607, 765 cm^{-1} ; ^1H NMR (CDCl_3 , 600 MHz, -40 $^\circ\text{C}$) δ 7.94 (1 H, d, J = 7.8 Hz), 7.34 (1 H, t, J = 7.5 Hz), 7.24 (1 H, t, J = 7.5 Hz), 7.205 (1 H, t, J = 7.5 Hz), 7.11 (1 H, d, J = 7.2 Hz), 7.02 (1 H, t, J = 7.5 Hz), 6.95 (1 H, t, J = 7.8 Hz), 6.84 (1 H, d, J = 8.4 Hz), 6.77 (1 H, s), 6.60 (3 H, broad), 6.35 (1 H, s), 3.83 (3 H, s), 3.54 (1 H, d, J = 13.2 Hz), 2.53 (1 H, d, J = 13.2 Hz), 1.33 (3 H, s), 1.04 (3 H, s); ^{13}C NMR (CDCl_3 , 150 MHz, -40 $^\circ\text{C}$) δ 187.1, 168.2, 159.0, 144.9, 144.2, 140.7, 140.6, 133.4, 131.9, 131.62, 131.58, 131.52, 131.0, 129.8, 128.7, 128.0, 127.7, 127.2, 126.3, 124.6, 123.4, 114.1, 111.0, 55.2, 47.2, 46.3, 35.5, 26.5; HRMS m/z calcd for $\text{C}_{28}\text{H}_{25}\text{O}_2$ (MH^+) 393.1849, found 393.1854. Recrystallization of **3.49** from diethyl ether/hexanes produced a crystal suitable for X-ray

structure analysis.

Propargylic Alcohol 3.47. The same procedure was repeated as described for **3.46** except that 0.130 g (0.684 mmol) of **3.45** was treated with the lithium acetylide derived from 0.159 g of **3.43** (0.685 mmol) and 0.42 mL of a 1.8 M solution of LDA (0.754 mmol) in hexanes to afford 0.262 g of propargylic alcohol **3.47** (0.622 mmol, 91% yield) as a yellow oil: IR 3500, 2216, 1692, 734 cm^{-1} ; ^1H NMR (CDCl_3 , 600 MHz) δ 7.55 (1 H, d, J = 8.4 Hz), 7.52–7.50 (2 H, m), 7.37–7.35 (2 H, m), 7.29 (1 H, td, J = 7.8, 1.8 Hz), 7.26 (1 H, td, J = 7.2, 1.2 Hz), 6.83–6.80 (2 H, m), 6.76 (1 H, d, J = 1.8 Hz), 6.65 (1 H, dd, J = 8.4, 2.4 Hz), 3.82 (3 H, s), 3.78 (3 H, s), 3.01 (1 H, d, J = 15.0 Hz), 2.63 (1 H, d, J = 15.0 Hz), 2.17 (1 H, s), 1.31 (3 H, s), 1.20 (3 H, s); ^{13}C NMR (CDCl_3 , 150 MHz) δ 160.5, 159.7, 144.4, 138.1, 133.2, 132.1, 131.8, 128.0, 127.6, 126.3, 125.2, 125.0, 115.3, 113.9, 112.4, 110.8, 93.4, 92.8, 87.0, 85.5, 81.4, 55.3, 55.2, 49.3, 44.6, 26.6, 21.5; HRMS m/z calcd for $\text{C}_{29}\text{H}_{27}\text{O}_3$ (MH^+) 423.1955, found 423.1963.

1,4-Naphthoquinone Methide 3.50. The same procedure was repeated as described for **3.49** except that 0.200 g (0.474 mmol) of **3.47** was treated with trifluoroacetic acid (0.162 g, 1.33 mmol) in dichloromethane to afford 0.082 g of **3.50** (0.389 mmol, 82% yield) as a yellow solid: mp 83–84 $^\circ\text{C}$; IR 1641, 1620, 1242 cm^{-1} ; ^1H NMR (CDCl_3 , 600 MHz, -20°C) δ 7.95 (1 H, d, J = 7.8 Hz), 7.20 (1 H, t, J = 7.5 Hz), 7.00–6.97 (2 H, m), 6.88 (1 H, d, J = 7.8 Hz), 6.86 (1 H, dd, J = 8.4, 2.4 Hz), 6.75 (1 H, d, J = 3.0 Hz), 6.64 (1 H, d, J = 9.0 Hz), 6.60 (1 H, dd, J = 9.0, 2.7 Hz), 6.53 (1 H, dd, J = 8.4, 2.4 Hz), 6.49 (1 H, dd, J = 8.4, 1.8 Hz), 6.35 (1 H, s), 3.82 (3 H, s), 3.79 (3 H, s), 3.52 (1 H, d, J = 13.2 Hz), 2.51 (1 H, d, J = 13.2 Hz), 1.32 (3 H, s), 1.02 (3 H, s); ^{13}C NMR (CDCl_3 , 150 MHz, -20°C) δ 187.0, 168.3, 159.2, 158.5, 145.0, 141.0, 140.9, 136.6, 133.6, 133.3, 132.4, 132.1, 131.9, 131.4, 129.9, 128.8, 126.1, 124.7, 123.2, 114.1, 113.6, 112.6, 111.2, 55.25, 55.17, 47.2, 46.5, 35.5, 26.4; HRMS m/z calcd for $\text{C}_{29}\text{H}_{27}\text{O}_3$ (MH^+) 423.1955, found 423.1963.

Propargylic Alcohol 3.48. The same procedure was repeated as described for **3.46** except that 0.134 g (0.705 mmol) of **3.45** was treated with the lithium acetylide derived from 0.173 g of **3.44** (0.706 mmol) and 0.36 mL of a 2.0 M solution of LDA (0.720 mmol) in hexanes to afford 0.276 g of **3.48** (0.634 mmol, 90% yield) as a yellow oil: ^1H NMR (CDCl_3 , 600 MHz) δ 7.58 (1 H, d, $J = 8.4$ Hz), 7.51 (2 H, td, $J = 8.4$, 1.8 Hz), 7.33–7.30 (2 H, m), 7.27 (1 H, td, $J = 7.2$, 1.2 Hz), 7.23 (1 H, td, $J = 7.2$, 1.2 Hz), 6.77 (1 H, d, $J = 2.4$ Hz), 6.68 (1 H, dd, $J = 8.4$, 2.4 Hz), 6.62–6.59 (2 H, m), 3.78 (3 H, s), 3.02 (1 H, d, $J = 15.6$ Hz), 2.98 (6 H, s), 2.65 (1 H, d, $J = 15.6$ Hz), 2.23 (1 H, s), 1.33 (3 H, s), 1.23 (3 H, s); ^{13}C NMR (CDCl_3 , 150 MHz) δ 160.4, 150.1, 144.4, 138.2, 132.9, 132.1, 131.6, 128.0, 127.0, 126.9, 125.2, 124.6, 112.3, 111.7, 110.7, 109.9, 94.8, 92.6, 86.4, 85.7, 81.4, 55.3, 49.3, 44.6, 40.1, 26.6, 21.48.

Propargylic Alcohol 3.53. The same procedure was repeated as described for **3.46** except that 0.190 g (0.931 mmol) of **3.52** was treated with the lithium acetylide derived from 0.202 g of **3.42** (1.00 mmol) and 0.61 mL of a 1.8 M solution of LDA (1.10 mmol) in hexanes to afford 0.354 g of **3.53** (0.873 mmol, 94% yield) as a yellow solid: mp 55–56 °C; IR 3400, 1695, 1613, 709 cm^{-1} ; ^1H NMR (CDCl_3 , 600 MHz) δ 7.94 (1 H, d, $J = 8.4$ Hz), 7.55–7.51 (2 H, m), 7.45–7.44 (2 H, m), 7.33–7.28 (5 H, m), 6.62 (1 H, d, $J = 3.0$ Hz), 6.59 (1 H, dd, $J = 8.4$, 3.0 Hz), 3.74 (3 H, s), 2.88–2.76 (2 H, m), 2.26 (1 H, s), 2.07 (1 H, ddd, $J = 13.5$, 10.2, 7.2 Hz), 1.67 (1 H, ddd, $J = 13.5$, 6.0, 4.2 Hz), 1.25 (3 H, s), 1.16 (3 H, s); ^{13}C NMR (CDCl_3 , 150 MHz) δ 159.1, 136.5, 132.2, 132.0, 131.8, 131.4, 130.2, 128.3, 128.2, 128.0, 127.9, 125.8, 125.4, 123.1, 113.4, 112.4, 95.5, 93.1, 88.3, 84.8, 75.0, 55.1, 37.8, 31.0, 26.1, 24.0, 23.7; HRMS m/z calcd for $\text{C}_{29}\text{H}_{26}\text{O}_2\text{Na}$ (MNa^+) 429.1825, found 429.1833.

1,4-Naphthoquinone Methide 3.54. The same procedure was repeated as described for **3.49** except that 0.180 g (0.443 mmol) of propargylic alcohol **3.53** was treated with trifluoroacetic acid (0.152 g, 1.33 mmol) in dichloromethane at room temperature for 20 min to afford 0.162 g of **3.54** (0.399 mmol, 90% yield) as a yellow solid: mp 80–81 °C; IR 1649, 1596, 694 cm^{-1} ; ^1H NMR (CDCl_3 , 600 MHz, -40°C) δ 7.92 (1 H, dd, $J = 7.8$, 1.2 Hz), 7.20 (2 H, t, $J = 7.5$ Hz), 7.12 (1 H, t, $J = 7.5$ Hz), 7.05 (1 H, d, $J = 7.8$ Hz), 6.95–6.89 (3 H, m), 6.86 (1 H, d, $J = 2.4$ Hz), 6.66 (1 H, dd, $J = 8.7$, 2.7 Hz), 6.63–6.61 (2 H, m), 6.59 (1 H, s), 3.85 (3 H, s), 3.56 (1 H, td, $J = 12.9$, 6.6 Hz), 2.82 (1 H, dd, $J = 12.6$, 6.0 Hz), 2.10 (1 H, dd, $J = 14.1$, 6.3 Hz), 1.74 (1 H, td, $J = 13.5$, 6.6 Hz), 1.23 (3 H, s), 0.43 (3 H, s); ^{13}C NMR (CDCl_3 , 150 MHz, -40°C) δ 187.3, 164.9, 159.6, 147.4, 142.7, 135.8, 134.6, 133.4, 133.0, 132.3, 132.2, 129.0, 127.6, 127.23, 127.17, 126.6, 124.2, 112.2, 112.0, 55.3, 44.4, 39.9, 36.4, 31.2, 28.4; HRMS m/z calcd for $\text{C}_{29}\text{H}_{27}\text{O}_2$ (MH^+) 407.2006, found 407.2013. Recrystallization of **9** from diethyl ether/hexanes produced a crystal suitable for X-ray structure analysis.

7-Methoxy-3,3-dimethyl-4-chromanone (3.55). To a solution of 7-hydroxy-3,3-dimethyl-4-chromanone (0.220 g, 1.15 mmol) and potassium carbonate (0.166 g, 1.20 mmol) in 5 mL of *N,N*-dimethylformamide was added iodomethane (0.204 g, 1.44 mmol). The mixture was heated at 80 °C for 1 h, and then the cooled mixture was diluted with 10 mL of water. The reaction mixture was extracted with diethyl ether (3 $\times$ 10 mL). The combined organic extracts were washed with brine and water, dried over sodium sulfate, and concentrated. Flash column chromatography (silica gel/40% diethyl ether in hexanes) provided 0.203 g of **3.55** (0.985 mmol, 86% yield) as a yellow oil: IR 1686, 1611, 1118 cm^{-1} ; ^1H NMR (CDCl_3 , 600 MHz) δ 7.83 (1 H, d, $J = 9.0$ Hz), 6.59 (1 H, dd, $J = 9.0$, 2.4 Hz), 6.40 (1 H, d, $J = 2.4$ Hz), 4.13 (2 H, s), 3.83 (3 H, s), 1.19 (6 H, s); ^{13}C NMR (CDCl_3 , 150 MHz) δ 196.1, 165.7, 163.1, 129.4, 113.4, 110.0, 100.5, 77.1, 55.6, 41.3, 20.6; HRMS m/z calcd for $\text{C}_{12}\text{H}_{14}\text{O}_3\text{Na}$ (MNa^+) 229.0835, found 229.0839.

Propargylic Alcohol 3.56. The same procedure was repeated as described for **3.46** except that 0.100 g (0.485 mmol) of **3.55** was treated with the lithium acetylide derived from 0.101 g of **3.42** (0.500 mmol) and 0.31 mL of a 1.8 M solution of LDA (0.550 mmol) in hexanes to afford 0.188 g of **3.56** (0.461 mmol, 95% yield) as a yellow oil: IR 3461, 2216, 1617, 754 cm^{-1} ; ^1H NMR (CDCl_3 , 600 MHz) δ 7.77 (1 H, d, J = 8.4 Hz), 7.55 (1 H, dd, J = 7.2, 1.8 Hz), 7.53 (1 H, dd, J = 7.2, 1.8 Hz), 7.43 (2 H, dd, J = 8.1, 1.5 Hz), 7.34–7.28 (5 H, m), 6.37 (1 H, d, J = 3.0 Hz), 6.35 (1 H, dd, J = 8.4, 2.4 Hz), 4.22 (1 H, d, J = 10.8 Hz), 3.84 (1 H, d, J = 10.8 Hz), 3.73 (3 H, s), 2.41 (1 H, s), 1.21 (3 H, s), 1.18 (3 H, s); ^{13}C NMR (CDCl_3 , 150 MHz) δ 186.6, 161.0, 153.7, 132.2, 132.1, 131.7, 130.1, 128.4, 128.3, 127.9, 126.0, 124.9, 123.0, 117.5, 107.7, 101.1, 93.29, 93.28, 88.1, 85.3, 71.6, 71.4, 55.3, 37.1, 22.1, 19.2; HRMS m/z calcd for $\text{C}_{28}\text{H}_{24}\text{O}_3\text{Na}$ (MNa^+) 431.1618, found 431.1630.

1,4-Naphthoquinone Methide 3.57. The same procedure was repeated as described for **3.49** except that 0.120 g (0.294 mmol) of propargylic alcohol **3.56** was treated with trifluoroacetic acid (0.107 g, 0.938 mmol) in dichloromethane at room temperature for 20 min to afford 0.110 g of **3.57** (0.270 mmol, 92% yield) as a yellow oil: IR 1703, 1655, 1600, 1115, 756 cm^{-1} ; ^1H NMR (CDCl_3 , 600 MHz) δ 7.95 (1 H, dd, J = 7.8, 1.2 Hz), 7.18 (1 H, ddd, J = 8.1, 7.2, 1.2 Hz), 7.13 (1 H, tt, J = 7.2, 1.2 Hz), 7.09 (1 H, dm, J = 7.8, 0.6 Hz), 7.07 (2 H, t, J = 7.8 Hz), 6.92 (1 H, ddd, J = 7.8, 7.2, 1.2 Hz), 6.84 (2 H, d, J = 7.2 Hz), 6.79 (1 H, dd, J = 2.4, 0.6 Hz), 6.62–6.61 (2 H, m), 6.59 (1 H, s), 4.13 (2 H, s), 3.85 (3 H, s), 0.97 (6 H, s); ^{13}C NMR (CDCl_3 , 150 MHz) δ 186.6, 162.4, 161.7, 157.3, 146.8, 142.6, 141.9, 134.1, 133.4, 132.8, 132.6, 132.4, 131.2, 129.2, 127.6, 127.4, 126.65, 126.59, 124.5, 111.2, 106.5, 83.1, 55.5, 41.7, 29.4; HRMS m/z calcd for $\text{C}_{28}\text{H}_{25}\text{O}_3$ (MH^+) 409.1798, found 409.1805.

Propargylic Alcohol 3.59. The same procedure was repeated as described for **3.46** except that 0.160 g (0.908 mmol) of **3.58** was treated with the lithium acetylide derived from 0.200 g of **3.42** (0.990 mmol) and 0.55 mL of a 1.8 M solution of LDA (0.99 mmol) in hexanes to afford 0.188 g of **3.59** (0.827 mmol, 92% yield) as a yellow oil: IR 3418, 2218, 1487, 753 cm^{-1} ; ^1H NMR (CDCl_3 , 600 MHz) δ 7.88 (1 H, dd, $J = 7.8, 1.2$ Hz), 7.56 (1 H, dd, $J = 7.8, 1.2$ Hz), 7.54 (1 H, dd, $J = 7.2, 1.2$ Hz), 7.42 (2 H, dd, $J = 8.1, 1.5$ Hz), 7.34–7.28 (5 H, m), 7.20 (1 H, ddd, $J = 8.1, 7.5, 1.8$ Hz), 6.84 (1 H, dd, $J = 8.4, 1.2$ Hz), 6.81 (1 H, td, $J = 7.8, 1.2$ Hz), 4.23 (1 H, d, $J = 10.2$ Hz), 3.89 (1 H, d, $J = 10.8$ Hz), 2.47 (1 H, s), 1.22 (3 H, s), 1.20 (3 H, s); ^{13}C NMR (CDCl_3 , 150 MHz) δ 152.6, 132.2, 132.1, 131.7, 130.0, 129.1, 128.4, 128.31, 128.29, 127.9, 126.0, 124.8, 124.7, 123.0, 120.8, 116.7, 93.3, 93.1, 88.1, 85.6, 71.9, 71.3, 36.9, 22.0, 19.2; HRMS m/z calcd for $\text{C}_{27}\text{H}_{22}\text{O}_2\text{Na}$ (MNa^+) 401.1512, found 401.1513.

1,4-Naphthoquinone Methide 3.60. The same procedure was repeated as described for **3.49** except that 0.090 g (0.238 mmol) of propargylic alcohol **3.59** was treated with trifluoroacetic acid (0.082 g, 0.714 mmol) in dichloromethane at room temperature for 60 min to afford 0.028 g of a yellow oil containing 75% of **15** (0.056 mmol, 23% yield) and 25% of an unidentified inseparable product **3.59**: ^1H NMR (CDCl_3 , 600 MHz,) δ 7.67 (1 H, dd, $J = 7.8, 0.6$ Hz), 7.55 (1 H, dd, $J = 7.8, 0.6$ Hz), 7.50–7.48 (2 H, m), 7.41–7.37 (2 H, m), 7.32–7.30 (4 H, m), 7.13 (1 H, ddd, $J = 8.4, 6.9, 1.5$ Hz), 6.75 (1 H, dd, $J = 8.4, 1.2$ Hz), 6.67 (1 H, ddd, $J = 7.8, 7.2, 1.2$ Hz), 6.47 (1 H, s), 3.95 (2 H, s), 1.11 (6 H, s); HRMS m/z calcd for $\text{C}_{27}\text{H}_{22}\text{O}_2\text{Na}$ (MNa^+) 401.1512, found 401.1514.

Propargylic Alcohol 3.62. The same procedure was repeated as described for **3.46** except that 0.133 g (0.692 mmol) of **3.61** was treated with the lithium acetylide derived from 0.140 g of **3.42** (0.693 mmol) and 0.39 mL of a 1.8 M solution of LDA (0.69 mmol) in hexanes to afford 0.267 g of **3.62** (0.679 mmol, 98% yield) as a yellow oil: IR 3403, 2221,

1382, 1117 cm^{-1} ; ^1H NMR (CDCl_3 , 600 MHz) δ 7.65 (2 H, d, $J = 9.0$ Hz), 7.56 (1 H, dd, $J = 7.2, 1.8$ Hz), 7.51 (1 H, dd, $J = 7.2, 1.8$ Hz), 7.46 (2 H, dd, $J = 7.8, 1.8$ Hz), 7.35–7.27 (5 H, m), 6.74 (2 H, d, $J = 8.4$ Hz), 3.75 (3 H, s), 2.37 (1 H, br s), 1.08 (9 H, s); ^{13}C NMR (CDCl_3 , 150 MHz) δ 158.8, 134.3, 132.20, 132.17, 131.7, 128.9, 128.4, 128.3, 128.0, 127.9, 125.8, 125.2, 123.1, 112.4, 96.5, 93.1, 88.3, 84.4, 79.3, 55.2, 39.8, 25.6; HRMS m/z calcd for $\text{C}_{28}\text{H}_{26}\text{O}_2\text{Na}$ (MNa^+) 417.1825, found 417.1826.

1,4-Naphthoquinone Methide 3.63. The same procedure was repeated as described for **3.49** except that 0.030 g (0.076 mmol) of **3.62** was treated with trifluoroacetic acid (0.026 g, 0.228 mmol) in dichloromethane at room temperature for 60 min to afford 0.008 g of **3.63** (0.019 mmol, 25% yield) as a yellow oil: ^1H NMR (CDCl_3 , 600 MHz) δ 7.98 (1 H, dd, $J = 7.5, 1.5$ Hz), 7.31–7.28 (3 H, m), 7.21–7.17 (5 H, m), 6.98 (1 H, ddd, $J = 8.4, 7.2, 1.2$ Hz), 6.90 (1 H, d, $J = 7.8$ Hz), 6.82 (2 H, d, $J = 8.4$ Hz), 6.72 (1 H, s), 3.80 (3 H, s), 1.00 (9 H, s); HRMS m/z calcd for $\text{C}_{28}\text{H}_{27}\text{O}_2$ (MH^+) 395.2006, found 395.2007.

Propargylic Alcohol 3.65. The same procedure was repeated as described for **3.46** except that 0.200 g (0.943 mmol) of **3.64** was treated with the lithium acetylide derived from 0.230 g of **3.42** (1.14 mmol) and 0.63 mL of a 1.8 M solution of LDA (0.56 mmol) in hexanes to afford 0.371 g of **3.65** (0.895 mmol, 95% yield) as a yellow oil: IR 3366, 2931, 1707, 1606, 1247 cm^{-1} ; ^1H NMR (CDCl_3 , 600 MHz) δ 7.66 (2 H, dd, $J = 8.4, 1.2$ Hz), 7.64 (2 H, d, $J = 9.0$ Hz), 7.56 (1 H, dd, $J = 7.2, 1.2$ Hz), 7.39 (1 H, dd, $J = 7.8, 1.8$ Hz), 7.34–7.21 (8 H, m), 6.73 (1 H, d, $J = 6.6$ Hz), 3.72 (3 H, s), 2.88 (1 H, s); ^{13}C NMR (CDCl_3 , 150 MHz) δ 159.0, 145.1, 137.3, 132.2, 132.0, 131.8, 128.4, 128.3, 128.28, 128.2, 128.0, 127.55, 127.5, 126.1, 126.0, 124.9, 123.0, 113.6, 95.8, 93.4, 88.2, 85.7, 74.7, 55.2; HRMS m/z calcd for $\text{C}_{30}\text{H}_{22}\text{O}_2\text{Na}$ (MNa^+) 437.1512, found 437.1513.

Ketone 3.66. The same procedure was repeated as described for **3.49** except that 0.350 g

(0.845 mmol) of **3.65** was treated with trifluoroacetic acid (0.291 g, 2.54 mmol) in dichloromethane at room temperature for 6 h to afford 0.156 g of **3.66** (0.380 mmol, 45% yield) as a yellow solid: IR 2918, 1701, 1603, 1227, 699 cm^{-1} ; ^1H NMR (CDCl_3 , 600 MHz) δ 7.66–7.52 (8 H, m), 7.47 (2 H, d, J = 6.6 Hz), 7.41 (2 H, d, J = 6.6 Hz), 7.18 (1 H, td, J = 7.2, 1.2 Hz), 7.14 (1 H, td, J = 7.8, 1.2 Hz), 7.01 (1 H, dd, J = 9.0, 2.4 Hz), 6.81 (1 H, d, J = 2.4 Hz), 6.27 (1 H, d, J = 7.8 Hz), 3.71 (3 H, s); ^{13}C NMR (CDCl_3 , 150 MHz) δ 192.2, 159.9, 144.1, 140.7, 138.6, 137.9, 136.9, 136.3, 136.0, 134.0, 133.1, 130.6, 129.8, 129.5, 129.4, 128.6, 128.55, 128.3, 128.1, 127.9, 126.6, 123.7, 123.6, 117.6, 107.2, 55.2; HRMS m/z calcd for $\text{C}_{30}\text{H}_{21}\text{O}_2$ (MH^+) 413.1536, found 413.1537.

Propargylic Alcohol 3.68. The same procedure was repeated as described for **3.46** except that 0.170 g (0.806 mmol) of **3.67** was treated with the lithium acetylide derived from 0.170 g of **3.42** (0.842 mmol) and 0.048 mL of a 1.8 M solution of LDA (0.86 mmol) in hexanes to afford 0.298 g of **3.68** (0.725 mmol, 90% yield) as a yellow oil: ^1H NMR (CDCl_3 , 600 MHz) δ 7.75 (1 H, d, J = 7.8 Hz), 7.65 (1 H, d, J = 7.8 Hz), 7.48 (2 H, td, J = 7.8, 1.2 Hz), 7.36 (1 H, td, J = 7.8, 1.2 Hz), 7.32–7.21 (8 H, m), 7.12 (1 H, d, J = 2.4 Hz), 6.73 (1 H, dd, J = 8.4, 2.4 Hz), 3.83 (3 H, s), 2.69 (1 H, s); ^{13}C NMR (CDCl_3 , 150 MHz) δ 161.2, 148.1, 140.7, 139.4, 138.8, 132.3, 131.7, 131.69, 129.5, 128.7, 128.24, 128.21, 128.18, 127.8, 126.1, 125.4, 124.9, 124.4, 123.1, 120.1, 113.8, 105.9, 93.4, 93.2, 87.9, 81.7, 74.8, 55.5.

Propargylic Alcohol 3.70. The same procedure was repeated as described for **3.46** except that 0.107 g (0.557 mmol) of **3.61** was treated with the lithium acetylide derived from 0.130 g of **3.43** (0.560 mmol) and 0.31 mL of a 1.8 M solution of LDA (0.560 mmol) in hexanes to afford 0.229 g of **3.70** (0.540 mmol, 97% yield) as a yellow oil: IR 3475, 2216 1606, 1509, 1247 cm^{-1} ; ^1H NMR (CDCl_3 , 600 MHz) δ 7.66 (2 H, d, J = 9.0 Hz), 7.53 (1 H, dd, J = 7.2, 1.2 Hz), 7.49 (1 H, dd, J = 7.2, 1.2 Hz), 7.38 (2 H, d, J = 9.0 Hz), 7.29 (1

H, td, $J = 7.8, 1.8$ Hz), 7.26 (1 H, td, $J = 7.5, 1.8$ Hz), 6.83 (2 H, d, $J = 9.0$ Hz), 6.75 (2 H, d, $J = 9.0$ Hz), 3.82 (3 H, s), 3.75 (3 H, s), 2.38 (1 H, br s), 1.08 (9 H, s); ^{13}C NMR (CDCl_3 , 150 MHz) δ 159.7, 158.8, 134.3, 133.2, 132.1, 132.0, 129.0, 128.0, 127.6, 126.2, 125.0, 115.2, 113.9, 112.4, 96.3, 93.3, 87.1, 84.6, 79.3, 55.3, 55.1, 39.8, 25.6; HRMS m/z calcd for $\text{C}_{29}\text{H}_{28}\text{O}_3\text{Na}$ (MNa^+) 447.1931, found 447.1931.

Ketone 3.71. The same procedure was repeated as described for **3.49** except that 0.086 g (0.203 mmol) of **3.70** was treated with trifluoroacetic acid (0.018 g, 0.157 mmol) in dichloromethane at room temperature for 4 h to afford 0.029 g of **3.71** (0.067 mmol, 33% yield) as a yellow liquid: IR 2249, 1675, 1601, 906, 726 cm^{-1} ; ^1H NMR (CDCl_3 , 600 MHz) δ 7.93 (2 H, d, $J = 9.0$ Hz), 7.60 (1 H, dd, $J = 7.5, 1.5$ Hz), 7.32 (1 H, td, $J = 7.8, 1.8$ Hz), 7.256 (1 H, td, $J = 7.8, 1.2$ Hz), 7.09 (1 H, d, $J = 7.8$ Hz), 6.91 (2 H, d, $J = 9.0$ Hz), 6.85 (2 H, d, $J = 8.4$ Hz), 6.66 (2 H, d, $J = 9.0$ Hz), 6.65 (1 H, s), 4.32 (2 H, s), 3.86 (3 H, s), 3.73 (3 H, s), 1.15 (9 H, s); ^{13}C NMR (CDCl_3 , 150 MHz) δ 197.7, 195.9, 163.3, 163.0, 158.3, 139.5, 134.3, 131.8, 130.8, 130.6, 130.1, 129.8, 129.5, 126.4, 125.3, 113.6, 112.7, 55.4, 55.1, 42.7, 37.3, 29.2; HRMS m/z calcd for $\text{C}_{29}\text{H}_{31}\text{O}_4$ (MH^+) 443.2217, found 443.2218. The stereochemistry of the carbon–carbon double bond in **20** was established by NOE measurements.

1-[2-(4-Methoxyphenyl)ethynyl]-2-[2-(trimethylsilyl)ethynyl]benzene **3.75**.

To a flask containing 0.126 g of dichlorobis(triphenylphosphine)palladium (0.180 mmol) and 0.060 g of CuI (0.32 mmol) was added via cannula a solution of 0.900 g of 1-bromo-2-[2-(trimethylsilyl)ethynyl]benzene (3.55 mmol) in 45 mL of triethylamine followed by a solution of 0.516 g of 1-ethynyl-4-methoxybenzene (3.90 mmol) in 30 mL of triethylamine under a nitrogen atmosphere. The resulting mixture was stirred vigorously at 75 °C for 12 h. The mixture was then filtered to remove solid particles, and the filtrate was concentrated. The residue was purified by flash column chromatography

(silica gel/3% diethyl ether in hexanes) to give 0.693 g of 1-[2-(4-methoxyphenyl)ethynyl]-2-[2-(trimethylsilyl)ethynyl]benzene (2.28 mmol, 64% yield) as a yellow oil: IR 2221, 2164, 1512, 1249, 1118 cm^{-1} ; ^1H NMR (CDCl_3 , 600 MHz,) δ 7.51–7.48 (4 H, m), 7.27 (1 H, td, $J = 7.5, 1.5$ Hz), 7.23 (1 H, td, $J = 7.2, 1.8$ Hz), 6.88 (2 H, d, $J = 9.0$ Hz), 3.84 (3 H, s), 0.27 (9 H, s); ^{13}C NMR (CDCl_3 , 150 MHz,) δ 159.8, 133.2, 132.3, 131.5, 128.2, 127.5, 126.5, 125.4, 115.5, 114.0, 103.6, 98.4, 93.6, 87.0, 55.3, 0.07; HRMS m/z calcd for $\text{C}_{20}\text{H}_{20}\text{OSiNa}$ (MNa^+) 327.1176, found 327.1182.

4-(2-((trimethylsilyl)ethynyl)phenyl)ethynyl-N,N-dimethyl-aniline 3.76.

To a flask containing 0.096 g of dichlorobis(triphenylphosphine)palladium (0.138 mmol) and 0.050 g of CuI (0.089 mmol) was added via cannula a solution of 0.840 g of 1-iodo-2-[2-(trimethylsilyl)ethynyl]benzene (2.80 mmol) in 60 mL of triethylamine followed by a solution of 0.400 g of 4-ethynyl-N,N-dimethylaniline (2.76 mmol) in 20 mL of triethylamine under a nitrogen atmosphere. The resulting mixture was stirred vigorously at 75 °C for 12 h. The mixture was then filtered to remove solid particles, and the filtrate was concentrated. The residue was purified by flash column chromatography (silica gel/20% diethyl ether in hexanes) to give 0.542 g of 4-(2-((trimethylsilyl)ethynyl)phenyl)ethynyl-N,N-dimethyl-aniline. (1.71 mmol, 62% yield) as a yellow oil; ^1H NMR (CD_3OD , 600 MHz,) δ 7.47 (1 H, d, $J = 8.4$ Hz), 7.45–7.42 (2 H, m), 7.25 (1 H, td, $J = 7.8, 1.2$ Hz), 7.19 (1 H, d, $J = 7.8, 1.2$ Hz), 6.66 (1 H, d, $J = 8.4$ Hz), 2.99 (6 H, s), 0.29 (9 H, s); ^{13}C NMR (CD_3OD , 150 MHz,) δ 152.1, 133.9, 133.3, 132.4, 129.6, 128.43, 128.4, 126.3, 113.2, 111.4, 105.2, 98.7, 96.2, 87.1, 40.6, 0.26.

7-Hydroxy-3,3-dimethyl-4-chromanone 3.81.

A solution of 7-hydroxy-4-chromanone (0.200 g, 1.22 mmol) and iodomethane (0.865 g, 6.09 mmol) in 20 mL of THF was added to a solution of potassium *tert*-butoxide (0.547 g,

4.88 mmol) in 60 mL of THF at $-78\text{ }^{\circ}\text{C}$ under a nitrogen atmosphere. After 6 h of stirring at $-78\text{ }^{\circ}\text{C}$, the resulting white slurry was allowed to warm to room temperature slowly and was filtered through a celite cake. The reaction mixture was treated with 50 mL of a saturated NH_4Cl solution and extracted with diethyl ether ($3 \times 30\text{ mL}$). The combined organic extracts were washed with brine and water, dried over sodium sulfate, and concentrated. Flash column chromatography (silica gel/40% diethyl ether in hexanes) provided 0.245 g of 7-hydroxy-3,3-dimethyl-4-chromanone (1.19 mmol, 98% yield) as a yellow solid: mp $128\text{--}129\text{ }^{\circ}\text{C}$; IR 3137, 1656, 1590, 1240 cm^{-1} ; ^1H NMR (CDCl_3 , 600 MHz,) δ 8.07 (1 H, br s), 7.80 (1 H, d, $J = 9.0\text{ Hz}$), 6.60 (1 H, dd, $J = 9.0, 2.4\text{ Hz}$), 6.45 (1 H, d, $J = 2.4\text{ Hz}$), 4.12 (2 H, s), 1.20 (6 H, s); ^{13}C NMR (CDCl_3 , 150 MHz,) δ 198.0, 163.8, 163.6, 130.0, 112.9, 111.1, 103.0, 76.8, 41.3, 20.7; HRMS m/z calcd for $\text{C}_{11}\text{H}_{12}\text{O}_3\text{Na}$ (MNa^+) 215.0679, found 215.0682.

Ketone 4.67 and ketone 4.68. A solution of indanone (0.213 g, 1.61 mmol) in THF (20 mL) was added dropwise to a stirred suspension of NaH (0.064g, 60% in mineral oil, 1.61 mmol) in 20 mL THF at $0\text{ }^{\circ}\text{C}$, and stirring was continued for 1 h. To this solution was added 0.300 g of 1-iodo-2-methoxyethane (1.61 mmol). After 1 h at room temperature, the mixture was heated to reflux for 6 h. Then the mixture was cooled to $0\text{ }^{\circ}\text{C}$ and quenched by ice-water. The reaction mixture was extracted with diethyl ether ($3 \times 50\text{ mL}$). The combined organic extracts were washed with brine and water, dried over sodium sulfate, and concentrated. Flash column chromatography (silica gel/10% diethyl ether in hexanes) provided 0.046 g of **4.67** (0.242 mmol, 15% yield) and 0.140 g of **4.68** (0.564 mmol, 35% yield) as yellow oil. **4.67**: ^1H NMR (CDCl_3 , 600 MHz) δ 7.50 (1 H, d, $J = 7.8\text{ Hz}$), 7.57 (1 H, td, $J = 7.8, 1.2\text{ Hz}$), 7.45 (1 H, d, $J = 7.8\text{ Hz}$), 7.36 (1 H, td, $J = 7.8, 1.2\text{ Hz}$), 3.58–3.55 (2 H, m), 3.39–3.34 (1 H, m), 3.34 (3H, s), 2.87 (1 H, dd, $J = 16.8, 4.2\text{ Hz}$), 2.79–2.75 (1 H, m), 2.28–2.23 (1 H, m), 1.75–1.65 (1 H, m); ^{13}C NMR (CDCl_3 , 150 MHz) δ 208.5, 153.6, 136.6, 134.6, 127.3, 126.5, 123.9, 70.8, 58.6, 44.8, 33.1, 31.2. **4.68**: ^1H NMR (CDCl_3 , 600 MHz) δ 7.74 (1 H, d, $J = 7.8\text{ Hz}$), 7.58 (1 H, td, $J = 7.8, 1.2$

Hz), 7.43 (1 H, d, $J = 7.8$ Hz), 7.36 (1 H, t, $J = 7.8$, Hz), 3.34–3.28 (4 H, m), 3.17 (2 H, s), 3.13 (6H, s), 2.03–1.98 (2 H, m), 1.90–1.85 (2 H, m); ^{13}C NMR (CDCl_3 , 150 MHz) δ 209.9, 152.9, 136.6, 134.7, 127.3, 126.3, 123.9, 70.0, 58.5, 50.1, 38.1, 37.0.

Ketone 4.71. A solution of ketone **4.70** (1.10 g, 7.48 mmol) in THF (20 mL) was added dropwise to a stirred suspension of NaH (0.390g, 60% in mineral oil, 9.75 mmol) in 30 mL THF at 0 °C, and stirring was continued for 1 h. To this solution was added 1.67 g of 1-iodo-2-methoxyethane (8.97 mmol). After 1 h at room temperature, the mixture was heated to reflux for 6 h. Then the mixture was cooled to 0 °C and quenched by ice-water. The reaction mixture was extracted with diethyl ether (3 $\times$ 50 mL). The combined organic extracts were washed with brine and water, dried over sodium sulfate, and concentrated. Flash column chromatography (silica gel/15% diethyl ether in hexanes) provided 1.04 g of **4.71** (5.09 mmol, 68% yield) as yellow oil: ^1H NMR (CDCl_3 , 600 MHz) δ 7.74 (1 H, d, $J = 7.8$ Hz), 7.57 (1 H, td, $J = 7.2, 1.2$ Hz), 7.42 (1 H, d, $J = 7.8$ Hz), 7.34 (1 H, td, $J = 7.8, 0.6$ Hz), 3.39–3.33 (2 H, m), 3.25 (1 H, d, $J = 17.4$ Hz), 3.15 (3H, s), 2.88 (1 H, d, $J = 16.8$ Hz), 2.00–1.95 (1 H, m), 1.87–1.81 (1 H, m), 1.21 (3H, s); ^{13}C NMR (CDCl_3 , 150 MHz) δ 210.62, 152.5, 135.7, 134.7, 127.3, 126.5, 124.2, 69.3, 58.4, 47.7, 40.4, 37.4, 24.3.

Propargylic alcohol 4.73. To 0.296 g (1.46 mmol) of **4.72** in 20 mL of THF under a nitrogen atmosphere at –78 °C was added 0.892 mL of a 1.8 M solution of lithium diisopropylamide (LDA, 1.60 mmol) in hexanes. After 30 min of stirring, a solution of 0.250 g of **4.71** (1.22 mmol) in 10 mL of THF was introduced via cannula, and the reaction mixture was allowed to warm to room temperature. After an additional 1 h, 30 mL of water was introduced, and the reaction mixture was extracted with diethyl ether (3 $\times$ 30 mL). The combined organic extracts were washed with brine and water, dried over sodium sulfate, and concentrated. Flash column chromatography (silica gel/20% diethyl

ether in hexanes) provided 0.479 g of **4.73** (1.18 mmol, 97% yield, 1:1 mixture of isomers) as a yellow oil. **Diastereomer 1**: ^1H NMR (CDCl_3 , 600 MHz) δ 7.72 (1 H, d, J = 7.8 Hz), 7.55–7.53 (2 H, m), 7.37–7.35 (2 H, m), 7.30–7.28 (3 H, m), 7.27–7.23 (3 H, m), 7.19 (1 H, d, J = 7.8 Hz), 7.14 (1 H, t, J = 7.2 Hz), 3.76 (1 H, td, J = 9.6, 2.4 Hz), 3.55 (1 H, m), 3.36 (3 H, s), 3.10 (1 H, d, J = 15.6 Hz), 2.65 (1 H, d, J = 15.6 Hz), 2.29–2.25 (1 H, m), 1.83–1.78 (1 H, m), 1.53 (1 H, br, s), 1.23 (3 H, s); **Diastereomer 2**: ^1H NMR (CDCl_3 , 600 MHz) δ 7.56–7.53 (1 H, m), 7.49–7.43 (4 H, m), 7.36–7.33 (3 H, m), 7.26–7.18 (4 H, m), 7.13 (1 H, d, J = 7.8 Hz), 4.21 (1 H, s), 3.59 (1 H, td, J = 9.6, 2.4 Hz), 3.41–3.38 (1 H, m), 3.34 (3 H, s), 3.03 (1 H, d, J = 15.6 Hz), 2.76–2.70 (1 H, m), 2.59 (1 H, d, J = 15.6 Hz), 1.61–1.55 (1 H, m), 1.03 (3 H, s); ^{13}C NMR (CDCl_3 , 150 MHz) δ 145.7, 140.5, 132.2, 131.9, 131.7, 128.3, 128.2, 127.9, 127.81, 127.8, 126.9, 125.5, 125.4, 124.9, 123.3, 123.25, 94.3, 92.9, 88.3, 86.4, 80.7, 69.9, 58.7, 52.3, 44.2, 36.2, 18.3.

Diacetylene 4.74. To a mixture of **4.73** (0.460 g, 1.13 mmol) and triethylsilane (0.395 g, 3.4 mmol) in 30 mL of dichloromethane was added 1.03 g of trifluoroacetic acid (9 mmol). After 0.5 h of stirring at room temperature, 2.5 g (23.5 mmol) of sodium carbonate was added followed by 50 mL of water. The organic layer was separated, washed with brine and water, dried over sodium sulfate, and evaporated under reduced pressure. The residue was purified by flash column chromatography (silica gel/10% diethyl ether in hexanes) to provide 0.420 g (1.07 mmol, 95%, 1:1 mixture of the diastereomer) of **4.74** as a white solid: ^1H NMR (mixture of diastereomers, CDCl_3 , 600 MHz) δ 7.55–7.48 (5 H, m), 7.46–7.41 (5 H, m), 7.32–7.26 (10 H, m), 7.17–7.15 (4H, m), 7.01–7.07 (2 H, m), 4.16 and 4.06 (2 H, two singlets), 3.61–3.55 (2 H, m), 3.38–3.29 (2 H, m), 3.30 (3 H, s), 3.15 (3 H, s), 3.02 (1 H, d, J = 15.0 Hz), 2.93 (1 H, d, J = 15.0 Hz), 2.72 (1 H, d, J = 15.0 Hz), 2.71 (1 H, d, J = 15.0 Hz), 2.09–2.05 (1 H, m), 2.00–1.85 (3 H, m); ^{13}C NMR (mixture of diastereomers, CDCl_3 , 150 MHz) δ 142.9, 142.4, 141.9, 141.7, 132.2, 132.1, 132.0, 131.95, 131.8, 131.7, 128.22, 128.21, 127.89, 127.87, 127.5,

127.1, 126.9, 126.62, 126.6, 126.2, 126.1, 125.7, 125.65, 124.7, 124.6, 124.5, 124.4, 123.3, 123.27, 92.93, 92.9, 92.8, 92.3, 88.49, 88.47, 84.0, 83.3, 70.1, 58.6, 58.3, 49.5, 48.4, 47.7, 47.5, 45.3, 44.0, 40.3, 36.5, 25.9, 21.8.

Hydrocarbon 4.76. To 0.340 g (0.87 mmol) of **4.74** in 20 mL of anhydrous toluene under a nitrogen atmosphere was added 1.92 mL of a 0.5 M solution of potassium *tert*-butoxide (0.96 mmol) in 2-methyl-2-propanol. The reaction mixture was then heated under 80 °C for 6 h. After the reaction mixture was allowed to cool to room temperature, 10 mL of water and 20 mL of dichloromethane were introduced, and the organic layer was separated, washed with brine and water, dried over sodium sulfate, and concentrated. The residue was purified by flash column chromatography (silica gel/10% diethyl ether in hexanes) to provide 0.265 g (0.68 mmol, 78%) of **4.74** as a yellow solid: ¹H NMR (CDCl₃, 600 MHz) δ 7.62–7.59 (2 H, m), 7.58–7.55 (2 H, m), 7.48–7.45 (2 H, m), 7.38–7.36 (1 H, m), 7.27 (2 H, t, *J* = 8.4 Hz), 7.24 (1 H, td, *J* = 7.2, 1.2 Hz), 7.05 (1 H, t, *J* = 8.4 Hz), 4.20 (1 H, d, *J* = 21.6 Hz), 4.15 (1 H, d, *J* = 21.6 Hz), 3.60 (1 H, d, *J* = 17.4 Hz), 3.40–3.36 (1 H, m), 3.28 (1 H, d, *J* = 16.8 Hz), 3.25–3.20 (1 H, m), 3.22 (3 H, s), 2.47–2.41 (1 H, m), 2.33–2.29 (1 H, m), 1.65 (3 H, s); ¹³C NMR (CDCl₃, 150 MHz) δ 145.2, 144.1, 142.8, 141.5, 139.7, 138.8, 136.9, 133.3, 131.0, 130.8, 130.2, 130.16, 129.0, 128.9, 127.6, 127.3, 126.9, 126.5, 124.9, 123.7, 121.5, 119.0, 70.3, 58.7, 46.5, 45.5, 39.5, 33.9, 27.5.

Iodide 4.77. To 0.230 g (0.588 mmol) of **4.76** in 10 mL of anhydrous chloroform under a nitrogen atmosphere at room temperature was added 1 mL of trimethylsilyl iodide, and then the reaction mixture was heated to 55 °C. After 48 h of stirring, the reaction mixture was concentrated in vacuo to remove excess trimethylsilyl iodide and chloroform. The residue was purified by flash column chromatography (silica gel/5% diethyl ether in hexanes) to provide 0.215g (0.441 mmol, 75%) of **4.77** as a yellow solid: ¹H NMR

(CDCl₃, 600 MHz) δ 7.62–7.54 (4 H, m), 7.46–7.42 (2 H, m), 7.37–7.35 (1 H, m), 7.28–7.23 (3 H, m), 7.04 (1 H, t, J = 7.2 Hz), 6.25 (1 H, d, J = 8.4 Hz), 4.18 (1 H, d, J = 21 Hz), 4.09 (1 H, d, J = 21.6 Hz), 3.50 (1 H, d, J = 17.4 Hz), 3.27 (1 H, d, J = 16.8 Hz), 3.10–3.05 (1 H, m), 2.82–2.73 (2 H, m), 2.62–2.60 (1 H, m), 1.66 (3 H, s); ¹³C NMR (CDCl₃, 150 MHz) δ 143.9, 143.5, 142.1, 141.4, 139.8, 138.6, 137.1, 133.5, 131.2, 131.1, 130.1, 129.0, 128.99, 127.7, 127.5, 127.0, 126.6, 125.0, 123.8, 121.8, 119.2, 50.2, 45.6, 44.5, 33.8, 26.9, 0.362.

Hydrocarbon 4.78. To a solution of iodide **4.77** (0.070 g, 0.144 mmol) in THF (20 mL) was added a solution of *t*-BuOK (0.017g, 0.15mmol) in 5 mL of THF. The reaction mixture was heated to 40 °C for 2 h and quenched with aq satd. NH₄Cl. The reaction mixture was extracted with diethyl ether (3 × 30 mL). The combined organic extracts were washed with brine and water, dried over sodium sulfate, and concentrated. Flash column chromatography (silica gel/10% diethyl ether in hexanes) provided 0.048 g of **4.78** (0.132 mmol, 92% yield) as a yellow solid: ¹H NMR (CDCl₃, 600 MHz) δ 7.72 (1 H, d, J = 7.2 Hz), 7.62 (1 H, br, s), 7.56–7.50 (2 H, m), 7.51 (1 H, d, J = 7.8 Hz), 7.44 (1 H, d, J = 14.4 Hz), 7.35 (1 H, t, J = 7.2 Hz), 7.32 (1 H, br, s), 7.20 (2 H, t, J = 7.2 Hz), 7.02 (1 H, t, J = 8.4 Hz), 6.77 (1 H, d, J = 7.2 Hz), 4.08 (1 H, t, J = 8.4 Hz), 3.59 (1 H, d, J = 17.4 Hz), 3.24 (1 H, d, J = 16.8 Hz), 2.74–2.65 (1 H, m), 2.31–2.27 (1 H, m), 1.64 (3 H, m), 1.52–1.43 (1 H, m), 1.28–1.21 (1 H, m); ¹³C NMR (CDCl₃, 150 MHz) δ 151.1, 148.0, 142.9, 142.87, 139.3, 138.45, 138.43, 136.8, 131.6, 131.4, 131.0, 129.9, 128.8, 128.5, 127.7, 127.5, 126.8, 126.7, 125.0, 123.1, 121.7, 119.2, 49.2, 43.4, 39.2, 37.5, 27.1, 26.1.

Propargylic alcohol 4.82. To 0.632 g (1.77 mmol) of **4.58** in 30 mL of THF under a nitrogen atmosphere at –78 °C was added 1.05 mL of a 1.8 M solution of lithium diisopropylamide (LDA, 1.90 mmol) in hexanes. After 30 min of stirring, a solution of 0.330 g of **4.71** (1.61 mmol) in 15 mL of THF was introduced via cannula, and the

reaction mixture was allowed to warm to room temperature. After an additional 1 h, 30 mL of water was introduced, and the reaction mixture was extracted with diethyl ether (3 × 50 mL). The combined organic extracts were washed with brine and water, dried over sodium sulfate, and concentrated. Flash column chromatography (silica gel/20% diethyl ether in hexanes) provided 0.868 g of **4.73** (1.55 mmol, 96% yield, 1:1 mixture of isomers) as a yellow oil. **Diastereomer 1**: ^1H NMR (CDCl_3 , 600 MHz) δ 7.59 (2 H, d, J = 7.8 Hz), 7.58–7.56 (1 H, m), 7.51–7.49 (1 H, m), 7.46–7.44 (1 H, m), 7.29–7.25 (2 H, m), 7.16–7.14 (2 H, m), 7.09–7.07 (1 H, m), 7.05 (1 H, t, J = 8.4 Hz), 4.18 (1 H, s), 3.59–3.54 (1 H, m), 3.40–3.36 (1 H, m), 3.34 (3 H, s), 3.01 (1 H, d, J = 15.0 Hz), 2.70–2.64 (1 H, m), 2.55 (1 H, d, J = 15.0 Hz), 1.53–1.49 (1 H, m), 1.01 (3 H, s); ^{13}C NMR (CDCl_3 , 150 MHz) δ 145.5, 140.6, 132.5, 132.4, 131.2, 129.7, 128.5, 127.9, 127.7, 127.3, 126.8, 126.7, 125.6, 124.9, 124.6, 123.3, 97.2, 94.6, 90.4, 86.3, 80.7, 69.9, 58.7, 52.3, 44.2, 36.2, 18.3; **Diastereomer 2**: ^1H NMR (CDCl_3 , 600 MHz) δ 7.68 (1 H, d, J = 13.2 Hz), 7.65–7.63 (1 H, m), 7.58–7.55 (1 H, m), 7.53 (2 H, d, J = 7.8 Hz), 7.34–7.32 (2 H, m), 7.21 (1 H, t, J = 7.8 Hz), 7.16–7.15 (1 H, m), 7.11 (1 H, t, J = 7.8 Hz), 7.00 (1 H, t, J = 7.8 Hz), 4.58 (3 H, s), 3.77–3.72 (1 H, m), 3.57–3.53 (1 H, m), 3.36 (3 H, s), 3.07 (1 H, d, J = 15.0 Hz), 2.64 (1 H, d, J = 15.0 Hz), 2.26–2.21 (1 H, m), 1.83–1.79 (1 H, m), 1.21 (3 H, s); ^{13}C NMR (CDCl_3 , 150 MHz) δ 145.1, 141.7, 132.8, 132.5, 131.2, 129.7, 128.7, 128.6, 127.8, 127.1, 126.7, 126.6, 125.5, 125.1, 124.8, 124.7, 97.1, 94.9, 90.7, 84.2, 80.8, 69.1, 58.5, 50.9, 45.4, 36.8, 24.4.

Diacetylene 4.83. To a mixture of **4.82** (0.843 g, 1.50 mmol) and triethylsilane (0.744 g, 6.4 mmol) in 30 mL of dichloromethane was added 0.37 g of trifluoroacetic acid (3.2 mmol). After 0.5 h of stirring at room temperature, 1.5 g (14.1 mmol) of sodium carbonate was added followed by 50 mL of water. The organic layer was separated, washed with brine and water, dried over sodium sulfate, and evaporated under reduced pressure. The residue was purified by flash column chromatography (silica gel/10%

diethyl ether in hexanes) to provide 0.769 g (1.41 mmol, 94%, 1:1 mixture of the diastereomer) of **4.83** as a white solid: ^1H NMR (mixture of diastereomers, CDCl_3 , 600 MHz) δ 7.66–7.62 (2 H, m), 7.57–7.54 (4 H, m), 7.52–7.48 (2 H, m), 7.45 (1 H, d, $J = 7.2$ Hz), 7.40 (1 H, d, $J = 7.2$ Hz), 7.33–7.29 (4H, m), 7.16–7.12 (4 H, m), 7.08–7.05 (2 H, m), 7.03–6.99 (2 H, m), 4.14 and 4.04 (2 H, two singlets), 3.61–3.51 (2 H, m), 3.38–3.29 (2 H, m), 3.31 (3 H, s), 3.17 (3 H, s), 3.02 (1 H, d, $J = 15.6$ Hz), 2.91 (1 H, d, $J = 15.6$ Hz), 2.72 (1 H, d, $J = 15.6$ Hz), 2.70 (1 H, d, $J = 15.0$ Hz), 2.07–2.02 (1 H, m), 2.05–1.88 (3 H, m); ^{13}C NMR (mixture of diastereomers, CDCl_3 , 150 MHz) δ 142.7, 142.2, 141.9, 141.7, 132.6, 132.56, 132.5, 132.47, 131.3, 129.6, 128.6, 127.5, 127.3, 127.0, 126.9, 126.6, 126.5, 126.4, 126.3, 125.0, 124.9, 124.8, 124.6, 124.5, 124.46, 97.5, 97.47, 93.2, 92.8, 90.5, 90.4, 83.8, 83.1, 70.1, 70.07, 58.6, 58.3, 49.6, 48.5, 47.7, 47.5, 45.3, 44.0, 40.4, 36.5, 25.9, 21.9.

Hydrocarbon 4.84. To 0.400 g (0.708 mmol) of **4.83** in 30 mL of anhydrous toluene under a nitrogen atmosphere was added 1.55 mL of a 0.5 M solution of potassium *tert*-butoxide (0.77 mmol) in 2-methyl-2-propanol. The reaction mixture was then heated under 110 °C for 6 h. After the reaction mixture was allowed to cool to room temperature, 20 mL of water and 20 mL of dichloromethane were introduced, and the organic layer was separated, washed with brine and water, dried over sodium sulfate, and concentrated. The residue was purified by flash column chromatography (silica gel/10% diethyl ether in hexanes) to provide 0.328 g (0.58 mmol, 82%) of **4.84** as a yellow solid: ^1H NMR (CDCl_3 , 600 MHz) δ 7.82 (2 H, dd, $J = 9.0, 3.0$ Hz), 7.57 (1 H, d, $J = 7.8$ Hz), 7.41 (1 H, t, $J = 8.4$ Hz), 7.31–7.27 (3 H, m), 7.13–7.09 (2 H, m), 6.57 (1 H, d, $J = 7.8$ Hz), 4.21 (1 H, d, $J = 21.0$ Hz), 4.16 (1 H, d, $J = 21.0$ Hz), 3.58 (1 H, d, $J = 17.4$ Hz), 3.35–3.30 (1 H, m), 3.29 (1 H, d, $J = 16.8$ Hz), 3.18–3.13 (1 H, m), 3.14 (3 H, s), 2.43–2.38 (1 H, m), 2.31–2.27 (1 H, m), 1.68 (3 H, s); ^{13}C NMR (CDCl_3 , 150 MHz) δ 146.4, 144.2, 143.3, 140.9, 140.0, 139.9, 137.2, 133.3, 132.4, 132.3, 130.5, 129.1, 128.8, 127.8, 127.3, 127.1,

126.0, 125.1, 122.3, 120.1, 119.3, 70.2, 58.6, 46.7, 45.6, 39.7, 34.1, 27.5.

Iodide 4.85. To 0.530 g (0.967 mmol) of **4.84** in 10 mL of anhydrous chloroform under a nitrogen atmosphere at room temperature was added 1.1 mL of trimethylsilyl iodide, and then the reaction mixture was heated to 55 °C. After 48 h of stirring, the reaction mixture was concentrated in vacuo to remove excess trimethylsilyl iodide and chloroform. The residue was purified by flash column chromatography (silica gel/5% diethyl ether in hexanes) to provide 0.492 g (0.764 mmol, 79%) of **4.85** as a yellow solid: ¹H NMR (CDCl₃, 600 MHz) δ 7.82 (2 H, dd, J = 8.4, 0.6 Hz), 7.59 (1 H, d, J = 7.8 Hz), 7.41 (1 H, t, J = 7.8 Hz), 7.32–7.27 (3 H, m), 7.12 (1 H, t, J = 7.8 Hz), 7.10 (1 H, d, J = 8.4 Hz), 6.56 (1 H, d, J = 7.8 Hz), 4.20 (1 H, d, J = 21.6 Hz), 4.12 (1 H, d, J = 21.0 Hz), 3.50 (1 H, d, J = 17.4 Hz), 3.29 (1 H, d, J = 17.4 Hz), 3.09–3.03 (1 H, m), 2.80–2.75 (1 H, m), 2.72–2.67 (1 H, m), 2.62–2.59 (1 H, m), 1.69 (3 H, s); ¹³C NMR (CDCl₃, 150 MHz) δ 144.6, 143.9, 142.6, 140.7, 140.1, 139.7, 137.4, 133.5, 132.4, 132.3, 130.5, 129.2, 129.1, 128.0, 127.5, 127.2, 125.9, 125.8, 125.1, 122.3, 120.4, 119.5, 50.3, 45.7, 44.6, 34.0, 26.8, 0.23.

Hydrocarbon 4.86. To a solution of iodide **4.85** (0.320 g, 0.497 mmol) in THF (20 mL) was added a solution of *t*-BuOK (0.056g, 0.500mmol) in 5 mL of THF. The reaction mixture was heated to 40 °C for 2 h and quenched with aq satd. NH₄Cl. The reaction mixture was extracted with diethyl ether (3 $\times$ 30 mL). The combined organic extracts were washed with brine and water, dried over sodium sulfate, and concentrated. Flash column chromatography (silica gel/10% diethyl ether in hexanes) provided 0.243 g of **4.86** (0.472 mmol, 95% yield) as a yellow solid: ¹H NMR (CDCl₃, 600 MHz) δ 7.87 (1 H, d, J = 7.8 Hz), 7.73 (1 H, d, J = 7.8 Hz), 7.56 (1 H, d, J = 7.8 Hz), 7.39 (1 H, t, J = 8.4 Hz), 7.29–7.25 (2 H, m), 7.23 (1 H, d, J = 6.6 Hz), 7.16 (1 H, d, J = 8.4 Hz), 7.12 (1 H, t, J = 7.8 Hz), 6.66 (1 H, d, J = 8.4 Hz), 4.10 (1 H, t, J = 8.4 Hz), 3.62 (1 H, d, J = 16.8 Hz),

3.27 (1 H, d, J = 16.8 Hz), 2.74–2.70 (1 H, m), 2.34–2.29 (1 H, m), 1.69 (3 H, m), 1.53–1.48 (1 H, m), 1.22–1.18 (1 H, m); ^{13}C NMR (CDCl_3 , 150 MHz) δ 151.1, 148.0, 142.9, 142.87, 139.3, 138.45, 138.43, 136.8, 131.6, 131.4, 131.0, 129.9, 128.8, 128.5, 127.7, 127.5, 126.8, 126.7, 125.0, 123.1, 121.7, 119.2, 49.2, 43.4, 39.2, 37.5, 27.1, 26.1.

Buckybowl 4.87 and 4.89. To a flask containing 0.176 g of **4.86** (0.341 mmol) and 0.060 g of dibromobis(triphenylphosphine)palladium (0.075 mmol) under a nitrogen atmosphere were added via cannula 0.559 mL of DBU (2.74 mmol) in 15 mL of DMF. The resulting mixture was stirred vigorously at 150 °C for 72 h. The reaction mixture was then allowed to cool to rt before 30 mL of water, 15 mL of a 2 M HCl solution, and 50 mL of diethyl ether were introduced. The organic layer was separated, dried over sodium sulfate, and concentrated. The residue was purified by a short silica gel plug to provide 0.057 g of **4.87** and **4.89** as yellow solids. Both dicyclization and monocyclization products are not stable on silica gel column, so the mixture can not be separated on a flash chromatography column. The crude NMR shows that the mixtures include 0.039 g of **4.87** and 0.018 g of **4.89**. The structure of cyclization products were analyzed and confirmed by 1D TOCSY and 1D NOESY. All non-aromatic protons were assigned to corresponding products. **4.87**: ^1H NMR (CDCl_3 , 600 MHz) δ 4.82 (1 H, dd), 3.59 (1 H, d), 2.59–2.52 (1 H, m), 2.54 (1 H, d), 1.79 (3 H, s), 1.60–1.55 (1 H, m), 1.15–1.10 (1 H, m), (-0.18)–(-0.24) (1 H, m); **4.89**: ^1H NMR (CDCl_3 , 600 MHz) δ 4.18 (1 H, dd), 3.72 (1 H, d), 3.11 (1 H, d), 2.76–2.69 (1 H, m), 2.19–2.14 (1 H, m), 1.72 (3 H, s), 1.30–1.20 (1 H, m), 0.99–0.91 (1 H, m),

Ketone 4.93. A solution of ketone **4.92** (0.900 g, 5.23 mmol) in THF (20 mL) was added dropwise to a stirred suspension of NaH (0.163 g, 6.80 mmol) in 30 mL THF at 0 °C, and stirring was continued for 1 h. To this solution was added 1.17 g of 1-iodo-2-methoxyethane (6.28 mmol). After 1 h at room temperature, the mixture was

heated to reflux for 7 h. Then the mixture was cooled to 0 °C and quenched by ice-water. The reaction mixture was extracted with diethyl ether (3 × 50 mL). The combined organic extracts were washed with brine and water, dried over sodium sulfate, and concentrated. Flash column chromatography (silica gel/20% diethyl ether in hexanes) provided 0.746 g of **4.93** (3.24 mmol, 62% yield) as yellow oil: ¹H NMR (CDCl₃, 600 MHz) δ 7.73 (1 H, d, *J* = 7.8 Hz), 7.57 (1 H, td, *J* = 7.8, 1.2 Hz), 7.42 (1 H, d, *J* = 7.8 Hz), 7.34 (1 H, td, *J* = 7.8, 1.2 Hz), 5.65–5.57 (1 H, m), 5.09–5.05 (1 H, m), 5.00–4.97 (1 H, m), 3.34–3.27 (2 H, m), 3.12 (1 H, d, *J* = 16.8 Hz), 3.11 (3H, s), 3.07 (1 H, d, *J* = 17.4 Hz), 2.44–2.39 (1 H, m), 2.34–2.30 (1 H, m), 2.07–2.02 (1 H, m), 1.89–1.84 (1 H, m); ¹³C NMR (CDCl₃, 150 MHz) δ 209.9, 152.8, 136.6, 134.7, 133.4, 127.3, 126.3, 123.8, 118.5, 68.9, 58.4, 51.1, 42.1, 36.9, 36.6.

Propargylic alcohol 4.94. To 1.09 g (3.06 mmol) of **4.58** in 30 mL of THF under a nitrogen atmosphere at –78 °C was added 1.78 mL of a 1.8 M solution of lithium diisopropylamide (LDA, 3.20 mmol) in hexanes. After 30 min of stirring, a solution of 0.640 g of **4.71** (2.78 mmol) in 10 mL of THF was introduced via cannula, and the reaction mixture was allowed to warm to room temperature. After an additional 1 h, 30 mL of water was introduced, and the reaction mixture was extracted with diethyl ether (3 × 40 mL). The combined organic extracts were washed with brine and water, dried over sodium sulfate, and concentrated. Flash column chromatography (silica gel/20% diethyl ether in hexanes) provided 1.60 g of **4.94** (2.72 mmol, 98% yield, 1:1 mixture of isomers) as a yellow oil. **Diastereomer 1:** ¹H NMR (CDCl₃, 600 MHz) δ 7.60 (2 H, d, *J* = 7.8 Hz), 7.59–7.56 (1 H, m), 7.53–7.51 (1 H, m), 7.47–7.44 (1 H, m), 7.29–7.27 (2 H, m), 7.16–7.14 (2 H, m), 7.07–7.03 (2 H, m), 5.84–5.76 (1 H, m), 5.02 (1 H, dd, *J* = 10.2, 1.8 Hz), 4.97 (1 H, dd, *J* = 16.8, 1.8 Hz), 4.26 (1H, s), 3.58–3.53 (1 H, m), 3.36–3.32 (1 H, m), 3.33 (3H, s), 2.84 (1 H, d, *J* = 15.6 Hz), 2.79 (1 H, d, *J* = 15.6 Hz), 2.67–2.60 (1 H, m), 2.49–2.44 (1 H, m), 2.03–1.98 (1 H, m), 1.61–1.56 (1 H, m); ¹³C NMR (CDCl₃, 150

MHz) δ 145.5, 140.2, 135.1, 132.5, 132.4, 131.2, 129.8, 128.5, 128.1, 127.8, 127.2, 126.8, 126.7, 125.6, 124.7, 124.5, 123.2, 117.7, 97.1, 94.6, 90.4, 86.4, 80.9, 69.6, 58.8, 54.8, 40.4, 34.4, 33.3; **Diastereomer 2** : ^1H NMR (CDCl_3 , 600 MHz) δ 7.67 (1 H, d, $J = 7.8$ Hz), 7.64–7.62 (1 H, m), 7.58–7.55 (1 H, m), 7.52 (2 H, d, $J = 7.8$ Hz), 7.36–7.31 (2 H, m), 7.19 (1 H, td, $J = 7.2, 1.2$ Hz), 7.13–7.09 (2 H, m), 6.99 (1 H, t, $J = 8.4$ Hz), 5.67–5.60 (1 H, m), 4.87 (1H, s), 4.86 (1 H, dd, $J = 10.2, 2.4$ Hz), 4.76 (1 H, dd, $J = 16.8, 1.8$ Hz), 3.73 (1 H, td, $J = 9.6, 2.4$ Hz), 3.51–3.47 (1 H, m), 3.31 (3H, s), 2.88 (1 H, d, $J = 15.6$ Hz), 2.81 (1 H, d, $J = 15.6$ Hz), 2.73–2.69 (1 H, m), 2.16–2.08 (2 H, m), 1.89 (1 H, ddd, $J = 15.0, 5.4, 1.8$ Hz); ^{13}C NMR (CDCl_3 , 150 MHz) δ 145.3, 141.2, 134.9, 132.8, 132.4, 131.2, 129.7, 128.8, 128.6, 127.8, 127.1, 126.7, 125.6, 124.9, 124.7, 124.5, 117.7, 97.0, 94.9, 90.7, 84.8, 81.0, 68.7, 58.5, 54.1, 41.0, 38.9, 33.3.

Diacetylene 4.95. To a mixture of **4.94** (1.33 g, 2.27 mmol) and triethylsilane (1.10 mL, 6.80 mmol) in 50 mL of dichloromethane was added 1.34 mL of trifluoroacetic acid (18.1 mmol). After 0.5 h of stirring at room temperature, 4.5 g (42.3 mmol) of sodium carbonate was added followed by 50 mL of water. The organic layer was separated, washed with brine and water, dried over sodium sulfate, and evaporated under reduced pressure. The residue was purified by flash column chromatography (silica gel/20% diethyl ether in hexanes) to provide 1.23 g (2.16 mmol, 95%, mixture of the diastereomer) of **4.95** as a white solid: ^1H NMR (mixture of diastereomers, CDCl_3 , 600 MHz) δ 7.66–7.63 (2 H, m), 7.58–7.55 (4 H, m), 7.52–7.48 (2 H, m), 7.44 (1 H, d, $J = 7.2$ Hz), 7.41 (1 H, d, $J = 7.2$ Hz), 7.34–7.29 (4H, m), 7.14–7.11 (4 H, m), 7.09–7.05 (2 H, m), 7.02 (1 H, t, $J = 8.4$ Hz), 7.01 (1 H, d, $J = 8.4$ Hz), 6.00–5.92 (1 H, m), 5.80–5.73 (1 H, m), 5.08–5.05 (3 H, m), 4.29 (1H, s), 4.22 (1H, s), 3.70–3.65 (1 H, m), 3.59–3.54 (1 H, m), 3.36–3.30 (1 H, m), 3.26–3.19 (1 H, m), 3.28 (1H, s), 3.70–3.65 (1 H, m), 3.12 (1H, s), 2.94 (1 H, d, $J = 15.6$ Hz), 2.93 (1 H, d, $J = 16.2$ Hz), 2.87 (1 H, d, $J = 15.6$ Hz), 2.77 (1 H, d, $J = 16.2$ Hz), 2.51–2.47 (1 H, m), 2.40–2.38 (1 H, m), 2.25–2.21 (1 H, m),

2.05–1.87 (5 H, m); ^{13}C NMR (mixture of diastereomers, CDCl_3 , 150 MHz) δ 142.54, 142.5, 141.5, 141.2, 135.1, 135.0, 132.6, 132.5, 132.46, 132.4, 131.2, 129.6, 128.6, 127.54, 127.5, 127.3, 127.27, 127.1, 127.05, 126.6, 126.5, 126.47, 126.2, 125.0, 124.9, 124.5, 124.4, 124.36, 124.3, 117.9, 117.4, 97.5, 97.4, 93.1, 92.9, 90.5, 90.4, 83.7, 83.6, 69.8, 69.6, 58.6, 58.3, 50.2, 50.0, 47.47, 46.8, 43.7, 41.8, 39.1, 38.0, 35.7.

Hydrocarbon 4.96. To 0.820 g (1.44 mmol) of **4.95** in 40 mL of anhydrous toluene under a nitrogen atmosphere was added 3.16 mL of a 0.5 M solution of potassium *tert*-butoxide (1.58 mmol) in 2-methyl-2-propanol. The reaction mixture was then heated under 110 °C for 6 h. After the reaction mixture was allowed to cool to room temperature, 30 mL of water and 50 mL of dichloromethane were introduced, and the organic layer was separated, washed with brine and water, dried over sodium sulfate, and concentrated. The residue was purified by flash column chromatography (silica gel/20% diethyl ether in hexanes) to provide 0.740 g (1.30 mmol, 90%) of **4.96** as a yellow solid: ^1H NMR (CDCl_3 , 600 MHz) δ 7.82 (2 H, d, J = 8.4 Hz), 7.58 (1 H, d, J = 7.2 Hz), 7.40 (1 H, t, J = 8.4 Hz), 7.31–7.27 (3 H, m), 7.12 (1 H, t, J = 7.8 Hz), 7.09 (1 H, d, J = 8.4 Hz), 6.57 (1 H, d, J = 7.8 Hz), 5.62–5.54 (1 H, m), 5.90 (1 H, dd, J = 17.4, 1.8 Hz), 4.93 (1 H, d, J = 9.6 Hz), 4.21 (1 H, d, J = 22.2 Hz), 4.17 (1 H, d, J = 22.2 Hz), 3.50 (1 H, d, J = 17.4 Hz), 3.42 (1 H, d, J = 16.8 Hz), 3.29–3.24 (1 H, m), 3.11–3.06 (1 H, m), 3.10 (3 H, s), 2.88–2.85 (1 H, m), 2.77–2.72 (1 H, m), 2.47–2.42 (1 H, m), 2.33–2.88 (1 H, m); ^{13}C NMR (CDCl_3 , 150 MHz) δ 144.4, 144.1, 143.4, 140.8, 140.0, 139.8, 138.0, 134.3, 133.6, 132.4, 132.3, 130.5, 129.0, 128.9, 127.9, 127.3, 127.1, 125.9, 125.85, 125.1, 122.3, 120.1, 119.2, 118.0, 69.9, 58.6, 50.2, 44.5, 41.9, 38.7, 34.3.

Ether 4.97. To 0.050 g (0.088 mmol) of **4.96** in 10 mL of anhydrous chloroform under a nitrogen atmosphere at room temperature was added 0.1 mL of trimethylsilyl iodide, and then the reaction mixture was heated to 55 °C. After 48 h of stirring, the reaction mixture was concentrated in vacuo to remove excess trimethylsilyl iodide and chloroform. The

residue was purified by flash column chromatography (silica gel/20% diethyl ether in hexanes) to provide 0.036 g (0.064 mmol, 73%) of **4.97** as a yellow solid: ^1H NMR (CDCl_3 , 600 MHz) δ 7.82 (2 H, d, $J = 8.4$ Hz), 7.58 (1 H, d, $J = 7.2$ Hz), 7.42 (1 H, t, $J = 7.8$ Hz), 7.32–7.27 (3 H, m), 7.12–7.27 (2 H, m), 6.55 (1 H, d, $J = 7.8$ Hz), 4.27 (2 H, s), 4.17 (1 H, dd, $J = 11.4, 3.6$ Hz), 3.90–3.82 (2 H, m), 3.52 (2 H, s), 2.62 (1 H, td, $J = 13.2, 4.8$ Hz), 2.26 (1 H, t, $J = 13.2$ Hz), 1.75 (1 H, d, $J = 13.8$ Hz), 1.66 (1 H, dd, $J = 13.8, 1.8$ Hz), 1.32 (3 H, d, $J = 6.0$ Hz); ^{13}C NMR (CDCl_3 , 150 MHz) δ 146.6, 144.1, 142.6, 140.7, 140.3, 139.9, 136.9, 133.4, 132.4, 130.5, 129.2, 129.0, 127.8, 127.4, 127.1, 126.0, 125.1, 122.3, 120.2, 119.5, 70.8, 65.4, 47.5, 43.2, 43.0, 35.1, 34.2, 22.2.

Alcohol 4.98. To a mixture of 0.180 g (0.315 mmol) of **4.96** and 0.030 g of 2,6-bis(1,1-dimethylethyl)-4-methyl-Pyridine in 20 mL of anhydrous chloroform under a nitrogen atmosphere at room temperature was added 0.1 mL of trimethylsilyl iodide, and then the reaction mixture was heated to 55 °C. After 48 h of stirring, the reaction mixture was concentrated in vacuo to remove excess trimethylsilyl iodide and chloroform. The crude mixture was dissolved in 30 mL of dichloromethane. The organic solvent was washed with brine and water, dried over sodium sulfate, and concentrated. The residue was purified by flash column chromatography (silica gel/20% diethyl ether in hexanes) to provide 0.152 g (0.274 mmol, 87%) of **4.98** as a yellow solid: ^1H NMR (CDCl_3 , 600 MHz) δ 7.82 (2 H, t, $J = 7.8$ Hz), 7.57 (1 H, d, $J = 7.8$ Hz), 7.40 (1 H, t, $J = 7.8$ Hz), 7.32–7.27 (3 H, m), 7.13–7.08 (2 H, m), 6.56 (1 H, d, $J = 7.8$ Hz), 5.65–5.57 (1 H, m), 5.12 (1 H, d, $J = 16.8$ Hz), 4.96 (1 H, d, $J = 10.2$ Hz), 4.21 (2 H, s), 3.58–3.53 (1 H, m), 3.52 (1 H, d, $J = 17.4$ Hz), 3.41 (1 H, d, $J = 17.4$ Hz), 3.42–3.37 (1 H, m), 2.92–2.88 (1 H, m), 2.79–2.75 (1 H, m), 2.49–2.43 (1 H, m), 2.29–2.24 (1 H, m), 1.22 (1 H, br s); ^{13}C NMR (CDCl_3 , 150 MHz) δ 144.3, 144.0, 143.2, 140.7, 139.9, 139.8, 137.9, 134.2, 133.7, 132.34, 132.32, 130.5, 129.2, 129.0, 128.0, 127.4, 127.2, 125.9, 125.85, 125.1, 122.3, 120.2, 119.3, 118.1, 60.1, 50.3, 44.4, 41.9, 41.8, 34.4.

Methanesulfonate 4.99. To 0.340 g (0.619 mmol) of **4.98** in 30 mL of methylene chloride at 0 °C was added 0.50 ml (6.19 mmol) of triethylamine followed by 0.39 mL (4.95 mmol) of methanesulfonyl chloride. The solution was stirred for 1 h before 20 ml of a 1.0 M solution of hydrochloric acid was added. The organic layer was separated, and the aqueous layer was extracted with methylene chloride (3 x 20 mL). The combined organic layer was washed with brine and water, dried over sodium sulfate and concentrated in vacuo. The residue was purified by column chromatography (silica gel/10% ethyl acetate in hexanes) to provide 0.375 g (0.588 mmol, 95%) of **4.99** as a yellow solid: ^1H NMR (CDCl_3 , 600 MHz) δ 7.82 (2 H, d, J = 7.8 Hz), 7.58 (1 H, d, J = 7.8 Hz), 7.41 (1 H, t, J = 7.8 Hz), 7.33–7.29 (3 H, m), 7.13 (1 H, t, J = 7.2 Hz), 7.10 (1 H, d, J = 7.8 Hz), 6.56 (1 H, d, J = 7.8 Hz), 5.64–5.56 (1 H, m), 5.14 (1 H, d, J = 16.8 Hz), 5.00 (1 H, d, J = 10.2 Hz), 4.21 (1 H, d, J = 21.6 Hz), 4.13 (1 H, d, J = 21.6 Hz), 4.02–3.94 (2 H, m), 3.57 (1 H, d, J = 17.4 Hz), 3.46 (1 H, d, J = 17.4 Hz), 2.92–2.88 (1 H, m), 2.81–2.76 (1 H, m), 2.61–2.56 (1 H, m), 2.54–2.50 (1 H, m), 2.34 (3 H, s); ^{13}C NMR (CDCl_3 , 150 MHz) δ 143.8, 143.0, 140.5, 140.1, 139.6, 137.9, 133.8, 133.6, 132.5, 132.4, 130.7, 129.5, 129.1, 128.2, 127.6, 127.3, 125.9, 125.7, 125.1, 122.4, 120.3, 119.6, 118.7, 67.9, 50.1, 44.5, 41.9, 37.9, 36.3, 34.2.

Iodide 4.100. To 0.450 g (0.0708 mmol) of **4.99** in 60 mL of anhydrous chloroform at room temperature was added 0.530 g (3.50 mmol) of sodium iodide and 0.094 g (0.7 mmol) of lithium iodide, and then the reaction mixture was heated to reflux. After 24 h of stirring, the reaction mixture was cooled to room temperature and concentrated in vacuo to remove acetone. 50 mL of water and 50 mL of methylene chloride was added to the solid mixtures. The organic layer was separated, and the aqueous layer was extracted with methylene chloride (3 x 20 mL). The combined organic layer was washed with brine and water, dried over sodium sulfate and concentrated in vacuo. The residue was purified by

column chromatography (silica gel/10% diethyl ether in hexanes) to provide 0.422 g (0.630 mmol, 89%) of **4.100** as a yellow solid: ^1H NMR (CDCl_3 , 600 MHz) δ 7.82 (2 H, d, $J = 8.4$ Hz), 7.59 (1 H, d, $J = 7.2$ Hz), 7.40 (1 H, t, $J = 8.4$ Hz), 7.32–7.26 (3 H, m), 7.13 (1 H, t, $J = 7.8$ Hz), 7.10 (1 H, d, $J = 7.8$ Hz), 6.56 (1 H, d, $J = 7.8$ Hz), 5.61–5.54 (1 H, m), 5.11 (1 H, d, $J = 16.8$ Hz), 4.96 (1 H, d, $J = 10.2$ Hz), 4.19 (1 H, d, $J = 16.8$ Hz), 4.13 (1 H, d, $J = 21.0$ Hz), 3.49 (1 H, d, $J = 17.4$ Hz), 3.32 (1 H, d, $J = 16.8$ Hz), 3.03–2.99 (1 H, m), 2.87–2.78 (2 H, m), 2.75–2.71 (1 H, m), 2.66–2.55 (2 H, m); ^{13}C NMR (CDCl_3 , 150 MHz) δ 143.8, 142.8, 140.7, 140.0, 139.7, 138.2, 133.8, 133.7, 132.4, 132.35, 130.6, 129.4, 129.1, 128.0, 127.5, 127.3, 125.9, 125.8, 125.2, 122.4, 120.4, 119.4, 118.4, 53.9, 44.6, 43.9, 40.9, 34.2, 0.026.

Hydrocarbon 4.101. To a solution of iodide **4.100** (0.120 g, 0.180 mmol) in THF (20 mL) was added a solution of *t*-BuOK (0.023 g, 0.200 mmol) in 2 mL of THF. The reaction mixture was heated to 40 °C. After 2 h of stirring, the reaction mixture was added another solution of *t*-BuOK (0.062 g, 0.540 mmol) in 5 mL of THF, followed by a solution of iodine (0.046 g, 0.180 mmol) in 2 mL of THF. With extra 5 h of stirring, the reaction mixture was quenched with aq satd. NH_4Cl , and then extracted with diethyl ether (3×40 mL). The combined organic extracts were washed with brine and water, dried over sodium sulfate, and concentrated. Flash column chromatography (silica gel/10% diethyl ether in hexanes) provided 0.064 g of **4.101** (0.119 mmol, 66% yield) as a yellow solid: ^1H NMR (CDCl_3 , 600 MHz) δ 7.83 (1 H, dd, $J = 8.4, 1.2$ Hz), 7.77–7.73 (2 H, m), 7.37 (1 H, t, $J = 8.4$ Hz), 7.30–7.25 (3 H, m), 7.19 (1 H, d, $J = 8.4$ Hz), 7.15 (1 H, t, $J = 7.8$ Hz), 6.77 (1 H, d, $J = 7.8$ Hz), 6.33–6.31 (1 H, m), 5.88–5.80 (1 H, m), 5.07 (1 H, dd, $J = 17.4, 1.8$ Hz), 5.02 (1 H, dd, $J = 10.8, 2.4$ Hz), 3.77 (1 H, d, $J = 15.6$ Hz), 3.29 (1 H, dd, $J = 18.6, 4.8$ Hz), 3.13 (1 H, d, $J = 15.6$ Hz), 2.83 (1 H, dd, $J = 18.6, 3.0$ Hz), 2.58–2.53 (1 H, m), 2.51–2.47 (1 H, m); ^{13}C NMR (CDCl_3 , 150 MHz) δ 143.5, 142.6, 142.1, 139.3, 138.8, 136.9, 134.5, 134.3, 132.8, 132.2, 132.1, 131.1, 130.5, 130.4, 128.4, 128.2, 128.0,

127.5, 126.4, 125.6, 123.1, 122.7, 121.7, 120.5, 120.3, 117.9, 47.0, 43.7, 41.3, 39.4.

Hydrozone 4.103. A mixture of 1-indanone **4.66** (0.500 g, 3.78 mmol), *N,N*-dimethylhydrazine (1.5 mL) and acetic acid (one drop) were placed in a sealed reaction vial equipped with a magnetic bar and heated under microwave irradiation at 140°C for 20 minutes. The reaction mixture was then concentrated under reduced pressure to remove excess *N,N*-dimethylhydrazine and the crude on purification over a short pack of basic alumina column using 5% EtOAc in petroleum ether gave 0.657 g of hydrazone **4.103** (quant.) as a yellow oil: ^1H NMR (CDCl_3 , 600 MHz) δ 7.55 (1 H, d, $J = 7.2$ Hz), 7.33 (1 H, t, $J = 7.2$ Hz), 7.29 (1 H, d, $J = 7.8$ Hz), 7.23 (1 H, t, $J = 7.8$ Hz), 3.05–3.02 (2 H, m), 2.91–2.88 (2 H, m), 2.64 (6 H, s); ^{13}C NMR (CDCl_3 , 150 MHz) δ 148.3, 138.7, 130.5, 126.8, 125.4, 122.0, 47.0, 28.8.

Ketone 4.67. A solution of hydrozone **4.103** (1.04g, 6.00 mmol) in THF (20 mL) was added dropwise to a solution of LDA (6.2 mmol) in anhydrous THF (20 mL) via cannula at -40°C and the reaction mixture was slowly warmed to 0°C for 2 h. 1-iodo-2-methoxyethane (1.12g, 6.00 mmol) in anhydrous THF (15 mL) was then added dropwise to it and the reaction mixture was slowly warmed to 40°C and stirred for additional 6 h. It was quenched by addition of saturated aqueous NH_4Cl solution and extracted with diethyl ether (50 mL x 3). The combined organic layer was washed with saturated brine solution and dried over Na_2SO_4 . Filtration and solvent evaporation under reduced pressure afforded the crude product which was passed through a short pack of basic alumina column using 5% EtOAc in hexane to remove the most polar impurities. The product thus obtained was then mixed with MeOH (50 mL) and 2N aqueous HCl (30 mL) solution at room temperature and stirred vigorously for 12 h. MeOH was removed under reduced pressure and the aqueous layer was extracted with diethyl ether. The combined organic layer washed with saturated aqueous sodium bicarbonate solution followed by saturated brine solution and dried over anhydrous Na_2SO_4 . Evaporation of

solvent followed by purification over silica gel column using 5% EtOAc in hexane gave 0.695 g (3.66 mmol, 61%) of **4.67** as colorless oil: ^1H NMR (CDCl_3 , 600 MHz) δ 7.50 (1 H, d, $J = 7.8$ Hz), 7.57 (1 H, td, $J = 7.8, 1.2$ Hz), 7.45 (1 H, d, $J = 7.8$ Hz), 7.36 (1 H, td, $J = 7.8, 1.2$ Hz), 3.58–3.55 (2 H, m), 3.39–3.34 (1 H, m), 3.34 (3H, s), 2.87 (1 H, dd, $J = 16.8, 4.2$ Hz), 2.79–2.75 (1 H, m), 2.28–2.23 (1 H, m), 1.75–1.65 (1 H, m); ^{13}C NMR (CDCl_3 , 150 MHz) δ 208.5, 153.6, 136.6, 134.6, 127.3, 126.5, 123.9, 70.8, 58.6, 44.8, 33.1, 31.2.

Enol ether 4.104. A suspension of methoxymethyl(triphenylphosphoniumchloride) (0.418g, 1.22 mmol) in THF (20 ml) was cooled to $-20\text{ }^\circ\text{C}$ and *t*-BuOk (0.109g, 1.22 mmol) in 10 mL THF was slowly added dropwise to give an orange solution. After 10 minutes a solution of ketone **4.67** (0.100g, 0.478 mmol) in THF (10 mL) was added dropwise and the mixture was stirred for 30 mins and then was warmed to ambient temperature and stirred for an additional hour. The mixture was filtered through a celit plug and the filtrate concentrated *in vacuo*. The residue was precipitated with EtOAc/hexane (1:2, 50 mL) and filtrated. The filtrate was concentrated and the residue purified by flash chromatograph (10-15% EtOAc in hexane gradient elution) to give enol ether **4.104** (0.92g, 0.420 mmol, 88%, mixture of *Z/E* diastereomer) as a yellow oil: ^1H NMR (mixture of diastereomers, CDCl_3 , 600 MHz) δ 7.81 (1 H, d, $J = 7.8$ Hz), 7.25 (1 H, d, $J = 7.2$ Hz), 7.20–7.16 (3 H, m), 7.14–7.08 (3 H, m), 6.65 (1 H, d, $J = 1.8$ Hz), 6.15 (1 H, d, $J = 1.8$ Hz), 3.75 (3 H, s), 3.71 (3 H, s), 3.55–3.50 (1 H, m), 3.48–3.42 (3 H, m), 3.36 (3 H, s), 3.34 (3 H, s), 3.32–3.26 (1 H, m), 3.20–3.12 (2 H, m), 3.08–3.04 (1 H, m), 3.20–3.12 (2 H, m), 2.72–2.65 (2 H, m), 2.09–2.02 (1 H, m), 1.84–1.77 (1 H, m), 1.75–1.70 (1 H, m), 1.67–1.61 (1 H, m); ^{13}C NMR (mixture of diastereomers, CDCl_3 , 150 MHz) δ 143.5, 143.2, 142.3, 140.7, 139.9, 139.5, 126.5, 126.4, 126.3, 126.1, 125.2, 125.17, 125.0, 124.5, 123.2, 118.3, 71.2, 70.5, 60.3, 60.1, 60.08, 58.6, 58.57, 58.4, 37.6, 37.1, 36.8, 36.4, 34.3.

Aldehyde 4.105. *p*-Toluenesulfonic acid monohydrate (0.026 g, 0.140 mmol) was added to a solution of the enol ethers **4.104** (0.150 g, 0.688 mmol) in aqueous dioxane (20 mL, dioxane : H₂O = 3 : 1), and the mixture was stirred under reflux for 14 h . It was then cooled to room temperature, diluted with water (20 ml), and extrated with ether (30 mL x 3). The combined organic extracts were washed with aqueous sodium bicarbonate and brine, dried with Na₂SO₄ and evaporated. Flash chromatograph of the residue over silica gel with 15% EtOAc-hexane gave 0.112 g (0.550 mmol, 80%) of **4.105** as colorless oil: ¹H NMR (CDCl₃, 600 MHz) δ 9.634 (1 H, d, *J* = 3.6 Hz), 7.30–7.25 (2 H, m), 7.25–7.20 (2 H, m), 3.72 (1 H, dd, *J* = 7.8, 3.6 Hz), 3.54–3.48 (2 H, m), 3.35 (3 H, s), 3.27–3.22 (1 H, dd, *J* = 16.2, 8.4 Hz), 3.00–2.94 (1 H, m), 2.79–2.74 (1 H, dd, *J* = 15.6, 8.4 Hz), 1.96–1.86 (2 H, m); ¹³C NMR (CDCl₃, 150 MHz) δ 200.9, 143.9, 138.3, 128.0, 126.8, 125.0, 124.7, 70.9, 63.7, 58.5, 38.7, 38.0, 34.6.

Alkyne 4.106. K₂CO₃ (0.215 g, 1.56 mmol) was added to a ice-cooled solution of aldehyde **4.105** (0.160 g, 0.784 mmol) and diazophosphonate (0.224 g, 1.17 mmol) in MeOH (10 mL). The resulting solution was stirred for 1h at 0 °C then for 16h at RT. The mixture was treated with a saturated aqueous solution of NH₄Cl (10 mL). MeOH was removed under reduced pressure and the aqueous layer was extracted with diethyl ether (3 x 30 mL). The combined organic layer saturated brine solution and dried over anhydrous Na₂SO₄. Evaporation of solvent followed by purification over silica gel column using 5% EtOAc in hexane gave 0.108 g (0.539 mmol, 72%) of **4.106** as colorless oil: ¹H NMR (CDCl₃, 600 MHz) δ 7.39 (1 H, d, *J* = 8.4 Hz), 7.25–7.17 (3 H, m), 3.67–3.65 (1 H, m), 3.59 (1 H, t, *J* = 7.2 Hz), 3.39 (3 H, s), 3.12–3.06 (1 H, m), 2.64–2.56 (2 H, m), 2.25 (1 H, d, *J* = 2.4 Hz), 2.19–2.14 (1 H, m), 1.88–1.82 (1 H, m); ¹³C NMR (CDCl₃, 150 MHz) δ 142.7, 142.1, 127.2, 126.7, 124.3, 123.9, 85.3, 71.4, 69.9, 58.6, 46.6, 42.3, 37.9, 34.0.

Diacetylene 4.107. To a mixture of 1,3-dibromo-2-((2-iodophenyl)ethynyl)benzene (0.185 g, 0.402 mmol), Pd(PPh₃)₂Cl₂ (0.021 g, 0.030 mmol), and CuI (0.010 g, 0.053 mmol) in 20 mL of triethylamine under a nitrogen atmosphere was added via cannula a solution of alkyne **4.106** (0.080 g, 0.400 mmol) in 5 mL of triethylamine. The resulting mixture was heated to 35 °C for 12 h before it was allowed to cool to room temperature. The reaction mixture was concentrated in vacuo. The black residue was dissolved in 100 mL of dichloromethane and then washed with brine and water. The organic layer was separated, dried over sodium sulfate, and concentrated. Purification by silica gel column using 5% EtOAc in hexane gave 0.159 g (0.300 mmol, 75%) of **4.107** as colorless oil: ¹H NMR (CDCl₃, 600 MHz) δ 7.65–7.64 (1 H, m), 7.55 (2 H, d, *J* = 8.4 Hz), 7.51–7.48 (1 H, m), 7.46 (1 H, d, *J* = 7.8 Hz), 7.32–7.29 (1 H, m), 7.17 (1 H, t, *J* = 7.2 Hz), 7.15 (1 H, t, *J* = 7.2 Hz), 7.10 (1 H, t, *J* = 7.2 Hz), 7.00 (1 H, t, *J* = 8.4 Hz), 3.94 (1 H, d, *J* = 9.6 Hz), 3.56 (2 H, t, *J* = 6.6 Hz), 3.32 (3 H, s), 3.10 (1 H, dd, *J* = 15.6, 7.8 Hz), 2.75–2.68 (1 H, m), 2.66–2.62 (1 H, m), 2.23–2.17 (1 H, m), 1.89–1.82 (1 H, m); ¹³C NMR (CDCl₃, 150 MHz) δ 143.0, 142.2, 132.6, 132.4, 131.2, 129.6, 128.6, 127.5, 127.3, 127.0, 126.6, 126.5, 126.2, 125.1, 124.5, 124.2, 97.5, 95.5, 90.6, 80.9, 71.6, 58.5, 46.9, 43.7, 38.0, 34.2.

Hydrocarbon 4.108. To 0.080 g (0.150 mmol) of **4.107** in 10 mL of anhydrous toluene under a nitrogen atmosphere was added 0.33 mL of a 0.5 M solution of potassium *tert*-butoxide (0.15 mmol) in 2-methyl-2-propanol. The reaction mixture was then heated under 80 °C for 2 h. After the reaction mixture was allowed to cool to room temperature, 10 mL of water and 20 mL of dichloromethane were introduced, and the organic layer was separated, dried over sodium sulfate, and concentrated. Purification by silica gel column using 5% EtOAc in hexane gave 0.008 g (0.015 mmol, 10%) of **4.107** as white solid: ¹H NMR (CDCl₃, 600 MHz) δ 7.83–7.80 (2 H, m), 7.57 (1 H, d, *J* = 7.2 Hz), 7.42–7.39 (1 H, m), 7.31–7.26 (2 H, m), 7.13–7.08 (1 H, m), 6.57 (1 H, d, *J* = 7.8 Hz), 4.20 (1 H, d, *J* = 21 Hz), 4.06 (1 H, d, *J* = 21 Hz), 4.07–4.02 (1 H, m), 3.71 (1 H, dd, *J* =

17.4, 8.4 Hz), 3.65–3.56 (2 H, m), 3.40 (3 H, s), 3.27 (1 H, dd, $J = 16.8, 3.6$ Hz), 2.66–2.60 (1 H, m), 2.00–1.94 (1 H, m); ^{13}C NMR (CDCl_3 , 150 MHz) δ 144.3, 143.6, 141.0, 139.9, 138.1, 133.9, 132.3, 130.5, 129.1, 128.6, 127.8, 127.3, 127.1, 126.0, 125.9, 125.2, 122.3, 120.0, 119.3, 71.2, 58.8, 40.2, 37.7, 34.6, 33.7.

2-(4-methoxybenzyloxy)-3-methylnaphthalen-1-ol (4.121). To a stirred solution of allene **4.117** (1.14 g, 6.50 mmol) in THF (100 mL) was added dropwise a 1.6 M solution of *n*-BuLi (4.06 mL, 6.50 mmol) in hexane under N_2 at -78°C . After stirring was continued for 1 h at -78°C , benzocyclobutanone **4.113** (0.760 g, 6.44 mmol) in 5 mL of THF was added dropwise to this solution. Stirring was continued for 1 h at -78°C and then warmed up to room temperature. The mixture was quenched with a solution of TFA (12.0 mmol in 1:1THF/water) and extracted with diethyl ether. The combined extracts was washed with brine and water, dried over Na_2SO_4 , and concentrated in *vacuo*. The residue was purified by flash chromatography (silica gel/20% diethyl ether in hexanes) to provide **4.121** (1.79 g, 6.12 mmol, 95 %) as a yellow oil: ^1H NMR (CDCl_3 , 600 MHz) δ 8.10–8.08 (1 H, m), 7.70–6.68 (1 H, m), 7.41–7.36 (4 H, m), 7.24 (1 H, s), 6.94 (2 H, d, $J = 9.0$ Hz), 5.91 (1 H, s), 4.90 (2 H, s), 3.83 (3 H, s), 2.52 (3 H, d, $J = 0.6$ Hz); ^{13}C NMR (CDCl_3 , 150 MHz) δ 160.0, 143.6, 140.1, 131.2, 130.5, 130.0, 129.1, 126.7, 125.4, 124.3, 123.2, 121.7, 120.2, 114.3, 75.5, 55.3, 17.1.

Hydroxyketone 4.122. To a stirred solution of allene **4.117** (1.49 g, 8.47 mmol) in THF (100 mL) was added dropwise a 1.6 M solution of *n*-BuLi (5.29 mL, 8.47 mmol) in hexane under N_2 at -78°C . After stirring was continued for 1 h at -78°C , benzocyclobutanone **4.113** (1.00 g, 8.47 mmol) in 10 mL of THF was added dropwise to this solution. The reaction mixture was stirred for 1 h at -78°C , then added a solution of TFA (16.0 mmol in 1:1THF/water). When the reaction is complete, the mixture was extracted with diethyl ether (3 x 100 mL). The combined extracts was washed with brine

and water, dried over Na₂SO₄, and concentrated in *vacuo*. The residue was purified by flash chromatography (silica gel/20% diethyl ether in hexanes) to provide **4.122** (1.35 g, 7.79 mmol, 92 %) as a yellow oil: ¹H NMR (CDCl₃, 600 MHz) δ 7.78 (1 H, d, *J* = 7.8 Hz), 7.64 (1 H, td, *J* = 7.8, 1.2 Hz), 7.46 (1 H, d, *J* = 7.8 Hz), 7.41 (1 H, t, *J* = 7.8 Hz), 5.89 (1 H, dd, *J* = 17.4, 10.8 Hz), 5.40 (1 H, d, *J* = 17.4 Hz), 5.21 (1 H, d, *J* = 10.8 Hz), 3.39 (1 H, d, *J* = 16.8 Hz), 3.29 (1 H, d, *J* = 16.8 Hz), 3.12 (1 H, br s); ¹³C NMR (CDCl₃, 150 MHz) δ 205.4, 150.9, 138.0, 136.0, 133.8, 128.1, 126.7, 125.0, 115.1, 80.9, 41.2.

Methoxyketone 4.123. A solution of hydroxyketone **4.122** (0.200 g, 1.15 mmol) in anhydrous THF (10 mL) was added dropwise to a suspension of sodium hydride [60% suspension in mineral oil] (55 mg, 1.38 mmol) in anhydrous THF (20 mL) at 0 °C. After being stirred for 1 h, iodo methane (0.22 mL, 3.45 mmol) was slowly added to it. The resulting solution was then slowly warmed to room temperature and stirred for 24 h. It was quenched with saturated aqueous NH₄Cl solution and extracted with diethyl ether (3 x 20 mL). The combined extracts was washed with brine and water, dried over Na₂SO₄, and concentrated in *vacuo*. The residue was purified by flash chromatography (silica gel/10% diethyl ether in hexanes) to provide 0.214 g of **4.123** (1.14 mmol, 99 %) as yellow oil: ¹H NMR (CDCl₃, 600 MHz) δ 7.76 (1 H, d, *J* = 7.2 Hz), 7.61 (1 H, td, *J* = 7.8, 1.2 Hz), 7.44 (1 H, d, *J* = 7.8 Hz), 7.41 (1 H, t, *J* = 7.2 Hz), 5.93 (1 H, dd, *J* = 17.4, 10.8 Hz), 5.36 (1 H, d, *J* = 17.4 Hz), 5.21 (1 H, d, *J* = 10.8 Hz), 3.37 (3 H, s), 3.35 (1 H, d, *J* = 18.0 Hz), 3.20 (1 H, d, *J* = 18.0 Hz); ¹³C NMR (CDCl₃, 150 MHz) δ 202.5, 150.5, 136.0, 135.6, 134.7, 127.9, 126.5, 124.8, 118.0, 85.4, 52.5, 37.4.

Propargylic alcohol 4.124. To 0.392 g (1.10 mmol) of **4.58** in 30 mL of THF under a nitrogen atmosphere at -78 °C was added 0.67 mL of a 1.8 M solution of lithium diisopropylamide (LDA, 1.20 mmol) in hexanes. After 30 min of stirring, a solution of 0.200 g of **4.123** (1.06 mmol) in 5 mL of THF was introduced via cannula, and the reaction mixture was allowed to warm to room temperature. After an additional 1 h, 30

mL of water was introduced, and the reaction mixture was extracted with diethyl ether (3 × 40 mL). The combined organic extracts were washed with brine and water, dried over sodium sulfate, and concentrated. Flash column chromatography (silica gel/20% diethyl ether in hexanes) provided 0.569 g of **4.124** (1.04 mmol, 98% yield) as a yellow oil; ¹H NMR (CDCl₃, 600 MHz) δ 7.68 (1 H, d, *J* = 7.8 Hz), 7.56–7.52 (2 H, m), 7.51–7.49 (2 H, m), 7.32–7.23 (7 H, m), 7.14 (1 H, t, *J* = 7.2 Hz), 6.14 (1 H, dd, *J* = 17.4, 10.8 Hz), 5.56 (1 H, d, *J* = 17.4 Hz), 5.51 (1 H, d, *J* = 10.8 Hz), 3.28 (1 H, d, *J* = 15.6 Hz), 3.17 (1 H, d, *J* = 15.6 Hz), 3.20 (3 H, s), 2.45 (1 H, s); ¹³C NMR (CDCl₃, 150 MHz) δ 144.0, 140.4, 135.6, 132.3, 131.8, 131.76, 129.1, 128.3, 128.2, 128.1, 127.8, 127.2, 126.1, 125.3, 125.1, 124.4, 123.2, 120.6, 93.3, 91.9, 91.7, 88.2, 86.0, 81.2, 51.9, 34.8.

Diacetylene 4.126. To a mixture of **4.124** (0.150 g, 0.385 mmol) and triethylsilane (0.19 mL, 1.15 mmol) in 20 mL of dichloromethane was added 0.22 mL of trifluoroacetic acid (3.08 mmol). After 0.5 h of stirring at room temperature, 0.500 g (4.7 mmol) of sodium carbonate was added followed by 20 mL of water. The organic layer was separated, washed with brine and water, dried over sodium sulfate, and evaporated under reduced pressure. The residue was purified by flash column chromatography (silica gel/10% diethyl ether in hexanes) to provide 0.075 g (0.20 mmol, 52%) of **4.126** as a white solid: ¹H NMR (CDCl₃, 600 MHz) δ 7.53–7.49 (2 H, m), 7.47 (1 H, d, *J* = 7.2 Hz), 7.40 (2 H, d, *J* = 7.2 Hz), 7.32–7.25 (5 H, m), 7.19 (2 H, d, *J* = 4.2 Hz), 7.11–7.08 (1 H, m), 6.16 (1 H, dd, *J* = 17.4, 11.4 Hz), 5.21 (1 H, d, *J* = 17.4 Hz), 5.51 (1 H, d, *J* = 10.8 Hz), 4.55 (1 H, s), 3.36 (3 H, s), 3.26 (1 H, d, *J* = 15.6 Hz), 3.15 (1 H, d, *J* = 15.6 Hz); ¹³C NMR (CDCl₃, 150 MHz) δ 140.8, 139.5, 137.2, 132.2, 131.9, 131.8, 128.2, 128.17, 127.8, 127.6, 127.5, 127.2, 126.0, 125.8, 124.6, 124.1, 123.3, 117.2, 93.0, 91.4, 90.1, 88.4, 84.3, 52.7, 48.3, 40.5.

Propargylic alcohol 4.129. To 0.069 g (0.700 mmol) of ethynyltrimethylsilane **4.128** in

10 mL of THF under a nitrogen atmosphere at $-78\text{ }^{\circ}\text{C}$ was added 0.38 mL of a 1.8 M solution of lithium diisopropylamide (LDA, 0.700 mmol) in hexanes. After 30 min of stirring, a solution of 0.100 g of **4.123** (0.532 mmol) in 5 mL of THF was introduced via cannula, and the reaction mixture was allowed to warm to room temperature. After an additional 1 h, 10 mL of water was introduced, and the reaction mixture was extracted with diethyl ether ($3 \times 20\text{ mL}$). The combined organic extracts were washed with brine and water, dried over sodium sulfate, and concentrated. Flash column chromatography (silica gel/20% diethyl ether in hexanes) provided 0.143 g of **4.129** (0.500 mmol, 94% yield) as a yellow oil; ^1H NMR (major diastereomer, CDCl_3 , 600 MHz) δ 7.56–7.54 (1 H, m), 7.30–7.27 (3 H, m), 6.97 (1 H, dd, $J = 17.4, 10.8\text{ Hz}$), 5.61–7.54 (2 H, m), 3.24 (1 H, d, $J = 15.6\text{ Hz}$), 3.23 (3 H, s), 3.15 (1 H, d, $J = 15.6\text{ Hz}$), 0.22 (9 H, s); ^{13}C NMR (CDCl_3 , 150 MHz) δ 143.8, 140.5, 135.4, 129.2, 127.3, 125.2, 124.1, 120.7, 92.2, 91.6, 80.8, 67.9, 51.9, 34.8, -0.006.

Alkyne 4.130. To a solution of trimethylsilyl-alkyne **4.129** (0.303 g, 1.06 mmol) in a premixed mixture of acetone-water-dichloromethane (4:1:7, 20 mL) was added silver triflate (0.038 g, 0.150 mmol). The resulting mixture was then stirred at room temperature. Once the starting materials disappeared, an aqueous saturated solution of ammonium chloride (10 mL) was added. The reaction mixture was extracted with dichloromethane ($3 \times 10\text{ mL}$). The combined organic extracts were washed with brine and water, dried over sodium sulfate, and concentrated. Flash column chromatography (silica gel/25% diethyl ether in hexanes) provided 0.202 g of **4.130** (0.940 mmol, 89% yield) as a yellow oil; ^1H NMR (CDCl_3 , 600 MHz) δ 7.56 (1 H, dd, $J = 6.6, 1.8\text{ Hz}$), 7.31–7.25 (3 H, m), 6.07 (1 H, dd, $J = 17.4, 10.8\text{ Hz}$), 5.60 (1 H, dd, $J = 10.8, 1.2\text{ Hz}$), 5.56 (1 H, dd, $J = 17.4, 1.2\text{ Hz}$), 3.26 (1 H, d, $J = 16.2\text{ Hz}$), 3.25 (3H, s), 3.18 (1 H, d, $J = 16.2\text{ Hz}$), 2.72 (1H, s); ^{13}C NMR (CDCl_3 , 150 MHz) δ 143.6, 140.2, 135.1, 129.3, 127.3, 125.1, 124.0, 120.9, 91.6, 82.2, 80.5, 75.3, 52.0, 34.6.

Allenic bromide 4.131. To 0.0130 g (0.607 mmol) of **4.130** in 20 mL of THF at $-40\text{ }^{\circ}\text{C}$ was added 0.5 mL (7 mmol) of pyridien followed by 0.1 mL (1.3 mmol) of thionyl bromide. The solution was allowed to warm to $0\text{ }^{\circ}\text{C}$ in 1 h before it was quenched with an aqueous saturated solution of ammonium chloride. The organic layer was separated. The aqueous layer was extracted with diethyl ether (3 x 20 mL). The combined organic extracts were washed with brine and water, dried over sodium sulfate, and concentrated. Flash column chromatography (silica gel/15% diethyl ether in hexanes) provided 0.119 g of **4.131** (0.431 mmol, 71% yield) as a yellow oil: ^1H NMR (major diastereomer, CDCl_3 , 600 MHz) δ 7.40–7.38 (1 H, m), 7.29–7.23 (3 H, m), 6.52 (1 H, s), 6.10 (1 H, dd, $J = 17.4, 10.8$ Hz), 5.44 (1 H, dd, $J = 17.4, 0.6$ Hz), 5.33 (1 H, dd, $J = 10.8, 0.6$ Hz), 3.31 (1 H, d, $J = 17.4$ Hz), 3.25 (3 H, s), 3.23 (1 H, d, $J = 17.4$ Hz); ^{13}C NMR (major diastereomer, CDCl_3 , 150 MHz) δ 198.3, 141.8, 139.0, 138.4, 135.2, 129.8, 127.5, 125.0, 124.2, 116.3, 87.4, 77.3, 51.5, 43.8.

Hydrocarbon 4.138. To a mixture of 0.280 g (0.600 mmol) of **4.132** in 10 mL of THF at $-78\text{ }^{\circ}\text{C}$ was added dropwise 0.38 mL (0.600 mmol) of a 1.6 M solution of butyllithium in hexanes. The solution was stirred at $-78\text{ }^{\circ}\text{C}$ for 10 min before 0.600 mL of 1.0 M solution (0.600 mmol) of zinc chloride in diethyl ether was introduced to form **4.136**. The solution was allowed to warm to $-40\text{ }^{\circ}\text{C}$ and stirred for 1 h. In a separated flask, 0.110 g (0.40 mmol) of **4.131** and 0.020 g (0.017 mmol) of tetrakis(triphenylphosphine)palladium were dissolved in 10 mL of THF. The mixture was stirred at room temperature for 15 min before it was transferred via cannula into the flask containing the zinc reagent **4.136**. The reaction mixture was stirred at room temperature for overnight and was quenched with an aqueous saturated solution of ammonium chloride. The organic layer was separated. The aqueous layer was extracted with diethyl ether (3 x 20 mL). The combined organic extracts were washed with brine and water, dried over sodium sulfate, and concentrated.

Flash column chromatography (silica gel/15% diethyl ether in hexanes) provided 0.176 g of **4.138** (0.304 mmol, 76% yield) as a yellow oil: ^1H NMR (major diastereomer, CDCl_3 , 600 MHz) δ 7.75 (1 H, d, $J = 9.0$ Hz), 7.50–7.46 (2 H, m), 7.42–7.37 (2 H, m), 7.34–7.31 (3 H, m), 7.27 (1 H, d, $J = 8.4$ Hz), 7.11 (1 H, t, $J = 7.8$ Hz), 6.22–6.16 (1 H, m), 5.37–5.33 (1 H, m), 5.22–5.19 (1 H, m), 4.20 (1 H, d, $J = 22.2$ Hz), 4.07 (1 H, d, $J = 22.8$ Hz), 3.79 (1 H, d, $J = 17.4$ Hz), 3.51 (1 H, d, $J = 17.4$ Hz), 3.15 (3 H, s).

Figure 5.1. ORTEP drawings for the crystal structures of two diastereomers of 2.8a

Figure 5.2. ORTEP drawings for the crystal structures of **3.66**

Figure 5.3. ORTEP drawings for the crystal structures of **4.97**

2.8a

2.2c

1.314
1.201

2.156

2.616
2.641

3.016
2.990

3.777

6.632
6.642
6.646
6.757
6.760
7.260
7.285
7.288
7.297
7.293
7.301
7.309
7.312
7.321
7.428
7.432
7.442
7.444
7.523
7.526
7.535
7.539
7.542
7.545
7.551
7.555
7.559

ppm

-0

1

2

3

4

5

6

7

8

9

77.211
77.000
76.789

55.260
55.216
47.368
46.851

145.011
141.247
140.974
136.835
133.684
132.390
132.212
131.698
129.825
128.809
126.186
124.896
123.333
114.396
111.536

159.643
158.980

168.376

186.782

ppm

3.54, rt

1.202

4.124

6.449
6.453
6.589
6.593
6.604
6.607

7.260

7.796
7.811

8.070

ppm

-0

1

2

3

4

5

6

7

8

9

1.188

3.831

4.129

6.395
6.399
6.576
6.580
6.591
6.595

7.260

7.827
7.842

2.691

~~3.829~~

77.215
77.000
76.788

4.74
Two diastereomer

4.82
Mixture of diastereomer

4.82
Mixture of diastereomer

4.84

4.85

4.85

77.211
76.996
76.785

144.621
143.932
142.566
140.708
140.067
139.739
137.363
133.472
132.394
132.310
130.539
129.206
129.137
127.978
127.464
127.209
125.949
125.829
125.147
122.320
120.400
119.467

50.334
45.667
44.614
33.979
26.842
0.230

ppm

0

20

40

60

80

100

120

140

160

180

200

A

B

1D NOESY

1D TOCSY

1D TOCSY

1D NOESY

Seldec ^1H NMR

Seldecoupled ^1H NMR spectra

B **A**

4.94
Diastereomer 1

4.94
Diastereomer 2

4.95
Mixture of Diastereomer

77.211
77.000
76.785

144.344
144.020
143.226
140.719
139.914
139.801
137.870
134.234
133.713
132.339
132.317
130.514
129.191
129.016
128.000
127.406
127.155
125.909
125.854
125.082
122.302
120.203
119.292
118.083

60.106
50.258
44.425
41.867
41.838
34.354

ppm

0

20

40

60

80

100

120

140

160

180

200

77.211
77.000
76.789

143.510
142.603
142.093
139.327
138.799
136.864
134.533
134.310
132.787
132.153
132.106
131.079
130.441
130.379
128.386
128.229
127.956
127.490
126.379
125.555
123.078
122.659
121.693
120.516
120.316
117.857

46.953
43.649
41.335
39.382

ppm

0 20 40 60 80 100 120 140 160 180 200

4.104
Mixture of Diastereomers

77.215
77.000
76.789

38.686
37.958
34.558

58.510

63.724

70.912

127.974
126.754
124.969
124.717

138.274

143.878

200.908

ppm

0

20

40

60

80

100

120

140

160

180

200

4.122

4.122

77.211
77.000
76.789

4.130
mixture of diastereomers

4.137

Publications

- Wen, B.; Petersen, J. L.; Wang, K. K. "Synthesis of 4,5-diheteroarylphenanthrenes and their dinuclear ruthenium(II) bis(2,2':6',2''-terpyridine) complexes possessing severe helical twists" *Chem. Commun.* **2010**, 46, 1938-1940.
- Wang, K. K.; Cui, H.; Wen, B. "Synthesis of bowl-shaped and basket-shaped fullerene fragments via benzannulated enyne-allens" in *Fragments of fullerene and carbon nanotubes: designed synthesis, unusual reactions, and coordination chemistry*; Petrukhina, M. A and Scott, L. T., Eds.; John Wiley & Sons, Inc, **2010**, in print.
- Wen, B.; Petersen, J. L.; Wang, K. K. "Synthesis of 1,4-naphthoquinone methides via acid-catalyzed cascade cyclizations of benzannulated enediynyl alcohols" *Org. Lett.* **2010**, Published on Web. DOI: 10.1021/ol102793a

Presentations

- Wen, B.; Petersen, J. L.; Wang, K. K. "Synthesis of 4,5-diheteroaryl phenanthrenes possessing severe helical twists" 236th ACS national meeting, Philadelphia, PA : Aug 2008.
- Wen, B.; Parbin, E. S.; Wang, K. K. "Synthesis of a partially hydrogenated 4H-cyclopenta [def]phenanthrene via a benzannulated enediynyl alcohol" 238th ACS national meeting, Washington, DC : Aug 2009.
- Wen, B.; Petersen, J. L.; Wang, K. K. "Synthesis of *p*-benzoquinone methides via benzannulated enediynyl alcohols" 240th ACS national meeting, Boston, MA : Aug 2010.